LIPPINCOTT MANUAL®

The Washington Manual® of Surgery

8TH EDITION

Mary E. Klingensmith
Paul E. Wise

RESIDENT EDITORS

Cathleen M. Courtney
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Matthew R. Schill
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Department of Surgery
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School of Medicine
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Wolters Kluwer

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SCHOOL OF MEDICINE

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Foreword

Welcome to the eighth edition of *The Washington Manual™ of Surgery.* Over the past 100 years, the most important focus of our Department of Surgery has been medical education of students, residents, fellows, and practicing surgeons. This commitment is clearly evident in the current edition of *The Washington Manual™ of Surgery.*

The educational focus of our Department of Surgery has a rich tradition. The first full-time head of the Department of Surgery at Washington University was Dr. Evarts A. Graham (1919–1951). Dr. Graham was a superb educator. Not only was he an outstanding technical surgeon, but his insightful comments at conferences and ward rounds were well known and appreciated by a generation of surgeons who learned at his elbow. Dr. Graham was a founding member of the American Board of Surgery and made many seminal contributions to the management of surgical patients. His work in the development of oral cholecystography actually helped establish the Mallinckrodt Institute of Radiology at Washington University. Dr. Graham was among the first to identify the epidemiologic link of cigarette smoking to lung cancer and was instrumental in raising public health consciousness about the deleterious effect on health from cigarette smoke.

Dr. Carl Moyer (1951–1965) succeeded Dr. Graham. Dr. Moyer is still regarded as a legendary educator at Washington University. He was particularly known for his bedside teaching techniques, as well as for linking pathophysiology to patient care outcomes. Dr. Walter Ballinger (1967–1978) came from the Johns Hopkins University and incorporated the Halsted tradition of resident education. Dr. Ballinger introduced the importance of laboratory investigation and began to foster development of the surgeon/scientist in our department. Dr. Samuel A. Wells (1978–1997) is credited with establishing one of the most accomplished academic departments of surgery in the United States. Not only did he recruit world-class faculty, but he increased the focus on research and patient care. Dr. Wells also placed great emphasis on educating the future academic leaders of surgery.

As in previous editions, this eighth edition of *The Washington Manual™ of*

Surgery combines authorship of residents, ably assisted by faculty coauthors and our senior editor, Dr. Mary Klingensmith, who is vice-chair for education in our department. Dr. Klingensmith is joined in this edition by a new senior editor, Dr. Paul Wise. This combination of resident and faculty participation has helped to focus the chapters on issues that will be particularly helpful to the trainee in surgery. This new edition of the manual provides a complete list of updated references that will serve medical students, residents, and practicing surgeons who wish to delve more deeply into a particular topic. This manual does not attempt to extensively cover pathophysiology or history, but it presents brief and logical approaches to the management of patients with comprehensive surgical problems. In each of the chapters, the authors have attempted to provide the most up-to-date and important diagnostic and management information for a given topic, as well as algorithms for quick reference. We have attempted to standardize each of the chapters so that the reader will be able to most easily obtain information regardless of subject matter.

The eighth edition has undergone a reorganization of chapters with an emphasis on clarity and consistency. As with the past edition, evidence-based medicine has been incorporated into each of the chapters, with updated information and references to reflect current knowledge and practice. All of the sections have been updated and rewritten to reflect the most current standards of practice for each topic. These updates have been carefully edited and integrated so that the volume of pages remains approximately the same. Our goal is to keep this volume concise, portable, and user-friendly. I am truly indebted to Drs. Klingensmith and Wise for their passion for education and devotion to this project. Additionally, I am proud of the residents in our Department of Surgery at Washington University who have done such an outstanding job with their faculty coauthors in this eighth edition. I hope that you will find *The Washington Manual™ of Surgery* a reference you commonly utilize in the care of your patient with surgical disease.

Timothy J. Eberlein, MD
St. Louis, Missouri

Preface

As with the previous editions, this eighth edition of *The Washington Manual™ of Surgery* is designed to complement *The Washington Manual of Medical Therapeutics*. Written by resident and faculty members of the Department of Surgery at Washington University in St. Louis, we present a brief, rational approach to the management of surgical conditions and topics relevant to surgeons. The text is directed to the reader at the second- or third-year surgical resident level, although all residents, surgical and nonsurgical attendings, medical students, physician assistants, nurse practitioners, and others who provide care for patients with surgical conditions will find this *Manual* of interest and assistance. The book provides a succinct discussion of surgical diseases, with algorithms for addressing problems based on the opinions of the authors. Although multiple approaches may be reasonable for some clinical situations, this *Manual* attempts to present a single, effective approach for each. We have limited extensive details on diagnosis and therapy as this is not meant to be an exhaustive, detailed surgical reference. Coverage of pathophysiology, the history of surgery, and extensive reference lists have been excluded from most areas.

The first edition of this *Manual* was published in 1997, followed by editions in 1999, 2002, 2005, 2007, 2012, and 2016. As with editions in the past, we have attempted to focus on relevant and timely topics. This eighth edition continues to provide multiple choice review questions at the end of each chapter so that readers can self-assess their knowledge and practice for in-training or other examinations. We have added chapters on “Radiology,” “Trauma Resuscitation and Adjuncts,” and “Intraoperative Considerations” to complement the other chapters in this edition. A separate chapter on appendiceal diseases has been added, and many chapters have been consolidated and reorganized to best reflect the nature of today’s surgical practice. For example, we are including more information on HIPEC as well as operating on the pregnant patient in this edition. In addition, chapters have again been updated with evidence-based medicine, with the latest information and treatment algorithms in each section. As with previous editions, the eighth edition includes updates on each topic as

well as new material and citations.

This is a resident-prepared *Manual*, and each chapter was updated and revised (or authored) by a resident with assistance from faculty coauthors. Editorial oversight for the *Manual* was shared by four senior resident coeditors (Cathleen Courtney, MD, Chapters 10, 13, 15–20, 43, 45, and 47–48; Kerri Ohman, MD, Chapters 21, 27–31, 38–42, and 46; Matthew Schill, MD, Chapters 1–8, 11–12, 14, and 36–37; and Jennifer Yu, MD, MPHS, Chapters 9, 22–26, 32–35, 44, and 49–50). The tremendous effort of all involved—resident and faculty authors, and particularly the above-noted senior resident coeditors—is reflected in the quality and consistency of the chapters.

We are indebted to the former senior editor of this work, Gerard M. Doherty, MD, who developed and oversaw the first three editions of this *Manual*, then handed over the role to M.E.K. as an exceptionally well-organized project. M.E.K. was proud to continue the effort through the next four editions with P.E.W. now joining as Co-Editor. We are grateful for the continued tremendous support from Wolters Kluwer Health, who have been supportive of the effort and have supplied dedicated assistance. Keith Donnellan has been a tremendously helpful Acquisitions Editor, with Sean McGuire as Development Editor and Tim Rinehart as Editorial Coordinator, keeping us on point and on schedule.

Finally, we are grateful to have the fantastic mentorship and leadership of Timothy J. Eberlein, MD, our Department Chair of over 20 years. His continued support and dedication has been tremendous, and his leadership of the Department of Surgery at Washington University in St. Louis has been nothing short of inspiring. Finally, to our families, we deeply thank you for your love, support, and encouragement; we wouldn’t be who we are without you!

We hope you enjoy the latest edition of *The Washington Manual™ of Surgery*!

M.E.K. and P.E.W.

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1 Preoperative Evaluation and Care

C. Alston James and Mary E. Klingensmith

I. PREOPERATIVE EVALUATION AND CARE

A. General Evaluation of the Surgical Patient. The goals of preoperative evaluation are to (1) identify the patient's medical problems and functional status; (2) determine if further information is needed to characterize the patient's medical status; (3) estimate the patient's level of risk for the planned procedure; and (4) establish if the patient's condition is medically optimized. Much of this can be accomplished with a thorough history and physical examination. For minor surgical procedures and procedures on young, healthy patients, routine diagnostic testing is often unnecessary. For patients with existing comorbidities, or in patients undergoing certain complex procedures, preoperative laboratory studies and imaging should be decided on an individual basis.

B. Specific Considerations in Preoperative Management

1. **Cardiovascular disease** is one of the leading causes of death after noncardiac surgery. In a cohort study looking at the 8,351 patients who were included in the PeriOperative ISchemic Evaluation (POISE) trial (noncardiac surgery), 5% of patients suffered a perioperative MI. Most of these MIs occurred within 48 hours of surgery (74%) and the majority did not experience ischemic symptoms (65%). The 30-day mortality rate was 11.6% among patients who had a perioperative MI, compared with 2.2% among those who did not (*Ann Intern Med*. 2011;154(8):523–528). Risk stratification for major adverse cardiac events (MACE, defined as death, Q-wave MI, and need for revascularization) by the operating

surgeon, anesthesiologist, and consulting internist is important.

a. Risk factors. A number of patient factors have been identified and are associated with perioperative cardiac morbidity and mortality. These include age above 70 years, unstable angina, recent (prior 6 months) MI, untreated CHF, diabetes mellitus, valvular heart disease, cardiac arrhythmias, peripheral vascular disease, and functional impairment. Factors related to the surgical procedure under consideration also convey risk. In their most recent guidelines published in 2014, the American Heart Association has condensed procedures into two risk levels: *low* risk (MACE risk <1%) and *elevated* risk (MACE risk >1%). The category of intermediate risk is no longer used, as the management of patients undergoing these and elevated risk procedures is similar.

TABLE 1-1 Revised Cardiac Risk Index[a]

Risk Factor	Comment
High-risk surgery	Intrathoracic, intraperitoneal, major vascular
Ischemic heart disease	History of myocardial infarction, positive exercise stress test, angina, nitrate therapy, electrocardiogram with abnormal Q waves
History of CHF	History of CHF, pulmonary edema, or paroxysmal nocturnal dyspnea, bilateral rales, S_3 gallop, chest x-ray showing pulmonary vascular redistribution
History of cerebrovascular disease	History of transient ischemic attack or stroke
Preoperative insulin therapy for diabetes	
Preoperative serum	

creatinine >2 mg/dL

[a]Rates of major cardiac complication with 0, 1, 2, or 3 of these factors were 0.4%, 0.9%, 7.0%, and 11.0%, respectively.

Adapted from Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043–1049.

b. Cardiac risk indices/calculators. Several tools have been created to aid in predicting preoperative risk of a MACE. The Revised Cardiac Risk Index is one such tool, and its criteria are shown in Table 1-1. The American College of Surgeons NSQIP Surgical Risk Calculator combines cardiac and noncardiac factors to calculate the risk of overall postoperative complications and can be found at riskcalculator.facs.org.

c. Functional status. Patients with poor functional status are at significantly elevated risk of perioperative cardiac events. This can usually be assessed from a patient's activities of daily living (ADLs) and is often expressed in metabolic equivalents (METs), with 1 MET equaling the resting oxygen consumption of an average 40-year-old male (Table 1-2). Functional capacity can be classified as excellent (>10 METs), good (7 to 10 METs), moderate (4 to 6 METs), or poor (<4 METs). Moderate functional capacity is classified as the ability to perform usual ADLs.

d. Preoperative testing. Specific preoperative workup is based on several factors including medical history, urgency of surgery, risk of surgical procedure, patient functional status, and goals of care. A treatment algorithm derived from ACC/AHA 2014 guidelines that guides the preoperative cardiac workup is shown in Figure 1-1. When it is determined that a patient requires further testing prior to surgery, a multidisciplinary approach including a cardiologist is employed to determine which noninvasive or invasive measure should be taken to optimize the patient. Interestingly, the recently published 2017 guidelines from the Canadian Cardiovascular Society (CCS) advocate for the use of preoperative biomarkers (BNP and pro-BNP) instead of functional

status as the key discriminator for the need for further testing. Ongoing studies are designed to address this question (*Can J Cardiol*. 2017;33(1):17–32).

TABLE 1-2 Assessment of Functional Status

Functional Capacity	MET Range	Example Activities
Poor	<4	Sleeping, writing, watching TV, walking 2–3 mph on flat land, golfing with a cart
Moderate	4–7	Climbing a flight of steps, slow bicycling, sexual activity
Good	7–10	Jogging, calisthenics
Excellent	>10	Rope jumping

e. Preoperative management

(1) Patients with pacemakers should have their pacemakers turned to the uninhibited mode (e.g., DOO) before surgery. In addition, bipolar cautery should be used when possible in these patients. If unipolar cautery is necessary, the dispersive electrode should be placed away from the heart.

(2) Patients with internal defibrillators should have these devices turned off during surgery.

(3) Perioperative beta-blockade should be considered as part of a thorough evaluation of each patient's clinical and surgical risk. Preoperative evaluation should involve identification of active cardiac conditions that would require intensive management and may result in delay or cancelation of nonemergent operations. Over the past 15 years, there has been conflicting and poorly supported evidence regarding the efficacy of beta-blockers in reducing perioperative cardiac events. However, recent studies, including the POISE trial, suggest that beta-

blockers reduce perioperative ischemia and may reduce the risk of MI and cardiovascular death in high-risk patients (*Lancet*. 2008;371:1839–1847). Routine administration of higher-dose, long-acting metoprolol on the day of surgery should be avoided in beta-blocker naïve patients, as its use is associated with an overall increase in mortality. Beta-blockers should ideally be started in appropriate patients days to weeks before elective surgery. Preoperatively, each patient's dose should be titrated to achieve adequate heart rate control to benefit from beta-blockade while avoiding the risks of hypotension and bradycardia (*Circulation*. 2009;120:2123–2151).

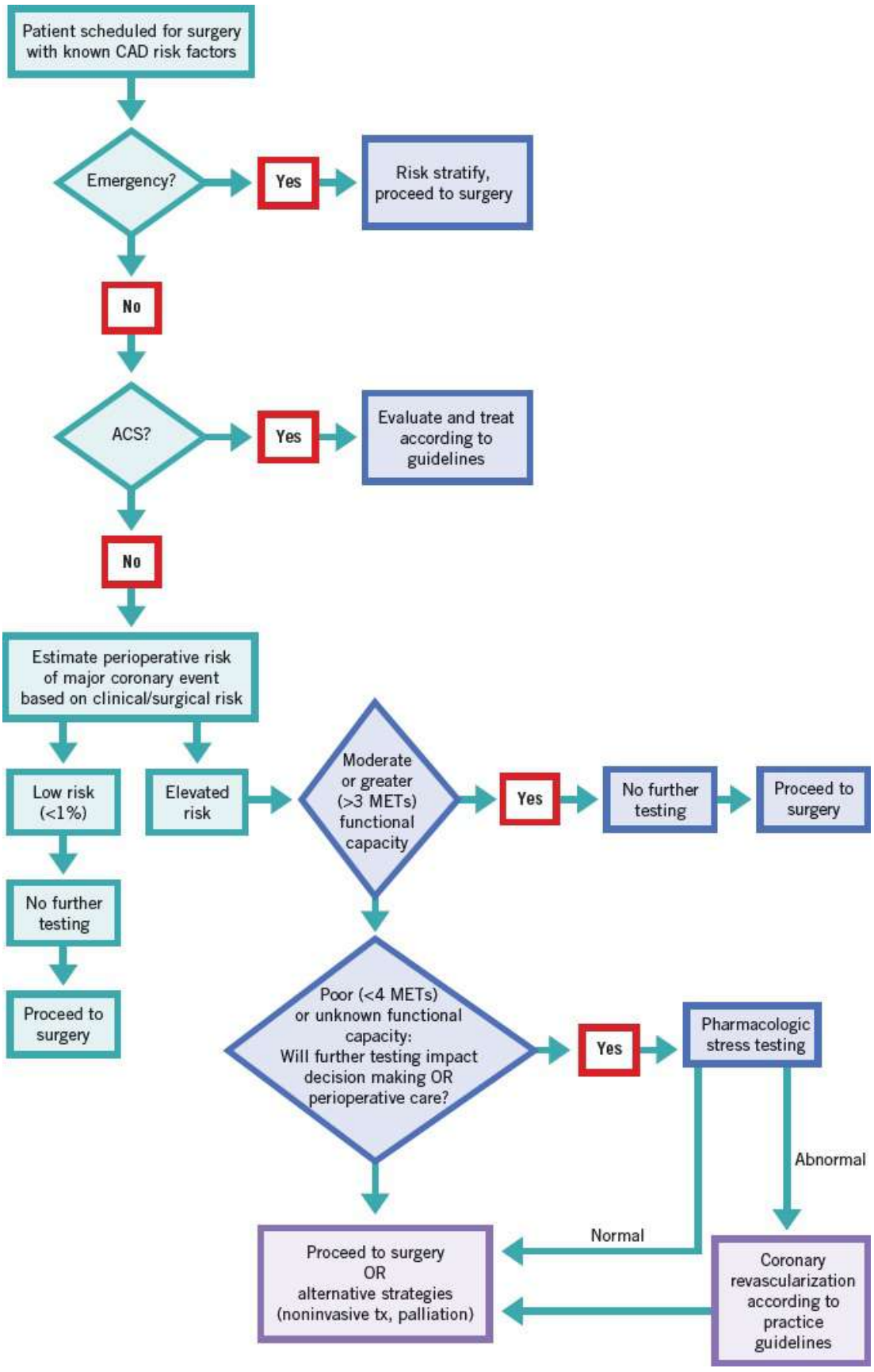

Patient scheduled for surgery with known CAD risk factors
Emergency?
Yes
Risk stratify, proceed to surgery
No
ACS?
Yes
Evaluate and treat according to guidelines
No
Estimate perioperative risk of major coronary event based on clinical/surgical risk
Low risk (<1%)
No further testing
Proceed to surgery
Elevated risk
Moderate or greater (>3 METs) functional capacity
Yes
No further testing
Proceed to surgery
Poor (<4 METs) or unknown functional capacity: Will further testing impact decision making OR perioperative care?
Yes
Pharmacologic stress testing
Abnormal
Normal
Proceed to surgery OR alternative strategies (noninvasive tx, palliation)
Coronary revascularization according to practice guidelines

FIGURE 1-1 Algorithm for preoperative workup of cardiac disease. (Adapted from Flelisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Col Cardiol*. 2014;64(22):e77–e137.)

(4) Patients with recent angioplasty or stenting. Over the past two decades, use of coronary angioplasty and stenting has increased dramatically. Several studies have shown a high incidence of cardiovascular complications when noncardiac surgery is performed shortly after coronary angioplasty or stenting. Current guidelines (ACC/AHA 2016) are to delay noncardiac surgery at least 6 weeks after coronary angioplasty or placement of bare metal stents for stable ischemic disease as these require at least 1 month of dual antiplatelet therapy (DAPT), aspirin 81 mg, and clopidogrel. In contrast, DAPT should be continued for at least 6 to 12 months following placement of newer-generation drug-eluting stent (DES, first generation rarely if ever used clinically), which can affect timing of elective operations. If coronary stents were placed for PCI following acute or recent ACS, then DAPT should be continued for 12 months. For all patients, the risk of bleeding and thrombosis need to be weighed against each other. Surgery in an open body space, such as the abdomen, is possible on patients taking these medications, albeit with an elevated bleeding risk.

2. Pulmonary disease

a. Preoperative evaluation and screening

(1) History. Pre-existing lung disease confers a dramatically increased risk of perioperative pulmonary complications. Risk factors for pulmonary complications include chronic obstructive pulmonary disease, smoking, asthma, obstructive sleep apnea, advanced age, obesity, surgical site located near the diaphragm, and functional status.

(2) Physical examination should be performed carefully, with attention paid to signs of lung disease (e.g., wheezing, prolonged expiratory–inspiratory ratio, clubbing, or use of accessory muscles of respiration).

(3) Diagnostic evaluation

(a) A chest x-ray (CXR) should only be performed for acute symptoms related to pulmonary disease, unless it is indicated for the specific procedure under consideration.

(b) An **arterial blood gas (ABG)** can be considered in patients with a history of lung disease or smoking to provide a baseline for comparison with postoperative studies, but is not reliable to accurately predict postoperative pulmonary complications.

(c) Preoperative pulmonary function testing is controversial and probably unnecessary in stable patients with previously characterized pulmonary disease undergoing nonthoracic procedures.

b. Preoperative prophylaxis and management

(1) Pulmonary toilet. Increasing lung volume by the use of preoperative incentive spirometry is potentially effective in reducing pulmonary complications.

(2) Antibiotics do not reduce pulmonary infectious complications in the absence of preoperative infection. Elective operations should be postponed in patients with respiratory infections. If emergent surgery is required, patients with acute pulmonary infections should receive intravenous (IV) antibiotic therapy.

(3) Cessation of smoking. All patients should be encouraged to and assisted in smoking cessation before surgery. There has been debate over timing of smoking cessation, in particular over whether smoking cessation within weeks of surgery may paradoxically increase pulmonary complications. This concern, however, is not supported by evidence, and current guidelines favor smoking cessation prior to surgery regardless of time frame.

(4) Bronchodilators. In the patient with obstructive airway disease and evidence of a significant reactive component, bronchodilators may be required in the perioperative period. Elective operation should be postponed in the patient who is actively wheezing.

3. Renal disease

a. Preoperative evaluation of patients with existing renal insufficiency

(1) Evaluation

(a) History. Patients with hypertension or diabetes and CRI are at a substantially increased risk of perioperative morbidity and mortality. The timing and quality of the patient's last dialysis session, the amount of fluid removed, and the preoperative weight provide important information about the patient's volume status. In nonanuric patients, the amount of urine made on a daily basis should also be documented.

(b) Physical examination should be performed to assess the volume status. Elevated jugular venous pulsations or crackles on lung examination can indicate intravascular volume overload.

(c) Diagnostic testing

(i) Laboratory data. Serum electrolyte and bicarbonate levels should be measured, as well as blood urea nitrogen (BUN) and creatinine. A complete blood cell count (CBC) should be obtained to evaluate for significant anemia or a low platelet level. Normal platelet numbers can mask platelet dysfunction in patients with chronic uremia.

(2) Management

(a) Timing of dialysis. Dialysis should be performed within 24 hours of the planned operative procedure.

(b) Intravascular volume status. Cardiac events are the most common cause of death in patients with CRI. Both hypovolemia and volume overload are poorly tolerated, and invasive monitoring in the intra- and postoperative periods may assist in optimizing fluid balance.

b. Preventing perioperative renal dysfunction

(1) Risk factors. Patients without pre-existing CRI ranges may be at risk of developing postoperative acute renal failure (ARF), depending on certain patient and procedure risk factors. Incidence of postoperative ARF ranges from 1.5% to 2.5% for

cardiac surgical procedures to more than 10% for patients undergoing repair of supraceliac abdominal aortic aneurysms (AAAs). Other risk factors for the development of ARF include elevated preoperative BUN or creatinine, CHF, advanced age, intraoperative hypotension, sepsis, aortic cross-clamping, intravascular volume contraction, and use of nephrotoxic and radionuclide agents.

(2) Prevention

(a) Intravascular volume expansion. Adequate hydration is the most important preventive measure for reducing the incidence of ARF.

(b) Radiocontrast dye administration. Patients undergoing radiocontrast dye studies have an increased incidence of postoperative renal failure. Fluid administration (1 to 2 L of isotonic saline) alone appears to confer protection against ARF. Additional commonly used but unproven measures for reducing the incidence of contrast dye-mediated ARF include the use of low-osmolality contrast agents, a bicarbonate drip, and oral N-acetylcysteine.

(c) Other nephrotoxins—including aminoglycoside antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and various anesthetic drugs—can predispose to renal failure, as well, and should be avoided in patients at high risk for postoperative renal failure.

4. Infectious complications. Infectious complications are a major cause of morbidity and mortality following surgery. They may arise at the surgical site itself or in other organ systems. It is impossible to overemphasize the importance of frequent handwashing or antiseptic foam use by all health care workers to prevent the spread of infection. In addition to impacting the patient, rates of postsurgical infections are closely monitored by hospitals and health care providers, and are increasingly being used as a metric by which hospitals, departments, and surgeons are measured.

a. Assessment. Risk factors for infectious complications after surgery can be grouped into procedure- and patient-specific risk factors.

(1) Procedure-specific risk factors include the type of operation,

the degree of wound contamination (whether the case is classified as clean, clean–contaminated, contaminated, or dirty), and the duration and urgency of the operation.

(2) Patient-specific risk factors include age, diabetes, obesity, immunosuppression, malnutrition, pre-existing infection, smoking, and other chronic illness.

b. Prophylaxis

(1) Surgical site infection. Several modifiable factors under control of various members of the surgical team have been identified as preventable contributors to surgical site infections. Updated guidelines addressing strategies for the prevention of SSI was published in *JAMA* recently and is listed here in the form of a checklist, shown in Table 1-3 (*JAMA Surg*. 2017;152(8):784–791). Perioperative antibiotic recommendations for specific procedures are shown in Table 1-4.

TABLE 1-3 Recommendations for Prevention of Surgical Site Infection

Parenteral Antimicrobial Prophylaxis

- Prophylactic systemic antibiotics used according to guidelines timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made. (Category IB—strong recommendation, accepted practice.)
- In clean and clean–contaminated procedures, do not administer additional prophylactic antimicrobial agent doses after the surgical incision is closed in the operating room.

Nonparenteral Antimicrobial Prophylaxis

- Do not apply antimicrobial agents (i.e., ointments, solutions, or powders) to the surgical incision for the prevention of SSI. (Category IB—strong recommendation; low-quality evidence.)
- Application of autologous platelet-rich plasma is not necessary for the prevention of SSI. (Category II—weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)
- Consider the use of triclosan-coated sutures for the prevention of SSI.

(Category II—weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)

Glycemic Control

- Implement perioperative glycemic control and use blood glucose target levels less than 200 mg/dL in patients with and without diabetes. (Category IA—strong recommendation; high- to moderate-quality evidence.)
- No recommendation/unresolved issue—no RCTs evaluating the use of optimal hemoglobin A1c target levels or narrower blood glucose target levels.

Normothermia

- Maintain perioperative normothermia (Category IA—strong recommendation; high- to moderate-quality evidence.)
- No recommendation/unresolved issue—no identified RCTs evaluating strategies to achieve and maintain normothermia, the lower limit of normothermia, or the optimal timing of normothermia.

Oxygenation

- For patients with normal pulmonary function undergoing general anesthesia with endotracheal intubation, administer increased fraction of inspired oxygen (FiO_2) during surgery and after extubation in the immediate postoperative period. Maintain perioperative normothermia and adequate volume replacement to optimize tissue oxygen delivery. (Category IA—strong recommendation; moderate-quality evidence.)
- No recommendation/unresolved issue—uncertain trade-offs between benefit and harms regarding increased FiO_2 via endotracheal intubation during only the intraoperative period, only the postoperative period, or the optimal target level, duration, and delivery method of FiO_2 for the prevention of SSI.

Antiseptic Prophylaxis

- Advise patients to shower or bathe (full body) with soap (antimicrobial or nonantimicrobial) or an antiseptic agent on at least the night before the operative day. (Category IB—strong recommendation; accepted practice.)
- Perform intraoperative skin preparation with an alcohol-based antiseptic agent unless contraindicated. (Category IA—strong

recommendation; high-quality evidence.)

- The use of plastic adhesive drapes with or without antimicrobial properties is not necessary for the prevention of SSI. (Category II—weak recommendation; high- to moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)
- Application of a microbial sealant immediately after intraoperative skin preparation is not necessary for the prevention of SSI. (Category II—weak recommendation; low-quality evidence suggesting a trade-off between clinical benefits and harms.)
- Consider intraoperative irrigation of deep or subcutaneous tissues with aqueous iodophor solution for the prevention of SSI. Intraperitoneal lavage with aqueous iodophor solution in contaminated or dirty abdominal procedures is not necessary. (Category II—weak recommendation; moderate-quality evidence suggesting a trade-off between clinical benefits and harms.)
- No recommendations/unresolved issue—did not identify RCTs that evaluated soaking prosthetic devices in antiseptic solutions prior to implantation, RCT evidence was insufficient to evaluate the trade-offs between benefits and harms of repeated applications of antiseptic agents to patient's skin immediately before closing the surgical incision for the prevention of SSI.

Blood Transfusion

- Do not withhold transfusion of necessary blood products from surgical patients as a means to prevent SSI. (Category IB—strong recommendation; accepted practice.)

Adapted from Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017;152(8): 784–791.

TABLE 1-4 Recommendations for Antibiotic Prophylaxis

Operation	Likely Pathogens	Recommended Antibiotics
Cardiac: prosthetic valve and other	Staphylococci, corynebacteria,	Vancomycin and cefazolin Vancomycin and

procedures	enteric gram-negative bacilli	aztreonam
Thoracic	Staphylococci	Cefazolin Vancomycin
Vascular: peripheral bypass or aortic surgery with prosthetic graft	Staphylococci, streptococci, enteric gram-negative bacilli, clostridia	Cefazolin Vancomycin and aztreonam[a]
Orthopedic: total joint replacement or internal fixation of fractures	Staphylococci	Cefazolin Vancomycin
Gastrointestinal		
Upper GI and hepatobiliary	Enteric gram-negative bacilli, enterococci, clostridia	Cefazolin Cefotetan Cefoxitin
Colorectal	Enteric gram-negative bacilli, anaerobes, enterococci	Cefoxitin Cefotetan Ertapenem Cefazolin and metronidazole
Appendectomy (no perforation)	Enteric gram-negative bacilli, anaerobes, enterococci	Cefoxitin Cefotetan
Obstetrics/gynecology	Enteric gram-negative bacilli, anaerobes, group B streptococci,	Cefotetan Cefoxitin Cefazolin Clindamycin and

	enterococci	gentamicin

[a]IV, intravenous.

From Casabar E, Portell J. *The Tool Book: Drug Dosing and Treatment Guidelines, Barnes-Jewish Hospital*. 12th ed. St. Louis, MO: Department of Pharmacy, Barnes-Jewish Hospital; 2014.

(2) Respiratory infections. Risk factors and measures for preventing pulmonary complications are discussed in Section I.B.2.

(3) Genitourinary infections may be caused by instrumentation of the urinary tract or placement of an indwelling urinary catheter. Preventive measures include avoiding catheterization for short operations, sterile insertion of the catheter, and removal of the catheter on postoperative day 1. Some operations that include a low pelvic dissection will require longer catheterization because of local trauma.

5. Diabetes mellitus. Diabetic patients are at increased risk of morbidity and mortality. Vascular disease is common in diabetics, and MI, often with an atypical presentation, is the leading cause of perioperative death among diabetic patients.

a. Preoperative evaluation. All diabetic patients should have their blood glucose measured in preop holding and intraoperatively to prevent unrecognized hyperglycemia or hypoglycemia.

(1) Patients with diet-controlled diabetes mellitus can be maintained safely without food or glucose infusion before surgery.

(2) Oral hypoglycemic agents should be discontinued the evening before scheduled surgery. Long-acting agents such as chlorpropamide or glyburide should be discontinued 2 to 3 days prior.

(3) Insulin-dependent diabetics require insulin and glucose preoperatively to prevent ketosis and catabolism. Patients undergoing major surgery should receive one-half of their morning insulin dose and 5% dextrose IV. Subsequent insulin administration by either subcutaneous (SC) sliding-scale or insulin infusion is guided by frequent blood glucose

determinations. SC insulin pumps should be inactivated the morning of surgery.

6. **Surgery in the elderly.** The US population is aging, which means that operative teams are taking care of a greater number of older patients. With this experience comes an appreciation for the difference between a patient's chronologic and biologic age. Recently, the concept of frailty has been introduced to address this finding, and has proven to be an excellent tool for predicting perioperative morbidity in elderly surgical patients. A joint statement from the American College of Surgeons and the American Geriatrics Society first recommended frailty assessment as part of the preoperative assessment for older surgical patients in 2012 (*JACS*. 2012;215(4):453–466), with a recent update in 2016 to address the remainder of perioperative care (*JACS*. 2016;222(5):930–947).
   a. **Assessment.** Frailty screening can serve not only as a prognostic tool for early identification of high-risk patients, but also has the potential to identify patients who may benefit from preoperative therapy. Preoperative physical and cognitive therapy, often called prehabilitation, is designed to improve patients' functional status and ultimately improve their perioperative outcomes.
      (1) Frailty screening
         (a) Patients most likely to benefit from screening are seniors (>65 years old) undergoing intermediate- or high-risk surgical procedures (i.e., those with a cardiac risk higher than 1%).
         (b) Multiple screening tools exist (frailty index, FRAIL scale, etc.); however, none have been shown as superior.
   b. **Application.** Once made, a diagnosis of frailty can then impact several phases of patient care (*J Clin Anesth*. 2018;47:33–42).
      (1) Shared decision making
         (a) Surgery is higher risk in the frail population; therefore, a frailty diagnosis makes it essential to establish upfront goals of care and confirm that these are in keeping with anticipated surgical outcomes.
      (2) Prehabilitation
         (a) Although no established, standardized preoperative exercise

therapy regimen currently exists, there is a growing body of evidence to suggest that in select patient populations preoperative interventions can improve patients' perioperative morbidity and mortality.

(3) Interdisciplinary geriatric comanagement

(a) Similarly, inpatient geriatric comanagement programs are an increasingly popular strategy that have been shown to improve perioperative morbidity and mortality. Although the majority of this data is in orthopedic fracture surgery, there is promising initial data from its application in other surgical fields.

CHAPTER 1: PREOPERATIVE EVALUATION AND CARE

Multiple Choice Questions

1. **Which of the following factors is associated with the highest elevated cardiac risk?**

   a. Diabetes controlled with metformin and glyburide
   b. Mild renal impairment with a preoperative creatinine level of 1.7 mg/dL
   c. History of a transient ischemic attack 9 months ago
   d. History of hypertension controlled with three medications

2. **Classify the functional status of a patient who is able to golf with a cart and climb two flights of steps but unable to jog or do push-ups:**

   a. Poor
   b. Moderate
   c. Good
   d. Excellent

3. **Which of the following is a recommendation endorsed by the Centers for Disease Control and Prevention to reduce the risk of surgical site infection?**

   a. Hair removal from surgical site by shaving
   b. Tight glucose control perioperatively with goal of <180 mg/dL
   c. Core body temperature maintained above 35.5°C
   d. Use of increased FiO_2 both during and immediately postoperatively in patients who had general anesthesia with endotracheal intubation

4. **Which of the following patients would require pharmacologic stress testing prior to surgery?**

   a. A patient presenting with sepsis from perforated diverticulitis who has known coronary artery disease
   b. A patient with history of coronary artery disease and three-vessel

CABG with moderate functional status presenting for elective knee replacement

c. A diabetic set to undergo peripheral arterial bypass who has no dyspnea on exertion but for whom claudication limits walking to ~10 paces

d. An elderly male with coronary artery disease and diabetes who is able to bicycle several miles without dyspnea and is scheduled for major liver resection

5. Which of the following is an indication for postoperative hemodialysis?

a. A potassium level of 6.2 in an oliguric patient with no ECG changes

b. Removal of fluid in an intubated and anuric patient with pulmonary edema

c. Oliguria and sepsis in a patient with creatinine 2× baseline and a moderate metabolic acidosis

d. A severely under-resuscitated patient with creatinine on 6.8

6. A 53-year-old male undergoes emergent exploratory laparotomy for perforated sigmoid diverticulitis. He is not septic and makes urine throughout the case, but the procedure lasts for 5 hours and the patient receives over 4 L of intravenous crystalloid. When should this patient's Foley catheter be removed following surgery?

a. Immediately following the procedure

b. On postoperative day 1

c. On postoperative day 3 if no hematuria is present and ureteral injury ruled out

d. When patient is ambulatory

7. Which of the following patients would most likely benefit from frailty screening?

a. 56-year-old female with colon cancer, preparing for laparoscopic left hemicolectomy

b. 80-year-old male with basal cell carcinoma, preparing for MOHS surgery of left scalp

c. 45-year-old female with biliary colic, preparing for laparoscopic cholecystectomy
d. 73-year-old male with a left upper lobe lung cancer, preparing for left upper lobectomy

2 Intraoperative Considerations

Matthew R. Schill and Michael M. Awad

Despite the vast breadth of general surgery and its subspecialties, the general principles of planning and executing operations share many similarities regardless of the operative approach. Attention to detail in the planning and execution of a patient's surgical care facilitates the best possible outcome for the patient and improves the working environment for the surgical team. This chapter presents a conceptual framework for planning and executing an operation (Table 2-1). Not all of these principles are applicable to every case, but they serve as a useful checklist for surgeons and surgical trainees.

PLANNING OPERATIONS

I. TEAMWORK AND INTERDISCIPLINARY COOPERATION.

Surgeons strive to provide excellent and safe care for patients. However, even the best surgeon cannot do this in isolation. Comprehensive surgical care requires the knowledge and skills of multiple other professionals, including anesthesiologists and nurse anesthetists, perioperative nurses and surgical technologists, and the support of hospital-based ancillary services. In leading the patient's care team through the course of the operation and recovery, the surgeon must ensure clear dialogue with others in the operating room. The use of individuals' **names** facilitates effective communication, especially at large institutions where the surgical team may change on a daily basis. **Closed-loop communication** is a technique for safe communication where every request or question is met with an answer. A **culture of safety** encourages any individual on the team to speak up if they observe risks or problems.

II. PREOPERATIVE PERIOD

A. Preoperative evaluation is covered in detail in Chapter 1, Preoperative Evaluation and Care. From the perspective of planning an elective operation, it is the responsibility of the surgeon to personally interview and examine the patient, establish or confirm the diagnosis, independently review and interpret testing, and generate a surgical plan. This can occur in the office, the hospital ward, or the emergency department. Different approaches are balanced, considering not only technical feasibility but also a determination of the potential risks of the operation and means to reduce them. In oncology, the technical possibility of curative resection is referred to as **resectability** and the patient's ability to withstand the stress of surgery is referred to as **operability**. Other physicians such as the patient's primary care physician, anesthesiologists, and cardiologists may aid in this effort, but ultimately the responsibility for risk stratification lies with the surgeon. Consultation with an anesthesiologist is routinely obtained prior to major surgery. Risk calculators such as that provided by the American College of Surgeons National Surgical Quality Improvement Program (http://riskcalculator.facs.org) may be helpful in estimating a patient's risk of significant morbidity and mortality.

TABLE 2-1 Framework for Conceptualizing an Operation

Preoperative period
Positioning
Preparation
Access
Exploration
Dissection
Resection
Reconstruction
Closure

B. Once the surgeon develops a plan for the patient's operation, this is presented to the patient in the form of an **informed consent** discussion. The law requires that a patient or his or her surrogate and the surgeon both discuss the proposed operation and sign a form attesting that they did so. The indication for the operation, the anticipated risks, the expected benefits, and alternative treatments must be discussed in such a way that a reasonable person would be able to make an informed decision. The discussion must be calibrated to the patient's degree of medical literacy. Conducting these discussions well is an important part of the art of surgery. It is helpful to ask the patient to describe in his or her own words what operation will be performed to ensure that he or she understands. When a major operation is planned, the patient's preferences regarding cardiopulmonary resuscitation, ventilator support, and other life-sustaining treatments should be discussed and a surrogate decision maker identified, should the patient become incapacitated. Copies of any advance directives should be placed in the patient's chart. The best time for this discussion to occur is during the initial consultation; the worst time is after a major complication.

C. As the date of the operation approaches, the surgeon and any surgical trainees (fellows, residents, and medical students) involved in the case should review the patient's history and imaging, the operative approach, potential technical pitfalls, and rescue strategies. It is best practice to discuss the plan prior to the day of surgery.

D. On the day of surgery, a member of the surgical team interviews and examines the patient. The history and physical examination must be updated; if the office consultation occurred more than 30 days prior to surgery, the history and physical must be redone, both for completeness and billing compliance purposes. In the preoperative holding area, the surgeon, anesthesia team, and operating room nurse meet the patient and review the planned procedure and site. If there could be any question about the location or laterality of the operative site, it should be marked. The patient is then transported to the operating room.

E. In the operating room, a "sign-in" briefing is performed. This consists of identification of the patient, verification of the site and operation to be performed, pitfalls including allergies or anticipated blood loss, and the safety of the equipment for anesthesia and surgery. Except in life-threatening emergencies, the room should be quiet during the induction

of anesthesia.

III. POSITIONING

A. After anesthesia is induced, the patient is positioned. Positioning is a key technical maneuver; correct positioning protects the patient and can often allow gravity to assist in retraction, particularly in laparoscopic surgery. The patient should be secured to the operating table by straps at two or more points to prevent falls. Pressure points including the elbows, wrists, and heels should be padded to reduce the risk of pressure sores. Limbs should be kept in neutral positions when possible to prevent neurapraxia.

B. Common positions for operations in general surgery include supine, lithotomy, lateral, and prone jackknife. **Supine** position is conceptually simple, but the positioning of the arms and legs bears consideration. It is common to place the arms supinated and abducted as this facilitates access for the anesthesia team and allows the surgeons to stand closer to the patient. If fluoroscopy is planned, the arm nearest the door should be tucked adducted against the body. Tucking the arms can facilitate pelvic surgery as well. Some surgeons abduct the legs to facilitate a laparoscopic approach to the upper abdomen. Flexing the hips and knees and abducting the hips produce the commonly used **lithotomy** position, which provides simultaneous exposure of the perineum and abdomen. Padding the lateral aspect of the knee is important for preventing injury to the peroneal nerve. **Lateral** positioning is used for thoracotomy and operations on the back; careful attention to padding of the hip, shoulder, and axilla is required. Flexion of the bed helps open the ribcage on the operative side. **Prone jackknife** position is commonly used for anorectal surgery but presents special challenges for the anesthesia provider due to the face pointing downward. Operations on the anterior neck are facilitated by extension of the neck with care taken to avoid injuring the cervical spine.

C. During the process of positioning the patient, thought should be given to planned changes in positioning. Abdominal operations, whether laparoscopic or open, frequently employ **Trendelenburg** (head down) and reverse Trendelenburg positioning and rotation of the bed. It is important to ensure that space is free around the bed to permit this. Many open abdominal operations employ self-retaining retractors which

can be fixed to the bed. It is important to verify that there is space available for this (typically just caudal to the axilla on the assistant's side of the table). Equipment and personnel should be positioned around the patient in a convenient manner. Typically, the operating surgeon stands opposite the pathology. For any laparoscopic or endoscopic case, screens should be positioned so that all team members can see.

D. Most operations employ monopolar electrosurgical devices. The return electrode should be placed far from the operative field on a broad, flat patch of skin, usually on the thigh or back. This electrode must be placed away from metallic implants and implanted electrical devices.

IV. PREPARATION

A. After positioning, the surgical site is prepared. Excess hair is removed to prevent its being pulled into the wound. This should be performed using mechanical clippers, not by shaving, as this has a lower rate of infection. Antiseptic agents are then used to disinfect the skin. Common agents include 4% chlorhexidine gluconate and 10% povidone-iodine. Chlorhexidine is more commonly used but the solution contains alcohol and is flammable until completely dry. It is also quite irritating to mucous membranes and open wounds. Povidone-iodine temporarily discolors tissues, and allergies to it are common. After the prep is dried, draping is performed. Draping should cover all of the operating table in a sterile fashion, leaving the surgical site and any areas the surgical team may need to access exposed. As an example, for a laparoscopic hernia repair, both groins should be prepped in addition to the abdomen. Appropriate exposure must be balanced with prevention of hypothermia.

B. The surgical team wears hats and masks and performs hand hygiene, either by traditional scrubbing or by using an alcohol- and chlorhexidine-based gel. Sterile gowns and gloves are donned. The use of two pairs of gloves is recommended for prevention of body fluid contamination and needlestick injury.

C. Prior to skin incision, a "time-out" is performed, which can be abbreviated under emergent circumstances. All team members state their name and role. The patient's identity, planned operation, prophylactic antibiotics if indicated, anticipated critical events, and availability of preoperative imaging are confirmed. The use of briefings and time-outs

has been shown in a multicenter prospective study to reduce postoperative mortality by 47% (*N Engl J Med*. 2009;360:491–499).

GENERAL PRINCIPLES OF SURGICAL PROCEDURES

V. ACCESS

A. Most operations commence by entering or creating a potential space around the target anatomy. This can consist of making an incision large enough to directly see and operate through (**open** surgery), making a small incision and introducing a camera into a potential space (**laparoscopic** or **thoracoscopic** surgery), passing a flexible endoscope via a natural orifice (**endoscopic** surgery), or percutaneously introducing a sheath into a vessel (**endovascular** surgery). It is critical to avoid unintended injury to other structures while obtaining access.

B. Open abdominal operations are performed through one of several abdominal incisions, each of which has its own strengths and weaknesses.

1. The workhorse incision is the **midline laparotomy**, performed between the xiphoid process and the pubic symphysis. Care is taken to carry the incision through the linea alba rather than the rectus abdominis to simplify closure. It is uncommon to open the full midline except in trauma, as most elective operations can be performed using only a portion of this extensible incision. The peritoneal cavity is usually entered bluntly just superior to the umbilicus.

2. Subcostal incisions were traditionally used for open cholecystectomy; bilateral subcostal incisions with midline extension provide optimal exposure of the upper abdomen and are used for liver transplantation.

3. **Paramedian** incisions have fallen out of favor due to the risk of hernia and potential loss of nervous supply to the rectus muscle.

4. The **Pfannenstiel** incision is comprised of a transverse skin incision just above the pubis with a lower midline fascial incision and offers improved cosmesis for pelvic surgery.

5. Muscle-splitting incisions, such as the **McBurney** incision in the right lower quadrant for appendectomy, are occasionally used.

6. **Retraction** allows the edges of an incision to be moved relative to the

underlying anatomy to facilitate exposure. Handheld retractors facilitate rapid changes in exposure but can be fatiguing for assistants. Self-retaining retractors such as the simple Balfour or the bed-mounted Bookwalter and Omni systems are ideal for longer cases.

C. Laparoscopic surgery requires insufflation of the peritoneal cavity with CO_2 to create working space and the use of a rigid scope for visualization. Laparoscopic access can be obtained either by cutting down to the peritoneum under direct visualization (the **Hasson** technique) or by percutaneous introduction of a **Veress** needle followed by trocar placement. Common sites for routine entry are either above or below the umbilicus or at Palmer point in the left upper quadrant. Additional ports are placed under laparoscopic visualization so as to be able to **triangulate** the target anatomy. Further technical details of laparoscopic surgery as well as **robotic** surgery are discussed in Chapter 30, Endoscopic, Laparoscopic, and Robotic Surgery.

D. Flexible endoscopy has been used for diagnostic and therapeutic purposes by surgeons for decades. In recent years there has been growing interest in performing more complex surgical procedures via this approach. Advanced endoscopy performed in the operating room often requires special equipment including energy devices and endoscopic instrumentation. Although diagnostic endoscopy is routinely performed under moderate sedation, advanced endoscopic surgical procedures are typically performed under general anesthesia. Further details regarding endoscopic surgery are discussed in Chapter 30.

E. Endovascular approaches have revolutionized vascular surgery and are increasingly utilized in cardiac surgery. Endovascular access is routinely obtained with the aid of **ultrasound**, and procedures are performed using x-ray **fluoroscopy**. Such procedures can be performed in a standard operating room with a “C-arm” portable fluoroscope, in a cardiac catheterization laboratory, or in an interventional radiology suite. Hybrid operating rooms with fixed fluoroscopic equipment, a catheterization laboratory table, and ample space for open surgical instruments as well as wires and catheters, provide an ideal environment for combined open and endovascular techniques. Appropriate positioning of equipment, the use of a radiolucent operating table, and appropriate radiation protection for surgeons and operating room staff

are key considerations in planning this approach. Details of specific procedures are discussed in Chapters 36 to 41.

VI. EXPLORATION

A. After access to the target anatomy is obtained, the next phase of any operation is **exploration.** Exploration is the systematic examination of the potential space containing the target anatomy to ensure that no iatrogenic injury was made during access, to detect unexpected pathology, and to confirm the preoperative diagnosis. A helpful mnemonic for this is to look down, look around, and then to look forward. Examples include the systematic exploration of the abdomen in trauma laparotomy, diagnostic laparoscopy prior to committing to a cancer resection, exploration for splenules during splenectomy for idiopathic thrombocytopenia, and angiography prior to an endovascular procedure. Both visualization and **palpation** (in open and laparoscopic surgery) are useful tools.

B. Once exploration has concluded, the surgeon must decide whether to proceed with the planned operation and if any alterations to the preoperative plan are necessary. If changes to the plan are made, these should be communicated to the rest of the operating room team in timely fashion.

VII. DISSECTION

A. After exploration, the next phase of most operations is **dissection**. As the beginning medical student quickly discovers in the anatomy laboratory, many named anatomic structures are hidden behind adipose and loose fibrous connective tissue and must be separated from this surrounding tissue prior to completing the intended operation. In reoperative or irradiated fields, dense fibrous scar tissue can present significant obstacles, even for experienced surgeons.

B. Sharp dissection involves the use of sharp instruments (scissors, knife) or electrosurgical devices to divide tissue. Sharp dissection can be performed quickly when the underlying anatomy is confidently known. When the underlying anatomy is unknown, sharp dissection must be performed cautiously, “layer by layer,” to avoid lacerating deeper structures. Structures should be divided under tension, which is

provided by the surgeon exerting **traction** while an assistant exerts **countertraction**.

C. Blunt dissection involves the use of blunt instruments to spread or peel fibrofatty tissues away from named anatomic structures. Blunt dissection should be performed without excessive force and in a systematic fashion.

D. The concept of a **tissue plane** is critical to dissection. A common pitfall for the beginning surgical resident is dissecting in random fashion without making progress. Dissection is more straightforward when a potential space is developed in linear fashion between two named structures. Successful dissection relies both on **visual** and **tactile** cues which are learned with experience.

E. Knowledge of both **normal** and **variant anatomy** is necessary for safe dissection. Failure to recognize anatomic variations contributes to many preventable surgical complications. This knowledge is gained both by preparation and experience. Pre- and intraoperative imaging are helpful adjuncts.

F. It is routine for the surgeon leading the operation to bluntly dissect structures while the first surgical assistant divides structures sharply, places ties, and aids in retraction. **Anticipation** of subsequent steps of the operation allows the assistant to be more effective.

G. Hemostasis is the control of bleeding. In the routine course of dissection, capillary beds, arterioles, and venules are routinely divided. Many of these vessels will retract and stop bleeding on their own, but many will not. Various techniques are used to achieve hemostasis:

1. **Direct pressure** compresses small vessels, facilitating coverage of the vessel injury by thrombus. Capillary bleeding from the skin edge can often be placed under sufficient direct pressure simply by closing a wound.
2. **Energy devices.** Monopolar electrosurgical devices, often referred to as “the Bovie,” are routinely used to stop tiny bleeding vessels. Grasping the vessel with forceps prior to applying energy facilitates more effective vessel sealing. Bipolar electrosurgical devices have less thermal spread, and advanced bipolar devices can control larger vessels. Ultrasonic devices are also effective. Further details may be found in the SAGES Fundamental Use of Surgical Energy course

(http://www.fuseprogram.org).

3. **Ligation** is the process of passing a suture or tie around a blood vessel and tying it down securely. In general, named vessels should be ligated prior to dividing them, and it is prudent to doubly ligate named arteries, with at least one suture ligature (in which the suture is passed through the vessel wall prior to tying it around the vessel).
4. **Topical hemostatic agents** promote thrombosis. These are useful for bleeding refractory to the above techniques, especially in coagulopathic patients. Specific products are discussed in Chapter 6, Hemostasis, Anticoagulation and Transfusion.

H. Just as after exploration, the end of the dissection phase of the operation, with final delineation of the relevant anatomy, represents another point at which the surgeon decides whether to proceed with the planned operation.

VIII. RESECTION

A. Resection is the removal of abnormal or diseased tissue. Although this term is most commonly applied to malignancy, the same concept can be relevant to closed-space infections, ischemia, and degenerative disease. Most operations include resection, followed by reconstruction. Some operations are extirpative, meaning that they only consist of removing something; appendectomy is an example. Other operations are only reconstructive, such as repair of a gunshot wound to the liver.

B. Margin is a key concept in any resection. In oncology, margin is defined as the distance between cancer cells and the edge of the resected specimen. The specific margin required markedly varies by tumor type and location. The same concept is involved in benign disease, although its prognostic significance is less well defined. Infected, ischemic, or necrotic tissue must be debrided to a margin of viable tissue to produce a good result.

C. Contamination should be avoided during any resection. In general, tumors should be left intact until removal from the operative field in order to prevent inoculation of the operative field with cancer cells. Similarly, efforts should be made to prevent spillage of pus, succus, or stool into the operative field to prevent postoperative infections.

D. Pathologic examination of resected specimens is routinely performed.

This serves to confirm the diagnosis, to provide additional prognostic information in some cases, and to check for unsuspected findings, such as occult malignancy. If the diagnosis or margin is in question and would alter intraoperative management, intraoperative pathologic evaluation of a **frozen section** of the specimen may be obtained.

IX. RECONSTRUCTION

A. After or in lieu of resection, most operations involve reconstruction. **Reconstruction** is the arrangement of tissues to restore a functional physiologic state.

B. In gastrointestinal and vascular surgery, reconstruction often involves an **anastomosis**, a sutured or stapled connection between two hollow structures. Anastomoses must be **patent**, allowing free passage of luminal contents, and must not **leak**. Anastomoses must be well perfused, performed using meticulous technique, and constructed without tension to ensure success.

C. In unstable patients, reconstruction is often deferred to a later date. This concept of **damage control** surgery is discussed further in Chapter 12, Abdominal Trauma.

X. CLOSURE

A. After the intended operation is nearly complete, the surgeon notifies the anesthesia and nursing staff, and then closes the wound. At first glance this appears straightforward, but the surgeon and operating room team make several safety checks during the process of closure.

1. **Hemostasis** is obtained, as above. “Run-down” blood carried by gravity into the wound can obscure sources of bleeding, so bleeding should be controlled in top-down fashion. Irrigation can provide additional insight into the location of bleeding as well.
2. The surgical site should be checked to ensure that any sutures and staple lines are intact.
3. **Surgical drains** should be considered. The use of drains varies markedly by procedure and surgeon preference. Closed spaces are drained in an attempt to prevent hematoma or seroma formation, and the drains are removed when the output becomes scant. Intraperitoneal drains are used to monitor the character of drainage

from a particular location, and if no complications arise, they are typically removed once the patient has returned to a regular diet regardless of the volume of drainage. In recent years, the benefit of routine use of intra-abdominal drains has been called into question in many areas of general surgery.

4. Surgical instruments, towels, sponges, and other items are meticulously counted by two members of the operating room staff. An item unintentionally left inside the patient is potentially disastrous. If there are discrepancies in the count, x-rays should be obtained and read prior to closing the wound. Retractors, trocars, insufflated gas, and other items facilitating access are removed.
5. Finally, the wound itself is closed. In general, at least two layers are used, one in the fascia and one in the skin. Very small wounds, such as small laparoscopic port sites, do not require fascial closure. Fascial closure must be secure to prevent dehiscence and the potential for evisceration. Sutures should be snug but not so tight as to cause ischemia when postoperative edema develops. Laparotomies have traditionally been closed using sutures with 1 cm depth and 1 cm spacing, but a recent randomized trial showed that the use of smaller bites may be superior for prevention of incisional hernia (*Lancet*. 2015;386:1254–1260).
6. The skin may be closed using sutures or staples. In general, staples are used for routine laparotomy closure at our institution. Buried absorbable monofilament suture in running subcuticular fashion is routinely used for clean wounds in cosmetically important locations. Nonabsorbable mattress sutures placed in interrupted fashion are used for wounds which may be exposed to tension.
7. Closure of the skin at the time of surgery facilitates healing by primary intention. Contaminated or infected wounds may be allowed to heal on their own, that is, by secondary intention, or closed in delayed fashion. Further details may be found in Chapter 15, Wound Care.

B. After closure, a **dressing** is placed in sterile fashion. The dressing should have an absorbent component next to the wound with an impermeable covering. The postoperative dressing is left in place for 48 hours in order to allow the wound to epithelialize prior to being exposed to contamination. Skin adhesive is used instead of a sterile dressing for

some clean wounds. Infected wounds are treated with simple dressings changed frequently or with negative pressure wound therapy.

C. Finally, the patient is permitted to emerge from anesthesia. Unless the patient is critically ill, extubation is performed in the operating room. The anesthesia team carefully monitors the patient for hemodynamic instability, emesis, delirium, and other potential problems.

D. A **debriefing** is then performed. The team reviews what operation was done, any unexpected issues from all perspectives (surgery, anesthesia, nursing), and the patient's postoperative plan. A brief operative note and postoperative orders are written prior to leaving the operating room. The patient is then transported to the postanesthesia care unit or the intensive care unit (ICU), where a representative from the surgical, anesthesia, and operating room nursing teams gives a scripted **handoff** to the recovery room nurse or ICU team. It is tempting to perform a cursory handoff after a long operation, but clear communication of the history, operative course, findings, and plan to those who will be taking care of the patient postoperatively is critical to ensuring a good outcome.

XI. SUMMARY.

This chapter provides a general overview of the conduct of operations. A systematic approach understood by all individuals involved with the patient's care facilitates safe and efficient patient care.

CHAPTER 2: INTRAOPERATIVE CONSIDERATIONS

Multiple Choice Questions

1. **Which of the following has been shown to reduce operative mortality by over 40%?**

   a. Using bites smaller than 1 cm to close fascia after a laparotomy
   b. Preoperative briefing, time-out, and debriefing
   c. Reviewing the patient's imaging prior to an operation
   d. Routine placement of surgical drains

2. **Who bears final responsibility for assessing a patient's risk of complications?**

   a. Surgeon
   b. Anesthesiologist
   c. Primary care physician
   d. Family

3. **The operative plan should be reassessed at the end of which stage of an operation?**

   a. Access
   b. Dissection
   c. Resection
   d. All of the above

4. **Which phase of an operation is sometimes omitted?**

   a. Resection
   b. Access
   c. Closure
   d. Dissection

5. **Which abdominal incision is no longer commonly used?**

   a. Midline
   b. Paramedian
   c. Subcostal

d. Pfannenstiel

3

Common Postoperative Problems

Jessica L. Hudson, Melissa K. Stewart, and Isaiah R. Turnbull

This chapter explores common postoperative problems and initial stages of their management. The evaluation of postoperative patients should begin with an assessment of clinical stability ("A, B, C's" of airway, breathing, and circulation). The next consideration should be the need to transfer to a higher level of care. The stable patient can be efficiently evaluated and treated on the inpatient ward. Patients with new-onset failure of more than one organ system (e.g., new respiratory insufficiency *and* new renal failure) or patients with an acute problem that does not respond to initial intervention (e.g., hypovolemia unresponsive to fluid challenge) should be considered for transfer to an intensive care unit (ICU). This chapter offers descriptions of commonly encountered postoperative pathologies and their initial workup and treatment.

I. NEUROLOGIC COMPLICATIONS

A. Diagnostic Considerations. The physiologic changes from surgical stress can affect neurologic function. The patient in postoperative day 0 is recovering from general anesthesia, the effects of which can last up to 48 hours. In addition, patients are placed in unfamiliar surroundings, are woken throughout the night, and are administered powerful medications to which they may not have been previously exposed. When evaluating neurologic concerns, initial differentiation should be made between the patient with altered sensorium characterized by somnolence, confusion, disorientation, and other deficits in executive function and the patient with focal neurologic changes such as slurred speech, changes in sensation or motor function, or cranial nerve deficits. This delineation

will guide development of a differential diagnosis. Altered sensorium primarily results from systemic problems such as hypoxemia, shock, or delirium. Focal neurologic deficits are concerning for an acute neurologic process such as stroke.

B. Basic Differential Diagnosis: respiratory insufficiency (hypoxia/hypercarbia), hypoglycemia, stroke, hypotension, arrhythmia, seizure, delirium, alcohol withdrawal, infection, medication side effect, and electrolyte abnormalities.

C. Initial Workup. A full set of vital signs including pulse oximetry and a finger-stick blood glucose should be immediately obtained. For somnolent patients, consider inadvertent or unknown extra administration of narcotic agents; a dose of 0.04 mg of naloxone is a reasonable treatment in this setting. A complete blood cell count and a comprehensive metabolic profile should be obtained to evaluate for hemorrhage, early signs of infection, and electrolyte disturbances. An arterial blood gas (ABG) can be obtained to determine if the patient needs positive pressure ventilation to recover from carbon dioxide narcosis. An electrocardiogram (ECG) should be obtained to evaluate for arrhythmias and MI. All patients with new focal neurologic findings should undergo an emergent computed tomographic (CT) scan of the head to evaluate for intracranial hemorrhage; although, ischemic stroke may not be evident on acute CT imaging.

D. Special Considerations

1. **Immediately postoperative patients** will likely be drowsy but should be arousable to voice or light touch. Common causes of somnolence in the acute perioperative period are narcotic overdose and hypoxemia. If the patient's respiratory rate is depressed, stimulate him or her and encourage deep breathing. If the patient is obtunded in the early postoperative period, consider naloxone injection and continuous infusion. If the patient responds to stimulation with combativeness, he or she is usually calmed with reorientation. The amnestics administered during general anesthesia can cause a patient to repeatedly lose orientation. A close friend or family member can be effective in reorientation.
2. **Elderly patients** have less neurologic reserve and are the largest population to suffer from mental status changes. Their other organ systems are also delicate, often requiring ICU admissions that may

prompt delirium. The effects of sedative and pain medications can be quite prolonged in this population and additional administration should only be done with careful consideration.

E. Perioperative Stroke

1. **Presentation.** Strokes usually present with acute onset of focal neurologic dysfunction, manifesting as unilateral weakness or clumsiness, sensory loss, speech disorder, diplopia, or vertigo. Massive strokes can present with altered mental status, but mildly altered sensorium alone without focal neurologic changes is unlikely to represent a stroke.
2. **Examination.** A thorough neurologic examination should be part of the initial encounter.
3. **Unique evaluation.** CT scan of the head should be obtained urgently to rule out hemorrhagic stroke. For patients with focal neurologic changes or imaging findings concerning for stroke, emergent consultation from a neurologist is warranted. Further studies including echocardiography, carotid ultrasound, ECG, and magnetic resonance imaging (MRI) may be needed.
4. **Treatment.** General supportive measures include supplemental oxygen and intravenous (IV) fluid. Aspirin (325 mg orally) should be given immediately in ischemic stroke. Thrombolysis has been proven effective in improving outcomes from ischemic strokes, but it may be contraindicated in postoperative patients and should only be initiated in close consultation with a neurologist and the surgeon.

F. Seizures

1. **Precipitating factors.** Most seizures in postoperative patients occur due to perioperative medication changes in patients with a history of seizures. Common causes of new seizure in postoperative patients are metabolic derangements including electrolyte abnormalities (i.e., hyponatremia and hypocalcemia), alcohol withdrawal, hypoglycemia, fever, and drugs (i.e., imipenem).
2. **Examination.** Complete physical and neurologic examination should focus on ABCs and then on any sequelae of seizure, including trauma, aspiration, or rhabdomyolysis. A careful patient history will help determine whether a true seizure was witnessed. If so, its type, characteristics (i.e., general vs. focal), and similarity to any previous

seizures should be noted. A focally abnormal neurologic examination, especially in the setting of a new-onset focal seizure, suggests a possible cerebrovascular event.

3. **Unique evaluation.** Serum chemistries should include calcium and magnesium. Serum levels of anticonvulsants should be measured in patients who normally take these medications. Patients with new-onset seizures who do not have identifiable metabolic or systemic causes warrant further evaluation with a head CT scan followed by a lumbar puncture and EEG.
4. **Treatment:**
   a. **The patient's airway** should be stabilized initially with a soft oral or nasal airway. Endotracheal intubation may ultimately be required to protect the airway. Cardiopulmonary parameters should be monitored and IV access established immediately.
   b. **A single, nonrecurring seizure** with identifiable metabolic or systemic causes usually requires only correction of the underlying abnormality.
   c. **Recurrent seizures** warrant neurologic consultation. A regimen beginning with a 15- to 20-mg/kg load of phenytoin, given parenterally in three divided doses, and followed by maintenance dosing of 5 mg/kg/day in three divided doses is typically prescribed. Status epilepticus, defined as a seizure lasting more than 5 minutes or a series of multiple, continuous seizures without return to baseline mental status, is a medical emergency and a neurology consult should be obtained immediately. Treatment regimens include:
      (1) **Lorazepam** (2 to 4 mg IV at a rate of 2 mg/min) should be given for generalized convulsions lasting longer than 5 minutes. Either lorazepam or fosphenytoin may be given intramuscularly in emergent situations. Results are usually seen within 10 minutes.
      (2) **Fosphenytoin** (prescribed in phenytoin equivalents) administered parenterally is the first choice to supplement benzodiazepines in this setting and should be started concurrently.
      (3) **Phenobarbital** is a second-line agent and should be used when

fosphenytoin is contraindicated (e.g., heart block) or ineffective. A loading dose of 20 mg/kg IV can be given at 100 mg/min. Maintenance doses of 1 to 5 mg/kg/day IV or orally are required to achieve therapeutic plasma levels. Institution of a phenobarbital coma should be considered if status epilepticus continues.

G. Delirium

1. **Presentation.** Symptoms include impaired memory, altered perception, and paranoia, often alternating with periods of lucency. Altered sleep patterns result in drowsiness during the day with wakefulness and agitation at night (i.e., sundowning). Disorientation and combativeness are common.
2. **Evaluation.** Generally considered a diagnosis of exclusion, management begins with eliminating the possibility of an underlying physiologic or metabolic derangement, with particular attention paid to infection. Infection should be evaluated with a CBC and urinalysis. Hypoxemia and hypercarbia should be assessed by ABG. Other testing, including ECG or CXR, is dictated by clinical suspicion. Medications should be reviewed carefully, paying particular attention to anticholinergic agents, opiate analgesics, and antihistamines.
3. **Treatment.** Mood-altering medications including narcotics and anticholinergics should be minimized and any metabolic abnormalities corrected. Benzodiazepines, antihistamines such as diphenhydramine, and sleep aids such as zolpidem and eszopiclone, ought to be strictly avoided. Good sleep hygiene is also important and should be encouraged by keeping the lights off at night and on during the day, minimizing night-time lab draws and nursing care, and getting the patient out of bed during waking hours. Patients also benefit from an exterior view when possible. For recalcitrant delirium, quetiapine 25 to 50 mg at bedtime has been shown to be an effective adjunct (*J Hosp Med*. 2013;8:215–220). Haloperidol (1 to 5 mg orally or intramuscularly) can also be used for hyperactive delirium. In some cases, physical restraints might be necessary to prevent self-harm, but should be used as a last resort and in concert with pharmacologic treatment.

H. Alcohol Withdrawal

1. **Presentation.** Symptoms of minor withdrawal can begin 8 hours after

blood alcohol levels normalize and are characterized by insomnia, anxiety, tachycardia, tachypnea, fever, and hypertension. These symptoms peak at 72 hours. Alcohol withdrawal seizures occur 12 to 48 hours after normalization of blood alcohol level. They are usually brief and self-limited. Delirium tremens (DT) typically occurs 72 to 96 hours or longer after cessation of alcohol intake and is characterized by disorientation, hallucinations, and autonomic lability, inclusive of tachycardia, hypertension, fever, and diaphoresis. Mortality for hospitalized patients with DT is 1% to 4%. Patients with acute DT should be monitored in an ICU (*N Engl J Med*. 2014; 371:2109–2113).

2. **Evaluation.** The diagnosis is clinical in nature. While one should have a high index of suspicion, in absence of a strong social history, alcohol withdrawal should also be considered a diagnosis of near exclusion.
3. **Treatment:**
   a. **Nutritional supplements.** Thiamine 500 mg IV for 3 days followed by 100 mg orally every day should be given to all suspected alcoholic patients to prevent development of Wernicke encephalopathy. Many chronic alcoholics have hypomagnesemia; if present, magnesium sulfate should be administered to patients with normal renal function. Folate 1 mg should be given daily.
   b. **Benzodiazepines**—such as chlordiazepoxide, 25 to 100 mg orally every 6 hours; oxazepam, 5 to 15 mg orally every 6 hours; or diazepam, 5 to 20 mg orally or IV every 6 hours—can be used as prophylaxis in alcoholics who have a history of withdrawal or to alleviate symptoms of minor withdrawal. Benzodiazepines are most helpful in preventing recurrent seizures. Patients with DT should be given diazepam, 5 to 10 mg IV every 10 to 15 minutes, to control symptoms yet avoid oversedation. The dose of benzodiazepines should be reduced in patients with liver impairment. Moderate alcohol intake with meals can be a simple way to prevent and treat alcohol withdrawal but should be used with caution.
   c. **Clonidine** 0.1 mg orally four times a day or **atenolol** 50 to 100 mg orally a day, can be used to treat tachycardia or hypertension resulting from autonomic hyperactivity with close hemodynamic

monitoring.

II. CARDIOVASCULAR COMPLICATIONS

A. Postoperative Hypotension

1. **Diagnostic considerations.** In the postoperative patient, hypotension should immediately raise concerns of postoperative bleeding. A full set of vital signs should be obtained, as should a CBC. Severe hypovolemia can cause hypotension and is usually preceded by oliguria and tachycardia. The notable exception to this is the patient on beta-blockade, in whom tachycardia is blunted. In the early postoperative period (postop days 0 to 2), hypovolemia from bleeding or under resuscitation is the most common cause of hypotension. Later in the hospital course, sepsis must be strongly considered.
2. **Basic differential diagnosis.** Bleeding, underresuscitation, sepsis, anesthetics, analgesics (especially epidural catheters), and administration of antihypertensive medication.
3. **Treatment.** In postoperative patients without a history of congestive heart failure (CHF), an initial fluid challenge is usually warranted. A Foley catheter should be placed to monitor urine output and the patient should have adequate IV access for resuscitation. If an epidural catheter is in place, the infusion should be slowed or discontinued completely. In patients with an upper extremity central venous catheter (internal jugular or subclavian) a measurement of central venous oxygen saturation can be helpful in distinguishing between septic and hypovolemic shock. If hypotension is not quickly resolved by IV fluid infusion, blood transfusion or drug cessation, as indicated, the patient should be transferred to a higher level of care.

B. Hypertension

1. **Diagnostic considerations.** Postoperative hypertension should be defined by the patient's preoperative blood pressure (BP). Chronic hypertension causes a shift in the cerebral autoregulatory system that may not allow for adequate cerebral perfusion at normotensive BPs. A reasonable goal of therapy for acute postoperative hypertension is within 10% of the patient's normal BP.
2. **Basic differential diagnosis:** essential hypertension, hypertensive urgency, pain, ethanol withdrawal, hypoxemia, hypothermia, and

acidosis.

3. **Treatment.** Underlying causes of hypertension such as acute pain or alcohol withdrawal should be identified and addressed. Initial treatment for hypertension should be to resume home antihypertensive agents when possible. Acute hypertension can be managed with labetalol (10 to 20 mg IV every 10 minutes, to a total dose of 300 mg), hydralazine (10 to 20 mg IV every 6 hours), or clonidine (0.1 mg orally every 6 hours), as limited by the heart rate. Patients with hypertensive urgency or emergency should be transferred to an ICU for further care.

C. Myocardial Ischemia and Infarction (MI)

1. **Presentation.** The presentation of myocardial ischemia in the postoperative patient is often subtle. Frequently, perioperative MI is silent or presents with dyspnea, hypotension, or atypical pain. Close questioning of the patient on the pain characteristics often narrows the differential significantly. Postoperative MIs classically occur on postoperative day 2 and any new development of chest pain should prompt a full workup for MI.
2. **Basic differential diagnosis:** MI, pulmonary embolism (PE), pleuritis, pneumonia, pericarditis, incisional pain, aortic dissection, pneumothorax, pneumomediastinum, and GERD.
3. **Evaluation.** Most chest pain complaints warrant a new set of vital signs, serum electrolytes, hemoglobin, and a CXR. An ECG is necessary in virtually all cases of postoperative chest pain, and it should be compared to prior tracings. Sinus tachycardia is one of the most common rhythms associated with MI. An elevated troponin I level in the setting of ECG changes is diagnostic of MI. A series of three samplings of troponin I 6 to 9 hours apart has a sensitivity and specificity of greater than 90% for detecting myocardial injury (*N Engl J Med*. 2009;361:868–877). However, clinical factors such as global shock and renal failure can lead to false positives. Further diagnostic evaluation, including echocardiography should be pursued as indicated by the initial workup.
4. **Treatment.** If the troponin level is elevated or there are ECG findings consistent with ischemia (ST-segment or new conduction system changes), an emergent cardiology consultation should be obtained. The patient should be placed on telemetry and have oxygen applied

to keep saturations >90%. Morphine may be administered to manage the pain and to decrease the sympathetic drive (1 to 4 mg IV every hour), and nonenteric coated aspirin administration can be lifesaving (325 mg). In the absence of hypotension, initial management for cardiac chest pain includes sublingual nitroglycerin (0.4 mg) every 5 minutes until the pain resolves. Hemodynamically stable patients without CHF, significant bradycardia, and/or heart block should also receive beta-blockade, usually metoprolol 15 mg IV in 5-mg doses every 5 minutes, as this has been shown to improve patient outcomes (*Am J Cardiology*. 1999; 84:76). Patients with any sign of hemodynamic changes should be urgently transferred to an ICU pending expert consultation.

D. Congestive Heart Failure (CHF)

1. **Presentation.** CHF exacerbations typically present with shortness of breath or hypoxia. Physical examination often reveals signs of fluid overload. CHF can occur in the immediate postoperative period as a result of excessive intraoperative administration of fluids or 24 to 48 hours postoperatively related to mobilization of fluids that are sequestered in the extracellular space. Patients frequently have a history of asymptomatic heart failure.
2. **Evaluation.** Bedside evaluation includes pulse oximetry and assessment of net fluid balance and weight for the preceding days. Laboratory studies include troponin I, B-type natriuretic peptide (BNP), ABG, CBC, electrolytes, and renal function tests. CXR and ECG are frequently indicated.
3. **Differential diagnosis:** pneumonia, atelectasis, PE, reactive airway disease (asthma, COPD exacerbation), and pneumothorax.
4. **Treatment** is aimed at maximizing cardiac perfusion and efficiency.
   a. **Supplemental oxygen** should be administered. Mechanical ventilation is indicated in patients with refractory hypoxemia.
   b. **Diuresis** should be initiated with furosemide (20 to 40 mg IV push), with doses up to 200 mg every 6 hours as necessary. Furosemide drips can be effective in promoting adequate diuresis. Fluid intake should be limited, and serum potassium should be monitored closely. If contraction alkalosis occurs, acetazolamide may be substituted for furosemide.

c. **Arterial vasodilators.** To reduce afterload and help the failing heart in the acute setting, ACE inhibitors can be used to lower the systolic BP to 90 to 100 mm Hg. Negative inotropes such as calcium channel blockers and beta-blockade should be avoided.

d. **Inotropic agents.** Digoxin increases myocardial contractility and can be used to treat patients with mild failure. Patients with florid failure may need invasive monitoring and continuous inotrope infusion.

III. PULMONARY COMPLICATIONS

A. Dyspnea

1. **Diagnostic considerations:** Shortness of breath is often thought of as being a primary respiratory problem, but it can be a symptom of systemic illness such as CHF and PE. Differential diagnoses include atelectasis, lobar collapse, pneumonia, CHF, COPD, asthma exacerbation, pneumothorax, PE, and aspiration. Shortness of breath can also be a result of MI, intra-abdominal complications, systemic sepsis, and fever. Additional factors that help to differentiate disease entities include smoking history, fever, chest pain, and the time since surgery.
2. **Examination** may reveal jugular venous distention, abnormal breath sounds (wheezing, crackles), asymmetry, and increased respiratory effort.
3. **Evaluation.** CBC, pulse oximetry, ABG, and CXR are mandatory for all persistently dyspneic patients. ECG should be obtained for any patient older than 30 years with significant dyspnea or tachypnea to exclude myocardial ischemia and in any patient who is dyspneic in the setting of tachycardia.
4. **Treatment:**
   a. **Atelectasis** commonly occurs in the first 36 hours after operation and typically presents with dyspnea and hypoxia. Therapy is aimed at reexpanding the collapsed alveoli. For most patients, deep breathing, coughing, and incentive spirometry are adequate. Postoperative pain should be controlled so that pulmonary mechanics are not impaired. In patients with atelectasis or lobar collapse, chest physical therapy and nasotracheal suctioning might

be required. In rare cases, bronchoscopy can aid in clearing mucus plugs that cannot be cleared using less invasive measures.

b. Gastric aspiration usually presents with acute dyspnea and fever. CXR might be normal initially but subsequently demonstrates a pattern of diffuse interstitial infiltrates. Therapy is supportive, and antibiotics are typically not given empirically.

c. Pneumothorax is treated with tube thoracostomy. If tension pneumothorax is suspected, immediate needle decompression should precede controlled placement of a thoracostomy tube.

d. Volume overload, pneumonia, and PE are discussed elsewhere in this chapter.

B. COPD and Asthma Exacerbations

1. Reactive airways are common in postoperative smokers and asthmatic patients. The local trauma of an endotracheal tube can induce bronchospasm.

2. Presentation may include wheezing, dyspnea, tachypnea, hypoxemia, and possibly hypercapnia.

3. Treatment:

a. Acute therapy includes administration of supplemental **oxygen** and **inhaled beta-adrenergic agonists** (albuterol, 3.0 mL [2.5 mg] in 2-mL normal saline every 4 to 6 hours via nebulization). Beta-adrenergic agonists are indicated primarily for acute exacerbations rather than for long-term use.

b. Anticholinergics such as ipratropium bromide (Atrovent, two puffs every 4 to 6 hours) can also be used in the perioperative period, especially if the patient has significant pulmonary secretions.

c. Patients with severe asthma or COPD may benefit from **parenteral steroid therapy** (methylprednisolone, 50 to 250 mg IV every 4 to 6 hours) as well as **inhaled steroids** (beclomethasone metered-dose inhaler, two puffs four times a day), but steroids require 6 to 12 hours to take effect.

IV. RENAL COMPLICATIONS

A. Oliguria is defined as urine output of less than 0.5 mL/kg/hr. The most common early perioperative cause of oliguria is hypovolemia from underresuscitation or bleeding. Other important considerations include

preoperative renal dysfunction, home diuretic use, and perioperative urinary retention due to general anesthesia. Initial evaluation should include serum electrolytes, hematocrit/hemoglobin level, and a bladder ultrasound to assess for urinary retention. Persistent oliguria necessitates Foley catheter placement. For patients with normal cardiac and renal function, a fluid challenge with 0.5 to 1 L of crystalloid IV can be diagnostic and therapeutic for hypovolemia.

B. Urinary Retention. Perioperative patients are at risk for acute urinary retention. Urinary retention can present as failure to void or with acute pain due to an overdistended bladder. In the perioperative patient, failure to void within 6 hours should prompt a workup for oliguria as described above, including a bladder ultrasound. Patients with subjective symptoms of bladder distension or patients with greater than 500 mL of urine on bladder ultrasound should undergo catheterization. An initial trial of bladder decompression with immediate removal of the catheter ("straight cath") is reasonable, although others advocate for a short duration (24 hours) of bladder decompression with an indwelling Foley catheter. Treatment with alpha-blockade (tamsulosin 0.4 mg daily) may decrease the probability of a second episode of urinary retention (*Rev Urol*. 2005;7 Suppl 8:S26–S33).

C. Acute Kidney Injury (AKI)

1. **Presentation:** AKI is defined by an increase in serum creatine level by 0.3 mg/dL or 1.5-fold above baseline in the setting of oliguria. The etiologies of AKI can be classified as prerenal, intrinsic renal, and postrenal (Table 3-1).
   - **a. Prerenal azotemia** results from decreased renal perfusion that might be secondary to hypotension, intravascular volume contraction, or decreased effective renal perfusion.
   - **b. Intrinsic renal** causes include drug-induced acute tubular necrosis, pigment-induced renal injury, radiocontrast dye administration, acute interstitial nephritis, rhabdomyolysis, and prolonged ischemia from suprarenal aortic cross-clamping.

TABLE 3-1 Laboratory Evaluation of Oliguria and Acute Renal Failure

Category	FE_{Na} (%)	FE_{Ur} (%)	U_{Na}	U_{Osm}	RFI	U_{Cr}/P_{Cr}
Prerenal	<1	≤35	<20	>500	<1	>40
Renal (intrinsic)	>1	>50	>40	<350	>1	<20
Postrenal	>4	NA	>40	<50	>1	<20

FE_{Na}, fractional excretion of sodium; FE_{Ur}, fractional excretion of urea; NA, not applicable; RFI, renal failure index; U_{Cr}/P_{Cr}, urine–plasma creatinine ratio; U_{Na}, urine sodium in mmol/L; U_{Osm}, urine osmolality in mOsm/kg.

c. Postrenal causes can result from obstruction of the ureters or bladder. Operations that involve dissection near the ureters, such as colectomy, colostomy closure, or total abdominal hysterectomy, have a higher incidence of ureteral injuries. In addition to ureteral injuries or obstruction, obstruction of the bladder from mechanical (enlarged prostate, obstructed urinary catheter) or functional (narcotics, anticholinergics) means can contribute to postrenal AKI.

2. **Evaluation.** Urinalysis with microscopy and culture (as indicated) can help in differentiating between etiologies of AKI. Additionally, urinary indices including fractional excretion of sodium (FE_{Na}), renal failure index, and fractional extraction of urea (FE_{Ur}) help to classify AKI into the above listed categories. In the setting of diuretic administration, FE_{Ur} is favored over FE_{Na}. Renal ultrasonography can be used to exclude obstructive uropathy, assess the chronicity of renal disease, and evaluate the renal vasculature with Doppler ultrasonography. Radiologic studies using IV contrast are contraindicated in patients with suspected AKI due to potential exacerbation of renal injury.

3. **Treatment:**

a. Prerenal. In most surgical patients, oliguria is caused by hypovolemia. Initial management includes a fluid challenge (i.e., a normal saline bolus of 500 mL). Patients felt to be adequately resuscitated and/or patients with underlying CHF may benefit from invasive monitoring and optimization of cardiac function.

b. Intrinsic renal. Treat the underlying cause, if possible, manage volume status, and avoid nephrotoxic agents.

c. Postrenal. Ureteral injuries or obstruction can be treated with percutaneous nephrostomy tubes and generally are managed in consultation with a urologist. Urinary retention and urethral obstruction can be managed with a Foley catheter or, if necessary, a suprapubic catheter.

d. In all cases, careful attention to intravascular volume is paramount. Patients should be weighed daily and have carefully recorded intakes and outputs. Hyperkalemia, metabolic acidosis, and hyperphosphatemia are common problems in patients with AKI and should be managed as discussed in Chapter 4. Medication doses should be adjusted appropriately and potassium removed from maintenance IV fluids.

e. Dialysis. Indications for dialysis include intravascular volume overload, electrolyte abnormalities (especially hyperkalemia), metabolic acidosis, and complications of uremia (encephalopathy, pericarditis).

V. GASTROINTESTINAL COMPLICATIONS

A. Postoperative Nausea and Vomiting

1. **Presentation.** On postoperative days 0 to 1, postanesthesia nausea can affect up to 30% of patients (*Anesthesiology*. 1992;77:162). Other common causes of nausea in the early perioperative period include medication side effects (especially from opiate analgesics), perioperative gastroparesis, and paralytic ileus. Patients who have undergone extensive intra-abdominal procedures and are more than 24 hours out from anesthesia should be evaluated for the underlying causes of nausea before administration of antiemetics. Up to 20% of these patients will suffer an ileus requiring nasogastric decompression (*Dis Colon Rectum*. 2000;43:61).
2. **Treatment.** Aggressive management with antiemetics can be employed. Multimodal therapy with ondansetron, promethazine, prochlorperazine, scopolamine, and dexamethasone can be required.

B. Postoperative Paralytic Ileus

1. **Presentation.** Paralytic ileus typically presents with obstipation,

persistent nausea despite antiemetic use, intolerance of oral diet, belching, and abdominal distension/discomfort.

2. **Differential diagnosis:** bowel obstruction, constipation, Ogilvie syndrome, intra-abdominal infection, and retroperitoneal bleeding.
3. **Evaluation.** Upright and lateral decubitus radiographs of the abdomen should be obtained to evaluate for dilated stomach and loops of bowel. Air should be seen in the colon, thus helping to differentiate from bowel obstruction. When this imaging is insufficient to rule out obstruction, abdominal CT with oral contrast is both sensitive and specific (90% to 100%), though is less reliable for partial versus complete small bowel obstructions. If the diagnosis remains uncertain, an upper gastrointestinal study with water-soluble contrast material may be necessary.
4. **Treatment.** Patients with an ileus should be made NPO and started on IVF. Strong consideration should be made for placing a decompressive nasogastric tube, even in the absence of emesis or gastric distension on plain film. A patient with an NG tube in place who complains of nausea should have the NG tube manipulated until functioning properly. This may even require replacement with a larger-bore NG tube. Deficiencies of potassium and magnesium as well as excess opioids can prolong ileus. Since the etiology is nonmechanical, patience must then be employed as one awaits return of bowel function. Should the ileus persist beyond 7 days, a TPN consultation should be placed.

VI. INFECTIOUS COMPLICATIONS

A. Diagnostic Considerations. Infection can manifest with obvious signs such as erythema, induration, drainage, necrosis, or tenderness on examination. Infection can also manifest with more subtle symptoms such as chills, malaise, hypothermia, and/or unexplained leukocytosis. While due attention to the multitude of peri- and postoperative infections complications is paramount, it is beyond the scope of this chapter. The discussion below is designed to serve as an initial starting point and will touch briefly on management of specific infectious pathologies.

B. Generalized Fever

1. **Presentation.** In the immunocompetent adult, fever is defined as a

body temperature greater than 38.5°C. Evaluation of fever should take into account the amount of time that has passed since the patient's most recent operation.

a. **Intraoperative fever** may be secondary to malignant hyperthermia, a transfusion reaction, or a pre-existing infection.

b. **Fever in the first 24 hours** usually occurs as a result of atelectasis. A high fever (>39°C) is commonly the result of a streptococcal or clostridial wound infection, aspiration pneumonitis, or a pre-existing infection. However, fever in this time period can also be seen in trauma or burn patients as a part of an expected inflammatory response.

c. **Fever that occurs more than 72 hours after surgery** has a broad differential diagnosis, including but not limited to the following: wound infection (including fascial or muscle), pneumonia, gastroenteritis, infection colitis (including *Clostridium difficile*), abscess, peritonitis, UTI, infected prosthetic materials or catheters, deep venous thrombosis (DVT), thrombophlebitis, drug allergy, or devastating neurologic injury. In immunocompromised hosts, viral and fungal infections should also be considered. Transfusion reactions can also be confused for infection due to the presence of fever, though the treatment is vastly different and will not be discussed here.

2. **Evaluation.** The new onset of fever or leukocytosis without an obvious source of infection requires a thorough history and physical examination, including inspection of all wounds, tubes, and catheter sites, and obtainment of CBC, urinalysis, and CXR. Gram stain/cultures of the blood, sputum, urine, and/or wound should be dictated by the clinical situation. Imaging such as an ultrasound or CT should be chosen based on clinical context, usually to evaluate for a deep space infection in the cavity where surgery was performed.

3. **Treatment.** Empiric antibiotics may be initiated after collection of cultures, with therapy directed by clinical suspicion, but are not always warranted. Therapy usually begins with broad-spectrum IV antibiotics and narrows as more information is known about the infectious pathogen.

C. Surgical Site Infections (SSI) are the second leading cause of nosocomial infections, leading to significant patient care costs, longer

length of hospital stays, and increased rates of readmission. They typically present with erythema, pain, induration, and/or drainage. Fever and leukocytosis may be present.

1. **Prevention** of SSI begins with appropriate selection of prophylactic antibiotics (Table 3-2). Consideration should be given to the classification of the preoperative field, which places a patient at increased risk for SSI despite antibiotic therapy (Table 3-3). Finally, the Surgical Care Improvement Project (SCIP) is a quality improvement partnership aimed at reducing significant surgical complications and improving surgical outcomes nationally. Of the 2018 SCIP core measurement, 6 of the 11 indicators relate to infection prevention.
2. **Treatment** is to open the wound to allow drainage, with culture if possible. Parenteral antibiotics are used only if extensive erythema or a deeper infection is present and are not required for superficial infections. Wound infections in the perineum or after bowel surgery are more likely to be caused by enteric pathogens and anaerobes. More aggressive infections involving underlying fascia require operative débridement and broad-spectrum IV antibiotics. Streptococcal wound infections present with severe local erythema and incisional pain. Penicillin G or ampicillin is effective adjuvant treatment. Patients with a severe necrotizing clostridial infection present with tachycardia and signs of systemic illness, pain, and crepitus near the incision. Treatment includes emergent operative débridement and metronidazole (500 mg IV every 6 hours) and clindamycin (600 to 900 mg IV every 8 hours).

TABLE 3-2 Recommendations for Antibiotic Prophylaxis

Nature of Operation	Likely Pathogens	Recommended Antibiotics	Adult Dose Before Surgery[a]
Cardiac: prosthetic valve and other procedures	Staphylococci, corynebacteria, enteric gram-	Vancomycin and Cefazolin Vancomycin and	1–1.5 g IV 1–3 g IV 1–1.5 g IV

Device insertion	negative bacilli	Aztreonam[a] Cefazolin or Vancomycin	1–2 g IV 1–3 g IV 1–1.5 g IV
Thoracic	Staphylococci	Cefazolin Vancomycin[a]	1–3 g IV 1–1.5 g IV
Vascular: peripheral bypass or aortic surgery with prosthetic graft	Staphylococci, streptococci, enteric gram-negative bacilli, clostridia	Cefazolin Vancomycin and Aztreonam[a]	1–3 g IV 1–1.5 g IV 1–2 g IV
Abdominal wall hernia	Staphylococci	Cefazolin Clindamycin[a]	1–3 g IV 900 mg IV
Orthopedic: total joint replacement or internal fixation of fractures	Staphylococci	Cefazolin +/− Vancomycin Vancomycin and Aztreonam[a]	1–3 g IV 1–1.5 g IV 1–1.5 g IV 1–2 g IV
Gastrointestinal			
Upper GI and hepatobiliary	Enteric gram-negative bacilli, enterococci, clostridia	Cefotetan Cefoxitin Clindamycin and Gentamicin[a] Ciprofloxacin and Metronidazole[a]	1–2 g IV 1–2 g IV 900 mg IV 5 mg/kg IV 400 mg IV 500 mg IV
Colorectal	Enteric gram-negative bacilli, anaerobes, enterococci	Cefoxitin Cefotetan Ertapenem Cefazolin and Metronidazole[a]	1–2 g IV 1–2 g IV 1 g IV 1–3 g IV 500 mg IV
Appendectomy (no perforation)	Enteric gram-negative bacilli,	Cefoxitin Cefotetan	1–2 g IV 1–2 g IV

	anaerobes, enterococci	Ciprofloxacin and Metronidazole[a]	400 mg IV 500 mg IV
Obstetrics/gynecology	Enteric gram-negative bacilli, anaerobes, group B streptococci, enterococci	Cefotetan Cefoxitin Cefazolin Clindamycin and Gentamicin[a]	1–2 g IV 1–2 g IV 1–3 g IV 900 mg IV 1.5–5 mg/kg IV

[a]Indicated for patients with penicillin/cephalosporin allergy.

For vancomycin, dose of 1 g is recommended for patients <80 kg, 1.5 g is recommended for ≥80 kg.

For cefazolin, cefotetan, cefoxitin, and aztreonam, pre- and intraoperative dosing of 1 g is suggested for patients weighing <80 kg, 2 g for patients weighing ≥80 kg and <120 kg, and 3 g for patients weighing ≥120 kg.

In obese patients, single-dose gentamicin should be dosed at 5 mg/kg of adjusted body weight (ABW = IBW + 0.4[TBW − IBW]).

IV, intravenous.

Casabar E, Portell J. *The Tool Book: Drug Dosing and Usage Guidelines, Barnes-Jewish Hospital*. 12th ed. St. Louis, MO: Department of Pharmacy, Barnes-Jewish Hospital; 2014.

D. Respiratory Infections. Pneumonia is diagnosed by the presence of fever, leukocytosis, purulent sputum production, and an infiltrate on CXR. After Gram stain and culture of the sputum and blood are performed, empiric antibiotics are started and aimed at nosocomial organisms in postoperative patients. Steps to help prevent pneumonia in the postoperative patient include incentive spirometry/pulmonary toilet, adequate pain control, early ambulation, and early extubation. Consideration should be given to viral causes of pneumonia as well.

E. Clostridium Difficile Infection (CDI)

1. **Presentation.** CDI may present in any patient who has received antibiotics, even after prophylactic perioperative dosing. CDI should be thought of as a spectrum of disease severity which then guides treatment:

TABLE 3-3 Classification of Surgical Wounds

Wound Class	Definition	Examples of Typical Procedures	Wound Infection Rate (%)	Usual Organisms
Clean	Nontraumatic, elective surgery; no entry of GI, biliary, tracheobronchial, respiratory, or GU tracts	Wide local excision of breast mass	2	*Staphylococcus aureus*
Clean–contaminated	Respiratory, genitourinary, GI tract entered but minimal contamination	Gastrectomy, hysterectomy	<10	Related to the viscus entered

Contaminated	Open, fresh, traumatic wounds; uncontrolled spillage from an unprepared hollow viscus; minor break in sterile technique	Ruptured appendix; resection of unprepared bowel	20	Depends on underlying disease
Dirty	Open, traumatic, dirty wounds; traumatic perforated viscus; pus in the operative field	Intestinal fistula resection	28–70	Depends on underlying disease

GI, gastrointestinal; GU, genitourinary.

a. Mild: diarrhea, minimal symptoms

b. Moderate: IV fluids needed, abdominal pain, mucus or blood in stool, WBC <15k, serum creatinine <1.5 mg/dL, low-grade fever, colitis on endoscopy

c. Severe: hypotension, peritonitis, WBC ≥15k*, serum creatinine ≥1.5 mg/dL*, fever <38.5°C (*attributed to CDI)

d. Fulminant (previously referred to as severe complicated): toxic megacolon, colonic ischemia, transfusion requirement from colonic bleeding, ileus, pressor requirements, perforation

2. **Evaluation.** A diagnosis of CDI requires a positive stool *C. difficile* A or B toxin assay and clinically significant diarrhea *or* ileus. There should be a low threshold for performing an assay for the *C. difficile* toxin in postoperative patients with unexplained and new onset of less than three unformed stools in 24 hours. Repeat testing should not be performed within 7 days during the same diarrheal episode.
3. **Treatment.** Initial therapy includes fluid resuscitation, cessation of

unnecessary antibiotics, stopping promotility or antidiarrheal agents, and preemptive contact isolation precautions. Successful treatment is demonstrated by decreased stool output to baseline and resolution of symptoms. Refractory CDI is defined as persistent symptoms despite 6 days of adequate treatment. Recurrence is classified as return of symptoms within 60 days after completion of full course of treatment plus either toxin-positive stool or findings of pseudomembranes on colonoscopy. Factors associated with high risk for recurrence are age >65 years plus either severe CDI or concomitant antibiotics use at time of CDI diagnosis.

Important changes were made to the CDI treatment algorithm in 2018 and are reflected below (*CID*. 2018;66:987–994). Notably, metronidazole is now considered to be inferior to oral vancomycin for both nonsevere and severe CDI and is no longer recommended as first-line therapy. Fidaxomicin has entered the algorithm but its use is frequently restricted due to cost.

a. First-time nonfulminant CDI with low risk of recurrence or complications requires administration of oral vancomycin (125 mg every 6 hours for 10 days). If intolerant of vancomycin or symptoms persist, oral fidaxomicin can be considered, but fidaxomicin should not be used for empiric treatment of CDI.

b. First-time nonfulminant CDI with high risk for recurrence or complications should prompt consultation with infectious disease as fidaxomicin may soon be first-line therapy.

c. Fulminant CDI is treated with oral or per tube vancomycin (500 mg every 6 hours) in combination with IV metronidazole (500 mg every 8 hours). In the presence of ileus, these measures should be supplemented by rectal or cecal vancomycin enemas (500 mg in 100-mL normal saline). Little data exist to support the use of cecostomies or diverting loop ileostomies to facilitate administration of vancomycin enemas. Consultations should be sought from gastroenterology, infectious disease, and colorectal/general surgery. In severe cases, subtotal colectomy with rectal preservation may be required.

d. In the case of **CDI recurrence**, infection disease consultation is now recommended at the first recurrence. The preferred treatment is oral fidaxomicin 200 mg twice daily for 10 days, though

outpatient prescription drug coverage may be limited and oral vancomycin taper and pulsed regimens exist. Subsequent episodes of recurrence usually require a prolonged, tapered course of oral vancomycin or fidaxomicin. Fecal microbiota transplant can be considered in patients with multiple recurrences who have failed antibiotics.

F. Intra-abdominal abscesses often present with asymptomatic leukocytosis but may also present with fever, abdominal pain/tenderness, or ileus. If generalized peritonitis is present, laparotomy is indicated. If the inflammation appears to be localized, a CT scan of the abdomen and pelvis should be obtained. The primary management of an intra-abdominal abscess is drainage. Depending on size and location, percutaneous drainage under radiologic guidance is preferable. In other situations, operative débridement and drainage are required. Empiric antibiotic therapy should cover enteric pathogens and anaerobes. Empiric antifungal coverage should be considered in patients with severe sepsis or shock who have undergone recent GI surgery, have a recent history of TPN, have yeast present on Gram stain, or present with necrotizing pancreatitis. Consider broader coverage in patients with known MRSA or VRE. Duration of empiric treatment should not exceed 4 to 7 days and should be deescalated as soon as possible.

G. Genitourinary infections are the most common nosocomial infection in the postoperative patient. Foley catheters are a major risk factor, and the likelihood of suffering from a UTI has been shown to increase if catheters are left in place for more than 2 days. Treatment begins with obtaining a urine specimen for urinalysis and culture, followed by removal of the Foley catheter. After the urine is cultured, simple lower tract infections can be managed with oral antibiotics. Ill patients or those with pyelonephritis require more aggressive therapy.

H. Prosthetic device–related infections may present with fever, leukocytosis, and systemic bacteremia. Infection of prosthetic valves may present with a new murmur. Management may require removal of the infected device and the use of long-term antibiotics.

I. Catheter-related infections also are diagnosed by the presence of fever, leukocytosis, and systemic bacteremia. Local erythema and purulence may be present around central venous catheter insertion sites. Management includes removal of the catheter and IV antibiotic

coverage. In rare instances, the risk associated with line removal outweighs the benefits, therefore salvage treatment is initiated (i.e., hemodialysis catheters, pheresis catheters, implanted ports). Line salvage should be undertaken only with the guidance of an infectious disease consultant.

J. Fungal infections (primarily with *Candida* species) occur most commonly with long-term antibiotic administration and indwelling catheters. Evaluation of persistent fever without an identified bacterial source should include several sets of routine and fungal blood cultures, removal of all IV catheters, and examination of the retina for *Candida endophthalmitis*. Therapy includes fluconazole, micafungin, or amphotericin B.

VII. THROMBOTIC COMPLICATIONS

A. Deep Venous Thrombosis (DVT)

1. **Presentation.** Symptoms of DVT vary greatly, although classically they include pain and swelling of the affected extremity distal to the site of venous obstruction. DVTs may sometimes present as an unexplained leukocytosis or fever, particularly in patients who have poor functional status or have had prolonged ICU stays.
2. **Examination.** Findings may include edema, erythema, warmth, a palpable cord, or calf pain with dorsiflexion of the foot (Homans sign). Physical examination alone is notoriously inaccurate in the diagnosis of DVT.
3. **Evaluation** is primarily with noninvasive studies of the venous system, most notably B-mode ultrasonography plus color Doppler (duplex scanning). Reported sensitivity and specificity of this test for the detection of proximal DVT are greater than 90% with nearly 100% positive predictive value. This modality is less reliable in the detection of infra-popliteal thrombi, and a negative study in symptomatic patients should be followed by repeat examination in 48 to 72 hours to evaluate for proximal propagation of clot. Patients in whom a negative study contrasts with a strong clinical suspicion may require contrast venography, once the gold standard for diagnosis of DVT.
4. **Treatment.** The key to DVT management is prevention. Guidelines exist to risk stratify patients for DVT in order to guide mechanical

and chemical prophylaxis (Table 3-4). Guidelines recommend against IVC filter placement for primary VTE prevention and against routine surveillance venous compression ultrasound. Additionally, fondaparinux has been removed from the algorithm because when compared to low–molecular-weight heparin (LMWH), it does not reduce DVT events but does lead to more major bleeding events. Low-dose aspirin should not be an alternative for pharmacologic prophylaxis in nonorthopedic patients. Figure 3-1 represents a suggested algorithm for DVT prevention.

B. Pulmonary Embolism (PE)

1. **Presentation.** PE is a very common postoperative occurrence, and autopsy studies demonstrate that it is more common than clinicians appreciate (*Chest*. 1995;108:978). Chest pain with a sensation of shortness of breath and hypoxemia should raise the possibility of PE. Symptoms of PE are neither sensitive nor specific, but most commonly include tachypnea and tachycardia, mental status changes, dyspnea, pleuritic chest pain, and cough/hemoptysis. Patients with massive PE may experience syncope, ECG changes, and cardiovascular collapse. PE should be considered in any postoperative patient with unexplained dyspnea, hypoxia, tachycardia, or dysrhythmia.

TABLE 3-4 Levels of Thromboembolism Risk and Recommended Thromboprophylaxis in Hospital Patients

Risk Level	Type of Patient	Symptomatic DVT Risk w/o Prophylaxis (%)	Suggested Thromboprophylaxis Options
Very low	Most outpatient/same day surgery	<0.5	Early and aggressive ambulation
Low	Minor surgery in mobile patients	~1.5	Mechanical prophylaxis with

	Medical patients who are fully mobile		IPC Mechanical prophylaxis with IPC
Moderate	Most general, cardiothoracic, nononcologic, gynecologic, or urologic surgery Medical patients who are on bed rest, “sick”	~3	LMWH *or* LDUH *or* mechanical prophylaxis with IPC LMWH *or* LDUH *or* mechanical prophylaxis with IPC
	Moderate VTE risk plus high bleeding risk		Mechanical prophylaxis with IPC until risk decreases, *then* chemical prophylaxis
High	Major trauma, bariatric surgery, pneumonectomy, spinal cord injury, TBI, or craniotomy	~6	LMWH *or* LDUH *AND* mechanical prophylaxis with IPC *or* elastic stockings
	High VTE risk plus high bleeding risk High risk plus oncologic, abdominal, or pelvic surgery		Mechanical prophylaxis with IPC until risk decreases, *then* chemical prophylaxis extended duration LMWH (4 wk) *AND* mechanical prophylaxis with

	IPC *or* elastic stockings while hospitalized

TBI, traumatic brain injury; IPC, intermittent pneumatic compression; LDUH, low-dose unfractionated heparin; LMWH, low–molecular-weight heparin; VTE, venous thromboembolism.
Adapted from Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2012;141(2):e227S–277S.

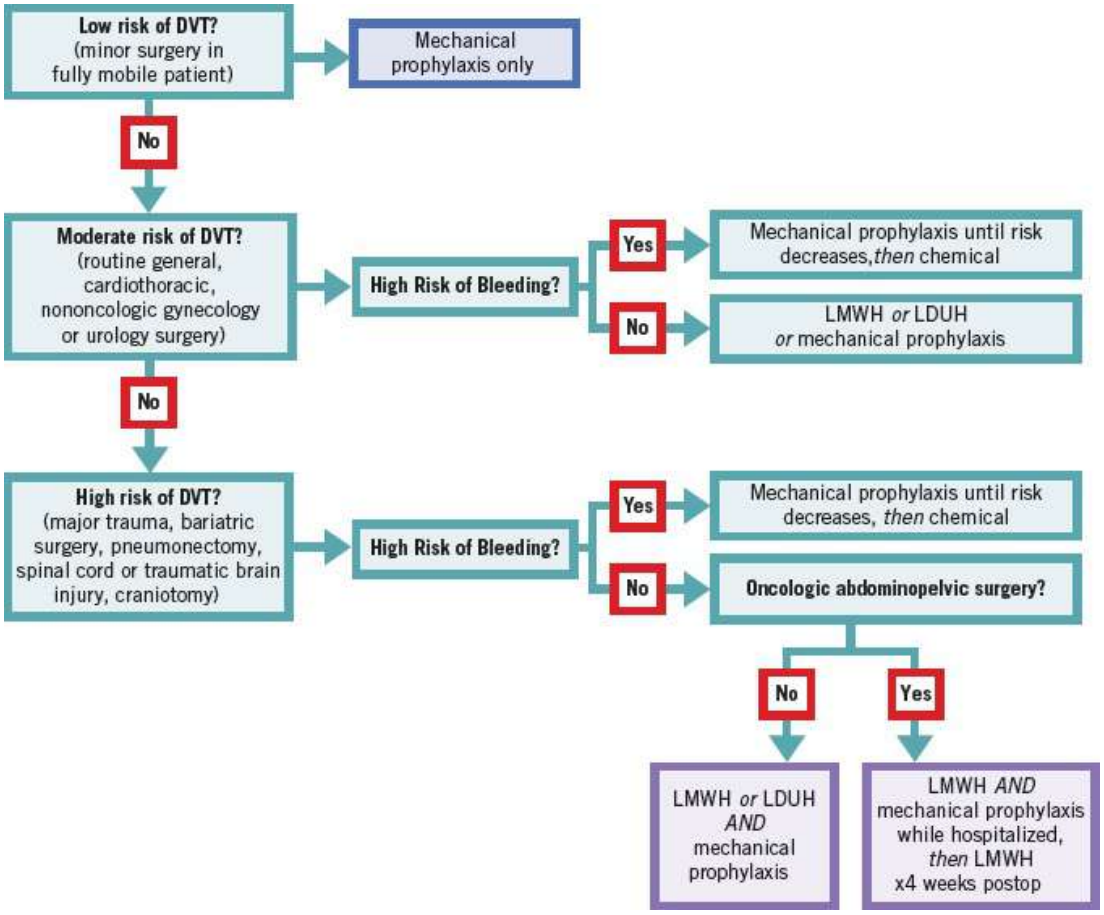


FIGURE 3-1 Algorithm for prevention of DVT in surgical patients.

2. Evaluation:

a. Preliminary studies. Findings that are suggestive of PE include arterial oxygen desaturation; nonspecific ST-segment or T-wave changes on ECG; and atelectasis, parenchymal abnormalities, or pleural effusion on CXR. Such classic signs as $S_1Q_3T_3$ on ECG or a prominent central pulmonary artery with decreased pulmonary

vascularity (Westermark sign) on CXR are uncommon. ABG determination is a helpful adjunctive test, for a decreased arterial oxygen tension (PaO_2) (<80 mm Hg), an elevated alveolar–arterial oxygen gradient, or a respiratory alkalosis may support clinical suspicion. Data obtained from these initial studies may corroborate clinical suspicion but none of these is sensitive or specific for PE. D-dimer assays have a high negative predictive value; however, positive values, particularly in the setting of recent surgery, are less helpful.

b. Spiral CT scan is becoming the primary diagnostic modality for PE over the previous gold standard of pulmonary angiography. The advantages of CT scans for PE include increased sensitivity, the ability to simultaneously evaluate other pulmonary and mediastinal abnormalities, greater after-hours availability, and the ability to obtain a CT venogram with the same dye load. This study subjects the patient to a contrast dye load and requires a large IV (18 g or higher) in the antecubital vein. There are still wide variations in technology and institutional expertise with this modality, with reported sensitivities ranging from 57% to 100% and specificity ranging from 78% to 100%. If the patient is in extremis, consider intubating prior to obtaining the CT.

c. A **V/Q scan** that demonstrates one or more perfusion defects in the absence of matched ventilation defects is abnormal and may be interpreted as high, intermediate, or low probability for PE, depending on the type and degree of abnormality. V/Q scans alone are neither sensitive nor specific for PE, and their interpretation may be difficult in patients with pre-existing lung disease, especially COPD. Nevertheless, high-probability scans are 90% predictive and suffice for diagnosis of PE. In the appropriate clinical setting, a high-probability V/Q scan should prompt treatment. Likewise, a normal scan virtually excludes PE (96%). Scans of intermediate probability require additional confirmatory tests.

3. Treatment:

a. Supportive measures include oxygen administration to correct hypoxemia and use of IV fluids to maintain BP. Hypotensive patients with high clinical suspicion of PE (i.e., high-risk patients,

patients with acute right heart failure or right ventricular ischemia on ECG) require immediate ICU transfer, where hemodynamic monitoring and vasoactive medications may be required.

b. Anticoagulation with IV unfractionated heparin (UFH) or subcutaneous LMWH should be started immediately with a target-activated partial thromboplastin time (PTT) of 50 to 80 seconds. Oral warfarin can be started concurrently while heparin is continued until a therapeutic INR is achieved. Anticoagulation should continue for 6 months unless risk factors persist or DVT recurs.

c. Systemic thrombolytic therapy is not indicated in the routine treatment of PE in surgical patients because the risk of hemorrhage in individuals with recent (<10 days) surgery outweighs the uncertain long-term benefits of this therapy. Catheter-directed thrombolytic therapy may be indicated in certain clinical settings.

d. Surgical patients with shock secondary to angiographically proven **massive PE that is refractory to anticoagulation** should be considered for either transvenous embolectomy, open pulmonary embolectomy, or percutaneous removal via extracorporeal venous bypass. These aggressive measures have varying degrees of success and morbidity.

e. Inferior vena caval filter placement is indicated when a contraindication to anticoagulation exists, a bleeding complication occurs while receiving anticoagulation, or a DVT or PE recurs during anticoagulation therapy.

CHAPTER 3: COMMON POSTOPERATIVE PROBLEMS

Multiple Choice Questions

1. **An otherwise healthy 65-year-old man is 16 hours postoperative from laparoscopic left colectomy for stage II colon adenocarcinoma. You are called by the nurse because over the last 3 hours his urine output has been less than 15 cc/hr. On evaluation, he reports feeling moderately anxious. His heart rate is 102 bpm and his blood pressure is 120/80. His physical examination is unremarkable. The appropriate immediate next step(s) in the workup and treatment of the patient include:**

   a. Measure hematocrit
   b. Give a 1-L fluid bolus
   c. Return to the operating room for reexploration
   d. a, b, and c
   e. a and b

2. **The appropriate maximum duration of antibiotic coverage after routine uncomplicated general surgery is:**

   a. A single dose given in the operating room
   b. IV antibiotics until the patient is afebrile and has a normal white blood cell count
   c. A single intraoperative dose of antibiotics then oral antibiotics until discharge
   d. 24 hours
   e. 48 hours

3. **A 75-year-old female is in the postoperative care unit after a left hemicolectomy. You are called to evaluate her because she is suddenly disoriented and agitated. What is your next step?**

   a. Naloxone administration
   b. Arterial blood gas
   c. Electrocardiogram
   d. Vital signs and pulse oximetry

e. Computed tomographic scan

4. **Which of the following causes of hypovolemia usually will not be present in a postoperative day 0 patient?**

   a. Bleeding
   b. Anesthetic/analgesics
   c. Antihypertensive medications
   d. Underresuscitation
   e. Sepsis

5. **A 50-year-old male undergoes a right inguinal hernia repair as an outpatient. Six hours later, he is unable to void despite multiple attempts. What is the next step in his care?**

   a. Fluid challenge with 1-L normal saline
   b. Foley insertion for 14 days
   c. Tamsulosin (Flomax)
   d. Bladder scan, consider Foley placement
   e. Discharge home

6. **A 68-year-old male status post a total abdominal colectomy with end ileostomy is postoperative day 2 when his creatinine increases from 1.2 to 1.8. His urine output is low normal and you decide to check FeNa, which comes back equal to 0.8%. What is his diagnosis?**

   a. Postrenal failure
   b. Antibiotic nephrotoxicity
   c. Urinary tract infection
   d. Prerenal failure
   e. Intrinsic renal failure

4 Nutrition

Kristen M. Seiler and Sara A. Buckman

Nutrition plays a vital and often underappreciated role in recovery from surgery. While most healthy patients can tolerate several days of starvation, patients affected by major trauma, surgery, sepsis, or other critical illnesses require nutritional intervention earlier. Poor nutrition has deleterious effects on wound healing and immune function, which increases postoperative morbidity, mortality, and hospital length of stay. Identification of those at risk for malnutrition is made through ongoing clinical assessments by vigilant clinicians. Appropriate understanding of dietary components, digestive organ physiology, and metabolism is necessary to determine nutritional adequacy in surgical patients. Once this is understood, a clinician can begin to calculate daily calorie need, with appropriate composition, according to the patient's condition. The following is by no means an exhaustive analysis, but should provide a sufficient quick reference guide for the practicing general surgeon. Excellent resources for further reading include the American Society for Parenteral and Enteral Nutrition (ASPEN, www.nutritioncare.org), the North American Surgical Nutrition Summit (*JPEN J Parenter Enteral Nutr*. 2013;37:99S–105S), the Society of Critical Care Medicine (www.sccm.org), and the Enhanced Recovery After Surgery (ERAS) Society (www.erassociety.org).

I. CLINICAL ASSESSMENT OF NUTRITIONAL STATUS

A. History and Physical Examination. Every good clinical assessment begins with obtaining a thorough history from the patient. The Nutritional Risk Screening (NRS-2002) is a validated method of detecting patients that would benefit from nutritional support which considers impaired nutritional status (recent and/or chronic weight loss, body mass index [BMI], and nutritional intake over the preceding week), severity of disease (as a surrogate for stress metabolism), and

patient age (*Clin Nutr*. 2003;22:321–336). In addition to this and other screening tools, any elicited history of anorexia, nausea, vomiting, dysphagia, odynophagia, or diarrhea should prompt further investigation. Furthermore, a complete history of current medications is essential to alert caretakers to potential underlying deficiencies as well as drug–nutrient interactions.

Ideally, assessment of nutritional status should occur during the first clinical encounter wherein the possibility of surgery is discussed, as a growing number of studies highlight the benefit of nutritional optimization, or "**prehabilitation**," in patients preparing for surgery who are at high risk for malnutrition (*JPEN J Parenter Enteral Nutr*. 2013;37:5S–20S). Furthermore, the use of **immunonutrition** containing arginine, fish oil, antioxidants, and nucleotides is recommended for *all* patients preparing for major elective surgery, regardless of nutrition status (*JPEN J Parenter Enteral Nutr*. 2013;37:99S–105S). Supplementation is provided using commercially available formulas, and timing relative to surgery affects outcomes such as infectious complications, length of stay, anastomotic dehiscence, and noninfective complications (*JPEN J Parenter Enteral Nutr*. 2014;38:53–69).

Physical examination may identify muscle wasting (especially thenar and temporal muscles), loose or flabby skin (indicating loss of subcutaneous fat), and peripheral edema and/or ascites (a result of hypoproteinemia) in malnourished patients. Generalized edema is especially obvious in **kwashiorkor**, which develops in prolonged starvation of dietary protein, or severe stress (e.g., major burn or prolonged sepsis) causing depletion of visceral protein stores. This is contrasted to **marasmus**, which is characterized by chronic inadequate protein *and* calorie intake resulting in losses in weight, body fat, and skeletal muscle mass, while visceral protein stores typically remain normal. Though ICD-10 coding criteria for malnutrition exist, it is often underdiagnosed and underdocumented. According to ASPEN, two out of six of the following criteria must be met for a clinical diagnosis of malnutrition: weight loss, insufficient energy intake, subcutaneous fat loss, muscle mass loss, localized or general fluid accumulation (may mask weight loss), and diminished functional status (measured by hand grip strength) (*J Acad Nutr Diet*. 2012;112:730–738). Severity of each feature is used to determine the overall severity of malnutrition, with the

definition of "severe" varying according to disease etiology (e.g., starvation, chronic disease, or acute disease or injury).

Subtler findings of nutritional deficiency include skin rash, pallor, glossitis, gingival lesions, hair changes, hepatomegaly, neuropathy, and dementia. In addition to global malnutrition, clinical signs/symptoms of specific vitamin and trace element deficiencies are presented below (Tables 4-1 and 4-2).

B. Laboratory and Imaging Tests. Laboratory tests of malnutrition include albumin, prealbumin, and transferrin. Low levels of all can be expected with malnutrition. However, one must keep in mind that these tests are nonspecific, and low levels can also reflect systemic illness and capillary leak. In these cases, a C-reactive protein (CRP), white blood cell count, and blood glucose level—as well as clinical indicators such as fever or tachycardia—may be useful adjuncts for interpretation of nutrition status based on laboratory data. Additionally, acute changes in nutritional status may be better assessed by prealbumin (which has a half-life of ~48 hours), rather than albumin (which has a half-life of ~21 days). Of note, all of these metrics are most useful in the preoperative evaluation of nutrition status; use of these values for ongoing nutritional assessment in hospitalized or critically ill patients is either controversial or contraindicated (*JPEN J Parenter Enteral Nutr*. 2013;37:99S–105S).

Imaging tests can also provide valuable information on nutritional status, particularly in patients requiring serial imaging. Volumetric and/or compositional analysis of specific muscle groups can be measured using computed tomography (CT), MRI, or ultrasonography (*JPEN J Parenter Enteral Nutr*. 2014;38:940–953).

TABLE 4-1 Vitamins

Vitamin	Function	Deficiency State
Fat Soluble		
A (Retinol)	Rhodopsin synthesis	Xerophthalmia, keratomalacia
D (Cholecalciferol)	Intestinal calcium	Rickets (children),

	absorption, bone remodeling	osteomalacia (adults)
E (α-Tocopherol)	Antioxidant	Hemolytic anemia, neurologic damage
K (Naphthoquinone)	τ-Carboxylation of glutamate in clotting factors	Coagulopathy (deficiency in factors II, VII, IX, and X)

**Problems with fat digestion and absorption can result in deficiency of vitamins A, D, E, and K. Vitamin K is also produced by enteric microbiota.*

Water Soluble

B_1 (Thiamine)	Decarboxylation and aldehyde transfer reactions	Beriberi, neuropathy, fatigue, heart failure

Bodily thiamine stores are relatively small, making deficiency common in hospitalized patients, and especially those with a history of alcoholism. As such, early thiamine supplementation, especially in the ICU, can be useful in the prevention of altered mental status and lactic acidosis. Furthermore, since thiamine is needed to breakdown glucose, supplementation should proceed glucose delivery in at risk patients, to prevent **Wernicke–Korsakoff syndrome* (Attaluri P, Castillo A, Edriss H, Nugent K. Thiamine deficiency: an important consideration in critically ill patients. *Am J Med Scii*. 2018;356:382–390).

B_2 (Riboflavin)	Oxidation–reduction reactions	Dermatitis, glossitis
B_3 (Niacin)	Oxidation–reduction reactions	Pellagra (**d**ermatitis, **d**iarrhea, **d**ementia, **d**eath)
B_6 (Pyridoxine)	Transamination and decarboxylation reactions	Neuropathy, glossitis, anemia
B_7 (Biotin)	Carboxylation reactions	Dermatitis, alopecia

B_9 (Folate)	DNA synthesis	Megaloblastic anemia, glossitis
B_{12} (Cyanocobalamin)	DNA synthesis, myelination	Megaloblastic anemia, neuropathy
**Vitamin B_{12} requires intrinsic factor (produced by gastric parietal cells) for absorption.*		
C (Ascorbic acid)	Hydroxylation of hormones, hydroxylation of proline in collagen synthesis, antioxidant	Scurvy

Modifications and supplementary information from authors are indicated by asterisks and italicized text.

Adapted from Atluri P, Karakouisis GC, Porrett PM, et al. Vitamins. In: *The Surgical Review: An Integrated Basic Science and Clinical Science Study Guide*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:252.

TABLE 4-2 Trace Elements

Trace Element	Function	Deficiency
Chromium	Promotes normal glucose utilization in combination with insulin	Glucose intolerance, peripheral neuropathy
Copper	Component of enzymes	Hypochromic microcytic anemia, neutropenia, bone demineralization, diarrhea
Fluorine	Essential for normal structure of bones and teeth	Caries

Iodine	Thyroid hormone production	Endemic goiter, hypothyroidism, myxedema, cretinism
Iron	Hemoglobin synthesis	Hypochromic microcytic anemia, glossitis, stomatitis
Manganese	Component of enzymes, essential for normal bone structure	Dermatitis, weight loss, nausea, vomiting, coagulopathy
Molybdenum	Component of enzymes	Neurologic abnormalities, night blindness
Selenium	Component of enzymes, antioxidant	Cardiomyopathy
Zinc	Component of enzymes involved in metabolism of lipids, proteins, carbohydrates, nucleic acids	Alopecia, hypogonadism, olfactory and gustatory dysfunction, impaired wound healing, acrodermatitis enteropathica, growth arrest

Adapted from Atluri P, Karakouisis GC, Porrett PM, et al. Vitamins. In: *The Surgical Review: An Integrated Basic Science and Clinical Science Study Guide*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:252.

II. DIETARY COMPONENTS AND DIGESTIVE ORGAN PHYSIOLOGY.

Essential dietary components are described below. Macronutrients are required in large quantities, and micronutrients are required in small quantities. Understanding the role that each organ plays in digestion and absorption of nutrients is critical, especially when assessing a patient who has had gastrointestinal (GI) resection or bypass, or a medical condition affecting the alimentary tract.

A. Macronutrients

1. **Carbohydrates** are the primary energy source for the body, and should provide 45% to 65% of calories in a typical diet. Each gram of enteral and parenteral carbohydrate provides 4 kcal and 3.4 kcal of energy, respectively. The latter is less owing to hydration of parenteral formulations. The functional unit of carbohydrate is glucose. **Carbohydrate digestion** is initiated by the action of salivary amylase, and absorption is generally completed within the first 1 to 1.5 m of small intestine. Salivary and pancreatic amylases cleave starches into oligosaccharides, which are hydrolyzed into monosaccharides by mucosal oligosaccharidases. They are then transported across the mucosa in a carrier-mediated manner. Diseases that result in generalized mucosal flattening (e.g., celiac sprue, Whipple disease, and hypogammaglobulinemia) may therefore cause diminished uptake of carbohydrates.
2. **Fats** should provide 20% to 35% of calories in a typical diet. Each gram of fat provides 9 kcal of energy. The functional unit of fat is lipid. **Fat digestion** is complex and utilizes nearly the entire GI tract. Fat in the duodenum stimulates cholecystokinin and secretin release, leading to gallbladder contraction and pancreatic enzyme release, respectively. Pancreatic secretions contain a combination of lipase, cholesterol esterase, and phospholipase A_2. In the alkaline environment of the duodenum, lipase hydrolyzes triglycerides to one monoglyceride and three fatty acids. Bile salts emulsify these fats into micelles, thereby facilitating absorption across the intestinal mucosal barrier by creating a hydrophilic outer coating. Of note, short- and medium-chain fatty acids enter circulation via the portal vein, while long-chain fatty acids undergo esterification and enter circulation via lymphatics, as chylomicrons. Bile salts are reabsorbed in the terminal ileum to maintain the bile salt pool (i.e., **enterohepatic circulation**). Consequently, major pancreatic or ileal resection may lead to fat malabsorption. Essential fatty acids include linoleic acid and linolenic acid, and deficiencies in these can lead to infection, poor wound healing, scaly rash, sparse hair growth, and thrombocytopenia.
3. **Protein** should provide 10% to 35% of calories in a typical diet, and each gram of protein provides 4 kcal of energy. The functional unit of protein is amino acid. **Protein digestion** is initiated by gastric pepsin.

Pancreatic trypsinogen is activated to form trypsin upon exposure to enterokinase (found throughout the duodenal mucosa). Trypsin then activates other proteolytic precursors to digest protein into small peptides. Once digested, almost 50% of protein absorption occurs in the duodenum, and complete protein absorption is achieved by the mid-jejunum. GI mucosa digests small peptides into amino acids, which are then released into portal circulation.

B. Micronutrients. Micronutrients are involved in wound healing and healthy immune function, and can serve as cofactors and enzymatic catalysts. Deficiencies can have a multitude of detrimental effects (Tables 4-1 and 4-2).

III. METABOLISM

A. General Principles of Metabolism. As a general principle, metabolism can be thought of as two opposing processes: anabolism and catabolism. Feeding drives synthesis and storage (anabolism), whereas starvation drives mobilization of energy (catabolism) from bodily stores. In the fed (anabolic) state, hyperglycemia triggers **insulin release**, leading to glycogen synthesis and storage in the liver and muscle, and the deposition of triglycerides in adipocytes.

In the starved (catabolic) state, about 12 hours worth of glycogen is available in the liver and skeletal muscles, which can provide a steady supply of blood glucose between meals. This is critical, as the brain and red blood cells rely almost exclusively on a steady supply of glucose to function.

After glycogen is depleted, **glucagon release** occurs, causing hepatic gluconeogenesis from amino acids (primarily alanine, derived from skeletal and visceral muscle breakdown). Glucagon also promotes ketone body formation from lipids, which the brain can utilize. After ~10 days of starvation, ketoacids become the primary fuel source for the brain, heart, skeletal muscle, and renal cortex, which have a protein-sparing effect. The kidney is also capable of producing glucose during periods of prolonged starvation.

B. Metabolism During Physiologic Stress. During **physiologic stress** (surgery, burn, major trauma) glucocorticoids and catecholamines are released. These hormones induce the release of glucose and lipids from peripheral stores, which accentuate the catabolic state induced by simple

starvation. Because surgery induces a hypercatabolic state, one can expect a significant rise in urinary nitrogen excretion (beyond that seen in simple starvation), a reflection of increased protein utilization. For this reason, while patients who are nonstressed should receive 0.8 to 1.2 g/kg/day of protein, those who are critically ill generally require 1.2 to 1.5 g/kg/day, and burn, septic, and obese patients can require up to 1.5 to 2.5 g/kg/day.

Indeed, **nitrogen balance** can serve as an important clinical indicator of patient nutritional status. As feeding and wound healing begin after surgery, the patient will gradually transition from the catabolic to anabolic state, and this will be reflected by a shift of the nitrogen balance from negative to positive (assuming there is appropriate protein supplementation). Protein is ~16% nitrogen by composition (or 1 g of nitrogen per every 6.25 g of protein). To determine adequacy of protein supplementation, nitrogen balance can be calculated as follows (considering 4 g of insensible nitrogen losses daily):

$$\text{Nitrogen balance} = (\text{g protein intake over 24 h}/6.25) - (\text{g urinary nitrogen excretion over 24 h} + 4\ \text{g})$$

IV. DAILY CALORIE NEED. The simplest method of determining *basal* daily calorie need is based on BMI (weight in kg/[height in m]^2). Stratification of BMI values is shown in Table 4-3.

Normal, nonstressed patients require ~25 kcal/kg/day. Patients suffering from severe metabolic stress or burn, on the other hand, require ~35 to 40 kcal/kg/day, and patients with moderate physiologic stress will fall somewhere in between. Keep in mind that obese patients should have their daily calorie intake calculated using adjusted body weight (ABW), to avoid overfeeding. To calculate ABW, one must first calculate ideal body weight (IBW):

TABLE 4-3 Stratification of BMI Values

BMI Categories (kg/m^2)	
Underweight	<18.5

Normal	18.5–24.9
Overweight	25–29.9
Obese	30–39.9
Morbid obesity	>40

$$\text{IBW for men} = 50\ \text{kg} + 2.3\ \text{kg for each inch over 5}' \text{ in height}$$
$$\text{IBW for women} = 45.5\ \text{kg} + 2.3\ \text{kg for each inch over 5}' \text{ in height}$$
$$\text{ABW} = \text{IBW} + 0.4\ (\text{actual weight} - \text{IBW})$$

Other methods of determining daily calorie need are based on measuring energy expenditure. **Indirect calorimetry** remains the gold standard in measuring energy expenditure in the clinical setting. It measures CO_2 production and O_2 consumption during rest and exercise at steady state, to calculate total energy expenditure (TEE). Additionally, **respiratory quotient (RQ)** represents the ratio of expired CO_2 to O_2 consumed (RQ = CO_2 eliminated/O_2 consumed), and is useful in determining basal metabolic rate. This ratio can also provide valuable information regarding the primary energy substrate being utilized: An RQ of 1, 0.8, and 0.7 indicates primarily glucose, protein, and fat utilization, respectively, while an RQ >1 signifies overfeeding. Of note, dietary modification to minimize CO_2 production—that is, limiting carbohydrates—can assist with weaning from the ventilator.

V. ROUTE AND TIMING OF PERIOPERATIVE NUTRITION. Surgical patients present a unique set of challenges to clinicians who must determine when, how, and what to feed them.

A. Route of Feeds. The two routes for nutrition delivery are enteral and parenteral.

1. **Enteral feeds.** Enteral administration of nutrition is the preferred route, since it is the most physiologic, least invasive, and inexpensive. Enteral feeding maintains the GI tract cytoarchitecture and mucosal integrity (via trophic effects), absorptive function, and

normal microbial flora. This results in less bacterial translocation and endotoxin release from the intestinal lumen into the bloodstream.

a. **Oral feeds.** Safe administration of an oral diet requires that the patient has an intact chewing/swallowing mechanism along with a functioning alimentary tract and appropriate mental alertness and orientation. Patients with difficulty swallowing may be candidates for modified diets such as mechanical soft, or pureed.

b. **Assisted enteral feeds.** For patients unable to tolerate and/or receive adequate nutrition via oral feeds, assistive devices such as nasogastric, nasoduodenal or jejunal, gastrostomy, and jejunostomy tubes can be considered. Selection of such a device depends on anticipated duration of need and patient/anatomical factors. For example, **tracheobronchial aspiration** of tube feeds may occur with patients who are fed into the stomach or proximal small intestine and can lead to major morbidity. Patients at particular risk are those with central nervous system abnormalities and those who are sedated. Precautions include assessment of gastric residuals as well as head of bed elevation. **High gastric residuals** as a result of outlet obstruction, dysmotility, intestinal ileus, or bowel obstruction may limit the usefulness of nasogastric or gastrostomy feeding tubes. Treatment of this problem should be directed at the underlying cause. Gastroparesis frequently occurs in diabetic or head-injured patients. Promotility agents such as metoclopramide or erythromycin may aid in gastric emptying. If gastric retention prevents the administration of sufficient calories and intestinal ileus or obstruction can be excluded, a nasojejunal or jejunostomy feeding tube may be necessary. **Clogging** can usually be prevented by careful routine flushing of the feeding tube. Instillation of a mixture of bicarbonate and pancreatic enzymes is useful for unclogging feeding tubes. Tubes should be flushed both before and after medication administration and liquid medications should be used whenever possible due to the possibility of crushed meds clogging tubes. Use of feeding tubes requires enteral feeding products (discussed below).

2. **Parenteral feeds.** Parenteral feeds are reserved for patients who require nutritional support but cannot meet their needs through enteral feeding.

a. **Peripheral parenteral nutrition (PPN)** is administered through a peripheral IV catheter. The osmolarity of PPN solutions is generally limited to 900 mOsm (∼12% dextrose solution) to avoid phlebitis. Consequently, unacceptably large volumes (>2,500 mL) are necessary to meet the typical patient's nutritional requirements. Temporary nutritional supplementation with PPN may be useful in selected patients, but is not typically indicated.

b. **Total parenteral nutrition (TPN)** is administered via central venous access (preferably placed in either the subclavian or internal jugular vein) and provides complete nutritional support. Long-term TPN use is associated with several complications including **catheter-related complications** (which can be minimized by strict aseptic technique and routine catheter care), and **cholestatic liver disease**. Cholestatic liver disease may ultimately lead to biliary cirrhosis, which is treated with transplantation. The solution, volume of administration, and additives are individualized on the basis of an assessment of the nutritional requirements. A practical approach to TPN composition and administration is provided below.

3. **Timing of feeds.** Within general surgery, timing of feeds is primarily dictated by the location and invasiveness of an abdominal or alimentary tract surgery. In the absence of contraindications (bowel discontinuity, ischemia, obstruction, and acute peritonitis), early enteral feeding is generally recommended. Relative contraindications include multiple high-output fistulas, shock or sepsis, and severe malabsorption (*JPEN J Parenter Enteral Nutr*. 2013;37:99S–105S). Of note, **open abdomen** guidelines advocate early enteral feeding (after resuscitation is complete), since this is associated with increased fascial closure rates, decreased complication rates, and decreased mortality (*J Trauma Acute Care Surg*. 2012;73:1380–1387). Furthermore, **paralytic ileus** (a common event following open abdominal surgery) is not a contraindication to feeding and several strategies have been developed to shorten the duration of paralytic ileus. These include the use of epidural analgesia and peripherally acting μ-opioid receptor antagonists such as alvimopan (to minimize the effects of narcotics on gut motility) and the ERAS pathway, which includes not only nutritional recommendations, but also a

comprehensive set of guidelines for multimodal perioperative management to speed recovery and shorten the duration of hospital stay. These guidelines also call to question the surgical dogma that patients need be NPO beginning at midnight prior to surgery, and instead favor the use of carbohydrate-rich beverages up to 2 hours prior to surgery (with certain exceptions such as diabetes), to preserve glycogen stores and improve postoperative insulin resistance (*Clin Nutr*. 2012;31:783–800). While the colorectal guidelines are most commonly referenced by general surgeons, the ERAS Society produces guidelines for a variety of surgical specialties (www.erassociety.org).

VI. COMPOSITION AND ADMINISTRATION OF ENTERAL AND PARENTERAL FORMULAS

A. Enteral Feeding Composition. Numerous enteral formulas are commercially available, and these can be classified as standard, elemental, or semielemental. Standard solutions provide 1 to 2 kcal/mL.

1. **Standard (polymeric) formulas** contain nonhydrolyzed macronutrients and can be tailored to patient diseases (renal insufficiency, hepatic insufficiency, pulmonary insufficiency, bariatric, diabetic, immune modulating, etc.). It is recommended that the standard formulas be used as first line with diabetic patients and also those with hepatic or renal insufficiency (*Nutr Clin Pract*. 2015;30:72–85).
2. **Elemental/semielemental formulas** contain hydrolyzed macronutrients appropriate for patients with malabsorptive disorders.

Of note, it is not uncommon to encounter **diarrhea** in formula-fed patients. Diarrhea may result from an overly rapid increase in the volume of hyperosmolar tube feedings. If other causes of diarrhea are excluded, the volume or concentration of tube feedings should be decreased. Soluble fiber may also be added, but should be used with caution within the first 7 days after an intestinal operation. If no improvement occurs, a different formula should be used. Antidiarrheal agents such as loperamide should be reserved for patients with severe diarrhea who have had infectious etiologies excluded.

B. Enteral Feeding Administration. It is recommended to start with a full-strength formula at a slow rate, which is steadily advanced.

Conservative initiation and advancement are recommended for patients who are critically ill, those who have not been fed for some time, and those receiving a high osmolarity or calorie-dense formula.

1. **Bolus feedings** are reserved for patients with gastrostomy feeding tubes. Feedings are administered by gravity, begin at 50 to 100 mL every 4 hours, and are increased in 50-mL increments until goal intake is reached (usually 240 to 360 mL every 4 hours). Tracheobronchial aspiration is a potentially serious complication because feedings are prepyloric. This type of feeding should be avoided in those with a high risk of aspiration, disorders of glucose metabolism, or fluid management concerns. To reduce the risk of aspiration, the patient's head and body should be elevated to 30 to 45 degrees during feeding and for 1 to 2 hours after each feeding. The feeding tube should be flushed with approximately 30 mL of water after each use. Free water volume can be adjusted as needed to treat hypo- or hypernatremia.
2. **Continuous infusion** administered by a pump is generally required for nasojejunal, gastrojejunal, or jejunal tubes. Feedings are initiated at 20 mL/hr and increased in 10- to 20-mL/hr increments every 4 to 6 hours until the desired goal is reached, with 30 mL of water flushes every 4 hours. Feedings should be held or advancement should be slowed if abdominal distension or pain develops. For some patients, the entire day's feeding can be cycled over 8 to 12 hours at night to allow the patient mobility free from the infusion pump during the day.
3. Routine measurement of **gastric residual volume** (GRV) has historically been used to monitor enteral feeding tolerance and guide feeding strategies in critically ill patients. However, recent literature has called this practice into question, citing little evidence to support withholding feeds for GRV <500 mL and, furthermore, noting the risks for undernutrition posed by withholding feeds for GRV in the absence of additional indicators of feeding intolerance. These include signs or symptoms of obstruction, abdominal distention, nausea, emesis, and diarrhea (*JPEN J Parenter Enteral Nutr*. 2016;40:159–211, *Am Surg*. 2018;84:831–835).

C. Parenteral Nutrition Composition. Pharmacists and nutrition support specialists are important allies in the initiation and monitoring of TPN.

Safe and effective use of TPN can be quite complex and guidelines have been established for hospital-wide policies and procedures in the administration of TPN (*Nutr Clin Pract*. 2018;33:295–304), as well as nutritional optimization/composition, and monitoring in critically ill patients (*JPEN J Parenter Enteral Nutr.* 2014;38:334–377, *Clin Nutr.* 2009;28:387–400). As such, the following are general guidelines to TPN that should be tailored to meet specific patient needs:

1. **TPN solutions** provide ~1 kcal/mL and are generally administered as a three-in-one admixture of amino acids (10%, 4 kcal/g); dextrose (70%, 3.4 kcal/g); and lipid emulsion of soybean, safflower, or olive oil (20%, 9 kcal/g). Alternatively, the lipid emulsion can be administered as a separate IV "piggyback" infusion.
2. **Additives.** Other elements can be added to the basic TPN solutions.
3. **Electrolytes** (sodium, potassium, chloride, acetate, calcium, magnesium, phosphate) should be adjusted daily. The number of cations and anions must balance: This is achieved by altering the concentrations of chloride and acetate. The calcium:phosphate ratio must be monitored to prevent salt precipitation.
4. **Medications** such as H_2-receptor antagonists and insulin can be administered in TPN solutions. Regular insulin should initially be administered subcutaneously on the basis of the blood glucose level. After a stable insulin requirement has been established, insulin can then be administered via TPN solution—generally at two-thirds the daily subcutaneous insulin dose. Please note that, in critically ill patients, strict glucose control is associated with increased mortality; the preferred blood glucose target is <180 mg/dL (*N Engl J Med*. 2009;360:1283–1297).
5. **Vitamins and trace elements** are added daily using a commercially prepared mixture that includes copper, chromium, selenium, manganese, and zinc. Vitamin K is not included in most multivitamin mixtures, to prevent unintentional administration to patients on warfarin, and must be added separately.

D. Parenteral Nutrition Administration

1. **Continuous infusion of TPN** is most commonly used. A new three-in-one admixture bag of TPN is administered daily at a constant infusion rate over 24 hours. Additional maintenance IV fluids are

unnecessary and total infused volume should be kept constant while nutritional content is increased. Serum electrolytes should be obtained and TPN adjusted until the patient can be maintained on a stable regimen.

2. **Cyclic administration of TPN** solutions may be useful for selected patients, including (1) those who will be discharged from the hospital and subsequently receive home TPN, (2) those with limited IV access who require administration of other medications, and (3) those who are metabolically stable and desire a period during the day when they can be free of an infusion pump. Cyclic TPN is administered for 8 to 16 hours, most commonly at night. This should not be done until metabolic stability has been demonstrated for patients on standard, continuous TPN infusions.
3. **Discontinuation of TPN** should begin when the patient can consistently satisfy 60% of their calorie and protein needs with oral intake or enteral feeding, and 100% of daily fluid needs. The calories provided by TPN can be decreased in proportion to calories from the patient's increasing enteral intake. To discontinue TPN when hypoglycemia is a concern, the infusion rate should be halved for 1 hour, halved again the next hour, and then discontinued. Tapering in this manner prevents rebound hypoglycemia from hyperinsulinemia. It is not necessary to taper the rate if the patient demonstrates glycemic stability when TPN is abruptly discontinued (i.e., cycled TPN) or receives less than 1,000 kcal/day.

VII. SPECIAL CONSIDERATIONS

A. Refeeding syndrome is a potentially lethal complication in patients who are severely malnourished. As these patients are fed, energy synthesis begins, which depletes the body of its limited phosphorous stores, leading to hypophosphatemia. Further, insulin production induces intracellular shift of potassium and magnesium leading to hypokalemia and hypomagnesemia. Symptoms of these electrolyte abnormalities ensue the most significant and immediately lethal, of which is arrhythmia and acute heart failure.

B. Dumping Syndrome. Procedures that reduce the reservoir capacity of the stomach, compromise the pyloric sphincter, or alter secretion of GI hormones can produce a "dumping syndrome" postoperatively. When

undigested, hyperosmolar food reaches the jejunum, fluid shifts into the intestine to equalize osmotic pressure, leading to nausea, diaphoresis, tachycardia, bloating, abdominal cramping, and diarrhea. Dietary modifications to prevent dumping syndrome include small, frequent meals and limiting beverages and liquids at meals, in addition to limiting the intake of simple carbohydrates and sugars. Fiber is gradually introduced and may help slow gastric emptying.

C. Low-residue diet provides <10 g/day of dietary fiber. It is used to prevent the formation of an obstruction when there is intestinal narrowing, delayed intestinal transit, reduced fiber in the colon pre- and postoperatively, and to allow bowel rest in times of colonic inflammation and/or irritation. Patients who benefit from a low-fiber diet include those going through an acute phase of inflammatory bowel disease (IBD), diverticulitis, or radiation enteritis.

D. Chyle Leak. Patients with a chyle leak should avoid dietary long-chain fatty acids, but can tolerate short- and medium-chain fatty acids, as these are directed into circulation via the portal vein rather than lymphatic circulation.

E. Renal Insufficiency. Consider limiting fluid, protein, phosphorous, and potassium. Patients that are on dialysis will have different requirements than those that are not on dialysis. The type of dialysis (continuous renal replacement therapy or hemodialysis) will help determine the limitations.

F. Hepatic Insufficiency. Consider limiting protein, fluid, and sodium.

G. Pulmonary Insufficiency. Consider limiting carbohydrates and increasing fats (to minimize CO_2 production), especially during ventilator weaning.

H. Cancer Cachexia. Malnourishment in cancer is common for a number of reasons. Examples include GI tumors that directly affect nutrition delivery and absorption, treatment effects, and metastatic disease burden. Furthermore, cancer can induce unique metabolic and neurohormonal responses that negatively affect appetite, satiety, energy levels, and muscle mass—independent of tumor type or stage—a syndrome known as cancer cachexia (CC). CC is associated with poor prognosis and cancer therapy response, making recognition and treatment imperative. Strategies for management include appetite

stimulants, anabolic agents, cytokine inhibitors, and nutrient supplements (*Nutr Clin Pract*. 2017;32:599–606).

CHAPTER 4: NUTRITION

Multiple Choice Questions

1. **A 36-year-old female undergoes an uncomplicated laparoscopic cholecystectomy. Her preoperative weight is 198 lb (89.8 kg) and she is 5 ft 6 in (167.6 cm) tall. What weight should be used to calculate her calorie needs?**

   a. 198 lb (89.8 kg)
   b. 130.7 lb (59.3 kg)
   c. 140.7 lb (63.8 kg)
   d. 157.6 lb (71.5 kg)
   e. 163.6 lb (74.2 kg)

2. **A 55-year-old emaciated alcoholic male presents with a 2-day history of chest pain after forceful vomiting. He is taken to the OR for a thoracotomy after he is found to have an esophageal rupture. A jejunal feeding tube is placed and he is started on tube feeds on POD 1, when he develops confusion, shallow breathing, and pulmonary edema. What electrolyte abnormalities do you expect to see?**

   a. Hypophosphatemia, hypokalemia, hypomagnesemia
   b. Hyperphosphatemia, hypokalemia, hypomagnesemia
   c. Hypernatremia, hyperkalemia, hyperphosphatemia
   d. Hypernatremia, hypokalemia, hypophosphatemia
   e. Hyperkalemia, hypophosphatemia, hypomagnesemia

3. **A 42-year-old female is admitted to the ICU after being operated on for a perforated duodenal ulcer. Her past medical history is significant for steroid-dependent COPD. Given the degree of contamination in her abdomen, the decision is made to wait at least 1 week before obtaining a UGI and starting enteral feeds. She will be started on TPN and has vascular access with a right IJ triple-lumen catheter. She is currently on low-dose norepinephrine and mechanically ventilated. She weighs 50 kg and is 150 cm tall. She does not have any renal or hepatic**

dysfunction. What should the composition of her TPN be?

a. 35 kcal/kg/day, 0.8 g/kg/IBW of protein/day
b. 30 kcal/kg/day, 1.5 g/kg/IBW of protein/day
c. 30 kcal/kg/day, 2.5 g/kg/IBW of protein/day
d. 25 kcal/kg/day, 0.8 g/kg/IBW of protein/day
e. 25 kcal/kg/day, 2.5 g/kg/IBW of protein/day

4. For the above patient, what is her target blood glucose level?

a. <100 mg/dL
b. <150 mg/dL
c. <180 mg/dL
d. <120 mg/dL
e. There is no blood glucose goal

5. A 60-year-old TPN-dependent male with short-gut syndrome and diarrhea presents with a nonhealing leg wound. Which trace element may he need supplementation with?

a. Manganese
b. Fluorine
c. Selenium
d. Copper
e. Zinc

5 Fluid, Electrolytes, and Acid–Base Disorders

Matthew T. Grant and Tiffany M. Osborn

I. INTRODUCTION.

The surgical patient is at risk for multiple derangements of fluid balance and electrolyte composition. As a result, knowing how to manage these derangements is essential for optimal postop management.

A. Definition of Body Fluid Compartments.

Water constitutes 50% to 70% of lean body weight. Total-body water is divided into an intracellular fluid compartment and an extracellular fluid compartment, which consists of an intravascular compartment and an interstitial compartment, as illustrated in Figure 5-1. The extracellular and intracellular compartments have distinct electrolyte compositions. The principal extracellular cation is Na^+, and the principal extracellular anions are Cl^- and HCO_3^-. In contrast, the principal intracellular cations are K^+ and Mg^{2+}, and the principal intracellular anions are phosphates and negatively charged proteins.

B. Osmolality and Tonicity.

Osmolality refers to the number of osmoles of solute particles per kilogram of water and is comprised of both effective and ineffective components. Effective osmoles cannot freely permeate cell membranes and are therefore restricted to either the intracellular or extracellular fluid compartments. The asymmetry in effective osmoles between these compartments causes the movement of water across the cell membrane. The effective osmolality of a solution is equivalent to its tonicity, and in turn, tonicity is the parameter the body attempts to regulate.

II. PARENTERAL FLUID THERAPY

A. Principles of Fluid Management. A normal individual consumes an average of 2,000 to 2,500 mL of water daily. Daily water losses include approximately 1,000 to 1,500 mL in urine and 250 mL in stool. The minimum amount of urinary output required to excrete the catabolic end products of metabolism is approximately 800 mL. An additional 750 mL of insensible water loss occurs daily via the skin and respiratory tract. Insensible losses increase with hypermetabolism, fever, and hyperventilation. The composition of commonly used parenteral fluid is presented in Table 5-1.

1. **Maintenance.** Maintenance fluids should be administered at a rate that is sufficient to maintain a urine output of 0.5 to 1 mL/kg/hr in adults. Maintenance fluid requirements can be approximated on the basis of body weight as follows: 100 mL/kg/day for the first 10 kg, 50 mL/kg/day for the second 10 kg, and 20 mL/kg/day for each subsequent 10 kg. Maintenance fluids in general should contain Na^+ (1 to 2 mmol/kg/day) and K^+ (0.5 to 1 mmol/kg/day [e.g., D5 0.45% NaCl + 20 to 30 mmol K^+/L]).

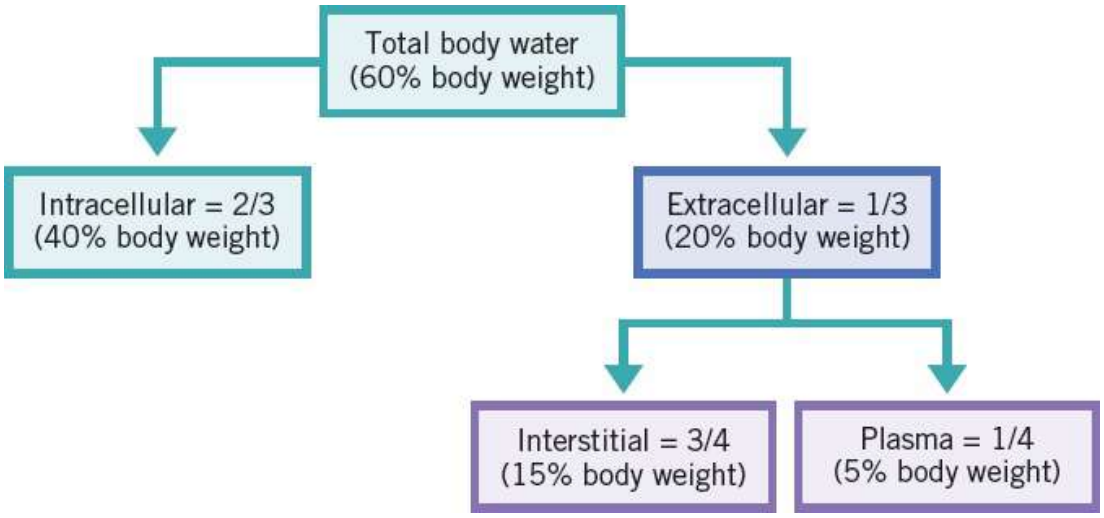


FIGURE 5-1 Body fluid compartments.

2. **Intraoperative fluid management** requires replacement of preoperative deficit as well as ongoing losses. Intraoperative losses include maintenance fluids for the length of the case, hemorrhage, and "third-space losses." With nonemergent bleeding, crystalloid or colloid may be employed. Unless the patient has a known or suspected reason to need albumin replacement, crystalloid is typically

the first-line agent, moving to colloid if the patient is refractory to crystalloid-based resuscitation. One exception when albumin should not be employed, is in the acute trauma patient with traumatic brain injury.

First-line replacement for significant, acute, or ongoing blood loss, is blood. However, under emergent situations, there may not be sufficient time to cross match the patient and universal donor transfusion protocols should be employed while cross-matched blood is being processed. Although blood replacement should equate to what is lost, frequently total blood loss is difficult to quantitate, especially with extensive bleeding prior to operating room arrival. Endpoints can be determined through physiologic parameters (blood pressure, urine output) in conjunction with lab assessment, and dynamic parameters (echocardiography, NICOM, stroke volume changes).

Intraoperative insensible and third-space fluid losses depend on incision size, extent of tissue trauma, and preoperative physiology. Small incisions with minor tissue trauma (e.g., inguinal hernia repair) result in third-space losses of approximately 1 to 3 mL/kg/hr. Medium-sized incisions with moderate tissue trauma (e.g., uncomplicated sigmoidectomy) result in third-space losses of approximately 3 to 7 mL/kg/hr. Larger incisions and operations with extensive tissue trauma and dissection (e.g., pancreaticoduodenectomy) can result in third-space losses of approximately 9 to 11 mL/kg/hr or greater. Patients who have on going third spacing prior to operating room arrival can expect exacerbation of fluid shifts during and after operative intervention. Thus monitoring of resuscitation endpoints are helpful to ensure volume requirements are appropriately addressed.

TABLE 5-1 **Composition of Common Parenteral Fluids**[a]

Solution	Volume[b]	Na^+	K^+	Ca^{2+}	Mg^{2+}	Cl^-	HCO_3 (as Lactate)	Dextrose (g/L)	mOsm/L
Extracellular fluid	—	142	4	5	3	103	27	—	280–310
Lactated Ringer	—	130	4	3	—	109	28	—	273
0.9% NaCl	—	154	—	—	—	154	—	—	308
0.45% NaCl	—	77	—	—	—	77	—	—	154
D5W	—	—	—	—	—	—	—	50	252
D5/0.45% NaCl	—	77	—	—	—	77	—	50	406
D5LR	—	130	4	3	—	109	28	50	525
3% NaCl	—	513	—	—	—	513	—	—	1,026
7.5% NaCl	—	1,283	—	—	—	1,283	—	—	2,567
6% hetastarch	500	154	—	—	—	154	—	—	310
10% dextran-40	500	0/154[c]	—	—	—	0/154[c]	—	—	300
6% dextran-70	500	0/154[c]	—	—	—	0/154[c]	—	—	300
5% albumin	250, 500	130–160	<2.5	—	—	130–160	—	—	330
25% albumin	20, 50, 100	130–160	<2.5	—	—	130–160	—	—	330
Plasma protein fraction	250, 500	145				145			300

[a]Electrolyte concentrations in mmol/L.

[b]Available volumes (mL) of colloid solutions.

[c]Dextran solutions available in 5% dextrose (0 Na^+, 0 Cl^-) or 0.9% NaCl (154 mmol Na^+, 154 mmol Cl^-).

D5LR, 5% dextrose in lactated Ringer solution; D5/0.45% NaCl, 5% dextrose per 0.45% NaCl; D5W, 5% dextrose in water.

3. **Postoperative fluid management** requires careful evaluation of the patient and should generally be titrated to maintain an adequate urine output (0.5 to 1.0 mL/kg/hr). Sequestration of extracellular fluid into the sites of injury or operative trauma can continue for 12 or more hours after operation. GI losses that exceed 250 mL/day from nasogastric tube suction should be replaced with an equal volume of crystalloid. Mobilization of perioperative third-space fluid losses typically begins 2 to 3 days after operation. In general, gastric losses should be replaced with D5 ½ NS with 20 mEq K and pancreatic, biliary, largest intestine losses (e.g., diarrhea) and small intestine losses should be replaced with Lactated Ringer (LR) solution.

B. Crystalloids are solutions that contain sodium as the major particle. Crystalloids are inexpensive and used for volume expansion, maintenance infusion, and correction of electrolyte disturbances.

1. **Isotonic crystalloids** include LR solution and 0.9% NaCl (NS). Isotonic crystalloids distribute uniformly throughout the extracellular fluid compartment so that after 1 hour of active resuscitation, only 25% of the total volume infused remains in the intravascular space. LR is designed to mimic extracellular fluid and is considered a balanced salt solution. This solution provides a HCO_3^- precursor and is useful for replacing GI losses and extracellular fluid volume

deficits. In general, LR and NS can be used interchangeably. Larger volumes of normal saline in resuscitation have been associated with higher incidences of hyperchloremic metabolic acidosis, acute kidney injury, and increased endothelial permeability. Electrolytes should be rechecked during resuscitation especially if volumes over 6 L are necessary.

2. **Hypertonic saline solutions** alone and in combination with colloids, such as dextran, have generated interest as resuscitation fluids for patients with shock or burns. These fluids were initially appealing because, relative to isotonic crystalloids, smaller quantities are required for resuscitation. However, coagulation imbalances were reported in trauma patients initially resuscitated with hypertonic solutions (*Shock*. 2015;44:25–31) The side-effect profile of hypertonic solutions include hypernatremia, hyperosmolality, hyperchloremia, hypokalemia, and central pontine demyelination with rapid infusion. Although useful in specific patient populations such as cerebral edema, they should not be used as a resuscitation tool at this time.
3. **Hypotonic solutions** (D5W, 0.45% NaCl) distribute throughout the total-body water compartment, expanding the intravascular compartment by as little as 10% of the volume infused. For this reason, hypotonic solutions should not be used for volume expansion. They are used to replace free water deficits (as in hypernatremia).

C. Colloid solutions contain high–molecular-weight substances that remain in the intravascular space. Early use of colloids in the resuscitation regimen may result in more prompt restoration of tissue perfusion and may lessen the total volume of fluid required for resuscitation.

Albumin studies are conflicting and meta-analyses often combine multiple patient populations (ages: adult, child; illness severity: nonacute, severe illness), comparator fluids, timing, and albumin concentrations making synthesis challenging. As a supplemental or maintenance fluid, albumin is not effective for general populations. The SAFE (saline versus albumin fluid evaluation) study, which randomized 6,997 patients in the ICU to receive either 4% albumin or normal saline over several days, found no significant difference in outcomes, including mortality and organ failure, between the two groups (*N Engl J*

Med. 2004;350:2247–2256). Another study where albumin was used as a supplemental fluid in hypooncotic patients targeting a serum albumin level, benefit was seen only in septic shock populations (*N Engl J Med*. 2014;370:1412–1421).

The majority of resuscitation data report albumin survival benefit in septic shock patients, especially within the first 6 to 24 hours. (*PloS One* 2014;9:e114666). However, reported benefit is less consistent in severe sepsis without shock. (*Crit Care* 2014;18:702).

Other populations where outcomes are reported improved with albumin are spontaneous bacterial peritonitis (*Clin Gastroenterol Hepatol* 2013;11:123–130), cirrhotics with hepatic encephalopathy (*J Hepatol* 2013;59:1184–1192), and patients requiring large volume paracentesis.

Since colloid solutions are substantially more expensive than crystalloids, their routine use is controversial. The most recent *Surviving Sepsis* guidelines advocate the use of crystalloids as the initial fluid of choice in the resuscitation of patients with septic shock and advise albumin for continued resuscitation when shock is refractory to crystalloids.

1. **Albumin preparations** ultimately distribute throughout the extracellular space, although the initial location of distribution is the vascular compartment. Preparations of 25% albumin (100 mL) and 5% albumin (500 mL) expand the intravascular volume by an equivalent amount (450 to 500 mL). Albumin 25% is indicated in the edematous patient to mobilize interstitial fluid into the intravascular space. They are not indicated in the patient with adequate colloid oncotic pressure (serum albumin >3.0 mg/dL, total protein >5 mg/dL), for augmenting serum albumin in chronic illness when not acutely ill (cirrhosis or nephrotic syndrome), or as a nutritional source.
2. **Dextran** is a synthetic glucose polymer that expands the intravascular volume by an amount equal to the volume infused. Side effects include renal failure, osmotic diuresis, coagulopathy, and laboratory abnormalities (i.e., elevations in blood glucose and protein and interference with blood cross-matching). There is no clear benefit to the use of dextrans over crystalloid solutions (*Ann Intensive Care*. 2014;4:38).

3. **Hydroxyethyl starch (hetastarch)** is a synthetic molecule resembling glycogen that is available as a 6% solution in 0.9% NaCl. Hetastarch, like 5% albumin, increases the intravascular volume by an amount equal to or greater than the volume infused. Meta-analysis, however, found that fluid resuscitation with hydroxyethyl starch is associated with an increased incidence of mortality, renal failure, and increased use of renal replacement therapy (*JAMA*. 2013;309(12):1229). Currently, hydroxyethyl starch is not recommended.

III. DIAGNOSIS AND TREATMENT OF COMMON ELECTROLYTE DISORDERS

A. Sodium

1. **Physiology.** Solute concentration inside and outside the cell must be equal. Cell volume is affected by sodium concentration (osmolality). "Tonicity" describes how plasma may affect cells. Hypertonicity causes cells to shrink while hypotonicity causes them the swell. Hypernatremia denotes hypertonicity. Clinical manifestations of significant hyponatremia or hypernatremia are primarily neurologic. Rapid plasma sodium concentration alterations can cause severe neurologic alterations that can become permanent or result in death. Normal Na^+ concentration is 135 to 145 mmol/L (310 to 333 mg/dL).
2. **Hyponatremia.** If infused or ingested water exceeds renal free water excretion capacity, plasma sodium will decrease rapidly. Potential sources of significant Na^+ loss include sweat, urine, and gastrointestinal secretions (Table 5-2).
   a. **Clinical manifestations.** Symptoms associated with hyponatremia are predominantly neurologic and result from hypoosmolality, and include lethargy, confusion, nausea, vomiting, seizures, and coma. Chronic hyponatremia is often asymptomatic until the serum Na^+ concentration falls below 110 to 120 mEq/L (253 to 276 mg/dL). An acute drop in the serum Na^+ concentration of 120 to 130 mEq/L (276 to 299 mg/dL), may also be symptomatic.
   b. **Causes, diagnosis, and treatment.** The diagnostic approach to hyponatremia is illustrated in Figure 5-2, and a treatment algorithm is detailed in Figure 5-3. It is first necessary to measure the serum osmolality to evaluate patients with hyponatremia to

determine if there is an associated tonicity imbalance.

(1) Isotonic hyponatremia. Hyperlipidemic and hyperproteinemic states result in an isotonic expansion of the circulating plasma volume and cause a decrease in serum Na^+ concentration, although total-body Na^+ remains unchanged. Isotonic, sodium-free solutions of glucose, mannitol, and glycine are restricted initially to the extracellular fluid and may similarly result in transient hyponatremia. Isotonic hyponatremia corrects with resolution of the underlying disorder.

(2) Hypertonic hyponatremia. Hyperglycemia increases concentration of extracellular solutes making the ECF hypertonic as compared to the intracellular fluid. To balance the osmotic difference, fluid shifts from the intracellular compartment to the extracellular compartment thereby diluting serum Na^+ concentration. Rapid infusion of hypertonic solutions of glucose, mannitol, or glycine may have a similar effect on Na^+ concentration. Hypertonic hyponatremia corrects with resolution of the underlying disorder.

TABLE 5-2 Composition of Gastrointestinal Secretions

Source	Volume (mL/24 hr)[a]	Na^+ (mmol/L)[b]	K^+ (mmol/L)[b]	Cl^- (mmol/L)[b]	HCO_3 (mmol/L)[b]
Salivary	1,500 (500–2,000)	10 (2–10)	26 (20–30)	10 (8–18)	30
Stomach	1,500 (100–4,000)	60 (9–116)	10 (0–32)	130 (8–154)	0
Duodenum	(100–2,000)	140	5	80	0
Ileum	3,000	140 (80–150)	5 (2–8)	104 (43–137)	30
Colon	(100–9,000)	60	30	40	
Pancreas	(100–800)	140 (113–185)	5 (3–7)	75 (54–95)	115
Bile	(50–800)	145 (131–164)	5 (312)	100 (89–180)	35

[a]Average volume (range).

[b]Average concentration (range).

Reprinted with permission from Faber MD, Schmidt RJ, Bear RA, et al. Management of fluid, electrolyte, and acid-base disorders in surgical patients. In: Narins RG, ed. *Clinical Disorders of Fluid and Electrolyte Metabolism*. New York: McGraw-Hill; 1994:1424.

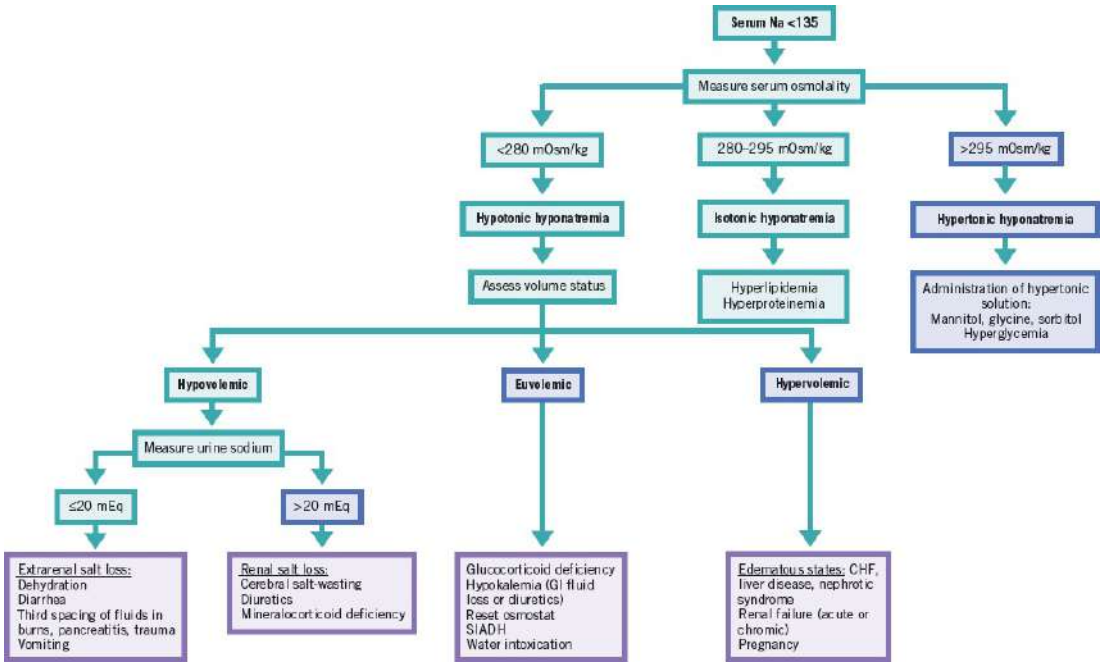


FIGURE 5-2 Diagnostic approach for hyponatremia. CHF, congestive heart failure; GI, gastrointestinal; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

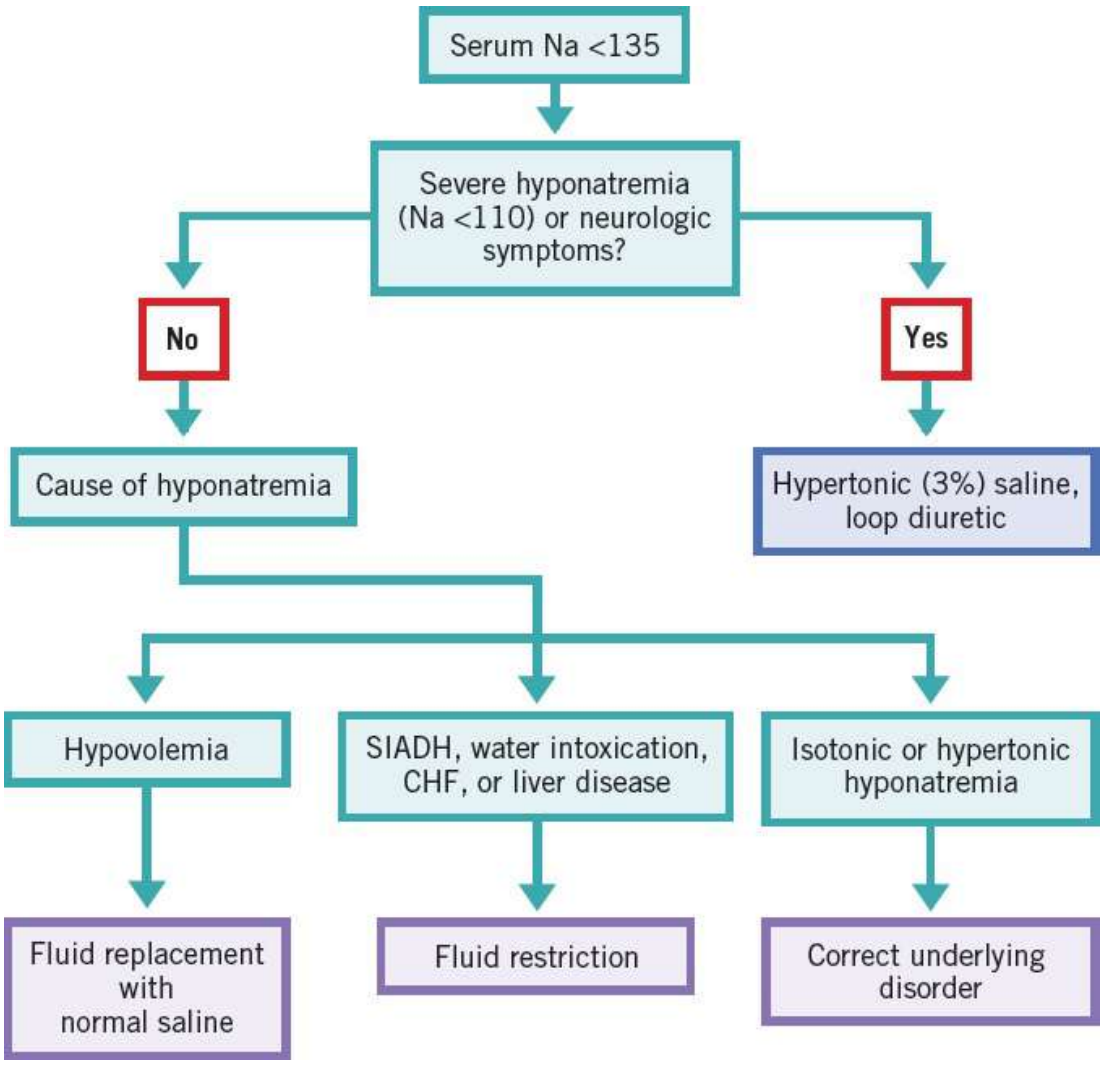


FIGURE 5-3 Treatment algorithm for hyponatremia. CHF, congestive heart failure; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

(3) Hypotonic hyponatremia is classified on the basis of extracellular fluid volume.

(a) Hypovolemic hyponatremia in the surgical patient occurs most commonly when sodium-rich fluid losses (e.g., from the GI tract, skin, or lungs) are inappropriately replaced with an insufficient volume of hypotonic fluid (e.g., D5W and 0.45% NaCl). Hypovolemic hyponatremia can be managed with administration of 0.9% NaCl to correct volume deficits and replace ongoing losses.

(b) Hypervolemic hyponatremia. The edematous states of congestive heart failure, liver disease, and nephrosis occur

in conjunction with inadequate circulating blood volume. This serves as a stimulus for the renal retention of sodium and water. Disproportionate accumulation of water results in hyponatremia. Hypervolemic hyponatremia may respond to water restriction (1,000 mL/day) to return Na^+ to greater than 130 mmol/L (299 mg/dL). In cases of severe congestive heart failure, optimizing cardiac performance may assist in Na^+ correction. If the edematous hyponatremic patient becomes symptomatic, plasma Na^+ can be increased to a safe level by the use of a loop diuretic (furosemide, 20 to 200 mg intravenously every 6 hours) while replacing urinary Na^+ losses with 3% NaCl. Hypertonic saline should not be administered to these patients without concomitant diuretic therapy. Administration of synthetic brain natriuretic peptide (BNP) is also useful therapeutically in the setting of acute heart failure because it inhibits Na^+ reabsorption at the cortical collecting duct and inhibits the action of antidiuretic hormone (ADH) on water permeability at the inner medullary collecting duct.

(c) Isovolemic hyponatremia

(i) Water intoxication typically occurs in the patient who consumes large quantities of water and has mildly impaired renal function (primary polydipsia). Alternatively, it may be the result of the administration of large quantities of hypotonic fluid in the patient with renal failure. Water intoxication responds to fluid restriction (1,000 mL/day).

(ii) Hypokalemia, either from GI fluid loss or secondary to diuretics, may result in isovolemic hyponatremia due to cellular exchange of K^+ and Na^+.

(iii) Reset osmostat. Normally, the serum “osmostat” is set at 285 mOsm/L. In some individuals with chronic disease (e.g., cirrhosis), the osmostat is “reset” downward, thus maintaining a lower serum osmolality. These patients respond normally to water loads with suppression of ADH secretion and excretion of free water.

(iv) Syndrome of inappropriate ADH (SIADH) is characterized by low plasma osmolality (<280 mOsm/L), hyponatremia (<135 mmol/L), low urine output with concentrated urine (>100 mOsm/kg), elevated urine sodium (>20 mEq/L), and clinical euvolemia. The major causes of SIADH include pulmonary disorders (e.g., atelectasis and respiratory failure), central nervous system disorders (e.g., trauma and meningitis), drugs (e.g., cyclophosphamide and cisplatin), and ectopic ADH production (e.g., small-cell lung carcinoma). For SIADH, water restriction (1,000 mL/day) should be attempted initially. The addition of a loop diuretic (furosemide) or an osmotic diuretic (mannitol) may be necessary.

(4) Transurethral resection syndrome refers to hyponatremia with cardiovascular and neurologic manifestations, which infrequently follow transurethral resection of the prostate. This syndrome results from intraoperative absorption of significant amounts of irrigation fluid.

(5) Hyponatremia treatment. A systematic review of hyponatremia guidelines reported five sets of guidelines and five consensus statements (*BMC Medicine* 2014, 12:231). Although there were differences, we provide recommendations based upon the preponderance of agreement. Evaluation of hyponatremia includes determining symptoms, chronicity and the cause to direct therapy. Acute hyponatremia usually involves a sodium drop within 24 to 48 hours. In surgical patients it is usually associated with postoperative hypotonic fluid administration. In acute hyponatremia, normal cerebral compensatory mechanisms are overwhelmed resulting in the risk of cerebral edema and herniation when levels fall from normal to 120 mEq/L.

Patients with severe symptomatic hyponatremia including seizures, severe confusion, coma, or signs of cerebral edema require immediate treatment with 100 mL of hypertonic saline (3% NaCl) over 10 minutes repeating up to three times based on symptoms. The initial correction goal varies across

recommendations. Acute hyponatremia goals in a symptomatic patient range between a sodium correction of 1 and 6 mmol/L over the first hour or two. Goals for chronic hyponatremia sodium correction range between 1 and 5 mmol/L over the first hour or two. If the patient is actively seizing, we suggest a correction goal 2 to 3 mmol/L/hr over the first 2 to 3 hours to a goal of seizure ablation. After seizures have abated, the 24-hour sodium goal is an increase of 6 to 8 mmol/L. Without osmotic demyelination risk characteristics, sodium correction goals are reported up to 10 mmol/L. However, we suggest a goal of 6 to 8 in the first 24 hours knowing there is some reserve if we exceed the goal. The patient's volume status should be carefully monitored over this time, and the serum Na^+ should be measured frequently (every 1 to 2 hours). The use of a loop diuretic (furosemide, 20 to 200 mg intravenously every 6 hours) may increase the effectiveness of 3% NaCl administration.

In asymptomatic, acute hyponatremia patients, treatment is focused on the underlying etiology. In asymptomatic, chronic, hyponatremia, treatment centers around volume status with normal saline administration for hypovolemia and fluid restriction with possible salt restriction and loop diuretics in euvolemia and hypervolemia.

Osmotic demyelination syndrome (ODS) or central pontine demyelination most commonly occurs with rapid correction of chronic hyponatremia. Patients at increased risk are those with liver transplants, a history of alcoholism, hypokalemia, or female gender. In asymptomatic hyponatremia, some guidelines recommend a maximum of 8 mEq/L sodium correction over 24 hours and a maximum of 6 mEq/L in patient with risks for ODS.

3. **Hypernatremia.** Plasma sodium will increase if excessive amounts of concentrated sodium are ingested or infused or when sizeable losses of electrolyte-free water are not replaced (osmotic diuresis in glycosuria).
   a. **Clinical manifestations.** Symptoms of hypernatremia include lethargy, weakness, and irritability and may progress to

fasciculations, seizures, coma, and irreversible neurologic damage.

b. Diagnosis and treatment. Patients are categorized on the basis of their extracellular fluid volume status. The diagnostic and treatment approaches to hypernatremia are illustrated in Figure 5-4.

(1) Hypovolemic hypernatremia. Common causes in the surgical patient include diuresis, as well as GI, respiratory, and cutaneous (e.g., burns) fluid losses. Chronic renal failure and partial urinary tract obstruction also may cause hypovolemic hypernatremia.

(a) Replacement of free water is the main goal of treatment. The **water deficit** associated with hypernatremia can be estimated using the following equation:

$$\text{Water deficit(L)} = 0.60 \times \text{TBW (kg)} \times \left[\frac{\text{serum } Na^+ \left(\frac{\text{mmol}}{\text{L}}\right)}{140} - 1\right]$$

where TBW is the total body weight.

Rapid correction of hypernatremia can result in cerebral edema and permanent neurologic damage. Consequently, only one-half of the water deficit should be corrected over the first 24 hours, with the remainder being corrected over the following 2 to 3 days. Oral fluid intake is acceptable for replacing water deficits. If oral intake is not possible, D5W or D5 0.45% NaCl can be substituted.

(2) Hypervolemic hypernatremia in the surgical patient is most commonly iatrogenic and results from the parenteral administration of hypertonic solutions (e.g., $NaHCO_3$, saline, medications, and nutrition). It can also be the result of aldosteronism, Cushing disease (secondary hypercortisolism), or mineralocorticoid excess. In cases of hypervolemic hypernatremia, free water replacement can be supplemented with a loop diuretic.

(3) Isovolemic hypernatremia

(a) Hypotonic losses. Evaporative losses from the skin and respiratory tract, in addition to ongoing urinary free water losses, require the administration of approximately 750 mL of electrolyte-free water (e.g., D5W) daily to parenterally maintained afebrile patients. Inappropriate replacement of these hypotonic losses with isotonic fluids is the most common cause of isovolemic hypernatremia in the hospitalized surgical patient.

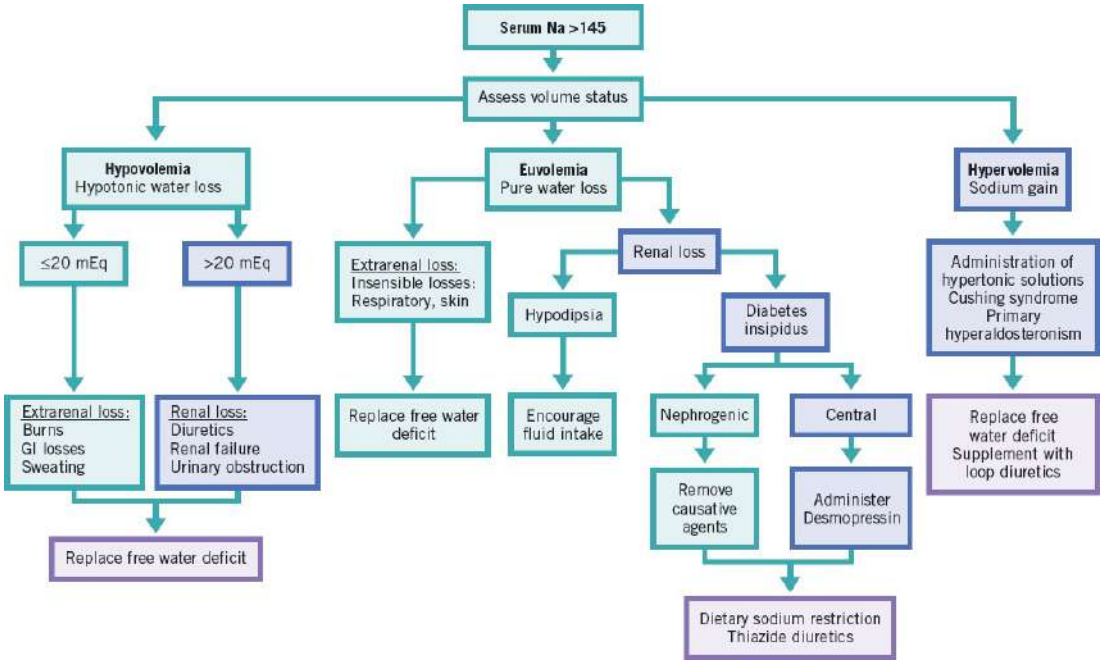


FIGURE 5-4 Diagnostic and treatment algorithm for hypernatremia. GI, gastrointestinal.

(b) Diabetes insipidus is characterized by hypernatremia >147 mEq/L, polyuria and polydipsia in association with hypotonic urine (urine osmolality <200 mOsm/kg or a specific gravity of <1.005) and a high plasma osmolality (>287 mOsm/kg). *Central diabetes insipidus* (CDI) describes a defect in the hypothalamic secretion of ADH while *nephrogenic diabetes insipidus* (NDI) describes renal insensitivity to normally secreted ADH. CDI can be treated with desmopressin acetate-synthetic ADH. NDI treatment requires removal of any potentially offending drug and correction of electrolyte abnormalities. If these measures are

ineffective, dietary sodium restriction in conjunction with a thiazide diuretic may be useful (hydrochlorothiazide, 50 to 100 mg/day orally).

(c) Therapeutic. Hypertonic saline may be administered for deliberate hypernatremia to control elevated intracranial pressure (ICP) and cerebral edema after head injury.

B. Potassium

1. **Physiology.** K^+ is the major intracellular cation, with only 2% of total-body K^+ located in the extracellular space. The normal serum concentration is 3.3 to 4.9 mmol/L (12.9 to 19.1 mg/dL). Approximately 50 to 100 mmol (195 to 390 mg/dL) K^+ is ingested and absorbed daily. Ninety percent of K^+ is renally excreted, with the remainder eliminated in stools.

2. **Hypokalemia**

   a. **Clinical manifestations.** Mild hypokalemia (K^+ >3 mmol/L [11.7 mg/dL]) is generally asymptomatic. Symptoms occur with severe K^+ deficiency (K^+ <3 mmol/L [11.7 mg/dL]) and are primarily cardiovascular. Early electrocardiogram (ECG) manifestations include ectopy, T-wave depression, and prominent U waves. Severe depletion increases susceptibility to reentry arrhythmias.

   b. **Causes.** K^+ depletion from inadequate intake alone is rare. Common causes of K^+ depletion in the surgical patient include GI losses, renal losses, and cutaneous losses (e.g., burns). Other causes of hypokalemia include conditions associated with acute intracellular K^+ uptake, such as insulin excess, metabolic alkalosis, myocardial infarction, delirium tremens, hypothermia, and theophylline toxicity. Hypokalemia may also occur in refeeding syndrome.

   c. **Treatment.** In mild hypokalemia, oral replacement is suitable. Typical daily therapy for the treatment of mild hypokalemia in the patient with intact renal function is 40 to 100 mEq (156 to 390 mg) potassium chloride in single or divided doses. Parenteral therapy is indicated in the presence of severe depletion, significant symptoms, or oral intolerance. K^+ concentrations (administered as chloride, acetate, or phosphate) in peripherally administered intravenous fluids should not exceed 40 mmol/L (156 mg/dL), and

the rate of administration should not exceed 20 mmol (78 mg)/hr. However, higher K^+ concentrations (60 to 80 mmol/L [234 to 312 mg/dL]) administered more rapidly (with cardiac monitoring) are indicated in cases of severe hypokalemia, for cardiac arrhythmias, and in the management of diabetic ketoacidosis.

3. Hyperkalemia

a. Causes and diagnosis. Hyperkalemia may occur with normal or elevated stores of total-body K^+. Pseudohyperkalemia is a laboratory abnormality that reflects K^+ release from leukocytes and platelets during coagulation. Spurious elevation in K^+ may result from hemolysis. Abnormal redistribution of K^+ from the intracellular to the extracellular compartment may occur as a result of insulin deficiency, β-adrenergic receptor blockade, acute acidemia, rhabdomyolysis, cell lysis (after chemotherapy), digitalis intoxication, reperfusion of ischemic limbs, and succinylcholine administration.

b. Clinical manifestations. Mild hyperkalemia is generally asymptomatic. Signs of significant hyperkalemia are, most notably, ECG abnormalities: Symmetric peaking of T waves, reduced P-wave voltage, and widening of the QRS complex. If untreated, severe hyperkalemia ultimately may cause a sinusoidal ECG pattern.

c. Treatment

(1) Mild hyperkalemia (K^+ = 5 to 6 mmol/L [19.5 to 23.4 mg/dL]) can be treated conservatively by the reduction in daily K^+ intake and, if needed, the addition of a loop diuretic (e.g., furosemide) to promote renal elimination. Any medication that is capable of impairing K^+ homeostasis (e.g., nonselective β-adrenergic antagonists, angiotensin-converting enzyme inhibitors, K^+-sparing diuretics, and nonsteroidal anti-inflammatory drugs) should be discontinued, if possible.

(2) Severe hyperkalemia (K^+ >6.5 mmol/L [25.4 mg/dL])

(a) Temporizing measures produce shifts of potassium from the extracellular to the intracellular space.

(i) Calcium gluconate 10% (5 to 10 mL intravenously over 2 minutes) should be administered to patients with

profound ECG changes who are not receiving digitalis preparations. Calcium functions to stabilize the myocardium.

(ii) NaHCO3 (1 mmol/kg or 1 to 2 ampules [50 mL each] of 8.4% $NaHCO_3$) can be infused intravenously over a 3- to 5-minute period. This dose can be repeated after 10 to 15 minutes if ECG abnormalities persist.

(iii) Dextrose (0.5 g/kg body weight) infused with insulin (0.3 unit of regular insulin/g of dextrose) transiently lowers serum K^+ (the usual dose is 25-g dextrose, with 6 to 10 units of regular insulin given simultaneously as an intravenous bolus).

(iv) Inhaled β-agonists (e.g., albuterol sulfate, 2 to 4 mL of 0.5% solution [10 to 20 mg] delivered via nebulizer) have been shown to lower plasma K^+, with a duration of action of up to 2 hours.

(b) Therapeutic measures to definitively decrease total-body potassium by increasing potassium excretion:

(i) Sodium polystyrene sulfonate (Kayexalate) is a Na^+–K^+ exchange resin. A decrease in serum K^+ level typically occurs 2 to 4 hours after administration; however, we caution its use in surgical patients, as it has been associated with bowel necrosis.

(ii) Hydration with 0.9% NaCl in combination with a loop diuretic (e.g., furosemide, 20 to 100 mg intravenously) should be administered to patients with adequate renal function to promote renal K^+ excretion.

(iii) Dialysis is definitive therapy in severe, refractory, or life-threatening hyperkalemia.

C. Magnesium

1. **Physiology.** Mg^{2+} (normal serum concentration: 1.3 to 2.2 mEq/L or 0.65 to 1.10 mmol/L) is predominantly an intracellular cation. Renal excretion and retention play the major physiologic role in regulating body stores. Mg^{2+} is not under direct hormonal regulation.
2. **Hypomagnesemia**
   a. **Clinical manifestations.** Symptoms of hypomagnesemia are

predominantly neuromuscular and cardiovascular. With severe depletion, altered mental status, tremors, hyperreflexia, and tetany may be present. The cardiovascular effects of hypomagnesemia are similar to those of hypokalemia and include T-wave and QRS-complex broadening as well as prolongation of the PR and QT intervals. Ventricular arrhythmias most commonly occur in patients who receive digitalis preparations. We recommend maintaining a patient's magnesium at the upper limit of normal (2 to 2.5 mEq/L) to prevent QT prolongation and arrhythmias.

b. Causes. Hypomagnesemia on the basis of dietary insufficiency is rare. Common etiologies include excessive GI or renal Mg^{2+} loss. Urinary loss occurs with marked diuresis, primary hyperaldosteronism, renal tubular dysfunction (e.g., renal tubular acidosis), chronic alcoholism, or as a drug side effect (e.g., loop diuretics, cyclosporine, amphotericin B, aminoglycosides, and cisplatin). Hypomagnesemia may also result from shifts of Mg^{2+} from the extracellular to the intracellular space, particularly in conjunction with acute myocardial infarction, alcohol withdrawal, or after receiving glucose-containing solutions. After parathyroidectomy for hyperparathyroidism, the redeposition of calcium and Mg^{2+} in bone may cause dramatic hypocalcemia and hypomagnesemia. Hypomagnesemia is usually accompanied by hypokalemia and hypophosphatemia and is frequently encountered in refeeding syndrome and in the trauma patient.

c. Treatment

(1) Parenteral therapy is preferred for the treatment of severe hypomagnesemia (Mg^{2+} <1 mEq/L or 0.5 mmol/L) or in symptomatic patients. In cases of life-threatening arrhythmias, 1 to 2 g (8 to 16 mEq) of $MgSO_4$ can be administered over 5 minutes, followed by a continuous infusion of 1 to 2 g/hr for the next several hours. The infusion subsequently can be reduced to 0.5 to 1 g/hr for maintenance. In less urgent situations, $MgSO_4$ infusion may begin at 1 to 2 g/hr for 3 to 6 hours, with the rate subsequently adjusted to 0.5 to 1 g/hr for maintenance. Mild hypomagnesemia (1.1 to 1.4 mEq/L or 0.5 to 0.7 mmol/L) in an asymptomatic patient can be treated

initially with the parenteral administration of 50 to 100 mEq (6 to 12 g) of $MgSO_4$ daily until body stores are replenished. Treatment should be continued for 3 to 5 days, at which time the patient can be switched to an oral maintenance dose.

(2) Oral therapy. Magnesium oxide is the preferred oral agent. Each 400-mg tablet provides 241 mg (20 mEq) of Mg^{2+}. Other formulations include magnesium gluconate (each 500-mg tablet provides 27 mg [2.3 mEq] of Mg^{2+}) and magnesium chloride (each 535-mg tablet provides 64 mg [5.5 mEq] of Mg^{2+}). Depending on the level of depletion, oral therapy should provide 20 to 80 mEq of Mg^{2+}/day in divided doses.

(3) Prevention of hypomagnesemia in the hospitalized patient who is receiving prolonged parenteral nutritional therapy can be accomplished by providing 0.35 to 0.45 mEq/kg of Mg^{2+}/day (i.e., by adding 8 to 16 mEq [1 to 2 g] of $MgSO_4$ to each liter of intravenous fluids).

3. Hypermagnesemia

a. Clinical manifestations. Mild hypermagnesemia (Mg^{2+} 5 to 6 mEq/L or 2.5 to 3 mmol/L) is generally asymptomatic. Severe hypermagnesemia (Mg^{2+} >8 mEq/L or 4 mmol/L) is associated with depression of deep tendon reflexes. Paralysis of voluntary muscles; hypotension; sinus bradycardia; and prolongation of PR, QRS, and QT intervals can occur at much higher levels.

b. Causes. Hypermagnesemia occurs infrequently, is usually iatrogenic, and is seen most commonly in the setting of renal failure or treatment of preeclampsia.

c. Treatment. Cessation of exogenous Mg^{2+} is necessary. Calcium gluconate 10% (10 to 20 mL over 5 to 10 minutes intravenously) is indicated in the presence of life-threatening symptoms to antagonize the effects of Mg^{2+}. A 0.9% NaCl (250 to 500 mL/hr) infusion with loop diuretic (furosemide, 20 mg intravenously every 4 to 6 hours) in the patient with intact renal function promotes renal elimination. Dialysis is the definitive therapy in the presence of intractable symptomatic hypermagnesemia.

D. Phosphorus

1. Physiology. Extracellular fluid contains less than 1% of total-body

stores of phosphorus at a concentration of 2.5 to 4.5 mg/dL (0.81 to 1.45 mmol/L). Phosphorus balance is regulated by a number of hormones that also control calcium metabolism. As a consequence, derangements in concentrations of phosphorus and calcium frequently coexist. Phosphate is necessary to produce ATP, which cells use for energy, and is thus critical to many metabolic processes. The average adult consumes 800 to 1,000 mg of phosphorus daily, which is predominantly excreted through the kidneys.

2. Hypophosphatemia

a. Clinical manifestations. Moderate hypophosphatemia (phosphorus 1 to 2.5 mg/dL or 0.32 to 0.81 mmol/L) is usually asymptomatic. Severe hypophosphatemia (phosphorus <1 mg/dL or 0.32 mmol/L) may result in respiratory muscle dysfunction, diffuse weakness, and flaccid paralysis.

b. Causes

(1) Decreased intestinal phosphate absorption results from vitamin D deficiency, malabsorption, and the use of phosphate binders (e.g., aluminum-, magnesium-, calcium-, or iron-containing compounds).

(2) Renal phosphate loss may occur with acidosis, alkalosis, diuretic therapy (particularly acetazolamide), during recovery from acute tubular necrosis, during hyperglycemia as a result of osmotic diuresis, and after large liver resections (*Ann Surg*. 2009; 249(5):824–827).

(3) Phosphorus redistribution from the extracellular to the intracellular compartment occurs principally with respiratory alkalosis and administration of nutrients such as glucose (particularly in the malnourished patient). This transient decrease in serum phosphorus is of no clinical significance unless there is a significant total-body deficit. Significant hypophosphatemia may also occur in malnourished patients after the initiation of total parenteral nutrition (refeeding syndrome) as a result of the incorporation of phosphorus into rapidly dividing cells.

(4) Hypophosphatemia may develop in **burn patients** as a result of excessive phosphaturia during fluid mobilization and

incorporation of phosphorus into new tissues during wound healing.

c. **Treatment.** Adequate repletion of phosphorus is especially important in critically ill patients, who are more likely to experience adverse physiologic consequences from hypophosphatemia, including the inability to be weaned from the ventilator, organ dysfunction, and death. Phosphorus replacement should begin with intravenous therapy, especially for moderate (1 to 1.7 mg/dL) or severe (<1 mg/dL) hypophosphatemia (*J Am Coll Surg*. 2004;198:198–204) (Table 5-3). Risks of intravenous therapy include hyperphosphatemia, hypocalcemia, hypotension, hyperkalemia (with potassium phosphate), hypomagnesemia, hyperosmolality, metastatic calcification, and renal failure. A 5 to 7 days of intravenous repletion may be required before intracellular stores are replenished. Once the serum phosphorus level exceeds 2 mg/dL (0.65 mmol/L), oral therapy can be initiated with a sodium–potassium phosphate salt (e.g., Neutra-Phos, 250 to 500 mg [8 to 16 mmol phosphorus] orally four times a day; each 250-mg tablet of Neutra-Phos contains 7 mmol each of K^+ and Na^+).

TABLE 5-3 Phosphorus Repletion Protocol

Phosphorus Level (mg/dL)	Weight 40–60 kg	Weight 61–80 kg	Weight 81–120 kg
1	30 mmol Phos IV	40 mmol Phos IV	50 mmol Phos IV
1–1.7	20 mmol Phos IV	30 mmol Phos IV	40 mmol Phos IV
1.8–2.2	10 mmol Phos IV	15 mmol Phos IV	20 mmol Phos IV

If the patient's potassium is <4, use potassium phosphorus.

If the patient's potassium is >4, use sodium phosphorus.

IV, intravenous; Phos, phosphorus.

Adapted from Taylor BE, Huey WY, Buchman TG, et al. Effectiveness of a protocol based on patient weight and serum phosphorus levels in repleting hypophosphatemia in a surgical ICU. *J Am Coll Surg*. 2004;198:198–204.

3. Hyperphosphatemia

a. Clinical manifestations, in the short term, include hypocalcemia and tetany. In contrast, soft tissue calcification and secondary hyperparathyroidism occur with chronicity.

b. Causes include impaired renal excretion and transcellular shifts of phosphorus from the intracellular to the extracellular compartment (e.g., tissue trauma, tumor lysis, insulin deficiency, or acidosis). Hyperphosphatemia is also a common feature of postoperative hypoparathyroidism.

c. Treatment of hyperphosphatemia, in general, should eliminate the phosphorus source, remove phosphorus from the circulation, and correct any coexisting hypocalcemia. Dietary phosphorus should be restricted. Urinary phosphorus excretion can be increased by hydration and diuresis (acetazolamide, 500 mg every 6 hours orally or intravenously). Phosphate binders (aluminum hydroxide, 30 to 120 mL orally every 6 hours) minimize intestinal phosphate absorption and can induce a negative balance of greater than 250 mg of phosphorus daily, even in the absence of dietary phosphorus. Hyperphosphatemia secondary to conditions that cause phosphorus redistribution (e.g., diabetic ketoacidosis) resolves with treatment of the underlying condition and requires no specific therapy. Dialysis can be used to correct hyperphosphatemia in extreme conditions.

E. Calcium

1. Physiology. Serum calcium (8.9 to 10.3 mg/dL or 2.23 to 2.57 mmol/L) exists in three forms: Ionized (45%), protein bound (40%), and in a complex with freely diffusible compounds (15%). Only free ionized Ca^{2+} (4.6 to 5.1 mg/dL or 1.15 to 1.27 mmol/L) is physiologically active. Daily calcium intake ranges from 500 to 1,000 mg, with absorption varying considerably. Normal calcium metabolism is under the influence of parathyroid hormone (PTH) and vitamin D. PTH promotes calcium resorption from bone and reclamation of calcium from the glomerular filtrate. Vitamin D

increases calcium absorption from the intestinal tract.

2. Hypocalcemia

a. Clinical manifestations. Tetany is the major clinical finding and may be demonstrated by Chvostek sign (facial muscle spasm elicited by tapping over the branches of the facial nerve). The patient may also complain of perioral numbness and tingling. In addition, hypocalcemia can be associated with QT-interval prolongation and ventricular arrhythmias.

b. Causes and diagnosis. Hypocalcemia most commonly occurs as a consequence of calcium sequestration or vitamin D deficiency. Calcium sequestration may occur in the setting of acute pancreatitis, rhabdomyolysis, or rapid administration of blood (citrate acting as a calcium chelator). Transient hypocalcemia may occur after total thyroidectomy, secondary to vascular compromise of the parathyroid glands and after parathyroidectomy. Hypocalcemia may occur in conjunction with Mg^{2+} depletion, which simultaneously impairs PTH secretion and function. Acute alkalemia (e.g., from rapid administration of parenteral bicarbonate or hyperventilation) may produce clinical hypocalcemia with a normal serum calcium concentration due to an abrupt decrease in the ionized fraction. As 40% of serum calcium is bound to albumin, hypoalbuminemia may decrease total serum calcium significantly—a fall in serum albumin of 1 g/dL decreases serum calcium by approximately 0.8 mg/dL (0.2 mmol/L). Ionized Ca^{2+} is unaffected by albumin. As a consequence, the diagnosis of hypocalcemia should be based on ionized, not total serum, calcium.

c. Treatment

(1) Parenteral therapy. Asymptomatic patients do not require parenteral therapy. Symptoms such as overt tetany, laryngeal spasm, or seizures are indications for parenteral calcium. Approximately 200 mg of elemental calcium is needed to abort an attack of tetany. Initial therapy consists in the administration of a calcium bolus (10 to 20 mL of 10% calcium gluconate over 10 minutes) followed by a maintenance infusion of 1 to 2 mg/kg elemental calcium/hor. Calcium chloride contains three times more elemental calcium than calcium gluconate; one 10-

mL ampule of 10% calcium chloride contains 272 mg (13.6 mEq) elemental calcium, whereas one 10-mL ampule of 10% calcium gluconate contains only 90 mg (4.6 mEq) elemental calcium. The serum calcium level typically normalizes in 6 to 12 hours with this regimen, at which time the maintenance rate can be decreased to 0.3 to 0.5 mg/kg/hr. In addition to monitoring calcium levels frequently during therapy, one should check Mg^{2+}, phosphorus, and K^{+} levels and replete as necessary.

(2) Oral therapy. Calcium salts are available for oral administration (calcium carbonate, calcium gluconate). Each 1,250-mg tablet of calcium carbonate provides 500 mg of elemental calcium (25.4 mEq), and a 1,000-mg tablet of calcium gluconate has 90 mg (4.6 mEq) of elemental calcium. In chronic hypocalcemia, with serum calcium levels of 7.6 mg/dL (1.9 mmol/L) or higher, the daily administration of 1,000 to 2,000 mg of elemental calcium alone may suffice. When hypocalcemia is more severe, calcium salts should be supplemented with a vitamin D preparation. Daily therapy can be initiated with 50,000 IU of calciferol, 0.4 mg of dihydrotachysterol, or 0.25 to 0.50 mg of 1,25-dihydroxyvitamin D_3 orally. Subsequent therapy should be adjusted as necessary.

3. Hypercalcemia

a. Clinical manifestations. Mild hypercalcemia (calcium <12 mg/dL or <3 mmol/L) is generally asymptomatic. The hypercalcemia of hyperparathyroidism is associated infrequently with classic parathyroid bone disease and nephrolithiasis. Manifestations of severe hypercalcemia include altered mental status, diffuse weakness, dehydration, adynamic ileus, nausea, vomiting, and severe constipation. The cardiac effects of hypercalcemia include QT-interval shortening and arrhythmias.

b. Causes and diagnosis. Causes of hypercalcemia include malignancy, hyperparathyroidism, hyperthyroidism, vitamin D intoxication, immobilization, long-term total parenteral nutrition, thiazide diuretics, and granulomatous disease. The finding of an elevated PTH level in the face of hypercalcemia supports the

diagnosis of hyperparathyroidism. If the PTH level is normal or low, further evaluation is necessary to identify one of the previously cited diagnoses.

c. Treatment of hypercalcemia depends on the severity of the symptoms (Fig. 5-5). Mild hypercalcemia (calcium <12 mg/dL or <3 mmol/L) can be managed conservatively by restricting calcium intake and treating the underlying disorder. Volume depletion should be corrected if present, and vitamin D, calcium supplements, and thiazide diuretics should be discontinued. The treatment of more severe hypercalcemia may require the following measures:

(1) NaCl 0.9% and loop diuretics may rapidly correct hypercalcemia. In the patient with normal cardiovascular and renal function, 0.9% NaCl (250 to 500 mL/hr) with furosemide (20 mg intravenously every 4 to 6 hours) can be administered initially. The rate of 0.9% NaCl infusion and the dose of furosemide should subsequently be adjusted to maintain a urine output of 100 to 150 mL/hr. Serum Mg^{2+}, phosphorus, and K^{+} levels should be monitored and repleted as necessary. The inclusion of KCl (20 mmol) and $MgSO_4$ (8 to 16 mEq or 1 to 2 g) in each liter of fluid may prevent hypokalemia and hypomagnesemia. This treatment may promote the loss of as much as 2 g of calcium over 24 hours.

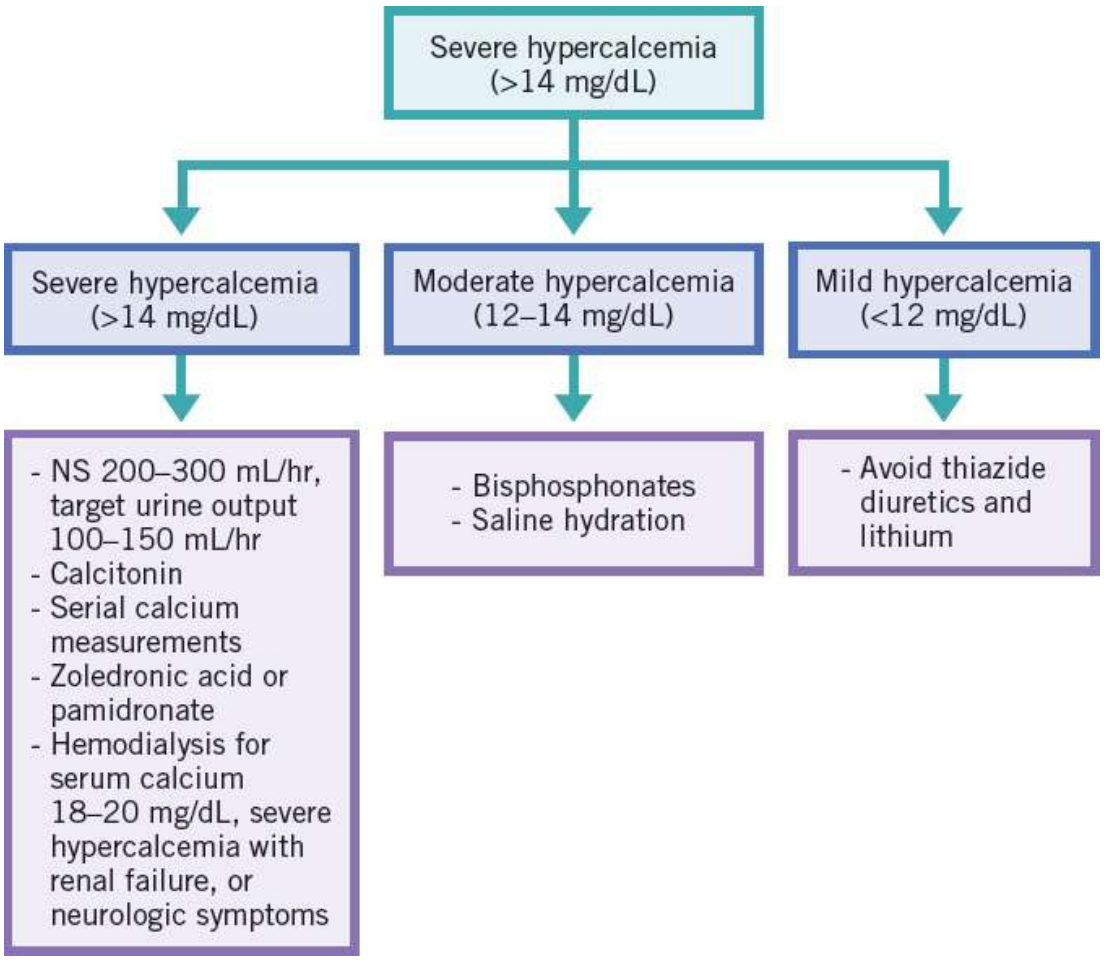


FIGURE 5-5 Basic treatment algorithm for hypercalcemia. Treatment specifics for unique causes of hypercalcemia is beyond the scope of this chapter.

(2) Salmon calcitonin, in conjunction with adequate hydration, is useful for the treatment of hypercalcemia associated with either malignancy or primary hyperparathyroidism. Salmon calcitonin can be administered either subcutaneously or intramuscularly. Skin testing by subcutaneous injection of 1 IU is recommended before progressing to the initial dose of 4 IU/kg intravenously or subcutaneously every 12 hours. A hypocalcemic effect may be seen as early as 6 to 10 hours after administration. The dose may be doubled if unsuccessful after 48 hours of treatment. The maximum recommended dose is 8 IU/kg every 6 hours.

(3) Pamidronate disodium, in conjunction with adequate hydration, is useful for the treatment of hypercalcemia associated with malignancy. For moderate hypercalcemia

(calcium 12 to 13.5 mg/dL or 3 to 3.38 mmol/L), 60 mg of pamidronate diluted in 1 L of 0.45% NaCl, 0.9% NaCl, or D5W should be infused over 24 hours. For severe hypercalcemia, the dose of pamidronate is 90 mg. If hypercalcemia recurs, a repeat dose of pamidronate can be given after 7 days. The safety of pamidronate for use in patients with significant renal impairment is not established.

(4) Plicamycin (25 mg/kg, diluted in 1 L of 0.9% NaCl or D5W, infused over 4 to 6 hours each day for 3 to 4 days) is useful for treatment of hypercalcemia associated with malignancy. The onset of action is between 1 and 2 days, with a duration of action of up to 1 week.

IV. ACID–BASE DISORDERS

A. Diagnostic Approach

1. General concepts

a. Acid–base homeostasis represents equilibrium among the concentration of H^+, partial pressure of CO_2 (Pco_2), and HCO_3^-. Clinically, H^+ concentration is expressed as pH.

b. Initial evaluation of acid–base disorders should include an arterial blood gas and serum electrolytes (Fig. 5-6). Normal blood pH is 7.35 to 7.45. **Acidemia** refers to pH of less than 7.35, and **alkalemia** refers to pH of greater than 7.45.

2. Compensatory response to primary disorders. Disorders that initially alter $Paco_2$ are termed *respiratory acidosis* or *alkalosis.* Alternatively, disorders that initially affect plasma HCO_3^- concentration are termed *metabolic acidosis* or *alkalosis.* Primary metabolic disorders stimulate respiratory responses that act to return the ratio of Pco_2 to HCO_3^- (and therefore the pH) toward normal, and vice versa. By convention, these compensating changes are termed *secondary, respiratory,* or *metabolic* compensation for the primary disturbance. The amount of compensation to be expected from either a primary respiratory or metabolic disorder is presented in Table 5-4. Significant deviations from these expected values suggest the presence of a mixed acid–base disturbance.

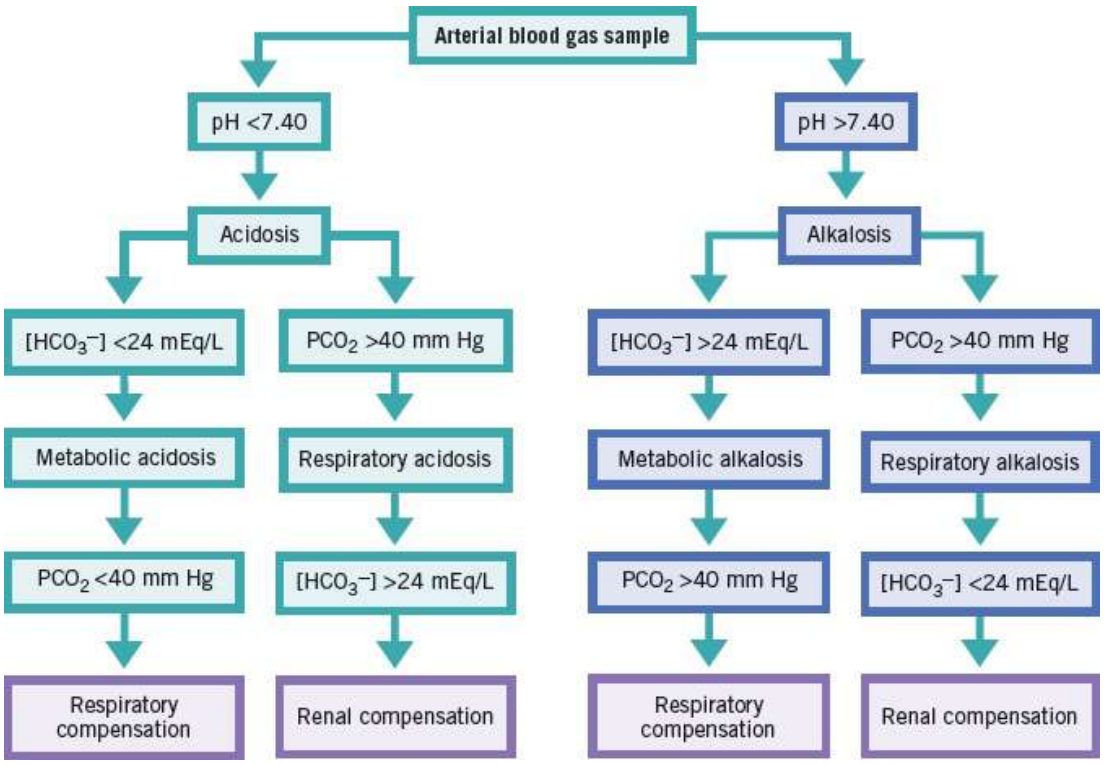


FIGURE 5-6 Diagnostic algorithm for acid–base disorders.

TABLE 5-4 Expected Compensation for Simple Acid–Base Disorders

Primary Disorder	Initial Change	Compensatory Response	Expected Compensation
Metabolic acidosis	HCO_3^- decrease	Pco_2 decrease	Pco_2 decrease = $1.2 \times \Delta HCO_3^-$
Metabolic alkalosis	HCO_3^- increase	Pco_2 increase	Pco_2 increase = $0.7 \times \Delta HCO_3^-$
Respiratory acidosis	Pco_2 increase	HCO_3^- increase	Acute: HCO_3^- increase = $0.1 \times \Delta Pco_2$ Chronic: HCO_3^- increase = $0.35 \times \Delta Pco_2$

Respiratory alkalosis	Pco_2 decrease	HCO_3^- decrease	Acute: HCO_3^- decrease = $0.2 \times \Delta Pco_2$ Chronic: HCO_3^- decrease = $0.5 \times \Delta Pco_2$

B. Primary Metabolic Disorders

1. **Metabolic acidosis** results from the accumulation of nonvolatile acids, reduction in renal acid excretion, or loss of alkali. The most common causes of metabolic acidosis are listed in Table 5-5. The appropriate diagnosis depends on the clinical setting and laboratory tests. It is useful diagnostically to classify metabolic acidosis into increased or normal AG metabolic acidosis. **The anion gap** (AG; normal = 12 ± 2 mmol/L) represents the anions, other than Cl^- and HCO_3^-, which are necessary to counterbalance Na^+ ionically (all values are in mmol/L): $AG = Na^+ - [Cl^- + HCO_3^-]$. For causes of increased and normal (hyperchloremic) AG metabolic acidosis, see Table 5-5.

   a. Treatment of metabolic acidosis must be directed primarily at the underlying cause of the acid–base disturbance. Bicarbonate therapy should be considered in patients with moderate-to-severe metabolic acidosis only after the primary cause has been addressed. The HCO_3^- deficit (mmol/L) can be estimated using the following equation:

$$HCO_3^- \text{ deficit}\left(\frac{\text{mmol}}{\text{L}}\right) = \text{body weight (kg)} \times 0.4 \times \left[\text{desired } HCO_3^-\left(\frac{\text{mmol}}{\text{L}}\right) - \text{measured } HCO_3^-\left(\frac{\text{mmol}}{\text{L}}\right)\right]$$

TABLE 5-5 Causes of Metabolic Acidosis

Increased anion gap
Increased acid production
Renal tubular dysfunction
Ketoacidosis
Diabetic
Alcoholic
Starvation
Lactic acidosis
Toxic ingestion (salicylates, ethylene glycol, methanol)
Renal failure
Normal anion gap (hyperchloremic)
Renal tubular acidosis
Hypoaldosteronism
Potassium-sparing diuretics
Loss of alkali
Diarrhea
Ureterosigmoidostomy
Carbonic anhydrase inhibitors
Administration of HCl (ammonium chloride, cationic amino acids)

In nonurgent situations, the estimated HCO_3^- deficit can be repaired by administering a continuous intravenous infusion over 4 to 8 hours. A 50-mL ampule of 8.4% $NaHCO_3$ solution, which provides 50-mmol HCO_3^-, can be added to 1 L of D5W or 0.45%

of NaCl. In urgent situations, the entire deficit can be repaired by administering a bolus over several minutes. The goal of HCO_3^- therapy should be to raise the arterial blood pH to 7.20.

2. Metabolic alkalosis (Table 5-6)

a. Causes

(1) Chloride-responsive metabolic alkalosis in the surgical patient is typically associated with extracellular fluid volume deficits. The most common causes of metabolic alkalosis in the surgical patient include inadequate fluid resuscitation or diuretic therapy (e.g., contraction alkalosis), acid loss through GI secretions (e.g., nasogastric suctioning and vomiting), and the exogenous administration of HCO_3^- or HCO_3^- precursors (e.g., citrate in blood). Posthypercapnic metabolic alkalosis occurs after the rapid correction of chronic respiratory acidosis. Under normal circumstances, the excess in bicarbonate that is generated by any of these processes is excreted rapidly in the urine. Consequently, maintenance of metabolic alkalosis requires impairment of renal HCO_3^- excretion, most commonly due to volume and chloride depletion. Since replenishment of Cl^- corrects the metabolic alkalosis in these conditions, each is classified as Cl^--responsive metabolic alkalosis.

TABLE 5-6 Causes of Metabolic Alkalosis

Associated with extracellular fluid volume (chloride) depletion
Vomiting or gastric drainage
Diuretic therapy
Posthypercapnic alkalosis
Associated with mineralocorticoid excess
Cushing syndrome
Primary aldosteronism

Bartter syndrome
Severe K^+ depletion
Excessive alkali intake

(2) Chloride-unresponsive metabolic alkalosis is encountered less frequently in surgical patients and usually results from mineralocorticoid excess.

b. Diagnosis. Although the cause of metabolic alkalosis is usually apparent in the surgical patient, measurement of the urinary chloride concentration may be useful for differentiating these disorders. A urine Cl^- concentration of less than 15 mmol/L suggests inadequate fluid resuscitation, ongoing GI loss from emesis or nasogastric suctioning, diuretic administration, or posthypercapnia as the cause of the metabolic alkalosis. A urine Cl^- concentration of greater than 20 mmol/L suggests mineralocorticoid excess, alkali loading, concurrent diuretic administration, or the presence of severe hypokalemia.

c. Treatment principles in metabolic alkalosis include identifying and removing underlying causes, discontinuing exogenous alkali, and replacing Cl^-, K^+, and volume deficits. Rapid correction of this disorder usually is not necessary because metabolic alkalosis generally is well tolerated.

(1) Initial therapy should include the correction of volume deficits (with 0.9% NaCl) and hypokalemia.

(2) Edematous patients. Chloride administration does not enhance HCO_3^- excretion because it does not correct the reduced effective arterial blood volume. Acetazolamide (5 mg/kg/day intravenously or orally) facilitates fluid mobilization while decreasing renal HCO_3^- reabsorption.

(3) Dialysis can be considered in the volume-overloaded patient with renal failure and intractable metabolic alkalosis.

C. Primary Respiratory Disorders

1. Respiratory acidosis occurs when alveolar ventilation is insufficient to excrete metabolically produced CO_2. Common causes in the

surgical patient include respiratory center depression (e.g., drugs and organic disease), neuromuscular disorders, and cardiopulmonary arrest. Chronic respiratory acidosis may occur in pulmonary diseases, such as chronic emphysema and bronchitis. Chronic hypercapnia may also result from primary alveolar hypoventilation or alveolar hypoventilation related to extreme obesity (e.g., Pickwickian syndrome) or from thoracic skeletal abnormalities. The diagnosis of acute respiratory acidosis usually is evident from the clinical situation, especially if respiration is obviously depressed. Appropriate therapy is correction of the underlying disorder. In cases of acute respiratory acidosis, there is no indication for $NaHCO_3$ administration.

2. **Respiratory alkalosis** is the result of acute or chronic hyperventilation. The causes of respiratory alkalosis include acute hypoxia (e.g., pneumonia, pneumothorax, pulmonary edema, and bronchospasm), chronic hypoxia (e.g., cyanotic heart disease and anemia), and respiratory center stimulation (e.g., anxiety, fever, gram-negative sepsis, salicylate intoxication, central nervous system disease, cirrhosis, and pregnancy). Excessive ventilation may also cause respiratory alkalosis in the mechanically ventilated patient.

D. Mixed Acid–Base Disorders. When two or three primary acid–base disturbances occur simultaneously, a patient is said to have a mixed acid–base disorder. As summarized in Table 5-4, the respiratory or metabolic compensation for a simple primary disorder follows a predictable pattern. Significant deviation from these patterns suggests the presence of a mixed disorder. Table 5-7 lists some common causes of mixed acid–base disturbances. The diagnosis of mixed acid–base disorders depends principally on evaluation of the clinical setting and on interpretation of acid–base patterns. However, even normal acid–base patterns may conceal mixed disorders.

TABLE 5-7 Common Causes of Mixed Acid–Base Disorders

Metabolic acidosis and respiratory acidosis
Cardiopulmonary arrest

Severe pulmonary edema
Salicylate and sedative overdose
Pulmonary disease with superimposed renal failure or sepsis
Metabolic acidosis and respiratory alkalosis
Salicylate overdose
Sepsis
Combined hepatic and renal insufficiency
Metabolic alkalosis and respiratory acidosis
Chronic pulmonary disease, with superimposed: Diuretic therapy Steroid therapy
Vomiting
Reduction in hypercapnia by mechanical ventilation
Metabolic alkalosis and respiratory alkalosis
Pregnancy with vomiting
Chronic liver disease treated with diuretic therapy
Cardiopulmonary arrest treated with bicarbonate therapy and mechanical ventilation
Metabolic acidosis and alkalosis
Vomiting superimposed on: Renal failure Diabetic ketoacidosis Alcoholic ketoacidosis

CHAPTER 5: FLUID, ELECTROLYTES, AND ACID–BASE DISORDERS

Multiple Choice Questions

1. **In which group of patients is there a clinically proven reduction in mortality following the resuscitation with hypertonic saline?**

   a. A 65-year-old female with mild-to-moderate dehydration
   b. A 35-year-old male with moderate hyponatremia from psychogenic polydipsia
   c. A 40-year-old female with traumatic hemorrhagic shock following a motor vehicle accident and splenic laceration
   d. A 5-year-old child with renal insufficiency
   e. Hypertonic saline has not been shown to decrease mortality in any patient population

2. **A patient with severe sepsis secondary to cholangitis has received 4 L of crystalloid resuscitation over the last 6 hours. His MAP remains below 65, but he is fluid responsive. Which of the following fluids should be administered?**

   a. 0.9% NS, 1 L over 1 hour
   b. 0.45% NS, 2 L over 1 hour
   c. 5% albumin, 500 cc over 1 hour
   d. Dextran 40, 500 cc over 2 hours
   e. Hetastarch, 6% solution, 1 L over 1 hour

3. **A patient with a known history of coronary artery disease presents to the emergency room with shortness of breath and extensive lower extremity edema. Initial laboratory studies reveal a sodium of 124 mmol/L. Initial therapy includes which of the following:**

   a. Administration of 1 L of 0.9 NS
   b. Fluid restriction to 1 L of free water per day
   c. Administration of 500 cc 3% NaCl
   d. Fluid restriction to 2 L of free water per day

e. Administration of 500 cc lactated Ringer solution

4. **You are caring for a head injured patient in the intensive care unit who has a large volume urine output and who, you suspect, may have central diabetes insipidus. What confirmatory test can you order in order to support your diagnosis?**

   a. Urine specific gravity
   b. Serum sodium and urine sodium
   c. 24-hour urine for electrolytes
   d. Serum potassium and urine sodium
   e. Serum glucose level

5. **You are informed by the laboratory that a patient you are caring for has a potassium of 6.0 on routine laboratory tests. What is the correct order of steps to manage this issue?**

   a. Order a confirmatory whole-blood K level, order an ECG, administer insulin and glucose
   b. Order an ECG, order a confirmatory whole-blood K level, administer insulin and glucose
   c. Order an ECG, administer insulin and glucose, place a dialysis catheter, order a confirmatory whole-blood K
   d. Order an ECG, place a dialysis catheter, administer albuterol, administer insulin and glucose, order a confirmatory whole blood K
   e. Consult renal service for dialysis management, order an ECG, administer insulin and glucose

6. **Which of the following is a manifestation of hypomagnesemia?**

   a. Flaccid paralysis
   b. Renal insufficiency
   c. Insomnia
   d. Ventricular arrhythmias
   e. Vertigo

7. **What is the most common cause of metabolic alkalosis in the postoperative patient?**

   a. General anesthetic reaction

b. Urinary losses
c. Associated hypomagnesemia
d. Acute blood loss
e. Inadequate fluid resuscitation

8. Bicarbonate therapy for metabolic acidosis is appropriate for which of the following patients?

a. A 36-year-old hemodynamically stable patient with salicylate poisoning
b. A 65-year-old female who remains severely acidemic despite correction of her lactic acidosis and underlying anemia
c. A 22-year-old trauma patient who has exsanguinated from acute blood loss and is now receiving ACLS protocol
d. A 72-year-old male in renal failure with mixed acid–base disorder
e. A 44-year-old male who has just arrived to the emergency department with an acidemia of unknown origin

9. You are caring for a patient who recently had a thyroidectomy. She complains of perioral numbness and has a positive Chvostek sign. While sending her blood for laboratory examination, she has a seizure. What treatment is indicated?

a. 0.9 NS, 1 L bolus
b. 0.9 NS, 1 L bolus, and a loop diuretic therapy
c. 20 mL of calcium gluconate intravenously over 20 minutes
d. Oral calcium carbonate
e. 4 IU/kg subcutaneous salmon calcitonin

10. You have a postsurgical patient who is dehydrated with hypernatremia. You calculate a free water deficit of 3 L. How much free water should be given in the first 24 hours?

a. 1 L
b. 1.5 L
c. 2 L
d. 2.5 L
e. It is safe to correct the entire deficit over 24 hours

6 Hemostasis, Anticoagulation, and Transfusions

Rahul R. Handa, Isaiah R. Turnbull, and Omer Ismail

I. HEMOSTASIS. There are two primary goals of hemostasis: (1) to prevent bleeding from defects in vessel walls via the temporary formation of localized, stable clot and (2) repair of injured vessel walls.

A. Mechanisms of Hemostasis. Hemostasis is centered on the **creation and destruction of a fibrin-cross-linked platelet plug (thrombus).** Thrombus formation is limited to the area of vessel injury and is temporary in nature. This involves a complex interplay of thrombotic, anticoagulant, and fibrinolytic processes that occur simultaneously. Injury, disease, medications, among several other factors affect homeostatic balance, resulting in life-threatening hemorrhagic or thrombotic complications.

1. **Thrombus formation** occurs in response to endothelial damage in the vessel wall that exposes collagen and tissue factor (TF) to circulating blood (*N Engl J Med*. 2008;359:938–949). Two critical yet interdependent events occur simultaneously, resulting in a stable, fibrin-cross-linked thrombus:

   a. **Primary hemostasis: Platelet plug formation.** Injury to the endothelium results in transient vasoconstriction, mediated by neural stimulation and endothelin. von Willebrand Factor (vWF), released from both the endothelial cells as well as platelets, binds to exposed subendothelial collagen. Platelets bind to vWF via glycoproteins (GP; GPIb-V-IX, and GPVI) resulting in a critical shape change in the platelet itself, leading to release of adenosine

diphosphate (ADP) and thromboxane A2 (TXA2). ADP stimulates the expression of GP IIb/IIIa on platelets, which is essential for platelet aggregation via fibrinogen.

b. **Secondary hemostasis: Coagulation and stabilization of the platelet plug.** Like primary hemostasis, secondary hemostasis is also triggered by disruption of the endothelium and uncovering of TF. In this process, the relatively weak platelet plug during primary hemostasis is stabilized by clotting factors. Importantly, TF is the sole initiator of thrombin generation and therefore fibrin formation. Fibrin is generated via thrombin as the end-product of activation of serine proteases known as coagulation "factors." This coagulation network has traditionally been divided into intrinsic and extrinsic pathways (Fig. 6-1).

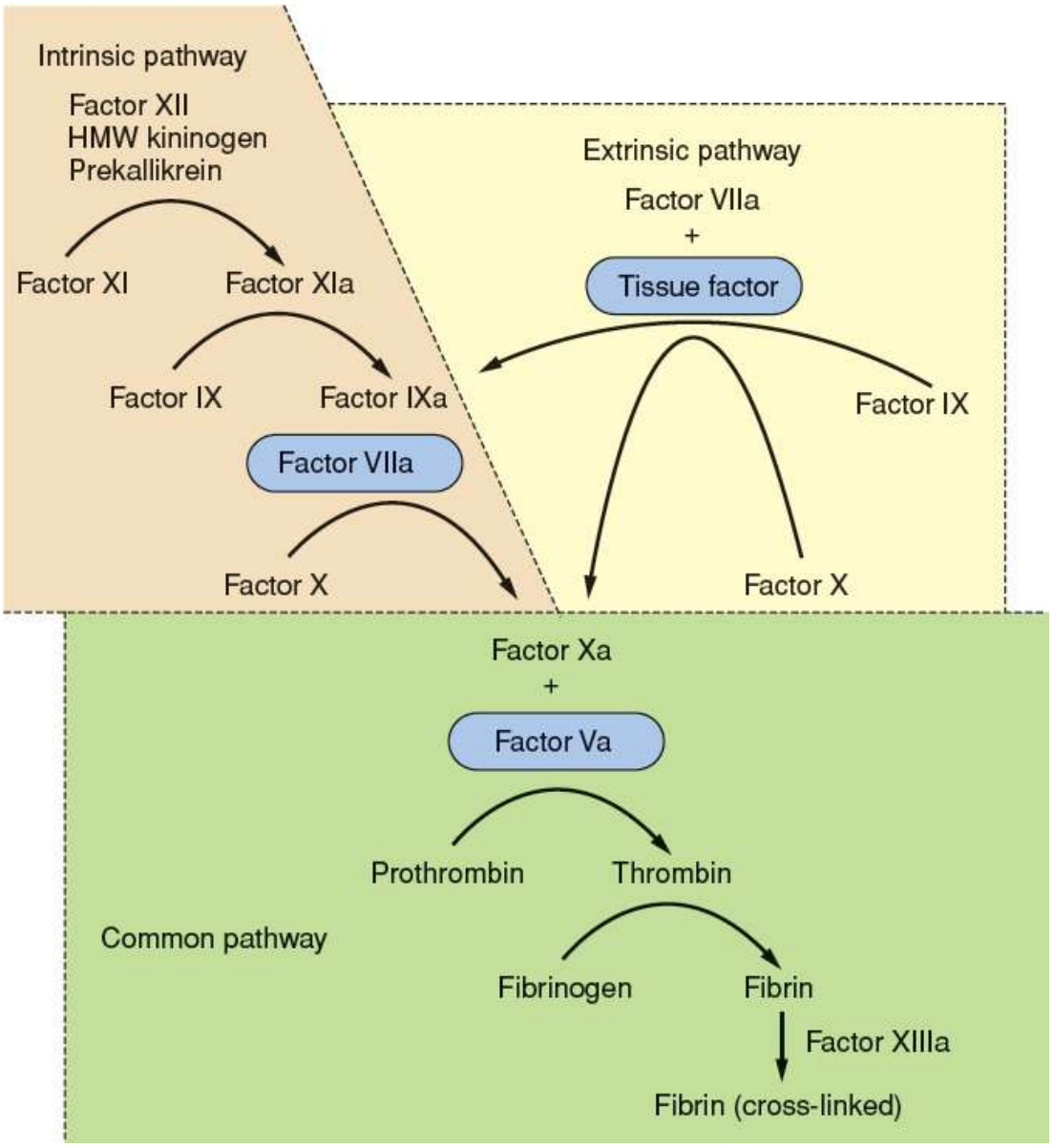


FIGURE 6-1 Secondary Hemostasis.

2. **Endogenous anticoagulants** restrict coagulation to the specific area of vascular injury and prevent pathologic thrombosis.
   a. **The endothelium** serves as a physical barrier sequestering subendothelial factors (TF, collagen) from platelets and circulating coagulation factors. Endothelial cells actively release antiplatelet factors and express surface enzymes which degrade platelet-activating factors. Intact endothelial cells are also coated with thrombomodulin (see below) and heparin-like glycosaminoglycans that facilitate antithrombin (AT) activation.

b. **Antithrombin (AT, previously known as ATIII)** inhibits coagulation by binding clotting factors and producing complexes that are cleared from the circulation. **Heparin** markedly accelerates AT-induced factor inhibition, increasing factor clearance, and leading to anticoagulation.

c. **The thrombomodulin–protein C–protein S system** begins with thrombomodulin binding with thrombin, creating "anticoagulant thrombin," accelerating protein C, a vitamin K–dependent proenzyme. Activated protein C inactivates factors Va and VIIIa in the presence of protein S.

d. **Other anticoagulant factors** include tissue factor pathway inhibitor (TFPI) and help inactivate clotting complexes.

3. **Fibrinolysis** is the process by which thrombus is both dissolved and remodeled. Plasminogen (a plasma zymogen) is incorporated into a developing thrombus. Tissue plasminogen activator (tPA) converts plasminogen to its active form, plasmin, which breaks down clot and allows for wound healing. Negative feedback in this system occurs via several pathways (e.g., alpha-2-antiplasmin, PAI-1, TAFI, etc.).

B. Laboratory Evaluation of Hemostasis. A detailed history and physical examination constitute the most important screening tools for disorders of hemostasis in surgical patients. Although surgical patients may have hereditary disorders of hemostasis, acquired defects and medications affecting hemostasis remain most common. Laboratory values can be used to evaluate endogenous function of primary and secondary hemostasis.

1. **Primary hemostasis** can be evaluated by:

a. **Quantitative evaluation of platelet function**

(1) **Platelet count**

(a) Abnormalities in platelet number should be confirmed with a **peripheral smear.**

(2) **Bone marrow biopsy**

(a) Can be obtained to check **megakaryocytes**, in conditions such as **ITP, TTP**, and **multiple myeloma**.

b. **Qualitative evaluation of platelet function.** No single test is adequate for screening for platelet dysfunction due to limited sensitivity, and many functions of platelets being separate targets

of drugs.

(1) Bleeding time is the length of time it takes for a superficial cut to stop. It is considered an in vivo test that is currently rarely used as a screening tool for both congenital and acquired disorders of primary hemostasis in labs that do not perform other tests.

(2) Evaluation of platelet aggregation can be assessed by a number of commercially available tests that employ different principles to help quantify aggregation. As the technology improved, processing time and accessibility to these tests improved.

(a) Light transmission platelet aggregation (LTA) is of the older generation tests that used photo-optical measurement of transillumination as the platelets in a sample clumped together. While it is sensitive to antiplatelet therapies, it is time consuming and requires high sample volume that is assessed manually.

(b) Impedance whole-blood aggregometry (WBA) employs electrochemistry to quantify activated platelets that stick to the surface of electrodes by their surface receptors. As such the analysis is rapid requiring a small sample and no manipulation and is available as a POCT (multiple electrode aggregometry [MEA]).

(c) Lumiaggregometry measures the release of adenine nucleotides from platelet granules and platelet aggregation. It is used mainly as a screening test to detect specific deficiencies in the number, content, and secretion of dense granules and defects of plasma membrane receptors.

(d) VerifyNow evaluates the capacity of activated platelets to bind to fibrinogen-laced beads and platelet agonists relative to the number of activated GPIIb/IIIa receptors. It is being used in the acute setting to monitor antiplatelet therapies.

(e) Plateletworks is a WB POC assay that measures the platelet count before and after aggregation to monitor the platelet response to antiplatelet agents. A disadvantage of this test is that it should be performed within a few minutes of blood sampling and as such is best suited for operating and

procedure areas.

(3) Evaluation of platelet adhesion upon exposure to shear stress and aggregation in the presence of an agonist has yielded several promising tests.

(a) Platelet function analyzer (PFA) differentiates intrinsic platelet defects from those due to antiplatelet therapy with ASA. It is sensitive to many variables that influence platelet function including low platelet count, hematocrit, and thrombocytopathies. Currently it is being used to assess the therapeutic effectiveness of antiplatelet therapy and perioperatively to guide blood transfusion.

(b) IMPACT: Cone and Plate(Let) Analyzer is a POC test that evaluates in vitro activation and adhesion of platelets by applying shear stress to platelets by the spinning of a cone on a plate. It is able to diagnose platelet defects and to monitor and evaluate the efficacy of dual antiplatelet therapy.

(c) The Global Thrombosis Test is also a rapid POC test that reports the thrombotic status and has been used as a screening tool in acute and critical care settings.

(4) Platelet function can also be assessed by:

(a) Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) (see below).

(b) Flow cytometry analysis of platelets is an effective and widely used technique to evaluate the in vivo functional status. Because it involves multiple assays for several purposes including assessing the activation state, evaluation of thrombopoiesis, diagnosis of specific disorders, and antiplatelet agent monitoring, it is used for the diagnosis of inherited (Glanzmann thrombasthenia, Bernard–Soulier syndrome), acquired platelet dysfunctions (e.g., HIT) and storage pool disease. It is the most used method for monitoring the efficacy of antiplatelet drugs. It is an expensive test, requiring specialized operators and devices, and prone to artifact.

(c) Activated platelets are a major source of thromboxane in the

body. The evaluation of thromboxane metabolites using ELISA is used to assess platelet function in different diseases, detect defects of thromboxane production, and to monitor aspirin therapy.

(5) The focus on LTA for standardization of testing has moved to POCT systems given the convenience it provides and is therefore being studied more for validation, reliability, and quality control testing.

2. Secondary hemostasis can be evaluated by the:

a. Prothrombin time (PT) and **international normalized ratio (INR)**

(1) Assesses the **extrinsic** and **common** pathways and is most sensitive to factor VII deficiency. Test reagents vary in their responsiveness to warfarin-induced anticoagulation. Therefore, **INR** is used as a surrogate value to standardize PT reporting between laboratories.

b. Partial thromboplastin time (PTT)

(1) Measures the function of the **intrinsic** and **common** pathways.

c. Activated clotting time (ACT)

(1) A measure of the clotting time of **whole blood**. A blood sample is added to a diatomite-containing tube, leading to activation of the **intrinsic** pathway. ACT is used to assess coagulation status in patients requiring high doses of heparin (e.g., prior to placing vascular clamps in cardiovascular surgery). Automated systems are available for real-time intraoperative use, during which accurate and rapid determination of the patient's state of anticoagulation is necessary. Normal ACT is less than 130 seconds, with therapeutic target values ranging from 250 to 350 seconds for noncardiac vascular procedures, and greater than 480 seconds for cardiopulmonary bypass.

d. Factor assays

(1) Factor Xa activity may be used to assess the effect of **low–molecular-weight heparin (LMWH).**

(2) Factor VIII and IX levels are used in the preoperative planning for patients with **hemophilia.**

(3) Fibrinogen level is used in the assessment of patients with

DIC or those **receiving thrombolysis.**

(4) Fibrin degradation products (FDP) can be measured to give insight into disease processes characterized by increased fibrinogen turnover, including **DIC** and **thromboembolic events.** In addition, this value is often measured to help guide in the administration of **fibrinolytic therapy.**

(5) D-dimer levels reflect fibrinolysis, and thus the utility of this laboratory value in surgical patients is less clear given its nonspecific elevation in response to inflammation (surgery).

3. Global hemostasis can be evaluated by viscoelastic hemostatic assays (VHA)

a. TEG/ROTEM

(1) Traditional in vitro tests such as PT/INR, PTT, and ACT are useful in the diagnosis and management of bleeding diathesis; however, *abnormal values obtained in a test tube are not always indicative or representative of underlying hemostatic perturbation.*

(2) TEG and TEM are assays used to provide broad functional assessments of the coagulation system in *real time*.

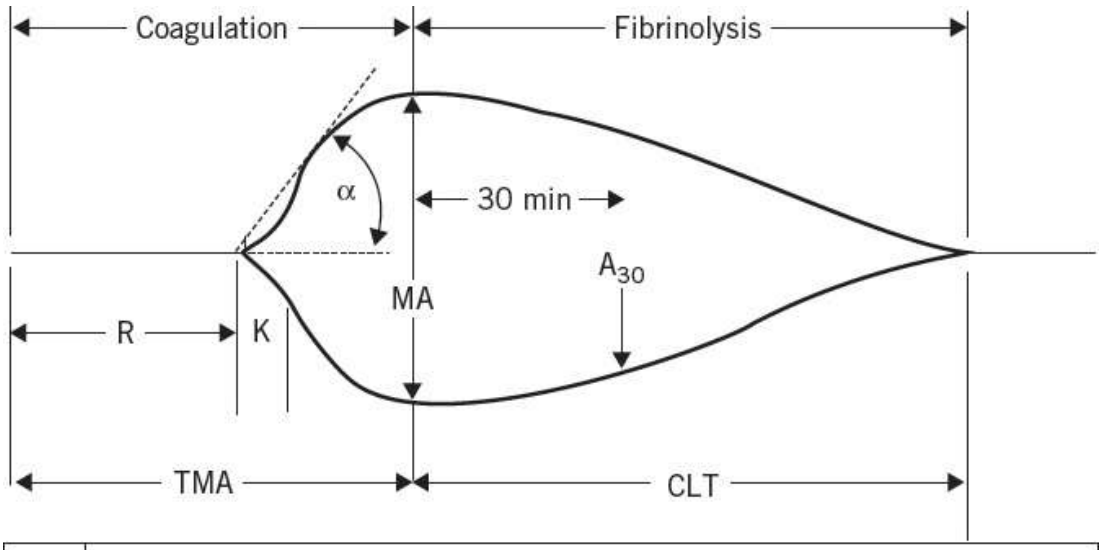
(3) Briefly, a small amount of whole blood is added to a cup in which a pin is immersed in the blood. Either the cup (TEG) or pin (TEM) rotates radially and transmits kinetic information to a sensor, indicating the dynamic state of clot formation and breakdown within the sample (Fig. 6-2).

(4) The graph plots the state of the clot in relation to time:

(a) Clot initiation: time for first fibrin formation (reaction R time—TEG, Activated clotting time ACT—rTEG, Clotting time CT— ROTEM)

(i) Prolonged by hypocoagulability

(ii) Treatment: factor replacement with fresh frozen plasma (FFP), PCC, fibrinogen



R	Period of latency from when blood is placed into the TEG analyzer until the initial fibrin formation. Represents the enzymatic portion of coagulation.
K	Measures the speed to reach a certain level of clot strength (20 mm above baseline). This represents clot kinetics.
α	Measures the rapidity of fibrin built up and cross-linking (clot strengthening). This represents fibrinogen level.
MA	Maximum amplitude, is a direct function of the maximum dynamic properties of the fibrin and platelet binding via GPIIb/IIIa and represents the ultimate strength of the fibrin clot. This represents platelet function/aggregation.
LY30	Measures the rate of amplitude reduction 30 min after MA. This represents clot lysis.

FIGURE 6-2 Thromboelastogram (TEG).

(b) Kinetics of fibrin polymerization

(i) Time to 20 MM (K time, alpha angle—TEG, Clot formation time CFT Rotem)

(ii) Depends on platelet count and fibrinogen level

(iii) Treatment: platelet transfusion, fibrinogen

(c) Clot strength every 5 minutes (Amplitude Ax, Maximum amplitude MA—TEG, Clot amplitude CA, Maximum clot formation MCF—ROTEM)

(i) Depends on platelet–fibrinogen interaction and factor XIII

(ii) Differentiated by adding platelet inhibitor to assess fibrinogen function (FF in TEG and FIBTEM in ROTEM)

(iii) Reduced MA/MCF with normal fibrinogen: transfuse platelets

(iv) Reduced MA/MCF with low fibrinogen: transfuse

cryoprecipitate or fibrinogen concentrate

(d) Measurement of clot lysis: percentage of clot reduction compared to maximal strength (Ly—TEG; Clot lysis CL, Lysis index Li, Maximal lysis ML—ROTEM)

(i) Clot strength reduction is normal due to platelet retraction phenomenon but beyond a threshold it is considered abnormal

(ii) Ly-30 >8% or Li30 >15% indicates fibrinolysis

(iii) Consider antifibrinolytics (tranexamic acid)

(5) Further details of TEG/ROTEM interpretation are shown in Table 6-1.

(6) VHA are generally insensitive to antiplatelet drugs and standard ROTEM is sensitive to DOACs at therapeutic doses except apixaban.

(7) The use of VHA in management of acute hemorrhage is of ongoing research. Its role in prediction and diagnosis of bleeding and coagulopathy is being studied in separate fields (obstetrics, cardiac surgery, trauma, and transplant surgery) as the normal ranges for TEG and ROTEM differ in each setting.

(8) Algorithm-guided approaches to transfusion that utilize laboratory and POC values have been shown to be safe and decrease the number of blood products transfused in cardiac surgery (*Br J Anesth*. 2004;92:178).

(9) While algorithms are available for the different therapy groups studies assess, their outcomes are still pending. As such the evidence-based guidelines are currently lacking.

C. Disorders of Primary and Secondary Hemostasis

1. **Disorders of primary hemostasis.** These disorders can be categorized as quantitative or qualitative in nature, and involve the dysfunction of platelets. They present with **mucosal bleeding** (epistaxis, hemoptysis, hematuria, etc.) and **skin bleeding** (easy bruising, petechiae, purpura, and ecchymoses). **Intracranial bleeding** occurs with severe quantitative platelet disorders.

TABLE 6-1 VHA Interpretation

	Clot Initiation	Clot Strength		Clot Lysis
Test Result Shows	Prolonged R, ACT, or CT	Reduced MA/MCF, Normal Fibrinogen	Reduced MA/MCF, Low Fibrinogen	Ly-30 >8% Li30 >15%
What does this mean?	Low clotting factors and/or low fibrinogen level Warfarin use Heparin use DOAC use (not apixaban)	Low platelets	Low fibrinogen	VHA detected fibrinolysis
Therapy recommended	FFP (PCC might be considered)	Platelets	Cryoprecipitate or fibrinogen concentrate	Consider additional antifibrinolytics
Therapy groups				
Obstetric	FFP if R or CT above the normal range. PCC is not recommended	No data are available to guide platelet transfusion	Cryoprecipitate or fibrinogen concentrate if FIBTEM <7 mm or <12 mm in severe bleeding	No data are available for guiding antifibrinolytic therapy
Liver	FFP if results above normal range (PCC might be considered)	EXTEM MCF <35 mm	FIBTEM <7 mm	Fibrinolysis at reperfusion may correct spontaneously. Antifibrinolytics are indicated in most other circumstances
Cardiac	FFP if >15% above ULN	Platelets	Cryoprecipitate or FgC	
Trauma	FFP if results ≥ULN PCC not recommended	Give platelets if MA/MCF at lower end or below the normal range while ff or FIBTEM normal	Cryoprecipitate or FgC if FIBTEM or ff at lower end or below the normal range	TEG LY30 ≥3% indicates clinically important lysis

Modified from *Br J Haematol*. 2018;182:789–806.

a. Quantitative abnormalities

(1) Thrombocytopenia is defined as a platelet count of **less than 140,000/mL**. If platelet function is normal, thrombocytopenia is infrequently the cause of bleeding unless counts are below 50,000/mL. Severe spontaneous bleeding may occur with platelet counts under 10,000/mL.

(2) Drug-induced thrombocytopenia occurs when pharmacologic therapy results in increased platelet destruction. Common offenders include antibiotics (e.g., penicillin, linezolid, and sulfonamides), thiazide diuretics, and chemotherapeutic agents. Increased destruction is most commonly secondary to an immune mechanism in which platelets are destroyed by complement activation following formation of drug–antibody

complexes.

(3) Immune thrombocytopenic purpura has multiple etiologies, including various drugs and viruses. Antiplatelet antibodies cause thrombocytopenia and its sequelae.

(4) Dilutional thrombocytopenia occurs with rapid blood product replacement for massive hemorrhage.

(5) Other causes of thrombocytopenia include disseminated intravascular coagulation (DIC), sepsis, thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), dialysis, and hematopoietic disorders.

(6) Thrombocytosis is defined as a **platelet count greater than 600,000/mL**. Essential thrombocytosis is caused by myeloproliferative disease. Secondary thrombocytosis occurs after splenectomy or with iron deficiency, malignancy, or chronic inflammatory disease.

b. Qualitative abnormalities

(1) Hereditary defects of platelet function include:

(a) von Willebrand disease (vWD, see below)

(b) Bernard–Soulier syndrome

(c) Glanzmann thrombasthenia

(d) Storage pool defects

(2) Acquired defects of platelet function are caused by uremia, liver disease, or cardiopulmonary bypass.

(3) Heparin-induced thrombocytopenia (HIT) is a unique form of drug-induced thrombocytopenia. Two different forms have been recognized:

(a) HIT type I is a nonimmune, heparin-associated thrombocytopenia that typically begins **within 4 days** of initiation of heparin therapy. The incidence ranges from 5% to 30%.

(b) HIT type II is a **severe, immune-mediated syndrome** caused by **heparin-dependent antiplatelet antibodies (anti-PF4–heparin complex)** occurring **5 to 10 days after initial exposure** to heparin but within hours after reexposure. Platelet counts are often less than 100,000/mL or drop by more than 30% from baseline. In a minority of

cases, thrombotic events may ensue, including extensive arterial and venous thrombosis (*N Engl J Med*. 2006;355:809–817).

(c) Laboratory testing

(i) HIT is a **clinical diagnosis**, although there exist associated laboratory findings.

(ii) Enzyme-linked immunosorbent assay (ELISA, HIT panel) is a sensitive test that is useful for screening but has low specificity.

(iii) Serotonin release assay (SRA) may suggest the diagnosis if associated clinical features are present. SRA is the gold standard due to its high sensitivity and specificity and often used as a confirmatory test.

(d) Treatment

(i) In **HIT type I, heparin cessation may not be necessary.**

(ii) If **HIT type II** is suspected, **all heparin products should be stopped immediately** until the diagnosis is refuted. This includes occult sources of heparin (e.g., flushes and heparin-coated catheters).

(iii) Since thrombotic complications can ensue even after heparin cessation, anticoagulation with nonheparin anticoagulants such as direct thrombin inhibitors is recommended unless clinically contraindicated. Platelet transfusion will exacerbate the process and is contraindicated.

(iv) Bivalirudin is a common pharmacologic alternative used in these situations, until laboratory evaluation has resulted.

(v) Note that if HIT is diagnosed, warfarin administration can potentiate a hypercoagulable state and has been associated with the development of venous limb gangrene. Warfarin therapy causes an initial decrease in antithrombotic, vitamin K–dependent factors protein C and protein S, resulting in hypercoagulation given uninhibited activated thrombin.

2. Disorders of secondary hemostasis

a. Inherited factor deficiencies

(1) vWD is the most common inherited bleeding disorder, with a prevalence as high as 1% of the general population.

(2) Hemophilia is an inherited factor deficiency of either factor VIII (hemophilia A) or factor IX (hemophilia B, Christmas disease). Factor activity assays confirm the diagnosis and are an indicator of disease severity.

b. Acquired factor deficiencies

(1) Vitamin K deficiency leads to the production of inactive, noncarboxylated forms of **factors II (prothrombin), VII, IX, X, and proteins C and S.** Vitamin K deficiency can occur in patients without oral intake for 1 week or longer, with biliary obstruction and malabsorption, or in those receiving antibiotics or warfarin.

(2) Liver dysfunction leads to complex alterations in coagulation through decreased synthesis of most clotting and anticlotting factors with the notable exceptions of factor VIII and vWF (derived from the endothelium). Coagulopathy is worsened by associated uremic platelet dysfunction, as well as thrombocytopenia from portal hypertension–associated hypersplenism.

(3) Sepsis overstimulates the coagulation cascade resulting in decreased levels of anticoagulant factors such as protein C, protein S, and AT. This imbalance in hemostasis causes the formation of microvascular thrombi, which further amplifies injury resulting in distal tissue ischemia and hypoxia.

c. Inherited hypercoagulable disorders are defined as either type I (loss of inhibition) or type II (gain of procoagulant). These disorders put patients at risk of both venous and arterial thrombosis and may require lifelong anticoagulation.

(1) Type I (loss of inhibition)

(a) Antithrombin (ATIII) deficiency is an autosomal-dominant disorder which presents with recurrent venous and occasionally arterial thromboembolism, usually in the second decade of life.

(b) Protein C deficiency and protein S deficiency may result in venous thrombosis. In a state of protein C or S deficiency, factors Va and VIIIa are not adequately inactivated, thereby allowing uninhibited coagulation. Aside from the hereditary subtype, protein C deficiency is encountered in patients with liver failure and in those who are receiving warfarin therapy. In individuals with diminished protein C activity, effective heparin anticoagulation must be confirmed before warfarin initiation because warfarin transiently lowers protein C levels further and potentially worsens the hypercoagulable state manifested as warfarin-induced skin necrosis (see below).

(2) Type II (gain of procoagulant)

(a) Factor V Leiden (activated protein C resistance) is the most common hereditary hypercoagulability disorder. Factor V Leiden is a genetic mutation in factor V which renders the protein resistant to breakdown by activated protein C, resulting in venous thrombosis.

(b) Prothrombin G20210A is a mutation of the prothrombin gene at nucleotide 201210 which causes heterozygous carriers to have a 30% higher level of plasma prothrombin compared to those without the mutation.

(c) Hyperhomocysteinemia is an autosomal recessive disorder resulting in elevated homocysteine levels, which has been implicated in the formation of thrombus.

d. Acquired hypercoagulable disorders

(1) Antiphospholipid antibodies are immunoglobulins that are targeted against antigens composed in part of platelet and endothelial cell phospholipids. Antiphospholipid antibody disorders may be detected by lupus anticoagulant, anticardiolipin, or other antiphospholipid antibodies. Patients with these antibodies are at risk for arterial and venous thrombosis, recurrent miscarriages, and thrombocytopenia.

(2) Other acquired hypercoagulable states include malignancies, pregnancy, use of estrogen therapy, intravascular hemolysis (e.g., hemolytic anemia), and the localized propensity for

thrombosis in arteries that have recently undergone endarterectomy, angioplasty, or placement of prosthetic vascular grafts.

3. **Disorders of global hemostasis**

   a. **DIC** has many inciting causes, including sepsis, extensive trauma, or burns. The pathogenesis involves inappropriate generation of thrombin within the vasculature, leading to platelet activation, formation of fibrin thrombi, and increased fibrinolytic activity. DIC often presents with complications from microvascular thrombi that involve the vascular beds of the kidney, brain, lung, and skin. In some patients, the consumption of coagulation factors, particularly fibrinogen, and the activation of the fibrinolytic pathway can lead to bleeding. Laboratory findings in DIC include thrombocytopenia, hypofibrinogenemia, increased FDPs, and prolonged PTT. Therapy is focused on treatment of the underlying cause. Correction of coagulopathy is guided by the underlying cause.

II. ANTIPLATELET AGENTS, ANTICOAGULATION, AND FIBRINOLYTIC THERAPY

A. Antiplatelet Therapy

1. **Aspirin (ASA)** irreversibly acetylates cyclooxygenase, inhibiting platelet synthesis of TXA2, and causing decreased platelet function. It is often used in the prevention and treatment of acute transient ischemic attacks, stroke, myocardial infarction, and coronary and vascular graft occlusion.
2. **Clopidogrel (Plavix)** irreversibly inhibits platelet function by binding to the ADP receptor, which normally promotes aggregation and secretion. It is used to decrease thrombotic events in percutaneous coronary and vascular stenting and in patients with unstable angina.
3. **GP IIb/IIIa inhibitors**, including abciximab (ReoPro), tirofiban (Aggrastat), and eptifibatide (Integrilin), function by blocking platelet adhesion to fibrin. These agents are used in preventing coronary artery thrombosis after coronary angioplasty or in unstable angina. Although they have relatively short half-lives (0.5 to 2.5 hours), the bleeding time may remain elevated for longer periods.
4. **Other** medications such as **dextran** are used to reduce perioperative

thrombotic events such as bypass graft occlusion because of their ability to decrease platelet aggregation and adhesion. Also, **nonsteroidal anti-inflammatory drugs (NSAIDs)** such as ibuprofen and ketorolac inhibit cyclooxygenase, reversibly inhibiting platelet aggregation. This may result in clinically relevant bleeding, particularly in patients taking warfarin, aspirin, or clopidogrel (*Ann Intern Med*. 2014;18:161).

5. Reversal of antiplatelet therapy guidelines are limited to stopping the agent.

a. Platelet transfusions given to patients with intracranial hemorrhage on antiplatelet therapy was found to be ineffective in stopping the bleed and was associated with increased mortality within 3 months after administration.

b. Desmopressin (DDAVP) may be used, but evidence is inconsistent.

B. Pharmacologic Anticoagulation

1. Anticoagulant medication is used to prevent and treat thrombosis and thromboembolic events. Before therapy is instituted, careful consideration must be given to the risk of thromboembolism versus anticoagulation-induced bleeding complications. Table 6-2 summarizes selected anticoagulant medications. Relative contraindications to anticoagulation therapy include recent surgical intervention, severe trauma, intracranial or other sites of active bleeding, and in patients with an increased risk of falling.

2. Heparin

a. Unfractionated heparin

(1) Administration:

(a) Prophylactic: Administered subcutaneously. Typical dose is 5,000 units every 8 hours. In obese patients, the dose is 7,500 units every 8 hours.

(b) Therapeutic: Administered parenterally.

(i) PTT should be measured before initiation of heparin, 6 hours after initiation of the drip and 6 hours after each change in dosing.

(ii) Use of heparin boluses is not generally recommended for surgical patients.

(iii) Platelet counts should be measured daily until a

maintenance dose of heparin is achieved and periodically thereafter to monitor for development of HIT.

(2) Complications

(a) Bleeding: Gastrointestinal bleeding that occurs while a patient is therapeutically anticoagulated suggests an occult source and warrants further evaluation.

(b) HIT, *discussed in detail above.*

(3) Heparin clearance is rapid and dose dependent. Initially, heparin is cleared by the reticuloendothelial system. Once saturated, clearance is renally dependent and takes longer.

(4) Reversal: Achieved rapidly with intravenous protamine sulfate.

(a) Should be used with caution because it can induce complications such as anaphylactoid reactions and systemic hypotension from splanchnic vasodilation.

(b) Each milligram of protamine sulfate reverses approximately 100 units of heparin. PTT or ACT can be used to assess the adequacy of the reversal.

TABLE 6-2 **Anticoagulant Medications**

Drug	Mechanism	Metabolism	Dose for DVT Prophylaxis	Dose for Therapeutic Anticoagulation	Therapeutic Target	Reversal Agent
Heparin	Potentiates antithrombin: IIa, Xa, IXa, XIa, XIIa inhibition	Hepatic, RES, and 50% renal excretion	5,000-U SC twice to thrice daily	Bolus = 80 μ/kg Infusion = 18 μ/kg/hr; adjust to target PTT	aPTT = 60–80 s	Protamine: start with 25–50 mg
LMWH (e.g., enoxaparin [Lovenox])	Potentiates antithrombin: Xa inhibition	Mainly renal excretion	40 mg SC once daily	1 mg/kg SC twice daily	Chromogenic anti-Xa assay: 0.6–1 anti-Xa U/mL	None
Fondaparinux (Arixtra)	Potentiates antithrombin: Xa inhibition	Renal	2.5 mg SC once daily	5 or 7.5 or 10 mg SC once daily	Chromogenic anti-Xa assay 0.6–1 anti-Xa U/mL	None
Rivaroxaban (Xarelto)	Direct Xa inhibition	Likely liver	10 mg PO once daily		Chromogenic anti-Xa assay 0.6–1 anti-Xa U/mL	None
Apixaban (Eliquis)	Direct Xa inhibition	Liver	5 mg PO BID		Chromogenic anti-Xa assay 0.6–1 anti-Xa U/mL	None
Warfarin (Coumadin)	Prevents carboxylation of X, IX, VII, II, protein C and S	Hepatic, marked genetic variability		2–10 mg PO daily; adjust to target INR	INR = 2–4	Vitamin K: 1–10 mg PO or plasma; start with 2–4 units
Lepirudin (Refludan)	Direct thrombin inhibition	Renal		Bolus = 0.4 mg/kg Infusion = 0.15 mg/kg/hr; adjust to target PTT	aPTT = 60–80 (1.5–2.5 times control)	None
Bivalirudin (Angiomax)	Direct thrombin inhibition	Proteolytic cleavage and renal (20%)		Bolus = 1 mg/kg Infusion = 0.2 mg/kg/hr; adjust to target PTT	aPTT = 60–80 s	None
Desirudin (Iprivask)	Direct thrombin inhibition	Renal	10–15 mg SC twice daily		Prolongs the aPTT	None
Argatroban (Acova)	Direct thrombin inhibition	Hepatic		Infusion = 2 μg/kg/min; adjust to target PTT	aPTT = 60–80 s; may prolong INR	None
Dabigatran etexilate (Pradaxa)	Direct thrombin inhibition	Renal (unchanged) and some conjugation with glucuronic acid	150 mg PO once daily	150 mg PO twice daily	Prolongs aPTT	None

b. Low–molecular-weight heparin (LMWH)

(1) LMWH preparations include enoxaparin, dalteparin, and tinzaparin. The anticoagulant effect of LMWH is predominantly due to factor Xa inhibition, which normally potentiates AT.

(2) Use of LMWH results in less thrombin inhibition than unfractionated heparin.

(3) Advantages of LMWH include a more predictable

anticoagulant effect, less platelet interaction, and a longer half-life.

(4) Renal clearance: adjustments need to be made for patients in renal insufficiency and should not be given to patients in renal failure.

(5) Because LMWH has a longer half-life and no effective antidote, it must be used with caution in surgical patients and in those in whom a bleeding risk has been substantiated.

3. Direct thrombin inhibition (DTI)

a. Direct thrombin inhibitors are a class of compounds that bind to free and fibrin-bound thrombin. These agents inhibit thrombin activation of clotting factors, fibrin formation, and platelet aggregation.

b. Lepirudin (recombinant hirudin)

(1) Binds irreversibly to thrombin, providing effective anticoagulation. It is approved in patients with HIT but may be considered in other severe clotting disorders.

(2) Bivalirudin is a truncated form of recombinant hirudin that targets only the active site of thrombin. It is FDA approved for HIT as well as for use during percutaneous coronary angioplasty and stenting. Because these agents are cleared by the kidneys, they should not be used in patients with renal failure.

c. Argatroban

(1) Synthetic thrombin inhibitor that is also approved for treatment of HIT. It is cleared by the liver and should not be used in patients with hepatic failure.

d. Dabigatran (Pradaxa)

(1) Administered orally

(2) Indications:

(a) Atrial fibrillation: reduces incidence of stroke and systemic embolism in nonvalvular Afib.

(b) DVT and PE: both for prophylactic and therapeutic purposes.

(3) Pharmacokinetics

(a) Metabolized in liver then binds to free and clot-bound

thrombin inhibiting fibrinogen conversion and feedback activation of factors VII, XI, and V.

(4) Monitoring rarely performed given reliable dose-proportional pharmacokinetics. INR results vary and do not correlate with anticoagulation effect. Dilute thrombin time is the test performed. A normal time excludes dabigatran effect. An elevated aPTT may suggest therapeutic effect but does not rule out an effect. Ecarin clotting time may also be tested.

(5) Reversal:

(a) Idarucizumab (Praxbind): FDA-approved humanized monoclonal antibody fragment for use in emergent/urgent surgical procedures, or life-threatening or uncontrolled bleeding.

(b) Hemodialysis may be used when idarucizumab is not available.

(c) PCC and cryoprecipitate may be used.

4. Factor Xa inhibition

a. Indirect factor Xa inhibitors (fondaparinux) are small, synthetic, heparin-like molecules that enhance AT-mediated inhibition of factor Xa. Fondaparinux has been shown to be effective in preventing DVT after hip and knee replacement. Monitoring of coagulation parameters is usually not necessary.

b. Direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban, and betrixaban) selectively block the active site of factor Xa free or bound to prothrombinase complex; thereby indirectly inhibits platelet aggregation.

(1) Rapid onset: peak plasma concentrations within 2 hours

(2) Half-life 12 hours

(3) Fewer food/drug interactions when compared to warfarin

(4) Indications: for patients with

(a) nonvalvular atrial fibrillation

(b) DVT prophylaxis in patients receiving hip and knee surgery

(c) DVT/PE treatment

(5) Monitoring:

(a) This class of anticoagulants does not require monitoring

(b) Clotting time tests are invariably prolonged

(c) Standardized assay kits are not widely available

(d) A normal PT/INR or normal anti-factor Xa excludes significant rivaroxaban levels

(6) Reversal: Andexanet competes with native factor Xa to bind to Xa inhibitors. FDA approved for life-threatening or uncontrolled bleeding associated to rivaroxaban and apixaban.

5. Warfarin (Coumadin)

a. Background

(1) Warfarin is an oral vitamin K antagonist that causes anticoagulation by inhibiting vitamin K–mediated carboxylation of factors II, VII, IX, and X as well as proteins C and S. The vitamin K–dependent factors decay with varying half-lives, so the full warfarin anticoagulant effect is not apparent for 5 to 7 days. When immediate anticoagulation is necessary, heparin or another agent must be used initially.

b. Administration

(1) Therapy is usually initiated with a loading dose of 5 to 10 mg/day for 2 days, followed by dose adjustment based on daily INR results. Elderly patients, those with hepatic insufficiency, and those who are receiving parenteral nutrition or broad-spectrum antibiotics should be given lower initial doses. A daily dose of warfarin needed to achieve therapeutic anticoagulation ranges from 2 to 15 mg/day. An INR of 2 to 3 is considered therapeutic for most indications, however patients with prosthetic heart valves should be maintained at an INR of 2.5 to 3.5. Once a stable INR is obtained at a given warfarin dose, it can be monitored biweekly or monthly.

c. Complications

(1) The risk of clinically significant bleeding in patients who are treated with warfarin is estimated to be approximately 10% per year. The bleeding risk correlates directly with the INR. Warfarin-induced skin necrosis, caused by dermal venous thrombosis, occurs in patients with pre-existing protein C and S factor deficiencies who receive warfarin initiation without other systemic anticoagulation. In these patients, warfarin causes a prothrombotic state, as protein C and S levels are the

first to significantly decrease. Warfarin can also produce significant birth defects and fetal death and should not be used during pregnancy. Changes in medications and diet may affect warfarin or vitamin K levels and require more vigilant INR monitoring and dose adjustment.

d. Reversal

(1) Warfarin reversal requires up to 1 week after discontinuation of therapy. Vitamin K can be used to reverse warfarin anticoagulation within 1 to 2 days, but the effect can last for up to 1 week longer. The appropriate vitamin K dose depends on the INR and the urgency with which correction must be accomplished. For patients with bleeding or extremely high INR levels (>10), 10 mg of vitamin K should be administered intravenously. In addition, FFP or factor concentrates can be administered to patients with ongoing hemorrhage or in need of rapid reversal.

C. Fibrinolytic Therapy

1. Thrombolytic therapy is most often used for clinically significant arterial and venous thromboses. **Tissue plasminogen activator (tPA, alteplase)** or a recombinant analog (reteplase), as well as urokinase (Abbokinase), is used for lysis of catheter, venous, and peripheral arterial thrombi.

2. Antifibrinolytics: **Tranexamic acid** is a lysine analog which is commonly used orally for menstrual bleeding. It binds plasminogen, reducing its activation into plasmin. It is frequently used intravenously during cardiac and orthopedic operations. Its use in trauma is an area of active investigation.

III. TRANSFUSION THERAPY AND REVERSAL OF COAGULOPATHY.

The risks and benefits of transfusion therapy must be considered carefully in each situation. Informed consent should be obtained before blood products are administered. The indications for transfusion should be noted in the medical record. Before elective procedures that are likely to require blood transfusion, the options of autologous or directed blood donation should be discussed with the patient in time to allow for the collection process.

A. Red Blood Cell Transfusion

1. Indications

a. RBC transfusions are used to treat anemia and improve the oxygen-carrying capacity of the blood. A hemoglobin level of 7 to 8 g/dL is adequate for tissue oxygenation in most normovolemic patients. However, therapy must be individualized based on the clinical situation rather than a hemoglobin level.

2. Transfusions in critically ill patients

a. Critically ill patients may be at increased risk for the immunosuppressive complications of transfusions and may benefit from a more restrictive transfusion protocol. This was demonstrated in the Transfusion Requirements in Critical Care (TRICC) trial, a randomized, controlled trial that showed significantly lower mortality rates with a restrictive transfusion strategy (transfusion for hemoglobin less than 7 g/dL) (*N Engl J Med*. 1999;340:409–417). Patients with active cardiac ischemia or infarction may benefit from a higher hemoglobin level of >10 g/dL to improve oxygen delivery (*Am Heart J*. 2013;165(6):964–971).

3. Preparation

a. Before administration, both donor blood and recipient blood are tested to decrease transfusion reactions. **Blood typing** tests the recipient's RBCs for antigens (A, B, and Rh) and screens the recipient's serum for the presence of antibodies to a panel of known RBC antigens. Each unit to be transfused is then **cross-matched** against the recipient's serum to check for preformed antibodies against antigens on the donor's RBCs. In an emergency situation, type O/Rh-negative blood that has been prescreened for reactive antibodies may be administered prior to blood typing and cross-matching. After blood typing, type-specific blood can be given.

4. Administration (Table 6-3)

a. Packed RBCs should be administered through a standard filter (170 to 260 mm) and an 18-gauge or larger intravenous catheter. The rate is determined by the clinical situation. Typically, each unit of blood must be administered within 4 hours to prevent infection. Patients are monitored for adverse reactions within the first 5 to

10 minutes of the transfusion and frequently thereafter.

5. **Alternatives to homologous transfusion** may provide advantages in safety and cost when used in elective procedures with a high likelihood of significant blood loss.
   a. **Autologous predonation** is the preferred alternative for elective transfusions. Up to 20% of patients still require allogeneic transfusion, however, and transfusion reactions may still result from clerical errors in storage.
   b. **Isovolemic hemodilution** is a technique in which whole fresh blood is removed and crystalloid is simultaneously infused in the immediate preoperative period. The blood is stored at room temperature and reinfused after acute blood loss has ceased. Moderate hemodilution (hematocrit 32% to 33%) is as effective as autologous predonation in reducing the need for allogeneic transfusion, and it is much less costly.

TABLE 6-3 Blood Products

Blood Product	Volume (mL)	Additional Factors	Expected Response	Common Use
PRBC 1 unit	200–250	Fibrinogen: 10–75 mg Clotting factors: none	Increase: 1 mg/dL Hgb 3% HCT	ABLA MTP Surgical blood loss
Platelets SDP (apheresis) RDP[a]	300–500 50 per unit	Fibrinogen: 2–4 mg/mL (360–900 mg) Clotting factors: equivalent of 200–250 mL of plasma (hemostatic level) "6 pack" of pooled RDP similar to SDP	Increase: 30–60 K/mm^3 Increase: 7–10 K/mm^3 per unit	Plt count <10 K MTP Bleeding with known qualitative plt defect
FFP[b] 1 unit	180–300	Fibrinogen: 400 mg Clotting factors: 1 mL contains 1 active unit of each factor (II, V, VII, IX, X, XI)	Decrease: PT/INR PTT	Coagulopathy Warfarin overdose DIC
Cryo 10 pack		Fibrinogen: 1,200–1,500 Clotting factors: VIII, vWF, XII	Decrease: PT/INR PTT Increase: fibrinogen level	vWD DIC Hemophilia A

[a]4 to 10 RDP units are pooled prior to transfusion.

[b]Duration of FFP effect is approximately 6 hours. INR of FFP is 1.6 to 1.7.

ABLA, acute blood loss anemia; Cryo, cryoprecipitate; FFP, fresh frozen plasma; Hgb, hemoglobin; HCT, hematocrit; MTP, massive transfusion protocol; PRBC, packed red blood cells; plt, platelet; RDP, random donor platelets; SDP, single donor platelets.

   c. **Intraoperative autotransfusion (i.e., cell saver)** is a process by which blood from the operative field is returned to the patient, thus decreasing allogeneic transfusion requirements. Equipment to separate and wash recovered RBCs is required. Contraindications include known neoplasm and/or enteric or purulent contamination.

d. **Erythropoietin** may be effective in decreasing allogeneic transfusion requirements when given preoperatively. The appropriate dose can be calculated based on anticipated transfusion requirements and is administered weekly over 2 to 4 weeks. Adjunctive use with autologous predonation has not consistently been shown to be effective. Chronic anemia, particularly anemia due to renal disease, is usually treated with erythropoietin (50 to 100 U/kg subcutaneously three times a week) rather than with transfusions. Erythropoietin should be used with caution in critically ill patients since it is associated with an increased risk of thrombotic events (*N Engl J Med*. 2007;357:965–976).

B. Transfusion Products for Coagulopathy

1. **FFP** contains all the coagulation factors. However, factors V and VIII may not be stable through the thawing process and are not reliably recovered from FFP. Therefore, it can be used to correct coagulopathies that are due to deficiencies of any other coagulation factor and is particularly useful when multiple factor deficiencies exist (e.g., liver disease or massive transfusion). Effects are immediate and typically last about 6 hours.
2. **Cryoprecipitate** is the cold-insoluble precipitate of fresh plasma and is rich in factor VIII and vWF as well as fibrinogen, fibronectin, and factor XIII. Cryoprecipitate may be used as second-line therapy in vWD or hemophilia, but is most often used to correct fibrinogen deficiency in DIC or during massive transfusion.
3. **Recombinant human factor VIIa (rhFVIIa, NovoSeven)** is an FDA-approved treatment for hemophilia in which factors VIII or XI are affected. The recommended dose for this indication is 90 to 120 mg/kg, which can be repeated every 2 hours for 24 hours.
4. **Factor concentrates** are an emerging option for rapid reversal of anticoagulation. These agents **(e.g., prothrombin complex concentrate [PCC])** contain high levels of factors II, IX, and X. Factor VII may also be a component of these products or may be administered separately. In addition to providing rapid reversal, these agents require lower volumes than FFP administration and thus may reduce cardiac complications in patients with CHF or dysrhythmias.
5. **Platelet transfusions** are used to control bleeding that is caused by

thrombocytopenia or platelet dysfunction and to prevent spontaneous bleeding in situations of severe thrombocytopenia. For minor surgical procedures, the transfusion threshold is often increased to a platelet count of less than 50,000/mL. Preparations, volumes, and expected response are summarized in Table 6-3.

C. Complications Associated With Transfusion of Blood Products

1. Infection

a. Current methods of blood screening have greatly reduced the transmission rate of viral disease. Hepatitis B, hepatitis C, HIV, and CMV transmission have all been reported. Although exceedingly rare, there have been cases in which blood products infected with bacteria and/or parasites have been transfused.

2. Transfusion reactions

a. Allergic reactions are the most common type of transfusion reactions and occur when the patient reacts to donated plasma proteins in the blood. Symptoms are usually mild, although rarely severe reactions can cause bronchospasm or laryngospasm, which should prompt immediate discontinuation of the infusion.

b. Febrile nonhemolytic reactions involve the development of a high fever during or within 24 hours of a transfusion. This reaction is mediated by the body's response to WBCs in donated blood. General malaise, chills, nausea, or headaches may accompany the fever. Because fever can be the first manifestation of a more serious transfusion reaction, this situation must be promptly evaluated. Patients with a previous history of a febrile reaction should receive leukoreduced blood products.

c. Acute immune hemolytic reactions are the most serious transfusion reactions, in which patient antibodies react to transfused RBC antigens causing intravascular hemolysis. This typically occurs with ABO or Rh incompatibility. Symptoms include nausea, chills, anxiety, flushing, and chest or back pain. Anesthetized or comatose patients may show signs of excessive incisional bleeding or oozing from mucous membranes. The reaction may progress to shock or renal failure with hemoglobinuria. If a transfusion reaction is suspected, the infusion should be stopped immediately. Identities of the donor unit and

recipient should be rechecked because clerical error is the most common cause. Also, a repeat cross-match should be performed.

d. Delayed hemolytic reactions result from an amnestic antibody response to antigens other than the ABO antigens to which the recipient has been previously exposed. Transfused blood cells may take days or weeks to hemolyze after transfusion. Typically there are few signs or symptoms other than a falling RBC count or elevated bilirubin. Specific treatment is rarely necessary, but severe cases should be treated like acute hemolytic reactions, with volume support and maintenance of urine output.

e. Transfusion-related acute lung injury (TRALI) may be one of the most common causes of morbidity and mortality associated with transfusion. TRALI typically occurs within 1 to 2 hours of transfusion but can occur any time up to 6 hours later. Support can vary from supplemental oxygen to intubation and ventilation. Although most cases resolve on their own, severe cases can be fatal.

f. GVHD can occur after transfusion of immunocompetent T cells into immunocompromised recipients or human leukocyte antigen (HLA)–identical family members. GVHD presents with a rash, elevated liver function tests, and pancytopenia. It has an associated mortality of greater than 80%. Irradiation of donor blood from first-degree relatives of immunocompetent patients and all blood for immunocompromised patients prevents this complication.

g. Volume overload after blood transfusion can occur in patients with poor cardiac or renal function, or as a component of the **transfusion-associated circulatory overload (TACO)** phenomenon. Careful monitoring of the volume status and judicious use of diuretic therapy can reduce the risk of this complication.

h. Alloimmunization occurs in 50% to 75% of patients receiving repeated platelet transfusions and presents as a failure of the platelet count to increase significantly after a transfusion. This occurs in immunocompetent individuals who mount an immune response to platelet-specific antigens which include class I HLA. Therefore, in patients who need long-term platelet therapy, HLA-

matched single-donor platelets slow the onset of alloimmunization.

i. **Posttransfusion purpura** is a rare complication of platelet transfusions seen in previously transfused individuals and multiparous women. It is usually caused by antibodies that develop in response to a specific platelet antigen Pl^{A1} from the donor platelets. This condition presents with severe thrombocytopenia, purpura, and bleeding occurring 7 to 10 days after platelet transfusion. Although fatal bleeding can occur, the disease is typically self-limiting. Plasmapheresis or an infusion of intravenous immunoglobulin may be helpful.

D. Massive Transfusion

1. Massive transfusion is defined as the **transfusion of blood products that are greater in volume than a patient's normal circulating blood volume in a period of less than 24 hours.** This creates several risks not encountered with a lesser volume or rate of transfusion.

   a. **Coagulopathy** might arise as a result of platelet or coagulation factor depletion. This has led to the use of transfusion ratios in the trauma setting that involve the transfusion of platelets and FFP in concert with packed red blood cells (PRBCs).

   b. **Hypothermia** can result from massive volume resuscitation with chilled blood products but can be prevented by using blood warmers. Hypothermia can lead to cardiac dysrhythmias and coagulopathy.

   c. **Citrate toxicity** can develop after massive transfusion in patients with hepatic dysfunction. Hypocalcemia can be treated with intravenous administration of 10% calcium gluconate.

   d. **Electrolyte abnormalities,** including acidosis and hyperkalemia, can rarely occur after massive transfusions, especially in patients with pre-existing hyperkalemia.

2. Many centers have established **massive transfusion protocols (MTPs)** which make use of these ratios. Although no definitive ratios are standardized, ratios of 1:1 or 1:2 FFP:PRBC are common. The algorithm for MTP at Barnes–Jewish Hospital is shown in Figure 6-3. In it, prepacked boxes serve to maintain the proper ratio of clotting factor and platelets to RBCs during situations requiring rapid volume

expansion. Additionally, they remove confusion and human error that may result when actively calculating proper ratios during an emergency.

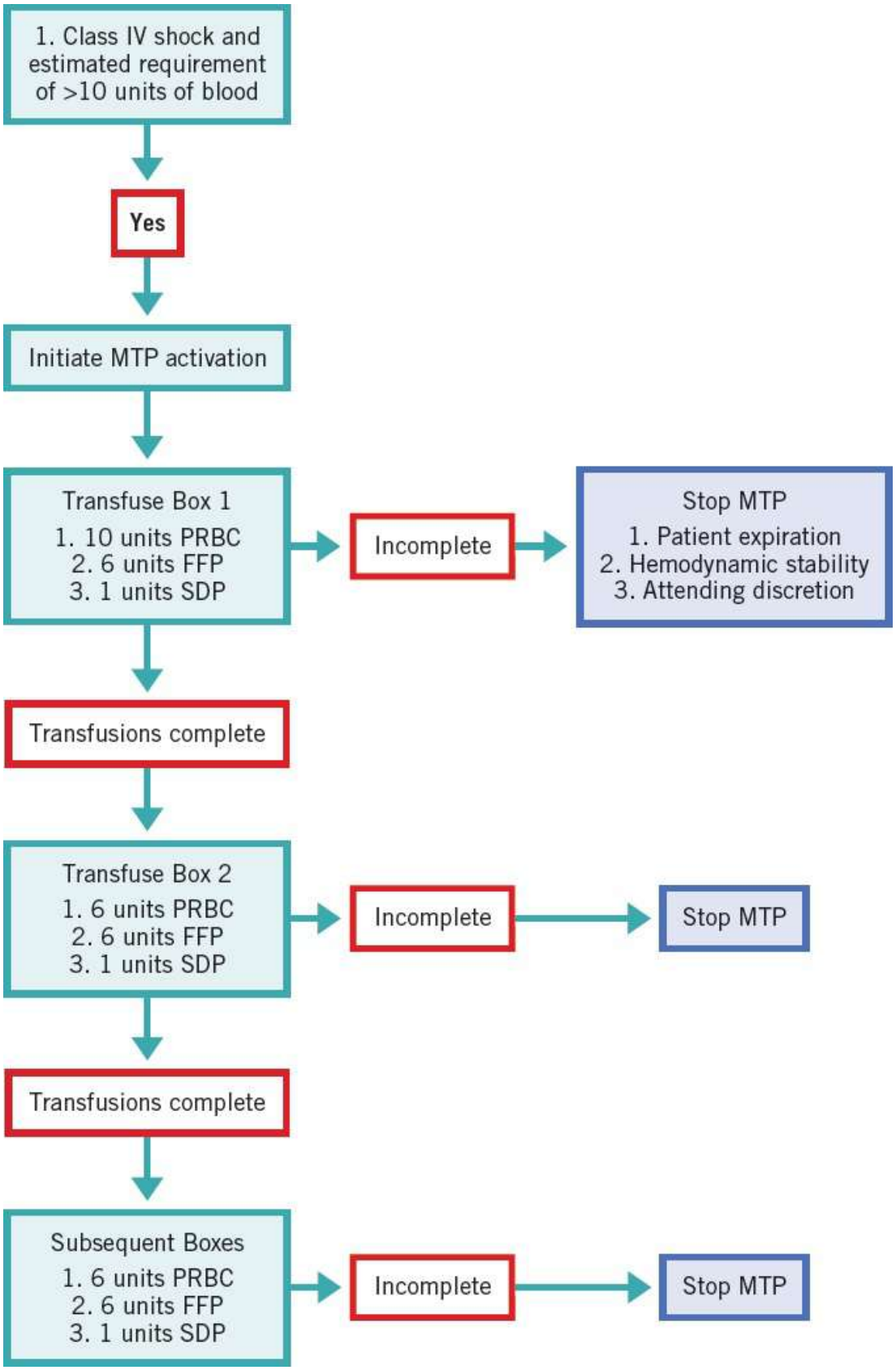


FIGURE 6-3 Barnes–Jewish Hospital massive transfusion protocol (MTP) algorithm.

IV. LOCAL HEMOSTATIC AGENTS. Local hemostatic agents promote hemostasis by providing a matrix for thrombus formation, and these agents can aid in the intraoperative control of mild-to-moderate surgical bleeding, such as that from needle punctures, vascular suture lines, or areas of extensive tissue dissection. Generally speaking, gelfoam, surgicel, and helistat are reasonable agents when direct pressure can be applied, including for superficial solid organ injuries as part of hepatorrhaphy or splenorrhaphy. Avitene, hemotene, topical thrombin, tisseel, and evicel are best used when there is more diffuse bleeding from a large dissection bed (i.e., following a retroperitoneal dissection). Floseal is particularly useful for areas where there is a small cavity with mild hemorrhage (such as a penetrating hepatic injury), as it can be used to fill the cavity as it is injected. Bleeding that is pulsatile, visibly discrete, or severe in nature will not respond to topical hemostatics. Anastomotic bleeding usually is best controlled with local pressure or a simple suture. Each agent is described below.

A. Gelatin sponge (e.g., Gelfoam) can absorb many times its weight of whole blood by capillary action and provides a platform for coagulation. Gelfoam itself is not intrinsically hemostatic. It resorbs in 4 to 6 weeks without a significant inflammatory reaction.

B. Oxidized cellulose (e.g., Surgicel) is a knitted fabric of cellulose that allows clotting by absorbing blood and swelling into a scaffold. Its slow resorption can create a foreign body reaction.

C. Collagen sponge (e.g., Helistat) is produced from bovine tendon collagen and promotes platelet adhesion. It is slowly resorbed and creates a foreign body reaction similar to that of cellulose.

D. Microfibrillar collagen (e.g., Avitene and Hemotene) can be sprayed onto wounds and anastomoses for hemostasis, particularly in areas that are difficult to reach. It stimulates platelet adhesion and promotes thrombus formation. Since microfibrillar collagen can pass through autotransfusion device filters, it should be avoided during procedures that utilize the cell saver.

E. Topical thrombin can be applied to the various hemostatic agents or to dressings and placed onto bleeding sites to achieve a fibrin-rich hemostatic plug. Topical thrombin, usually of bovine origin, is supplied as a lyophilized powder and can be applied directly to dressings or

dissolved in saline and sprayed onto the wound. Topical thrombin can be used effectively in anticoagulated patients.

F. Gelatin matrices (e.g., Floseal) are often used in combination with topical thrombin intraoperatively. Typically, bovine thrombin (5,000 units) is sprayed onto the matrix, which is then applied to the site of bleeding.

G. Fibrin sealants (e.g., Tisseel and Evicel) are prepared by combining human thrombin and human fibrinogen. These components are separated prior to administration and are mixed during application to tissue via a dual-syringe system. An insoluble, cross-linked fibrin mesh is created which provides a matrix for thrombus formation.

CHAPTER 6: HEMOSTASIS, ANTICOAGULATION, AND TRANSFUSIONS

Multiple Choice Questions

1. A 57-year-old male who developed atrial fibrillation is noticed to have a drop in his platelets to 60,000/**μL 7 days after initiation of a heparin drip. He goes on to develop lower extremity swelling, and the presence of a new DVT is confirmed with ultrasound. What if any changes should be made to address his anticoagulation regimen and thrombocytopenia?**

   a. Continue heparin drip
   b. Discontinue all anticoagulation and place an IVC filter
   c. Start the patient on a bivalirudin drip
   d. Start platelet transfusion
   e. Obtain a hematology consult

2. **A 45-year-old male is septic and found to have DIC with hypofibrinogenemia. Which of the following products would be appropriate to administer?**

   a. FFP
   b. PRBCs
   c. DDAVP
   d. Cryoprecipitate
   e. Whole blood

3. **Patients with hemophilia A:**

   a. Commonly present with spontaneous bleeding
   b. Should receive factor IX prior to surgery
   c. May produce factor VIII inhibitors
   d. Are deficient in platelet membrane receptors
   e. Are mostly female

4. **Which of the following is not an absolute contraindication to fibrinolytic therapy?**

a. Intolerable ischemia
b. Active bleeding
c. Recent stroke or neurosurgical procedure
d. Intracranial neoplasm
e. Active menses

5. Which of the following facts concerning von Willebrand disease is correct?

a. It is the third most common inherited bleeding disorder.
b. It is characterized by low levels of vWF alone.
c. It is characterized by ineffective vWF alone.
d. Type 2 is treated with DDAVP.
e. Type 3 is treated with cryoprecipitate.

6. Which of the following concerning factor XIIIa is correct?

a. It is involved in the activation of platelets.
b. It is involved in the cross-linking of fibrin.
c. It is not involved in coagulation cascade.
d. It is deficient in Christmas disease.
e. It is found in the prothrombinase assembly which involves factors Va, Xa, and calcium.

7. A deficiency of all of the following will result in hypercoagulability except:

a. Prekallikrein
b. Protein C
c. Protein S
d. Plasminogen
e. Antithrombin III

8. Which of the following is correct regarding antithrombin III?

a. It is a necessary cofactor for heparin.
b. It is activated by argatroban.
c. It is secreted by endothelial cells.
d. Its synthesis is affected by warfarin.
e. It is inhibited by fondaparinux.

9. Which of the following regarding the prothrombinase complex is correct?

a. It is inhibited by heparin.
b. It is inhibited by argatroban.
c. It does not require ionized calcium.
d. It is inhibited by clopidogrel.
e. It is inhibited by aspirin.

10. Cryoprecipitate includes:

a. Factor II
b. Factor VII
c. Factor IX
d. Factor X
e. vWF

7 Anesthesia

Megan O. Kelly and Tracey W. Stevens

Thorough preoperative assessment of the surgical patient is an integral component of comprehensive anesthesia care and critical to patient safety. It includes a complete history including previous anesthetic complications, physical examination including airway and vascular access evaluation, optimization of patient comorbidities, and perioperative management of home medications. Please see Chapter 1 for a detailed discussion of preoperative patient evaluation.

I. ANESTHESIA TECHNIQUES AND MEDICATIONS. Anesthesia care can be categorized into four types: local, regional, monitored anesthesia care (mac), and general anesthesia. Multimodal anesthesia strategies use combinations of these techniques to improve patient outcomes while minimizing adverse effects of anesthetic medications (e.g., less sedation, earlier ambulation, faster return of bowel function).

A. Basic anesthesia **monitoring** standards apply to patients undergoing all types of anesthesia. Minimum standards for patient monitoring include the following methods for continuous evaluation of oxygenation, ventilation, circulation, and temperature:

1. Oxygenation

a. Oxygen analyzer measurement of inspired gas

b. Pulse oximetry with variable pitch pulse tone and low-threshold alarm

2. Ventilation

a. Continuous end-tidal CO_2 analysis when endotracheal tube or laryngeal mask is used, noninvasive analysis with moderate or deep sedation

3. Circulation

a. Blood pressure (BP)

b. Pulse

c. Continuous electrocardiogram

4. **Body temperature** when clinically significant changes are anticipated (American Society of Anesthesiologists (ASA) Standards for Basic Anesthesia Monitoring, October 2015; https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring).

B. Local anesthesia refers to sensory nerve impulse blockade by injection or application near the surgical site. Local anesthetics are categorized into two groups: **aminoesters (one i)** include tetracaine, procaine, cocaine, and chloroprocaine; **aminoamides (two i's)** include lidocaine, bupivacaine, ropivacaine, and mepivacaine. Characteristics of commonly used local anesthetic agents are summarized in Table 7-1.

TABLE 7-1 Local Anesthetics for Infiltration[a]

Agent	Maximum Dose (mg/kg)		Length of Action (hr)	
	Plain	With Epinephrine[a]	Plain	With Epinephrine[b]
Procaine	7	9	0.5	0.5–1
Lidocaine	4	7	0.5–1	2
Mepivacaine	4	7	0.75–1.5	2
Bupivacaine	2.5	3	2–4	3–4
Ropivacaine	3	4	2–4	3–4
Tetracaine	1.5		24	

[a]See Chapter 36 Local Anesthetics in *Miller's Anesthesia*, Saunders, 2015 for dosing recommendations for regional anesthesia applications.

[b]1:200,000.

1. Mechanism of action

a. The **mechanism of action** of local anesthetics is blockade of voltage-gated sodium channels (increasing action potential threshold) thereby inhibiting sodium influx, neuronal depolarization, and axonal conduction.

b. Local tissue acidosis (e.g., from infection) slows the onset and decreases intensity of analgesia by causing local anesthetic molecules to become positively charged and less able to diffuse into the neuron.

2. Toxicity (dose dependent, except for hypersensitivity reactions)

a. Central nervous system (CNS) toxicity includes mental status changes, dizziness, perioral numbness, metallic taste, tinnitus, and visual disturbances. Seizures can result from overdose or inadvertent intravascular injection.

b. Cardiovascular toxicity ranges from decreased cardiac output to hypotension and cardiovascular collapse. Most local anesthetics cause CNS toxicity before cardiovascular toxicity. Bupivacaine (Marcaine) is an exception; its intravascular injection can cause severe cardiac compromise.

c. Treatment of **local anesthetic systemic toxicity (LAST)** involves airway support and ventilation with 100% oxygen which should always be available. Benzodiazepines are preferred for seizure suppression; propofol should be avoided in patients with cardiovascular instability as it lowers systemic vascular resistance and can cause hypotension. Modified BLS and ACLS protocols should be followed for cardiac arrhythmia management, with avoidance of vasopressin, Ca^{2+} channel blockers, and beta-blockers and reduction of individual epinephrine doses to <1 mcg/kg. **Lipid emulsion therapy** should be used based on the clinical severity and rate of progression of LAST, and is given as a 1.5 mL/kg IV bolus of 20% lipid emulsion followed by continuous infusion at 0.25 mL/kg/min. Bolus doses may be repeated up to two times, with a recommended upper limit of 10 mL/kg over the first 30 minutes (American Society of Regional Anesthesia Checklist for Treatment of LAST, *Reg Anesth Pain Med*. 2012;37(1):16–18).

d. Hypersensitivity reactions, although rare, have been described with **ester**-based local anesthetics and are attributed to the

metabolite p-aminobenzoic acid (PABA). True amide-based local anesthetic anaphylactic reactions are rare.

(1) Signs and symptoms include urticaria, bronchospasm, hypotension, and anaphylactic shock.

(2) Treatment is similar to that for hypersensitivity reactions from other etiologies. Urticaria is treated with diphenhydramine, 25 to 50 mg IV. Bronchospasm is treated with inhaled bronchodilators (e.g., albuterol) and oxygen. Hypotension is treated with fluid resuscitation and vasopressors or small incremental doses of epinephrine. Anaphylactic cardiovascular collapse should be treated with epinephrine, 0.5 to 1 mg, administered as an IV bolus.

3. Epinephrine (1:200,000, 5 µg/mL) is mixed with local anesthetic solutions to prolong neural blockade duration and reduce systemic drug absorption. Its use is **contraindicated** where arterial spasm would cause tissue necrosis (e.g., nose, ears, fingers, toes, and penis) and in patients with arrhythmias, unstable angina, poorly controlled hypertension, or uteroplacental insufficiency.

C. Regional anesthesia refers to neuroaxial or peripheral nerve blockade with local anesthetic to inhibit the sensation of pain in a certain area of the body.

1. General considerations

a. Supplements to regional anesthesia. Local infiltration by the surgeon may be required if there is an incomplete block. IV sedation using short-acting agents can also be helpful. Conversion to general anesthesia may be required when a regional technique provides inadequate analgesia or surgical positioning is not tolerated.

b. Ultrasound imaging is coming to replace landmark-based and nerve stimulation techniques as a guidance tool for peripheral nerve blockade, resulting in more consistent blockade and decreased complications.

2. Neuroaxial blockade

a. Spinal anesthesia involves the injection of low-dose local anesthetic solution into the subarachnoid space at the level of the lumbar spine.

(1) Level of analgesia is affected by multiple variables. The agent's **baricity** (density of anesthetic compared to that of cerebrospinal fluid) and the **position** of the patient immediately after injection are the major determinants of level. The **total dose** and **volume injected** are also important.

(2) Onset and duration of analgesia are primarily determined by the **specific characteristics of the local anesthetic** used. Variability in the length of analgesia is significant, ranging from as little as 30 minutes (lidocaine) to up to 6 hours (tetracaine with epinephrine).

(3) Complications

(a) Hypotension occurs as a result of sympatholytic-induced vasodilation. It is more severe in hypovolemic patients or those with pre-existing cardiac dysfunction. Treatment includes IV fluids, vasopressors, and positive inotropic and chronotropic drugs. Leg elevation and Trendelenburg positioning can be used to increase venous return to the heart. It is advisable to administer 500 to 1,000 mL of crystalloid prior to spinal block to avoid hypotension.

(b) High spinal blockade. Inadvertently high levels of spinal blockade may result in hypotension (blocking dermatomes T1–T4: preganglionic cardioaccelerator nerves), dyspnea (loss of chest proprioception or intercostal muscle function, diaphragmatic paralysis due to C3–C5 blockade), or apnea (decreased medullary perfusion secondary to hypotension). Treatment consists of ventilatory support and/or intubation, IV fluids, and chronotropic and inotropic support.

(c) Headache can result from leakage of CSF at the dural puncture site. A postural component is always present (i.e., symptoms worsened by sitting up or standing). The use of smaller-caliber needles has reduced the frequency of this complication. Treatment includes bed rest, abdominal binders, oral or IV fluids, oral analgesics, and caffeinated beverages. Severe refractory headache may require placement of an epidural blood patch to prevent ongoing leakage of CSF.

(d) CNS infection after spinal anesthesia, although extremely

rare, may result in meningitis, epidural abscess, or arachnoiditis.

(e) Permanent nerve injury is exceedingly rare and seen with the same frequency as in general anesthesia.

(f) Urinary retention with bladder distention can occur in patients with spinal anesthesia whose bladders are not drained by urethral catheters.

(4) Contraindications

(a) Absolute contraindications to spinal anesthesia are lack of consent, localized infection at the planned puncture site, increased intracranial pressure, sepsis, and coagulopathy.

(b) Relative contraindications include hypovolemia, pre-existing CNS disease, chronic low back pain, platelet dysfunction, and preload-dependent valvular lesions such as aortic and mitral stenosis.

b. Epidural anesthesia is similar to spinal anesthesia except that the needle remains in the epidural space (between the ligamentum flavum and dura mater) and is not advanced through the dura. A flexible catheter is often advanced into the space to allow for repeat bolus doses or continuous infusion of local anesthetics and opioids.

(1) Level of analgesia is primarily determined by the **volume** of injection, as well as by patient **position**, **age,** and **area of placement.**

(2) Onset and duration of analgesia

(a) Epidural anesthesia has slower onset of action than spinal anesthesia because the local anesthetic solution must diffuse farther. The rate of onset of sympathetic blockade and hypotension also is slowed providing for fewer acute hemodynamic effects compared to spinal anesthesia.

(b) The **dosing interval** and **duration of action** depend on the agent used.

(3) Complications are similar to those of spinal anesthesia and also include:

(a) Postoperative epidural-associated hypotension

Management includes:

(i) IV fluid bolus

(ii) Decrease epidural infusion rate

(iii) Initiation of vasopressor (e.g., phenylephrine)

(iv) Evaluation for other causes of postoperative hypotension (e.g., bleeding, sepsis)

(b) Postdural puncture (spinal) headache (PDPH) may result from inadvertent perforation of the dura. Treatment is the same as with spinal anesthesia.

(c) Unintended dural puncture may be managed by withdrawing the catheter and repeating the procedure at a different level or by intrathecal placement of the epidural catheter, which avoids a repeat procedure, ensures adequate anesthesia, and may reduce the incidence of CSF leak and PDPH. Care must be taken to avoid high block and inappropriate drug administration.

(d) Intravascular catheter placement (usually in epidural veins) is potentially devastating due to the potential for intravascular injection of local anesthetic and risk of systemic toxicity. The ability to aspirate blood or hypertension and tachycardia in response to a 3-mL 1.5% lidocaine with 1:200,000 epinephrine test dose warrants removal and re-siting of the epidural catheter placement.

(e) Epidural hematoma is rare and usually occurs in patients with coexisting coagulopathy. Emergent laminectomy may be required to decompress the spinal cord and avoid permanent neurologic injury.

(4) Combined spinal and epidural anesthesia

(a) A **small-gauge spinal needle** is placed through an epidural needle once the epidural space has been located. The dura is punctured only by the spinal needle for administration of anesthetic to the subarachnoid space prior to placement of the epidural catheter. This procedure combines the quick onset of spinal analgesia with the continuous dosing advantages of epidural analgesia.

3. Peripheral nerve blockade—upper extremity

a. Brachial plexus blockade. Upper extremity blockade is achieved

by local anesthetic injection into the brachial plexus sheath by one of the several approaches.

(1) Interscalene blockade targets the brachial plexus trunks and is used for shoulder and upper arm surgery because it reliably blocks the shoulder. The lower trunk is often missed, thus interscalene blockade is unsuitable for distal arm surgery. Ipsilateral recurrent laryngeal nerve, stellate ganglion, and phrenic nerve blockade can result in hoarseness, Horner syndrome, and dyspnea from diaphragmatic paralysis, respectively.

(2) Supraclavicular blockade targets the divisions and is used for arm surgery. Risks are similar to interscalene blockade. The risk of pneumothorax is reduced with ultrasound guidance.

(3) Infraclavicular blockade targets the cords. It is suitable for arm and hand surgery. Phrenic nerve block is unlikely and it is therefore the preferred option for patients with severe pulmonary disease.

(4) Other regional techniques for upper extremity anesthesia include **axillary blockade**, distal blocks of the **radial, median, and ulnar nerves**, **digital blockade**, and **intravenous regional anesthesia (Bier block).**

4. Peripheral nerve blockade—lower extremity

a. Femoral nerve blockade is used for anterior thigh, femur, and knee surgery by blocking the femoral nerve at the groin. Complications are rare but include femoral arterial puncture and hematoma.

b. Common techniques for anesthesia of the lower extremity include **popliteal nerve**, **saphenous nerve**, and **ankle** blocks.

5. Miscellaneous regional anesthesia techniques

a. Intercostal nerve block is indicated after thoracotomy or before chest tube placement. Local anesthetic is injected just below the rib in the posterior axillary line, usually for a distance of five interspaces surrounding the interspace of interest. Complications include pneumothorax and intravascular injection. Injection into the nerve sheath with retrograde spread to the spinal cord can produce a high spinal or epidural block.

b. Paravertebral nerve block targets the spinal nerves at the level of the paravertebral space. It is most commonly performed at the thoracic level for breast surgery, thoracotomy, or rib fractures.

c. Transversus abdominis plane (TAP) block targets the cutaneous branches of the low thoracic and lumbar spinal nerves that travel in the plane between the transversus abdominis and internal oblique muscles. It can be done at the time of laparotomy from inside the abdomen, or ultrasound guided externally.

d. Erector spinae plane (ESP) block is a recently described technique that has been used to provide analgesia in the chest when performed at the level of T5 and is being evaluated for efficacy of abdominal analgesia when performed at the level of T7. The block is performed using ultrasound guidance to target the plane just inferior to the erector spinae muscle and superior to the transverse process. Local anesthesia is injected into this space which can also accommodate indwelling catheters for use in the postoperative period (*Anaesthesia*. 2017;72:452–460).

e. Readers are referred to the New York Society of Regional Anesthesia website for excellent reviews of regional anesthesia techniques (www.nysora.com).

D. MAC describes a multimodal approach to anesthesia for procedures that do not require general anesthesia. MAC involves a combination of local and/or regional anesthesia of the operative site with mild sedation and analgesia. Full monitors are applied and supplemental oxygen is administered via nasal cannula or face mask. Patients maintain spontaneous respirations and the ability to respond to the anesthesia provider. Vigilance is key to ensure the avoidance of apnea and airway obstruction. Medications commonly used during MAC are summarized in Table 7-2.

E. General Anesthesia. A balanced approach to general anesthesia provides unconsciousness, amnesia, analgesia, and skeletal muscle relaxation.

1. **Premedication** is often used in the immediate preoperative period for anxiolysis and amnesia. Common agents include benzodiazepines (e.g., midazolam) or opioids (e.g., fentanyl).
2. **Induction of general anesthesia.** IV agents are most widely used

owing to rapid onset and ease of administration. All patients must be fully monitored and preoxygenated with 100% oxygen before induction.

a. Propofol, a phenol derivative (1 to 3 mg/kg IV), is a common agent for induction and maintenance of anesthesia. Onset of action is immediate. Propofol decreases systemic vascular resistance and BP and should be used with caution in patients with hypotension or active coronary ischemia. The incidence of postoperative nausea and vomiting (PONV) is low. The pharmacokinetics is not changed by chronic, hepatic, or renal failure. Pain on injection can be attenuated with a low-dose IV lidocaine injection.

b. Etomidate, an imidazole derivative (0.3 mg/kg IV), has an onset of 30 to 60 seconds and has mild direct hemodynamic depressant effects. Adrenal insufficiency may result from a single administration.

c. Ketamine, a phencyclidine derivative (1 to 4 mg/kg IV), provides dissociative anesthesia and is also an excellent analgesic. It increases cardiac output and BP in patients who are not catecholamine depleted and is an ideal induction agent for patients with bronchospasm as it has bronchodilatory properties and does not cause respiratory depression. It does, however, raise intracranial pressure and should not be used in head trauma patients. Premedication with midazolam can prevent the side effects of emergence delirium and hallucinations. It is often used in pediatrics with the advantage that it can be given **intramuscularly.**

TABLE 7-2 Medications for Short-Term Sedation and Analgesia During Procedures

Agent	Route	Dose (as Needed)	Comments
Dexmedetomidine (Precedex)	IV	1 mcg/kg over 10 min, then 0.2–1 mcg/kg/hr	May cause bradycardia and hypotension, transient

			hypertension during loading
Fentanyl	IV	25–50 mcg q5–10 min	Opioids provide analgesia with unpredictable sedative effects
Ketamine (Ketalar)	IV/IM	0.2–0.8 mg/kg IV q10–15 min 4–6 mg/kg IM	Provides sedation and analgesia, coadminister midazolam to reduce emergence reactions
Midazolam (Versed)	IV	0.5–1 mg q15 min	Benzodiazepines do not provide analgesia
Propofol (Diprivan)	IV	10–20 mg over 3–5 min q10 min, or 25–75 mcg/kg/min	May cause hypotension, especially with bolus dosing

IV, intravenous; q, every.

3. **Neuromuscular blockade** (muscle relaxation) is achieved with acetylcholine receptor antagonists that act on postsynaptic receptors in the neuromuscular junction to produce muscle relaxation. Agents are categorized as either depolarizing or nondepolarizing (Table 7-3). Blockade can facilitate endotracheal intubation and may improve operating conditions for many surgical procedures. Its use, however, increases the intraoperative awareness risk and postoperative neuromuscular weakness. It should only be used when clinically indicated and normal neuromuscular function should be ascertained prior to extubation or stopping the anesthetic. While nerve monitors

are not a standard ASA monitoring requirement, they should be used whenever neuromuscular blockade is performed.

a. Depolarizing agent in current clinical use is **succinylcholine,** a rapidly acting (60 seconds) and rapidly metabolized agent that allows return of neuromuscular function in 5 to 10 minutes. In certain patients, the normally mild hyperkalemic response can be exaggerated, possibly leading to cardiac arrest. Its use is therefore usually contraindicated in patients with severe burns, trauma, paralysis, neuromuscular disorders, or prolonged bed rest. It can also cause increased intraocular, intracranial, and gastric pressures. It is contraindicated in those with a personal or family history of **malignant hyperthermia.** Prolonged neuromuscular blockade can occur in patients with pseudocholinesterase deficiency.

TABLE 7-3 Agents Producing Neuromuscular Blockade

Agent	Initial Dose (mg/kg)	Duration (min)	Elimination	Associated Effects
Depolarizing				
Succinylcholine	1–1.5	3–5	Plasma cholinesterase	Fasciculations, increase or decrease in heart rate, transient hyperkalemia, malignant hyperthermia trigger agent
Nondepolarizing				
Atracurium	0.2–0.4	20–35	Ester hydrolysis	Histamine release
Cisatracurium	0.1–0.2	20–35	Ester hydrolysis	
Vecuronium	0.1–0.2	25–40	Hepatic and renal	Histamine release
Rocuronium	0.6–1.2	30	Hepatic and renal	
Pancuronium	0.04–0.1	45–90	Primarily renal	Increase in heart rate, mean arterial BP, and cardiac output

BP, blood pressure.

b. Nondepolarizing agents can be divided into short, intermediate, and long acting (Table 7-3). Associated hemodynamic effects and elimination pathways vary. These agents are distinguished from succinylcholine by reversibility and no risk of malignant hyperthermia.

c. Reversal of neuromuscular blockade with **acetylcholinesterase inhibitors** (neostigmine, 0.06 to 0.07 mg/kg, and edrophonium,

0.1 mg/kg) or **sugammadex** (2 mg/kg with reappearance of second twitch, 4 mg/kg with zero twitches; a binding agent that forms a complex with rocuronium or vecuronium and does not affect acetylcholine) is performed before extubation to ensure full return of respiratory muscle function and protective airway reflexes. The diaphragm is less sensitive to muscle relaxants than the muscles of the head and neck; therefore, a spontaneously ventilating patient **may still be unable to protect the airway**. Dosage response should be monitored by a peripheral nerve stimulator (train-of-four) to assess twitches. Strength can also be assessed by having the patient raise their head from the bed for 5 seconds or more. A muscarinic anticholinergic agent such as atropine or glycopyrrolate is used to counteract the side effects of these reversal agents.

4. **Airway management.** Ventilation during general anesthesia may be spontaneous, assisted, or controlled.
   a. **Mask ventilation** with spontaneous respiratory effort can be used during short procedures that do not require neuromuscular relaxation. Nasopharyngeal and oral airways can relieve obstruction and make mask ventilation more effective.
   b. **Endotracheal intubation** allows for control of ventilation and protects against aspiration. Although frequently performed orally with the laryngoscope, intubation can also be accomplished nasally and, in anatomically challenging patients, can be performed with the aid of a fiberoptic bronchoscope. Newer optical and video laryngoscopes are also helpful devices in difficult intubations.
   c. **Supraglottic airway devices** are alternative airway support devices that are positioned above the larynx. The laryngeal mask airway (LMA), the most commonly used supraglottic device, is inserted blindly into the pharynx to form a low-pressure seal around the laryngeal inlet. Although supraglottic devices allow ventilation with gentle positive pressure, they do not definitively protect the airway from aspiration. Their use is contraindicated in nonfasted patients, morbidly obese patients, and patients with obstructive or abnormal lesions of the oropharynx.
   d. **Management of the difficult airway.** Several adjuncts to

endotracheal intubation may facilitate management of the difficult airway, including supraglottic devices, intubating stylets, optical or video laryngoscopy, fiberoptic bronchoscopy, and invasive airway access (American Society of Anesthesiologists Difficult Airway Algorithm (p. 257), *Anesthesiology*. 2013;118(2):251–270; Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults Algorithm (p. 828), *Br J Anaesth*. 2015;115(6):827–848).

e. Rapid sequence intubation (RSI) is an algorithm that guides the approach to endotracheal intubation in emergent scenarios and in patients at increased risk for aspiration (nonfasted, patients with delayed gastric emptying, reflux, pregnancy, bowel obstruction) (RSI Algorithm (p. 1408), *Chest*. 2005;127(4):1397–1412).

5. Maintenance of anesthesia

a. Inhalational agents

(1) Volatile anesthetics include **isoflurane, sevoflurane**, and **desflurane**. They provide unconsciousness and amnesia with less cardiovascular depression than previously used agents. Isoflurane has a relatively slow rate of metabolism. Sevoflurane is nonirritating to the airway and is the preferred agent for inhalational induction. Desflurane is less fat soluble and therefore metabolized more quickly; however, it is a pungent airway irritant and should not be used for induction or in patients with severe reactive airway disease.

(2) Nitrous oxide by itself cannot provide surgical anesthesia. When combined with other inhalational agents, it reduces the required dose and subsequent side effects of the other agents. Nitrous oxide is extremely soluble and readily diffuses into any closed gas space, increasing its pressure. As a result, this agent should not be administered to patients with intestinal obstruction, suspected pneumothorax, or those undergoing neurosurgical or ophthalmologic procedures.

b. Intravenous agents may be used alone (total intravenous anesthesia [TIVA]) or as a supplement to inhalational agents for anesthesia maintenance, and include opioids, benzodiazepines, propofol, **dexmedetomidine**, and ketamine. TIVA carries an increased risk of intraoperative awareness, and the use of

electroencephalogram (EEG) or processed EEG (e.g., bispectral index) monitoring is recommended.

6. Recovery from general anesthesia

a. The **goal** at the conclusion of surgery is to provide a smooth, rapid return to consciousness, with stable hemodynamics and pulmonary function, protective airway reflexes, and continued analgesia.

b. Patients recover from the effects of anesthesia in the **postanesthesia care unit (PACU)**. Patient readiness for PACU discharge can be evaluated with tools such as the **Aldrete Post Anesthetic Recovery Score** (*Anesth Analg*. 1970;49:924–934).

7. Complications of general anesthesia

a. Intraoperative awareness describes intraoperative consciousness and/or explicit recall of intraoperative events, and places patients at risk of developing psychological sequelae. Risk factors include the use of TIVA, neuromuscular blockade, and anesthetic underdosing due to technical, surgical, or patient-related factors. Management includes recognition and avoidance of risk factors and prompt referral for psychological evaluation in patients reporting awareness.

b. Delayed emergence from general anesthesia may be attributable to residual medication effect, hypercarbia or hypoxia, hypoglycemia, hypothermia, electrolyte abnormalities, or neurologic complications. Treatment may include a trial of naloxone, flumazenil, or physostigmine for medication reversal, followed by laboratory and radiologic evaluation for alternative causes.

c. Malignant hyperthermia is an autosomal dominant—most commonly related to mutation of *RYR1* gene—hypermetabolic skeletal muscle disorder characterized by intracellular hypercalcemia and rapid adenosine triphosphate consumption. An acute episode is a life-threatening emergency. This condition is initiated by exposure to a triggering agent, such as volatile anesthetics or succinylcholine. Signs and symptoms may occur in the operating room for more than 24 hours postoperatively and include tachycardia, tachypnea, hypertension, hypercapnia, hyperthermia, acidosis (metabolic with/without respiratory

component), and skeletal muscle rigidity. Treatment involves immediate cessation of triggering agents and administration of **dantrolene** (1 mg/kg IV up to a total dose of 10 mg/kg). Acidosis and hyperkalemia should be monitored and treated appropriately. Intensive care monitoring for 48 to 72 hours is indicated after an acute episode of malignant hyperthermia to evaluate for recurrence, acute tubular necrosis, pulmonary edema, and disseminated intravascular coagulation. Readers are referred to the Malignant Hyperthermia Association of the United States (www.mhaus.org, (800) 644-9737 for 24-hour emergency assistance).

d. Hypothermia occurs by increased heat losses due to peripheral vasodilation during general anesthesia. Hypothermia is more pronounced in the elderly and may lead to prolonged emergence, cardiac arrhythmias, and coagulopathy. Treatment should be preventative, including warming the operating room prior to the patient's arrival and minimizing unnecessary patient exposure prior to draping. Active warming with forced-air convective warmers is effective, but care should be taken to avoid use on ischemic extremities.

e. Laryngospasm may occur due to noxious stimulation of the vocal cords by the endotracheal tube, blood, or other oral secretions. Forceful apposition of the vocal cords restricts or completely prevents airflow through the larynx. This can cause airway compromise and leads to negative-pressure pulmonary edema. Treatment involves the use of positive-pressure ventilation by mask to break the spasm. Succinylcholine may be required in refractory cases to allow successful ventilation.

f. PONV occurs in approximately 30% of patients undergoing general anesthesia, and is more common in preadolescents, women, and obese patients. Cortical (pain, hypotension, hypoxia), visceral (gastric distention, visceral traction), vestibular, and chemoreceptor trigger zone (opioids) afferent stimuli can all play a role in the mechanism. Medications including opioids, etomidate, inhalational gases, and reversal agents such as neostigmine have also been implicated. Commonly used agents for the treatment of PONV include **ondansetron,**

prochlorperazine, promethazine, and **diphenhydramine**. Agents better used for prophylaxis of PONV include **dexamethasone** and transdermal **scopolamine.**

g. Postanesthesia shaking/shivering related to pain and perioperative hypothermia may be uncomfortable and/or painful to the patient and significant metabolic effects may result, including acidosis and myocardial ischemia resulting from increased metabolic demand. The clonic component from residual inhalational anesthetic is exacerbated by hypothermia. Shivering may be relieved by administration of **meperidine** or other opioids, although these are less effective.

h. Urinary retention, although not uncommon with spinal anesthesia, occurs in only 1% to 3% of cases involving general anesthesia. It most commonly occurs after pelvic operations and in conjunction with benign prostatic hypertrophy (BPH). Early urinary catheter removal, early ambulation, and resumption of BPH medications may reduce the occurrence. Treatment may require urinary catheter placement.

i. Nerve injury can occur secondary to improper positioning of the patient on the operating table or insufficient padding of dependent regions. Resulting nerve palsies can be long lasting and debilitating. Prophylactic padding of sensitive regions and attention to proper positioning remain the most effective preventative therapies.

II. POSTOPERATIVE ANALGESIA AND COMPLICATIONS

A. Postoperative analgesia is provided to minimize patient discomfort and anxiety, attenuate the physiologic stress response to pain, facilitate optimal pulmonary toilet, and enable early ambulation. Analgesics can be administered by the oral, IV, or epidural route. Consultation with a dedicated pain management service is recommended for patients whose postoperative pain is difficult to manage.

1. **Opioids** are the most commonly used agents for postoperative analgesia. **Fentanyl, morphine**, and **hydromorphone** are most often administered in IV form by nursing staff or via a **patient-controlled analgesia (PCA)** device. With PCA, the patient has the ability to self-deliver analgesics within preset safety parameters. Continuous

"basal" infusions are rarely used in the surgical population due to the risk of respiratory compromise with opioid toxicity. **Hydrocodone** and **oxycodone** are most often administered by the oral route.

2. **Nonnarcotic adjuncts** for postoperative analgesia include **acetaminophen**, nonsteroidal anti-inflammatory drugs (NSAIDs; e.g., **ketorolac** and **ibuprofen**), and **gabapentin**.
3. **Epidural continuous infusion local anesthetic devices and peripheral nerve infusions** are also useful adjuncts for postoperative pain caused by thoracotomy, extensive abdominal incisions, or extremity procedures (see Section 1.C. Regional anesthesia).
4. **Side effects and complications**

a. Oversedation and respiratory depression

(1) Arousable, spontaneously breathing patients should be given supplemental oxygen and be monitored closely for signs of respiratory depression until mental status improves. Medications for pain or sedation should be decreased accordingly.

(2) Unarousable but spontaneously breathing patients should be treated with oxygen and **naloxone**, 0.04 mg IV repeated every 30 to 60 seconds until the patient is arousable. Excess naloxone may result in severe pain and/or severe hypertension with possible pulmonary edema. Adequate ventilation should be confirmed by arterial blood gas measurement. Current opioid administration should be stopped and the regimen decreased. In addition to continuous pulse oximetry, the patient should be monitored closely for potential recurrence of sedation as the half-life of naloxone may be shorter than the opioid.

b. Apnea

(1) Treatment involves immediate supportive mask ventilation and possible intubation if no improvement in clinical status. Naloxone administration should be considered.

c. Nausea and vomiting (see Section 1.7 Complications of General Anesthesia).

d. Pruritus

(1) Symptomatic relief may be provided with diphenhydramine or

hydroxyzine.

e. **Serotonin toxicity** can result from combination of **monoamine oxidase inhibitors** (e.g., isocarboxazid, phenelzine) with **phenylpiperidine-derivative opioids** such as meperidine, tramadol, methadone, and fentanyl. This interaction may result in severe hemodynamic swings, respiratory depression, seizures, diaphoresis, hyperthermia, and coma. Meperidine has been most frequently implicated and should be avoided.

CHAPTER 7: ANESTHESIA

Multiple Choice Questions

1. **A 40-year-old male undergoes elective right inguinal hernia repair under local anesthesia. Immediately following anesthetic injection under the external oblique aponeurosis, the patient becomes unconscious, hypotensive, and convulsive. Which of the following is correct about the management of local anesthetic systemic toxicity?**

   a. Propofol is preferred for seizure suppression.
   b. Vasopressin should be used to counteract vascular tone reduction.
   c. Cardiovascular collapse should be treated with epinephrine according to ACLS protocol.
   d. Lipid emulsion therapy should be implemented based on clinical severity and rate of progression of symptoms.
   e. Monitoring may be discontinued 2 hours after treatment for local anesthetic toxicity.

2. **A 65-year-old man with coronary artery disease and chronic obstructive pulmonary disease on 2 L of home oxygen is being prepared for operative fixation of a right distal humerus fracture. Which of the following regional anesthesia techniques is preferred to reduce risk of postoperative pulmonary complications in this patient?**

   a. Cervical blockade
   b. Interscalene blockade
   c. Supraclavicular blockade
   d. Infraclavicular blockade
   e. Axillary blockade

3. **Which of the following muscles demonstrates the earliest recovery from neuromuscular blockade following administration of an anticholinesterase reversal agent?**

   a. Adductor pollicis

b. Diaphragm
c. Geniohyoid
d. Pharyngeal
e. Flexor hallucis

4. **Minutes after receiving induction with sevoflurane and succinylcholine, a 23-year-old male undergoing elective inguinal hernia repair develops a temperature of 39.2çC, heart rate of 148 bpm, blood pressure of 186/104 mm Hg, and muscle rigidity. Which of the following is the most appropriate FIRST step in management?**

a. Administration of IV dantrolene
b. Hyperventilation with 100% oxygen
c. Cessation of volatile anesthetics
d. Obtain STAT potassium level and electrocardiogram
e. Obtain family medical history

5. **Which of the following is a risk factor for intraoperative awareness during general anesthesia?**

a. Use of neuromuscular blockade
b. Use of inhalational anesthesia
c. Older patient age
d. Elective surgery
e. Hypothyroidism

6. **In which of the following situations would succinylcholine be preferred to a nondepolarizing neuromuscular blocking agent?**

a. Severe burns
b. Rapid sequence intubation
c. Muscular dystrophy
d. Hyperkalemia
e. Family history of malignant hyperthermia

7. **You are finishing a case and instructed to inject local prior to closing. The patient is a 70-kg male and the available anesthetic is 1% lidocaine with epinephrine. What is the maximum dose?**

a. 28 mL
b. 21 mL
c. 49 mL
d. 30 mL

8 Critical Care

Robert M. MacGregor and Clare H. Ridley

INTRODUCTION

This chapter focuses on the monitoring of critically ill patients, the most common reasons for surgical ICU admissions (respiratory or circulatory failure) and sepsis. It also addresses the topics of sedation and analgesia, stress-induced ulcer prophylaxis, and the role of transfusion and glucose control in the critically ill.

I. MONITORING OF THE CRITICALLY ILL PATIENT

A. Temperature Monitoring. Critically ill patients should have their temperature measured at least every 4 hours. The fever cutoff is traditionally ≥38.5°C. Antipyretics as a strategy of temperature control should be avoided due to increased mortality (*Crit Care*. 2012;16:R33).

B. Electrocardiographic (ECG) Monitoring. Continuous ECG monitoring with telemetry allows for rapid detection of dysrhythmias and assessment of heart rate and rhythm.

C. Arterial Pressure Monitoring

1. **Indirect.** Blood pressure measurement should be performed at least hourly with a noninvasive blood pressure cuff or more often during vasoactive drip titration.
2. **Direct.** Intra-arterial catheters allow for the continuous measurement of arterial pressures and provide convenient access for frequent arterial blood–gas measurement, and blood draws for laboratory tests. They are utilized in patients with vasoactive medication requirements or a tenuous respiratory status. The most common site is the radial artery, chosen because of accessibility and collateral blood flow. Alternative sites are the axillary or brachial artery, both of which

have a similar incidence of complications (*Crit Care.* 2002;6:199–204; *Anesthesiology.* 2016;124:590–597). The common femoral artery can be used, though it is more inconvenient and usually only cannulated in an emergency. The extremity distal to the catheter should be assessed prior to and after insertion for signs of ischemia.

D. Central Venous Pressure (CVP) Monitoring. Central venous catheters provide access to measure CVP, $SCvO_2$, and to administer vasoactive medications and TPN. CVP is sometimes used as a surrogate for volume status and ventricular preload, though many question its use.

E. Pulmonary artery (PA) catheters determine CVP, cardiac output (CO), PA pressures, systemic vascular resistance (SVR), and mixed venous oxygen saturation (SvO_2). They can be used in unstable patients with rapid changes in hemodynamic status to assess responses to treatment with fluid and cardioactive agents. Importantly, the use of PA catheters has not been demonstrated to improve mortality, in part, due to error in interpretation and variations in management (*JAMA.* 2005;294:1625–1633). However, this has not been evaluated sufficiently through randomized controlled trials in surgical patients, specifically after cardiac surgery. Nonetheless, the ongoing popularity of PA catheters in cardiac surgery patients should be reconsidered in view of data from observational research suggesting lack of benefit (*Anesth Analg.* 2011;113:994–1002). Furthermore, the hemodynamic measurements of the PA catheter are operator dependent (e.g., volume and rate of saline injection) and error prone, especially when there is tricuspid regurgitation or intracardiac shunts. The mixed SvO_2 measurement is attractive as it requires no operator action and provides a useful indicator of adequacy of global oxygen delivery, though the value is falsely elevated in patients with AV fistulas.

1. **Complications.** Prior to PA catheter placement, a left bundle branch block must be ruled out because PA catheter placement can induce a transient **right bundle branch block**. Thus, PA catheter insertion with a left bundle branch block can cause life-threatening bradycardia. **Balloon rupture** results in the risk of air and balloon fragment emboli. Balloon rupture is confirmed by aspiration of blood from the balloon port. **PA perforation** presents with hemoptysis, typically after balloon inflation. Management of this life-threatening

complication requires positioning the patient with the involved side in the dependent position and emergent thoracic surgical consultation. Other complications include malposition (e.g., coronary sinus), right ventricular rupture, cardiac tamponade, and decreased CO.

F. Esophageal Doppler and pulse contour analysis have been introduced as less invasive alternatives to PA catheters for advanced hemodynamic monitoring. An esophageal Doppler measures descending aortic blood velocity and, based on assumptions regarding aortic diameter, calculates descending aortic blood flow, from which CO is extrapolated. Though it has shown utility, its utilization of the descending aorta for flow measurement assumes a constant and specific percentage of blood flow distributed to the heart, head, and upper extremities. Pulse contour analysis uses an arterial pressure waveform to calculate the stroke volume and CO, with multiple systems available.

G. Respiratory Monitoring

1. **Pulse oximetry** should be used in all critically ill patients to provide a continuous assessment of arterial oxygen saturation (SaO_2). An elevated carboxyhemoglobin falsely raises the measurement, and methemoglobinemia results in a persistent reading of 85%.
2. **Capnography** provides a quantitative, continuous assessment of expired CO_2 concentrations. A rise in $ETCO_2$ can indicate a decrease in alveolar ventilation or an increase in CO_2 production, as seen with sepsis and fever. An acute fall in $ETCO_2$ may indicate an increase in alveolar ventilation or an increase in dead space, as seen with massive pulmonary embolism (PE), endotracheal tube (ET), or mainstem bronchus obstruction.

H. Neurologic Monitoring

1. **Intracranial pressure monitoring.** See Chapter 10.
2. **Processed electroencephalogram monitors** (e.g., Bispectral Index and SedLine [BIS]) use proprietary algorithms to analyze the EEG waveform and provide a dimensionless number that is intended to indicate sedation or anesthetic depth. These monitors can be particularly useful in the ICU while patients are receiving neuromuscular blocking agents. The reliability of the BIS monitor to prevent recall has been questioned (*N Engl J Med.* 2008;358:1097–1108).

II. SEDATION AND ANALGESIA.

Sedation may be necessary for ICU patients who require invasive or poorly tolerated interventions. For example, sedation is frequently required to enable pressure-controlled ventilation (PCV). Pain should be treated to alleviate suffering and to promote deep breathing and early rehabilitation. However, both sedative and analgesic medications have side effects and should be given sparingly. Recent evidence suggests that time on the ventilator and rates of PTSD are improved when sedation is decreased. This can often be achieved by using a sedation scale, such as the Richmond Agitation–Sedation Scale (RASS) (Table 8-1). The dose of the chosen agent is then titrated by the nurse to maintain the sedation goal.

A. Control of Agitation

1. **Benzodiazepines** act through gamma-aminobutyric acid$_A$ (GABA$_A$) receptors. The two benzodiazepines commonly used for sedation are midazolam and lorazepam. **Midazolam** is hepatically metabolized and renally cleared, which may cause active metabolites to accumulate after prolonged infusions and take days to clear. **Lorazepam** has a slower onset and longer half-life. While it does not have active metabolites, it may still accumulate if used for a long duration and can result in propylene glycol toxicity at high doses. Benzodiazepines are associated with higher rates of delirium, especially in older patients (*Crit Care*. 2010;14:R38). Benzodiazepines are also indicated for alcohol or benzodiazepine withdrawal.
2. **Propofol** is short acting and acts through potentiation of GABA$_A$ receptors. Its lipophilicity facilitates rapid onset allowing it to cross the blood–brain barrier quickly. It has no analgesic properties and it is typically used with an opioid in postoperative patients. Propofol induces significant hypotension due to myocardial depression, vasodilation, and increased venous capacitance. Respiratory depression and bradycardia are also common side effects (*Crit Care Med*. 2014;42:1696). Profound hypotension has been described when propofol is administered to patients receiving rifampin (*Anesth Analg*. 2013;117:61–64). Prolonged use can lead to an elevation of triglycerides and subsequent pancreatitis. Although this is rare, triglyceride levels should be checked periodically. Propofol infusion

syndrome is a rare but lethal complication, presenting with arrhythmia, rhabdomyolysis, and lactic acidosis (*Injury.* 2014;452:245). It should be suspected when patients receiving propofol have an unexplained metabolic acidosis.

TABLE 8-1 Richmond Agitation–Sedation Scale (RASS)

Score	Characteristics
+4	Combative: Danger to self or staff
+3	Very agitated: Aggressive, pulling at tubes
+2	Agitated: Frequent nonpurposeful movements
+1	Restless: Anxious, movements vigorous but not aggressive
0	Calm and alert
−1	Drowsy: In response to voice; eye contact sustained >10 sec
−2	Light sedation: In response to voice; eye contact sustained <10 sec
−3	Moderate sedation: In response to voice; movement but without eye contact
−4	Deep sedation: In response to physical stimulation; any movement
−5	Unarousable: No response to verbal or physical stimulation

3. **Dexmedetomidine** is a centrally acting alpha$_2$-adrenoceptor agonist with sedative and analgesic properties. It is becoming increasingly popular as a sedative agent in the ICU as it might be associated with less delirium than other sedative agents, has analgesic properties, and does not depress respiration. Dexmedetomidine may be useful during a breathing trial to decrease anxiety while other anxiolytics are discontinued. As an agonist of the alpha$_2$-adrenoreceptor, similar to

clonidine, it may induce hypotension and bradycardia (*Crit Care Med.* 2014;42:1696–1702).

4. **Ketamine** is a dissociative anesthetic agent which activates the sympathetic nervous system and maintains mean arterial pressure and CO. For these reasons it may be used in patients with depressed cardiac function which may be present after cardiac surgery.

B. Management of Delirium. Delirium is a common manifestation of acute illness and is associated with increased mortality (*Crit Care.* 2010;14:R210). The cardinal features of delirium are waxing and waning inattention and disorganized thinking coupled with an acutely altered level of consciousness. Most patients have hypoactive delirium.

1. **Antipsychotics. Haloperidol** is an antipsychotic used to treat hyperactive delirium if the patient is self-destructive. Major toxicities include hypotension, prolongation of the QT interval, and extrapyramidal symptoms. **Quetiapine** is a second-generation antipsychotic which might be used as an alternative to haloperidol (*Crit Care Med.* 2010;38:419–427).
2. **Benzodiazepines** can be life saving for delirium tremens.
3. **Dexmedetomidine.** The role of dexmedetomidine for preventing and temporizing delirium has been suggested and is still under investigation. Its use in patients with agitated delirium receiving mechanical ventilation has been shown to increase ventilator-free hours at 7 days (*JAMA.* 2016;315:1460–1468).

C. Control of Pain. See Chapter 7.

D. The use of a sedation protocol, titrated by the bedside nurse, has been shown to decrease the number of days on mechanical ventilation and the ICU length of stay (*Crit Care Med.* 1999;27:2609–2615). For patients who require long-term sedation and analgesia, a daily interruption of sedation to wakefulness produces decreased time on mechanical ventilation and shorter ICU stays (*N Engl J Med.* 2000;342:1477).

III. RESPIRATORY FAILURE

A. Etiology. Respiratory failure results from inadequate gas exchange caused by ventilation/perfusion (V/Q) mismatch, hypoventilation, or impaired systemic delivery/extraction. Dead space ventilation refers to airflow within the lung that does not equilibrate with blood–gas content; this occurs in chronic obstructive pulmonary disease and PE. In contrast,

intrapulmonary shunts result from perfusion of lung tissue that is poorly ventilated, such as severe pulmonary edema, acute respiratory distress syndrome (ARDS), or pneumonia. Hypoventilatory hypoxemia may be caused by a failure of mechanical ventilation, which results in hypercapnia and hypoxemia.

B. Diagnosis. Signs or symptoms of respiratory distress should prompt pulse oximetry and an ABG. Oxygen saturation readings less than 90% can be reflective of impaired tissue oxygenation. An acute rise in $PaCO_2$ accompanied by a decrease in pH (respiratory acidosis) implies a significant imbalance between carbon dioxide production and elimination. **It is important to note that adequate oxygenation does not guarantee adequate ventilation.** In addition to a physical examination and consideration of the patient's recent history, a chest x-ray, ECG, and chest CT with PE protocol should be considered.

C. Treatment. The urgency of the situation may necessitate management prior to a diagnosis. Treatment may consist of inhaled oxygen, noninvasive positive-pressure ventilation (NIPPV), endotracheal intubation, chest tube placement, or extracorporeal membrane oxygenation (ECMO).

1. **Oxygen therapy.** Supplemental oxygen can be administered to increase the alveolar oxygen concentration. At increasing concentrations of oxygen delivery, these methods include nasal cannula, simple face mask, or face mask with a reservoir (Table 8-2).
2. **Airway management.** If uncertainty exists about whether the airway is patent or protected from aspiration, ET intubation is indicated. **Unless the physician is skilled in artificial airway placement, bag-mask ventilation should be performed until an expert arrives.**
   a. **ET intubation.** Once placed, the adequacy of ventilation is confirmed with bilateral auscultation and a CO_2 indicator. A chest x-ray confirms correct ET tube position, midway between the clavicles and carina.
   b. **NIPPV.** Biphasic positive airway pressure (BiPAP) is a form of ventilation that is delivered by a tight-fitting mask over the mouth and nose. It is useful in patients with mild to moderate respiratory insufficiency of short duration and may prevent intubation in patients with rapidly reversible respiratory failure. BiPAP may

result in gastric distension, increasing the risk of aspiration.

c. Tracheostomy should be considered urgently in the presence of severe maxillofacial injury. It should also be considered electively if prolonged intubation is anticipated. Tracheostomy provides a more secure airway, improves patient comfort and oral hygiene, increases patient mobility, and enhances secretion removal. In one study, the placement of an early tracheostomy decreased the duration of mechanical ventilation and the length of ICU and hospital stay (*Crit Care Med.* 2005;33:2513–2520) while a more recent trial showed no difference in survival or ICU length of stay for early over late tracheostomy (*JAMA.* 2013;309:2121–2129). Timing of tracheostomy placement remains controversial. **If a tracheostomy is inadvertently removed prior to the development of an established tract, approximately 2 weeks, an orotracheal tube should be placed rather than blind attempts at tracheostomy replacement.** If orotracheal intubation is not possible, a bronchoscope can aid in tracheostomy reinsertion. If the tracheostomy tube is inadvertently placed in the pretracheal tissue, the subsequent attempts at ventilation will create subcutaneous emphysema.

TABLE 8-2 Oxygen Delivery Systems

Type	FiO_2 Capability (%)	Comments
Nasal cannula	24–48	Flow rates of 1–8 L/min; true FiO_2 uncertain and highly dependent on minute ventilation; simple, comfortable, and can be worn during eating or coughing
Simple face mask	35–55	Flow rates of 6–10 L/min
High-humidity mask	Variable from 28 to nearly 100	Flow rates should be 2–3 times minute ventilation;

		levels >60% may require additional oxygen bleed-in
Nonrebreather	90–95	Flow rates of 12–15 L/min; incorporates valve to reduce room air entrainment and rebreathing of expired air
Ventimask	24, 28, 31, 35, 40, or 50	Provides controlled FiO_2; useful in chronic obstructive pulmonary disease patients to prevent depression of respiratory drive; poorly humidified gas at maximum FiO_2

FiO_2, fraction of inspired oxygen.

d. Cricothyroidotomy is utilized to obtain an airway in emergent situations when attempts to ventilate by face mask or laryngeal mask airway (LMA), and ET tube placement are unsuccessful.

3. Modes of mechanical ventilation are divided into volume- or pressure-controlled modes. Volume-controlled modes deliver a set tidal volume ensuring adequate alveolar ventilation; airway pressure varies depending on lung compliance. Pressure-controlled modes deliver a set airway pressure; tidal volume varies depending on compliance (the change in volume divided by the change in pressure, D*V*/D*P*).

a. Volume-controlled modes

(1) Intermittent mandatory ventilation (IMV) delivers a preset tidal volume over a set time, and the pressure is varied. The ventilator is synchronized to assist with any patient-initiated breaths up to a set rate, but any additional breaths initiated by the patient will be unassisted. If the patient does not initiate

enough breaths to fulfill the set respiratory rate, the ventilator will initiate additional breaths. This is well tolerated with minimal sedation.

(2) **Assist-control (A/C) ventilation** delivers a preset tidal volume at a set rate over a set time. As the machine senses each inspiratory effort by the patient, it delivers the set tidal volume over a set time. If the patient's respiratory rate is below the machine's set rate, ventilator-initiated breaths are delivered to make up the difference. A/C ventilation minimizes the work of breathing because the ventilator assists all breaths; however, this mode is uncomfortable in the minimally sedated patient if the breaths are dyssynchronous.

b. Pressure-controlled modes

(1) **Pressure-support ventilation (PSV)** delivers a preset inspiratory pressure but at no set rate. Constant inspiratory pressure continues until the inspiratory flow falls below a predetermined level and the exhalation valve opens, delivering tidal volumes only when the patient is breathing spontaneously. Therefore, this mode is for spontaneously breathing patients. It does increase the amount of work necessary because each breath is patient initiated and the duration of pressure support is also dependent on ongoing patient effort. As such, PSV is effort cycled. Low pressures (5 to 8 cm H_2O) are set routinely to overcome the resistance caused by the ET tube and the inspiratory demand valves. This mode is often utilized to evaluate for extubation.

(2) **PCV** delivers a preset inspiratory pressure at a set rate with each breath delivered over a set time. As such, PCV is time cycled. This mode allows the physician to set the airway pressure and minimize barotrauma. The disadvantage is that the tidal volume varies depending on compliance and any increase in airway resistance can decrease the tidal volume to dangerously low levels. This mode is used in patients with poor lung compliance which requires a higher pressure.

c. Advanced ventilator settings. For patients in whom conventional mechanical ventilation fails to achieve adequate oxygenation,

open lung ventilation may be considered. It minimizes shearing forces due to alveolar collapse by stenting alveoli open at end expiration.

(1) Airway pressure release ventilation (APRV) is a pressure support mode that allows spontaneous breathing throughout the ventilation cycle. It is time cycled between two levels of positive airway pressure. This mode increases the mean airway pressure without increasing the peak. It is managed with four variables, a time at a high pressure (T_{high}) and lower pressure (T_{low}) and the pressure high (P_{high}) and low (P_{low}). It is set to have a higher T_{high} to recruit alveoli with ventilation occurring with spontaneous breaths over the P_{high} and during the pressure release to P_{low}. APRV is a partial ventilatory support modality that can deliver full work of breathing if necessary.

(2) High-frequency oscillatory ventilation (HFOV) uses higher rates (180 to 300/min) and smaller tidal volumes than conventional modes. Adjustable variables include oscillatory frequency (Hz), FiO_2, amplitude or power (tidal volume), and inspiratory time. When utilizing HFOV, often as the final option on the ventilator algorithm, the patient must be deeply sedated and paralyzed.

4. Ventilator management

a. FiO2 should be adjusted to ensure adequate oxygenation with the lowest possible levels to prevent pulmonary oxygen toxicity.

b. Tidal volume. It has been shown that a lung-protective strategy, during an abdominal operation, with lower-volume ventilation may improve clinical outcomes (*N Engl J Med.* 2013;369:428–437), whereas a strategy to prevent atelectasis with a high PEEP leads to increased vasoactive drug requirements during the operation without reducing postoperative complications (*Lancet.* 2014;384:495–503). With ARDS, a randomized trial demonstrated improved survival in patients who were ventilated with low tidal volumes (6 mL/kg ideal body weight) compared with high tidal volumes (12 mL/kg) (*N Engl J Med.* 2000;342:1301–1308). As a result, the tidal volume should be decreased to maintain plateau

pressures <30 cm H_2O to minimize barotrauma but >20 cm H_2O to minimize atelectasis.

c. Ventilatory rate. Once the tidal volume has been determined, the rate is chosen to provide adequate minute ventilation and adjusted to optimize arterial pH and $PaCO_2$.

d. Inspiratory–expiratory (I:E) ratio. The normal I:E ratio is 1:2 to 1:3. Longer expiratory times allow patients with obstructive lung disease to exhale fully and prevent breath stacking. Longer inspiratory times, which decrease peak airway pressures, are useful in patients with low pulmonary compliance. Inverse-ratio ventilation takes advantage of breath stacking, using I:E ratios from 1:1 to 4:1. This improves gas exchange by progressive alveolar recruitment with a higher mean airway pressure. It is used most commonly with PCV.

e. PEEP increases functional residual capacity and improves V/Q matching by opening terminal airways and recruiting alveoli. A PEEP of 5 cm H_2O is considered minimal; higher levels are used with hypoxemia. PEEP levels >15 cm H_2O significantly increase the risk of barotrauma and spontaneous pneumothorax. **Continuous positive airway pressure (CPAP)** is PEEP applied to the spontaneously ventilating patient without additional inspiratory support.

f. Sedation and neuromuscular paralysis are often necessary in mechanically ventilated patients to control anxiety, synchronize breathing, and allow for rest. However, a recent clinical trial demonstrated that patients who receive no sedation have more ventilator-free days and shorter ICU lengths of stay (*Lancet.* 2010;375:475–480). The minimum sedation necessary should be used. The need for paralysis is rare, except in patients with severe respiratory failure and decreased pulmonary compliance. An evaluation of patients with severe ARDS found that a continuous infusion of cisatracurium was associated with improved survival (*N Engl J Med.* 2010;363:1107–1116). If paralytics are necessary, the patient must be adequately sedated and the paralytic should be discontinued as soon as possible. The extent of paralysis should routinely be assessed with neuromuscular monitoring, and

adequacy of anesthesia should be ensured with a processed electroencephalogram.

g. Prone positioning is a rescue strategy for patients with severe ARDS. Patients are placed in a prone position for a scheduled period of time daily. Theoretical benefits include recruitment of dorsal lung units, improved mechanics, decreased V/Q mismatch, and increased secretion drainage (*JAMA.* 2005;294:2889–2896). The PROSEVA study demonstrated a survival advantage with early use of prolonged prone positioning for patients with severe ARDS (*N Engl J Med.* 2013;368:2159–2168).

h. Weaning from mechanical ventilation. The patient who has required prolonged ventilatory support may need several days to weeks to wean because of marginal respiratory muscle strength and the time required for lung recovery. In general, hemodynamic instability and high work of breathing are contraindications to weaning. Reduction in the FiO_2 to 0.40 and PEEP to 5 cm H_2O is accomplished first. At Washington University in Saint Louis, patients receive daily PSV trials to assess suitability for extubation. A common tool is the rapid shallow breathing index (RSBI), calculated as respiratory rate/tidal volume, with a value >105 suggesting that discontinuation of assisted ventilation is unlikely to succeed.

5. Complications

a. ET tube dislodgment and patient self-extubation can become an emergency. For this reason, restraint of the patient's upper extremities is frequently required.

b. ET tube cuff leaks lead to a decreased airway pressure and return of expired volume. It may indicate that the ET tube needs to be advanced or exchanged.

c. Respiratory distress may occur during mechanical ventilation due to an acute change in the patient's status or ventilator malfunction. The first priority is to switch to bag ventilation using 100% oxygen to ensure adequate ventilation and oxygenation. Increased airway pressures may indicate obstruction of the tube with secretions, a kink, bronchospasm, pneumothorax, inadequate sedation, or migration of the ET tube into a mainstem bronchus.

Check the ET tube for patency; if there is a partial obstruction, use large-volume saline lavage to clear the tube. If the obstruction is complete, remove the ET tube and reintubate the patient. Listen closely for any change in breath sounds consistent with a pneumothorax, new lung consolidation, or pleural fluid collection. A less common but important cause of respiratory distress is PE. The results of an ABG and a chest x-ray are frequently helpful. In addition, a CT or bronchoscopy can be performed.

d. Barotrauma from high peak airway pressures can lead to subcutaneous emphysema, pneumomediastinum, and pneumothorax. A pneumothorax that develops while on positive-pressure ventilation is at risk for becoming a tension pneumothorax and is treated with a tube thoracostomy.

e. Oxygen toxicity refers to high intra-alveolar oxygen concentration causing lung damage. The precise mechanism is unknown, but likely involves oxidation of cell membranes due to oxygen radicals. FiO_2 should be weaned as soon as possible.

f. Tracheoinnominate fistula is caused by erosion of a tracheostomy tube into the innominate artery. It leads to accumulation of blood within the airway and hemorrhage. Emergent treatment consists of insertion of a finger into the tracheostomy and applying ventral pressure to compress the artery. Orotracheal intubation should be performed and a thoracic surgical consult obtained. This complication can be minimized by maintaining a cuff pressure <25 mm Hg.

6. ECMO may be the only remaining option if all other ventilator modes fail. It can be utilized as either veno-venous (VV) for pulmonary support or as veno-arterial (VA) for pulmonary and cardiac support. This method of support, with its necessary anticoagulation, is fraught with complications. In the critical care setting, it may be necessary as temporary support for a patient with reversible myocardial damage after surgery (Chapter 36). Another potential indication is VV-ECMO for ARDS, with a survival to discharge of 63% (*Lancet.* 2009;374:1351–1363).

IV. CIRCULATORY FAILURE: SHOCK

A. Shock is defined by global tissue hypoxia and occurs when the supply

of oxygen is insufficient to meet metabolic demands.

B. Classification and Recognition of Shock. Early recognition and prompt intervention is critical (Table 8-3). The patient's recent history, laboratory values, and physical examination are usually sufficient for determining the etiology.

1. **Hypovolemic shock** results from loss of circulating blood volume caused by acute hemorrhage, fluid depletion, or dehydration. Patients are peripherally vasoconstricted, tachycardic, and have low jugular venous pressure.
2. **Distributive shock** is a hyperdynamic state consisting of tachycardia, vasodilation, decreased SVR, and increased CO. The most common causes include sepsis, neurogenic shock, adrenal insufficiency, and liver failure. **Neurogenic shock** results from interruption of the spinal cord at or above the thoracolumbar sympathetic nerve roots, which produces loss of sympathetic tone, causing vasodilation. Patients are peripherally vasodilated and tachycardic. Jugular venous pressure is low.

TABLE 8-3 Clinical Parameters in Shock

Shock Classification	Skin	Jugular Venous Distention	Cardiac Output	Pulmonary Capillary Wedge Pressure	Systemic Vascular Resistance	Mixed Venous Oxygen Content
Hypovolemic	Cool, pale	↓	↓	↓	↑	↓
Cardiogenic	Cool, pale	↑	↓	↑	↑	↓
Septic						
Early	Warm, pink	↑↓	↑	↓	↓	↑
Late	Cool, pale	↓	↓	↓	↑	↑↓
Neurogenic	Warm, pink	↓	↓	↓	↓	↓

3. **Obstructive shock** results from etiologies that prevent adequate CO but are not intrinsically cardiac in origin. This may be caused by PE, tension pneumothorax, or cardiac tamponade. Jugular venous pressure is elevated while the peripheral tissues demonstrate vasoconstriction.
4. **Cardiogenic shock** results from inadequate CO due to intrinsic cardiac failure. Diagnosis may require echocardiography. These patients typically are peripherally vasoconstricted and tachycardic with an elevated jugular venous pressure.

C. Interventions Common to All Types of Shock. The goal of therapy is to ensure adequate oxygen delivery. Because oxygen delivery is proportional to SaO_2, hemoglobin concentration, and CO, each should be optimized.

1. **SaO2.** Supplemental oxygen should be administered or an airway placed to achieve a SaO_2 >92%.
2. **Hemoglobin concentration.** For most critically ill patients, a transfusion threshold of 7 g/dL is appropriate, except with an ongoing

myocardial infarction or severe ischemic cardiomyopathy (*N Engl J Med*. 1999;340:409–417).

3. **CO.** A continuous cardiac monitor provides the heart rate and indirect clues about stroke volume. The atrial contraction provides approximately 15% to 25% of preload; therefore, atrial fibrillation can significantly reduce CO. Other tachyarrhythmias decrease diastolic ventricular filling and may reduce CO despite the elevated HR, typically occurring at an HR >140. With the exception of the patient in pulmonary edema, patients in circulatory shock should initially receive 10 to 20 mL/kg bolus of a crystalloid solution.
4. Palpable pedal pulses and urine output exceeding 1 mL/kg/hr indicate good CO. A metabolic acidosis can reflect the depth of circulatory compromise and the adequacy of resuscitation. Infusion of sodium bicarbonate should be reserved for patients with a pH of less than 7.15 because it may worsen intracellular pH as it is converted to CO_2 at the tissue level.

D. Specific Therapy

1. **Hypovolemic shock.** Therapy focuses on control of ongoing loss and restoration of intravascular volume. Patients with blood losses of up to 20% can be resuscitated using crystalloid solutions. However, because salt solutions equilibrate with the interstitial space, volume replacement requires three times the estimated volume deficit. Patients in whom diaphoresis, ashen facies, and hypotension develop have lost 30% or more of their blood volume and require transfusion. To achieve rapid infusion rates, short, large-bore intravenous catheters in a peripheral vein are best. If this is not possible, an 8.5-Fr sheath in a central vein is highly effective. In addition, if intravenous attempts are unsuccessful, intraosseous access can be quickly obtained. **A multilumen central line is not effective for rapid volume resuscitation due to its high resistance to flow (resistance is proportional to catheter length and inversely proportional to catheter lumen radius raised to the fourth power).** Hypothermia is aggravated by rapid infusion of room temperature crystalloid and refrigerated blood, impairing oxygen unloading and compromising coagulation; therefore fluids and blood products should be warmed. With adequate volume resuscitation, vasoactive agents can usually be avoided.

2. **Distributive shock**

   a. **Septic shock (see Section V.C).**

   b. **Systemic inflammatory response syndrome (SIRS)** may result from noninfectious causes of inflammation. Treatment is supportive until the inflammatory process resolves.

   c. **Critical illness–related corticosteroid insufficiency (CIRCI)** can result from adrenal insufficiency or glucocorticoid resistance. The diagnosis and treatment of adrenal insufficiency in septic shock are evolving. The use of corticosteroids is not without risk as it does increase the risk of infection (*N Engl J Med.* 2008;358:111–124). Per ACCM 2008 guidelines, adrenal insufficiency is best diagnosed by an increase in cortisol level of <9 μg/dL after a cosyntropin stimulation test or random total cortisol level <10 μg/dL. These guidelines state that patients with primary adrenal insufficiency or those with septic shock refractory to fluid resuscitation and vasopressors, without performing a cosyntropin stimulation test, should be treated with moderate-dose hydrocortisone due to a faster resolution of shock seen in multiple studies and a survival advantage (*Crit Care Med.* 2008;36:1937–1949). Corticosteroids in the critically ill remain a topic of controversy. A recent meta-analysis evaluating the use of steroids for septic shock did not show a survival advantage, though again, there was faster resolution of shock (*Anesth Analg.* 2014;118:346–357). Future studies will need to clarify the utility of corticosteroids and any subgroups where they are beneficial.

   d. **Neurogenic shock.** The initial intervention is volume infusion. A peripheral vasoconstrictor, phenylephrine or norepinephrine, is administered to increase vascular tone if hypotension is refractory to volume infusion. Dopamine is used in patients with neurogenic shock and bradycardia. Because patients with spinal shock tend to equilibrate body temperature with their environment, fluids and room temperature must be kept warm.

3. **Obstructive shock.** Tension pneumothorax is treated by needle decompression followed by tube thoracostomy. Pericardial tamponade is treated by needle decompression, often with catheter placement for drainage. The treatment of a PE varies based on the degree of hemodynamic compromise. Options include systemic

anticoagulation, thrombolysis, and surgical clot removal. IVC filters are used in patients with a contraindication to anticoagulation or with progression of thrombus on therapeutic anticoagulation.

4. **Cardiogenic shock.** Management is directed toward maintaining adequate myocardial perfusion and CO with volume expansion and vasoactive medications (see Table 8-4). Initial treatment is often guided by CVP measurements or PA catheter data, while the precipitating cause is identified and treated. CVP in this setting is useful for assessment of RV function and not as a marker of volume status (*Chest.* 2008;134:172–178). Intra-aortic balloon counterpulsation may be necessary before and during recovery from definitive surgical treatment. If perfusion remains inadequate, the only remaining option is mechanical circulatory support.

TABLE 8-4 Inotropes and Vasoactive Drugs and Their Specific Actions

Class and Drug	Blood Pressure	Systemic Vascular Resistance	Cardiac Output	Heart Rate	Inotrope: Low Dose	Inotrope: High Dose	Renal Blood Flow	Coronary Blood Flow	MvO_2
Alpha only									
Phenylephrine	↑↑	↑↑↑	↓	↓	±	±	↓↓↓	±↑↑	↑
Alpha and beta									
Norepinephrine	↑↑↑	↑↑↑	↑↑↑	↑±	↑	↑	↓↓↓	↑↑	↑↑
Epinephrine	↑↑↑	↑↑↑	↑↑↑	↑↑↑	↑↑	↑↑↑	↓±	↑↑	↑↑↑
Dopamine	↑↑	↑↑	↑↑↑	↑↑	±	↑↑	↑↑↑	↑↑	↑↑
Beta only									
Dobutamine	±	↓↓↓	↑↑↑	↑↑	↑↑↑	↑↑↑	±	↑↑↑	↑↑↑
Beta-blocker									
Metoprolol	↓	↓	↓↓	↓↓↓	↓↓	↓↓↓	±	↓↓	↓↓
Other									
Nitroglycerine	±↓	↓↓	↑↑	±	±	±	±↑	↓	↓↓
Hydralazine	↓↓	↓↓↓	↑↑	↑↑	±	±	±↑	↓	↓↓
Nitroprusside	↓↓↓	↓↓↓	↓↓↓	±↑	±	±	↑↑	±	↓↓

MvO_2, mixed venous oxygen saturation.

V. SEPSIS

A. Definition. Sepsis is defined as SIRS with a documented or presumed infection. The clinical definition of SIRS requires two of the following: Body temperature >38°C or <36°C, heart rate >90 beats/min, respiratory

rate >20/min or $PaCO_2$ <32, and WBC count >12 or <4 or >10% bands. Severe sepsis is multiple-organ dysfunction or hypoperfusion (septic shock) resulting from infection.

B. Diagnosis

1. Cultures should be obtained as part of the initial evaluation, at least one of which should be drawn percutaneously, prior to the initiation of antibiotics. This will allow a more specific antibiotic regimen once susceptibilities return.

C. Treatment

1. Infection

a. Antibiotic therapy

(1) Broad-spectrum intravenous antibiotics should be initiated within the first hour (*Chest.* 2000;118:146–155). The use of antifungal therapies and agents directed at highly resistant gram-negative rods, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococcus, and resistant pneumococcus should be guided by the clinical situation and local susceptibility patterns.

(a) The following increase risk for infection with resistant organisms:

(i) Prior antibiotic treatment.

(ii) Prolonged hospitalization.

(iii) Presence of invasive devices.

(2) For a hospitalized patient who becomes septic with a presumed pneumonia, a common initial broad-spectrum regimen consists of vancomycin and cefepime. For intra-abdominal infections, therapies commonly start with vancomycin and piperacillin/tazobactam with the possible addition of an antifungal.

b. Source control, drainage, debridement, or removal of the infectious source, is imperative.

2. Circulatory support

a. Volume resuscitation. Early goal-directed therapy consists of volume resuscitation for a CVP of 8 to 12, MAP >65, UOP >0.5 mL/kg/hr, and mixed SvO_2 >70% (*N Engl J Med.* 2001;345:1368–1377). This has been practiced for septic patients for a decade;

however, a recent randomized trial showed no difference in survival with this protocol over standard medical judgment (*N Engl J Med.* 2014;370:1683–1693). Volume resuscitation remains a cornerstone, but can be used more judiciously.

b. Vasoactive medications. Septic patients who fail to achieve rapid hemodynamic stability with fluids are started on a vasoactive medication. Most practitioners favor norepinephrine for its vasoconstrictive properties as well as its ability to increase CO. Dopamine is still used by some, but it is associated with higher rate of dysrhythmias (*N Engl J Med.* 2010;362:779–789; *Shock.* 2010;33:375–380). The addition of low-dose vasopressin increases MAP, SVR, and urine output in septic patients who are hyporesponsive to catecholamines. This may spare patients from high-dose norepinephrine, although its impact on survival is unclear.

VI. UPPER GASTROINTESTINAL HEMORRHAGE PROPHYLAXIS.

Patients in the ICU are at increased risk for stress-induced mucosal ulceration and GI hemorrhage. Risk factors include head injury (Cushing ulcers); burns (Curling ulcers); prolonged mechanical ventilation; history of peptic ulcer disease; NSAIDS or steroids; and the presence of shock, renal failure, portal hypertension, or coagulopathy. An H_2-receptor antagonist should be used to maintain mucosal integrity in these patients. Proton-pump inhibitors are preferred by some, and they should be used in patients who bleed despite H_2-receptor antagonists. The use of stress ulcer prophylaxis for a patient without an above-listed risk factor should be avoided due to an increased risk of *Clostridium difficile*–associated diarrhea (*J Crit Care*. 2014;696:E11-5).

VII. ANEMIA.

The prospective Transfusion Requirements in Critical Care (TRICC) trial reported that **transfusing all patients to a hemoglobin of 10 mg/dl either has no effect or may actually decrease survival in the critically ill** (*N Engl J Med.* 1999;340:409–417). A restrictive transfusion strategy (hemoglobin <7 mg/dl) is recommended in critically ill patients; except in those with acute coronary syndrome, severe hypoxemia, or active hemorrhage. A randomized controlled trial demonstrated that administration of recombinant erythropoietin did not reduce the rate of

transfusion or reduce mortality in critically ill patients, but increased the risk of thrombotic events (*N Engl J Med.* 2007;357:965–976).

VIII. BLOOD GLUCOSE CONTROL. A study of randomly assigned surgical patients to tight glucose control (blood glucose goal: 80 to 110 mg/dL) versus conventional control (blood glucose goal: 180 to 200 mg/dl) showed nearly a twofold decrease in mortality in the tight glucose control group and reduced in-hospital mortality, bloodstream infections, acute renal failure, number of red cell transfusions, and critical illness polyneuropathy (*N Engl J Med.* 2001;345:1359–1367). however, a follow-up study in medical patients did not demonstrate such a benefit (*N Engl J Med.* 2006;354:449–461). hypoglycemia remains a major risk of tight glucose control and has been associated with increased mortality. A goal blood sugar of less than 140 mg/dL seems safe and beneficial; further studies are required to determine the response of different patient populations to varying intensities of insulin.

IX. MEDICATIONS. Commonly used drugs and doses (Table 8-5).

TABLE 8-5 Drugs Commonly Used in the Intensive Care Unit

Drug	Dilution (Concentration)	Loading Dose	Dose	Comments
Diltiazem	125 mg/125 mL 0.9% NaCl or D5W (1 mg/mL)	0.25 mg/kg (followed by 0.35 mg/kg if needed)	5–15 mg/hr	May cause hypotension
Dobutamine	250 mg/100 mL 0.9% NaCl (2,500 µg/mL)		2–20 µg/kg/min	Selective inotropic (beta) effect; may cause tachycardia and arrhythmias
Dopamine	400 mg/250 mL 0.9% NaCl or D5W (1,600 µg/mL)		Dopa, 1–3 µg/kg/min; alpha, 3–10 µg/kg/min; beta, 10–20 µg/kg/min	Clinical response is dose and patient dependent; may cause arrhythmias and tachycardia
Epinephrine	5 mg/500 mL 0.9% NaCl or D5W, or 4 mg/100 mL 0.9% NaCl or D5W		0.01–0.05 µg/kg/min	Mixed alpha and beta effects; use central line; may cause tachycardia and hypotension
Esmolol	2.5 g/250 mL 0.9% NaCl or D5W (10 mg/mL)	500 µg/kg/min for 1 min (optional)	50–300 µg/kg/min	Selective $beta_1$-blocker; $T_{1/2}$ 9 min; not eliminated by hepatic or renal routes; may cause hypotension
Heparin	25,000 units/250 mL 0.45% NaCl (100 units/mL)	60 units/kg	14 units/kg/hr	Obtain PTT every 4–6 hr until PTT is 1.5–2 times control; may cause thrombocytopenia

Lidocaine	2 g/500 mL D5W (4 mg/mL)	1 mg/kg (can repeat two times if needed)	1–4 mg/min	Dose should be decreased in patients with hepatic failure, acute MI, CHF, or shock
Nitroglycerin	50 mg/250 mL D5W (200 µg/mL)		5–20 µg/min	Use cautiously in right-sided MI
Nitroprusside	50 mg/250 mL D5W (200 µg/mL)		0.25–10 µg/kg/min	Signs of toxicity include metabolic acidosis, tremors, seizures, and coma; thiocyanate may accumulate in renal failure
Norepinephrine	8 mg/500 mL D5W (16 µg/mL)		0.01–0.1 µg/kg/min	Potent alpha effects; mainly $beta_1$ effects at lower doses; use central line
Phenylephrine	10 mg/250 mL 0.9% NaCl or D5W (40 µg/mL)		10–100 µg/min	Pure alpha effects; use central line; may cause reflex bradycardia and decreased cardiac output
Vasopressin	20 units/100 mL NS (0.2 units/mL)		0.04 units/min	Do not titrate; higher doses may cause myocardial ischemia

CHF, congestive heart failure; D5W, 5% dextrose in water; MI, myocardial infarction; PTT, partial thromboplastin time; $T_{1/2}$, terminal half-life.

CHAPTER 8: CRITICAL CARE

Multiple Choice Questions

1. **A patient develops significant hemoptysis and shortness of breath minutes after insertion of a pulmonary artery catheter into a branch of the left pulmonary artery and measurement of the wedge pressure. Management should be:**

   a. Emergent tracheostomy.
   b. Thrombolytics followed by systemic anticoagulation or IVC filter placement.
   c. Changing to pressure-controlled ventilation with a reverse I:E ratio.
   d. Placing the patient with the side of the PA catheter in left lateral decubitus position and urgent thoracic surgery consult.
   e. Placing the patient with the side of the PA catheter in right lateral decubitus position and urgent thoracic surgery consult.

2. **Concerning the sedated patient for mechanical ventilation:**

   a. Sedation should be deep in order to minimize any discomfort when there is no chance of extubation.
   b. The chosen method of sedation and goal level of sedation should be communicated to the bedside nurse who will titrate dosage.
   c. For patients receiving neuromuscular blockade, a BIS of <90 is considered sufficient.
   d. Due to a lack of analgesic properties, propofol often leads to hypertension.
   e. Ketamine should be avoided in patients who have depressed cardiac function.

3. **A 72-year-old male has been admitted to the surgical ICU for 16 days after surgical repair of a spontaneous duodenal perforation due to steroids for his SLE. He developed pneumonia and has required mechanical ventilation since his operation. He underwent tracheostomy placement on POD 6. Yesterday he had a small amount of blood from his tracheostomy which stopped spontaneously. He now develops significantly more hemoptysis**

through his tracheostomy and his respiratory status is rapidly decompensating. Your next step should be to:

a. Remove the tracheostomy, place your finger through the tracheostomy site, and apply pressure to the innominate artery. The patient should be intubated.
b. Urgent CT to evaluate for potential PE followed by systemic anticoagulation or thoracic surgical consult for emergent thrombectomy.
c. Urgent ENT consult for bleeding likely from the nasopharynx.
d. Tube thoracostomy placement.
e. Transfuse 2 units of PRBCs through a level I infuser into a large peripheral IV followed by FFP and platelets as with a massive transfusion protocol.

4. **The ventilator mode airway pressure release ventilation (APRV) or BiLevel:**

a. Increases the peak airway pressure to open alveoli.
b. Provides additional time for ventilation to eliminate CO_2.
c. Usually utilizes an I:E of 1:2.
d. Increases the mean airway pressure without increasing the peak.
e. Requires a paralyzed patient.

5. **A tracheostomy is placed for a patient who is anticipated to have a prolonged ventilatory course. He does better than anticipated and is weaned from the ventilator to tracheostomy collar 2 days after placement. He is in bed and during a roll his tracheostomy collar gets caught and pulls his tracheostomy tube out. His respiratory status declines quickly. The next step is:**

a. Bag-mask ventilation over the tracheostomy site.
b. Replacement of the tracheostomy tube and bag-mask ventilation until an appropriate oxygen saturation is reached.
c. Intubation from above with appropriate sedation.
d. Bronchoscopy to clear any mucus plugs.
e. Blocking the tracheostomy site to prevent air leakage so the patient can breathe normally.

6. A patient who comes into the emergency department with unknown history is hypotensive. Initial physical examination findings are increased jugular venous distention and cool skin. After PA catheter placement you see decreased cardiac output with increased wedge pressure and increased systemic vascular resistance. This patient is most likely suffering from:

a. Hypovolemic shock.
b. Neurogenic shock.
c. Late septic shock.
d. Early septic shock.
e. Cardiogenic shock.

7. Steroid administration for septic shock:

a. Should be given if the cosyntropin stimulation test has a δ >9 μg/dL.
b. Should not be given if the random total cortisol level is <10 μg/dL.
c. Has been shown to decrease duration of sepsis and improve survival in all studies.
d. Should be high-dose dexamethasone.
e. Should be given to patients who do not respond to volume and vasoactive medications without evaluation of cortisol level.

8. A patient on a mechanical ventilator for ARDS has required increasing pressure for oxygenation. He suddenly develops respiratory distress with desaturation, tachycardia, and hypotension. Initially you increase the FiO_2 and the pressure, but the situation continues to deteriorate. On physical examination, you note severely diminished breath sounds on the right and you notice the CVP is much higher. Your next step is:

a. Bronchoscopy to remove a mucus plug.
b. Needle decompression followed by tube thoracostomy.
c. Volume resuscitation and more advanced ventilator settings.
d. Chest CT scan to evaluate for PE.
e. Decompressive laparotomy for abdominal compartment syndrome.

9. Stress ulcer prophylaxis:

a. Should be administered only in patients with risk factors admitted to the ICU.
b. Should be administered to all patients admitted to the ICU.
c. Should be given to patients who have an NG tube.
d. Does not increase the risk of *C. difficile* infection.
e. Is not necessary in patients receiving corticosteroids.

10. For which of the following patients, currently in the ICU, is blood transfusion indicated?

a. A 26-year-old male admitted after a motorcycle accident with femur fracture s/p ORIF POD 2 with a hemoglobin of 7.4 mg/dL with low UOP.
b. A 76-year-old patient with ESRD who underwent brachiocephalic graft placement complicated by a postoperative pneumonia with a hemoglobin of 8.2.
c. An 84-year-old male POD 2 after a femoral–popliteal bypass complicated by postoperative NSTEMI and a hemoglobin of 7.9 mg/dL.
d. A 56-year-old male after left hemicolectomy with the intraoperative course complicated by significant blood loss with a hemoglobin of 8.6 mg/dL and a small norepinephrine requirement.
e. A 94-year-old female admitted after hepaticojejunal bypass for a mass obstructing the duodenum with a hemoglobin of 8.2 mg/dL.

9 Trauma Resuscitation and Adjuncts

Emily J. Onufer and Jason A. Snyder

Injury remains a leading cause of death and disability around the world. Trauma deaths have a **trimodal distribution**: (1) immediate death occurring at the time of injury due to devastating wounds; (2) early death occurring within the first few hours of injury due to major intracranial, thoracic, abdominal, pelvic, and extremity injuries; and (3) late death occurring days to weeks after the initial injury due to secondary complications (sepsis, acute respiratory distress syndrome, systemic inflammatory response syndrome, or multiple organ dysfunction/failure). This chapter outlines an overall approach to trauma care, based on Advanced Trauma Life Support (ATLS) guidelines. Initial hospital care has two main components: the primary and secondary surveys. The goal of the **primary survey** is to identify and treat those injuries that can result in early death within the first few minutes of injury. The goal of the **secondary survey** is to initiate and maintain the resuscitation of physiologic functions, catalogue all injuries sustained, and institute appropriate therapy and supportive measures.

I. PREHOSPITAL CARE.

Prehospital care of the trauma patient is provided by a wide range of emergency medical service (EMS) personnel with varying levels of training (first responders, emergency medical technicians, and paramedics). These professionals are responsible for performing the three major functions of prehospital care: (1) assessment of the injury scene, (2) stabilization and monitoring of injured patients, and (3) safe and rapid transportation of critically ill patients to the appropriate trauma center.

A. EMS Evaluation

The **MVIT** (*m*echanism, *v*ital signs, *i*njury inventory, *t*reatment) system of reporting is one method of communicating data to the trauma team in an efficient and organized manner. The **mechanism of trauma** can help

determine the pattern and severity of injuries sustained in the event (Table 9-1). **Vital signs**, including level of consciousness and voluntary movement, give insight into the clinical trajectory of the patient and are a key element in leveling trauma. Important prehospital observations (e.g., prolonged extrication, crushed under a heavy object, significant exposure) alert the trauma team to critical secondary injuries, including rhabdomyolysis, traumatic asphyxia, and hypothermia, which can have a profound impact on outcome.

B. Prehospital Treatment

This is aimed at stabilization of the injured patient and involves securing an airway, providing adequate ventilation with administration of oxygen, assessing and supporting circulation, and stabilizing the spine via immobilization on a backboard and with a properly fitting hard cervical collar. Any patient suspected of having injuries to the cervical spine must be placed in a rigid collar.

TABLE 9-1 Mechanism of Trauma With Possible Associated Injuries

Mechanism	Impact	Possible Associated Injuries
Front-end car collision	Direct impact between driver's knees and dashboard	• Patellar fracture • Posterior knee dislocation (with popliteal artery injury) • Femoral shaft fracture • Posterior acetabular rim fracture
Feet-first fall from significant height	Axial loading	• Calcaneal fracture • Lower extremity long bone fracture • Acetabular injury • Lumbar spine compression fracture
Pedestrian struck by	Impact on car	• Injury to tibia and fibula

motor vehicle	bumper, windshield, hood, or pavement	(striking bumper) • Head injury (striking windshield/hood) • Injury to upper extremity (extended arm hitting pavement)

Child struck by motor vehicle	Impact on car bumper, windshield, hood, or pavement	• Waddell triad:
		  • Femur fracture (striking bumper)
		  • Abdominal solid organ injury (liver or spleen; striking fender)
		  • Opposite side head injury (landing on pavement)

C. Preparation of the Trauma Bay

Mobilization of all trauma team personnel and resources is essential prior to the trauma patient's arrival. Team leaders should assign roles, and those who are likely to have patient contact should wear proper standard precaution devices. Additionally, airway equipment, warmed IV fluids, and other needed supplies should be strategically placed. Protocols to ensure prompt response by laboratory and radiology personnel should be activated.

II. Primary Survey.

The primary survey is a systematic, rapid evaluation for immediate threats to life, following the **mnemonic ABCDE** (***a*irway with cervical spine control, *b*reathing and ventilation, *c*irculation and hemorrhage control, *d*isability, *e*xposure and *e*nvironmental control**). Concurrently with the primary survey, a rudimentary history is obtained (if possible). This history follows the acronym **AMPLE** (*a*llergies, *m*edications, *p*ast medical/surgical history, *l*ast oral intake, *e*vents surrounding the injury).

A. Airway.

Establishing a patent airway is the highest priority in order to prevent irreversible brain damage and should always be secured under cervical spine control. A patient who is able to respond verbally has a patent airway, and those who cannot are assumed to have an obstructed

airway until proven otherwise. Every trauma patient initially should have oxygen administered (via nasal cannula or bag-valve-facemask) and pulse oximeter placed.

1. **Basic maneuvers.** Simple suctioning can remove blockages caused by mechanical obstruction. In the semiconscious or unconscious patient, the tongue itself can occlude the airway and the jaw-thrust maneuver displaces the tongue anteriorly from the pharyngeal inlet. In the unconscious patient, the placement of an oropharyngeal airway (or, in the absence of head trauma, a nasopharyngeal airway) can mechanically displace the tongue anteriorly. In the semiconscious patient, the nasopharyngeal airway can be used (in the absence of facial trauma). Both devices, however, can cause significant irritation of the upper aerodigestive tract, with resultant vomiting, and thus should be avoided in fully conscious patients.
2. **Tracheal intubation** is indicated in any patient in whom concern for airway integrity exists (e.g., unconscious or semiconscious patients, patients with mechanical obstruction secondary to facial trauma or debris, combative and hypoxic patients). The preferred method of intubation is via the orotracheal route using **rapid sequence induction** (**RSI**) (Fig. 9-1). Once the airway is secured, additional placement of an orogastric tube can also help prevent subsequent emesis and aspiration.
3. **Cricothyrotomy** is the method of choice for establishing a surgical airway in adults after unsuccessful orotracheal attempts or with massive facial trauma. The cricothyroid membrane is easily palpated between the cricoid cartilage and the larynx. Being both superficial and relatively avascular, it provides rapid, easy access to the trachea. A 1.5-cm longitudinal skin incision is made over the membrane and after spreading of the soft tissues, a small transverse incision is made in it. The hole is expanded using a scalpel handle or tracheal spreader. A 6.0-mm endotracheal or tracheostomy tube is inserted into the trachea through the cricothyrotomy, the balloon is inflated, and the tube sutured into place. Cricothyrotomy is contraindicated in children younger than 12 years of age because of their small cricothyroid membranes and proximity to the vocal cords. In this situation, percutaneous transtracheal ventilation is an alternative.
4. **Percutaneous transtracheal ventilation** can provide a temporary

airway until a formal surgical airway can be obtained, especially in young children. A small cannula (usually a 14-gauge intravenous catheter) is placed through the cricoid membrane. The cannula is connected to oxygen tubing containing a precut side hole. Temporary occlusion of the side hole provides passage of oxygen into the lungs via the cannula. Exhalation occurs passively through the vocal cords. Alveolar oxygen concentrations are transiently maintained for approximately 30 to 45 minutes.

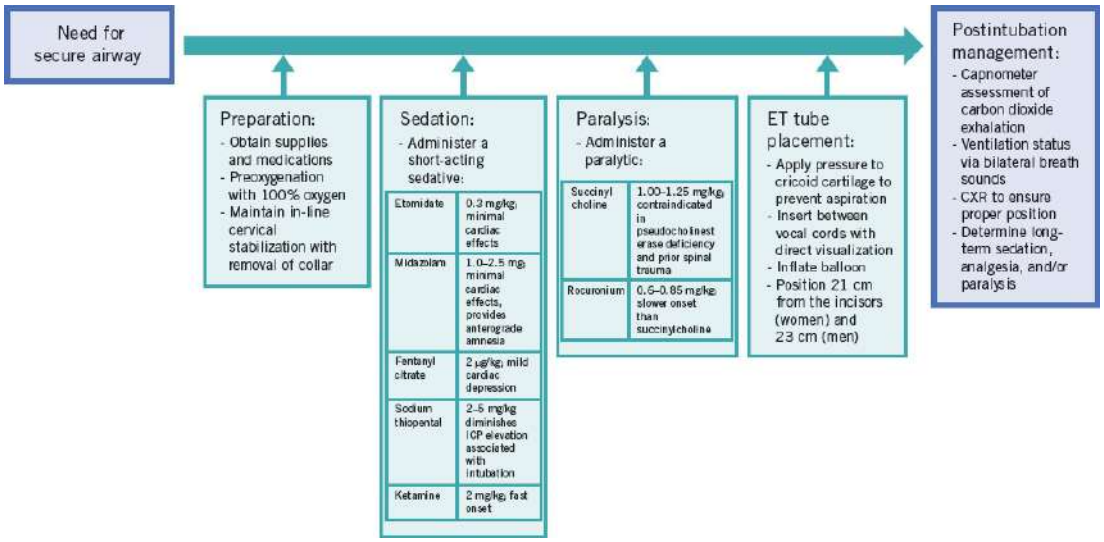


FIGURE 9-1 Rapid sequence intubation to achieve endotracheal intubation.

B. Breathing. Once an airway is established, attention is directed at assessing the patient's oxygenation and ventilation status. A patent airway does not always ensure adequate breathing. Signs of dysfunctional breathing can include: abnormal or unequal breath sounds, accessory muscle usage, or abnormal chest wall motion. In the unstable patient, treatment should be immediate and not be delayed for imaging studies.

1. **Pneumothorax or hemothorax.** There are three types of pneumothoraces—tension, open, and simple. Signs of a tension pneumothorax include the absence of breath sounds, hyperresonance in the lung field, tracheal deviation away from the side of the abnormality, and associated hypotension due to decreased venous return. Absent or decreased breath sounds in a lung field without tracheal deviation usually indicate a simple pneumothorax or

hemothorax on the affected side. Immediate needle decompression is indicated for a symptomatic pneumothorax. Any chest wound communicating with the pleural space that is greater than two-thirds the diameter of the trachea will preferentially draw air into the thorax ("sucking chest wound"), thus deemed an open pneumothorax. These must be covered with a partially occlusive bandage secured on *three* sides, forming a one-way valve and preventing development of a tension pneumothorax. Prompt tube thoracostomy should follow placement of the partially occlusive dressing.

a. Needle decompression. Needle decompression involves placement of a 14-gauge intravenous catheter in the second intercostal space in the midclavicular line or through the 4th intercostal space in the midaxillary line. A tube thoracostomy should promptly follow decompression. A chest x-ray should be obtained only after the chest tube placement is complete.

b. Tube thoracostomy. Treatment for a pneumothorax or hemothorax consists of a **tube thoracostomy** (28 to 32 Fr for a pneumothorax, 32 to 36 Fr for a hemothorax). The patient is positioned at a 30- to 45-degree angle in a semidecubitus position by placing a bump under the affected side, if possible based on spinal clearance. The patient's ipsilateral arm is extended and secured above the head in order to expose the axillary area. The tube should typically be placed in the "safe triangle" delineated by the lateral border of the pectoralis major muscle, the anterior border of the latissimus dorsi muscle, and an imaginary line at the level of the nipple. With the skin prepped and draped, assuming time and patient status permits, lidocaine is infiltrated into the 4th or 5th intercostal space at the anterior axillary line at the location of the intended incision. A 2- to 3-cm transverse incision is then made through the skin and subcutaneous tissue and a curved clamp is used bluntly to dissect an oblique tract to the rib. The clamp is advanced over the top of the rib to puncture and spread the parietal pleura with care taken not to stab the clamp into the lung parenchyma. An efflux of air or fluid is usually encountered. A finger is introduced into the tract to ensure passage into the pleural space and to lyse any adhesions at the point of entry, being wary of potentially fractured ribs. The thoracostomy tube is then introduced into the pleural space and is

directed posteriorly or basally for a dependent effusion and apically for a pneumothorax. The tube is advanced until the last hole on the tube is clearly inside the thoracic cavity. When the tube is positioned properly and functioning adequately, it is secured to the skin and covered with an occlusive dressing to prevent air leaks. A U-stitch around the tube may be placed for use as a purse-string suture to close the tract once the tube is removed. The chest tube should be connected to an underwater seal-suction device adjusted to −20 cm water suction. A chest radiograph is obtained to assess for lung reexpansion and tube position.

2. **Flail chest.** Paradoxical chest wall motion with spontaneous respirations indicates a flail chest (three or more ribs with two or more fractures per rib). Pulmonary contusion often accompanies such an injury. Chest x-ray often reveals the extent of fractures and underlying lung injury. Treatment involves adequate pain control (often with epidural analgesia), aggressive pulmonary toilet, and respiratory support. Many of these patients will require early mechanical ventilatory support. Intensive care unit (ICU) monitoring is recommended for elderly or debilitated patients.
3. **Tracheobronchial disruption.** Severe subcutaneous emphysema with respiratory compromise can suggest tracheobronchial disruption. The tube thoracostomy placed on the affected side will reveal a rolling air leak, and the collapsed lung may fail to reexpand. Bronchoscopy is diagnostic. Treatment involves intubation of the unaffected bronchus followed by operative repair.

C. Circulation. The goal of this portion of the primary survey is to identify and treat the presence of shock, defined as the inadequate delivery of oxygen and nutrients to tissue. Initially, all active external hemorrhage is controlled with direct pressure or tourniquets, and obvious fractures are stabilized. The pulse is characterized, and a blood pressure (BP) is obtained. The skin perfusion is determined by noting skin temperature and evaluating capillary refill. Over time, end-organ perfusion during a trauma resuscitation is estimated using mental status and urine output as markers. The etiologies of shock seen in the traumatically injured patient can be divided into three broad categories: hemorrhagic, cardiogenic, and neurogenic.

1. **Hemorrhagic shock.** This is the most common type of shock and occurs as a result of decreased intravascular volume secondary to hemorrhage (Table 9-2). In its severe form, it can manifest as a rapid pulse; decreased pulse pressure; diminished capillary refill; and cool, clammy skin. Therapy involves controlling external or internal hemorrhage and restoring intravascular volume.

TABLE 9-2 Associated Features and Classification of Hemorrhagic Shock

Features	Class I	Class II	Class III	Class IV
Blood loss (mL)	Up to 750	750–1500	1500–2000	>2000
Blood loss (% blood volume)	Up to 15%	15–30%	30–40%	>40%
Pulse rate	<100	>100	>120	>140
Blood pressure (mm Hg)	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Urinary output (mL/hr)	>30	20–30	5–15	Negligible

   a. **External hemorrhage control.** Control of external hemorrhage is best achieved with direct pressure to the bleeding site or upstream vascular supply. Additionally, **tourniquets** can be placed by EMS in the field to reduced blood loss from extremities. Common areas of external hemorrhage that can easily be missed include the posterior scalp, axillae, perineum, and posterior trunk.

   b. **Access.** The patient should have **two large-bore IV lines** placed (14- or 16-gauge), preferably in the antecubital fossae. If a peripheral IV catheter cannot be placed secondary to venous collapse, **central venous access** should be obtained with an 8.5-Fr catheter (cordis catheter) placed via the Seldinger technique into

the femoral vein. The subclavian and internal jugular veins should be reserved for those patients in whom major venous intra-abdominal injury or pelvic fractures could prevent venous return from the femoral vein. A blood specimen should be simultaneously obtained for cross-matching and for any other pertinent labs.

c. Resuscitation. Rapid resuscitation without hemorrhage control worsens the "lethal triad" of hypothermia, acidosis, and coagulopathy; permissive hypotension (SBP goal 80 to 90 mm Hg) has been proven to increase survival in trauma patients (*J Trauma*. 2015;78(4):687–695). Resuscitation should consist of an initial bolus of warm 2 L crystalloid solution (children should receive an initial bolus of 20 mL/kg). Then hemostatic resuscitation begins with the very early use of blood products to prevent dilutional coagulopathy and treat intrinsic acute traumatic coagulopathy. Institutional protocols should be established to determine massive transfusion ratios. The PROPPR trial suggests that blood products should be administered in a 1 PRBC:1 platelet:1 fresh frozen plasma ratio (*JAMA*. 2015;313(5):471–482). If time has not allowed proper cross-matching, type-O blood should be used. Premenopausal women should receive Rh negative (Rh−) blood. Men and postmenopausal women can receive either Rh− or Rh+ blood. In addition to hemorrhage, trauma can also lead to transient hyperfibrinolysis. In the CRASH-2 trial, tranexamic acid (TXA), an antifibrinolytic, was found to improve survival when administered early in patients with known or suspected massive hemorrhage (*Lancet*. 2010; 376(9734):23–32).

d. Internal hemorrhage control.

(1) Pelvic hemorrhage. If blood loss is suspected secondary to severe pelvic trauma, a **pelvic binder** or a sheet should be placed around the greater trochanters of the femurs.

(2) The emergency department thoracotomy (EDT) allows for identification and control of both intrathoracic and subdiaphragmatic hemorrhage and is a procedure of last resort in a moribund patient. Indications for this procedure are divided into strongly recommended and conditionally

recommended (Table 9-3; *J Trauma*. 2015;79(1):159–173). Position the patient supine with the left arm elevated and then perform a left anterolateral thoracotomy at the fifth intercostal space from the left sternocostal junction to the latissimus dorsi muscle. Continue sharp transection of the intercostal muscles and open the pleura. Place a Finochietto retractor between the ribs and spread for exposure. Elevate the left lung medially to locate and dissect the descending aorta and place a vascular clamp across it. If cardiac injury is suspected, open the pericardial sac longitudinally to preserve the phrenic nerve and evacuate any blood clots, then, proceed to repair the injury. If no injury is identified, begin cardiac massage. If there is active bleeding in the pulmonary hilum, apply the vascular clamp. Any pulmonary lacerations should also be clamped. If there is an associated injury in the contralateral thoracic cavity, extend the incision across the sternum using a Lebsche knife, and through the contralateral rib space, creating a bilateral anterolateral thoracotomy ("clamshell" incision) and assess for injuries.

TABLE 9-3 EAST Recommendations to Perform EDT

Strongly Recommended	Conditionally Recommended
• Patients who arrive pulseless *with signs of life after penetrating thoracic injury*	• Patients who arrive pulseless *without signs of life after penetrating thoracic injury* • Patient who arrive pulseless *with or without signs of life after penetrating extrathoracic injury* • Patients who arrive pulseless *with or without signs of life* after *blunt injury*

EAST, Eastern Association for the Surgery of Trauma; EDT, emergency department thoracotomy.

(3) Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a minimally invasive technique using a balloon

catheter to occlude the aorta for control of noncompressible torso hemorrhage. There is currently limited high-grade evidence for its use, but the American College of Surgeons Committee on Trauma recommends its use for critical patients with hemorrhage below the diaphragm unresponsive to resuscitation and patients who arrived in arrest from subdiaphragmatic injury. The balloon should be inflated in the distal thoracic aorta (zone 1) to control intra-abdominal or retroperitoneal hemorrhage or those in arrest. For those with pelvic, junctional, or lower extremity hemorrhage, the balloon catheter should be inflated at the distal abdominal aorta (zone 3). To place the REBOA, access must be obtained with a 7 Fr or larger sheath via the common femoral artery. Ultrasound (US) guidance or cutdown is advised to avoid cannulation of the superficial femoral artery, which can lead to limb loss. Prolonged balloon inflation can cause end-organ ischemia or spinal cord injury from ischemia; therefore, definitive hemorrhage control must be performed immediately. The use of REBOA is currently limited to certified institutions and trained physicians. An appropriately placed femoral arterial line can be easily upsized to a REBOA.

2. **Cardiogenic shock** occurs when the heart is unable to provide adequate cardiac output to perfuse the peripheral tissues, either by (1) extrinsic compression of the heart leading to decreased venous return or (2) myocardial injury. Extrinsic compression is most commonly secondary to tension pneumothorax or hemothorax or cardiac tamponade (from a penetrating injury) and presents with cool/pale skin, hypotension, distended jugular veins, and transient response to an initial IV fluid bolus. Rapid diagnosis can be obtained with the use of US. Treatment of pneumothorax or hemothorax is described above. Treatment for cardiac tamponade consists of pericardial drainage via **pericardiocentesis** and repair of the injury, usually of a proximal great vessel or cardiac wound. To perform a pericardiocentesis, obtain a 16- to 18-gauge, 6 in or longer over-the-needle catheter attached to an empty syringe. Insert the needle 1 to 2 cm inferior to the left of the xiphochondral junction at a 45-degree angle to the skin and advance cephalad, aiming to the left scapula.

Withdraw as much nonclotted blood as possible, while watching for abnormalities in the electrocardiogram (ECG) monitor indicating contact with the ventricular muscle. These patients always require subsequent definitive repair. Patients in cardiogenic shock secondary to myocardial injury present similarly. Diagnosis of a myocardial infarction is via ECG and troponin levels. Therapy should follow Advanced Cardiac Life Support (ACLS) guidelines, keeping in mind that anticoagulants may need to be avoided until active bleeding related to the trauma has been excluded. Severe blunt cardiac injury is another etiology, usually occurring in the setting of high-speed motor vehicle crashes. An ECG and possibly an echocardiogram are essential. Therapy ranges from close monitoring with pharmacologic support in an ICU to operative repair.

3. **Neurogenic shock** occurs as a result of central nervous system injury causing an increase in venous capacitance leading to decreased venous return due to loss of peripheral sympathetic tone. Patients present with warm skin, absent rectal tone, and inappropriate bradycardia. They often respond to an initial IV fluid bolus but will eventually require pharmacologic support (phenylephrine, 30 to 60 μg/min, titrating to BP goal) to help restore sympathetic tone.

D. Disability. The goal of this phase of the primary survey is to identify and treat life-threatening neurologic injuries, and priority is given to evaluating level of consciousness and looking for lateralizing neurologic signs. The level of consciousness is quickly assessed using the **AVPU system** (ascertaining whether the patient is ***a***wake, opens eyes to ***v***oice, opens eyes to ***p***ainful stimulus, or is ***u***narousable) and the Glasgow Coma Scale score is determined (Table 9-4). A thorough neurologic exam includes evaluation of pupillary response, ability to follow commands, and gross asymmetry of limb movement to painful stimuli. Severe neurologic injuries require urgent evaluation and are either intracranial or spinal in origin.

TABLE 9-4 Glasgow Coma Scale Based on ATLS Guidelines, 10th Edition

Scale	Score

Eye Opening (E)	
Spontaneous	4
To sound	3
To pressure	2
None	1
Nontestable	NT
Verbal Response (V)	
Oriented	5
Confused	4
Words	3
Sounds	2
None	1
Nontestable	NT
Best Motor Response (M)	
Obeys commands	6
Localizing	5
Normal flexion	4
Abnormal flexion	3
Extension	2
None	1
Nontestable	NT

1. **Intracranial injuries.** Herniation (uncal or cerebellar) is often the final common pathway leading to death. Uncal herniation is often associated with a “blown” (fixed, dilated) pupil on the side of herniation secondary to compression. As this compression begins, the pupil assumes an ovoid shape. Such a finding can alert the trauma

team to impending herniation and the need for immediate intervention with acute therapy focusing on maximizing cerebral perfusion pressure (CPP) to provide an adequate supply of glucose and oxygen to the injured tissue. *CPP* is defined as the difference between mean arterial pressure (MAP) and intracranial pressure (ICP): CPP = MAP − ICP. Therefore, maximization of CPP (>60 to 70 mm Hg) is achieved when the BP is adequate (MAP > 70 to 80 mm Hg) and the ICP is normal (<10 to 15 mm Hg in adults).

a. MAP. The patient should be kept euvolemic or hypervolemic with pharmacologic support as needed to maintain an adequate BP. Hypoxia is especially detrimental in traumatic head injuries, and all efforts to maintain adequate oxygenation should be made during trauma resuscitations.

b. ICP. In the trauma setting, early and rapid delineation of intracranial injuries by computed tomography (CT) scan is important, as it allows for early decisions regarding the need for ICP monitoring. If there is concern for elevated ICP, mannitol (1 g/kg) or hypertonic saline should be emergently administered. ICP monitoring is usually accomplished via the placement of a subarachnoid pressure monitor ("bolt"). An intraventricular catheter placed in the nondominant lateral ventricle can also be used and has the advantage of draining CSF, if needed. General measures used to prevent an increase in the ICP include elevating the head of the bed to 30 to 45 degrees and maintaining the patient's head in the midline position to prevent obstruction of jugular venous outflow.

2. **Spinal cord injuries.** Acute injury to the spinal cord can result in neurogenic shock, which should be treated appropriately. In addition, spinal cord trauma produces debilitating neurologic loss of function. The appropriate acute management of such deficits remains somewhat controversial. There is no added benefit to steroid treatment (*Cochrane Database Syst Rev*. 2012; 1:CD001046).

3. **Neurosurgical consultation.** A neurosurgeon should be consulted immediately in all patients with severe neurologic injuries. Early radiologic evaluation of the CNS to exclude resectable intracranial mass lesions is also critical.

E. Exposure. The last component of the primary survey is exposure with

environmental control. Its purpose is to allow for complete visual inspection of the injured patient while preventing excessive heat loss. The patient is disrobed and visually inspected, including logrolling to examine the back, splaying of the legs to examine the perineum, and elevation of the arms to inspect the axillae. Rectal examination should be performed to assess for rectal tone and blood. Additionally, all penetrating wounds should be counted and marked with a radio-opaque marker on the skin. The exposed patient loses heat rapidly, so the resuscitation room should be kept warm and the patient promptly covered with warm blankets. All resuscitation IV fluids should be warmed.

III. ADJUNCTS TO THE PRIMARY SURVEY

A. Chest and Pelvic Radiographs. Radiographs serve as useful adjuncts to diagnose potentially fatal injuries and allow for assessment of suspected pathologies based on the patient's history and pertinent findings on primary survey. Radiographs should not delay treatment (e.g., needle decompression, pelvic binder placement) if warranted based on mechanism and presentation.

1. **Chest radiograph.** Chest radiographs should be read in a stepwise fashion.
   - **a. Trachea and bronchi.** First assess for position of an endotracheal tube, if placed. The presence of interstitial or pleural air can indicate tracheobronchial injury. Tracheal lacerations present with pneumomediastinum, pneumothorax, or pneumoperitoneum with subcutaneous emphysema along the neck. Bronchial disruptions present with a massive pneumothorax with a persistent air leak on placement of a tube thoracostomy.
   - **b. Pleural spaces and lung parenchyma.** First assess the pleural spaces for abnormal collections of fluid (hemothorax) or air (pneumothorax). A pneumothorax most often presents as a lucent area in the apex devoid of bronchial or vascular markings. Then assess the lung parenchyma for infiltrates (pulmonary contusion, aspiration) or areas of consolidation (hematoma from laceration). Be aware that over- or underlying external structures (e.g., backboards, ECG leads) can obscure the lung apices and should be cleared away, if possible.

c. **Mediastinum.** First assess the mediastinum for air or blood between tissue planes, indicating injury. Air or blood in the pericardium leads to an enlarged silhouette. If suspected based on mechanism and exam, a widened mediastinum is concerning for aortic rupture, and should lead to a CT angiogram of the chest to assess the mediastinal vessels.

d. **Diaphragm.** To assess for rupture, the diaphragm should be examined for elevation, obliteration, or irregularity. Examine for an air- or OG/NG tube-containing stomach or mass-like density (bowel, omentum, spleen, etc.) above the diaphragm.

e. **Bony thorax.** Assess the clavicles, scapulae, sternum, and ribs for fractures. Clavicular, scapular, sternal fracture, and 1st to 3rd rib fractures are associated with great-vessel injury. The 4th to 12th ribs should be carefully examined for two or more contiguous ribs fractured in two places, indicating flail chest. Lower rib fractures (9th to 12th) can be associated with spleen, liver, or kidney injuries.

f. **Soft tissues.** Assess soft tissues for disruption of tissue planes and presence of subcutaneous air.

g. **Tubes, lines, and foreign bodies.** Assess placement and position of all lines and tubes placed. Assess location of foreign bodies and correlate this with physical exam; this is especially important to know when a bullet appears to have crossed the midline, which is highly concerning for possible great-vessel injury. Radio-opaque markers placed adjacent to bullet or penetrating injury holes at the skin level can assist with trajectory determination.

2. **Pelvic radiograph.** The pelvic radiograph is vital to assess for large pelvic fractures that could lead to massive internal hemorrhage, particularly in the unstable patient.

a. **Bony pelvis.** Assess all pelvic bones and bilateral femurs for fracture. An open-book pelvic fracture in a patient with hypotension should be treated with immediate placement of a pelvic binder.

b. **Tubes, lines, and foreign bodies.** Similar to above, assess placement and position of all lines and tubes placed. Assess location of foreign bodies and correlate this with physical exam;

this is especially important in situations where a projectile may have crossed midline, resulting in possible vascular injury.

B. Focused Assessment With Sonography in Trauma (FAST) Exam. The FAST exam is a noninvasive way to identify hemorrhage using a bedside US and helps triage whether the patient should go to the operating room, the CT scanner, or the angiography suite. The FAST exam is particularly important in the unstable blunt trauma patient—identification of free fluid in these patients should direct these patients to the OR (Fig. 9-2). Images are obtained of the (1) pericardial sac using a subxiphoid or parasternal view, (2) hepatorenal fossa using a midaxillary view at the 10th or 11th rib space, (3) splenorenal fossa using a midaxillary view at the 8th or 9th rib space, and (4) pelvis or pouch of Douglas using a suprapubic view.

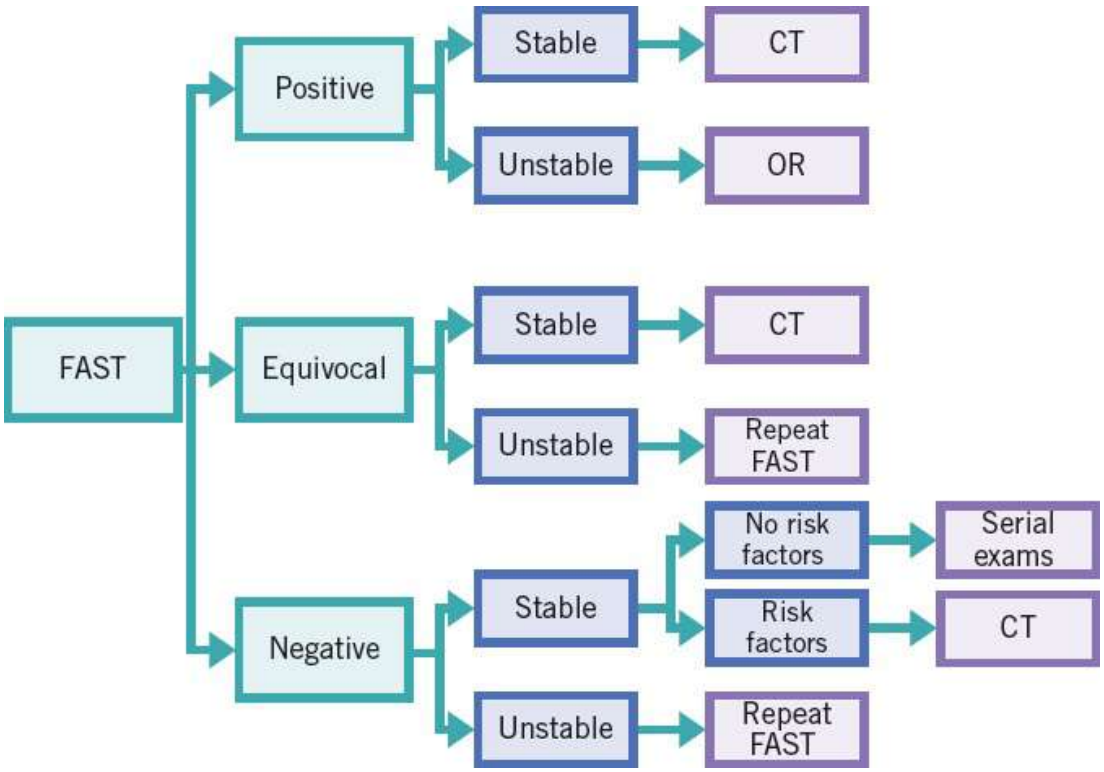


FIGURE 9-2 FAST algorithm for blunt abdominal trauma.

C. Invasive Monitoring

1. **Respiratory status.** Arterial blood gas and end-tidal CO_2 monitoring can both assist with assessing respiratory status.
2. **Urine output.** Unless contraindicated, a Foley should be placed.

Catheterization allows for assessment for hematuria, indicating possible retroperitoneal trauma. Also, it allows continuous monitoring of renal perfusion (adequate resuscitation volume replacement should produce a urinary output of 0.5 mL/kg/hr in adults and 1 mL/kg/hr in children). Contraindications for Foley placement without radiographic confirmation of an intact urethra include blood at the urethral meatus or a high-riding, mobile, or nonpalpable prostate.

IV. SECONDARY SURVEY. The secondary survey follows the primary survey. It is a complete head-to-toe examination of the patient designed to inventory all injuries sustained in the trauma. Thoroughness is the key to finding all injuries, and a systematic approach is required. Diagnostic evaluation is necessary for making decisions about subsequent interventions.

CHAPTER 9: TRAUMA RESUSCITATION AND ADJUNCTS

Multiple Choice Questions

1. **A 30-year-old female is in a motor vehicle crash and presents with a blood pressure of 170/80, heart rate of 60, and respiratory rate of 18. She is noted to have decorticate posturing, is moaning, and has unequal pupillary response. Which is the cause of this presentation?**

   a. Acute subdural hematoma
   b. Hypoxemia
   c. Diffuse axonal injury
   d. Spinal injury
   e. Drug overdose

2. **A 32-year-old male sustains multiple gunshots to the abdomen and is brought to the emergency department. His blood pressure and heart rate on arrival are 120/90 mm Hg and 110 bpm, respectively. He has lost approximately 1 L of blood from the wounds per the paramedics. What class of hemorrhagic shock is he in, and what would you use to resuscitate him?**

   a. Class 2, crystalloid
   b. Class 3, blood products
   c. Class 4, blood products
   d. Class 3, crystalloid
   e. Class 1, blood products

3. **A 35-year-old male was in a motor vehicle accident. He has a GCS of 14 and his vital signs are the following: blood pressure 85/65, heart rate 120, oxygen saturation 97% on room air. FAST exam is negative, and his left leg is noted to be severely deformed and angulated at the midthigh. What is the most likely cause of his hypotension?**

   a. Intracranial hemorrhage
   b. Pelvic fracture

c. Femur fracture
d. Cardiac contusion
e. Intra-abdominal hemorrhage

4. **A 20-year-old male fell from a ladder at work. He presents to the emergency room moaning and opening his eyes to pain. He withdraws his right leg to pain but his left arm is in flexion. What is his Glasgow Coma Scale Score?**

a. 7
b. 8
c. 9
d. 10
e. 11

5. **Which patient has the most appropriate indication for an emergency thoracotomy?**

a. 32-year-old male in a motor vehicle crash who lost pulse in the field 30 minutes prior to arrival
b. 40-year-old female suffering from an abdominal stab wound who arrives to the emergency department without pulse and has no signs of life
c. 20-year-old male who was shot in the chest and lost pulse in the ambulance
d. 18-year-old female who has large bruising to the chest after a motor vehicle crash with paramedics performing over 20 minutes of CPR
e. 80-year-old female found down on the floor after an unwitnessed fall who has a weak pulse and heart rate in the 30s

10

Head, Neck, and Spinal Trauma

Erin G. Andrade and Bradley D. Freeman

INTRODUCTION

This chapter focuses on the initial evaluation and management of head, neck, and spinal trauma in the emergent setting.

I. TRAUMA EVALUATION FOR THE HEAD. Evaluation of head injury involves a basic neurologic exam to determine cognitive function during the primary survey and a thorough head, ear, eye, nose, and throat (HEENT) exam during the secondary survey.

Primary Survey:

During the disability portion of the primary, cognitive function is assessed.

Glasgow Coma Scale (GCS): A scale based on eye (1 to 4), verbal (1 to 5), and motor (1 to 6) response to stimuli that is used to assess level of consciousness. It ranges from 3 in a completely unresponsive patient to 15 in a patient who is awake and responding appropriately.

Secondary Survey

A. Facial Bone and Skull Exam. Systematic palpation and visual inspection assess for lacerations and fractures, which may be noted with bony deformity, instability, or step offs.

B. Eye Exam. Eyes are inspected for pupillary size and response, globus structure, and orbit structure to assess for signs of trauma, such as periorbital hematomas or conjunctival hemorrhage. Unilateral pupillary dilatation may herald the onset of early brain herniation. Periorbital hematoma (raccoon eyes) may signify basal skull fractures. Extraocular

movement exam assesses for entrapment.

C. Nasal Exam. The nares should be assessed for septal deviation, bleeding, and CSF rhinorrhea (a sign of a basal skull fracture).

D. Ear Exam. The ears should be assessed for ruptured tympanic membranes, hemotympanum, and otorrhea. The latter two are both signs of a basal skull fracture.

E. Oral Cavity Exam. The oral cavity should be assessed for missing dentition, mucosal or glossal violations, and foreign bodies.

II. RADIOGRAPHIC EVALUATION OF HEAD INJURIES

A. Noncontrasted CT head should be obtained in cases of penetrating head trauma to determine trajectory. In the setting of blunt head trauma, a noncontrasted head CT is generally obtained for patients with GCS <13. For patients with GCS 13 to 15, the Canadian CT Head Rule is used to determine who warrants head CT. If any of the criteria in the table are present, noncontrasted head CT is indicated (see Table 10-1). The indications for imaging in patients on anticoagulation are the same; however, these patients should undergo a longer observation period prior to discharge to rule out delayed hemorrhage.

TABLE 10-1 Canadian CT Head Rule

Canadian CT Head Rule (Initial GCS 13–15)[a]
Age ≥65
GCS <15 after 2 hrs
Open/depressed skull fracture
Signs of basal skull fracture
>Two episodes of emesis
Amnesia ≥30 min
Significant mechanism (peds vs. auto, ejected passenger, fall ≥3 ft or 5 stairs)

[a]The Canadian CT rule applies to patients who present with a GCS of 13–15, loss of consciousness, amnesia, or confusion, and any of the manifestations in the table (*JAMA*. 2005;294(12):1511–1518).

B. Facial Trauma. Patients with significant craniofacial soft-tissue injury or clinical signs of facial fractures, such as, bony deformity, instability, or step offs, require radiographic evaluation to determine bony integrity. Facial CT has generally supplanted facial plain films for this purpose.

III. TYPES OF HEAD INJURIES

A. Epidural hematomas (EDHs) classically present with a "lucid interval" after injury, followed by rapid deterioration. This sign is inconsistent and nonspecific, however, and may also be seen with other forms of severe brain injury. EDHs typically result from laceration of the middle meningeal artery due to fracture of the squamosal portion of the temporal bone. Other vessels that are frequently involved include the middle meningeal vein, venous sinuses, and diploic vein. They appear on noncontrasted head CT scan as biconvex hyperdensities that typically respect the suture lines (Fig. 10-1A,B).

B. Acute subdural hematomas (aSDHs) appear on noncontrasted head CT as hyperdense crescents representing blood interspersed between the brain surface and dura (Fig. 10-1C). Often, aSDHs result from high-speed acceleration or deceleration trauma and portend severe underlying intracranial injury. These injuries result from shearing/tearing forces applied to small bridging (emissary) veins that drain the underlying neural tissue into the dural sinuses.

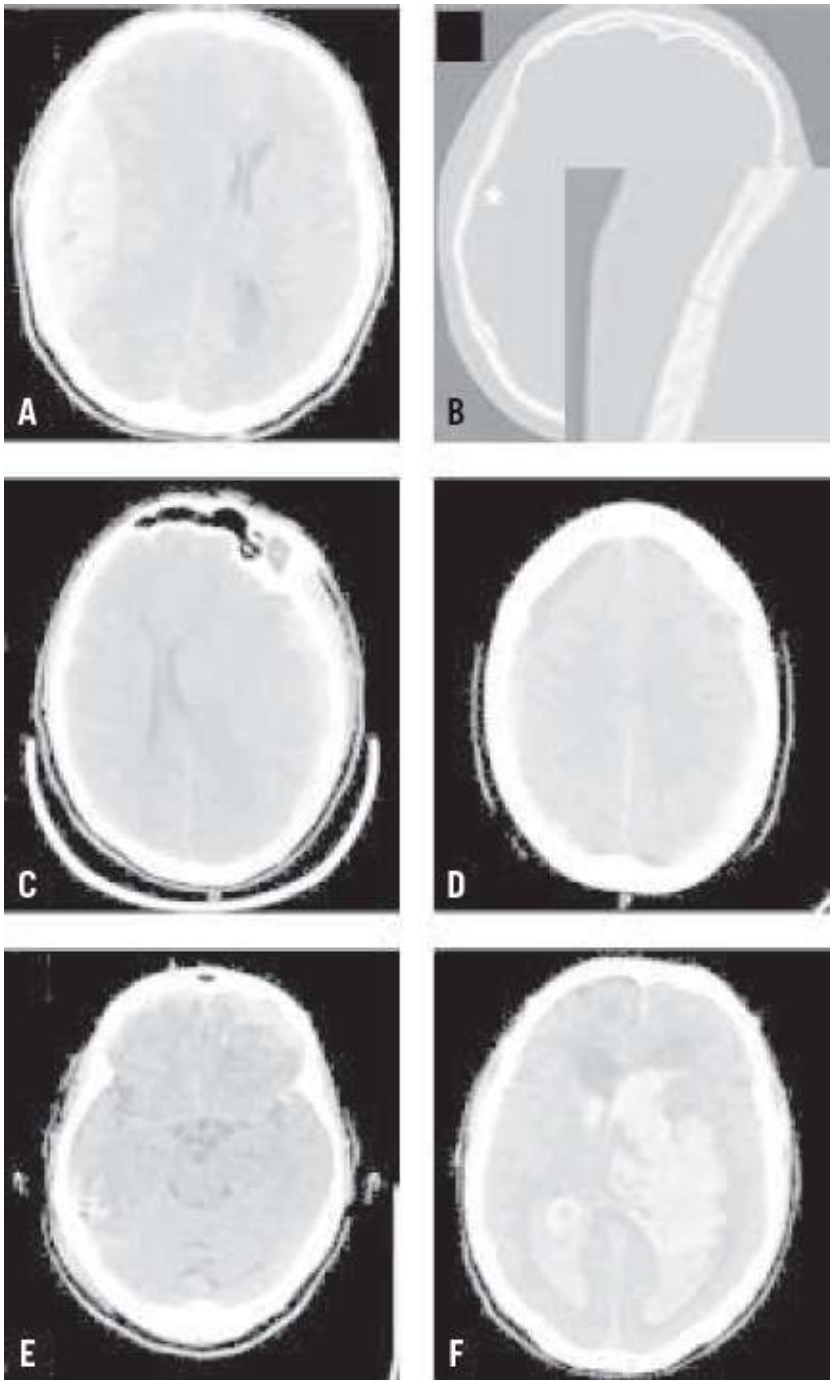


FIGURE 10-1 Noncontrast head CTs showing **(A)** large right-sided epidural hematoma with mass effect and midline shift, **(B)** bone windows from panel "A" demonstrating associated linear temporal bone fracture (*asterisk*, see inset), **(C)** left-sided acute subdural hematoma with significant midline shift, **(D)** bilateral mixed-density subdural hematomas with both acute (hyperdense) and chronic (hypodense) components, **(E)** bilateral frontal and right-sided temporal hemorrhagic contusions with surrounding edema (hypodense), and (**F**) large left-sided basal ganglia intraparenchymal hemorrhage (nontraumatic, likely related to hypertension) with intraventricular extension resulting in acute hydrocephalus.

C. Chronic SDHs (cSDHs) can present days to weeks after the initial head injury, especially in the elderly and alcoholic populations. cSDHs may cause focal neurologic deficits, mental status changes, metabolic abnormalities, and/or seizures or may be asymptomatic. Noncontrasted head CT typically shows a crescentic collection tracking between the dura and the brain but unlike an aSDH the fluid is hypodense (Fig. 10-1D).

D. Cerebral contusions manifest on noncontrasted head CT scan as small, punctate hyperdensities that are commonly located in the basal frontal and temporal lobes (Fig. 10-1E). Small contusions are better visualized on MRI. Contusions occur during blunt trauma to the head or with acceleration/deceleration injuries. In many cases, damage occurs when the brain comes into contact with the sharp bony ridges on the interior skull base. Contusions may be observed in a "coup" pattern, whereby injury to the cerebral cortex occurs in the region immediately underlying the site of impact as the brain collides with the inert table of the skull. Alternatively, a "countercoup" pattern occurs when the brain comes into contact with the opposite side of the skull following the initial impact.

E. Intraparenchymal hemorrhages (IPHs) are identified on noncontrasted head CT as focal areas of hyperdensity, typically with hypodense surrounding areas of edema (Fig. 10-1F). In addition to trauma, they may be caused by hypertension, coagulopathy, hemorrhagic transformation of ischemic stroke or tumor, venous outflow obstruction, ruptured aneurysms, or vascular malformations. Typically, laceration of larger cerebral vessels is the inciting event and may progress to brain herniation in severe cases. Extension of bleeding into the ventricular system may result in **intraventricular hemorrhage** with increased risk of communicating or noncommunicating hydrocephalus due to impaired cerebrospinal fluid (CSF) reabsorption by the arachnoid granulations or focal blockade of CSF flow, respectively.

F. Skull and facial fractures may be suspected on physical exam and confirmed on head or facial CT. They may be caused by blunt or penetrating trauma. They are classified as open versus closed and depressed versus nondepressed.

IV. MANAGEMENT OF INTRACRANIAL HEMORRHAGE. This section

focuses on the initial management of head injuries. For a more in-depth discussion of this topic, please refer to the guidelines for the surgical management of TBI (*J Neurosurg Sci*. 2014;58(4):249–259). Neurosurgical consultation should be sought immediately when these injuries are identified.

A. Monitoring and Treatment of Elevated Intracranial Pressure (ICP). In the noninjured individual, ICPs range from 5 to 15 mm Hg. In the setting of head injury, ICPs may become elevated. ICP monitoring is recommended if serial neurologic examinations cannot be used as a reliable indicator of progressive intracranial pathology because of the severity of the injury, sedation, or mental status. The goal of monitoring is to maintain ICP <20 mm Hg and cerebral perfusion pressure (CPP = mean arterial pressure [MAP] − ICP) between 60 and 70 mm Hg. Therapeutic interventions for elevated ICP are listed in Table 10-2. Initial steps in the management of elevated ICP include sedation, pain control, osmotic diuretics, head of bed elevation, and hyperventilation (Fig. 10-2).

B. Maintain Adequate CPP. As noted above, CPP is the difference between MAP and ICP. Thus, adequate blood pressure must be maintained in the setting of elevated ICP, in order to perfuse the brain. This is accomplished through control of any sources of hemorrhage, maintenance of normovolemia, and vasopressor use. Hypotension (systolic blood pressure <90 mm Hg) is associated with poor outcomes in severely head-injured patients.

TABLE 10-2 Therapies for Intracranial Hypertension

Therapeutic Modality	Usage
Mannitol	• Dose: 0.25–1 g/kg IV every 2–6 hrs in hemodynamically stable patients with adequate renal function • Monitor electrolytes • Keep serum osmolarity <320 • Strict I and O
	• Dose: 250 mL bolus IV every 6 hrs (30–60 mL IV

Hypertonic saline 3%	q6h if 23.4% hypertonic saline is used) or continuous infusion 1 mL/kg/hr • Place central line • Keep Na <160
Hyperventilation ($PaCO_2$ 30–35 mm Hg)	• Limit use to acute and emergent situations, until other interventions take effect • This may worsen cerebral ischemia
Sedation	• To prevent agitation, pain, and patient–ventilator dyssynchrony
Metabolic suppression (barbiturate coma)	• Usually reserved for refractory ICP • Adequate hemodynamic monitoring is needed to prevent hypotension
Surgical decompression	Consider for patients with: • Mass lesions • Uncontrollable ICPs • Deteriorating neurologic examination
Temperature control	• Avoid fevers (antipyretics, cooling blankets, etc.) • Hypothermia (32–34°C) can be considered for patients with refractory ICP
Other	• Elevate the head of the bed to 30 degrees • CSF drainage by ventriculostomy

C. Coagulopathy should be corrected as expeditiously as possible. The goal of therapy is minimizing intracranial hematoma expansion. Anticoagulants should be discontinued. International normalized ratio (INR) and partial thromboplastin time (PTT) should be maintained at ≤1.4 and <40 seconds, respectively, and platelets should be kept ≥100,000. For patients with warfarin-associated ICH, patients should be reversed with prothrombin complex concentrate (PCC), which contains factors II, VI, IX, and X. PCC should also be considered in patients taking Xa (i.e., apixaban, rivaroxaban) inhibitors. For patients on dabigatran, a factor II inhibitor, idarucizumab can be used to reverse

coagulopathy. For full recommendations on reversal of coagulopathy in patients on anticoagulants, please see the hematology chapter.

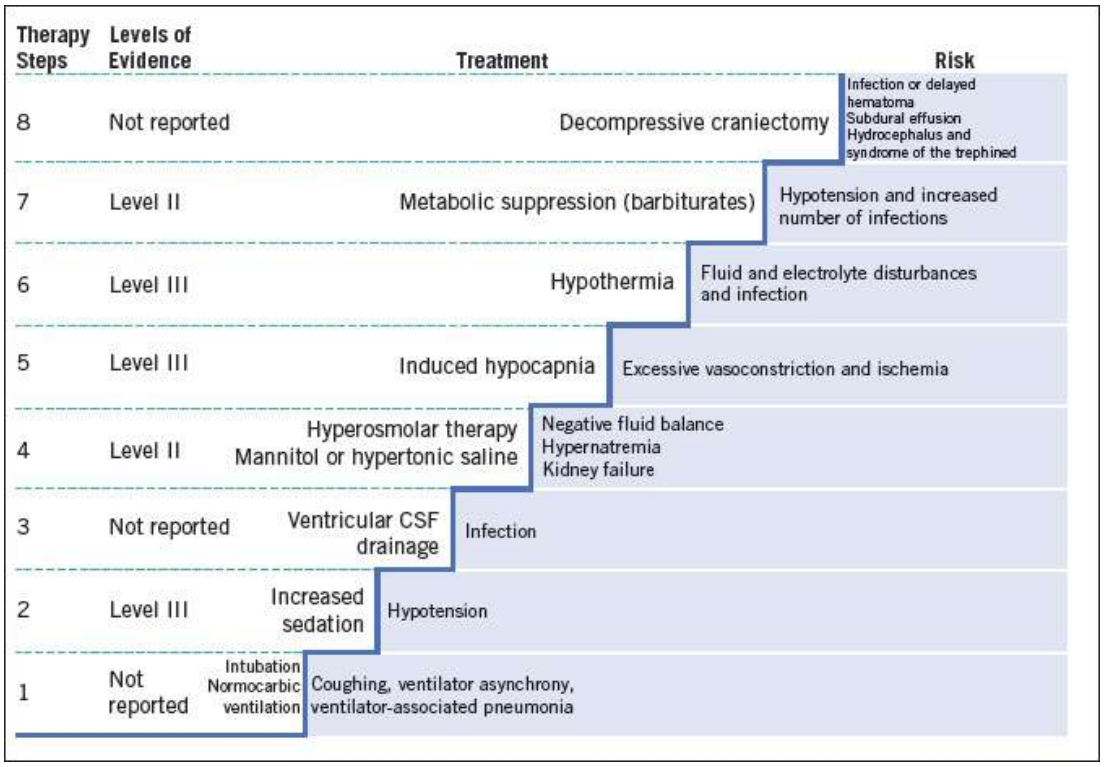


FIGURE 10-2 Staircase approach for managing intracranial hypertension. (Adapted from Stocchetti N, Maas A. Traumatic intracranial hypertension. *N Engl J Med*. 2014;370:2121–2130, with permission.)

V. MANAGEMENT OF SKULL FRACTURES. Management of skull fractures should be deferred to a neurosurgical consultant. In general, closed, nondepressed, linear skull fractures are managed nonoperatively. Simple depressed skull fractures, which have no skin or galeal disruption, are also usually managed nonoperatively. Patients with open, depressed skull fractures may require elevation and debridement of depressed bony fragments as well as devitalized tissue, followed by a course of antibiotics.

VI. TRAUMA EVALUATION OF THE NECK AND SPINE

A. The soft tissue of the **neck** should be inspected for signs of vascular injury, such as an expanding hematoma, a pulsatile mass, or ecchymoses. Stridor, dysphonia, and crepitus on exam are suspicious for laryngeal trauma. **Penetrating neck injuries** are classified as superficial

(no platysma fascia violation) or deep (if the platysma fascia is violated). Deep injuries are categorized based on the following anatomic landmarks:

TABLE 10-3 Zones of Penetrating Neck Injury

Zone	Operative Approach
1	Median sternotomy with possible extension along sternocleidomastoid or supraclavicular incision
2	Transverse cervical collar incision or anterior sternocleidomastoid incision
3	Preferably endovascular, difficult to control operatively, need to dislocate mandible

1. **Zone I**, the thoracic inlet, from the manubrium to the cricoid cartilage
2. **Zone II**, the mid neck, from the cricoid cartilage to the angle of the mandible
3. **Zone III**, the upper neck, from the angle of mandible to the base of the skull. These zones were historically used to guide operative management and/or diagnostic workup. This approach has been largely supplanted by the liberal use of axial imaging in the setting of penetrating neck trauma. Patients with penetrating neck injuries who are hemodynamically stable should undergo CT angiography (CTA) to determine the trajectory of the injury and to plan the operative approach (Table 10-3). In the unstable patient, ATLS algorithms should be followed to secure an airway and attempt tamponade of any active bleeding. If patients are not sufficiently stable to undergo diagnostic imaging, they should undergo emergent neck exploration.

B. Cervical and Thoracolumbar Spine. Patients with potential cervical spine injuries require cervical spine immobilization. To examine the cervical spine, the cervical collar should be removed and the neck must be maintained in a neutral position. The cervical spine should be assessed for posterior midline tenderness and palpated for deformities. The remainder of the spine should be examined for obvious deformity,

step off, and point tenderness. Weakness, paralysis, asymmetry, and loss of sensation in the extremities should be noted. Assessing reflexes and rectal sphincter tone completes the examination. If there is no posterior midline tenderness and the patient is awake and alert, ask the patient to flex and extend neck and rotate side to side. If these motions do not cause pain, the collar can be removed. Many patients are unable to fully participate in the exam due to altered mental status or distracting injuries. These patients should be maintained in cervical spine immobilization and logrolled until spinal injuries are excluded.

VII. RADIOGRAPHIC EVALUATION

A. Penetrating Neck Injury. For hemodynamically unstable patients with penetrating neck injury, emergent neck exploration is indicated. For the stable patient with a penetrating neck injury, regardless of the zone, a CTA is the initial recommended radiographic study. It delineates the location of potential vascular or aerodigestive injuries and the tract of the injury, and it aids in operative planning. If an esophageal injury is suspected and CTA is equivocal, esophagoscopy and esophagography may be performed. Bronchoscopy should be performed if tracheal injury is suspected (Fig. 10-3).

B. Blunt Neck Injury. Guidelines such as the Canadian C-Spine Rule and NEXUS are used to determine who can be clinically cleared and who should undergo imaging (Table 10-4). If NEXUS criteria are met, cervical spine imaging is generally not indicated. For the Canadian C-Spine Rule, see Figure 10-4. CTA should be obtained if patients meet Denver criteria for blunt cerebrovascular injury (BCVI) as listed in Table 10-5. BCVI to the carotid or vertebral arteries carries significant morbidity, including the possibility of cerebral hemorrhage or stroke (CVA). Such injuries are commonly a result of hyperextension or hyperflexion with rotation of the neck or a direct blow to the cervical region.

C. Thoracolumbar Spine. Patients with back pain, thoracolumbar spine tenderness, neurologic deficits, or known or suspected high-energy mechanisms in which spinal trauma might be sustained should be screened with a CT scan of the axial spine to include the thoracic, lumbar, and sacral regions. A CT scan should be considered for patients with a known or suspected injury to the cervical spine, or any other

region of the spine, due to the high incidence of concurrent spinal injuries. For patients with penetrating spinal injuries, a CT scan can be performed to localize retained foreign bodies (*J Trauma*. 2012;73(5):S326–S332).

VIII. TYPES OF SPINAL INJURIES. The spinal column is divided into the anterior, middle, and posterior columns. The **anterior column** contains the anterior longitudinal ligament, anterior half of the annulus fibrosus and vertebral body. The **middle column** consists of the posterior ligament, posterior half of the annulus fibrosus and vertebral body, and the **posterior column** consists of the ligamentum flavum, articulating facets, lamina, and spinous processes. As a generalized rule, an injury affecting one column is stable; however, an injury affecting two or more columns is unstable.

A. Compression Fractures. These injuries usually occur as a result of axial loading forces on the spinal column, resulting in height loss of the anterior portion of the vertebral body. These are usually stable injuries due to the fact that only one column is usually affected. In some patients, there is a greater than 50% loss in height of the anterior vertebral body, which places the posterior column under significant strain. These patients may be considered for C-collar/thoracic brace versus surgical fixation procedures on an individualized basis.

B. Burst Fractures. These fractures involve both the anterior and middle columns and occur as a result of axial loading. Burst fractures are potentially unstable and carry a high incidence of associated neurologic injuries. Management of these injuries is individualized.

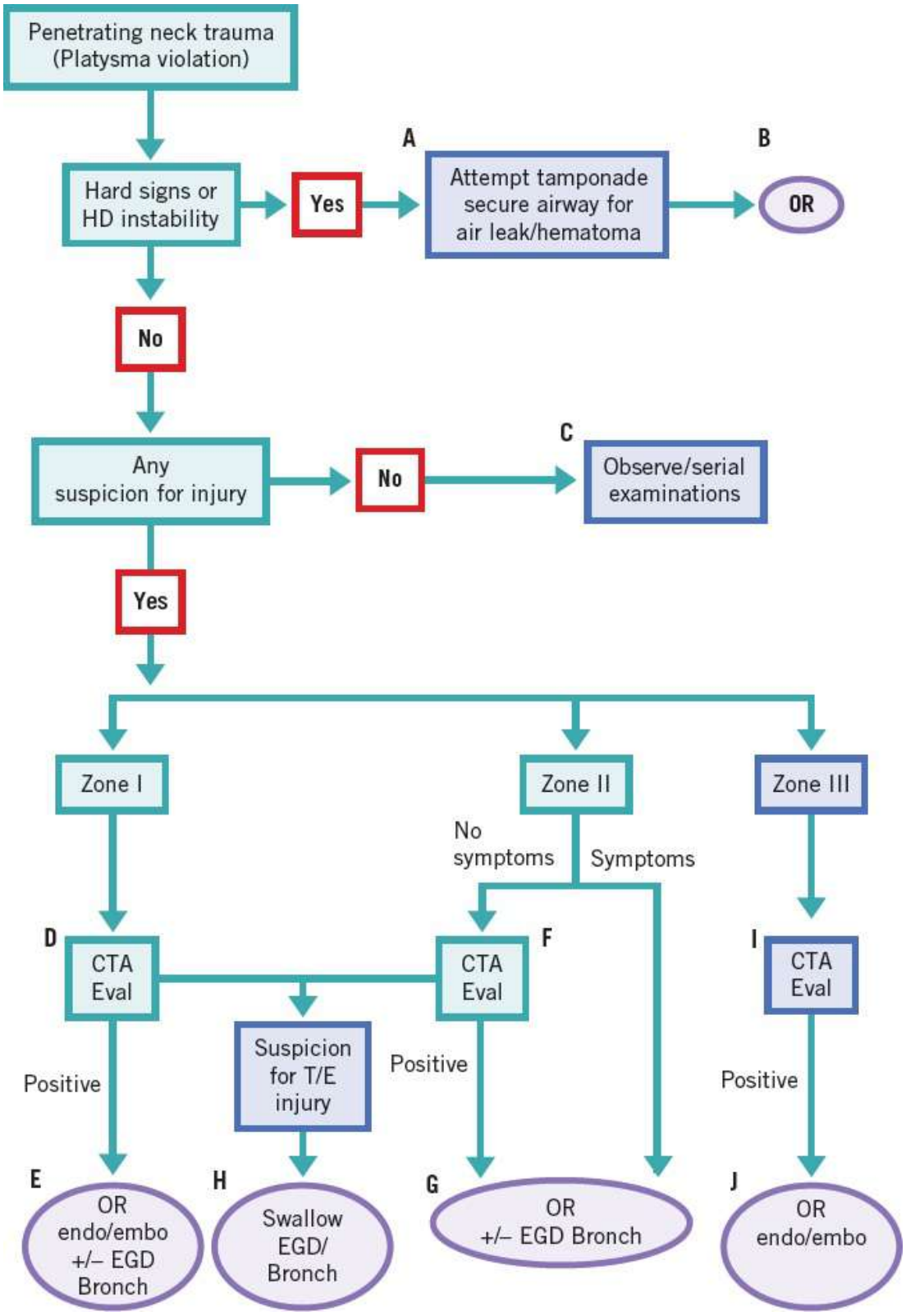
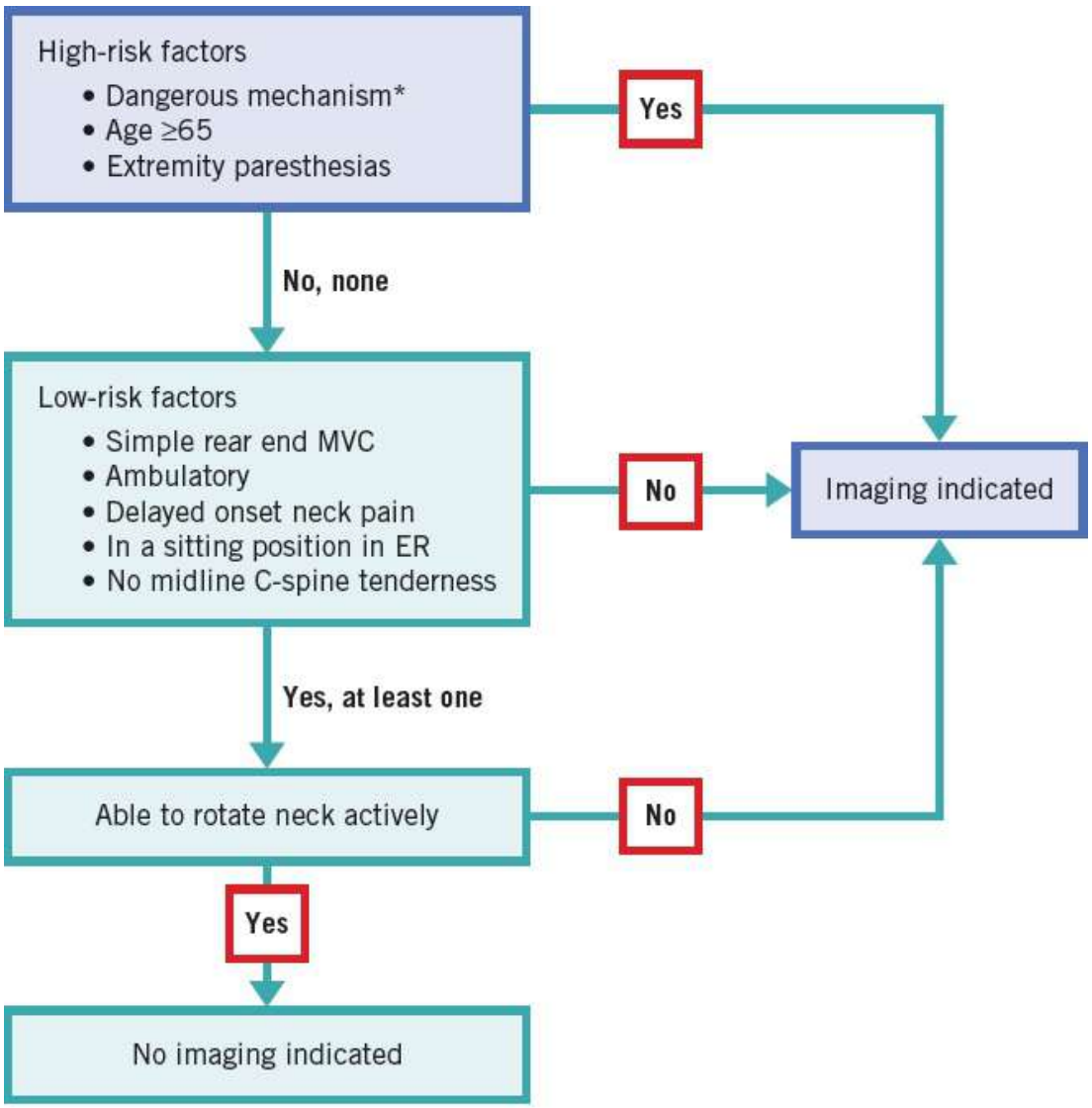


FIGURE 10-3 Western Trauma Association management algorithm for penetrating neck trauma. (Adapted from Sperry JL, Moore EE, Coimbra R, et al. Western Trauma Association critical decisions in trauma: penetrating neck trauma. *J Trauma Acute Care Surg*.

2013;75(6):936–940, with permission.)

TABLE 10-4	NEXUS Criteria
No posterior midline cervical tenderness	
No evidence of intoxication	
A normal level of alertness	
No focal neurologic deficit	
No painful distracting injuries	



*Dangerous mechanism: fall from ≥3 feet or 5 stairs, axial load to head, high-speed MVC (≥60 mph), ejection, or rollover, motorized recreational vehicles or bicycle struck.

FIGURE 10-4 Canadian C-Spine criteria. (Modified from Stiel IG, Wells GA, Vandemheen KL. The Canadian C-Spine Rule for radiography in alert and stable trauma patients. *JAMA.* 2001;286(15):1841–1848.)

TABLE 10-5 Updated Denver Screening Criteria for BCVI

Signs and Symptoms

- Arterial hemorrhage from neck/nose/mouth
- Cervical bruit in patient <50 years old
- Expanding cervical hematoma
- Focal neurologic defect: TIA, hemiparesis, vertebrobasilar symptoms, Horner syndrome

- Neurologic deficit inconsistent with head CT
- Ischemic stroke on CT or MRI

Risk Factors

High-energy transfer mechanism with:

- LeForte II or III fracture
- Cervical spine fracture with subluxation, fractures extending into the transverse foramen, or fractures of C1–C3
- Basilar skull fracture with carotid canal involvement
- Near hanging with anoxic brain injury
- Diffuse axonal injury with GCS ≤6

Burlew et al. (2011).

C. Penetrating injuries to the neck and torso may result in fractures of the spine or penetration of the spinal canal. While these injuries are often stable, indications for surgery include deterioration of neurologic status, spinal compression, or cauda equina syndrome, as well as complications related to presence of a foreign body.

CHAPTER 10: HEAD, NECK, AND SPINAL TRAUMA

Multiple Choice Questions

1. **A 25-year-old male presents with a stab wound to the neck at the level of the cricoid cartilage. Primary survey reveals a patent airway, equal breath sounds, and palpable femoral pulses. He is hemodynamically stable. Secondary survey reveals no additional injury. What is the next step in management?**

   a. CTA of the neck
   b. Emergent neck exploration
   c. Bronchoscopy
   d. Esophagoscopy
   e. Contrast esophagram

2. **A 68-year-old male presents to your emergency department after high-speed motor vehicle crash. His GCS was 13 in the field but is 15 on arrival. He exhibits no focal neurologic deficits and has no midline C-spine tenderness. Which of the following is the appropriate imaging workup?**

   a. Noncontrast CT head only
   b. CTA of the head and neck
   c. Noncontrast CT head and C-spine
   d. No imaging indicated
   e. Noncontrast C-spine CT

3. **An 84-year-old female with a history of atrial fibrillation on dabigatran presents to your emergency department after slipping and falling on her icy driveway. She is hemodynamically stable with a GCS of 10. CT head reveals a subdural hematoma. What is your next step in management of her anticoagulation?**

   a. Fresh frozen plasma
   b. Vitamin K
   c. Platelets
   d. Idarucizumab

e. Packed red blood cells

4. **A 66-year-old intoxicated male presents to your emergency department after a motor vehicle crash. The patient is not cooperative and vehemently denies any cervical spine tenderness. What is the appropriate next step to minimize the potential for cervical spine injury?**

   a. Reassess the patient when he is sober
   b. Place a cervical collar on the patient
   c. Obtain a plain x-ray of the C-spine
   d. Obtain a C-spine CT
   e. Obtain a C-spine MRI

5. **A 54-year-old male presents with a gunshot wound to his neck, which occurred during an attempted robbery. The patient's voice is inaudible and he is noted to have a significant hematoma of his neck. His blood pressure is 60/palp and his HR is 125 bpm. What is the appropriate next course of action?**

   a. CTA of the neck
   b. Bronchoscopy
   c. Endoscopy
   d. Secure airway and attempt tamponade
   e. Transfuse blood products

11

Chest Trauma

Jason M. Gauthier and Grant V. Bochicchio

INTRODUCTION

Thoracic injury is a contributing factor in as many as 75% of all trauma-related deaths. Unfortunately, a large proportion of these patients die before reaching the hospital. Among those reaching the trauma bay, the prompt diagnosis and management of injuries to the heart, lungs, great vessels, and other mediastinal structures is essential for patient survival. Therefore, a sound understanding of the common injuries following blunt and penetrating chest trauma is critical in successfully treating these patients.

TRAUMA EVALUATION

Every hemodynamically stable patient with suspicion for thoracic trauma should undergo plain chest radiography following the ATLS primary survey. Based on the results of the initial chest x-ray, as well as the overall stability of the patient, further workup and management can be directed with an algorithmic approach (Fig. 11-1). Prompt recognition and treatment of a hemothorax and/or pneumothorax can be life-saving and is the only intervention required in a large proportion of chest trauma victims. Computed tomography (CT) has become a valuable imaging modality as well, as it can usually be obtained quickly and easily. The use of chest CT should be based on patient stability and the mechanism of injury. The Focused Assessment with Sonography for Trauma (FAST) examination is another valuable tool in the workup of patients with chest trauma, as the subxiphoid view can help diagnose traumatic pericardial effusion and tamponade quickly in the trauma bay. Ultrasound examination is being increasingly utilized in the emergency setting, and some series have shown that it can diagnose pneumothorax with an even greater sensitivity than the traditional upright chest x-ray.

I. PENETRATING THORACIC INJURIES.

As many as 40% of all penetrating injuries involve the thorax. These occur most frequently from gunshot wounds and stabbings, representing 10% of all major traumas in the United States (*J Trauma*. 1990;30(11):1356–1365). Although less common than blunt thoracic trauma, penetrating trauma to the chest is more lethal, with 15% to 30% of all penetrating injuries to the chest requiring thoracotomy.

A. Chest Wall Injuries.

Penetrating injuries to the chest wall are often less significant than those seen in blunt thoracic trauma. Low-velocity injuries, such as those suffered from a stab to the chest, may result in intercostal artery laceration, pulmonary laceration, and/or fracture of a single rib. High-velocity penetrating trauma (i.e., a gunshot wound to the chest) may result in more significant chest wall injury, such as soft tissue loss, multiple rib fractures, and severe damage to the pulmonary parenchyma.

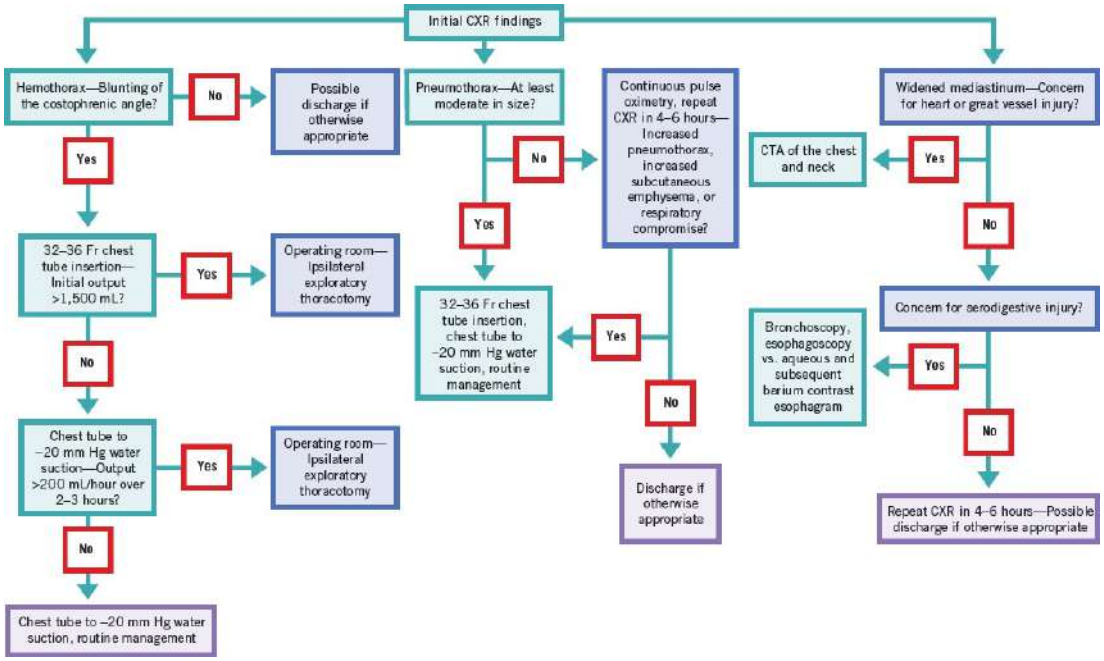


FIGURE 11-1 An algorithmic approach to a stable patient with chest trauma based on initial chest x-ray findings.

1. **Open pneumothorax.** An open pneumothorax ("sucking chest wound") may develop following significant chest wall trauma when a soft tissue defect ≥2/3 the circumference of the trachea is present. In this condition, air is preferentially drawn into the pleural space

through the chest wall when negative intrathoracic pressure is generated during inspiration; this occurs because the chest wall defect provides less resistance to the flow of air than the trachea itself, creating a wound that appears to be “sucking” into the chest. Initial management includes supplemental oxygen or intubation if oxygenation or ventilation is inadequate and thoracostomy tube placement at a site remote from the wound. Definitive treatment requires operative closure. If operative repair is not an immediate option, an occlusive dressing taped on three sides provides a temporizing flap valve effect, in which air escapes from the pleural space during expiration but does not enter during inspiration.

B. Lung Injuries. Injury to the lungs occurs in 65% to 90% of all penetrating trauma to the chest, resulting in pulmonary laceration, pneumothorax, hemothorax, and/or pulmonary contusion. Concomitant injury to other intrathoracic structures may also occur and demands a high level of suspicion.

1. **Pneumothorax and hemothorax.** It should be assumed that a traumatic pneumothorax has a component of hemothorax. The initial management of a hemopneumothorax diagnosed by chest x-ray in the stable patient includes drainage via a 32- to 36-Fr tube thoracostomy. Subsequent need for thoracotomy is determined via an algorithmic approach (Fig. 11-1).

   a. **Tension pneumothorax.** Tension physiology must be suspected in the unstable patient with chest trauma. Following pulmonary laceration, a progressive accumulation of air in the pleural cavity may pressurize the space such that the mediastinum deviates to the contralateral hemithorax, thereby obstructing venous return to the heart. Although easily recognizable on chest x-ray (Fig. 11-2), tension pneumothorax is a clinical diagnosis, as outlined in Table 11-1. Without rapid diagnosis and treatment, these early signs are followed by obstructive shock and subsequent traumatic arrest, usually with pulseless electrical activity. As such, chest trauma accompanied by the triad of absent breath sounds, tachycardia, and hypotension refractory to fluid resuscitation merit immediate decompression. In the field, this may be accomplished with a large-bore angiocatheter inserted in the second intercostal space at the midclavicular line. Subsequent ipsilateral tube thoracostomy

provides definitive decompression and directs further management (Fig. 11-1).

2. **Pulmonary contusion.** When the lung parenchyma absorbs force from a penetrating injury, alveolar hemorrhage and tissue edema may occur, resulting in a pulmonary contusion. Respiratory complications typically peak 24 hours postinjury and frequently cause difficulty with oxygenation and ventilation, at times requiring mechanical ventilation. Providers must anticipate worsening respiratory function after diagnosing a pulmonary contusion and closely monitor the patient until the condition improves.

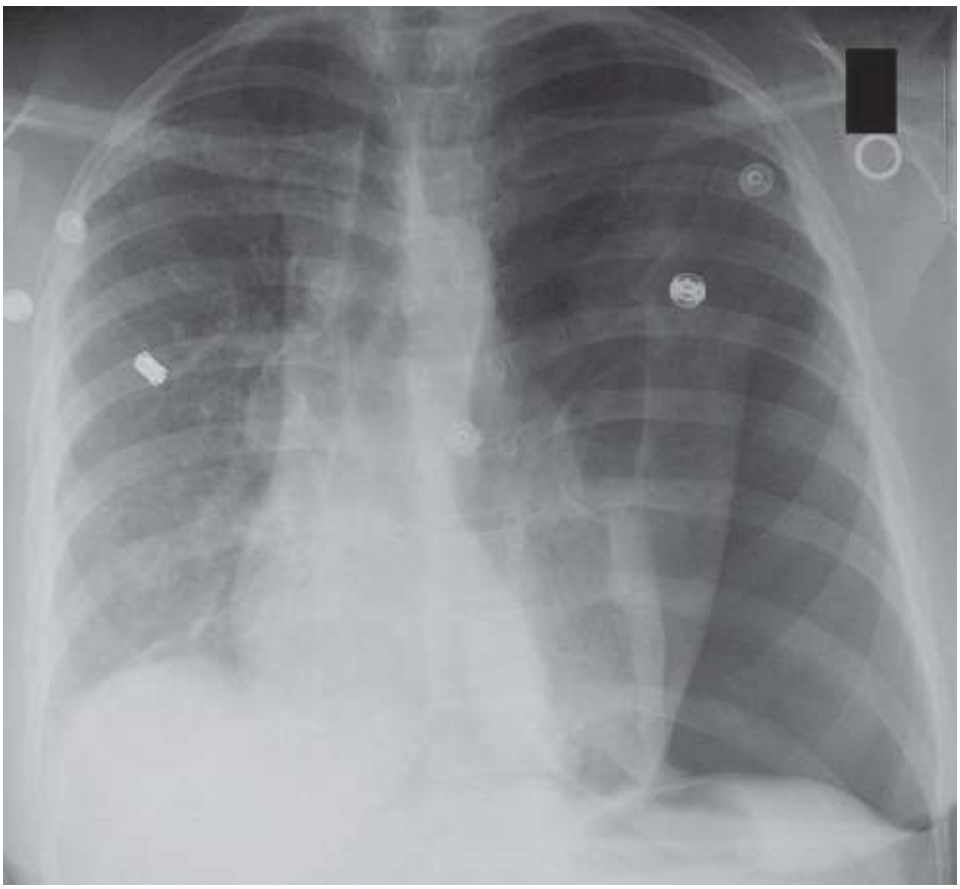


FIGURE 11-2 Plain chest x-ray of a patient with tension pneumothorax demonstrates tracheal deviation and shift of the mediastinum away from the side of the tension. Depression of the ipsilateral hemidiaphragm is also noted. (Photo courtesy of open access clinicalcases.org CC-BY-SA-2.5.)

TABLE 11-1 Clinical Signs of Tension Pneumothorax

Tachycardia
Tachypnea
Hypoxia
Absent breath sounds over the ipsilateral hemithorax
Tracheal deviation toward the contralateral hemithorax
Hypotension refractory to fluid resuscitation
Hyperexpansion of the chest
Hyperresonance on percussion
Decreased chest excursion with respiration
Distended neck veins or increased CVP[a]
Increased airway pressure

[a]May be normal or low in hypovolemic states.

3. **Late complications.** Late complications of penetrating injury to the lung may include empyema, intrapulmonary abscess, retained hemothorax, or bronchopleural fistula, all of which may be amendable to treatment with video-assisted thoracoscopic surgery (VATS), as discussed below.

C. Heart and Great Vessels. Major injuries to the heart and great vessels occur in approximately 4% of patients with penetrating chest injuries and are associated with a high mortality rate. These injuries are rarely encountered as part of a trauma activation, as over 80% of these patients expire in the field. However, of those that survive transport to a Level I trauma center, one large series has demonstrated better than 25% survival (*Arch Surg*. 2011;146(9):1061–1066). Overall, gunshot wounds to the heart are more universally fatal, with an overall mortality of greater than 90%. In contrast, stab wounds to the heart are said to carry an overall 67% mortality.

1. **Pathophysiology of cardiac trauma.** Penetrating cardiac injury is associated with anterior chest trauma between the midclavicular lines, though it may occur outside of these anatomical landmarks. The right ventricle is the most commonly injured chamber due to its anterior position in the chest cavity, followed by the left ventricle. Atrial injuries are both less common and less severe, though they contribute to a higher overall mortality when involved in a multichamber injury. Penetrating cardiac injuries can cause obstructive or hemorrhagic shock, depending on the integrity of the pericardial sac. Due to the poor compliance of the pericardium, a sudden accumulation of as little as 50 mL of blood may cause tamponade physiology. Beck's triad is the classic presentation of acute pericardial tamponade, consisting of hypotension, diminished heart sounds, and distended neck veins. In the case of coronary artery disruption, cardiogenic shock can further complicate management.
2. **Diagnosis.** In the hemodynamically stable patient with suspicion for an occult penetrating cardiac injury, transesophageal echocardiography is the diagnostic modality of choice. However, many of these injuries can be more readily identified with transthoracic echocardiography. The presence of pericardial fluid on echocardiography warrants emergent operative exploration. Another diagnostic and potentially therapeutic modality is emergent subxiphoid pericardial exploration. This procedure must be performed in the operating room under general anesthesia, making it ideal for patients already in need of an exploratory laparotomy for other injuries. The diaphragm is exposed via a subxiphoid approach and incised longitudinally to expose the pericardium. A 1-cm longitudinal pericardial incision is then made under direct vision. The presence of straw-colored fluid within the pericardium constitutes a negative examination. Blood within the pericardium mandates prompt exploration for definitive repair.
3. **Treatment.** In hemodynamically unstable patients with suspected penetrating injury to the mediastinum, the preferred operative approach is via median sternotomy, which provides access to the proximal aorta, superior vena cava, right subclavian, innominate and carotid arteries, and heart. If injury to the left subclavian artery is identified or suspected, a supraclavicular extension ("trapdoor") of

the median sternotomy is often required. The left subclavian artery may also be accessed through a left anterolateral thoracotomy, which may be required for distal injuries. Atrial and ventricular cardiac wounds are repaired using monofilament sutures (cardiorrhaphy). If definitive management must be delayed for any reason, either skin staples or a Foley catheter inserted into the wound may be used as temporizing measures. Care must be taken to avoid injury to coronary arteries during the repair. Wounds adjacent to major branches of the coronary circulation require horizontal mattress sutures placed beneath the artery (Fig. 11-3). Distal coronary artery branches may be ligated. Early consultation with a cardiothoracic surgeon is essential, especially in cases requiring complex repairs or cardiopulmonary bypass. Patients in extremis may require resuscitative thoracotomy in the emergency department as a life-saving diagnostic and therapeutic measure, as is discussed below.

D. Diaphragm. Injuries to the diaphragm may be difficult to diagnose, particularly when occurring on the right side. Up to 31% of patients may demonstrate no abdominal tenderness and 40% may have normal chest radiographs. Among all asymptomatic patients with penetrating chest injuries, the risk of occult diaphragm injury is reported to be 7%. When left unrepaired, diaphragmatic injury is associated with a high risk of bowel herniation (*J Trauma*. 2003;55(4):646–650).

E. Aerodigestive System. Injury to the tracheobronchial tree and the esophagus are more common in the setting of penetrating than blunt trauma. Given the close proximity of these structures, penetrating wounds involving the tracheobronchial tree are associated with concurrent esophageal and major vascular injuries in approximately 30% of cases. Large injuries can often be diagnosed clinically. Patients with an airway injury may present with hypoxia, inability to ventilate, hemoptysis, and/or subcutaneous emphysema. Chest x-ray can reveal disruption of the tracheobronchial tree, subcutaneous emphysema, pneumomediastinum, or air and fluid in the pleural space.

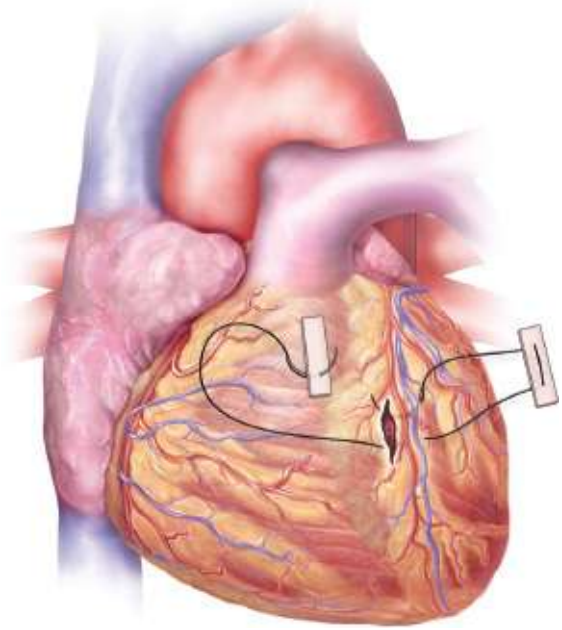


FIGURE 11-3 Horizontal mattress repair of a penetrating cardiac injury. Monofilament suture closure of the wound passing underneath the coronary artery avoids subsequent myocardial ischemia.

1. If a **tracheobronchial injury** is suspected, control of the unstable airway is first priority. If possible, intubation should be done over a flexible bronchoscope with access to the supplies for an emergent tracheostomy should this be unsuccessful. Once the airway is stabilized, the tracheobronchial tree should be evaluated for injury via bronchoscopy. Consultation with a thoracic surgeon is recommended if tracheobronchial injury exists. The operative approach is dictated by the location of the injury. Upper tracheal injuries require a median sternotomy. Distal tracheal or right bronchial injuries are repaired via a right thoracotomy. Left bronchial injuries mandate a left thoracotomy. Many penetrating injuries can be debrided and repaired primarily. Tracheal defects involving up to two rings can usually be approximated after adequate mobilization. Transections resulting from blunt injuries usually require debridement of the tracheobronchial segment with anastomosis.
2. Traumatic **esophageal injury** is associated with a very high mortality rate and requires prompt attention; the diagnosis of esophageal injury, however, should not delay repair of life-threatening airway or cardiovascular injuries. Esophagoscopy is the diagnostic modality of choice and can identify small mucosal injuries, but requires that the

patient be sedated and is best done in the operating room. Therefore, esophagography using oral contrast is often used in hemodynamically stable patients with suspected esophageal injury. As in the case of tracheobronchial injuries, the operative approach for esophageal injuries is determined by the level of injury. A right thoracotomy provides excellent exposure for most thoracic esophageal injuries, particularly those in the midesophagus. A left thoracotomy is recommended for distal esophageal injuries. In the unstable patient injury exclusion and esophageal diversion may be necessary; primary repair, however, should be undertaken whenever possible. Primary repair is done using an absorbable synthetic suture and can be buttressed with a vascularized flap (i.e., pleural or pericardial) or fundoplication in the case of distal injuries. Drain placement and gastric decompression are highly recommended. Esophageal resection is avoided at all cost, as this is associated with a high rate of morbidity and mortality. In a hemodynamically stable patient, more options exist for esophageal repair, such as primary repair with wide pleural drainage, complex flap closure, or creation of an esophageal conduit.

II. BLUNT THORACIC INJURIES. Blunt thoracic injury directly accounts for 20% to 25% of deaths resulting from trauma, representing over 16,000 deaths annually in the United States. Over 70% of these injuries are the result of motor vehicle collisions (MVCs). Blunt thoracic injuries are identified in 40% to 50% of all unrestrained drivers following MVC, and greater than 25% of drivers who die as a result of MVC have sustained blunt thoracic trauma. Patients who present following a blunt trauma injury should promptly undergo ATLS with specific focus on the ABCs. As discussed above, chest x-ray is the first diagnostic tool used to evaluate the injured thorax in the trauma bay and serves to direct management (FIG. 11-1).

A. Chest Wall Injuries. The chest wall is injured in 70% of blunt trauma to the chest, ranging from a soft tissue contusion to severe injuries that limit ventilation. **Rib fractures** are among the most common chest wall injuries and may cause acute respiratory failure, particularly in the elderly. **Flail chest** is one particularly severe injury that occurs when a portion of the rib cage fractures under extreme force and becomes

detached from adjacent ribs; this requires fracture of at least three adjacent ribs in at least two places, which may be seen as paradoxical movement of the affected portion of chest wall during inspiration. Underlying pulmonary contusion is extremely common in patients with flail chest and contributes to respiratory failure. Occasionally, operative repair of the flail segment is required to liberate patients from supplemental oxygen or mechanical ventilation. Open reduction and internal fixation of rib fractures is being increasingly used following significant chest wall trauma. While the exact indications are still being defined, the procedure has been shown to have a clear benefit in patients with severe flail chest injury. Importantly, even one or two simple rib fractures may cause respiratory insufficiency, particularly in the elderly population. Early placement of epidural catheters can help with aggressive pulmonary hygiene and has been shown to prevent complications, such as respiratory insufficiency and pneumonia. Most trauma surgeons advocate for aggressive early placement of epidural catheters in patients with significant chest wall trauma without any contraindications. Other bony structures of the thoracic cage that may be injured following blunt trauma include the sternum, clavicles, and scapulae, all of which may require surgical repair. Occasionally, a chest wall hematoma may develop secondary to disruption of subcutaneous and intramuscular blood vessels. Chest wall hematomas can usually be managed expectantly, though these may occasionally warrant decompression and/or angioembolization.

B. Lung Injuries. As in penetrating injuries to the chest, pneumothorax and/or hemothorax may be seen following blunt thoracic trauma. In this setting, hemopneumothorax is usually secondary to broken ribs causing laceration of the lung parenchyma and intercostal vessels. Rarely, acutely increased intrathoracic pressure can lead to bleb rupture and pneumothorax in patients with pre-existing emphysematous disease. The treatment for hemopneumothorax caused by blunt trauma is the same as that caused by penetrating trauma, with similar late complications as well (see Section I.B.1).

C. Blunt Cardiac Injury (BCI). The heart is injured in roughly 7% of blunt thoracic trauma. BCI accounts for up to 20% of deaths from MVC. BCI may be seen in as many as 75% of trauma patients who sustain multiple injuries or severe thoracic injuries. Findings that would lead a

clinician to be concerned for BCI include midanterior chest pain or tenderness, sternal fracture, a mechanism of major blunt force directly to the chest, and ongoing signs or symptoms of cardiac pathology.

1. **Diagnosis.** A complete understanding of injury mechanism along with a high index of suspicion is necessary for the diagnosis of BCI. Due to its anterior position in the mediastinum deep to the sternum, the right side of the heart (right ventricle and atrium) is injured more frequently in blunt trauma. Following routine chest x-ray, the first diagnostic test that should be performed to evaluate a patient for BCI is an electrocardiogram (EKG). Although there is no pathognomonic rhythm associated with BCI, electrical abnormalities including a new arrhythmia, bundle branch block, ST changes, and even unexplained tachycardia should prompt further investigation with continued cardiac monitoring and echocardiography. The Eastern Association for the Surgery of Trauma (EAST) guidelines now recommend that troponin I be measured routinely for all patients with a suspected BCI, though the optimal timing remains to be determined (*J Trauma*. 2012;73(5): S301–S306; see below and Table 11-2).
2. **Classification.** The American Association for the Surgery of Trauma (AAST) grades cardiac injuries I to VI with grade VI injuries being the most severe (http://www.aast.org/blunt-cardiac-injury). Myocardial contusion is the most common category of injury, commonly resulting in echocardiography changes and/or elevation in cardiac enzymes. Pericardial injury may occur as well as a result of a sudden high energy impact to the chest or an increase in intra-abdominal pressure. Rupture of the pericardium can result in cardiac evisceration and torsion of the great vessels, causing life-threatening obstructive shock. Valvular injuries (most commonly the aortic and mitral) are rare, but may lead to cardiogenic shock or acute pulmonary edema. New murmurs in the setting of blunt chest trauma should prompt investigation for an injured valve, which is best diagnosed on echocardiography. Very rarely, direct impact to a coronary artery may lead to thrombus formation and myocardial ischemia, sometimes manifesting as a new arrhythmia. BCI may also lead to cardiac chamber rupture. While chamber rupture is uncommon, it is often fatal. Survivors will present to the ED in obstructive shock from cardiac tamponade or hypovolemic shock

from bleeding, depending on the integrity of the pericardial sack.

3. **Treatment.** Due to the significant morbidity and relative frequency associated with this injury, the EAST has developed evidence-based guidelines for the evaluation and treatment of myocardial contusion in BCI (Table 11-2).

D. Blunt Traumatic Aortic Injury (BTAI). Blunt injury to the aorta is the second most common cause of traumatic death, with the majority of patients dying before even reaching the hospital. Among those that reach the hospital alive, 50% will die within the following 24 hours (*J Trauma*. 2015;78(1):136–146). While many of these injuries can be definitively treated in a delayed fashion, a rapid diagnosis of those that warrant immediate intervention is required to ensure patient survival.

TABLE 11-2 East Guidelines for the Evaluation of Blunt Cardiac Injury (BCI)

Level I

(1) Admission EKG should be obtained in all patients where there is suspected BCI.

Level II

(1) If the admission EKG is abnormal, the patient should be admitted for continuous EKG monitoring for 24–48 hours.
(2) If the admission EKG and troponin I value are normal, BCI is ruled out. However, the patient with a normal EKG but elevated troponin should be kept for observation/monitoring.
(3) If the patient is hemodynamically unstable, an echocardiogram should be obtained.
(4) The presence of a sternal fracture does not predict the presence of BCI and should not prompt monitoring if EKG and troponin I value are normal.
(5) Creatinine phosphokinase with isoenzyme analysis should not be performed, as it is not useful in predicting which patients will have complications from BCI.
(6) Nuclear medicine scans add little compared with echocardiography and should not be routinely performed.

Level III

(1) Elderly patients with known cardiac disease, unstable patients, and those with abnormal admission EKGs can be safely operated on provided that they are closely monitored.

(2) Troponin I should be measured routinely for patients with suspected BCI and, if elevated, should prompt further monitoring and serial measurements.

(3) Cardiac CT or MRI can be helpful in differentiating acute myocardial infarction from BCI in trauma patients with abnormal EKG, troponin I, and/or echocardiography.

1. **Diagnosis.** BTAI occurs in the setting of severe acceleration/deceleration forces and must be ruled out quickly when a patient presents following such a mechanism of injury. Widened mediastinum on chest x-ray, bright red blood return from the thoracostomy tube, or hemodynamic instability should raise suspicion for aortic injury. CT angiography should be done, situation permitting, when concern for a BTAI exists; this study carries a nearly 100% sensitivity for diagnosing BTAI, which rivals the traditional gold standard of formal angiography (*J Trauma Acute Care Surg*. 2015;78(1):136–146). The area of injury is most commonly at the level of the left subclavian artery takeoff, where the aorta is fixed at the ligamentum arteriosum.
2. **Treatment.** Immediate repair was traditionally considered the gold standard in order to maintain distal perfusion and decrease the risk of rupture. However, studies over the last two decades have shown that delayed repair of BTAI with strict blood pressure control results in decreased mortality and paraplegia. It is thought that patients who survive long enough to make it to the trauma bay are likely suffering from a partial-thickness tear which can be temporized by preventing hypertension and overresuscitation. Furthermore, some patients will present with multiple severe, life-threatening injuries that must be addressed immediately. If laparotomy or sternotomy are required, then these life-saving measures should be done first with attention later turned to the BTAI. Endovascular repair is the treatment of choice unless contraindications exist, such as small aortic diameter or injury in a location not amendable to placement of a stent graft.

III. PROCEDURES

A. VATS is a minimally invasive method of operating within the thoracic cavity. Recent data suggests that the early use of VATS (3 to 7 days postinjury) to address the indications discussed below leads to fewer complications and decreased length of hospital stay (*J Trauma*. 2011;70(2):510–518).

1. **Indications.** Any patient with a retained hemothorax or pneumothorax after a well-placed thoracostomy tube is likely to benefit from VATS. Other indications include persistent air leak, posttraumatic emphysema, intrapulmonary abscess, foreign body removal, or diagnostic purposes. Evidence suggests that VATS is most beneficial when done in the first 3 to 7 days. It should be noted that any patient with active bleeding, hemodynamic instability, or massive bleeding (>1,500 mL of blood immediately or 200 mL/hr for 2 to 3 hours) after placing a thoracostomy tube should receive an urgent thoracotomy in the operating room rather than VATS.
2. **Technique.** The surgical technique is similar to laparoscopic surgery of the abdomen. One or more port sites are created in the chest wall, preferably using a previously established thoracostomy tube track, and operations in the thoracic cavity are conducted with the aid of a camera. The thoracic cavity should be thoroughly inspected for the presence of injuries missed on prior imaging. Upon completion of the operation, a thoracostomy tube is placed under thoracoscopic guidance to optimize postoperative drainage of the pleural place.
3. **Complications.** Injury to the thoracic organs, namely the lung, can occur during VATS, resulting in additional bleeding or postoperative air leak. Postoperative infection, pain control, and pulmonary complications are certainly of concern as well, though these occur at lower rates when compared to thoracotomy.

B. Resuscitative Thoracotomy. Resuscitative thoracotomy is performed in a final attempt to salvage a certain subset of patients presenting in extremis to the emergency department. The goals are to control intrathoracic hemorrhage, relieve cardiac tamponade, cross-clamp the thoracic aorta, and restore cardiac output.

1. **Indications.** The indications for resuscitative thoracotomy have been refined over time. The current indication includes any patient with penetrating chest trauma and hemodynamic deterioration (systolic

blood pressure <60 mm Hg) or cardiopulmonary arrest occurring within the emergency department or shortly before arrival. In addition, it can be used to gain access to the descending aorta for cross-clamp in certain cases of penetrating abdominal trauma fulfilling the same criteria.

2. **Technique.** Resuscitative thoracotomy is performed via a left anterolateral thoracotomy in the fifth or sixth intercostal space. The skin, subcutaneous tissues, and intercostal muscles are sharply divided. A Finochietto retractor is placed to spread the ribs and aid in exposure. First, the pericardium is identified and incised vertically and anterior to the phrenic nerve. Any clot or debris is removed from around the heart. The heart is then inspected for injury, and if identified, repaired as previously described. After cardiorrhaphy, air is evacuated from the heart by needle aspiration and the adequacy of cardiac filling is assessed to determine intravascular volume status. In the absence of associated pulmonary vascular or great-vessel injury, vigorous volume resuscitation is undertaken. If peripheral vascular access is insufficient, direct infusion into the right atrium can be performed. During volume resuscitation, open cardiac massage can be employed to provide adequate circulation. In severely hypovolemic patients, the descending thoracic aorta may be exposed and cross-clamped to maintain coronary and cerebral perfusion. The aorta should also be clamped if any intra-abdominal hemorrhage is suspected. After restoration of circulatory volume, the underlying cardiac rhythm is assessed, and internal cardioversion used when appropriate. After a successful resuscitation the patient should be transported to the operating room for definitive repair and wound closure.

3. **Complications.** Complications of resuscitative thoracotomy are many, including lung laceration, transection of the phrenic nerve while performing pericardiotomy, injury to the coronary vessels during cardiorrhaphy, and esophageal trauma while clamping the descending thoracic aorta. Therefore, care must be taken during each step of the procedure to avoid causing additional injuries. Furthermore, a member of the trauma team sustains a needlestick or sharp injury in roughly 10% of resuscitative thoracotomies. Given that this procedure is most commonly performed in a patient

population at high risk of carrying blood-borne disease, the risk to the trauma team is not insubstantial and must be considered.

IV. CONCLUSION. Injury to the chest and its contents represents a significant portion of traumatic injuries and deaths. Attention to mechanism of injury and a high index of suspicion for life-threatening thoracic injuries is crucial when caring for the traumatically injured patient. While the majority of thoracic trauma can be managed expectantly or with a thoracostomy tube, certain injuries are immediately life-threatening and require an early, accurate diagnosis and intervention.

CHAPTER 11: CHEST TRAUMA

Multiple Choice Questions

1. **A 34-year-old male is brought to the emergency department after sustaining a GSW to the right chest. Upon arrival, his HR is 125 and SBP is 80. His trachea is deviated to the left and breath sounds on the right are absent. He is awake and agitated. Which of the following is the first step in management?**

   a. Left-sided thoracotomy
   b. Right-sided thoracotomy
   c. CT scan of the chest and abdomen
   d. Needle decompression of the right chest
   e. Endotracheal intubation via direct laryngoscopy

2. **In the above patient, a right-sided thoracostomy tube is inserted. Which of the following resultant findings would prompt an immediate trip to the operating room?**

   a. 500 mL initial output of blood or 100 mL output of blood over the following 4 hours
   b. 1,500 mL initial output of blood or 200 mL/hr output over the following 2 to 3 hours
   c. Bubbling in the water seal chamber consistent with an air leak
   d. 2 L total output over the following 24 hours
   e. A rush of air upon making the thoracostomy tube incision in the chest

3. **A 25-year-old female is brought to the emergency department after suffering a stab wound just to the left of the sternum. Upon arrival, she becomes pulseless. Which of the following is a component of a resuscitative thoracotomy?**

   a. Right thoracotomy in the fifth intercostal space
   b. Ultrasound of the left chest
   c. Incision in the pericardium anterior to the phrenic nerves
   d. Cross-clamp of the abdominal aorta

e. Pericardial window with incision inferior to the xiphoid process

4. **A 50-year-old woman is involved in an MVC and strikes her chest on the steering wheel. Which of the following should be ordered to evaluate for blunt cardiac injury (BCI)?**

   a. Electrocardiogram
   b. CT angiogram of the aortic arch
   c. Sestamibi scan of the heart
   d. Chest x-ray
   e. Dobutamine stress test

5. **On primary survey, the patient above is noted to have crepitus of her neck and upper chest. Which of the following will help best determine whether she has an aerodigestive injury?**

   a. Abdominal CT
   b. Chest x-ray
   c. Esophagram with water-soluble contrast
   d. FAST examination
   e. Plain x-ray of the neck and C-spine

6. **Tension pneumothorax and cardiac tamponade are examples of which of the following?**

   a. Cardiogenic shock
   b. Distributive shock
   c. Hemorrhagic shock
   d. Obstructive shock
   e. Neurogenic shock

12

Abdominal Trauma

Joseph C. Fusco and Douglas J. Schuerer

I. GENERAL APPROACH TO ABDOMINAL TRAUMA IN THE TRAUMA BAY.

The abdomen extends from the diaphragm to the pelvic floor, corresponding to the space between the nipples and the inguinal creases on the anterior aspect of the torso. The mechanism of injury often provides important clues to the potential organs injured and dictates further workup.

A. Stab Wounds. Only one-third of stab wounds to the anterior abdomen penetrate the peritoneal cavity and cause significant injury. Options to evaluate for injuries include local wound exploration, laparoscopy or laparotomy, computed tomography (CT), Focused Abdominal Sonography for Trauma (FAST), diagnostic peritoneal lavage (DPL), and admission with observation.

B. Gunshot Wounds (GSWs). GSWs within the surface markings of the abdomen have a high probability of causing a significant intra-abdominal injury and therefore traditionally require immediate laparotomy, but this imperative has been challenged for those patients with stable hemodynamics and no peritoneal signs on physical examination. In a large retrospective study of patients with abdominal GSWs, selective nonoperative management was reported to result in a significant decrease in the percentage of unnecessary laparotomies (*Ann Surg*. 2001;234:395). Current recommendations for nonoperative management of penetrating trauma include the use of triple-contrast CT (which accurately predicts the need for laparotomy) and serial examination. The majority of these patients can be discharged after 24 hours of observation (*J Trauma*. 2010;68: 721–733).

C. Blunt Trauma. In the patient sustaining blunt abdominal trauma, physical signs of significant organ involvement are often lacking. As a

result, a number of algorithms have been proposed to exclude the presence of serious intra-abdominal injury.

1. An immediate celiotomy is required for an **unstable patient with injuries confined to the abdomen.**
2. **In the awake, unimpaired patient without abdominal complaints,** combining hospital admission and serial abdominal examinations is a cost-effective strategy for excluding serious abdominal injury, as long as the patient is not scheduled to undergo an anesthetic that would interfere with observation. However, such patients are rare in the trauma setting.
3. If an **unstable patient has multiple injuries** and there is uncertainty about whether the abdomen is the source of shock, a FAST examination may be useful. If a patient is fairly stable and access to CT is readily available, head and abdomen/pelvis CT scans can be obtained. DPL may be useful in patients with head injuries requiring immediate operative therapy. In many large centers, a CT scan can be obtained as readily as the performance of a DPL.
4. If a **stable patient has multiple injuries** and the abdomen may harbor occult organ involvement that is not immediately life threatening, a CT evaluation is necessary. In addition to identifying the presence of intra-abdominal injury, CT scanning can provide information helpful for determining the probability that a laparotomy will be therapeutic. Laparoscopy has also been proposed as an adjunct in this situation.

II. IMAGING MODALITIES

A. Trauma Ultrasonography. Many trauma centers now use FAST as an initial radiographic screening evaluation for all traumas following the primary survey. As the name implies, it is a focused examination designed to identify free intraperitoneal fluid and/or pericardial fluid. An ultrasound machine is used to take multiple views of six standard areas on the torso: (1) right paracolic gutter, (2) Morrison pouch, (3) pericardium, (4) perisplenic region, (5) left paracolic gutter, and (6) suprapubic region. It is most useful in evaluating patients with blunt abdominal trauma, especially those who are hypotensive. It may not be as useful in evaluating children or patients with penetrating trauma. However, if a FAST examination is negative, it does not exclude major

intra-abdominal injury.

B. CT. The care of injured patients has been significantly changed by the use of CT scanning. Unnecessary laparotomy is associated with significant morbidity and cost. Because of CT, an increasing amount of both blunt and penetrating trauma has been safely managed nonoperatively. Although triple-contrast CT (oral, IV, rectal) has been traditionally used, more recent evidence suggests that single-contrast CT scanning with a high-resolution, multislice scanner may obviate the need for oral and rectal contrast.

III. TRAUMA RESUSCITATION AND OPERATIVE MANAGEMENT.

Trauma patients should immediately have two large-bore IV lines placed (14 or 16 gauge), with the antecubital veins being the preferred sites. Laboratory samples can be efficiently sent at the time of initial venous access, the most important of which is a Type and Screen. All hypotensive trauma patients should be assumed to be in hemorrhagic shock until proven otherwise (Table 12-1), and should be resuscitated with blood products as soon as possible, preferably in a 1:1:1 ratio of pRBC:FFP:Platelets. A massive transfusion protocol (MTP) should be in place at each institution and activated in this setting. Crystalloid, colloid, and hypertonic saline should be avoided. Permissive hypotension and balanced resuscitation prior to definitive control of bleeding reduces overall transfusion requirements and coagulopathy (*J Trauma*. 2011;70:652–663). However, the target blood pressure should be tailored to the patient's age and medical history, as elderly patients may not tolerate the same degree of hypotension as younger patients.

TABLE 12-1 Estimated Blood Loss by Initial Hemodynamic Variables

	Class I	Class II	Class III	Class IV
Blood loss (mL)	Up to 750	750–1,500	1,500–2,000	>2,000
Blood loss (% blood volume)	Up to 15%	15–30%	30–40%	>40%
Pulse rate	<100	>100	>120	>140
Blood pressure (mm Hg)	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Urinary output (mL/hr)	>30	20–30	5–15	Negligible

Successful operative management of trauma in a hemodynamically unstable patient requires a team approach, with close communication between the attending surgeon, surgical assistants, anesthesiologist, circulating nurse, and surgical technologist. The surgeon should clearly communicate the plan to the rest of the team. Close communication with the anesthesiologist about the hemodynamic status of the patient is important to determine if the operation should be temporarily interrupted (damage control laparotomy).

Once in the operating room, the patient should be placed in a supine position with both arms outstretched at 90 degrees. A Foley catheter and gastric tube should be placed, and the patient should be prepped and draped widely from the chin to both knees. A single dose of a broad-spectrum antibiotic with aerobic and anaerobic coverage should be given, keeping in mind that the initial dosage may need to be increased and repeated after transfusion of 10 units of blood products (*J Trauma*. 2012;73:S321–S325).

Initial access to the intra-abdominal cavity should begin with a generous midline incision. The small bowel should be eviscerated and all four quadrants should be rapidly packed off with laparotomy pads. Management of individual injuries will be discussed in the next section.

IV. MANAGEMENT OF SPECIFIC INJURIES

A. Diaphragmatic Injuries occur most commonly as a result of

penetrating thoracic or abdominal trauma. Blunt trauma, however, can produce rupture secondary to rapid elevation of intra-abdominal pressure. Frequently, diagnosis is made during laparotomy, but injury can occasionally be recognized on radiographic studies (e.g., chest x-ray or CT). Therapy entails primary repair using permanent sutures in an interrupted figure-of-eight fashion. Immediate repair prevents the long-term complications associated with diaphragmatic hernias.

B. Abdominal Esophageal Injuries are managed much like thoracic esophageal injuries (see Chapter 11). In addition to primary repair and drain placement, the fundus of the stomach can be used to buttress the site via a partial wrap (e.g., a Dor fundoplication).

C. Gastric Injuries. Injuries to the stomach occur most often in the setting of penetrating trauma. Bloody drainage from a gastric tube should raise the possibility of gastric injury. Diagnosis is usually made at laparotomy. Simple lacerations can be repaired in one layer using a synthetic absorbable suture. Massive devitalization may require formal resection with restoration of GI continuity via gastroenterostomy. In such cases, vagotomy is helpful in reducing the risk of a marginal ulcer.

D. Hepatic Injuries. The use of CT in blunt trauma has increased the diagnosis of occult liver injuries, making the liver the most commonly injured abdominal solid organ.

1. **Penetrating trauma.** Although some centers advocate nonoperative management for penetrating trauma isolated to the liver in a hemodynamically normal patient (*J Trauma*. 2010;68:721–733), the diagnosis of penetrating hepatic injury is usually made with exploratory laparotomy. Hemorrhage in the setting of hepatic trauma can be massive, and familiarity with maneuvers to gain temporary and definitive control of such bleeding is essential. Rapid mobilization of the injured lobe with perihepatic compression can often provide initial hemostasis. Complex injuries that are controlled with packing may be best managed with a damage control approach, including ICU admission and resuscitation, followed by return to the operating room in 24 to 48 hours. Other methods to control hemorrhage include a Pringle maneuver, total vascular isolation, and atriocaval shunt. Definitive hemostasis can then be obtained with a combination of cautery, chromic suture, topical hemostatic agents, finger fracture and ligation, and omental packing. Consultation with

interventional radiology for evaluation of and intervention upon arterial bleeding after packing or as a part of damage control should be considered. Formal anatomic resection should be avoided because of its high associated morbidity and mortality. Finally, closed suction drains should be placed near the wound to help to identify and control biliary leaks.

2. **Blunt trauma.** CT with IV contrast is the recommended diagnostic modality for evaluation of the stable patient suspected of having blunt hepatic trauma. The unstable patient requires operative exploration and control of hemorrhage as described. The stable patient without an alternate indication for laparotomy should be admitted for close hemodynamic monitoring and serial hematocrit determinations. Operative intervention should be promptly undertaken for hemodynamic instability. Evidence of ongoing blood loss in the hemodynamically stable patient warrants angiographic evaluation and embolization of the bleeding source.

E. Gallbladder Injuries. Injury to the gallbladder frequently coexists with hepatic, portal triad, and pancreaticoduodenal trauma. Treatment consists of cholecystectomy. The gallbladder also provides an effective means of assessing biliary tree integrity via cholangiography.

F. Common Bile Duct Injuries are most often a result of penetrating trauma. Like gallbladder injuries, they often occur in association with other right upper quadrant organ trauma. Most often, diagnosis is apparent at the time of laparotomy, but occult injuries can occur. Intraoperative cholangiography, therefore, is warranted when biliary involvement is suspected. Primary repair of the injured duct over a T-tube is the preferred management.

G. Duodenal Injuries frequently coexist with devastating GI and abdominal vascular trauma and, as a result, can represent a diagnostic and therapeutic challenge. The type and severity of duodenal injury determine management.

1. **Duodenal hematoma.** Intramural duodenal hematomas usually occur after blunt trauma to the upper abdomen. Patients present with abdominal pain, nausea, and vomiting. Diagnosis is made with CT or upper GI fluoroscopy using Gastrografin. Therapy consists of long-term nasogastric decompression and nutritional support (parenteral or enteral distal to the level of injury). The majority of duodenal

hematomas are effectively treated in this manner, but operative evacuation may be indicated if obstruction persists for more than 14 days and CT reimaging confirms persistent hematoma.

2. **Duodenal perforation** can be difficult to diagnose. Patients often complain only of vague back or flank pain, and symptoms can evolve slowly. Plain radiographic signs suggestive of perforation include evidence of retroperitoneal gas, blurring of the right psoas muscle, and leftward scoliosis. Upper GI fluoroscopy using water-soluble contrast may also show evidence of a leak. The diagnostic modality of choice, however, is CT using oral and IV contrast, with the oral contrast administered in the trauma bay. Operative therapy depends on the degree of injury, but complete mobilization of the duodenum (Kocher maneuver) is essential for proper visualization and repair. Most defects (approximately 80%) can be repaired primarily in two layers, with a transverse closure to avoid luminal narrowing. Closed suction drainage placed around the repair is strongly recommended to control any anastomotic leak. Nasoduodenal decompression should be initiated. Alternatively, antegrade or retrograde (preferred) tube duodenostomy can be performed in conjunction with tube gastrostomy and feeding jejunostomy, the so-called triple tube drainage (*J Trauma*. 1979;19:334–339).
3. **Complex duodenal injuries** are an operative challenge, and management remains controversial, especially in the presence of tissue devitalization. Whenever possible, debridement with primary repair should be performed. The repair should be protected via triple-tube drainage or pyloric exclusion with diverting gastrojejunostomy. For large defects not amenable to primary closure, a retrocolic Roux-en-Y duodenojejunostomy is an option. Finally, pancreaticoduodenectomy (Whipple procedure) should be reserved only for the most complex injuries, including duodenal devascularization or severe combined injuries involving the pancreatic head and bile duct. This procedure has a very high morbidity and mortality in the trauma setting.

H. Pancreatic Injuries. Injuries to the pancreas often occur as a result of penetrating trauma. Isolated pancreatic trauma is rare, and typically the liver or stomach is also involved. CT is the best diagnostic imaging modality available, and importantly, pancreatic enzymes are not helpful

for diagnosis. Treatment focuses on determining the presence and location of major ductal involvement. Adequate exploration entails performing a Kocher maneuver and transecting the gastrohepatic and gastrocolic ligaments to inspect the body and tail of the pancreas. Injuries in which the pancreatic duct is intact are treated with closed suction drainage. Transection of the pancreatic duct requires more extensive procedures involving debridement and/or resection combined with closed suction drainage of the pancreatic bed. Severe injury to the head of the pancreas, especially in conjunction with duodenal and biliary trauma, may require pancreaticoduodenectomy but usually not during the initial operation.

I. Splenic Injuries. The spleen is the second most commonly injured solid organ in abdominal trauma. An algorithm for management of splenic trauma is presented in Figure 12-1.

1. **Penetrating trauma.** Penetrating splenic injuries are usually diagnosed at laparotomy. Management depends on complete mobilization of the spleen. Initial hemostasis is possible through manual compression. Minor injuries contained within the splenic capsule do not require any intervention. Bleeding from small capsular lacerations can be controlled with direct pressure or topical hemostatic agents. More complex injuries are treated according to the hemodynamic status of the patient. In the stable patient, splenorrhaphy can be employed in an attempt to preserve immune function (requiring salvage of 40% of the splenic mass). Devitalized tissue should be debrided and the wound closed with absorbable horizontal mattress sutures (usually 2-0 chromic). Alternatively, the spleen can be wrapped in an absorbable mesh. Partial resection is indicated for isolated superior or inferior pole injuries. In unstable patients or in patients for whom splenic salvage fails, splenectomy should be performed in an expeditious manner. All patients undergoing emergent splenectomy require postoperative immunization against *Streptococcus pneumoniae, Haemophilus influenzae*, and *Neisseria meningitidis*. It is recommended that vaccines be given 14 days following trauma splenectomy; however, vaccines should be given prior to discharge from the hospital if concerns exist that the patient will be lost to follow-up.
2. **Blunt trauma.** Most blunt splenic injuries are initially treated with

nonoperative observation. CT remains the diagnostic modality of choice. All hemodynamically stable patients without an alternate indication for laparotomy should undergo close observation with continuous monitoring of vital signs and serial hematocrit determinations. Patients with CT evidence of a contrast "blush" or evidence of continuing blood loss who remain stable should undergo embolization. Patients who are hemodynamically unstable or are failing nonoperative management (e.g., require continuing transfusion) should undergo operative exploration.

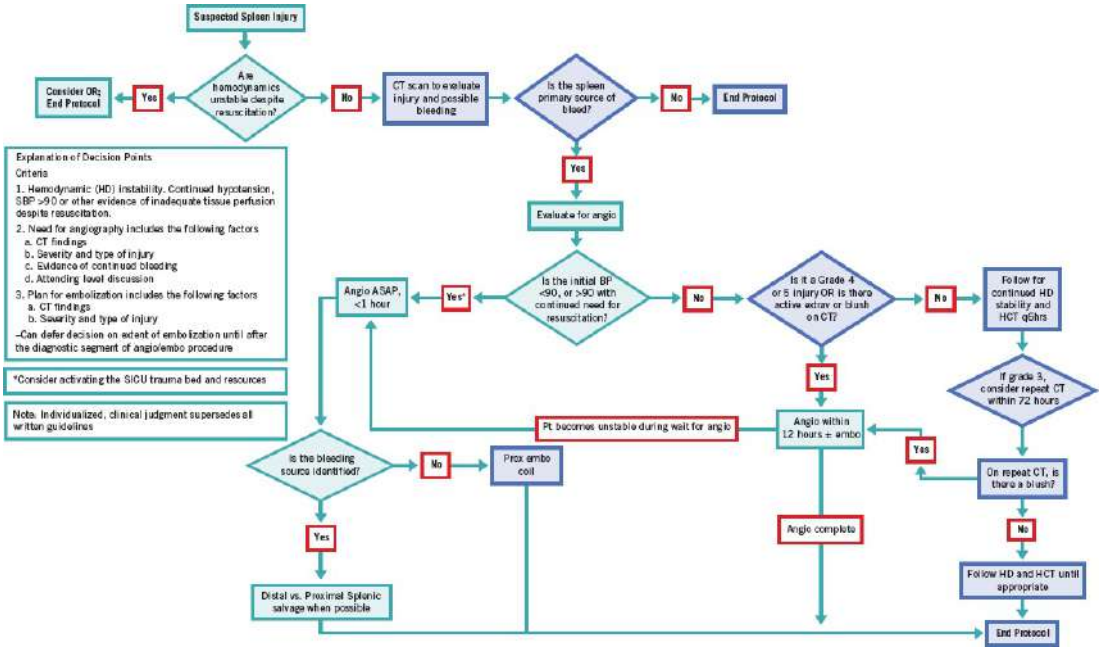


FIGURE 12-1 Splenic trauma algorithm.

J. Small-bowel Injuries. The small bowel is prone to both penetrating and blunt trauma. Treatment consists of primary repair or segmental resection with anastomosis.

K. Large-bowel Injuries. Most colonic injuries occur due to penetrating trauma and are diagnosed at the time of laparotomy. Primary repair, therefore, should be considered in all penetrating colonic injuries unless the patient experiences prolonged intraoperative hypotension (*J Trauma*. 2001;50:765–775).

L. Rectal Injuries. Penetrating trauma is also responsible for most rectal injuries and often occurs in association with genitourinary or pelvic vascular trauma. Proctoscopy is useful for diagnosis. Primary repair of

intraperitoneal rectal and accessible extraperitoneal injuries is indicated. Selective use of diverting colostomy should be considered based on the hemodynamic status of the patient or in the setting of inaccessible injuries (*J Trauma*. 2006;60:508–514).

M. Vascular Injuries. Abdominal vascular trauma is rare, but often lethal when associated with penetrating mechanisms. Mortality ranges from 20% to 60%, with early deaths resulting from hemorrhage and late deaths related to multisystem organ failure (*Clinical Review of Vascular Trauma* 2014;213–214). Presentation is dependent upon whether there is free rupture as compared to tamponade within a hematoma. The former causes volume-unresponsive hemorrhagic shock, while the latter presents either with hemodynamic stability or with transient responsiveness to fluid resuscitation. When abdominal vascular injuries are suspected, immediate large-bore intravenous access and appropriate resuscitation with blood products in a 1:1:1 ratio are essential. Adjuncts including active body rewarming and fluid warmers are aimed at maintaining normothermia.

1. **Free intraperitoneal bleeding.** Patients with free intraperitoneal bleeding are often unstable and without immediate surgical intervention rapidly deteriorate. The patient should be widely prepped from the chin to the knees, and the abdomen is opened from xiphoid to pubis. Rapid packing of all four quadrants is performed in order to allow for restoration of circulating blood volume via transfusions. If packing fails to control blood loss, there are three alternative interventions that can be attempted. First, supraceliac control of the aorta can be attained by dividing the gastrohepatic ligament and dividing the right crus of the diaphragm while retracting the stomach and esophagus. Second, a left anterolateral thoracotomy just above the fifth rib space can be utilized to access the aorta after dividing the inferior pulmonary ligament and retracting the lung anteriorly. These maneuvers then involve manual compression either with the surgeon’s hand or with a T-bar at the hiatus. Finally, aortic control can be achieved with a resuscitative balloon occlusion of the aorta (REBOA). The REBOA balloon is inserted via a femoral puncture and can be positioned based on the location of suspected bleeding.
2. **Contained retroperitoneal hematoma.** The retroperitoneum is

divided into three zones. The management and approach to contained hematomas in the retroperitoneum depend on several factors: mechanism of injury, location, and suspected vascular injury.

a. **Central abdominal hematomas (zone I).** Zone I contains the aorta, IVC, celiac, and superior and inferior mesenteric arteries. All central abdominal hematomas require evaluation as they are usually due to injury to the aorta, IVC, or their major branches, while all penetrating injuries in this zone must be explored. Blunt injuries may be better approached first with packing with further evaluation prior to exploration.

b. **Flank hematomas (zone II).** Zone II is in the paracolic gutters bilaterally containing the renal vessels and the kidneys. Unless they are rapidly expanding, pulsatile, or ruptured, they should not be explored if they are discovered at the time of laparotomy. Penetrating injuries must be explored unless a preoperative CT shows only minimal lateral kidney damage.

c. **Pelvic hematomas (zone III).** Zone III begins at the sacral promontory and contains the iliac arteries and veins. Penetrating injuries in this zone more than likely require exploration. Central pelvic hematomas in the setting of blunt trauma are usually due to pelvic fractures. If they are discovered at laparotomy, they should not be explored unless iliac arterial injury is suspected (loss of ipsilateral groin pulse, rapidly expanding hematoma, or pulsatile hematoma), rupture has occurred, or there is concomitant ureteral injury. Unstable pelvic fractures in association with hypotension should undergo some form of external stabilization (e.g., bed sheet, pelvic binder, or C-clamp). Formal external fixation should follow as soon as possible. If the patient continues to be hemodynamically unstable, the patient should go to the operating room emergently for preperitoneal pelvic packing. If the patient responds to resuscitation, a CT scan should be performed. Pelvic angiography with selective embolization is the preferred intervention for patients in whom major pelvic fractures are the suspected source of ongoing bleeding. It should also be considered in patients with major pelvic fractures when CT imaging reveals evidence of arterial extravasation in the pelvis or when bleeding in the pelvis cannot be controlled at laparotomy.

V. ABDOMINAL TRAUMA IN PREGNANCY. Trauma is responsible for approximately 50% of all deaths in pregnant women, most commonly due to motor vehicle collisions, although both falls and abuse are major causes as well. A gravid uterus displaces the majority of the intra-abdominal organs and thus relatively protects the mother from penetrating abdominal injury. In general, pregnant patients should be managed similarly to nonpregnant patients, following the dictum that the best way to take care of the fetus is to take care of the mother. Thus, concerns for fetal well-being should not preclude any urgent operative or radiologic investigations. For all pregnancies of 20 weeks of gestation or greater, or unknown gestation, fetal heart monitoring and urgent obstetrical consultation should be obtained. If possible, the mother should be placed in left lateral decubitus position to off-load pressure on the IVC and should be given supplemental oxygen. Placental abruption is the most common cause of fetal demise and typically presents with vaginal bleeding. If the patient expires in the trauma bay or operating room and the fetus is at least 26 weeks of gestation, postmortem caesarean section should be performed expediently.

CHAPTER 12: ABDOMINAL TRAUMA

Multiple Choice Questions

1. **A 22-year-old male suffers a GSW to his right buttock. He is hemodynamically normal with a benign abdominal examination. CT scanning is suggestive of an extraperitoneal rectal injury. Proctoscopy finds blood in the rectal vault, but you cannot clearly identify the level of injury. At laparotomy, you find no evidence of intraperitoneal injury. What is the best next step?**

   a. Diversion with end colostomy, distal rectal washout, and presacral drainage
   b. Diversion with end colostomy alone
   c. Mobilization of distal rectum with identification and suture repair of injury
   d. Abdominoperineal resection
   e. Nothing further and close the abdomen

2. **A 14-year-old female was riding her bicycle and accidentally rode into a ditch, resulting in her abdomen hitting her handlebars. In the trauma bay, she complains of nausea, vomiting, and abdominal pain radiating to her midback. She is hemodynamically normal and only has mild epigastric tenderness. CT scan demonstrates a 3-cm duodenal hematoma, nearly occluding the lumen of the first portion of the duodenum. What is the next best step?**

   a. Exploratory laparotomy with drainage of hematoma
   b. Whipple procedure (pancreaticoduodenectomy)
   c. Nasogastric drainage and TPN
   d. Pyloric exclusion with gastrojejunostomy
   e. Primary resection and anastomosis

3. **A 19-year-old male arrives at the trauma bay. EMS states that he was the unrestrained driver in a rollover MVC and was ejected from the vehicle. The patient was intubated by them at the scene for combativeness. He has bilateral breath sounds, HR is 150, BP**

80/palp, and SaO_2 100%. He has bony crepitus over his chest and multiple bruises over his abdomen. His pelvis is stable and he has no obvious deformities in his extremities. His CXR and pelvic x-rays are normal. You send off laboratory samples and start infusing uncrossed matched type O positive blood. What is the next best step to try to identify the source of his hypotension?

a. FAST
b. CT chest/abdomen/pelvis
c. Immediate laparotomy
d. Empiric bilateral chest tubes
e. DPL

4. **A morbidly obese 40-year-old male suffered a right flank GSW. He is hemodynamically normal and has a benign abdominal examination. On physical examination, you find a bullet hole on his midright flank and another hole more posteriorly on his right midback. What is the next best step?**

a. Immediate laparotomy
b. FAST
c. DPL
d. CT Abdomen/Pelvis
e. Admission for serial abdominal examinations

5. **A 64-year-old female was a restrained passenger in a high-speed MVC. She complains of RUQ pain but does not have peritonitis. Her HR is 100, BP 140/70. CT scan demonstrates a Grade IV liver injury with no evidence of contrast extravasation. Hgb is 13.5. What is the next best step?**

a. Admit to the floor, daily CBCs and serial abdominal examinations
b. Admit to the ICU, Foley, q6h CBCs and serial abdominal examinations
c. Immediate laparotomy and liver packing
d. Angiography and embolization
e. Repeat CT in 24 hours

6. **A 64-year-old female was a restrained passenger in a high-speed MVC. She complains of RUQ pain and has peritonitis. Her HR is 120, BP 90/50. On laparotomy, you find a liter of blood in her abdomen and a deep laceration involving the right hemiliver that is actively bleeding. You are able to control the bleeding with laparotomy packs; however, the anesthesiologist now tells you that the patient's pH is 7.1, her temperature is 34°C, and her INR is 2.5. What is your next best step?**

   a. Right hepatectomy
   b. Argon beam coagulation of the raw liver surfaces
   c. Blunt-tipped chromic mattress sutures to the bleeding liver edges
   d. Damage control laparotomy with plans for returning to the OR in 24 to 48 hours
   e. Electrocautery

7. **A 22-year-old female was just involved in a motorcycle accident and now arrives in the trauma bay hypotensive and in shock. You have adequate IV access and a type and screen is sent. The nurse asks you what kind of fluids you want to give. You answer:**

   a. Type O negative uncrossmatched blood
   b. Type O positive uncrossmatched blood
   c. Lactated Ringer
   d. Normal saline
   e. 5% albumin

8. **A 36-year-old male was intoxicated and fell off his ATV, landing on his left side. In the trauma bay, his HR is 130, BP 70/30. On laparotomy, you find a shattered spleen, which you remove. You find no other injury and close his abdomen. It is now postop day 3 and the patient is ready to go home. It is important to give him vaccines against which of the following organisms prior to discharge?**

   a. *Streptococcus pneumoniae, Haemophilus influenzae,* and *Neisseria gonorrhoeae*
   b. *Streptococcus pneumoniae, Haemophilus influenzae,* and *Neisseria meningitidis*

c. *Staphylococcus aureus, Haemophilus influenzae,* and *Neisseria meningitidis*
d. *Staphylococcus aureus,* Influenza, and *Neisseria meningitidis*
e. *Klebsiella pneumoniae, Haemophilus influenzae,* and *Neisseria meningitides*

9. A 70-year-old female living in a nursing home wandered off and fell down a flight of stairs. She complains of pelvic pain. Her HR is 110, BP 90/50. Her pelvic x-ray shows an open-book pelvic fracture. What is your next step?

a. OR for preperitoneal pelvic packing
b. IR for angioembolization
c. Placement of a pelvic binder
d. CT abdomen/pelvis
e. OR for ORIF of the pelvis

10. You are in the operating room with a patient who suffered a GSW to his anterior abdomen. You find a small defect of the sigmoid colon (<50% of diameter) along the antimesenteric border, with scant stool within the abdominal cavity. You find no other injuries and the anesthesiologist tells you the patient is hemodynamically stable. What is your next step?

a. End colostomy and drain placement
b. Resection of involved colon and primary anastomosis
c. Resection of involved colon and damage control laparotomy
d. Primary repair with diverting loop ileostomy
e. Primary repair alone

13

Extremity Trauma

Trina Ghosh and Christopher M. McAndrew

TREATMENT OF ORTHOPEDIC INJURIES

I. INITIAL ASSESSMENT

A. Priorities of Management. Assessment and management of ABCs (*a*irway, *b*reathing, and *c*irculation) and following ATLS guidelines take precedence over extremity injuries. Polytrauma patients do benefit from early identification and treatment of extremity and pelvic trauma.

B. History. In addition to a regular history and physical with a medical history, the mechanism of injury, especially the relative energy associated with the injury (e.g., low-energy fall vs. high-energy motor vehicle crash), is important. An orthopedic history should also include preinjury functional level, including occupation or hobbies, ambulatory status, and hand-dominance in the case of upper-extremity injuries.

C. Examination

1. Examination of the extremity includes inspection, palpation, range of motion, strength, stability, sensory, and body region specific tests. Patients with severe trauma or with multiple injuries will often have missed extremity injuries, especially in the hand and foot (*Patient Saf Surg*. 2008;2:20). Inspect the extremities for bruising, swelling, lacerations, abrasions, deformity, and asymmetry. Systematically palpate all extremities, noting tenderness, crepitus, and deformity of the underlying bone. In suspected cervical spine (C-spine) injury, maintain immobilization in a cervical collar. Logroll the patient to examine and palpate the spine.

2. Control bleeding with direct pressure. Tourniquets should be reserved for life-threatening exsanguinations only and should be placed as distally as possible.

3. **Vascular exam.** Assess by checking pulses (palpable or Doppler), capillary refill, temperature, color, and comparing to the contralateral side.
4. **Sensorimotor evaluation** (**Table 13-1**). A motor evaluation in the setting of acute spinal cord injury or peripheral nerve injury is critical, and serial examinations are often required. A sensory examination includes light touch in dermatomal and peripheral nerve distributions. In upper-extremity or C-spine trauma, two-point discrimination or a light touch 10–10 test of the fingers should be assessed and compared to the uninjured extremity.

II. RADIOLOGIC EXAMINATION. Radiologic assessment typically consists of x-rays with two to three views depending on the location, usually AP, lateral, and oblique views (Table 13-2). A complete evaluation includes obtaining imaging of the joints above and below the injury, which may be affected by the initial trauma. Plain films can assess for retained foreign bodies such as needles or teeth. Certain injuries (articular injuries and pelvic injuries) often necessitate further advanced imaging with computed tomography.

TABLE 13-1 Peripheral Nerve Examination

Nerve	Sensory	Motor	Muscle
Deep peroneal (DP)	Web space between great and second toe	Ankle and great toe dorsiflexion	Tibialis anterior (TA), extensor hallucis longus (EHL)
Superficial peroneal (SP)	Lateral dorsum of foot	Eversion of hindfoot	Peroneus brevis and longus
Tibial (T)	Plantar surface of foot	Ankle and great toe plantar flexion	Gastrocnemius and soleus (GS), flexor hallucis longus (FHL)

Axillary (A)	Lateral deltoid	Shoulder abduction	Deltoid
Radial (R)	Dorsal web space between thumb and index	Extension of thumb IP joint	Extensor pollicis longus (EPL)
Median (M)	Two-point discrimination of thumb, index, long	Abduct thumb perpendicular to palm, flex index DIP joint	Abductor pollicis brevis (APB), flexor digitorum profundus to index (FDP2)
Ulnar (U)	Two-point discrimination of ring, small	Spread fingers apart, flex small finger DIP joint	Interossei (IO), flexor digitorum profundus to small (FDP5)

IP, interphalangeal; DIP, distal interphalangeal.

TABLE 13-2 Imaging Examinations for Orthopedic Injuries

Conditions	X-ray	Advanced Imaging
Clavicle fracture	Two views of the clavicle + CXR to evaluate the clavicle length of the contralateral side	
Proximal humerus fracture	AP glenohumeral joint, scapular Y, axillary view	

Scapula fracture	AP, scapular Y, and axillary lateral view	CT
Shoulder dislocation	See proximal humerus	
AC dislocation	See proximal humerus and clavicle	
Sternoclavicular dislocation		CT to evaluate displacement and visualize adjacent neurovascular structures
Humeral shaft fracture	Two orthogonal views of the humerus, including the shoulder and elbow joints	
Distal humerus fracture	Orthogonal views of the elbow	
Radial head fracture	Three views of the elbow joint	
Distal phalanx fracture	Two views of the hand	
Olecranon fracture	Three views of the elbow	
Elbow dislocation	AP and lateral radiographs of the elbow	
Radius and ulna fracture	AP and lateral radiographs for the forearm, elbow, and wrist	

Distal radius fracture	Three views of the wrist	CT to evaluate comminuted intra-articular fractures
Scaphoid fracture	Four views of the wrist	
Pelvic fracture	AP pelvis, with inlet and outlet views	CT to evaluate pelvic, sacral, and lumbar fractures
Pubic rami fracture	AP pelvis, inlet and outlet views	
Acetabular fracture	Oblique views of the pelvis	CT
Femoral neck and intertrochanteric	AP pelvis, AP and lateral hip	MRI or bone scan if history suggests fracture, but none seen on x-ray
Femoral shaft fracture	AP and lateral of the femur, including thigh and knee joints	
Hip dislocation	Pelvic films to evaluate for acetabular, femoral head, or hip fractures; check for component positioning, loosening, or periprosthetic fractures in hip replacements	

Knee and tibia	Four views of the knee	
Patella fracture	Four views of the knee	
Tibial plateau fracture	AP and lateral, and views of the knee and ankle	CT scan
Tibial shaft fracture	AP and lateral views of the tibia, including both ankle and knee joints	
Knee dislocation	Four views of the knee	Angio/CT angio to evaluate for vascular injury; MRI to evaluate for ligamentous injury
Pilon fracture	Three views of the ankle and foot films to evaluate for associated food fractures	
Ankle fracture/dislocation	Three views of the ankle	
Calcaneus fracture	Three views of the ankle and foot	Lumbar spine films to evaluate for associated lumbar fractures
Talus fracture/dislocation	Three views of the ankle and foot	CT scan
Metatarsal fracture	Three views of the foot	MRI or bone scan if concern for stress fracture

Lisfranc fracture	Three views of the foot

III. FRACTURES AND DISLOCATIONS

A. General Management Principles

1. **Dislocation.** All dislocated joints, especially in the setting of neurovascular compromise, should be reduced emergently. Successful reduction reduces the risk of neurovascular compromise and degree of soft-tissue injury (e.g., pressure necrosis). Traction and postreduction radiographs are essential to confirm reduction and to evaluate for associated fractures previously not visualized because of deformity. Persistently diminished or absent pulses in spite of reduction require further evaluation.
2. **Fractures** should be described as open or closed, simple versus comminuted, nondisplaced versus displaced, intra-articular versus extra-articular. The angle of the fracture should be described as transverse versus oblique versus spiral. The angulation and rotation of the distal fragment should be described as well.
3. **Splinting.** Plaster or fiberglass is used with padding over the prominent surfaces to prevent pressure ulcers. In the acute situation, the splint should not be circumferential to allow for swelling.

TABLE 13-3 Salter–Harris Classification of Growth Plate Injuries

Type 1	Fracture through the growth plate without any metaphyseal or epiphyseal involvement
Type 2	Fracture through the growth plate is associated with a metaphyseal fracture
Type 3	Fracture through the growth plate is associated with an epiphyseal fracture
Type 4	Fracture through the metaphysis, across the growth plate, and exiting the epiphysis
Type 5	Severe crush injury to the growth plate

4. Pediatric versus adult

a. Pediatric: Children, especially those with open growth plates, have a greater potential for bony remodeling than adults, and therefore a greater amount of malalignment is acceptable. In children, to decrease the risk of permanent deformity, at least a limited reduction is often necessary.

b. Adults: In the adult, the inability to achieve and obtain an acceptable reduction is a relative indication for surgical treatment. Throughout this chapter, we will focus primarily on management of injuries in adult patients unless otherwise specified.

c. Physeal plate injuries ("growth plate") are common because this is the weakest part of the bone. The Salter–Harris classification categorizes these fractures into five types of increasing severity and likelihood of future growth disturbance (Table 13-3 and Fig. 13-1).

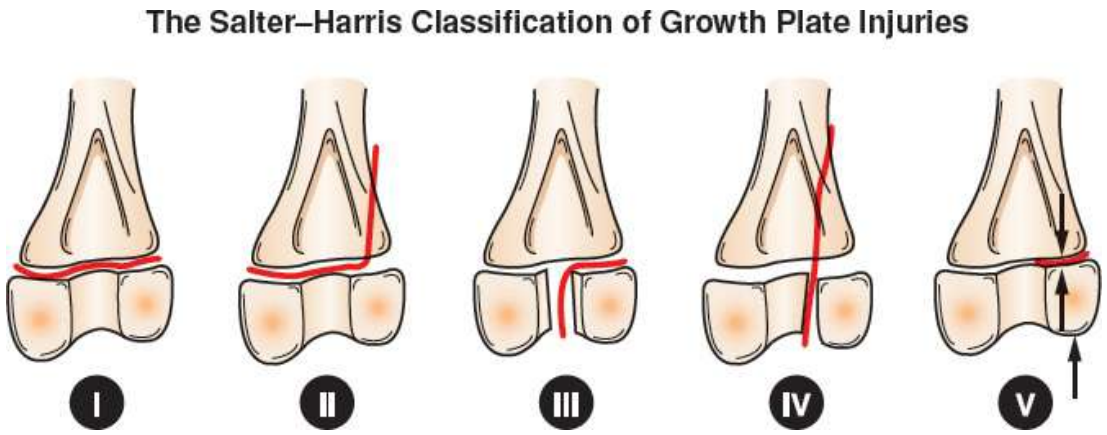


FIGURE 13-1 The five types of Salter–Harris growth plate injuries.

IV. SOFT-TISSUE INJURY

A. Principles of Management. In general, isolated soft-tissue injuries, such as ligament sprains and muscle strains, are treated with *r*est, *i*ce, *c*ompression bandage, and *e*levation (RICE therapy) with or without immobilization.

1. Skin lacerations/defects. All devitalized tissue should be debrided. The wound should be thoroughly irrigated. If the wound cannot be closed due to excessive tension, it should be covered with a moist

saline dressing, and a delayed primary closure or skin grafting should be planned.

2. **Muscle**
   a. **Mechanism.** Strains of the musculotendinous unit are usually secondary to violent contraction or excessive stretch. Injury spans the range from stretch of the fibers to a complete tear with loss of function.
   b. **Physical examination.** Swelling, tenderness, and pain with movement occur. RICE-type treatment of the involved muscle is adequate for most such injuries.
3. **Tendon.** Lacerated, ruptured, or avulsed tendons, especially those of the upper extremity, should be surgically repaired because such injuries result in loss of function. Examination reveals loss of motion or weakness. Open wounds with a tendon laceration are debrided, irrigated, and closed primarily with early planned repair of the tendon in the operating room (OR). Grossly contaminated wounds require operative debridement. Splints are applied with the extremity in a functional position in an attempt to prevent further tendon retraction.
4. **Ligament.** Ligament sprains range from mild stretch to complete tear and are commonly sports related. Pain, localized tenderness, and joint instability may be present on examination. Radiographs may reveal joint incongruence. If the joint is clinically or radiographically unstable, treatment involves immobilization in a reduced position. If no evidence of instability is present, treatment based on the RICE principle is used, and early range of motion is encouraged.

V. SPECIFIC INJURIES BY ANATOMIC LOCATION

A. Shoulder

1. **Fractures**
   a. **Clavicle.** Injury typically occurs via a fall or direct blow to the shoulder and presents with a visible or palpable deformity is often present at the fracture site. Most clavicle fractures heal with nonoperative treatment, managed with a sling. Severe displacement/deformity, particularly if associated with soft-tissue compromise, is a surgical indication.
   b. **Proximal humerus fractures** typically result from a low-energy

fall usually seen in the elderly. **Physical signs** include decreased range of motion, swelling, ecchymosis, and pain. The neurovascular examination is critical to evaluate possible associated injury to the brachial plexus. **Typical management** if the fracture is nondisplaced and stable is a sling and early, controlled mobilization. Comminution and displacement increases the risk of humeral head avascular necrosis and may require surgery. In the elderly, a primary shoulder arthroplasty may be considered if stabile internal fixation cannot be achieved. If there is associated neurovascular compromise, these should be taken emergently to the OR for open reduction.

c. Scapula fractures typically occur via high-energy chest trauma. **Physical signs** include tenderness to palpation over the scapula. Patients should be observed for signs of pneumothorax or other chest trauma when scapula fractures are present. **Treatment** is typically with a sling unless intra-articular glenoid displacement mandates surgical treatment.

2. Dislocations

a. Shoulder dislocations (glenohumeral dislocation)

(1) Mechanism. Anterior shoulder dislocations (most common, ~85%) occur with forced shoulder abduction and/or external rotation. Posterior shoulder dislocations are associated with seizure and electrical shock.

(2) Presentation. Shoulder dislocation presents with decreased and painful range of motion and the humeral head may be palpable anteriorly or posteriorly.

(3) Management. Reduction is performed under sedation with axial traction and bringing the arm into full abduction above the head. Care should be taken with the elderly to avoid iatrogenic fracture. The arm is then immobilized in the position of greatest stability: internal rotation for anterior dislocations and external rotation for posterior dislocations.

b. Acromioclavicular (AC) dislocations (“a separated shoulder”)

(1) Mechanism. Fall onto or a direct blow to the shoulder.

(2) Presentation. Variable deformity can be seen. Side-to-side asymmetry should be assessed. Pain with cross-body adduction

and tenderness to palpation is common.

(3) Management. AC joint dislocations can be treated with a sling and early motion in most cases. Significant displacement and deformity may require surgical treatment, especially if associated with soft-tissue compromise.

c. Sternoclavicular dislocations

(1) Mechanism. High-energy direct loads through the shoulder or upper chest.

(2) Presentation. Localized pain, swelling, and tenderness are seen. Hoarseness, dyspnea, dysphagia, or engorged neck veins are red flags for posterior sternoclavicular joint dislocations with neurovascular compromise and should prompt emergent evaluation and treatment.

(3) Management. Anterior sternoclavicular dislocation can be treated with a sling or shoulder immobilizer, whereas posterior dislocations commonly require reduction because of potential neurovascular and airway compromise. This should be done in the OR under general anesthesia with general or thoracic surgery backup in case of injury to the lung or great vessels.

B. Arm and Elbow

1. Humeral shaft fractures

a. Mechanism. Fall onto an outstretched arm.

b. Physical signs include deformity of the upper arm, pain, and ecchymosis. A careful neurovascular examination should be performed because the radial nerve is especially vulnerable to injury even in closed injuries due its proximity with the humeral shaft (*J Bone Joint Surg Br*. 2005;87:1647–1652).

c. Management. Closed fractures are placed in a coaptation splint or Sarmiento brace. Indications for surgical fixation include open fractures, injuries to multiple extremities, concurrent injury below the elbow (“floating elbow”), or a body habitus that is not amenable to bracing. Radial nerve palsy is not an indication for operative treatment of humerus fractures in isolation, but exploration of the nerve is recommended if associated with open fractures, stab/lacerating injuries, or changes in examination following manipulation.

2. Distal humerus fractures

a. Mechanism. Fall onto an outstretched hand or directly onto the elbow. Supracondylar humerus fractures are the most common fractures seen in children.

b. Physical signs include swelling, pain, ecchymosis, and decreased elbow range of motion. In children, displaced supracondylar fractures are frequently associated with peripheral nerve injuries. Patients should undergo serial examinations to rule out the development of compartment syndrome.

c. Management. Supracondylar fractures in children can be treated in a splint acutely if they are nondisplaced but require percutaneous pinning and casting if they are displaced. In adults, displacement of or neurovascular compromise with supracondylar fractures are indications for surgical treatment.

3. Radial head fractures

a. Mechanism. Fall onto an outstretched arm.

b. Typical physical signs include tenderness to palpation and pain with forearm rotation.

c. Typical management. Radial head fractures with minimal involvement of the articular surface (<30%) can be treated nonoperatively with early range-of-motion exercises. Compromise of elbow or forearm stability is a surgical indication.

4. Elbow dislocations (ulnohumeral)

a. Mechanism. Fall onto an outstretched hand.

b. Examination reveals pain, swelling, bruising, and deformity with loss of elbow range of motion. Posterior dislocations are most common.

c. Treatment consists of prompt reduction and assessment of stability through gentle passive range of motion. Stable dislocations benefit from early, controlled motion, whereas unstable elbows may require surgical stabilization.

C. Forearm, Wrist, and Hand

1. Radius and ulna fractures

a. Mechanism. Fall onto the outstretched arm. A direct blow can cause a midshaft fracture of the ulna caused by a forceful blow to the forearm positioned for protection, often during an assault.

b. Examination reveals deformity, pain, and focal tenderness. Variable amounts of swelling can be seen, and compartment syndrome occurs in 2% to 3% of cases. Acute carpal tunnel syndrome can occur with distal fractures due to swelling and hematoma.

c. Management. In children, most diaphyseal and wrist fractures can be managed with closed reduction and splinting. In adults, shaft fractures that involve both bones are almost always treated with open reduction/internal fixation (ORIF) after initial closed reduction and splinting. Associated acute carpal tunnel syndrome or forearm compartment syndrome is a surgical emergency.

2. Distal radius fractures

a. Mechanism. Fall on an outstretched hand.

b. Physical signs include pain, deformity, swelling, ecchymosis, and focal tenderness. Similar to diaphyseal fractures, there can be an associated compartment syndrome or acute carpal tunnel syndrome.

c. Management. Many can be treated with splinting and cast immobilization for 4 to 6 weeks. Displacement and shortening are indications for surgical treatment.

3. Scaphoid fractures

a. Mechanism. Fall on an outstretched hand.

b. Physical signs include local swelling, pain with motion, and tenderness in the “anatomic snuffbox.”

c. Management. Nondisplaced scaphoid fractures are treated with a thumb spica splint. Suspected scaphoid fractures, with pain in the anatomic snuffbox but no fracture seen on x-ray, should be treated as nondisplaced fractures and immobilized in the ER. Displaced fractures are at risk of nonunion and avascular necrosis and benefit from surgical treatment.

4. Metacarpal and distal phalanx fractures

a. Mechanism. Crush injury or axial load onto a closed fist.

b. Physical signs include swelling and bruising, often with less knuckle prominence; the most common fracture is of the distal fifth metacarpal, otherwise known as a “boxer’s fracture.”

c. Management involves reduction and splinting with fingers in the

intrinsic plus position (wrist in 20 to 30 degrees of extension, the metacarpophalangeal [MCP] joints in 60 to 90 degrees of flexion, and the interphalangeal [IP] joints in full extension. The thumb should be abducted with the MCP extended), followed by reexamination for rotational deformity. **Indications for operative intervention:** Reduction is not maintained after closed reduction, contaminated open fractures, associated soft-tissue injuries, malalignment (uncorrected rotated, angulated, or shortened deformities of the digit), and articular incongruity >1 mm.

5. Distal phalanx fractures

a. Mechanism is typically a crush injury.

b. Physical signs. These are typically associated with lacerations of the fingertip or nail-bed injuries.

c. Management. While these are technically open fractures, they can be adequately irrigated and debrided in the ER and do not require a formal I&D in the OR. If there is any question of a nail-bed injury, the nail should be removed. Preformed finger splints are used to immobilize the fracture. For complete work-up and management of hand injuries refer to Chapter 44.

D. Pelvic Fractures

1. Disruptions of the pelvic ring

a. Mechanism. Pelvic ring injuries typically result from high-energy mechanisms, such as motor vehicle collisions or a fall from height.

b. Physical signs. Crepitus, pelvic instability, or pain with iliac wing compression or distraction should alert the examiner to possible pelvic ring injury. The patient should be inspected for soft-tissue injury, including a degloving injury. Rectal and vaginal examinations are performed to check for blood, open communication with a fracture, or a high-riding prostate. Blood at the urethral meatus at time of catheterization is a sign of lower urogenital injury. Retrograde urethrogram should be obtained to identify these injuries and define their location. Pelvic bleeding may result in a loss of 2 to 3 L of blood or more, and signs of hypovolemic shock should be treated with aggressive fluid and blood product replacement. High-energy pelvic fractures rarely

occur in isolation, and associated injuries are likely.

c. Management. The initial treatment consists of adherence to ATLS protocols. Maintenance of adequate intravascular volume and systolic blood pressure is essential in the hemodynamically unstable patient. In the persistently unstable patient, sources of bleeding other than the pelvis should be ruled out followed by emergent stabilization of the pelvis with a linen sheet or pelvic binder in patients with volume expanding pelvic ring injuries (AP compression "open book" and vertical shear). Angiogram and embolization of bleeding pelvic vessels should be considered for those patients who remain hemodynamically unstable after volume control and stabilization of the pelvis with a sheet/binder (*J Trauma*. 2002; 53:303–308).

2. Pubic rami fractures

a. Mechanism. Same level falls in an elderly patient.

b. Physical signs include groin pain and pain with weightbearing.

c. Management. These patients are allowed to bear weight as tolerated, but they often initially have significant pain with weightbearing. Physical therapy and mobilization is important to prevent secondary morbidity.

3. Acetabular fractures

a. Mechanism. High-energy trauma such as a motor vehicle collision or fall from height.

b. Physical signs include hip pain and pain with logroll. In cases with an associated hip dislocation, the limb may be shortened and internally rotated. A sciatic palsy is also possible with a posterior hip dislocation.

c. Management. Skeletal traction may be indicated for fractures of the acetabulum, depending on the size and location of the fracture and an associated dislocation. Fractures involving the weightbearing portion of the acetabulum are usually treated with surgical reduction and fixation.

E. Hip and Femur

1. Hip fractures (femoral neck and intertrochanteric fractures)

a. Mechanism. Low-energy falls onto the hip in the elderly.

b. Physical signs. Shortening of the limb may be seen in addition to

pain with motion and the inability to bear weight. Displaced hip fractures are associated with a typical presentation: a shortened, externally rotated lower extremity. A high index of suspicion must be maintained in the elderly after a low-energy fall presenting with complaints of groin or medial thigh pain (site of referred pain from the hip joint) because these may be the only signs of a nondisplaced hip fracture.

c. Management. Displaced femoral neck fractures in the young require urgent anatomic reduction and internal fixation to reduce the risk of avascular necrosis. In the elderly, surgical treatment is generally the rule for hip fractures. Stable femoral neck fractures are usually treated with internal fixation (most commonly, percutaneous screws) and unstable femoral neck fractures with hip arthroplasty (hemi- or total hip arthroplasty).

2. Femoral shaft fractures

a. Mechanism. High-energy mechanisms, most commonly motor vehicle accidents.

b. Physical signs. Patients usually have gross deformity and instability.

c. Management. Initial management involves long-leg splinting or skeletal traction. Most are treated with intramedullary nailing soon after the injury to allow early mobilization and decrease the risk of additional complications. In the unstable, multiply injured patient, external fixation may be the initial treatment to minimize adverse systemic effects caused by instrumentation of the medullary canal (*J Trauma*. 2009;67(3):602–605).

3. Hip dislocations

a. Mechanism. High-energy motor vehicle crash, often associated with acetabular fracture. In patients with a previous hip replacement, dislocation is typically atraumatic.

b. Physical signs. Posterior dislocations (most common) cause limb shortening with an adducted and internally rotated posture. Sciatic nerve function should be assessed for palsy with posterior dislocations (the peroneal division is most commonly affected).

c. Management. Once a hip dislocation is identified in a native hip, immediate closed reduction followed by additional imaging

should be performed to reduce the risk of avascular necrosis. Adequate sedation and muscle relaxation are essential for successful reduction without iatrogenic fracture. Assessment of stability and postreduction neurologic examination are necessary. Postreduction radiographs, including AP, lateral, and Judet views, are needed to confirm reduction and assess for associated fractures.

F. Knee and Tibia

1. Supracondylar femur fractures

a. Mechanism. Can be low energy in the elderly, generally high energy in younger patients.

b. Physical signs are deformity and swelling around the knee.

c. Management. These fractures are initially reduced and splinted in the ER. Almost all of these will require operative treatment.

2. Patellar fractures

a. Mechanism. Patella fractures are commonly caused by a direct fall onto the knee or striking a dashboard.

b. Physical signs. Patella fractures often have a palpable defect, and patients have an associated inability to perform a straight-leg raise.

c. Management. Patella fractures with displacement, joint incongruity, or loss of active knee extension require surgical treatment. Nondisplaced fractures can be treated with a knee immobilizer and weightbearing as tolerated.

3. Tibial plateau fractures

a. Mechanism. Motor vehicle collision, fall from a height, direct blow, and pedestrian versus car are all common.

b. Physical signs include knee effusions, swelling in the lower leg, ecchymosis, and deformity. Tibial plateau fractures should be carefully monitored for compartment syndrome.

c. Management. Tibial plateau fractures are treated with splinting and early motion if they are nondisplaced and stable, but they require surgical treatment for articular incongruity, significant displacement, deformity, or instability. When significant soft-tissue swelling is present, plateau fractures are treated with a temporary, spanning external fixator across the knee until swelling

decreases to the point that ORIF is appropriate (*J Trauma*. 2009;67(3):602–605).

4. Tibial shaft fractures

a. Mechanism. Motor vehicle and motorcycle collisions, falls from height, and gunshot wounds are all common mechanisms.

b. Physical signs. Gross deformity and instability is usually present. The subcutaneous location of the tibia predisposes to open fractures. Nerve function, pulses, and foot perfusion should be compared with the contralateral side. The patients should be carefully monitored for compartment syndrome.

c. Management. Stable tibial shaft fractures can be treated with casting; however, most are treated with intramedullary nailing to allow early weightbearing and joint motion. Open tibial shaft fractures may require multiple surgical debridements and soft-tissue coverage.

5. Knee dislocations

a. Mechanism. Knee dislocations are the result of very-high-energy injuries and require multiple ligamentous disruptions to occur. In extremely obese persons, these can occur with a same level fall or even walking on uneven surfaces.

b. Physical examination. Knee dislocations present with deformity, shortening, ligamentous instability, and often signs of significant neurovascular compromise. Check side-to-side differences in pulse examination serially. Knee dislocations that have reduced spontaneously are easy to miss in the acute setting, and the knees should be examined for ligamentous instability in the setting of high-energy trauma.

c. Management. Knee dislocations require immediate, emergent reduction. These should be reduced even before radiographs are taken if possible. The incidence of concomitant vascular injury is approximately 30%, and pedal pulse examination has a low sensitivity (79%) for detecting significant vascular injury (*J Trauma.* 2004;56:1261–1265). Ankle-brachial index (ABI) testing and, possibly, arteriography can be used for further evaluation. If vascular repair is necessary, a spanning external fixator can be placed to stabilize the knee. After any vascular repair,

prophylactic fasciotomy should be considered. Delayed ligamentous reconstruction may be necessary to restore knee stability (*J Bone Joint Surg Am*. 2009;91:2946–2957).

G. Distal Tibia and Ankle

1. Pilon fractures

a. Mechanism. Distal tibial intra-articular fractures (pilon fractures) are associated with an axial loading mechanism such as falls from a height or floor board injury from a motor vehicle accident.

b. Physical signs include deformity, instability, swelling, and ecchymosis about the ankle. Note soft-tissue injury, which is often significant with pilon injuries, including location of fracture blisters and whether the blisters are blood filled (marker of deeper injury).

c. Management. Pilon fractures with significant shortening, comminution, or soft-tissue injury are best managed initially with closed reduction and placement of a spanning external fixator. External fixation is then maintained until soft-tissue swelling resolves and the leg can tolerate an open procedure. Soft-tissue management is critical in the presence of these injuries (*Clin Orthop Relat Res*. 2000;375:78–90).

2. Ankle fractures

a. Mechanism. Ankle fractures are commonly caused by a twisting mechanism.

b. Physical signs include deformity and instability of the lower leg and ankle joint. A neurovascular examination should be performed and documented.

c. Management. Stable, nondisplaced fractures of the ankle can be treated with immobilization and protected weightbearing. Unstable fractures (one with both medial and lateral injuries) and fractures with joint subluxation benefit from operative treatment. All fractures should be reduced in the ER with postreduction radiographs demonstrating adequate joint and fracture reduction. If adequate joint reduction cannot be achieved or maintained, early surgical treatment is indicated.

3. Ankle sprains are commonly caused by inversion or eversion of the foot. Patients present with swelling, ecchymosis, and maximal

tenderness along the injured ligaments. Radiographs are normal or reveal cortical avulsions. Initial treatment with RICE is usually adequate, followed by physical therapy for proprioceptive training to reduce the risk of reinjury.

4. **Ruptured Achilles tendon** usually occurs during running, jumping, or vigorous activity, with sudden pain and difficulty in walking. Examination can reveal a palpable defect, weak plantar flexion, and, in cases of complete rupture, no passive ankle plantar flexion on squeezing the patient's calf (positive Thompson sign). Treatment consists of either nonoperative management in a splint with the ankle plantar flexed or direct surgical repair. Previous literature has supported operative treatment to decrease the risk of rerupture, but this has not been found in more recent literature with modern nonoperative treatment courses (*J Bone Joint Surg Am*. 2015;97:1187–1195).

H. Foot

1. Calcaneus fractures

a. Mechanism. They are usually the result of an axial load such as a fall from height.

b. Physical signs. Calcaneal fractures are associated with swelling, heel widening, tenderness, and ecchymosis. Associated fractures are common, especially in the thoracolumbar spine, due to axial loading.

c. Management. Calcaneal fractures should be placed in a well-padded splint. Significant subtalar joint depression and comminution may require ORIF once soft-tissue swelling allows.

2. Talus fractures

a. Mechanism. Talus fractures (the second most common) are also generally higher energy (motor vehicle collision or falls) and are usually caused by forced dorsiflexion (e.g., slamming on the brake at the time of impact).

b. Physical signs. Talus fractures can also present with swelling, and when they are associated with a dislocation of the tibiotalar joint and/or the subtalar joint, a significant deformity can be present.

c. Management. Talus fractures can be treated with cast immobilization if they are nondisplaced, but most talus fractures

are treated with ORIF to decrease the risk of nonunion and avascular necrosis.

3. **Metatarsal fractures**
   a. **Mechanism.** Metatarsal fractures can be seen with lower-energy trauma. Stress fractures can occur in runners or others who have recently increased their distance or activity.
   b. **Physical signs.** Stress fractures may present only with tenderness to palpation at the level of the injury.
   c. **Management.** Most metatarsal fractures can be treated nonoperatively with splinting. Transverse fractures of the proximal fifth metatarsal diaphysis (Jones fracture), due to being in a vascular watershed region, are prone to healing complications and require more aggressive treatment than other metatarsal fractures, including either strict nonweightbearing with cast immobilization or surgery. An avulsion of the base of the fifth metatarsal, in contrast, is treated with a controlled ankle motion boot and early weightbearing.
4. **Toe fractures.** Toe injuries are best treated by "buddy taping" to the adjacent digit and giving the patient a hard-soled shoe for more comfortable ambulation. Distal phalanx fractures with nail-bed injuries or soft-tissue lacerations are treated the same as similar injuries in the fingers.
5. **Talar dislocations**
   a. **Mechanism.** The level of energy is similar to that for calcaneal and talar fractures. Talar dislocation occurs with forced foot inversion.
   b. **Physical signs.** With talar dislocations, there is often significant deformity. Dislocation of the talar body can commonly impinge on adjacent neurovascular structures and can be entrapped by tendons.
   c. **Management.** Talar dislocations are treated with emergent reduction to decrease the risk of avascular necrosis, neurovascular injury, and skin compromise. Soft-tissue interposition can prevent closed reduction, in which case open reduction is required.
6. **Lisfranc dislocations**
   a. **Mechanism.** Lisfranc injuries are disruptions of the tarsal–metatarsal joints by either dislocation or fracture dislocation and

are caused by a bending or twisting force through the midfoot.

b. Physical signs. Lisfranc injuries are associated with significant swelling and midfoot tenderness. Compartment syndrome of the foot may be present.

c. Management. Lisfranc injuries are splinted, iced, and elevated in preparation for eventual operative treatment. An attempt at closed reduction should be made to help decrease soft-tissue injury.

VI. OTHER ORTHOPEDIC CONDITIONS

A. Compartment syndrome is characterized by an increase in tissue pressure within a closed osteofascial space sufficient to compromise microcirculation, leading to irreversible damage to tissues within that compartment and soft-tissue necrosis. This occurs in association with prolonged limb ischemia/reperfusion, external pressure, fractures, and burns (*Open Orthop J*. 2012;6:535–543).

1. **Examination.** Signs and symptoms of compartment syndrome include pain (especially with passive motion), pressure, paralysis, paresthesia, pulselessness, and pallor (the so-called six *P*s). The earliest and most important sign is pain out of proportion to the injury, particularly an increasing and disproportionate narcotic demand and unexpectedly poor response to appropriate pain medication, and/or pain with passive motion of involved muscles or tendons traversing the involved compartment. A high index of suspicion is necessary for early diagnosis because "hard signs" like nerve dysfunction or pulselessness occur late in the process. Serial compartment pressure measurements should be considered in obtunded patients with risk factors. A difference between diastolic blood pressure and compartment pressure of <30 mm Hg is diagnostic of compartment syndrome (*J Bone Joint Surg Br*. 1996;78:99–104). In the awake patient, compartment syndrome is a clinical diagnosis.
2. **Treatment.** Fasciotomy of all involved compartments is necessary when compartment syndrome is diagnosed. Prophylactic fasciotomy should also be performed after repair of traumatic vascular injuries (particularly those presenting with ischemia).

B. Open Fractures and Joints. Lacerations or wounds near fractures or joints can communicate and should be carefully evaluated. If exposed

bone is not evident, wounds should be carefully probed to determine whether communication with the fracture is present. Air in the joint on x-ray and fat droplets in blood from the wound also confirm communication with a joint or fracture, respectively.

1. **Treatment** consists of assessing the wounds, removing any obvious gross contamination, applying moist saline dressings, reducing the fracture or joint, and splinting the extremity. Tetanus prophylaxis and IV antibiotics should be administered. Open fractures are classified according to the amount of soft-tissue injury, which provide prognosis for development of infection (*J Bone and Joint Surg*. 1976;58-A:453–458). First-generation cephalosporins are given for all open fractures, unless allergy requires an alternate antibiotic. Debridement of the open fracture and stabilization (either temporary or permanent) should be done urgently, but previously taught time frames (6 to 8 hours) have not been shown to affect the outcomes following open fracture. While there is no proven time frame to operative debridement shown to decrease the risk of infection, decreasing the time to the definitive treating trauma center and decreasing the time from injury to first IV antibiotic dose has been shown to decrease the risk of infection (*J Bone Joint Surg Am*. 2010;92:7–15). Operative debridement should be performed as soon as possible after the patient is resuscitated and appropriate OR personnel are available for a thorough wound debridement and skeletal stabilization.

C. Acute Nerve Injuries. Nerve injury may occur via sharp transection or following gunshot or open blunt trauma. Refer to Chapter 44 for complete details of the assessment and management of peripheral nerve injuries.

D. High-pressure Injection Injuries. These typically occur in laborers in the upper extremity or hand. Grease or paint is injected at up to 10,000 lb/in^2. External wounds are predictably small puncture wounds. Management involves urgent and thorough debridement and decompression.

E. Upper-extremity Traumatic Amputation. A team approach is needed to evaluate for possible reimplantation, and all necessary consultants should be contacted early.

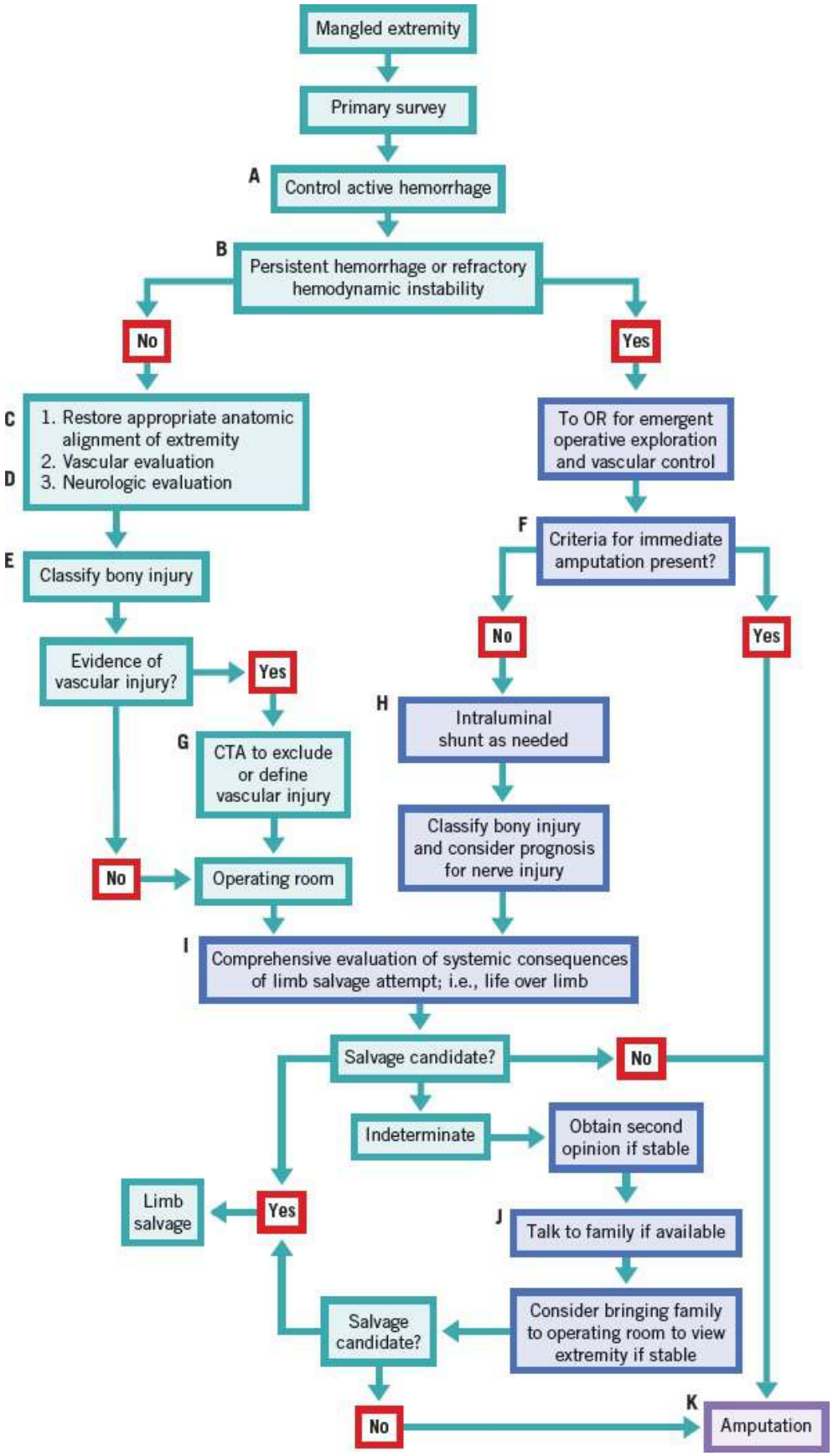

Mangled extremity
Primary survey
A
Control active hemorrhage
B
Persistent hemorrhage or refractory hemodynamic instability
No
Yes
C
1. Restore appropriate anatomic alignment of extremity
D
2. Vascular evaluation
3. Neurologic evaluation
To OR for emergent operative exploration and vascular control
F
Criteria for immediate amputation present?
E
Classify bony injury
No
Yes
Evidence of vascular injury?
Yes
H
Intraluminal shunt as needed
G
CTA to exclude or define vascular injury
Classify bony injury and consider prognosis for nerve injury
No
Operating room
I
Comprehensive evaluation of systemic consequences of limb salvage attempt; i.e., life over limb
Salvage candidate?
No
Indeterminate
Obtain second opinion if stable
Limb salvage
Yes
J
Talk to family if available
Consider bringing family to operating room to view extremity if stable
Salvage candidate?
K
No
Amputation

FIGURE 13-2 Algorithm for management of patients with mangled extremities. (From Scalea TM, DuBose J, Moore EE, et al. Western Trauma Association critical decisions in trauma: management of the mangled extremity. *J Trauma Acute Care Surg*. 2011;72(1):86–93, with permission.)

1. **Management.** The proximal stump should be cleaned, and a compression dressing should be applied. Tourniquets are not used. Amputated parts should be wrapped in moist gauze, placed in a bag, and cooled by placing on ice (taking care to avoid freezing damage), and sent to the OR before the patient for preparation. Reimplantation is most likely to be successful with a sharp amputation and is typically not likely possible with crush injuries or other injuries with a wide zone of injury. Timing is of essence, and a rapid and efficient evaluation is critical. Indication for reimplantation of fingers includes injury in a child, involvement of the thumb, multiple involved digits, and injury distal to the middle phalanx.

F. The Mangled Extremity. The mangled extremity is one that has sustained significant injury to the vascular, bony, soft-tissue, and/or nerve structures. Management of these injuries has to take into account the patient's clinical status on presentation, the ability to revascularize the limb within a timely fashion, and the overall presumed functional status of the limb if it is able to be salvaged. Outcomes following these severe injuries have been associated with multiple psychosocial factors and may not be independently related to the decision to salvage the limb or proceed with amputation. Figure 13-2 is one proposed algorithm for the management of mangled extremity (*J Trauma Acute Care Surg*. 2012;72:86).

CHAPTER 13: EXTREMITY TRAUMA

Multiple Choice Questions

1. **Diagnosis of compartment syndrome of the leg in an obtunded patient is made by measuring a difference of less than 30 mm Hg between the compartment pressure and:**

   a. Systolic blood pressure
   b. Diastolic blood pressure
   c. Mean arterial pressure
   d. Cerebral perfusion pressure

2. **A 22-year-old man injured in a motor vehicle accident is hypotensive and tachycardic. Anteroposterior pelvis radiograph reveals an anteroposterior compression-type pelvic ring injury. In addition to resuscitation, what is the next most appropriate step in management?**

   a. Pelvic angiography
   b. CT of the pelvis
   c. Application of a pelvic sheet or binder
   d. Emergent open reduction and internal fixation
   e. Focused assessment with sonography for trauma (FAST examination)

3. **A 27-year-old male presents with thoracic contusions, a left femur shaft fracture, and initial lactate of 5.1. Following temporary stabilization with skeletal traction, the patient is resuscitated overnight in the ICU and is intubated for pulmonary failure. The following morning the patient has a lactate of 4.7. What is the recommended treatment for the patient's femur fracture on postinjury day 1?**

   a. Reamed intramedullary nail fixation
   b. Unreamed intramedullary nail fixation
   c. Open reduction and internal fixation with plates and screws
   d. External fixation

e. Conversion of skeletal traction to a hip spica cast

4. **Intramedullary nail fixation of femur fractures in under-resuscitated multitrauma patients is associated with which complication?**

   a. Malunion
   b. Fat embolism syndrome
   c. Acute respiratory distress syndrome
   d. Acute blood loss anemia
   e. Nonunion

5. **A 23-year-old female presents following MVC with an open humerus shaft fracture. On examination, she is unable to extend her wrist, fingers, and thumb. Definitive treatment of her extremity injury should include:**

   a. Cleansing in the ER with saline, wet-to-dry dressings, coaptation splint converted to functional brace
   b. External fixation of the humerus
   c. Debridement and irrigation of the wound with exploration of the radial nerve, followed by internal fixation of the fracture
   d. Debridement and irrigation of the wound with exploration of the ulnar nerve, followed by internal fixation of the fracture
   e. Debridement and irrigation of the wound with exploration of the median nerve, followed by internal fixation of the fracture

14

Burns

Kelly Koch and John P. Kirby

INTRODUCTION

Burns result from thermal injury to the skin. They compromise the skin's function as a barrier to injury and infection and as a regulator of body temperature and fluid loss. Like trauma, mortality from burns occurs in a bimodal pattern: immediately after the injury or weeks later from sepsis and multiorgan failure. Detailed guidelines for the management of burns may also be found in the American Burn Association Consensus Statements (*J Burn Care Res*. 2013;34:4).

I. ASSESSMENT AND MANAGEMENT OF BURN INJURIES (Fig. 14-1)

A. Mechanism of Injury. Identify burn source, duration of exposure, time of injury, and environment. Burns sustained in a closed environment, such as a structure fire, often produce inhalation injury in addition to thermal trauma. Explosions can cause barometric injury to the eardrums and lungs and may also cause blunt trauma.

B. Primary survey should follow the guidelines established by the American College of Surgeons' Advanced Trauma Life Support Course. Burn patients should be evaluated and treated as victims of multisystem trauma because there is significant morbidity associated from missed injuries secondary to an explosion, falls, and so forth.

1. **Airway** assessment and security are the foremost priority. Inhalation injury should be suspected if the patient was burned in an enclosed structure or explosion. Physical signs include hoarseness, stridor, facial burns, singed facial hair, expectoration of carbonaceous sputum, and presence of carbon in the oropharynx. The decision to

intubate the trachea for airway protection should be made early and is preferable to cricothyroidotomy in the edematous and swollen neck.

2. **Breathing** is evaluated for effort, depth of respiration, and auscultation of breath sounds. Wheezing or rales suggest either inhalation injury or aspiration of gastric contents. Most severely burned patients develop early pulmonary insufficiency and respiratory failure. The use of lower tidal volumes, permissive hypercapnia, and the “open lung” approach to ventilation can significantly improve outcomes (*N Engl J Med*. 2000;342:1301).
3. **Circulation.** Aggressive and prompt fluid resuscitation is a cornerstone of early burn management. Burn injury causes a combination of hypovolemic and distributive shock characterized by the release of inflammatory mediators, dynamic fluid shifts from the intravascular compartment to the interstitium, and exudative and evaporative water loss from the burn injury. Full-thickness circumferential extremity or neck burns require escharotomy if circulation distal to the injury is impaired.

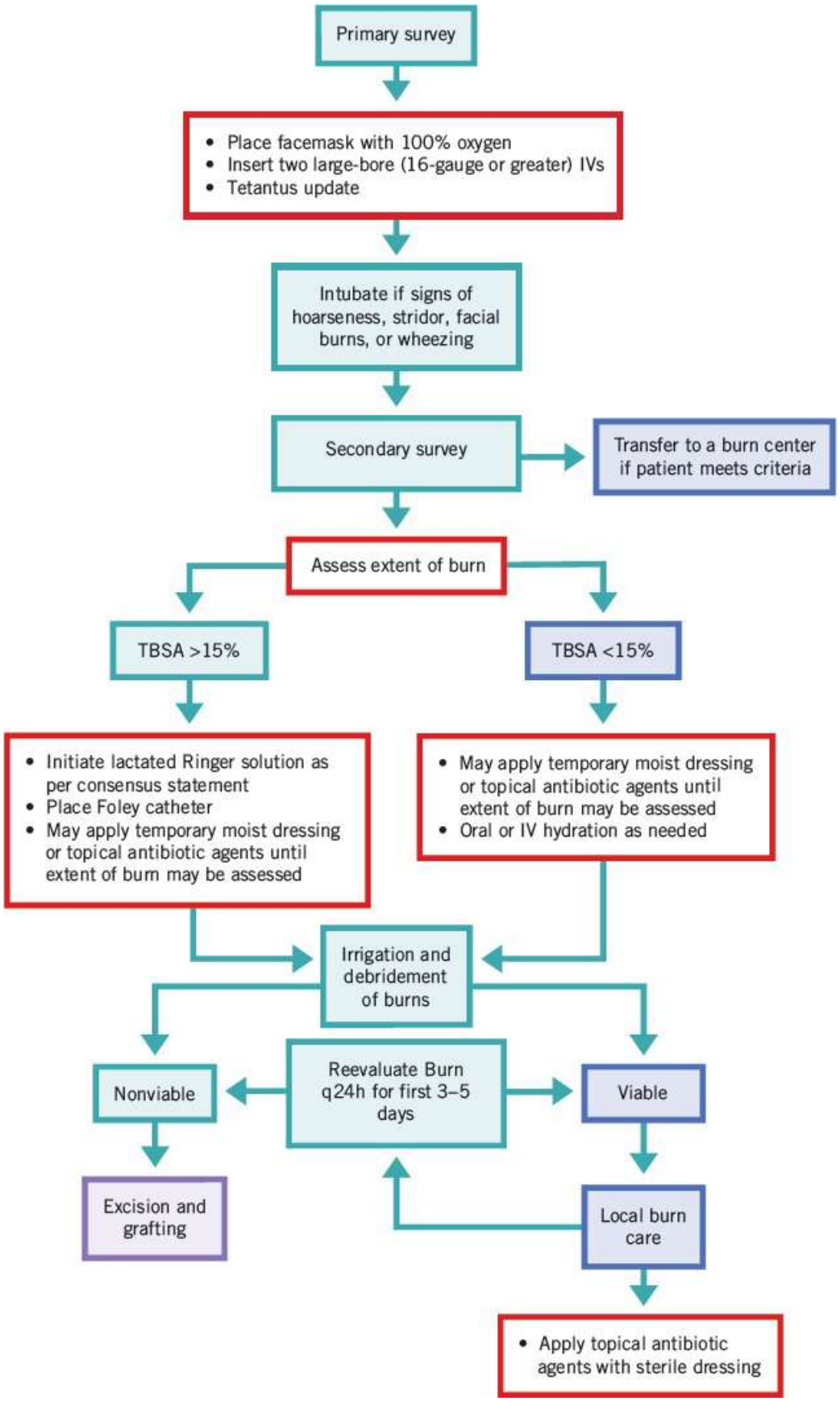

Primary survey
• Place facemask with 100% oxygen
• Insert two large-bore (16-gauge or greater) IVs
• Tetantus update
Intubate if signs of hoarseness, stridor, facial burns, or wheezing
Secondary survey
Transfer to a burn center if patient meets criteria
Assess extent of burn
TBSA >15%
TBSA <15%
• Initiate lactated Ringer solution as per consensus statement
• Place Foley catheter
• May apply temporary moist dressing or topical antibiotic agents until extent of burn may be assessed
• May apply temporary moist dressing or topical antibiotic agents until extent of burn may be assessed
• Oral or IV hydration as needed
Irrigation and debridement of burns
Nonviable
Reevaluate Burn q24h for first 3–5 days
Viable
Excision and grafting
Local burn care
• Apply topical antibiotic agents with sterile dressing

FIGURE 14-1 Algorithm for the evaluation and management of burns.

4. **Exposure.** Remove all clothing to halt continued burn from melted synthetic compounds or chemicals and to assess the full extent of body surface involvement in the initial examination. Irrigate injuries with water or saline to remove harmful residues. Remove jewelry to prevent injury resulting from increasing tissue edema.

C. Burn-specific Secondary Survey

1. **Depth of burn.** Burns should be classified and managed based on which layer of skin to which they extend (see Table 14-1).
2. **Percentage of body surface area (BSA) estimation.** The accurate and timely assessment of BSA is a critical aspect of the initial evaluation of burned patients. It will determine whether transfer to a specialized burn center is required as well as the magnitude of initial fluid resuscitation and nutritional requirements (*J Burn Care Res*. 2007;28:42).
   a. **Small areas:** The area of patient's hand (including palm and extended fingers) equals 1% of BSA (*Burns*. 2001;27:591).
   b. **Large areas:** "Rule of nines." Regions of the body approximating 9% BSA or multiples thereof are shown in Figure 14-2. Note that infants and babies have a proportionally greater percentage of BSA in the head and neck region and less in the lower extremities than adults (*Burns*. 2000;26:156).

D. Transfer to a burn center should follow the guidelines of the American Burn Association (www.ameriburn.org). These criteria reflect multiple studies showing that age and BSA burn percentage remain the two most important prognostic factors. Criteria include:

1. Partial-thickness burns greater than 10% BSA.
2. Any full-thickness burn.
3. Burns that involve the face, hands, feet, genitalia, perineum, or major joints.
4. Any inhalation, chemical, or electrical injury (including lightning).
5. Burn injury in patients with pre-existing medical conditions that could complicate management, prolong recovery, or affect mortality.
6. Burns in combination with significant associated mechanical trauma. Note, if the traumatic injury poses a greater threat to life, the patient

should be stabilized at a trauma center before transfer to a burn unit.

7. Burned children in hospitals without qualified personnel or equipment for the care of children.
8. Patients requiring specialized rehabilitation, psychological support, or social services (including suspected neglect or child abuse).

II. MANAGEMENT

A. Resuscitation. A surgical consultation is initiated for all patients with major injury.

1. **Oxygen** should be provided to patients with all but the most minor injuries. A 100% oxygen high-humidity facemask for those with possible inhalation injury assists the patient's expectoration from dry airways and treats carbon monoxide poisoning.

TABLE 14-1 Treatment Algorithm for the Three Clinically Important Burn Depths[a]

Burn Depth[b]	Level of Injury	Clinical Features	Treatment	Usual Result
Superficial partial-thickness	Papillary dermis	Blisters Erythema Capillary refill Intact pain sensation	Tetanus prophylaxis Cleaning (e.g., with chlorhexidine gluconate) Topical agent (e.g., 1% silver sulfadiazine) Sterile gauze dressing[c] Physical therapy Splints as necessary	Epithelialization in 7–21 days Hypertrophic scar rare Return of full function
Deep partial-thickness	Reticular dermis	Blisters pale white or yellow color Absent pain sensation	As for superficial partial-thickness burns Early surgical excision and skin grafting an option	Epithelialization in 21–60 days in the absence of surgery Hypertrophic scar common Earlier return of function with surgical therapy
Full-thickness	Subcutaneous fat, fascia, muscle, or bone	Blisters may be absent Leathery, in classic, wrinkled appearance over bony prominences No capillary refill Thrombosed subcutaneous vessels may be visible Absent pain sensation	As for superficial partial-thickness burns Wound excision and grafting at earliest feasible time	Functional limitation more frequent Hypertrophic scar mainly at graft margins

[a]Epidermal (first-degree) burns present clinically with cutaneous erythema, pain, and tenderness; they resolve rapidly and generally require only symptomatic treatment.
[b]No clinically useful objective method of measuring burn depth exists; classification depends on clinical judgment.
[c]Sterile gauze dressings are frequently omitted on the face and neck.
Reprinted with permission from Monafo WW. Initial management of burns. *N Engl J Med*. 1996;335:1581–1586.

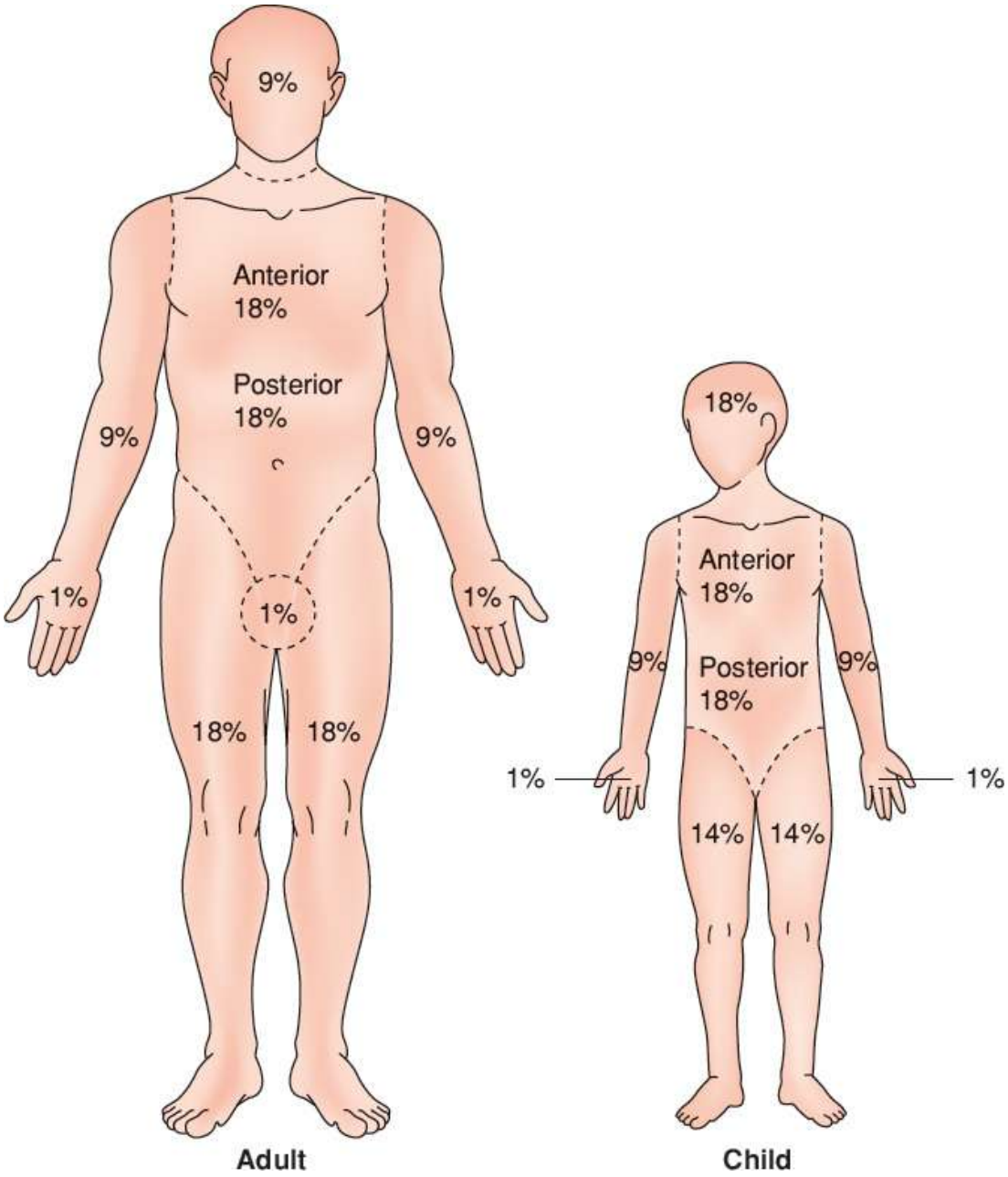


FIGURE 14-2 Estimation of percent area burned in adults and children using the rule of nines.

2. **Intravenous access.** All patients with burns of 15% or greater BSA require intravenous fluids. Two 16-gauge or larger peripheral venous catheters should be started immediately to provide circulatory volume support. An intravenous catheter may be placed through the burn if other sites are unavailable and may be sutured in place. Avoid lower-extremity catheters, if possible, to prevent phlebitic complications.

3. **Fluid.** Improved survival in the era of modern burn care is largely attributable to early and aggressive volume resuscitation. Intravenous fluid in excess of maintenance fluids is administered to all patients with burns of 20% or greater BSA in adults and children. Fluid resuscitation based on the consensus formula is widely used as an initial estimation of likely fluid resuscitation needs and has decreased the occurrence of burn-induced shock (*J Burn Care Res*. 2008;29:257).
   a. **Consensus formula.** The estimated crystalloid requirement for the first 24 hours after injury is calculated on the basis of patient weight (determined early after the burn as a baseline) and BSA burn percentage. Lactated Ringer solution volume in the first 24 hours = 2 to 4 mL × %BSA (second-, third-, and fourth-degree burns only) × body weight (kg). One-half of the calculated volume is given in the first 8 hours after injury, and the remaining volume is infused over the next 16 hours with adjustments being made as clinical conditions and size/depth of burns evolve. Fluid resuscitation calculations are based on the time of injury. Avoid overresuscitation as this can lead to an increase in congestive complications such as intra-abdominal hypertension and ACS. For children weighing 30 kg or less, 5% dextrose in one-quarter normal saline maintenance fluids should supplement the consensus formula to compensate for ongoing evaporative losses and quickly depleted glycogen stores.
   b. **Colloid-containing solutions** for resuscitation remains an ongoing debate. Some studies show they should be avoided as an intravenous therapy until after the first 24 hours postburn, at which time capillary leak diminishes. Some providers opt for a compromise, augmenting resuscitation with albumin later in the first 24 hours and in patients with large burns.

B. Additional Management

1. **Foley catheter** is used to monitor hourly urine production as an index of adequate tissue perfusion. In the absence of underlying renal disease, a minimum urine production rate of 1 mL/kg/hr in children (weighing ≤30 kg) and 0.5 mL/kg/hr in adults is the guideline for adequate intravenous infusion.
2. **Nasogastric tube** insertion with low suction is performed if patients

are intubated or develop nausea, vomiting, and abdominal distention consistent with adynamic ileus.

3. **Continuous pulse oximetry** to measure oxygen saturation is useful. One caveat is that falsely elevated levels can be observed in carbon monoxide poisoning.
4. **Laboratory evaluation** includes a baseline complete blood cell count, type and crossmatch, electrolytes and renal panel, β-human chorionic gonadotropin (in women), arterial carboxyhemoglobin, arterial blood–gas evaluation, and urinalysis. An electrocardiogram is useful initially, particularly in elderly patients or those with electrical burns. Fluid and electrolyte fluxes during resuscitation and later mobilization of third-space edema can result in arrhythmias and interval electrocardiogram changes.
5. **Tetanus prophylaxis.** If a patient's last booster was administered greater than 5 years prior, 0.5 mL of tetanus toxoid is given intramuscularly. If immunization status is unknown, 250 to 500 units of human tetanus immunoglobulin (Hyper-Tet) are given intramuscularly.

C. Wound Care

1. **Early irrigation and debridement** are performed using normal saline and sterile instruments to remove all loose epidermal skin layers. In general, it is safe to leave small blisters overlying superficial partial-thickness burns intact because they permit healing in a sterile environment and offer some protection to the underlying dermis. However, in larger and deeper partial-thickness burns, debridement of burn blisters should be done to relieve tension and purge inflammatory mediators. Nonviable tissue in the burn wound should be debrided early because the dead tissue provides a bacterial medium putting the patient at risk for both local and systemic infections.
2. **Topical antimicrobial agents** are the mainstay of local burn wound management (Table 14-2). Prior to the use of topical antimicrobial agents, the most common organisms causing burn wound infections were *Staphylococcus aureus* and group A streptococci. Subsequent to the development of topical agents, gram-negative organisms, particularly *Pseudomonas aeruginosa*, and fungi are the most common causes of invasive burn wound sepsis (*J Burn Care Res*.

2011;32:324). Systemic antibiotics are not administered prophylactically. A 500-mg biopsy of suspicious eschar and underlying unburned tissue is required to diagnose an invasive infection. Wound infection is defined by more than 10^5 organisms per gram of tissue. Treatment requires infected eschar excision and appropriate topical/systemic antibiotic therapy.

3. **Dressings**

   a. **Biologic dressings** include allograft (cadaver skin) and xenograft (pig skin). These dressings provide the advantages of ease of acquisition and application while providing barrier protection and a biologic bed under which dermis can granulate.

   b. **Synthetic dressings** have become an attractive alternative for early wound coverage. **Biobrane** is a collagen-coated silicone membrane that prevents moisture loss, but, therefore, can trap infection. It is relatively painless and can be easily peeled from the wound after epithelialization. **Trancyte** is similar to Biobrane, but also has growth factors from cultured fibroblasts to theoretically aid wound healing. **Integra** consists of an epidermal analogue (silastic film) and a dermal analogue (collagen matrix), making it useful for full-thickness burns. Once adequate vascularization is seen through the silicone layer, the film is removed, and an ultrathin autograft is placed onto the artificial dermis, which allows more rapid reharvesting from the donor site (*J Burn Care Rehabil*. 2003;24:42).

D. Operative Management

1. **Escharotomy** may be necessary in full-thickness circumferential burns of the neck, torso, or extremities when increasing tissue edema impairs peripheral circulation or when chest involvement restricts respiratory efforts.

TABLE 14-2 Topical Antimicrobial Agents for Burns

Agent	Advantages	Disadvantages
Silver sulfadiazine (Silvadene)	Broad spectrum (gram positive, gram negative, some	*Pseudomonas* residence Poor eschar

	fungal) Nonirritating Easy to use Few adverse side effects Formulated as a cream, which minimizes water and heat loss, thereby diminishing caloric requirements	penetration Occasional transient leukopenia 3–5 days after use (harmless, resolves regardless of cessation of treatment)
Mafenide acetate (Sulfamylon)	Broad spectrum (includes *Pseudomonas* and *Enterococcus* species) Good eschar penetration	Painful Allergic rash Can cause metabolic acidosis via carbonic anhydrase inhibition, limiting its use to small, full-thickness burns
Polymyxin B sulfate (Polysporin), neomycin, bacitracin, mupirocin	Painless Allows wound observation Tolerated well on facial burns Do not discolor skin Mupirocin-improved activity against methicillin-resistant *Staphylococcus aureus* and gram-negative bacteria	Poor gram-negative coverage Poor eschar penetration
Silver nitrate	Painless, application as a soaked gauze Good antimicrobial coverage	Stains tissue gray to black (makes wound monitoring difficult) Hypotonic (causes

	Safe in sulfa allergy	severe electrolyte abnormalities)
Acticoat	Easy application Good antimicrobial coverage from impregnated silver ions	Expensive Can only be left in place for 3 days

2. **Early tangential excision of burn eschar** to the level of bleeding capillaries should follow the resuscitation phase. A meta-analysis of six randomized control trials found decreased mortality and decreased length of hospital stay in burn patients with early excision (*Burns*. 2006;32:145). For each trip to the operating theater, consider limiting burn excision to less than 20% BSA or 2 hours of operating time.
3. **Early excision and grafting** has been shown to benefit survival, blood loss, incidence of sepsis, and length of stay compared with serial debridement (*Burns*. 2006;32:145). Split-thickness skin grafts are harvested at a thickness of 0.012 to 0.015 in (*Clin Dermatol*. 2005;23:332). For cosmetically sensitive areas, autografts are not meshed, or, if necessary, meshed at a narrow ratio (≤2:1). Grafts are secured with absorbable sutures or staples. For very large wounds, split-thickness skin grafts can be meshed up to 4:1 and may be overlaid with meshed allograft tissue. However, cosmesis is poor, and graft take rates may be compromised.

E. Nutrition. Severe burns induce a hypermetabolic state proportional to the size of the burn up to 200% the normal metabolic rate. The daily estimated metabolic requirement (EMR) in burn patients can be calculated from the Curreri formula: EMR = [25 kcal × body weight (kg)] + (40 kcal × %BSA). In children, formulas based on BSA are more appropriate. Protein losses in burn patients from both an increased oxidation rate and burn wound extravasation should be replaced by supplying 1.5 to 2 g/kg of protein per day (*Lancet*. 2004;363:1895).

1. **Enteral feedings** are the preferred route when tolerated and can be administered through an enteral feeding tube positioned in the duodenum. For severe burns, early feeding within the first 24 hours

has been shown to decrease the catabolic response, reduce infectious complications, and decrease the length of ICU stay (*J Burn Care Res*. 2011;32:104).

2. **Total parenteral nutrition** should be initiated after fluid resuscitation only if the patient is unable to tolerate enteral feeding.
3. **Daily vitamin supplementation** in adults should include 1.5 g of ascorbic acid, 500 mg of nicotinamide, 50 mg of riboflavin, 50 mg of thiamine, and 220 mg of zinc.

F. Critical Care Considerations

1. **Stress ulcer prophylaxis** (e.g., H_2 blockers or proton-pump inhibitors) should be provided for patients who have major burns (Eastern Association for the Surgery of Trauma Stress Ulcer Prophylaxis Guidelines. 2008. https://www.east.org/education/practice-managementguidelines/stress-ulcer-prophylaxis).
2. **Venous thromboembolism (VTE).** Burn patients are at increased risk for VTE and should receive pharmacologic prophylaxis (*Burns*. 2004;30:591).
3. **Sepsis.** In patients who survive the first 24 hours after injury, burn sepsis is the leading cause of mortality (*Burns*. 2006;32:545). The evidence-based recommendations of the Surviving Sepsis Campaign (*Crit Care Med*. 2008;36(1):296) include antibiotic therapy, source control, crystalloid resuscitation, vasopressor use, a hemoglobin transfusion trigger of 7 g/dL, an open-lung/low-tidal-volume ventilatory strategy, and maintenance of blood glucose less than 180 mg/dL.

III. BURN MECHANISMS: SPECIAL CONSIDERATIONS

A. Patient age is a major determinant on outcome. Infants and elderly patients are at highest risk. Burns are a common form of child abuse. Physical examination findings include stocking/glove injury patterns, lack of splash marks, and dorsally located contact burns of the hands (*Forensic Sci Int*. 2009;187:81). Elderly patients often have comorbid medical problems and decreased physiologic reserve.

B. Inhalation Injuries. Thermal injury to the airway generally is limited to the oropharynx or glottis. Gases containing substances that have

undergone incomplete combustion (particularly aldehydes), toxic fumes (hydrogen cyanide), and carbon monoxide can cause tracheobronchitis, pneumonitis, and edema. Mortality may be increased by as much as 20% in these patients. Management of **minor inhalation injury** is by delivery of humidified oxygen. **Major injuries** require endotracheal intubation for airway protection, preferably with a large-bore tube (7.5 to 8 mm) to facilitate pulmonary toilet of viscous secretions. Bronchodilators can be given to treat bronchospasm whereas nebulized heparin and *N*-acetylcysteine can limit cast formation. Extubation is performed as soon as possible to prevent pneumonia because coughing clears pulmonary secretions more effectively than suctioning. **Carbon monoxide** exposure is suggested by a history of exposure in a confined space with symptoms of nausea, vomiting, headache, mental status changes, and cherry-red lips. Carbon monoxide binds to hemoglobin with an affinity 249 times greater than that of oxygen, resulting in extremely slow dissociation unless the patient is administered supplemental oxygen (40-minute half-life with 100% oxygen via nonrebreathing mask). The arterial **carboxyhemoglobin** level is obtained as a baseline. If it is elevated (>5% in nonsmokers or >10% in smokers), oxygen therapy should continue until normal levels are achieved. Consideration for adjunctive hyperbaric oxygen treatment in CO poisonings and burns should be according to guidelines as set forth by the Undersea & Hyperbaric Medical Society Indications Report.

C. Electrical Injuries. Factors influencing severity include the voltage (high is >1,000 V), resistance, type of current, current pathway through the body, and duration of contact with an electrical source (*Annu Rev Biomed Eng*. 2000;2:477). Electrical current passes in a straight line between points of body contact with the source and the ground. In most cases, these injuries respond to resuscitation and usually do not cause permanent damage (*Ann Intern Med*. 2006;145:531). Severity of injury frequently is underestimated when only the entrance and exit wounds are considered. High-voltage injury, which is commonly seen in workers operating near power lines, can present with full-thickness, charred skin at the entrance and exit wounds, with full arrest, and with fractures sustained while current is passed through the body or during a fall. **Complications** include cardiopulmonary arrest (more common with alternating current), thrombosis, associated fractures related to fall or

severe muscle contraction, spinal cord injury, and cataracts. **Rhabdomyolysis** may occur and result in myoglobin release from injured cells of deep tissues. Precipitation of protein in the renal tubules can cause acute renal failure. Dark urine is the first clinical indication of myoglobinuria, and intravenous lactated Ringer solution should be administered to maintain a urine output greater than 2 mL/kg/hr.

D. Chemical injury may result from contact with alkali, acid, or petroleum compounds. Removal of the offending agent is the cornerstone of treatment. Dry chemicals should be brushed off or aspirated into a closed suction container before irrigating with **copious** amounts of water for at least 20 to 30 minutes. Alkali burns penetrate more deeply than acid burns and require longer periods of irrigation. Neutralizing the chemicals is not recommended because the resulting reaction generates heat, which can exacerbate the injury. All chemical injuries to the eye are potentially blinding and require copious irrigation with several liters of water and prompt referral to an ophthalmologist (*BMJ*. 2004;328:36). Tar can cause ongoing burns which can be quite deep if not removed promptly. Treat them by cooling the tar with cold water followed by removing any remaining tar with adhesive remover.

E. Cold Injuries

1. **Hypothermia** is defined as a core body temperature less than 35°C. Mild hypothermia is classified as a core body temperature of 32° to 35°C; moderate hypothermia is 30°C; and severe hypothermia is less than 30°C. Signs of hypothermia include reduced levels of consciousness, dysrhythmias, and skin that appears cold, gray, or cyanotic. Core body temperature should be monitored by means of an esophageal or rectal probe. The heart becomes increasingly irritable at core temperatures below 34°C, and cardiac monitoring should be routine in all hypothermic patients. Asystole may occur below 28°C, and cardiopulmonary resuscitation should be started and maintained until the patient is rewarmed to at least 36°C. Rewarming can be passive or active. **Passive rewarming** involves using blankets to cover the body and head. The warming rate ranges between 0.5° and 2°C per hour. **Active external warming** includes the use of heating blankets or a heated forced-air system, which can increase rewarming rates by 1°C per hour as compared with simple cotton blankets. **Active internal rewarming** can be started immediately in the case of

severe hypothermia and includes the use of warmed intravenous fluids and oxygen, together warming at a rate of 1° to 2°C per hour. Although rarely used, active invasive rewarming methods can warm faster, at a rate 1° to 4°C per hour. Examples of this approach include warmed peritoneal lavage, thoracostomy lavage, and bladder lavage. Extracorporeal rewarming of blood via a continuous venovenous bypass circuit or heated hemodialysis can rewarm at a rate of 1° to 2°C every 5 minutes.

2. **Frostbite** results from the formation of intracellular ice crystals and microvascular occlusion. Factors affecting severity are temperature, duration of exposure, and environmental conditions promoting rapid heat loss such as wind velocity, moisture, immobilization, and open wounds. The fingers, toes, and ears are most commonly injured, particularly when reduced tissue perfusion has resulted from other causes such as shock.

   a. Classification

   (1) First degree: Hyperemia and edema, without skin necrosis.

   (2) Second degree: Superficial vesicle formation containing clear or milky fluid surrounded by hyperemia, edema, and partial-thickness necrosis.

   (3) Third degree: Hemorrhagic bullae and full-thickness necrosis.

   (4) Fourth degree: Gangrene with full-thickness involvement of skin, muscle, and bone.

   b. Treatment consists of rapid rewarming in a warm water bath between 40° and 42°C until the tissue perfusion returns, which also may help to minimize tissue loss. Splinting and elevation of the frostbitten extremity may reduce edema and promote tissue perfusion. Because mechanical pressure or friction can injure the tissue further, massage and weightbearing are discouraged. Escharotomy may be required for severe injury. Early amputation is not recommended because improvement in tissue viability can occur weeks after injury.

CHAPTER 14: BURNS

Multiple Choice Questions

1. **A patient receives a scald burn to his arm after spilling hot tea. The burn is red and blistered and is painful to touch. What is the depth of this burn?**

   a. First degree
   b. Second degree
   c. Third degree
   d. Fourth degree

2. **A 42-year-old patient presents with second-degree burns to the anterior surface of both legs and anterior torso. What is his total percentage body surface area burn?**

   a. 18%
   b. 36%
   c. 45%
   d. 54%
   e. 63%

3. **What is the most common organism to cause burn sepsis?**

   a. *Escherichia coli*
   b. Group A streptococci
   c. *Staphylococcus epidermidis*
   d. Enterococcus
   e. Pseudomonas

4. **What is a side effect of mafenide acetate?**

   a. Metabolic acidosis
   b. Neutropenia
   c. Hyponatremia
   d. Thrombocytopenia
   e. Gastrointestinal upset

5. A 42-year-old man city worker presents after sustaining an electrical burn. He has contact burns on his hands and feet. His EKG shows normal sinus rhythm. What is this patient at risk for?

a. Respiratory distress
b. Renal failure
c. Hyperthermia
d. Hypothermia
e. Infection

15

Wound Care

Erin G. Andrade and Laurie J. Punch

INTRODUCTION

Acute wound healing is the normal orderly process that occurs after injury and often requires minimal practitioner intervention. *Chronic* wound healing *does not* follow that orderly progression of healing and often necessitates a variety of interventions to facilitate complete healing.

ACUTE WOUND HEALING

I. Physiology of the Acute Wound. Disruption of tissue integrity initiates a sequence of events directed at restoring the injured tissue to a healed, normal state. Normal wound healing occurs in an orderly fashion and is a balance of repair and regeneration of tissue.

A. Early Wound Healing

1. **Hemostasis.** Tissue trauma commonly causes bleeding. Vasoconstriction immediately follows, and the coagulation cascade is initiated. This process contains hemorrhage and stimulates fibrin. The fibrin matrix further activates **platelets** and also serves as the initial scaffold for wound healing. In later phases of wound healing, the fibrin matrix facilitates cell attachment and serves as a reservoir for cytokines.
2. **Inflammatory phase** (days 1 to 4). Injury immediately activates three plasma-based systems: the coagulation cascade, the complement cascade, and the kinin cascade. Proinflammatory factors attract leukocytes and facilitate their migration out of the intravascular space and into the wound. **Polymorphonuclear leukocytes** (**PMNs**) are the dominant inflammatory cells in the

wound for the first 24 to 48 hours, which phagocytize bacteria and damaged tissue, and also release cytokines such as TNF-alpha and interleukin-1 that further stimulate the inflammatory response and local vasodilation. The inflammatory phase progresses with the infiltration of circulating **monocytes** into the wound. Monocytes migrate into the extravascular space through capillaries and differentiate into **macrophages**. Macrophages are activated by locally produced cytokines and are essential for normal healing. They phagocytize bacteria and damaged tissue, secrete enzymes for the degradation of tissue, and release cytokines for inflammatory cell recruitment and fibroblast proliferation. The inflammatory phase lasts a well-defined period of time in primarily closed wounds (~4 days), but it continues indefinitely to the end point of complete epithelialization in wounds that close by secondary or tertiary intention.

B. Intermediate wound healing involves mesenchymal cell migration and proliferation, angiogenesis, and epithelialization.

1. **Fibroblast migration** occurs 2 to 4 days after wounding. Chemotactic cytokines influence fibroblasts to migrate into the wound from undamaged tissue.
2. While the wound is infiltrated by mesenchymal cells, **angiogenesis** takes place to restore the vasculature that has been disrupted by the wound.
3. **Epithelialization** restores the barrier between the wound and the external environment. Epithelialization of wounds occurs via the migration of epithelial cells from the edges of the wound and from remaining epidermal skin appendages. Migration of epithelial cells occurs at the rate of 1 mm/day in clean, open wounds. Primarily closed wounds have a contiguous epithelial layer at 24 to 48 hours.

C. Late wound healing involves the deposition of collagen and other matrix proteins and wound contraction. The primary function of the fibroblast at this stage becomes protein synthesis.

1. **Collagen** is the main protein secreted by fibroblasts. It provides strength and structure to the wound. Collagen is synthesized at an accelerated rate for 2 to 4 weeks, greatly contributing to the tensile strength of the wound. Oxygen, vitamin C, alpha-ketoglutarate, and iron are important cofactors for the cross-linkage of collagen fibers.

2. **Wound contraction** is a decrease in the size of the wound without an increase in the number of tissue elements that are present. It involves movement of the wound edge toward the center of the wound through the contraction of myofibroblasts. Wound contraction begins 4 to 5 days after wounding and continues for 12 to 15 days or longer if the wound remains open.
3. The final wound-healing event is **scar formation and remodeling.** It begins at approximately 21 days after wounding. During scar remodeling, collagen is broken down and replaced by new collagen that is denser and organized along the lines of stress. By 6 months, the wound reaches 80% of the bursting strength of unwounded tissue. It is important to note that a well-healed wound never achieves the strength of unwounded tissue. This process reaches a plateau at 12 to 18 months, but it may last indefinitely.

CHRONIC WOUND HEALING

I. PHYSIOLOGY OF THE CHRONIC WOUND. A chronic wound is a wound that fails to heal in a reasonable amount of time due to a disruption of the normal process of acute wound healing. Most chronic wounds are slowed or arrested in the inflammatory or proliferative phases of healing and have increased levels of matrix metalloproteinases, which bind up or degrade the various cytokines and growth factors at the wound surface.

A. Intrinsic or local factors are abnormalities within the wound that prevent normal wound healing. Examples include the following:

1. **Foreign bodies** increase duration of inflammatory process as body fights material recognized as nonself.
2. **Necrotic tissue** increases wound bioburden and prevents new tissue growth.
3. **Repetitive trauma** to the wound prevents wound healing from progressing, as each injury restarts the inflammatory process.
4. **Hypoxia/ischemia** prevents wound healing through decreased nutrient delivery. Also, oxygenases are important in collagen deposition and superoxide production.
5. **Venous insufficiency** causes distention and damage to capillaries, which triggers an inflammatory response.

6. Active **infection** prolongs the inflammatory reaction.
7. Growth factors are involved in signaling pathways of inflammation, migration, and maturation. Thus, **growth factor deficiency** can lead to stagnation of wound healing.
8. **Excessive matrix protein degradation** inhibits cell–matrix interactions necessary for cell function.
9. **Radiation.**

B. Extrinsic or systemic factors also contribute to abnormal wound healing. Optimization of these factors is critical to healing a chronic wound: (1) diabetes mellitus, (2) use of steroids and antineoplastic drugs, (3) smoking, (4) collagen vascular disease, (5) repetitive trauma, and (6) chronic disease states in the kidney and liver.

C. Biofilms represent a chronic infection in which bacteria are both more resistant and less invasive. They are groups of cells held together by an extracellular matrix that grow adherent to a surface, such as medical implants, catheters, and chronic wounds. They are resistant to antibiotics and contribute to the prolonged inflammatory phase in chronic wounds.

II. SPECIAL CATEGORIES OF CHRONIC WOUNDS

A. Diabetic Foot Ulcers

1. **Evaluation.** The quality of the peripheral circulation, the extent of the wound, and the degree of sensory loss should be recorded. See Figure 15-1 for an example of a diabetic foot ulcer. Web spaces and nails should be examined for evidence of mycotic infection. Neuropathic, arthropathic, and vasculopathic ulcers occur on the plantar surface of the metatarsals and extend to the metatarsal head, leaving exposed cartilage. Evaluation of diabetic foot ulcers should include plain x-rays of the foot (Fig. 15-2) to evaluate for osteomyelitis, ankle-brachial index measurements for vascular insufficiency, and the Semmes–Weinstein monofilament test for neuropathy.
2. **Treatment.** Critical to treatment of any diabetic foot wound is complete offloading of the ulcer with an appropriate diabetic shoe or other orthotic device as well as documentation that the patient is neuropathically insensate.
   a. **Clean wounds** are treated with minimal debridement and damp

gauze or hydrogel-based dressing changes. Hydrogel dressings may be more effective than damp gauze (*Cochrane Database Syst Rev*. 2010;20:CD003556). Exudative wounds may benefit from alginate, hydrocolloid, or negative-pressure wound therapy (NPWT) that removes excess wound exudate, which inhibits wound healing. Close follow-up is essential.

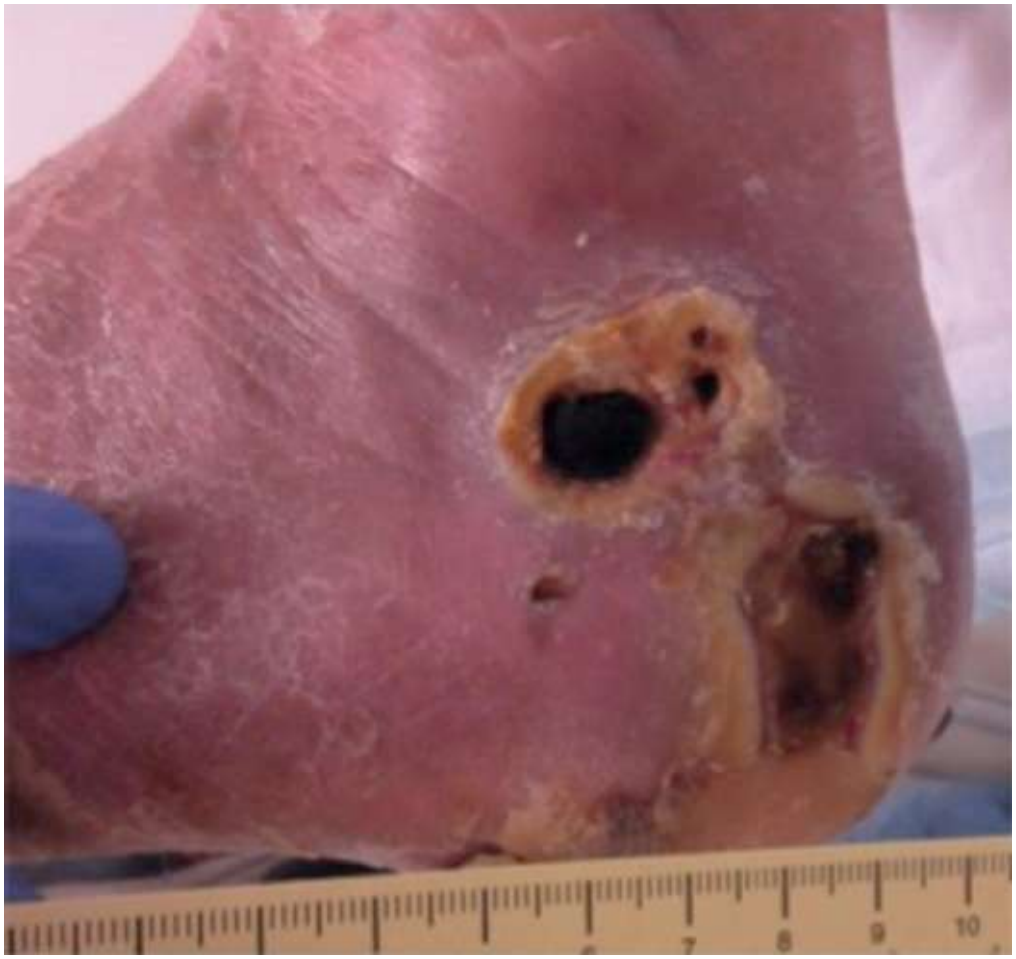


FIGURE 15-1 Diabetic foot ulcer in a patient with low grade fever and active wound drainage.

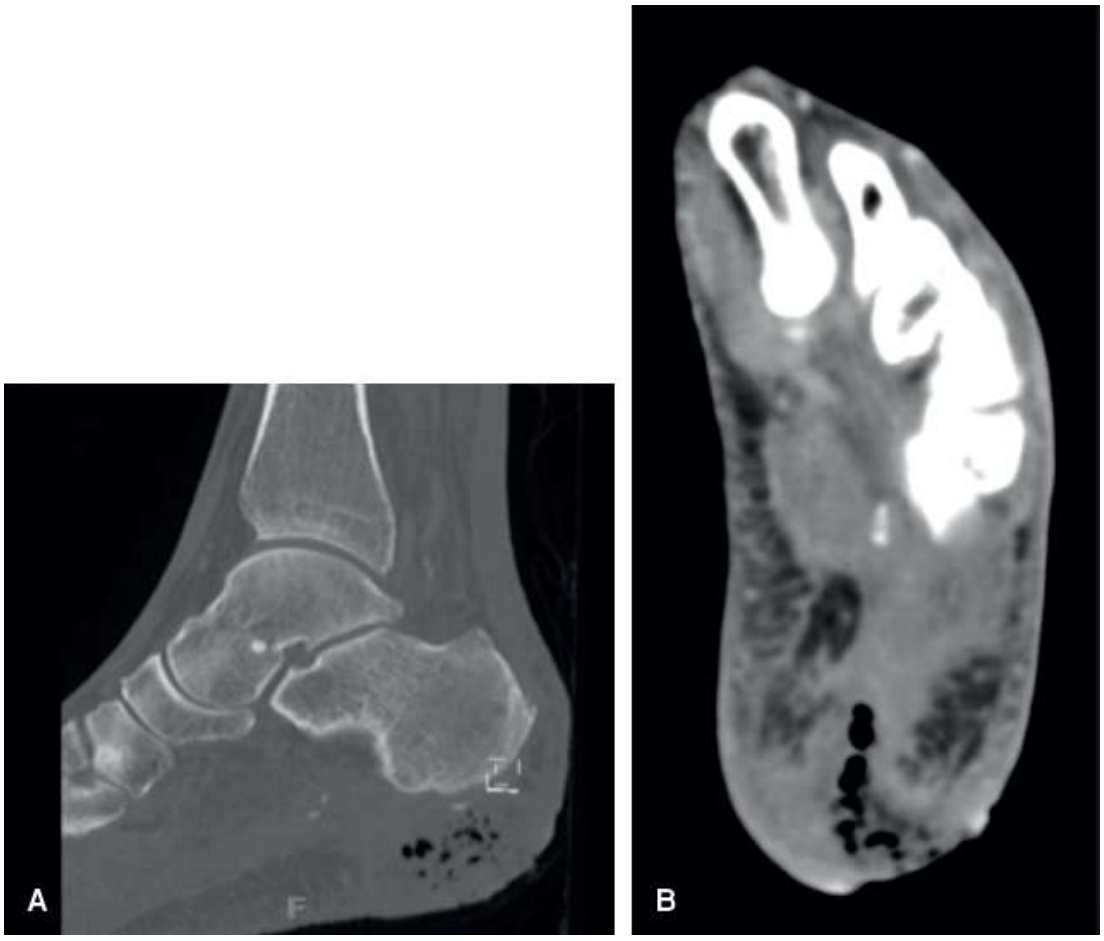


FIGURE 15-2 **A,B:** Sagittal and axial CT images of a diabetic foot.

b. Infected wounds are diagnosed based on clinical signs of infection. Plain x-rays or CT scan may show osteomyelitis or gas in the soft tissues (Fig. 15-2A,B). Patients with a suspected infected diabetic foot ulcer should be admitted for inpatient wound care and broad-spectrum antibiotic therapy. Infected wounds require a thorough exploration with drainage of all abscess cavities and debridement of infected, necrotic, or devitalized tissues. The clean wound can then be managed with local wound care as described above.

c. Antibiotic therapy. For infected wounds, initial antibiotic therapy should be broad spectrum directed at both gram-positive and gram-negative organisms. In the acute phase parenteral treatment is indicated. Wound cultures should be obtained prior to initiation of antibiosis. Duration of antibiosis depends on severity of infection. For mild infections limited to the soft tissue 1 to 2

weeks of therapy is sufficient, whereas moderate or severe infections require 2 to 4 weeks of total antibiotic therapy. For osteomyelitis involving viable bone, 4 to 6 weeks of IV therapy may be indicated. Consultation with an infectious disease specialist is helpful in guiding therapy (*Clin Infect Dis.* 2012;54:e134).

d. Prevention remains one of the most important elements in the management of the diabetic foot. Meticulous attention to hygiene and daily inspection for signs of tissue trauma prevent the progression of injury. Podiatric appliances or custom-made shoes are helpful in relieving pressure on weight-bearing areas.

B. Leg Ulcers

1. **Arterial insufficiency ulcers** tend to occur distally on the tips of the patient's toes or near the lateral malleolus. The surrounding skin is thin, shiny, and hairless. Patients frequently complain of claudication or rest pain; however, some patients may have sufficient neuropathy that they lack any pain symptoms even in critical limb ischemia. Peripheral pulses are diminished or absent. When arterial ulcers are suspected, a vascular evaluation should be obtained. Critical to treatment of these wounds is restoration of arterial inflow (see Chapter 39). After optimization of arterial inflow, devitalized tissue can be resected to facilitate healing.

   Neglected chronic arterial insufficiency can result in dry or wet gangrene. Wet gangrene can lead to an ascending necrotizing infection while dry gangrene can convert to wet at any time. If infection is suspected, obtain wound cultures, debride infected tissue, and institute appropriate antibiosis.

2. **Venous stasis ulcers** are among the most common types of leg ulcers and typically occur on the medial leg in the supramedial malleolar location. A patient with a venous stasis ulcer usually has a history of ulceration and associated leg swelling or of deep venous thrombosis. See Chapter 40 for a complete description of venous stasis ulcers and their treatment.

C. Pressure Ulcers

1. **Pathophysiology.** Prolonged pressure applied to soft tissue over bony prominences, usually caused by paralysis or immobility associated with severe illness, leads to ischemic ulceration and tissue

breakdown. Muscle tissue seems to be the most susceptible. The prevalence of pressure ulcers ranges from 6% to 18.5% in the acute care setting and 28.8% to 32.9% in the long-term acute care setting (*Clin Nurs Res*. 2018;27:643; *J Wound Ostomy Continence Nurs*. 2017;44:20). Pressure ulcers increase in-hospital mortality rates more than twofold as well as increase the risk of hospital readmissions (*J Am Geriatr Soc*. 2012;60:1603). Ulcers frequently develop over the occiput, sacrum, greater trochanter, and heels. Pressure ulcers are described by stages (Table 15-1). When a full-thickness injury to the skin has occurred, one cannot adequately stage the wound until the eschar is incised and the actual depth is determined. See Figure 15-3 for an example of an unstageable ischial and greater trochanter pressure ulcer. The examiner must also look for underlying bony breakdown and osteomyelitis.

2. Prevention

a. Skin care. Skin should be kept well moisturized but protected from excessive contact with extraneous fluids. Barrier products may reduce the risk of pressure ulcers by protecting skin against excessive moisture.

TABLE 15-1 National Pressure Ulcer Advisory Panel Classification Scheme

Stage	Description
I	Nonblanchable erythema of intact skin; wounds generally reversible at this stage with intervention
II	Partial-thickness skin loss involving epidermis or dermis; may present as an abrasion, blister, or shallow crater
III	Full-thickness skin loss involving damage or necrosis of subcutaneous tissue but not extending through underlying structures or fascia

IV	Full-thickness skin loss with damage to underlying support structures (i.e., fascia, tendon, or joint capsule)
Unstageable	Full-thickness tissue loss with actual depth of ulcer unknown due to slough and/or eschar in wound bed
Suspected deep tissue injury	Localized area of discolored skin or blood-filled blister due to damage of underlying tissue

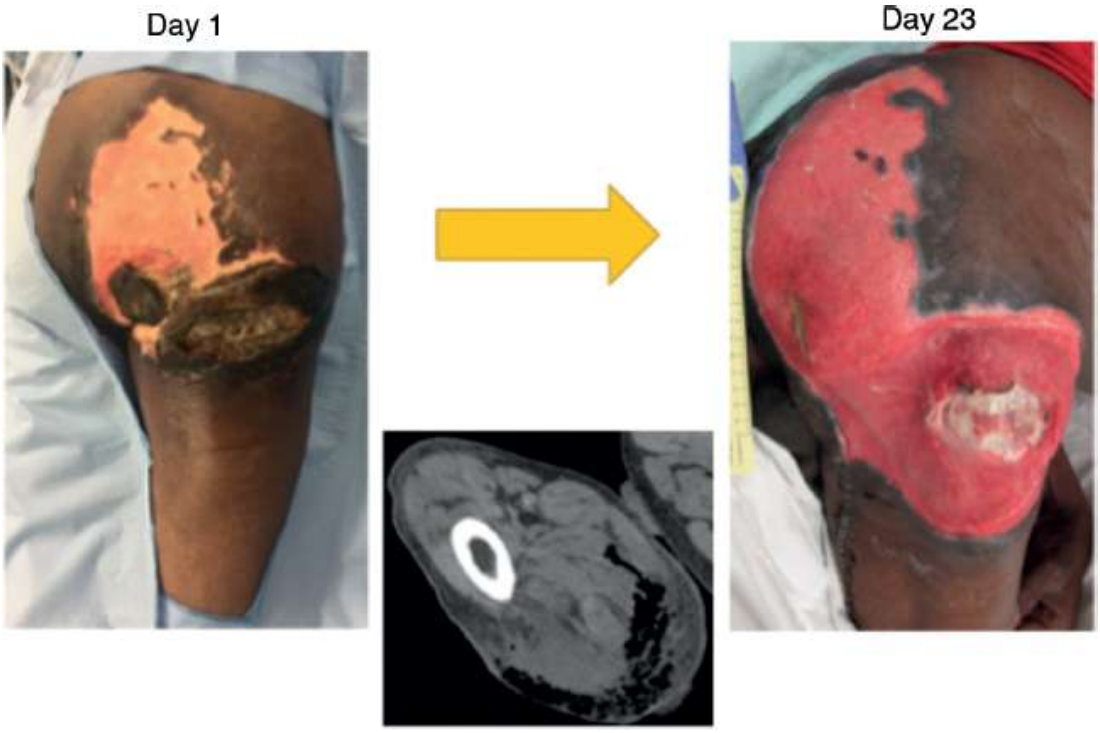


FIGURE 15-3 Ischial and greater trochanter unstageable pressure ulcer with necrotizing infection. Day 1 indicates initial presentation with eschar (unstageable pressure ulcer) overlying the necrotizing infection seen on CT scan. Day 23 shows good granulation tissue, many days after sharp debridement.

b. Frequent repositioning. High-risk patients should be repositioned at a minimum every 2 hours, either while seated or in bed.

c. Appropriate support surfaces. Adequate support surfaces redistribute pressure from the bony prominences that cause pressure ulcers.

d. Static support surfaces. Foam, air, gel, and water-overlay support

surfaces are appropriate for low-risk patients.

e. Dynamic support surfaces. These are support modalities that are powered and actively redistribute pressure. These include alternating and low air-loss mattresses. These surfaces are appropriate for high-risk patients.

f. Nutrition. High-risk patients should also undergo nutritional screening to ensure that caloric and protein goals are met.

3. Treatment

a. Debridement. Eschar and necrotic tissue should be debrided unless contraindicated. Sharp debridement of small wounds can be done at the bedside. Larger wounds require operative debridement. Once the bulk of eschar and devitalized tissue is removed, debridement can be continued with wet-to-damp gauze dressings or with enzymatic debridement with topical agents such as collagenase.

b. Wound cleansing. The base of uninfected ulcers should be cleaned with saline irrigation or a commercially available wound cleanser at each dressing change. Antiseptic solutions such as hydrogen peroxide, povidone–iodine, or Dakin solution should not be routinely used as they are toxic to tissues and impede healing. For actively infected wounds, a short course (3 to 5 days) of damp-to-dry dressing changes with one-fourth strength Dakin solution may facilitate local bacterial control. However, topical antiseptic solutions cannot take the place of appropriate debridement and systemic antibiotic therapy.

c. Dressing. Dressings should be selected to ensure the wound base remains moist while keeping the surrounding skin dry. Wet-to-damp gauze and hydrocolloid dressings are appropriate. NPWT is also useful for pressure ulcers and may facilitate closure as compared to traditional dressings (*Br J Nurs*. 2004;13:135).

d. Control of infection and bacterial colonization. All open ulcers are colonized with bacteria. Surface colonization is best controlled with topical wound cleansing. Superficial colonization does not require antibiotic therapy. Evidence of active infection (purulence, surrounding cellulitis, or foul odor) should prompt reexploration of the wound with debridement of any necrotic or infected tissue.

Bacterial infection >10^5 organisms per gram of tissue can impair wound healing. Quantitative tissue cultures should be obtained from wounds that fail to heal. The underlying bone should be evaluated for osteomyelitis with appropriate imaging.

e. Nutrition. Successful treatment of pressure ulcers requires adequate nutrition. Patients should be provided with 30 to 35 kcal/kg body weight and 1.25 to 1.5 g protein/kg body weight (*National Pressure Ulcer Advisory Panel Quick Reference Guide*; 2014. https://www.npuap.org/resources/educational-andclinical-resources). These estimates should be adjusted for factors such as recent weight changes, BMI, and renal failure or other comorbid conditions.

4. Surgical treatment. Most pressure ulcers heal spontaneously when pressure is relieved. *This remains the most important factor in their healing.* The healing process may require up to 6 months. Unless the patient was only temporarily immobilized, recurrences are common. Surgical management may include simple closure, split-thickness skin grafting, or creation of a musculocutaneous flap; but these measures should be reserved for well-motivated patients in whom a real reduction in risk factors for recurrence is possible.

WOUND CLOSURE AND CARE

I. TYPES OF WOUND CLOSURE

A. Primary intention occurs when the wound is closed by direct approximation of the wound margins. Direct approximation of the edges of a wound provides the optimal treatment on the condition that the wound is clean, the closure can be done without undue tension, and the closure can occur in a timely fashion. Primary intention also describes the healing of wounds created in the operating room that are closed at the end of the operative period. Epithelialization of surgical incisions occurs within 24 to 48 hours of closure. CDC guidelines dictate that a sterile dressing should be left in place during this susceptible period to prevent bacterial contamination.

B. Secondary intention, or spontaneous healing, occurs when a wound is left open and is allowed to close by epithelialization and contraction. Contraction is a myofibroblast-mediated process that aids in wound

closure by decreasing the circumference of the wound. This method is commonly used in the management of wounds that are treated beyond the initial 6-hour window or for contaminated or infected wounds with a bacterial count of $>10^5$/g of tissue. These wounds are characterized by prolonged inflammatory and proliferative phases of healing that continue until the wound has either completely epithelialized or been closed by other means.

C. Tertiary intention, or delayed primary closure, is a useful option for managing wounds that are too heavily contaminated for primary closure but appear clean and well vascularized after 4 to 5 days of open observation so that the cutaneous edges can be approximated at that time. During this period, the normally low arterial partial pressure of oxygen (PaO_2) at the wound surface rises and the inflammatory process in the wound bed leads to a minimized bacterial concentration, thus allowing a safer closure than could be achieved with primary closure and a more rapid closure than could be achieved with secondary wound healing.

II. OPEN WOUND CARE OPTIONS. Please find below a brief overview of open wound care product categories. It remains an area of intense research, clinical, and commercial interest in which availability and indications of both established and new products can be expected to change during the publication cycle of this manual. The clinician would do well to weigh each patient's response to treatment, the indications and risks of any particular product, and need for further treatment.

A. Topical Ointments. Petroleum-based ointments that contain one or several antibiotics prevent adherence of dressings to wounds and, by maintaining moisture of the wound environment, they accelerate epithelialization and healing of primarily approximated wounds.

B. Impregnated Gauze. Gauze that is impregnated with petrolatum is used for the treatment of superficial, partial-thickness wounds. As petroleum is hydrophobic, it acts to maintain moisture and prevent excessive fluid loss. In the case of Xeroform, it also provides mild deodorizing. It can also be used as the first layer of the initial dressing on a primarily closed wound to prevent adherence of dry dressing. The use of this type of gauze is contraindicated when infection of the wound is suspected and inhibition of wound drainage would lead to adverse

consequences.

C. Gauze Packing. The practice of packing an open wound with gauze prevents dead space, facilitates drainage, and provides varying degrees of debridement. The maximum amount of debridement is seen when the gauze is packed into the wound dry and removed after absorption and evaporation have taken place, leaving a dry wound with adherent gauze, which on removal extracts superficial layers of the wound bed (dry-to-dry dressing). This dressing is seldom indicated. Wounds that are in need of great amounts of debridement usually benefit most from sharp debridement in the operating room or at the bedside; dry-to-dry dressings are painful and violate the principle of maintaining a moist environment for the wounds. Wet-to-moist dressings provide a much gentler debridement, are less painful, and can include sterile normal saline or various additives. Dakin solution (in full [0.5% sodium hypochlorite], half, or quarter strength) can be used to pack infected open wounds for a brief period when antimicrobial action is desirable. Because of its cytotoxic effects, the use of Dakin solution is not indicated except in infected wounds for a short period during the inflammatory phase (*Ann Plastic Surgery*. 2014;73:254).

D. Hydrogels. These water- or glycerin-based gels (e.g., IntraSite) can be used in shallow or deep, open wounds. The gel promotes healing by gently rehydrating necrotic tissue, facilitating its debridement, absorbing exudate produced by the wounds, and maintaining a moist wound environment. A nonadherent, nonabsorbent secondary dressing is applied over the gel, and dressings should be changed every 8 hours to 3 days, depending on the condition of the wound.

E. Hydrocolloids. These occlusive, adhesive wafers provide a moist and protective environment for shallow wounds with light to moderate exudate. They can remain in place for 3 to 5 days and can be used under compression dressings to treat venous stasis ulcers.

F. Alginates. Complex carbohydrate dressings composed of glucuronic and mannuronic acid, derived from brown seaweed, are formed into ropes or pads that are highly absorbent (e.g., Kaltostat). Alginates are absorbable and are useful for the treatment of deep wounds with heavy exudate because they form a gel as they absorb wound drainage.

G. Adhesive Films. These plastic membranes (e.g., Tegaderm) are self-adhering and waterproof, yet are permeable to oxygen and water vapor.

They are appropriate for partial-thickness wounds, such as split-thickness skin graft donor sites or superficial abrasions. They can also be used as secondary dressings on wounds that are being treated with hydrocolloids or alginates.

H. Collagen-Containing Products. A number of collagen-containing products are available in powder, sheet, or fluid form. They are available as pure collagen, typically types 1 and 3, or combined with other materials such as calcium alginate (Fibracol). Some chronic wounds may respond better to collagen than to other dressing materials (*J Am Col Certif Wound Spec*. 2010;2:50).

I. Hydrofibers represent a newer dressing category of strands; they are some of the most absorptive materials available for packing in a heavily draining wound. In addition to decreasing exudate, they are impregnated with silver and report decreases in wound infection and biofilm rates (*J Wound Care*. 2016;25:134).

J. Growth Factors. Human recombinant platelet-derived growth factor (PDGF) is the only U.S. Food and Drug Administration-approved clinically available growth factor. Topically applied to a granulating wound, it promotes granulation tissue formation, angiogenesis, and epithelialization. A saline-moistened gauze dressing is applied daily at midday to help keep the wound bed moist. Although initial approval was for the treatment of diabetic plantar foot ulcers, the drug is often used on other wound types. Epidermal growth factor (EGF) is in clinical trials for the treatment of venous stasis ulcers and diabetic foot ulcers. Small trials of recombinant human basic fibroblast growth factor (rh-bFGF) have shown improved healing in pressure ulcers, diabetic foot ulcers, and second-degree burns (*Wound Repair Regen*. 2014;22:569).

K. Skin Substitutes. There are many different types of biologically active materials and skin substitutes and a comprehensive review of their properties and use is beyond the scope of this chapter. The indication and usage of these products is guided by their biologic and material properties. Skin substitutes can be used to facilitate healing of chronic open wounds; provide temporary or permanent wound coverage; and bridge skin, soft tissue, or fascial defects. The usage of individual products is guided by the manufacturer’s recommendations and the nature of the wound.

1. Xenograft products (Permacol, EZ Derm, Matriderm, Oasis) are

derived from animal tissues and consist of a collagen and/or proteoglycan matrix designed to promote influx of fibroblasts.

2. **Allogeneic products** are acellular tissue substitutes derived from cadaveric sources (AlloDerm, Strattice, Graftjacket, GammaGraft) that can be used to provide wound coverage. Each of these products is differently processed and material properties guide usages including wound coverage and hernia repair.
3. **Bioengineered living tissues** are composites of a structural mesh and cultured keratinocytes. Cells can be derived from neonatal sources (Dermagraft, TransCyte, Apligraf, OrCel) or autologous skin (Epicel, Laserskin, Epidex, Hyalograft). These advanced products bring living, biologically active cells into the wound bed.

L. NPWT. Negative pressure created by vacuum-assisted closure devices (Wound VAC or Blue Sky or institutionally created dressings) appears to stimulate capillary ingrowth and the formation of granulation tissue in open wounds while keeping a relatively clean wound environment. NPWT is effective in the management of wounds as diverse as diabetic foot wounds, pressure ulcers, open abdomen, closed incisions, and wounds including prosthetic mesh, exposed bone or tendon (*Diabetes Care*. 2008;31:631; *Plast Reconstr Surg*. 2006;117:127S; *J Trauma Acute Care Surg*. 2012;73:629; *J Clin Orthop Trauma*. 2016;7:256). A meta-analysis of randomized controlled trials of NPWT over closed incisions showed a reduction in dehiscence, seroma formations, and skin necrosis compared with standard care (*Adv Skin Wound Care*. 2018;31:421). NPWT has been reported to be successful in managing enteroatmospheric fistulae and increasing fistula closure rates (*Int Wound J*. 2018;15:722). NPWT is contraindicated when there are exposed major blood vessels, untreated osteomyelitis, or cancer within the wound, and it is relatively contraindicated in anticoagulated patients.

M. NPWT With Instillation. NPWT with instillation has the additional benefit of episodic irrigation that decreases the viscosity of wound exudate and reduces biofilm formation (*Int Wound J*. 2008;5:399). Studies comparing NPWT to NPWT with instillation have not shown significantly different results but there is a trend toward earlier wound healing and decreased hospital length of stay (*J Wound Care*. 2016;25:475). Expert consensus recommends NPWT with instillation use in complex wounds with invasive infection or extensive biofilm

(*Wounds*. 2015;27:S2). It is contraindicated in untreated osteomyelitis, malignancy within the wound, and possible connection to thoracic or abdominal cavity.

N. Metallic Silver-impregnated Dressings. The broad antimicrobial properties of silver have long been recognized. Silver-impregnated dressings are used extensively for burns, chronic leg ulcers, diabetic, and traumatic injuries. A variety of silver-based dressings are available with specific indications determined by the manufacturer.

III. HYPERBARIC OXYGEN TREATMENT. Local hypoxia in wound tissue may contribute to delayed healing. Hyperbaric oxygen treatment (HBOT) has been found to increase healing of diabetic foot ulcers as well as reduce the risk of diabetic amputations (*PMR*. 2009;1:471). Standard treatment protocols are based on appropriate debridement and wound care in conjunction with 90 min/day at 2 ATA (atmosphere absolute) of oxygen. The undersea and hyperbaric medical society (UHMS) has recognized the use of HBOT for chronic wounds, diabetic ulcers, and burns (Hyperbaric Oxygen Therapy Indications Manual 2014, http://www.UHMS.org).

CHAPTER 15: WOUND CARE

Multiple Choice Questions

1. **When does a well-healed wound reach the original strength of uninjured issue?**

   a. 5 days
   b. 2 weeks
   c. 1 month
   d. 6 months
   e. Never

2. **A 58-year-old diabetic man presents with a 2 ë 2 cm ulcer on the lateral aspect of big toe. He complains of chronic pain in his foot at rest and when walking. There are no signs of erythema or drainage. What is the best initial step in management?**

   a. Noninvasive vascular studies
   b. Antibiotics
   c. Debridement
   d. Amputation

3. **After debridement of the sacral decubitus ulcer, the wound bed appears clean without any signs of infection. Once all apparent devitalized tissue is removed, what is the next step in treatment?**

   a. Nothing further is required
   b. Normal saline wet to moist dressing changes
   c. Dakin wet to moist dressing changes
   d. Hydrogen peroxide damp-to-dry dressing changes
   e. Musculocutaneous flap

4. **After taking a 24-year-old male with a gunshot wound to the abdomen to the operating room, it is discovered that he has a significant sigmoid colon injury with gross spillage. He is given a Hartman colostomy, and his fascia is closed while the skin is left open. How will this wound heal?**

a. It will not heal
b. Primary intention
c. Secondary intention
d. Tertiary intension
e. Quaternary intention

5. **What are the benefits of negative pressure wound therapy (NPWT)?**

a. Keeps wound clean
b. Increases angiogenesis
c. Decreases edema
d. Increases granulation tissue growth
e. All of the above

16

Acute Abdomen

Ali J. Khiabani and Obeid N. Ilahi

INTRODUCTION

Acute abdomen is defined as the recent or sudden onset of severe abdominal pain. It is the most common emergent general surgical problem and has a vast differential diagnosis, including both intra- and extraperitoneal processes. A thorough history and physical examination in conjunction with selective diagnostic testing are of paramount importance in the evaluation of the patient with acute abdominal pain.

I. PATHOPHYSIOLOGY. This chapter focuses on intra-abdominal etiologies of abdominal pain; however, it is important to be cognizant of other sources of pain arising from other sites such as the abdominal wall (e.g., rectus sheath hematoma) or extra-abdominal organs (e.g., testicular torsion). Irritation of the peritoneum is responsible for the origin of pain arising from an intra-abdominal process. **Visceral pain** is poorly localized and triggered by inflammation; ischemia; and geometric changes such as distention, traction, and pressure, creating deep, dull, and vague pain. The general location of pain can correlate with the anatomic location of disease (Fig. 16-1). in contrast, **parietal pain** is in a distinct abdominal quadrant, causing sharp and severe pain that is well localized and occurs due to (a) peritoneal irritation by localized inflammation of an organ in contact with the parietal peritoneum, (b) chemical peritonitis from a perforated viscus, or (c) mechanical stimulation as from a surgical incision or trauma (Fig. 16-2). parietal pain can correlate with local or diffuse peritonitis and usually signifies the need for surgical treatment. **Referred pain** arises from a deep structure but is superficial at the painful site; examples include biliary tract pain which refers to the right inferior scapular area, renal colic referring down to the ipsilateral groin, or a

ruptured aortic aneurysm or pancreatitis radiating to the back. **Epigastric:** foregut-derived structures (stomach to second portion of duodenum, liver, biliary tract, pancreas, spleen). **Periumbilical:** midgut-derived structures (second portion of duodenum to proximal two-thirds of transverse colon). **Suprapubic:** hindgut-derived structures (distal transverse colon to anal verge).

II. EVALUATION.

A thorough history and physical examination with ancillary imaging and laboratory tests can guide the diagnostic and treatment process (Fig. 16-3).

A. History of present illness

provides a chronological description of the progression of the patient's signs and symptoms (Table 16-1).

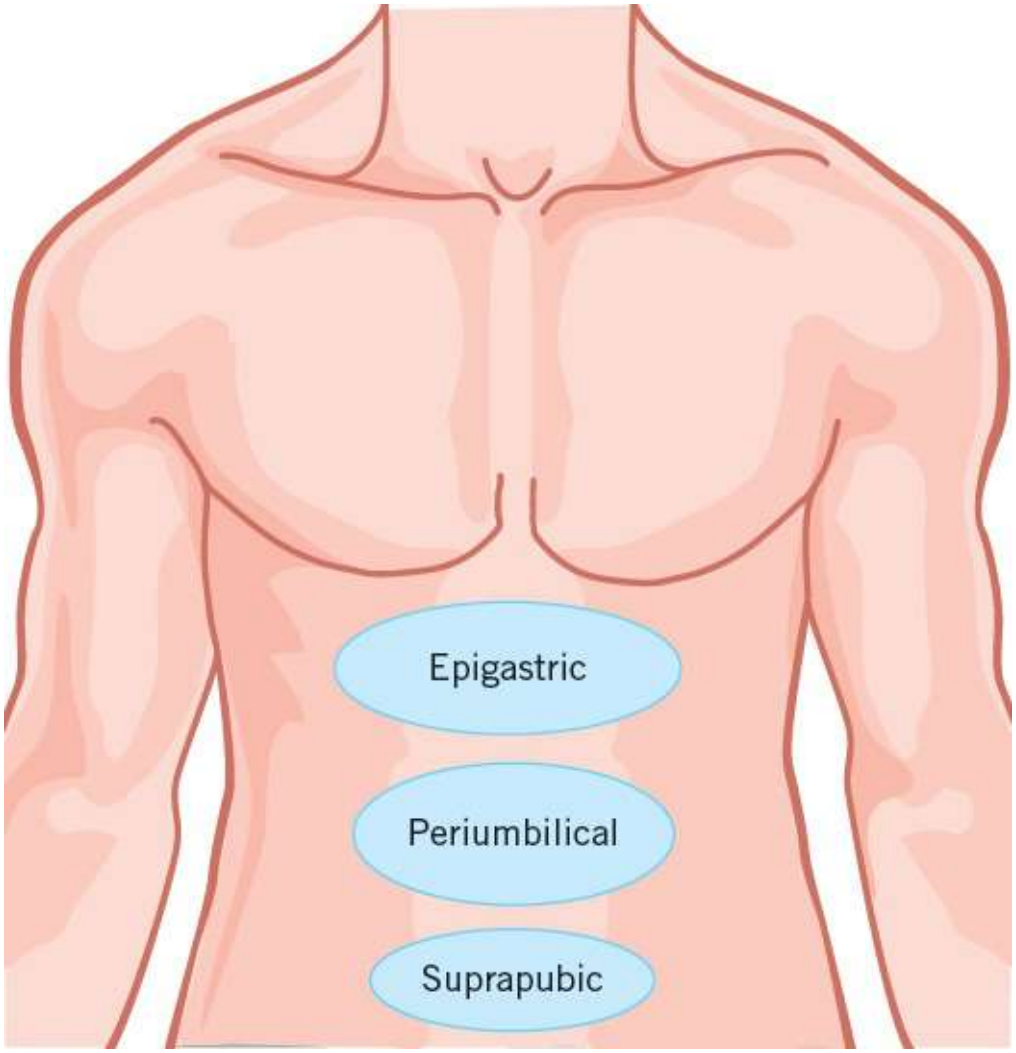


FIGURE 16-1 Visceral pain distribution correlates with location of intra-abdominal disease.

B. Past Medical History

1. Medical conditions precipitating intra-abdominal pathology

- **a.** Peripheral vascular disease (PVD) or coronary artery disease (CAD) may predispose patients to abdominal vascular disease, such as AAA or mesenteric ischemia.
- **b.** Cancer history should raise suspicion for bowel obstruction or perforation from progression or recurrence.

2. Surgical history

- **a.** Following abdominal surgeries patients may develop adhesions predisposing them to bowel obstructions.
- **b.** If a patient has had a prior abdominal surgery, it is important to be aware of anatomic variations (ex: bowel resections, organ transplantation).

C. Organ-System Review

1. History of diabetes, CAD, or PVD presenting with vague abdominal symptoms may have myocardial ischemia.

2. Pneumonia may present with upper abdominal pain and be associated with cough and fevers.

3. In women, a thorough gynecologic history is important to rule out ruptured ovarian cysts, ectopic pregnancy, and pelvic inflammatory disease.

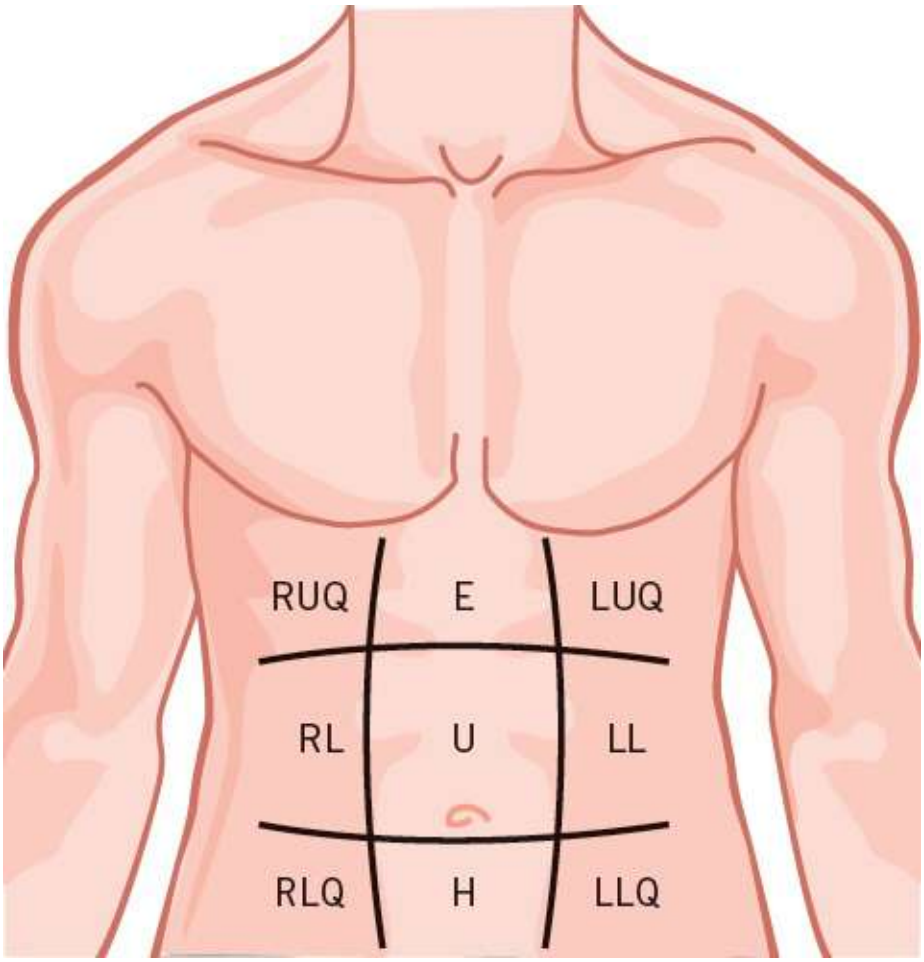


FIGURE 16-2 Parietal pain distribution, when localized, may correlate with inflammatory processes involving the underlying intra-abdominal structures. *RUQ*, right upper quadrant (biliary, gastric, pancreatic); *E*, epigastric (gastric, pancreatic, biliary, hernia); *LUQ*, left upper quadrant (splenic, gastric, duodenal, biliary, pancreatic); *RL*, right lumbar (renal, colonic, hernia); *U*, umbilical (pancreatic, appendiceal, gastric, small bowel, hernia); *LL*, left lumbar (renal, colonic); *RLQ*, right lower quadrant (appendiceal, colonic, pelvic, hernia); *H*, hypogastric (bladder, appendiceal, colonic, pelvic); *LLQ*, left lower quadrant (colonic, pelvic, hernia).

D. Medications

1. Nonsteroidal anti-inflammatory medications, such as aspirin or ibuprofen increase the risk of complicated peptic ulcer disease, namely, bleeding, obstruction, and perforation.
2. Corticosteroids often mask classic signs of inflammation such as fever and peritoneal signs.
3. Antibiotics may either attenuate abdominal symptoms due to treatment of the underlying disease process, or cause diarrhea/abdominal pain from antibiotic-induced pseudomembranous

colitis.

E. Physical Examination

1. Overall appearance

a. Diffuse peritonitis. Acutely ill patients tend to lie quietly on their sides in fetal position to minimize stimulation to the abdomen.

b. Colic tends to cause patients to be restless or writhing in pain, as they are unable to find a comfortable position.

2. Vital signs

a. Fever suggests inflammatory or infectious process; marked fevers >39°C suggests the presence of abscess, cholangitis, or pneumonia.

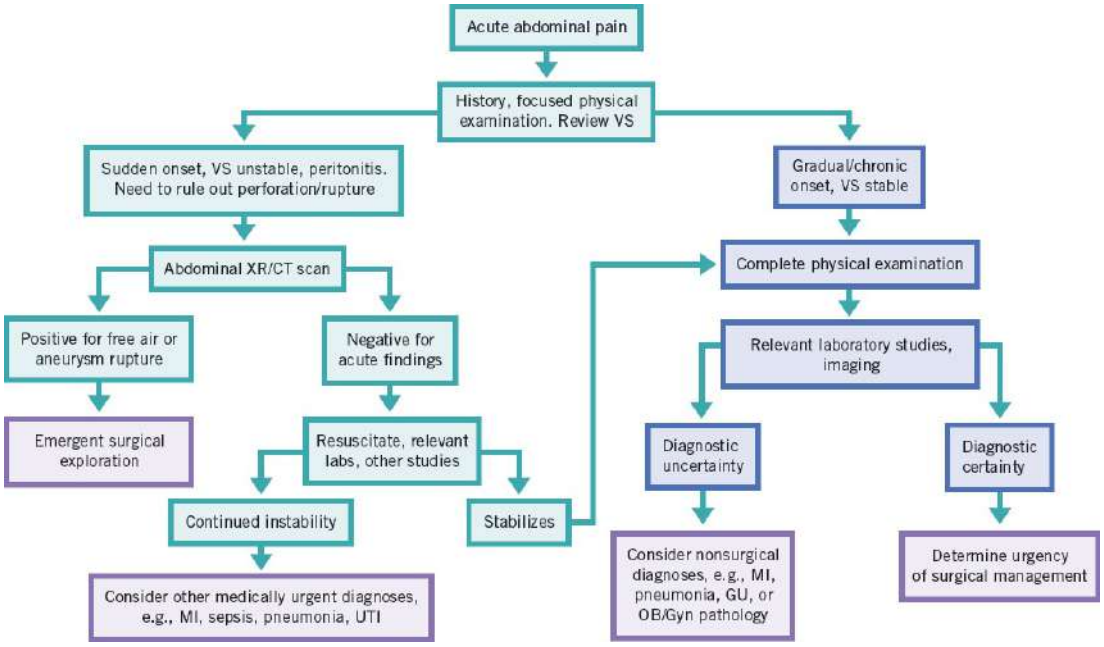


FIGURE 16-3 Diagnostic algorithm for the evaluation of acute abdominal pain.

TABLE 16-1 Findings to Elicit During History Taking, and Differential Diagnoses to Consider

Findings on History	Differential Diagnosis
Onset/Duration	
• Sudden (within seconds)	Perforated viscus, ruptured aneurysm, myocardial infarction, acute mesenteric occlusion

• Rapid acceleration (within minutes)	• Colic syndromes: biliary, ureteral, bowel obstruction • Inflammatory: appendicitis, pancreatitis, diverticulitis • Ischemic: mesenteric ischemia, bowel strangulation, volvulus
• Gradual (over hours)	• Inflammatory: appendicitis, cholecystitis • Obstructive: nonstrangulated bowel obstruction, urinary retention • Other mechanical: ectopic pregnancy, tumors
Character	
• Colicky, waxing, and waning	Hyperperistalsis of smooth muscle against mechanical obstruction (SBO, renal stone) Exception is biliary colic—constant, intense, lasting 30 min to hr
• Severe, persistent, steadily increasing	Infectious or inflammatory process
Location	Specific organs localizing to their respective quadrants, refer to Figure 16-2
Alleviating/Aggravating Factors	Diffuse peritonitis—worse with movement Colic—unable to find a comfortable position Obstruction—transient relief from vomiting Peptic ulcer—transient relief from food intake

Associated Symptoms	
• Nausea/vomiting	Vomiting after pain—appendicitis Vomiting before pain—gastroenteritis/food poisoning Bilious—distal to duodenum Hematemesis—peptic ulcer, gastritis
• Fevers/chills	Inflammation/infection
• Anorexia	Common symptom in acute abdominal pain

b. Hypotension and/or tachycardia signal hypovolemia or sepsis.

3. Abdominal examination should be done systematically. Analgesia administered prior to examination may alter findings but does not decrease diagnostic accuracy (*Ann Emerg Med*. 2006;48:150).

a. Inspection should be carried out for distention, scars, masses, or skin changes.

b. Auscultation may reveal high-pitched bowel sounds of obstruction or the absence of sounds from ileus or diffuse peritonitis.

c. Percussion may reveal tympanitic sounds from bowel distention or fluid wave of ascites; it is also useful for localizing tenderness and peritoneal irritation when it is clearly present so as to expose the patient to deep palpation.

d. Palpation should be performed with the patient supine.

(1) Begin at a site remote from the reported site of pain.

(2) Note areas of tenderness and guarding.

(3) Peritonitis can be evoked by rocking the patient's pelvis or shaking the bed and assessing for pain.

(4) Pain out of proportion to examination is classic for mesenteric ischemia.

(5) Search for hernias and palpable masses.

(6) Consider referred pain patterns.

e. Rectal examination should be done routinely in all patients with suspected GI bleeding, obstruction, or lower abdominal/pelvic pathology.

(1) Rectal mass may be an obstructing cancer; note fraction of circumference involved, mobility, and distance from anal verge.

(2) Occult blood in stool specimen indicates GI bleeding.

f. Pelvic examination must be performed in all women of child-bearing age with lower abdominal pain.

(1) Note appearance of the cervix and any discharge.

(2) Bimanual examination should be performed for cervical motion tenderness, adnexal tenderness, or masses.

g. Testicular/scrotal examination must be performed in all males with abdominal pain.

(1) Testicular torsion produces painful, swollen, and tender testicles that retract upward in the scrotum.

(2) Epididymitis may coexist with urinary tract infection (UTI), with the epididymis and vas deferens becoming swollen and tender.

F. Laboratory Evaluation

1. Complete blood count with differential

a. Leukocytosis indicates the likelihood of an infectious source.

b. Left shift on the white count differential points to an inflammatory process in the setting of a normal WBC count.

c. Hematocrit can be elevated from volume contraction due to dehydration; conversely, it may be low from occult blood loss.

2. Electrolyte profile

a. Hypokalemic, hypochloremic metabolic alkalosis classically appears in patients with prolonged vomiting and volume depletion.

b. Metabolic acidosis with a low serum bicarbonate level suggests general tissue hypoperfusion, and may suggest an underlying ischemic process.

c. Elevated BUN or creatinine suggests volume depletion.

3. Liver function panel

a. Mild transaminitis (<two times normal), elevation of alkaline phosphatase and total bilirubin are seen in acute cholecystitis.

b. Moderate transaminitis (>three times normal) in the setting of acute

right upper quadrant (RUQ) pain is most likely an obstructing stone in the common bile duct. Transaminitis precedes elevation of total bilirubin or alkaline phosphatase in the acute setting.

c. Marked transaminitis (>1,000 IU/L) is likely due to acute hepatitis or ischemia.

4. Pancreatic enzymes, amylase and lipase, are measured when pancreatitis is suspected. The degree of elevation does not correlate with the severity of pancreatitis.

a. Mild hyperamylasemia can be nonspecific, also being elevated in sialadenitis, perforated ulcer, cholecystitis, or bowel obstruction.

b. Elevation of lipase is more specific for pancreatic parenchymal disease.

5. Lactic acid level is measured when intestinal ischemia is suspected.

a. Serum lactate is a general indicator of tissue hypoxia due to the absence or reduced perfusion.

b. Mild lactic acidosis is seen in patients with arterial hypotension.

c. Ongoing elevation despite resuscitation is concerning for progressive tissue ischemia.

6. Urinalysis assesses urologic causes of abdominal pain.

a. Bacteriuria, pyuria, and presence of leukocyte esterase suggest the presence of UTI. Recurrent UTI in males is unusual and warrants further evaluation.

b. Hematuria is seen with nephrolithiasis and renal or urothelial cancer.

7. Urine human chorionic gonadotropin (hCG) must be obtained in all women of child-bearing age. A positive urine test should be followed by quantitated serum levels.

a. Low level (<4,000 mIU) usually accompanies ectopic pregnancy.

b. Higher levels (>4,000 mIU) indicate intrauterine pregnancy, usually detectable on ultrasound (US).

G. Radiographic evaluation, while an important component of a diagnostic workup, should be used selectively to minimize cost and potential morbidity to the patient. These modalities include abdominal x-rays, US, computed tomography (CT), magnetic resonance imaging (MRI), radionuclide imaging studies, and invasive radiographic techniques. Please see Chapter 47 for details on radiographic modalities and their

interpretation.

III. Differential Diagnosis. Common etiologies of acute abdominal pain are described in Table 16-2. In general, patients with peritonitis on physical exam should be taken urgently for surgical intervention. For specific management, see respective chapters.

TABLE 16-2 Acute Abdomen Common Differential Diagnoses

Diagnosis	Presentation	Laboratory Findings	Radiologic Findings
Appendicitis	• Progressive, persistent RLQ pain • Anorexia • Mild fever an tachycardia	Leukocytosis, pyuria, albuminuria, hematuria	• Ultrasound- diameter > mm, lack luminal compressibil presence appendicolith • CT scan- distended, thick-walled appendix wi streaking periappendic fat
Acute cholecystitis	• Postprandial epigastric or RUQ pain • Nausea/vomiting • Positive Murphy sign	Possible leukocytosis, elevation in liver enzymes, elevated bilirubin (may suggest obstructed common bile duct)	• Ultrasound- gallbladder wall thickening, pericholecys fluid, sonographic Murphy sig increased bi duct size

			• HIDA scan- nonfilling the gallbladder
Acute pancreatitis	• Severe epigastric pain radiating to the back • Tachycardia, fever, and hypotension, depending on the severity of the episode	Elevation of amylase, lipase, and serum transaminases	• Plain x-ray- may reveal sentinel loo or pancreat calcifications • CT scan with I contrast identify pancreatic necrosis fluid collectio
Perforated peptic ulcer	• Associated with the chronic use of nonsteroidal anti-inflammatory medications • Sudden onset, severe epigastric pain that progresses to peritonitis	Leukocytosis	Plain x-ray- free intraperitoneal air
Intestinal obstruction	• Sharp, crampy periumbilical pain with intervening pain-free periods • Nausea, vomiting, and obstipation • Abdominal	Leukocytosis and lactic acidosis	Plain x-ray— dilated loops o small bowel, air–fluid levels and paucity of gas distally in the colon and rectum

	distention, high-pitched or tinkling bowel sounds, and a variable degree of abdominal tenderness		
Mesenteric ischemia	• Sudden onset of severe, constant abdominal pain • Vomiting and diarrhea • Pain out of proportion to examination	Leukocytosis and lactic acidosis	Angiography ma confirm the diagnosis; however, radiologic studies are no indicated if peritonitis is present on physical examination
Ruptured abdominal aortic aneurysm	• Sudden onset of abdominal pain with varying manifestations of radiation to the flank or back • May present with shock • Tender, pulsatile abdominal mass on exam	Leukocytosis	• Plain x-rays- calcification the aortic wa • CT scan is th gold standar for diagnos (should on be performe in hemodynami stable patients)

CHAPTER 16: ACUTE ABDOMEN

Multiple Choice Questions

1. **An 84-year-old male presents after becoming unresponsive approximately 2 hours after complaining of abdominal pain. What is the first necessary step in management?**

   a. Transfuse 2 units of uncrossmatched blood
   b. Obtain IV access, laboratory values, and plain abdominal x-ray
   c. Intubate after induction
   d. Obtain CT scan with IV contrast
   e. Emergent laparotomy

2. **A 74-year-old demented female nursing home resident presents after 12 hours of abdominal pain and longstanding history of constipation. Temperature is 37.8çC, HR 101, BP 140/86. A plain radiograph is obtained, which shows a dilated lucency in the midabdomen, concerning for sigmoid volvulus without free intraperitoneal air, pneumatosis, or pneumobilia. What is the appropriate next step?**

   a. IV fluid resuscitation, bowel prep, colonoscopy
   b. Admit to surgical floor for serial abdominal examinations, minimize narcotics
   c. Exploratory laparotomy for extended right hemicolectomy
   d. Barium enema
   e. Immediate sigmoidoscopic reduction

3. **A 35-year-old man presents with abdominal pain and vomiting. Temperature is 38.3çC, HR 120, BP 100/54. He is uncooperative with abdominal examination, and is lying still in the fetal position. Which of the following ancillary test is most urgent in determining the cause of this patient's pain?**

   a. Plain chest and abdominal x-rays
   b. CT of the abdomen
   c. Serum electrolytes and liver function tests

d. Upper endoscopy
e. Drug screen and alcohol level

4. **A 65-year-old male with a known large abdominal aortic aneurysm who has regular interval follow-ups presents with acute abdominal pain and altered mental status. Temperature is 37.7çC, HR 115, BP 88/56. Hemoglobin is 7.6, serum bicarbonate 18, and creatinine 1.3. What is the most appropriate next step?**

a. CT scan with IV contrast to delineate aneurysm anatomy
b. Admission to ICU for resuscitation and intubation under anesthesia
c. Urgent aneurysm repair
d. US evaluation of aneurysm
e. Placement of central lines and aggressive IV fluid administration

17 Esophagus

Lauren M. Barron and Bryan F. Meyers

STRUCTURAL AND FUNCTIONAL DISORDERS OF THE ESOPHAGUS

I. HIATAL HERNIA

A. Epidemiology. Hiatal hernias are a common disorder. Most are asymptomatic; however, patients with a hiatal hernia are more likely to have symptoms related to persistent gastroesophageal reflux disease (GERD) (*Scand J Gastroenterol*. 1991;26(9):921–926).

B. The **type of hiatal hernia** is defined by the location of the gastroesophageal (GE) junction and the relationship of the stomach to the distal esophagus.

1. **Type I (sliding)** is the most common type of hiatal hernia, though usually asymptomatic. The distal esophagus and gastric cardia herniate up through the hiatus and *often present with reflux.*
2. **Type II** (**paraesophageal**) is a rare manifestation; the peritoneum and greater curvature of the stomach herniate along the distal esophagus. However, the GE junction remains anchored within the abdomen.
3. **Type III (combination of types I and II)** is more common than pure type II and involves the herniation of both the greater curvature of the stomach and the GE junction into the chest.
4. **Type IV** hiatal hernias occur when abdominal organs (e.g., colon or spleen) other than or in addition to the stomach herniate through the hiatus into the chest.

Type II, III, and IV hiatal hernias frequently produce postprandial pain or bloating, early satiety, breathlessness with meals, and mild dysphagia. The herniated stomach is susceptible to volvulus and can

develop ischemic longitudinal ulcers.

C. Diagnosis and Evaluation

1. A **chest x-ray** with a soft-tissue mass with or without an air–fluid level above the diaphragm suggests a hiatal hernia. Differential diagnosis includes mediastinal cyst, abscess, or a dilated obstructed esophagus. However, retrocardiac air–fluid levels on two-view plain radiograph are pathopneumonic for hiatal hernia.
2. A **barium swallow** confirms the diagnosis, delineates the type of hiatal hernia, and defines the anatomy (length and coexisting abnormalities such as strictures or ulcers). Patients with hiatal hernia are at increased risk for aspiration. For this reason, barium is the preferred agent for contrasted studies due to the risk of pneumonitis with aspirated water-soluble agents.
3. **Esophagogastroduodenoscopy (EGD)** is indicated in patients with symptoms of reflux or dysphagia to assess for the presence of esophagitis, stricture, or Barrett esophagus. EGD also establishes the location of the GE junction in relation to the hiatus. A sliding hiatal hernia is defined as existing when greater than 2 cm of gastric mucosa is present between the diaphragmatic hiatus and the mucosal squamocolumnar junction.
4. **Esophageal manometry** evaluates esophageal motility in patients who are being considered for operative repair and helps guide the operative approach for fundoplication.
5. **CT scan** is most valuable in the emergent setting to evaluate tissue viability and anatomy. In the nonemergent setting, CT is often useful for preoperative planning in patients with large type III or IV hernias or recurrent hernias.

D. Management

1. **Asymptomatic type I hernias:** No treatment.
2. **Symptomatic type I hernias** (GERD) should undergo a trial of medical therapy. Patients who should be evaluated for an **antireflux procedure** (see Section II) **and hiatal hernia repair** include patients who have **failed medical therapy**, have ongoing regurgitation or respiratory symptoms, have Barrett esophagus, and young patients who would require lifelong PPIs. Patients with atypical symptoms (chest pain or dysphagia) require further testing and continued

medical therapy.

3. Patients with a **type II, III, or IV hiatal hernia** should be **considered for repair** via a thoracic or abdominal approach. Operative principles include reduction of the hernia, resection of the sac, and closure of the hiatal defect. In type III hiatal hernias, the esophagus frequently is shortened, and a lengthening procedure (Collis gastroplasty) must be considered. **Type II** repair should include a fundoplication due to a 60% incidence of associated GERD and the potential to develop GERD symptoms postoperatively secondary to intraoperative dissection (*Am J Surg*. 1996;171(5):485–489).

II. GASTROESOPHAGEAL REFLUX (GERD)

A. Prevalence. Symptoms of heartburn and excessive regurgitation are relatively common in the United States, occurring daily in 18% to 28% of the population (*Gut.* 2014;63(6):871–880).

B. Pathophysiology in GERD relates to abnormal exposure of the distal esophagus to refluxed stomach contents. In 60% of patients, it is due to a mechanically defective lower esophageal sphincter (LES) (*Am J Surg*. 1988;155(1):104–111).

C. The classic **symptom** of GERD is posturally aggravated epigastric burning pain that is readily relieved by antacids. Other symptoms include regurgitation and dysphagia. Atypical symptoms may mimic laryngeal, respiratory, cardiac, biliary, pancreatic, or gastric disease.

D. Diagnosis and evaluation

1. **EGD** is the most direct method to evaluate symptomatic patients for objective evidence of GERD such as esophagitis and Barrett changes. **Esophagitis** is a clinical and pathologic diagnosis.
2. **Esophageal manometry** guides the selection of the best antireflux procedure by defining the location and function of the LES. It helps exclude achalasia, scleroderma, and diffuse esophageal spasm. Characteristics of a manometrically abnormal LES are (1) a resting pressure <6 mm Hg, (2) an overall length <2 cm, and (3) an abdominal length <1 cm.
3. **Esophageal pH testing** over a 24-hour period is the gold standard in the diagnosis of GERD. A DeMeester score less than 15.7 is normal.
4. **Upper GI radiography** is useful in for identifying anatomical abnormalities that may cause symptoms. However only 33% of

patients with GERD demonstrate spontaneous reflux on upper GI radiography, making this study insufficient as a diagnostic study.

5. A **gastric emptying study** can be useful in evaluating redo patients (vagus nerve injury) or symptoms of gastroparesis. Patients with gastroparesis may benefit additionally from a pyloric drainage procedure (i.e., pyloroplasty or pyloromyotomy).

E. Complications. Approximately 20% of patients with GERD have complications, including esophagitis, stricture, or Barrett esophagus.

F. Treatment

1. **Medical treatment** aims to reduce the duration and amount of esophageal exposure to gastric contents.
   a. **Behavioral recommendations** include remaining upright after meals for at least 1 hour, sleeping with an elevated head of the bed, and avoiding bending or straining.
   b. **Dietary alterations** are aimed at maximizing LES pressure and decreasing stomach acidity. Patients are instructed to lose weight, eat small, frequent meals, and to stop smoking. Fatty foods, alcohol, caffeine, chocolate, peppermint, and certain medications may exacerbate reflux.
   c. **Pharmacologic therapy** is indicated in patients who do not improve with postural or dietary measures and include **antacids, H2-receptor antagonists, and proton-pump inhibitors.**
2. **Surgical treatment** should be considered in patients who have symptomatic reflux despite optimal medical management and manometric evidence of a defective LES. Also, patients who have achieved relief with medical therapy but want to avoid a lifetime of medication may be candidates. However, they should be counseled that use of acid-reducing medications following surgery is not uncommon. Surgery consists of either a transabdominal or a transthoracic antireflux operation to replicate a competent LES and to keep the GE junction in the abdomen.
   a. A **laparoscopic, transabdominal approach** is preferred, although the transthoracic approach may be beneficial in redo cases with a shortened esophagus.
      (1) **Nissen fundoplication** (360-degree fundic wrap) is traditionally the most common surgical approach for GERD. It

is very effective at preventing reflux but is associated with an inability to vomit, gas bloating, and dysphagia. During surgery, care must be taken to ensure that the wrap is not too tight and placed appropriately around the distal esophagus.

(2) The **Toupet fundoplication** is a partial 270-degree posterior wrap, with the wrapped segment sutured to the crural margins and to the anterolateral esophageal wall. It is the preferred fundoplication for GERD patients with esophageal dysmotility and recent data suggests that it should be strongly considered for most patients due to a lower incidence of postoperative dysphagia and equivalent or better relief of GERD symptoms when compared with Nissen fundoplication (*Br J Surg*. 2018;105(11):1398–1407).

b. A **transthoracic approach** is a reasonable alternative in patients with esophageal shortening or stricture, coexistent motor disorder, morbid obesity, coexistent pulmonary lesion, or prior antireflux repair.

(1) Nissen fundoplication can be done via a transthoracic approach with similar results.

(2) The **Belsey Mark IV repair** consists of a 240-degree fundic wrap around 4 cm of distal esophagus. In cases of esophageal neuromotor dysfunction, it produces less dysphagia than with a 360-degree wrap. In cases of previous foregut surgery, large hernia, redo operation or extreme obesity, this approach has been reported as a safe alternative (*BMC Surg*. 2013;13(1):24). The ability to belch is preserved, thereby avoiding gas-bloat syndrome (*Surg Endosc*. 2003;17:1212).

(3) Collis gastroplasty is a technique used to lengthen a shortened esophagus (i.e., <3 cm of intra-abdominal esophagus after mobilization) to minimize tension on the antireflux repair. A gastric tube is formed from the upper lesser curvature of the stomach in continuity with the distal esophagus. The antireflux repair then is constructed around the “neo-esophagus.” A gastroplasty should be considered preoperatively in patients with gross ulcerative esophagitis or stricture, failed prior antireflux procedure, or total intrathoracic stomach (*Surg Clin N Am*. 2005;85:433).

c. Complications of antireflux repairs may result from overly tight wraps or excessive tension on the repair.

(1) Postoperative dysphagia can result from a fundoplication that is too tight, misplaced or slipped fundoplication, or a complete fundoplication in the setting of poor esophageal contractile function.

(2) Recurrent reflux after surgery is increasingly common as time progresses, due to natural loosening of the wrap and may require medical therapy. However, reflux immediately after surgical repair may suggest an inadequate or disrupted repair.

(3) Gas bloating can occur if the fundoplication is too tight or if there is unrecognized gastric outlet obstruction.

III. FUNCTIONAL ESOPHAGEAL DISORDERS

A. Motor disorders of esophageal skeletal muscle result in defective swallowing and aspiration.

B. Motor Disorders of Esophageal Smooth Muscle and LES

1. Primary dysmotility

a. Achalasia is rare but is the most common primary esophageal motility disorder. Achalasia is characterized by loss of effective esophageal body peristalsis and failure of the LES to relax with swallowing, resulting in esophageal dilation. The characteristic pathology is alteration in the ganglia of Auerbach plexus.

(1) Symptoms include progressive dysphagia (~100%); regurgitation immediately after meals (>70%); odynophagia (30%); and aspiration with resultant bronchitis and pneumonia (10%). Some patients experience chest pain due to esophageal spasms.

(2) Diagnostic chest x-ray often shows a fluid-filled, dilated esophagus, and absence of a gastric air bubble. A **barium esophagogram** demonstrates tapering ("bird's beak") of the distal esophagus and a dilated proximal esophagus. **Esophageal manometry** is the **definitive diagnostic test** for achalasia. Characteristic manometric findings include the absence of peristalsis, mirror-image contractions, and limited or absent relaxation of the LES with swallowing. **Endoscopy**

rules out benign strictures or malignancy. When these symptoms are caused by malignant obstruction, the syndrome is referred to as pseudoachalasia.

(3) Medical treatment decreases the LES tone and includes nitrates and calcium-channel blockers.

(4) Surgical treatment with a **modified Heller esophagomyotomy** has been shown to produce excellent results in >90% of patients (*J Thorac Cardiovasc Surg*. 2010;140:962). A concomitant antireflux procedure (270-degree or 180-degree fundoplication) with the esophagomyotomy helps avoid late stricture due to GERD caused by the incompetent LES (*J Clin Gastroenterol*. 2008;42:603–609).

(5) Peroral endoscopic myotomy (POEM) consists of endoscopically creating a submucosal tunnel; then dividing the circular muscle layer of distal esophagus, LES, and proximal stomach, keeping the mucosa intact. Dysphagia outcomes, postoperative pain, and symptomatic GERD are similar to laparoscopic Heller/fundoplication (*Medicine (Baltimore)*. 2016;95(6):e9609). While POEM is highly effective in relieving symptoms of achalasia, patients can experience significant GERD postoperatively.

b. Diffuse esophageal spasm is characterized by loss of the normal peristaltic coordination of the esophageal smooth muscle.

(1) The primary **symptoms** are severe spastic pain, dysphagia, regurgitation, and weight loss.

(2) The **diagnosis** is confirmed with esophageal manometry, which demonstrates spontaneous activity, repetitive waves, and prolonged, high-amplitude contractions.

(3) Treatment with calcium-channel blockers and nitrates, but these may not be beneficial. Surgical treatment is very rare and may consist of a long esophagomyotomy and often a concomitant antireflux procedure.

c. Nutcracker esophagus is characterized manometrically by prolonged, high-amplitude peristaltic waves associated with chest pain that may mimic cardiac symptoms. Treatment with calcium-

channel blockers and long-acting nitrates has been helpful.

2. **Secondary dysmotility** represents the esophageal response to inflammatory injury or systemic disorders. Inflammation can produce fibrosis, which can lead to loss of peristalsis and esophageal contractility.
   a. The most common cause of secondary dysfunction is **GERD**, resulting in erosive esophagitis and stricture formation. Intensive medical treatment of the reflux is essential before operation. Most surgeons prefer a Collis gastroplasty and a Toupet or Belsey antireflux procedure for these patients because of the presence of esophageal shortening and impaired peristalsis.
   b. **Progressive systemic sclerosis** produces esophageal manifestations in 60% to 80% of patients, and often the esophagus is the earliest site of GI involvement. Smooth muscle atrophy and fibrosis results in absent contractions in the mid-distal esophagus. However, contractility is preserved within the striated muscle of the proximal esophagus.

IV. ESOPHAGEAL STRICTURES.

Esophageal strictures are either benign or malignant. **Benign strictures** are either congenital or acquired.

A. Congenital webs represent a failure of appropriate canalization of the esophagus during development and can occur at any level.

B. Acquired Strictures

1. **Esophageal rings** or **webs** occur at all levels. An example is **Schatzki ring**, which occurs in the lower esophagus at the junction of the squamous and columnar epitheliums due to GERD. A hiatal hernia is always present though esophagitis is rarely present. Treatment generally consists of medical management of reflux with periodic dilation for symptoms of dysphagia.
2. **Strictures** of the esophagus can result from any esophageal injury, including chronic reflux, previous perforation, infection, or inflammation.

C. Symptoms associated with a stricture begin when the lumen narrows beyond 12 mm and consist of progressive dysphagia to solid food.

D. Evaluation and treatment of a stricture begins with the categorical **exclusion of malignancy**. The diagnosis of stricture usually is based on

a **barium swallow. Esophagoscopy** is essential to assess the location, length, size, and distensibility of the stricture and to obtain appropriate biopsies or brushings. Because a peptic stricture secondary to reflux always occurs at the squamocolumnar junction, biopsy of the esophageal mucosa below a high stricture should demonstrate columnar mucosa. If squamous mucosa is found, the presumptive diagnosis of a malignant obstruction should be made. Most benign strictures are amenable to **dilation** to relieve symptoms, then focus is directed to correcting the underlying etiology. **Resection** can be required for recurrent or persistent strictures or if malignancy cannot be ruled out.

V. ESOPHAGEAL DIVERTICULA. Esophageal diverticula are acquired conditions of the esophagus found primarily in adults.

A. A **pharyngoesophageal (or Zenker) diverticulum** is a **pulsion diverticulum**. It is the most common type of symptomatic diverticulum. A hypertensive upper esophageal sphincter (UES) or uncoordinated pharyngeal contraction and opening of the UES results in increased pharyngeal intraluminal pressure. Herniation of only the mucosa and submucosa results in this false diverticulum. **Symptoms** include progressive cervical dysphagia, halitosis, cough on assuming a recumbent position, and spontaneous regurgitation of undigested food. **Diagnosis** with a barium swallow should prompt **surgical correction** with cricopharyngeal myotomy and diverticulectomy or diverticulopexy.

B. A **traction** (midesophageal or parabronchial) **diverticulum** occurs rarely in the middle third of the esophagus and is a true (full thickness) diverticulum. It occurs secondary to mediastinal inflammatory diseases (histoplasmosis or tuberculosis). Symptoms are rare, but when present, they may prompt operative excision of the diverticulum and adjacent inflammatory mass.

C. An **epiphrenic diverticulum** is associated with underlying esophageal motility disorder and can be located at almost every level but typically occurs in the **distal 10 cm** of the thoracic esophagus. Many patients are asymptomatic, and the **diagnosis** is made with a contrast esophagogram, though endoscopy and esophageal function studies are needed to define the underlying pathophysiology. **Operative treatment** is indicated for patients with progressive or incapacitating symptoms and consists of diverticulectomy or diverticulopexy, along with an extramucosal

esophagomyotomy.

TRAUMATIC INJURY TO THE ESOPHAGUS

I. ESOPHAGEAL PERFORATION

A. Overall, perforation is associated with a 20% mortality rate

1. Intraluminal causes

a. Instrumentation injuries represent 75% of esophageal perforations and most commonly occur at anatomical narrowings of the esophagus.

b. Foreign bodies can cause acute perforation, or more commonly follow an indolent course with late abscess formation in the mediastinum or development of empyema.

c. Ingested caustic substances, such as alkali chemicals, can produce coagulation necrosis of the esophagus.

d. Cancer of the esophagus may lead to perforation.

e. Barotrauma induced by external compression, forceful vomiting (Boerhaave syndrome), seizures, childbirth, or lifting can produce esophageal perforation. Almost all of these injuries occur in the distal esophagus on the left side.

2. Extraluminal causes

a. Penetrating injuries to the esophagus can occur from stab wounds or, more commonly, gunshot wounds.

b. Blunt trauma may produce an esophageal perforation related to a rapid increase in intraluminal pressure or compression of the esophagus between the sternum and the spine.

c. Operative injury to the esophagus during an unrelated procedure occurs infrequently, but may occur during spine surgery, aortic surgery, or mediastinoscopy.

B. Signs and symptoms include dysphagia, pain, and fever and quickly progress to sepsis if left undiagnosed or untreated. **Cervical perforations** may present with neck stiffness and subcutaneous emphysema. **Intrathoracic perforation** present with chest pain, subcutaneous emphysema, dyspnea, and a pleural effusion (right sided in proximal perforations, left in distal perforations). **Intra-abdominal perforations** present with peritonitis.

C. Diagnosis of perforation is suggested by pneumomediastinum, pleural effusion, pneumothorax, atelectasis, and soft-tissue emphysema on **chest x-ray** or mediastinal air and fluid on **computed tomography** (**CT**) **scan.** Rapid evaluation with **water-soluble contrast (Gastrografin) or dilute barium contrast esophagography** (10% false-negative rate) is **mandatory.** Intramural perforation after endoscopic procedures appears to have a thin collection of contrast material parallel to the esophageal lumen without spillage into the mediastinum. **Esophagoscopy** is used primarily as an adjunctive study and can miss sizable perforations.

D. Initial management includes: (1) adequate **drainage** of the leak, (2) intravenous **antibiotics,** (3) aggressive fluid **resuscitation,** (4) adequate **nutrition**, (5) **relief** of any distal obstruction, (6) **diversion** of enteric contents past the leak, and (7) **restoration** of GI integrity. Patients are kept NPO, a nasogastric tube is carefully placed, and they receive intravenous hydration and broad-spectrum antibiotics.

E. Definitive management generally requires operative repair, although a carefully selected group of nontoxic patients with a locally contained perforation may be observed. Esophageal stent placement and appropriate drainage has been effective for spontaneous perforations and anastomotic leaks (*Ann Surg*. 2014;259(5):852–860).

1. **Cervical and upper thoracic perforations** usually are treated by cervical drainage alone or in combination with esophageal repair.
2. **Thoracic perforations** should be closed primarily and buttressed with healthy tissue, and the mediastinum should be drained widely. If primary closure is not possible, options include wide drainage alone or in conjunction with resection, or with exclusion and diversion in cases of severe traumatic injury to the esophagus.
3. **Abdominal esophageal perforations** typically require an upper abdominal midline incision to correct.
4. **Perforations associated with intrinsic esophageal disease** (e.g., carcinoma, hiatal hernia, or achalasia) require addressing the perforation and surgically correcting the associated esophageal disease.

II. CAUSTIC INGESTION. Liquid alkali solutions (e.g., **drain cleaners, lye**) are responsible for most of the serious caustic esophageal and gastric

injuries, producing coagulation necrosis in both organs. Acid ingestion is more likely to cause isolated gastric injury.

A. Initial management is directed at hemodynamic stabilization and evaluation of the airway and extent of injury.

1. **Evaluate for airway compromise**, burns may require tracheostomy.
2. **Fluid** resuscitation and broad-spectrum **antibiotics.**
3. **Do not induce vomiting,** place on NPO, and give patients an oral suction device.

B. Evaluation with **water-soluble contrast esophagography** and gentle **esophagoscopy** should be done early to assess the severity and extent of injury and to rule out esophageal perforation or gastric necrosis.

C. Management

1. Without perforation, **management is supportive**, with acute symptoms generally resolving over several days.
2. **Perforation, unrelenting pain**, or **persistent acidosis** mandate surgical intervention. A transabdominal approach is recommended to allow evaluation of the patient's stomach and distal esophagus.
3. **Late complications** include the development of **strictures** and an increased risk (×1,000) of **esophageal carcinoma.**

ESOPHAGEAL TUMORS

I. BENIGN ESOPHAGEAL NEOPLASMS. Benign esophageal neoplasms are rare, the most common lesions are mesenchymal tumors (leiomyomas and some GI stromal tumors) and polyps.

A. Clinical features depend primarily on the location of the tumor within the esophagus. **Intraluminal** tumors, like polyps, cause esophageal obstruction, and patients present with dysphagia, vomiting, and aspiration. **Intramural** tumors, like leiomyomas, are typically asymptomatic, but can produce dysphagia or chest pain if large enough.

B. Diagnosis usually involves a combination of barium swallow, esophagoscopy, and perhaps CT scanning or magnetic resonance (MR) scan studies.

C. Treatment of all symptomatic or enlarging tumors is **surgical removal.** Intraluminal tumors can usually be removed endoscopically. Intramural tumors usually can be enucleated from the esophageal muscular wall

without entering the mucosa.

II. BARRETT ESOPHAGUS.

Barrett esophagus is a complication of chronic gerd; histologically demonstrates intestinal-type metaplasia. The columnar epithelium may replace the normal squamous epithelium circumferentially, or it may be asymmetric and irregular.

A. Prevalence. Barrett esophagus is diagnosed in approximately 2% of all patients undergoing esophagoscopy and in 10% to 15% of patients with esophagitis. Most patients diagnosed with Barrett esophagus are middle-aged White men.

B. Symptoms of Barrett esophagus arise from chronic GERD including heartburn (50%), dysphagia (75%), and bleeding (25%) (*Ann Surg*. 1983; 198:554).

C. Diagnosis requires endoscopy and correlation between endoscopic and histologic appearances.

D. Complications

1. **Esophageal ulceration and stricture** are more likely to occur in patients with Barrett esophagus than in those with GERD alone.
   a. **Barrett ulcers, like gastric ulcers**, penetrate the metaplastic columnar epithelium. They occur in up to 50% of patients with Barrett esophagus.
   b. A **benign stricture** occurs in 30% to 50% of patients with Barrett esophagus. The stricture is located at the squamocolumnar junction, which may be found proximal to the GE junction.
2. The metaplastic columnar epithelium of Barrett esophagus is prone to development of **dysplasia**, detected by biopsy. Low-grade dysplasia is present in 5% to 10% of patients with Barrett esophagus. **Malignant degeneration** from benign to dysplastic to malignant epithelium occurs in Barrett esophagus.
3. **Adenocarcinomas** above the normal GE junction are characteristic of malignant degeneration in Barrett esophagus. The risk of development of adenocarcinoma in Barrett esophagus is 50 to 100 times that of the general population; yet adenocarcinoma is still a rare event in a Barrett patient. Approximately 0.12% to 0.43% per year will progress from Barrett to adenocarcinoma (*Best Pract Clin Gastroenterol*. 2015;29(1):125–138).

E. Treatment (Fig. 17-1)

1. Uncomplicated Barrett esophagus in **asymptomatic** patients requires endoscopic surveillance and biopsy annually or even less frequently in the absence of dysplasia.
2. Uncomplicated Barrett esophagus in **symptomatic** patients should be managed like GERD patients and should have periodic endoscopic surveillance with four-quadrant biopsies. Elimination of reflux with an **antireflux procedure** may halt progression of the disease, heal ulceration, and prevent stricture formation but will not reverse the columnar metaplasia of Barrett.
3. **Barrett ulcers** usually heal with medical therapy. Frequently, 8 weeks of treatment with a PPI are necessary to achieve complete healing. Ulcers that fail to heal or recur despite 4 months of medical therapy are an indication for rebiopsy and antireflux surgery.

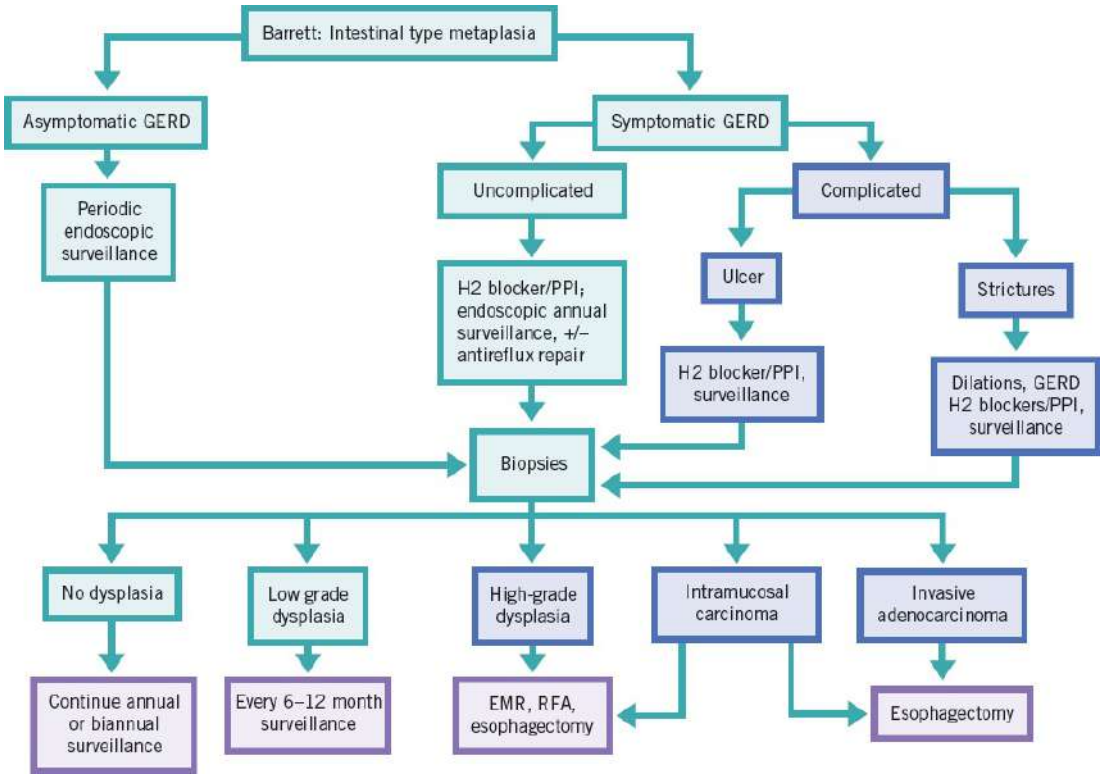


FIGURE 17-1 Algorithm for surveillance and management of Barrett esophagus.

4. **Strictures** associated with Barrett esophagus are managed with periodic esophageal dilation combined with medical management. Recurrent or persistent strictures warrant an antireflux operation

combined. Rarely, undilatable strictures require resection.

5. **Dysplasia**
   a. **Low-grade dysplasia** requires frequent (every 3 to 6 months) surveillance esophagoscopy and biopsy. Medical therapy for GERD is recommended in these patients, even when asymptomatic.
   b. **High-grade dysplasia** is pathologically indistinguishable from carcinoma in situ and was recently an indication for esophagectomy. Nonresective options are increasingly utilized such as endoscopic mucosal resection (EMR) and radiofrequency ablation. Resection via esophagectomy is reserved for failure of these less-invasive approaches.
6. **Adenocarcinoma** in patients with Barrett esophagus is an indication for esophagogastrectomy. Early detection offers the best opportunity to improve survival after resection, which is 20% at 5 years for all patients with cancer but far higher in those detected by surveillance and screening.

III. ESOPHAGEAL CARCINOMA

A. Epidemiology.

Adenocarcinoma and squamous cell carcinoma of the esophagus represents 1% of all cancers in the United States. It is more common in men (4:1) and most frequently diagnosed between ages 65 and 74.

1. **Risk factors** for **squamous cell carcinoma** include African American race; alcohol and cigarette use; achalasia; caustic esophageal injury; and geographic locations of China, South Africa, France, and Japan.
2. **Risk factors** for **adenocarcinoma** include White race, GERD, Barrett esophagus, obesity, and cigarette smoking.

B. Pathology

1. **Squamous cell carcinoma** is multicentric and most frequently involves the middle third of the esophagus.
2. **Adenocarcinoma** constitutes the majority of malignant esophageal tumors in the United States. It typically exhibits extensive proximal and distal submucosal invasion, is not multicentric, and commonly involves the distal esophagus.

3. **Less common malignant esophageal tumors** include small-cell carcinoma, melanoma, leiomyosarcoma, lymphoma, and esophageal involvement by metastatic cancer.

C. Most patients with early-stage disease are asymptomatic or may have symptoms of reflux, dysphagia, odynophagia, and weight loss. Hoarseness, abdominal pain, persistent bone pain, hiccups, and respiratory symptoms may indicate a more advanced stage. Approximately 50% of presenting patients have unresectable primary tumors or distant metastasis at the time of diagnosis.

D. Diagnosis is suggested by a barium swallow or CT with IV and PO contrast demonstrating esophageal mass or stricture and confirmed with esophagoscopy and biopsy.

E. Staging. Esophageal adenocarcinoma and squamous cell carcinoma are staged differently; squamous cell carcinoma has the additional variable of anatomical location (Table 17-1). Evaluation for lymph node and distant-organ metastatic disease is performed by PET-CT. Endoscopic ultrasonography is most accurate for determining the depth of wall invasion and the involvement of peritumoral lymph nodes in patients without evidence of M1 disease on PET-CT. Lesions above the carina in M0 disease require bronchoscopy to evaluate the airway for involvement.

F. Treatment

1. **Surgical resection** remains a mainstay of curative treatment of patients with localized disease. Total esophagectomy with a cervical esophagogastric anastomosis and subtotal resection with a high intrathoracic anastomosis have become the most common resections and produce the best long-term functional results as well as the best chance for cure. Options for **esophageal replacement** include the stomach, colon, and jejunum.
   a. **Complications of esophagectomy** patients include aspiration pneumonia, anastomotic leak, and atrial fibrillation.
      (1) Respiratory complications, including pneumonia, can be reduced by using retrograde drainage of the conduit (retrograde tube gastrostomy), instead of a nasogastric tube (*Ann Thorac Surg*. 2011;92(2):499–503).
      (2) Management of an **anastomotic leak** is based on the size of the

leak, the location of the anastomosis, and the clinical status of the patient.

(a) Cervical anastomotic leaks can usually be managed by opening the incision to allow drainage. Occasionally, the leak tracks below the thoracic inlet into the mediastinum, necessitating evaluation of ischemic injury to the stomach and wider debridement and drainage.

(b) Intrathoracic anastomotic leaks are associated with a high mortality rate and large or poorly drained leaks require operative exploration.

2. **Adjuvant therapy** with preoperative chemotherapy or chemoradiotherapy may enhance local control and resectability. For localized squamous carcinoma of the thoracic esophagus, preoperative chemoradiation followed by resection is the preferred approach (National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers Version 1.2019, MARCH 14, 2019). Optimal treatment of squamous cell esophageal cancers remains controversial with the current literature suggesting that chemoradiotherapy may be a definitive therapy option rather than only an adjuvant for surgically fit patients (*World J Surg Oncol*. 2018;16). Patients with dysphagia and or severe malnutrition may require feeding tube placement to optimize nutrition during neoadjuvant therapy.
3. **Radiotherapy** is used worldwide for attempted cure and palliation of patients with squamous cell esophageal cancer deemed unsuitable for resection. The 5-year survival rate is 5% to 10%.

TABLE 17-1 **TNM (Tumor, Node, Metastasis) Staging System for Esophageal Cancer**

Definition of TNM

T: Primary Tumor

TX	Carcinoma in situ/high-grade dysplasia
T0	No evidence of primary tumor
Tis	High-grade dysplasia, defined as malignant cells confined to the epithelium by the basement membrane
T1	Tumor invades the lamina propria, muscularis mucosa, or submucosa
T1a	Tumor invades the lamina propria or muscularis mucosa
T1b	Tumor invades the submucosa
T2	Tumor invades the muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Pleura, pericardium, diaphragm, or adjacent peritoneum
T4b	Other adjacent structures, e.g., aorta, vertebral body, airway

N: Regional Lymph Nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional node metastasis
N1	1–2 regional lymph nodes
N2	3–6 regional lymph nodes
N3	>6 regional lymph nodes

M: Distant Metastasis

M0	No distant metastasis
M1	Distant metastasis

G: Histologic Grade

GX	Grade cannot be assessed—stage grouping as G1
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated

L: Location for Squamous Cell Carcinoma (Location defined by epicenter of esophageal tumor)

X	Location unknown
Upper	Cervical esophagus to lower border of azygos vein
Middle	Lower border of azygos vein to lower border of inferior pulmonary vein
Lower	Lower border of inferior pulmonary vein to stomach, including GE junction

Adenocarcinoma Stage Grouping

Stage	T	N	M	G
0	Tis	0	0	N/A
IA	1	0	0	X–1
IB	1a	0	0	2
	1b	0	0	X or 1–2
IC	1	0	0	3
	2	0	0	1–2
IIA	2	0	0	X or 3
IIB	1	1	0	Any
	3	0	0	Any
IIIA	1	2	0	Any
	2	1	0	Any
IIIB	2	2	0	Any
	3	1–2	0	Any
	4a	0–1	0	Any
IVA	4a	2	0	Any
	4b	0–2	0	Any
	Any	3	0	Any
IVB	Any	Any	M1	Any

Squamous Cell Carcinoma Stage Grouping					
Stage	**T**	**N**	**M**	**G**	**Location**
0	Tis	0	0	N/A	Any
IA	1a	0	0	X or 1	Any
IB	1a	0	0	2–3	Any
	1b	0	0	1–3	Any
	2	0	0	1	Any
IIA	2	0	0	X or 2–3	Any
	3	0	0	Any	Lower
	3	0	0	1	Upper, middle

Squamous Cell Carcinoma Stage Grouping					
Stage	**T**	**N**	**M**	**G**	**Location**
IIB	3	0	0	2–3	Upper, middle
	3	0	0	X	Any
	3	0	0	Any	X
	1	1	0	Any	Any
IIIA	1	2	0	Any	Any
	2	1	0	Any	Any
IIIB	2	2	0	Any	Any
	3	1–2	0	Any	Any
	4a	0–1	0	Any	Any
IVA	4a	2	0	Any	Any
	4b	0–2	0	Any	Any
	Any	3	0	Any	Any
IVB	Any	Any	1	Any	Any

National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers (Version 2.2018).

4. **Palliative treatment** is used to relieve obstruction and mitigate dysphagia.

a. **Radiotherapy and chemotherapy** work best in patients with squamous cell carcinoma above the carina. Adenocarcinoma is less responsive to radiation.
b. **Intraluminal prostheses** intubate the esophagus and stent the obstruction. Potential complications include perforation, erosion or migration of the stent, and obstruction of the tube.
c. **Endoscopic laser techniques** (photodynamic therapy) can restore an esophageal lumen successfully 90% of the time, with only a 4% to 5% perforation rate.

CHAPTER 17: ESOPHAGUS

Multiple Choice Questions

1. **A 62-year-old female has a newly diagnosed type III hiatal hernia with 40% of the stomach noted to be in the chest. She presents with dysphagia, postprandial epigastric pain, and breathlessness when eating. She is evaluated for treatment. Which of the following is the most appropriate option?**

   a. PPI
   b. Watch and wait
   c. Hiatal hernia repair with a Collis gastroplasty (lengthening procedure)
   d. Hiatal hernia repair with a Dor procedure
   e. Toupet fundoplication

2. **Which of the following procedures reduces the incidence of postoperative dysphagia in patients with GERD that also have abnormal esophageal motility?**

   a. Laparoscopic Nissen fundoplication
   b. Transthoracic Nissen fundoplication
   c. Extensive mobilization of the esophagus
   d. Collis gastroplasty
   e. Toupet fundoplication

3. **Which of the following is the most common symptom of achalasia?**

   a. Aspiration events
   b. Pneumonia
   c. Postprandial regurgitation
   d. Odynophagia
   e. Dysphagia

4. **A 65-years-old female presents with atypical chest pain; she has been ruled out for an MI three times in the past year and is otherwise healthy. To rule out esophageal causes she undergoes**

a manometry study, which shows prolonged high-amplitude peristaltic waves. Which of the following is the most likely diagnosis?

a. Variant achalasia
b. Achalasia
c. Nutcracker esophagus
d. Esophageal spasm
e. Hiatal hernia

5. Which of the following conditions can be treated by enucleation from the esophageal muscular wall?

a. Esophageal polyps
b. Esophageal leiomyomas
c. Esophageal squamous cell carcinoma
d. Esophageal adenocarcinoma
e. High-grade esophageal dysplasia

18 Stomach

Bradley A. Krasnick and William G. Hawkins

DISORDERS OF THE STOMACH

I. PEPTIC ULCER DISEASE. Peptic ulcer disease (PUD) is characterized by ulceration of the stomach or proximal duodenum due to an imbalance between mucosal defense and aggravating factors such as acid secretion, *Helicobacter pylori* infection, alcohol, and nonsteroidal anti-inflammatory drug (NSAID).

A. Epidemiology. Occurs at annual incidence of 1% to 2% and lifetime prevalence of ~10%, making it one of the most common GI conditions in the United States.

B. Location. Duodenal ulcers are typically located at the antral–pylorus junction and gastric ulcers usually fall within one of the five categories (Modified Johnson Classification).

1. Type 1: Located along the lesser curvature, normal/decreased acid secretion, along with *H. pylori* injection in majority (60% to 70%).
2. Type 2: Body of stomach/ incisura and duodenal, high acid secretion (15%).
3. Type 3: Prepyloric, associated with high acid secretion (20%).
4. Type 4: Proximal stomach/cardia, low mucosal protection, as well as normal or decreased acid secretion.
5. Type 5: Anywhere in stomach, medication induced (often associated with NSAIDs and/or steroids).

C. Pathogenesis

1. ***H. pylori* infection** is associated with 95% of duodenal ulcers and 75% of gastric ulcers and leads to chronic antral gastritis, increased acid and gastrin secretion, and decreased mucosal resistance to acid.

2. **NSAID** use increases the risk PUD fivefold due to suppression of prostaglandin production (*Rheum*. 2010;49:ii3–ii10).
3. **Cigarette smoking** doubles the risk of PUD formation.
4. **Acid hypersecretion.** Vagal input stimulates postganglionic fibers to secrete GRP, which works in concert with stomach distention and digested protein products to lead to gastrin release from G cells in the antrum. Gastrin, along with histamine released from ECL cells, and continued vagal input leads to gastric body parietal cells to release acid (HCl). Gastrin, histamine, and HCl release is inhibited by somatostatin from D cells. Disorders in this pathway (e.g., a gastrin-secreting tumor) can lead to increased HCl.

D. Presentation in uncomplicated disease is characterized by burning, gnawing, intermittent epigastric pain relieved by food or antacid ingestion for duodenal ulcers, but exacerbated for gastric ulcers. Associated symptoms include nausea, vomiting, and mild weight loss.

E. Diagnosis is made by **esophagogastroduodenoscopy** (**EGD**) as it is the most sensitive and specific test. Once PUD is confirmed, further testing is performed to determine its etiology.

1. ***H. pylori infection*** can be detected noninvasively by **radiolabeled urea breath test, stool antigen testing**, or **serologic antibody testing** (serology is unable to assess for eradication). Antral tissue can be assessed by direct **histologic examination** (gold standard), **rapid urease testing**, or in vitro **culture**.
2. **Fasting serum gastrin levels** are obtained if the patient has no history of NSAID use, is *H. pylori* negative, or has recurrent ulcers despite adequate treatment, multiple ulcers, ulcers in unusual locations, or complicated PUD. **Zollinger–Ellison syndrome** (**ZES**) is a rare condition caused by gastrin hypersecretion from a gastrinoma. ZES is associated with **multiple endocrine neoplasia type I** (**MEN I**) in 20% of patients.
3. **Endoscopic biopsy** of gastric ulcers is indicated to rule out malignancy if the patient has atypical signs or symptoms (weight loss, malaise, anemia, obstruction) or if the ulcer has an atypical appearance (associated mass, folds around ulcer). In addition, if the ulcer remains after a course of medical management, biopsy is indicated.

F. Treatment has shifted from primarily surgical to medical, as *H. pylori* eradication has become the cornerstone of PUD treatment.

1. Medical therapy

a. *H. pylori* eradication includes an acid-reducing medication (PPI preferred, H2 blocker) with two antibiotics (often clarithromycin + amoxicillin or metronidazole) administered for 10 to 14 days (triple therapy). One in five patients fail initial therapy for *H. pylori*, and goes on to receive further medical treatment (*Rev. Gastro. Disord*. 2005;5(2):67).

b. NSAID-associated PUD is treated by discontinuing all NSAID use and starting antisecretory therapy. If the NSAID must be continued, PPIs are most effective for facilitating ulcer healing.

c. Smoking cessation promotes ulcer healing, but compliance rates are low.

d. Follow-up endoscopy for gastric ulcers given risk of malignancy.

2. Surgical therapy for uncomplicated PUD is nearly obsolete given the advent of PPIs. Indications include bleeding (acute/chronic), perforation, obstruction, failure of medical therapy (intractability), and inability to exclude malignancy.

a. Duodenal ulcers

(1) Truncal vagotomy and antrectomy (gold standard) with Billroth I (gastroduodenostomy) or Billroth II (gastrojejunostomy) reconstruction: Maximal acid suppression with lowest ulcer recurrence rates (1% to 2%) but highest postoperative morbidity (15% to 30%) and mortality (1% to 2%) rates.

(2) Truncal vagotomy with pyloroplasty with recurrence rate of 5% to 15% and operative mortality <1%.

(3) Highly selective vagotomy (HSV): Lowest postoperative morbidity (3% to 8%) and mortality rates (<1%), but technically demanding and has higher recurrence rates (5% to 15%).

b. Nonhealing or treatment refractory gastric ulcers are treated with wedge excision or antrectomy with inclusion of the ulcer. Concurrent acid-reducing operation is reserved for acid hypersecreting patients (types II and III) or patients with refractory PUD despite maximal medical therapy.

II. COMPLICATED PEPTIC ULCER DISEASE. Complicated PUD refers to hemorrhage, perforation, or obstruction in the setting of PUD. While the global prevalence of PUD has declined, complicated disease and the rate of emergency surgery have remained stable.

A. Hemorrhage is the leading cause of death with estimated 5% to 10% mortality. After resuscitation and IV PPI therapy, EGD is performed. Although bleeding stops spontaneously in 75% of patients, recurrent bleeding may occur in high-risk individuals or if clot, visible vessel, or active bleeding are observed during EGD. Consideration should also be given to arteriography with angioembolization in select cases. **Indications for surgery** include repeated episodes of bleeding, continued hemodynamic instability, ongoing transfusion requirement of more than 4 to 6 units of packed red blood cells over 24 hours, and more than one unsuccessful endoscopic intervention. In most centers surgery is reserved for failure of endoscopic management (clips, cautery, epinephrine, sclerosing agents).

1. **Bleeding duodenal ulcers** are usually located on the posterior duodenal wall within 2 cm of the pylorus and erode into the gastroduodenal artery. Bleeding is controlled by duodenotomy and three-point ligation of the bleeding vessels.
2. **Bleeding gastric ulcers** are managed by biopsy followed by oversewing or wedge excision of the ulcer in unstable patients, or by acid-reducing procedures if stable.

B. Perforated peptic ulcers present with sudden onset of severe abdominal pain but may be less dramatic in hospitalized, elderly, or immunocompromised patients. Examination reveals fever, tachycardia, abdominal wall rigidity, and possible peritonitis. Laboratory evaluation demonstrates leukocytosis, and abdominal x-ray may demonstrate free subdiaphragmatic air. Treatment is aggressive fluid resuscitation, broad-spectrum antibiotics followed by prompt operation. Nonoperative treatment can be considered in poor operative candidates in whom the perforation has been present for more than 24 hours, the pain is well localized, and there is no evidence of extravasation on upper GI water-soluble contrast study (*Dig Surg*. 2010;27:161).

1. **Perforated duodenal ulcers** require omental patching (Graham patch), peritoneal washout, and postoperative *H. pylori* eradication. Vagotomy is seldom performed, thus long-term antacid treatment is

required. If the patient is stable, an acid-reducing procedure (preferably truncal vagotomy and pyloroplasty) may be added if the patient is *H. pylori* negative or has failed medical therapy.

2. **Perforated gastric ulcers** are treated by simple wedge resection to eliminate the perforation and exclude malignancy. If resection cannot be performed due to a juxtapyloric location, multiple biopsies are taken and omental patching is performed.

C. Gastric outlet obstruction (GOO) may result from fibrosis and scarring in chronic PUD or from edema, spasm, and pyloric dysmotility in acute disease. Patients present with recurrent vomiting of poorly digested food, dehydration, and hypochloremic hypokalemic metabolic alkalosis. Management consists of correction of volume and electrolyte abnormalities, nasogastric decompression, and intravenous antisecretory agents. EGD is performed to evaluate the nature of the obstruction and to rule out malignancy, and endoscopic hydrostatic balloon dilation can be performed at the same time. **Indications for surgical therapy** include persistent obstruction after 7 days of nonoperative management and recurrent obstruction. Antrectomy to include the ulcer and truncal vagotomy is the ideal operation for most patients.

III. GASTRIC ADENOCARCINOMA. Gastric adenocarcinoma is the fifth most common cancer and third leading cause of cancer death worldwide, but is a relatively uncommon malignancy (14th) in the United States. In the United States only 25% of patients present with localized disease, resulting in an overall 5-year survival rate of 28% (*SEER Cancer Statistics*, www.seer.cancer.gov/statistics).

A. Risk factors include male gender, family history, low socioeconomic status, polyposis syndromes, diets high in nitrates, salted or pickled foods, previous gastric resection, Ménétrier disease, HNPCC, smoking, *H. pylori* infection, blood group A, and chronic atrophic gastritis. Gastric adenomatous polyps are also precancerous lesions and should be differentiated from the more common non-premalignant hyperplastic polyp (75% of gastric polyps). All polyps >1 to 2 cm should be removed. Aspirin, fresh fruits and vegetables, selenium, and vitamin C may be protective.

B. Classification. Ninety-five percent of gastric cancers are adenocarcinomas, arising from mucus-producing cells in the gastric

mucosa.

1. The **Lauren classification** system is most widely used and divides gastric cancers into two subtypes:
   a. **Intestinal-type cancers** are glandular and arise from the gastric mucosa. They occur more commonly in elderly men and in the distal stomach and are associated with *H. pylori* and other environmental exposures that lead to chronic gastritis, intestinal metaplasia, and dysplasia. Hematogenous metastatic spread to distant organs is seen.
   b. **Diffuse-type cancers** arise from the lamina propria and are associated with an invasive growth pattern with rapid submucosal spread of signet ring cells. They occur more commonly in younger patients, females, and in the proximal stomach. Transmural and lymphatic spread is common, with early metastases.
2. As part of the Cancer Genome Atlas (**TCGA**) project, an updated classification schema was created (*Nature*. 2014;513:202).
   a. **Microsatellite unstable** (**MSI-H**, 20%) characterized by mismatch repair gene MLH1 silencing, leading to a high mutation rate.
   b. **Epstein-Barr virus positive** (**EBV**, 10%) tumors seen more so in male patients, often in the stomach fundus or body. Tumors often overexpress PD-L1.
   c. **Chromosomally unstable** (**CIN**, 50%) tumors characterized by intestinal histology, with high somatic copy number variation, and p53 and RAS mutations.
   d. **Genomically stable** (**GS**, 20%) tumors have low somatic copy number variation. Often have CDH1 mutations and diffuse histology.

C. Presentation: nonspecific signs and symptoms such as epigastric abdominal pain, weight loss, nausea, vomiting, anorexia, and fatigue. Dysphagia is associated with proximal gastric cancers, whereas GOO is more typical of distal cancers. Classic physical findings such as enlarged supraclavicular nodes (Virchow node) and infiltration of the umbilicus (Sister Mary Joseph node) represent metastatic and incurable disease. Perforation and hemorrhage present in the minority and portend advanced disease.

D. Diagnosis is most commonly made by EGD. During EGD, six to eight

biopsies should be taken. **Screening examination** is not cost-effective for the US population, except for certain high-risk patients—such as those with hereditary diffuse gastric cancer who harbor a germline CDH1 mutation. In Japan and Korea, where incidence is high, mass screening is performed starting at 40 to 50 years of age, resulting in increased detection of early-stage cancer and improved survival (*Surg Clin North Am*. 2017;26(2):163).

E. Staging: The American Joint Committee on Cancer and International Union against Cancer (AJCC/UICC) jointly developed a staging system that is most widely used worldwide (Table 18-1).

1. **CT scan** of the chest, abdomen, and pelvis with oral and IV contrast is the best initial noninvasive modality for detecting locoregional and metastatic disease. **Positron emission tomography** (**PET**)**/CT** can detect nodal and distant metastatic disease not apparent on CT alone —although only 50% of gastric carcinomas are PET avid.
2. **EUS** is indicated for further staging in patients with locoregional disease and delineates depth of tumor invasion in the gastric wall and adjacent structures. EUS has been found to be a good predictor of advanced (T3/4 or >N0 disease) disease, with a positive predictive value for advanced disease of 76%, and a negative predictive value for low-risk disease (T1-2, N0) of 91% (*Ann Surg Onc*. 2007;14(6):1853).
3. **Laparoscopic staging** can detect occult distant metastases in 31% of patients (*Am J Surg*. 2006;191(1):134). Peritoneal washings with cytology should be performed for clinical stage T3+ or N+ patients.
4. **Treatment.** Curative intent therapy often relies on the combination of surgery and chemotherapy for local/locoregional disease (Fig. 18-1).
   a. **Surgical therapy** necessitates complete resection with negative microscopic margins (≥4 cm) for T1b-T3 tumors and en bloc resection for T4 tumors (*J Am Coll Surg*. 2004;199:880).

TABLE 18-1 **TNM (Tumor, Node, Metastasis) Pathological Staging of Gastric Carcinoma**

T: Primary Tumor	
T0	No evidence of primary tumor

Tis	Carcinoma in situ
T1a	Invasion of lamina propria, muscularis mucosae
T1b	Invades submucosa
T2	Invasion of muscularis propria
T3	Invades subserosal connective tissue
T4a	Perforates serosa (visceral peritoneum)
T4b	Invasion of adjacent structures
N: Regional Lymph Nodes	
N0	No regional node metastasis
N1	Metastasis in 1 to 2 regional lymph nodes
N2	Metastasis in 3 to 6 regional lymph nodes
N3a	Metastasis in 7 to 15 regional lymph nodes
N3b	Metastasis in 16 or more regional lymph nodes
M: Distant Metastasis	
M0	No distant metastases
M1	Distant metastases
G: Histologic Grade	
GX	Cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated, Undifferentiated

Stage Grouping

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T1	N1	M0
	T2	N0	M0
Stage IIA	T1	N2	M0

	T2	N1	M0
	T3	N0	M0
Stage IIB	T1	N3a	M0
	T2	N2	M0
	T3	N1	M0
	T4a	N0	M0
Stage IIIA	T2	N3a	M0
	T3	N2	M0
	T4a	N1-2	M0
	T4b	N0	M0
Stage IIIB	T1-2	N3b	M0
	T3-4a	N3a	M0
	T4b	N1-2	M0
Stage IIIC	T3	N3b	M0
	T4a	N3b	M0
	T4b	N3a-b	M0
Stage IV	Any T	Any N	M1

(1) Proximal tumors comprise nearly half of all cancers and require total gastrectomy or proximal subtotal gastrectomy. Total gastrectomy with Roux-en-Y esophagojejunostomy is preferred to avoid reflux esophagitis and impaired gastric emptying. Tumors of the GE junction may require esophagogastrectomy.

(2) Midbody tumors comprise 15% to 30% and generally require total gastrectomy.

(3) Distal tumors are approached by subtotal gastrectomy, which has a similar outcome but decreased complications versus total gastrectomy (*Ann Surg*. 1999;230:170).

(4) **Early gastric cancers** confined to the mucosa (T1a), that are ≤2 cm and have clear margins, no lymphovascular invasion, and are well to moderately differentiated on pathology have limited propensity for lymph node metastasis and may be treated by **endoscopic mucosal resection** (**EMR**) (*Curr Opin Gastro*. 2016;32(6):492).

(5) **Laparoscopic gastric resections** have advantages of reduced pain, shorter hospitalization, and improved quality of life (*J Clin Oncol*. 2014;32:627).

b. Lymphadenectomy entails removal of ≥15 nodes, with a D2 lymphadenectomy being preferred in the Western hemisphere, and conferring improved survival over D1 dissection (*Arch. Surg*. 2008;143(7):671; *Lancet Onc*. 2010;11:439). A D2 lymphadenectomy includes a D1 dissection (perigastric nodes) + celiac, left gastric, common hepatic, and splenic artery lymph nodes.

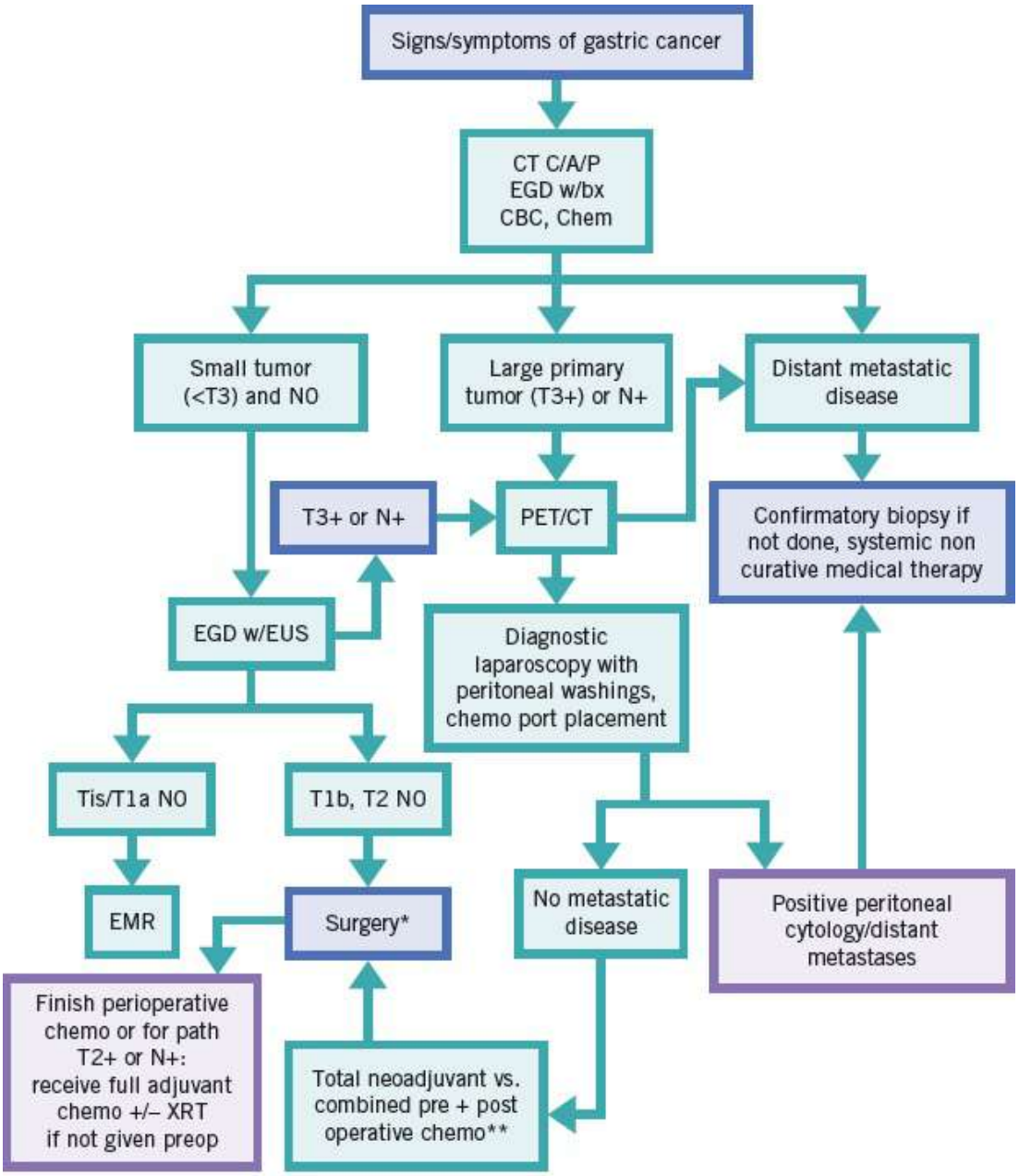


FIGURE 18-1 Gastric cancer diagnosis and treatment algorithm.

c. Systemic therapy is important because the majority of patients with locoregional disease are at high risk for local or systemic recurrence following curative surgery.

(1) Perioperative systemic chemotherapy improves overall and disease-free survival rates in patients with resected gastric cancer treated with epirubicin/cisplatin/5-fluorouracil (ECF)

chemotherapy. In the MAGIC Trial, perioperative ECF therapy, consisting of three cycles of **neoadjuvant** and three cycles of **adjuvant** chemotherapy, led to 36% versus 23% 5-year survival in resected gastric cancer (*N Engl J Med*. 2006;355(1):11). Potential benefits of delivering chemotherapy in the **neoadjuvant** setting include increased tumor downstaging and R0 resection rate, as well as the ability to guide therapeutic response and prognosis (*J Gastro Oncol*. 2015;6(5):534). Alternatively, **adjuvant chemoradiotherapy** can be given alone with good results (*J Clin Oncol*. 2012;30:2327).

(2) Patients with **advanced/metastatic disease** can now benefit from multiple new avenues of therapy. Patients with tumors overexpressing HER2 (20%), trastuzumab can be given with chemotherapy, and improve survival for advanced disease by nearly 3 months (*Lancet*. 2010;376(9742):687). In a recent Phase II trial of anti-PD-1 therapy for metastatic gastric cancer, in a small number of patients with EBV+ and MSI-H tumors, 100% and 86% of EBV+ and MSI-H patients, respectively, responded to therapy, two of which achieved complete response (*Nature Med*. July 2018;24(7):968–977).

d. Palliative procedural therapy is important due to overall low historic cure rates from systemic therapy. Patients with peritoneal disease, hepatic or nodal metastases, or other poor prognostic factors benefit most from endoscopic palliation.

IV. Primary Gastric Lymphoma. Primary gastric lymphoma (PGL) accounts for fewer than 5% of gastric neoplasms but two-thirds of all primary GI lymphomas. PGLs are **diffuse large B cell lymphomas** (55%) or gastric mucosa-associated lymphoid tissue (**MALT**) **lymphomas** (40%).

A. Presentation: typically in the sixth decade with epigastric pain, weight loss, anorexia, nausea, and vomiting.

B. Diagnosis: EGD, EUS, CT of chest/abdomen/pelvis, bone marrow biopsy, and biopsy of enlarged peripheral lymph nodes.

C. Treatment: Low-grade PGLs, so-called **MALT lymphomas**, are associated with *H. pylori* infection and first-line therapy is *H. pylori*

eradication. For early-stage disease no other therapy is needed beyond *H. pylori*, while chemotherapy is added for more advanced disease. Treatment for diffuse large B cell lymphoma is chemotherapy (*Lancet*. 2010;376;287). Surgical resection is reserved for failures or complications of medical therapy (*Ann Surg*. 2004;240(1):28).

V. GASTROINTESTINAL STROMAL TUMORS. Gastrointestinal stromal tumors (**GISTs**) are the most common sarcomatous tumor of the gi tract, with the most common gi tract location being the stomach (60%), although they only account for ~3% of gastric malignancies. They arise from intestinal pacemaker cells—so-called interstitial cells of cajal. Most patients are >50 years old, with a slight male predominance. Gists frequently display prominent extraluminal growth and can attain large sizes before becoming symptomatic.

A. Presentation: asymptomatic masses found incidentally, vague abdominal pain secondary to mass effect, and hemorrhage.

B. Diagnosis: EGD/EUS demonstrates a round, smooth submucosal tumor. GISTs are staged according to tumor size and histologic frequency of mitoses (low grade ≤5 mitoses/5 mm^2 versus high grade >5 mitoses/5 mm^2). Staging is accomplished by CT A/P, with chest imaging reserved for larger (>2 cm)/high-grade lesions.

C. Treatment: Open or laparoscopic surgical resection with 2 cm margins of grossly normal gastric wall. For tumors <2 cm with no high-risk EUS features, regular surveillance can be considered. En bloc resection of structures involved by local invasion should be attempted, but lymphadenectomy is not indicated. Local recurrence, as well as metastases via hematogenous spread are common. Most GISTs express the **c-kit** receptor, a tyrosine kinase that acts as a growth factor receptor. **Imatinib** (**Gleevec**) is a small-molecule inhibitor of the c-kit receptor that is first-line therapy for metastatic or recurrent GIST and can also be used to downsize bulky disease prior to resection. Imatinib should be given in the adjuvant setting for intermediate or high-risk disease: >5 cm tumor and/or >10 mitoses (*Lancet*. 2009;373:1097; *JAMA*. 2012;307(12):1265). Prior to imatinib therapy, tumors should be sent for *KIT* (CD117) and *PDGFRA* gene testing, whereby *KIT* exon 11 mutation predicts a 90% response rate to imatinib, *KIT* exon 9 mutation predicts a 50% response rate, PDGFRA mutation leads to variable

response depending on exact mutation, and wild type *KIT* and *PDGFRA* genes predicts <50% response rate (National Comprehensive Cancer Network. Neuroendocrine tumors of the gastrointestinal tract, Version 1.2019, March 5, 2019).

VI. GASTRIC CARCINOIDS. Gastric carcinoids are rare neuroendocrine tumors (NETs) comprising <2% of all gastric neoplasms. Carcinoid tumors arise from ecl cells, and can be subdivided into three types: **type 1**—most common type and associated with elevated gastrin and pernicious anemia or chronic atrophic gastritis (95% 5-year survival), **type 2**—elevated gastrin in association with zes and men i (70% to 90% 5-year survival), and **type 3**—occur independent of gastrin and metastasize in 50% of cases (<35% 5-year survival) (*am. j. gastroent*. 1995;90:338).

A. Diagnosis: EGD with biopsy, along with serum gastrin, constitutes standard workup.

B. Treatment: Small lesions can be resected endoscopically or via wedge resection, while larger/ multiple lesions may require subtotal or total gastrectomy. In some cases of type 1 and 2 carcinoids, surveillance can be employed. For type 3 carcinoids EUS should be added, with D1 or D2 lymphadenectomy included if suspicious nodes are present.

VII. POSTGASTRECTOMY SYNDROMES. Postgastrectomy syndromes are caused by changes in gastric emptying and may occur in up to 20% of patients who undergo gastric surgery, depending on the extent of resection, disruption of the vagus nerves, status of the pylorus, type of reconstruction, and presence of mechanical or functional obstruction. Most are treated nonoperatively and resolve with time.

A. Nutritional disturbances occur in 30% of patients, either as a result of functional changes or postgastrectomy syndromes. Prolonged **iron, folate, vitamin B12, calcium, and vitamin D deficiencies** can result in anemia, neuropathy, dementia, and osteomalacia, but can be prevented with supplementation.

B. Dumping syndrome results from rapid emptying of a high-osmolar carbohydrate load into the small intestine and is most common after Billroth II reconstruction due to loss of reservoir capacity and pylorus function.

1. Early dumping occurs within 30 minutes of eating and is

characterized by nausea, epigastric distress, explosive diarrhea, and vasomotor symptoms. It is caused by a rapid shift of extracellular fluid into the bowel lumen in response to a hyperosmolar load entering the small intestine from the stomach.

2. **Late dumping** is primarily vasomotor and occurs 2 to 3 hours after eating. The hormonal response to high simple carbohydrate loads results in hyperinsulinemia and reactive hypoglycemia, which leads to adrenal axis activation with catecholamine release. Symptoms are relieved by carbohydrate ingestion.
3. **Treatment** is primarily nonsurgical and results in improvement in nearly all patients over time. Meals are decreased in volume but increased in frequency, liquids should be ingested 30 minutes after eating solids, and simple carbohydrates should be avoided. If reoperation is necessary, conversion to Roux-en-Y gastrojejunostomy is preferred.

C. Alkaline reflux gastritis is most commonly associated with Billroth II gastrojejunostomy and is characterized by epigastric pain, nausea, and bilious emesis. Pain is not relieved by vomiting or associated with meals. EGD reveals inflamed, friable gastric mucosa and may demonstrate bile reflux into the stomach, which can be confirmed by hydroxy iminodiacetic acid (HIDA) scan. **Nonoperative therapy** consists of frequent meals, antacids, and cholestyramine, but is usually ineffective. **Surgery** to divert bile flow from the gastric mucosa is the only proven treatment. The creation of a long-limb (45 cm) Roux-en-Y gastrojejunostomy is preferred (*Gastroenterol Clin North Am.* 1994;23:281).

D. Roux stasis syndrome may occur in up to 30% of patients after Roux-en-Y gastroenterostomy. It results from functional obstruction due to disruption of the normal propagation of pacesetter potentials in the Roux limb from the proximal duodenum as well as altered motility in the gastric remnant. It is characterized by chronic abdominal pain, nausea, and vomiting that is aggravated with eating. Promotility agents can be trialed. Paring down of the gastric remnant or near-total gastrectomy to remove the atonic stomach can improve gastric emptying and is useful in patients with refractory Roux stasis.

E. Loop syndromes result from mechanical obstruction of either the **afferent** or **efferent** limbs of the Billroth II gastrojejunostomy.

Evaluation includes plain abdominal x-rays, CT scan, upper GI contrast studies, and EGD. Relief of the obstruction may require adhesiolysis, revision of the anastomosis, bowel resection, or conversion of Billroth II to Billroth I or Roux-en-Y gastrojejunostomy.

1. **Afferent loop syndrome** can be acute or chronic. In the **acute form** the afferent bowl limb is obstructed in the 1 to 2 weeks postoperatively, resulting in abdominal pain and cramping. Examination may reveal a fluid-filled abdominal mass, and laboratory findings may include elevated bilirubin or amylase. Duodenal **stump blowout** may result from progressive afferent limb dilation, leading to peritonitis, abscess, or fistula formation. In the urgent setting, jejunojejunostomy can effectively decompress the afferent limb. A **chronic form** of afferent loop syndrome results from partial mechanical obstruction of the afferent limb. Patients present with postprandial right upper quadrant pain relieved by forceful bilious emesis that is not mixed with recently ingested food. Longstanding stasis of the afferent limb can lead to bacterial overgrowth and subsequent bile salt deconjugation in the obstructed loop, causing **blind loop syndrome** (steatorrhea and vitamin B_{12}, folate, and iron deficiency) by interfering with fat and vitamin B_{12} absorption (*Surg Clin. North Am*. 2017;97(2):277).
2. **Efferent loop syndrome** results from intermittent obstruction of the efferent limb of the gastrojejunostomy. Patients complain of abdominal pain and bilious emesis months to years after surgery, similar to the situation seen with proximal small bowel obstruction. An upper GI contrast study with failure of contrast to enter the efferent loop is diagnostic.

F. Postvagotomy diarrhea occurs in 20% after truncal vagotomy and is thought to result from alterations in gastric emptying and vagal denervation of the small bowel and biliary tree. The diarrhea is typically watery, episodic, and not related to oral intake. Treatment includes antidiarrheal medications and decreasing excessive intake of fluids or foods that contain lactose. Symptoms usually improve with time, and surgery is rarely indicated.

G. Gastric atony may occur after vagotomy, as gastric emptying is slowed. Scintigraphy is commonly used to establish diagnosis. Patients

may present with early satiety, postprandial fullness, nausea, abdominal pain, and vomiting (*Am J Gastroent*. 2013;108(1):18). It is important to establish absence of any mechanical obstruction. In addition, other causes of delayed gastric emptying (gastroparesis) such as diabetes, electrolyte imbalance, and neuromuscular disorder must be excluded. Treatment depends on etiology (e.g., blood glucose control for diabetes), but often begins with dietary management and a promotility agent. Nonpharmacotherapy can include botulinum toxin injection, gastric pacemaker placement, or completion gastrectomy. A newer surgical option for refractory gastroparesis, with promising initial results, is peroral pyloromyotomy (POP, *Ann Surg*. 2018;268(3):421).

CHAPTER 18: STOMACH

Multiple Choice Questions

1. **A patient with gastric outlet obstruction and prolonged emesis has which electrolyte disturbance?**

   a. Hyperchloremic, hyperkalemic metabolic acidosis
   b. Hyperchloremic, hypokalemic metabolic acidosis
   c. Hypochloremic, hyperkalemic metabolic alkalosis
   d. Hypochloremic, hypokalemic metabolic alkalosis
   e. Hyponatremic, hypokalemic metabolic acidosis

2. **What is the typical first-line therapy for low-grade MALT lymphoma of the stomach?**

   a. Chemotherapy
   b. Radiation
   c. Total gastrectomy
   d. Wedge resection of lesion without reconstruction
   e. *H. pylori* eradication

3. **What is the preferred surgical therapy for hemodynamically unstable patients with bleeding duodenal ulcers?**

   a. Graham patch
   b. Duodenotomy and three-point ligation of the bleeding vessel
   c. Duodenotomy, three-point ligation of the bleeding vessels, highly selective vagotomy
   d. Duodenotomy, three-point ligation of the bleeding vessels, truncal vagotomy, pyloroplasty
   e. Duodenal resection with reconstruction

4. **What is true regarding gastrointestinal stromal tumors?**

   a. Local recurrence is uncommon after resection
   b. Lymphadenectomy should be attempted given high propensity of lymph node metastasis
   c. Imatinib is first-line therapy for metastatic or recurrent disease with

the most common KIT and PDGFRA mutations

d. En bloc resection of involved structures should not be attempted

e. Tumors are highly radiosensitive

5. What is true among the treatment principles for gastric cancer?

a. Distal tumors comprise the majority of gastric cancers

b. There is a low risk of recurrence of disease

c. Lymphadenectomy is not required in early-stage disease

d. A minimum of 15 lymph nodes should be resected during lymphadenectomy

e. Early gastric cancers always require total gastrectomy

19

The Surgical Management of Obesity

Katharine Caldwell and J. Christopher Eagon

INTRODUCTION

Obesity is a disease process that has reached epidemic proportions worldwide, with the highest prevalence in the United States, where nearly 40% of the adult population is obese and 5% is morbidly obese (CDC, 2018. www.cdc.gov/obesity/data/adult.html). Obesity is also becoming increasingly prevalent in the pediatric and adolescent population. Severe or morbid obesity in adults is **defined** as a body mass index [BMI = weight (kg)/height (m^2)] equal to or greater than 40, which generally correlates with an actual body weight 100 lb greater than ideal body weight. In children, severe obesity is defined as a BMI that is equal to or greater than 120% of the 95th percentile or equal to or greater than 35 kg/m^2 (whichever is lower).

The **etiology** of morbid obesity is poorly understood with o debate as to the role of genetic, psychosocial, and environmental influences.

Morbid obesity is associated with a number of weight-related comorbidities. Patients with **central** obesity (android or “apple” fat distribution) are at higher risk for development of obesity-related complications than those with **peripheral** obesity (gynecoid or “pear” fat distribution), due to increased visceral fat distribution, producing increased intra-abdominal pressure and increasing fat metabolism (with subsequent hyperglycemia, hyperinsulinemia, and peripheral insulin resistance). Table 19-1 lists some of the medical complications associated with morbid obesity (*Arch Intern Med*. 2000;160(7):898–904). In addition to the aforementioned comorbidities, obesity increases mortality (*N Engl J Med*. 2007;357(8):741–752).

TREATMENT

Treatment of morbid obesity is of paramount importance due to medical sequelae associated with obesity, nearly all of which are reversible on resolution of the obese state.

A. Medical Therapy

1. Medical therapy including physician-guided weight loss or pharmacotherapy has limited short-term and nearly no proven long-term success. In patients with morbid obesity, lifestyle modifications alone have been shown to create 5% to 10% weight loss at 6 months, but negligible weight loss at 1 year of maintenance and negligible effects on comorbidities (*Surg Obes Relat Disord*. 2010;6:347). However, in patients with BMI less than 27, lifestyle changes alone may be sufficient. Lifestyle modifications including changes in diet and exercises remain first-line treatment, however the NIH consensus congress has recognized that for the morbidly obese, medical treatment is nearly uniformly unsuccessful.

TABLE 19-1 Complications of Morbid Obesity

Cardiac	Pulmonary
Hypertension Sudden cardiac death (myocardial infarction) Coronary artery disease Deep venous thrombosis Heart failure Venous stasis	Obesity hypoventilation syndrome Asthma Obstructive sleep apnea
Metabolic	**Musculoskeletal**
Type II diabetes Hyperlipidemia Hypercholesterolemia Nonalcoholic steatohepatitis	Degenerative joint disease Lumbar disc disease Osteoarthritis Ventral hernias
Gastrointestinal	**Genitourinary/Gynecologic**

Cholelithiasis Gastroesophageal reflux disease	Stress incontinence Polycystic ovarian syndrome Menstrual irregularities
Infectious	**Neurologic**
Fungal infections Necrotizing soft tissue infections	Pseudotumor cerebri Stroke

2. **Pharmacotherapy** is second-tier therapy used in patients with BMI greater than 27 in combination with lifestyle changes. Currently, sibutramine, a presynaptic norepinephrine and serotonin reuptake inhibitor that functions as an appetite suppressant, and orlistat, a lipase inhibitor that reduces lipid absorption, are the only approved drugs for weight loss treatment. Weight loss with these agents is 6% to 10% at 1 year, but relapse rates after discontinuation of the drugs are high. Additionally, many patients have difficulty with compliance due to adverse effects.

B. Bariatric surgery is the most effective approach for achieving durable weight loss in the morbidly obese. Multiple studies have confirmed the superiority of surgery to nonsurgical approaches in achieving and maintaining weight reduction in the morbidly obese (*N Engl J Med*. 2004;351:2683).

1. **Indications:** Patients who have failed intensive efforts at weight control using medical means are candidates for bariatric surgery if they have a BMI index greater than 40 or greater than 35 with weight-related comorbidities. In addition, patients who have a BMI index greater than 30 with poorly controlled diabetes or metabolic syndrome may be offered bariatric surgery although long-term data demonstrating benefit is still lacking. Proposed **contraindications** include untreated or uncontrolled severe psychiatric illness, binge-eating disorders, active alcohol or drug abuse, prohibitive operative risks secondary to severe medical disease, as well as the inability to comprehend the nature of the surgical intervention or comply with required postoperative nutritional and lifestyle changes. Further, patients actively pregnant or intending to get pregnant within 12 to 18 months postoperatively should not undergo bariatric surgery (*Surg Obes Relat Dis*. 2005 1(3):371–381).

2. **Preoperative evaluation:** A bariatric multidisciplinary team including primary care physicians, dietitians, physical therapists, anesthesiologists, nurses, and psychiatrists or psychologists evaluates a patient's weight history, dietary habits, motivation, social history, and comorbid medical conditions prior to surgery.

C. Benefits of bariatric surgery include its demonstrated effectiveness in long-term weight reduction and reversal of the disease processes associated with severe obesity. Hypertension completely resolves in 62% of patients and resolves or improves in 79% (*Surg Obes Relat Dis*. 2009;5(3):387–405). Diabetes is completely resolved in 77% of patients and resolves or improves in 86% (*JAMA*. 2017;317(6):635–636). Obstructive sleep apnea resolves or improves in 85% of patients and hyperlipidemia improves in 70%. The quality of life is markedly better. Most importantly, recent studies demonstrate reduced mortality rates in morbidly obese patients undergoing bariatric surgery compared to matched controls and most strikingly an 80% reduction in annual mortality among diabetics who underwent bariatric surgery (*N Engl J Med*. 2007;357(8):741–752).

Bariatric surgical procedures can generally be divided into two types: **Restrictive procedures,** which limit the amount of food that can be ingested, and **malabsorptive procedures**, which limit the absorption of nutrients and calories from ingested food by bypassing predetermined lengths of small intestine. Though once performed via an open technique, bariatric procedures are now primarily performed by laparoscopic technique when possible by a skilled surgeon due to improved patient tolerance with laparoscopic techniques. Open bariatric procedures are still performed for inability to tolerate insufflation, failure of laparoscopic techniques, or difficult reoperations. The standard operations used to produce weight loss in the morbidly can be found in Table 19-2.

D. Adjustable gastric banding (AGB) involves laparoscopic placement of a silicone band with an inflatable balloon around the proximal stomach by division of the peritoneum at the angle of His and creation of a tunnel posterior to the stomach. The band is connected to a reservoir that is implanted over the rectus sheath. The patient undergoes serial adjustments to inflate the band and create a small proximal gastric pouch. Anticipated excess weight loss at the 1-year mark will approach

50% to 60% (*J Am Soc Bariatr Surg*. 2007;3(5):496–502).

E. Sleeve gastrectomy (SG) was originally developed as the first component of a duodenal switch (DS) operation and is now performed alone as a purely restrictive procedure for the treatment of morbid obesity. It does not produce malabsorption and is technically easier to perform than BPD or Roux-en-Y gastric bypass (RYGB). Preliminary reports have demonstrated 60% to 70% excess weight loss at 1 year (*Obes Surg*. 2007;17(8):1069–1074).

The SG procedure is performed by the surgeon first taking down the greater curve from within 4 to 6 cm of the pylorus up to the angle of His, exposing the right crus. Using a 30- to 40-Fr bougie, the stomach is then divided from the antrum to the angle of His preserving the left gastric vessels.

TABLE 19-2 Bariatric Surgical Procedures

Restrictive Procedures
Adjustable gastric banding (AGB) Laparoscopic sleeve gastrectomy (LSG)
Restrictive and Malabsorptive Procedures
Roux-en-Y gastric bypass (RYGB)
Primarily Malabsorptive Procedures
Biliopancreatic diversion (BPD) Duodenal switch (DS)

F. RYGBP is the most popular bariatric surgical procedure performed in the United States. The RYGB anatomy is visualized in Figure 19-1**.** To perform the procedure, a Roux limb is created by division of the jejunum at 30 to 40 cm beyond the ligament of Treitz with a stapler. The length of the Roux limb is determined by the patient's BMI; a 75 cm limb is used for patients with lower BMIs and a 150 cm limb for those with BMI >50. Weight loss varies with Roux limb length.

Additional staple fires are used to create a jejunojejunal anastomosis. The mesenteric defect is then closed in a running fashion. The Roux

limb is passed in a retrocolic or antecolic approach. The antecolic limb is then passed antegastric, while the retrocolic limb can then be passed ante- or retrogastric. The peritoneum between the spleen and GE junction is divided. The lesser sac is entered and a stapler is used to create an approximately 15 cc gastric pouch. A gastrojejunal anastomosis is created using a combination of stapled and sutured closure. The mesenteric defect is then closed to prevent Roux limb herniation through the transverse colon mesentery.

Gastric bypass results in weight loss superior to that achieved with restrictive procedures, with mean excess weight loss of 70% (*Surgery*. 2006;140(4): 524–529).

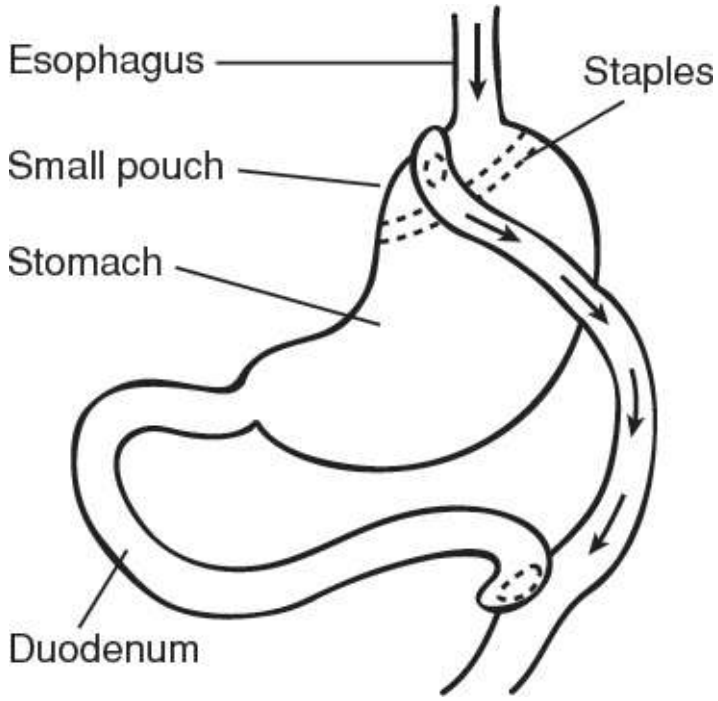


FIGURE 19-1 Roux-en-Y anatomy.

G. Biliopancreatic diversion (BPD) is an additional procedure less frequently performed for morbidly obese patients. This procedure is done at select centers for the superobese and those who have failed to maintain weight loss following gastric bypass or restrictive procedures. The BPD anatomy is visualized in Figure 19-2**.** First, the surgeon measures the terminal ileum to 50 cm and marks this area with a stitch as the common channel. An additional 200 cm of ileum is measured and divided. The proximal end of this is then anastomosed to the TI at the

level of marking and the mesenteric defects are closed. A distal gastrectomy is performed and the duodenum is stapled and divided distal to the pylorus. Finally, the proximal end of the 200 cm limb of ileum is anastomosed to the proximal stomach. Long-term outcomes indicate excess weight loss of 75% at 1 year but nutritional deficiencies are more common than for RYGB (*Obes Surg*. 2006;16(9):1138–1144).

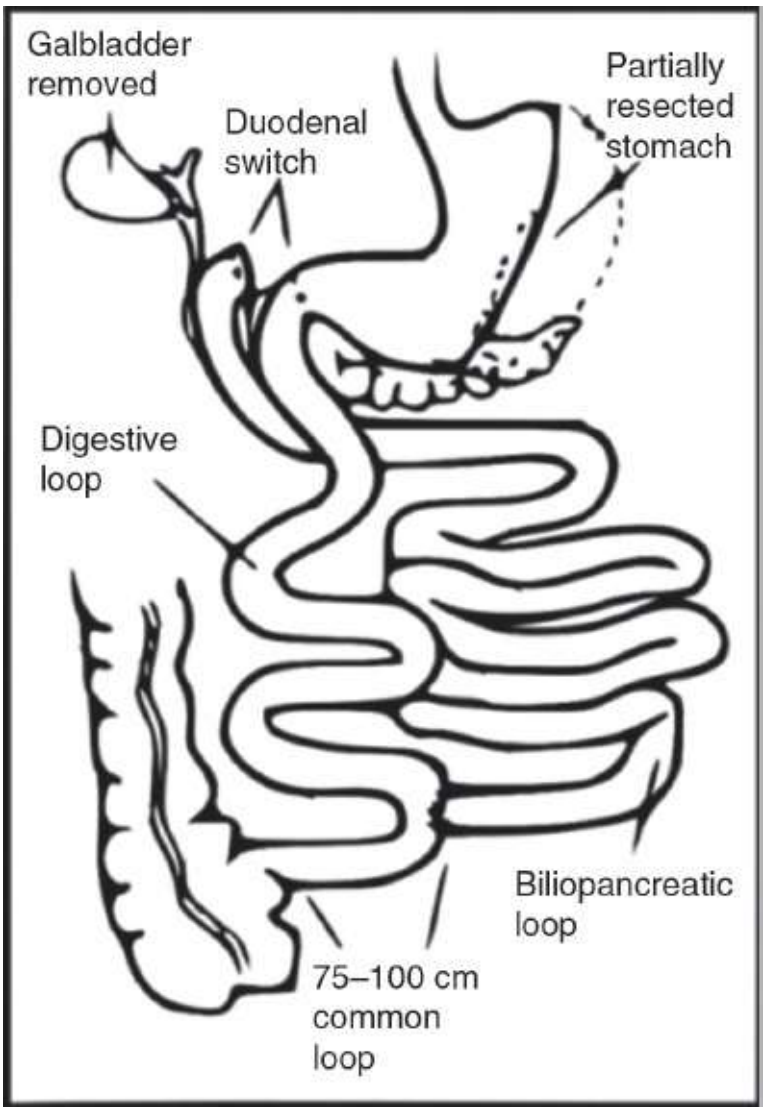


FIGURE 19-2 Biliopancreatic diversion anatomy.

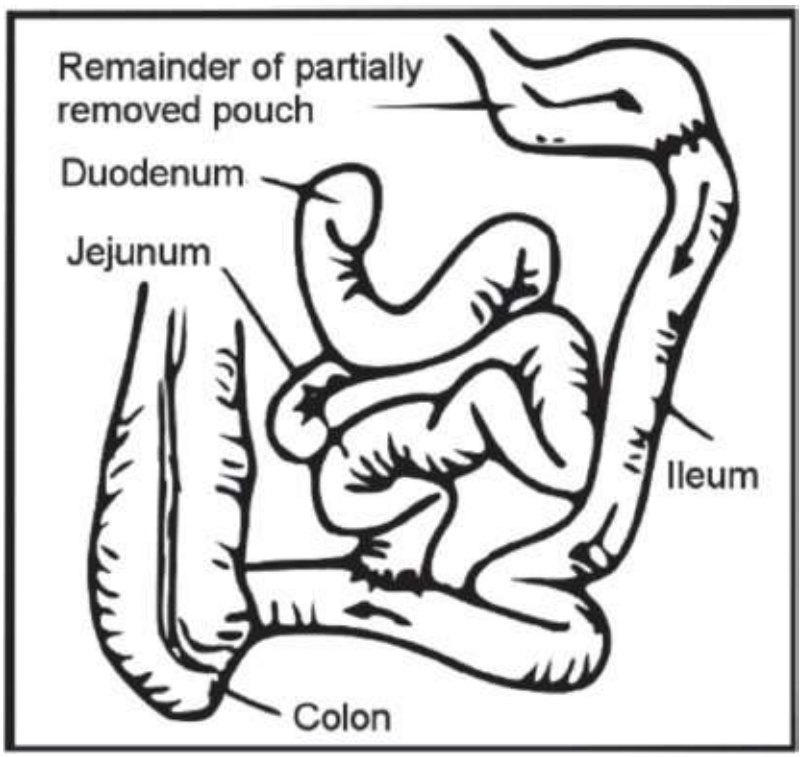


FIGURE 19-3 Duodenal switch anatomy.

H. DS is an additional procedure performed at select centers for the superobese. The first step of a DS procedure is performance of a SG, as described above. In some cases this is performed as the first stage of a two-stage operation. The duodenum is then divided 2 cm beyond the pylorus. A 100 cm common channel is measured from the terminal ileum. An additional 150 cm of terminal ileum are measured and a duodenoileostomy is created. The biliopancreatic limb is then reanastomosed at the common channel. DS anatomy is visualized in Figure 19-3**.** Long-term outcomes indicate excess weight loss of 75% at 1 year, but as with BPD, nutritional deficiency risk exceeds that of RYGB (*Semin Laparosc Surg*. 2002;9(2):125–129).

POSTOPERATIVE MANAGEMENT

Typical **postoperative management** includes postoperative analgesia, frequent measurements of intake and output, monitoring for tachycardia which can be the only evidence of postoperative leak in this population, as well as gradual advancement of diet from NPO to a high-protein liquid diet. Aggressive pulmonary management with early institution of continuous positive airway

pressure (when indicated) is necessary to prevent hypoxemia. Early ambulation is highly encouraged and mechanical and pharmacologic venous thromboembolism prophylaxis is recommended for all patients due to high risk of deep venous thrombosis. Careful monitoring of postoperative blood pressure and blood glucose measurements are performed, as many patients will require down-titration of their antihypertensive and diabetic agents. Nonsteroidal anti-inflammatory drugs should be avoided following many types of bariatric surgery due to its association with marginal ulcers and perforations.

Close follow-up for adequate weight loss, improvement or resolution of comorbidities, in addition to close metabolic and nutritional monitoring is crucial. All patients should be encouraged to engage in physical activity for at least 30 minutes daily, take smaller more frequent meals chewed thoroughly, and avoid high-fat or high-sugar liquids which could precipitate dumping syndrome and impede weight loss. Of note, inadequate weight loss following bariatric surgery should warrant further evaluation to determine the etiology (including surgical failure potentially requiring revision or poor compliance with nutritional or lifestyle requirements). Lifelong nutritional supplementation with multivitamins, iron, calcium, vitamin D, and vitamin B_{12} is indicated (*Endocr Pract*. 2013;19(2):337–372).

COMPLICATIONS

Bariatric surgery has become increasingly safe in the last decades with improved understanding of the physiology of the obese patient and improved surgical procedures. However, surgeons must be mindful of postoperative complications as signs are often subtle and nonspecific. Any severe or persistent gastrointestinal complaints warrant further examination, typically employing radiographic imaging studies and possible surgical intervention (Fig. 19-4).

Dumping syndrome results from patients' inability to regulate gastric emptying of simple carbohydrates or other osmotic loads. Patients usually complain of sweating, dizziness, palpitations, abdominal pain, nausea, vomiting, and/or diarrhea. Treatment may involve dietary measures including high-protein diets, acarbose and somatostatin analogues, or surgical reintervention for refractory cases (*Best Pract Res Clin Gastroenterol*. 2014;28(4):741–749).

Anastomotic leaks are a serious complication associated with high morbidity and mortality rates. Clinical findings include tachycardia, leukocytosis, and fever. Typical findings of peritonitis and sepsis may be absent until late in the

patient's clinical course. Management of leaks is time dependent and can include surgical closure of the defect, drainage, or placement of an intraluminal stent.

Small bowel obstructions typically present with abdominal pain, nausea and vomiting, and minimal bowel function. Etiologies include edema and/or hematoma in the early postoperative period and adhesions, abdominal wall hernias, intussusceptions, and internal hernias in the late postoperative period. Possible locations for internal hernias following a RYGB include the opening of the transverse mesocolon, the small bowel mesenteric defect at the jejunojejunostomy site, and the space between the transverse mesocolon and Roux limb mesentery (known as a Peterson hernia) (*J Hosp Med*. 2012;7(2):156–163). Treatment of obstruction in an unstable patient is prompt surgical exploration.

Gallstone formation is a common late complication following bariatric surgery. Therefore, regular use of ursodeoxycholic acid during the rapid weight loss period is recommended (*Obes Surg*. 2016; 26:990–994).

Nutritional deficiencies are a risk after any procedure with a malabsorptive component and the risk increases with the amount of small intestine bypassed. The most common postop deficiencies seen are iron and B_{12} deficiency. However, folate deficiency and calcium deficiencies are also seen. BPD and DS procedures carry the additional risk of fat-soluble vitamin deficiencies and protein deficiency. All patients require careful postoperative monitoring and lifelong supplementation.

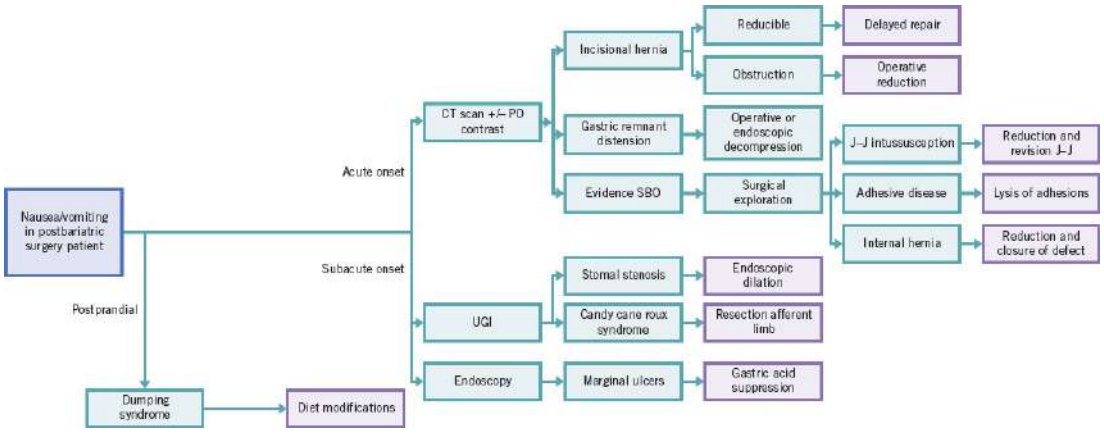


FIGURE 19-4 Workup of nausea/vomiting in postbariatric surgery patient.

Specific considerations should also be taken into account based on the type of operation performed:

A. AGB

1. Benefits: No risk of leak, low risk of metabolic disturbance due to no changes in GI tract anatomy.
2. Risks: Band slippage, band erosion, leakage or kinking of tubing, increased reflux

B. Laparoscopic Sleeve Gastrectomy

1. Benefits: technical simplicity, pylorus preservation leads to no risk of dumping syndrome, low risk metabolic disturbances.
2. Risks: leak from gastric staple line, reflux, gastric outlet obstruction due to stenosis, increased reflux.

C. Roux-en-Y Gastric Bypass

1. Benefits: increased weight loss versus restrictive procedures, improved gastric reflux.
2. Risks: G-J stenosis, malabsorption leading to nutritional deficiencies (primarily iron and B_{12} deficiencies), marginal ulcer risk, internal limb obstruction, anastomotic leak.

D. Biliopancreatic Diversion

1. Benefits: Improved percentage of excess weight loss and improved maintenance over RYGB, excellent resolution of obesity-related comorbidities.
2. Risks: Difficult procedure, marginal ulcer risk, anastomotic leak, malabsorption leading to high risk for vitamin and protein deficiencies.

E. Duodenal Switch

1. Benefits: Improved percentage of excess weight loss and improved maintenance over RYGB, excellent resolution of obesity-related comorbidities, pylorus preserved leading to low risk of ulcers.
2. Risks: Difficult procedure, anastomotic leak, malabsorption leading to high risk for vitamin and protein deficiencies.

CHAPTER 19: THE SURGICAL MANAGEMENT OF OBESITY

Multiple Choice Questions

1. **A 50-year-old woman with a history of poorly controlled diabetes presents for evaluation for bariatric surgery. Her BMI is 33 kg/m^2 and has fluctuated from 31 to 34.3 with physician-supervised diet and exercise over the past year. She has unsuccessfully tried multiple weight loss programs in the previous 7 years and now seeks surgical management. What treatment plan is appropriate for this patient?**

   a. Continue physician-supervised diet and exercise program as she has seen some benefit and follow-up in 1 year
   b. Recommend bariatric surgery after appropriate multidisciplinary preoperative evaluation as patient meets the indication for surgery
   c. Bariatric surgery is not recommended at this time as patient's BMI index is not considered "severely obese" and no follow-up needed
   d. Recommend multidisciplinary evaluation now with bariatric surgery offered when patient's BMI goes above 35 kg/m^2
   e. None of the above

2. **A 29-year-old woman reports severe abdominal pain along with persistent nausea and vomiting 4 days after Roux-en-Y gastric bypass. On evaluation, she is tachycardic with a blood pressure of 100/65. Examination reveals severe upper abdominal tenderness to palpation and CT scan reveals distended small bowel loops. What is the most appropriate next step in management?**

   a. Intravenous fluid resuscitation and prompt surgical exploration
   b. Intravenous fluid resuscitation and serial abdominal examinations
   c. Change analgesic and antiemetic medications in an effort to improve symptoms
   d. Obtain upper gastrointestinal study with Gastrografin in an effort to further localize the area of obstruction
   e. None of the above

3. **A 37-year-old woman presents 10 weeks after her laparoscopic adjustable gastric banding with severe heartburn, nausea, and persistent vomiting for the past week. She reports compliance with the postoperative diet and exercise regimen recommended and notes that her band was tightened at her last office visit 2 weeks prior to her presentation. On examination, she is tachycardic and has mild epigastric tenderness to palpation. What is the most appropriate next step?**

   a. Obtain a CT abdomen with oral and IV contrast
   b. Make patient NPO and place nasogastric tube
   c. Start esomeprazole today and reassess in 2 weeks
   d. Advise patient to eat smaller portions at each meal
   e. Immediate removal of all the fluid from the adjustable band

4. **A 52-year-old woman presents 3 months after her sleeve gastrectomy, with a 5-cm painless and easily reducible periumbilical bulge that is exacerbated by Valsalva maneuvers. She notes that it does not bother her although it has been increasing in size and is cosmetically unappealing. She remains compliant with her postsurgical diet and exercise and reports adequate weight loss. What is the best management plan at this time?**

   a. Recommend surgical repair now given the risk of incarceration or strangulation of hernia
   b. Decrease frequency of exercise to avoid worsening the problem and defer surgical management at this time until weight loss has stabilized and nutritional status is optimized
   c. Recommend surgical repair immediately after admission to optimize patient's nutritional status
   d. Defer surgical management at this time until weight loss has stabilized and nutritional status is optimized
   e. None of the above

5. **A 45-year-old woman presents with a 3-week history of epigastric pain and occasional nausea 1 year after undergoing her Roux-en-Y gastric bypass. During workup, upper endoscopy**

reveals a 1.5-cm ulceration near the gastrojejunostomy. Which of the following is(are) associated with this condition?

a. Nonsteroidal anti-inflammatory drugs
b. *Helicobacter pylori* infection
c. Smoking
d. Poor tissue perfusion due to ischemia at the anastomosis
e. All of the above

20

Small Intestine

Darren R. Cullinan and Paul E. Wise

I. SMALL-BOWEL OBSTRUCTION.

Mechanical obstruction of the small intestine (SI) can be complete, with total occlusion of the lumen, or partial, allowing some distal passage of gas or fluid. In a strangulated obstruction, the involved SI has vascular compromise leading to infarction and eventual perforation of the intestinal wall. No clinical or laboratory values are pathognomonic for strangulated obstruction, although characteristic findings include constant, as opposed to only crampy, abdominal pain, fever, leukocytosis, and acidosis. **Ileus** implies failure of peristalsis and thus a functional "obstruction" without mechanical obstruction. Recent abdominal operations, electrolyte disturbances, trauma, peritonitis, systemic infections, bowel ischemia, and medications can cause ileus.

A. Etiology

1. **Adhesions** from previous abdominal operations (or rarely isolated congenital adhesions/bands) are the *most common* cause in US adults, accounting for 60% to 70% of small-bowel obstructions (SBOs).
2. **Incarcerated hernias** are the second most common cause of SBOs in industrialized nations and the most common cause of SBO worldwide. In children and patients without prior abdominal operations, hernias are the most common cause of SBO.
3. **Intussusception** occurs when one portion of bowel (the intussusceptum) telescopes into another (the intussuscipiens). Tumors, polyps, enlarged mesenteric lymph nodes, or a Meckel diverticulum may serve as lead points of the intussusceptum, especially in adults, who require further workup when it occurs. Intussusception in children is often of unclear etiology and can usually be treated nonoperatively.

4. **Volvulus**, or the rotation of a segment of bowel around its vascular pedicle, is often caused by adhesions or congenital anomalies such as intestinal malrotation.
5. **Strictures** secondary to ischemia, inflammation (Crohn disease, CD), radiation, or prior surgery may cause SBO.
6. **Gallstone ileus** occurs as a complication of cholecystitis. Fistulization between the biliary tree and the small bowel (cholecystoduodenal or choledochoduodenal fistula) allows one or more gallstones to travel distally and obstruct the lumen, typically at the ileocecal valve.
7. **External** or **intrinsic compression** from tumors, abscesses, hematomas, or other masses can cause SBO.
8. **Foreign bodies** typically pass without incident. Items presenting with obstruction may require operation if they cannot be retrieved endoscopically.

B. Diagnosis

1. **Signs and symptoms.** Proximal SBOs present with early bilious **emesis.** Distal obstructions present later with thicker, more feculent emesis. Early in the disease course, **nausea** may be observed in the absence of vomiting. **Abdominal distention** typically increases the more distal the obstruction. **Abdominal pain** is poorly localized and often colicky in nature. **Obstipation** is observed once the distal bowel (past a complete obstruction) is evacuated. With a persistent obstruction, **hypovolemia** progresses due to impaired intestinal absorption, increased secretion, and fluid losses from emesis.
2. **Physical examination.** Abnormal **vital signs** are generally indicative of hypovolemia (e.g., tachycardia and hypotension). **Abdominal examination** may reveal distension, prior surgical scars, masses, or hernias. Peritonitis mandates prompt surgical treatment due to the concern for bowel strangulation and/or perforation.
3. **Laboratory evaluation.** In the early stages of SBO, laboratory values may be normal. As the process progresses, laboratory values commonly reflect dehydration demonstrating hypochloremic, hypokalemic contraction alkalosis. Elevated white blood cell (WBC) count and/or serum lactate levels are concerning for possible strangulation.

4. **Radiologic evaluation. Abdominal plain films** may demonstrate dilated loops of SI, air–fluid levels, and paucity of colorectal gas. These findings may be absent in early, proximal, and/or closed-loop obstructions. Pneumatosis intestinalis or portal venous gas suggests strangulated obstruction and necrosis. Free intra-abdominal air indicates hollow viscus perforation. Air in the biliary tree and a radiopaque gallstone in the right lower quadrant are pathognomonic of gallstone ileus. Paralytic ileus appears as gaseous distention uniformly distributed throughout the stomach, SI, and colon. **Computed tomography (CT)** can localize and characterize the obstruction and provides information regarding etiology of SBO and presence of other intra-abdominal pathologies.
5. **Differential diagnosis. Mesenteric vascular ischemia** can produce colicky abdominal pain, especially after meals. Acute occlusion often presents with marked leukocytosis and severe abdominal pain out of proportion to physical findings. **Colonic obstruction** can easily be confused with a distal SBO. A CT or water-soluble contrast enema can aid in diagnosis. Radiography of primary **hypomotility** disorders reveals gas throughout the entire GI tract with particular distention of the small bowel.

C. Treatment of SBO is evolving and includes prevention at initial laparotomy.

1. **Prevention.** The highest risk of adhesive SBO occurs after ileal pouch-anal anastomosis, open colectomy, and open gynecologic operations. Excluding acute appendicitis, laparoscopic as opposed to open techniques result in fewer adhesions. A systematic review and meta-analysis of 28 clinical trials of adhesion barriers showed that using oxidized regenerated cellulose led to a decreased incidence of adhesions and hyaluronate carboxymethylcellulose reduced the need for reoperation due to adhesive SBO without increasing the risk of postoperative complications (*Lancet*. 2014;383:48–59).
2. **Strangulated** obstruction or peritonitis requires prompt operative intervention. Mortality associated with gangrenous bowel approaches 30% if operation is delayed beyond 36 hours but is improved when surgical intervention is prompt. Fluid/electrolyte resuscitation and nasogastric (NG) tube decompression are crucial in the preoperative preparation of the patient.

3. **Nonstrangulated** obstructions can be treated nonoperatively if the patient is clinically stable. Fluid resuscitation and NG decompression are the primary therapy for any SBO. A trial of nonoperative management requires close observation with serial abdominal examinations every 4 to 6 hours, preferably by the same person. If the patient develops signs of shock or peritonitis, or fails to improve within a few days, laparotomy is indicated. Early evaluation of patients with a water-soluble oral contrast agent may be useful in differentiating patients who will spontaneously resolve their obstruction from patients who require operative intervention resulting in a shorter length of stay (*J Trauma Acute Care Surg*. 2017;(83):47–54). A sample treatment algorithm is given in Figure 20-1.

   In patients with SBO secondary to incarcerated hernia, attempts to reduce the hernia with mild sedation and manual pressure is warranted if the symptoms were present less than 24 to 48 hours. If successful, the patient requires close monitoring for evidence of bowel infarction or perforation. Severe initial tenderness, erythema or ecchymosis at the hernia site, or symptoms >48 hours increase suspicion for strangulation. That, or inability to reduce the hernia, requires urgent operation. A trial of nonoperative therapy is also indicated for SBO in the early postoperative state and for patients with multiple prior SBOs, "frozen"/hostile abdomen, abdominal irradiation, CD, or carcinomatosis.

4. **Operative intervention** is generally performed via midline incision, though a standard groin incision can be used for incarcerated inguinal or femoral hernias. The goal is to identify and treat the origin of obstruction. Extensive adhesiolysis and bowel resection may be necessary. If adjacent bowel viability is questionable, a second-look operation within 24 to 48 hours may be required. Enteroenteric or enterocolic anastomosis can bypass an unresectable obstructing lesion. Placement of a gastrostomy tube for palliative decompression should be considered in select cases, such as carcinomatosis or unresectable obstructing cancer that cannot be bypassed.

II. MECKEL DIVERTICULUM. Meckel diverticulum is the most common congenital anomaly of the GI tract and occurs from failure of the vitelline or omphalomesenteric duct to obliterate by the sixth week of fetal

development. It is a true diverticulum containing all layers of the bowel wall and located on the antimesenteric border of the ileum, usually 2 feet from the ileocecal valve. This is part of the "*rule of twos*" for these diverticula, including a 2% incidence, a 2:1 male:female ratio, 2 in in length, typically presenting before 2 years of age, and often containing two types of mucosa: intestinal and heterotopic (commonly gastric or pancreatic).

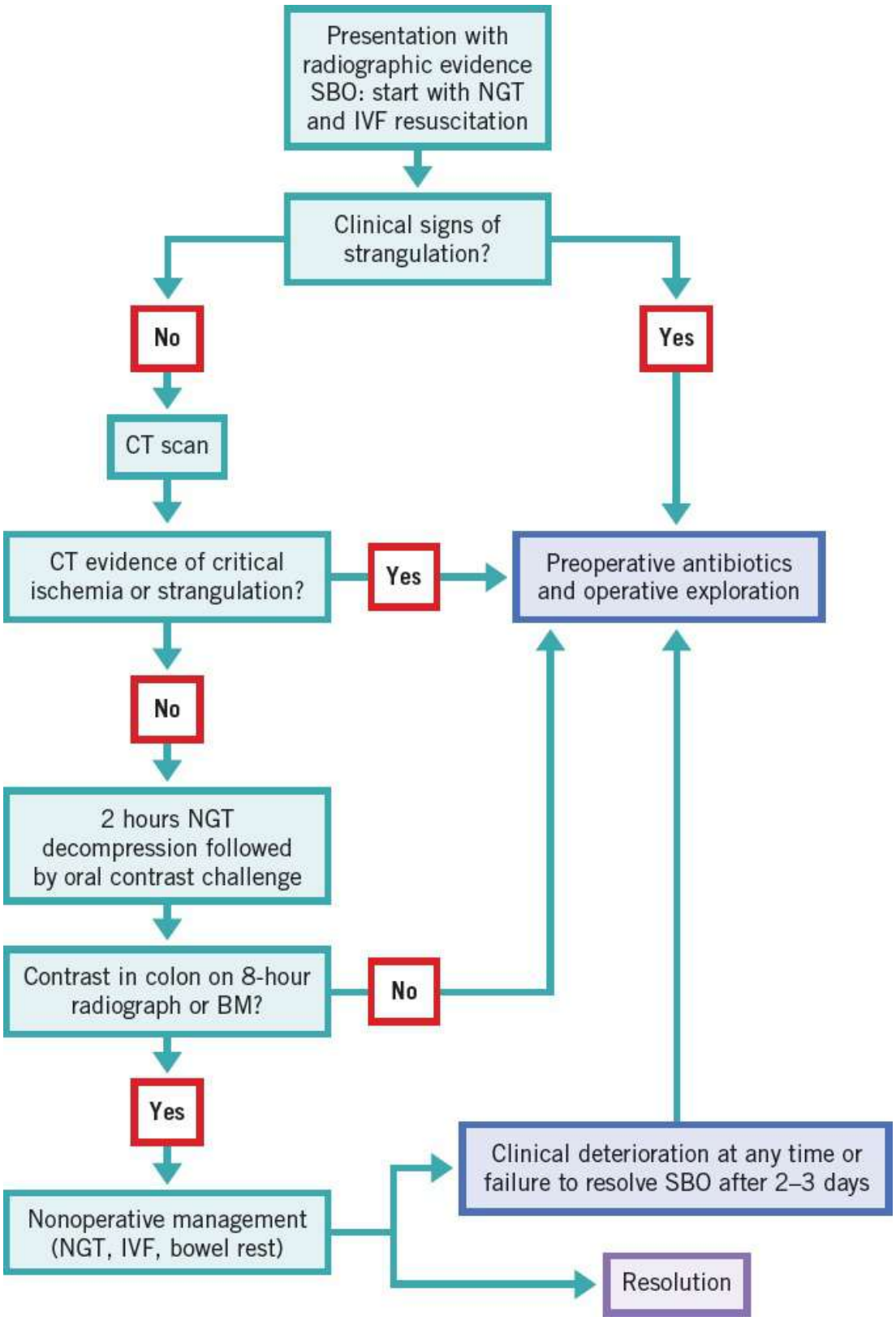


FIGURE 20-1 Algorithm for management of small-bowel obstruction. SBO, small-bowel obstruction; NGT, nasogastric tube; IVF, intravenous fluid; oral contrast challenge, water-

soluble oral contrast administration; BM, bowel movement.

A. Presentation. The vast majority are *asymptomatic.* Painless, episodic **bleeding** is the most common presenting symptom. The source is typically a peptic ulcer of adjacent normal ileum on the mesenteric border of the bowel caused by acid secretion from gastric mucosa within the diverticulum. Intussusception or incarcerated hernia (Littré hernia) causing **intestinal obstruction** is the second most common presentation. Obstruction can also occur due to volvulus of small bowel around a fibrous band connecting the diverticulum to the anterior abdominal wall. **Meckel diverticulitis** occurs in 20% of symptomatic patients and is often mistaken for acute appendicitis.

B. Diagnosis. In adults, clinical diagnosis of a Meckel diverticulum is extremely difficult except in the presence of bleeding. A **Meckel scan** is a radionucleotide study based on te uptake of Tc-99m pertechnetate by ectopic gastric mucosa. In children, this test is the most accurate (90%) for diagnosing a Meckel diverticulum but is less accurate (46%) in adults because of reduced prevalence of ectopic gastric mucosa within the diverticulum. In the presence of bleeding, a **tagged red blood cell scan** can also be useful. **Contrast studies**, such as small bowel follow through (SBFT) and enteroclysis, are diagnostic in up to 75% patients. **CT** and **sonography** are typically of little value because distinguishing between a diverticulum and intestinal loops can be very difficult unless Meckel diverticulitis is present.

C. Treatment. Resection is indicated in symptomatic patients. For patients who present with obstruction, simple diverticulectomy can be performed. Segmental small-bowel resections should be performed for acute diverticulitis, a wide-based diverticulum, volvulus with necrotic bowel, or bleeding from a mesenteric ulcer. **Incidental diverticulectomy** during surgery for other abdominal pathology is *not indicated.* Lifelong morbidity associated with the presence of a Meckel diverticulum is extremely low.

III. ENTERIC FISTULAS.

A fistula is defined as an abnormal communication between two epithelialized surfaces. Fistulas are categorized according to anatomy, output, and etiology.

A. Anatomic Considerations. *External* fistulas are most common and

connect an internal organ system with the skin (an enterocutaneous fistula [ECF]) or the atmosphere if an open wound without skin is present (an enteroatmospheric fistula [EAF]). *Internal* fistulas connect two hollow structures of the same or different organ system. Examples include colovesicular and enteroenteric fistulas. Physiologic categorization of fistulas is centered on the *output* and is divided into *high* (>500 mL/day), *moderate* (200 to 500 mL/day), and *low* (<200 mL/day) output fistulas. *Proximal* fistulas, located in the stomach, duodenum, or jejunum, are usually associated with high outputs of ≥3 L/day leading to profound dehydration, malnutrition, and electrolyte disturbances. *Distal* fistulas of the ileum or colon tend to be lower output, associated with fewer complications, and more often close with nonoperative treatment.

B. Pathophysiology. The overall mortality for all enteric fistulas is 5% to 20%. Loss of GI contents leads to **hypovolemia** as well as **acid/base** and **electrolyte abnormalities**. High-output fistulas release large volumes of fluid that cannot be adequately replaced by enteral means, leading to dehydration and intravascular volume depletion. Malnutrition is often due to both insufficient caloric intake and functional exclusion of portions of the GI tract limiting absorptive capacity.

C. Etiology

1. **Abdominal operations** are the leading cause of fistula formation. The risk is greatest for operations performed for inflammatory bowel disease (IBD), ischemia, malignancy, or extensive intestinal adhesions. Malnutrition and immunosuppression significantly increase the risk of fistula formation as well.
2. **CD** is a common cause of ECF and enteroenteric fistulas.
3. **Diverticular disease** results in fistula formation when localized abscesses drain into adjacent organs. Common examples include colovesical and colovaginal fistulas. Internal fistulas should be suspected in patients with diverticular disease who exhibit persistent or recurrent urinary tract infections or sepsis.
4. **Malignant** fistulas form when tumors perforate or invade adjacent structures. Healing does not occur if cancer is present, and resection is often the only means of cure.
5. **Radiation enteritis** predisposes to fistula formation after an

operation, regardless of the temporal proximity of radiation exposure.

6. **Trauma** to the abdomen or pelvis may also cause fistulas. Missed enteric injuries, or those repaired in a contaminated field, are prone to leak and subsequent fistula formation.
7. **Other causes** of SI fistulas include a foreign body (mesh, suture), vascular compromise, and infectious diseases (amebiasis, tuberculosis, or *Actinomyces*).

D. Diagnosis

1. **Imaging.** Initial diagnosis usually includes a CT with oral and IV contrast to help characterize the location of the fistula as well as to evaluate for associated intra-abdominal abscesses or undrained fluid collections. Additional imaging may include fistulography, where contrast is injected into the fistula to provide visualization of all tracts and sites of enteral communication. Oral contrast studies, such as an upper GI with SBFT, can demonstrate contrast extravasation through the fistula, but are less sensitive than fistulogram. A contrast enema is often helpful in the evaluation of rectal or colonic fistulas.
2. **Endoscopy** is useful to assess the bowel for underlying pathology, such as peptic ulceration, IBD, or cancer.

E. Spontaneous Closure.

Common conditions under which fistulas fail to close can be remembered with the aid of the mnemonic "FRIENDS": Foreign body, Radiation, Inflammation or Infection, Epithelialization, Neoplasm or lack of Nutrition, Distal obstruction, and/or Steroids (immunosuppression). Approximately 40% of ECFs will close spontaneously in 4 to 6 weeks with adequate nutritional support and control of sepsis. Increased rates of closure are seen in fistulas with low output, long tracts (>2 cm), small orifices (<1 cm^2), and in the absence of malnutrition, abscess, sepsis, or active IBD. Delaying reoperation allows adhesions to attenuate and the patient to recover nutritional status and general health. For small fistulas, reoperation should be delayed at least 4 to 6 months from the time of last laparotomy. Improved home intravenous (IV) therapy, parenteral nutrition (TPN), wound care, and somatostatin analogs (see below) have allowed longer periods of waiting for spontaneous fistula closure to be possible.

F. Nonoperative Treatment

1. **Fluid resuscitation and electrolyte correction.** The initial phase of

ECF/EAF management focuses on correction of hypovolemia and electrolyte imbalance and accurate measurement of fistula output. IV fluid administration is typically necessary because adequate enteral replacement of fistula output is difficult.

2. **Sepsis control** is critical as sepsis remains the primary determinant of fistula mortality. Sepsis accompanies a large percentage of fistulas and is caused by undrained enteric leaks or abscesses. Percutaneous abscess drainage should be performed if present. **IV antibiotics** directed against bowel flora are indicated when infection is present. Reoperation for *source control* may be required to manage continuous bacterial seeding from the GI tract. **Infected wounds** are opened and packed to allow complete drainage, debridement, and healing by secondary intention.
3. **Nutritional support.** Nutritional support is essential to facilitate spontaneous closure and to optimize the patient for surgery if the fistula does not heal on its own.
   a. **Complete bowel rest.** Initial NPO status reduces fistula drainage and simplifies the evaluation and stabilization of the patient.
   b. **Enteral feeding** is preferred as long as fistula output does not increase significantly. Patients with low-output colonic or distal SI fistulas are often safely fed with standard enteral formulas. However, if the available bowel is short, elemental feeding may maximize absorption. In patients with a proximal fistula, feeding distal to the fistula is typically effective (e.g., feeding jejunostomy tube for a gastric fistula).
   c. **TPN** provides nourishment when enteral feeding is not possible. Indications include intolerance to enteral nutrition, high-output fistulas, and proximal fistulas where distal enteral access is not possible. Complications of TPN include biliary stasis, hepatic dysfunction, trace element (zinc, copper, chromium) and essential fatty acid deficiencies, and venous catheter-related complications, such as infections.
4. **Decrease of fistula output.** H_2-receptor antagonists or proton-pump inhibitors are used to reduce gastric and duodenal fistula output and provide stress ulceration prophylaxis. Somatostatin and its analogs have mixed results in decreasing fistula output and fistula closure.

5. **Skin protection.** Fistula effluent is corrosive to the skin and must be controlled. For low-output fistulas, dressings may be used to simply absorb effluent but may impede healing and cause skin breakdown if prolonged contact occurs. Barrier/ostomy devices are useful as they isolate the effluent away from the skin and allow for quantification of output. Vacuum-assisted wound closure devices may help control skin irritation and speed fistula closure. Early involvement of an enterostomal therapist is critical in the management of fistula patients.

G. Operative treatment is indicated when a fistula fails to heal with nonoperative management, or when sepsis cannot be controlled. The goals of surgery are to eradicate the fistula tract and to restore the epithelial continuity of the associated organ systems.

1. **Gastric fistulas** can arise from anastomotic breakdown or ulcer perforation. Most low-output gastric fistulas close spontaneously, such as after removal of a gastrostomy tube. In cases where surgery is needed, primary repair with serosal and/or omental patch placement is usually successful.
2. **Duodenal fistulas** typically close spontaneously with nonoperative management. When operative intervention is required, primary closure of small duodenal wall disruptions may be performed, but a duodenal stricture may result with primary closure of large defects. In these cases, duodenal wall integrity may be restored by a serosal patch using another segment of bowel. Alternatively, a Roux-en-Y duodenoenterostomy may be performed.
3. **Small-bowel fistulas** typically require bowel resection and primary reanastomosis. For enteroenteric or other internal fistulas, openings that are in close proximity to the involved region are resected en bloc. Short bowel is a risk (see below).
4. **Large-bowel fistulas** are associated with high spontaneous closure rates. If operative closure is required, resection with primary reanastomosis is preferred. A proximal, diverting loop ileostomy should be considered in the setting of malnutrition or suboptimal anastomosis.
5. **Enteral feeding tubes** placed at the time of definitive repair may facilitate postoperative management and maintenance of nutrition.

IV. SHORT-BOWEL SYNDROME.

Short-bowel syndrome (SBS) is a malabsorptive state and symptom complex following massive SI resection. In adults, the normal length of the SI varies from 300 to 600 cm and correlates directly with body surface area. Adults with less than 200 cm of functional bowel or less than 30% of the initial SI length are at high risk of developing SBS. With an end stoma, resection resulting in <100 cm of intact SI generally leads to SBS. However, in patients with an intact ileocecal valve and one-third of the colon, SBS may not develop until <75 cm SI remains. Children tend to develop SBS when <30% of normal SI length for age remains. Infants may survive resection of up to 85% of their bowel because of enhanced adaptation and growth. SBS may be seen with greater lengths of remaining SI if an underlying disease, such as CD or radiation enteritis, is present. Because the ileum has specialized absorptive function, complete resection is not well tolerated. On the contrary, the entire jejunum can usually be resected without serious adverse nutritional sequela.

A. Etiology.

In children, the most common etiologies for SBS include necrotizing enterocolitis, congenital intestinal atresia, midgut volvulus, and gastroschisis. The leading causes of massive intestinal resection in adults and elderly patients are mesenteric ischemia, trauma, IBD, strangulated hernia, SI or mesenteric neoplasms, volvulus, and portal vein thrombosis.

B. Pathophysiology.

SBS is characterized by diarrhea, dehydration, electrolyte disturbances, steatorrhea, malnutrition, and weight loss.

1. **Adaptation.** The SI undergoes several adaptive changes in response to massive SI resection in an attempt to counteract the development of SBS. Slower transit and increased nutrient absorption occurs through functional adaptations. If colon is present, adaptation manifests as increased colonic absorption and colonocyte degradation of carbohydrates into short-chain fatty acids (SCFA), which increases caloric uptake up to 50%. With resection of the jejunum, the distal SI has the greatest adaptive potential and can assume nearly all of the absorptive properties of the proximal gut.
2. **Fluid and electrolyte response.** Of the 7 to 10 L of fluid presented daily to the SI, only 1 to 2 L are delivered into the colon. Significant quantities of electrolytes are absorbed in this process. The colon, if present, can absorb a significant amount of the increased fluid it

encounters with SBS.

3. **Malabsorption and malnutrition. Gastric hypersecretion** causes increased acid load, injures distal bowel mucosa, and leads to hypermotility and impaired absorption. Altered bilirubin metabolism after ileal resection increases the risk of **cholelithiasis** secondary to decreased bile salt. Delivery of bile acids into the colon also produces a reactive, often severe watery diarrhea. **Hyperoxaluria** results from excessive fatty acids in the colonic lumen binding intraluminal calcium and leads to calcium oxalate **nephrolithiasis**. Loss of the ileocecal valve permits reflux of colonic bacteria into the SI leading to **bacterial overgrowth** and colonization that impairs digestion and absorption of nutrients. Rapid intestinal transit, hyperosmolar contents in the distal SI, disruption of the enterohepatic bile acid circulation, and bacterial overgrowth all promote **steatorrhea** and **diarrhea**. Unabsorbed fats in the colon further inhibit absorption of water and electrolytes and stimulate secretion.

C. Acute Phase Treatment. The primary goal in the acute phase (initial 4 weeks) is stabilization as metabolic, respiratory, and cardiovascular derangements frequently accompany massive small-bowel resection. Close monitoring of fluid balance and serum electrolytes are critical. **Prolonged ileus** is common. TPN should be provided until GI function resumes. Early initiation of nutritional support promotes a positive nitrogen balance, wound healing, and adaptation of remnant bowel. Enteral nutrition has positive trophic effects on bowel mucosa and should be initiated. Feeding tubes placed at laparotomy are often necessary. Initial feeds should be gradual, continuous, low volume, low fat, and isosmotic.

D. Maintenance Phase Treatment. Maintenance therapy in SBS focuses on long-term nutritional goals, support of adaptation that takes place over the first 1 to 2 years, and addressing various clinical issues that arise.

1. **Nutritional support** with supplemental electrolytes (potassium, magnesium), vitamins (A, D, E, K, B_{12}), trace elements and minerals (zinc, selenium, and iron), and essential fatty acids (linoleic acid) should be given parenterally until adequate enteral absorption is achieved. A glucagon-like peptide (GLP-2) analogue, teduglutide, is a novel therapy shown to increase adaptation and decrease TPN

dependence (*J Parenter Enteral Nutr*. 2017;41(6):946–951). The use of growth hormone and glutamine remain controversial (*Cochrane Database Syst Rev*. 2010(6):CD006321).

2. **Diarrhea** is often multifactorial and dietary modifications can improve symptoms. Medications such as H_2-receptor blockers, bile chelating resins (cholestyramine), antisecretory medications (loperamide, somatostatin analogs), and low-dose narcotics (diphenoxylate hydrochloride and atropine [Lomotil], codeine, or tincture of opium) are useful for decreasing output.
3. **Late complications** are common and include nephrolithiasis, cholelithiasis, nutritional deficiencies (anemia, bone disease, and coagulopathy), liver dysfunction, as well as TPN and central access–related complications. Anastomotic leaks, fistulas, strictures, and late bowel obstructions can also occur well beyond the early postoperative period and commonly require reoperation.

E. Surgical Therapy. Various surgical procedures have been described for the management of SBS but have not been widely adopted. Intestinal lengthening procedures may decrease TPN dependence, increase oral caloric intake, and reverse liver disease. The most common procedures are "serial transverse enteroplasty" (STEP) and the Bianchi procedure, both with similar efficacy. Isolated small-bowel transplants or multivisceral transplantations are additional options for SBS.

V. NEOPLASMS.

Small-bowel neoplasms are relatively uncommon. Benign neoplasms are often discovered incidentally, and malignant tumors account for <2% of all GI cancers. Most malignant tumors eventually become symptomatic with weight loss, abdominal pain, obstruction, perforation, or hemorrhage. Small-bowel neoplasms can also be a lead point for intussusception.

A. Benign Tumors. Benign SI masses are more common than malignant.

1. **Leiomyoma** is the most common benign SI neoplasm and arises from mesenchymal cells. These tumors grow submucosally and project into the bowel lumen. On contrast studies, they appear as smooth, eccentric filling defects with normal-appearing mucosa. Histopathologic examination is needed to distinguish benign from malignant stromal tumors. Treatment consists of segmental bowel resection.

2. **Adenomas** can occur sporadically as solitary lesions, or in association with familial adenomatous polyposis syndrome. Adenomas can cause intermittent pain secondary to obstruction, intussusception, or bleeding. Three subtypes include simple tubular, Brunner gland, and villous adenomas. The duodenum is the most common site for all three types of adenomas. Tubular and Brunner gland adenomas have low malignant potential and may be treated with endoscopic polypectomy. Villous adenomas have significant malignant potential. If complete endoscopic resection is not possible, transduodenal excision with adequate margins is appropriate. Villous adenomas of the jejunum or ileum require small-bowel resection if endoscopic resection is not possible or incomplete.
3. **Hamartomas** may be spontaneous, but most arise in patients with Peutz–Jeghers syndrome, an autosomal-dominant syndrome characterized by mucocutaneous hyperpigmentation and multiple GI polyps. Operative intervention is indicated only for symptoms (obstruction, intussusception, bleeding), and all polyps larger than 1 cm should be resected. Multiple resections can lead to SBS, so local excision or endoscopic treatment of noncancerous polyps is preferred. These patients are at increased risk for de novo SI and/or colonic adenocarcinoma (arising separately from the hamartomas) and therefore require frequent endoscopic screening.
4. **Other benign tumors. Lipomas** occur most often in the ileum and have no malignant potential. **Hemangiomas** are associated with Osler–Weber–Rendu disease (or hereditary hemorrhagic telangiectasia) and present with bleeding. **Neurofibromas and fibromas** are less common tumors that can cause intussusception. **Endometriosis** implants appear as puckered, bluish-red, serosal-based nodules that can cause GI bleeding or obstruction.

B. Malignant Tumors

1. **Adenocarcinoma** is the most common malignant SI tumor, with 40% in the duodenum and then with decreasing frequency distally through the SI. Risk factors for development of adenocarcinoma include villous adenomas, polyposis syndromes, CD, and hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome. Presenting symptoms depend on the location of the primary tumor. Periampullary tumors present with painless jaundice, duodenal

obstruction, or bleeding. Distal tumors tend to present with abdominal pain and weight loss from progressive obstruction. *Diagnosis* is made via CT and endoscopy with or without ERCP for biopsy. *Treatment* consists of en bloc resection with the associated mesenteric nodal basin. Tumors of the terminal ileum are resected with the right colon as well. Carcinomas of the duodenum usually require pancreaticoduodenectomy. The 5-year survival rate for duodenal adenocarcinoma is 56% for node-positive and 83% for node-negative disease. Patients with metastatic disease at the time of diagnosis rarely survive past 6 months. Adjuvant 5-fluorouracil–based chemotherapy regimens are often used, but data on their efficacy are lacking.

2. **Gastrointestinal stromal tumors** (GISTs) arise from mesodermal-derived components of the bowel and are equally distributed along the length of the intestine. These tumors grow extraluminally and cause symptoms late in their course. Hemorrhage into either peritoneum or bowel lumen may result when these tumors outgrow their blood supply and necrose. Mutations of **c-kit** (CD117, a tyrosine kinase) allow diagnosis by immunohistochemistry. Histologic grade and tumor size are predictors of survival. Tumors >2 cm should be resected; however, there is no consensus on resection for tumors <2 cm. Surgical treatment of SI GIST includes segmental resection with negative margins. Lymphadenectomy is unnecessary as tumors rarely metastasize to lymph nodes. Risk factors for recurrence include tumor size, a high mitotic rate, or tumor rupture. Traditional chemoradiation is not effective for GIST. However, the tyrosine kinase inhibitor *imatinib mesylate* (***Gleevec***) effectively inhibits the overactive tyrosine receptor c-kit found on all GIST cells. Adjuvant imatinib therapy has been shown to cause radiographic and histologic regression of metastatic lesions as well as improves recurrence-free survival in intermediate and high-risk GIST in patients with imatinib-sensitive mutations (*JAMA Oncol*. 2018;4(12):e184060).
3. **Primary small-bowel lymphomas** are most common in the ileum due to relatively large amounts of gut-associated lymphoid tissue. Virtually all SI lymphomas are non-Hodgkin, B-cell lymphomas (NHL) that arise either de novo or in association with a pre-existing systemic condition such as celiac disease, CD, or

immunosuppression. The presentation is highly variable. Imaging can help make a diagnosis, but operation is frequently required for histologic confirmation. Surgery may also be indicated in the setting of bowel obstruction, bleeding, or perforation. In general, treatment of SI lymphoma is based on the subtype and treated similarly to lymphoma arising in the periphery.

4. **Neuroendocrine tumors (NET)** arise from enterochromaffin cells of intestinal crypts. Most intestinal NETs occur within 2 feet of the ileocecal valve. SI NETs are more likely to metastasize when compared to appendiceal or rectal NET. Patients typically remain asymptomatic until advanced disease causes local complications of GI obstruction, pain, or bleeding, or the systemic carcinoid syndrome.
   a. **Carcinoid syndrome** implies hepatic metastatic spread. Hormones released by carcinoid tumors are normally metabolized by the liver and produce no symptoms; however, hepatic metastases drain into the systemic circulation causing *diarrhea* and *flushing* of the face, neck, and upper chest. Tachycardia, hypotension, bronchospasm, and coma may be observed. In long-standing carcinoid syndrome, patients develop right heart endocardial and valvular fibrosis.
   b. **Diagnosis** of NET is made by measuring a 24-hour urinary 5-hydroxyindoleacetic acid (5-HIAA), the breakdown product of serotonin secreted by the tumor. Serum chromogranin A measurement is another diagnostic test for GI NET with high sensitivity (80% to 100%), but lower specificity than urine 5-HIAA levels.
   c. **Tumor localization.** Multiphasic CT scan is recommended for all patients. MRI is helpful in further elucidating potential hepatic metastases but may underestimate the tumor burden. 111-In pentetreotide, or OctreoScan, is useful at providing whole-body images and thus detection of metastastic disease, however, 68-Ga DOTATATE PET/CT is preferred due to higher spatial resolution.
   d. The **treatment** of NET is operative. The entire bowel should be inspected as 30% of cases have synchronous lesions. Jejunal and ileal tumors are treated with segmental resection including adjacent mesentery. Small tumors (<1 cm) of the third or fourth

portions of the duodenum can be either locally excised or included in a segmental resection. Large duodenal tumors and periampullary tumors require pancreaticoduodenectomy. Locally advanced disease with involvement of adjacent organs or peritoneum requires aggressive resection to delay occurrence of mesenteric desmoplastic reaction, hepatic metastases, and carcinoid syndrome. Solitary and accessible liver lesions should be resected. Adjuvant cytotoxic chemotherapy and radiotherapy are of little benefit. The somatostatin analog **octreotide** offers excellent palliation of carcinoid syndrome symptoms in patients with unresectable disease. In patients with metastatic midgut NET the radiolabeled somatostatin analogue, ^{177}Lu-Dotatate, has shown increased progression-free survival compared to long-acting octreotide (*NEJM*. 2017;376:125–135).

e. Small-bowel NETs are generally indolent tumors and **prognosis** is correlated with stage of the tumor. Patients with early stage disease have 10-year disease-specific survival over 90%, while patients who present with metastatic disease have a 42% 10-year disease-specific survival (*J Clin Oncol*. 2013;31(30):3776–3781).

5. Metastases can spread to the small bowel and palliative resection may be appropriate if required for symptom relief. Several primary cancers are known to metastasize to the SI including melanoma, colorectal, gynecologic, breast, stomach, lung, prostate, and renal cancers. Median survival is poor. Cases should be considered individually. Palliative gastrostomy with or without TPN may be appropriate in advanced cases where nonoperative management is chosen.

VI. Crohn Disease.

CD is an idiopathic, chronic, granulomatous IBD that can affect any part of the GI tract from mouth to anus. CD is incurable, slowly progressive, and characterized by episodes of exacerbation and remission. Incidence of CD varies by geography with lower rates in Asia and the Middle East and higher rates in Europe and North America. A population-based study found that the incidence of CD was 10.7 cases per 100,000 person-years and has been increasing over time (*Clin Gastroenterol Hepatol*. 2017;15(6)857–863).

A. Etiology.

The cause of CD is unknown, but is believed to involve both

genetic and environmental factors. CD is 25 times more common among patients with a family history and has a concordance rate of 60% in monozygotic twins. Environmental aspects, such as smoking, also increase the risk of developing CD. Pathogenesis likely relates to a defective mucosal barrier and/or dysregulated intestinal immunity leading to chronic inflammation within the intestinal wall. Intestinal dysbiosis has been recognized in CD, but it is unknown if it is a cause or effect of the disease.

B. Bowel Involvement. The *terminal ileum* is the most common site of disease. Disease affecting both small and large intestine occurs in 55% of patients. **Small-bowel only** disease occurs in 30% of patients whereas colonic-only disease occurs in 15%. **Perianal** involvement commonly coexists with more proximal forms, thus isolated **anorectal** disease is rare.

C. Histology. CD is characterized by *transmural inflammation.* Grossly, the bowel is thickened with creeping fat, corkscrew vessels, and a shortened fibrotic mesentery with lymphadenopathy. Mucosal changes include pinpoint hemorrhages, aphthous ulcers, deep linear fissures, crypt abscesses, and *cobblestoning.* These findings commonly occur segmentally, causing *skip lesions* along the intestine rather than being continuous. *Granulomas* are found in the bowel wall in 40% to 60% of patients.

D. Clinical Presentation. CD has a highly variable presentation. Physical examination is performed with special attention to the abdominal and anorectal areas. No physical signs are pathognomonic for CD, although the appearance of the perineum may be highly suggestive. **Diarrhea** occurs in almost all patients. Patients with ileal disease may present with SBO symptoms or have steatorrhea secondary to bile salt deficiency. **Abdominal pain** typically is colicky, worse after meals, relieved by defecation, and poorly localized. **Weight loss** occurs as a result of decreased oral intake, malabsorption, protein-losing enteropathy, and/or steatorrhea. Children with CD may develop vitamin and mineral deficiencies and growth retardation. **Constitutional symptoms** such as malaise and fever are common. **Anorectal** disease is common and may precede intestinal symptoms. **Extraintestinal manifestations** can be numerous, including conjunctivitis, iritis, uveitis, pyoderma gangrenosum, erythema nodosum multiforme, arthritis, ankylosing

spondylitis, and even sclerosing cholangitis.

E. Endoscopy. Lower, and sometimes upper, endoscopy is crucial for determination of location and severity of disease as well as diagnostic biopsies. Those with long-standing (>7 to 10 years) colitis are at increased risk for adenocarcinoma, and surveillance colonoscopy for cancer is important.

F. Imaging. Radiologic imaging in CD is especially useful to evaluate for SI disease. This can be done with upper GI SBFT or CT enterography (CTE). Magnetic resonance enterography (MRE) is gaining popularity as an imaging modality in CD as it avoids radiation exposure in patients who will likely require multiple evaluations over the course of their life.

G. Treatment

1. **Medical management** is important to palliate symptoms, correct nutritional disturbances, and reduce inflammation. Disease location, severity, and complications dictate therapeutic recommendations. Mild-to-moderate disease can be treated as an outpatient with oral aminosalicylates. Initiation of antibiotics (ciprofloxacin, metronidazole) is indicated in patients who do not tolerate aminosalicylates or do not improve with aminosalicylate therapy. Oral prednisone may be used for patients who are unresponsive to the above measures, or for those presenting with more severe initial symptoms (but not requiring hospitalization). Budesonide is a glucocorticoid with a high first-pass hepatic metabolism that is an alternative to prednisone for patients with active ileitis or right-sided Crohn colitis. Hospitalization is required for patients who present with severe or fulminant disease. Inpatient treatment includes bowel rest, TPN, and IV glucocorticoids. Patients who are steroid dependent or steroid resistant may require treatment with immunomodulator or biologic therapies. Immunomodulators include azathioprine, 6-mercaptopurine, and methotrexate. Biologic therapies include antitumor necrosis factor-alpha (anti-TNF) antagonists, anti-integrin antibodies, and anti-interleukin antibodies. Anti-TNFs are effective in treatment of moderate to severe luminal CD, including infliximab, adalimumab, and certolizumab. Anti-integrin antibodies, such as natalizumab and vedolizumab, are generally second-line biologics and act by blocking leukocyte migration to sites of inflammation. Ustekinumab is a second-line biologic which blocks interleukin (IL)

receptors IL-12 and IL-23 on T-cells, natural killer cells, and antigen presenting cells.

2. **Surgical therapy** is indicated when medical therapy has failed or to address complications such as high-output fistulas, perforation, intra-abdominal abscess, severe colitis, bleeding, or obstruction from fibrotic strictures.

   a. At the time of operation, the most important principle is to correct the complication while *preserving bowel length* to prevent SBS. Resection to histologically negative margins does not reduce the likelihood of disease recurrence; therefore, grossly normal margins are accepted. In the absence of free perforation, large abscesses, massively dilated bowel, severe malnutrition, or high-dose immunosuppression, primary anastomosis is safe. Laparoscopic resections are safe alternatives to open procedures. SI strictures of appropriate length and type can be treated with stricturoplasty to preserve bowel length.

   b. *Appendectomy.* Patients who are being explored for presumed acute appendicitis and are found to have Crohn ileitis should undergo appendectomy if the cecum is not inflamed. Conventional teaching has been that the terminal ileum should not be removed at that time unless absolutely necessary.

H. Prognosis. CD is a chronic, pan-intestinal disease that currently has no cure and requires chronic, lifelong treatment, with operation reserved for severe complications. Further study of the pathways involved may shed light on pathogenesis and lead to more effective medical treatments.

CHAPTER 20: SMALL INTESTINE

Multiple Choice Questions

1. **A 29-year-old male presents to the emergency department with complaints of abdominal pain, nausea, and bilious vomiting for 2 days. He has no significant past medical history, and his past surgical history is significant for an open appendectomy for perforated appendicitis. CT scan demonstrates dilated loops of small bowel with a transition point in the right lower quadrant and is negative for free air or fluid. The most likely etiology for this patient's condition is:**

   a. Intussusception
   b. Malignancy
   c. Adhesions
   d. Crohn disease
   e. Gallstone ileus

2. **A 45-year-old male presents to the emergency department with complaints of abdominal pain, nausea, and bilious vomiting for 2 days. His last bowel movement was 3 days ago. His past medical history is significant for hypertension and diabetes, and his past surgical history is significant for an open appendectomy for perforated appendicitis and open ventral hernia repair. His initial vitals in the emergency room are: Temperature 39°C, heart rate 115, blood pressure 90/54, respirations 22, O_2 saturation 92% on room air. On physical examination, he has a well-healed lower midline incision, abdomen is firm, moderately distended, and has diffuse tenderness to palpation of his abdomen with rebound and guarding. CT scan demonstrates dilated loops of small bowel with a transition point in the right lower quadrant and a moderate amount of free fluid in the pelvis. You place an NG tube and begin IV fluid resuscitation. The next best step in the treatment of this patient would be:**

   a. Admission for close monitoring
   b. Urgent laparotomy

c. Obtain an upper GI study with small bowel follow through using water-soluble contrast
d. Reassurance and discharge with follow-up in 1 week
e. Urgent colonoscopy

3. **A 70-year-old male presents to the emergency department with abdominal pain, nausea, and bilious vomiting. He also complains of a painful bulge in his left groin that has been present for 4 hours. His past medical history is significant for hypertension, chronic obstructive pulmonary disease, and hypothyroidism. He has no past surgical history. His initial vitals in the emergency room are: Temperature 37.5°C, heart rate 80, blood pressure 165/90, respirations 14, O_2 saturation 93% on room air. On physical examination, he is moderately distended, and has mild tenderness to palpation throughout his abdomen, and a firm, painful bulge in his left groin above the inguinal ligament. There are no overlying skin changes in his groin. You start IV fluid resuscitation. The next best step in the treatment of this patient would be:**

a. Attempt manual reduction in the ED with light sedation
b. Obtain a CT scan of the abdomen
c. Discharge the patient with a follow-up appointment in 1 week
d. Urgent laparotomy
e. Elective inguinal hernia repair

4. **A 60-year-old female presents to the emergency room with signs and symptoms of bowel obstruction. On CT scan, a mass is visualized in the jejunum with dilation of the small bowel proximal to the mass and several lesions in the liver concerning for metastasis. You perform a laparotomy and segmental bowel resection and core biopsy of a liver lesion. Final pathology reveals cells that are c-kit positive. Which of the following is the best chemotherapeutic regimen for this patient?**

a. Imatinib mesylate (Gleevec)
b. 5-FU and oxaliplatin
c. Cyclophosphamide + doxorubicin + vincristine + prednisone

(CHOP)
d. Trastuzumab (Herceptin)
e. Octreotide

5. **A 45-year-old male with widely metastatic small-bowel neuroendocrine tumor has symptoms of flushing and diarrhea. Which of the following drugs would be useful to control his symptoms?**

a. 5-FU and oxaliplatin
b. Sunitinib malate (Sutent)
c. Octreotide
d. Tincture of opium
e. Diphenoxylate hydrochloride and atropine

6. **A 10-year-old girl with short-bowel syndrome secondary to congenital malrotation and volvulus presents to the emergency department with fevers of 39.5°C, tachycardia, and hypotension. She receives TPN via a tunneled central venous catheter. Her physical examination is unremarkable. WBC is 12. Chest x-ray demonstrates her central line, and abdominal plain films demonstrate a normal gas pattern, no free air. The most likely acute diagnosis for this patient is:**

a. Hyperthyroidism
b. Central venous catheter–associated blood stream infection
c. Intra-abdominal abscess
d. Pneumonia
e. Small-bowel perforation

21 Surgical Diseases of the Liver

David G. Brauer, Kathryn J. Fowler, and William C. Chapman

ANATOMY AND PHYSIOLOGY

I. SEGMENTAL AND SURGICAL ANATOMY. Grossly, the liver appears to be separated into a right and left liver based on the position of the falciform ligament. However, **Cantlie line**, extending from the gallbladder fossa to the inferior vena cava (IVC), is the true functional plane between the left and right liver. French surgeon Claude **Couinaud** delineated the functional anatomy of the liver into eight segments with distinct arterial, venous, and biliary inflow and outflow. The **Brisbane Terminology** has further standardized segmental and surgical anatomy (Table 21-1). Second-order resections are referred to as sectionectomies, and first-order resections are referred to as left or right hepatectomies or hemihepatectomies. A trisectionectomy refers to the right hemiliver plus the left medial section (segments IV to VIII) or the left hemiliver plus the right anterior section (segments II to V, VIII).

II. ANATOMIC FEATURES

A. Inflow

1. **Arterial.** The **hepatic artery** supplies approximately 25% of the vascular inflow to the liver. The normal course of the hepatic artery is from the celiac axis to the **common hepatic artery** to the **proper hepatic artery**, which runs anteriorly and medially within the porta hepatis before bifurcating into the left and right liver. Variations of the origin of the left and right hepatic arteries are common.

   a. A **replaced** (or accessory) **right hepatic artery** arises from the

superior mesenteric artery in up to 20% of cases and courses posterior and lateral to the portal vein.

b. A **replaced** (or accessory) **left hepatic artery** arises from the left gastric artery in around 15% of cases and runs in the gastrohepatic ligament.

2. **Venous.** The **portal vein** supplies approximately 75% of the vascular inflow to the liver. The left portal vein routinely branches external to the liver parenchyma.

B. Outflow

1. **Venous.** Conventionally, three **hepatic veins** drain the liver into the IVC. The **right hepatic vein** drains segments V through VIII. The **middle hepatic vein** drains segment IV and, to some extent, segments V and VIII. The **left hepatic vein** drains segments II and III. Drainage of the caudate lobe is directly into the IVC. In most cases, the **left** and **middle hepatic veins** join prior to their insertion into the IVC. **Accessory right hepatic veins** are a common variant and often enter the IVC inferior to the hepatic confluence, and primarily drain segment VI.

TABLE 21-1 Brisbane Terminology of Liver Anatomy and Resections

Segment	Second-Order Division	First-Order Division
I (Caudate)		
II	Left lateral section	Left liver or left hemiliver
III		
IV	Left medial section	
V	Right anterior section, along with section VIII	Right liver or right hemiliver
VI	Right posterior	

	section
VII	
VIII	Right anterior section, along with section V

2. **Biliary.** The **common bile duct** lies anterior and lateral in the porta. Similar to the portal vein, the **left hepatic duct** takes a longer extrahepatic course than the **right hepatic duct.**

C. Ligamentous Attachments. The liver is held in place by several ligaments. The **left** and **right triangular ligaments** provide attachment to the diaphragm. The **coronary ligaments** are extensions of the triangular ligaments anteriorly. The **falciform ligament** extends anteriorly from the umbilical fissure within the left hemiliver; its free edge becomes the **round ligament**, also called the **ligamentum teres**, which contains the **remnant umbilical vein.** On the underside of the liver, the **ligamentum venosum**, the remnant of the fetal ductus venosus, is attached between the left portal vein and the round ligament. A number of other ligaments represent attachments between surrounding organs including the **gastrohepatic** and **hepatoduodenal ligaments.**

III. PHYSIOLOGY

A. Bilirubin. Bilirubin is a product of heme catabolism. Heme is transported bound to albumin and is conjugated to glucuronic acid by glucuronyl transferase, making it water-soluble **conjugated bilirubin,** which is then excreted in bile.

B. Bile. The liver makes approximately 1 L of bile a day, which is an alkaline fluid composed of a number of substances including lipids, cholesterol, and bile acids produced from cholesterol, including cholic acid and chenodeoxycholic acid. Greater than 90% of excreted bile salts are absorbed in the terminal ileum, which are then transported back to the liver (**enterohepatic circulation**).

C. The liver controls a number of essential metabolic processes including gluconeogenesis, glycogenolysis, and protein metabolism.

IV. LABORATORY TESTING

A. Alkaline phosphatase is an enzyme found throughout the body but at higher concentrations in the liver, bones, and small intestine. It is used as an indirect marker of cholestasis, particularly for diseases like primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC).

B. Gamma-glutamyltranspeptidase (GGT) participates in the transfer of amino acids. Similar to alkaline phosphatase, this enzyme is found in many other organs but primary hepatic disease, including cellular injury and cholestasis, is a major source of GGT elevation. GGT elevation in the setting of hepatic disease occurs earlier and persists longer than elevations in alkaline phosphatase.

C. The **aminotransferases, aspartate transaminase** (AST) and **alanine transaminase** (ALT), are responsible for the transformation of ketoglutarate to pyruvate and oxaloacetate. AST is found in the liver and other tissues including skeletal muscle and the kidneys, whereas ALT is primarily hepatic in origin. Elevations of these enzymes are indicative of cellular injury.

D. Measures of Liver Function

1. **Albumin** is the most abundant plasma protein and is synthesized in the liver.
2. **Prothrombin time** is the time to coagulation once serum is exposed to tissue factor. Coagulation in this setting relies on factor VII within the extrinsic pathway and common factors including II, V, and X. Because the majority of clotting factors are synthesized in the liver, prolonged prothrombin time is indicative of hepatic dysfunction. Prothrombin time is standardized using the International Normalized Ratio (INR).
3. **Grading**
   a. The **Child–Pugh score** was originally used to predict surgical mortality and is now widely used to classify the severity of liver failure and to predict survival. The model gives points for increasing severity of hepatic dysfunction (elevated bilirubin, hypoalbuminemia, and prothrombin time prolongation) and clinical signs (ascites and encephalopathy). Scores range between 5 and 15, which stratify patients into prognostic classes: Class A (5–6, least severe), B (7–9, moderately severe), or C (10–15, most

severe).

b. The **Model for End-Stage Liver Disease**, or **MELD**, is a scoring system employed by the United Network for Organ Sharing (UNOS) for prioritization on the liver transplant wait list. The MELD score was originally developed to predict mortality following **transjugular intrahepatic portosystemic shunts** (TIPS) and has since been modified, with adjustment for serum sodium (MELD-Na) added in 2016 (*N Engl J Med.* 2008;359(10):1018–1026). The equation incorporates serum bilirubin, INR, and serum creatinine into a total score ranging from 7 to 40. Patients with scores of 10 or higher should generally be referred to a hepatologist for further management and consideration of organ transplantation.

E. Tumor Markers

1. **Alpha-fetoprotein (AFP)** is normally produced by the fetal liver and yolk sac. Elevations of AFP may occur in patients with cirrhosis, however levels over 400 mcg/L in this setting are concerning for **hepatocellular carcinoma** (HCC) in high-risk patients. In the setting of normal background liver, levels greater than 10 mcg/L should raise suspicion for HCC if seen in conjunction with a mass on imaging. However, many HCCs do not secrete AFP, and AFP elevations can be seen in other tumors including gonadal cell tumors.
2. **CA 19-9** is regularly used in the workup and surveillance of **cholangiocarcinoma**, although the sensitivity and specificity are highly variable, as it may be expressed in benign conditions like cholangitis or in other cancers including pancreatic cancer. Furthermore, 7% to 10% of the population does not express the allele responsible for producing CA 19-9. As a tumor marker, it may be most reliable if elevated at the time of diagnosis and used to follow the effect of treatment or detect recurrence. It may also be a helpful cholangiocarcinoma screening tool for patients with PSC, though the threshold for positivity would be higher due to background inflammation.

V. LIVER FAILURE AND CIRRHOSIS

A. Liver biopsy is not necessary in the presence of overwhelming clinical, imaging, and laboratory data suggesting cirrhosis, although it can

confirm the diagnosis and identify or suggest a cause. Biopsies can be obtained surgically, percutaneously, or via a transjugular route. The severity of liver disease can be documented pathologically through a number of grading systems that stratify the severity of inflammation and fibrosis (reviewed in *J Hepatol.* 2007;47(4):598–607).

B. Portal Hypertension. The gold standard for the diagnosis of portal hypertension is measurement of the **hepatic venous pressure gradient,** that is, the difference between free and wedged hepatic venous pressures. This is performed through a jugular puncture with advancement of a catheter through the IVC and hepatic veins to the level of the liver periphery. A value of 8 mm Hg or greater is diagnostic of portal hypertension and suggests intrinsic liver disease. Varices develop at or above a value of 10 mm Hg. Reduction of the gradient to below 12 mm Hg is considered a therapeutic target.

BENIGN PATHOLOGY

I. MASSES

A. Hemangioma

1. **Presentation.** Hemangiomas are the most common benign liver tumor. They receive blood supply from branches of the hepatic artery. Accelerated growth has been associated with high-estrogen states including pregnancy, puberty, and use of oral contraceptive pills or androgens. Grossly, they are flat, red-blue, well circumscribed, soft, and compressible. Pathologic examination reveals hamartomatous outgrowths of endothelium. Clinically, these are rarely symptomatic and are frequently found incidentally during examinations for unrelated reasons. Malignant degeneration does not occur and rupture is extremely rare.
2. **Diagnosis.** Ultrasound (US) is sensitive although not specific; findings include well-demarcated, lobulated, homogeneous, hyperechoic mass. In patients with any underlying risk factors, diagnostic imaging should be done to confirm. On multiphase contrast-enhanced CT and MRI, hemangiomas demonstrate one of three classic patterns of enhancement: flash filling, peripheral **centripetal enhancement** progressing to confluence over time, or if large, they may have a central zone that fails to fill completely.

Recognition of peripheral nodular interrupted puddling of contrast and distinction from peripheral rim enhancement (more commonly seen in metastatic disease) is essential (Fig. 21-1). Marked T2 hyperintensity (bright signal) is a classic feature on MRI.

3. **Management.** Asymptomatic lesions can be observed. Interventions are often reserved only for rare cases including hemorrhage or where there is diagnostic uncertainty. These can be enucleated under careful vascular control. Hemorrhage can be treated with embolization, however if hemorrhage is present, the diagnosis should be questioned.

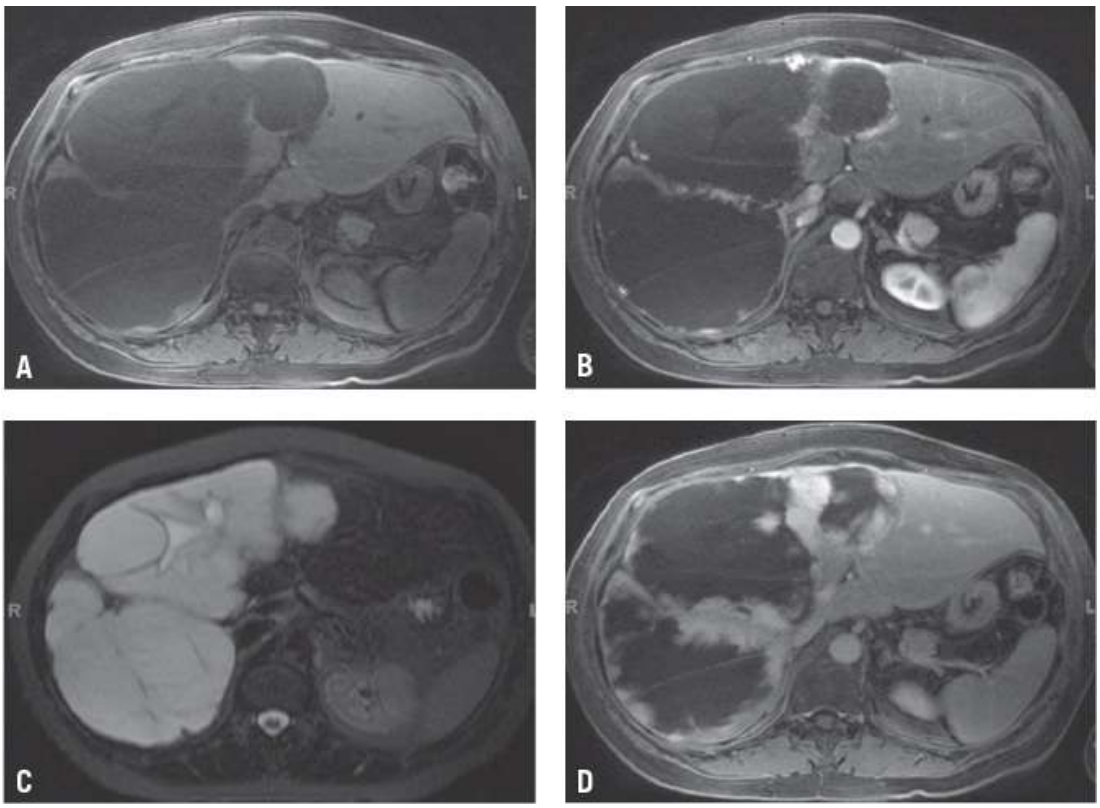


FIGURE 21-1 Large cavernous hemangioma. Characteristic peripheral interrupted puddling that progresses during dynamic imaging (**A,B,D**) along with the characteristically bright signal intensity on T2-weighted imaging (**C**) provides a definitive diagnosis of hemangioma on MRI.

B. Focal Nodular Hyperplasia (FNH)

1. **Presentation.** FNH is the second most common benign hepatic tumor and is thought to result from hyperplasia in response to hyperperfusion from a congenital arterial malformation. These lesions are identified predominantly in women of child-bearing age,

although the association between FNH and hormonal exposure is not as strong as that for hepatic adenomas. Grossly, these are often solitary lesions that are well circumscribed, lobulated, and unencapsulated. Pathologic examination reveals bland hepatocytes, bile duct proliferation, and malformed vessels. Clinically, these are rarely symptomatic, with pain, palpable mass, or rupture occurring very rarely.

2. **Diagnosis.** US is often insufficient for identification of these lesions, as they are isoechoic with surrounding normal liver. Due to its vascular supply, FNH has a **homogeneous enhancement on the arterial phase** of a CT or MRI examination, and if large, may possess a **central "stellate" fibrous scar** that has delayed enhancement on MRI with hepatobiliary phase imaging (Fig. 21-2). MRI with gadoxetate disodium (Eovist, Bayer) or gadobenate dimeglumine (MultiHance, Bracco) is considered the diagnostic imaging test of choice with reports of near 100% specificity for diagnosis of FNH. Older methods, such as technetium Tc-99m sulfur colloid scans are no longer standard of care.
3. **Management.** As these are often incidentally found and are benign, there is essentially no role for resection except in cases of symptoms (e.g., pain) or with diagnostic uncertainty despite adequate imaging with hepatobiliary phase MRI.

C. Hepatic Adenoma

1. **Presentation.** Hepatic adenomas are benign proliferations of hepatocytes. They are frequently found in young women due to a significant **association with synthetic estrogen and progesterone use** such as that found in oral contraceptive pills. Grossly, these adenomas are usually solitary, round, well-circumscribed, unencapsulated lesions. Pathologic examination reveals sheets of normal hepatocytes separated by dilated sinusoids but, importantly, **they do not contain bile ductules, a key finding distinguishing adenomas from FNH.** Clinically, adenomas can be identified incidentally or frequently are identified on workup for vague abdominal pain/discomfort as well as fullness. More acute episodes of pain occur with **spontaneous rupture and hemorrhage.** Bleeding can occur at high rates (over 50% of patients) depending on the size and location of the lesions (*Br J Surg.* 2014;101(7):847–855).

Rupture is more likely in men, particularly those using steroids, and in pregnant women, due to growth influenced by increased estrogen.

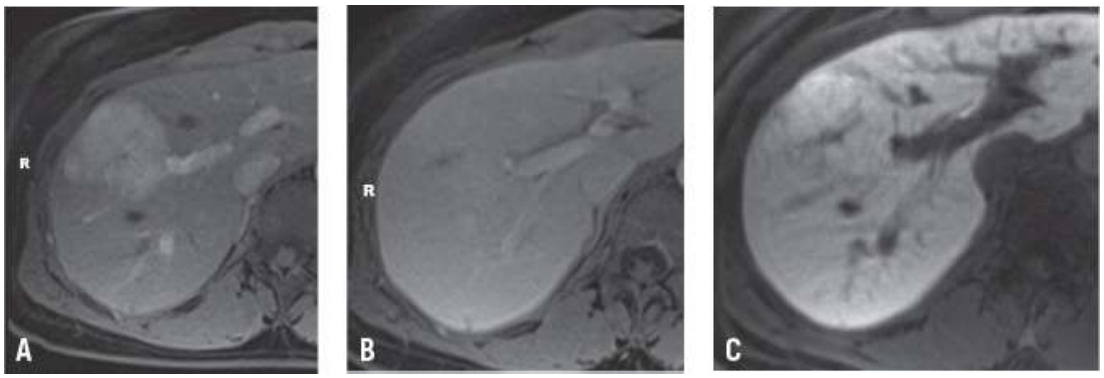


FIGURE 21-2 Focal nodular hyperplasia (FNH). Arterial phase hyperenhancement (**A**) and equilibration during portal venous (**B**) or later postcontrast phases, along with retention of contrast similar or brighter than the background liver during the hepatobiliary phase (**C**), are classic features of FNH. MRI performed with hepatobiliary contrast agents can provide definitive diagnosis of FNH.

2. **Diagnosis.** Heterogeneity as the result of hemorrhage, necrosis, and fat content are defining features of hepatic adenomas. On multiphasic MRI or CT, these lesions often hyperenhance on arterial phase and show variable enhancement patterns including washout or delayed central enhancement during portal venous and delayed phase imaging. Due to the fat content and lack of bile ducts, MRI is considered an ideal diagnostic imaging modality, with adenomas having characteristic chemical shift imaging appearance compatible with lipid and lack of gadoxetate disodium contrast retention on hepatobiliary phase imaging, which differentiates them from FNH.
3. **Management.** Adenomas without a history of rupture can be managed with surveillance and cessation of hormonal exposure. Rupture can be managed with arterial embolization. Due to the low malignant potential, surgical management requires a complex discussion with patients and is reserved for lesions with a history of significant rupture and hemorrhage, particularly intra-abdominal hemorrhage, as well as lesions greater than 5 cm (*Gastroenterology.* 2009;137(5):1698–1705).

D. Bile Duct Hamartoma. These lesions are frequently seen incidentally at laparotomy or laparoscopy. They appear as peripherally located, firm, smooth, small (1 to 5 mm), white nodules that can raise suspicion for

metastatic processes on initial operative exploration. Although benign, distinguishing them from malignancy may be essential; so frozen section biopsy can be obtained as appropriate.

II. ABSCESSES AND CYSTIC DISEASE

A. Pyogenic abscesses are frequently the result of hematogenous spread of nonhepatic sources of bacterial infection or direct introduction through instrumentation or biliary–enteric anastomoses.

1. **Presentation.** The majority of cases arise from direct spread of bacteria via the biliary tree in clinical scenarios such as cholangitis or biliary empyema. Responsible organisms are representative of their source: intra-abdominal infections likely lead to multi-organism gram-negative or anaerobic infections, while bacteremia likely leads to single-organism infections, many of which are gram positive. Immunocompromised patients, including those on chemotherapy, are more likely to develop fungal abscesses. Patients with pyogenic abscesses of the liver present with fever and abdominal pain.
2. **Diagnosis.** Laboratory work can reveal a leukocytosis and elevated alkaline phosphatase, which is more frequently elevated than AST or ALT, though this is nonspecific. Additional diagnostics should include imaging: chest x-ray may reveal an elevated right hemidiaphragm and an associated right pleural effusion, and US and cross-sectional imaging can be used to characterize the size and location of disease as well as the presence of biliary duct stones or strictures that may require extraction or stenting.
3. **Management.** Although **initiation of system antibiotics** and resuscitation for possible sepsis are important early interventions, pyogenic liver abscesses **usually require drainage**. Percutaneous drainage is usually preferred, and aspirated fluid is sent for culture to guide antibiotic selection. The duration of antibiotics may be rather prolonged and can be dictated by resolution of the abscess based on signs and symptoms, monitoring drain output, and on serial imaging of the abscesses. Operative drainage may be required for cases where percutaneous access may not be safe or due to anatomy, feasibility of drainage, a high number of abscesses, or where clinical improvement is not achieved through systemic antibiotics alone.

B. Amebic abscesses are caused by hematogenous spread via the portal

system of gastrointestinal infection by the protozoan *Entamoeba histolytica*.

1. **Presentation.** These can present as persistent fever with right upper quadrant pain. On examination, patients may have hepatomegaly and point tenderness over the liver. Intestinal manifestations of amebiasis such as diarrhea may also be present.
2. **Diagnosis.** The diagnosis can be made with serologic tests for antibodies. Needle aspiration can be performed when the diagnosis is unclear, yielding "anchovy paste" fluid, a combination of proteinaceous debris and necrotic hepatic tissue. Imaging reveals a cystic hypoechoic or hypoenhancing mass with a rim of peripheral enhancement. Chronic or treated lesions may be calcified.
3. **Management.** Treatment is usually achieved with metronidazole orally or intravenously for 7 to 10 days. Additional treatment should be undertaken for gastrointestinal intraluminal exposure including paromomycin. Rarely, complications including erosion of the cyst into surrounding structures or rupture into the peritoneal cavity can occur.

C. Echinococcal cysts (hydatid cysts) are the most common hepatic cystic lesions throughout the world, more so in developing nations. Multiple strains exist, all carried by an animal host and with unique geographic ranges.

1. **Presentation.** Signs and symptoms include right upper quadrant pain and hepatomegaly.
2. **Diagnosis.** Imaging is the preferred diagnostic test; aspiration should not be performed as the initial diagnostic test, as spillage of cyst contents can result in spread of the organisms throughout the peritoneal cavity. A number of serologic tests can be performed, including indirect hemagglutination and enzyme-linked immunosorbent assays.
3. **Management.** Definitive management is through careful cyst aspiration, which can include cyst injection with scolicidal medication (hypertonic saline or alcohol). Careful resection to prevent spillage should be performed if necessary, and patients should be treated perioperatively with albendazole.

D. Intrahepatic biliary cysts, also called simple cysts, are found in

greater than 10% of the population and are more common with age.

1. **Presentation.** Often presenting as incidental findings in the absence of symptoms, these simple cysts do not require additional management and can be observed. Cysts can result in increased abdominal girth, abdominal discomfort, and early satiety. These can also compress adjacent hepatic parenchyma without significant effect on overall synthetic function.
2. **Diagnosis.** The diagnosis of cysts is frequently limited to imaging, with US or MRI being most specific, showing homogeneous hypodense lesions with smooth rounded borders. Cysts may be septated or complex in the setting of prior hemorrhage. Laboratory testing is likely to be normal, and cyst fluid analysis is rarely performed in the absence of concerning symptoms or imaging findings.
3. **Management.** Although cysts can be drained, they frequently recur. Operative management includes fenestration, in which the cyst is unroofed, or complete enucleation. If the cysts contain bile, a communication to the biliary system should be identified and closed. Enucleation or resection of the entire cyst should be performed if there is clinical concern for neoplastic cystic lesions including cystadenoma or cystadenocarcinoma, which are rare, and the entire cyst wall should be evaluated by pathology. Irregular or abnormally thickened walls and mural nodules should increase suspicion of a tumor or malignancy. Liver transplantation may be necessary for rare cases of marked hepatomegaly in the setting of symptomatic polycystic disease not amenable to fenestration or resection.

MALIGNANT PATHOLOGY

I. METASTATIC DISEASE.

Metastatic disease is the most common malignancy affecting the liver in the united states. Many gastrointestinal cancers metastasize to the liver via the portal drainage of the gi tract.

A. Colorectal Cancer (CRC)

1. **Presentation.** By far, the single most common primary malignancy responsible for metastases to the liver is CRC. Fifty percent of all patients with CRC present with or develop hepatic metastases during the course of their disease. Foci of intrahepatic disease should be

suspected with high-stage tumors and are identified on staging or surveillance cross-sectional imaging. They rarely contribute to symptoms or other outward signs.

2. **Diagnosis** is regularly made with cross-sectional imaging, either contrasted CT or MRI, at the time of diagnosis or surveillance. These masses appear as homogeneous hypoattenuating lesions, often best appreciated on portal venous phase imaging.
3. **Management.** Surgical resection is associated with 5-year survival of up to 50%, much greater than the 5-year survival for patients not undergoing resection, which is usually less than 20% (*J Clin Oncol.* 2009;27(22):3677–3683). Therefore, optimal management of disease is to achieve complete resection when feasible. Preoperative planning should include updated staging to rule out additional sites of hepatic or extrahepatic metastatic disease, recurrence, or metachronous disease. Resection should aim for microscopically negative margins (R0 resection) without any preference for anatomic versus nonanatomic resection. In the case of synchronous primary colorectal and metastatic hepatic disease, the two sites of disease can be resected simultaneously or sequentially, with no inferior strategy in terms of morbidity or mortality (*Br J Surg.* 2014;101(6):605–612). For patients with a high tumor burden or for tumors in close proximity to vital structures, bridging the patient to surgery can be attempted with additional systemic therapy or procedural treatments such as radiofrequency ablation (RFA) or chemoembolization (see sections Surgical Management, Additional Treatments). Postoperatively, repeat physical examinations, cross-sectional imaging, and CEA levels should be obtained every 3 to 4 months for the first 2 years, then every 6 months through 5 years after diagnosis. For patients who experience intrahepatic recurrence, repeat resections can be performed if adequate functional liver remnant would remain and the patient's overall health and prognosis is acceptable.

B. Neuroendocrine Tumors. Metastases to the liver from primary tumors of the gastrointestinal system can happen in up to 75% of patients with neuroendocrine tumors and confer a poorer prognosis (less than 50% 5-year overall survival compared with greater than 75% for patients without metastases) (*HPB.* 2010;12:361–379). Once these tumors deposit in the liver, they can become symptomatic since factors

produced by the primary tumors are limited to the portal circulation and metabolized, but factors from intrahepatic disease can be released systemically and result in symptoms including flushing, diarrhea, and/or nausea. Indications for resection of these metastases can therefore include symptomatic palliation in addition to treatment in the setting of limited effective chemotherapeutic options and improved long-term survival. R0 (negative margins) resection has not been associated with improved survival.

II. HEPATOCELLULAR CARCINOMA (HCC). HCC is the most common primary liver tumor, with an annual incidence in the United States of approximately 6 cases per 100,000 individuals (*Hepatology.* 2014;60(5):1767–1775). HCC is one of the few cancers with a rising incidence, attributable to increased rates of cirrhosis from a number of primary diagnoses including hepatitis C, as well as PBC, PSC, autoimmune hepatitis, alcohol abuse, nonalcoholic steatohepatitis (NASH), and hereditary disorders such as hemochromatosis. Hepatitis B viral infection is a major risk factor as well, even in the absence of cirrhosis.

A. Presentation. Presenting symptoms for HCC are vague and may include weight loss, weakness, and dull, persistent epigastric or right upper quadrant pain.

B. Diagnosis. HCC may be associated with laboratory abnormalities although these can be difficult to interpret in the setting of chronic liver disease. For high-risk patients (particularly those with chronic hepatitis B or cirrhosis), screening with US with or without AFP is recommended (*Hepatology.* 2018;67(1):358–380); elevations of AFP are not specific but should prompt additional studies. Imaging is critical to the surveillance and diagnosis of HCC. HCC is unique in that **pathologic diagnosis is not necessary; the diagnosis and subsequent treatment decisions can be made based on imaging alone in most cases**. On multiphasic CT or MRI, HCC exhibits hyperenhancement relative to the background liver on the arterial phase with contrast washout (hypoenhancement) relative to the background liver in the portal venous or delayed phases (Fig. 21-3). The specificity of the imaging diagnosis for HCC nears 100% when applied using explicit criteria in sufficiently at-risk patients. These criteria have been standardized by the **Liver**

Reporting and Data System (LI-RADS), established by the American College of Radiology, and recently adopted by the American Association for Study of Liver Disease (AASLD) (*Hepatology.* 2018;67(1):358–380). Categories range from "definitely benign" (LR-1) to "definitely HCC" (LR-5) based on a number of features including size/growth, arterial phase hyperenhancement, "washout," and delayed enhancing capsule appearance.

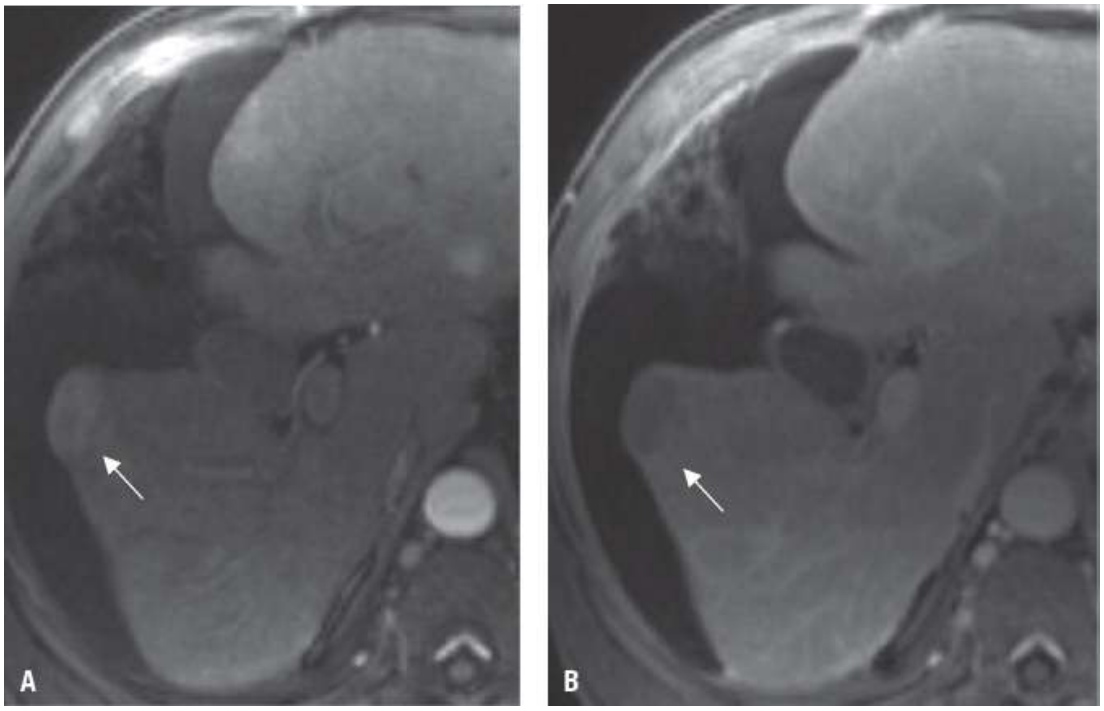


FIGURE 21-3 Hepatocellular carcinoma (HCC)—multiphase liver MRI shows mass hyperenhancement on arterial phase image (**A,** *arrow*) and washout appearance on portal venous phase image (**B,** *arrow*) relative to background liver. Dynamic multiphase imaging is essential for demonstrating features of HCC. These features in combination allow for noninvasive definitive diagnosis of HCC.

C. Management. Without treatment, HCC has a poor prognosis. Treatment options depend on resectability and the patient's overall condition including his or her suitability for transplantation, if available.

1. **Anatomic surgical resection** can be a successful treatment strategy for patients with normal background liver or with early cirrhosis without portal hypertension (Child–Pugh class A). This pool of patients may be quite small, depending on the prevalence of hepatitis B viral infection in the population. Careful assessment of future liver remnant (FLR) should be undertaken, and pathologic assessment of

the baseline function of the surrounding liver through biopsy should be considered. Surgeons should aim for complete anatomic resections with negative margins to 1 cm. Five-year overall survival rates after resection for HCC are greater than 50%, although recurrence rates are quite high (*Br J Surg.* 2012;99(12):1622–1629).

2. **Orthotopic liver transplantation (OLT)** is considered an ideal treatment option for patients with HCC as it removes the malignancy in addition to the background liver that is already predisposed to metastatic or metachronous disease. A number of standardized criteria for OLT have been proposed, with the Milan criteria being most common. Mazzaferro et al. demonstrated that patients pathologically staged with a single tumor less than 5 cm or patients with three or fewer tumors with the largest measuring less than 3 cm without vascular invasion or metastases experienced 4-year actuarial survival of 75%, with recurrence-free survival of 83% (*N Engl J Med.* 1996;334(11):693–699). These criteria, now referred to as the **Milan criteria**, are equivalent to T2 stage and have been adopted by UNOS as a primary metric for transplant eligibility. Many centers are enrolling patients in protocols as a bridge to transplantation, with regional therapy being utilized most commonly, including intra-arterial therapy (transarterial chemoembolization [TACE] or yttrium-90 [Y-90]), or direct ablation (see sections Surgical Management, Additional Treatments).
3. Treatment options for patients who are not candidates for resection or transplantation are limited to palliative options of systemic therapy and/or hepatic-directed therapies. Conventional cytotoxic chemotherapies have not shown adequate effectiveness as neoadjuvant or adjuvant treatments. Sorafenib, a tyrosine kinase inhibitor, has shown modest benefit in patients with advanced HCC (*N Engl J Med.* 2008;359:378–390), with median survival prolongation of 2.8 months in such patients.
4. Fibrolamellar HCC is a rare form of liver cancer diagnosed in younger patients without background liver disease. These malignancies are more often resectable and may have a better prognosis than HCC.

III. CHOLANGIOCARCINOMA. This is the second most common primary

hepatic malignancy, with an incidence of 2 cases per 100,000 persons in the united states (*Hepatology.* 2014;60(5):1767–1775). Intrahepatic or mass-forming cholangiocarcinoma (ICC) accounts for 10% of all cholangiocarcinoma and may arise from second-order or smaller intrahepatic ducts. More commonly, cholangiocarcinoma involves the larger extrahepatic ducts as a periductal infiltrating variant: 65% of ICCs are located distally in the bile duct and are treated like periampullary tumors, usually with Whipple resection, and 25% of ICCs are hilar and typically require combined liver and biliary tract resection in patients with resectable tumors. Patients with more advanced disease may present with a combination of periductal infiltrating tumor and an intrahepatic mass. A rare variant of cholangiocarcinoma is the intraductal or papillary variant, which is associated with a better prognosis than the other variants.

A. Presentation. Unlike extrahepatic cholangiocarcinomas, patients with mass-forming ICC are less likely to present with jaundice and may instead have dull right upper quadrant pain, weight loss, and laboratory abnormalities including elevated alkaline phosphatase. Patients with PSC are at increased risk for cholangiocarcinoma.

B. Diagnosis. While ICC may have a characteristic appearance on imaging, unlike HCC, the imaging diagnosis is not considered definitive by itself. Often, tissue biopsy is performed for diagnostic confirmation, particularly if the tumor is arising in the setting of cirrhosis and distinction between HCC and ICC is relevant for transplantation planning. Diagnostic imaging with multiphase contrast-enhanced MRI/MRCP or CT is recommended. The imaging features of ICC are like those seen with metastatic adenocarcinoma, including peripheral or rim arterial phase hyperenhancement, delayed central enhancement, peripheral washout appearance, and targetoid appearance on hepatobiliary phase imaging and diffusion (*Abdom Radiol.* 2018;43(1):149–157). When arising in the absence of background liver disease, correlation with any extrahepatic primary malignancy, tumor markers, and potentially tissue sampling is recommended. When arising in a patient with cirrhosis, these features are described by LI-RADS as LR-M (probable or definite malignancy, not specific for HCC), and biopsy or multidisciplinary discussion to determine next steps would be appropriate. Other features that may favor ICC include peripheral capsular retraction, ductal dilation, severe ischemia/necrosis, and

marked diffusion restriction. Histology of both periductal infiltrating and mass-forming ICC may demonstrate the presence of dense fibrous matrix often with peripheral cellularity and diffuse spreading/infiltrating margins. Periductal infiltrating tumors often arise in the setting of background PSC and may present as a new dominant stricture, nodular soft tissue associated with a duct, or new vascular encasement and occlusion with associated biliary duct dilation. MRCP and liver MRI/CT can also be helpful in defining the extent of bile duct involvement (Bismuth–Corlette) and of vascular involvement for possible surgical planning.

C. Management. Resection is the only potential curative therapy. However, resection is not possible in many cases due to the central location of these tumors. As with other cholangiocarcinomas, radiation therapy and chemotherapy with gemcitabine plus cisplatin are commonly employed, although overall prognosis remains poor (*Br J Cancer.* 2009;101(4):621–627 and *J Clin Oncol.* 2015;33(24):2617–2622).

SURGICAL MANAGEMENT

I. TECHNIQUES OF HEPATIC TRANSECTION. Multiple techniques for hepatic resection have been described, with a similarly high number of surgical devices available for use. Despite the approach, care should be taken to perform safe transection with control of vascular structures in combination with techniques to prevent posthepatectomy bile leak or hemorrhage. Techniques include combinations of clamp–crush, electrocautery, water dissector, and devices employing US, radiofrequency, or other electrosurgical sealing techniques. Vessels or bile duct branches are then divided using these devices or ties, clips, or staples.

A. The **Pringle maneuver** (isolation of the portal triad) and subsequent **cross-clamping** of hepatic inflow can greatly aid in control of bleeding. This can be helpful in reducing overall blood loss but should be used sparingly, as extended periods of inflow occlusion can lead to hepatic injury, ischemia, and systemic reperfusion injury. The ideal duration of inflow occlusion is difficult to study although several groups recommend no more than 15 to 20 minutes at a time, with at least 5

minutes between periods of Pringle clamping and cumulative clamp time of under 120 minutes.

B. Intraoperative hemodynamic management of patients undergoing liver surgery should be thoroughly discussed before and throughout a case in conjunction with anesthesia providers. Depending on a center's practice patterns and the anticipated extend of resection, arterial blood pressure monitors and central venous access may be necessary prior to the start of a case, and postoperative observation in intermediate or intensive care units should be considered. Low target central venous pressures (5 mm Hg or less) have been shown to reduce blood loss and blood transfusions (*J Am Coll Surg.* 1998;187(6):620–625). Providers must be mindful of the potential consequences of this approach on renal perfusion.

C. Minimally invasive hepatectomy through laparoscopy has become increasingly common, with excellent results, including lower morbidity and length of stay compared to patients undergoing open procedures (*J Gastrointest Surg.* 2016;20(9):1608–1617). Patient selection and surgeon experience play an important role in optimizing outcomes and selecting the safest surgical approach.

II. COMPLICATIONS

A. Posthepatectomy bile leak is defined as a bilirubin concentration in drain fluid at least three times that of the serum bilirubin concentration on or after postoperative day 3, or the need for radiologic or operative intervention due to biliary collections or bile peritonitis (*Surgery.* 2011;149(5):680–688). This complication occurs in up to 10% of patients and is a major cause of postoperative morbidity and extended length of stay.

B. Posthepatectomy liver failure is a major cause of perioperative mortality and represents the impaired ability of the remnant liver to perform synthetic, excretory, and detoxifying functions. It is defined as an elevated INR and hyperbilirubinemia above normal on or after postoperative day 5; if these values are elevated preoperatively, increasing INR and bilirubin on or after postoperative day 5 is used (*Surgery.* 2011;149(5):713–724).

III. ADDITIONAL TREATMENTS

A. Portal vein embolization (PVE) can aid in increasing the FLR. FLR can be increased by about 10% at 1-month postprocedure, with additional growth thereafter, depending on underlying liver function (*J Am Coll Surg.* 2014;291(4):620–630). In cases of resectable lesions on both sides of the liver, alternative strategies must be sought to achieve an adequate FLR and appropriate treatment. Two-stage hepatectomy can be performed, where one affected side is resected and, with an interval of time and systemic therapy as necessary for the underlying pathology, the second side may be amenable to resection with sufficient FLR. **Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS)** is a newer approach to improving the FLR and to allow marked increases in the FLR in a short duration. First, portal vein ligation is performed, but with hepatic artery inflow preservation to the planned future site for resection, along with hepatic transection (phase I). Following adequate hepatic hypertrophy, usually in 1 to 2 weeks, a second surgery is performed to resect the diseased liver (phase II).

B. A number of other procedures can be done to treat liver lesions. These can be performed by surgeons or other proceduralists such as interventional radiologists. These include TACE, RFA, Y-90 radioembolization, and stereotactic body radiation. These may be used as definitive treatments, particularly in patients who are not surgical candidates, or as a bridge to surgery or transplant.

CHAPTER 21: SURGICAL DISEASES OF THE LIVER

Multiple Choice Questions

1. **A 30-year-old female is referred to your office for a second opinion after diagnosis of an incidental hepatic mass, found on CT scan as part of a workup for vague abdominal pain at an outside hospital. You are able to view her imaging: an MRI shows a 3-cm mass in the right hemiliver, with heterogeneous appearance and no retention of an administered hepatocyte-specific contrast agent (gadoxetate disodium). The lesion is not hyperintense on T2-weighted imaging. What diagnosis should you favor?**

   a. Simple biliary cyst
   b. Focal nodular hyperplasia
   c. Hemangioma
   d. Hepatic adenoma
   e. Hepatocellular carcinoma

2. **You are called to evaluate a 30-year-old male in the emergency room. He presented with fever and right upper quadrant pain. When obtaining his history, he informs you that he has had some diarrhea and recently traveled in rural Mexico. You obtain an ultrasound showing a cystic mass in the right liver. Serologic testing confirms an amebic abscess. What is the next best treatment plan?**

   a. Aspiration
   b. Cyst injection with alcohol
   c. Hepatic resection
   d. Albendazole
   e. Metronidazole

3. **A patient is referred to you by your hospital's colorectal surgery group. This is a 60-year-old female who had a rectal cancer resected 2 years ago and now has multiple hepatic lesions identified on surveillance CT scan. She has few other**

comorbidities and good baseline functional status. Her imaging shows six discrete lesions, all around 3 cm: four are in the right hemiliver and two are in segment IV. None are amenable to wedge resection. Resection with a right trisectionectomy would leave her with an estimated future liver remnant under 20%. Which of the following would be an *inadequate* treatment option?

a. Trisectionectomy
b. Portal vein embolization followed by trisectionectomy
c. Right hepatectomy and radiofrequency ablation of the lesions in segment IV
d. Two-stage resection with right hepatectomy and systemic chemotherapy followed by possible resection of the lesions in segment IV
e. ALPPS procedure

4. **The same patient as in question 3 elects to undergo two-stage resection. You see her back in clinic for a repeat examination prior to the second stage. At this visit, she reports she has not tolerated systemic chemotherapy well and has issues with itching, jaundice, and "mildly" elevated liver enzymes. Surveillance imaging of her liver shows persistent lesions as well as fatty infiltration, increased nodularity, and poor hypertrophy of the remaining segments. She is very motivated for the second stage of surgery. What is the next best step?**

a. Proceed with surgery
b. Liver biopsy
c. Continue systemic therapy and reimage in 3 months
d. Cessation of all therapies
e. Portal vein embolization

5. **You are evaluating a patient with liver failure due to alcohol-induced cirrhosis in a hepatology clinic. No recent laboratory data exist for this patient in your medical records and you want to calculate a MELD score. Which selection has the appropriate combination of lab values to calculate MELD?**

a. Bilirubin, INR, albumin
b. Bilirubin, INR, albumin, sodium
c. Bilirubin, INR, creatinine, sodium
d. Bilirubin, INR, creatinine, alkaline phosphatase
e. INR, creatinine, alkaline phosphatase

22 Surgical Diseases of the Biliary Tree

Matthew S. Strand and Adeel S. Khan

I. CHOLELITHIASIS

A. Asymptomatic Gallstones

1. **Presentation.** The incidence of cholelithiasis is approximately 6% in men and 9% in women. Asymptomatic gallstones are usually discovered on routine imaging studies or incidentally at laparotomy for unrelated problems.
2. **Management.** Prophylactic cholecystectomy is generally not indicated in patients with asymptomatic gallstones. However, it may be warranted in patients who are at risk for developing gallbladder cancer (e.g., porcelain gallbladder), those undergoing gastric bypass, or patients with hereditary hemolytic anemias.

B. Symptomatic Gallstones

1. **Presentation. Biliary colic** is the main symptom and is caused by temporary obstruction of the gallbladder outlet by a gallstone. Pain is classically provoked by a fatty meal, but may wake the patient from sleep. Typically, the pain lasts 30 minutes to several hours and localizes to the epigastrium or right upper quadrant (RUQ), with occasional referred pain to the back or right shoulder. Associated symptoms include nausea and vomiting. Fever is typically absent.
2. **Diagnosis.** Physical signs can include RUQ tenderness, however most patients have few abdominal findings on examination between attacks. Stones are diagnosed by ultrasound (US) visualization of echogenic structures with posterior acoustic shadows within the gallbladder. Unless the patient has acute or chronic cholecystitis, gallstones are usually the only sonographic finding. The bile ducts should be assessed for dilation or choledocholithiasis.

3. **Treatment. Laparoscopic cholecystectomy** (**LC**) is the appropriate treatment for the majority of patients with symptomatic gallstones, as described below.

C. Acute calculous cholecystitis is initiated by obstruction of the **cystic duct** by a gallstone, just as with biliary colic, except that the gallstone becomes impacted resulting in outlet obstruction, dyskinesia, increased luminal pressure, and inflammation of the gallbladder.

1. **Diagnosis** can be made according to the **Tokyo Guidelines** by a combination of local and systemic signs of inflammation, correlated with imaging findings (Table 22-1). Local inflammatory signs include RUQ pain and tenderness as well as **Murphy sign**, which is inspiratory arrest during deep palpation of the RUQ. Systemic signs include fever and leukocytosis. Jaundice is rare and usually suggests biliary obstruction, either due to choledocholithiasis, cholangitis, or external compression of the CBD by a gallstone (**Mirizzi syndrome**). Leukocytosis is usually between 12,000 and 20,000 cells/μL; a more severe leukocytosis suggests complications, such as gangrene, perforation, or cholangitis. Liver function tests (LFTs) should be obtained and may be abnormal if choledocholithiasis or biliary obstruction is present. Traditionally, US has been the imaging study of choice when cholecystitis is suspected and may reveal **gallbladder wall thickening** (>5 mm), **pericholecystic fluid**, and a **sonographic Murphy sign**, which is tenderness over the gallbladder when compressed by the US probe. Computed tomographic (CT) scanning is frequently performed to evaluate acute abdominal pain, though it is less sensitive than US. Signs of acute cholecystitis on CT include gallbladder wall thickening, pericholecystic fluid, edema, and emphysematous changes. **Radionuclide cholescintigraphy** with hepatic 2,6-dimethyliminodiacetic acid (HIDA) may be useful in equivocal cases but is not often needed. Nonfilling of the gallbladder after 4 hours may be diagnostic of acute cholecystitis on a HIDA study, though prolonged fasting, chronic cholecystitis, and sphincter of Oddi dysfunction (SOD) can cause false-positive results.

TABLE 22-1 Severity Grading for Acute Cholecystitis

Grade	Criteria

Mild (grade 1)	Acute cholecystitis that does not meet criteria for a more severe grade
Moderate (grade 2)	The presence of one or more of the following: • Leukocytosis >18,000 cells/mm^3 • Palpable tender mass in the right upper quadrant • Duration >72 hr • Marked local inflammation including biliary peritonitis, pericholecystitis abscess, hepatic abscess, gangrenous cholecystitis, and emphysematous cholecystitis
Severe (grade 3)	Presence of any organ dysfunction (e.g., hypotension, mental status changes, respiratory failure, acute renal failure, hepatic or hematologic dysfunction)

From Yokoe M, Hata J, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci*. 2018;25(1):45–51.

2. **Management.** Initial steps for patients with acute cholecystitis include intravenous fluids and parenteral antibiotics. For mild and moderate acute cholecystitis, early LC is recommended. For patients with severe acute cholecystitis or significant medical comorbidities, **percutaneous cholecystostomy** can be performed as a temporizing measure, with either delayed cholecystectomy after resolution of inflammation, or percutaneous stone extraction if surgical risk remains prohibitively high. Numerous trials have compared early versus delayed (6 weeks) LC for acute cholecystitis. A meta-analysis of outcomes in over 1,600 patients showed that LC within 7 days of symptom onset resulted in a lower incidence of wound infection and a shorter hospital stay than delayed LC, with no difference in mortality, morbidity, biliary injury, or conversion to open operation (*Br J Surg*. 2015;102(11):1302–1313). Controversy still exists about the relationship between operation in the acute phase of inflammation and bile duct injury. As a general rule of thumb, early LC is indicated

for patients with <72 hours of symptoms once fully resuscitated, and for any low risk patient, regardless of symptom duration.

D. Choledocholithiasis is usually due to gallstones that originate in the gallbladder and pass through the cystic duct into the common bile duct (CBD).

1. **Diagnosis. Jaundice** is the most common manifestation of uncomplicated choledocholithiasis, often accompanied by a history of biliary colic. LFTs reveal elevation in bilirubin and alkaline phosphatase. US usually demonstrates stones in the bile duct and bile duct dilation, though visualization of the CBD may be limited by bowel gas or patient habitus. The diagnosis may be confirmed by noninvasive means through MRI/**MRCP** or by more invasive methods utilizing cholangiography, either via **endoscopic retrograde cholangiopancreatography** (**ERCP**) or **percutaneous transhepatic cholangiography** (**PTC**). The latter techniques have the advantage of potentially being both diagnostic and therapeutic. Occasionally, the diagnosis of choledocholithiasis is made by **intraoperative cholangiography** (**IOC**) at the time of cholecystectomy.
2. **Management** depends on available expertise and clinical picture. Choledocholithiasis in the absence of cholangitis should be managed with stone retrieval via ERCP and cholecystectomy. Patients with US evidence of a CBD stone, bilirubin levels >4 mg/dL, clinical ascending cholangitis, or dilated CBD on US with a bilirubin >1.8 mg/dL are considered high risk for having choledocholithiasis and should undergo ERCP prior to interval LC (*Ann Surg.* 1994;220(1):32–39). For intermediate risk patients, management is controversial. Most patients can undergo LC with IOC. If stones are seen, administration of IV **glucagon**, use of irrigation to flush the CBD, blind passage of balloon catheters or stone baskets, or CBD exploration via **choledochoscopy** can be attempted depending on expertise available. If clearance of the CBD is unsuccessful, postoperative ERCP is indicated. For patients who are not candidates for cholecystectomy, ERCP with **sphincterotomy** (**endoscopic sphincterotomy** [**ES**]) and stone removal is the treatment of choice. Placement of a percutaneous cholecystostomy tube and extraction of gallstones can also be considered, though the risk of additional gallstone formation remains.

E. Biliary pancreatitis is caused by obstruction of the pancreatic duct by a gallstone that has been expelled by the gallbladder and into the CBD. Small (~2 mm) stones pose the greatest risk as they can easily pass through the cystic duct compared to larger stones. The management of severe pancreatitis is discussed elsewhere in this manual. After resolution of pancreatitis, cholecystectomy is indicated during the index admission to prevent additional episodes, though occasionally severe pancreatitis may preclude this. IOC should be conducted at the time of cholecystectomy to confirm that the CBD is free of stones. In patients in whom cholecystectomy is contraindicated, ES may be protective against further attacks of pancreatitis.

F. Gallstone ileus (see also in Chapter 20) is a rare cause of small bowel obstruction (SBO) in which a gallstone erodes through the gallbladder into adjacent bowel, most commonly the duodenum, creating a cholecystoenteric fistula. The stone migrates distally and most commonly lodges at the ileocecal valve. **Rigler triad** of air in the biliary tree, SBO, and ectopic gallstone may be present on abdominal x-ray. Treatment is exploratory laparotomy and removal of the obstructing gallstone by milking it back to an enterotomy made in healthy intestine. The entire bowel should be searched for other stones, and cholecystectomy with fistula closure should be performed if the patient is stable and inflammation is minimal, otherwise the fistula may be left in place and potentially addressed at a later time, if necessary.

G. Laparoscopic Cholecystectomy

1. **Indications.** LC is widely available, has low complication rates, and is associated with excellent recovery. Contraindications include peritonitis, acute cholangitis, and inability to tolerate general anesthesia.
2. **Technique.** Conclusive identification of the cystic duct and artery is essential to prevent iatrogenic biliary injury. The **Critical View of Safety Technique** pioneered at Washington University in St. Louis comprises three criteria that should be met prior to division of the putative cystic duct and artery (see Fig. 22-1) (*J Am Coll Surg.* 1995;180(5):638–639). First, the **triangle of Calot is dissected free** of fat, fibrous, and areolar tissue. Second, the **lower one-third of the gallbladder must be dissected off the liver bed**. Third, **only two structures** (i.e., the cystic duct and artery) **are seen entering the**

gallbladder. Once these criteria have been met, the critical view has been achieved and these structures may be safely divided and the gallbladder removed from the liver bed. IOC may be used to assist with anatomical definition, especially when the critical view is not achieved. When the ductal and vascular structures in the triangle of Calot cannot be safely identified, a **subtotal cholecystectomy** should be considered which involves removal of the anterior wall of the gallbladder and leaving a drain near the residual infundibulum. The cystic duct can be sutured closed from inside the gallbladder (**reconstituting subtotal cholecystectomy**) or left as is (**fenestrating subtotal cholecystectomy**). Patients with jaundice, cholangitis, pancreatitis, or imaging evidence of choledocholithiasis should undergo IOC. In the absence of this, CBD stones are less likely and IOC is not required, though some surgeons perform IOC routinely. IOC can also be used to clarify anatomical relationships, if needed.

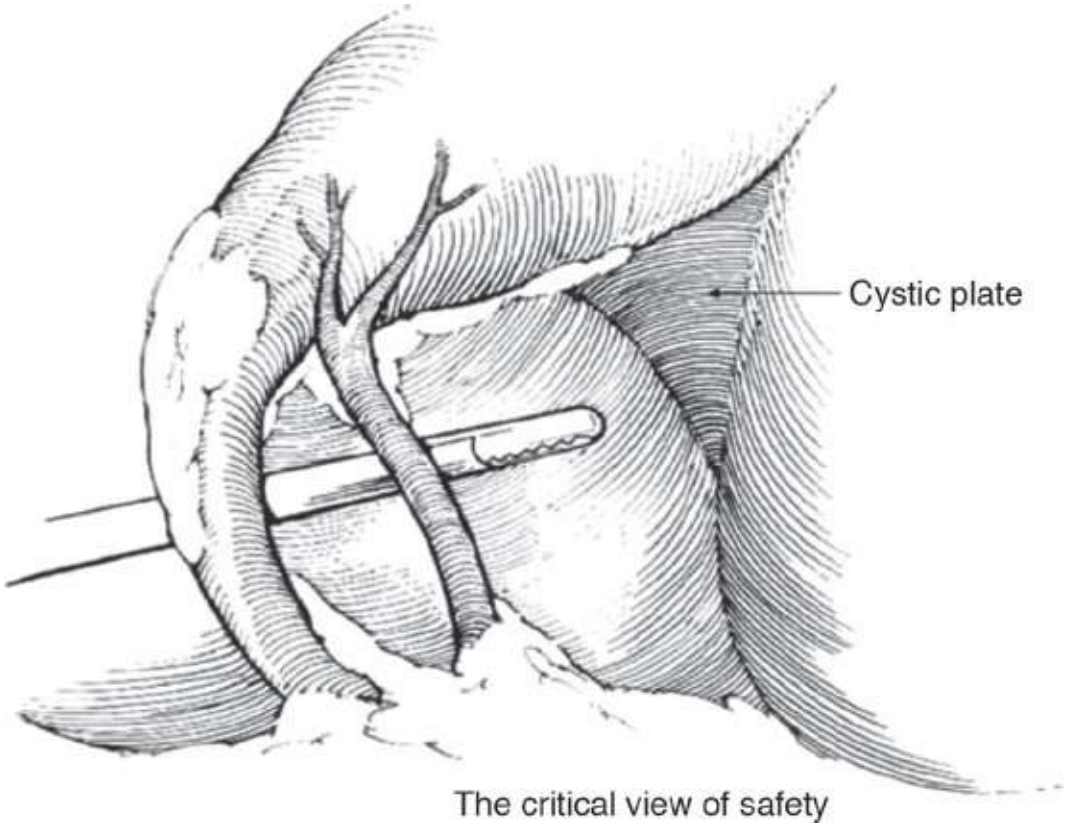


FIGURE 22-1 Demonstrating the critical view of safety technique: Calot's triangle is dissected free of all excess tissue, the base of the liver bed is exposed at the cystic plate (noted), and the only two structures entering the gallbladder are the cystic duct and artery. (Strasberg SM, Soper N. *J Am Coll Surg*. 1995;180(5):638–639.)

3. **Complications.** LC has historically been associated with a higher incidence (~2.5/1,000) of major bile duct injury than open cholecystectomy, though recent studies seem to show equivalent rates. Nonetheless, biliary injury during LC is a serious problem that is further discussed below. Bowel or hepatic arterial injury is very rare. Spilled and retained gallstones can rarely lead to complications such as abscess and fistula formation.

H. Open cholecystectomy is performed in patients who have contraindications to LC or those who require conversion from LC. Conversion to an open operation in the face of a difficult laparoscopic procedure should never be viewed as a surgical failure but rather as a way to avoid potential injury to the patient. Emergent cholecystectomy, male sex, age greater than 60 years, obesity, severe gallbladder inflammation, choledocholithiasis, and prior upper abdominal surgery are risk factors for conversion to open cholecystectomy.

II. ACALCULOUS CHOLECYSTITIS

A. Presentation. Acalculous cholecystitis typically occurs in severely ill hospitalized patients, especially those with a history of hypotension. It is also seen in those with prolonged NPO status, dependence on parenteral nutrition, episodes of systemic sepsis, or multiorgan system failure. Presentation depends largely on the patient's concurrent medical conditions and should be considered in the differential diagnosis during the infectious workup of a severely ill patient. Alert patients may be symptomatic, but afflicted individuals are often intubated or incapacitated due to concurrent medical illness, hence a high index of suspicion is required for diagnosis.

B. Diagnosis. In sedated patients, leukocytosis and abnormal LFTs, although variable, may be the only indications of acalculous cholecystitis, thus imaging is relied upon heavily for diagnosis. US is almost universally the first test of choice, but if the diagnosis is unclear, HIDA or cross-sectional imaging (CT or MRI) can be used to improve the diagnostic index. In difficult cases, **percutaneous cholecystostomy** may be both diagnostic and therapeutic because an infected gallbladder can be decompressed and inciting stones extracted.

C. Management of acalculous cholecystitis involves parenteral antibiotics, NPO status, and treatment of any comorbidities. Initial treatment

involves decompression of the gallbladder, typically with percutaneous cholecystostomy. Definitive treatment is interval cholecystectomy.

III. BENIGN STRICTURES AND BILE DUCT INJURIES. Stricture or injury may occur in association with a number of conditions, including pancreatitis, choledocholithiasis, primary sclerosing cholangitis (PSC), prior hepatic transplantation, trauma, or iatrogenic injury after instrumentation or operation. LC is the leading cause of iatrogenic bile duct injuries and subsequent benign strictures. Biliary malignancy may masquerade as a benign stricture. Attempts to differentiate between the two etiologies should be made prior to surgery because the patient may not be a candidate for a curative resection if an advanced cancer is found.

A. Risk factors for intraoperative bile duct injury during LC include acute and chronic inflammation, presence of a large impacted stone, variant anatomy, and emergency surgery. Technical factors include such issues as inadvertent injury to the bile ducts with electrocautery, failure to develop the critical view of safety, lack of operator experience, or inadequate maintenance of laparoscopic instruments.

B. Classification. A widely accepted classification scheme has been developed at Washington University in St. Louis (*J Am Coll Surg.* 1995;180:101–125). Type A injuries are cystic duct leaks or leaks from small ducts in the liver bed. Type B and C injuries involve an aberrant right hepatic duct. Type B represents an occluded segment, whereas type C involves open drainage from a transected duct. Type D injuries are lateral injuries to the extrahepatic bile ducts. Type E injuries (subtypes 1 to 5) are derived from the **Bismuth classification** and represent transections or occlusions at various levels of the CBD, with higher numbers representing higher level of injury.

C. Presentation depends on the type of injury. Only 25% of major bile duct injuries are recognized at the time of the initial procedure. Intraoperative signs of a major ductal injury include unexpected bile leakage or abnormal IOC. If an injury is not recognized intraoperatively, the patient usually presents with symptoms within 1 week and almost always within 3 to 4 weeks of operation. Patients with a bile leak often present with RUQ pain, fever, and sepsis secondary to **biloma** while those with biliary occlusion present with jaundice.

D. Diagnosis. Imaging with CT or MRI is useful for detecting abdominal

bile collections that require percutaneous drainage. **MRCP with angiography** is now often the initial imaging test of choice because of its ability to define the biliary anatomy as well as any associated vascular injuries. Ongoing bile leaks can also be diagnosed by HIDA scan. ERCP and/or PTC are often needed for diagnostic and therapeutic purposes including biliary decompression in cases of bile duct occlusion or for stenting for strictures or leaks.

E. Management depends on the presentation. If the injury is identified at the time of the initial procedure, the surgeon should only proceed to open exploration to control life-threatening hemorrhage or to perform bile duct repair if trained in complex techniques in hepatobiliary surgery. Otherwise, the patient should be resuscitated, a drain should be placed in the RUQ, and the patient should be referred immediately to a hepatobiliary specialist. Minor, nonsegmental injuries to bile duct and cystic duct stump leaks may be successfully managed with ERCP with sphincterotomy and stenting. Occlusive injuries require decompression of the proximal system via PTC. Ideally, if a reparable injury is identified early, the procedure should be done within the first few days after the initial operation when inflammation is minimal. In delayed diagnosis, temporization for at least 8 weeks with internal and external biliary decompression can allow the acute inflammation to resolve. If there is a concern about a concomitant vascular injury, definitive repair should be delayed to allow for ischemic demarcation of the injured duct, which should be excised and not incorporated into the repair. Control of sepsis, percutaneous drainage, and adequate nutrition should be optimized before definitive repair.

F. Operative repair depends on the extent and level of injury, but is often best accomplished with a Roux-en-Y hepaticojejunostomy after debridement of the bile duct to viable tissue. All bile ducts must be accounted for, and an adequate blood supply must be apparent for each. A tension-free mucosa-to-mucosa anastomosis with fine absorbable suture is desired. Excellent long-term outcomes have been described, with anastomotic stricture the most common, yet infrequent, complication.

IV. ACUTE CHOLANGITIS

A. Presentation. *Acute cholangitis* is a bacterial infection of the biliary

tree associated with obstruction of the ductal system, most commonly from choledocholithiasis. Benign and malignant strictures of the bile ducts or at biliary-enteric anastomoses, or occlusion of indwelling stents or tubes, are additional causes. Patients present with a spectrum of disease severity, ranging from subclinical illness to acute toxic cholangitis. Fever is present in >90% of patients. **Charcot triad** (fever, jaundice, and RUQ pain) is present in only 50% to 70% of patients, and **Reynolds pentad** (Charcot triad with hemodynamic instability and mental status changes) in less than 10% of patients, mostly in the elderly and those with a septic course.

B. Diagnosis. Laboratory data demonstrate leukocytosis and LFT derangements suggesting cholestasis. US or CT can reveal gallstones and biliary dilation, but definitive diagnosis is made by ERCP or PTC. These studies are diagnostic and therapeutic because they demonstrate the level of obstruction and allow culture of bile, removal of stones or indwelling foreign bodies, and placement of drainage catheters, if necessary.

C. Treatment. Initial management of cholangitis includes IV hydration and antibiotic coverage of gram-negative and anaerobic organisms, followed by biliary decompression, usually with either ERCP or PTC. If unavailable, operative intervention to decompress the biliary tree is indicated, though it should usually be limited to extraction of obvious stones and insertion of a T-tube into the CBD. Cholangitis in patients with indwelling tubes or stents generally requires stent removal and replacement. Definitive operative therapy for benign or malignant biliary tract strictures should be deferred until a later date.

V. BILIARY DYSKINESIA. Biliary dyskinesia is seen in patients with typical symptoms of biliary colic but without evidence of gallstones. Other causes of RUQ pain should be ruled out. Diagnosis relies on calculation of a gallbladder ejection fraction from a HIDA scan. An ejection fraction of <35% is suggestive of biliary dyskinesia. Though cholecystectomy results in improvement or relief of symptoms in more than 90% of patients with reduced gallbladder ejection fraction, patients with a normal ejection fraction still had relief of symptoms in 85% of cases, making the utility of ejection fraction unclear for determining operative candidacy (*Aliment Pharmacol Ther.* 2003;18(2):167).

VI. SPHINCTER OF ODDI DYSFUNCTION.

SOD is a diagnosis of exclusion that may present with either biliary or pancreatic manifestations. In biliary SOD, patients have biliary pain, but no gallstones. In some cases, cholecystectomy has been performed but biliary pain persists. Episodes of pain correlate with elevated LFTs and a dilated CBD. Patients with suspected SOD that meet **Rome IV criteria** should undergo sphincter of Oddi manometry, with a pressure >40 mm hg or a nonrelaxing sphincter indicative of dysfunction. Treatment is ES.

VII. PRIMARY SCLEROSING CHOLANGITIS

A. Presentation. PSC is an autoimmune cholestatic disorder characterized by a progressive fibrous stricturing in the bile ducts. PSC afflicts 1% to 5% of those with inflammatory bowel disease (IBD), and approximately 75% of patients with PSC have or will develop IBD. PSC is a risk factor for **cholangiocarcinoma**, affecting up to 10% to 20% of patients. Prolonged disease ultimately leads to progressive hepatic failure, characterized by relapses and remissions. Jaundice with pale, acholic stools and dark urine forms the initial clinical picture. With advanced disease, pain in the RUQ, pruritus, fatigue, and weight loss often accompany bouts of cholangitis. Overall, the median length of time from diagnosis to hepatic failure, resulting in death or liver transplantation, is 10 to 12 years.

B. Diagnosis. Physical examination may reveal jaundice and hepatosplenomegaly. Alkaline phosphatase level is almost always elevated, usually out of proportion to the bilirubin, while transaminases are usually mildly elevated. **Perinuclear antineutrophil cytoplasmic antibodies** (**pANCA**) are present in the serum of 80% of patients who have PSC and are highly suggestive but not specific. Cholangiography via ERCP or PTC is the gold standard for diagnosis and demonstrates diffuse and irregular narrowing of the entire biliary tree, with short, annular strictures giving a beaded appearance. CT, MRI, or MRCP may also be helpful.

C. Treatment. Immunosuppressants such as corticosteroids, azathioprine, cyclosporine, and methotrexate may offer symptomatic improvement, however, none of these alters the natural history of the disease. Because of risk for cholangiocarcinoma, close surveillance of patients is needed. The diagnosis is difficult because cholangiocarcinomas also masquerade

as strictures. A dominant biliary stricture or elevated or rising tumor markers (e.g., CA 19-9) should raise the suspicion of cholangiocarcinoma in a PSC patient. PSC has been effectively palliated with endoscopic or percutaneous dilation of strictures, with limited role for surgical resection or bypass in the absence of cholangiocarcinoma. Extensive, diffuse stricture disease with end-stage cirrhosis is an indication for orthotopic liver transplantation (OLT). OLT improves survival and quality of life, and early referral for transplantation is indicated to decrease the risk of developing cholangiocarcinoma. However, disease recurrence can still occur even after liver transplant.

VIII. CHOLEDOCHAL CYSTS. Choledochal cysts are congenital dilations of the biliary tree that may occur in any bile duct but characteristically involve the **common hepatic duct** and CBD. Diagnosis and treatment are essential because the cysts predispose to choledocholithiasis, cholangitis, portal hypertension, and cholangiocarcinoma, which develop in up to 30% of cysts. An anatomic **classification scheme** has identified five distinct types (Table 22-2). Clinical course ranges from biliary obstruction manifesting in neonates to jaundice and abdominal pain in older children. Cysts may be entirely asymptomatic. Initial diagnosis is often made with US and/or CT, but additional evaluation of the cyst should be performed with specific biliary imaging such as ERCP or MRCP. Treatment is primarily surgical and depends on the cyst type (Table 22-2).

IX. BENIGN BILE DUCT TUMORS. Benign bile duct tumors, usually adenomas, are rare and arise from the ductal glandular epithelium and are found most commonly at the ampulla or CBD. These lesions have malignant potential and therefore should be excised. Most patients present with intermittent obstructive jaundice, often accompanied by RUQ pain. Treatment involves complete resection of the tumor with a margin of duct wall. Endoscopic removal or ampullectomy may be feasible for smaller distal lesions, but larger lesions or lesions extending proximally into the CBD or pancreatic duct should be surgically resected via pancreaticoduodenectomy (Whipple), segmental bile duct resection, or hepatectomy, depending on where the tumor is located in the biliary tree. Patients who are not surgical candidates still benefit from sphincterotomy or partial resection to alleviate biliary obstruction.

TABLE 22-2 Choledochal Cyst Classification

Cyst Type	Frequency	Anatomy	Treatment
I	50–85%	Fusiform dilation of the CBD	Excision with Roux-en-Y hepaticojejunostomy
II	2%	Saccular cysts of the extrahepatic bile ducts	Simple excision
III	1–5%	Cysts of the intraduodenal portion of the CBD	Endoscopic unroofing or excision with sphincterotomy
IV	15–35%	Multiple intra- and extrahepatic cysts	Excision with Roux-en-Y hepaticojejunostomy
V (Caroli disease)	20%	Multiple intrahepatic cysts	Resection (if isolated to a portion of the liver) or transplantation

X. CHOLANGIOCARCINOMA

A. Presentation. Jaundice, followed by weight loss and pain, is the most frequently encountered clinical feature at presentation. Cholangiocarcinomas arise from the bile duct epithelium and can occur anywhere along the course of the biliary tree. They are classified according to anatomic location: intrahepatic (20%), extrahepatic upper duct (also called **hilar** or **Klatskin tumor**, 40%), and extrahepatic lower duct (40%), further described in the **Bismuth classification** scheme (Table 22-3). Tumors are locally invasive, spreading along bile ducts, and often metastasize to regional lymph nodes, the liver, and the

peritoneum. Predisposing conditions include male gender, PSC, choledochal cysts, intrahepatic stones, and parasitic infestations such as *Clonorchis* species.

B. Diagnosis. Carbohydrate antigen 19-9 (**CA19-9**) is the most commonly used marker in the diagnosis of cholangiocarcinoma, though inflammation and cholestasis may also elevate the levels. Abdominal MRI or MRCP is the imaging modality of choice and can demonstrate the tumor in relation to the portal structures and is sensitive for intrahepatic metastases. US or CT may be helpful, especially if MR is contraindicated or not tolerated. ERCP is valuable for diagnosing extrahepatic tumors via biliary brushings or biopsy and can also be used for preoperative biliary decompression, which has the advantage of improving liver function prior to resection but carries the risk of cholangitis and increased postoperative infection. Only the less-affected hemiliver should be decompressed so that it remains infection free and hypertrophies while the undrained side atrophies. The side to be resected should be drained only if cholangitis is present or with significant hyperbilirubinemia (>10 mg/dL). A tissue diagnosis is not necessary before proceeding with resection or transplantation, especially in the setting of a characteristic radiographic lesion and elevated CA 19-9 levels. Transperitoneal biopsy should not be undertaken if the patient is a potential liver transplant candidate since it will preclude transplant at some centers.

TABLE 22-3 Bismuth–Corlette Classification of Hilar Cholangiocarcinoma

Type I	Tumor remains below the confluence of the right and left hepatic ducts
Type II	Tumor involves the confluence of the right and left hepatic ducts
Type III	Tumor involves *either* the right *or* the left hepatic duct and extends to secondary radicals
Type IV	Tumor involves secondary radicals of *both* the right *and* left hepatic ducts

C. Treatment. Resection remains the primary treatment of cholangiocarcinoma, although only 15% to 20% are resectable at presentation. Intrahepatic tumors are best treated with hepatectomy. Resectability is assessed with a goal of 1-cm tumor-free margins and maintenance of an adequate **future liver remnant** (**FLR;** discussed in Chapter 21). If there is risk of insufficient FLR, volume optimizing strategies such as preoperative **portal vein embolization** can be used to promote hyperplasia of the FLR. For hilar tumors, surgical resection typically involves removal of the bile duct bifurcation, ipsilateral hemiliver and often the caudate lobe, especially with left-sided tumors. The goal of resection is to obtain an R0 resection (complete, margin-negative resection). Biliary reconstruction is performed as a Roux-en-Y hepaticojejunostomy. Whipple operation may be necessary in some cases to obtain a negative distal CBD margin. Vascular involvement is not an absolute contraindication to resection because portal venous resection and reconstruction may be possible. **Contraindications** to resection include bilateral intrahepatic ductal spread, extensive involvement of the main trunk of the portal vein, bilateral arterial or portal venous involvement, vascular involvement with evidence of contralateral ductal spread, and significant lymph node involvement or distant spread. **OLT** with neoadjuvant chemoradiation is currently considered for carefully selected patients in selected U.S. centers for early-stage, unresectable perihilar cholangiocarcinomas with excellent results in this highly selected population. Tumors in the middle of the extrahepatic bile duct may be approached with segmental bile duct excision, cholecystectomy, and portal lymphadenectomy. However, more often than not, a Whipple operation or liver resection is also required to achieve R0 resection. Distal bile duct cholangiocarcinomas are treated the same as pancreatic head malignancies with a Whipple operation in the absence of locally advanced or metastatic disease.

D. Palliation for patients with unresectable disease involves surgical, radiologic, or endoscopic biliary decompression. Biliary decompression via endoscopic or percutaneous internal stenting is often the first choice. When encountered at laparotomy, internal biliary drainage is best achieved by choledochojejunostomy for lower duct lesions.

XI. GALLBLADDER CANCER

A. Presentation. Gallbladder cancer is the most common malignancy of the biliary tract. It has a poor prognosis with a median survival of 5 to 8 months. There is a strong correlation with gallstones (95%). Histologically, nearly all gallbladder cancers are adenocarcinomas, and concomitant cholecystitis is frequently present. Tumors spread primarily by direct extension into liver segments IV and V but also via lymphatics along the cystic duct to the CBD. Because of its generally advanced stage at presentation, few patients with a preoperative diagnosis of gallbladder cancer have resectable tumors. Polyps 1.5 cm or greater in diameter have a 46% to 70% prevalence of cancer, whereas in those smaller than 1 cm, the risk of malignancy is <5% (*Arch Surg*. 198;123(1):26). Malignant polyps also tend to be sessile in nature and echogenic on US. Prophylactic cholecystectomy should be considered for polyps >1 cm in size or those meeting morphologic criteria. Other risk factors include porcelain gallbladder, PSC, and anomalous pancreatobiliary junction anatomy.

B. Diagnosis. Approximately one-third of these tumors are diagnosed incidentally during cholecystectomy, found in 0.3% to 1% of all cholecystectomy specimens. Symptoms of stage I and II gallbladder cancer are often due to gallstones rather than the cancer, whereas stage III and IV cancers present with weight loss and symptoms of CBD obstruction. Suggestive US findings include thickening or irregularity of the gallbladder, a polypoid mass, or diffuse wall calcification indicative of porcelain gallbladder. Tumor markers (CA 19-9) may be elevated in patients with gallbladder cancer.

C. Treatment. Mucosal disease confined to the gallbladder wall (Tis and T1a tumors) is often identified after routine LC. Because the overall 5-year survival rate is as high as 80%, cholecystectomy with negative margins is adequate therapy. Patients with a preoperative suspicion of gallbladder cancer should undergo open cholecystectomy because port site recurrences and late peritoneal metastases (associated with bile spillage) have been reported. T2 tumors have invaded the muscularis and may be treated by radical cholecystectomy that includes the gallbladder, the gallbladder bed of the liver, the hepatoduodenal ligament, and nodal tissue including paraduodenal, peripancreatic, hepatic artery, and celiac lymph nodes. Lymph node metastases or

extension of disease beyond the gallbladder wall into adjacent hepatic parenchyma (T3–T4 disease) requires more radical resection. Depending on the extent of local invasion, extirpation may range from wedge resection of the liver adjacent to the gallbladder bed to **trisectionectomy**. Improvement in survival has been demonstrated after radical resection. Because of the aggressive nature of this malignancy, adjuvant chemoradiation is often recommended; however, efficacy is limited. Extensive liver involvement or discontiguous metastases preclude surgical resection. Jaundice may be palliated by percutaneous or endoscopically placed biliary stents. Duodenal obstruction can be surgically bypassed if present.

CHAPTER 22: SURGICAL DISEASES OF THE BILIARY TREE

Multiple Choice Questions

1. **A 70-year-old male with no significant medical problems presents to the emergency room at midnight with right subcostal pain, nausea, and vomiting for the last 48 hours. He is afebrile and normotensive, but tender to palpation in the right upper quadrant of the abdomen without peritonitis. His WBC is 15, and he has no other laboratory abnormalities. A CT of the abdomen shows a distended gallbladder with minimal fat stranding around it and no other significant findings. What is the next best step?**

   a. Order an abdominal sonogram to confirm acute cholecystitis
   b. Order a HIDA scan to confirm acute cholecystitis
   c. Initiate antibiotics that cover the usual gut flora and start intravenous fluids
   d. Take the patient emergently to the operating room for laparoscopic cholecystectomy
   e. Consult interventional radiology for a percutaneous cholecystostomy tube

2. **An inpatient consultation was placed for a 30-year-old obese woman who recently gave birth via C-section and presented to the hospital with acute abdominal pain, nausea, and vomiting. She is nontoxic at presentation with tenderness to her epigastrium and has laboratory data showing no leukocytosis, a bilirubin of 1.5 mg/dL, mild elevations of amylase and lipase, and an abdominal ultrasound showing numerous small gallstones without gallbladder wall thickening, pericholecystic fluid, CBD stone, or dilation. After pain control, initiating NPO status, and fluid resuscitation, what is the next best step?**

   a. Consultation to gastroenterology for an ERCP to evaluate the common bile duct and perform a sphincterotomy
   b. Obtain an MRCP to evaluate the biliary tree
   c. Schedule the patient for open cholecystectomy after resolution of

biochemical evidence of jaundice and pancreatitis

d. Schedule the patient for laparoscopic cholecystectomy after resolution of abdominal pain

e. Discharge the patient after resolution of symptoms and laboratory abnormalities

3. A 60-year-old male with coronary artery disease and congestive heart failure with an ejection fraction of 25% is in the medical intensive care unit recovering from an ST-elevated myocardial infarction complicated by hospital-acquired pneumonia. Recently, the patient became febrile with respiratory distress requiring mechanical ventilation. He has a leukocytosis of 17,000 cells/mm^3, a bilirubin level of 2.3 mg/dL, and an abdominal ultrasound showing a dilated gallbladder with wall thickening and local inflammation, but with no stones or any dilation of the intra- or extrahepatic ducts. After initiation with antibiotics, what is the next best step in managing this patient?

a. Perform a percutaneous biliary drain to decompress the biliary tree

b. Perform a laparoscopic cholecystectomy with possible cholangiography

c. Perform an ERCP to decompress the biliary system

d. Obtain an MRCP to delineate the biliary anatomy and level of obstruction

e. Perform a cholecystostomy tube

4. During workup for symptomatic cholelithiasis in a 50-year-old male, an ultrasound showed an incidental mass in the gallbladder. After laparoscopic cholecystectomy, pathology reports adenocarcinoma that resides in the lamina propria. Which of the following is the best management for this patient?

a. Counseling for extended resection of the gallbladder fossa as well as periportal lymph node dissection

b. Serial annual ultrasound examination for 5 years

c. MRCP to evaluate the biliary system for additional pathology

d. Obtain serial CA19-9 and CEA levels

e. Pathologic examination of the cystic duct margin, and if negative,

no further intervention

5. **A surgeon at a small ambulatory surgical center reports that during laparoscopic cholecystectomy for acute cholecystitis he thinks the common bile duct was transected. The procedure is not yet completed and he calls a hepatobiliary surgeon at a tertiary care center asking from the operating room for advice regarding further management. What should be the next recommendation?**

   a. Place a percutaneous drain near the dissection, close the incisions, and transfer the patient to the specialist
   b. Perform an intraoperative cholangiogram to evaluate the level of injury
   c. Complete the cholecystectomy and schedule the patient to be evaluated by the hepatobiliary surgeon in clinic
   d. Convert to an open procedure and attempt a choledochojejunostomy
   e. Convert to an open procedure and attempt a primary repair of the injury

6. **A 58-year-old female with biliary colic undergoes ultrasound demonstrating a 2.2 cm gallbladder polyp. CT scan is performed without any additional findings. No prior abdominal operations. The appropriate management is:**

   a. Percutaneous biopsy
   b. Radical cholecystectomy
   c. Laparoscopic cholecystectomy
   d. Repeat ultrasound in 6 months
   e. PET scan

23

Pancreas

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INTRODUCTION

The pancreas has four sections moving from right to left: The head/uncinate, neck, body, and tail. It is a **retroperitoneal** organ, lying obliquely across the upper abdomen with the tail more superior than the head. The head or proximal pancreas is cradled by the C-loop of the duodenum. The neck lies anterior to the mesenteric vessels and portal vein. The body, which is generally accepted to begin at the left border of the superior mesenteric vein (SMV), lies posterior to the stomach and anterior to the splenic vein. The distal pancreas ends in the tail which sits near the splenic hilum, anterior to the left adrenal gland. The pancreas receives its blood supply from both the celiac trunk and the superior mesenteric artery (SMA). The arterial supply of the pancreatic head is provided by the superior pancreaticoduodenal arteries (from the gastroduodenal artery) and the inferior pancreaticoduodenal arteries (from the SMA). The distal pancreas receives its arterial supply from branches of the splenic artery; including the superior (dorsal) pancreatic, greater pancreatic, and transverse pancreatic arteries. Venous drainage is primarily by the pancreaticoduodenal and splenic veins, which drain into the portal vein. Lymphatic drainage from the anterior portion of the pancreatic head and neck occurs via the pancreaticoduodenal and pyloric lymph node groups, whose efferent lymphatics connect to the celiac and hepatic lymph node basins. The posterior aspect of the pancreatic head and neck, as well as the uncinate process, drains via the retropancreatic lymphatic system following the posterior pancreaticoduodenal vessels to the celiac and hepatic or the superior mesenteric lymph nodes. Lymphatics draining the body and tail of the pancreas converge with channels running with the splenic vessels and primarily drain into the celiac nodal plexus. The pancreatic surface in direct contact with the retroperitoneum may drain directly into posterior abdominal

wall or perineural lymphatic channels (*Clinical Anatomy.* 2014;28(4):527–537).

The pancreas forms from ventral and dorsal outpouchings of the duodenum, each with its own duct entering the duodenum. In the most common final pattern, the ventral duct (Wirsung) joins with the dorsal duct (Santorini) at the neck of the pancreas, with regression of the dorsal duct in the pancreatic head. Several other patterns are possible, but the most important is pancreas divisum in which there are two separate ductal systems: a ventral system which drains through the ampulla of Vater and a dorsal system which drains through a second duodenal ampulla located about 1 cm proximal to the ampulla of Vater.

I. ACUTE PANCREATITIS. Acute pancreatitis is an inflammatory illness of variable severity. Approximately 80% of cases are **interstitial edematous acute pancreatitis**, characterized by acute inflammation of the pancreatic parenchyma and peripancreatic tissues, which usually is self-limited and associated with "mild" transitory clinical manifestations. In contrast, 20% of patients develop **necrotizing acute pancreatitis**, characterized by inflammation and pancreatic parenchymal necrosis, which is associated with a much higher morbidity and a substantial mortality rate (*Gut.* 2013;62:102). Occasionally, inflammation and necrosis are accompanied by pancreatic parenchymal hemorrhage (**acute hemorrhagic pancreatitis**). The exact mechanism by which various factors induce acute pancreatitis is unclear. However, it seems that the initial insult is **unregulated activation of trypsin within pancreatic acinar cells,** leading to autodigestion and an inflammatory cascade that may progress to SIRS (*Lancet.* 2008;371(9607):143–152). In severe cases, autodigestion extends beyond the pancreas into the retroperitoneum digesting peripancreatic tissues, causing fat necrosis and erosion of blood vessels with hemorrhage. Entry of enzymes into the blood stream may cause respiratory and renal injury and other effects.

A. Etiology. The two most common causes of acute pancreatitis in the United States are **gallstones (40% to 45%)** and **alcoholism (30% to 35%),** collectively accounting for nearly 80% of cases. Endoscopic retrograde cholangiopancreatography (ERCP) accounts for another 2% to 5% of cases. Other causes include **metabolic abnormalities** (e.g., hypercalcemia or hypertriglyceridemia), **drugs** (e.g., azathioprine, sulfamethoxazole–trimethoprim, furosemide, opiates, and valproic acid), **toxins** (e.g., scorpion stings and organophosphates), **infections**

(e.g., mumps, Coxsackie virus B, Epstein–Barr virus, cytomegalovirus, rubella, and *Ascaris* species), **neoplasms** (e.g., benign and malignant), **trauma, autoimmune disorders** (e.g., IgG4-associated lymphoplasmacytic pancreatitis, Sjögren syndrome, systemic lupus erythematosus [SLE], primary biliary cirrhosis [PBC], and autoimmune pancreatitis), or may be **idiopathic.**

B. Diagnosis

1. **Physical examination** typically reveals **epigastric pain,** often radiating to the back. Classically, the abdomen is doughy to palpation. However, irritation from intraperitoneal pancreatic enzymes occasionally results in impressive peritoneal signs, simulating other causes of an acute abdomen. Nausea, vomiting, and low-grade fever are common, as are tachycardia and hypotension secondary to hypovolemia. Hypoxemia, renal failure, hypocalcemia, hyperglycemia, and respiratory failure are evidence of severe systemic effects. Flank ecchymosis **(Gray Turner sign)**, periumbilical ecchymosis **(Cullen sign), or inguinal ecchymosis (Fox's sign)** is due to tracking of retroperitoneal hemorrhage and is always a manifestation of severe pancreatitis. However, these signs are present in only 1% to 3% of cases and do not usually develop until 48 hours after the onset of symptoms.
2. **Laboratory studies**
   a. **Serum amylase** levels rise within a few hours of onset of symptoms and may return to normal over the following 3 to 5 days. Persistent elevations of amylase levels for longer than 10 days suggest complications, such as pseudocyst formation. However, there is no correlation between amylase level and severity of inflammation. In addition, hyperamylasemia can be found in a variety of other clinical conditions including renal failure, intestinal obstruction, sialadenitis, and malignancy.
   b. **Serum lipase** generally is considered more sensitive (95%), and remains elevated for a longer period of time, which can be useful in patients with a delayed presentation.
   c. **Acute-phase proteins** such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukin 6 (IL-6) may be measured as markers of severity.

d. Serum calcium levels may fall as a result of complexing with fatty acids (saponification or fat necrosis) produced by activated lipases as well as from hypoalbuminemia.

e. Hepatic function panel (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin, alkaline phosphatase) should be checked to assess for concomitant biliary disease or as an etiology of pancreatitis (gallstone disease) although normal values do not rule out biliary etiologies.

3. Radiologic imaging complements clinical history and examination because no single modality provides a perfect diagnostic index of severity.

a. Ultrasound (US) is quite user dependent, and the pancreas is not visualized in up to 40% of patients due to overlying bowel gas and body habitus. The primary utility of US in acute pancreatitis is to evaluate for biliary etiology (e.g., gallstones).

b. Computed tomography (CT) has a sensitivity and specificity of 90% and 100%, respectively, and is the gold standard for the disease. Iodinated contrast enhancement is essential to detect the presence of pancreatic necrosis. CT findings include parenchymal enlargement and edema, necrosis, blurring of fat planes, peripancreatic fluid collections, bowel distention, and mesenteric edema. A pleural effusion and atelectasis, especially on the left side, are also common. In general, CT imaging is indicated for patients in whom the diagnosis is in question, for severely ill patients in whom necrosis is more likely, and for any patient who exhibits clinical deterioration or fails to improve with medical management.

c. Magnetic resonance imaging (MRI) is a useful substitute for CT scan in patients who are allergic to iodinated contrast or who are in acute renal failure, with sensitivity 83% and specificity 91%. In addition, MRI/MR cholangiopancreatography (MRCP) is better than CT at visualizing cholelithiasis, choledocholithiasis, and anomalies of the pancreatic and common bile ducts.

d. ERCP is not routinely indicated for the evaluation of patients during an attack of acute pancreatitis and is a subject of some controversy. **Indications for ERCP** are as follows:

(1) Patients with **jaundice, suspected biliary pancreatitis, and possible cholangitis** who are not clinically improving by 24 hours after admission should undergo endoscopic sphincterotomy and stone extraction. However, the literature is clear that early routine endoscopic intervention for gallstone pancreatitis does not beneficially influence morbidity or mortality (*Cochrane Database Syst Review.* 2012;5:CD009779).

(2) Patients with no identifiable cause to rule out occult common bile duct stones, strictures, or neoplasms.

(3) Suspected pancreatic ductal disruption, such as with traumatic pancreatitis.

C. Prognosis. Because the associated mortality of fulminant acute pancreatitis approaches 40% and randomized studies have shown that early aggressive supportive care improves outcomes, attempts have been made to identify clinical parameters that predict patients at higher risk of developing poorer outcomes.

1. **Ranson criteria** (Table 23-1) constitute the most frequently utilized predictor of mortality associated with acute pancreatitis. The limitation of this assessment tool is that a score cannot be calculated until 48 hours after admission.
2. **CT Severity Index (CTSI)** is a prognostic scale based on CT findings, including peripancreatic fluid collections and extent of pancreatic necrosis. It was originally described by Balthazar et al. (*Radiology.* 1994;174:331–336) and then modified to a simpler model by Mortele et al. (*Am J Roent.* 2004;183:1261–1265) (Tables 23-2 and 23-3).

TABLE 23-1 Ranson Criteria

Admission	
Age	>55 yr
White blood cell count	>16,000/μL
Blood glucose	>200 mg/dL

Serum lactate dehydrogenase	>350 IU/L
Aspartate aminotransferase	>250 IU/L
Initial 48 hr	
Hematocrit decrease	>10%
Blood urea nitrogen elevation	>5 mg/dL
Serum calcium	<8 mg/dL
Arterial PO_2	<60 mm Hg
Base deficit	>4 mEq/L
Estimated fluid sequestration	>6 L

Mortality

Number of Ranson Signs	Approximate Mortality (%)
0–2	0
3–4	15
5–6	50
>6	70–90

TABLE 23-2 CT Severity Grading Index (CTSI) Scoring Based on Imaging Characteristics

Scoring for pancreatic necrosis

0 Points	No pancreatic necrosis
2 Points	≤30% pancreatic necrosis
4 Points	>30% necrosis
Evaluation of pancreatic morphology, not including necrosis	
0 Points (grade A)	Normal pancreas
2 Points (grade B/C)	Focal or diffuse enlargement of the gland, including contour irregularities and inhomogeneous attenuation with or without peripancreatic inflammation
4 Points (grade D/E)	Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis
Additional 2 points	Extra pancreatic complications including one or more of the following: pleural effusion, ascites, vascular complications, parenchymal complications, or gastrointestinal tract involvement

3. The **Acute Physiology and Chronic Health Evaluation (APACHE) II,** using a total of 14 variables, can be calculated at admission and updated daily to allow continual reassessment. More recently, the APACHE IV score, using 52 variables, has also been validated in acute pancreatitis with a score >44 predicting mortality in 100% of cases (*Pancreas.* 2015;44(8):1314–1319). However, these scores are somewhat cumbersome and difficult to calculate that limits their everyday use.

TABLE 23-3 Prognosis Based on CTSI Score

Index	Predicted Morbidity (%)	Predicted Mortality (%)
0–3	8	3
4–6	35	6

4. **Multiple Organ Dysfunction Score (MODS) and Sequential Organ Failure Assessment (SOFA)** have been shown to be important predictors of disease severity in critically ill patients and have been extended to patients with severe acute pancreatitis and are predictive of mortality and development of complications (*Br J Surg.* 2009;96(2):137–150).
5. **Bedside Index for Severity in Acute Pancreatitis (BISAP)** is a validated 5-point scoring system assigning a point for presence of serum BUN >25 mg/dL, impaired mental status, systemic inflammatory response syndrome (SIRS), age >60 years, or presence of pleural effusion within the first 24 hours. Observed mortality was <1% in patients with low BISAP scores (<2), while scores ≥3 correlated with worse prognosis (5% to 22% mortality) (*Gut.* 2008;57:1698–1703).

D. Complications

1. **Necrotizing pancreatitis** occurs in about 10% to 20% of acute pancreatitis cases, and its presence correlates with prognosis. It may be present at initial presentation or develop later in the clinical course. Necrosis is diagnosed on CT as failure to enhance with intravenous contrast. It is often associated with large fluid collections in the lesser sac.
2. **Infected pancreatic necrosis** occurs in 5% to 10% of cases and is the cause of most late deaths (>14 days). Whether pancreatic necrosis visualized on CT scan is infected cannot be determined by imaging; however, gas in the areas of necrosis is suggestive. The gold standard for diagnosing infected pancreatic necrosis is fine-needle aspiration (FNA), but this is rarely necessary as treatment is based on clinical status and blood cultures.
3. Acute pseudocyst (see Section VII).
4. **Visceral pseudoaneurysm** is a rare complication, and is most common in patients with necrotizing pancreatitis. The most common arteries involved are the splenic, gastroduodenal, and left gastric arteries. Rupture is a life-threatening emergency and usually presents with signs and symptoms of upper gastrointestinal bleeding.

Angiography is the first step in management and can be both diagnostic and therapeutic (*Am J Surg.* 2005;190(3):489–495).

5. Because of the proximity of the splenic, superior mesenteric, and portal veins, **venous thrombosis** is not uncommon in patients with acute pancreatitis. Anticoagulation for splanchnic vein thrombosis of a variety of etiologies, including acute pancreatitis, has been shown to be safe and effective in a prospective cohort study (*JAMA Intern Med.* 2015;175(9):1474–1480).

E. Treatment. End-organ failure is associated with poorer outcomes. Therefore, the initial approach to managing acute pancreatitis focuses on supporting patients with aggressive fluid resuscitation and close monitoring.

1. Supportive care

a. Volume resuscitation with isotonic fluids is crucial; urinary output is monitored with a Foley catheter targeting greater than 0.5 mL/kg/hr. During the course of resuscitation, patients should be maintained on continuous pulse oximetry as patients often require large-volume fluid resuscitation and frequent monitoring of electrolytes.

b. Gastric rest with nutritional support. Nasogastric decompression is performed to decrease neurohormonal stimulation of pancreatic secretion. Acute pancreatitis is a hypercatabolic state, and nutritional support has been shown to have a significant impact on outcomes in critically ill patients. Enteral feeding is generally preferred to parenteral nutrition. Early enteral feeding in patients with severe acute pancreatitis is associated with lower rates of infection, surgical intervention, and length of stay (*BMJ.* 2004;328:1407).

c. Analgesics are required for pain relief.

d. Respiratory monitoring and arterial blood gases are usually necessary in severe pancreatitis to assess oxygenation and acid–base status. Hypoxemia is common, even in mild cases of acute pancreatitis given the volume of fluid resuscitation and the potential for development of sympathetic effusions. Pulmonary complications occur in up to 50% of patients.

e. Antibiotics. The routine use of antibiotic prophylaxis in acute

pancreatitis, especially in mild to moderate cases, is not supported in the literature. Conflicting data exist regarding antibiotics in severe cases, as there are small prospective, randomized trials demonstrating significantly lower rates of septic complications in patients receiving antibiotics (*Ann Surg.* 2006;243:154) and subsequent data from a randomized controlled trial (RCT) that found differences in infection or surgical intervention (*Ann Surg.* 2007;245:674). However, a meta-analysis demonstrated no difference in mortality, infected necrosis, or overall infections with antibiotic therapy (*Cochrane Database Syst Rev.* 2010;5:CD002941). When infection is confirmed or suspected, patients should be treated with broad-spectrum systemic antibiotics that cover gram-negative bacteria and, depending on length of hospitalization, common hospital-acquired pathogens, including fungal organisms, as superinfection can be seen commonly.

2. **Interventional and surgical treatment** is necessary in a small percent of cases. Fluid collections and/or pancreatic necrosis may need to be treated. The indications are clinical deterioration, sepsis, hypotension, and evidence of gastrointestinal obstruction due to the collections. Debridement of necrotic pancreas should be delayed to at least 18 to 20 days after onset of attack to allow sequestration of the necrosis. In severely ill patients, percutaneous or endoscopic drainage using multiple and/or large drains is often used as a first step. Resection of necrosis by endoscopic or minimally invasive or open surgery is performed as a second procedure several weeks later if necessary (*NEJM.* 2010;362(16):1491–1502; *Br J Surg.* 2011;98(1):18–27). Open surgery was once the mainstay of treatment but is needed uncommonly today. Rarely, surgery is needed for bleeding or organ perforation.
3. **Treatment of gallstone pancreatitis.** In mild cases of acute pancreatitis, laparoscopic cholecystectomy with operative cholangiogram is indicated on the index admission or soon thereafter in healthy patients. Delay has resulted in the occurrence of a second attack, which may be more severe. In patients with severe gallstone pancreatitis, cholecystectomy should be performed when general and local conditions permit. Operative cholangiography is needed to rule

out persistent choledocholithiasis, although since acute pancreatitis is caused by small stones only 10% are found to have residual stones at the time of surgery. In patients not fit for surgery, endoscopic sphincterotomy may protect against further attacks of pancreatitis (*Pancreatology.* 2013;13(4):1–15).

II. CHRONIC PANCREATITIS

A. Etiology. Alcohol (EtOH) abuse is the most common cause (70%); however, other etiologies include idiopathic, metabolic (hypercalcemia, hypertriglyceridemia), drug-related, traumatic, genetic (PRSS1, SPINK1, cystic fibrosis), and congenital abnormalities (sphincter of Oddi dysfunction or pancreas divisum). It also appears that tobacco abuse plays an important role in the development of chronic pancreatitis and particularly in patients with EtOH-related disease (*Arch Intern Med.* 2009;169:1035–1045). A history of recurrent acute pancreatitis is present in some but not all patients with chronic pancreatitis.

B. Pathophysiology. Chronic pancreatitis is characterized by diffuse scarring and strictures in the pancreatic duct and commonly leads to endocrine or exocrine insufficiency, although substantial glandular destruction must occur before secretory function is lost. Most patients who develop diabetes already have pancreatic exocrine insufficiency and steatorrhea. Reduced food intake due to pain in addition to malabsorption lead to malnutrition.

C. Diagnosis is based on history and examination, complemented by appropriate investigative studies. **Upper midepigastric pain radiating to the back** often postprandial is the cardinal symptom and is present in 85% to 90% of cases, and it becomes progressively worse over time. Changes in bowel habits and bloating are other common early symptoms, followed later by steatorrhea and diabetes as the disease progresses. Weight loss is common, and food fear may be present. Upper abdominal tenderness may be present. Less common findings include jaundice secondary to stricture of the common bile duct, enlarged spleen secondary to thrombosis of the splenic vein, or ascites secondary to a pancreatic peritoneal fistula.

1. Laboratory tests

a. Amylase and lipase levels are elevated in acute pancreatitis but rarely are useful in chronic pancreatitis and are **commonly**

normal due to progressive loss of pancreatic function.

b. Pancreatic secretin stimulation tests assess pancreatic exocrine function by quantifying duodenal bicarbonate concentrations via nasoduodenal or endoscopic means following IV administration of secretin. While cumbersome, secretin stimulation testing has proven to be a highly sensitive (90% to 100%) and specific (>90%) test for the diagnosis of chronic pancreatitis (*Gastrointest Endosc*. 2003;57:37–40).

c. Pancreatic endocrine function. Fasting and 2-hour postprandial blood glucose levels or glucose tolerance tests may be abnormal in 14% to 65% of patients with early chronic pancreatitis and in up to 90% of patients when calcifications are present. Serum trypsinogen levels correlate with residual acinar cell mass and levels <20 ng/mL indicate severe pancreatic insufficiency (*Dig Dis Sci*. 2017;62(7):1702–1712).

d. A 72-hour quantitative collection for estimation of daily fecal fat is relatively simple and cost efficient but plays a limited role in the definitive diagnosis of chronic pancreatitis as it lacks specificity, and patients must have a high degree of pancreatic insufficiency to have a positive test. Fecal elastase-1 levels are more specific with sensitivity approaching 100% and specificity of 93% for severe pancreatic endocrine insufficiency (*Dig Dis Sci.* 2017;62(7):1702–1712).

2. Radiologic studies

a. Plain films of the abdomen may show diffuse calcification of the pancreas in 30% to 40% of patients.

b. Transabdominal US has low sensitivity and is subject to limitations related to user dependency, body habitus, and overlying bowel gas, and plays a limited role in the diagnosis of chronic pancreatitis.

c. CT is 80% sensitive and 75% to 90% specific for the diagnosis of parenchymal or ductal disease. Common findings include ductal dilation, strictures, calcifications, atrophy, and cystic lesions. CT is also useful to evaluate for mass lesions and sequelae of chronic pancreatitis.

d. MRI is less sensitive than CT for detection of calcification. MR

pancreatography is more sensitive in visualizing dilated ducts and strictures but loses sensitivity relative to ERCP in evaluating side branch disease (i.e., small duct disease).

e. ERCP provides the greatest detail of pancreatic duct anatomy, demonstrating strictures and areas of dilation. The presence of both may give the characteristic "chain of lakes" appearance. ERCP may also be beneficial for evaluation of pancreatic mass lesions, cytology, and can be therapeutic. There are drawbacks, however, in that images must be interpreted by specialized individuals, and there is a 3% to 7% risk of causing acute pancreatitis.

f. Endoscopic ultrasound (EUS). EUS has come to play a more important role in the diagnosis of biliary obstruction. Criteria for the diagnosis of chronic pancreatitis is based on EUS characteristics, such as lithiasis within the main pancreatic duct (MPD) and parenchymal honeycombing, referred to as the Rosemont criteria (*Gastrointest Endosc.* 2009;69(7):1251–1261).

D. Complications

1. **Common bile duct obstruction** may result from transient obstruction from pancreatic inflammation and edema or from stricture of the intrapancreatic common bile duct. When present, **strictures** are often **2 to 4 cm long and smooth** ("rat-tail") and must be distinguished from malignancy.
2. **Intestinal obstruction.** Duodenal obstruction can occur due to acute pancreatic inflammation, chronic fibrotic reaction, pancreatic pseudocyst, or neoplasm. Rarely, the colon may become obstructed.
3. **Pancreaticoenteric fistulas** result from spontaneous drainage of a pancreatic abscess cavity or pseudocyst into the stomach, duodenum, transverse colon, or biliary tract. They are often asymptomatic but may become infected or result in hemorrhage.
4. **Pancreaticopleural fistulas** often have communication from the distal duct traversing the esophageal hiatus.
5. **Pseudocyst** (see below).
6. **Splenic vein thrombosis** (see below).
7. **Pancreatic carcinoma.** Chronic pancreatitis has been suggested to increase the risk of pancreatic carcinoma by two- to threefold.

E. Treatment

1. Medical management

a. Malabsorption or steatorrhea. Most patients will experience improvement in steatorrhea and fat absorption with pancreatic enzyme supplementation. In addition, there is some evidence that adequate enzyme supplementation improves pain control.

b. Diabetes initially is responsive to careful attention to overall good nutrition and dietary control; however, use of oral hypoglycemic agents or insulin therapy often is required.

c. Narcotics are often required for pain relief. A multimodal approach should be used as patients with chronic pancreatitis receiving chronic narcotics demonstrate a 12% to 20% abuse/addiction rate (*Pain Medicine.* 2008;9(4):444–459). In selected patients, tricyclic antidepressants and gabapentin may be effective.

d. Abstinence from alcohol and smoking cessation result in improved pain control in a majority of patients and should be encouraged (*J Gastroenterol.* 2007;42(2):101–119).

e. Cholecystokinin antagonists and somatostatin analogs have been considered for treatment of chronic pancreatitis but have yet to show improvements in pain control.

f. Tube thoracostomy or repeated paracentesis may be required for pancreatic pleural effusions or pancreatic ascites. Approximately 40% to 65% of patients respond to nonsurgical management within 2 to 3 weeks.

2. Endoscopic therapy.

Endoscopic sphincterotomy, stenting, stone retrieval, and lithotripsy have all been used with moderate success in the management of patients with ductal complications from chronic pancreatitis. Endoscopic celiac plexus block may improve symptoms in patients with severe pain. However, in a small RCT, surgical decompression of the pancreatic duct via pancreaticojejunostomy resulted in significantly improved pain and quality of life compared to endoscopic interventions in patients with chronic pancreatitis (*N Engl J Med.* 2007;356(7):676–684).

3. Surgical principles

a. Indications for surgery. By far the most common indication is unremitting pain, but others include the inability to rule out

neoplasm and the management of complications (pseudocyst, aneurysm, stricture, and fistula).

b. Choice of procedure. The goals of surgical therapy are drainage and/or resection of the diseased pancreas to alleviate pain and complications associated with chronic pancreatitis. Most modern procedures combine drainage with some resection of the pancreas.

c. Drainage/resection procedures

(1) The **Frey procedure** is a major modification of earlier operations which removed duct stones, opened ductal strictures in the body of the gland, and then provided new drainage of the duct by lateral pancreaticojejunostomy (Puestow, Partington–Rochelle). These operations and the Frey procedure are best suited for patients with dilated ducts. The earlier operations often failed because the pancreatic duct in the head of the gland was not drained adequately. In the Frey procedure, the proximal pancreatic duct is also cleared by extensive coring of the head of the gland. This is the most common procedure performed at Washington University in St. Louis and throughout North America. The Frey procedure has been shown to provide excellent pain control and patient satisfaction in chronic pancreatitis.

(2) The **Beger procedure** is a duodenum-preserving resection of most of the pancreatic head. This operation preserves a small amount of pancreatic tissue within the C-loop of the duodenum and also in front of the portal vein. The pancreas is then transected at the pancreatic neck. This procedure has also demonstrated excellent long-term results (*Ann Surg.* 1999;230(4):512–519); however, the procedure is more technically difficult because it requires dissection along the SMV. It is rarely performed in North America.

d. Pancreatectomy

(1) Pancreaticoduodenectomy (PD, Whipple procedure) is indicated in cases in which the pancreatitis disproportionately involves the head of the pancreas, the pancreatic duct is of small diameter, or cancer in the head of the pancreas cannot be ruled out. The Whipple has been shown to be inferior to both the Beger (*Int J Pancreatol.* 2000;27(2):131–142) and Frey

(*Ann Surg*. 1998;228:771) procedures for this indication.

(2) Distal subtotal pancreatectomy is commonly used for disease in the tail of the gland. It is also employed in patients with previous ductal injury from blunt abdominal trauma who sustained fracture of the pancreas or stenosis of the duct at the midbody level.

(3) Total pancreatectomy is performed only as a last resort in patients whose previous operations have failed and who appear to be capable of managing an apancreatic state. Some centers have combined this procedure with islet cell transplantation. The latter seems particularly applicable in cases of juvenile pancreatitis.

(4) Celiac plexus block can be achieved surgically by either ganglionectomy or direct injection of sclerosing agents. However, endoscopic injection is used most commonly today, though its effect is only temporary.

III. PANCREATIC DUCTAL ADENOCARCINOMA

A. Incidence and Epidemiology. Pancreatic cancer is the third leading cause of cancer-related mortality in the United States. Most patients have incurable disease at the time of diagnosis, and the overall 5-year survival is approximately 8%. The median age at diagnosis is 65 years. The survival of resected patients is 20% to 25%.

B. Risk Factors. An increased risk of pancreatic ductal adenocarcinoma (PDAC) has been associated with smoking, family history, intraductal papillary mucinous neoplasms (IPMNs), hereditary disorders (hereditary nonpolyposis colon cancer [HNPCC], von Hippel–Lindau disease [VHL], Peutz–Jeghers syndrome, familial breast cancer [BRCA2], familial atypical multiple mole melanoma [FAMMM]), and chronic pancreatitis.

C. Pathology. PDAC accounts for the majority of pancreatic malignancies (90%). Seventy percent of PDAC occur at the head, 20% in the body, and 10% in the tail.

D. Diagnosis. Symptoms associated with pancreatic cancer are almost always gradual in onset and are nonspecific.

1. History and examination. In cancer of the head of the pancreas, bile duct obstruction, which occurs frequently, leads to the classical

presentation of painless jaundice, pruritus, dark urine, and pale stools. Malaise, nausea, fatigue, and weight loss are common, and some patients do have epigastric or back pain. Epigastric abdominal pain improved with leaning forward (Ingelfinger sign) is also sometimes present. In cancer of the distal pancreas, pain and weight loss are the predominant symptoms. Some patients present only with steatorrhea when the pancreatic duct alone is obstructed. New-onset diabetes within the year prior to diagnosis is found in 15% of patients with pancreatic cancer. Trousseau sign (migratory thrombophlebitis) has been associated with pancreas cancer.

2. Laboratory tests

a. Elevated serum bilirubin with >50% direct-reacting bilirubin.

b. Elevated alkaline phosphatase.

c. Prolonged obstruction may lead to mild increase in AST and ALT.

(a, b, and c are seen with biliary obstruction)

d. Tumor markers. Serum CA19-9 is often elevated (>37 U/mL) in patients with pancreatic cancer but may be falsely elevated in cases of nonmalignant biliary obstruction. Approximately 15% of patients with pancreatic cancer will demonstrate normal CA19-9 levels (≤37 U/mL) and low levels (<100 U/mL) correlate with resectable disease. Normalization or reduction in pretreatment serum CA19-9 levels can be useful in assessing disease response and correlates with prognosis (*Curr Mol Med.* 2015;13(3):340–351). Carcinoembryonic antigen (**CEA**) is elevated (>5 ng/mL) in 40% to 50% of patients with pancreas cancer.

3. Radiologic studies

a. CT imaging should be a fine-cut (≤3 mm slices), “pancreatic protocol CT” including two contrast phases (arterial and venous) to allow for assessment of the relationship of the mass to vascular structures as this is crucial to determine resectability. Pancreatic cancer on CT usually appears as a hypoattenuating mass that distorts the normal architecture of the gland, often paired with findings of a dilated pancreatic and biliary ductal system (the so-called “double-duct” sign). Preoperative assessment of tumor resectability using the National Comprehensive Center Network (NCCN) guidelines classifies pancreatic adenocarcinoma into

three categories (Table 23-4):

(1) **Resectable.** No distant metastases; no arterial tumor contact (celiac axis [CA], common hepatic artery [CHA], and SMA); no tumor contact with the SMV or portal vein (PV); ≤180-degree contact with vein contour irregularity.

(2) **Borderline resectable.** No distant metastases; solid tumor arterial contact without extension to CA or CHA allowing for complete resection and reconstruction; tumor contact with the CA or SMA ≤180 degrees; tumor contact with the CA >180 degrees without aortic involvement and an uninvolved GDA (permitting modified Appleby procedure), tumor contact with variant arterial anatomy (as it effects surgical planning); solid tumor contact with the SMV or PV >180 degrees; contact ≤180 degrees with contour irregularity of the vein or thrombosis but amenable to complete vein resection and reconstruction; solid tumor contact with the IVC.

(3) **Unresectable.** Distant metastases (including nonregional lymph nodes) or solid tumor contact of the CA or SMA >180 degrees; unreconstructable SMV/PV due to tumor involvement or occlusion (bland or tumor thrombus); tumor contact with the most proximal draining jejunal branch of the SMV (for head/uncinate lesions).

b. EUS and ERCP, especially the former, play an important role in patients in whom a mass is not seen on CT, obtaining tissue diagnosis when necessary (e.g., to determine candidacy for neoadjuvant therapy or when the diagnosis is in doubt). In addition, ERCP can be performed for drainage of biliary obstruction. Preoperative stenting in patients suitable for surgery at the time of presentation is controversial as it has been associated with an increase in postoperative complications (*NEJM*. 2010;362(2):129–137). However, it is advisable in patients whose bilirubin is very high and in those whose surgery will be delayed due to neoadjuvant therapy or treatment of comorbidities.

c. MRI and MRCP can provide information similar to that in conventional CT.

d. Staging laparoscopy is used sparingly in cancer of the head of the

pancreas where palliative operations are useful. A high suspicion for metastatic disease would be an indication (e.g., high CA19-9). It is advisable for cancers of the distal pancreas where peritoneal metastases are common and surgical palliation is not performed.

E. Treatment

1. Resection

a. PD (Whipple procedure) consists of en bloc resection of the head of the pancreas, distal common bile duct, duodenum, jejunum, and gastric antrum. Pylorus-sparing PD has been advocated by some, but there are no data demonstrating improved survival or lower morbidity (*Cochrane Database Syst Rev*. 2011;(5):CD006053). There has been a sharp decline in morbidity and mortality in specialized centers, with a 30-day mortality of less than 3%.

TABLE 23-4 NCCN 2019 Imaging Criteria for Resectability of Pancreatic Adenocarcinoma

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2019
Pancreatic Adenocarcinoma
NCCN Evidence Blocks™

NCCN Guidelines Index
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Discussion

CRITERIA DEFINING RESECTABILITY STATUS

Resectability Status	Arterial	Venous
Resectable	No arterial tumor contact (celiac axis [CA], superior mesenteric artery [SMA], or common hepatic artery [CHA]).	No tumor contact with the superior mesenteric vein (SMV) or portal vein (PV) or ≤180° contact without vein contour irregularity.
Borderline Resectable[a]	Pancreatic head/uncinate process: •Solid tumor contact with CHA without extension to CA or hepatic artery bifurcation allowing for safe and complete resection and reconstruction. •Solid tumor contact with the SMA of ≤180° •Solid tumor contact with variant arterial anatomy (ex: accessory right hepatic artery, replaced right hepatic artery, replaced CHA, and the origin of replaced or accessory artery) and the presence and degree of tumor contact should be noted if present, as it may affect surgical planning. Pancreatic body/tail: •Solid tumor contact with the CA of ≤180° •Solid tumor contact with the CA of >180° without involvement of the aorta and with intact and uninvolved gastroduodenal artery thereby permitting a modified Appleby procedure [some panel members prefer these criteria to be in the unresectable category].	•Solid tumor contact with the SMV or PV of >180°, contact of ≤180° with contour irregularity of the vein or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing for safe and complete resection and vein reconstruction. •Solid tumor contact with the inferior vena cava (IVC).
Unresectable[a]	•Distant metastasis (including non-regional lymph node metastasis) Head/uncinate process: •Solid tumor contact with SMA >180° •Solid tumor contact with the CA >180° Body and tail: •Solid tumor contact of >180° with the SMA or CA •Solid tumor contact with the CA and aortic involvement	Head/uncinate process: •Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus) •Contact with most proximal draining jejunal branch into SMV Body and tail: •Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus)

[a]Solid tumor contact may be replaced with increased hazy density/stranding of the fat surrounding the peri-pancreatic vessels (typically seen following neoadjuvant therapy); this finding should be reported on the staging and follow-up scans. Decision on resectability status should be made in these patients, in consensus at multidisciplinary meetings/discussions.

Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.
All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PANC-C

b. Distal pancreatectomy. The procedure of choice for lesions of the body and tail of the pancreas is distal pancreatectomy. Distal pancreatectomy consists of resection of the pancreas, generally at the SMV laterally to include the spleen. We have described a technique that provides a more radical resection with improved R0 resection rates, the radical antegrade modular pancreatosplenectomy (RAMPS), when compared to traditional series, which is the procedure of choice for malignant tumors of the distal pancreas at our institution (*J Hepatobiliary Pancreat Sci.* 2016;23(7):432–441).

c. Minimally invasive pancreatectomy is emerging as a feasible strategy for patients with overall survival, rate of R0 resection, and adjuvant therapy being similar to open procedures in a large meta-analysis (*Eur J Surg Oncol.* 2019;45(5):719–727).

2. Postoperative considerations. Delayed gastric emptying, pancreatic fistula, and wound infection are the three most common complications of PD.

a. Delayed gastric emptying (20%) almost always subsides with conservative treatment.

b. Pancreatic fistula (20%) may be reduced by meticulous attention to the blood supply of the pancreaticoenteric duct-to-mucosa anastomosis (*J Am Coll Surg.* 2002;194:746). Most surgeons routinely place abdominal drains, with a recent Cochrane Review citing modest-quality evidence that routine drain placement may slightly reduce 90-day mortality (*Cochrane Database Syst Rev.* 2018;6:CD010583).

c. Surgical site infection (10% to 15%).

d. Superficial incisional infection (<5%).

e. Organ space infection (10% to 12%).

f. Hemorrhage (<10%). While relatively rare, postpancreatectomy hemorrhage accounts for up to 38% of postoperative deaths. Bleeding is most commonly from the gastroduodenal artery stump or pseudoaneurysm at its origin from the hepatic artery. Diagnosis and treatment is managed by angiography with embolization or covered stent (*AJR.* 2011;196:192–197).

g. Death following pancreatectomy is <3% in the modern era when

the procedure is performed at a high volume center.

3. **Radiotherapy and Chemotherapy**

   a. **Adjuvant therapy**

      (1) Chemotherapy in the adjuvant setting using gemcitabine (ESPAC-1) or 5-fluorouracil plus leucovorin (CONKO-001) has demonstrated a survival benefit compared to observation alone in several clinical trials (ESPAC-1 and CONKO-001). More recently, adjuvant therapy using a modified FOLFIRINOX regimen was shown to improve survival compared to gemcitabine (*N Engl J Med.* 2018;379(25):2395–2406).

      (2) Chemoradiation following pancreatic cancer resections remains controversial with no prior clinical trials demonstrating a survival benefit with radiotherapy. More recently, the LAP07 trial using 3D conformal radiation therapy in locally advanced pancreatic cancer also failed to show an improvement in survival (*JAMA.* 2016;315(17):1844–1853). Advances in radiation include using intensity-modulated (IMRT) and stereotactic body radiotherapy (SBRT).

   b. **Neoadjuvant therapy** remains controversial. Neoadjuvant therapy avoids unnecessary surgery in patients with aggressive tumor biology that have disease progression during treatment. However, in upfront resectable disease, a meta-analysis found no benefit to neoadjuvant therapy. In patients with borderline resectable or advanced local disease, neoadjuvant treatment improved R0 and overall resection rates (*Cancer Med.* 2017;6(6):1201–1219).

F. Prognosis. Surgical resection increases survival compared to patients with similar stage disease who do not undergo resection. Overall 5-year survival rates are approximately 20% to 25% for patients after resection. In patients with small tumors, negative resection margins, and no evidence of nodal metastases, the 5-year survival rate is as high as 40%. Median survival for unresectable locally advanced disease is 12 months, and for hepatic metastatic disease it is 6 months.

G. Pseudotumors of the Pancreas

1. **Inflammatory and fibrosing conditions** of the pancreas may form dense, fibrotic masses, and segmental fibrosis that are difficult to

differentiate from carcinoma preoperatively. **Lymphoplasmacytic sclerosing pancreatitis** is often misdiagnosed as pancreatic cancer. Patients are typically young (i.e., age 30 to 50) and may have other associated autoimmune disorders (Sjögren's, ulcerative colitis, sclerosing cholangitis). Biopsy may only reveal plasma cells on pathologic review. When compared to patients with pancreatic cancer of all stages, these patients may have increased levels of serum IgG4, which can aid in making this diagnosis (*Ann Surg Oncol.* 2008;15(4):1147–1154).

IV. NEUROENDOCRINE NEOPLASMS OF THE PANCREAS.

See **Chapter 33**.

V. RARE NEOPLASMS OF THE PANCREAS

A. Acinar cell carcinoma is more common in men, and treatment is resection. Prognosis is slightly better than with pancreatic adenocarcinoma, but recurrence is common.

B. Solid pseudopapillary tumor is most commonly seen in young females, especially those who are African American. These tumors are typically large at presentation and are less frequently metastatic. Treatment is resection, and prognosis is generally favorable.

C. Metastatic tumors to the pancreas are most commonly renal cell carcinomas (RCC). Less common primaries include ovarian, colon, and melanoma. When isolated to the pancreas, resection in the setting of RCC has been associated with 60% 5-year survival (*J Am Coll Surg.* 2010;211(6):749–753).

D. Lymphoma can be primary or metastatic to the pancreas. Treatment is combined multimodality therapy with chemotherapy and radiation without surgical resection.

VI. CONGENITAL ABNORMALITIES

A. Failure of the ventral and dorsal pancreatic buds to fuse during the sixth week of development results in pancreatic divisum, the most common congenital abnormality of the pancreatic gland (4% to 14%). In this condition, the dorsal duct of Santorini becomes the means of pancreatic drainage from the bulk of pancreatic tissue (body, tail, and superior portion of head) (*J Clin Med Res.* 2018;10(5):370–375). Pancreas

divisum is associated with an increased risk of pancreatitis. Minor papilla sphincterotomy may improve outcomes in patients with recurrent pancreatitis. Patients with severe symptomatic pancreas divisum may require surgical resection.

B. Malrotation of the ventral primordium during the fifth week results in annular pancreas, where a thin, flat band of normal pancreatic tissue surrounds the second part of the duodenum. The annular pancreas usually contains a duct that connects to the MPD. Annular pancreas may cause duodenal obstruction usually early in life but sometimes later in life. The treatment of choice is duodenoduodenostomy or duodenojejunostomy.

VII. CYSTIC DISEASES

A. Pancreatic Pseudocyst. It is important to distinguish pseudocysts from tumors, cystic pancreatic neoplasms, and other fluid collections. An acute pancreatic fluid collection follows in approximately 25% of patients with acute pancreatitis. It is characterized by acute inflammation, cloudy fluid, a poorly defined cyst wall, and necrotic but sterile debris, and many resolve spontaneously. Pseudocysts differ from true cysts in that the wall is reactive inflammatory tissue as opposed to an epithelial-lined sac that secretes fluid. By definition, a fluid collection appearing in the first 4 weeks after the onset of pancreatitis is an *acute fluid collection;* after 4 weeks, it becomes an *acute pseudocyst* (*Gut.* 2013;62102–62111). Pseudocysts become chronic and may require treatment months after the acute attack has subsided.

1. **Causes.** Pseudocysts develop after disruption of the pancreatic duct with or without proximal obstruction, usually occurring after an episode of acute pancreatitis.

2. **Diagnosis**

   a. Clinical presentation. The most common complaint is recurrent or persistent upper abdominal pain. Other symptoms include nausea, vomiting, early satiety, anorexia, weight loss, back pain, and jaundice. Physical examination may reveal upper abdominal tenderness and a mass.

   b. Laboratory tests

   (1) Amylase. Serum concentrations are elevated in approximately 50% of cases.

(2) **Liver function tests** occasionally are elevated and may be useful if biliary obstruction is suspected.

(3) **Cystic fluid analysis** is discussed in the diagnosis sections c to e below.

c. Radiologic studies. CT is the radiographic study of choice for initial evaluation of pancreatic pseudocysts. CT scan findings that determine prognosis include the following:

(1) Pseudocysts **smaller than 4 cm** usually resolve spontaneously.

(2) Pseudocysts with **wall calcifications** generally do not resolve.

(3) Pseudocysts with **thick walls** are resistant to spontaneous resolution.

d. MRI and MRCP can be useful to delineate ductal anatomy and are not associated with the risks of pancreatitis and infection as with ERCP. However, MRCP is not as sensitive for small duct involvement as ERCP.

e. ERCP allows for the determination of pancreatic duct anatomy and influences therapeutic intervention. Approximately 50% of pseudocysts have ductal abnormalities identified by ERCP, such as proximal obstruction, stricture, or communications with the pseudocyst. ERCP itself risks infection of a communicating pseudocyst.

3. Complications

a. Infection is reported in 5% to 20% of pseudocysts and requires external drainage.

b. Hemorrhage results from erosion into surrounding visceral vessels. The most common arteries are the splenic (45%), gastroduodenal (18%), and pancreaticoduodenal (18%) arteries. Immediate angiographic embolization has emerged as the initial treatment of choice.

c. Obstruction. Compression can occur anywhere from the stomach to the colon. The arteriovenous system also can be subject to compression, including the vena caval and portal venous system. Hydronephrosis can result from obstruction of the ureters (rare). Biliary obstruction can present as jaundice, cholangitis, and rarely biliary cirrhosis.

d. Rupture occurs in fewer than 3% of cases. Approximately one-half

of patients can be treated nonsurgically, with total parenteral nutrition and symptomatic paracentesis or thoracentesis. However, rupture is occasionally a surgical emergency.

e. Enteric fistula can occur spontaneously and usually results in resolution of the cyst.

4. Treatment depends on symptoms, age, pseudocyst size, and the presence of complications. **Pseudocysts smaller than 6 cm and present for less than 6 weeks have low complication rates.** The chance of spontaneous resolution after 6 weeks is low, and the risk of complications rises significantly after 6 weeks.

a. Nonoperative. If the pseudocyst is new, asymptomatic, and without complications, the patient can be followed with serial CT scans or US to evaluate size and maturation.

b. Percutaneous drainage can be considered for patients in whom the pseudocyst does not communicate with the pancreatic duct and for those who cannot tolerate surgery or endoscopy. External drainage is indicated when the pseudocyst is infected and does not have a mature wall.

c. Excision, including resection, is only performed in unusual settings including bleeding, systemic sepsis, and concern for malignancy.

d. Internal drainage. Cystoenteric drainage is the procedure of choice in uncomplicated pseudocysts requiring intervention. Drainage can be undertaken by either surgical or endoscopic means. Endoscopic cystogastrostomy or cystoduodenostomy has a 60% to 90% success rate and is the initial treatment of choice. Endoscopic therapy also allows transsphincteric stenting in the case of duct–cyst communication. If drainage cannot be accomplished by endoscopic methods, surgical methods include Roux-en-Y cystojejunostomy, loop cystojejunostomy, cystogastrostomy, and rarely cystoduodenostomy. A biopsy of the cyst wall should be obtained to rule out neoplasia in the cyst.

B. True pancreatic cysts are most commonly asymptomatic and found incidentally on imaging studies with an incidence of 3% to 15% depending on imaging modality. Pancreatic cystic neoplasms account for 10% to 15% of all pancreatic cysts and include IPMNs, mucinous cystic neoplasms (MCNs), serous cystadenomas (SCAs), and solid

pseudopapillary neoplasms (SPNs).

C. Intraductal papillary mucinous neoplasm (IPMN) communicates with the pancreatic ductal system and are classified into three groups based on ductal involvement, which is important for determining subsequent management per the revised Fukuoka consensus guidelines *(Pancreatology.* 2017;17(5): 738–753). The three types of IPMN are main duct (MD-IPMN), branched suck (BD-IPMN), and mixed type IPMN.

1. **Epidemiology.** IPMNs account for >50% of all resected cystic pancreatic neoplasms. They have a slight male predominance and are usually diagnosed in the seventh decade of life.

2. **Diagnosis**

   a. **Imaging** with a pancreatic protocol CT or gadolinium-enhanced MRI with MRCP should be performed to evaluate pancreatic cystic lesions. MRI/MRCP may provide superior resolution of ductal communication and avoids radiation exposure in patients requiring frequent surveillance imaging. Findings of any "*high-risk stigmata*" are suggestive of malignancy and include:

      (1) Obstructive jaundice with a cystic lesion in the head of the pancreas

      (2) Enhancing mural nodules ≥5 mm

      (3) MPD dilation ≥10 mm

   b. **EUS** is indicated to further assess lesions in patients with any of the following "*worrisome features*":

      (1) Cyst size >3 cm

      (2) Enhancing mural nodule <5 mm

      (3) Thickened/enhancing cyst wall

      (4) MPD 5 to 9 mm

      (5) Abrupt change in MPD caliber with distal pancreatic atrophy

      (6) Lymphadenopathy

      (7) Increased serum CA19-9 levels (>37 U/mL)

   c. **Ultrasound-guided FNA** at the time of EUS may also aid in diagnosis. Aspiration of viscous fluid with an elevated CEA (>192 ng/mL) and high amylase levels (suggestive of MPD communication) are consistent with mucinous neoplasm of the pancreas. Cytology, DNA molecular analysis (high-amplitude

KRAS mutation), and elevated CA19-9 levels in the cyst fluid may be suggestive of malignant transformation.

3. **Treatment.** Surgery should be strongly considered in the medically fit patient with any "high-risk stigmata," cytology suggestive of malignancy, or symptoms related to pancreatic mass (pancreatitis, pain, obstructive jaundice). In the absence of these features, management per consensus guidelines is determined by IPMN subtype. When indicated, standard oncologic resection (PD or distal pancreatectomy) with lymph node dissection should be performed. The use of intraoperative frozen section is recommended to confirm the resection margin is free of high-grade dysplasia or invasive carcinoma, although the presence of low-grade dysplasia at the margin does not require further intervention (*Surgery.* 2011; 149(1):79–86).
   - **a.** Main duct IPMN carries a high incidence of malignancy with >70% having high-grade dysplasia or invasive carcinoma in a large retrospective study and warrants resection in selected medically fit patients (*Ann Surg.* 2015;261(5):976–983). While MPD dilation >10 mm is a clear indication for pancreatectomy, surgical resection for MPD dilation of 5 to 9 mm remains controversial but should be considered in young, healthy patients with life expectancy >10 years. Surgery should remove all tumor, and intraoperative frozen section is recommended to confirm that the resection margin is free of high-grade dysplasia or invasive carcinoma, although the presence of low-grade dysplasia at the margin does not require further intervention (*Surgery.* 2011;149(1):79–86).
   - **b.** Side branch IPMNs are less likely to evolve to invasive disease and management by current consensus guidelines indicates resection be considered for cysts >3 cm, mural nodules >5 mm, symptomatic patients, and cytology concerning for malignancy. Lesions without these findings may undergo routine surveillance imaging.
   - **c.** Mixed IPMNs have similar malignant risk and surgical management as main duct IPMN.

D. Mucinous Cystic Neoplasms (MCNs)

1. **Epidemiology.** MCNs are considered premalignant lesions that

account for approximately 25% of all resected cystic pancreatic neoplasms. They are most commonly located in the pancreatic body or tail and occur almost exclusively in middle age women. Most are asymptomatic and identified incidentally.

2. **Diagnosis.** MCNs are mucin-producing cystic lesions that do not communicate with the pancreatic ductal system. Histologically, they have a columnar epithelium lining with an ovarian-type stroma. Cyst fluid analysis reveals viscous fluid with an elevated CEA level (>192 IU) and low amylase levels.
3. **Treatment.** MCNs undergo an adenoma–adenocarcinoma sequence of evolution and invasive cancer is present in 17.5% of resected MCN. Malignancy is associated with larger size (>4 cm) and advanced age (>55). Five-year survival was 100% for noninvasive MCN and 57% for patients with malignant lesions (*Ann Surg.* 2008;247(4):571–579). As there is a clear survival advantage for those patients who undergo resection prior to the development of invasive cancer, pancreatectomy is recommended for all patients with MCN.

E. Serous Cystadenoma (SCA)

1. **Epidemiology.** SCAs are benign lesions that account for 16% of all resected cystic neoplasms. They are most commonly located in the pancreatic head, and the majority (75%) is diagnosed in women, usually in the fifth or sixth decade of life. Symptoms correlate with size (>4 cm); however, most lesions are asymptomatic.
2. **Diagnosis.** Lesions are characterized by an epithelial lining and are microcystic (“honeycomb” appearance) with a calcified central scar present in 30% of lesions on imaging studies. Cyst fluid analysis reveals nonviscous fluid with low CEA (<5 IU) and amylase levels.
3. **Treatment.** Surgery is reserved for symptomatic lesions. Asymptomatic SCAs do not require treatment and no additional surveillance imaging is required.

F. Solid-pseudopapillary neoplasm (SPN) is a rare neoplasm of the pancreas with low malignant potential and overall good clinical outcomes. Most are asymptomatic and found incidentally on imaging studies. Classic appearance on CT imaging demonstrates solid and cystic components with some having peripheral calcifications. Surgical

resection is the definitive treatment option (*Arch Pathol Lab Medicine.* 2017;141:990–995).

G. Other rare cystic pancreatic lesions include acinar cell cystadenocarcinoma, cystic choriocarcinoma, cystic teratoma, and angiomatous neoplasms. All lesions with carcinoma noted on preoperative biopsy or with a concern for malignancy should undergo resection if tolerated.

CHAPTER 23: PANCREAS

Multiple Choice Questions

1. **A 65-year-old female presents to clinic with an incidental finding of a 5-cm cystic pancreatic head mass with calcified central scar. Endoscopic ultrasound (EUS)-guided fine needle aspirate (FNA)-guided aspirate of the fluid reveals a low CEA and amylase level with no evidence of malignancy on cytology. What is the most likely diagnosis?**

   a. Pancreatic adenocarcinoma
   b. Intraductal papillary mucinous neoplasm
   c. Mucinous cystic neoplasm
   d. Serous cystadenoma
   e. Pancreatic pseudocyst

2. **A 45-year-old female presents with abdominal pain and an elevated amylase and lipase. The rest of her laboratory values are remarkable for a mildly elevated AST of 100 and elevated white blood cell count of 15,000. On hospital day 3, her pain is resolved and she is tolerating a regular diet. Which of the following should be performed prior to discharge?**

   a. ERCP
   b. RUQ ultrasound
   c. Amylase and/or lipase
   d. CT scan of abdomen
   e. Serum ethanol level

3. **A 73-year-old male is referred for evaluation of an incidentally discovered 2-cm cyst in the tail of his pancreas. On examination the patient has no abdominal pain, and his laboratory values are unremarkable. He undergoes an endoscopic ultrasound which shows a cystic lesion that appears to communicate with the pancreatic duct, originating from a side branch. Which of the following is the next step in management?**

a. Distal pancreatectomy
b. Total pancreatectomy
c. Observation
d. Enucleation
e. Biopsy

4. **A 35-year-old female is found to have an incidentally discovered 3-cm cystic lesion in the tail of her pancreas on a CT scan. She undergoes an endoscopic ultrasound which reveals a 3.5-cm cyst without communication with the pancreatic duct. Analysis of cyst fluid reveals high levels of mucin. What is the next step in the management of this patient?**

a. Distal pancreatectomy
b. Repeat CT scan in 1 year
c. MRCP
d. Total pancreatectomy
e. Endoscopic drainage

5. **A 59-year-old male is 2 weeks out from a pancreaticoduodenectomy for pancreatic adenocarcinoma complicated by a pancreatic fistula. He presents to the ED with new onset of bloody output in his drain. He is tachycardic to the 110s, but otherwise looks well. His Hgb is 10. What is the best course of management for this patient?**

a. CT scan
b. ERCP
c. Angiogram
d. Exploratory laparotomy
e. Remove the drain

6. **A 60-year-old physically fit female with painless jaundice and a 20-lb weight loss presents for evaluation of a 2-cm hypodense mass in the head of the pancreas on CT scan. The patient was referred to you from a gastrointestinal medicine colleague, who performed an endoscopic ultrasound with biopsy and ERCP with stent. The biopsy is suspicious for malignancy. By imaging, the lesion appears to be clearly resectable without evidence of**

malignancy. Which of the following is the most appropriate management of this patient?

a. Repeat endoscopic ultrasound with biopsy
b. Pancreaticoduodenectomy
c. Total pancreatectomy
d. MRI pancreatogram
e. Neoadjuvant chemoradiation

24 Spleen

Roheena Z. Panni and M. Majella Doyle

I. INTRODUCTION

A. Splenic Anatomy. The spleen is the largest reticuloendothelial organ in the body and arises from the primitive mesoderm as an outgrowth of the left side of the dorsal mesogastrium by the fifth week of gestation. The spleen assumes an important hematopoietic role until the fifth month of gestation, and even after birth, splenic erythropoietic function may persist in some hematologic disorders. The spleen resides in the left upper quadrant of the abdomen with the diaphragmatic surface facing posterosuperiorly, and it generally weighs 1,000 to 1,500 g. Of particular clinical relevance, the spleen is suspended in position by several ligaments and peritoneal folds which attach it to the colon (splenocolic ligament), the stomach (gastrosplenic ligament), the diaphragm (phrenosplenic ligament), and the kidney, adrenal gland, and tail of the pancreas (splenorenal ligament). The gastrosplenic ligament contains the short gastric vessels. The remaining ligaments are avascular, with rare exceptions, such as in patients with portal hypertension (Fig. 24-1). The most common anomaly of splenic embryology is the development of an accessory spleen which can be present in up to 20% of the population. Over 80% of accessory spleens are found in the region of the splenic hilum and vascular pedicle.

B. Splenic Function. The spleen has important hematopoietic, host defense, and cleansing functions and has a highly vascularized red pulp which is interspersed with areas of white pulp. The spleen can serve as an extramedullary site for hematopoiesis, if required. Erythrocytes in large numbers are destroyed intravascularly throughout the body. The released hemoglobin is then bound to haptoglobin, which is ultimately scavenged from the circulation in the spleen.

II. SURGICAL DISEASES OF THE SPLEEN

A. Indications for Splenectomy. Splenectomy is therapeutic for a large host of conditions, including both benign and malignant disease processes (Table 24-1).

1. Congenital:

a. ***Hereditary spherocytosis*** is an inherited autosomal dominant disorder which involves dysfunction or deficiency in one of the erythrocyte membrane proteins (*spectrin, ankyrin, band 3 protein,* or *protein 4.2*) which results in destabilization of the cell membrane. The spherocytes are sequestered and destroyed in the spleen which induces hemolytic anemia. Signs and symptoms include anemia, jaundice (indirect hyperbilirubinemia), and pigmented gallstones. The mean corpuscular volume is typically normal or slightly decreased. Diagnosis is confirmed by the presence of spherocytes on peripheral blood smear, positive osmotic fragility test, and decreased eosin-5-maleimide binding. Treatment includes folate supplementation and splenectomy for moderate to severe cases. It is the most common hemolytic anemia for which splenectomy is indicated.

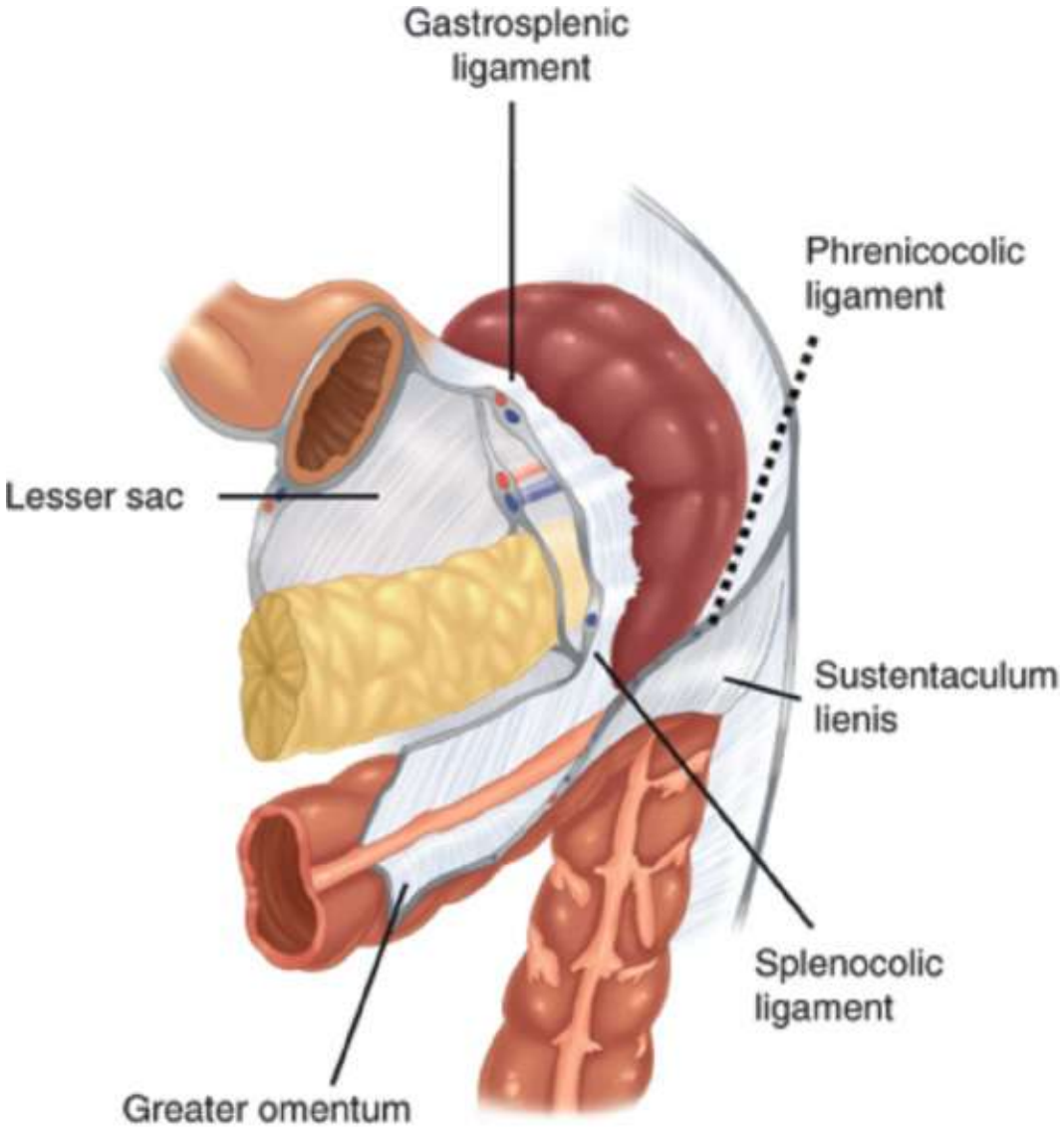


FIGURE 24-1 Suspensory ligaments of the spleen. (Data from Poulin EC, Thibault C. The anatomical basis for laparoscopic splenectomy. *Can J Surg*. 1993;36:484–488.)

b. ***Hereditary elliptocytosis*** results from genetic defects in skeletal membrane proteins of erythrocytes. The cell elongates as it circulates so that far fewer red blood cells (RBCs) are sequestered or destroyed when transiting the splenic parenchyma. In moderate to severe disease (more than 50% of RBCs are affected) patients present with anemia. In symptomatic patients, splenectomy may be curative.

c. ***RBC enzyme deficiencies*** associated with hemolytic anemia may be classified into two groups: deficiencies of enzymes involved in glycolytic pathways, such as pyruvate kinase (PK) deficiency, and

deficiencies of enzymes needed to maintain a high ratio of reduced to oxidized glutathione in the RBC, protecting it from oxidative damage, such as glucose-6-phosphate dehydrogenase (G6PD) deficiency. In both scenarios, patients with severe disease can develop splenomegaly, and splenectomy can alleviate transfusion requirements. As with other disorders that cause hemolytic anemia in children, splenectomy should be delayed if possible until at least 4 years of age to reduce the risk of post-splenectomy infection.

TABLE 24-1 Indications for, and Response to, Splenectomy in Various Diseases and Conditions

Disease/Condition	Indications for Splenectomy	Response to Splenectomy
Congenital hematologic disorders		
Hereditary spherocytosis Pyruvate kinase deficiency Sickle cell disease Thalassemia	Hemolytic anemia, recurrent transfusions, intractable leg ulcers	Improves or eliminates anemia, palliative only
Warm-antibody autoimmune hemolytic anemia	Failure of medical (steroid) therapy	60–80% response rate, recurrences common
Myeloproliferative and myelodysplastic disorders		
Acute myeloid leukemia, chronic myeloid leukemia, polycythemia vera	Symptomatic splenomegaly	Relief of abdominal pain and early satiety
Myelofibrosis		76% clinical response at 1 yr, high risk of hemorrhagic, thrombotic,

		and infectious complications (26%)
Lymphoproliferative disorders		
Chronic lymphocytic leukemia	Cytopenias and anemia	75% response rate
Non-Hodgkin lymphoma	Cytopenias, symptomatic splenomegaly	Improved complete blood count values, relief of symptoms
Platelet disorders		
Idiopathic thrombocytopenic purpura (ITP) Thrombotic thrombocytopenic purpura (TTP)	Failure of medical therapy, recurrent disease	75–85% rate of long-term response, curative in TTP
Infectious disorders		
Splenic abscesses Symptomatic parasitic cysts	Therapy of choice	Curative
Other disorders		
Gaucher disease, Niemann–Pick disease, amyloidosis, sarcoidosis	Hypersplenism or symptomatic splenomegaly	Improves cytopenias; does not correct underlying disease
Felty syndrome	Neutropenia	80% durable response rate
Splenic artery aneurysm	Splenectomy best for distal lesions	Curative

	near splenic hilum	
Portal hypertension	Portal or sinistral hypertension due to splenic vein thrombosis	Palliative

2. Acquired

a. ***Warm-antibody autoimmune hemolytic anemia*** is characterized by the destruction of RBCs by autoantibodies against antigens at 37°C. Clinical presentation includes mild jaundice and symptoms and signs of anemia. One-third to one-half of patients present with splenomegaly, and sometimes the spleen is palpable on physical examination. A positive result on direct Coombs test confirms the diagnosis by distinguishing autoimmune from other forms of hemolytic anemia. Treatment of severe symptomatic anemia requires RBC transfusion, however the mainstay treatment of symptomatic and unstable patients is corticosteroids. Therapy should continue until a response is noted by a rise in hematocrit and fall in reticulocyte count, which generally occurs within 3 weeks. Splenectomy is performed in nonresponders and is considered after failure of steroids or anti-CD20 antibody administration.

b. ***Hemoglobinopathies*** sickle cell disease is inherited in an autosomal codominant fashion, and the underlying abnormality is the mutation of adenine to thymine in the sixth codon of the β-globin gene. Deoxygenated HbS is insoluble and becomes polymerized and sickled. Due to recurrent vaso-occlusive episodes, these patients often have functional asplenia. The most common indications for splenectomy are recurrent acute sequestration crises, splenic abscess, and hypersplenism, and it remains largely a palliative procedure.

c. ***Thalassemia*** is prevalent in Mediterranean populations. In thalassemia, the primary defect is absent or reduced hemoglobin chains which leads to underproduction of hemoglobin and an excess of unpaired hemoglobin subunits. Treatment includes RBC transfusions to maintain a hemoglobin level above 9 mg/dL along

with chelation therapy. In complex cases where transfusion requirements are excessive and patients have painful splenic infarction, splenectomy is indicated. These patients are at high risk for postsplenectomy infectious complications due to an underlying coexisting immune deficiency.

3. **Platelet disorders** (Thrombocytopenias):
   a. ***Idiopathic thrombocytopenic purpura*** (***ITP***) is an autoimmune disorder characterized by low platelet counts due to premature removal of platelets secondary to opsonization by antiplatelet immunoglobulin G autoantibodies produced by the spleen. Patients present with petechiae or ecchymosis, but some also experience major bleeding, most commonly menorrhagia, hematuria, melena or epistaxis. The incidence of major intracranial hemorrhage is approximately 1%, and it usually occurs early in the disease course. Approximately half of the patients who present with ITP are children, and most pediatric cases are acute and remit regardless of therapy. Children often present at a young age (peak age approximately 5 years) with sudden onset of petechiae or purpura several days to weeks after an infectious illness. In contrast, adults experience a more chronic form of disease with an insidious onset. The first line of **ITP treatment** is oral prednisone at a dosage of 1.0 to 1.5 mg/kg per day. Fifty percent to 70% patients respond initially but frequently relapse. IV immunoglobulin is indicated for internal bleeding when platelet counts remain less than 5,000/mm^3, when extensive purpura exists, or to preoperatively boost platelets. Splenectomy results in 65% long-term remission (>5 years) and remains the treatment of choice in patients with platelets less the 30,000/mm^3 or with a high risk of bleeding (Fig.24-2). Most patients will achieve a response to splenectomy within 10 days postoperatively (*Am J Surg.* 2004;187:720–723). Alternatives to splenectomy include Rituximab (anti-CD20 monoclonal antibody) and thrombopoietin receptor agonists which have shown efficacy as second-line agents (*Blood.* 2012;120:960–969). When the short- and long-term outcomes after laparoscopic splenectomy are assessed in patients with ITP, the conversion rate to open surgery was 5.6%, and the immediate nonresponder rate was 8.2%.

However, in these patients, a clinical response was achieved in 72% of the patients on 5-year long-term follow-up (*Am J Hematol.* 2009;84:743–748). Urgent splenectomy, in conjunction with aggressive medical therapy, may play a role in the rare circumstance of severe, life-threatening bleeding in both children and adults with ITP.

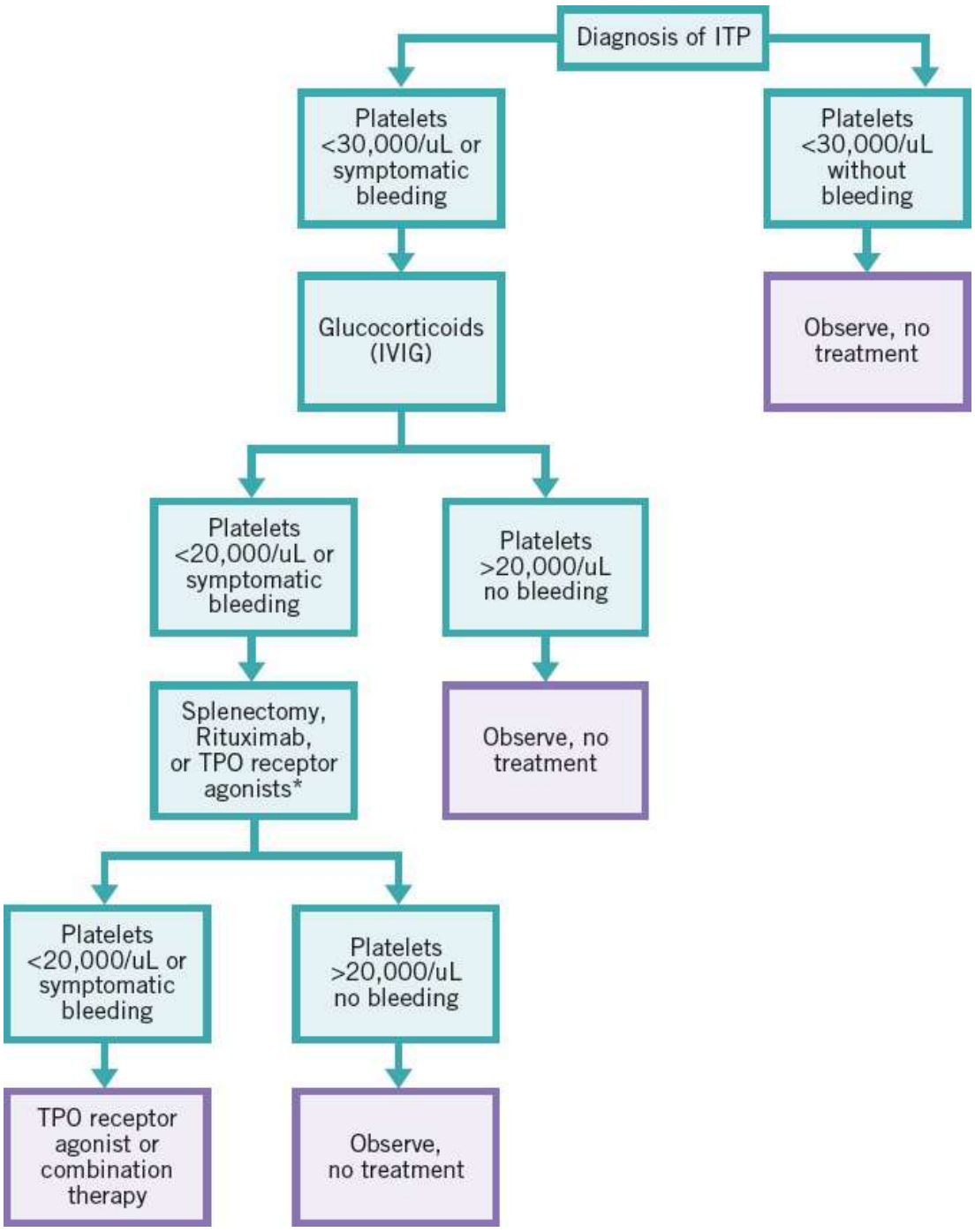


FIGURE 24-2 Simplified approach to the treatment of patients with ITP. Clinical symptoms and patients' concerns must be taken into account, and the decision for which management modality to use first (splenectomy, rituximab, or a thrombopoietin receptor agonist) is determined by patient and physician preference. The treatment of serious bleeding also requires additional therapy including platelet transfusions. ITP, idiopathic thrombocytopenia purpura; IVIG, intravenous immune globulin; TPO, thrombopoietin receptor agonist.

b. ***Thrombotic thrombocytopenic purpura*** (***TTP***) is a serious systemic disease resulting in the pentad of thrombocytopenia, microangiopathic hemolytic anemia, altered mental status, renal failure, and fever. It is a result of decreased ADAMT13, a protease responsible for cleaving von Willebrand factor, leading to platelet aggregation and thrombosis of the microvasculature. TTP may be distinguished from autoimmune causes of thrombocytopenia, such as Evans syndrome (ITP and autoimmune hemolytic anemia) or systemic lupus erythematosus, by a negative result on Coombs test. It is more common in adults and is usually idiopathic or drug related (e.g., cyclosporine, gemcitabine, clopidogrel, quinine). First-line **TTP treatment** includes plasmapheresis, which improves initial response and 6-month survival compared with plasma infusion (*N Engl J Med.* 1991;325:393–397). Steroid therapy in addition to plasmapheresis is used in the treatment of relapse. Second-line agents include rituximab, cyclosporine, and increased frequency of plasmapheresis. Plasma exchange consists of the daily removal of a single volume of the patient's plasma and its replacement with fresh-frozen plasma until the thrombocytopenia, anemia, and associated symptoms are corrected. Therapy is then tapered over 1 to 2 weeks. Splenectomy plays a key role for patients who experience relapse or who require multiple plasma exchanges to control symptoms, and it is generally well tolerated without significant morbidity. Furthermore, splenectomy has only shown benefit when used in conjunction with plasmapheresis in order to achieve durable remission (*Br J Haematol.* 2005;130:768–776).

4. Myeloproliferative and myelodysplastic disorders

a. ***Chronic myelogenous leukemia*** (CML) is a myelodysplastic disorder of the primitive pluripotent stem cells in the bone marrow that results in a significant increase in erythroid, megakaryocytic,

and pluripotent progenitors in the peripheral blood smear. Genetically it is characterized by the *bcr–abl* fusion oncogene, known as the *Philadelphia chromosome.* This oncogene results in a constitutively active tyrosine kinase, and thus first-line therapy utilizes the tyrosine kinase inhibitor (TKI) imatinib mesylate (Gleevec). Alternative TKI treatments (*dasatinib* and *nilotinib*) are used in cases of intolerance or suboptimal response. Stem cell transplantation is used for cases of treatment failure in eligible patients (*Blood.* 2006;108:1809–1820). In the management of CML, early splenectomy has no effect on disease progression or overall survival, however, it increased the rate of thromboembolic events and vascular accidents (*Cancer.* 1984;54;333–338). Splenectomy is indicated only for palliation of symptomatic splenomegaly (pain control, early satiety, etc.) or hypersplenism that significantly limits therapy.

b. ***Polycythemia vera*** is a clonal, chronic, progressive myeloproliferative disorder characterized by an increase in RBC mass, leukocytosis, thrombocytosis, and splenomegaly. Physical findings include ruddy cyanosis, hepatomegaly, splenomegaly, and hypertension. Treatment ranges from phlebotomy and aspirin administration to the use of chemotherapeutic agents. Splenectomy is not helpful in the early stages and is most useful with late-stage disease when patients have developed severe splenomegaly-related symptoms. Splenectomy can result in severe thrombocytosis, causing thrombosis or hemorrhage, which requires perioperative antiplatelet, anticoagulation, and myelosuppressive treatment.

c. ***Myelofibrosis*** is a chronic, malignant hematologic disease associated with bone marrow fibrosis, extramedullary hematopoiesis, splenomegaly, and the presence of RBC and white blood cell (WBC) progenitors in the bloodstream. Asymptomatic patients are closely followed, whereas symptomatic patients undergo therapeutic intervention targeted to their symptoms. Allogeneic bone marrow transplantation in younger, high-risk patients is the only curative treatment. Supportive therapy for clinically symptomatic anemia includes steroids, danazol, erythropoietin, or blood transfusion (*Clin Adv Hematol Oncol.*

2008;6:278,281–282). Splenomegaly-related symptoms are best palliated with splenectomy, but the cytopenias frequently recur. In addition, these patients are at increased risk for postoperative hemorrhage and thrombotic complications after splenectomy.

5. Lymphoproliferative disorders

a. ***Non-Hodgkin lymphoma*** (***NHL***) includes a wide range of disorders ranging from indolent to highly aggressive and includes a variety of clinical presentations. Splenomegaly exists in some forms. As with other malignant processes, splenectomy is indicated for palliation of hypersplenism and cytopenias or for diagnosis in patients with suspected persistent or recurrent disease after systemic therapy. Splenectomy plays an important role in the diagnosis and staging of patients with isolated splenic lymphoma. In these cases, improved survival has been shown in patients undergoing splenectomy.

b. ***Hairy cell leukemia*** is an uncommon blood disorder, representing only 2% of all adult leukemias, and is characterized by splenomegaly, pancytopenia, and large numbers of abnormal lymphocytes in the bone marrow. The lymphocytes have cytoplasmic projections which can be identified on peripheral smear. Splenectomy does not correct the underlying disorder, but cell counts do return to normal with some alleviation of symptoms as well. Splenectomy was previously regarded as the primary therapy for this disease, but improvements in systemic chemotherapy (e.g., rituximab, pentostatin, cladribine) have reduced the role of splenectomy, which is reserved only for refractory disease.

c. ***Hodgkin lymphoma*** historically had required splenectomy for diagnostic staging. However, due to refinements in imaging techniques and progress in the methods of treatment, splenectomy for Hodgkin lymphoma is rare. Indications for surgery are similar to those for NHL.

d. ***Chronic lymphocytic leukemia*** (***CLL***), a B-cell leukemia, is the most common of the chronic leukemias and is characterized by the accumulation of mature but nonfunctional lymphocytes. Primary therapy is medical, with palliative splenectomy reserved for those patients with symptomatic splenomegaly to improve

cytopenias and severe hypersplenism.

6. Neutropenia

a. ***Felty syndrome*** involves the triad of rheumatoid arthritis, splenomegaly, and neutropenia. It exists in approximately 3% of all patients with rheumatoid arthritis, two-thirds of whom are women. The size of the spleen varies from nonpalpable to massively enlarged. The primary treatment is corticosteroids, but refractory cases may require splenectomy to reverse the neutropenia. After splenectomy, >80% of patients show a durable increase in WBC count. Besides symptomatic neutropenia, other indications for splenectomy include transfusion-dependent anemia and profound thrombocytopenia.

7. Nonhematologic conditions

a. ***Trauma*** is the most common indication for splenectomy. In the unstable trauma patient, the procedure is traditionally performed via laparotomy. With current imaging modalities, grading of splenic injuries allows for conservative management in selected patients (*J Trauma.* 2008;207(5):646–655).

b. ***Incidental splenectomy*** occurs when the spleen is iatrogenically injured during an intra-abdominal procedure. Injury may result from a retractor placed in the left upper quadrant or during mobilization of the splenic flexure. Small injuries such as capsular tears may be controlled with hemostatic agents or electrocautery, but injuries resulting in significant blood loss may require splenectomy to achieve rapid hemostasis.

c. ***Wandering spleen*** is an uncommon abnormality in which the spleen floats inside the abdominal cavity due to anomaly of embryogenesis. The wandering spleen is not normally attached to adjacent viscera in the splenic fossa which may lead to splenic torsion and infarction. Splenectomy or splenopexy is indicated.

d. ***Splenic artery aneurysm*** is the most common visceral artery aneurysm and is typically an incidental finding. It occurs more commonly in females and is associated with a high incidence of rupture during pregnancy with significant maternal and fetal mortality. Indications for intervention include aneurysm size ≥2 cm, females of child-bearing age who may become pregnant, and

inflammatory pseudoaneurysms.

e. ***Primary infections*** of the spleen are infrequent. *Parasitic infections* account for more than two-thirds of splenic cysts worldwide but are rare in the United States. The majority are hydatid cysts caused by *Echinococcus* species. They are typically asymptomatic but may rupture or cause symptoms due to splenomegaly. The primary treatment is splenectomy, with careful attention not to spill the cyst contents. The cyst may be aspirated and injected with hypertonic saline prior to mobilization if concern about rupture exists.

f. ***Splenic abscesses*** are rare, but potentially lethal if not accurately diagnosed and treated. Two-thirds arise from seeding of the spleen by a distant site, most commonly endocarditis and urinary tract infections. Abdominal CT and/or ultrasound (US) imaging are the diagnostic modalities of choice. CT images reveal a low intensity lesion that does not enhance with contrast. The most common organisms are aerobic microbes (*Streptococci*, *Escherichia coli*), but other microorganisms have also been isolated (*Mycobacterium tuberculosis, Salmonella typhi*). Treatment includes broad-spectrum antibiotics for 14 days. Splenectomy is the operation of choice, but percutaneous and open drainage are options for patients who cannot tolerate splenectomy.

g. ***Cystic lesion*** of the spleen may be either true cysts or pseudocysts, but this differentiation is difficult to make preoperatively. ***True cysts*** (or primary cysts) have an epithelial lining and are most often congenital. Rare true cysts include epidermoid and dermoid cysts. ***Pseudocysts*** (or secondary cysts) lack an epithelial lining and make up more than two-thirds of nonparasitic cysts. They typically result from traumatic injury and will resorb. Treatment of splenic cysts depends on the size of the lesion and associated symptoms. Most are typically asymptomatic, but they may present with left upper abdominal or shoulder pain. If smaller than 5 cm, the cysts can be followed with US and often resolve spontaneously. Larger cysts risk rupture and require cyst unroofing or splenectomy. Percutaneous aspiration is associated with infection and recurrence and therefore not indicated. Laparoscopic management of splenic cysts yields shorter hospital

length of stay and fewer complications with no adverse effects (*Surg Endosc*. 2007;21:206–208).

h. ***Tumors and metastasis.*** Sarcoma is the most common primary tumor of spleen. Most metastases to the spleen are carcinomas, commonly lung cancer. If isolated splenic metastasis is confirmed, a laparoscopic splenectomy with intact spleen retrieval should be considered.

B. Preoperative Preparation for Splenectomy

1. ***Imaging:*** CT or MRI may be required in patients with concern for malignancy or clinical splenomegaly to accurately estimate splenic size and evaluate for hilar adenopathy that may complicate a laparoscopic approach. Right upper quadrant US is indicated for preoperative assessment of gallstone disease in patients with hemolytic or sickle cell anemias for planning of possible concomitant cholecystectomy.
2. ***Vaccination:*** Infection is the most common complication after splenectomy, and vaccination for encapsulated organisms is the mainstay of preventive therapy. Asplenic patients are at higher risk of infection caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, *Neisseria meningitidis* (*J Clin Pathol.* 2001;54(3):214–218).
3. ***Transfusions:*** Patients with hematologic disease, particularly those with autoimmune disorders, often have autoantibodies and are difficult to cross-match. Thus, blood should be typed and screened at least 24 hours prior to surgery, and patients with splenomegaly should have 2 to 4 units of packed RBCs cross-matched and available for surgery. Patients with severe thrombocytopenia (particularly those with counts <10,000/μL) should have platelets available for transfusion, which are administered intraoperatively after ligation of the splenic artery so they will not be quickly consumed by the spleen. Most patients with thrombocytopenia from ITP can undergo splenectomy safely without platelet transfusion even in the setting of very low platelet counts.
4. ***Deep vein thrombosis*** (**DVT**) ***prophylaxis:*** DVT after splenectomy in cases involving splenomegaly and myeloproliferative disorders is not uncommon, and the reported incidence of portal vein thrombosis (PVT) may reach 40% for patients presenting with both

splenomegaly and myeloproliferative disorders. The risk factors for DVT should be evaluated for each patient, and sequential compression devices and subcutaneous administration of heparin (5,000 U) or low–molecular-weight heparin, should be initiated for patients undergoing splenectomy (*Am Surg.* 2009;75:363–368; *Blood.* 2011;117:3494–3504).

5. ***Other considerations:*** Perioperative treatment with stress-dose steroids should be considered for patients receiving steroids preoperatively, and oral steroids should be continued postoperatively. These can be tapered gradually once a hematologic response to splenectomy occurs.

C. Splenectomy Techniques

1. ***Open splenectomy*.** Several clinical scenarios favor an open approach for splenectomy, including trauma, massive splenomegaly, ascites, portal hypertension, multiple prior operations, extensive splenic irradiation, and possible splenic abscess. Either an upper midline or a left subcostal incision can be utilized, though when significant splenomegaly is present, a midline incision is usually preferred. Splenic attachments including the splenocolic, gastrohepatic, and splenophrenic ligaments as well as the lateral peritoneal attachments are then divided. After mobilization, isolation of splenic artery and vein at the hilum is performed. Each vessel is individually ligated to prevent formation of arteriovenous fistula and care is taken to prevent injury to the tail of the pancreas. A drain is not routinely required unless injury to the pancreatic tail is suspected.
2. ***Laparoscopic splenectomy*** has been shown to be safe and effective under most conditions and is now considered the gold standard for elective splenectomy in patients with normal-sized spleens. Contraindications to the laparoscopic approach are listed in Table 24-2. Laparoscopic splenectomy is associated with decreased intraoperative blood loss, shorter hospital stay and lower morbidity compared to open splenectomy (*Arch Surg.* 1999;134(11):1263–1269; *Surgery.* 2003;134(4):647–655). Splenomegaly increases the complexity of the laparoscopic approach. Most moderately enlarged spleens (<1,000 g weight or 15 to 20 cm in length) can be removed in a minimally invasive fashion, often without a hand-port device. In general, massive splenomegaly (spleens greater than 30 cm in

craniocaudal length and weighing >3,000 g) should be approached in an open fashion because of the reduced working space and increased difficulty in manipulating the spleen.

TABLE 24-2 Contraindications for Laparoscopic Splenectomy

Absolute Contraindications	Relative Contraindication
Massive splenomegaly (>30 cm)	Moderate splenomegaly (>23 cm)
Portal hypertension	Severe, uncorrectable cytopenia
Splenic trauma (unstable patient)	Splenic vein thrombosis
	Splenic trauma (stable patient)
	Bulky hilar adenopathy
	Morbid obesity
	Pregnancy
	Extensive previous surgeries

3. ***Robotic splenectomy*** offers a unique three-dimensional visualization. The overall outcomes of robotic approach are very similar to standard laparoscopy, although not as cost effective.
4. ***Partial splenectomy*** is indicated to minimize the risk of postsplenectomy sepsis in children, in lipid storage disorders with splenomegaly (Gaucher disease), and certain cases of blunt and penetrating splenic trauma. Both open and laparoscopic approaches have been well described. The spleen must be adequately mobilized, and the splenic hilar vessels attached to the targeted segment should be ligated and divided, with the spleen then transected along the devascularized line of demarcation.

D. Splenectomy Complications

1. ***Intraoperative complications***
   a. ***Hemorrhage*** is the most common intraoperative complication (open: 2% to 3%, laparoscopic: 5%) of splenectomy, which can

occur during the hilar dissection or from a capsular tear during retraction. Bleeding during laparoscopic splenectomy may necessitate conversion to a hand-assisted or open approach. Strong consideration should be given to splenorrhaphy in minor injuries. Overall, the patient's hemodynamic condition is the primary determinant of whether splenic salvage can be attempted.

b. ***Pancreatic injury*** occurs in up to 6% of splenectomies, whether open or laparoscopic. A retrospective review of one center's experience with laparoscopic splenectomy found pancreatic injury in 16% of patients, of which half were simply isolated instances of hyperamylasemia (*J Surg.* 1996;172(5):596–599). If pancreatic parenchymal injury is suspected during laparoscopic splenectomy, a closed suction drain should be placed adjacent to the pancreas, and a drain amylase obtained prior to removal after the patient is eating a regular diet.

c. ***Colonic injuries*****.** Due to the close proximity of the splenic flexure to the lower pole of the spleen, it is possible to injure the colon during mobilization, but it is rare. Mechanical bowel preparation is not indicated preoperatively. Identification and primary repair are appropriate.

d. ***Gastric injuries*** can occur by direct trauma or can result from thermal injury during division of the short gastric vessels. Use of energy devices too close to the greater curvature of the stomach can result in a delayed gastric perforation. High index of suspicion and low threshold to oversew any areas of concern is warranted.

e. ***Diaphragmatic injury*** has been described during the mobilization of the superior splenic pole, especially with perisplenitis, and is of no consequence if recognized and repaired. In laparoscopic splenectomies, careful dissection of the splenophrenic ligament can minimize its occurrence. The pleural space should be evacuated under positive-pressure ventilation prior to closure to minimize the pneumothorax.

2. ***Early postoperative complications***

a. ***Pulmonary complications*** develop in nearly 10% of patients after open splenectomy, and these range from atelectasis to pneumonia and pleural effusion which are significantly less common with the laparoscopic approach (*Surgery.* 2003;134:647–653).

b. ***Subphrenic abscess*** occurs in 2% to 3% of patients after open splenectomy but is uncommon after laparoscopic splenectomy (0.7%). Treatment usually consists of percutaneous drainage and IV antibiotics.

c. ***Ileus*** can occur after open splenectomy, but a prolonged postoperative ileus should prompt the surgeon to search for concomitant problems such as a subphrenic abscess or PVT.

d. ***Wound problems*** such as hematomas, seromas, and wound infections are common after open splenectomy (4% to 5%). Splenectomy utilizing minimally invasive techniques is associated with wound complications that are usually minor and less frequent (1% to 2%).

e. ***Thrombocytosis and thrombotic complications*** can occur after either open or laparoscopic splenectomy. The presumed causes of thrombosis after splenectomy may relate to the occurrence of thrombocytosis, alterations in platelet function, and a low-flow/stasis phenomenon in the ligated splenic vein. As a result, splenomegaly is a major risk factor for splenic/PVT. Symptomatic PVT occurs more commonly than expected (8% to 12.5%) and can result in extensive mesenteric thrombosis if not recognized promptly and treated expeditiously (*Surg Endosc.* 2004;18:1140–1143).

3. ***Late postoperative complications***

a. ***Overwhelming postsplenectomy infection*** (***OPSI***) can occur at any point in an asplenic or hyposplenic patient's lifetime. The estimated mortality with OPSI averages 0.73/1,000 patient years (*Ann Intern Med.* 1995;122:187–188). Patients present with nonspecific flu-like symptoms rapidly progressing to fulminant sepsis, consumptive coagulopathy, bacteremia, and ultimately death within 12 to 48 hours. Encapsulated bacteria, especially *S. pneumoniae*, *H. influenzae* type B, and *N. meningitidis*, are the most commonly involved organisms. Successful treatment of OPSI requires early supportive care and high-dose third-generation cephalosporins. OPSI appears to have a higher incidence in children, particularly below the age of 5. All patients who have had a splenectomy should be vaccinated and educated about the risk of OPSI (Table 24-3).

b. ***Splenosis*** is the presence of disseminated intra-abdominal splenic tissue, which usually occurs after splenic rupture. Care should be taken during splenic morcellation to avoid bag rupture and spillage of splenic tissue.

TABLE 24-3 Centers for Disease Control and Prevention Vaccine Recommendations for Asplenic Patients

Vaccine	Recommendation
Tetanus (Td/Tdap)	One dose every 10 yr
Human papillomavirus	Three doses for women through age 26 years (0, 2, 6 months)
Measles, mumps, rubella	One or two doses
Varicella	Two doses (0, 4–8 weeks)
Zoster	One dose
Influenza	One dose annually
Pneumococcal polysaccharide	One or two doses
Hepatitis A	Two doses (0, 6–12 months or 0, 6–18 months)
Hepatitis B	Three doses (0, 1–2 months, 4–6 months)
Meningococcal	One dose

E. Antibiotics and the Asplenic Patient. Early antibiotic therapy for the asplenic patient can be considered in three contexts: deliberate therapy for established or presumed infections, prophylaxis in anticipation of invasive procedures (e.g., dental procedures), and general prophylaxis. Daily prophylactic antibiotics (oral penicillin) have been recommended after operation in all children younger than 5 years and in

immunocompromised patients because these patients are unlikely to produce adequate antibodies in response to pneumococcal vaccination. Some also advocate continuation of prophylactic antibiotics into at least young adulthood, though this is not as widely practiced.

CHAPTER 24: SPLEEN

Multiple Choice Questions

1. **The most common organism leading to overwhelming postsplenectomy infection (OPSI) is:**

   a. *Streptococcus pneumoniae*
   b. *Haemophilus influenza* (type B)
   c. Streptococcus B
   d. *Staphylococcus aureus*
   e. *Escherichia coli*

2. **Which of the following is the correct set of vaccines to administer to a patient who is asplenic?**

   a. Pneumococcal, pertussis, MMR, meningococcal, and influenza
   b. Pneumococcal, herpes zoster, meningococcal, and influenza
   c. Pneumococcal, *Haemophilus influenzae*, meningococcal, and influenza
   d. Pertussis, *Haemophilus influenzae*, meningococcal, and influenza
   e. Pneumococcal, influenza, MMR, and herpes zoster

3. **The most common etiology of splenic abscess is:**

   a. Hematogenous spread
   b. Secondary infection of hematoma
   c. Local extension of colonic perforation
   d. Local extension of pancreatic abscess
   e. Secondary infection of cyst

4. Which of the following are **not features of the post splenectomy patient?**

   a. Target cells
   b. Schistocytes
   c. Pappenheimer bodies
   d. Howell–Jolly bodies
   e. Leukocytosis that may persist for months

5. **Which of the following individuals is at least risk for postsplenectomy sepsis?**

   a. 6 year old who underwent elective splenectomy for hereditary spherocytosis
   b. 40 year old who underwent elective splenectomy for lymphoma
   c. 13 year old who underwent emergent splenectomy for blunt trauma
   d. 35 year old who underwent emergent splenectomy for blunt trauma
   e. 22 year old who underwent elective splenectomy for thalassemia

6. **Which of the following concerning thrombotic thrombocytopenic purpura (TTP) is true?**

   a. Rituximab is standard first-line treatment
   b. Splenectomy is limited to patients who do not respond to medical management
   c. Plasmapheresis improves survival compared with plasma infusions
   d. It is associated with severe deficiency of ADAMTS-13
   e. Results in a hemolytic anemia with a positive Coombs test

7. **The most common indication for elective splenectomy is:**

   a. Hodgkin lymphoma
   b. Thrombotic thrombocytopenic purpura
   c. Sickle cell anemia
   d. Idiopathic thrombocytopenic purpura
   e. Hereditary spherocytosis

8. **A 25-year-old female presents with incidental finding of a proximal 2.5 cm splenic artery aneurysm. Which of the following therapies would be most appropriate?**

   a. Conservative management with routine surveillance
   b. Aneurysm exclusion and in situ reconstruction with vein graft
   c. Aneurysm exclusion and in situ reconstruction with PTFE
   d. Resection with splenectomy
   e. Proximal and distal ligation of the splenic artery

9. **A 55-year-old female who underwent splenectomy 7 days ago for myelofibrosis and massive splenomegaly presents with**

abdominal pain, fever, and WBC of 17,000. CT of the abdomen reveals a small amount of pneumatosis in the small bowel and ascites.

The most likely etiology is:

a. Nonocclusive mesenteric ischemia
b. Portal vein thrombus
c. Perforated viscus
d. SMA occlusion
e. *Clostridium difficile* colitis

10. The most common site of an accessory spleen is:

a. Splenorenal ligament
b. Mesentery of the small bowel
c. Bifurcation of the aorta
d. Gastrohepatic ligament
e. Splenic hilum

25 Abdominal Transplantation

Jessica Lindemann and Jason R. Wellen

INTRODUCTION TO PHYSIOLOGIC IMMUNITY

Our immune system did not evolve to stymie the efforts of transplant surgeons, but rather to evade microbes that aim to overrun us. To understand why tissues from one individual are rejected by another, one has to appreciate the components of our immune system in its physiologic state.

I. THE IMMUNE SYSTEM ENCOMPASSES TWO COMPLEMENTARY ARMS

A. The innate immune system recognizes general distress as well as conserved moieties from ubiquitous pathogens, such as lipopolysaccharides of gram-negative bacteria. The response is **direct, nonspecific, and lacks memory.**

1. Mediators

a. The **complement cascade** is a soluble group of proteins whose activation promotes the formation of the **membrane attack complex** (MAC). This embeds itself within cell membranes of pathogens causing disruption and cell lysis. In addition, byproducts of the complement cascade opsonize pathogens, which promote phagocytosis by **antigen-presenting cells** (APCs).

b. Natural killer cells recognize cells that lack a self-**major histocompatibility complex** (MHC) and are part of the body's immunosurveillance for cancer.

B. The **adaptive immune system** recognizes specific, pathogenic antigens in the context of the MHC, which helps the immune system distinguish "self" from "non-self." Foreign antigens presented in the context of the MHC are targets of the adaptive immune system. In humans, these

complexes are referred to as **human leukocyte antigens** (**HLA**) and are located on chromosome 6.

1. Classes of HLA

a. Class I (**A**, **B**, **C**) are present on all nucleated cells and are targets for cytotoxic (CD8) T-cells.

b. Class II (**DR**, **DP**, **and DQ**) are present on APCs and are targets for helper (CD4) T-cells. They trigger an antibody (humoral) mediated immune response.

The most important HLA in solid organ transplantation are A, B, and DR. Since each person has two MHC complexes, one on each copy of chromosome 6, everyone has a total of six HLA antigens that are relevant to organ transplantation.

2. Adaptive immune responses

a. Cell mediated. Antigens in the peripheral tissues are presented to T-cells located in lymph nodes and the spleen. The **T-cell receptor** (TCR) recognizes a specific antigen in the context of the MHC. Formation of the TCR is the result of DNA rearrangement that occurs within the thymus during fetal development. Following rearrangement, T-cells are selected based on their ability to bind self-MHC without activating a response. MHC encountered in the tissues not involved in thymic education activates an immune response. ***This is the basis of alloreactivity.***

(1) Helper T-cells (**CD4**) recognize exogenous antigens presented in the context of MHC class II on the surface of APCs (B-cells, dendrites, and macrophages). Activation releases IL-2, which causes B-cell maturation into plasma cells and IL-4, which causes maturation of cytotoxic T-cells.

(2) Cytotoxic T-cells (**CD8**) recognize endogenous (i.e., TB, viruses) pathogens presented in the context of MHC class I.

b. Antibody mediated (**humoral**). B-cells (bone) activate antibody-mediated (humoral) immunity. IL-4 from helper T-cells transforms B-cells into **plasma cells**, which secrete antibodies specific to the offending pathogen.

TRANSPLANT IMMUNOLOGY

A. Isografts. Tissue transfer from genetically identical individuals (i.e.,

twins).

B. Xenografts. Tissue transfer between species.

C. Allografts. Tissue transfer among members of the same species.

1. Alloreactivity/histocompatibility

a. ABO blood compatibility is necessary for all transplants, except liver.

b. HLA-A, **-B**, **-DR** are the most important for compatibility; HLA-DR is the most important overall.

(1) Cross-matching detects preformed antibodies against donor HLA. It involves mixing recipient serum with donor lymphocytes.

(2) Panel reactive antibodies (PRA) help to predict the likelihood of a positive cross-match. It is determined by testing the potential recipient's serum against a panel of cells of various HLA specificities in a manner similar to the cross-match. The percentage of specificities in the panel with which the patient's sera react is the PRA. Patients who have been exposed to other HLAs via blood transfusion, pregnancy, or prior transplantation will have higher PRAs.

TRANSPLANT REJECTION

I. TYPES OF REJECTION

A. Hyperacute rejection is the result of preformed anti-HLA antibodies that bind the allograft endothelium to initiate a cascade of events culminating in vascular thrombosis and ischemic necrosis. The only therapeutic option is to remove the allograft immediately. This is extraordinarily uncommon in the modern era of cross-matching.

B. Accelerated rejection is caused by sensitized T-cells that produce a secondary immune response. This generally occurs within 1 week of transplantation. Treatment includes pulse steroids and muromonab-CD3 (OKT3).

C. Acute cellular rejection (ACR) is cell mediated and involves T-lymphocytes (cytotoxic and helper). This typically occurs 1 week to 1 month after transplantation. There are two basic treatment modalities: High-dose methylprednisolone and an antilymphocyte preparation.

D. Chronic rejection is a poorly understood phenomenon that can occur weeks to years after transplantation. Emerging evidence suggests that the humoral immune response is an important contributor. Plasmapheresis, IV immunoglobulin, and rituximab have been used to treat antibody-mediated rejection.

IMMUNOSUPPRESSION

Immunosuppressive drugs are used for induction, maintenance therapy, and treatment of rejection. In general, steroids and antithymocyte agents are used for induction with the primary aim of lymphocyte depletion and immune system downregulation. An ideal maintenance therapy regimen includes a calcineurin inhibitor (CNI), an antiproliferative agent, and steroids. In the treatment of rejection, it is important to choose medications that target the underlying mechanism. Doses given below are typical for kidney transplant recipients, however, specific combinations of medications and dosages are tailored for the patient and organ transplanted.

I. CLASSES OF IMMUNOSUPPRESSIVE DRUGS (FIG. 25-1)

A. Corticosteroids (prednisone, methylprednisolone/Solu-Medrol) play the broadest role in immunomodulation, acting on lymphocytes to prevent proliferation and on neutrophils to prevent migration, dampening the inflammatory response. They are used for induction, maintenance, and treatment of rejection.

1. Induction: Methylprednisolone up to 1 g IV initial dose followed by taper.

2. Maintenance: Prednisone: 1 mg/kg QD for days 1 to 3, 20 mg QD for days 4 to 14, reduce by 5 mg weekly until 5 mg QD.

3. Rejection (early/mild): Methylprednisolone 7 mg/kg IV QD for 3 days or prednisone 3 mg/kg PO QD divided into 2 to 4 doses for 3 to 5 days, then resume previous steroid dose.

Toxicities include poor wound healing, hyperglycemia, infections, cataracts, hypertension, weight gain, and bone disease.

B. Antiproliferative Agents/Antimetabolites

1. Azathioprine (Imuran) is a purine analog that alters DNA and RNA synthesis inhibiting T- and B-lymphocyte proliferation. Used for maintenance therapy:

a. 1 to 2 mg/kg PO QD in combination with other immunosuppressive medications.

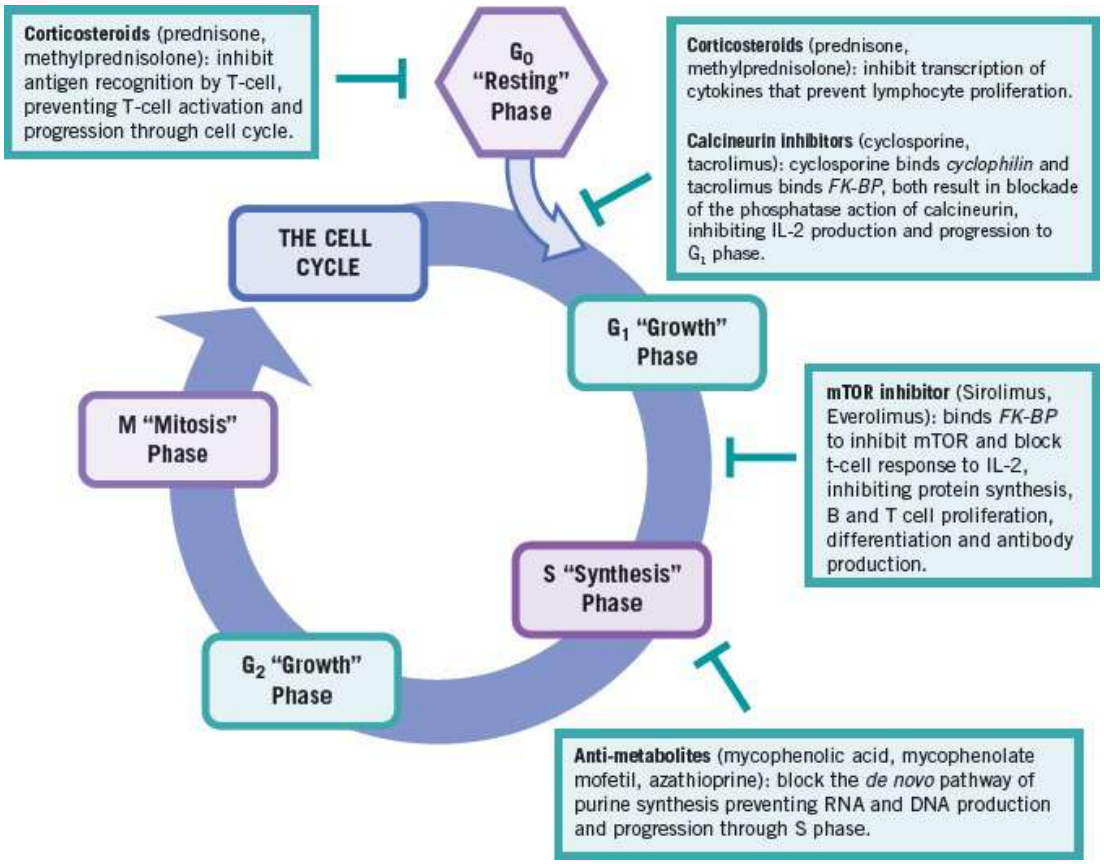


FIGURE 25-1 Classes of immunosuppressant medications and sites of action within the cell cycle.

b. 2 to 3 mg/kg PO QD if used alone, max dose 200 mg/day.

Myelosuppression manifested as leukopenia and thrombocytopenia are its main toxicities.

2. Mycophenolic acid (CellCept, Myfortic) selectively inhibits lymphocyte proliferation resulting in suppression of T- and B-lymphocytes. Used for maintenance therapy:

a. Mycophenolate mofetil (CellCept): 1 to 3 g PO per day, divide over two doses.

b. Mycophenolic acid (Myfortic): 360 to 1,080 mg PO BID. Use 360 mg BID with tacrolimus, leukopenia, diarrhea, or in first week posttransplant.

Toxicities include GI disturbance and leukopenia.

C. CNIs

1. Cyclosporine (CsA, Sandimmune, Neoral, Gengraf) inhibits IL-2 production preventing the initiation of T-cell proliferation. Used for maintenance therapy:

a. 2 to 3 mg/kg PO BID as starting dose, titrate to trough of 300 ng/mL then target trough of 150 ng/mL from 6 weeks posttransplant.

Nephrotoxicity, hypertension, tremors, seizures, hyperkalemia, hyperuricemia, hypercholesterolemia, gingival hyperplasia, and hirsutism are the main toxicities.

2. Tacrolimus (FK506, Prograf) acts similarly to CsA but is 10 to 100 times more potent. Used for maintenance therapy:

a. 0.1 mg/kg PO BID, titrate dose for target trough level 5 to 7 ng/mL.

A trough level above 15 ng/mL is considered toxic. Toxicities are similar to CsA, but include more GI and neurologic changes.

D. mTOR Inhibitors

1. Sirolimus (Rapamune) is an anti-T-cell agent that inhibits the mTOR molecule, blocking T-cell signal transduction. Used as maintenance therapy:

a. 6 mg PO loading dose on posttransplant day 1, followed by 2 mg PO QD, titrate to trough of 8 to 12 ng/mL for first year. Dosing adjustments are made based on concomitant use of a CNI.

Toxicity includes thrombocytopenia, hyperlipidemia, oral ulcers, anemia, proteinuria, and impairment of wound healing.

2. Everolimus (Zortress): mechanism of action and toxicities similar to sirolimus, but with greater bioavailability. Increasingly used for maintenance therapy in combination with low-dose tacrolimus to minimize CNI toxicity.

a. 1 mg PO BID, titrate to trough level between 3 and 8 ng/mL.

E. Costimulation Blockade. Belatacept (Nulojix) prevents costimulation required for T-cell activation resulting in T-cell antigen-specific tolerance (anergy). FDA approved in 2011 for maintenance therapy in renal transplant, used only off label in liver transplantation:

1. 10 mg/kg IV loading dose posttransplant day 1, second dose on days 4 and 5 then once monthly 5 mg/kg IV.

Associated with posttransplant lymphoproliferative disorder

(PTLD) and should be avoided in patients who are EBV seronegative or who have received lymphocyte-depleting therapy.

F. Antithymocyte Antibodies (Fig. 25-2)

1. Thymoglobulin causes rapid T-cell depletion. It is the most commonly used antithymocyte antibody in the United States and is derived from rabbit serum after exposure to human thymocytes or T-cells. Used as induction therapy or as rescue therapy following ACR, with premedication to avoid cytokine release syndrome:

a. Premedication: diphenhydramine 50 mg PO, acetaminophen 650 mg PO, hydrocortisone 200 mg IV, given 1 hour before infusion.

b. Induction: 4.5 mg/kg IV over 4 to 6 hours given on days 0, 1, and 2 posttransplant.

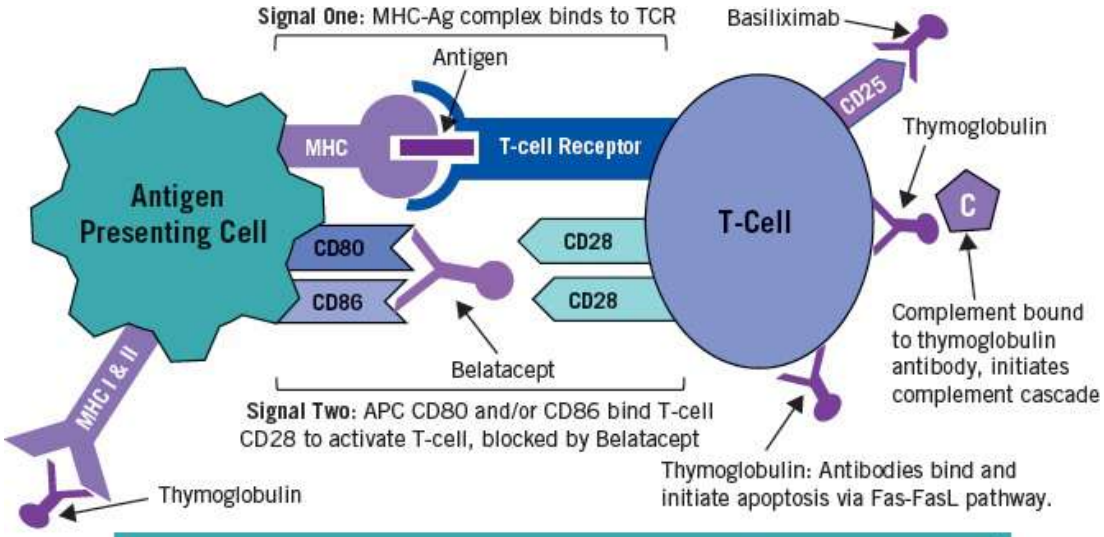
c. Rejection: 2 to 3 mg/kg IV over 4 to 6 hours for 3 and 4 days.

Side effects include allergic reaction, leukopenia, and increased CMV infection and lymphomas.

2. Basiliximab (Simulect): binds to T-cell IL-2 receptor (CD25) only and is also used for induction therapy, but much less often than thymoglobulin and usually reserved for patients with low risk of rejection and preoperative leukopenia, thrombocytopenia, and/or hypotension.

a. 20 mg IV QD on days 1 and 4 posttransplant.

Side effects are minimal due to its specificity in binding.



Co-stimulation Blockade (Belatacept): blocks the binding of APC CD80 and/or CD86 to T-cell CD28, preventing Signal Two and inhibiting T-cell activation. Belatcept is a fusion protein composed of the Fc component of human IGg1 and CTLA-4 (CD27 analog) that competitively binds with CD80 and CD86.

Antithymocyte Antibodies (Thymoglobulin, Basiliximab): Thymoglobulin is a polyclonal antibody that causes rapid lymphocyte depletion via complement-dependent lysis and apoptosis. It also modulates T-cell activation and homing functions, interferes with APC function and induces regulatory T-cells and Natural Killer cells. Basiliximab is a non-T-cell depleting monoclonal antibody that competitively binds CD25, the IL-2 receptor on T-cells, preventing T-cell proliferation and activation of B cells by T-cells.

MHC – major histocompatibility complex, Ag – antigen, TCR – T-cell receptor, C – complement, APC – antigen presenting cell

FIGURE 25-2 Mechanism of action for costimulation blockade and antithymocyte antibodies.

II. COMPLICATIONS OF IMMUNOSUPPRESSION

A. Bacterial Infections. Pneumonia and urinary tract infections (UTIs) occur fairly commonly after transplantation. Infectious complications from opportunistic organisms are now uncommon because of appropriate prophylactic strategies.

B. Viral Infections

1. **Cytomegalovirus** (**CMV**) infection can occur at any time but is most common 1 to 4 months posttransplant in the absence of prophylaxis. CMV may infect the recipient's liver, lungs, or GI tract. Signs and symptoms include fever, chills, malaise, anorexia, nausea, vomiting, cough, abdominal pain, hypoxia, leukopenia, and elevation in liver transaminases. CMV peripheral blood PCR or serologic assays are the most common tools for diagnosis. Prophylaxis may be useful in any patient who receives a CMV-positive allograft because many of these patients develop a significant CMV infection if left untreated.

Treatment consists of decreasing immunosuppression and administering ganciclovir, which inhibits DNA synthesis.

2. **Epstein–Barr virus** (**EBV**) can infect B-cells at any time after transplantation and may be associated with the development of PTLD, a type of lymphoma usually of monoclonal B-cell origin. Infiltration of the hematopoietic system, central nervous system (CNS), lungs, or other solid organs may occur. The patient usually presents with fever, chills, sweats, enlarged lymph nodes, and elevated uric acid. Diagnosis is made by physical examination, EBV serology, computed tomography (CT) scan of the head, chest, and abdomen (to evaluate lymph nodes or masses), and biopsy of potential sites or lesions. Treatment consists of reducing or withdrawing immunosuppression.
3. **Herpes simplex virus** (**HSV**) causes characteristic ulcers on the oral mucosa, in the genital region, and in the esophagus. Renal transplant patients, if not on ganciclovir, are given prophylactic acyclovir. Active HSV infections are treated by decreasing the patient's immunosuppression and instituting acyclovir therapy.
4. **BK virus** is a member of the polyoma virus family. Approximately 90% of individuals are seropositive. BK viruria develops in 30% of kidney transplant recipients and progresses to viremia in 15% of recipients within the first year. Persistent viremia leads to BK nephropathy, which occurs in up to 10% of kidney transplant recipients during the first year. There is no known effective treatment.

C. Fungal infections can range from asymptomatic colonization to lethal invasive infections. Oral **candidiasis** can be prevented and treated with oral nystatin or fluconazole. Esophageal candidiasis can be treated with a short course of intravenous amphotericin B or fluconazole. Serious fungal infections are treated with intravenous amphotericin B, although use of less nephrotoxic agents such as caspofungin and anidulafungin is increasing.

D. Malignancies. Cancers that occur at a higher frequency in transplant recipients include squamous cell carcinoma, basal cell carcinoma, Kaposi sarcoma, lymphomas, hepatobiliary carcinoma, and cervical carcinoma.

ORGAN ALLOCATION

Over 120,000 individuals in the United States are currently waiting for organ donation. The gap between supply and demand grows daily, so a system exists that allocates solid organs to individuals based on two overarching themes:

A. Justice. Each candidate is given fair consideration based on individual circumstances and medical need.

B. Utility. The system tries to maximize the number of transplants performed and the survival of both patients and allografts.

The **United Network of Organ Sharing** (**UNOS**) is the organization contracted by the federal government to oversee organ allocation in the United States. Fifty-eight local Organ Procurement Organizations (OPOs) serve 11 UNOS regions.

I. LIVER ALLOCATION. Livers are allocated based on the Model for End-Stage Liver Disease (**MELD**) scoring system which predicts 3-month mortality in patients with liver disease. The MELD score is derived from a logarithmic formula that incorporates the values for bilirubin, serum creatinine, and the international normalized ratio (INR) and ranges from 6 to 40 (www.unos.org). For patients with an initial MELD score greater than 11, the MELD score is recalculated with an adjustment formula for serum sodium (Na), as hyponatremia was found to be an independent predictor of mortality in liver transplant candidates (*New Engl J Med.* 2008;359:1018–1026). Incorporating Na into the MELD score increases its predictive accuracy, particularly in patients with ascites (*Gastroenterology.* 2006;130:1652–1660). Livers are allocated to appropriate patients with the highest MELD scores. Special exception points may be granted, such as in cases of hepatocellular carcinoma (HCC), hilar cholangiocarcinoma, hepatopulmonary syndrome, or hepatorenal syndrome. Children receive a Pediatric End-Stage Liver Disease (PELD) score.

II. KIDNEY ALLOCATION. In 2014, an Organ Procurement and Transplant Network (OPTN) policy was implemented to increase utilization of available kidneys, reduce regional variability in access to transplantation and maximize the number of years individual recipients have a functioning graft (https://optn.transplant.hrsa.gov/governance/policies/). It includes an estimated posttransplant survival (EPTS) score for the recipient and kidney donor profile index (KDPI), with priority given to

candidates with less common blood types and a high calculated PRA score. Waiting-list times are also included. EPTS is calculated based on age, time on dialysis, diabetes status, and history of previous solid organ transplant. It estimates the number of years of benefit from a transplant.

KDPI is calculated for deceased donor kidneys only and provides a measure of donor quality to assist the transplant team in determining the suitability of donor kidney offers for potential recipients. It includes 10 donor factors and results in a score reported as a percent.

KDPI is derived from the Kidney Donor Risk Index (KDRI), which is a measure of relative risk of graft failure. The reference population for KDRI is all deceased donor kidneys transplanted in the United States from the previous calendar year. The KDPI is then determined using the KDRI-to-KDPI Mapping Table (https://optn.transplant.hrsa.gov/media/2150/kdpi_mapping_table.pdf). The lower the KDPI, the longer the predicted graft survival. For example, a deceased donor kidney with a KDPI of 90% has a relative risk of graft failure (KDRI) greater than 90% of all recovered kidneys from the prior calendar year. Recipient consent is required to receive a kidney with a KDPI >85%.

KDPI was primarily included in the new policy to facilitate "longevity matching" within the kidney allocation system through which transplant candidates in the top 20% of calculated EPTS receive priority for kidneys from donors with KDPIs of 20% or less. However, it should not be used in isolation when determining whether to use a kidney for transplantation. Recipient factors and other donor factors not included in the calculation should be considered. Additionally, KDPI was developed using kidney transplant outcomes in an adult population and should be used with caution in the pediatric recipient, though the original analysis for KDRI included pediatric donors (*Transplantation.* 2009;88(2):231–236).

ORGAN DONATION

I. TYPES OF ORGAN DONATION

A. Living Donation. Given the significant number of candidates on the transplant waiting list, living donation is an important means for increasing the donor pool and has become an integral part of renal

transplant practice. Advantages of living-donor transplantation include improved short- and long-term graft survival (1-year survival >95%), improved immediate allograft function, planned operative timing to allow for medical optimization (and, often, avoidance of dialysis). The evaluation of potential living donors includes assessment of their overall health, comorbid conditions and psychosocial influences. Compatibility with their intended recipient is determined though ABO blood typing and HLA histocompatibility. Donors who are not compatible with their intended recipient may still donate through paired exchange and ABO-incompatible protocols.

B. Deceased Donation

1. **Heart beating** (Donation after brain death, DBD). Strict criteria for establishing brain death include irreversible coma and the absence of brain stem reflexes (i.e., pupillary, corneal, vestibulo-ocular, and gag reflexes). Other useful diagnostic tests include blood flow scan, arteriography, and an apnea test.
2. **Non-heart beating** (Donation after cardiac death, DCD) refers to those potential organ donors who do not meet strict brain death criteria but who are considered to have nonrecoverable devastating neurologic insults. Life support is discontinued in the operating room, and organ procurement is initiated after a specified interval following cardiac asystole. While effectively increasing the donor pool, 16% to 28% of DCD livers have biliary complications, including ischemic cholangiopathy (*World J Gastroenterol.* 2014;20(20):6159–6169). However, there is a growing body of evidence to suggest that in high volume centers and selected recipients, comparable outcomes can be achieved (*Liver Transpl.* 2018;24(6):279–789).

II. SUITABILITY FOR TRANSPLANTATION

A. Contraindications

1. **Active infection.** While evidence of HIV or TB are absolute contraindications to organ donation, patients with localized infections such as UTIs and pneumonia, in the absence of dissemination, are routinely given consideration. Even in the presence of bacteremia, appropriate initiation of antibiotic therapy ensures a small risk of transmission.
2. **Cancer.** With the exception of primary CNS tumors, active cancer,

whether treated or not, is an absolute contraindication to organ donation. While the blood–brain barrier protects CNS tumor cells from widespread dissemination in the heavily immunosuppressed patient, this is not the case for other malignancies. Depending on the type of cancer, patients may be listed after a cancer-free wait time ranging from 2 to 5 years.

B. General Considerations

1. **Age.** As experience with less than ideal donors has grown, it has become apparent that arbitrary limits on donor age are unnecessary. Good allograft function has been achieved with kidney and liver donors with advanced age.
2. **Overall health.** As the donor pool ages, systemic diseases that can have an effect on specific organ function must be taken into consideration. Hypertension and atherosclerosis can hinder the suitability of kidney allografts, while obesity with hepatic steatosis limits the suitability of liver allografts.
3. **Social behaviors.** While all donors are tested for HIV, hepatitis, and other viral infections, donors who engage in high-risk behaviors may still transmit an infection if donation were to occur within the window period prior to seroconversion. Potential recipients are counseled regarding these socially high-risk donors and given the option whether to consider organs allocated from this group.

ORGAN PROCUREMENT AND PRESERVATION

Initial dissection aims to control the abdominal aorta and inferior mesenteric vein (IMV) for the placement of cannulae. Identification of hepatic hilar structures aids later dissection in the cold. After cross-clamping the supraceliac aorta, the abdominal viscera are then flushed and cooled with University of Wisconsin (UW) preservation solution or histidine–tryptophan–ketoglutarate (HTK). The organs are packed with ice while the solution infuses. Evacuation of blood is into the chest via the inferior vena cava (IVC). The donor liver is removed with its diaphragmatic attachments, a cuff of aorta surrounding the celiac axis and the superior mesenteric artery (SMA), and a portion of the supra- and infrahepatic IVC. The liver is packaged in preservation solution and surrounded by iced saline during transportation.

The donor kidneys are removed separately or en bloc. The ureters are

dissected widely to minimize devascularization and are divided near the bladder.

The pancreas may also be removed for transplantation, with the pancreas, duodenum, and spleen removed en bloc. The blood supply for the pancreas allograft comes from the donor splenic artery and SMA, and outflow is via the portal vein (Fig. 25-3).

With the advent of modern preservation solutions, donor livers can be preserved for up to 12 hours before reperfusion (kidneys up to 40 hours), with a low incidence of allograft dysfunction. Ideally, cold ischemia time is minimized to less than 6 hours for livers and 24 hours for kidneys.

ORGAN TRANSPLANTATION

I. KIDNEY

A. End-stage renal disease (ESRD) is the consequence of multiple disease processes; however, diabetes, hypertension, and polycystic kidney disease account for majority of cases (Table 25-1).

1. Keys to successful transplantation

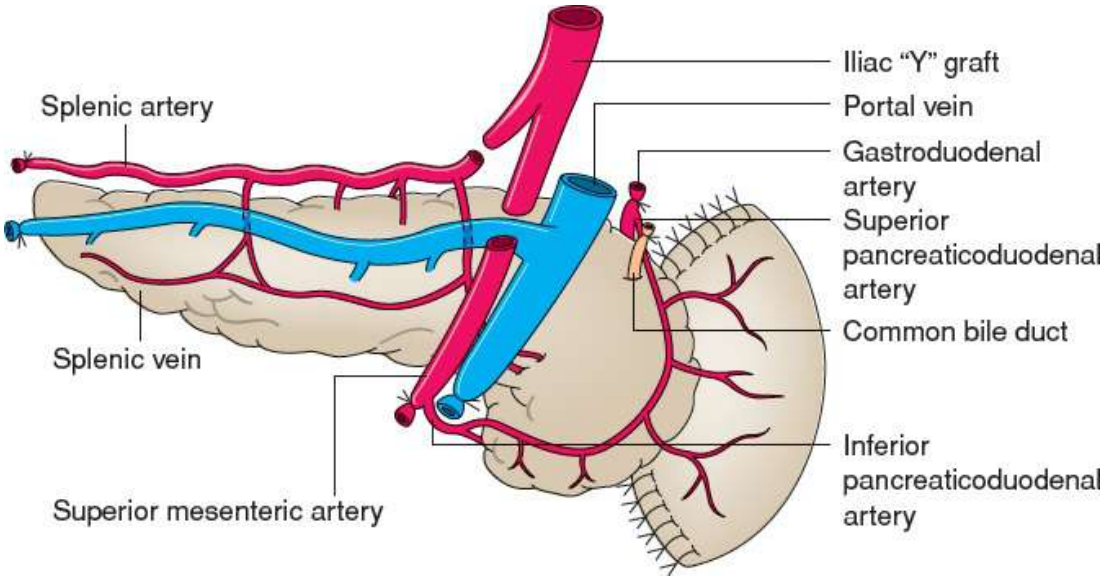


FIGURE 25-3 Anatomy of a pancreatic allograft. (From Sung R. *Pancreas and Islet Transplantation. Greenfield's Surgery: Scientific Principles and Practice*. Philadelphia, PA: Lippincott Williams and Wilkins; 2011.)

a. Recipient selection. The evaluation identifies coexisting problems or disease entities that must be addressed to improve the outcome of the transplant. Family history is important because it may

provide information about the patient's kidney disease and allows a discussion about potential living donors.

b. Recipient operation. In the operating room, a Foley catheter is inserted, and the patient's bladder is irrigated with antibiotic-containing solution. A central venous pressure (CVP) line is inserted, and a first-generation cephalosporin is administered. The transplant renal vein and artery typically are anastomosed to the external iliac vein and artery, respectively. A heparin bolus of 3,000 units may be administered before clamping the iliac vessels. Before reperfusion of the kidney, mannitol (25 g) and furosemide (100 mg) are administered intravenously, and the patient's systolic blood pressure (BP) is maintained above 120 mm Hg, with a CVP of at least 10 mm Hg to ensure optimal perfusion of the transplanted kidney. The ureter can be anastomosed to either the recipient bladder or the ipsilateral ureter, although the bladder is preferred. Establishing an antireflux mechanism is essential for preventing posttransplantation reflux pyelonephritis. This is accomplished by performing an **extravesical ureteroneocystostomy** (**Lich**). A double-J ureteral stent is commonly used.

TABLE 25-1 Causes of Renal Failure Requiring Transplantation

Type	Characteristics
Congenital	Aplasia, obstructive uropathy
Hereditary	Alport syndrome (hereditary nephritis), polycystic kidney disease, tuberous sclerosis
Neoplastic	Renal cell carcinoma, Wilms tumor
Progressive	Diabetic neuropathy, chronic pyelonephritis, Goodpasture syndrome (antiglomerular basement membrane disease), hypertension, chronic glomerulonephritis, lupus nephritis, nephrotic syndrome, obstructive uropathy, scleroderma, amyloidosis

Traumatic	Vascular occlusion, parenchymal destruction

c. Postoperative considerations

(1) IV fluid replacement. In general, the patient should be kept euvolemic or mildly hypervolemic in the early posttransplantation period with a goal of 130 mm Hg systolic BP to ensure adequate perfusion to the new allograft. Hourly urine output is replaced with one-half normal saline on a milliliter-for-milliliter basis because the sodium concentration of the urine from a newly transplanted kidney is 60 to 80 mEq/L (60 to 80 mmol/L).

(2) Renal allograft function or nonfunction. If the patient's urine output is low in the early postoperative period (<50 mL/hr), perfusion to the new allograft must be assessed. After adequate volume resuscitation, low-dose (≤5 mg/hr) dopamine infusion may be added to augment vasomotor tone and perfusion pressure. Early poor function of a transplanted kidney is most commonly due to reversible acute tubular necrosis (ATN) secondary to reperfusion injury. Before the diagnosis of ATN can be made, however, noninvasive studies (renal Doppler ultrasonography [US] or technetium-99m renal scan) demonstrating vascular patency and good renal blood flow in the absence of hydronephrosis or urinary leak must be obtained. If adequate renal blood flow is confirmed, dialysis can be continued until allograft function recovers.

d. Complications

(1) Lymphoceles are lymph collections that occur because of lymphatic leaks in the retroperitoneum. They present one week to several weeks after transplantation and are best diagnosed by US. Most are asymptomatic and are found incidentally. Treatment of symptomatic lymphoceles consists of drainage into the peritoneum, via laparoscopic or open methods.

(2) Renal artery and vein thrombosis. Arterial and venous thromboses most often occur in the first 1 to 3 days after transplantation. If the transplant kidney had been functioning initially but a sudden cessation of urine output occurs, graft

thrombosis should be suspected. A rapid rise in serum creatinine, graft swelling, and local pain ensues. The diagnosis is made by technetium-99m renal scan or Doppler US. Unless the problem is diagnosed and repaired immediately, the graft will be lost and transplantation nephrectomy will be required.

(3) Urine leak. The etiology of urine leak is usually anastomotic leak or ureteral sloughing secondary to ureteral blood supply disruption. Urine leaks present with pain, rising creatinine, and possibly urine draining from the wound. A renal scan demonstrates radioisotope outside the urinary tract. Urine leaks are treated by placing a bladder catheter to reduce intravesical pressure and subsequent surgical exploration.

(4) Rejection is infrequent and inversely correlated with degree of HLA matching. Treatment of ACR is pulse steroids. Antithymocyte preparations can be used in situations involving steroid resistant rejection and plasmapheresis should be considered for antibody-mediated rejection.

e. Graft surveillance. After the initial 3-month period, when ACR becomes less of a risk, tacrolimus and steroid doses are tapered. Chronic long-term immunosuppression can be maintained at lower levels than those required for induction. Rarely, immunosuppression can be discontinued completely.

II. LIVER

A. Indications include complications attributable to end-stage liver disease (ESLD) (Table 25-2). While hepatitis C has been the leading contributor to ESLD, nonalcoholic steatohepatitis (NASH) has become increasingly prevalent. In the largest single institution experience, OLT for NASH increased fivefold from 2002 to 2011 (*Ann Surg.* 2012;256(4):624–633). Although outcomes were comparable with other indications for OLT, there are significantly more healthcare resources consumed by this group of recipients.

TABLE 25-2 Most Common Indications for Orthotopic Liver Transplantation

Adults

Chronic hepatitis C	Primary biliary cirrhosis
Alcoholic liver disease	Primary sclerosing cholangitis
Chronic hepatitis B	Autoimmune hepatitis
Children	
Extrahepatic biliary atresia	Primary hepatic tumors
α_1-Antitrypsin deficiency	Metabolic liver disease
Cystic fibrosis	

1. **Transplantation for hepatic malignancy.** Cirrhosis is a risk factor for HCC. Given that most patients who develop HCC die from their underlying cirrhosis rather than from metastatic disease, it was reasoned that transplantation may be a potentially curative approach to the primary tumor as well as the underlying pathology. The **Milan criteria** are outcome driven and establish guidelines for considering OLT in patients who present with **early stage I or II HCC** and underlying cirrhosis (Table 25-2). Given the concern for HCC progression while awaiting transplantation, candidates receive MELD exception points beyond what is calculated from their cirrhosis, but only after the first 6 months of being listed. At 6 months, candidates with an approved extension receive an MELD of 28, which increases with each extension to a maximum MELD score of 34.

B. Recipient Operation. OLT comprises three distinct sequential phases. The *first phase* involves the dissection and removal of the recipient's diseased liver. The *second phase*, known as the anhepatic phase, refers to the period starting with devascularization of the recipient's liver and ending with revascularization of the newly implanted liver. During the anhepatic phase, venovenous bypass (VVB) may be used (Fig. 25-4). VVB shunts blood from the portal vein and infrahepatic IVC to the axillary, subclavian, or jugular veins. Alternatively, many transplant surgeons will create a temporary portocaval shunt, which has the advantages of VVB with much less risk and cost. Maintenance of venous return from the kidneys and lower extremities results in a

smoother hemodynamic course, allows time for a more deliberate approach to hemostasis, reduces visceral edema and splanchnic venous pooling, and lowers the incidence of postoperative renal dysfunction. The liver allograft is implanted by anastomosing first the suprahepatic and then the infrahepatic IVC. The portal vein anastomosis is performed, and blood flow to the liver is reestablished. Finally, the hepatic arterial anastomosis is performed. If the recipient hepatic artery is not suitable for anastomosis, a donor iliac arterial graft can be used as a conduit from the infra- or suprarenal aorta. The *third phase* includes biliary reconstruction and abdominal closure. Biliary continuity is established via a duct-to-duct anastomosis or a choledochojejunostomy. A duct-to-duct anastomosis is preferable, but may not be possible when there is a donor–recipient bile duct size discrepancy or a diseased recipient bile duct (e.g., with primary sclerosing cholangitis, biliary atresia, or secondary biliary cirrhosis).

C. Postoperative Considerations

1. **Hepatic allograft function.** Monitoring of hepatic allograft function begins intraoperatively after revascularization. Signs of satisfactory graft function include hemodynamic stability and normalization of acid–base status, body temperature, coagulation studies, maintenance of glucose metabolism, and bile production. Reassessment of allograft function continues postoperatively, initially occurring every 12 hours. Satisfactory function is indicated by an improving coagulation profile, decreasing transaminase levels, normal blood glucose, hemodynamic stability, adequate urine output, bile production, and clearance of anesthesia. Early elevations of bilirubin and transaminase levels may be indicators of preservation injury. The peak levels of aspartate transaminase (AST) and alanine transaminase (ALT) are usually less than 2,000 units/L, and should decrease rapidly over the first 24 to 48 hours postoperatively. Persistent transaminitis should prompt a liver US to assess vessel patency and flow.

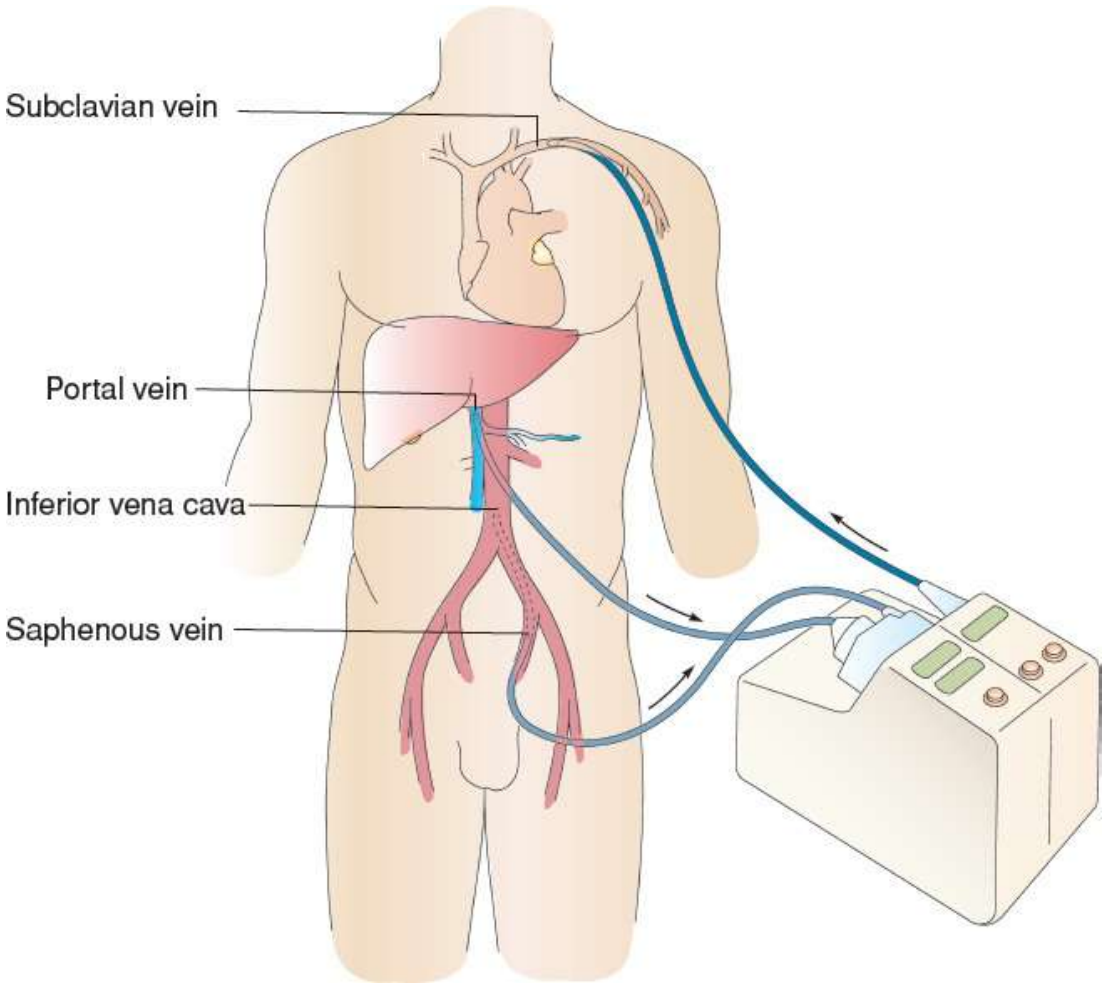


FIGURE 25-4 Hepatic transplantation with venovenous bypass. (From Welling T, Pelletier S. *Hepatic Transplantation. Greenfield's Surgery: Scientific Principles and Practice*. Philadelphia, PA: Lippincott Williams and Wilkins; 2011.)

D. Complications

1. **Primary nonfunction** is characterized by hemodynamic instability, poor quantity and quality of bile, renal dysfunction, failure to regain consciousness, increasing coagulopathy, persistent hypothermia, and lactic acidosis in the face of patent vascular anastomosis (as demonstrated by Doppler US). The incidence is approximately 1% and without retransplantation, death ensues.
2. **Hepatic artery thrombosis** in the early posttransplantation period may lead to fever, hemodynamic instability, and rapid deterioration, with a marked elevation of the transaminases. An associated bile leak may be noted soon after liver transplantation due to loss of the main vascular supply of the bile duct. Acute thrombosis may be treated by

attempted thrombectomy; however, this is usually unsuccessful and retransplantation is needed.

3. **Portal vein stenosis or thrombosis** is rare. When it occurs, the patient's condition may deteriorate rapidly, with profound hepatic dysfunction, massive ascites, renal failure, and hemodynamic instability. Although surgical thrombectomy may be successful, urgent retransplantation is often necessary.
4. **Biliary stricture** is diagnosed by cholangiography. A single short bile duct stricture may be treated by either percutaneous or retrograde balloon dilation. A long stricture, ampullary dysfunction, or failed dilation necessitates revision of the biliary anastomosis.

III. PANCREAS

A. Indications. Most patients who are evaluated for a pancreas transplant in conjunction with kidney transplantation are type I diabetics with concomitant nephropathy. Ninety-five percent of all pancreas transplants are performed in conjunction with a kidney transplant. Whole-organ pancreas transplantation represents the only therapeutic option for long-term insulin independence.

B. Graft Selection

1. **Simultaneous kidney–pancreas transplantation** (**SPK**) may be considered in insulin-dependent diabetic patients who are dialysis dependent (or imminent) and have a creatinine clearance of less than 30 mL/min. Since alloreactivity among donor organs is concordant, an advantage of combined transplantation includes the ability to monitor pancreas rejection by monitoring renal rejection.
2. **Pancreas after kidney transplantation** (**PAK**). Patients with living donors can be listed separately for deceased pancreas transplantation; however, since the organs are immunologically distinct, pancreas allograft monitoring is more difficult and outcomes are worse.
3. **Pancreas alone transplantation** (**PAT**). Few patients with complications from type I diabetes who are not uremic are considered for pancreas only transplantation. Patients must be brittle diabetics who have experienced life-threatening hypoglycemic episodes.
4. **Pancreatic islet cell transplantation** is still investigational and has not received widespread acceptance. Pancreatic islet cells are isolated and injected into the portal vein for engraftment in the liver. The

major problems have been in obtaining enough islet cells to attain glucose homeostasis and failing to achieve long-term insulin independence.

C. Recipient Operation. The most widely accepted technique of pancreatic transplantation in the United States uses whole-organ pancreas with venous drainage into the systemic circulation and enteric exocrine drainage. Some centers advocate portal venous drainage. Under cold-storage conditions, the portal vein is isolated. If it is too short to allow for a tension-free anastomosis, an extension autograft is placed using donor iliac vein. The SMA and splenic artery then are reconstructed with a donor iliac artery Y-bifurcation autograft (Fig. 25-3). Only the second portion of the duodenum is retained with the pancreas. Then the portal vein is anastomosed to the iliac vein or the SMV, and the donor common iliac artery graft is anastomosed to the recipient's external iliac artery. The duodenal segment of the transplant is then opened, and a duodenojejunostomy is created. Alternatively, the duodenal segment can be anastomosed to the bladder. The pancreas transplant is placed in the right paracolic gutter, and if kidney transplantation is to be performed, it is done on the left side.

D. Postoperative Considerations

1. **Serum glucose** is followed during and after the transplantation. IV insulin infusions should not be needed from the time in the operating room or are stopped within the first few hours after pancreas transplantation.
2. **Rejection** of the pancreas transplant is suggested by a rise in serum amylase or a fall in urinary amylase. Rejection of pancreas and kidney transplants usually occurs in parallel but may be discordant. The diagnosis of kidney rejection is suggested by a rise in creatinine, which is then confirmed by biopsy. Biopsy of the pancreas transplant is performed percutaneously. Rejection is treated with corticosteroids or antilymphocyte preparations.
3. **Graft-related complications.** Besides rejection, complications of pancreas transplantation include metabolic acidosis and dehydration. These are due to the loss of sodium and bicarbonate into the urine from the transplanted duodenum. Other common complications include pancreatitis, UTIs, urethritis, and anastomotic leak from the duodenocystostomy. Infections with CMV also may occur.

IV. INTESTINE

A. Indications. The Centers for Medicare and Medicaid Services (CMS) recognize intestinal transplantation as the standard of care for patients who have failed total parental nutrition (TPN) therapy for intestinal failure. The leading cause of intestinal failure is loss of intestinal length resulting in malabsorption. Long-term TPN therapy is associated with significant morbidity and mortality and has 3- and 5-year survival rates of 70% and 63%, respectively (*N Engl J Med.* 2009;361:10). Complications of long-term TPN include cholestatic liver disease, line infections, and central vein stenosis/thrombosis. Indications for intestinal transplant include the life-threatening complications associated with TPN therapy (Table 25-3). Timing of referral to an intestinal center can be difficult and is aided by a patient-centered, clinical algorithm (*Nat Rev Gastroenterol Hepatol.* 2015;12(2):108–120; Fig. 25-5).

B. Types of Grafts

1. **Isolated intestinal allograft.** Transplantation of the jejunoileum.
2. **Composite liver and intestinal graft.** In cases of severe hepatic dysfunction, composite grafts are necessary. Inclusion of the pancreas and duodenum facilitates en bloc procurement and engraftment (*N Engl J Med.* 2009;361:10).

TABLE 25-3 Failure of Parenteral Nutrition, as Defined by the Centers for Medicare and Medicaid Services

Impending or overt liver failure due to TPN-induced liver injury
Thrombosis of two or more central veins
Two or more episodes per year of catheter-related systemic sepsis that requires hospitalization
A single episode of line-related fungemia, septic shock, or acute respiratory distress syndrome
Frequent episodes of severe dehydration despite intravenous fluid supplementation in addition to TPN

TPN, total parenteral nutrition.

From Fishbein TM. Intestinal transplantation. *N Engl J Med*. 2009;361(10):998–1008, with permission.

3. **Multivisceral graft.** Exenteration of the native foregut allows en bloc engraftment of donor stomach, duodenum, pancreas, small intestine, and liver. Inclusion of the colon is sometimes performed and is currently under investigation.

C. Recipient Operation. Patients who receive isolated intestinal allografts have vascular anastomoses created between the donor SMV and the recipient portal vein, and between the donor SMA and the recipient aorta. Vascular reconstruction for patients who receive combined liver–intestinal grafts parallels that for patients undergoing a standard OLT.

D. Postoperative Considerations

1. **Graft function.** Most recipients wean from TPN and achieve nutritional autonomy after transplantation (OPTN/SRTR 2011 Annual Data Report). Experienced centers report 1-year patient survival between 86% and 93%, which is on par with other solid organs (*Am J Transplant.* 2014;14:1976–1984). Unfortunately, these results do not persist as 3- and 5-year survival rates are a modest 61% and 47%, respectively (*N Engl J Med.* 2009;361:10). Patients who receive an intestinal transplant seem to enjoy a better quality of life (QOL) than those who remain on TPN (*Am J Transplant.* 2014;14:1976–1984). Factors that diminish QOL after transplantation include persistent g-tube or ostomies and repeat hospitalizations.
2. **Infection.** The foremost clinical conundrum that faces intestinal transplant surgeons is distinguishing infectious enteritis from allograft rejection. Both present similarly and have masquerading features on biopsy specimens. Adenovirus, calicivirus, *Clostridium difficile,* and CMV must all be distinguished from rejection.
3. **Renal dysfunction.** Intestinal transplant recipients are at a higher risk of nephrotoxicity from CNIs because of the higher dose used for immunosuppression. Recent use of antithymocyte antibody induction therapy associated with decreased target levels of tacrolimus is anticipated to preserve renal function of future recipients (*Am J Transplant.* 2014;14:1976–1984).

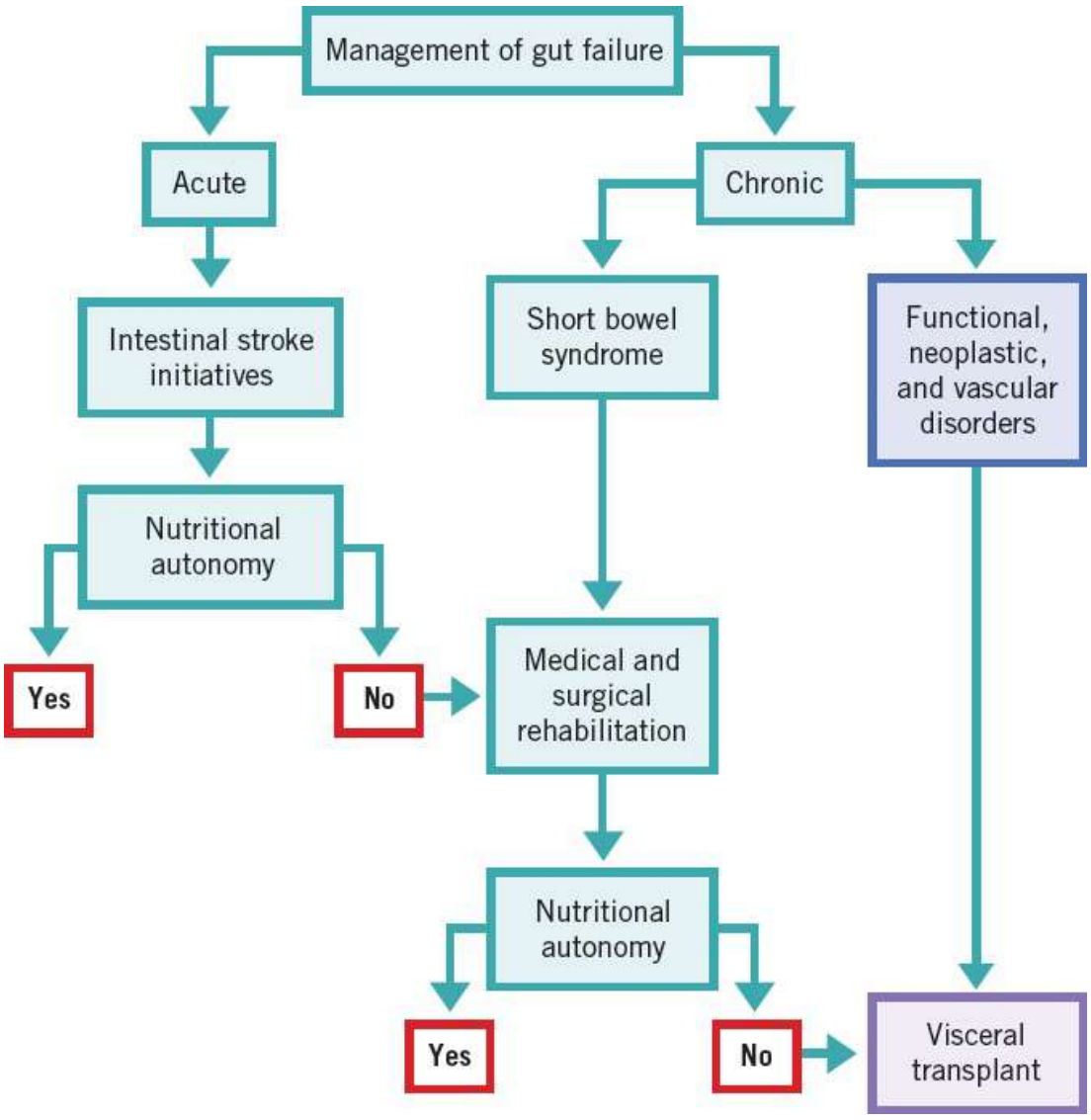


FIGURE 25-5 Decision making algorithm in the management of intestinal failure. (From Abu-Elmagd K. The concept of gut rehabilitation and the future of visceral transplantation. *Nat Rev Gastroenterol Hepatol*. 2015;12:(2)108–120, with permission.)

4. **Graft rejection.** Rates of ACR were significantly reduced with the introduction of antithymocyte antibodies into induction protocols, but rejection rates still remain high at between 33% and 50% (*N Engl J Med*. 2009;361:10). Given the lack of a reliable noninvasive marker of rejection, intestinal stomas created during transplantation give an access to serial endoscopic biopsies for graft surveillance.
5. **Cost.** Similar to renal transplantation, intestinal transplantation becomes cost effective over continuous TPN after 2 years (*Gastroenterology.* 2006;130:s158–s162).

CHAPTER 25: ABDOMINAL TRANSPLANTATION

Multiple Choice Questions

1. **During preoperative evaluation of a 33-year-old male with ESRD from polycystic kidney disease, his mother comes forward and wishes to donate one of her kidneys to her son. What factors are taken into consideration when evaluating potential living donors?**

   a. Blood type
   b. HLA type
   c. Comorbid conditions
   d. Psychosocial influences
   e. All of the above

2. **A 65-year-old male is 3 days status post orthotopic liver transplant. On rounds you note new bilious output from his surgical drain. This finding along with a persistent transaminitis should prompt an evaluation for:**

   a. Portal vein thrombosis
   b. Enterocutaneous fistula
   c. Hepatic arterial thrombosis
   d. Rejection
   e. All of the above

3. **A 55-year-old male with cirrhosis from HCV visits your office to discuss his recent surveillance imaging. “They told me I have a few spots on my liver.” What findings would preclude this patient from being considered for transplantation for HCC?**

   a. Single 4.5 cm lesion
   b. 3 lesions: 2.5 cm, 2 cm, 3.5 cm
   c. 2 lesions: 2.5 cm, 2 cm
   d. Single 3 cm lesion
   e. All of the above are contraindications for transplantation

4. **A 45-year-old female with type I diabetes complicated by**

nephropathy and ESRD is referred to your office for kidney transplant evaluation. She asks you whether she would benefit from a combined kidney–pancreas transplant. Which of the following statements regarding whole-organ pancreas transplantation are true?

a. It is usually performed alone without concomitant kidney transplantation
b. It is the only therapeutic modality that can achieve long-term insulin independence
c. Compared to islet cell transplantation, there is a greater chance of requiring insulin after whole-organ pancreas transplantation
d. Sequela of diabetes, such as neuropathy and retinopathy are unaffected after pancreas transplantation
e. All of the above

5. **A 55-year-old male is 2 days status post orthotopic liver transplant. Despite normalization of his coagulation profile and bilirubin level, his transaminases are persistently elevated. Which noninvasive test would be most appropriate in the workup of this patient?**

a. MRCP
b. CT angiography
c. KUB
d. Liver duplex ultrasound
e. No further testing is indicated at this time

6. **Three days following deceased donor renal transplantation, your patient begins to complain of swelling and tenderness over her graft. Despite having adequate urine output over the last 12 hours, you notice a moderate rise in her serum creatinine. Which study would be most helpful in making the diagnosis?**

a. Ultrasound of the graft
b. Nuclear medicine scan
c. Retrograde urethrogram
d. CT scan
e. MRI

7. **A 45-year-old female with intestinal failure secondary to short gut syndrome is hospitalized with her third serious line infection in the last 12 months. Which of the following are indications for intestinal transplantation?**

   a. Frequent episodes of dehydration despite IV fluid supplementation with TPN
   b. Two or more serious line-related infection per year, one line-related fungal infection or episode of shock due to line sepsis
   c. Loss of two or more central venous access sites
   d. Peripheral nutrition associated liver disease (PNALD)
   e. All of the above

8. **A 55-year-old female with ESRD secondary to Alport syndrome is undergoing evaluation for kidney transplantation. Which of these factors should not raise her PRA?**

   a. Previous pregnancy
   b. History of blood transfusion
   c. Previous transplant
   d. Prior blood donation
   e. All of the above will raise one's PRA

26

Appendix

Ina Chen and Sean C. Glasgow

I. ANATOMY AND HISTOPATHOLOGY

A. The appendix is a vestigial organ located on the inferior border of the cecum. The base of the appendix can be found by following the three teniae coli of the ascending colon to their point of convergence. The tip of the appendix is usually found intraperitoneal and anterior to the cecum. Anatomical variations of the tip include retrocecal, pelvic, and retroperitoneal, and patients with these variants may present with noncanonical symptoms of acute appendicitis.

B. The arterial supply of the appendix is the appendicular artery, a branch of the ileocolic artery, and is located in the mesoappendix along with the lymphatic drainage.

C. As a true diverticulum of the colon, the wall of the appendix is composed of all the layers of the colonic wall: mucosa, submucosa, muscularis, and serosa. The appendix can be histologically differentiated from the colon by the presence of lymphoid aggregates in the submucosa.

II. APPENDICITIS

A. Epidemiology. Appendicitis is one of the most common diagnoses encountered by the general surgeon. Approximately 250,000 cases are diagnosed each year in the United States, with the highest incidence occurring in patients 10 to 19 years of age (23.3 per 10,000 population). The lifetime risk of developing acute appendicitis is 8.6% for males and 6.7% for females (*Am J Epidemiol.* 1990;132(5):910–925).

B. Pathophysiology. Appendicitis is caused by luminal obstruction (e.g., lymphoid hyperplasia, fecalith, tumor) followed by increased intraluminal and intramural pressure. Venous drainage is impaired,

resulting in wall ischemia, inflammation, and superimposed infection. If left untreated, the appendix may become necrotic and perforate, forming a periappendiceal phlegmon or abscess.

C. Presentation. Classic presentation begins with the onset of periumbilical pain caused by stimulation of the visceral pain response. As the appendix continues to engorge, irritation of the parietal peritoneum can cause somatic pain in the right lower quadrant (RLQ). Anorexia, nausea/vomiting, and low-grade fever may follow. Onset of symptoms generally occurs within 24 hours from the development of acute appendicitis. Variant locations of the appendiceal tip may lead to unique presentations of acute appendicitis. Patients with pelvic appendices may present with suprapubic pain, urinary discomfort, and diarrhea. Inflamed retroperitoneal appendices are more likely to present as back and/or flank pain rather than abdominal pain.

D. Physical Examination. In a typical presentation of appendicitis, palpation of **McBurney point,** located 1/3 of the distance from the anterior iliac spine to the umbilicus, may reveal focal peritoneal signs. Patients with variant locations of their appendiceal tips may present with suprapubic or back/flank tenderness. A palpable mass is uncommon but may indicate a periappendiceal phlegmon or abscess. It is important to perform a complete abdominal examination in a patient who presents with acute abdominal pain to rule out other etiologies. The following maneuvers may also be performed to elicit pain from acute appendicitis, usually localizing to the right side.

1. **Obturator sign.** The patient lies supine with hips and knees flexed. A positive sign occurs when pain develops as the examiner internally rotates the leg on the side of inflammation. This is secondary to irritation of the obturator muscle.
2. **Psoas sign.** The patient lies in the left lateral decubitus position with knees extended. The examiner extends the right leg at the hip. Pain is elicited if the inflamed appendix irritates the psoas muscle. This can occur with retroperitoneal appendicitis.
3. **Rovsing sign.** A positive Rovsing sign is the development of worsening RLQ abdominal pain with palpation of the left lower quadrant (LLQ). Palpation of the LLQ will stretch the whole peritoneum, causing the inflamed appendix to contact and irritate the parietal peritoneum in the RLQ.

E. Laboratory Evaluation

1. **Complete blood cell count.** WBC count >10,000 cells/μL is present in most appendicitis patients. More severe leukocytosis may indicate progression to necrosis or perforation.
2. **Urinalysis** is frequently abnormal in patients with advanced appendicitis, especially in patients with suprapubic appendicitis and secondary bladder irritation.
3. **Serum electrolytes, BUN, creatinine.** Abnormalities may indicate dehydration and will require urgent correction.
4. **Serum or urine pregnancy test** must be performed in all ovulating females to guide diagnosis and management, as well as evaluate for obstetric etiologies of pain.

F. Imaging

1. **Computed tomography (CT)** imaging is the most commonly ordered radiographic test to diagnose acute appendicitis. Positive CT findings include a distended, thick-walled appendix with inflammatory streaking of periappendiceal fat; appendicoliths/fecaliths may be present. Patients with perforated appendicitis may have a periappendiceal phlegmon or abscess. The major disadvantage of CT is exposure to ionizing radiation, so alternative imaging modalities need to be considered for patients who will not tolerate this exposure (e.g., pregnant women, young children) (Fig. 26-1).

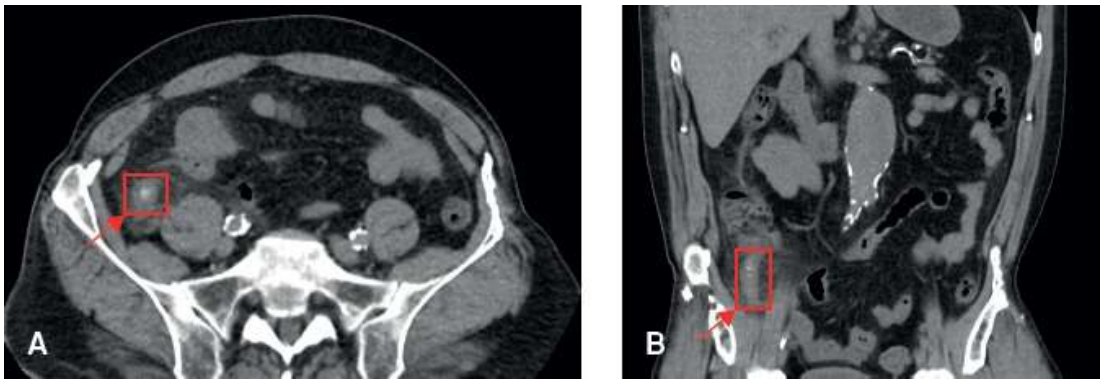


FIGURE 26-1 Axial **(A)** and coronal **(B)** computerized tomography (CT) images of patient with unperforated appendicitis. Acute appendicitis can be diagnosed on CT imaging by the presence of thickened appendiceal wall, fecalith, and/or periappendiceal fat stranding.

2. **Ultrasound (US)** is most useful in patients for whom CT imaging is

contraindicated. Findings consistent with acute appendicitis include an appendiceal diameter >6 mm, lack of luminal compressibility, and the presence of an appendicolith. Appendiceal perforation is more difficult to diagnose on US than CT. Additionally, the quality and accuracy of US are highly variable and depend on the patient's body habitus and the operator's technical skills.

3. **Magnetic resonance imaging (MRI)** is an alternative cross-sectional imaging modality that is useful in evaluating patients with equivocal findings on US. In a small retrospective study, the overall sensitivity of MRI was close to 100%; it is, therefore, particularly useful in excluding acute appendicitis (*Radiology*. 2006;238(3):891–899). Moreover, MRI in pregnant patients suspected of having acute appendicitis can lower the rate of negative appendectomy and perforation (*Radiology*. 2009;250(3):749–757).

G. Treatment

1. An appendicitis treatment algorithm is available in Figure 26-2. Initial treatment involves intravenous (IV) **fluid resuscitation** to achieve adequate urine output and correct any electrolyte abnormalities.
2. For patients with uncomplicated appendicitis who immediately proceed to operation, a single preoperative dose of **antibiotics** is sufficient for surgical wound prophylaxis. A second-generation cephalosporin, such as cefoxitin or cefotetan, is the most common choice.
3. **Appendectomy** is the current standard of care for uncomplicated acute appendicitis. Surgeon preference generally drives the decision to perform a laparoscopic versus open appendectomy. However, laparoscopic appendectomy has many advantages over open appendectomy, including shorter length of stay, reduced postoperative pain, and lower rate of postoperative complications (*Ann Surg*. 2004;239(1):43–52). Laparoscopic appendectomy is now widely practiced and has become the standard operation offered to patients with acute appendicitis.

   a. Laparoscopic appendectomy

   (1) The patient is positioned supine with left arm tucked. A Foley catheter is placed to decompress the bladder. Three ports are placed: 10 mm at the umbilicus, 5 mm at the LLQ, and 5 mm at

the suprapubic midline. The patient is placed in Trendelenburg with the right side up to improve visualization of the RLQ.

(2) The appendix is located by following the three teniae coli of the ascending colon distally to their convergence point.

(3) The appendix is carefully lifted with a Babcock clamp to expose the mesoappendix. A window is created in the mesoappendix near the base of the appendix and an endoscopic stapler is introduced.

(4) The appendix is stapled across its base and separated from the cecum. The mesoappendix is also divided, sealing the appendicular artery within.

(5) The appendix is placed in a specimen bag within the abdomen and removed though the 10-mm umbilical port.

(6) Any purulent fluid is suctioned and the RLQ is carefully irrigated.

b. Open appendectomy

(1) A transverse incision over McBurney point is made. The external and internal oblique and transversus abdominis muscle layers are split in the direction of their fibers.

(2) The cecum is identified and teniae coli are traced to the appendix.

(3) The mesoappendix is divided, the appendiceal base ligated, and the appendix excised and delivered through the wound.

4. For patients with perforated appendicitis, immediate appendectomy is rarely indicated. Instead, patients are started on IV antibiotics covering gram-negative rods, gram-positive cocci, and anaerobes. Periappendiceal abscesses are **percutaneously drained,** if technically feasible, to achieve source control. Duration of antibiotic therapy depends on whether source control has been achieved. According to guidelines published by the Surgical Infection Society, antibiotic therapy should not exceed 5 to 7 days; patients who do not clinically improve will need to be reevaluated for a source control intervention or for another diagnosis (*Surg Infect (Larchmt).* 2017;18(1):1–76). For patients with adequately drained abscess, data from a randomized controlled trial suggest that a shorter course of antibiotics, up to 4 days, is sufficient (*NEJM*. 2015;372(21):1996–2005). An interval

appendectomy, though not routine, can be considered 6 to 12 weeks later to prevent recurrent appendicitis. However, a meta-analysis evaluating the treatment of perforated appendicitis revealed the rate of recurrent appendicitis is low at 8.9%, with most occurring within 6 months of initial diagnosis (*Ann Surg.* 2007;246(5):741–748). Whether or not an interval appendectomy is performed is determined individually and relies on a thorough discussion between the patient and the surgeon.

5. **Nonoperative management of uncomplicated appendicitis.** Studies evaluating short-term outcomes of nonoperative management have shown that patients treated nonoperatively do *not* have a higher complication rate than those who underwent appendectomy (*Lancet.* 2011;377(9777):1573; *J Am Coll Surg*. 2016;223(6):814–824). Additionally, a randomized controlled trial comparing nonoperative management to open appendectomy found that up to 2/3 of patients can be treated with antibiotics and do not require operation within a 5-year follow-up period (*JAMA.* 2018;320(12):1259–1265). However, since there is currently no predictive model that can identify these patients, and appendectomy is a relatively safe operation, surgery remains the gold standard. Moreover, no study has compared antibiotics alone to appendectomy in high-risk patients who would benefit most from avoiding an operation. Nonoperative management is currently offered as an alternative to only a small minority of patients with either a prior history of surgical complications or mild presentation of acute appendicitis.
6. **Negative appendectomy.** Negative appendectomy, or the discovery of a normal appendix during appendectomy for presumed appendicitis, has become less common due to more accurate diagnostic imaging (*Ann Surg.* 2008;284(4):557–563). When a normal-appearing appendix is encountered upon entry into the abdomen, the surgeon may use the laparoscope to evaluate for other etiologies. A retrospective review of negative appendectomy cases found that the most common identifiable diagnosis in men misdiagnosed with acute appendicitis was colonic diverticulitis; in women, it was ovarian cyst (*Am J Surg.* 2011;201(4):433–437). There are no clear guidelines on whether to remove a normal-appearing appendix; the benefits of preventing appendicitis and detecting occult

appendiceal neoplasms need to be balanced with the risk of postoperative complications.

III. APPENDICITIS IN SPECIAL POPULATIONS

A. Appendicitis in Pregnancy

1. The incidence of appendicitis in pregnancy is approximately 1/1,500. It is the most common nongynecologic surgical emergency during pregnancy (*Am J Obstet Gynecol.* 2000;182(5):1027–1029).
2. The clinical presentation of acute appendicitis in pregnant patients is generally similar to that of nonpregnant patients. While RLQ abdominal pain is the most common symptom, the appendix may be displaced superior to McBurney point by the gravid uterus. Additionally, leukocytosis can also be a normal finding in pregnancy. If diagnostic imaging is needed, CT is relatively contraindicated given the risks of ionizing radiation to the fetus. Ultrasonography is preferred. MRI can be performed if US findings are equivocal.
3. Appendectomy is safe during pregnancy and is the preferred treatment of acute appendicitis in pregnant women, regardless of the trimester of pregnancy. Observational studies have found that pregnant women treated with surgery had a lower risk of adverse maternal and fetal outcomes compared to untreated or nonoperatively treated women (*Am J Surg.* 2005;190(3):467–473; *Ann Surg.* 2017;266(2):260–266). Laparoscopic appendectomy, with a few key modifications regarding patient positioning and trocar placement, is safe and feasible for most pregnant patients. Fetal monitoring should be considered.

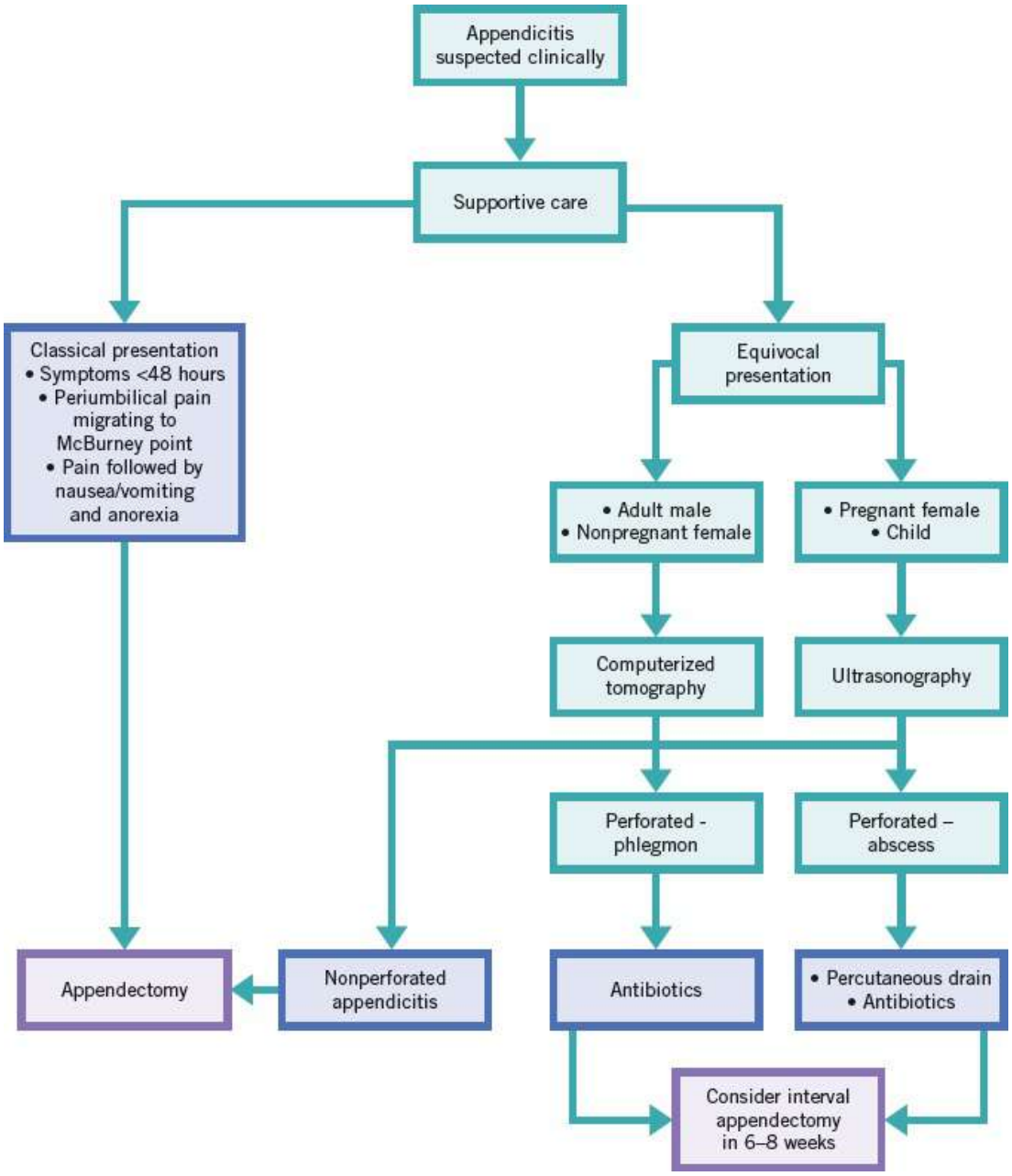


FIGURE 26-2 Appendicitis algorithm.

B. Appendicitis in Children

1. Appendicitis is the most common indication for emergency abdominal operation in childhood. Incidence increases with age in the pediatric population, with the highest incidence in the 10- to 19-year age group (*Am J Epidemiol.* 1990;132(5):910–925). The most common cause of appendicitis in children is lymphoid hyperplasia.
2. Presentation of appendicitis will vary with age. Children <5 years of

age are more likely to present with nonspecific symptoms such as diffuse abdominal pain, irritability, and diarrhea, leading to delay in diagnosis and a higher prevalence of perforation. Adolescents have a similar presentation to that of adults.

3. Due to increased risk of ionizing radiation in pediatric patients, CT imaging is not as widely used as in adults. Many institutions implement a stepwise protocol that prioritizes clinical evaluation and US over CT. Studies have found that these algorithms decrease the use of CT without sacrificing diagnostic accuracy (*Radiology.* 2011;259(1):231–239; *Ann Surg.* 2016;264(3):474–481).

IV. APPENDICEAL NEOPLASMS

A. Carcinoid Tumor. Carcinoid tumor (i.e., well-differentiated **neuroendocrine tumor**) is the most common appendiceal neoplasm, accounting for up to 2/3 of all appendiceal tumors. Carcinoids are derived from neuroendocrine cells, which are found in the submucosa of the appendiceal wall.

1. **Clinical features.** Most appendiceal carcinoids are asymptomatic. Tumors can cause obstruction and lead to appendicitis; therefore, many tumors are detected incidentally in appendectomy specimens. Tumors that metastasize to the liver release **serotonin** into the systematic circulation, causing **carcinoid syndrome**; these patients can present with flushing, diarrhea, bronchoconstriction, and valvular heart disease (see also Chapter 20).
2. **Treatment.** A review of patients with appendiceal carcinoids in the Surveillance, Epidemiology, and End Results (SEER) database found that lymph node metastases were present in 15% of patients with tumors smaller than 1 cm, 47% of patients with tumors between 1 cm and 2 cm, and 84% of patients with tumors larger than 2 cm (*J Surg Oncol.* 2001;104(1):41–44). Therefore, the surgical management of appendiceal carcinoids is mostly determined by size. For tumors smaller than 1 cm, appendectomy is curative. Tumors larger than 2 cm require formal right hemicolectomy to evaluate for and treat lymph node metastases. The best surgical management of tumors of intermediate size can be determined by considering the tumor's location and histopathologic characteristics.

B. Appendiceal Mucinous Neoplasms. Mucinous neoplasms are

epithelial tumors characterized by their production of mucin. These tumors are categorized based on histology: low-grade appendiceal mucinous neoplasms (LAMN) and high-grade (HAMN). Malignant lesions are called **mucinous adenocarcinoma** (*Am J Surg Pathol.* 2016;40(1):14–26).

1. **Clinical presentation.** Mucinous tumors can obstruct the appendiceal lumen, causing the appendix to develop into a mucin-filled structure. If the appendix remains unruptured, symptoms can mimic acute appendicitis. If rupture occurs, deposits of mucin-secreting tumors can disseminate throughout the peritoneal cavity generating mucinous ascites; this condition is called **pseudomyxoma peritonei (PMP).**
2. **Treatment.** Surgical resection should be pursued for all appendiceal mucinous neoplasms to prevent rupture and to rule out concomitant malignancy. Additional treatment is determined by pathology. Unruptured appendices with LAMN or HAMN on histopathology do not require additional surgery. Mucinous adenocarcinomas require a formal oncologic resection. Ruptured mucinous neoplasms with the development of PMP are aggressively managed with **cytoreductive surgery (CRS)** and **hyperthermic intraperitoneal chemotherapy (HIPEC).**
    a. **CRS** involves resecting all visible tumor deposits within the peritoneal cavity. This may include visceral and peritoneal resections, including but not limited to cholecystectomy, hysterectomy and oophorectomy, and colon resections. Due to circulation of peritoneal fluid, tumor deposits are most commonly found along the diaphragm and within the pelvis. Once CRS is complete, **HIPEC** is instilled into the peritoneal cavity. The most commonly used agents for PMP caused by appendiceal mucinous neoplasms are **mitomycin** and **oxaliplatin**. HIPEC allows the delivery of highly concentrated agents to an isolated cavity, maximizing antitumor effects within the abdomen while limiting systemic adverse effects.
    b. CRS and HIPEC have excellent outcomes in PMP caused by appendiceal mucinous tumors. Patients who undergo CRS and HIPEC at specialized centers have a median survival of 16.3 years; 63% remain disease free at 10 years (*J Clin Oncol.*

2012;30(20):2449–2456). Completeness of CRS is the most important procedure-associated predictor of survival; therefore, all visible tumor deposits should be excised if feasible, even if extensive organ resections are required. A retrospective study evaluating patients who underwent extensive CRS, defined as having >3 organ resections or >2 anastomoses, found that, while intraoperative blood loss and hospital length of stay were greater compared to patients with nonextensive CRS, there was no difference in long-term morbidity or mortality. Moreover, oncologic outcomes were not compromised (*Ann Surg Oncol.* 2012;20(4):110–114).

C. Adenocarcinoma. Adenocarcinomas of the appendix are extremely rare and are often discovered incidentally in appendectomy specimens (Fig. 26-3). There are three types of appendiceal adenocarcinomas: mucinous (described above), intestinal/colonic, and signet ring cell. Colonic/intestinal and signet ring cell types are treated like their colonic counterparts and, therefore, are resected with a formal right colectomy. Adjuvant chemotherapy regimens are extrapolated from those of colonic adenocarcinoma (i.e., 5-fluorouracil based); however, given the rarity of appendiceal adenocarcinomas, the survival benefit from adjuvant chemotherapy has not been established.

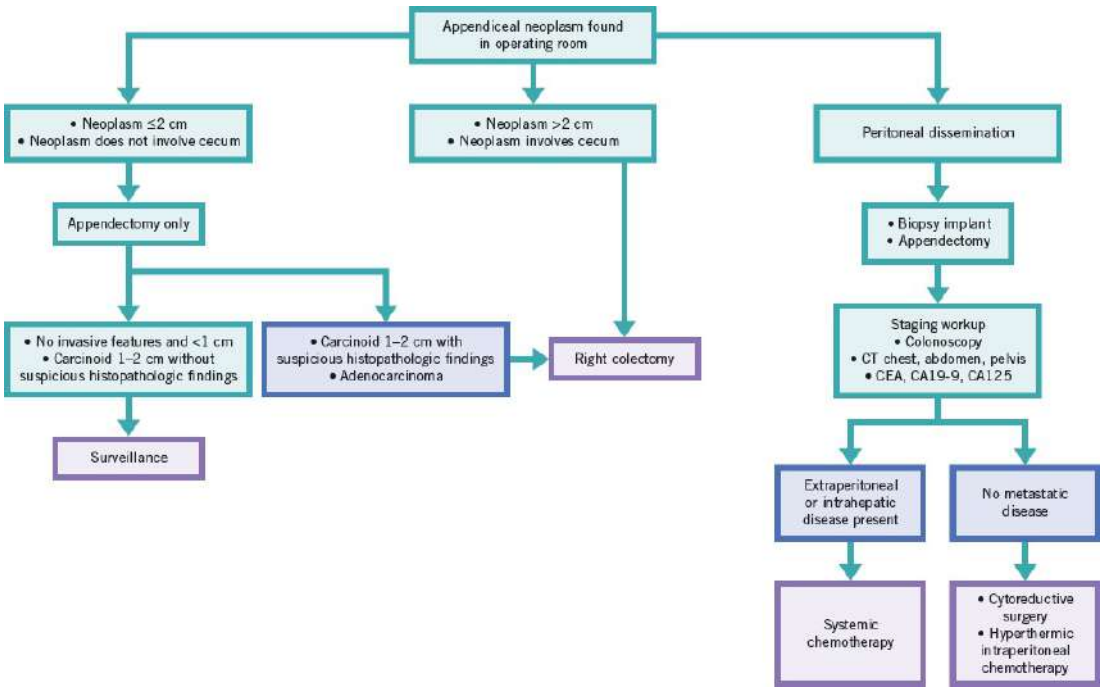


FIGURE 26-3 Incidental appendiceal neoplasm algorithm.

CHAPTER 26: APPENDIX

Multiple Choice Questions

1. **A 16-year-old male has a 10-hour history of periumbilical pain and anorexia that is now localized to the right lower quadrant. On examination, he has tenderness medial and superior to the anterior superior iliac spine. Which of the following explains the localized nature of his pain?**

   a. Localized ileus from appendiceal inflammation
   b. Inflammation of the visceral peritoneum
   c. Localized pain is unequivocal for perforation
   d. Referred pain from appendiceal inflammation
   e. Irritation of the parietal peritoneum

2. **A 30-year-old woman is 24 weeks pregnant and presents with a 5-hour history of abdominal pain. On examination, she has point tenderness over the right iliac fossa. Pelvic examination is normal. Her laboratory examination is remarkable for WBC 14. You suspect a diagnosis of acute appendicitis. What is the next best diagnostic step?**

   a. Diagnostic laparoscopy
   b. MRI of the abdomen and pelvis
   c. US of the right iliac fossa
   d. Transvaginal US to monitor the fetus
   e. CT scan of the abdomen and pelvis

3. **The patient described above undergoes the appropriate diagnostic workup and acute nonperforated appendicitis is diagnosed. All of the following are part of the management of acute appendicitis in pregnant women EXCEPT:**

   a. Tocolytic therapy prior to further treatment to protect the fetus
   b. Intravenous antibiotics
   c. Urgent laparoscopic appendectomy
   d. Urgent open appendectomy

e. Preoperative bowel rest

4. **An 18-year-old female presents to the emergency department for evaluation of right lower quadrant pain that started approximately 1 week ago. Her temperature is 38.3çC and her abdominal examination reveals mild right lower quadrant tenderness. Her labs are significant for WBC 15 and a negative urine pregnancy test. CT imaging shows a 3-cm rim-enhancing fluid collection anterior to the cecum. Which of the following is the most appropriate treatment?**

   a. Prescribe 10-day course of oral antibiotics and instruct patient to return in 6 to 8 weeks for interval appendectomy
   b. Admit patient for 10-day course of IV antibiotics and close monitoring
   c. Admit patient for percutaneous drainage of the abscess and antibiotics
   d. Urgent laparoscopic appendectomy with irrigation and drain placement
   e. IV antibiotics and serial CT scans every 24 to 48 hours

5. **You are consulted by the emergency department to evaluate a 19-year-old man with acute abdominal pain. The patient reports the pain started around his umbilicus approximately 12 hours ago and is now most severe in the RLQ. You have a high suspicion for acute appendicitis and elect to take this patient to the operating room for laparoscopic appendectomy, foregoing diagnostic imaging. Upon entry into the abdomen, you note the appendix appears grossly normal. However, the cecum and terminal ileum are severely inflamed. The abdomen otherwise looks normal. What is the most appropriate next step?**

   a. Continue with appendectomy and refer the patient to a gastroenterologist
   b. Leave the appendix, close the abdomen, and refer the patient to a gastroenterologist
   c. Resect cecum, appendix, and terminal ileum *en bloc*
   d. Biopsy an area of inflammation and send for frozen section to

determine the best surgical option

e. Biopsy an area of inflammation for pathology and close the abdomen

6. **A 45-year-old man presents to the emergency department with right lower quadrant pain, fever, nausea, and anorexia. Given high clinical suspicion for acute appendicitis, the patient is taken immediately to the operating room for a laparoscopic appendectomy. On entry into the abdomen, the appendix is noted to appear normal except for a 3-cm mass at the tip. What is the next best step?**

a. Continue with laparoscopic appendectomy only

b. Perform right colectomy

c. Perform right colectomy with removal of at least 30 cm of terminal ileum

d. Close and refer to medical oncology for neoadjuvant chemotherapy

e. Close and perform regular CT scans for surveillance

27

Colon and Rectum

Coen L. Klos, Richard Tsai, and Steven R. Hunt

I. DISORDERS OF COLONIC PHYSIOLOGY

A. Normal Colonic Physiology. The primary function of the colon is to act as the final arbiter of bowel fluid and sodium resorption, as well as to provide a means for moving stool and coordinating defecation. The colon normally resorbs 1,000 to 1,500 mL of fluid per day but can reabsorb up to 5 to 6 L if necessary, primarily via passive means. Sodium and chloride are also conserved by active transport in exchange for potassium and bicarbonate. The integrity and function of the colonic mucosa is heavily dependent on the intraluminal microflora. Colonic bacteria participate in digestion via fermentation of complex carbohydrates, producing **short chain fatty acids** (**SCFA**), of which **butyrate** is the primary energy source for the colonocyte. Normal colon motility is characterized by **segmental contractions** that mix stool and **mass movements** that occur 3 to 4 times per day and move stool through the colon.

B. Functional constipation is diagnosed by meeting at least two of the **Rome IV criteria**. Additionally, patients must not meet criteria for **irritable bowel syndrome** (IBS), and loose stools should rarely be present without the use of laxatives.

1. Straining for >25% of defecations.

2. Lumpy or hard stools in >25% of defecations.

3. Sensation of incomplete evacuation for >25% of defecations.

4. Sensation of anorectal obstruction/blockage for >25% of defecations.

5. Manual maneuvers to facilitate for >25% of defecations (e.g., digital evacuation, support of the pelvic floor).

6. <3 defecations per week.

a. Etiologies include medications (e.g., narcotics, anticholinergics, antidepressants, calcium-channel blockers), chronic laxative abuse, hypothyroidism, hypercalcemia, dietary factors (low fluid or fiber intake), inactivity, and neurologic disorders (e.g., Parkinson disease, multiple sclerosis). Symptoms may also be caused by obstruction secondary to disorders such as malignant or benign stricture (e.g., inflammatory bowel disease [IBD], diverticulitis), pelvic floor dysfunction, and rectal prolapse, as well as intrinsic disorders of the colonic myenteric plexus (e.g., colonic inertia, Chagas disease, Hirschsprung disease).

b. Evaluation. The initial evaluation of constipation should include a complete history and physical, including a digital rectal examination (DRE). The initial diagnostic workup should include a laboratory evaluation of serum glucose, creatinine, calcium, and thyroid function tests to rule out metabolic or endocrine abnormalities such as diabetes mellitus, hypothyroidism, or hyperparathyroidism. A **contrast enema** or a full **colonoscopy** should be performed to rule out structural causes. Provided these tests are negative, patients are given a trial of high-fiber (25 to 30 g/day) diet and increased fluid intake. If this is not sufficient to resolve the problem, the next step is a **colonic transit study.** Patients continue high-fiber diet and ingest a capsule containing 24 radiopaque markers with abdominal x-rays obtained on days 3 and 5 after ingestion. Normal transit results in 80% of the rings in the left colon by day 3 and 80% of all the rings expelled by day 5. The persistence of >5 rings throughout the colon on day 5 indicates colonic inertia (Fig. 27-1). When the rings stall in the rectosigmoid region, functional anorectal obstruction (obstructed defecation) may be present and warrants further evaluation.

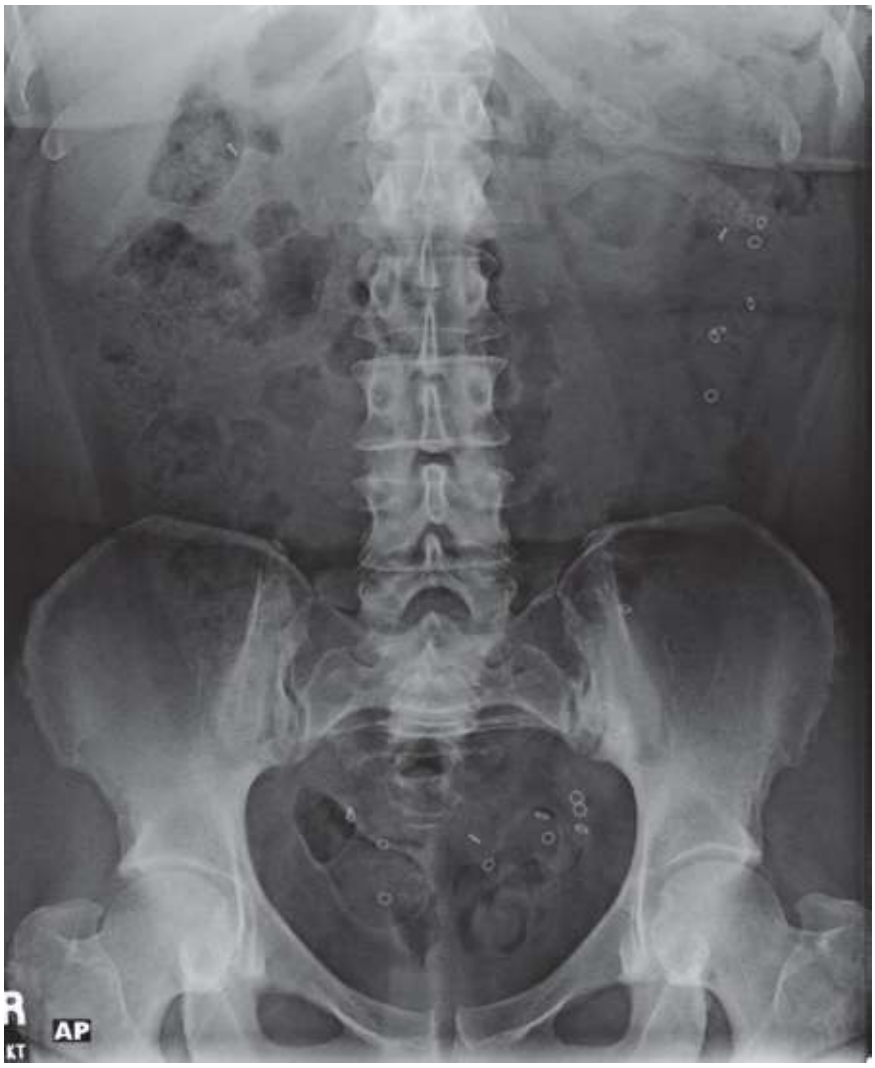


FIGURE 27-1 Colonic transit study: Single view abdominal radiograph demonstrating multiple ring-shaped densities compatible with radiopaque markers within the left colon and rectum.

c. Treatment of colonic inertia initially includes increased water intake, osmotic laxatives, fiber, exercise, and avoidance of predisposing factors. Other agents such as Lubiprostone or Linaclotide should be tried before operation is offered. In patients with debilitating symptoms refractory to nonoperative measures, **total abdominal colectomy (TAC)** with **ileorectal anastomosis (IRA)** or **end ileostomy** may prove curative. The risk of persistent symptoms and long-term complications after colectomy for inertia is relatively high compared to other indications, with series reporting recurrent constipation in as many as 33% of patents and

fecal incontinence in up to 52%. The patient should be thoroughly informed and understand these risks.

C. Colonic pseudo-obstruction is characterized by marked colonic distention, the absence of intestinal contractility, and the absence of mechanical obstruction. Critically ill or institutionalized patients are at the highest risk for this condition. In order to establish the diagnosis, mechanical obstruction must be excluded via imaging studies and/or colonoscopy. Initial management in patients without evidence of peritonitis or perforation consists of nasogastric decompression, bowel rest, correction of systemic contributing factors (e.g., shock, heart failure, metabolic derangements), and discontinuation of medications that decrease colonic motility (including narcotics, calcium-channel blockers, etc.). If these measures are not sufficient after 24 to 48 hours, neostigmine should be considered. Neostigmine is a parasympathomimetic agent that should only be given in a monitored setting as it may cause significant bradycardia. It is contraindicated if significant cardiac disease or asthma is present. Resolution of the condition frequently occurs within 10 minutes of administration. Second-line treatments include epidural anesthetic (sympathetic blockade) or colonoscopic decompression. Patients who fail medical treatment or those with evidence of perforation or peritonitis should undergo laparotomy with decompressing loop colostomy or resection of any ischemic or perforated segments with end ileostomy and mucous fistula, if needed.

D. Volvulus accounts for nearly 10–15% of colonic obstruction in the United States.

1. **Sigmoid volvulus** accounts for up to 60% of all cases and is most common in the elderly or institutionalized, as well as patients with neurologic disorders. It is an acquired condition resulting from sigmoid redundancy with narrowing of the mesenteric pedicle leading to twisting at the mesenteric base.

   a. Diagnosis is suspected when there is abdominal pain, distention, cramping, and obstipation. Abdominal x-ray may show a characteristic **inverted-U,** or "**bent inner tube**" **sign** (Fig. 27-2A). If the diagnosis is still in question, **water-soluble contrast enema** or **computed tomography** (**CT**) may be obtained. Contrast enema may show a **bird's beak deformity** at the

obstructed rectosigmoid junction, and CT may show a characteristic **mesenteric whirl.**

b. Treatment involves decompression via flexible or rigid **sigmoidoscopy** and placement of a rectal tube followed by elective sigmoid colectomy, as the risk of recurrence is as high as 40%, and emergent surgery is associated with higher mortality than elective surgery. If peritonitis is present, or sigmoidoscopy is unsuccessful, the patient should undergo exploration and **Hartmann procedure** (sigmoid colectomy and end-descending colostomy, blind rectal stump).

2. Cecal volvulus accounts for up to 30% of colonic volvulus, occurs in a younger population than sigmoid volvulus, and is likely due to congenital failure of appropriate cecal tethering. Cecal volvulus occurs as either a true axially rotated volvulus (90%) or anterosuperior folding-in or "**cecal bascule**" (10%).

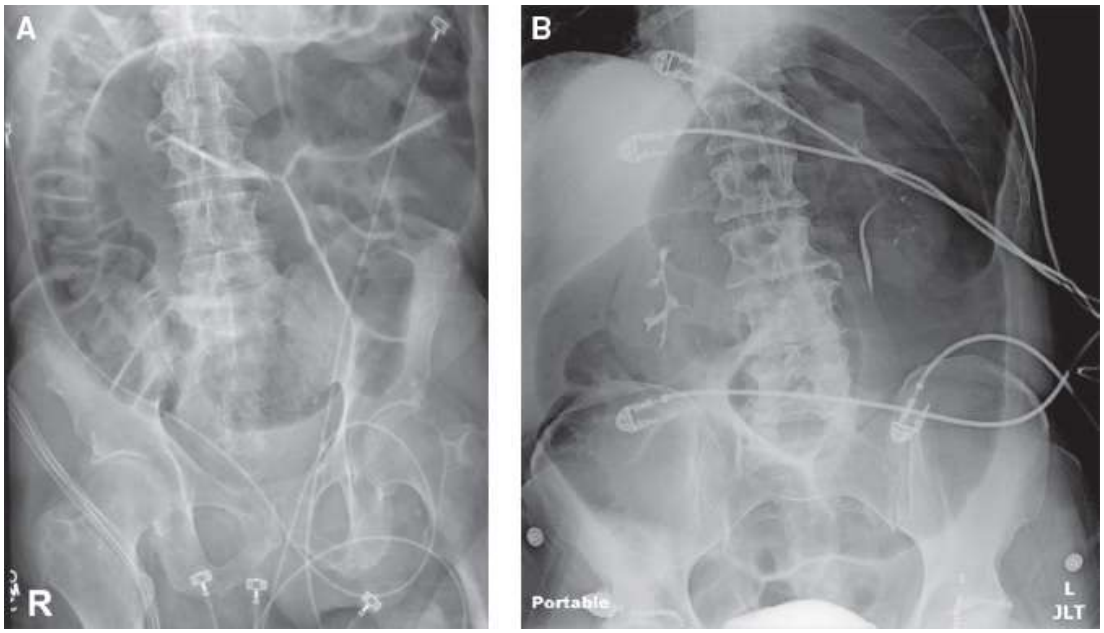


FIGURE 27-2 **A:** Supine abdominal radiograph showing sigmoid volvulus demonstrating a dilated loop of large bowel within the midabdomen with multiple folds pointing toward the right upper quadrant. Proximally, gas-filled loops of cecum and ascending colon are present. **B:** Supine abdominal radiograph showing cecal volvulus demonstrates dilated, gas-filled cecum within the left upper quadrant. Note that the large bowel emanates from the right lower quadrant, with gas seen distally in the sigmoid colon.

a. Diagnosis. Presentation is similar to that of distal small-bowel obstruction, with nausea, vomiting, abdominal pain, and

distention. Abdominal x-ray may show a **coffee bean-shaped**, air-filled cecum extending into the left upper quadrant (Fig. 27-2B). Water-soluble enema may be performed, but CT is recommended as it is generally more useful in the undifferentiated patient with abdominal pain.

b. Management involves urgent laparotomy and **ileocolectomy** with either primary anastomosis or ileostomy. **Cecopexy** alone has an unacceptably high rate of recurrence and colonoscopic decompression has limited utility.

3. Transverse and **splenic flexure volvulus** are extremely rare with clinical presentation similar to that of sigmoid volvulus. Diagnosis is made based on the results of abdominal x-ray and contrast enema or CT. Operative resection is usually required.

E. Diverticular Disease

1. General considerations. Colonic diverticula are an outpouching of the colonic mucosa and submucosa through interruptions in the muscular layer of the colon associated with weaknesses where the small mesenteric arteries penetrate the wall to supply the mucosa. Formation is related to high colonic intraluminal pressures and commonly associated with a low-fiber diet. The **incidence increases with age** to a 75% prevalence after the age of 80 years.

2. Complications

a. Diverticulitis develops in 10% to 20% of patients with diverticulosis.

(1) Patients most commonly present with abdominal pain. There is the potential for constipation or diarrhea, fevers, and dysuria. Pneumaturia or fecaluria may indicate a colovesicular fistula. Colovaginal fistula may be indicated by expulsion of gas or feces from the vagina.

(2) Evaluation and staging in the acute setting is done using CT scan. Colonoscopy and barium or water-soluble enemas are not recommended in the acute setting.

(3) Treatment is tailored to severity.

(a) Uncomplicated diverticulitis may involve fever and/or leukocytosis, but is **localized** and nonperforated. This can often be treated as an outpatient with oral antibiotics, liquid

diet slowly advanced as tolerated to low residue diet, and close follow-up.

(b) Complicated diverticulitis involves evidence of perforation and is generally graded in severity using the Hinchey classification which helps to guide treatment (Table 27-1).

(4) Radiologic-guided **percutaneous drainage** may be indicated in patients with localized abscess and lack of diffuse peritonitis.

(5) Surgical intervention for complicated diverticulitis can often be converted to an elective setting in patients with a localized abscess using percutaneous drainage. In patients with diffuse peritonitis, urgent/emergent surgical intervention is generally indicated and usually requires a Hartmann procedure. In selected circumstances (stable patients with minimal contamination), resection and primary anastomosis (with or without diverting loop ileostomy [DLI]) can be considered.

TABLE 27-1 Hinchey Classification of Complicated Diverticulitis

Grade	Description	Treatment
I	Localized pericolonic abscess	Conservative management with antibiotics, bowel rest, and monitoring. Can be treated as outpatient in stable, reliable patients
II	Pelvic abscess	Bowel rest, IV antibiotics, monitoring, image-guided drainage, possible surgical intervention
III	Purulent peritonitis	Bowel rest, IV antibiotics, surgery
IV	Fecal peritonitis	Bowel rest, IV antibiotics, surgery

(6) **Elective resection** for diverticulitis usually consists of a sigmoid colectomy. The decision to perform an elective colectomy is multifactorial and comes down to identifying those who are at higher risk for complications if they were to have a recurrent episode of diverticulitis. The frequency, duration, and intensity (e.g., requiring hospitalization versus managed as an outpatient) of attacks are taken into account but are not absolute indications for elective resection independently. Risk stratification by CT grading of documented attacks holds most promise; those with complicated and/or severe disease should be considered to be at high risk for long-term complications and elective resection should be considered. In addition, immunocompromised patients are at a higher risk for poor outcome, and elective resection is therefore often recommended (*Dis Colon Rectum*. 2014;57:284–294). When performing an elective sigmoid colectomy, the proximal resection margin is through uninflamed, nonthickened bowel, but there is no need to resect all diverticula in the colon. The distal margin extends to normal, pliable rectum, even if this means dissection beyond the anterior peritoneal reflection. With the increased use of CT imaging to diagnose acute diverticulitis, routine endoscopic evaluation after an episode of acute diverticulitis is not always justified (*Gastrointest Endosc*. 2014;79(3):378–389). At this time, however it is important that patients who are of appropriate age and/or those with suspicious CT findings (wall thickening, stricture, etc.) undergo a complete colonoscopic evaluation of the colon at some interval after an initial attack of diverticulitis in order to rule out malignancy, especially and ideally prior to elective resection.

b. Fistulization secondary to diverticulitis may occur between the colon and other organs, including the bladder, vagina, small intestine, and skin. Diverticulitis is the most common etiology of colovesical fistulas. In women, colovaginal and colovesical fistulas usually occur in those who have previously undergone hysterectomy. Colocutaneous fistulas are uncommon and are

usually easy to identify. Coloenteric fistulas are likewise uncommon and may be entirely asymptomatic or result in diarrhea of various severity. Fistula takedown and repair is usually performed at the time of sigmoid resection.

F. Lower Gastrointestinal Bleeding (LGIB). LGIB is generally self-limiting; however, up to 25% of patients require surgical intervention. The colon is the most common location for the source of LGIB, with only up to 15% located in the anorectal area and 5% in the small intestine. The most common cause of LGIB is diverticular disease (30%), followed by anorectal disease (up to 14% to 20%), ischemia (12%), colitides (9%), and neoplasia (10%). Angiodysplasia is a relatively rare cause of bleeding (3%) (*Surg Clin North Am*. 2014;94(1):55–63).

1. Management in the acute setting varies by the volume of bleeding. Patients with slow intermittent bleeding often do not require hospital admission, whereas those who present with **massive LGIB** (defined as any patient who requires >2 U of red blood cells in a 24-hour period) and hemodynamic instability should be adequately resuscitated in a monitored setting following a balanced transfusion protocol (see **Chapter 8**).

2. Once resuscitation has been initiated, it is critical to discern the site of bleeding as long as the patient remains stable. An emergent "blind" hemicolectomy is associated with a >50% incidence of rebleeding, and emergent subtotal colectomy for bleeding is associated with mortality rates up to 30%. The workup of LGIB therefore frequently involves the use of multiple different imaging and diagnostic modalities to localize the source of bleeding before any surgical intervention.

a. The history and physical are of some value to locating the source of bleeding. **Hematochezia** is usually associated with vigorous bleeding or a more distal source whereas **melena** is associated with an UGI or small-bowel (SB) source or slower, intermittent bleeding from the proximal colon. Recent weight loss or history of anemia may point to a chronic process, such as neoplasm or IBD. **Stigmata of portal hypertension** may be evident. Rectal examination should be performed early in all patients as this may rule out an anorectal source. Placing a nasogastric tube (NGT) and

assessing the tube output quality helps differentiate an UGI bleeding source as bilious output without blood significantly reduces the likelihood of a gastric source (but does not eliminate it). If the patient is on anticoagulant therapy, this should be put on hold and may require reversal.

b. Laboratory studies include a full panel of complete blood count, coagulation profile, basic metabolic profile, and hepatic function panel to indicate the degree of anemia and coagulopathy as well as identify possible liver or renal dysfunction.

c. Diagnosing the source and location of hemorrhage are key, as this will help to guide initial therapy and ultimately the need for, and type of, surgical intervention, if any.

(1) Endoscopy: EGD should be considered in any patient with massive LGIB or melena if an UGI source has not already been ruled out. **Colonoscopy** can be both diagnostic and therapeutic, as can EGD. Actively bleeding lesions may be injected with dilute epinephrine solution for vasoconstriction, cauterized or clipped. In stable patients who have no evidence of bleeding on EGD or colonoscopy with persistent transfusion requirement, **capsule endoscopy** or **SB "push" enteroscopy** should be considered.

(2) CT angiogram (**CTA**) has become the test of choice. It is relatively quickly obtained and can detect continuous bleeding with a sensitivity of up to 90% at rates >0.35 mL/min. It is more specific in identifying the anatomic location of bleeding when compared to a nuclear scan (see below). Caution must be used for patients with renal disease as the use of contrast may induce nephropathy.

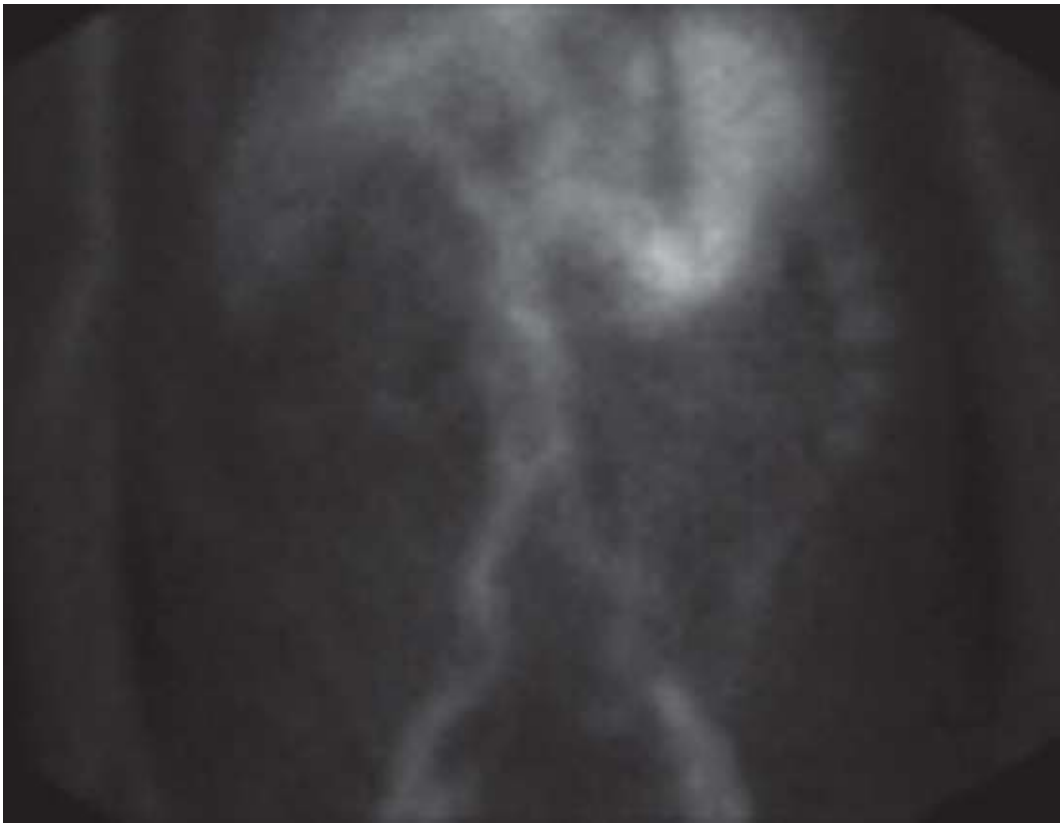


FIGURE 27-3 Technetium-99m tagged red blood cell scan demonstrating increased uptake within the distal transverse colon with antegrade propulsion of radiolabeled red blood cells. Findings are consistent with active extravasation (subsequent colonoscopy demonstrated a bleeding diverticulum).

(3) Nuclear scan using technetium-99m sulfur colloid or tagged RBCs can identify bleeding sources with rates as low as 0.1 to 0.5 mL/min. Tagged RBC scan can identify bleeding up to 24 hours after isotope injection but is not specific in identifying the anatomic location of the bleeding source (Fig. 27-3).

(4) Mesenteric angiography should be performed in patients with a positive nuclear scan or CTA to definitively localize (and hopefully treat) the source of bleeding. Angiography can localize bleeding exceeding 1 mL/min. It allows for therapeutic interventions such as vasopressin infusion (0.2 unit/min) or selective arterial embolization, which together achieve hemostasis in 85% of cases with an associated risk of ischemia to the treated bowel segment.

(5) In the rare patient with **continued bleeding from an obscure source**, diagnostic laparoscopy or laparotomy with

intraoperative endoscopy can be considered.

II. COLITIDES

A. IBD is an umbrella term that traditionally covers ulcerative colitis (UC), Crohn disease (CD), and "indeterminate colitis." The exact etiology of IBD has not been fully explained, but it is evident that both environmental and genetic components are involved. Extraintestinal manifestations can be associated with both UC and CD and include arthritis, primary sclerosing cholangitis (3%; see Chapter 22), pyoderma gangrenosum, erythema nodosum, iritis/uveitis (2% to 8%), and stomatitis. In addition, patients with IBD have an increased risk of thrombosis including portal and mesenteric venous thrombosis, as well as deep venous thrombosis and pulmonary embolus.

1. **UC** is an inflammatory process of the colonic mucosa. The disease **always involves the rectum and extends continuously for a variable distance proximally**. There is a slight male predominance. Patients can present with bloody diarrhea, tenesmus, abdominal pain, fever, and weight loss. As the duration of the inflammation increases, pathologic changes progress. Initially, mucosal ulcers and crypt abscesses are seen. Later, mucosal edema and pseudopolyps (islands of normal mucosa surrounded by deep ulcers) develop, and the end-stage pathologic changes show a flattened, dysplastic mucosa. Cancer must be considered in any colonic stricture in a patient with UC. The risk of colon cancer is increased in patients with UC and is related to duration of disease with risk increasing significantly after 20 years to approach almost 10%.
   a. **Diagnosis** is made by colonoscopy with biopsy and by the constellation of symptoms. Imaging studies can help to determine if the patient has SB disease or fistulae indicative of CD.
   b. **Medical management** revolves around therapy which induce and maintain remission of colonic inflammation. Patients with distal disease (**proctitis**) often respond to topical 5-aminosalicylic acid derivatives (5-ASA) in the form of enemas or suppositories. For those with more proximal disease, oral 5-ASA or sulfasalazine (**SSZ**) will induce remission in the majority of patients with mild or moderate disease. Patients unresponsive to topical and/or oral 5-ASA and SSZ can then be treated with oral corticosteroids and

transitioned back to 5-ASA or SSZ. Intravenous corticosteroids are given to those that are unresponsive to oral corticosteroids or are systemically ill with severe colitis. Azathioprine (AZA) and 6-mercaptopurine (6-MP) have been shown to help wean patients off steroids and can be used as maintenance therapy. Biologic therapy with TNF-α inhibitors (Infliximab) has been shown to decrease colectomy rates in studies with short-term follow-up (*Gastroenterology*. 2009;137(4):1250–1260). Long-term data shows that those with a good early response (within 3 months) are more likely to sustain this, resulting in lower long-term colectomy rates as well (*Aliment Pharmacol Ther*. 2017;45(4):519–532). Adalimumab has also been FDA approved for the treatment of UC and may be used as an alternative to Infliximab. Golimumab is a more novel TNF-α inhibitor that is currently being studied in clinical trials for its effectiveness in the treatment of UC.

c. Surgery is indicated in patients who have a high risk of malignancy, UC refractory to medical therapy (the most common indication), **toxic colitis**, or intractable bleeding. In the acutely ill patient, the operation of choice is **TAC with EI**. These patients, once recovered and healthy, can be considered for **ileal pouch anal anastomosis** (**IPAA**) and DLI, followed by DLI takedown at a later date once IPAA healing is confirmed. This is considered a **three-stage restorative proctocolectomy**. In patients who are subacutely ill or stable, a **two-stage approach** can be considered, consisting of initial total proctocolectomy (TPC) and IPAA with DLI followed by subsequent DLI closure. Some surgeons perform a **one-stage approach** in optimal UC patients. Regardless of approach, anticipated function after restorative proctocolectomy is approximately six bowel movements a day, often with the aid of bulking agents or antidiarrheals (>25%). Complications after IPAA include leak (thus the DLI), impaired continence, sexual dysfunction/infertility, pouchitis, and bowel obstruction. IPAA is contraindicated in patients with poor baseline continence or low anorectal malignancy; older patients and obese patients have worse outcomes with IPAA. In addition, CD or indeterminate colitis are relative contraindications for IPAA.

2. CD is a transmural inflammatory process that can affect any area of

the GI tract from the mouth to the anus. It has a female predominance. The disease has a segmental distribution, with **normal mucosa interspersed between areas of diseased bowel**. Common symptoms include diarrhea, abdominal pain, nausea and vomiting, weight loss, and fever. There can be an abdominal mass or perianal fistulas on physical examination. The **terminal ileum** is involved in up to 45% of patients at presentation. Common pathologic changes include fissures, fistulae, transmural inflammation, and granulomas. Grossly, the mucosa shows aphthous ulcers that often deepen over time and are associated with fat wrapping and bowel wall thickening. As the disease progresses, the bowel lumen narrows, and obstruction or perforation may result. SB CD is discussed in Chapter 20 and perianal CD is discussed in Chapter 28.

a. Diagnosis is made using colonoscopy, imaging, and the clinical picture. Unfortunately, patients with Crohn colitis (CC) will often present similarly to patients with UC, and up to one-third of patients with CC or UC will be diagnosed incorrectly prior to operative intervention. CC can be discerned from UC by the presence of perianal disease, “skip lesions,” ileal inflammation on colonoscopy, and the presence of SB involvement on imaging (enteroclysis/small bowel follow through series, CT, and/or MRI/MRE).

b. Medical management revolves around the use of immunosuppression to induce and maintain remission of the disease. In the setting of an acute flare and the presence of sepsis, source control should be obtained by drainage of any abscesses in addition to antibiotics. After the initial control of patients with steroids, patients are weaned using immunomodulators as listed above for UC. In addition, **budesonide**, a topical corticosteroid administered orally without systemic absorption, can be administered. Biologic therapy using **TNF-α inhibitors infliximab, certolizumab, natalizumab, and adalimumab** has proven to decrease steroid use **and prolong time to surgical intervention** in CD.

c. Surgical intervention is indicated in patients with medically refractory disease, acute systemic sepsis/perforation not amenable to percutaneous drainage, uncontrolled hemorrhage, failure to

thrive/malnutrition, and dysplasia/malignancy. Patients with segmental CD should be considered for limited resection. Colectomy with IRA should be considered for patients with colitis and rectal sparing with limited or no perianal disease. In the setting of total proctocolitis, patients will likely require TPC with EI. In some centers, IPAA is considered for isolated CC with no perianal or SB disease. While **stricturoplasty** has a role in the treatment of stricturing SB CD, stricturoplasty plays no role in the treatment of CC, as there is a 7% risk of malignancy over 20 years.

3. **Indeterminate colitis** is a term used for cases in which UC has not definitively been discerned from CC (10% to 15% of patients with IBD). More than half of patients with an initial diagnosis of indeterminate colitis will eventually be diagnosed with either UC or CD based on the clinical pattern and pathologic findings. The surgical approach for those patients who remain indeterminate is similar to those with UC, although higher rates of IPAA complications have been reported.

B. Ischemic colitis results from colon malperfusion due to global hypoperfusion (e.g., critical illness), venous or arterial thrombosis or embolization, iatrogenic inferior mesenteric artery (IMA) ligation after abdominal aortic aneurysm repair, and vasculopathy. It is **idiopathic** in the majority of patients. Patients are usually elderly and present with lower abdominal pain localizing to the left side with melena or hematochezia. CT may show bowel wall thickening that corresponds to submucosal hemorrhage and edema. Ischemic colitis can be distinguished from infectious colitis by the appearance of the mucosa on endoscopy. Watershed areas such as the splenic flexure (**Griffiths point**) and sigmoid colon (**Sudeck point**) are more prone to ischemia. In the presence of full-thickness necrosis or peritonitis, emergent resection with diversion is recommended. Patients without peritonitis or free air, but with fever or an elevated white blood cell count, may be treated with bowel rest, close observation, and IV antibiotics. Up to 50% of patients eventually develop focal colonic strictures, some then subsequently requiring resection.

C. Radiation proctocolitis results from (usually pelvic) irradiation for the treatment of various malignancies (e.g., cervical or prostate cancer).

Risk factors include a dose of greater than 6,000 cGy, vascular disease, diabetes mellitus, hypertension, prior low anterior resection, and advanced age. The early phase occurs within days to weeks from radiation therapy. Mucosal injury, edema, and ulceration develop, with associated nausea, vomiting, diarrhea, and tenesmus. The late phase occurs within weeks to years and is associated with tenesmus and hematochezia with bowel thickening and fibrosis. Ulceration with bleeding, stricture, and fistula formation may occur. Medical treatment may be successful in mild cases, with the use of stool softeners, steroid enemas, and topical 5-ASA products. If these measures fail, endoscopic ablation or transanal application of **4% formalin** to affected mucosa may be effective in patients with transfusion-dependent rectal bleeding. Patients with stricture or fistula require proctoscopy and biopsy to rule out locally recurrent disease or primary neoplasm. Strictures may be treated by endoscopic dilation, but often recur. Surgical treatment consists of proximal diversion and is reserved for medical failures, recurrent strictures, and fistulae. Resection may also be indicated, including for recurrent/primary malignancy.

D. Infectious Colitis

1. **Pseudomembranous colitis** is an acute diarrheal illness resulting from toxins produced by overgrowth of *Clostridium difficile* after antibiotic treatment (especially the use of clindamycin, ampicillin, or cephalosporins). Antibiotics already have been discontinued in one-fourth of the cases, and symptoms can occur up to 6 weeks after even a single dose. **Diagnosis** is made by detection of glutamate dehydrogenase (GDH) in combination with **toxin A** or **toxin B** on enzyme immunoassays in a liquid stool sample. If GDH is positive (highly sensitive) but toxin assays are negative a nucleic acid amplification test (NAAT) may be performed to detect genes associated with toxigenic strains such as *tcdB*. Alternatively, liquid stool may be sent immediately for NAAT. Proctoscopy demonstrates sloughing colonic mucosa or pseudomembranes, and CT often shows transmural colonic thickening. **Treatment** begins with stopping unnecessary antibiotics and starting oral vancomycin (125 mg, four times a day). Metronidazole may be used in nonsevere cases or if oral vancomycin is unavailable. For severe cases, if patients are unable to take oral medications, vancomycin enemas (500 mg in 250 mL

saline) may be useful. Rarely, pseudomembranous colitis presents with severe sepsis and colonic distention with **toxic megacolon** or perforation. In severe cases, laparotomy with TAC and EI is required.

2. **Other causes of colitis include bacteria (*Escherichia coli, Shigella*), amoebic colitis, CMV colitis, and actinomycosis,** however, these conditions are rare. Typically, they are diagnosed by fecal testing or culture and treatment is dictated based on these results. Actinomycosis is treated with appropriate antibiotic therapy, CMV colitis is treated with ganciclovir, and amoebic colitis is treated with oral metronidazole.
3. **Neutropenic enterocolitis (typhlitis)** after chemotherapy occurs most commonly in the setting of acute myelogenous leukemia after cytosine arabinoside therapy. Patients present with abdominal pain, fever, bloody diarrhea, distention, and sepsis. CT is usually diagnostic, often involving the right colon. Initial treatment includes bowel rest, total parenteral nutrition, granulocyte colony-stimulating factor (G-CSF), and broad-spectrum intravenous antibiotics. Laparotomy with right colectomy or TAC (depending on extent) and EI is required only if peritonitis develops.

III. NEOPLASTIC DISEASE

A. Colorectal neoplasms are typically diagnosed either by **screening studies** or symptomatic presentation: hematochezia, melena, anemia, abdominal pain, and constipation. Initiation and frequency of screening is recommended beginning at age 45 with special consideration outlined in Table 27-2 (*CA Cancer J Clin.* 2018;68:250–281). **Colonoscopy** is the gold standard screening test and has been shown to prevent cancer. The U.S. Preventive Services Task Force (USPSTF) recommends screening beginning at age 50 until age 75, does not recommend routine screening from age 76 to 85, and recommends against screening any patients over 85 years of age based on risk–benefit analysis. While complications are rare, there are risks associated with colonoscopy including perforation (0.04%), bleeding (0.1%), and mortality (0.2%).

TABLE 27-2 **Colorectal Cancer Screening Recommendations Based on Patient Risk**

Risk	Description	Modality	Age at Initiation
Average (75% of newly diagnosed colorectal cancer)	Sporadic	**1.** Colonoscopy every 10 yr **2.** Flexible sigmoidoscopy every 5 yr **3.** CT colonography every 5 yr **4.** High-sensitivity fecal occult blood test yearly **5.** Fecal immunochemical test yearly **6.** Multitarget stool DNA test every 3 yr	45
Family history (15–20%)	One first-degree relative with adenomatous polyps (AP) or CRC or two second-degree relatives with CRC	**1.** Colonoscopy every 10 yr **2.** Colonoscopy every 5 yr (if diagnosis was before age 60) **3.** CT colonography every 5 yr	40 or 10 yr prior to youngest relative's diagnosis (whichever is earliest)
Hereditary nonpolyposis colorectal cancer (HNPCC, 3–8%)	Genetic or clinical diagnosis of HNPCC or individuals with high risk of HNPCC	Colonoscopy every 1–3 yr, genetic counseling and consider genetic testing	21 yr

Familial adenomatous polyposis (FAP, 1%)	Genetic diagnosis of FAP or suspected FAP without diagnosis	Flexible sigmoidoscopy or colonoscopy every 1–2 yr, genetic counseling, consider genetic testing	Puberty
Inflammatory bowel disease (1%)	Chronic Crohn colitis or ulcerative colitis	Colonoscopy with random biopsies for dysplasia every 1–2 yr	Risk of cancer is significant 8 yr after the diagnosis of pancolitis and 12–15 yr after diagnosis of left-sided colitis

B. Polyps

1. Nonadenomatous polyps

a. Hamartomatous polyps make up <1% of all polyps diagnosed in adults and are associated with hereditary conditions including **Peutz–Jeghers syndrome, PTEN hamartoma tumor syndrome (PHTS), multiple endocrine neoplasia 2B, familial juvenile polyposis syndrome (JPS)**, and **neurofibromatosis type 1 (NF1).** Hamartomatous polyps of the colon can be categorized as the juvenile type or Peutz–Jeghers type and have only rare malignant potential. They are commonly pedunculated and >1 cm in size. Isolated colonic hamartomas are most often located in the sigmoid colon or rectum and present with bleeding and/or polyp prolapse. Less frequently these polyps are associated with anemia, diarrhea, obstruction, or mucoid stools. Treatment of hamartomas is via endoscopic resection, but large polyps sometimes require segmental colectomy.

b. Hyperplastic polyps are the most common colorectal neoplasm

(10 times more common than adenomas) and have an extremely limited malignant potential. Most are <0.5 cm in diameter, are found in the distal colon, and rarely need treatment. Right-sided lesions or lesions >1 cm should be removed and may be a marker of increased risk of adenoma.

2. **Adenomas** are dysplastic lesions with the ability to progress to malignancy and are thought to be the precursor of most colorectal cancers (CRCs). Risk of invasive malignancy is higher in villous adenomas than tubular, however all adenomas are treated with endoscopic or surgical removal. The risk of malignancy increases with size. Sessile polyps have a higher malignant risk than pedunculated polyps. If a polyp is not amenable to complete endoscopic removal, segmental colectomy should be considered.
   a. **Tubular adenomas** are usually sessile and account for roughly 85% of adenomas and can contain up to 25% villous elements.
   b. **Tubulovillous adenomas** account for 10% to 15% of adenomas and contain 25% to 50% villous features.
   c. **Villous adenomas** are usually sessile and account for 5% to 10% of adenomas. They contain predominantly villous architecture.
3. **Malignant polyps** contain foci of invasion into the submucosa and are considered T1 CRCs. The level of invasion is an important factor in the treatment of malignant polyps typically classified using the **Haggitt** (Table 27-3) and **Kudo** classifications (Table 27-4). These classification systems stratify the risk of lymph node metastasis. Those with low risk of lymph node involvement are treated with endoscopic removal. When the estimated risk of lymph node involvement is high, a segmental colectomy should be performed following oncologic principles. The Haggitt system classifies pedunculated polyps by the depth and location of stalk invasion. Sessile polyps per definition classify as Haggitt level 4. The Kudo classification further divides the submucosa into three levels from superficial to deep (SM1 to 3) as it relates to the muscularis propria. This classification is generally used when considering local resection of rectal polyps. In addition, lymphovascular invasion (LVI) and poor differentiation have been shown to increase the likelihood of lymph node metastases. Patients with an inadequate endoscopic resection margin (<2 mm), LVI, SM3 invasion, or poor differentiation should

undergo segmental colectomy. Surveillance after complete endoscopic removal of polyps with foci of invasive cancer without high risk features involves repeat endoscopy at 1 year per NCCN Guidelines for Colon Cancer Version 2.2018.

TABLE 27-3 Haggitt Classification of Malignant Polyps of the Colon and Rectum

Level	Description	Risk of Lymph Node Metastasis	Treatment
0	Noninvasive, high-grade dysplasia	<1%	Endoscopic removal with ≥2 mm margin
I	Focus of invasive cancer in head of pedunculated polyp	<1%	Endoscopic removal with ≥2 mm margin
II	Focus of invasive cancer in neck of pedunculated polyp	<1%	Endoscopic removal with ≥2 mm margin
III	Focus of invasive cancer in stalk of pedunculated polyp	<1%	Endoscopic removal with ≥2 mm margin
IV	Focus of invasive cancer in base of pedunculated polyp; **all sessile polyps**	Up to 25%	**See Kudo classification** (Table 27-4)

TABLE 27-4 Kudo Classification of Submucosal Invasion of Malignant Polyps of the Colon and Rectum

Level	Description	Treatment

SM1	Invasion of the superficial one-third of submucosa	Endoscopic removal with ≥2 mm margin; in distal rectum transanal full-thickness removal
SM2	Invasion of the middle one-third of submucosa	Endoscopic removal with ≥2 mm margin; in distal rectum transanal full-thickness removal
SM3	Invasion of the deep one-third of submucosa	Segmental colectomy

a. Malignant polyps of the proximal two-thirds of the rectum can be treated as colon polyps; however, there is some controversy regarding the treatment of malignant polyps of the distal one-third of the rectum as these lesions may have an increased risk of lymph node metastasis.

b. All T1 lesions of the distal rectum should be approached with at least transanal full-thickness excision using traditional transanal excision, Transanal Endoscopic Microsurgery (TEM) or Transanal Minimally Invasive Surgery (TAMIS) techniques.

C. Colon Cancer

1. There are approximately 150,000 new diagnoses of CRC each year, of which 70% to 75% are colon cancer. CRC is the fourth leading cause of cancer death worldwide and about one-third of patients will eventually die of their disease. See Table 27-5 for hereditary CRC syndromes.

2. The **clinical presentation** of colon cancer diagnosed in the setting of appropriate screening is usually asymptomatic and carries a very favorable prognosis. The most common presenting symptoms are abdominal pain, hematochezia, change in bowel habits, or anemia. **Right-sided** lesions more commonly present with asymptomatic anemia and abdominal pain, whereas **left-sided** lesions more often cause changes in bowel habits, rectal bleeding, and crampy abdominal pain associated with defecation. Obstruction, weight loss, and perforation are uncommon due to effective screening programs and are associated with advanced disease.

3. Diagnosis and staging

a. The majority of patients are diagnosed based on biopsy results from a mass or polyp encountered during colonoscopy. Every effort should be made to assess the remainder of the colon proximal to the biopsied mass to exclude synchronous disease. Patients who are severely ill from obstruction or perforation and require urgent colectomy should undergo a complete colonoscopy within approximately 3 to 6 months from this intervention, taking into account the time of completion of any adjuvant chemotherapy.

b. Standard staging studies include chest and abdominal/pelvic CT scan to evaluate the primary tumor as well as lung and liver, the most common sites of metastasis. **Routine PET/CT** has no proven benefit for staging index disease but has a role in detecting recurrent or metastatic disease unclear on routine CT. **MRI** may be useful if there are concerning hepatic lesions on CT. **Carcinoembryonic antigen** (**CEA**) should be drawn prior to initiating therapy as this can be used in follow-up, but it does not play a role in diagnosis or staging.

TABLE 27-5 Hereditary Colorectal Cancer (CRC) Syndromes

Syndrome	Percent of Total CRC Burden	Genetic Basis	Phenotype	Extracolonic Manifestations	Treatment	Notes
Familial adenomatous polyposis (FAP)	<1%	Mutations in tumor suppressor gene *APC* (5q21)	<100 adenomatous polyps; near 100% with CRC by age 40 yr	CHRPE, osteomas, epidermal cysts, periampullary neoplasms	TPC with end-ileostomy or IPAA or TAC with IRA and lifelong surveillance	Variants include Turcot (CNS tumors) and Gardener (desmoids) syndromes
Hereditary nonpolyposis colorectal cancer (HNPCC)	5–7%	Defective mismatch repair: *MSH2* and *MLH1* (90%), *MSH6* (10%)	Few polyps, predominantly right-sided CRC, 80% lifetime risk of CRC	At risk for uterine, ovarian, small intestinal, pancreatic malignancies	Genetic counseling; consider prophylactic resections, including TAH/BSO	High microsatellite instability (MSI-H) tumors, better prognosis than sporadic CRC
Peutz–Jeghers (PJS)	<1%	Loss of tumor suppressor gene *LKB1*/STK11 (19p13)	Hamartomas throughout GI tract	Mucocutaneous pigmentation, risk for pancreatic cancer	Surveillance EGD and colonoscopy q3yr; resect polyps >1.5 cm	Majority present with SBO due to intussuscepting polyp
Familial juvenile polyposis (FJP)	<1%	Mutated *SMAD4/DPC* (18q21)	Hamartomas throughout GI tract; >3 juvenile polyps; 15% with CRC by age 35 yr	Gastric, duodenal, and pancreatic neoplasms; pulmonary AVMs	Genetic counseling; consider prophylactic TAC with IRA for diffuse disease	Presents with rectal bleeding or diarrhea

AVM, arteriovenous malformation; CHRPE, congenital hypertrophy of retinal pigmented epithelium; CNS, central nervous system; EGD, esophagogastroduodenoscopy; GI, gastrointestinal; IPAA, ileal pouch–anal anastomosis; IRA, ileal–rectal anastomosis; TAC, total abdominal colectomy; TAH/BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy; TPC, total proctocolectomy.

c. Based on the modalities above in combination with pathology

assessment of the surgical specimen, the final colon cancer is stage can be summarized using the American Joint Committee on Cancer (AJCC) TNM staging system which takes into account the depth of invasion (T), lymph node status (N), and presence of distant metastases (M) (Table 27-6). Stage I tumors have a 90% 5-year survival. Stage II tumors have a 60% to 80% 5-year survival. Stage III tumors have a 60% 5-year survival. Stage IV tumors have a 5-year survival of 10%. Unfavorable characteristics include poor differentiation, pericolonic tumor deposits, multiple lymph node involvement, mucinous or signet-ring pathology, venous or perineural invasion, bowel perforation, aneuploid nuclei, and elevated CEA.

4. Surgical treatment

a. Preoperative preparation is focused on surgical site infection prevention, perioperative pain control, prevention of prolonged postoperative ileus and deep venous thrombosis. **Preoperative oral antibiotics, a mechanical bowel preparation**, and a prophylactic dose of **intravenous antibiotics** significantly decreases wound infections. We employ multimodal pain management techniques including patient-controlled analgesia, scheduled NSAIDs, gabapentin, oral acetaminophen, and regional block techniques. In opioid naïve patients alvimopan has been shown to decrease length of stay and speeds return of bowel function (*Ann Surg*. 2007;245(3):355–363). All patients receive perioperative prophylactic doses of either enoxaparin or heparin to prevent deep venous thrombosis.

TABLE 27-6 TNM Categories for Colorectal Cancer

T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)

T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into the pericolorectal tissues
T4	Tumor invades the visceral peritoneum or invades or adheres to adjacent organ or structure
T4a	Tumor invades through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades or is adherent to adjacent organs or structures
N	**Regional Lymph Nodes**
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the subserosa, mesentery, or nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional lymph nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive
M	**Distant Metastasis**
M0	No distant metastasis by imaging, etc.; no evidence of tumor in distant sites or organs
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastasis
M1b	Metastasis to two or more sites or organs is identified without

peritoneal metastasis

M1c Metastasis to the peritoneal surface is identified alone or with other site or organ metastasis

AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.

b. Colectomy may be approached laparoscopically, open, or robotically. For colonic lesions, this means ensuring an adequate proximal and distal margin, high ligation of the arterial pedicle for lymph node clearance, tension-free anastomosis, and good blood supply to the ensuing anastomosis or stoma. Retrieval of **at least 12 lymph nodes** is required to ensure appropriate staging. The laparoscopic approach to right, left, and sigmoid colon lesions has been found to be oncologically equal to open surgery with the added benefit of shorter recovery as reflected by multiple studies (*Lancet Oncol*. 2009;10(1):44–52). Lesions of the cecum and ascending colon should be resected via right colectomy. Lesions of the descending and sigmoid colon are removed via left colectomy. Transverse colon lesions are typically approached using an extended right colectomy.

c. In the **emergent** setting, intraoperative decisions may be necessary regarding appropriate therapy. This may include tumor resection with or without anastomosis or proximal diversion if the tumor is unresectable. If resection is not performed in the case of obstruction, the distal obstructed limb should be vented via loop ostomy or mucus fistula.

5. **Adjuvant chemotherapy** is currently recommended in patients with stage III and IV colon cancer. Adjuvant therapy should also be considered for patients with stage II disease who have inadequate lymph node retrieval (<12) or high risk features such as T4 stage, vascular invasion, and poor differentiation. In addition, patients with colon cancer that has high microsatellite instability (MSI-high), suggestive of a defect in a mismatch repair gene (MMR), tend to have a better oncologic outcome and have not been demonstrated to benefit from adjuvant chemotherapy. Current therapy involves the combination of 5-fluorouracil/leucovorin with either irinotecan (**FOLFIRI**) or oxaliplatin (**FOLFOX**). The role of targeted therapy

using vascular endothelial growth factor (VEGF) inhibitors (bevacizumab) or epidermal growth factor receptor (EGFR) inhibitors (cetuximab) has some benefit in the treatment of stage IV disease. Mutation status for KRAS should be established before starting EGFR-directed therapy as the presence of KRAS mutation is associated with a lack of response. Recently, some exciting progress has been made with the introduction of PD-1 blockade by pembrolizumab and/or nivolumab in the treatment of patients with advanced stage, MSI-high disease, overexpressing PD-L1. Phase 3 trials are currently in progress to further identify the ideal target group of patients for this novel treatment (*Eur J Cancer*. 2019;109:70–83).

6. **Follow-up** is crucial in the first 2 years after surgery, as this is when 90% of recurrences occur. Surveillance colonoscopy is recommended the first year after resection and then every 3 years until negative, at which time every 5 years is recommended. Advanced stage CRC should undergo yearly CTs of the chest, abdomen, and pelvis for 3 years. CEA should be followed, and rising levels should prompt a CT and possible colonoscopy if not recently performed.

D. Rectal Cancer

1. The evaluation and treatment of rectal cancer differs from that of colon cancer considering the following anatomic factors: (1) confinement of pelvis and sphincters; (2) proximity to urogenital structures and nerves; (3) dual blood supply and lymphatic drainage; and (4) transanal accessibility. The proximal extend of the rectum is at approximately 12 cm above the anal verge on rigid proctoscopy, but is above the third valve of Houston.
2. **Diagnosis and staging** of the rectum is done using the AJCC staging system for CRC as outlined above with additional considerations regarding local staging. DRE can give information on the size, height relative to the anorectal ring/sphincters, fixation, ulceration, local invasion, and lymph node status. Rigid or flexible sigmoidoscopy is important for precisely measuring the distance to the anal verge and dentate line. **Rectal cancer protocol magnetic resonance imaging (MRI)** is an integral part of staging rectal tumors to evaluate depth of invasion, the circumferential resection margin (**CRM**), and lymph node status, as this will help determine the need for preoperative

chemoradiation therapy (Fig. 27-4). **Endorectal ultrasound** (**EUS**) can be used for local staging as well, but does not assess CRM as well as MRI and is susceptible to user error. **Distant spread** is evaluated (as with colon cancer) with chest and abdominopelvic CT. It is helpful to have a preoperative CEA for patient follow-up.

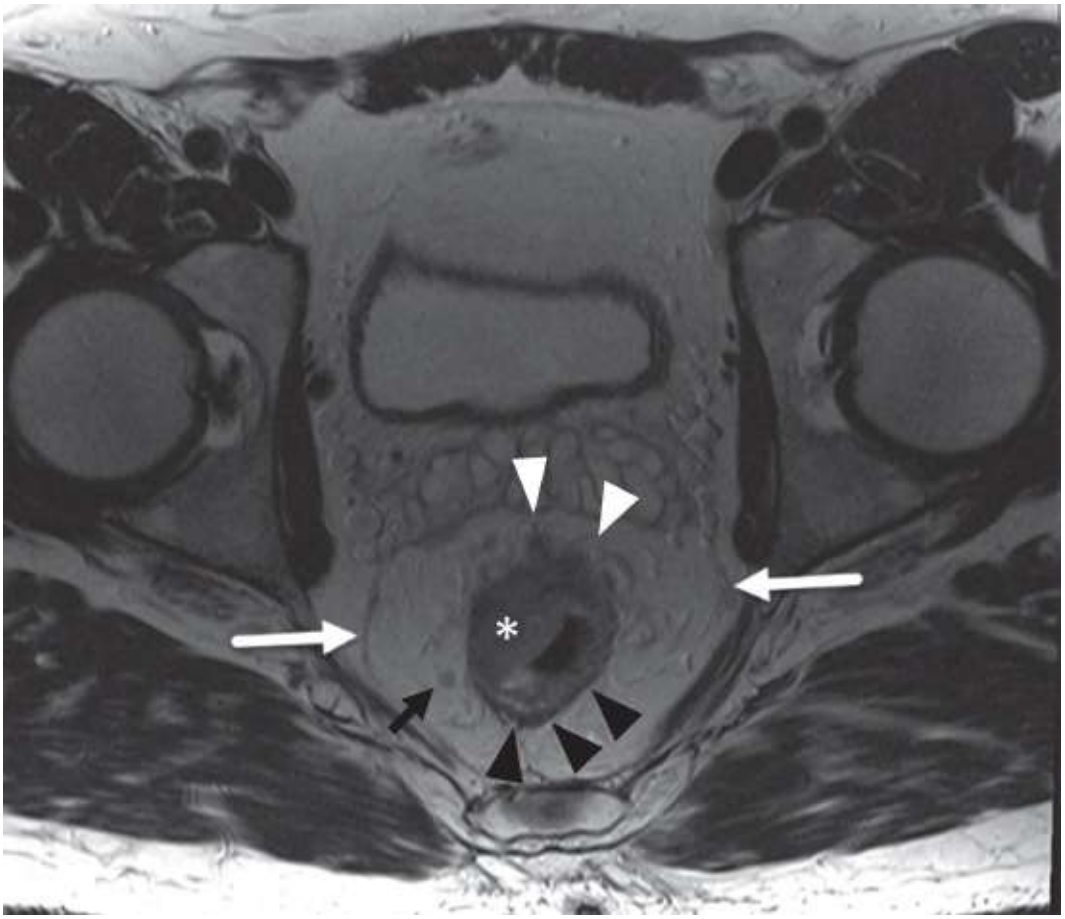


FIGURE 27-4 Pelvic MRI for rectal cancer: High-resolution, oblique axial, T2-weighted MRI image demonstrates a T2 hyperintense mass along the right and anterior aspect of the rectum (*), with nodular soft tissue extension (*white arrowheads*) through the T2 hypointense muscularis into the adjacent mesorectal fat. Normal T2 hypointense muscularis is seen along the posterior aspect of the rectum (*black arrowheads*). The findings are indicative of a T3 cancer. A small, indeterminate mesorectal lymph node is seen at the 8 o'clock position (*black arrow*). The circumferential resection margin is not involved (*white arrows*).

3. **Neoadjuvant chemoradiation** traditionally consists of 5-FU and leucovorin or capecitabine with concomitant radiation therapy (XRT, 54 Gy) given over 5 to 6 weeks. This is currently the standard in the United States for all patients with T3 or T4 lesions or node positive disease on imaging (MRI). Radiation therapy improves local control,

generating higher rates of sphincter-sparing resections and lower local recurrence rates, but it does not prolong survival. In addition, neoadjuvant radiation is associated with similar results while accompanied by significantly less toxicity than postoperative radiation (*Lancet Oncol*. 2011;12(6):575–582). Advancements in the administration of radiation therapy such as "short course" radiation (25 Gy given in five fractions), chemotherapy regimens, and optimization of timing of surgery after therapy provide promising results with increased complete clinical and pathologic response rates. Multiple centers now offer total neoadjuvant therapy (TNT), in which patients complete a course of radiation and receive systemic chemotherapy upfront, before surgical resection. Ongoing trials have yet to establish the optimal regimen, safety, and feasibility of organ-sparing treatment after complete response to neoadjuvant therapy (*Cancer*. 2017;123(9):1497–1506).

4. The **goal of surgical therapy** is to remove the cancer with adequate margins, **total mesorectal excision** (TME), lymph node clearance with high ligation of the arterial pedicle (IMA), and consideration of future continence and urogenital function. Patients with clinical or imaging evidence of sphincter involvement, incontinence, or concern for distal margin should undergo abdominoperineal resection (APR). Bowel preparation is similar to colon resection. Possible stoma sites including colostomy and proximal DLI should be marked preoperatively. **Preoperative ureteral stents** should be considered in patients who are at high risk of ureteral injury.
    a. **As with colectomy, proctectomy can be approached open, laparoscopically, or robotically.** Although there is ongoing discussion about the quality of oncologic resection with minimally invasive approaches, there is no conclusive evidence that oncologic outcome is inferior (*Cochrane Database Syst Rev*. 2014;(4):CD005200 and *World J Gastrointest Oncol*. 2018;10(11):449–464). Regardless of the approach undertaken, the principles of surgery are the same. The distal margin can be <2 cm in patients with distal tumors to preserve continence; however, it must be ensured that there is a negative margin. Based on current data, any patient with a T2 rectal cancer should undergo radical excision with LAR or APR. Optimal surgical treatment for

T1 rectal cancers should be determined on a case by case basis. Lesions that are well/moderately differentiated, less than 3 cm in size, less than 30% of the circumference of the bowel wall, mobile, nonfixed, SM1/SM2, without LVI or perineural invasion, and without clinical evidence of nodal involvement are amenable to transanal full-thickness excision, TEM or TAMIS techniques. Rectal cancer with extension into the bladder, sacrum, vagina, or other local pelvic structures can possibly be resected en bloc with the other involved organs for cure. It is important to remember the anatomic confines and anatomy of the pelvis as infertility, sexual dysfunction, and continence are affected by the parasympathetic and sympathetic nerves and are common complications. In addition, anastomotic leak is more common for coloproctostomy than colocolostomy, and leak testing in the operating room is recommended. Proximal diversion is recommended for any low or tenuous anastomosis, as leaks can have devastating consequences.

5. **Obstructing rectal cancers** should be evaluated by hypaque enema and/or colonoscopy in patients without clear signs of peritonitis. Endoluminal stents can be used as a short-term bridge to operative therapy, but they should be avoided in low- and midrectal tumors as stents are poorly tolerated in this location. To facilitate preoperative chemoradiation therapy in these patients, a diverting loop colostomy should be fashioned rather than stent placement.
6. **Rectal cancer** recurrence typically presents with pain, rectal bleeding, or on routine follow-up testing. Diagnosis is confirmed by examination and biopsy. Patients should then be worked up for systemic recurrence including CT and/or PET-CT. If there is no evidence of systemic recurrence, resection can be considered if patients are fit. Pelvic MRI is useful to evaluate the relationship to other pelvic structures. Preoperative therapy can be considered if patients have not received pelvic radiation previously. Curative resection of recurrent rectal cancer can lead to significant long-term survival (*Eur J Surg Oncol*. 2018;44(1):100–107).

E. Other Colorectal Tumors

1. **Lymphoma** is most often metastatic to the colorectum, but primary non-Hodgkin colonic lymphoma accounts for 10% of all GI lymphomas. The GI tract is also a common site of non-Hodgkin

lymphoma associated with human immunodeficiency virus. The most common presenting symptoms include abdominal pain, altered bowel habits, weight loss, and hematochezia. Biopsies are often not diagnostic because the lesion is submucosal. Surgery and/or chemotherapy should both be considered as a treatment option with the added staging benefit of surgical intervention as well as the potential to be curative without chemotherapy. Intestinal bypass, biopsy, and postoperative chemotherapy should be considered for locally advanced tumors.

2. **Retrorectal tumors** usually present with postural pain and a posterior rectal mass on physical examination and CT scan or are incidentally found on imaging for other reasons.
   a. The **differential diagnosis** includes congenital, neurogenic, osseous, and inflammatory masses. Chordomas are the most common malignant retrorectal tumor, and they are typically slow growing but difficult to resect for cure.
   b. **Diagnosis** is based on physical findings, CT, and MRI imaging. Biopsy should be performed selectively if it will assist in determining the need for, and type of, neoadjuvant therapy. Biopsies should not be performed transrectal or transvaginal. Formal resection, preferably from a perineal or transsacral approach, should be undertaken if there are symptoms or concern for malignancy.
3. **Neuroendocrine tumor**
   a. **Colonic carcinoids** account for 2% of GI carcinoids. Lesions less than 2 cm in diameter rarely metastasize, but 80% of lesions greater than 2 cm in diameter have local or distant metastases, with a median length of survival of less than 12 months. These lesions are treated with local excision if small and with formal resection if greater than 2 cm.
   b. **Rectal carcinoid** accounts for 15% of GI carcinoids. Lesions less than 1 cm in diameter have low malignant potential and can be treated with local transanal or endoscopic resection. With lesions 1 to 2 cm, more extensive resection should be considered based on the presence of symptoms at diagnosis and characteristics including muscular invasion and ulceration. Rectal carcinoids greater than 2 cm in diameter are treated with proctectomy.

c. The classic **"carcinoid syndrome"** is most commonly (90%) associated with a midgut carcinoid tumor (including the right colon and appendix). Hindgut carcinoids virtually always lack the ability to produce 5-hydroxytryptophan or serotonin and therefore even those with metastatic disease do not present with carcinoid syndrome.

IV. INTESTINAL STOMAS

A. Ileostomy creation and care was revolutionized with the description of the eversion technique by Brooke in 1952. The small intestine adapts to ileostomy formation within 10 days postoperatively. Average output is 500 mL/day, but may be up to 1,500 mL/day. Volumes above 1,000 mL/day may be pathologic and/or cause dehydration and electrolyte abnormalities. Stoma construction of either a loop ileostomy or end-ileostomy should be "Brooked" or everted 2 to 2.5 cm to create an easier stoma to pouch. Stoma creation should be within the rectus abdominis to decrease the risk of peristomal herniation. Preoperative marking of the planned site prevents improper placement near bony prominences, belt/pant lines, abdominal creases, and scars. Reversal of a loop ileostomy is relatively straightforward and rarely requires laparotomy. The enterotomy can safely be closed primarily in a hand sewn fashion or excised and reanastomosed with a stapled side-to-side, functional end-to-end technique providing similar outcomes.

B. Colostomy construction is typically associated with fewer electrolyte and physiologic derangements than an ileostomy. Left-sided or sigmoid colostomies are preferred to right-sided or transverse colostomies. Colostomies can be created in either a loop, end, or end-loop configuration. Common colostomy complications include stenosis, retraction, prolapse, and parastomal hernia. Stenosis/retraction may require local revision if symptomatic or difficult to maintain appliance seal. Parastomal hernia repair (usually with mesh or resiting) is indicated for the same reasons as other abdominal wall hernias. Colostomy prolapse, usually treated with local revision, does not require repair unless there is an inability to reduce the prolapse/ischemia, obstruction, or there are pouching issues. Obstipation/constipation can be assessed with digital exam and treated with stoma irrigation and/or hypaque enema, which can be diagnostic and therapeutic. End

colostomy takedown can be difficult, and all patients should undergo full colonoscopic evaluation including the distal defunctionalized colon/rectum to rule out stricture or mass prior to takedown.

CHAPTER 27: COLON AND RECTUM

Multiple Choice Questions

1. Which of the following is part of the Rome criteria for the diagnosis of constipation?

a. Three or fewer bowel movements per week
b. Manual maneuvers to assist with more than 50% of bowel movements
c. Fulfilling criteria of irritable bowel syndrome
d. Sensation of incomplete evacuation with 100% of bowel movements
e. Lumpy/hard stools with 75% of bowel movements

2. When administering neostigmine to a patient with Ogilvie syndrome, why is it important to ensure the patient is in a monitored setting?

a. Often there is a rapid response causing a large evacuation which can be difficult to manage
b. There is a high risk of hypotension due to vasovagal stimulation related to having a large bowel movement
c. Neostigmine can cause significant bradyarrhythmias potentially requiring cardioversion
d. There is a significant risk of perforation with the administration of neostigmine
e. Neostigmine causes a significant sympathetic nervous system stimulation, causing severe agitation

3. The most important aspect in the care of a patient with hemodynamically significant LGIB is which of the following?

a. Obtaining early tagged red blood cell scan
b. Ensuring appropriate resuscitation and stabilizing patient
c. Using fecal occult blood test to test for bleeding
d. Placing an NGT to rule out an upper GI source
e. Obtaining immediate upper and lower GI luminal contrast studies to assess for bleeding source

4. Definitive treatment of sigmoid volvulus is accomplished by:

a. Endoscopic decompression
b. Endoscopic decompression and placement of a long rectal tube
c. Sigmoidopexy
d. Sigmoidectomy
e. Total abdominal colectomy

5. The most common cause of lower GI bleed is:

a. Upper GI bleed
b. Colorectal cancer
c. Ischemic colitis
d. Ulcerative colitis
e. Diverticulosis

6. Hinchey IV diverticulitis demands operative therapy and is characterized by:

a. Pericolonic abscess 2 to 4 cm
b. Pericolonic abscess >4 cm
c. Purulent peritonitis
d. Fecal peritonitis
e. Pelvic abscess

7. An important distinguishing feature of Crohn disease when compared to ulcerative colitis is:

a. The lack of “skip” lesions
b. Response to biologic therapy
c. Perianal disease
d. The presence of pyoderma gangrenosum
e. The presence of arthritis

8. Surgical treatment of medically refractory ulcerative colitis includes:

a. Abdominoperineal resection with end colostomy
b. Total proctocolectomy with ileal pouch–anal anastomosis (IPAA)
c. Segmental colectomy involving the diseased area and colocolostomy

d. Total abdominal colectomy with ileorectal anastomosis
e. Ileocolic resection and primary anastomosis

9. A patient presents to the ED with abdominal pain and hematochezia after endovascular aortic aneurysm repair (EVAAR), how would you confirm your clinical suspicion?

a. Flexible sigmoidoscopy
b. Pelvic MRI
c. Barium enema
d. Acute abdominal series
e. Upper endoscopy/esophagogastroduodenoscopy (EGD)

10. The most common types of colonic polyps diagnosed on endoscopy are:

a. Adenomatous polyps
b. Malignant polyps
c. Hamartomatous polyps
d. Hyperplastic polyps
e. Inflammatory polyps

11. The Kudo classification of polyp invasion is important to the treatment of malignant colon and rectal polyps because:

a. The Kudo classification is more sensitive than the Haggitt classification for the diagnosis of malignancy
b. The Kudo classification assesses the depth of invasion into the stalk of a pedunculated polyp
c. The Kudo classification accurately predicts who needs adjuvant therapy after resection
d. The Kudo classification predicts the risk of lymph node metastasis and the need for surgical resection
e. The Kudo classification accurately predicts which polyps are technically amenable to endoscopic retrieval

12. An asymptomatic patient presents to your office for consultation regarding screening colonoscopy due to the fact that the patient's father was diagnosed with colon cancer. What is the most important

factor when considering initiating screening colonoscopy?

a. Recent weight loss
b. Smoking history
c. The stage of the patient's father's colon cancer at diagnosis
d. The age of the patient's father at colon cancer diagnosis
e. The patient's mother's diagnosis of breast cancer

13. On pathologic examination after right colectomy, a patient is diagnosed with a T3 tumor with 0 out of 9 lymph nodes negative. What do you tell this patient about his or her need for adjuvant therapy?

a. The patient does not need adjuvant therapy because there is only marginal benefit in patients with stage II disease
b. Adjuvant therapy should be considered because although the patient is stage II, there was inadequate lymph node harvest
c. The patient should consider not receiving adjuvant therapy because although the patient has stage III disease, they have low-risk stage III disease
d. The patient should consider adjuvant chemoradiation therapy for their stage II disease
e. The patient should receive adjuvant therapy because there is clearly a benefit for patients with stage III disease

14. To appropriately stage rectal cancer, patients need what imaging studies for initial assessment?

a. Chest CT, abdomen CT, pelvic MRI
b. Chest x-ray, abdomen and pelvis CT, PET/CT
c. Chest x-ray, abdomen and pelvis CT
d. Abdomen CT, pelvic MRI, PET/CT
e. Chest x-ray, abdomen and pelvis CT, pelvic MRI, PET/CT

15. The principles of surgical resection for the treatment of rectal cancer include which of the following?

a. Resection of Denonvilliers fascia to ensure an adequate anterior margin

b. Ensuring an intact and complete total mesorectal excision
c. Resection of the hypogastric nerves along the pelvic sidewall as this is a common site of recurrence
d. Performing an abdominoperineal resection for any patient with a tumor <5 cm from the dentate line due to the dual blood supply of the distal rectum
e. High ligation and node harvest from the superior mesenteric artery (SMA)

28

Anorectal Disease

William C. Chapman, Jr and Matthew G. Mutch

I. ANORECTAL ANATOMY AND PHYSIOLOGY

A. Anatomy

1. The **anal canal** is the distal-most portion of the gastrointestinal (GI) tract and extends from the anorectal ring—formed by the puborectalis and anal sphincter muscular sling (see below)—to the anal verge (i.e., transition zone between anoderm and skin). It essentially comprises a 4-cm "tube within a tube" of muscular sphincters that control defecation (Fig. 28-1).
2. The **epithelial lining** of the canal uniquely transitions from columnar, pink mucosa at the anorectal junction to pigmented squamous epithelium at the anal verge. The **dentate line** marks the point of epithelial transition from embryonic endoderm to ectoderm.
3. The dentate line also delineates the transition of **nervous innervation** from sympathetic and parasympathetic systems to the somatic, as well as the transition of **vascular and lymphatic supply** from the hypogastric to inferior hemorrhoidal systems.
4. Three major muscles form the underlying structure of the anal canal and enable the sphincteric function of the complex. The **internal anal sphincter** is the continuation of the circular smooth muscle of the rectum and is controlled by parasympathetic reflexes. The **external anal sphincter**, however, is striated skeletal muscle under somatic control that forms an elliptical tube around and distal to the internal sphincter. The **puborectalis** arises from the pubic symphysis and encircles the bowel at the anorectal junction, thus forming the anorectal ring.

B. Physiology

1. The **rectum functions as a capacitance organ,** with a reservoir of

650 to 1,200 mL compared to an average daily stool output of 250 to 750 mL.

2. The **anal sphincter mechanism** allows defecation and maintains continence. The internal sphincter (involuntary) accounts for 80% of resting pressure, whereas the external sphincter (voluntary) accounts for 20% of resting pressure and 100% of squeeze pressure. The external anal sphincter normally contracts in response to sensed rectal contents and relaxes during defecation.
3. **Defecation** has four components: (1) increased intra-abdominal pressure (Valsalva) propels stool forward from the distal colon/rectum; (2) mass movement of feces into the rectal vault; (3) distal rectal distention incites the **rectoanal inhibitory reflex (RAIR;** involuntary relaxation of the internal sphincter while the external sphincter contracts) leading to "**sampling,"** which allows for determination of contents as gas, liquid, or solid; and (4) voluntary relaxation of the external sphincter mechanism and puborectalis muscle allows expulsion of stool.

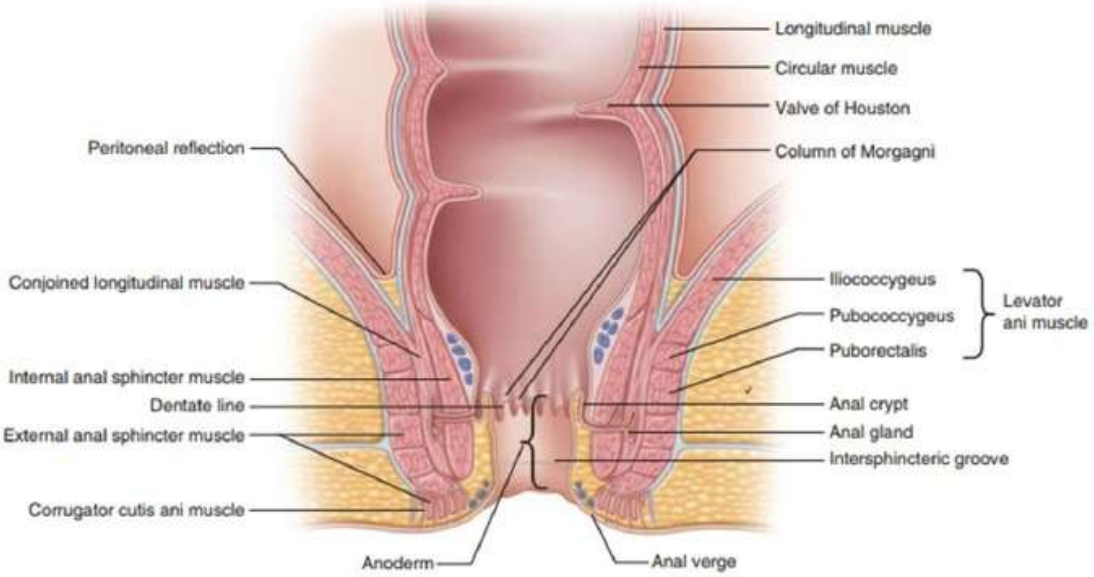


FIGURE 28-1 Coronal depiction of the anal canal highlighting the boundary landmarks (anorectal ring, anal verge), important mucosal anatomy, and components of the sphincter complex. (From Steele SR, Hull TL, Read TE, Saclarides TJ, Senagore AJ, Whitlow CB. *The ASCRS Textbook of Colon and Rectal Surgery.* 3rd ed. New York: Springer International Publishing; 2016, with permission.)

4. **Continence** requires normal capacitance, normal sensation at the

anorectal transition zone, puborectalis function for solid stool, external sphincter function for fine control, and internal sphincter function and hemorrhoidal pillars for resting pressure.

II. FUNCTIONAL ABNORMALITIES OF THE RECTUM

A. Incontinence—the inability to prevent elimination of rectal contents.

1. The **spectrum of disease** includes **anal seepage** (the leakage of postdefecation mucus or stool), **urgency** (the inability to maintain continence for an extended period of time), and **complete incontinence** (lack of any control of gas or stool). Differentiation becomes important when determining the aggressiveness of therapy.
2. **Etiologies** include (1) **mechanical defects,** such as sphincter damage (e.g., obstetric trauma, fistulotomy, scleroderma, radiation proctitis), (2) **neurogenic defects** (e.g., spinal cord injuries, pudendal nerve injury due to birth trauma or lifelong straining, systemic neuropathies such as multiple sclerosis), and (3) **stool content–related causes** (e.g., diarrhea).
3. **Evaluation** begins with a thorough history and physical examination that include visual and digital examination of gross tone or squeeze abnormalities and determining muscle bulk. The history should include any neurologic or medical disorders, prior anorectal surgery, vaginal deliveries, and medications. Testing should include multiple modalities. **Endoanal ultrasound** (EUS) assesses the internal and external sphincter for defects. **Anal manometry** quantitatively measures parameters of anal function, including resting and squeeze pressure (normal mean >40 and >80 mm Hg, respectively), sphincter length (4 cm in men, 3 cm in women), and minimal sensory volume of the rectum. **Pudendal nerve terminal motor latency** (PNTML) testing and EUS provide neural and anatomic information.
4. **Treatment** depends upon the spectrum of disease and underlying cause. Neurogenic and minor mechanical anal sphincter defects are initially treated using **dietary fiber** to increase stool bulk and **biofeedback** to strengthen muscle and improve early sensation. Major defects require **anal sphincter reconstruction**. **Sacral nerve stimulation** (SNS), used in patients with an intact sphincter complex or minimal defect, is emerging as the most durable treatment for fecal incontinence. SNS has shown improved continence and evacuation in

those with chronic constipation, although the mechanism of action remains unclear. Patients keep an incontinence journal before and after temporary leads are imbedded in the S2 to S4 nerve roots. If there is a marked improvement after 2 weeks, then a permanent device is placed.

B. Obstructed defecation is a group of disorders with pelvic floor outlet obstruction that leads to inability to evacuate rectal contents.

1. This group of defecatory disorders requires careful history-taking and workup to correctly diagnose. **Anal stenosis,** which often presents with frequent, thin stools and incomplete evacuation, is most commonly due to postsurgical scarring, radiation, chronic laxative abuse, recurrent anal ulcers, or trauma. **Nonrelaxation of the puborectalis,** however, presents with bloating and incomplete evacuation in the absence of stenosis. Persistent puborectalis distortion on defecography is diagnostic. **Rectocele** and **descending perineum syndrome** both result from chronic straining that damages the rectovaginal septum or pudendal nerve, respectively. These represent long-term sequelae of nonrelaxation of the puborectalis. Fecal impaction and stercoral ulceration are associated with all of these processes.
2. **Evaluation** includes (1) **video defecography** or dynamic pelvic MRI to evaluate fixation of the posterior rectum to the sacrum and relaxation of the puborectalis; (2) **anal manometry and surface EMG testing** to assess rectal sensation, ability to expel a balloon, and paradoxical contraction of the external sphincter with straining; and (3) **colonic transit study** to assess colonic motility.
3. **Treatment** is often multimodal and conservative. **Fiber, biofeedback, suppositories/enemas, and stool softeners** are used depending on the underlying etiology. Surgical correction (even diverting colostomy) is employed only as a last resort and results are inconsistent due to the functional—not mechanical—nature of the disorder.

C. Abnormal rectal fixation includes defects in the ligamentous attachments of the distal colon and rectum that lead to partial- or full-thickness rectal prolapse.

1. **Internal intussusception (internal rectal prolapse)** causes outlet obstruction with mucus discharge, hematochezia, tenesmus, and

constipation. The underlying pathophysiology involves the chronic straining caused by a **nonrelaxing puborectalis**. Proctoscopy demonstrates an inflamed, irritated rectal mucosa and/or a **solitary rectal ulcer** (SRU) that may develop at the lead point of the internal prolapse. This may mimic a rectal cancer so **biopsy** is required before offering any treatment. **Treatment** is as with obstructed defecation (see above), including biofeedback to retrain the function of the puborectalis. **Indications for surgery** are chronic bleeding, impending incontinence, and lifestyle-limiting symptoms. **Surgical options** are controversial. The most frequent procedure is **transabdominal rectopexy** (suture fixation of the rectum to the presacral fascia) with or without **resection** of the sigmoid colon if constipation is prominent. Chronic ischemia of the SRU causes entrapment of mucin-producing cells, eventually resulting in **colitis cystica profunda, which can be confused for cancer.**

2. **External rectal prolapse** is protrusion of full-thickness rectum through the anus. Symptoms include pain, bleeding, mucous discharge, and incontinence. Physical examination can distinguish rectal prolapse (**concentric mucosal rings**) from prolapsing internal hemorrhoids (deep radial grooves with a rosebud appearance). **Acute prolapse** needs urgent bedside reduction. If unsuccessful, reduction or resection in the operating room may be needed. **Risk factors** include increased age, female gender, institutionalization, antipsychotic medication, previous hysterectomy, and spinal cord injury. Evaluation includes physical examination to confirm full-thickness prolapse and exclude prolapsed hemorrhoids. Ideally, a **barium enema or colonoscopy** is needed to rule out concomitant colonic pathology. In general, abdominal procedures trade higher operative morbidity with lower recurrence rates relative to perineal-only operations. Continence improves in almost all patients, regardless of procedure.
   a. **Sigmoid resection and rectopexy** (**Frykman–Goldberg procedure**) shortens the redundant rectosigmoid colon with posterior sacral fixation. Prolapse recurs in less than 10% of patients following rectopexy with or without resection.
   b. **Ventral rectopexy** is a newer option in which the anterior plane is mobilized, a permanent mesh is secured to the anterior rectal wall

at the level of the pelvic floor, and then the mesh is anchored to the sacral promontory. Essentially, this procedure creates an artificial sling which tethers the rectum to the spine and reinforces the anterior rectal wall. Proponents cite lower complication rates, similar recurrence rates, and improved functional outcomes.

c. **Perineal proctectomy** (**modified Altemeier [full-thickness resection] or Delorme [mucosectomy and muscular plication] procedures**) is an alternative for patients with comorbidities or other contraindications to abdominal operation/approach. Recurrence rate is generally around 20%, although lower rates have been reported in retrospective, single-institution studies.

III. HEMORRHOIDS

A. The anal canal is lined by three columns of vascular cushions in the left lateral, right anterolateral, and right posterolateral locations that normally contribute to fecal continence. These cushions, which are called hemorrhoids when engorged and symptomatic, can cause a number of symptoms including bleeding, pain, stool leakage, and prolapse. The **etiology** of hemorrhoidal disease is typically multifactorial and related to hard stools, prolonged straining and constipation, increased intra-abdominal pressure, and/or prolonged lack of support of the pelvic floor.

B. Evaluation of the hemorrhoidal location of origin (either above or below the dentate line) is paramount for therapy selection. **Internal hemorrhoids,** which originate above the dentate line, are covered with mucosa and devoid of noxious nervous innervation. **External hemorrhoids,** however, arise below the dentate line and are covered with squamous epithelium, and therefore pain-sensing nerves innervate these tissues, often resulting in pain as a primary symptom. While history and physical examination suggest the origin, true localization requires full examination of the anal canal with anoscopy or proctoscopy.

C. Treatment is based on grading and severity of patient symptoms (Table 28-1); options include the following:

1. **Medical treatment** of grade 1 and 2 hemorrhoids includes **increased dietary fiber** and water to increase stool bulk, **stool softeners**, and

avoidance of straining during defecation. Additional medical treatments include **topical nitrates, calcium channel blockers**, or **astringents** (e.g., witch hazel) to reduce vascular congestion, and **topical anesthetics** can reduce pain.

TABLE 28-1 Classification and Treatment of Symptomatic Internal Hemorrhoids

Grade	Description	Treatments
I	Palpable, nonprolapsing enlarged venous cushions	Dietary fiber, stool softeners
II	Prolapse with straining and defecation, spontaneously reduce	Dietary fiber, stool softeners, elastic ligation
III	Protrude spontaneously or with straining, require manual reduction	Dietary fiber, stool softeners, elastic ligation, excisional hemorrhoidectomy, stapled hemorrhoidectomy
IV	Chronically prolapsed and cannot be reduced, often with dentate line released from internal position	Dietary fiber, stool softeners, excisional hemorrhoidectomy, stapled hemorrhoidectomy/hemorrhoidopexy

2. Refractory grade 2 and 3 hemorrhoids may be treated in the office by **elastic ligation.** The ligation must be 1 to 2 cm above the dentate line to avoid severe pain. One to two quadrants are ligated every 2 to 8 weeks in the office, and the patient is warned that the necrotic hemorrhoid may slough in 4 to 10 days with potential **bleeding** occurring at that time. Severe pain at the time of banding requires immediate removal, so testing of the mucosa for sensation prior to

placement is required. Patients on anticoagulation should have their anticoagulation stopped before banding, or banding is precluded for the bleeding risks. Other complications include **severe sepsis,** particularly in immunocompromised patients. Accidental full-thickness ligation of the rectum in the prolapsed patient is rare but reported. Typical presentation includes **severe pain, fever, and urinary retention** within 12 hours of ligation. Patients with this life-threatening complication should undergo examination under anesthesia (EUA), immediate removal of rubber bands, and debridement of any necrotic tissue, accompanied by broad-spectrum intravenous antibiotics. Overall, patients who undergo banding have a **30% recurrence rate**.

3. **Excisional hemorrhoidectomy** is reserved for symptomatic hemorrhoids not amenable to banding, larger-grade 3/4 hemorrhoids, mixed internal and external hemorrhoids, and thrombosed, incarcerated hemorrhoids with impending gangrene. The procedure is performed with the patient in the **prone flexed position, often with monitored anesthesia care/sedation and local anesthetic or spinal or general anesthesia.** The hemorrhoids are excised while protecting the underlying sphincters, and the resulting elliptical defects are completely closed with an absorbable suture (**Ferguson hemorrhoidectomy**). Complications include a 10% to 20% incidence of urinary retention (most common complication after pain), bleeding, infection, sphincter injury, and anal stenosis from excising excessive anoderm.
4. **Stapled hemorrhoidectomy/hemorrhoidopexy** is an alternative to traditional excisional hemorrhoidectomy for large, prolapsing, or bleeding grade 3 hemorrhoids with minimal external disease. This procedure is performed by a circumferential excision of redundant rectal mucosa approximately 5 cm superior to the dentate line using a specially designed circular stapler, ensuring avoidance of vaginal tissue in female patients. Stapled hemorrhoidectomy results in significantly less perioperative discomfort but carries a higher recurrence rate than surgical excision.
5. **Transanal hemorrhoidal dearterialization (THD)** uses a proctoscope with a Doppler transducer to selectively ligate branches of the superior hemorrhoidal artery. Sutured hemorrhoidopexy can be

performed concomitantly.

6. **Acutely thrombosed external hemorrhoids** are treated by excision of the thrombosed vein outside the mucocutaneous junction, which can be done in the office or emergency room with the wound left open. If the thrombosis is more than 48 to 72 hours old, the patient is treated with nonsurgical management first, reserving excisional hemorrhoidectomy for persistence of symptoms. The recurrence rate of thrombosed external hemorrhoids is significantly higher with nonoperative management (25%) than excision (6%).

IV. ANAL FISSURE

A. Fissure is a split in the anoderm lining the anal canal, exposing the submucosa and underlying sphincter complex. Symptoms include blood, tearing pain, and severe anal spasm with defecation. The **etiology** is usually hypertrophy or spasm of the distal one-third of the internal anal sphincter and exaggerated constriction of this muscle in response to the RAIR precluding spontaneous healing. Less common causes of fissures include Crohn's, malignancy, abscess or fistula, or infections such as herpes, chancroid, and syphilis.

B. Evaluation of anal fissure centers on determination of the location and severity of the lesion. Ninety percent occur in the posterior midline and 10% in the anterior midline with any alternate location raising suspicion of atypical etiology and consideration of infection assessment or biopsy. An external skin tag, or "**sentinel pile**," and **hypertrophied anal papilla** are often associated with **chronic fissures**.

C. Treatment is focused on decreasing internal sphincter hypertonicity and is largely limited to medical therapies including fiber supplementation, stool softeners, sitz baths, and topical calcium channel blockers or nitrates. Ninety percent of fissures will resolve with these therapies, but those that fail to respond after 6 to 8 weeks are treated with **lateral internal sphincterotomy (LIS)**, either chemical (with **botulinum toxin injection**) or surgical. While surgical LIS is over 95% successful, it is associated with ~10% rate of minor incontinence.

V. INFECTIOUS PATHOLOGY OF THE ANORECTUM

A. Anorectal Abscess

1. **Cryptoglandular abscess** results from infection of the **anal glands**

in the crypts at the dentate line. The initial abscess, which occurs in the intersphincteric space, can then spread (1) superficial to the external sphincter into the **perianal** space; (2) cephalad in the **intersphincteric plane;** (3) through the external sphincter into the **ischiorectal** space (which in turn may connect posteriorly via the deep postanal space, resulting in a **horseshoe abscess**); or (4) deep to the external sphincter into the **supralevator** space.

a. Diagnosis usually is obvious, with **severe anal pain and a palpable, tender, fluctuant mass**. An intersphincteric abscess yields only a painful bulge in the rectal wall and no external manifestations.

b. Treatment is surgical drainage. Intersphincteric abscesses are drained by an **internal sphincterotomy** over the entire length of the abscess. Draining an intersphincteric abscess externally may result in a supralevator fistula, which is technically challenging to repair. **Perianal and ischiorectal abscesses** are drained through the perianal skin with a small mushroom-shaped catheter placed to keep the abscess unroofed. **Supralevator abscesses,** originating from intersphincteric abscesses, should be drained into the rectum. **Antibiotic therapy is not necessary** unless the patient (1) is immunocompromised, (2) is diabetic, (3) has extensive cellulitis or systemic symptoms (e.g., sepsis), or (4) has valvular heart disease. Immunocompromised patients may present with anal pain without fluctuance because of the paucity of leukocytes. The painful indurated region must still be drained, and the underlying tissue must undergo biopsy and culture. **Drainage** alone is definitive therapy in **over 60% of patients.** The remainder will develop a chronic perianal fistula. It is not encouraged to search for an internal opening in the acute setting, often difficult to find at that time regardless.

2. Fistula-in-ano

a. Also known as perianal fistula, **fistula-in-ano** represents the chronic stage of cryptoglandular abscess. In addition to initial abscess formation, fistula **etiology** may also be related to trauma, Crohn disease, radiation, or cancer. Patients present with persistent or intermittent purulent and/or feculent drainage from an external perianal opening. The corresponding internal opening

within the anal canal usually follows **Goodsall rule** with few exceptions: fistulas with external openings anterior to a transverse plane through the anal canal penetrate toward the dentate line in a radial direction, whereas fistulas posterior to that plane curve so that the internal opening is in the posterior midline (Fig. 28-2). These fistulas may involve the sphincters in one of four configurations (Fig. 28-3).

b. Evaluation requires determination of the overall stability of the patient as well as the degree of perianal involvement of the fistula. In addition to physical examination, axial imaging with contrast can also delineate degree of pelvic involvement.

c. Treatment depends on the stability of the patient, the level that the fistula traverses the external sphincter, and pre-existing sphincter function. **Decompression of undrained abscess** is the first priority of management, especially in the setting of systemic sepsis. Placement of a soft, noncutting **seton** permits resolution of surrounding inflammation while preserving sphincter musculature, often acting as temporizing first-stage operation. **Fistulotomy,** dividing the overlying internal sphincter, may be performed for intersphincteric and low transsphincteric fistulas. For posterior midline fistulas, up to 50% of the sphincter can safely be divided. In women, anterior fistulas should never be treated with a fistulotomy because the risk of incontinence is too high. Therefore, anterior and high transsphincteric fistulas should be treated with sphincter-sparing techniques. **Fibrin glue injection** and **anal fistula plug** initially provided encouraging results, but, over time, the success of these techniques has ranged from 25% to 40%. The **ligation of intersphincteric fistula tract (LIFT)** procedure has gained acceptance with success rates of 60% to 75%. This procedure requires dissection in the intersphincteric plane, isolation of the fistula tract, and ligation of both sides of the tract. Endorectal advancement flaps remain the gold standard with success rates ranging from 70% to 90%. Recurrent or complex fistulas may even require temporary fecal diversion (i.e., ostomy) to facilitate healing.

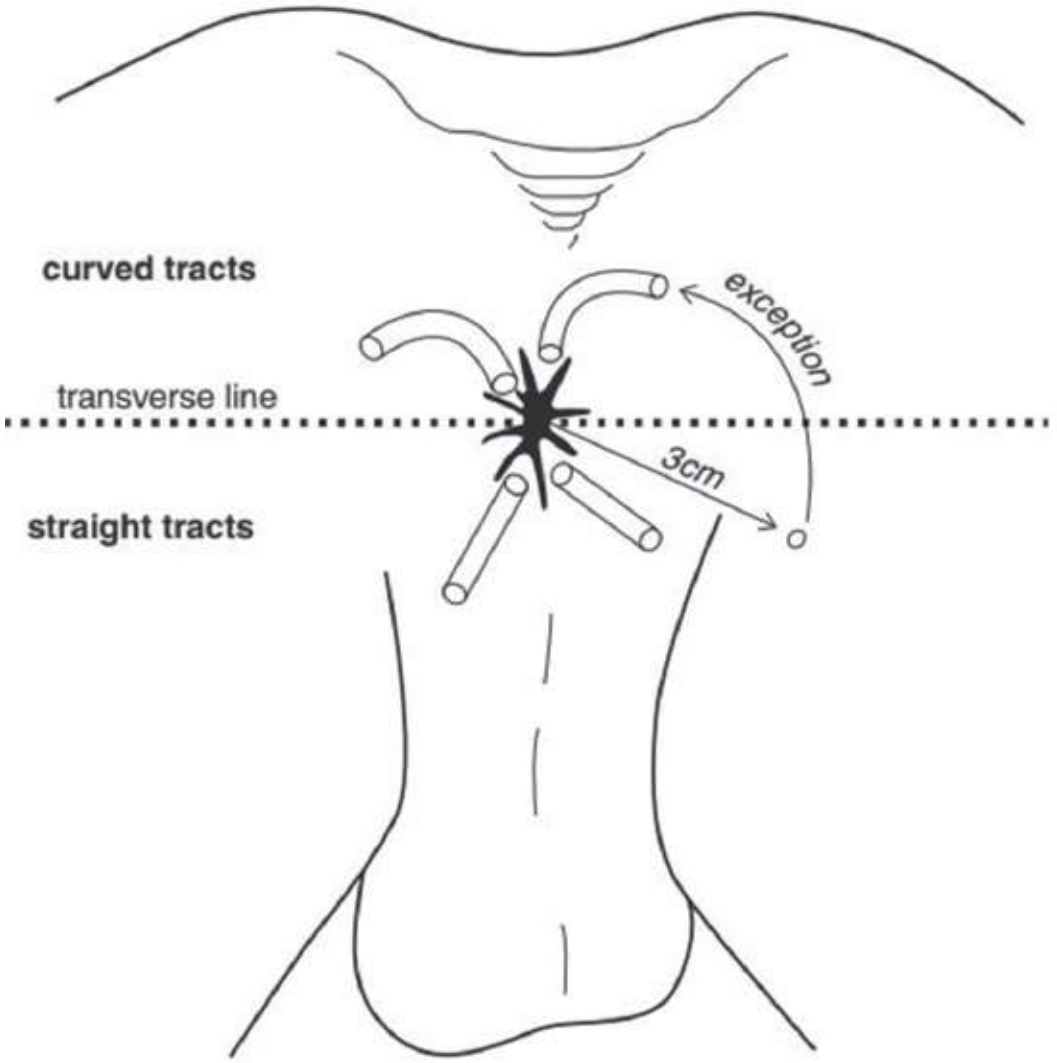


FIGURE 28-2 Goodsall rule. The anterior–posterior location of the external opening of the fistula helps to identify the internal opening of the fistula. (From Steele SR, Hull TL, Read TE, Saclarides TJ, Senagore AJ, Whitlow CB. *The ASCRS Textbook of Colon and Rectal Surgery.* 3rd ed. New York: Springer International Publishing; 2016, with permission.)

B. Necrotizing Anorectal Infection

1. Also known as **Fournier gangrene**, necrotizing perineal infections are deadly processes that require rapid intervention. Often originating with innocuous infections of synergistic GI flora (*Clostridia* and *Streptococcus*), patients will rapidly develop perianal pain and systemic toxicity.
2. On examination, **crepitus** or **pain out of proportion** to cutaneous findings should elicit concern. Hyponatremia may be found but is not always present.

3. Treatment requires **wide excision/debridement** of all nonviable tissue, and **IV antibiotics**. Mortality approximates 50%, and multiple resections may be required in a staged fashion. Definitive wound coverage often eventually requires skin grafting. Fecal diversion is rarely needed.

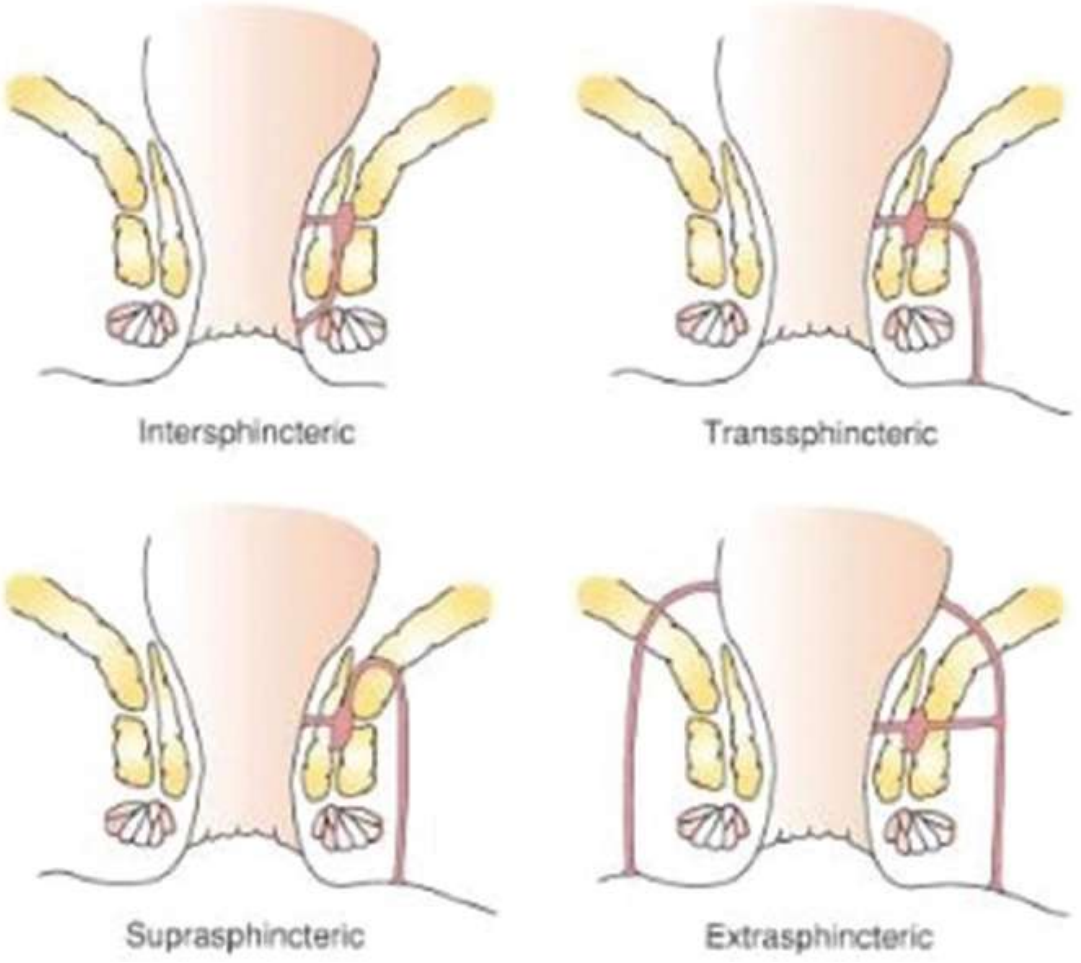


FIGURE 28-3 The four main anatomic types of fistula. (From Mulholland MW, Lillemoe KD, Doherty GM, et al. *Greenfield's Surgery: Scientific Principles and Practice.* 4th ed. New York: Lippincott Williams & Wilkins; 2005, with permission.)

C. Pilonidal Cyst

1. This infection usually occurs in **hair-containing sinus tracts** in the **intergluteal fold**. Patients often present with relapsing episodes of pain, drainage, and cellulitis. It is most common in **males in the second and third decades of life**.
2. Unless severe, these infections do not involve the anus or perianal

tissue. Physical examination is often pathognomonic. Radiographic evaluation is not warranted except in severe cases.

3. **Treatment** involves **incision, drainage, curettage, and marsupialization of the sinus tract(s)**. Care should be taken to treat all tracts and cysts. While secondary closure should be allowed in the setting of active inflammation (with recurrence rates up to 40%), primary closure with a rotation flap can be utilized electively for improved cosmesis and healing (e.g., Bascom or Limberg flaps).

D. Hidradenitis Suppurativa

1. **Apocrine** sweat glands of the groin and perineum serve as the nidus for the development of pustules, sinus tracts, scars, and nodules in this chronic, inflammatory skin disorder. Similar to fistula-in-ano, hidradenitis is characterized by **superficial fistulous tracts external to the anal verge**.
2. Definitive **treatment** involves excision of infected tissue. For more severe cases, chronic suppressive antibiotics may be required.

E. Pruritus Ani

1. "Anal itching" is actually a symptom more than a specific diagnosis. **Multiple etiologies** such as hemorrhoids, fissure, prolapse, rectal polyps, anal warts, and intraepithelial dysplasia commonly produce this symptom.
2. Both **evaluation** and **treatment** depend on the underlying cause. Failure to find an underlying cause should prompt investigation of dietary factors (e.g., coffee, alcohol). Children should be evaluated for **pinworms,** which, if found, are treated with piperazine citrate. However, as the **most common cause is overcleaning,** therapy often includes a high-fiber diet, minimizing wiping, avoiding the use of soaps and alcohol-containing products for cleaning, and barrier creams.

F. Condyloma Acuminatum

1. This **anorectal and urogenital wart** is caused by infection with **human papillomavirus** (**HPV**). The virus is sexually transmitted and presents with visible perianal growth, often accompanied by pruritus, anal discharge, bleeding, and/or pain.
2. Treatment includes both topical and surgical approaches. Importantly, biopsies should be taken liberally to ensure invasive malignancy is

not overlooked. Topical therapies include **trichloroacetic acid and imiquimod**, but not within the anal canal. Surgical excision can typically be achieved under local anesthesia but should be paired with **fulguration** of the wound bed. Of note, HPV can be aerosolized during the fulguration process, so careful attention must be paid to proper ventilation and protective masks.

VI. ANAL NEOPLASIA

A. Tumors of the Anal Margin

1. **Squamous cell carcinoma**–similar to cutaneous squamous carcinoma, this malignancy is well differentiated and keratinizing. Treatment includes **wide local excision** (WLE) or if large, involving the sphincter complex, or concomitant regional lymphadenopathy, chemoradiation as described by the **Nigro protocol for anal cancer** (60-Gy radiation concurrent with 5-FU and mitomycin C).
2. **High-grade squamous intraepithelial lesion III** (**Bowen disease**)—commonly seen in HIV+ or immunosuppressed patients, this precancerous lesion is typically identified with **high-resolution anoscopy with acetic acid** but can be found incidentally on condyloma biopsy. Treatment involves local excision of gross lesions and long-term surveillance for malignant degeneration.
3. **Paget disease** or intraepithelial adenocarcinoma, typically found in elderly patients, is an in situ neoplasm originating in apocrine sweat glands that presents with **pruritic, erythematous rash**. Biopsy proves the diagnosis, and treatment must include colonic evaluation to rule out synchronous malignancy as the source of cancerous tissue. Up to **50% of patients will have a coexisting visceral carcinoma**. WLE is the treatment of choice, though radical resection and colostomy are required for invasive disease.
4. **Basal cell carcinoma** (BCC) is a rare, male-predominant disease similar to cutaneous BCCs and is treated with WLE (see Chapter 32).

B. Anal Canal Tumors

1. **Epidermoid carcinoma**—nonkeratinizing malignancy arising from the columnar epithelium 6 to 12 mm proximal to the dentate line, this cancer usually presents with induration, pain, and bleeding. As up to 40% of these are malignant on presentation, full staging with CT and PET scans is paramount in initial evaluation. Treatment includes

Nigro protocol. Local disease recurrence (after 6 months after treatment) or lack of therapeutic response/persistent disease within 6 months of treatment warrants evaluation for resection (typically abdominoperineal resection, APR), which may require flap reconstruction of the perineum.

2. **Anal adenocarcinoma** can arise from the anal glands, although typically it's an extension of low rectal tumors. APR is standard therapy with or without neoadjuvant chemoradiation, though outcomes are poor regardless; so multidisciplinary approach is warranted.
3. **Melanoma**—accounting for 1% to 3% of anal malignancies, anorectal melanoma is a rare but deadly disease with 5-year survival less than 20%. Often initially diagnosed as a thrombosed hemorrhoid, anorectal melanoma is frequently advanced on presentation. However, for local disease, radical resection and local excision are both reasonable approaches with equivalent poor outcomes.

CHAPTER 28: ANORECTAL DISEASE

Multiple Choice Questions

1. **A 41-year-old woman has prolapsing tissue and bright red blood on the toilet paper after bowel movements. Physical examination reveals two large, pink nonreducible columns of mucosa protruding from her anal canal. Which is the most likely complication following surgical treatment of her anorectal disease?**

   a. Sphincter injury
   b. Bleeding
   c. Infection
   d. Urinary retention
   e. Anal stenosis

2. **A 68-year-old man has perianal mucus and pain. Physical examination reveals a posterior fistula. On examination under anesthesia, you discover the fistula crosses the internal and deep external anal sphincters with a small underlying abscess cavity. Which is the most appropriate treatment at this time?**

   a. Fistulotomy using electrocautery over the entire fistula tract
   b. Division of the internal sphincter using electrocautery and placement of seton encircling the external sphincter
   c. Diverting colostomy
   d. Antibiotics only
   e. Anal advancement flap

3. **A 36-year-old woman presents to clinic complaining of incontinence to soft stool at least once a week. She recently recovered from her fourth vaginal delivery, which was complicated by a third-degree perineal tear. On digital rectal examination, you note little change in tone when the patient attempts to contract her pelvic floor. Which component of the anal sphincter mechanism is most likely dysfunctional?**

a. The internal sphincter
b. The external sphincter
c. The sacral nervous plexus
d. The puborectalis muscle
e. The rectal–anal inhibitory reflex

4. **A 54-year-old woman has anal pain and blood on the toilet tissue after defecation. Physical examination reveals a 2- ë 2-cm ulcer within the anal canal. Biopsy of the ulcer returns as squamous cell carcinoma. Which of the following is the appropriate treatment?**

a. Low anterior resection with diverting ileostomy
b. Abdominoperineal resection
c. Primary chemoradiation therapy
d. Wide local excision, skin grafting, permanent colostomy
e. Wide local excision and primary closure

5. **A 75-year-old man has a perianal pruritic, erythematous rash. Biopsy reveals Paget disease. Which of the following is correct regarding Paget disease?**

a. Regardless of level of invasion, all patients require abdominoperineal resection.
b. Since Paget disease is an intraepithelial neoplasm, patients do not require colonoscopy.
c. Extramammary Paget disease is most common in 20- to 30-year-old women.
d. Fulguration with laser or electrocautery is the most effective treatment.
e. Wide local excision is the most appropriate treatment in noninvasive disease.

6. **A 26-year-old man has severe anal pain during and after bowel movements for the past 6 weeks. Physical examination reveals a split in the anoderm in the posterior midline with a skin tag just inferior to the wound. Which of the following is correct regarding this condition?**

a. Lateral sphincterotomy is associated with poor rates of resolution.
b. Fissurectomy is the mainstay of treatment.
c. Ninety percent of patients heal with medical treatment, including fiber, sitz baths, and topical nifedipine ointment.
d. An equal number of fissures occur posteriorly as anteriorly.
e. The anal fissure triad consists of internal hemorrhoid, sentinel skin tag, and fissure.

29 Hernias

Wen Hui Tan and Jeffrey A. Blatnik

I. INGUINAL HERNIA

A. Incidence. Inguinal hernia formation is a by-product of genetic and environmental factors, combined with individual patient factors such as immune status, comorbidities such as chronic obstructive pulmonary disease and thoracic or abdominal aortic aneurysm, personal habits (e.g., smoking), and changes in body mass index (*Surg Clin North Am.* 2008;88:179–201). Laparoscopic studies have reported rates of contralateral defects as high as 22%, with 28% of these going on to become symptomatic during short-term follow-up. The reported prevalence of inguinal hernias varies widely in the literature, and the true incidence of inguinal hernias is unknown. Instead, hernia repair statistics are used as a surrogate. The lifetime prevalence is estimated to be 25% in men and 2% in women. Inguinal hernias tend to be diagnosed at the extremes of age, and the male-to-female ratio is greater than 10:1. Two-thirds of inguinal hernias are indirect whereas nearly two-thirds of recurrent hernias are direct, especially after open repair. Inguinal hernias are more common on the right side than on the left (*N Engl J Med.* 2015;372:756–763). Approximately 10% of inguinal hernias will become incarcerated, and a portion of these may become strangulated. Recurrence rates after surgical repair are less than 1% in children and vary in adults depending on the method of repair.

B. Terminology and Anatomy

1. **The inguinal canal** (Fig. 29-1) is a tunnel that traverses the layers of the abdominal wall musculature, bounded on the lateral deep aspect by an opening in the transversalis fascia/transversus abdominis muscle (**internal inguinal ring**), and travels along the fused edges of the transversus abdominis/internal oblique/inguinal ligament and

iliopubic tract posteriorly and layers of the external oblique musculature anteriorly, ending on the medial superficial aspect at an opening in the external oblique aponeurosis (**external inguinal ring**). The inguinal canal houses the spermatic cord (males) or the round ligament (females) and is subject to hernia formation primarily due to decreased mechanical integrity of the internal ring and/or transversalis fascia, allowing intra-abdominal contents to encroach into this space and form the characteristic bulge of a groin hernia.

2. **Direct hernias** occur as a result of weakness in the posterior wall of the inguinal canal, which is usually a result of attenuation of the transversalis fascia. The hernia sac protrudes through **Hesselbach triangle**, which is the **space bounded by the inferior epigastric artery, the lateral edge of the rectus sheath, and the inguinal ligament**.

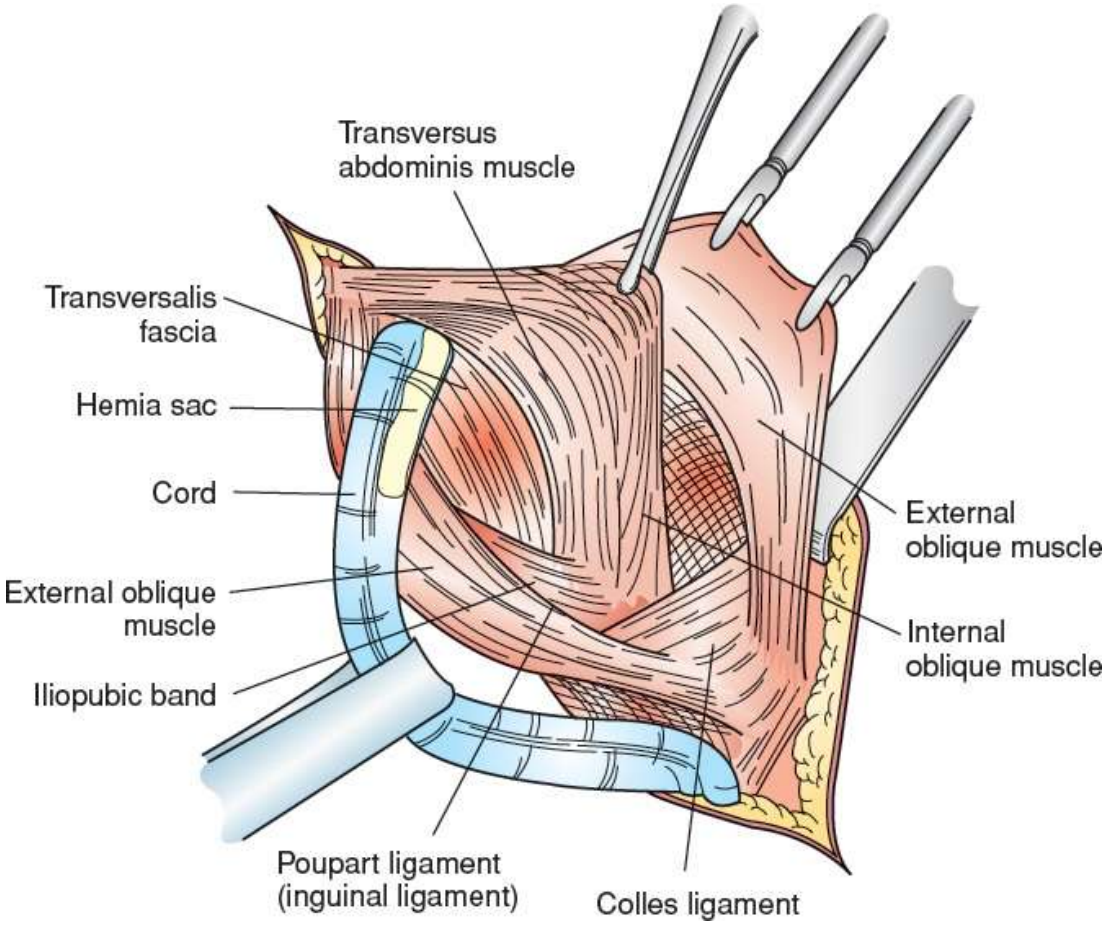


FIGURE 29-1 Inguinal hernia anatomy.

3. **Indirect hernias** pass through the internal inguinal ring lateral to the inferior epigastric vessels and Hesselbach triangle and follow the spermatic cord in males and the round ligament in females. During dissection, an indirect hernia sac is typically found on the anteromedial aspect of the spermatic cord. Indirect hernias may become incarcerated at either the internal or external ring. Indirect hernias are the **most common types of groin hernia** in both men and women.
4. **In combined** (**pantaloon**) **hernias**, direct and indirect hernias coexist and abdominal contents can protrude through both/either opening.
5. **Variants of inguinal hernias**
   a. **Sliding hernia:** (Usually indirect inguinal) denotes that a part of the wall of the hernia sac is formed by an intra-abdominal viscus (usually colon, sometimes bladder).
   b. **Richter hernia:** A portion of (rather than the entire circumference) of the bowel wall is incarcerated.
   c. **Littré hernia:** Contains a **Meckel diverticulum** (see also Chapter 20).
   d. **Amyand hernia:** An inguinal hernia that contains the **appendix**.
6. **Incarcerated inguinal hernias** cannot be reduced into the abdominal cavity and may or may not be symptomatic. **Strangulated** hernias are incarcerated with vascular compromise of the herniated contents and warrant urgent surgical evaluation. Frequently, intense pain is caused by ischemia of the incarcerated segment.

C. Diagnosis

1. **Clinical presentation**
   a. **Most inguinal hernias** present as an intermittent bulge that appears in the groin. In males, it may extend into the scrotal sac. Symptoms are usually related to exertion or long periods of standing. The patient may complain of unilateral discomfort without noting a mass. Often, a purposeful Valsalva maneuver can reproduce the symptoms and/or the presence of a bulge. In infants and children, a groin bulge is often noticed by caregivers during episodes of crying or defecation. Only in rare cases do patients present with bowel obstruction without the presence of a groin abnormality. All patients presenting with small-bowel obstruction

(SBO) must be questioned carefully and examined for all types of hernia (e.g., inguinal, umbilical, incisional, obturator, etc.) as a possible etiology of obstruction.

b. Physical examination. The main diagnostic maneuver for inguinal hernias is **palpation of the inguinal region**. The patient is best examined while standing and straining (cough or Valsalva). Hernias manifest as bulges with smooth, rounded surfaces that become more evident with straining. It may be necessary to invaginate the hemiscrotum to introduce an index finger through the external inguinal ring if the hernia is not apparent, but this maneuver is often uncomfortable for the patient and is unnecessary if an obvious bulge is present. It is difficult to determine whether the hernia is direct or indirect based solely on physical examination, although most hernias that extend into the scrotum are indirect. Incarcerated inguinal hernias present with pain, abdominal distention, nausea, and vomiting due to intestinal obstruction. Strangulated hernias will present with severe pain and possible skin changes over the surface of the hernia.

2. **Radiographic evaluation.** X-ray studies are rarely indicated. Ultrasonography (US) or computed tomographic (CT) scan may occasionally be used to diagnose an occult groin hernia, particularly in the obese patient. US is the preferred first-line imaging as it can be performed with the patient straining and without radiation exposure.

D. Differential Diagnosis. Inguinal hernias should be distinguished from femoral hernias, which protrude below the inguinal ligament. Inguinal adenopathy (e.g., inguinal bubo from lymphogranuloma venereum and chancroid), lipomas, hydrocele, epididymitis, testicular torsion, groin abscess, and vascular aneurysms/pseudoaneurysms all should be considered in the differential diagnosis. Typically, if the bulge appreciated on exam can be reduced, this is a good indication of a hernia.

E. Treatment

1. **Preoperative evaluation and preparation.** Most patients with inguinal hernias should be treated surgically, although watchful waiting may be appropriate for individuals with asymptomatic hernias or for elderly patients with minimally symptomatic hernias as the risk for acute incarceration or strangulation is very low (*J Am*

Coll Surg. 2006;203:458–468). When followed for 7 to 10 years, approximately 70% of male patients who elect for inguinal hernia observation will undergo operative repair, with the likelihood of undergoing repair being higher for men older than 65 years when compared to younger men, and the most common indication for operation was pain rather than acute strangulation (*Ann Surg*. 2013;258(3):508–515; *Br J Surg*. 2011;98:596–599). Therefore, surgical repair should be considered in patients with asymptomatic or minimally symptomatic inguinal hernia if they are an appropriate surgical candidate. Associated conditions that lead to increased intra-abdominal pressure such as chronic cough, constipation, or bladder outlet obstruction should be evaluated and remedied to the extent possible before elective herniorrhaphy. In incarcerated hernias with intestinal obstruction and possible strangulation, broad-spectrum antibiotics should be given and nasogastric decompression may be necessary. Correction of volume status and electrolyte abnormalities is also important when there is associated SBO.

2. **Reduction.** In uncomplicated cases, the hernia should reduce with palpation over the inguinal canal while the patient is supine. If this does not occur, the physician should apply gentle pressure over the hernia with the concavity of the palm of his/her hand and fingers and exert a steady but gentle pressure as follows: cranial and lateral for direct and indirect hernias, cranial and posterior for femoral hernias. If this is not successful, gentle traction over the mass with compression may allow bowel gas to leave the herniated segment, making the mass reducible. Sedation and Trendelenburg position may be required for reduction of an incarcerated hernia, but it may be difficult to distinguish between acute incarceration and strangulation, as the inguinal canal can become quite tender with or without ischemic contents. When an incarcerated hernia is reduced nonsurgically, the patient should be observed for the potential development of peritonitis caused by perforation or ischemic necrosis of a loop of strangulated bowel. Strong suspicion of strangulation (e.g., erythema over hernia site, pain out of proportion to examination) is a surgical emergency and should be evaluated even if the bowel contents are able to be reduced.

3. **Surgical treatment** (**Fig. 29-2**)

a. Choice of anesthetic. Local anesthesia with sedation and monitored anesthesia care (MAC), which has several advantages over general or regional (spinal or epidural) anesthesia, is the preferred anesthetic for elective open repair of small- to moderate-sized hernias. This approach results in better postoperative analgesia, a shorter recovery room stay, and a negligible rate of postoperative urinary retention. It is also the lowest-risk anesthetic for patients with underlying cardiopulmonary disorders. Commonly, a mixture of a short-acting agent (lidocaine 1%) and longer-acting agent (bupivacaine 0.25% to 0.50%) is used. Virtually all patients who undergo hernia repair under local anesthesia can be managed as outpatients unless associated medical conditions or extenuating social circumstances necessitate overnight observation in the hospital. In contrast, laparoscopic inguinal hernia repair is performed under general anesthesia to facilitate tolerance of pneumoperitoneum.

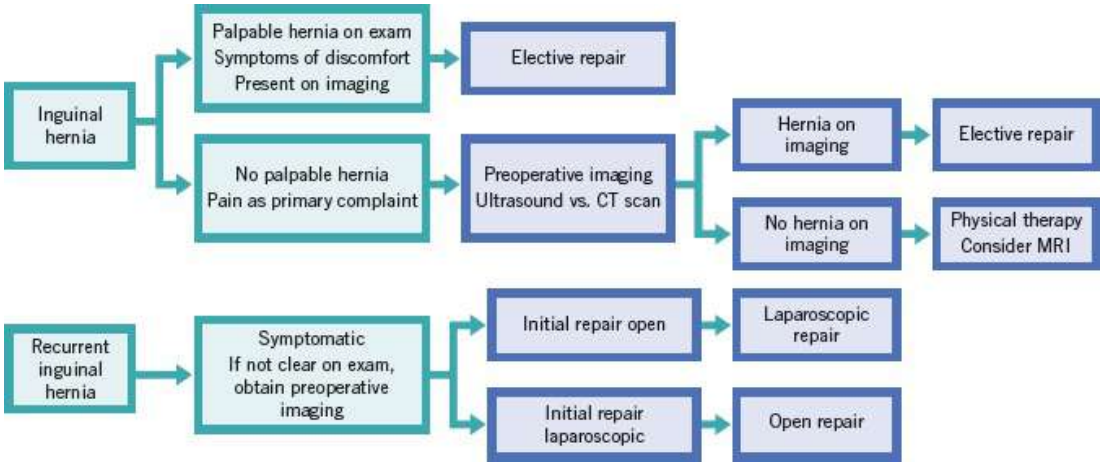


FIGURE 29-2 Considerations for inguinal hernia repair.

b. Treatment of the hernia sac. For indirect hernias, the sac (peritonealized abdominal contents) is dissected from the spermatic cord and cremasteric fibers (Fig. 29-1). The sac can either be ligated deep into the internal ring with an absorbable suture after reduction of herniated contents or invaginated back into the abdomen without ligation. The latter approach is thought to be associated with less postoperative pain because it avoids transection of innervated peritoneum (*Hernia*. 2014;18(2):199–

204). Care should be taken when dissecting large, indirect sacs that extend into the scrotum due to an increased risk of ischemic orchitis from vascular injury. Similarly, the testicle should not be translocated into the inguinal canal during hernia repair owing to the risk of ischemia or torsion. Cord lipomas are frequently encountered during repair and should be excised or reduced into the preperitoneal space to avoid future confusion with a recurrent hernia. Sliding hernia sacs can usually be managed by reducing the sac and attached viscera without sac ligation. Direct sacs are usually too broadly based for ligation and do not need to be opened. The redundant attenuated tissue is inverted and if the defect is small, it may be closed with a few interrupted sutures to facilitate placement of mesh.

c. Primary tissue repairs without mesh were the mainstay of hernia surgery prior to the development of synthetic-mesh approaches. While primary repair avoids placement of foreign prosthetic material, disadvantages of this approach include **higher recurrence rates** (5% to 10% for primary repairs and 15% to 30% for repair of recurrent hernias) due to tension on the repair and a slower return to unrestricted physical activity. Although the vast majority of hernias are now treated with a tension-free mesh repair, a primary tissue repair can be considered in contaminated wounds (e.g., if strangulated bowel is resected), as placement of synthetic material would be contraindicated. The principal features of the more commonly performed tissue repairs are as follows:

(1) Shouldice repair. In this repair, the pelvic floor is opened widely. The transversalis fascia is opened transversely from the internal ring towards the pubic tubercle (and partially excised if weakened). Retroperitoneal tissue, including fat, hernia sac, and peritoneum, is dissected off the posterior wall of the pelvic floor and the cremasteric muscle is resected. The Shouldice repair utilizes four imbricated layers of running nonabsorbable suture to reapproximate a superior flap of the pelvic floor (containing the transversus abdominis and internal oblique) to an inferior flap (containing the transversalis fascia edge, shelving edge of the inguinal ligament, and external oblique

aponeurosis). Closing the defect in multiple layers is thought to ensure that no one layer is under significant tension. The experience of the Shouldice Clinic (Thornhill, ON, Canada) with this repair has been excellent, with recurrence rates of less than 1%, but higher recurrence rates have been reported in nonspecialized centers.

(2) Bassini repair. The inferior arch of the transversalis fascia or conjoint tendon is approximated to the shelving portion of the inguinal ligament (iliopubic tract) with interrupted, nonabsorbable sutures. The Bassini repair is similar to the Shouldice repair, but utilizes only one layer of sutures. The Bassini repair has been used primarily for indirect hernias, including inguinal hernias in women.

(3) McVay repair. The transversalis fascia is sutured to Cooper ligament medial to the femoral vein and is then transitioned to the inguinal ligament at the level of, and lateral to, the femoral vein. This operation requires placement of a **relaxing incision** medially on the aponeuroses of the internal oblique muscle to avoid undue tension on the repair. Historically, this approach was used more commonly for direct hernias. The McVay repair closes the femoral space and therefore, unlike the Bassini repair, is **also effective for femoral hernias**.

d. Open tension-free repairs. The most common mesh inguinal hernia repairs performed today are the tension-free mesh hernioplasty (**Lichtenstein repair**) and the **patch-and-plug** technique.

(1) In the **Lichtenstein repair**, a piece of polypropylene mesh measuring approximately 6 × 3 in is used to reconstruct the inguinal floor (Fig. 29-3). The mesh is sutured to the transversalis fascia and conjoint tendon medially and to the inguinal ligament laterally. The mesh is slit at the level of the internal ring, and the two limbs are crossed around the spermatic cord and then tacked to the inguinal ligament, effectively creating a new internal ring. This repair avoids the approximation of attenuated tissues under tension, and recurrence rates with this technique have been consistently 1% or less. Moreover, because the repair is without tension,

patients are allowed to return to unrestricted physical activity in 2 weeks or fewer.

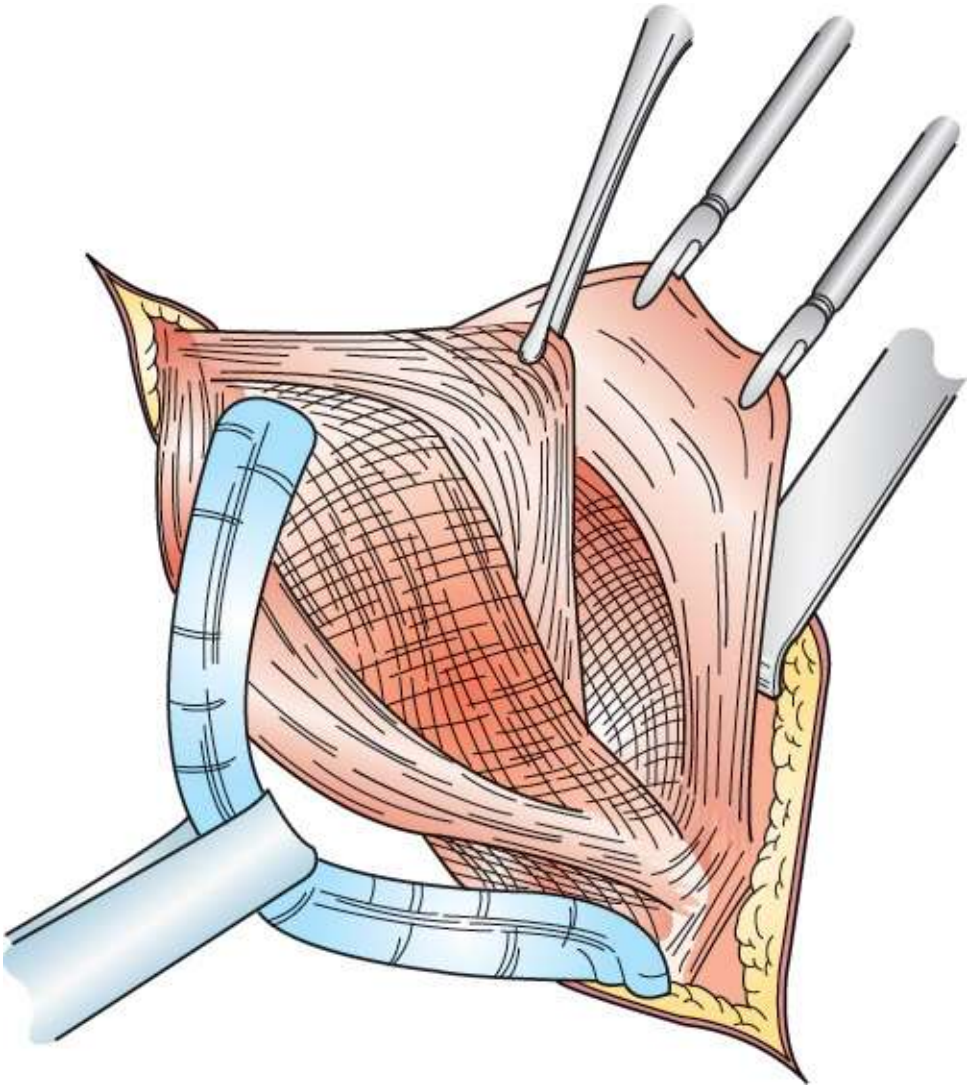


FIGURE 29-3 Lichtenstein tension-free hernia repair.

(2) The **mesh plug** technique entails placement of a preformed plug of mesh in the hernia defect (e.g., internal ring) that is then sutured to the rings of the fascial opening. An onlay piece of mesh is then placed over the inguinal floor, which may or may not be sutured to the fascia. Mesh plugs may be ideally suited for the repair of small, tight defects such as femoral hernias. The Prolene hernia system is another technique that involves the use of a bilayer mesh in which the posterior leaflet

is placed in the preperitoneal space and the anterior leaflet is sutured to the same layers as that in the Lichtenstein repair. Note that it is important to make an attempt to identify the **ilioinguinal nerve**, but it should not be skeletonized or exteriorized behind the external oblique aponeurosis as was done historically because of the risk of exposing the nerve to fibrosis around the mesh that could result in neuropathic groin pain. If, despite this, the nerve will potentially be exposed directly to the mesh, it may be preferable to resect it for 3 to 4 cm proximal to the internal ring and to allow the proximal end to retract into the muscle to minimize subsequent neuroma formation. Plug style repair has fallen out of fashion due to potential complications attributed to the plug such as migration and pain.

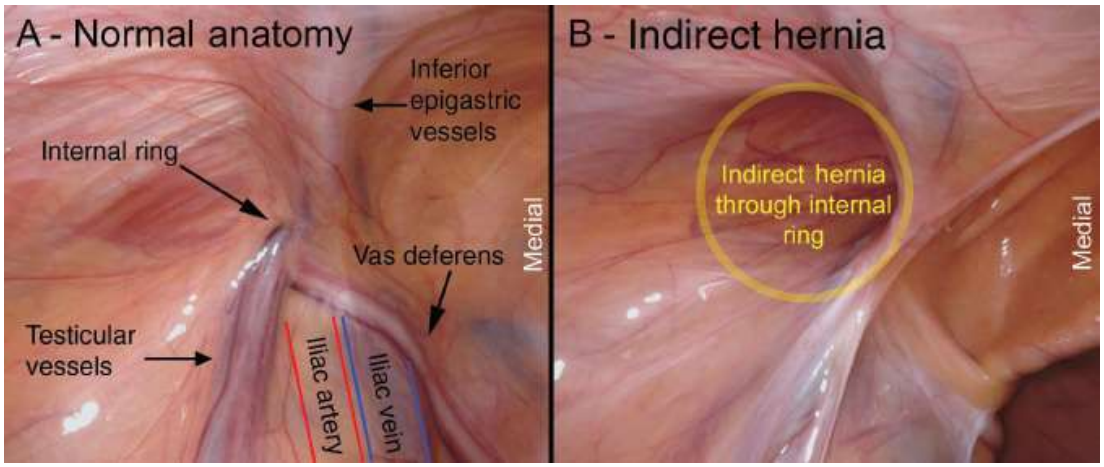


FIGURE 29-4 **A:** Laparoscopic view of normal inguinal anatomy (patient left). **B:** Laparoscopic view of indirect inguinal hernia.

e. Laparoscopic inguinal hernia repair. (Fig. 29-4) Laparoscopic hernia repair is typically advocated in the elective setting, but with increased experience its use has been introduced for the incarcerated and strangulated patient as it facilitates evaluation of the incarcerated contents. Contraindications to the laparoscopic approach include inability to tolerate general anesthesia and/or pneumoperitoneum or the presence of a hernia with a significant scrotal component as it is more difficult to reduce laparoscopically. The laparoscopic approach is also relatively

contraindicated in the patient who has previously undergone prostatectomy or other lower midline abdominal surgery due to scarring in the preperitoneal space. There are two approaches to laparoscopic repair of inguinal hernias:

(1) Transabdominal preperitoneal (**TAPP**) **repair.** In the TAPP technique, the peritoneal space is entered by conventional means at the umbilicus, the peritoneum overlying the inguinal floor is dissected away as a flap, the hernia is reduced, mesh is fixed over the internal ring opening in the preperitoneal space, and the peritoneum is reapproximated. The advantages of the TAPP approach are that a large working space is retained, familiar anatomic landmarks are visible, and the contralateral groin can be examined for an occult hernia.

(2) Totally extraperitoneal repair (**TEP**)**.** In the TEP technique, the preperitoneal space is developed with either a dissecting balloon inserted between the posterior rectus sheath and the rectus abdominis and directed toward the pelvis inferior to the arcuate ligament (Fig. 29-5) or can also be performed bluntly with the tip of the camera. The other ports are inserted into this preperitoneal space without entering the peritoneal cavity. The advantages of the TEP repair are that the peritoneum is not opened and, therefore, does not need to be closed and the operation is also typically faster to perform. Disadvantages include a smaller working space, and potentially more challenging exposure.

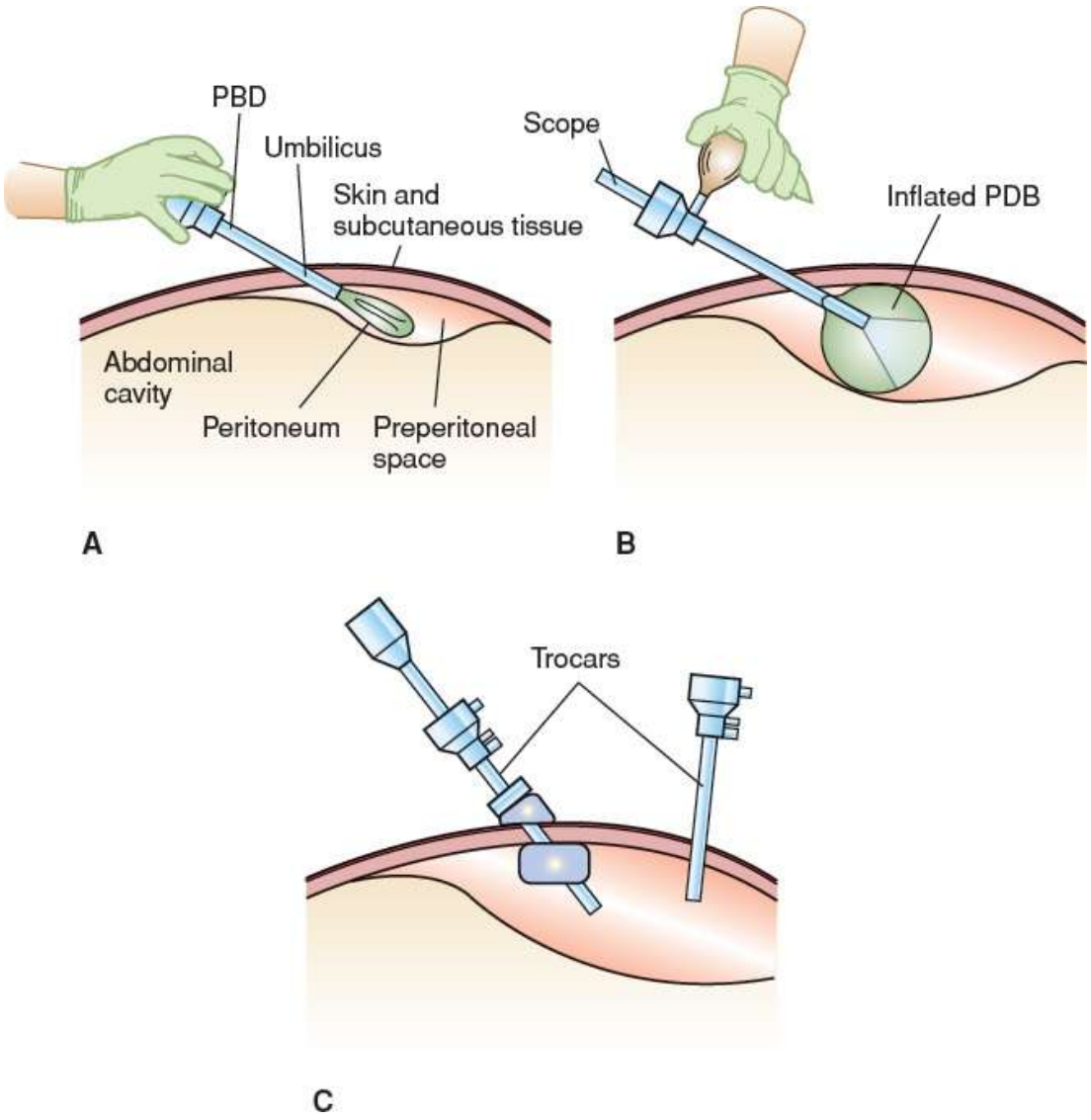


FIGURE 29-5 Laparoscopic total extraperitoneal approach with preperitoneal balloon dilation (PBD).

(3) Technique and outcomes. In either the TAPP or TEP technique, a large piece of mesh (6 × 4 in) is placed over the inguinal floor. Methods of fixation vary by surgeon preference and mesh choice, but traditionally fixation is performed (1) superiorly to the posterior abdominal wall fascia on either side of the inferior epigastric vessels, (2) inferiorly at the Cooper ligament, (3) medially to the midline fascia, and (4) superolaterally to the fascia above the internal ring. Staples/tacks must not be placed inferomedial to the internal ring or inferior to the iliopubic tract because of the risk of

injury to the external iliac vessels (“**triangle of doom”**) and ilioinguinal, genitofemoral, lateral femoral cutaneous, and femoral nerves (“**triangle of pain”**). Studies comparing laparoscopic and open approaches to inguinal hernia repair have shown that laparoscopic repair is associated with less postoperative pain and faster recovery than open repair. Operative times, complications, and recurrence rates (<3% for both laparoscopic and open repairs) have been similar. One persistent criticism of the laparoscopic approaches is an increased cost when compared to open inguinal hernia repairs. A NSQIP study of 5,468 inguinal hernia repairs (4,693 open and 775 laparoscopic) found that length of stay and perioperative outcomes were superior in the laparoscopic group; however, the mean laparoscopic inguinal hernia repair cost was $5,105 compared to $4,360. This discrepancy was mainly due to supply costs. However, as more hospitals implement cost-containment measures and surgeon experience increases, the equipment costs of laparoscopic hernia repair will likely decrease and length of stay may become a major factor in the patients’ overall cost (*Hernia*. 2016;20(3):399–404). Special circumstances in which laparoscopic repair may also be favored include: (1) recurrent hernias, (2) bilateral hernias, because both sides of the groin can be repaired with the same incisions, (3) in individuals with a unilateral hernia for whom a rapid recovery is critical (e.g., athletes and laborers), and (4) in obese patients.

f. Robotic inguinal hernia repair: In the past decade, robotic surgery has become increasingly popular. Benefits of robotic surgery include better visualization, improved ergonomics, and more degrees of freedom than traditional laparoscopic instrumentation. There are few studies that directly compare robotic inguinal hernia repair to traditional laparoscopy or open inguinal hernia repair. Initial criticisms of utilizing the robot in inguinal hernia repair include increased cost and operative time. However, more recent studies have found a rapid reduction in operative time as surgeons surmount the initial learning curve such that operative times are similar to times required to perform laparoscopic inguinal hernia

repair (*Surg Endo*. 2018;32(12):4850–4859). Direct (variable) costs may be comparable between the two, but that does not include capital costs of the robotic system itself or laparoscopic towers (*J Robot Surg*. 2016;10(3):239–244). Transition from open to minimally invasive approaches is one of the greatest strengths of robotic surgery for hernia repair.

(1) Complications. Surgical complications include hematoma, infection, nerve injury (ilioinguinal, iliohypogastric, genital branch of the genitofemoral, lateral femoral cutaneous, femoral), vascular injury (femoral vessels, testicular artery, pampiniform venous plexus), vas deferens injury, ischemic orchitis, and testicular atrophy. **Recurrence rates** after tension-free mesh repairs for primary hernias are **less than 2%**. As mesh-based repairs have resulted in a decreased recurrence rate, chronic pain has emerged as one of the more prominent postoperative complications. Management of postoperative pain requires a multidisciplinary team and evaluation for recurrent hernia.

(2) Recurrent inguinal hernias are more difficult to repair because scarring makes dissection difficult and because the hernia-producing disease process has continued to progress. Early recurrences within a few weeks or months of the initial repair suggest an inadequate initial repair and may reflect failure to identify an indirect hernia sac, whereas recurrence after 1 or more years suggests progression of the disease process that caused the initial hernia (e.g., increased intra-abdominal pressure, degeneration of tissues). Recurrences should generally be repaired because the defect usually is small with fixed edges that are prone to complications such as incarceration or strangulation. Most surgeons advocate utilizing the alternate approach to the initial repair for management of recurrent hernias.

g. Choice of prosthetic mesh in inguinal hernia repairs. The choice of mesh for inguinal hernia repair is expanding rapidly as manufacturers compete to produce the ideal prosthetic material. The ideal material provides a combination of adequate strength to prevent recurrence and flexibility to minimize chronic

postoperative pain and/or the sensation of a foreign body. Examples of the three basic classes of synthetic meshes available to surgeons for use in inguinal hernia repair are summarized in Table 29-1, however, this is not an exhaustive list. Randomized clinical trials demonstrate that the use of lightweight polypropylene meshes for Lichtenstein hernia repair does not increase recurrence rates and is associated with less postoperative pain and discomfort (*Hernia*. 2010;14:253–258). These results support the use of lightweight mesh materials in open inguinal hernia repair. In comparison, recent randomized data looking at lightweight mesh versus heavyweight mesh in laparoscopic repair has shown that heavyweight mesh may be favorable due to decreased pain and recurrence (*Ann Surg*. 2018;268(2):241–246).

TABLE 29-1 Weight Classes of Examples of Mesh Used in Inguinal Hernia Repair

	Marlex[a] (Heavyweight)	Prolene Soft[b] (Midweight)	Ultrapro[b] (Lightweight)
Material	Polypropylene	Polypropylene	Polypropylene, poliglecaprone
Weight (g/m^2)	95	45	28
Pore size (mm)	0.6	2.4	4
Burst strength (newtons)	1,218	590	576
Stiffness (newtons/cm)	59.1	49.1	43.2

[a]Davol, Inc., Cranston, RI.

[b]Ethicon, Inc., Somerville, NJ.

Adapted from Cobb WS, Burns JM, Peindl RD, et al. Textile analysis of heavy weight, mid-weight, and light weight polypropylene mesh in a porcine ventral hernia model. *J Surg Res*. 2006;136(1):1–7.

II. FEMORAL HERNIAS

A. Incidence. Femoral hernias constitute between 2% and 4% of all groin hernias, with >90% occurring in women. Approximately 25% of femoral hernias become incarcerated or strangulated, and a similar number are missed or diagnosed late.

B. Anatomy. The abdominal viscera and peritoneum protrude through the femoral canal into the upper thigh. The boundaries of the femoral canal are the lacunar ligament medially, the femoral vein laterally, the iliopubic tract anteriorly, and Cooper ligament posteriorly. It is thought that the presence of more rigid boundaries is a contributing factor to a higher rate of incarceration and strangulation in comparison with direct and indirect inguinal hernias.

C. Diagnosis

1. Clinical presentation

a. Symptoms. Patients may complain of an intermittent groin bulge or a groin mass that may be tender and typically is reported below the inguinal ligament. Femoral hernias have a high incidence of incarceration and SBO may be the presenting feature in some patients. Elderly patients, in whom femoral hernias occur most commonly, may not complain of groin pain even in the setting of incarceration. Therefore, an occult femoral hernia should be considered in the differential diagnosis of any patient with SBO, especially if there is no history of previous abdominal surgery.

b. Physical examination. The characteristic finding is a small, rounded bulge that appears in the upper thigh just below the inguinal ligament. An incarcerated femoral hernia usually presents as a firm, tender mass. The differential diagnosis is the same as that for inguinal hernia.

c. Radiographic evaluation. Radiographic studies are rarely indicated. Occasionally, a femoral hernia is found on a CT scan performed to evaluate an SBO.

D. Treatment. The surgical approach can be inguinal, preperitoneal, or femoral.

1. Inguinal approach. A **Cooper ligament repair** (**McVay**) using the inguinal canal approach allows reduction of the hernia sac with visualization from above the inguinal ligament and closure of the

femoral space. Occasionally, it may be necessary to divide the inguinal ligament to reduce the hernia. The repair can be performed with or without mesh.

2. **Preperitoneal approach.** A transverse suprainguinal incision permits access to the extraperitoneal **spaces of Bogros and Retzius**. The hernia is reduced from inside the femoral space, and the hernia defect is repaired preperitoneally, usually with mesh, but can be repaired primarily. This approach is especially useful for incarcerated or strangulated femoral hernias. Uncomplicated femoral hernias can also be repaired laparoscopically with traditional TAPP or TEP approaches.
3. **Femoral approach.** A horizontal incision is made over the hernia, inferior and parallel to the inguinal ligament. After the hernia sac is dissected free, it can be resected or invaginated. The femoral canal is closed by placing interrupted stitches to approximate Cooper ligament to the inguinal ligament or by using a plug of prosthetic material.
4. **Complications.** Complications are similar to those for inguinal hernia repair. The femoral vein may be especially susceptible to injury because it forms the lateral border of the femoral canal.

III. INTERNAL HERNIA

A. Incidence. Of patients who present with acute intestinal obstruction, less than 5% have an internal hernia. When internal hernias are complicated by intestinal volvulus, there is an 80% incidence of strangulation or gangrene.

B. Etiology. Internal hernias occur within the abdominal cavity owing to congenital or acquired causes. Congenital causes include abnormal intestinal rotation (paraduodenal hernias) and openings in the ileocecal mesentery (transmesenteric hernias). Other, less frequent types are pericecal hernias, hernias through the sigmoid mesocolon, and hernias through defects in the transverse mesocolon, gastrocolic ligament, gastrohepatic ligament, or greater omentum. Acquired causes include hernias through mesenteric defects created by bowel resections or ostomy formation. Internal hernia is also a common cause of SBO after laparoscopic Roux-en-Y gastric bypass surgery, as the small bowel can herniate through a residual mesenteric defect. Adhesive bands from

prior operations may also cause or contribute to mechanical obstruction.

C. Diagnosis

1. **Clinical presentation.** These hernias usually are diagnosed because an intestinal segment becomes incarcerated within the internal defect, resulting in SBO. Patients with congenital causes usually have not had prior abdominal surgery. The reported mortality in acute intestinal obstruction secondary to internal hernias is 10% to 16%. Symptoms are usually intestinal obstruction without evidence of an external hernia. When there is intestinal obstruction or intestinal strangulation, the diagnosis is based on clinical rather than on laboratory findings.
2. **Radiographic studies.** Plain abdominal films may show dilated loops of bowel and air–fluid levels as is common with SBO. An abdominal/pelvic CT scan is usually necessary to establish the diagnosis of an internal hernia preoperatively. A radiographic swirling of the mesentery is frequently seen on the scan.

D. Differential diagnosis includes other causes of intestinal obstruction, such as adhesions, external hernia, malignancy, gallstone ileus, and intussusception.

E. Surgical Treatment. The diagnosis of internal hernia is often made at laparoscopy or laparotomy for SBO. Intestinal loops proximal to the obstruction are dilated and edematous and collapsed and normal-appearing distal to it. Once the hernia is reduced, intestinal viability is assessed and nonviable intestine is resected. If a large percentage of bowel is of questionable viability, a limited bowel resection followed by a second-look laparotomy in 24 to 48 hours may preserve small bowel length. The hernia defect should be closed primarily with nonabsorbable suture to minimize the risk for recurrent herniation.

IV. ABDOMINAL WALL HERNIA

A. Incidence and Etiology

1. **Incisional hernias** occur at sites of previous incisions where there was division of abdominal wall fascia. Contributing risk factors include obesity, diabetes mellitus, prior wound infection, malnutrition, smoking, and technical errors in wound closure. Hernias occur in up to 20% to 30% of patients undergoing abdominal operations and are most commonly seen with midline incisions. Most

incisional hernias are now repaired with a mesh prosthetic via open or laparoscopic or robotic approach.

2. **Umbilical hernias** are congenital defects that may enlarge over time and become protuberant and symptomatic. Most newborn umbilical hernias close spontaneously by the second year of life. However, umbilical hernias are also common in adults, especially in the setting of obesity, prior pregnancy, or in patients with ascites. Small umbilical hernias can be present for years without causing symptoms and may even go unnoticed. Over time, however, these hernias can enlarge and become incarcerated, usually with preperitoneal fat or omentum. Small umbilical hernias can be closed primarily, but umbilical hernias greater than 2 cm should be repaired with a prosthetic mesh to reduce the risk for recurrence.
3. **Epigastric hernias** are hernias of the linea alba above the umbilicus. They occur more frequently in athletically active young men or women. When small or in obese individuals, epigastric hernias may be hard to palpate and difficult to diagnose. Usually, they produce epigastric pain that may be falsely attributed to other abdominal diagnoses. The diagnosis is made by palpation of a subcutaneous epigastric mass. Most epigastric hernias occur within a few centimeters of the umbilicus and are associated with a small (1 to 2 cm) fascial defect and are filled with preperitoneal fat.
4. **Spigelian hernias** protrude through the Spigelian fascia, near the termination of the transversus abdominis muscle along the lateral edge of the rectus abdominis near the junction of the linea semilunaris and linea semicircularis. Because the herniated visceral contents are intraparietal (between the abdominal wall muscles), these hernias can be difficult to diagnose and, therefore, are included in the differential diagnosis of obscure abdominal pain. US or CT scan can be useful confirmatory tools in patients with focal symptoms in the appropriate region. However, it is possible to miss a Spigelian hernia on CT scan as the patient is traditionally supine and abdominal contents have reduced. Laparoscopy can be utilized when there is a high level of suspicion.
5. The most common type of **lumbar hernia** is an incisional hernia from a previous retroperitoneal or flank incision. They can also be seen spontaneously after blunt abdominal trauma. Lumbar hernias

may also occur in two different triangles: The **Petit (inferior lumbar) triangle** and the **Grynfeltt–Lesshaft** (**superior lumbar**) **triangle**, although these hernias are quite rare. Petit hernias are located in an area limited posteriorly by the latissimus dorsi, anteriorly by the external oblique muscle, and inferiorly by the iliac crest; the floor is formed by the internal abdominal oblique muscle. **Grynfeltt–Lesshaft hernias** are bordered superiorly by the 12th rib, medially by the quadratus lumborum muscle, and laterally by the internal abdominal oblique muscle, while the floor and roof of the triangle are formed by the transversalis fascia and the external abdominal oblique muscle, respectively.

6. **Obturator hernias** are very rare hernias that occur predominantly in thin, older women and are difficult to diagnose. Patients classically present with bowel obstruction and focal tenderness on rectal examination. Pain along the medial aspect of the thigh with internal rotation of the thigh, known as the **Howship–Romberg sign**, results from **obturator nerve compression** and, when present, may aid in the clinical diagnosis.

B. Treatment and Operative Management. Small (<2 cm) epigastric, umbilical, obturator, and Spigelian hernias may be repaired primarily. Most incisional hernias as well as lumbar and obturator hernias require the use of a prosthetic mesh because of their size and high recurrence rates after primary repair. There are numerous factors to consider during repair (Table 29-2).

1. **Prosthetic mesh in abdominal wall hernia repairs.** The recurrence rate for ventral incisional hernia repair is 31% to 54% when primarily repaired. Long-term follow-up of a randomized controlled trial showed that the use of mesh results in a lower recurrence rate and less abdominal pain and does not result in more complications than primary repair (*Hernia*. 2006;10:236–242). The choice of mesh for incisional hernia repair should be based on location, mesh properties, and handling characteristics. Broadly speaking, there are dozens of commercially available meshes with varying base materials, barrier materials, pore sizes, and mechanical properties. In general, **uncoated polypropylene mesh** should not be placed in an intraperitoneal position because it can form dense adhesions to the intestine and precipitate fistulization. For intraperitoneal placement,

either microporous polytetrafluoroethylene (PTFE) mesh or a barrier-coated mesh should be used. **Microporous PTFE mesh** has a microporous architecture and hydrophobicity that prevent cellular penetration of intestine or abdominal viscera and may reduce the density of intraperitoneal adhesions. There are also several absorbable **barrier-coated meshes** with a polypropylene or polyester construction. Different types of mesh are summarized in Table 29-3. Currently, there are limited data to support the use of one product over another. What is clear, however, is that the use of mesh is superior to primary repair for incisional hernias.

TABLE 29-2 Factors for Consideration in Ventral and Incisional Hernia Repair

Patient Factors	Hernia Factors	Imaging
Age	Size of hernia	Defect size
BMI	Location of hernia	Single hole vs. Swiss cheese defect
Diabetes	Previous repairs	Amount of bowel in hernia
Smoking	Loss of domain	Quality of surrounding muscle
Symptoms (obstruction, pain)		Evidence of previous repairs (tacks, old mesh)
Overlying skin		
Surgical history		
Abdominal wall compliance		

2. Open repairs. The principles for ventral hernia repair include

dissection and identification of all defects and repair with nonabsorbable sutures placed in healthy tissue. Incisional hernias should be repaired with mesh prosthesis that should be anchored by nonabsorbable sutures placed at least 3 cm beyond the margins of the defect. A variety of mesh products are available for repair, including polypropylene, PTFE, Gore-Tex, and a composite mesh of polypropylene and PTFE. Several composite mesh products (Table 29-3), with absorbable barrier coating external to polypropylene or polyester mesh cores, are available to minimize tissue attachment to intra-abdominal structures. Numerous approaches that utilize separation of abdominal wall components and varying layers of mesh placement (e.g., onlay, see below) have been developed for the repair of large and complex abdominal wall hernias.

3. **Laparoscopic repairs.** The laparoscopic approach is another method for repair of incisional hernias. The repair involves intraperitoneal placement of a mesh prosthesis to cover the hernia defect and can be performed with or without primary defect closure. This approach requires adhesiolysis of the entire prior incision, reduction of herniated abdominal contents, and broad coverage with PTFE or a barrier-coated mesh. The mesh is anchored in place with sutures and tacks with a minimum of 4 to 5 cm overlap past the edge of the hernia defect on all sides. A pooled data analysis of 45 published series comparing open and laparoscopic ventral hernia repairs concluded that laparoscopic repair is associated with fewer wound-related (3.8% vs. 16.8%) and overall complications (22.7% vs. 41.7%) and has a lower rate of recurrence (4.3% vs. 12.1%) than open repairs (*Surg Endosc*. 2007;21:378–386). Contraindications to laparoscopic ventral hernia repair include inability to establish pneumoperitoneum safely, peritonitis or an acute abdomen with strangulated or infarcted bowel, or loss of abdominal domain.

TABLE 29-3 Commonly Used Biomaterials for Incisional Hernia Repair

	Product Trade Name	Manufacturer	Components
Absorbable	Sepramesh	Genzyme Corp.,	Polypropylene mesh

barrier composite meshes		Cambridge, MA	absorbable sodiu hyaluronate/carbo on the other side
	C-Qur	Atrium Medical, Hudson, NH	Lightweight polypro (Prolite) coated w acid
	Parietex	Covidien-Medtronic, Minneapolis, MN	Polyester mesh with collagen coating c absorbable PEG/
	ProGrip	Covidien-Medtronic, Minneapolis, MN	Self-gripping Pariete
	Proceed	Ethicon, Inc., Somerville, NJ	Polypropylene mesh with polydioxanon side with oxidized cellulose
	Ventralight ST	Bard-Davol, Warwick, RI	Polypropylene mesh barrier
Nonabsorbable, barrier composite mesh	Bard Composix	Bard-Davol, Warwick, RI	Macroporous bilaye polypropylene an PTFE
	Gore-Tex Dual Mesh	W.L. Gore & Associates, Flagstaff, AZ	PTFE with different the peritoneal (int parietal (abdomin of the mesh
Nonabsorbable synthetic mesh	Bard Soft Mesh	C.R. Bard, Inc., Murray Hill, NJ	Large pore monofila polypropylene
Absorbable synthetic mesh	Phasix	Bard-Davol, Warwick, RI	Knitted monofilamer using poly-4-hydr (P4HB), a biologic resorbable materi
	BioA	W.L. Gore &	Polyglycolic acid an

		Associates, Flagstaff, AZ	carbonate
Bioremodelable materials (aka biologic meshes)	Surgisis	Cook Biotech, Inc., West Lafayette, IN	Acellular, extracellul derived from porc intestinal submuc
	Alloderm	LifeCell Corp., Branchburg, NJ	Acellular dermal ma from cadaveric hu
	Flex HD	Musculoskeletal Transplant Foundation, Edison, NJ	Acellular dermal ma from cadaveric hu
	Strattice	LifeCell Corp., Branchburg, NJ	Acellular porcine de
	Permacol	Tissue Science Laboratories, Covington, NJ	Acellular, cross-linke matrix

PEG, polyethylene glycol; PTFE, polytetrafluoroethylene.

4. **Mesh location.** For laparoscopic ventral hernia repairs, the mesh is routinely placed intraperitoneally (underlay or intraperitoneal onlay [IPOM] repair). In open ventral hernia repairs, there are several locations where mesh can be implanted. In an onlay repair, the mesh is secured on top of the anterior fascia that is closed below the mesh. This repair is technically easier to perform, however, it is also associated with a higher number of wound complications because it requires raising subcutaneous flaps. In an inlay repair, the fascial defect is not closed. The mesh is placed in the hernia defect and the edges secured to the surrounding fascia. However, the mesh can be exposed to bowel, and there is less mesh–tissue overlap than in other forms of repair, increasing the chances of hernia recurrence. In a sublay repair, the mesh is placed in the retrorectus or preperitoneal space. This technique includes closure of the posterior rectus sheath beneath the mesh, allowing for the use of uncoated mesh, as it is excluded from the peritoneal cavity. The principles of this repair have been expanded to include transversus abdominis release for the repair

of giant ventral/incisional hernias. Of the techniques described above, sublay repairs often have lower rates of recurrence and surgical site infection.

CHAPTER 29: HERNIAS

Multiple Choice Questions

1. **Which of the following is true regarding inguinal hernias?**

   a. Inguinal hernia is more common in women than men
   b. Inguinal hernias are rarely bilateral
   c. Direct inguinal hernias are more common than indirect
   d. Recurrent hernias are more likely to be direct than indirect
   e. There is no difference in recurrence rate based on type of repair

2. **An 83-year-old thin woman with no history of abdominal surgery presents with symptoms of a small bowel obstruction. On physical examination, she has pain with medial (internal) thigh rotation. There is no palpable hernia in the groin. What is the most likely diagnosis?**

   a. Femoral hernia
   b. Inguinal hernia
   c. Spigelian hernia
   d. Obturator hernia
   e. Adhesive small bowel obstruction

3. **A 35-year-old woman presents with a 1-day history of abdominal pain, distension, and nausea. Physical examination reveals temperature of 38.5°C, heart rate 115, abdominal distention, and a tender bulge in the right groin with erythema. What is the most appropriate next step in management?**

   a. Ultrasound of the right groin
   b. CT scan of the abdominal/pelvis
   c. Admission, NG tube decompression, IV fluid resuscitation
   d. Laparoscopic inguinal hernia repair
   e. Open inguinal hernia repair

4. **A 28-year-old active man with an athletic build is being evaluated for a 5-cm wide incisional hernia from a previous exploratory laparotomy for trauma. Which of the following repairs is**

preferred for this patient?

a. Open repair with intra-abdominal placement of synthetic mesh
b. Laparoscopic repair with synthetic mesh
c. Open repair with retrorectus placement of synthetic mesh
d. Laparoscopic repair with barrier-coated synthetic mesh
e. Open repair with retrorectus placement of biologic mesh

5. **A 70-year-old man with a history of congestive heart failure and a prior open prostatectomy presents with a symptomatic but reducible right inguinal hernia. On examination, there is concern for a small asymptomatic left inguinal hernia. What is the most appropriate management strategy?**

a. Bilateral open inguinal hernia repair without mesh
b. Laparoscopic repair of right inguinal hernia with mesh and evaluation of left side
c. Laparoscopic repair of right inguinal hernia and coverage of left inguinal floor
d. Open repair of right inguinal hernia with mesh and watchful waiting of left side
e. Watchful waiting of right inguinal hernia and potential left inguinal hernia

30 Endoscopic, Laparoscopic, and Robotic Surgery

Bola Aladegbami and Michael M. Awad

INTRODUCTION

Minimally invasive surgical (MIS) techniques are a crucial component of surgical care with the goal to perform operations through small (or no) incisions when compared to traditional open operations. Benefits include shorter length of hospital stay, less postoperative pain, and lower rates of postoperative wound complications. The use of robot-assisted laparoscopic surgery continues to expand in a variety of surgical fields. In addition, surgeons provide diagnostic endoscopy to a large segment of patients in the United States and have been instrumental in pioneering a variety of endoscopic surgical techniques. For these reasons, a familiarity with basic principles of laparoscopic, robotic, and endoscopic surgery is critical for surgical trainees.

I. FLEXIBLE ENDOSCOPY AND ENDOSCOPIC SURGERY

A. Equipment and Troubleshooting. Flexible endoscopy is performed using a flexible **fiberoptic endoscope**, connected to a source of water or saline, a suction source, and an air or gas insufflator. Most modern endoscopes are operated with a **charged coupled device (CCD) chip camera**. Commonly used endoscopes also have working channels that allow instruments to be passed through the scope to the target where biopsies can be taken or interventions performed. The most commonly used endoscopes among surgeons are **gastroscopes** and **colonoscopes**. Gastroscopes are used for diagnostic **esophagogastroduodenoscopy** (EGD) and have a typical working length of 92.5 to 110 cm and a diameter of 9.0 to 9.2 mm and usually have a single working channel.

Colonoscopes are longer (133 to 170 cm) and thicker (11.1 to 13.7 mm diameter) and also have a working channel. Diagnostic endoscopy is performed by inserting an endoscope into the gastrointestinal (GI) tract and meticulously examining the target mucosa while advancing or withdrawing the scope. Room air or **carbon dioxide** (CO_2) is used (the latter used preferentially to facilitate postprocedure GI decompression) to dilate/insufflate the GI lumen to facilitate scope advancement and mucosal visualization. Irrigation is used to clean the tip of the endoscope or wash debris from segments of mucosa. All of these elements are subject to malfunction, and a systematic approach to troubleshooting is critical (Fig. 30-1).

B. Endoscopic Surgery. A variety of graspers, electrosurgical hemostatic devices, biopsy snares, ablative technologies, stents, clips, and other devices are available for use in interventional endoscopy. A full description of interventional endoscopy is beyond the scope of this chapter, but this expansion of technology has made possible a variety of endoluminal therapies for disorders that would have previously required open or laparoscopic operations. These include endoluminal therapies for reflux, complications of bariatric surgery, achalasia, gastroparesis, and esophageal/rectal tumors.

Problem	Check the Following
No light at distal end	1. Light source plugged in and turned on 2. Light source ignited 3. Not in "standby" mode 4. Lens at distal tip is dirty 5. Bulb burned out
Out of focus	1. Adjust focus ring 2. Fiberoptic scope—clean lens
No irrigation	1. Water bottle contains water 2. Water bottle connected to umbilical cord 3. Connection tight 4. Lid of water bottle screwed on tightly 5. Power turned on 6. Valve stuck or occluded
No insufflation	1. Umbilical cord firmly seated into light source and screwed in if necessary 2. Power turned on 3. Valve stuck or occluded
Clogged valve or nozzle	1. Take valve apart and clean 2. Flush channel of endoscope with cleaning solution, followed by clean water
Difficulty passing instrument	1. Check tip angulation; decrease angulation and try again 2. Ensure that the instrument is fully closed 3. Check size of instrument relative to instrument channel; try smaller-diameter instrument

FIGURE 30-1 Troubleshooting for endoscopy. (From Vitale GC, Davis BR. Flexible endoscopes: characteristics, troubleshooting, and equipment care. In: Soper NJ, Scott-Connor CEH, eds. *The SAGES Manual: Volume 1. Basic Laparoscopy and Endoscopy*. New York: Springer; 2012:497–507.)

C. Fundamentals of Endoscopic Surgery (FES) is a didactic curriculum and technical examination developed by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) to train surgical learners in the theory and technical skills necessary to perform diagnostic and interventional endoscopy. The didactic portion is a web-based modular curriculum similar to the model established with Fundamentals of Laparoscopic Surgery (FLS). Modules focus on technology, patient preparation, patient sedation, upper and lower diagnostic endoscopy, biopsy techniques, enteral access procedures,

hemostatic techniques, and endoscopic retrograde cholangiopancreatography (ERCP). A proctored written examination tests knowledge of these topics and is accompanied by a technical examination that assesses fundamental endoscopic skills on a simulator. Passage of the FES written and technical examination is a prerequisite for board eligibility in General Surgery in the United States.

II. LAPAROSCOPY

A. Patient Selection. Laparoscopy is used to perform a vast assortment of operations, and there are very few contraindications to its use. Absolute contraindications are limited to inability to tolerate general anesthesia or laparotomy, hemodynamic instability, uncorrected coagulopathy, or unavailability of an experienced laparoscopic surgeon competent in the procedure being attempted. Relative contraindications include bowel obstruction, severe cardiopulmonary disease, peritonitis, and loss of domain, including from extensive adhesions. Preoperative assessment for laparoscopic procedures should proceed as it would for a comparable open operation.

B. Basic Principles. Laparoscopy is strictly defined as the use of an endoscope to explore the abdominal cavity. Laparoscopy, as commonly defined among surgeons today, involves entry into the intraperitoneal cavity and establishment of pneumoperitoneum with CO_2 or, much less commonly, N_2O. Pneumoperitoneum creates working space for instruments that are inserted into the abdomen through plastic or metallic ports with valves that prevent loss of pneumoperitoneum. Visualization is achieved using a lighted rigid or semirigid endoscope connected to display monitors in the operating room. Laparoscopy is performed based on the principle of triangulation as follows: The camera port is placed centrally with working ports to either side, allowing the long rigid instruments to converge at the surgical target without colliding with the laparoscope or with one another.

C. Limitations. Surgeons performing laparoscopy should be aware of some special considerations unique to this technique. The surgical field is a three-dimensional space, but most laparoscopes project an image onto a traditional two-dimensional monitor, creating limited depth perception for the surgeon. Most laparoscopic instruments can rotate around their long axis, and some may have some degree of articulation

at the instrument tip, but they have significantly limited dexterity compared to the human hand and wrist. In addition, laparoscopic instruments can transmit some haptic input through the instrument shaft and handle to the operator's hand, but much of the haptic feedback that is central to appropriate tissue handling in open operations is lost during laparoscopy.

D. Equipment, Troubleshooting, and Techniques

1. **Room setup and positioning.** The basic setup includes an insufflator, gas tank or central gas supply, light source, camera, laparoscope, monitors, laparoscopic ports and trocars, laparoscopic instrumentation, and instruments for open conversion, if necessary. If intraoperative fluoroscopy or radiography is likely to be employed, the patient and equipment positioning should allow additional hardware to access the operating table. The patient, surgeon, and monitor should be positioned to place the operative field between the surgeon and the monitor. Patient position is dictated by the surgical procedure being performed. Most abdominal operations require the patient be placed in the supine position. This position is sometimes modified to split the legs and allow the surgeon to operate from between the legs to access the upper abdomen. Footboards, suction beanbags, and safety straps are often employed to secure the patient to the operating table, allowing for steep angles to be employed intraoperatively. Pelvic procedures in which a perineal approach may be required typically employ the lithotomy position. Lateral decubitus positioning is used to perform thoracoscopic or retroperitoneal procedures. Monitors should be positioned to allow the operating surgeon to view them clearly without turning their head and with a 15-degree downward gaze, minimizing neck extension and postural fatigue. The operating table height and port placement should allow the surgeon to keep both arms at their sides with their elbows flexed to 90 to 120 degrees. A preoperative safety and equipment checklist is essential prior to any laparoscopic operation (Fig. 30-2).
2. **Insufflation.** A pressure-limited insufflator is typically used in laparoscopic surgery. This device controls the flow of CO_2 into the abdominal cavity. Most insufflators display the pressure in the system, which reflects the pressure in the target body cavity when the

two are in continuity, as well as the flow rate of gas through the insufflator and the total volume of gas insufflated. The insufflator allows a target pressure to be selected and the rate of gas flow to be modulated. The minimum pressure that allows adequate working space should be employed. Loss of pneumoperitoneum or an increase in pressure can occur due to multiple factors (Fig. 30-2).

3. **Imaging system.** The typical laparoscopic imaging system consists of four basic components: A laparoscope, a light source, a camera plus camera controller, and a monitor. Imaging difficulties can be caused by any component in the system (Fig. 30-2). The laparoscope is a rigid or semirigid scope that is inserted into the patient through a port and contains either fiberoptic elements or CCD chip. The fiberoptic cables are connected to a high-energy light source and provide illumination to the surgical field. The CCD chip camera is more modern and captures an image from the laparoscope tip (rather than through cables), digitizes it, and projects it to a monitor. Laparoscopes vary in diameter, with larger-diameter scopes providing greater illumination. Most surgeons use a 10-mm scope, but 5-mm (and even 3-mm) laparoscopes are available for a variety of procedures. Laparoscopes can have flat tips (0-degree scopes) or angled tips (commonly 30- or 45-degree) to allow the field of view to be turned around the long axis of the scope.
4. **Energy sources.** A vast array of surgical instruments are available for use in laparoscopic as well as open operations, and a full discussion of energy sources is beyond the scope of this chapter. We direct the reader to the expertly curated SAGES' course on Fundamental Use of Surgical Energy (FUSE).

Problem	Cause	Solution
1. Poor insufflation/ loss of pneumoperitoneum	CO_2 tank empty Accessory port stopcock(s) not properly adjusted Leak in sealing cap or stopcock Excessive suctioning Loose connection of insufflator tubing at source or at port Hasson stay sutures loose Tubing disconnection from insufflator Flow rate set too low	Change tank Inspect all accessory ports. Open or close stopcock(s) as needed Change cap or cannula Allow time to reinsufflate Tighten connections Replace or secure sutures Connect tubing Adjust flow rate
2. Excessive pressure required for insufflation (initial or subsequent)	Veress needle or cannula tip not in free peritoneal cavity Occlusion of tubing (kinking, table joint, etc.) Port stopcock turned off Patient is "light" Cannula tip not in peritoneal space	Reinsert needle or cannula Inspect full length of tubing. Replace with proper size as necessary Fully open stopcock Give more muscle relaxant Advance cannula under visual control
3. Inadequate lighting (partial/ complete loss)	Loose connection at source or scope Light is on "manual minimum" Bulb is burned out Fiber optics are damaged Automatic iris adjusting to bright reflection from instrument Monitor brightness turned down Room brightness floods monitors	Adjust connector Go to "automatic" Replace bulb Replace light cable Reposition instruments, or switch to "manual" Readjust setting Dim room lights
4. Lighting too bright	Light is on "manual maximum" "Boost" on light source is activated Monitor brightness turned up	Go to "automatic" Deactivate "boost" Readjust setting
5. No picture on monitor(s)	Camera control or other components (V.C.R., printer, light source, monitor) not "on" Cable connector between camera control unit and/or monitors not attached properly Cable between monitors not connected Input select button on monitor doesn't match "video-in" choice	Make sure all power sources are plugged in and turned on Cable should run from "video-out" on camera control unit to "video-in" on primary monitor. Use compatible cables for camera unit and light source. Cable should run from "video-out" on primary monitor to "video-in" on secondary monitor Assure matching selections
6. Poor quality picture **a. fogging/haze** **b. flickering, electrical interference** **c. blurring, distortion**	Condensation on lens from cold scope entering warm abdomen Condensation on scope eyepiece, camera lens, coupler lens Moisture in camera cable–connecting plug Poor cable shielding Insecure connection of video cable between monitors Incorrect focus Cracked lens, internal moisture Too grainy	Gently wipe lens on viscera; use antifog solution, or warm water Detach camera from scope (or camera from coupler), inspect and clean lens as needed Use suction or compressed air to dry out moisture (don't use cotton tip applicators on multipronged plug) Replace cables as necessary Move electrosurgical unit to different circuit or away from video equipment Reattach video cable at each monitor Adjust camera focus ring Inspect scope/camera, replace if needed Adjust enhancement and/or grain settings for units with this option
7. Inadequate suction/irrigation	Occlusion of tubing (kinking, blood clot, etc.) Occlusion of valves in suction/ irrigator device Not attached to wall suction Irrigation fluid container not pressurized	Inspect full length of tubing. If necessary, detach from instrument and flush tubing with sterile saline Detach tubing, flush device with sterile saline Inspect and secure suction and wall source connector Inspect compressed gas source, connector, pressure dial setting
8. Absent or "weak" cauterization	Patient not grounded properly Connection between electrosurgical unit and instrument loose Foot pedal or hand switch not connected to electrosurgical unit Wrong output selected Connected to the wrong socket on the electrosurgical unit Instrument insulation failure outside of surgeon's view	Assure adequate grounding pad contact Inspect both connecting points Make connection Correct output choice Check that cable is attached to endoscopic socket Use new instrument and inspect insulation

FIGURE 30-2 Troubleshooting algorithm for laparoscopic surgery. (Airan M. Equipment setup and troubleshooting. In: Soper NJ, Scott-Connor CEH, eds. *The SAGES Manual: Volume 1. Basic Laparoscopy and Endoscopy*. New York: Springer; 2012:21–43.) (*continued*)

5. **Abdominal access.** Safe access to the abdomen is the crucial first step to any laparoscopic procedure. Two strategies to achieve access to the abdomen are generally used: the Veress needle (**"closed" technique**) and the Hasson cannula (**"open" technique**).

   a. Closed technique. The Veress needle is a 7- to 12-cm long 14-gauge needle attached to a valve and stopcock that allow gas to be insufflated through the needle. The needle has a sharp beveled tip

with a spring-loaded retractable blunt tip that projects beyond the sharp tip and retracts when pressed against a surface. To achieve safe access to the abdomen using a Veress needle, the appropriate site of Veress insertion is selected. In a patient without prior abdominal operations, a periumbilical insertion site is often used. In patients with prior midline abdominal surgery, alternative sites on the abdomen remote from the prior incision may be used (often the left upper quadrant or right lower quadrant is used as alternate site). A stab incision is made at the site of Veress insertion. It is recommended to lift the abdominal wall away from the underlying viscera prior to needle insertion (the authors prefer to use a Kocher clamp for this). The needle is then inserted into the abdomen, generally at an angle perpendicular to the abdominal wall, while held at the shaft for stability rather than its hub. The needle encounters resistance followed by a sensation of give at approximately two to three separate points as it crosses fascia and peritoneum. Once the Veress needle has entered the abdomen, its position may be confirmed by first aspirating using a syringe containing saline, and no blood or succus should be aspirated (see "Complications of abdominal access" below). Saline should then easily instill into the abdomen without any return of saline on subsequent aspiration. After instilling 3 to 5 cc of saline, the syringe should be removed with the stopcock open and the saline remaining in the Veress needle should flow easily into the abdomen. This constitutes the **"drop" test**. The insufflation tubing is then connected to the hub and the gas flow initiated at 1 to 2 L/min. The opening pressure should be no more than 10 mm Hg. Elevated initial pressure is caused by malposition of the Veress needle tip, either due to placement of the needle in the preperitoneal space or due to the needle tip abutting a structure or sitting in a pocket with limited continuity with the rest of the abdomen. If this occurs, the needle may be gently rotated and slightly advanced or withdrawn. If the pressure does not quickly drop to the expected level, the needle should be withdrawn and another attempt made. This may be repeated until an intra-abdominal position of the needle and normal insufflation are confirmed, or the site should be abandoned and a new site

attempted or an open operation performed (with attention paid to the prior attempted entry site for any underlying visceral injuries). Insufflation of the abdomen proceeds at 1 to 2 L/min for 1 minute, then the flow rate is increased to the maximal rate the insufflator can support until the intra-abdominal pressure reaches the set target of 12 to 15 mm Hg. Once the abdomen is adequately insufflated, the Veress needle is removed, the skin is incised at the camera port site, and the first trocar is inserted. This can be done blindly, or under direct vision using an optical trocar which has a clear tip and allows a scope to be inserted with the port. As the port is pushed into the abdomen, the layers of the abdominal wall and intraperitoneal space can be visualized and confirmed. Once the port is placed into the abdomen, the trocar is removed and the laparoscope inserted into the abdomen to reconfirm placement and perform an initial exploration. Particular attention is paid to the area directly below the initial port where injury may have been caused by the Veress needle or the trocar. Afterward, subsequent ports may be placed 8 to 10 cm apart under direct visualization using the principle of triangulation described above.

b. Open technique. The Hasson technique involves entry into the abdomen at the initial trocar site under direct vision, which can be useful when extensive intra-abdominal adhesions are anticipated. However, some surgeons preferentially use an open-access technique for all laparoscopic procedures. Open entry is usually performed at a periumbilical site, which is then used as the camera port, but in patients with prior midline incisions, an alternative site may be used, such as the left upper or right lower quadrants. After the skin is prepped, a 1- to 3-cm incision is made at the site of entry and carried down to the subcutaneous tissue using sharp dissection and electrocautery. On sweeping away of subcutaneous fat using retractors, the underlying fascia is exposed and pulled away from underlying viscera by elevating it vertically with clamps. The fascia is then carefully incised sharply or with electrocautery to expose the peritoneum. The peritoneum is then similarly elevated and opened. The abdominal cavity is then visualized and gently explored with a finger, and fascial sutures placed. The Hasson cannula, which has a blunt obturator to

prevent insertion trauma, a cone-shaped sleeve that sits in the fascial incision, and two struts that are fixed to the fascial stitches to hold the system in place, is then inserted into the intraperitoneal space. Some systems employ a balloon that sits over the intraperitoneal portion of the cannula and is inflated upon insertion, holding the system in place without fascial sutures when the sleeve is brought down into position. Once the cannula is positioned, the camera is inserted for an initial exploration of the abdomen and placement of subsequent ports as in the Veress technique. A limitation of the Hasson technique is the challenge faced when used in obese patients with thick abdominal walls.

c. Complications of abdominal access can occur, particularly during blind portions such as Veress needle or blind trocar insertion, including visceral or vascular injuries. If bowel contents or blood is aspirated during Veress insertion, the needle should be withdrawn and reinserted and laparoscopic access should proceed. Upon entry into the abdomen, bowel or other injured organs should be examined and managed per established protocols for traumatic injury to intraperitoneal organs. Veress needle stick to intra-peritoneal viscera should prompt close inspection, but in many cases may need only a simple repair or no intervention at all. Inadvertent intraluminal insufflation of the bowel with the Veress needle, however, can cause significant injury requiring bowel resection. The retroperitoneum should also be closely examined on abdominal exploration, particularly in situations where blood was encountered on initial Veress insertion. A stable hematoma in the mesentery or lateral retroperitoneum can usually be observed. However, central or rapidly expanding hematomas require exploration of the retroperitoneum.

(1) Trocar insertion can cause injuries far more severe than Veress insertion. Bowel and visceral injuries should be considered penetrating traumas and managed accordingly, and any central or rapidly expanding retroperitoneal hematoma should be explored. If a rush of blood is encountered on trocar insertion or open cannula placement, the surgeon must assume that a critical vascular injury has occurred and conversion to open must be performed immediately (without yet removing

the trocar, which may be partially tamponading the injury).

(2) **Abdominal wall hemorrhage** is a common complication of laparoscopic surgery that may be caused by injury to the epigastric arteries, veins, or their tributaries. These are often self-limited and cease with the tamponading effect of the port. If this fails to control the bleeding, control may be attempted using electrosurgical energy or with a transfascial suture.

6. **Port removal and closure.** At the conclusion of the operation, instruments and ports are removed under direct visualization, with the camera port being removed last after the abdomen is desufflated. Fascial incisions 5 mm or smaller do not need to be closed. Consider closure of 10-mm port site fascia, especially if the fascia has been dilated or cut to remove a large specimen or if the port is placed through a previous incision. Skin incisions are then closed.

7. **Physiologic effects of laparoscopy.** The increase in intra-abdominal pressure during laparoscopy may be associated with a variety of physiologic effects.

   a. **Cardiovascular.** Elevated intra-abdominal pressure leads to an increase in systemic vascular resistance due to compression of the venous structures and visceral arteries, as well as the resultant activation of the renin–angiotensin–aldosterone axis. Inferior vena cava compression leads to reduced preload and lower cardiac output. Cephalad displacement of the diaphragm causes increased intrathoracic pressure, which leads to increased pulmonary vascular resistance and may result in low blood pressure.

   b. **Respiratory.** Increased intra-abdominal pressure limits diaphragmatic excursion, decreasing pulmonary compliance, and functional residual capacity, and increasing thoracic pressure. These changes are associated with the development of atelectasis. In addition, absorption of insufflated CO_2 can contribute to hypercarbia and acidosis.

   c. **Renal.** Increased intra-abdominal pressure leads to a reduced glomerular filtration rate due to reduced afferent arterial flow and elevated renal venous pressure. This may lead to a transient reduction in urine output, which usually resolves when the pneumoperitoneum is released.

d. Neurologic. The increased intrathoracic and central venous pressure associated with pneumoperitoneum leads to a decrease in venous return from the brain. This leads to an increase in intracranial pressure and may contribute to temporary confusion on emergence from long laparoscopic operations.

E. FLS is a validated program developed by SAGES for the teaching and evaluation of knowledge and technical skills associated with laparoscopy. The program is composed of a didactic curriculum, a written examination, and a skill-based examination. The didactic portion is a web-based series of modules that learners are able to navigate and study at their own pace. These modules cover basic preoperative considerations, intraoperative considerations, basic laparoscopic procedures, postoperative care and complications, and an explanation of the technical skills portion of the examination. After studying the modules, the learner is examined in a proctored setting. The manual skills examination is performed in a laparoscopic trainer box and consists of five tasks: peg transfer, precision cutting, ligating loop, extracorporeal knot, and intracorporeal knot. Each task is scored for efficiency and has a time limit to complete the task. In addition, each task is scored for performance, with specifically defined task errors leading to lower scores. Passing the FLS written and technical examinations is now a prerequisite for eligibility for board certification in General Surgery in the United States.

III. Robot-Assisted Surgery.

It is used in a variety of fields, particularly general surgery, urologic surgery, and gynecologic surgery, among others. It holds great promise in the advancement of MIS, but also has significant current limitations.

A. Equipment and Basic Principles. Strictly speaking, current “robotic” surgical systems are not robots, as the term implies some degree of automation and current robotic surgical platforms do not perform any autonomous functions. More accurately, the most common robotic surgical platform (da Vinci Surgical System, Intuitive Surgical Inc., Sunnyvale, CA) can be described as a computer-assisted surgical system. On this platform the surgeon is seated at a console (“surgeon cart”) and manipulates hand-held controllers, whose motions are mapped directly to the surgical instrument tip. The instruments are

mounted to mechanical arms on a platform that is “docked” to the patient at the laparoscopic port sites (“patient cart”). The laparoscope is also attached to an arm of the patient cart and is controlled by the surgeon from the surgeon cart. Commonly used robotic surgical platforms employ a scope very similar to a traditional 10-mm high-definition laparoscope, but which captures two separate images that are projected to the binocular eyepieces the surgeon looks into at the surgeon cart, creating a three-dimensional display. In many cases, a nonrobotic assistant port is also placed, allowing an assistant surgeon to participate using traditional laparoscopic instruments. Abdominal access for robot-assisted laparoscopic surgery is achieved in much the same way as in traditional laparoscopy. Triangulation of the surgical target remains the guiding principle for port placement, though robotic ports are generally arranged along a straight line, rather than the “baseball diamond” configuration that is commonly used in laparoscopic surgery, to facilitate the action of the robotic arms.

B. Advantages. Robot-assisted laparoscopic surgery has a variety of benefits for operating surgeons compared to laparoscopy. Robotic instruments are wristed, allowing for more degrees of freedom compared to laparoscopic instruments. In addition, this configuration allows the movements of the surgeon to be scaled down when they are converted to instrument actions, allowing for finer movements than laparoscopic instruments can achieve. Robot-assisted surgery has also been shown to generate less ergonomic stress on surgeons than laparoscopic surgery, both objectively and subjectively.

C. Limitations. Robot-assisted laparoscopic surgery has several limitations. The robotic platform requires docking of the patient cart to the laparoscopic ports, limiting surgery to one or two body quadrants. However, the newest iteration of the da Vinci Surgical System (“Xi”) provides multiquadrant access, but overall, traditional laparoscopy still allows for greater freedom to explore the abdomen. In addition, the current surgeon cart provides minimal to no haptic feedback to the surgeon. This compels surgeons to increasingly rely on visual cues to safely manipulate tissue. Finally, robotic surgery carries additional expense compared to laparoscopy with no significant improvement in patient outcomes.

D. Future of Robotic Surgery. There are currently new FDA-approved

robotic platforms and future platforms on the horizon from companies that include TransEnterix, HeroSurg, Medrobotics, and Verb Surgical. These systems are attempting to further improve on robotic surgical technologies including advancements in haptics, multiquadrant mobility, single port access, as well as innovations in machine learning and image-guided surgery.

E. Fundamentals of Robotic Surgery. Fundamentals of Robotic Surgery (FRS, http://frsurgery.org/) is an educational curriculum for training and assessing surgical learners in the use of robot-assisted surgery. This program has been developed by a group of experts in robotic surgery and surgical education, and is modeled on the FLS program. The curriculum contains modules focusing on introducing learners to robotic surgical systems, learning about important psychomotor skills for robot-assisted surgery, and understanding the team-based approach and communication skills necessary to effectively perform robotic surgery.

CHAPTER 30: ENDOSCOPIC, LAPAROSCOPIC, AND ROBOTIC SURGERY

Multiple Choice Questions

1. **Which of the following is an absolute contraindication to laparoscopic surgery?**

   a. Small bowel obstruction
   b. Morbid obesity
   c. Peritonitis caused by perforation
   d. Uncontrolled coagulopathy
   e. Hypothermia

2. **Intra-abdominal pressure during laparoscopic surgery should be closest to:**

   a. 2 mm Hg
   b. 6 mm Hg
   c. 12 mm Hg
   d. 18 mm Hg
   e. 25 mm Hg

3. **After insufflating the abdomen using a Veress needle, a trocar is inserted just inferior to the umbilicus with an immediate rush of bright red blood. The next step of management should be:**

   a. Keep the trocar in place and perform a laparotomy
   b. Resume insufflation and insert the laparoscope to identify the injury
   c. Apply manual pressure to the abdomen
   d. Remove the trocar and perform a laparotomy
   e. Abort the operation and proceed to interventional radiology to attempt angiographic localization and control of the injury

4. **Which of the following is a benefit of robot-assisted laparoscopic surgery compared to traditional laparoscopy?**

   a. Reduced operative time
   b. Ergonomic advantages to the operating surgeon

c. Reduced blood loss
d. Improved haptic feedback compared to laparoscopic instruments
e. Expanded field of view compared to laparoscopic imaging systems

5. **Which of the following is a physiologic effect of pneumoperitoneum?**

a. Increased preload
b. Metabolic alkalosis
c. Increased pulmonary compliance
d. Decreased intracranial pressure
e. Decreased glomerular filtration rate

31 Breast

Leisha C. Elmore and Julie A. Margenthaler

I. ANATOMY

A. The Breast. Located between the subcutaneous fat and the fascia of the **pectoralis major** and **serratus anterior** muscles, the breast is bounded superiorly by the clavicle, inferiorly by the inframammary fold, and medially by the lateral edge of the sternum, with its lateral border lying along the anterior border of the latissimus dorsi. When anatomically describing the breast, it is traditionally divided into four quadrants: upper inner, upper outer, lower inner, lower outer. Suspensory ligaments (**Cooper ligaments**) run through the breasts from the deep fascia to the skin and may cause skin dimpling when associated with a malignancy.

1. **Vasculature.** Arterial supply is predominantly from the **internal thoracic artery** (**or internal mammary artery**) via perforating branches (perforators). Venous drainage is mainly through the **axillary vein.**
2. **Lymphatic drainage.** The superficial **Sappey plexus** converges with a deep lymphatic plexus, and they ultimately drain into the axillary (75%) and internal mammary (25%) lymph nodes.
3. **Innervation.** Lateral and anterior cutaneous branches of the second to sixth intercostal nerves provide sensory innervation.

B. The Axilla. The borders of the axilla are defined as the **axillary vein** superiorly, **latissimus dorsi** laterally, the **serratus anterior** muscle medially, the **subscapular and teres major** posteriorly, and the **pectoralis major and minor** anteriorly.

1. **Axillary lymph nodes** are classified according to their anatomic location relative to the pectoralis minor muscle.

   a. Level I nodes: *Lateral* to the pectoralis minor muscle.

b. Level II nodes: *Posterior* to the pectoralis minor muscle.

c. Level III nodes: *Medial* to the pectoralis minor muscle and most accessible with division of the muscle.

d. Rotter nodes: *Between* the pectoralis major and the minor muscles.

2. Axillary nerves. Three motor and several sensory nerves are located in the axilla. Preservation of all is preferred during an axillary lymph node dissection (ALND), however, direct tumor invasion may require resection along with the specimen.

a. The **long thoracic nerve** travels superior to inferior along the chest wall and medially within the axilla, innervating the **serratus anterior muscle.** Injury to this nerve causes a **"winged" scapula**.

b. The **thoracodorsal nerve** courses along the posterior border of the axilla superior to inferior on the subscapularis muscle and innervates the **latissimus dorsi**. Injury to this nerve causes weakness in arm adduction and medial rotation.

c. The **medial pectoral nerve** travels from the posterior aspect of the pectoralis minor muscle around the lateral border of the pectoralis minor to the posterior aspect of the pectoralis major muscle. It innervates the lateral third of the pectoralis major; injury to this nerve results in atrophy of the lateral pectoralis major muscle.

d. The **lateral pectoral nerve** arises from the brachial plexus and traverses the clavipectoral fascia and typically runs medial to the medial pectoral nerve to innervate the **pectoralis major.**

e. Intercostal brachial sensory nerves travel laterally in the axilla from the second intercostal space to the medial upper arm. Transection causes numbness in the posterior and medial surfaces of the upper arm.

II. CLINICAL ASSESSMENT

A. History. Patients seek medical attention most commonly for an abnormal mammogram, a breast mass, breast pain, nipple discharge, and/or skin changes. A history should include:

- Description and duration of signs and symptoms and their temporal relationship to pregnancy, menstrual cycle, or previous trauma
- Date of last menstrual period and regularity of the menstrual cycle
- Age of menarche

- Number of pregnancies and age at first full-term pregnancy
- Lactation history
- Age at natural or surgical menopause (e.g., oophorectomy)
- Previous history of breast biopsies and mammoplasties
- Mammogram history
- History of oral contraceptive and/or hormone replacement therapy (HRT)
- Personal and family history of breast and gynecologic cancer, including age at diagnosis. This should include at least two generations as well as any associated cancers, such as ovary, colon, prostate, gastric, or pancreatic to assess for hereditary cancer risk.

1. Assessment of cancer risks

a. Risk factors. Hormonal and environmental exposures, genetics, and certain types of breast tissue histology can all be associated with an increased risk for breast cancer (Table 31-1).

b. Hereditary breast cancer accounts for 5% to 10% of breast cancers. These tumors can be attributed to a mutation in a single, highly penetrant gene, and approximately 80% of hereditary breast cancers are the result of mutations in ***BRCA1*** and ***BRCA2***. Women with *BRCA1* mutations have an estimated risk of 85% for breast cancer by the age of 70 years, a 50% chance of developing a second primary breast cancer, and a 20% to 40% chance of developing ovarian cancer. *BRCA2* mutations carry a slightly lower risk for breast and ovarian cancer and account for 4% to 6% of all male breast cancers. Screening for *BRCA* gene mutations should be reserved for women who have a strong family history of breast or ovarian cancer, and referral for genetic counseling should be based on the National Comprehensive Cancer Network (NCCN) guidelines (*J Natl Compr Canc Netw*. 2014;12:1326–1338; www.nccn.org).

TABLE 31-1 Risk Factors for Breast Cancer and Approximate Strength of Association

Reproductive	Hormonal	Nutritional/Lifestyle/Body Habitus	Other
Early menarche	OC use (current vs.	Obesity (>30 BMI vs. <25)	Family

[+]	none) [+]	Premenopausal [−] Postmenopausal [+]	(mo siste
Age at first birth (>35 vs. <20) [++]	Estrogen replacement (10+ yr vs. none) [+]	Adult weight gain (postmenopausal) [++]	Family (firs rela
No. of births (0 vs. 1 child) [+]	Estrogen plus progesterone replacement (>5 yr vs. none) [++]	Alcohol (1 or more drink/day vs. none) [+]	Jewish (yes
Age at menopause (5-yr increment) [+]	High blood estrogens or androgens (postmenopause) [+++]	Height (>5 ft 7 in) [+]	Ionizir (yes
Breastfeeding (>1 yr vs. none) [−]	High blood prolactin [++]	Physical activity (>3 hr/wk) [−]	Benigr dise diag [++]
		Monounsaturated fat[c] (vs. saturated fat) [−]	Mamn den (hig cate lowe
		Low intake of fruits and vegetables[c] (specifically for ER-breast cancer) [+]	

[a]Two first-degree relatives who have a history of breast cancer before age 65 years versus no relative.

[b]First-degree relative who has a history of breast cancer before age 65 years versus no relative.

[c]Upper quartile (top 25%) versus lower quartile (lowest 25%).

[d]Clinically recognized chronic cystic, fibrocystic, or other benign breast disease versus none.

BMI, body mass index; OC, oral contraceptives;

[+] = relative risk (RR) 1.1–1.4; [++] = RR 1.5–2.9; [+++] = RR 3.0–6.9; [−] = RR 0.7–0.8.

Adapted with permission from Table 18.2 in Willett WC, Tamimi R, Hankinson SE, Hazra A, Eliassen AH, Colditz GA. *Chapter 18: Nongenetic Factors in the Causation of Breast Cancer,*

c. **Modeling breast cancer risk.** The **Gail model** is one of several prediction models—including the BOADICEA, BRCAPRO, Claus, and Tyrer–Cuzick models—that estimate the absolute risk (probability) that a woman in a program of annual screening will develop breast cancer over a defined age interval (*J Nat Cancer Inst*. 1989;81:1879–1886). A modified Gail model focusing only on the risk of invasive cancer has been used to define eligibility criteria for entry into chemoprevention trials. The National Surgical Adjuvant Breast and Bowel Project (NSABP) and the National Cancer Institute (NCI) offer an interactive online risk assessment tool (http://www.cancer.gov/bcrisktool). Additionally, a number of genome-based prediction tools have also been developed to help predict patients who may be at risk for recurrent malignancy. The most widely used is **Oncotype Dx**, which analyzes specific genes to develop a recurrence score. In women with early-stage breast cancer, this helps determine which patients would benefit from adjuvant chemotherapy.

B. Physical Examination. Complete clinical examination of a patient requires inspection of the bilateral breasts and axillae. Inspect the patient's breasts in both the **upright** and **supine** positions. With the patient in the upright position, examine with the patient's arms relaxed and then raised, looking for shape asymmetry, deformity, skin changes (e.g., erythema, edema, dimpling), nipple changes or discharge, and lymphadenopathy (axillary, supraclavicular, and infraclavicular). With the patient in the supine position, examine the entire breast systematically with the patient's ipsilateral arm raised above and behind the head. Clinical examination of the axilla is best completed with the arm positioned by the patient's side.

C. Breast Imaging

1. **Screening mammograms** are performed in the **asymptomatic** patient and consist of two standard views, mediolateral oblique (MLO) and craniocaudal (CC). **Tomosynthesis**, or three-dimensional mammography, became available in the United States in 2011 and improves the sensitivity and specificity of mammography, particularly for women with nonfatty breasts and in the assessment of

noncalcified lesions. Although the U.S. Preventative Task Force (USPTF) changed its screening recommendation in 2009 to annually for women beginning at age 50, the current recommendation from the NCI, the American Congress of Obstetricians and Gynecologists (ACOG), and the American Cancer Society (ACS) is **annual screening mammography for women aged 40 years and older.**

- (1) **BI-RADS (Breast Imaging Reporting and Data System)**. Breast lesions on mammograms are classified according to the American College of Radiology BI-RADS by the following scores:
- **0** = Needs further imaging; assessment incomplete
- **1** = Normal; continue annual follow-up (risk of malignancy: 1/2,000)
- **2** = Benign lesion; no risk of malignancy; continue annual follow-up (risk of malignancy: 1/2,000)
- **3** = Probably benign lesion; needs 4 to 6 months follow-up (risk of malignancy: 1–2/100)
- **4** = Suspicious for breast cancer; biopsy recommended. This category can be further subdivided into the following:
  - 4A = Low suspicion for malignancy (>2% to ≤10%)
  - 4B = Moderate suspicion for malignancy (>10% to ≤50%)
  - 4C = Finding of moderate concern of being cancer, but not as high as Category 5 (>50% to ≤95%)
- **5** = Highly suspicious for breast cancer; biopsy strongly recommended (≥95% are malignant)
- **6** = Known biopsy-proven malignancy

(2) **Malignant mammographic findings** include new or spiculated masses, clustered microcalcifications in linear or branching array, and/or architectural distortion.

(3) **Benign mammographic findings** that might be mistaken for malignancy include **radial scar** (biopsy needed), **fat necrosis** (i.e., oil cysts; biopsy may be needed), and **milk of calcium** (no biopsy needed). **Cysts** cannot be distinguished from solid masses by mammography, so **ultrasound** (US) is needed to make this distinction.

(4) **Screening in high-risk patients.** For patients with known *BRCA* mutations, annual mammograms and semiannual physical examinations should **begin at the age of 25 to 30**

years. In patients with a strong family history of breast cancer but undocumented genetic mutation, annual mammograms and semiannual physical examinations should begin **10 years earlier than the age at diagnosis of the youngest affected relative and no later than the age of 40 years.**

(5) **Magnetic resonance imaging** (**MRI**) is recommended for screening in select **high-risk patients** including those with an elevated lifetime risk per a validated risk assessment model, a personal or family history of *BRCA* mutations or other predisposing genetic syndromes (Li–Fraumeni, Cowden, or Bannayan–Riley–Ruvalcaba), or a history of chest wall radiation between the ages of 10 and 30 years.

2. Diagnostic Imaging

a. Diagnostic mammograms are performed in the **symptomatic** patient or to **follow-up an abnormality noted on a screening mammogram.** Additional views (spot-compression views or magnification views) may be used to further characterize any lesion. A normal mammogram in the presence of a palpable mass does *not* exclude malignancy and further workup should be performed with an US, MRI, and/or biopsy. **Contrast-enhanced digital mammography** is being adopted in some centers as an adjunct in the diagnostic setting and has been shown in some series to be more sensitive than standard mammography. This modality is particularly useful in patients who cannot tolerate an MRI due to the presence of medical devices or claustrophobia.

b. US can determine whether a lesion is **solid or cystic** and can define the size, contour, or internal texture of the lesion. US is not a useful screening modality by itself due to significant false-positive rates and significant time burden to accurately examine an entire breast. When used as an adjunct with mammography, US may improve diagnostic sensitivity of benign findings to greater than 90%, especially among **younger patients for whom mammographic sensitivity is lower** due to denser breast tissue. In patients with known cancer, US is sometimes used to detect additional suspicious lesions and/or to map the extent of disease.

c. MRI is useful as an adjunct to mammography to determine extent of disease, to detect multicentric disease in the dense breast, to

assess the contralateral breast, to evaluate patients with axillary metastases and an unknown primary (i.e., occult primary breast cancer), and in the diagnostic scenario where mammogram, US, and clinical findings are inconclusive. It is also useful for assessing chest wall involvement. Patients should be counseled about the relatively high false-positive rates associated with this modality (Fig. 31-1).

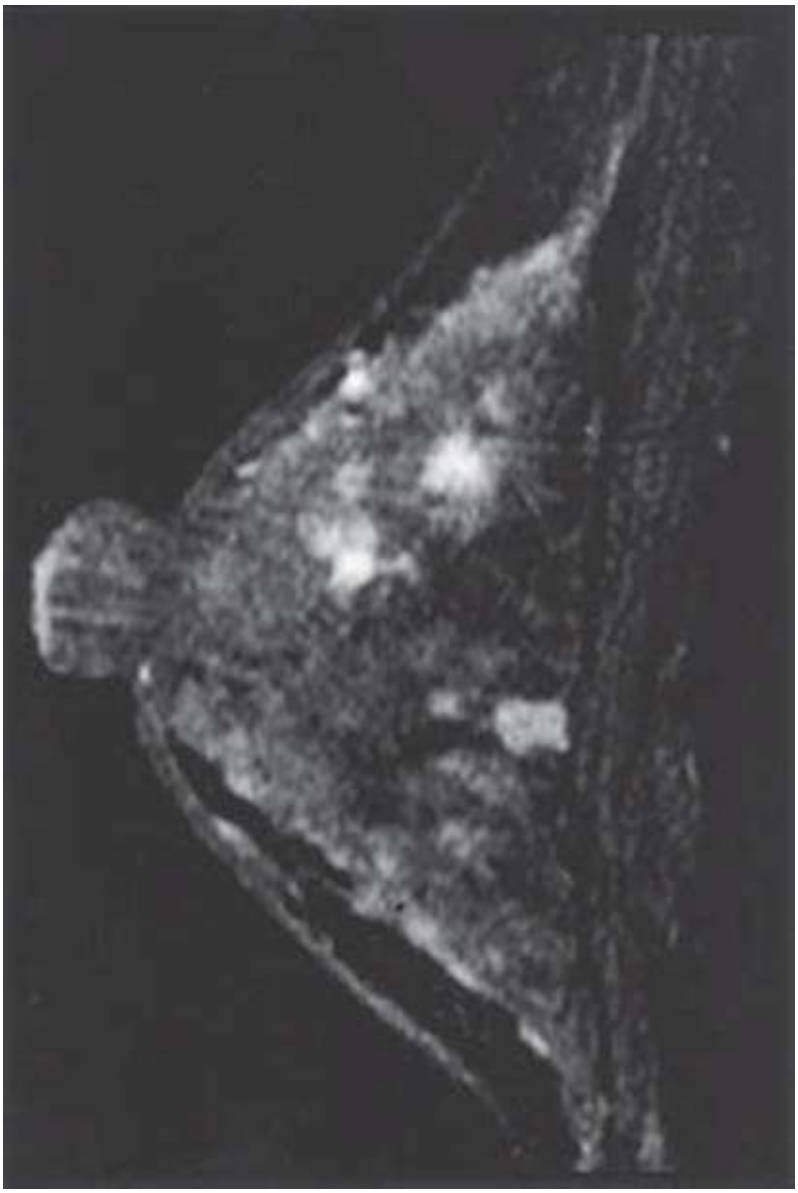


FIGURE 31-1 Magnetic resonance imaging (MRI)-detected multiple enhancing "lesions." (Reproduced with permission from Harris JR, Lippman ME, Osborne CK, et al., eds. *Diseases of the Breast*. Philadelphia, PA: Wolters Kluwer Health; 2014.)

D. Breast Biopsy

1. Palpable masses (Figs. 31-2 and 31-3)

a. Fine-needle aspiration biopsy (**FNAB**) is reliable and accurate, with sensitivity greater than 90%. FNAB can determine the presence of malignant cells and estrogen receptor (ER) and progesterone receptor (PR) status but does not give information on tumor grade or the presence of invasion. Nondiagnostic aspirates require an additional biopsy, either by surgical excision or core needle biopsy (*Am J Surg*. 1997; 174:371–385).

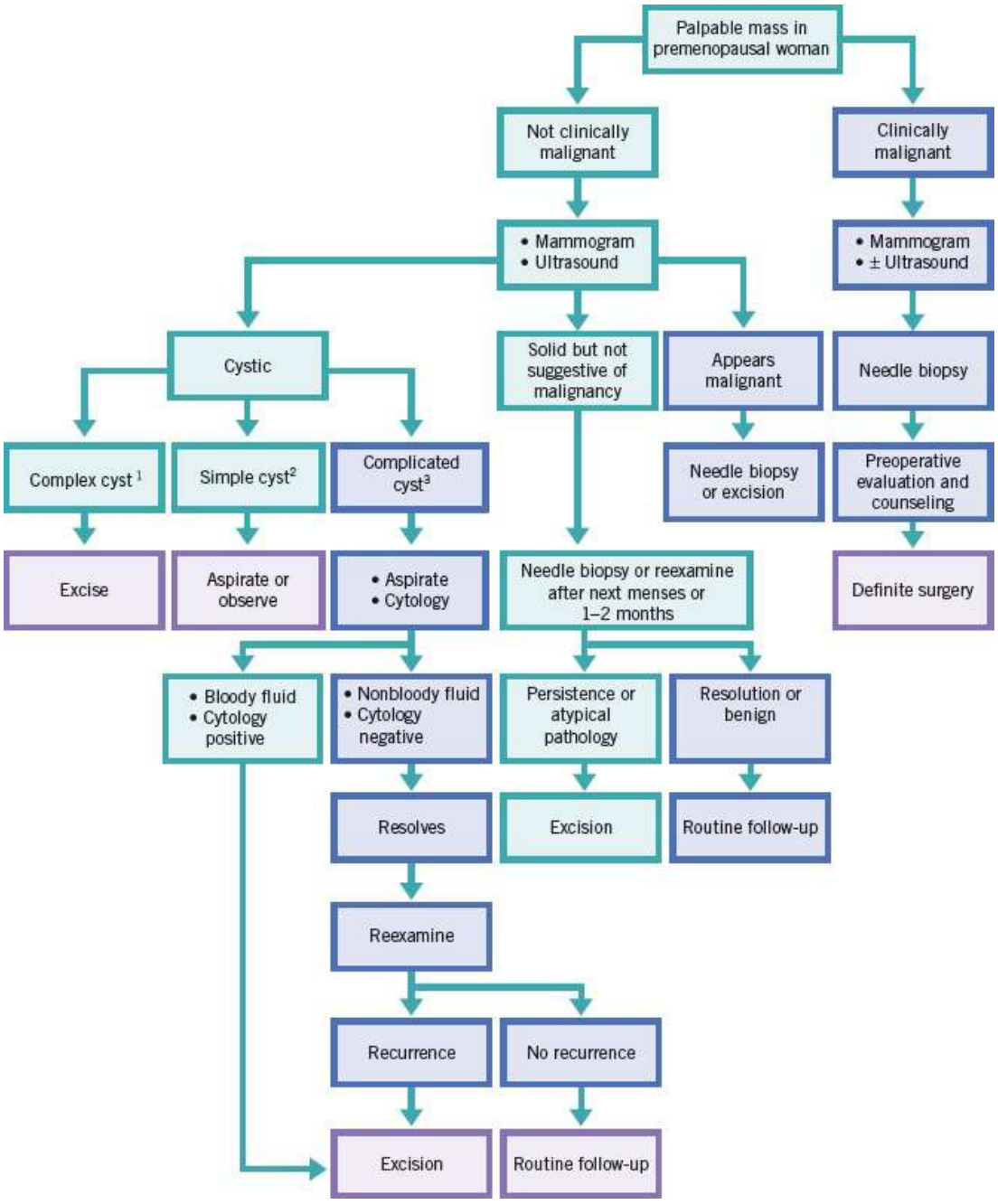


FIGURE 31-2 Algorithm for management of breast masses in premenopausal women. Based on American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) breast ultrasound reporting, cysts are: [1]complex if it has both cystic and solid components (BI-RADS 4); [2]simple if well-circumscribed margins, posterior acoustic enhancement, and no internal echoes suggesting simple fluid (BI-RADS 2); and [3]complicated if it has well-circumscribed margins, posterior acoustic enhancement, and low-level internal echoes suggesting protein, crystals, or other material (BI-RADS 3). (Reproduced with permission from Berek JS. *Berek & Novak's Gynecology*. Philadelphia, PA: Wolters Kluwer Health; 2012.)

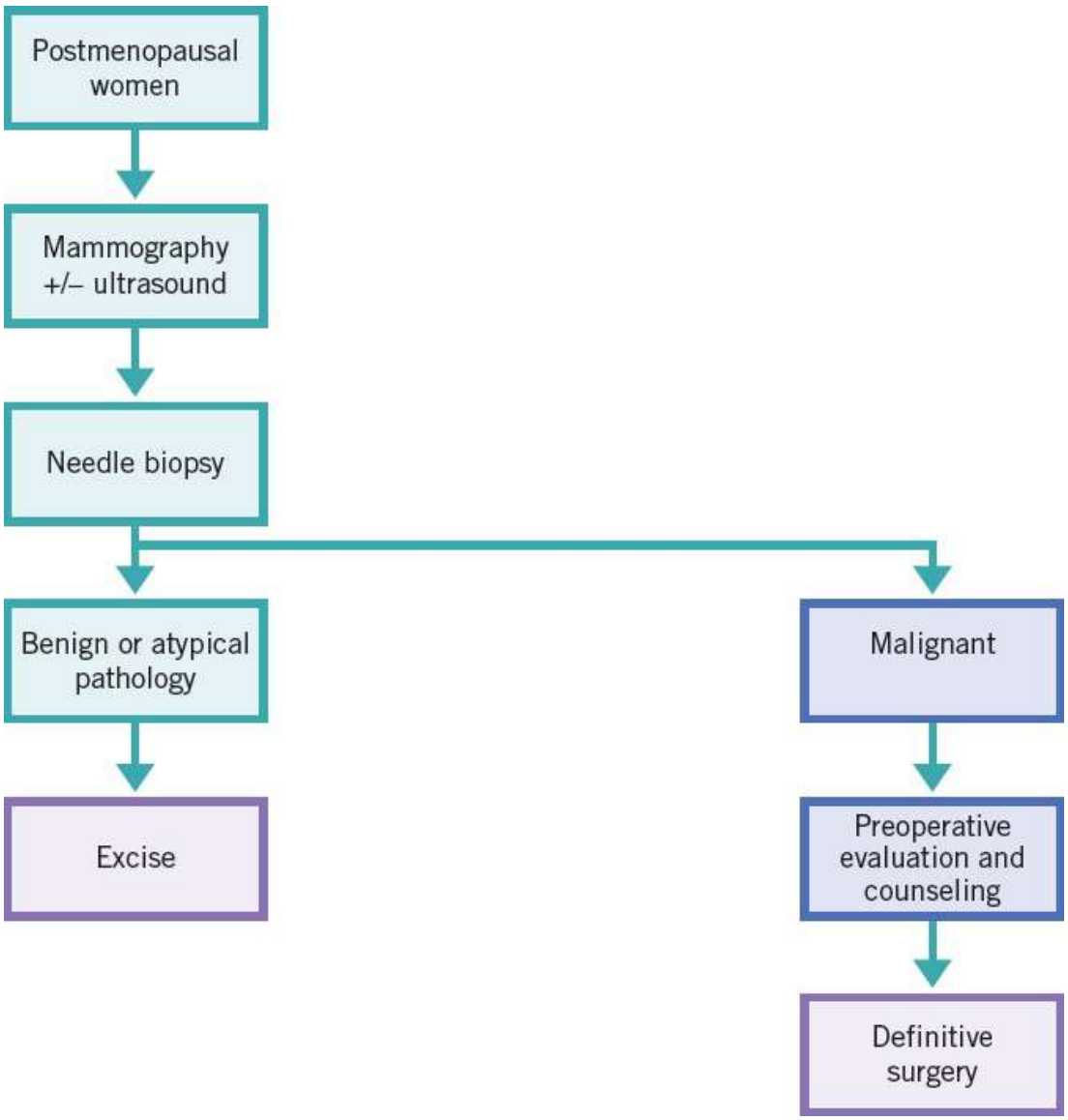


FIGURE 31-3 Algorithm for management of breast masses in postmenopausal women. (Reproduced with permission from Berek JS. *Berek & Novak's Gynecology*. Philadelphia, PA: Wolters Kluwer Health; 2012.)

b. Core needle biopsy is preferred over FNAB. It can distinguish between invasive and noninvasive cancer and provides information on tumor grade as well as receptor status. For indeterminate specimens, a surgical biopsy is necessary.

c. Excisional biopsy should primarily be used when a core biopsy cannot be done. In general, this should be an infrequent diagnostic method. It is performed in the operating room, and if feasible, incisions should be planned so that they can be incorporated into a

future mastectomy incision, if necessary. Masses should be excised as a single specimen and labeled to preserve three-dimensional orientations.

d. Incisional biopsy is indicated for the evaluation of a large breast mass suspicious for malignancy but for which a definitive diagnosis cannot be made by FNAB or core biopsy. For **inflammatory breast cancer** with skin involvement, an incisional biopsy can consist of a **skin punch biopsy.**

2. Nonpalpable lesions. Minimally invasive breast biopsy is the optimal initial tissue acquisition method and procedure of choice for obtaining a pathologic diagnosis of image-detected abnormalities. Correlation between pathology results and imaging findings is mandatory. Patients with histologically benign findings on percutaneous biopsy do not require open biopsy if imaging and pathologic findings are concordant. Patients with high-risk lesions on image-guided biopsy **(**e.g., **atypical ductal hyperplasia** [**ADH**]**, atypical lobular hyperplasia** [**ALH**]**, lobular carcinoma in situ** [**LCIS**]**, radial scar**) may have malignancy at the same site and should undergo a **surgical biopsy**.

a. Stereotactic core biopsy is used for nonpalpable mammographically detected lesions, such as microcalcifications that cannot be seen with US. In a vacuum-assisted approach, a **metallic marking clip** is usually placed through the probe after sampling is complete to allow for identification of the biopsy site if excisional biopsy or partial mastectomy becomes necessary. This is the preferred approach for lesions presenting with microcalcifications without a visible or palpable mass. Contraindications include lesions close to the chest wall or in the axillary tail and thin breasts that may allow needle strikethrough into the thorax. Superficial lesions and lesions directly beneath the nipple–areolar complex are also often not approachable with stereotactic techniques. Nondiagnostic and insufficient specimens necessitate **needle-localized excisional biopsy** (NLB; see below).

b. US-guided biopsy is generally easier to perform than stereotactic core biopsy and is the preferred method for lesions with a cystic component, as it can be used to aspirate the cyst as well as provide core biopsy specimens.

c. NLB. A needle and hookwire are placed into the breast adjacent to the concerning lesion under mammographic guidance. The patient is then brought to the operating room for an excisional biopsy. Using localization mammograms as a map, the whole hookwire, breast lesion, and a rim of normal breast tissue is removed en bloc. The specimen is oriented, and a radiograph is performed to confirm the presence of the lesion within the specimen.

III. BENIGN BREAST CONDITIONS

A. Fibrocystic Breast Change. **Fibrocystic breast change** (FBC) refers to a variety of pathologic features including stromal fibrosis, macro- and microcysts, apocrine metaplasia, hyperplasia, and adenosis (which may be sclerosing, blunt duct, or florid).

1. FBC is common and may present as breast pain, a breast mass, nipple discharge, and/or abnormalities on mammography.

2. Patients presenting with suspected FBC should be reexamined in a short interval, preferably on day 10 of the menstrual cycle, when hormonal influence is lowest, and the mass may have diminished in size.

3. A persistent dominant mass must undergo further radiographic evaluation and tissue sampling, where indicated, to exclude cancer.

B. Breast Cysts. Breast cysts frequently present as tender masses or as smooth, mobile, well-defined masses on palpation. **Aspiration can determine the nature of the mass (solid vs. cystic) but is not routinely necessary.** Cyst fluid color varies and can be clear, straw colored, or even dark green. If discovered by mammography and confirmed as simple cysts by US, **asymptomatic cysts can be observed. Symptomatic simple cysts should be aspirated.** If no palpable mass is present after drainage, the patient should be evaluated in 3 to 4 weeks. If the cyst recurs, does not resolve completely with aspiration, or yields bloody fluid with aspiration, then mammography or US should be performed to exclude intracystic tumor. Nonbloody clear fluid does not need to be sent for cytology.

C. Fibroadenoma. Fibroadenoma is the most common discrete mass in women younger than 30 years of age. They typically present as **smooth, firm, mobile masses**, and can be multiple in 20% of cases.

1. They may enlarge during pregnancy and involute after menopause.

2. They have well-circumscribed borders on mammography and US.

3. They may be managed nonoperatively if clinical and radiographic appearance is consistent with a fibroadenoma, and it is less than 2 cm. If the mass is symptomatic, greater than 2 cm, or enlarges, it should be excised to rule out a **malignant phyllodes tumor**.

D. Mastalgia. Most women (70%) experience some form of breast pain or discomfort during their lifetime. The pain may be **cyclic** (e.g., worse before a menstrual cycle) or **noncyclical**, which is more suspicious for malignancy, especially if focal and in association with a mass or bloody discharge. Benign disease is the etiology in the majority of cases. However, pain may be associated with cancer in up to 10% of patients. Once cancer has been excluded, most patients can be managed successfully with symptomatic therapy and reassurance as it resolves in up to 30% of women, though it does recur in 60%. In 15% of patients, the pain may be so disabling that it interferes with activities of daily living. A **well-fitting supportive bra** is an important first step in pain relief. **Topical nonsteroidal anti-inflammatory drugs** (**NSAIDs, e.g., diclofenac gel**) are considered first-line therapy, having been proven effective with minimal side effects in a randomized trial (*J Am Coll Surg*. 2003;196:525–530). Low-dose **tamoxifen** (an estrogen antagonist) has been shown to provide good pain relief in placebo-controlled trials with tolerable side effects (*Br J Surg*. 1988;75:845–846), although concerns over increased risks of endometrial cancer limit long-term use. **Danazol** (a derivative of testosterone), **bromocriptine, and gonadorelin analogs** have significant side effects, and their use should be limited to refractory cases. Many patients experience symptomatic relief by **reducing caffeine intake** or by **taking vitamin E** or **evening primrose oil**, although there is no scientific evidence supporting these lifestyle modifications.

1. **Superficial thrombophlebitis** of the veins overlying the breast (Mondor disease) may present as breast pain. Treatment is conservative with **NSAIDs** and **hot compresses.** Antibiotics are not generally indicated.
2. **Breast pain in pregnancy and lactation** can occur from engorgement, clogged ducts, trauma to the areola and nipple from pumping or nursing, or any of the aforementioned sources. Clogged ducts are usually treated with **warm compresses, soaks, and**

massage.

E. Nipple Discharge

1. **Lactation** is the most common physiologic cause of nipple discharge and may continue for up to 2 years after cessation of breastfeeding. In parous nonlactating women, a small amount of milk may be expressed from multiple ducts. This requires no treatment.
2. **Galactorrhea** is milky discharge unrelated to breastfeeding. Physiologic galactorrhea is the continued production of milk after lactation has ceased and menses has resumed and is often caused by continued mechanical stimulation of the nipples.
   a. **Drug-related galactorrhea** is caused by medications that affect the hypothalamic–pituitary axis by depleting dopamine (e.g., tricyclic antidepressants, reserpine, methyldopa, cimetidine, and benzodiazepines), blocking the dopamine receptor (e.g., phenothiazine, metoclopramide, and haloperidol), or having an estrogenic effect (e.g., digitalis). Discharge is generally **bilateral and nonbloody.**
   b. **Spontaneous galactorrhea** in a **nonlactating** patient may be due to a pituitary **prolactinoma**, and may be associated with amenorrhea. The diagnosis is established by measuring the **serum prolactin level** and performing a **computed tomography** (**CT**) **or MRI scan of the pituitary gland**. Treatment is **bromocriptine** or **resection** of the prolactinoma.
3. **Pathologic nipple discharge** is usually bloody (can be confirmed with guaiac test), spontaneous, unilateral, and/or originates from a single duct. Normal physiologic discharge is usually nonbloody, is from multiple ducts, can be a variety of colors (clear to yellow to green), and requires breast manipulation to produce. Cytologic evaluation is generally not useful.
   a. **Malignancy is the underlying cause in 10% of patients.**
   b. If not associated with a mass, the most likely etiologies are **benign intraductal papilloma** (peripheral papillomas put patients at slightly higher risk of malignancy), **duct ectasia,** and **fibrocystic changes.** In lactating women, serosanguineous or bloody discharge can be associated with duct trauma, infection, or epithelial proliferation associated with breast enlargement.

c. Patients with persistent spontaneous discharge from a single duct require a surgical **microdochectomy** (i.e., excision of a single duct and its associated lobule) using a ductogram or ductoscopy or **major duct excision** (i.e., excision of all retroareolar ducts).

F. Breast Infections

1. Mastitis

a. Lactational mastitis

(1) The most common causative organism is ***Staphylococcus aureus*.**

(2) It presents as a swollen, erythematous, and tender breast. Purulent discharge from the nipple is uncommon.

(3) In the early cellulitic phase, the treatment is **antibiotics**, and the frequency of **nursing or pumping should be *increased*.** Approximately 25% progress to abscess formation.

(4) **Breast abscesses** occur in the later stages and are often *not* fluctuant. The diagnosis is made by failure to improve on antibiotics, abscess cavity seen on US, or aspiration of pus. Treatment is **cessation of nursing** and **surgical drainage.**

b. Granulomatous mastitis

(1) Sudden onset of a painful breast mass that can mimic an abscess or malignancy with skin changes and ulceration. They often present with repeated symptoms with slow resolution with nonoperative management. Diagnosis is obtained via core needle biopsy of the mass.

(2) Management is supportive with NSAIDs and antibiotics if a concomitant abscess develops. Immunosuppression with steroids or methotrexate is indicated in select circumstances. Surgery is not generally recommended.

2. Nonpuerperal abscesses

Nonpuerperal abscesses result from duct ectasia with periductal mastitis, infected cysts, infected hematoma, or hematogenous spread from another source.

a. They usually are located in the peri/retroareolar area.

b. Anaerobes are the most common causative agent, although antibiotics should cover both **anaerobic and aerobic** organisms.

c. Treatment is **surgical drainage.**

d. Unresolved or recurring infection requires biopsy to exclude

cancer. These patients often have a chronic relapsing course with multiple infections requiring surgical drainage.

e. Repeated infections can result in a **chronically draining periareolar lesion or a mammary fistula** lined with squamous epithelium. Treatment is **excision of the central duct along with the fistula** once the acute infection resolves. The fistula can recur even after surgery.

G. Gynecomastia. Gynecomastia is hypertrophy of breast tissue in men that is usually secondary to an imbalance between the breast stimulatory effects of estrogen and the inhibitory effects of androgens.

1. **Pubertal** hypertrophy occurs in adolescent boys, is usually bilateral, and resolves spontaneously in 6 to 12 months.
2. **Senescent** gynecomastia is commonly seen after the age of 70 years as testosterone levels decrease.
3. **Drugs** associated with this are similar to those that cause galactorrhea in women, including digoxin, spironolactone, methyldopa, cimetidine, tricyclic antidepressants, phenothiazine, reserpine, and marijuana. Drugs used for androgen blockade, such as **luteinizing hormone releasing hormone analogues** for the treatment of prostate cancer and **5-alpha reductase inhibitors** (e.g., finasteride) for the management of benign prostatic hypertrophy may also result in gynecomastia.
4. Tumors can cause gynecomastia secondary to excess secretion of estrogens. These include testicular teratomas and seminomas, bronchogenic carcinomas, adrenal tumors, and tumors of the pituitary and hypothalamus.
5. Gynecomastia may be a manifestation of systemic diseases such as hepatic cirrhosis, renal failure, hyperthyroidism, and malnutrition.
6. During the workup of gynecomastia, cancer should be excluded by mammography and subsequently by biopsy if a mass is found. If workup fails to reveal a medically treatable cause, or if the enlargement fails to regress, **excision of breast tissue via a periareolar incision** can be performed.

H. High-Risk and Premalignant Conditions

1. **ADH** and **ALH** are proliferative lesions with cell atypia that arise within breast ducts and lobules, respectively. ADH confers a four to

five times increased relative risk of developing an invasive breast malignancy. Historically, ALH was thought to have a weaker association with malignancy, but a recent study suggested that both lesions confer equal levels of risk (*Cancer Prev Res*. 2014;7:211–217). If atypia is found on needle biopsy, **excisional biopsy** is warranted to rule out associated malignancy. If no malignancy is found on postoperative pathology, patients with these conditions can simply undergo surveillance with imaging and physician examination at increased intervals as compared to low-risk patients. **Chemoprevention with tamoxifen** is also an option.

2. **LCIS** is not considered a preinvasive lesion but rather an indicator for increased breast cancer risk of approximately 1% per year (∼20% to 30% at 15 years) (*J Natl Compr Canc Netw*. 2006;4:511–522).
   - **a.** It may be **multifocal** or **bilateral.**
   - **b.** The cancer that develops may be **invasive ductal** or **lobular** and may occur in either breast.
   - **c.** LCIS has loss of **E-cadherin** (involved in cell–cell adhesion), which can be stained for on pathology slides to clarify cases that are borderline ductal carcinoma in situ (DCIS) from LCIS.
   - **d. Pleomorphic LCIS** is a particularly aggressive subtype of LCIS that is treated more like DCIS; it tends to have less favorable biologic markers.
   - **e. Treatment options** are (1) lifelong close **surveillance,** (2) **bilateral total mastectomies** with immediate reconstruction for selected women with a strong family history after appropriate counseling, or (3) **chemoprevention** with **tamoxifen, raloxifene** (which has been validated in the postmenopausal setting), or an **aromatase inhibitor.**

IV. MALIGNANCY OF THE BREAST

A. Epidemiology. Breast cancer is the **most common noncutaneous cancer in women,** with a lifetime risk of **one in eight women.** In the United States in 2017, an estimated 252,710 new cases of invasive breast cancer and 63,410 new cases of noninvasive in situ carcinoma of the breast were diagnosed. In that same period, approximately 40,610 women died of breast cancer, making it the second-leading cause of cancer death in women, exceeded only by lung cancer (ACS. *Breast*

Cancer Facts & Figures 2017–2018. Atlanta, GA: ACS, Inc. 2017).

B. Staging. Breast cancer is staged by using the **American Joint Committee on Cancer** (**AJCC**) system, which is both a **clinical and pathologic staging system** and is based on the tumor, node, and metastasis (TNM) system (Tables 31-2 through 31-6). It is important to note that TNM staging is not applicable to breast sarcomas, lymphomas, or phyllodes tumors. Workup should include the following in addition to breast-specific imaging:

1. **Complete blood cell count** (CBC), **complete metabolic panel** (CMP) including **liver function tests** (**LFTs**)**,** and **chest x-ray.**
2. A **bone scan,** if the alkaline phosphatase or calcium level is elevated.
3. **CT of the abdomen** if LFTS are abnormal.
4. **Patients with clinical stage III or IV** disease should undergo bone scan and CT of the chest/abdomen/pelvis due to a high probability of distant metastases.

C. Tumor Biomarkers and Prognostic Factors. These should be evaluated on all tumor specimens. The **presence or absence of disease in axillary lymph nodes** is the single most important prognostic factor in breast cancer. **Tumor size** and **grade** (which is based on degrees of *glandular differentiation*, *mitotic count*, and *nuclear grade*) are the most reliable pathologic predictors of outcome for patients without axillary nodal involvement. **High grade** (i.e., **grade 3** on a scale of 1 to 3) is a poor prognostic factor.

1. **Hormone receptors.** Expression of **ER** and **PR** should be evaluated by immunohistochemistry. Intense ER and PR staining is a good prognostic factor.
2. ***Her2/neu (ERB2).*** *Her2/neu* is a member of the **epidermal growth factor receptor** (EGFR) family and is involved in cell growth regulation. Overexpression due to gene amplification is seen in approximately 30% of patients with breast cancer. *Her2/neu* expression is measured by **immunohistochemistry** and, if equivocal, by **fluorescence in situ hybridization** (**FISH**). Overexpression of *Her2/neu* is a poor prognostic factor, as it results in an increased rate of metastasis, decreased time to recurrence, and decreased overall survival. Patients with *Her2/neu*-amplified (HER2+) tumors are treated with targeted monoclonal antibody therapies, such as

trastuzumab (**Herceptin**) or **pertuzumab** (**Perjeta**). Pertuzumab, in combination with trastuzumab and docetaxel, has demonstrated significant efficacy in prolonging progression-free survival in metastatic HER2+ breast cancer (*Lancet Oncol*. 2013;14:461–471), and its efficacy in treating other stages is the subject of several ongoing clinical trials.

TABLE 31-2	AJCC Staging—Primary Tumor (T)[a]
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	DCIS
Tis (LCIS)	LCIS
Tis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)[b]
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma

T4c	Both T4a and T4b
T4d	Inflammatory carcinoma

[a]The T classification of the primary tumor is the same regardless of whether it is based on clinical or pathologic criteria, or both. Size should be measured to the nearest millimeter. If the tumor size is slightly less than or greater than a cutoff for a given T classification, it is recommended that the size be rounded to the millimeter reading that is closest to the cutoff. For example, a reported size of 1.1 mm is reported as 1 mm, or a size of 2.01 cm is reported as 2 cm. Designation should be made with the subscript "c" or "p" modifier to indicate whether the T classification was determined by clinical (physical examination or radiologic) or pathologic measurements, respectively. In general, pathologic determination should take precedence over clinical determination of T size.

[b]Invasion of the dermis alone does not qualify as T4.

DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

TABLE 31-3 AJCC Staging—Regional Lymph Nodes (N)

	Clinical
NX	Regional lymph nodes cannot be assessed (e.g., previously removed)
N0	No regional lymph node metastases
N1	Metastases to movable ipsilateral level I, II axillary lymph node(s)
N2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted OR Metastases in clinically detected[a] ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases
N2a	Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
N2b	Metastases only in clinically detected[a] ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases
N3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph

	node involvement OR Metastases in clinically detected[a] ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases OR Metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
N3a	Metastases in ipsilateral infraclavicular lymph node(s)
N3b	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
N3c	Metastases in ipsilateral supraclavicular lymph node(s)

[a]Clinically detected is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine-needle aspiration biopsy with cytologic examination. Confirmation of clinically detected metastatic disease by fine-needle aspiration without excision biopsy is designated with an (f) suffix, for example, cN3a(f). Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, for example, cN1. Information regarding the confirmation of the nodal status will be designated in site-specific factors as clinical, fine-needle aspiration, core biopsy, or sentinel lymph node biopsy. Pathologic classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathologic T assignment.

TABLE 31-4 AJCC Staging—Pathologic Lymph Node Status (pN)[a,b,c]

pNX	Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathologic study)
pN0	No regional lymph node metastasis identified histologically

Note: ITCs are defined as small clusters of cells ≤0.2 mm, or single tumor cells, or a cluster of <200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by IHC

methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

pN0(i−)	No regional lymph node metastases histologically, negative IHC
pN0(i+)	Malignant cells in regional lymph node(s) ≤0.2 mm (detected by H&E or IHC including ITC)
pN0(mol−)	No regional lymph node metastases histologically, negative molecular findings (RT-PCR)
pN0(mol+)	Positive molecular findings (RT-PCR), but no regional lymph node metastases detected by histology or IHC
pN1	Micrometastases OR Metastases in 1–3 axillary lymph nodes AND/OR Metastases in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected[b]
pN1mi	Micrometastases (>0.2 mm and/or >200 cells but none >2.0 mm)
pN1a	Metastases in 1–3 axillary lymph nodes, at least one metastasis >2.0 mm
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected[b]
pN1c	Metastases in 1–3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected
pN2	Metastases in 4–9 axillary lymph nodes OR Metastases in clinically detected[b] internal mammary lymph nodes in the *absence* of axillary lymph node metastases

pN2a	Metastases in 4–9 axillary lymph nodes (at least 1 tumor deposit >2 mm)
pN2b	Metastases in clinically detected[c] internal mammary lymph nodes in the *absence* of axillary lymph node metastases
pN3	Metastases in ≥10 axillary lymph nodes OR Metastases in infraclavicular (level III axillary) lymph nodes OR Metastases in clinically detected[c] ipsilateral internal mammary lymph nodes in the *presence* of one or more positive level I, II axillary lymph nodes OR Metastases in >3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected[b] OR Metastases in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in ≥10 axillary lymph nodes (at least 1 tumor deposit >2.0 mm) OR Metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	Metastases in clinically detected[c] ipsilateral internal mammary lymph nodes in the *presence* of one or more positive axillary lymph nodes OR Metastases in >3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected[b]
pN3c	Metastases in ipsilateral supraclavicular lymph nodes

[a]Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for "sentinel node," for example, pN0(sn).

[b]"Not clinically detected" is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.

[c]"Clinically detected" is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine-needle aspiration biopsy with cytologic examination.

AND, axillary node dissection; H&E, hematoxylin and eosin stain; IHC, immunohistochemical; ITC, isolated tumor cells; RT-PCR, reverse transcriptase/polymerase chain reaction.

Posttreatment ypN

- Posttreatment yp "N" should be evaluated as for clinical (pretreatment) "N" methods above. The modifier "sn" is used only if a sentinel node evaluation was performed after treatment. If no subscript is attached, it is assumed that the axillary nodal evaluation was by AND.
- The X classification will be used (ypNX) if no yp posttreatment sn or AND was performed.
- N categories are the same as those used for pN.

TABLE 31-5 AJCC Staging—Distant Metastases (M)

M0	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other nonregional nodal tissue that are ≤0.2 mm in a patient without symptoms or signs of metastases
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven >0.2 mm

Posttreatment yp M classification. The M category for patients treated with neoadjuvant therapy is the category assigned in the clinical stage, prior to initiation of neoadjuvant therapy. Identification of distant metastases after the start of therapy in cases where pretherapy evaluation showed no metastases is considered progression of disease. If a patient was designated to have detectable distant metastases (M1) before chemotherapy, the patient will be designated as M1 throughout.

3. Other **adverse tumor characteristics** include lack of expression of any tumor biomarkers, known as triple-negative breast cancer, **lymphovascular invasion** (**LVI**), and other indicators of a high proliferative rate (>5% of cells in the **S phase** of mitosis or >20% **Ki-67**).

D. Ductal Carcinoma In Situ (DCIS). DCIS is a lesion with malignant cells that have not penetrated the basement membrane of the mammary ducts.

1. **DCIS** is treated as a **malignancy** because it has the potential to develop into an invasive breast cancer.

- It is usually detected by mammography as **clustered pleomorphic calcifications** (Fig. 31-4).
- **Physical examination is normal** in the majority of patients.
- It may advance in a **segmental manner, with gaps between disease areas.**
- It can be **multifocal** (two or more lesions >5 mm apart within the same index quadrant) or **multicentric** (in different quadrants).

(1) Histology

(a) There are **five architectural subtypes:** papillary, micropapillary, solid, cribriform, and comedo (necrosis). Specimens are also grouped as ***comedo* versus *noncomedo***.

(b) The **high-grade subtype** is often associated with microinvasion, a higher proliferation rate, aneuploidy, gene amplification, and a higher local recurrence rate.

TABLE 31-6 AJCC Anatomic Stage/Prognostic Groups[a,b]

Stage	T	N	M
0	Tis	N0	M0
IA	T1[a]	N0	M0
IB	T0	N1mi	M0
	T1[b]	N1mi	M0
IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0

	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

[a]T1 includes T1mi.

[b]T0 and T1 tumors with nodal micrometastases only are excluded from stage IIA and are classified stage IB.

- M0 includes M0(i+).
- The designation pM0 is not valid; any M0 should be clinical. If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered stage IV and remains stage IV regardless of response to neoadjuvant therapy. Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.
- Postneoadjuvant therapy is designated with “yc” or “yp” prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

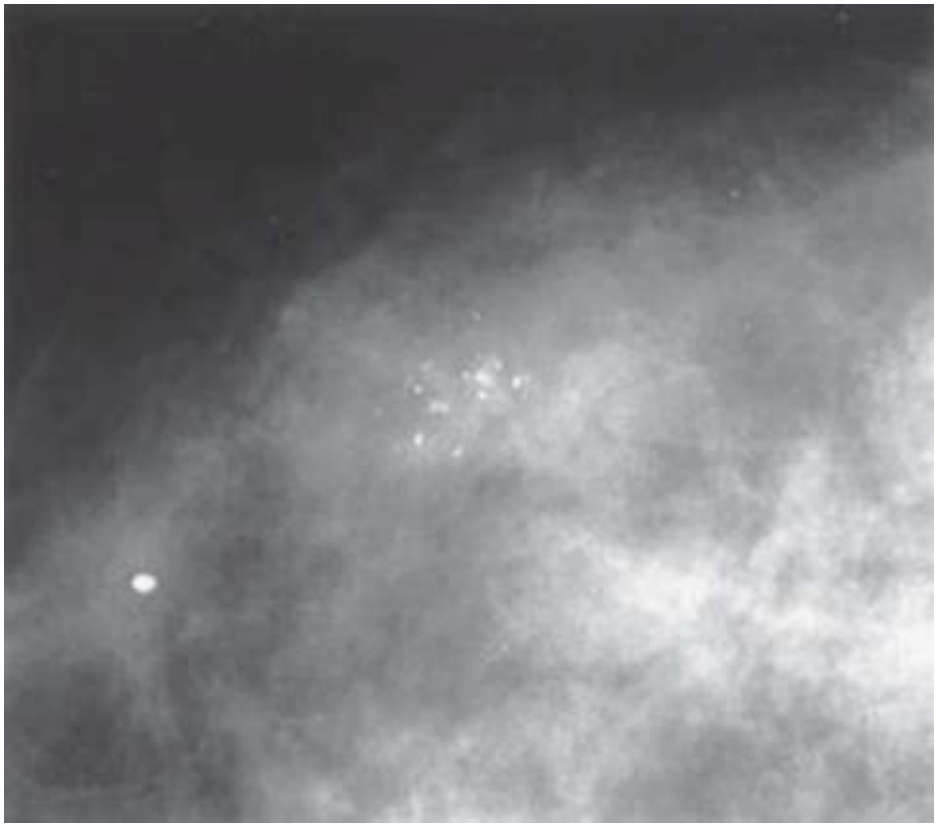


FIGURE 31-4 Mammogram of ductal carcinoma in situ (DCIS). (Reproduced with permission from Harris JR, Lippman ME, Osborne CK, et al., eds. *Diseases of the Breast*. Philadelphia, PA: Wolters Kluwer Health; 2014.)

(c) ER and PR expression levels should be assessed if hormone therapy is being considered.

(2) Treatment

(a) **Surgical excision alone** (via partial mastectomy) with **margins greater than 2 mm** was deemed sufficient in a consensus guideline released by the Society of Surgical Oncology, American Society for Radiation Oncology and the American Society of Clinical Oncology when followed by whole breast irradiation (*J Clin Oncol*. 2016;34:33; 4040–4046). The addition of adjuvant radiation reduces the local recurrence rate but does not impact survival. Approximately half of DCIS recurrences present as invasive ductal carcinomas. **Surgical options** depend on the extent of disease, grade, margin status, multicentricity of disease, and patient age.

(1) Partial mastectomy. For unicentric nonpalpable lesions, **needle localization** (sometimes with **bracketing**) is required to identify the area to be excised in most cases.

(2) Total (**simple**) **mastectomy** with or without immediate reconstruction is recommended for patients with multicentric lesions, extensive involvement of the breast (i.e., high tumor-to-breast-size ratio), or persistently positive margins with partial mastectomy.

(b) Assessment of axillary lymph nodes. Axillary dissection is not performed for pure DCIS.

(1) Sentinel lymph node biopsy (**SLNB**) may be considered when there is a reasonable probability of finding invasive cancer on final pathologic examination (e.g., >4 cm, palpable, comedo subtype, or high grade).

(2) Some surgeons perform SLNB in all patients with DCIS undergoing mastectomy because SLNB cannot be performed postmastectomy if an occult invasive cancer is found. This is an area of ongoing controversy and research.

(3) A positive sentinel node indicates invasive breast cancer and changes the stage of the disease. Historically, a **completion axillary dissection** was indicated for patients with a positive sentinel node, but the findings of the American College of Surgeons Oncology Group (ACOSOG) trial Z011, have contributed to a paradigm shift in the management of axillary disease (see later discussion in Management of the Axilla).

(c) Adjuvant therapy

(1) For pure DCIS, there is no added benefit from systemic chemotherapy because the disease is confined to the ducts of the breast. However, in those patients with **ER positive** (**ER+**) **DCIS,** adjuvant **tamoxifen** can reduce the risk of breast cancer recurrence by 36% over 5 years and the risk of developing a new contralateral breast cancer (NSABP B-24 trial, *J Clin Oncol*.

2012;30:1268–1273) but confers no survival benefit. **Aromatase inhibitors** (e.g., **anastrozole, exemestane, letrozole**), which block the peripheral conversion of androgens into estrogens by inhibiting the enzyme aromatase but do not affect estrogen produced by the ovaries, are sometimes used as an alternative in postmenopausal patients.

(2) Adjuvant radiation should be given to patients with DCIS treated with partial mastectomy to **decrease the rate** of **local recurrence** (NSABP B-17 trial, *J Natl Cancer Inst*. 2011;103:478–488). This is especially true for younger women with close margins or large tumors. However, there is no survival benefit. For older patients with smaller, widely excised DCIS of low or intermediate grade, the benefit of radiation therapy is less clear and adjuvant radiation may not be necessary (*Ann Surg Oncol*. 2013;20:3175–3179).

(d) The University of Southern California/Van Nuys Prognostic Index (Table 31-7) is a numerical algorithm used to determine which patients with DCIS are at greatest risk for recurrence and would therefore benefit from aggressive treatment. In order to achieve a local recurrence rate of less than 20% at 12 years, **surgical excision** alone is recommended for all patients scoring 4, 5, or 6 and patients who score 7 but have margin widths ≥3 mm; **surgical excision plus radiation therapy** for those who score 7 and have margins <3 mm, patients who score 8 and have margins ≥3 mm, and for patients who score 9 and have margins ≥5 mm; and **mastectomy** for patients who score 8 and have margins <3 mm, who score 9 and have margins <5 mm, and for all patients who score 10, 11, or 12 (*J Natl Cancer Inst Monogr*. 2010;2010(41):193–196).

TABLE 31-7 University of Southern California/Van Nuys Prognostic Index Scoring System[a]

	Score

	1	2	3
Size (mm)	≤15	>15–40	≥41
Margins (mm)	≤10	1–9	<1
Histology	Grade 1/2 without necrosis	Grade 1/2 with necrosis	Grade 3 with or without necrosis
Age	>60	40–60	<40

[a]A score, ranging from 1 for lesions with the best prognosis to 3 for lesions with the worst prognosis, is given for each of the four prognostic predictors, thus establishing a range of 4 (best prognosis) to 12 (worst prognosis) for total scores.

Modified from Silverstein MJ, Lagios MD. Choosing treatment for patients with ductal carcinoma in situ: fine tuning the University of Southern California/Van Nuys Prognostic Index. *J Natl Cancer Inst Monogr*. 2010;2010(41):193–196.

E. Invasive Breast Cancer

1. The most common **histology** identified includes **infiltrating ductal** (75% to 80%), **infiltrating lobular** (5% to 10%), **medullary** (5% to 7%), **mucinous** (3%), and **tubular** (1% to 2%).
2. Surgical options for **early-stage** (**T1–2, N1, or less clinical disease**) breast cancer:
   a. **Mastectomy** with or without reconstruction.
      (1) **Radical** (**Halsted**) **mastectomy** involves total mastectomy, complete ALND (levels I, II, and III), removal of the pectoralis major and minor muscles, and removal of all overlying skin. This surgical approach is largely historical and is rarely, if ever, performed in modern practice.
      (2) **Modified radical mastectomy** (MRM) involves total mastectomy and ALND. It is indicated for patients with clinically positive lymph nodes or a positive (i.e., with macrometastases) axillary node based on previous SLNB or FNAB.
      (3) **Total** (**simple**) **mastectomy with SLNB** is for patients with a clinically negative axilla. A **skin-sparing mastectomy** (preserves skin envelope and inframammary ridge) may be performed with immediate reconstruction, resulting in improved cosmesis. The nipple–areolar complex, a rim of

periareolar breast skin, and any previous excisional biopsy or partial mastectomy scars are excised. **Nipple-sparing mastectomy,** in which all of the skin including the nipple–areolar complex is left in place, may also be an option for select women. Patients must be counseled that the preserved nipple is often insensate and that nipple necrosis is not an infrequent complication of the procedure, occurring in an estimated 10% to 15% of patients (*Breast J*. 2014;20:69–73).

(4) Immediate reconstruction at the time of mastectomy should be offered to eligible patients. Options include latissimus dorsi myocutaneous flaps, transverse rectus abdominis myocutaneous (TRAM) flaps, and inflatable tissue expanders followed by exchange for saline or silicone implants. Immediate reconstruction has been shown not to affect patient outcome adversely nor delay chemotherapy, and the detection of subsequent recurrence is not delayed.

(5) Follow-up after mastectomy should involve physical examination every 3 to 6 months for 3 years, then every 6 to 12 months for the next 2 years, and then annually (*J Clin Oncol*. 2013;31:961–965). Mammography of the contralateral breast should continue yearly. Regular gynecologic follow-up is recommended for all women (N.B.: Tamoxifen increases risk of endometrial cancer).

b. Breast conservation therapy (**BCT, partial mastectomy** and SLNB [or ALND; see later discussion] followed by breast irradiation).

(1) Several trials have demonstrated that BCT with adjuvant radiation therapy has similar survival and recurrence rates to those for MRM (*J Clin Oncol*. 1992;10:976–983).

(2) Surgical margins should demonstrate **no tumor touching the inked specimen margins** based on consensus guidelines released by the Society of Surgical Oncology and American Society for Radiation Oncology (*Annals Surg Onc*. 2014;21:704–716).

(3) Contraindications for BCT. Not every patient is a candidate for BCT. It is contraindicated in patients who may be unreliable with follow-up or with the radiation therapy treatments that

take place 5 days a week for 5 to 6 weeks, when the extent of disease prevents adequate negative margins, when there is a high tumor-to-breast-size ratio that prevents adequate resection without major deformity, with persistently positive margins on re-excision partial mastectomy, and with the inability to receive adjuvant radiation (e.g., prior radiation to the chest wall, first- and second-trimester pregnancy in which the delay of radiation to the postpartum state is inappropriate, collagen vascular diseases such as scleroderma).

(4) For patients with large tumors who desire BCT, **neoadjuvant chemotherapy** and/or **neoadjuvant hormonal therapy** may be offered to attempt to reduce the size of the tumor to make BCT possible.

(5) Partial mastectomy incisions should be planned so that they can be incorporated into a mastectomy incision should that prove necessary. Incisions for partial mastectomy and either SLNB or ALND should be separate.

(6) Adjuvant radiotherapy decreases the breast cancer recurrence rate from approximately 35% to less than 10% at 12 years and is a required component of BCT (*N Engl J Med*. 1995;333:1456–1461).

(7) Follow-up after BCT. Physical examinations are the same as those for mastectomy (see earlier discussion). A posttreatment mammogram of the treated breast is performed no earlier than 6 months after completion of radiation therapy to establish a new baseline, after which annual bilateral mammograms can resume in conjunction with regular gynecologic follow-up (*J Clin Oncol*. 2013;31:961–965).

c. Management of the axilla. Approximately 30% of patients with clinically negative examinations will have positive lymph nodes in an ALND specimen. The presence and number of lymph nodes involved affect staging and thus prognosis. However, complications are not infrequent (see later discussion). Thus, SLNB was developed to provide sampling of the lymph nodes without subjecting patients to ALND.

(1) The **SLNB** procedure requires a multidisciplinary approach, including nuclear medicine, pathology, and radiology.

(a) Blue dye (either **lymphazurin or methylene blue**) is injected in the operating room and/or **technetium-labeled sulfur colloid** is injected in the nuclear medicine department, radiology suite, or sometimes by the surgeon. The combination of blue dye and radioisotope provides higher node identification rates and increases the sensitivity of the procedure relative to using either agent alone. The goal is to identify the primary draining lymph node(s) in the axillary nodal basin.

(b) A variety of injection techniques are used: **Intraparenchymal** versus **intradermal** (intradermal methylene blue will cause skin necrosis at the injection site), **peritumoral** versus **periareolar.**

(c) The SLN is identified by its blue color, by high activity detected by a handheld gamma probe, and/or by a blue lymphatic seen to enter a nonblue node. Palpable nodes are also sentinel nodes even if not blue or radioactive.

(d) More than one SLN is identified 20% to 30% of the time.

(e) Experienced surgeons (those who have performed at least 30 SLNB with ALND for confirmation) can identify the SLN in greater than 90% of patients, accurately predicting the patients' remaining axillary lymph node status in greater than 97% of cases.

(f) Historically, **standard completion ALND was recommended if an SLNB was positive for metastasis greater than or equal to 0.2 mm; furthermore, isolated tumor cells were to be considered N0 disease and not important in the determination of therapeutic decisions.** This remains the standard of care in many practices, but this surgical paradigm has recently been challenged by a number of studies, most significantly by the results of the **ACOSOG Z0011 trial.** This randomized trial compared the overall survival and local recurrence rates for patients with T1–2 tumors and limited SLN metastatic disease who received BCT and systemic therapy and either had ALND or no further axillary procedures (*JAMA*. 2011;305:569–575). There was no difference in the two groups, leading many to

defer completion ALND for this subgroup of patients. All patients underwent partial mastectomy, whole breast radiation, and systemic therapy, thus, the results cannot be generalized to all patients with a positive SLN. Nevertheless, this study contributed to growing concern that excess surgery is being performed for axillary disease. This concern has garnered further discussion following publication of the results of the **AMAROS trial,** a European randomized noninferiority trial that compared completion ALND to axillary radiation therapy for a positive SLN in patients with T1–2 primary breast cancer and no palpable lymphadenopathy; rates of local recurrence were statistically equivalent and radiation was associated with less lymphedema than ALND (*Lancet Oncol*. 2014;15:1303–1310). Furthermore, the prognostic significance of **isolated tumor cells** has been brought into question by the **Dutch MIRROR cohort study,** which demonstrated an association between disease-free survival and isolated tumor cells in women who had been diagnosed at a young age and in women with triple-negative cancer who did not undergo either ALND or axillary radiation (*N Engl J Med*. 2009;361:653–663).

(2) ALND. Patients with **clinically positive lymph nodes** should undergo ALND for local control. It involves:

(a) Removal of **level I** and **level II nodes** and, if grossly involved, level III nodes. Motor and sensory nerves are preserved unless there is direct tumor involvement.

(b) An ALND should remove **10 or more nodes.** The number of nodes identified is often pathologist dependent. Patients with **four or more positive lymph nodes** should undergo **adjuvant radiation to the axilla.** Selective patients with one to three positive nodes may also benefit from radiation therapy to the axilla.

(c) The most frequent **postoperative complications** are wound infections and seromas. Persistent seroma may be treated with **repeated aspirations or reinsertion of a drain.** Other complications include pain and numbness in the axilla and

upper arm, impaired shoulder mobility, and **lymphedema,** which occurs in approximately 10% to 40% of women undergoing axillary dissection. Radiation to the axilla increases the risk of this complication. The most effective therapy is **early intervention with intense occupational therapy with massage. Graded pneumatic compression devices and a professionally fitted compression sleeve** can also provide relief and prevent worsening of lymphedema. Blood draws, blood pressure cuffs, and intravenous lines should be avoided in the affected arm, mainly to avoid infection. Infections of the hand or arm should be treated promptly and aggressively with antibiotics and arm elevation because infection can damage lymphatics further and cause irreversible lymphedema. Lymphedema increases the risk of developing **angiosarcoma.**

(3) Management of the axilla in patients with nodal disease who undergo neoadjuvant chemotherapy is another area of active research. SLNB may be used in selected patients with a clinically negative axilla, but the accuracy of this practice has been called into question by the results of the **ACOSOG Z1071 trial** which evaluated the role of SLNB in patients with axillary disease prior to neoadjuvant chemotherapy. In this study, SLNB was followed by completion ALND to document accuracy of SLNB and false-negative rate (FNR). The FNR of SLNB was 12.6%; however, the FNR was significantly lower (10.8%) when mapping was completed using a radioactive isotope and blue dye when compared to a single modality (20.3%). Given the elevated FNR, the authors challenge the use of SLNB in patients with nodal disease prior to undergoing neoadjuvant chemotherapy (*JAMA*. 2014;310:1455–1461). Work is ongoing to determine the best method of axillary staging after neoadjuvant therapy and the impact on long-term outcomes.

3. **Adjuvant systemic therapy** is given in appropriate patients after completion of surgery.
   a. All node-positive patients should be considered for adjuvant chemotherapy.

(1) Regimens are guided by the tumor biomarkers. Typical regimens consist of four to eight cycles of a combination of **cyclophosphamide** and an **anthracycline** followed by a **taxane** administered every 2 to 3 weeks.

(2) Patients with **ER-positive tumors** receive **adjuvant hormonal therapy** for 5 to 10 years. **Tamoxifen** is given to premenopausal women, and **aromatase inhibitors** are given to postmenopausal women.

(3) In postmenopausal women older than 70 years, chemotherapy is performed less frequently. In postmenopausal women with ER+ tumors, tamoxifen or an aromatase inhibitor is frequently the sole adjuvant medical therapy.

(4) In patients with ***Her2/neu-positive tumors***, polychemotherapy is combined with biologic therapy targeting the Her2/neu protein (see earlier discussion).

b. Node-negative patients may have increased disease-free survival from adjuvant chemotherapy and/or hormonal therapy. An individualized approach is crucial and requires thorough discussion with the patient regarding the risks of recurrence without adjuvant therapy, the cost and toxicities of treatment, and the expected benefit in risk reduction and survival.

(1) Node-negative patients who are at **high risk** and benefit the most from adjuvant chemotherapy include those with **tumors greater than 1 cm, high tumor grade, *Her2/neu* expression, aneuploidy, elevated Ki-67 expression, high percentage of cells in S phase, LVI, and ER/PR-negative tumors.**

(2) The NSABP B-20 trial and the International Breast Cancer Study Group Trial IX showed that **polychemotherapy in combination with tamoxifen was superior to tamoxifen alone** in increasing disease-free and overall survival, especially in ER-negative patients, regardless of tumor size.

(3) The St. Gallen Consensus Panel in 1997 suggested that patients who have node-negative disease and whose tumors are 1 cm or less and ER positive may be spared adjuvant chemotherapy but still may benefit from adjuvant endocrine therapy.

4. Adjuvant radiation

a. Indications for adjuvant radiation to the chest wall and axilla **after mastectomy** include T3 and T4 tumors, attachment to the pectoral fascia, positive surgical margins, skin involvement, involved internal mammary nodes, inadequate or no axillary dissection, four or more positive lymph nodes, and residual tumor on the axillary vein. Presence of one to three positive axillary nodes is a relative indication (*N Engl J Med*. 1997;337:949–955). (See earlier discussion of radiation after BCT.)

b. Complications. Radiation to the chest wall can cause skin changes. Infrequent complications include interstitial pneumonitis, spontaneous rib fracture, breast fibrosis, pericarditis, pleural effusion, and chest wall myositis. Radiation to the axilla can increase the incidence of lymphedema and axillary fibrosis.

5. Locally advanced breast cancer (**LABC**)

a. LABC includes T3, T4, N2, and/or N3 clinical disease, and because up to 10% to 20% of these patients have distant metastasis at the time of presentation, all should receive a **bone scan** and **CT of the chest and abdomen** before treatment.

b. Noninflammatory LABC patients should receive **neoadjuvant chemotherapy** (often cyclophosphamide combined with an anthracycline [e.g., doxorubicin] and a taxane), followed by **surgery** and **radiation** as based on previously discussed criteria. Neoadjuvant chemotherapy also provides information regarding tumor response to treatment that may aid to guide further adjuvant therapy. Additional adjuvant chemotherapy is also necessary in select cases.

c. Inflammatory LABC (**T4d**) is characterized by erythema, warmth, tenderness, and edema (i.e., peau d'orange, Fig. 31-5), it is often misdiagnosed initially as mastitis and represents 1% to 6% of all breast cancers. **Skin punch biopsy** confirms the diagnosis, and in two-thirds of cases, tumor emboli are seen in dermal lymphatics. An **underlying mass** is present in 70% of cases. Associated **axillary adenopathy** occurs in 50% of cases. Approximately 30% of patients have distant metastasis at the time of diagnosis. Despite aggressive multimodal therapy, median survival is approximately 2 years, with a 5-year survival of only 5%.

d. Follow-up. Because of high risk for local and distant recurrence,

patients should be examined every 3 months by all specialists involved in their care.

6. **Locoregional recurrence.** Patients with locoregional recurrence should have a **metastatic workup** to exclude visceral or bony disease and should be considered for systemic chemotherapy or hormonal therapy.
   a. **Recurrence in the breast after BCT** requires total (simple) mastectomy. Provided that margins are negative, survival is similar to that for patients who received mastectomy initially.
   b. **Recurrence in the axilla** requires surgical resection followed by radiation to the axilla and systemic therapy.
   c. **Recurrence in the chest wall after mastectomy** occurs in 4% to 5% of patients. One-third of these patients have distant metastases at the time of recurrence, and greater than 50% will have distant disease within 2 years. Multimodal therapy is essential. For an isolated local recurrence, excision followed by radiotherapy results in excellent local control. Rarely, patients require radical chest resection with myocutaneous flap closure.

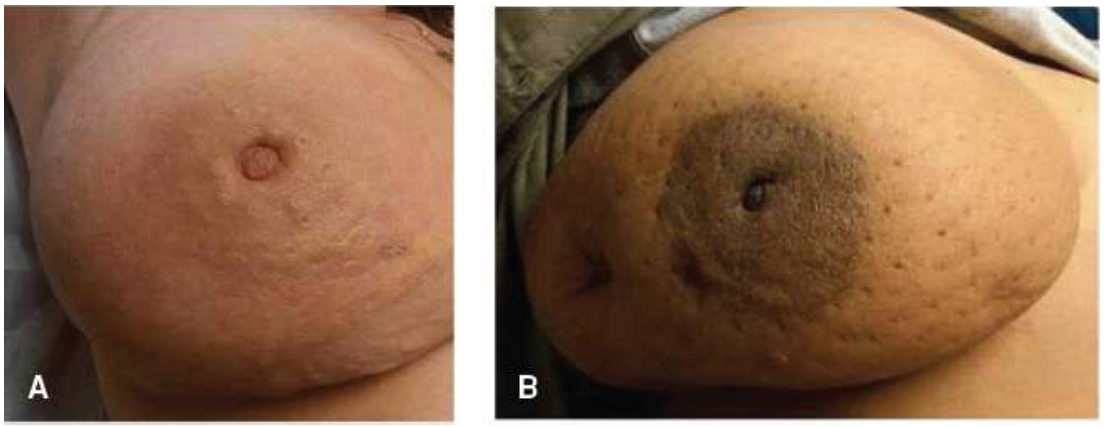


FIGURE 31-5 Classic clinical features of inflammatory breast cancer. (Reproduced with permission from Harris JR, Lippman ME, Osborne CK, et al., eds. *Diseases of the Breast*. Philadelphia, PA: Wolters Kluwer Health; 2014.)

V. SPECIAL CONSIDERATIONS

A. Breast Conditions During Pregnancy

1. **Bloody nipple discharge** may occur in the second or third trimester. It results from epithelial proliferation under hormonal influences and

usually resolves by 2 months postpartum. If it does not, standard evaluation of pathologic nipple discharge should be performed.

2. **Breast masses** occurring during pregnancy include galactoceles, lactating adenoma, simple cysts, breast infarcts, fibroadenomas, ***and*** carcinoma. Fibroadenomas may grow during pregnancy due to hormonal stimulation.
   - **a.** Masses should be evaluated by US, and a core needle biopsy should be performed for any suspicious lesion.
   - **b.** Mammography can be performed with uterine shielding but is rarely helpful due to increased breast density.
   - **c.** If a breast lesion is diagnosed as malignant, the patient should be given the **same surgical treatment** options, stage for stage, as a nonpregnant woman, and the **treatment should not be delayed** because of the pregnancy.
3. **Breast cancer during pregnancy** may be difficult to diagnose due to low levels of suspicion and increased breast nodularity and density.
   - **a.** It occurs in approximately 1 in 5,000 gestations and accounts for almost 3% of all breast cancers.
   - **b. Workup is the same as in nonpregnant women.** For advanced-stage disease, MRI scan or US may be used in lieu of CT for staging. Excisional biopsy can be safely performed under local anesthesia if there is some contraindication to the preferred core needle biopsy.
   - **c. Therapeutic decisions** are influenced by the clinical cancer stage and the trimester of pregnancy and must be **individualized.** The radiation component of BCT cannot be applied during pregnancy, and delaying radiation therapy is not ideal. For these reasons, **BCT is usually not recommended to patients in their first or second trimester. For patients in the third trimester, radiation can begin after delivery.** SLNB is being used more frequently as the commonly used radioisotope is approved for use during pregnancy.
   - **d. Chemotherapy** may be given by the mid-second trimester.

B. Paget Disease of the Nipple. This is characterized by eczematoid changes of the nipple–areolar complex. It is almost always **accompanied by malignancy** and in 60% of cases is associated with a

palpable mass. **Mammography** should be performed to identify other areas of involvement. If clinical suspicion is high, a pathologic diagnosis should be obtained by **wedge biopsy of the nipple and underlying breast tissue.** Burning, pruritus, and hypersensitivity may be prominent symptoms. Treatment should include **excision of the nipple–areolar complex** (i.e., a central lumpectomy) but is otherwise **dictated by the underlying malignancy.**

C. Breast Cancer in Men. This accounts for less than 1% of male cancers and less than 1% of all breast cancers. *BRCA2* mutations are associated with approximately 4% to 6% of these cancers. **Mammography** can be helpful in distinguishing gynecomastia from malignancy. Eighty-five percent of malignancies are infiltrating ductal carcinoma. **MRM** was traditionally the surgical procedure of choice, however, SLNB has been shown to be effective in men. Thus, **total** (**simple**) **mastectomy with SLNB** is a valid option in men. **Adjuvant hormonal, chemotherapeutic, and radiation treatment criteria are the same as in women.** Overall **survival per stage is comparable to that observed in women,** although men tend to present in later stages.

D. Phyllodes Tumors. Phyllodes tumors account for 1% of breast neoplasms. They present as large, smooth, lobulated masses and may be difficult to distinguish from fibroadenomas on physical examination. FNAB cannot reliably diagnose these tumors, therefore **at least a core needle biopsy is needed.** Ninety percent are benign; 10% are malignant, with biologic behavior similar to that of sarcomas. Treatment is **wide local excision** to tumor-free margins or total mastectomy. **Axillary assessment is not needed** in clinically node-negative patients. Historically, there was no role for adjuvant radiation therapy, but a retrospective review demonstrated an association between receipt of **radiation** and improved local control (*Int J Radiat Oncol Biol Phys*. 2008;70:492–500). Tumors greater than 5 cm in diameter and with evidence of stromal overgrowth may benefit from adjuvant chemotherapy with **doxorubicin and ifosfamide** (*Cancer*. 2000;89:1502–1511). Patients should be followed with **semiannual physical examinations** and **annual mammograms and chest radiographs.**

CHAPTER 31: BREAST

Multiple Choice Questions

1. **Which of the following patients should undergo radiation therapy as part of her breast cancer management?**

   a. A 25-year-old woman with 2 cm palpable left breast mass and history of non-Hodgkin lymphoma at 16
   b. An 80-year-old woman with 6 mm of ductal carcinoma in situ (DCIS) in her right breast
   c. A 32-year-old pregnant woman with T1 tumor and a suspicious lymph node on axillary ultrasound at 33 weeks of gestation
   d. A 41-year-old woman diagnosed with multicentric lobular carcinoma at 26 weeks of gestation
   e. A 36-year-old woman with LCIS

2. **Radiation therapy after partial mastectomy improves:**

   a. Rates of local recurrence
   b. Overall survival
   c. Risk of lymphedema after axillary lymph node dissection (ALND)
   d. Breast-cancer-specific survival
   e. The effectiveness of adjuvant chemotherapy

3. **First-line pharmaceutical treatment for mastalgia is:**

   a. Oral vitamin E
   b. Evening primrose oil
   c. Topical vitamin E
   d. Topical NSAIDs
   e. Tamoxifen

4. **A 32-year-old breastfeeding woman who is 2 weeks postpartum presents to the emergency department with a 2-day history of warmth and erythema over the inferomedial right breast. She is afebrile and her skin is red but not edematous. Your next step in management is:**

a. Incision and drainage (I&D)
b. Antibiotics, instruction to increase breastfeeding frequency
c. Antibiotics, instruction to breastfeed only using the contralateral breast
d. Antibiotics, instruction to cease all breastfeeding
e. Skin punch biopsy

5. Breast cancer in men:

a. Is associated with the *BRCA2* mutation in about 5% of cases
b. Is more lethal when compared to stage-matched female controls
c. Is less lethal when compared to stage-matched female controls
d. Is more likely to be infiltrating lobular carcinoma
e. Mandates radical mastectomy

6. The most common cause of pathologic nipple discharge is:

a. DCIS
b. Lobular carcinoma in situ (LCIS)
c. Intraductal papilloma
d. Invasive ductal carcinoma
e. Atypical ductal hyperplasia (ADH)

7. A 75-year-old man presents with a chief complaint of bilateral breast enlargement over the past 4 months. His past medical history is significant for a history of congestive heart failure, atrial fibrillation (for which he takes digitalis), hypertension, benign prostatic hypertrophy (for which he takes finasteride), and stage 3 chronic kidney disease. Your next step in management is:

a. To perform a punch biopsy in the clinic
b. Order a stereotactic core needle biopsy
c. Perform bilateral mastectomies immediately
d. To inform him there is nothing to be done
e. To call his primary care physician (PCP)

8. A 44-year-old G3P2 female whose mother was diagnosed with breast cancer at 65 comes to see you in clinic after being told that her most recent screening mammogram was read as

BIRADS 3, probably benign. How do you counsel her?

a. Tell her she has nothing to worry about
b. Ask her to come back and see you in 6 months with repeat mammography
c. Start her on low-dose tamoxifen
d. Obtain immediate breast MRI
e. Perform an ultrasound in clinic

9. A 41-year-old female with a known history of lobular carcinoma in situ (LCIS) found on an excisional biopsy 4 months ago presents to your clinic and would like to undergo bilateral prophylactic mastectomy with reconstruction. Options for managing LCIS include:

a. Chemoprevention with an estrogen antagonist
b. Chemoprevention with an aromatase inhibitor
c. Bilateral mastectomy
d. Close surveillance
e. All of the above

10. Pertuzumab:

a. Is an aromatase inhibitor used in the treatment of ER+ breast cancer
b. Is associated with progression-free survival in women with metastatic HER2+ cancer when used with cyclophosphamide
c. Is associated with progression-free survival in women with metastatic HER2+ cancer when used with trastuzumab and docetaxel
d. Is still an experimental drug and not yet available in the United States
e. Has shown a near 100% cure rate in metastatic HER2+ cancer

32 Skin and Soft Tissue Tumors

Julie G. Grossman and Ryan C. Fields

INTRODUCTION

While management of benign lesions is generally straightforward, management of malignant skin and soft tissue lesions, especially advanced forms, has become increasingly complex with the advent of new prognostic markers and therapeutic options. With more than 5 million Americans diagnosed annually, skin cancer represents the most common cancer in the United States, with its incidence exceeding that of lung, colon, breast, and prostate cancers combined. Fortunately, the vast majority of cases are curable, nonmelanoma skin cancers. Soft tissue sarcomas (STSs) are less common lesions that often require multimodal care.

I. SKIN LESIONS

A. General Assessment

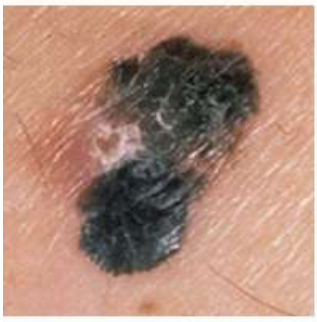
1. **History.** Pigmented lesions with a change in size, borders, and/or color are of concern for malignancy. Itching, bleeding, or ulceration requires assessment.
2. **Physical examination.** The color, size, shape, borders, elevation, location, firmness, and surface characteristics should be documented. Uniformly colored, small, round, circumscribed lesions are more likely to be benign while irregularly colored, larger, asymmetric lesions with indistinct borders and ulceration are worrisome for malignancy. These features can be remembered using the mnemonic ABCDE: Asymmetry, Borders, Color variation, Diameter, and Evolution (Fig. 32-1). Of note, melanoma can manifest as pigmented subungual or mucosal lesions or as an atypical, nonpigmented lesion. A complete skin examination and regional lymph node examination

is necessary.

3. **Biopsy** is warranted for lesions that have worrisome features or that change over time. Optimally, this is a full-thickness tissue biopsy, which encompasses the entire lesion with clinically negative margins and enough depth to ensure the lesion is not transected. This can be obtained via deep shave, punch, or excisional biopsy. Biopsy should include the thickest portion of the lesion, avoiding areas of crusting, ulceration, or necrosis. Excisional biopsies of the extremity must be oriented parallel to the long axis to facilitate possible need for subsequent definitive resection. Critical to the utility of the biopsy is the determination of the **Breslow depth**; hence superficial shave biopsies should be avoided while deep shave biopsies are usually adequate (*J Am Coll Surg*. 2011;212(4):454–460). Fine-needle aspiration (FNA) is the modality of choice for clinically positive lymph nodes.

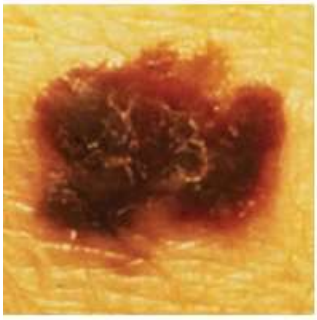
Melanoma

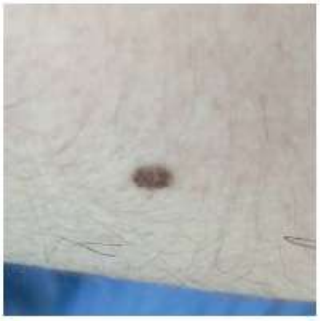
Normal



ASYMMETRY:

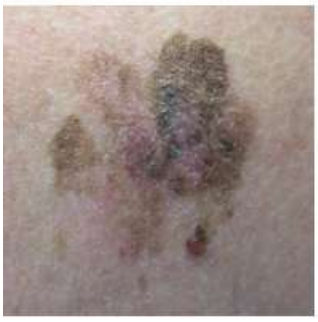
Melanomas tend to lack symmetry, unlike benign nevi





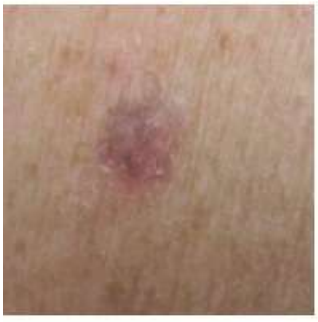
BORDER:

The borders of melanomas are typically indistinct, with blurred or jagged edges



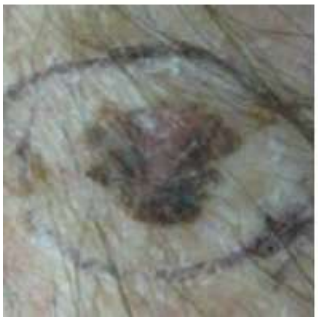
COLOR:

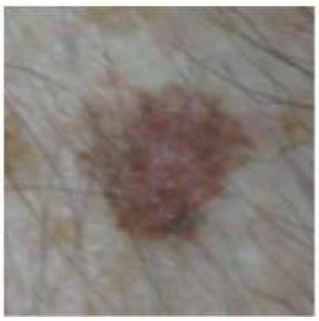
The color of a melanoma is often heterogeneous with tan, brown, black, red, blue, or white areas



DIAMETER:

Lesions larger than 6 mm are more concerning than smaller lesions





EVOLUTION:

A nevus that changes in shape, size, or color could represent a melanoma. The lesion pictured evolved from a red-tan lesion (right) to a darker brown lesion (left) over the course of 28 mo.

FIGURE 32-1 ABCDEs of melanoma.

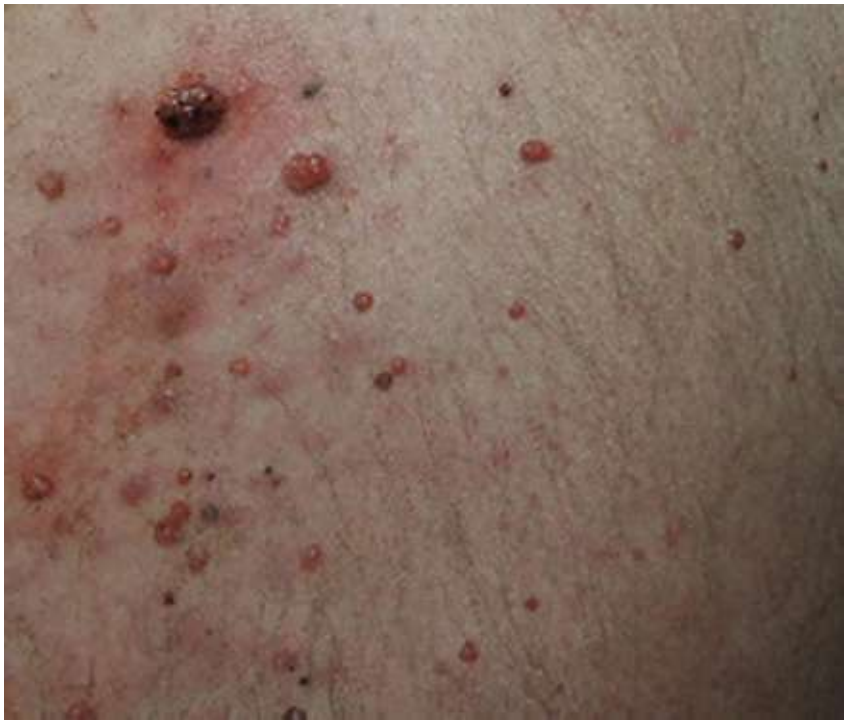


FIGURE 32-2 Cutaneous melanoma of the thigh with satellitosis.

B. Melanoma. The incidence of melanoma continues to rise at an epidemic rate. Melanoma represents the fifth-most common cancer in the United States.

1. **Lesions.** Most pigmented lesions are benign, but the majority of all melanomas arise from pigmented nevi. Amelanotic melanoma represents 2% of all melanomas. While malignant melanoma was historically classified into histologic subtypes (superficial spreading, nodular, lentigo maligna, and acral lentiginous), this convention does not carry prognostic significance when controlled for stage, Breslow depth, and presence of ulceration and mitoses. **In-transit metastases** or **satellite lesions** (Fig. 32-2) include regional spread of tumor via lymphatic vessels in the dermis or subcutaneous tissue, usually between the primary and regional nodal basin. This signifies a poor prognosis with a high risk of local recurrence and distant metastasis.
2. **Risk factors.** A history suggesting increased likelihood of melanoma includes assessment of risk factors and family history, including family or personal history of melanoma, red hair and blue eyes,

dysplastic nevi, high mole count, presence of actinic keratosis, xeroderma pigmentosum, immunosuppression (e.g., solid organ transplant, HIV, stem cell transplant), history of nonmelanoma skin cancer, multiple sunburns or tendency to burn, sun exposure, or tanning bed use. **Familial atypical multiple-mole melanoma (FAMMM) syndrome** is a syndrome with an increased risk for melanoma and pancreatic cancer and is defined by the following: (1) malignant melanoma in one or more first- or second-degree relatives, (2) a large number of melanocytic nevi, usually more than 50, and (3) melanocytic nevi with particular histopathologic features (architectural disorder with asymmetry, subepidermal fibroplasia, and lentiginous melanocytic hyperplasia with spindle or epithelial melanocyte nests). FAMMM syndrome may be caused by mutations in the *CDKN2A* gene (40% of cases) or *CDK4* gene (rare cases).

TABLE 32-1 American Joint Committee on Cancer TNM (Tumor, Node, Metastasis) Definitions of Melanoma

T Classification	Thickness (mm)	Ulceration Status
Tis	Melanoma in situ	—
T1	≤1.0	a. Breslow <0.8 mm without ulceration b. Breslow 0.8–1.0 mm without ulceration or ≤1.0 with ulceration
T2	1.1–2.0	a. Without ulceration b. With ulceration
T3	2.1–4.0	a. Without ulceration b. With ulceration
T4	>4.0	a. Without ulceration b. With ulceration
Regional Lymph Nodes (N)	**# of Nodes**	**Clinical Detectability/MSI Status**
N1	0–1	a. Clinically occult, no MSI b. Clinically detected, no MSI

		c. 0 nodes, MSI present
N2	1–3	a. 2–3 nodes clinically occult, no MSI b. 2–3 nodes clinically detected, no MSI c. 1 node clinical or occult, MSI present
N3	>1	a. >3 nodes, all clinically occult, no MSI b. >3 nodes, ≥1 clinically detected or matted, no MSI c. >1 node clinical or occult, MSI present

Distant Metastasis (M)	Serum LDH	Site
M1a–d	Not assessed	Skin/subcutaneous/nodule(a), lung(b), other visceral(c), brain(d)
M1a–d(0)	Normal	Skin/subcutaneous/nodule(a), lung(b), other visceral(c), brain(d)
M1a–d(1)	Elevated	Skin/subcutaneous/nodule(a), lung(b), other visceral(c), brain(d)

LDH, lactic dehydrogenase; MSI, microsatellites, satellites, or in-transit metastasis.

TABLE 32-2 American Joint Committee on Cancer Stage Groupings for Cutaneous Melanoma

	Clinical Staging[a]				Pathologic Staging[b]		
0	Tis	N0	M0	**0**	Tis	N0	M0
IA	T1a	N0	M0	**IA**	T1a	N0	M0
IB	T1b	—	—	**IB**	T1b	—	—
	T2a	—	—		T2a	—	—
IIA	T2b	N0	M0	**IIA**	T2b	N0	M0
	T3a	—	—		T3a	—	—
IIB	T3b	—	—	**IIB**	T3b	—	—
	T4a	—	—		T4a	—	—
IIC	T4b	—	—	**IIC**	T4b	—	—

III	Any T	≥N1	M0	**IIIA**	T1–2a	N1a	M0
	—	—	—		T1–2a	N2a	—
	—	—	—	**IIIB**	T0	N1b-c	M0
	—	—	—		T1–2a	N1b-c	—
	—	—	—		T1–2a	N2b	—
	—	—	—		T2b–3a	N1a-2b	—
	—	—	—	**IIIC**	T0	N2b-c	M0
	—	—	—		T0	N3b-c	—
	—	—	—		T1a-3a	N2c-3c	—
	—	—	—		T3b-4a	Any N	—
	—	—	—		T4b	N1a-2c	—
	—	—	—	**IIID**	T4b	N3a-c	M0
IV	Any T	Any N	M1	**IV**	Any T	Any N	M1

[a]Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

[b]Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy, except for pathologic stage 0 or stage IA patients, who do not need pathologic evaluation of their lymph nodes.

3. **Staging.** The American Joint Committee on Cancer (AJCC) TNM (tumor, node, metastasis) classification system (Tables 32-1 and 32-2) is the standard classification scheme. The **Breslow thickness**, a physical depth measurement of the primary tumor, is used to classify the tumor ("T classification"). Imaging, consisting of computed tomography (CT) chest, abdomen, and pelvis or positron emission tomography (PET)/CT, should be obtained for patients presenting with an advanced (T4b) primary tumor, stage III or higher patients, or for patients with symptoms concerning for advanced disease.

Additionally, a brain magnetic resonance imaging (MRI) should be considered for stage IIIC or above.

4. **Prognosis.** Tumor thickness is the most important factor in staging the tumor, both for overall survival and risk for nodal and distant metastasis (*J Clin Oncol*. 2001;19:3622). Tumors less than 1 mm thick have a 10-year survival of 92%, whereas lesions more than 4 mm thick have a 10-year survival of 50%. Other than Breslow depth, ulceration and mitotic rate are important histologic characteristics that are negative prognostic factors. Regional node metastasis severely worsens prognosis (5-year survival, 32% to 93%) while distant metastases have a dismal prognosis (5-year survival, <10%).

5. **Treatment**

   a. Surgery

   (1) Wide local excision (WLE) is the primary treatment for melanoma and melanoma in situ (MIS). The surgical margin depends on the Breslow tumor thickness. MIS should be excised with 5- to 10-mm margins, thin melanomas (Breslow thickness <1 mm) should have a margin of 1 cm, and lesions with thickness of 1 to 2 mm should have a margin of 1 to 2 cm. A 2-cm margin for thick (>2 mm) melanomas was confirmed in a randomized controlled trial (RCT) (*Lancet*. 2011;378(9803):1635). Wounds should be closed primarily, with flaps or skin grafts reserved for large defects.

   (2) Sentinel lymph node biopsy (SLNB) is based on the lymphatic drainage of the tumor to the initial regional lymph node(s). It is not therapeutic. SLNB status is the strongest prognostic factor with respect to overall and melanoma-specific survival. The histology of the SLN is highly reflective of the rest of the nodal basin—the incidence of a positive nonsentinel node in the setting of a negative sentinel node is less than 1% (*Arch Surg*. 1992;127(4):392). Routine SLNB is not recommended for patients with thin melanomas that are T1a (nonulcerated lesions <0.8 mm in Breslow thickness). SLNB may be considered for thin melanomas that are T1b (0.8- to 1.0-mm Breslow thickness or <0.8-mm Breslow thickness with ulceration) after a discussion on the benefits and risks. SLNB is recommended for lesions of T2 or above (*J Clin*

Oncol. 2018;36(4):399–413). Preoperative injection of radiotracer and intraoperative injection of blue dye have led to an SLN identification rate of 99% (*Semin Oncol*. 2007;34(6):498–508). Blue dye (isosulfan blue, Patent Blue V, or methylene blue) is injected intradermally at the primary site. Of note, methylene blue has been associated with soft tissue necrosis. All nodes that measure 10% or higher of the ex vivo radioactive count of the hottest SLN should be harvested.

(3) Completion lymph node dissection (CLND) was previously performed on all patients with a positive SLNB; however, it has not been shown to be associated with overall or melanoma-specific survival in two phase III studies. In "MSLT-II," an international prospective randomized trial, patients with positive SLNB were randomized to undergo either CLND or nodal basin ultrasound (US) surveillance. They demonstrated that CLND increased the rate of regional disease control and provided prognostic information but did not increase melanoma-specific survival among patients with SLN metastases (*N Engl J Med*. 2017;376:2211–2222). Similarly, "DeCOG" showed no difference in survival in patients treated with CLND compared with observation only (*Lancet Oncol.* 2016;17:757–767). If a patient has a positive SLN, CLND versus active nodal basin surveillance with US should be considered.

(4) Therapeutic lymph node dissection (TLND) is recommended for clinically and biopsy positive axillary and superficial inguinal lymph nodes unless unresectable distant metastases are present. These nodes should be biopsied, preferably by FNA. TLND can achieve 5-year survival rates of 20% to 40%. Surgical therapy of the inguinal region includes a superficial inguinal lymphadenectomy with extension to the deep ilioinguinal region, including the iliac and obturator lymph nodes, if there is radiographic evidence of lymph node involvement or **Cloquet's node** is positive. Also, this should be considered if there are clinically positive inguinofemoral nodes or three or more positive SLNs. Of note, currently there are clinical trials for neoadjuvant treatment in patients with clinical

stage III disease. In a randomized phase II trial, resectable clinical stage III or oligometastatic stage IV *BRAF* V600E or *BRAF* V600K-mutated melanoma was treated with neoadjuvant plus adjuvant dabrafenib and trametinib versus standard of care (upfront surgery and consideration for adjuvant therapy). Significantly more patients receiving neoadjuvant plus adjuvant dabrafenib and trametinib were alive without disease progression than those receiving standard of care (10 [71%] of 14 patients vs. none of 7 in the standard of care group) (*Lancet Oncol*. 2018;19:181–193).

(5) Complications of melanoma excision include functional disability, infection, and difficulty with wound healing. For patients who have undergone lymphadenectomy, lymphedema is a substantial problem. In MSLT-II, 24% of the patients in the CLND group reported lymphedema. It is treated with compression garments and physiotherapy.

(6) Resection of metastases. The surgical options for patients with metastatic melanoma can be divided into two categories: curative or palliative. Curative-intent surgery for metastatic melanoma should carefully weigh the risks and benefits of surgery. Favorable factors include long disease-free intervals, fewer metastatic sites, responsiveness to targeted and/or systemic therapy (see below), and good functional status. With the advent of more effective systemic therapy, surgery for refractory metastatic disease is becoming more common.

b. Regional therapy with **isolated limb perfusion (ILP)** or **isolated limb infusion (ILI)** of chemotherapy can be used for recurrent or in-transit extremity melanoma that is locally advanced and/or unresectable. ILP and ILI deliver high-dose regional chemotherapy to the affected extremity while minimizing systemic toxicity. ILI is simpler and less toxic than ILP, but its response rates are lower (*J Am Coll Surg*. 2009;208(5):706). A review of ILP and ILI including the agents used, technique employed, and treatment algorithms was published by Tyler et al. (*Surg Oncol Clin N Am*. 2011;20(1):79–103).

c. Intralesional therapy is indicated for unresectable satellite or in-transit metastasis. **Talimogene laherparepvec (TVEC)** is a

herpes simplex virus–derived oncolytic agent designed to selectively replicate within tumors and produce granulocyte macrophage colony-stimulating factor (GM-CSF) to enhance systemic antitumor immune responses. It has demonstrated a greater durable response rate than subcutaneous GM-CSF in advanced melanoma. TVEC was associated with a response rate lasting >6 months in patients with unresectable metastatic melanoma (*J Clin Oncol*. 2015;33(25):2780–2788; *ASCO Meeting Abstracts*. 2015;33:TPS9094). Intralesional injections of **interleukin 2 (IL-2)**, **bacillus Calmette–Guerin (BCG),** and **interferon (IFN)** are additional second-line options.

d. Local therapy can also be utilized for palliation of unresectable in-transit metastasis and consists of topical imiquimod, laser ablation, or radiation therapy.

e. Systemic therapy

(1) Immunotherapy, specifically **checkpoint inhibitors,** has revolutionized melanoma treatment. Blockade of inhibitory receptors, CTLA-4 and PD-1, enhances T-cell–mediated antitumor immune responses, leading to improved survival and durable response. Although not as effective as targeted molecular therapy (see below), they provide a longer duration of response. The EORTC 18071 trial compared adjuvant high-dose **ipilimumab**, a monoclonal antibody against CTLA-4, to placebo in resected stage III melanoma, demonstrating improved recurrence-free survival. High-dose ipilimumab is approved as adjuvant treatment in stage III disease. Therapy for metastatic and unresectable disease includes **pembrolizumab** or **nivolumab**, monoclonal antibodies against PD-1, and/or ipilimumab. In a randomized, double-blind, phase III trial, patients who were undergoing complete resection of stage IIIB, IIIC, or IV melanoma received either nivolumab or ipilimumab. Compared with patients who received adjuvant ipilimumab, those who received nivolumab had a higher rate of recurrence-free survival at 12 months (70% vs. 61%, respectively) and a lower rate of severe adverse effects (14% vs. 46%, respectively) (*N Engl J Med*. 2017;377:1824–1835). Further, it was demonstrated that combination therapy was

effective. In an RCT in patients with advanced melanoma, 3-year survival rate was higher with nivolumab and ipilimumab combined (55%) than with either nivolumab alone (52%) or ipilimumab alone (32%) (*N Engl J Med*. 2017;377:1345–1356). **IL-2** is considered second-line therapy for metastatic disease.

(2) Targeted molecular therapy. Testing for *BRAF* mutations is now standard for patients with advanced melanoma due to the advent of targeted therapies. *BRAF* is a proto-oncogene that has been found to be activated in about 40% of melanomas (*J Clin Oncol*. 2012;30(20):2522–2529). **Vemurafenib** and **dabrafenib** are small molecule inhibitors of *BRAF* that have shown clinical efficacy in patients with the V600 mutation. **Cobimetinib** and **trametinib** are small molecule inhibitors of *MEK*, an effector downstream of *BRAF*. Combination therapies with *BRAF* and *MEK* inhibitors have demonstrated improved efficacy over *BRAF* therapy alone for patients with V600 *BRAF* mutations (*N Engl J Med*. 2014;371(20):1877–1888; *N Engl J Med*. 2014;371(20):1867–1876).

C. Nonmelanoma Skin Cancers

1. **Basal cell carcinoma (BCC)** is the most common skin cancer. They are slow growing, may be large, disfiguring, and locally invasive, but rarely metastasize (<0.1%). Sun exposure is the most significant epidemiologic factor; consequently, this neoplasm is found most commonly on sun-exposed areas in fair-skinned patients older than 40 years.

   a. Lesions are flat, but indurated with a smooth, whitish, waxy surface and indistinct borders. The noduloulcerative form is most common and is characterized by shiny, translucent nodules with a central umbilication that often becomes ulcerated with pearly, rolled, telangiectatic edges.

   b. Treatment. A skin biopsy should be performed. The recurrence risk, high versus low, will determine the treatment plan. Table 32-3 summarizes these high-risk factors.

   (1) Surgical excision with a margin of 4 mm should be obtained; however high-risk lesions require wider margins. **Mohs micrographic surgery** is the gold standard for high-risk

lesions, cosmetically sensitive areas, and reexcision of positive margins. Excision with complete circumferential peripheral and deep margin assessment using intraoperative frozen sections is an alternative to Mohs.

(2) **Additional treatment options. Curettage with electrodesiccation (CED)** can be used in low-risk lesions in areas without hair growth. The main disadvantage of CED is that no specimen is available for margin evaluation. **Radiation therapy** is considered for nonsurgical candidates and after resection of tumors with extensive perineural involvement. Low-risk, superficial BCC where resection and radiation are not options can be treated with cryotherapy, topical 5-fluorouracil (5-FU), topical imiquimod, and/or photodynamic therapy. **Vismodegib** and **sonidegib**, hedgehog pathway inhibitors, are relatively new therapies that have shown efficacy in patients with inoperable and metastatic BCC (*N Engl J Med*. 2012;366(23):2171–2179; *Lancet Oncol*. 2015;16:716–728).

TABLE 32-3 High-Risk Factors for Local Recurrence or Metastases for Basal Cell Skin Cancer

Risk Factors
Area L ≥20 mm
Area M ≥10 mm
Area H, any size
Aggressive growth pattern
Poorly defined borders
Immunosuppression
Site of prior RT
Recurrent BCC
Perineural involvement

Area H, “mask areas” of face (central face, eyelids, eyebrows, periorbital, nose, lips, chin, mandible, preauricular and postauricular skin, temple, ear), genitalia, hands, feet; Area M, cheeks, forehead, scalp, neck, and pretibial; Area L, trunk and extremities.

2. **Squamous cell carcinoma (SCC)** is the second-most common skin cancer. Sunlight is the major etiology, and elderly men with a history of chronic sun exposure are at greatest risk. SCC is usually found on sun-exposed areas and may develop from draining sinuses, radiation, chronic ulcers, and scars (**Marjolin ulcer**).

   a. Lesions are small, firm, erythematous plaques with a smooth or verrucous surface and indistinct margins with progression to raised, fixed, and ulcerated lesions. Most are preceded by actinic keratoses that progress into slow-growing, locally invasive lesions. Although rare, nodal metastases do occur more frequently than in BCC.

   b. Treatment. Biopsy should be performed. The recurrence risk will determine the treatment plan. Table 32-4 summarizes the high-risk factors. Treatment is similar to BCC, except that low-risk lesions have surgical margins of 4 to 6 mm with high-risk patients requiring larger margins. Like in BCC, CED can be used in low-risk lesions. Radiation therapy is considered for nonsurgical candidates and after resection of tumors with extensive perineural involvement. Superficial therapies such as cryotherapy, topical 5-FU, topical imiquimod, and photodynamic therapy can be used in SCC in situ. For patients with metastatic SCC, systemic treatment includes cisplatin, cisplatin plus 5-FU, EGFR inhibitors (**cetuximab**), or immune checkpoint inhibitors (see above). An early clinical trial suggests that a new PD-1 inhibitor, **cemiplimab**, may be effective in patients with unresectable locally advanced or metastatic disease, with 50% response rates in advanced disease (*NEJM*. 2018;379:341–351).

TABLE 32-4 **High-Risk Factors for Local Recurrence or Metastases for Squamous Cell Skin Cancer**

Risk Factors
Area L ≥20 mm
Area M ≥10 mm
Area H, any size
Poorly defined borders

Recurrent SCC
Immunosuppression
Site of prior RT
Rapidly growing tumor
Neurologic symptoms
Poorly differentiated
Acantholytic, adenosquamous, desmoplastic, or metaplastic subtypes
≥2 mm depth
Perineural, lymphatic, or vascular involvement

Area H, “mask areas” of face (central face, eyelids, eyebrows, periorbital, nose, lips, chin, mandible, preauricular and postauricular skin, temple, ear), genitalia, hands, feet; Area M, cheeks, forehead, scalp, neck, and pretibial; Area L, trunk and extremities.

D. Merkel Cell Carcinoma. **Merkel cell carcinoma (MCC)** is a rare, neuroendocrine skin cancer. UV radiation, immunosuppression, and exposure to Merkel cell polyomavirus are predisposing factors. Similar to melanoma, the cancer often recurs locally and metastasizes to regional lymph nodes. Treatment consists of WLE with 1- to 2-cm margins down to the muscle fascia. SLNB is recommended for all clinically node-negative patients. CLND or TLND with or without radiation therapy should be performed for positive SLNB or clinically positive nodes confirmed by FNA or core biopsy, respectively. Because these lesions are highly radiosensitive, radiotherapy can be used for treatment of high-risk lesions or nodal basins or in patients who are unresectable or are otherwise not operative candidates. Advanced and metastatic MCC has substantial response rates to treatment with immunotherapy. In a clinical trial of patients with advanced MCC, response rate to PD-L1 inhibitor, **avelumab**, was 32% during a median follow-up of 10 months (*Lancet Oncol*. 2016;17(10):1374–1385). Additionally, **pembrolizumab**, has been shown to also be an effective first-line therapy in advanced MCC with an objective response rate of 56% (*N Engl J Med*. 2016;374:2542–2552).

E. Benign Skin Lesions

1. **Seborrheic keratoses** are benign skin growths that characteristically appear in older people as multiple, raised, irregularly rounded lesions

with a verrucous, friable, waxy surface, and variable pigmentation on the face, neck, or trunk. No treatment is indicated for most lesions. If treatment is desired, surgical excision, shave biopsy, CED, topical trichloroacetic acid, or cryotherapy with liquid nitrogen may be employed. Of note, the sudden development of multiple seborrheic keratoses in conjunction with acanthosis nigricans—the **Leser–Trelat sign**—can represent a paraneoplastic syndrome, which is most often associated with adenocarcinomas of the stomach and colon, as well as breast cancer, lymphoma, and leukemia.

2. **Actinic keratoses** result from sun exposure and are found predominantly in elderly, fair-skinned patients. Lesions are small, usually multiple, flat-to-slightly elevated with a scaly surface ranging from red to yellowish brown to black. Unlike seborrheic keratoses, these lesions have malignant potential, up to 20% become well-differentiated SCC, and thus should be treated. Treatments include excision, cryotherapy, dermabrasion, laser therapy, chemical peels, photodynamic therapy, and topical applications of imiquimod, 5-FU, ingenol mebutate, or diclofenac sodium.
3. **Nevi. Dysplastic nevi** have variegated color (tan to brown on a pink base), are large (5 to 12 mm), appear indistinct with irregular edges, and have macular and papular components. **Congenital nevi** (“birthmarks”) are associated with an increased risk of melanoma development, particularly for giant congenital nevi, which have diameters greater than 20 cm and are sometimes hairy. Biopsied nevi that reveal moderate or severe atypia should be excised to negative margins. **Spitz nevi** are pink-red papules, which are benign melanocytic lesions most often seen in childhood. Histologically, they closely resemble melanoma, often leading to misdiagnosis.

II. SOFT TISSUE MASSES

A. General Assessment

1. **History.** A focused history includes descriptions of location, duration, change in size, and presence of associated symptoms. A painless mass is the most common presentation. Any history of enlargement or color/shape change is concerning for malignancy. Pain may be a late symptom. Lesions can be misdiagnosed as hematomas, hemorrhoids, or muscle strain due to perceived antecedent trauma.

2. **Physical examination.** Key features are size, anatomic relationships with surrounding structures, borders, and mobility. A neurovascular examination of the affected area should be performed. If palpable, it is concerning if the lesion is hard, nodular, immobile against the skin, and felt to be involving deeper tissue.
3. **Radiologic evaluation**
   a. **MRI** is the best choice for imaging soft tissue masses to evaluate relationship to large nerves and other soft tissue structures and is the main imaging modality in the extremities, pelvis, and trunk. T2-weighted images and gadolinium enhancement can help distinguish edematous normal tissue from tumors.
   b. **CT** is more useful than MRI in evaluating relationship to vascular structures. CT-guided core needle biopsy is often used for deep tumors that are difficult to access without radiographic guidance. A chest CT is generally obtained for diagnosis of STS to evaluate for pulmonary metastases.
   c. **PET** is utilized for staging, prognosis, and response to chemotherapy by evaluating the maximum standardized uptake value (SUV_{max}) of F18-deoxyglucose. It aids in differentiation of necrotic tumor or scar versus metabolically active disease.
4. **Biopsy**
   a. **Core needle biopsy** is the preferred method of biopsy. It provides a section of intact tissue for histologic analysis, the same information as an excisional or incisional biopsy, without impacting the future surgical plan. Indeterminate results should be confirmed by a repeat core needle biopsy.
   b. **Incisional biopsy** may be performed by an experienced surgeon for masses greater than 3 cm. An incision oriented parallel to the long axis of the extremity should be made such that the resulting scar can be excised at subsequent operation. Meticulous hemostasis to prevent hemorrhage from spreading tumor is critical. Drains should be avoided, but if needed, drain sites should be placed for excision at subsequent operation.
   c. **Excisional biopsy** is usually only considered after multiple nondiagnostic core biopsies have been performed. It may be performed for tumors that are probably benign or less than 3 cm in

diameter (e.g., lipomas, dermatofibromas). An elliptical incision is made around the tumor oriented parallel to the long axis of the limb and along skin lines of minimal tension. Complete excision with a thin margin of normal tissue followed by primary closure should be performed whenever possible.

d. FNA is the least invasive method of tissue diagnosis, but also the least informative. FNA can determine the presence of malignancy and histologic type but often cannot determine grade. Indeterminate results should prompt definitive biopsy. It is most often used to confirm recurrence or metastasis.

B. Malignant Soft Tissue Tumors

1. **Dermatofibrosarcoma protuberans (DFSP)** is a cutaneous sarcoma of fibroblast origin that infrequently metastasizes but can recur locally. Because of the infiltrative nature of the tumor, WLE should include at least 2-cm margins. Radiation therapy can be employed for patients with positive margins when further resection is not feasible. Mohs microsurgery can be utilized for tissue conservation and cosmesis. Imatinib mesylate is recommended for patients with unresectable, recurrent, and metastatic disease who harbor a PDGFR translocation.
2. **Desmoid tumors** are nonmetastasizing, locally aggressive tumors that arise from connective tissue. Small asymptomatic tumors, located in areas that would not lead to functional limitations, can be observed. Large symptomatic tumors should be excised with a margin of normal tissue. Desmoids are radiosensitive, and radiation therapy can be used in multimodality treatment. Antiestrogen receptor agents (e.g., tamoxifen), nonsteroidal anti-inflammatory drugs (e.g., sulindac), chemotherapy, and tyrosine kinase inhibitors (TKI, e.g., **imatinib, sorafenib**) are currently being used in patients with unresectable, progressive, or recurrent disease. In a randomized phase III trial, patients with unresectable tumors or unacceptable surgical morbidity, progressive disease, and symptomatic disease were treated with sorafenib or placebo. Sorafenib resulted in significantly improved progression-free survival (PFS) compared with placebo. The median PFS with sorafenib was not reached, compared with a median PFS of 11.3 months in the placebo group (*J Clin Oncol.* 2018;36(15_suppl):11500–11500). Patients with a

desmoid tumor require colonoscopy to exclude familial adenomatous polyposis (FAP).

3. **Soft tissue sarcomas (STSs)** represent a heterogeneous group of malignant tumors derived from mesodermal tissues. STSs are uncommon, constituting approximately 1% of adult malignant neoplasms. While most of these tumors occur de novo, some are seen as part of syndromes such as neurofibromatosis, Werner syndrome, or Li–Fraumeni syndrome. Lymphedema and radiation have been shown to be causative in certain subtypes (*Am Surg*. 2006;72:665). Nodal metastases are rare in STS as dissemination usually occurs hematogenously. The epidemiology and natural history of this diverse group of malignancies have been reviewed in a series of 10,000 patients spanning 30 years at a single institution (*Ann Surg*. 2014;260(3):416–421).
   a. **Lesions**. Sarcomas are classified by histologic cell type of origin and grade. Pleomorphic undifferentiated sarcoma (previously malignant fibrous histiocytoma, 40%) is most common, followed by liposarcoma (25%). Patients typically present with an asymptomatic mass that becomes visible or palpable. Intra-abdominal and retroperitoneal tumors can become massive before symptoms prompt presentation.
   b. **Diagnosis**. Biopsy (core preferred) is obtained for diagnosis. Care is needed to orient biopsy approach to aid in definitive resection. For intra-abdominal or retroperitoneal masses, preoperative biopsy is only needed if there is concern for other diagnosis or malignancy. However, a biopsy is always needed prior to starting chemotherapy or radiation.
   c. **Staging** includes physical examination and CT or MRI to assess the size and extent of tumor. As hematogenous spread to the lungs is the most common form of metastasis, chest imaging is necessary with CT being the preferred modality. The AJCC staging system is based on tumor size and depth, nodal status, histologic grade, and metastasis. Of these, tumor grade is the major prognostic factor and is based on tumor cell differentiation, mitotic activity, and extent of necrosis.
   d. **Prognosis** is highly variable given the variety of histologic diagnoses. Almost 80% of metastases are to the lungs and occur

within 2 to 3 years of diagnosis. If pulmonary disease is resectable, overall survival is 30% at 3 years. In addition, tumor size, grade, tumor rupture during surgery, margins after resection, and anatomic location all influence local recurrence, overall survival, and tumor-free survival. Retroperitoneal and truncal STS have worse prognoses than extremity STS. While mortality from extremity STS is usually due to metastasis, retroperitoneal STS is usually fatal secondary to local recurrence.

e. Treatment

(1) Surgical resection with negative surgical margins is the primary treatment for patients with resectable disease. Resection should include the area of previous incision. Radiation and/or chemotherapy may be used in the neoadjuvant setting to improve the chances of an R0 resection. Reexcision should be performed for positive surgical margins, when possible, if it will not impact functional outcome. **Limb-sparing resection** combined with radiation therapy offers rates of survival equivalent to those achieved with amputation. Limb-sparing procedures have a psychological and functional advantage over amputations and are the procedures of choice for most tumors. Amputation is rarely necessary. **Retroperitoneal sarcomas** are considerably more difficult to treat because the tumors often involve vital structures. Overall and disease-free survival for retroperitoneal STS are 56.8% and 39.4%, respectively (*J Clin Oncol*. 2013;31(13):1649–1655). Organs associated with the tumor should be resected en bloc because 5-year recurrence rates are lower for en bloc resections than for cases of tumor resection alone (28% vs. 48%, respectively; *J Clin Oncol*. 2009;27:24). Postoperative radiation may be used but is associated with relatively high morbidity, often due to off-target effects. Preoperative radiation therapy has several advantages including direct targeting of the tumor, reduced off-target effects, and conversion of tumors from unresectable to resectable.

(2) Radiation. For the majority of high-grade STS, surgery combined with radiation therapy is more effective than either therapy alone. Surgery alone may be appropriate for small (<5

cm), superficial lesions with favorable histologic subtype and grade. Otherwise, adjuvant radiotherapy is generally indicated to improve local control. Preoperative radiation can also be used for large, deep-seated tumors for which the surgeon anticipates a possible positive margin. Brachytherapy (administration of radiation therapy via the implantation of radioactive beads) can also be used to improve localization to radiosensitive areas.

(3) Chemotherapy. There has been mixed data supporting the use of pre- and postoperative chemotherapy. Tumors at high risk for recurrence or metastasis, in addition to advanced, unresectable or metastatic disease should be considered for chemotherapy. The agents used are specific to the histologic subtype of STS. Doxorubicin, epirubicin, and ifosfamide are cornerstones of treatment; however, newer targeted agents and immunotherapy are being used with increasing success in a variety of STS.

(4) ILP and ILI with melphalan can be used to treat extremity STS, particularly in patients with either primary or recurrent unresectable disease. There is some suggestion of decreased local recurrence with definite downstaging of the tumor, but survival data are lacking (*Ann Surg Oncol*. 2007;14:230).

(5) Other therapies. Trabectedin (a small molecule inhibitor of DNA nucleotide excision repair), **pazopanib** (an oral TKI), **eribulin** (a microtubule-inhibiting agent), and **olaratumab** (a monoclonal antibody that blocks PDGFRα) are new therapies with some efficacy in select histologic subtypes for patients with advanced disease. A recent phase III trial evaluated **anlotinib**, a receptor TKI with potential antineoplastic and antiangiogenic activities. Patients with histologically proven advanced STS with intolerance or failure to anthracycline-based chemotherapy were randomized to anlotinib versus placebo. The median PFS was 6.27 months for patients receiving anlotinib compared to 1.47 months for patients receiving placebo (*J Clin Oncol*. 2018;36(Suppl 11):503). There is a current clinical trial evaluating this in the United States.

C. Benign Soft Tissue Lesions

1. **Cutaneous cysts** may be of epidermal, dermal, trichilemmal, or sebaceous duct origin. Symptomatic or infected cysts should be excised or drained. Asymptomatic cysts may be removed for diagnosis, prevention of infection, or cosmesis. Excision should include the entire cyst, its lining, and any skin tract or drainage site to prevent recurrence. All excised cysts should be sent for pathology review to exclude the rare case of cystic malignancy (e.g., porocarcinoma).
2. **Neurofibromas** are benign nerve sheath tumors. They are soft, pendulous, sometimes lobulated subcutaneous masses of variable size. Solitary tumors are common; however if a patient has multiple, one must consider neurofibromatosis type 1. They may be removed for pain, increase in size, concern for malignant degeneration, or cosmesis.
3. **Ganglion cysts** are subcutaneous cysts attached to the joint capsule or tendon sheath of the hands and wrists and are most common among young and middle-aged women. These lesions present as firm, round masses of the hand and wrist. Pain, limitation of movement, and nerve palsies are indications for treatment. These lesions can be aspirated. However, to prevent recurrence, which may occur in up to 40% of patients, surgical excision should include the capsular attachment and a small portion of the joint capsule.
4. **Lipomas** are benign tumors consisting of fat. They are soft, rubbery, and mobile subcutaneous masses of variable size. Malignant potential is near zero. Asymptomatic small tumors can be observed, but symptomatic or enlarging tumors are concerning and should be biopsied or removed. A complete gross resection should be performed to prevent recurrence.

CHAPTER 32: SKIN AND SOFT TISSUE TUMORS

Multiple Choice Questions

1. **For which of the following patients is sentinel lymph node biopsy (SLNB) indicated?**

   a. A 55-year-old male with 0.6-mm thick melanoma of the back with no ulceration and three mitoses/mm^2
   b. A 28-year-old female with melanoma in situ of the right back
   c. A 66-year-old male with 1.2-mm thick acral melanoma of the left lower extremity with left inguinal adenopathy
   d. A 54-year-old female with 3.2-mm thick right upper extremity melanoma with two pulmonary metastases
   e. A 35-year-old male with 1.4-mm thick melanoma of the back with no ulceration or mitoses

2. **A 68-year-old male presents with a growing, smooth, hypopigmented 2-cm lesion on the right cheek that he says occasionally stings and bleeds. The best next step is:**

   a. Mohs microsurgery
   b. Excisional biopsy
   c. FNA
   d. Punch biopsy
   e. Shave biopsy

3. **A 38-year-old firefighter is referred to your clinic with a nonhealing wound that arose after sustaining a burn injury 4 months ago. His past medical history is significant for diabetes mellitus type II controlled on insulin and a recent HgbA1c of 6.8%. He smokes about one pack weekly. He is otherwise healthy. He denies any fever but complains of oozing from his lower extremity wound. Examination of the left lower extremity reveals a 4-cm linear scar with a 1.5-cm central ulcer with serosanguineous drainage and mild local edema. Peripheral pulses are palpable. There is mild tenderness but no warmth or erythema. The best course of action is to:**

a. Prescribe topical mupirocin
b. Increase insulin dose
c. Advise smoking cessation
d. Obtain ankle–brachial indices
e. Biopsy wound edge

4. **A 44-year-old male is referred to your clinic after punch biopsy of a lesion on his left shoulder revealed a 2.1-mm thick superficial spreading-type melanoma. There is no clinically detectable lymphadenopathy. The most appropriate management is:**

   a. Wide local excision with 1-cm margins
   b. Wide local excision with 2-cm margins
   c. Wide local excision with 1-cm margins and sentinel lymph node biopsy
   d. Wide local excision with 2-cm margins and sentinel lymph node biopsy
   e. Wide local excision with 2-cm margins and left axillary lymph node dissection

5. **A 55-year-old female presents to your clinic with a 4-mm brown, homogeneous, round macular lesion with slightly indistinct border located on the right posterior calf. She states it is new within the last year. The most appropriate management is:**

   a. Observation
   b. Shave biopsy
   c. Excision with 1-cm margins
   d. Excisional biopsy
   e. Topical 5-fluorouracil for 2 to 6 weeks

6. **A 46-year-old male presents on referral from his primary physician to your clinic with a “lump” of the left posterior neck. He has noticed this since he was a child. He denies any associated symptoms or complaints. On examination, a 1-cm mobile, soft, round mass is palpable at the border of the left trapezius. Neurovascular examination is unremarkable. The most appropriate management is:**

a. Observation
b. Core needle biopsy
c. Surgical excision
d. Incisional biopsy
e. CT of the head and neck

7. **A 30-year-old male presents with an ulcerated pigmented lesion on his right arm and right axillary lymphadenopathy. CT scan shows innumerable lesions within his lungs. Both the arm lesion and lung axillary lymph nodes are biopsied. The pathology is melanoma. His tumor does not have a *BRAF* mutation. What is the next best treatment option?**

a. Combination nivolumab/ipilimumab
b. SLNB
c. Intralesional IL-2
d. Vemurafenib
e. Radiation

8. **A 42-year-old female presents with a 2- ë 4-cm enlarging right upper extremity mass. She is right handed and has had problems dropping things recently. Physical examination reveals the mass without overlying skin changes. Grip strength is weak. The best management option is:**

a. Refer for radiation therapy
b. Obtain MRI and chest CT
c. Perform core biopsy
d. Excise with wide margins and perform sentinel lymph node biopsy
e. Perform FNA

9. **A 63-year-old female presents with a lump in her left axilla that she has noticed for the last 4 months. She denies any skin lesions, recent infections, or fevers and physical examination is unremarkable except for axillary adenopathy. Mammogram obtained 3 weeks ago is unremarkable. The most appropriate next step is:**

a. Core needle biopsy

b. PET scan
c. Observe, follow-up in 1 month
d. 10-day course of Keflex
e. Radiation therapy

10. Which of the following is the most important prognostic factor for soft tissue sarcomas?

a. Histologic subtype
b. Age at presentation
c. Comorbidities
d. Necrosis
e. Grade

11. A 73-year-old female was recently diagnosed with a left distal femoral high-grade malignant fibrous histiocytoma abutting the distal superficial femoral artery measuring 7 cm. The best next step is:

a. Wide local excision
b. Left above-the-knee amputation
c. Chest CT
d. Isolated limb perfusion
e. Radiation therapy

12. A 44-year-old male is taken to the operating room for resection of a large retroperitoneal liposarcoma. He has no significant past medical history and preoperative laboratory studies were normal. After laparotomy, the tumor is discovered to encase the left renal artery and vein. The most appropriate course of action is:

a. Tumor debulking followed by adjuvant chemotherapy
b. Placement of clips, closure, and referral for radiation therapy
c. Closure and subsequent chemotherapy
d. Resection of the mass en bloc with the left kidney
e. Resection of the mass with a positive gross margin, percutaneous nephrostomy tube placement

33

Adrenal, Pituitary, and Hereditary Endocrine Syndromes

Jared McAllister and L. Michael Brunt

I. DISEASES OF THE ADRENAL GLAND AND PITUITARY

A. Embryology, Anatomy, and Physiology

1. **Embryology.** The **adrenal cortex** arises from the coelomic mesoderm around the fifth week of gestation. The **adrenal medulla** is populated by the neural crest cells originating from the neural ectoderm that migrate ventrally. The consequence of this migration is evident by the existence of **paragangliomas** (extra-adrenal pheochromocytomas) all along the paraspinal axis.
2. **Anatomy.** The adrenal glands are retroperitoneal structures that lie along the superior border of each kidney and are adjacent to the inferior vena cava (IVC) on the right and the aorta on the left. Each adrenal gland has arterial supply from three sources, but typically only a single source of venous drainage. Arterial supply is from the superior adrenal artery which derives from the inferior phrenic artery; the middle adrenal arteries, which arise directly from the aorta; and the inferior adrenal artery, which arises from the renal artery. Venous drainage occurs through a single central vein for each adrenal; the right adrenal vein drains directly into the IVC and the left adrenal vein drains into the left renal vein.
3. **Physiology.** The adrenal gland is histologically composed of four layers, each with their own biosynthetic products.

a. Adrenal cortex

(1) The **zona glomerulosa** is responsible for mineralocorticoid production, of which **aldosterone** is the primary product. Aldosterone production is stimulated by angiotensin II and increased levels of serum potassium. Aldosterone acts to increase circulating blood volume by increasing sodium and chloride reabsorption in the distal tubule of the kidney.

(2) The **zona fasciculata** produces the glucocorticoids, of which cortisol is the primary product. Cortisol production is stimulated by the release of **adrenocorticotropic hormone (ACTH**) by the anterior pituitary gland. ACTH itself is stimulated by the release of **corticotropin-releasing hormone (CRH)** by the hypothalamus. Glucocorticoids have extremely broad effects with the overall goal of inducing a catabolic state in the body in response to stress. Glucocorticoids increase blood glucose concentrations, stimulate lipolysis, enhance adrenergic stimulation of the cardiovascular system, and reduce the inflammatory response of the immune system.

(3) The **zona reticularis** produces the adrenal sex hormones androstenedione and dehydroepiandrosterone (DHEA). These hormones support the gonadal production of testosterone and estrogen.

b. Adrenal medulla

The **medulla** produces the catecholamines **norepinephrine** and **epinephrine** that act on peripheral α- and β-adrenergic receptors. α-Receptor stimulation produces peripheral vasoconstriction. β_1-Receptor stimulation targets the myocardium and increases heart rate and contractility. β_2-Receptor stimulation produces peripheral vasodilation.

B. Adrenal Incidentaloma (Fig. 33-1). Adrenal incidentaloma is the most commonly identified adrenal lesion. The prevalence is between 1% and 4% of abdominal computed tomography (CT) scans and increases with age from 0.1% in 20 to 29 year olds to 7% in patients over 70 (*Endocrine.* 2011;40:80–83). The important questions to address for an adrenal incidentaloma are (1) is the mass functional and secreting adrenal hormones and (2) is it malignant or potentially malignant? If the answer is yes to either of these, then adrenalectomy is indicated.

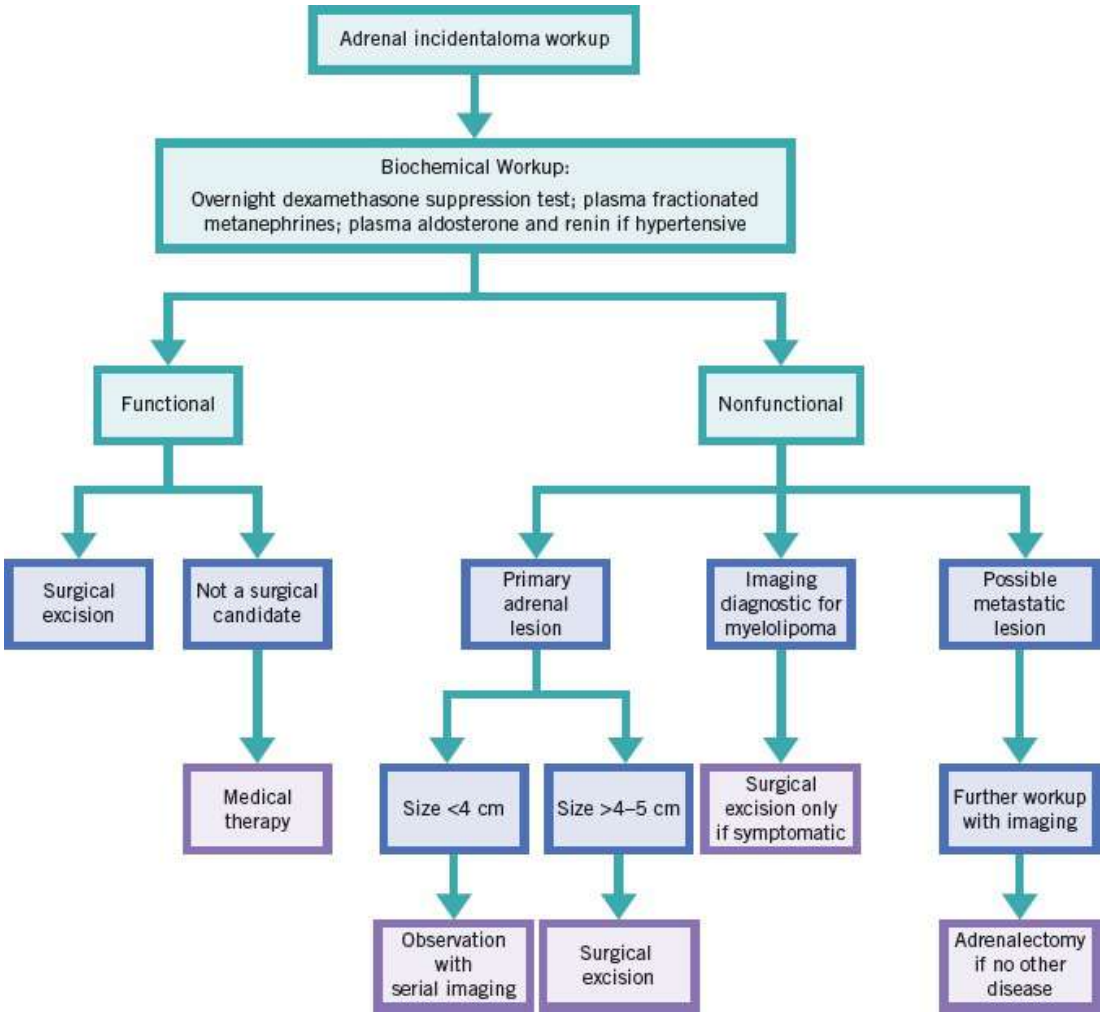


FIGURE 33-1 Algorithm for evaluation and treatment of adrenal incidentaloma.

1. Patients presenting with an adrenal mass should undergo a complete biochemical workup (*Endocr Pract.* 2009;15:450–453) that includes:
   a. Plasma **metanephrines** and **normetanephrines** and/or 24-hour urinary catecholamines and metanephrines to evaluate for a pheochromocytoma.
   b. **Overnight low-dose dexamethasone suppression test** to screen for hypercortisolism. 1 mg of dexamethasone is given at 11 pm, and an 8 am plasma cortisol is obtained. In normal individuals, cortisol should suppress to <1.8 mg/dL.
   c. Plasma **aldosterone** and plasma **renin** activity in hypertensive patients to evaluate for an aldosteronoma.
2. Malignant and benign adrenal masses can typically be distinguished on the basis of characteristic CT and magnetic resonance imaging

(MRI) features (Table 33-1) (*Cancer Imaging.* 2010;10:102–113).

a. Size is an important factor in detecting malignancy, with the risk of malignancy increasing for size >4 to 5 cm.

b. Other imaging characteristics suspicious for malignancy include irregular borders or local invasiveness, CT attenuation >10 Hounsfield units on noncontrasted CT, slower washout of contrast media on contrasted CT, and no loss of signal on opposed-phase chemical shift MRI.

c. Note that pheochromocytomas also have higher attenuation on CT, do not lose signal on chemical shift MRI, and can be large tumors (5 to 6 cm or larger).

d. Adrenal myelolipomas are also larger lesions that can be recognized radiographically by the presence of macroscopic fat.

3. Adrenal biopsy is rarely indicated for an adrenal incidentaloma and should never be done unless a pheochromocytoma has been excluded biochemically because it may precipitate a hypertensive crisis. The main role of adrenal biopsy is to obtain tissue diagnosis in unresectable adrenal metastases.

C. Functional Adrenal Masses

1. Cushing syndrome and hypercortisolism

a. Clinical manifestations. The clinical manifestations of Cushing syndrome include hypertension, central obesity (i.e., moon facies, prominent supraclavicular fat pads, buffalo hump), facial plethora, edema, muscle weakness, glucose intolerance, mood swings, irregular menses, osteoporosis, easy bruising, and purplish striae. Women may develop acne, hirsutism, and amenorrhea as a result of adrenal androgen excess.

b. Pathophysiology of excess circulating glucocorticoids.

(1) Iatrogenic. The most common cause of Cushing syndrome is iatrogenic from administration of exogenous glucocorticoids.

(2) Cushing disease. Hypersecretion of ACTH from the anterior pituitary gland (Cushing disease) is the most common pathologic cause (65% to 70% of cases) of endogenous hypercortisolism. The adrenal glands respond normally to the elevated ACTH, and the result is bilateral adrenal hyperplasia. Cushing disease is almost always caused by a pituitary

microadenoma. Transsphenoidal resection is the treatment of choice. Excessive release of CRH by the hypothalamus is a rare cause of hypercortisolism.

TABLE 33-1 Imaging Characteristics of Adrenal Masses

Adrenal Mass	Imaging Characteristics
Adrenocortical adenoma	Unilateral, <4–5 cm in diameter Round, homogeneous density with smooth border Low attenuation on CT scan (<10 HU) Rapid, intense contrast enhancement followed by early contrast washout (absolute percent washout >60%, relative percent washout >40%) Intracellular fat with signal loss on opposed-phase MRI images
Myelolipoma	Macroscopic fat on CT Calcification Hyperintense signal on T1 MRI
Pheochromocytoma	Hypervascularity with cystic areas in larger lesions Rapid, intense contrast enhancement with variable delayed washout High T2 MRI signal intensity (light-bulb sign)
Adrenocortical carcinoma	Unilateral, >4–5 cm Irregular shape, heterogeneous, central tumor necrosis, local invasion Calcification Increased attenuation on CT (>10 HU) Delay in contrast washout No loss of signal on opposed-phase MRI Elevated SUV on PET
Adrenal metastasis	Irregular shape, heterogeneous May be bilateral or with other metastatic disease Increased attenuation on CT (>10 HU) Delay in contrast washout No loss of signal on MRI Elevated SUV on PET

CT, computed tomography; HU, Hounsfield units; MRI, magnetic resonance image; PET, positron emission tomography; SUV, standardized uptake values.

(3) Cortisol-producing adrenal adenoma. Abnormal secretion of cortisol from a primary adrenal adenoma accounts for 10% to 20% of cases, with fewer cases due to adrenocortical carcinoma (ACCA). Primary adrenal neoplasms secrete corticosteroids independent of ACTH and, therefore, result in suppressed plasma ACTH levels and atrophy of the adjacent and contralateral adrenocortical tissue.

(4) Ectopic ACTH production. Ectopic ACTH production accounts for approximately 10% to 15% of cases. Tumors that produce ACTH ectopically include small cell lung carcinoma, carcinoid (neuroendocrine) tumor, pancreatic carcinoma, thymic carcinoma, medullary thyroid cancer, and other neuroendocrine neoplasms. Patients with ectopic ACTH-secreting neoplasms can present primarily with hypokalemia, glucose intolerance, and hyperpigmentation but with few other chronic signs of Cushing syndrome.

c. Diagnostic evaluation (Fig. 33-2). The first step in the diagnostic evaluation of suspected Cushing syndrome is to assess for increased cortisol secretion. If those tests are positive, then a plasma ACTH should be done to differentiate ACTH-dependent causes of Cushing's (pituitary or ectopic ACTH) from ACTH-independent causes (adrenal source). Finally, the source of the Cushing's should be localized.

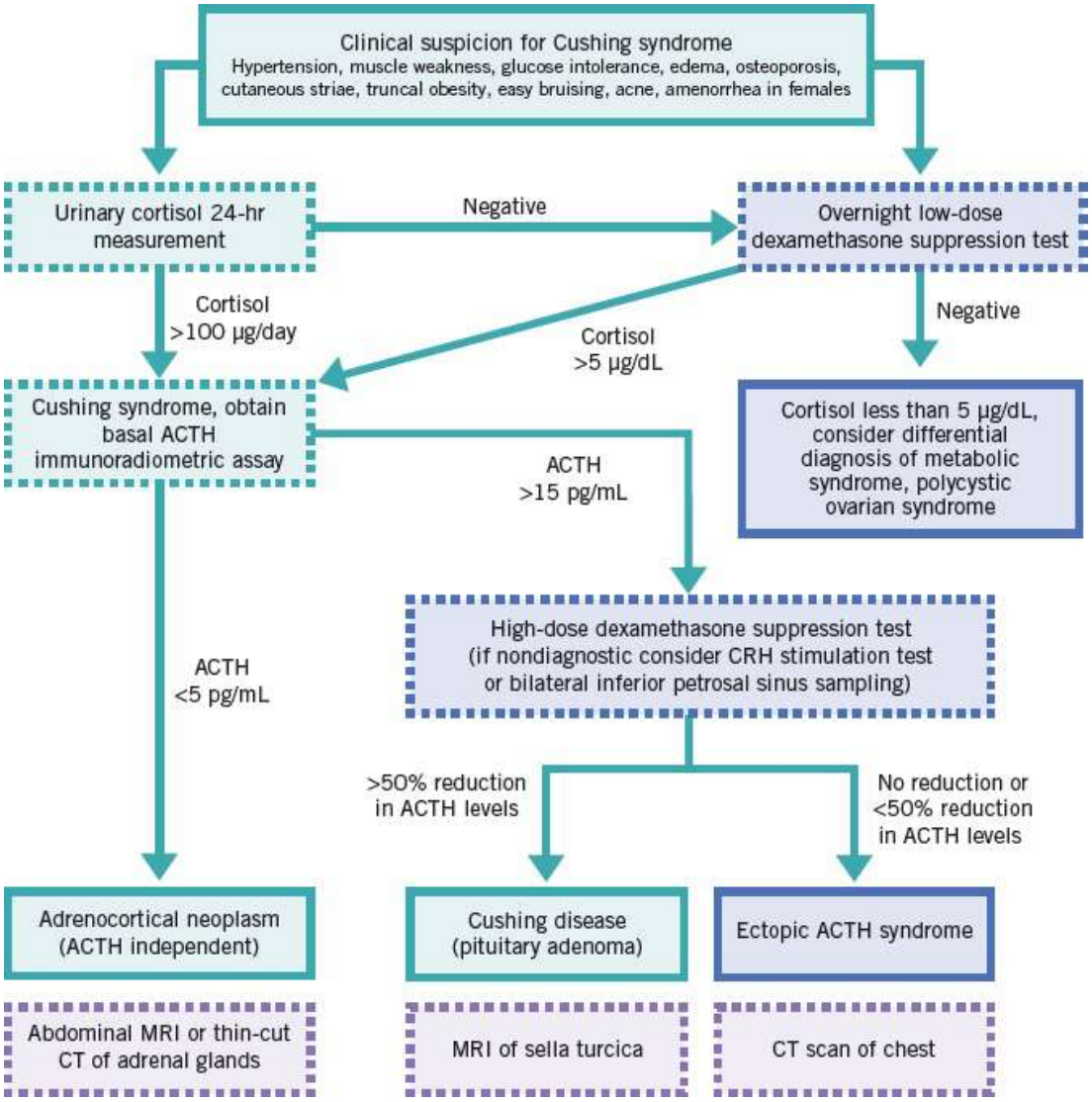


FIGURE 33-2 Diagnosis of Cushing syndrome is biochemical.

(1) Establishing the presence of hypercortisolism. First-line screening tests for Cushing syndrome include 24-hour urinary free cortisol, a low-dose dexamethasone suppression test, and late-night salivary cortisol. None of these tests have adequate sensitivity and specificity to diagnose Cushing syndrome alone. Generally, at least two abnormal results are required to make the diagnosis, and test choice should be tailored to the patient.

(a) 24-hour measurement of the urinary excretion of free cortisol gives a good representation of total cortisol secretion given the episodic and circadian rhythms that affect cortisol at a given moment. Values >62 >g/dL in the

setting of clinically suspected Cushing syndrome is highly correlated with a positive diagnosis, and one can proceed directly to determining the source (*N Engl J Med*. 2017; 376:1451–1459).

(b) Low-dose **overnight dexamethasone suppression test**. Dexamethasone 1 mg orally is administered at 11 pm, and plasma cortisol is measured at 8 am. Patients with autonomous hypercortisolism have lost the normal adrenal–pituitary feedback and should fail to suppress the morning plasma cortisol level below 1.8 >g/dL.

(c) Late-night salivary cortisol testing is based on the normal evening nadir of plasma cortisol that is lost in patients with Cushing syndrome. Samples are taken before 11 pm over several days. This test should be avoided in shift workers where circadian rhythm may be disturbed.

(2) Differentiation of ACTH-dependent from ACTH-independent causes. Plasma ACTH should be measured once hypercortisolism is documented or suspected. Suppression of plasma ACTH to <5 pg/mL is indicative of an ACTH-independent source due to an adrenocortical neoplasm. ACTH levels in Cushing disease usually range from the upper limits of normal to significantly above normal (15 to 500 pg/mL). The highest plasma levels of ACTH (1,000 pg/mL) have been observed in patients with ectopic ACTH syndrome.

(3) Localization of the source of hypercortisolism.

(a) ACTH-dependent Cushing syndrome. Pituitary MRI is generally the first step in distinguishing between pituitary and ectopic sources. In patients with tumors >6 mm in the anterior pituitary, further testing can be foregone. In those with smaller tumors or no abnormalities on pituitary MRI, **inferior petrosal sinus sampling (IPSS)** is performed. Simultaneous bilateral petrosal sinus and peripheral blood samples are obtained before and after peripheral intravenous injection of 1 μg/kg of CRH. Levels of ACTH in the inferior petrosal sinus are compared to peripheral plasma ACTH levels: A basal ratio of ≥2 or a ratio of ≥3 after CRH administration is 100% sensitive and specific for pituitary

adenoma. In patients with equivocal ACTH levels or MRI findings, CRH stimulation testing and high-dose dexamethasone suppression testing can be useful in determining the cause of hypercortisolism. Patients with suspected ectopic ACTH release should have a CT scan of the chest to identify possible small cell lung cancers.

(b) Patients with ACTH-independent hypercortisolism require thin-section CT or MRI imaging of the adrenals, both of which identify adrenal abnormalities with more than 95% sensitivity.

d. Surgical treatment of Cushing syndrome

(1) Transsphenoidal resection of an ACTH-producing pituitary tumor is successful in ≥80% of cases of Cushing disease. In patients who fail surgical treatment of pituitary Cushing's, laparoscopic bilateral adrenalectomy may occasionally be indicated.

(2) Treatment of ectopic ACTH syndrome involves resection of the primary lesion, if possible.

(3) Primary adrenal Cushing syndrome is treated by adrenalectomy. Rarely, the cause may be macro- or micronodular adrenal hyperplasia which is treated with **bilateral adrenalectomy**. All patients who undergo adrenalectomy for primary adrenal causes of Cushing syndrome require peri- and postoperative glucocorticoid replacement because the pituitary–adrenal axis is suppressed. Recovery of the pituitary–adrenal axis may take as long as 4 to 6 months following unilateral adrenalectomy.

2. Primary hyperaldosteronism. Primary hyperaldosteronism is a syndrome of hypertension and hypokalemia caused by hypersecretion of the mineralocorticoid aldosterone. Its prevalence is as high as 8% to 12% in hypertensive populations. Secondary aldosteronism is a physiologic response of the renin–angiotensin system to renal artery stenosis, cirrhosis, congestive heart failure, or even normal pregnancy.

a. Pathophysiology of primary hyperaldosteronism. There are four subtypes of primary hyperaldosteronism:

(1) **Aldosterone-producing adrenal adenoma (APA)** is the cause of primary aldosteronism in up to two-thirds of cases and is one of the few surgically correctable causes of hypertension.

(2) **Idiopathic hyperaldosteronism (IHA)** from bilateral cortical hyperplasia accounts for 30% to 40% of cases of primary aldosteronism and is best managed medically.

(3) **Aldosterone-producing adrenal carcinoma** is very rare.

(4) **Glucocorticoid-suppressible aldosteronism** may be familial and is rare. This condition is due to ACTH control of aldosterone secretion and responds to administration of exogenous corticosteroids.

b. Diagnosis

(1) **Screening for primary hyperaldosteronism** should be carried out in adults with young age of onset of hypertension, hypertension that is poorly controlled or requires multiple medications, and hypertension with associated hypokalemia. It should be noted the hypertension in these patients is predominately diastolic and is often refractory to standard medical therapy.

(2) **Laboratory diagnosis.** Screening for hyperaldosteronism consists of measurement of upright plasma aldosterone concentration (PAC) and plasma renin activity (PRA). A PAC:PRA ratio of >25–30 in conjunction with a primary aldosterone level >15 ng/dL and plasma renin <0.5 ng/mL/hr is diagnostic of primary hyperaldosteronism. Some investigators use a lower cutoff level for aldosterone in order to avoid missing affected patients, provided that the ratio is high and the aldosterone is >6 >g/dL. An inappropriate kaliuresis (>30 mEq/day) in the setting of hypokalemia also supports the diagnosis provided the patient is not on a low-salt diet. Drugs that stimulate renin such as spironolactone, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor antagonists (ARBs) can produce false-negative test results. β-Blockers, clonidine, and nonsteroidal anti-inflammatory drugs suppress renin and may result in false positives (*Horm Metab Res.* 2012;44:170–176). Primary hyperaldosteronism is confirmed by demonstration of lack of aldosterone suppression

with salt loading. This test is performed by having patients increase salt intake (two to three bags of salted potato chips or 6 g salt/day) for 72 hours and then measurement of 24-hour urine aldosterone on the third day which should not suppress to <12 ng/dL in patients with primary hyperaldosteronism. Alternatively, saline loading by administration of 2-L intravenous normal saline infusion over 4 hours can be carried out. Postinfusion aldosterone values >10 >g/dL make the diagnosis of PA very likely (*J Clin Endocrin Metab*. 2016;101:1889–1916).

c. Localization. Once the biochemical diagnosis has been established, the subtype of hyperaldosteronism should be determined.

(1) High-resolution thin-cut (3-mm) adrenal CT may show a unilateral adenoma with better spatial resolution than MRI. In some centers, the presence of a unilateral macroadenoma (>1 cm) and a normal contralateral adrenal is sufficient to recommend adrenalectomy, especially in patients less than age 35 to 40 years. It is important to note that incidental adrenal nodules are more common with increasing age and that, while aldosterone-producing adenomas are treated by surgical excision, bilateral hyperplasia is treated medically. Therefore, older patients and those with microadenomas as well as those with normal adrenals and bilateral nodules should undergo adrenal vein sampling (AVS) to determine if there is a unilateral increased source of aldosterone before proceeding to surgery.

(2) In AVS, simultaneous adrenal vein blood samples for aldosterone and cortisol are taken from both adrenal veins and the IVC. An aldosterone to cortisol ratio greater than 4:1 between sides supports a lateralizing source and management by adrenalectomy.

d. Treatment. Surgical removal of an APA through a posterior retroperitoneal endoscopic or laparoscopic transabdominal flank approach results in cure or substantial improvement in hypertension and hypokalemia in more than 90% of patients.

(1) Preoperatively, patients should have their hypertension controlled and electrolytes corrected. Patients with prolonged

hypertension prior to diagnosis are not often cured of hypertension but should be better controlled on less medication. Preoperatively, patients with aldosteronism can usually be managed medically with **spironolactone** (200 to 400 mg/day). Patients with IHA should be treated medically with spironolactone or **eplerenone**, a selective aldosterone antagonist. A potassium-sparing diuretic, such as **amiloride** (5 to 20 mg/day), and **calcium channel blockers** have also been used.

(2) It is critically important to stop spironolactone and any potassium diuretics once adrenalectomy has been performed in order to avoid severe hyperkalemia postoperatively. Plasma aldosterone and renin should be measured at follow-up to document biochemical cure.

3. Pheochromocytoma

a. The clinical manifestations of pheochromocytoma include paroxysms of pounding frontal headache, diaphoresis, palpitations, flushing, and/or anxiety related to the excess sympathetic stimulation from catecholamines. The most common sign is episodic or sustained hypertension, but pheochromocytoma accounts for only 0.1% to 0.2% of patients with sustained diastolic hypertension. Uncommonly, patients present with complications of prolonged uncontrolled hypertension (e.g., myocardial infarction, cerebrovascular accident, renal disease).

b. Pathophysiology of pheochromocytoma.

(1) Pheochromocytomas are neoplasms derived from the **chromaffin cells** of the sympathoadrenal system that engage in unregulated, episodic oversecretion of catecholamines.

(2) Approximately 85% to 90% of pheochromocytomas in adults arise in the adrenal medulla, whereas 10% to 15% arise in the **extra-adrenal chromaffin tissue**, including near the renal hilum, paravertebral ganglia, posterior mediastinum, organ of Zuckerkandl, and urinary bladder.

(3) Pheochromocytomas can occur in association with several hereditary syndromes, including multiple endocrine neoplasia (MEN) types 2A and 2B, von Hippel–Lindau syndrome,

neurofibromatosis type 1, and succinate dehydrogenase mutations. Tumors that arise in familial settings frequently are bilateral. Young patients with pheochromocytomas or patients with bilateral or extra-adrenal pheochromocytomas should undergo genetic testing. See Table 33-2 for a list of hereditary pheochromocytoma syndromes.

TABLE 33-2 Multiple Endocrine Neoplasia Syndromes

	MEN-1	MEN-2A	MEN-2B
Gene mutation	MENIN	RET	RET
Endocrinopathy	HPT Pituitary Pancreatic endocrine tumors	MTC Pheo HPT	MTC Pheo

HPT, hyperparathyroidism; MTC, medullary thyroid carcinoma; Pheo, pheochromocytoma.

c. Biochemical testing. The biochemical diagnosis of pheochromocytoma is made by demonstrating elevated levels of plasma metanephrines or 24-hour urinary catecholamines and metanephrines. If possible, antihypertensive medications (especially monoamine oxidase inhibitors) should be discontinued before the 24-hour urine collection, and creatinine excretion should be measured simultaneously to assess the adequacy of the sample.

d. Localization. Radiographic tests are used to demonstrate the presence of an adrenal mass.

(1) CT identifies 90% to 95% of pheochromocytomas >1 cm. Up to 30% to 40% of pheochromocytomas present as an incidental mass found on imaging done for other reasons. MRI scan can also be useful because T2-weighted images have a characteristic high intensity in patients with pheochromocytoma compared with adenomas (Fig. 33-3).

(2) In patients with biochemical evidence pheochromocytoma and negative CT and MRI, further imaging with scintigraphic or PET scanning can help identify occult tumors.

(a) Scintigraphic scanning after the administration of ^{123}I-meta-iodobenzylguanidine (MIBG) provides a functional and anatomic test of hyperfunctioning chromaffin tissue. MIBG scanning is very specific for both intra- and extra-adrenal pheochromocytomas but is expensive and somewhat difficult to use.

(b) 68-Ga DOTATATE PET scanning has the highest sensitivity and can be helpful in identifying occult tumors or metastatic disease in patients with high risk of metastatic disease (paraganglioma or large tumor).

e. Treatment. The treatment of benign and malignant pheochromocytomas is surgical excision.

(1) Preoperative preparation. Preparation for adrenalectomy for pheochromocytomas includes administration of α-adrenergic blockade to control hypertension and to permit reexpansion of intravascular volume. **Phenoxybenzamine** is a nonspecific α-blocker that is initiated and increased to 20 to 40 mg orally two to three times per day until the desired effect or prohibitive side effects are encountered. However, its use today is limited by the high cost of the medication (e.g., $9,000 for 100 10-mg capsules). Consequently, selective α-blockers such as doxazosin and calcium channel blockers are increasingly being used given their low cost and more favorable side effect profiles. The goal of therapy is to control hypertension and tachycardia, and some degree of postural hypotension is expected and is the desired end point. It is important for the patient to stay well hydrated as α-blockade proceeds and intravascular volume expands. β-Adrenergic blockade (e.g., metoprolol) may be added if reflex tachycardia or arrhythmias develop but should only be initiated after complete α-adrenergic blockade to avoid unopposed α-effect and precipitation of a hypertensive crisis.

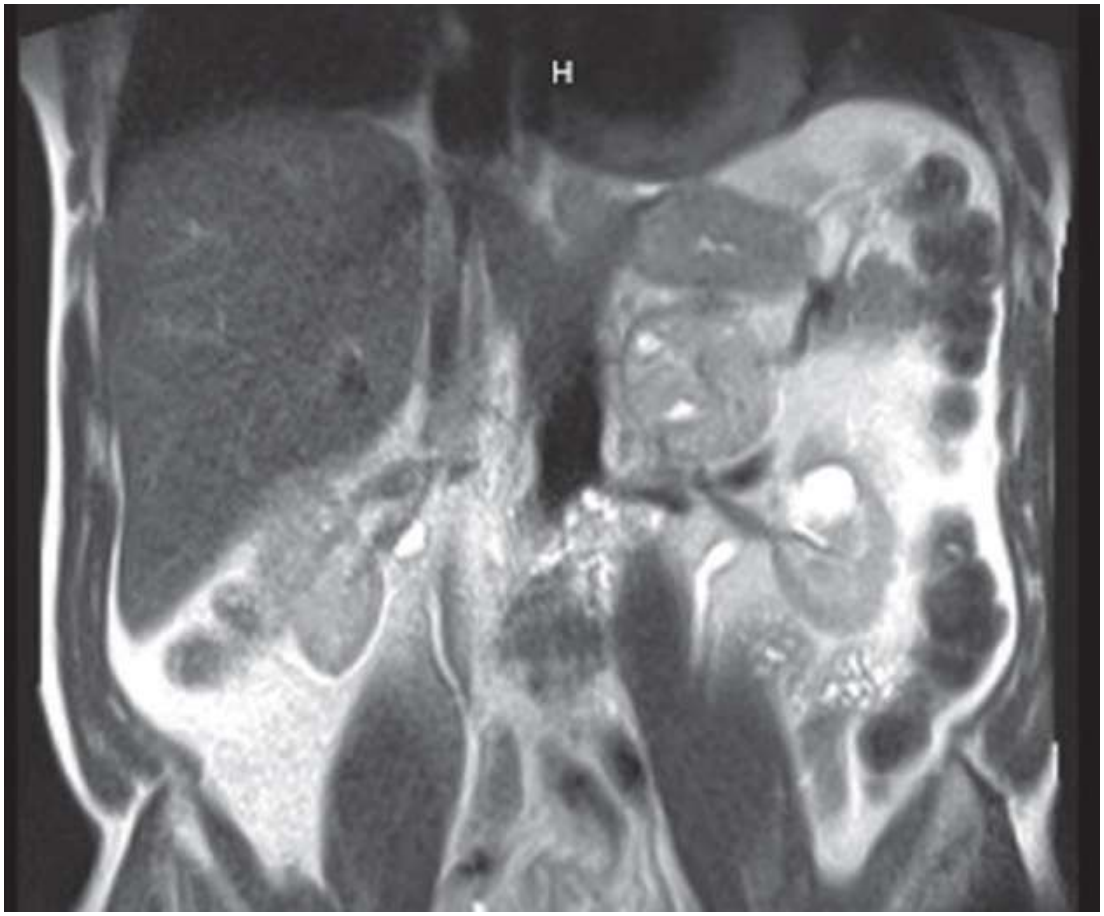


FIGURE 33-3 Magnetic resonance imaging (MRI) T2-weighted image showing typical appearance for pheochromocytoma.

(2) Intra-operative considerations: All patients should be monitored intraoperatively with an arterial line. Patients with large or very active pheochromocytomas, or who have significant comorbidities, may require central line placement. Intraoperative labile hypertension can occur during resection of pheochromocytoma. This can be prevented by minimal manipulation of the tumor but can be controlled most effectively with IV vasodilators (sodium nitroprusside or nitroglycerin). After the adrenal has been disconnected from its blood supply, many patients require transient pressor support for up to a few hours.

(3) Technical considerations. The preferred surgical approach is laparoscopic in the vast majority of patients. The lateral transabdominal flank approach is most commonly used, but a

posterior retroperitoneal endoscopic approach may be used for smaller tumors in nonobese patients. In patients with MEN type 2A or 2B and bilateral tumors, an effort should be made to preserve adrenal cortical function by carrying out a partial adrenalectomy.

(4) Post-operative considerations and follow-up: Most patients should be monitored in the surgical intensive care unit in the immediate postoperative period. Following pheochromocytoma excision, annual follow-up with measurement of plasma fractionated metanephrines is recommended for at least 5 years after adrenalectomy because of the risk of recurrence, even after resection of an apparently benign lesion.

D. Nonfunctional Adrenal Masses

1. **Adrenocortical adenomas** comprise the majority of adrenal incidentalomas. Adrenocortical adenomas are benign and nonfunctioning, with the majority having no clinical significance.
   - **a. Surgery** should be performed in patients with nonfunctional adrenal adenomas greater than 4 to 5 cm in diameter or if there is significant growth during follow-up (*Endocr Pract.* 2009;15:450–453).
   - **b. Tumors <4 cm should be monitored clinically and radiologically at 4 to 6 months after initial presentation and then annually for 2 years**. Any tumor that enlarges by more than 1 cm during the follow-up period should be removed. Biochemical testing should be performed annually for up to 5 years.
2. **Adrenal myelolipoma** is a benign tumor composed of mature fat and hematopoietic elements.
   - **a.** Myelolipomas have characteristic macroscopic fat on CT imaging.
   - **b.** Myelolipomas may enlarge over time. Routine follow-up imaging is not necessary except for large lesions. Surgical excision is only indicated for masses causing local mass-effect symptoms. Spontaneous retroperitoneal hemorrhage may occur with large masses. Approximately 4% of patients diagnosed with a myelolipoma will require adrenalectomy (*J Surg Oncol.* 2012;106:557–564).

3. **Adrenocortical carcinoma (ACCA)** is a rare but aggressive malignancy. Most patients with this cancer present with locally advanced stage III or IV disease.
   a. Syndromes of adrenal hormone overproduction may include hypercortisolism or virilization (Fig. 33-4). Any large adrenal cortical tumor >6 cm should be suspected to be an adrenal cancer. Most adrenal cancers are 10 cm or larger and may extend to surrounding structures, and associated tumor thrombus in the adrenal or renal veins may occur.

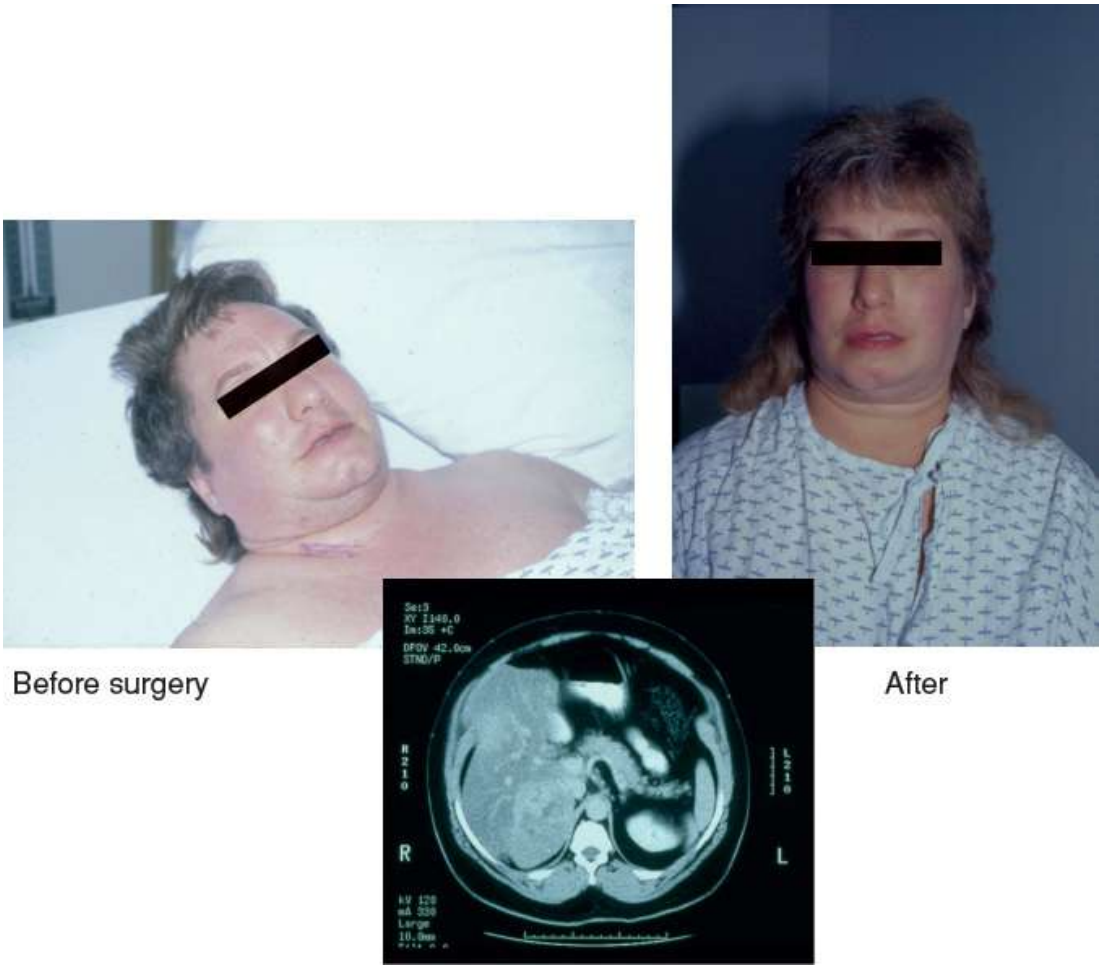


FIGURE 33-4 Adrenocortical carcinoma.

   b. Complete surgical resection is the only chance for cure of ACCA. Definitive diagnosis of ACCA requires operative and pathologic demonstration of nodal or distant metastases. A number of histologic criteria (**Weiss criteria**) are used for the histologic

diagnosis of ACCA. These include presence of necrosis, increased mitotic rate, nuclear grade, and invasion of vessels or adrenal capsule.

c. Frequently, patients with ACCA present with metastatic disease, most often involving the lung, lymph nodes, liver, or bone. Palliative surgical debulking of locally advanced or metastatic ACCA may provide these patients with symptomatic relief from some slow-growing, hormone-producing cancers. Chemotherapy with **mitotane** may be somewhat effective including as adjuvant therapy after complete resection. Overall, the prognosis for patients with ACCA is poor with survival rates of 15% to 20%.

4. Adrenal metastases are the most common malignant lesions involving the adrenal gland. Frequently, bilateral lesions are present.

a. Lung, breast, melanoma, colorectal, pancreatic, hepatocellular, and renal cell cancers all may metastasize to the adrenal glands.

b. Diagnosis of metastatic disease can often be made from the imaging appearance and a history of cancer. A need for pathologic confirmation of metastatic disease is rare and should mainly be done for unresectable metastases in order to direct therapy. **Biochemical testing for pheochromocytoma should *always* be performed prior to biopsy**.

c. Patients with bilateral metastatic disease should be evaluated for adrenal insufficiency.

d. Adrenalectomy for metastatic disease may be considered for an isolated adrenal lesion.

E. Acute Adrenal Insufficiency

1. Acute adrenal insufficiency is an emergency and should be suspected in physiologically stressed patients with a history of either adrenal insufficiency or exogenous steroid use. Adrenocortical insufficiency is most often caused by acute withdrawal of chronic corticosteroid therapy but can occur in the postoperative setting following adrenal surgery or from autoimmune destruction of the adrenal cortex, adrenal hemorrhage (**Waterhouse– Friderichsen syndrome**), or, rarely, infiltration with metastatic carcinoma. The diagnosis and treatment of acute adrenal insufficiency in patients in septic shock is very controversial. Two prospective randomized trials

have shown different effects in the use of hydrocortisone in patients with septic shock (*N Engl J Med.* 2003;348:727–734; *N Engl J Med.* 2008;358:111–124). Current Surviving Sepsis Guidelines call for the use of corticosteroids only in cases of septic shock where the blood pressure is not responsive to fluid administration or vasopressor therapy (*Crit Care Med.* 2013;41:580–637).

a. Signs and symptoms include fever, nausea, vomiting, severe hypotension, and lethargy. Characteristic laboratory findings of adrenal insufficiency include hyponatremia, hyperkalemia, azotemia, and fasting or reactive hypoglycemia.

b. Diagnosis. A **rapid ACTH stimulation test** is used to test for adrenal insufficiency. **Cosyntropin** (i.e., synthetic ACTH, 250 μg) is administered IV, and plasma cortisol levels are measured on completion of the administration and then 30 and 60 minutes later. Normal peak cortisol response should exceed 20 μg/dL.

c. Treatment of adrenal crisis must be immediate and based on clinical suspicion, before laboratory confirmation is available. IV volume replacement with normal or hypertonic saline and dextrose is essential, as is immediate IV steroid replacement therapy with 4 mg of dexamethasone. Thereafter, 50 mg of hydrocortisone is administered IV every 8 hours and is tapered to standard replacement doses as the patient's condition stabilizes. Mineralocorticoid replacement is not required until IV fluids are discontinued and oral intake resumes.

d. Prevention. Patients who have known adrenal insufficiency or have received supraphysiologic doses of steroid for at least 1 week in the year preceding surgery should receive 100 mg of hydrocortisone the evening before and the morning of major surgery, followed by 100 mg of hydrocortisone every 8 hours during the first postoperative 24 hours.

F. Operative Adrenalectomy

1. **Approach. Laparoscopic adrenalectomy** has become the standard of care for adrenal resection and is associated with shorter hospitalization, faster recovery, and lower morbidity compared to open surgery. The only absolute contraindication to a laparoscopic approach is local tumor invasion, but suspected adrenal cortical carcinomas >6 cm should also be approached in an open fashion

because of an increased risk of local recurrence when done laparoscopically. Experience and expertise with adrenalectomy should determine the operative approach in larger benign tumors such as large pheochromocytomas. Both laparoscopic transperitoneal adrenalectomy and retroperitoneal endoscopic adrenalectomy have been described with similar outcomes in terms of operative time, blood loss, length of hospitalization, time to oral intake, morbidity, and mortality (*Surgery.* 2013;153:111–119).

2. **Technique.** For transabdominal adrenalectomy, the patient is placed in a lateral decubitus position with the affected side up. All pressure points are well padded, and a roll is placed under the chest wall to protect the axilla. Four ports are placed in the subcostal region spaced 5 cm apart. Generally, only one 12-mm port is necessary, and the others are 5 mm. On the right side, the key steps include mobilization of the right lobe of the liver by division of the triangular ligament; dissection of the medial border of the adrenal and separation from the IVC; isolation, clipping, and division of the right adrenal vein; dissection of the inferior and superior attachments with control of small arterial branches; and finally, division of the posterior and lateral attachments. On the left side, the splenic flexure is mobilized followed by division of the splenorenal ligament. The plane between the tail of the pancreas and kidney is then developed, which should lead to the adrenal gland. It is important to positively identify the tail of the pancreas and splenic vessels in order to avoid injuring them. The medial and inferior/lateral borders of the adrenal are then defined and dissected. The left adrenal vein is located at the medial-inferior edge and is isolated, clipped, and divided. The remaining lateral, posterior, and superior attachments are then divided, and the specimen is placed in an impermeable entrapment bag and removed.

II. HEREDITARY ENDOCRINE TUMOR SYNDROMES (TABLE 33-2)

A. Multiple Endocrine Neoplasia Type I (MEN-1)

1. **MEN-1** is an autosomal-dominant syndrome characterized by tumors of the parathyroid glands, pancreatic islet cells, and pituitary gland. **Hyperparathyroidism** occurs in virtually all patients. Clinical evidence of **pancreatic islet cell** and **pituitary** tumors develops in 50% and 25% of patients, respectively. Lipomas, thymic or bronchial

carcinoid tumors, and tumors of the thyroid, adrenal cortex, and central nervous system (CNS) may also develop. The gene responsible for MEN-1, ***MENIN***, is located on chromosome 11q13 and appears to act through transcription factors. Genetic testing is available. Screening of affected family members should begin in their early teens, including yearly determinations of plasma calcium, glucose, gastrin, fasting insulin, vasoactive intestinal polypeptide (VIP), pancreatic polypeptide, prolactin, growth hormone, and β-human gonadotropin hormone levels.

a. Hyperparathyroidism. Because hyperparathyroidism is frequently the first detectable abnormality in patients with MEN-1, yearly calcium screening of asymptomatic kindred members is recommended. Patients with hyperparathyroidism and MEN-1 usually have generalized (4-gland) parathyroid enlargement. Surgery should consist of 3.5-gland parathyroidectomy or a total parathyroidectomy with autotransplantation of parathyroid tissue to the sternocleidomastoid muscle or forearm. This method achieves cure in more than 90% of cases and results in hypoparathyroidism in less than 5%. Graft-dependent recurrent hyperparathyroidism, however, is seen in up to 50% of cases and is managed by debulking of the autografted material.

b. Pituitary tumors occur in up to 40% of MEN-1 patients and most commonly are benign prolactin-producing adenomas. Patients may present with headache, diplopia, or symptoms referable to hormone overproduction. **Bromocriptine** inhibits prolactin production, may reduce tumor bulk, and may obviate the need for surgical intervention. **Transsphenoidal hypophysectomy** may be necessary if medical treatment fails.

c. Pancreatic islet cell tumors pose the most difficult clinical challenge and account for most of the morbidity and mortality of the syndrome. **Gastrinomas (i.e., Zollinger–Ellison syndrome, ZES**) are most common, but VIP-secreting tumors, insulinomas, glucagonomas, and somatostatinomas are also encountered. The pancreas is usually diffusely involved, with islet cell hyperplasia and multifocal tumors. Tumors may be found in the proximal duodenum and peripancreatic areas (**gastrinoma triangle**) and are virtually always malignant. The treatment goal is relief of

symptoms related to excessive hormone production and cure or palliation of the malignant process. Patients frequently require medical and surgical therapy.

B. Multiple Endocrine Neoplasia Type 2 (MEN-2)

1. MEN-2 is characterized by medullary thyroid carcinoma (MTC) and includes MEN-2A and MEN-2B. **Familial MTC (FMTC) was previously recognized as a distinct syndrome but is now considered a variant of MEN-2A**. These autosomal-dominant syndromes are caused by gain-of-function mutations in the ***RET* proto-oncogene**, which encodes a transmembrane tyrosine kinase receptor. Genetic testing should be performed on all suspected individuals. Because MTC occurs universally in all MEN-2 variants, **thyroidectomy is indicated for all RET-mutation carriers**. **Calcitonin** serves as a tumor marker for MTC and can be used to guide timing of thyroidectomy as well as postoperative monitoring for disease recurrence. When possible, prophylactic thyroidectomy should be performed prior to the presence of biochemical evidence of disease in order to reduce the risk of spread outside the thyroid that may lead to disease persistence or recurrence. The timing of prophylactic thyroidectomy is determined by the aggressiveness of MTC with specific RET mutations. Current guidelines call for prophylactic thyroidectomy in the first months to year of life for MEN-2B and codon M918T mutation; thyroidectomy before age 5 years for patients in the high-risk category (RET codon 634 and 883 mutations); and thyroidectomy beginning after 5 years of age for patients with elevated serum calcitonin levels in the moderate-risk group (RET codon 533, 609, 611, 618, 620, 630, 666, 768, 790, 804, 891, and 912 mutations) (*Thyroid.* 2015;25(6):567–610). A rising calcitonin level should prompt earlier intervention.
    a. **MEN-2A.** All patients with MEN-2A will develop MTC, but the course of MTC is variable and can be predicted based upon codon mutation. Mutations in codon 611, 618, 620, 634 expose patients to an increasing, cumulative age-related risk of lymph node metastasis, starting from the midteens and reaching a greater than 40% cumulative risk by the age of 20. MEN-2A with mutations in codons 768, 790, 804, or 891 is less aggressive and often presents with MTC in the second or third decade of life. The penetrance of

other features of the syndrome is variable. Pheochromocytomas arise in approximately 40% to 50% of patients, and hyperplasia of the parathyroid glands occurs in approximately 25% to 35%. Patients with MEN-2A also develop gastrointestinal manifestations, including abdominal pain, distention, and constipation as well as Hirschsprung disease. On genetic analysis, patients with MEN-2A and Hirschsprung disease (MEN-2A-HD) share common mutations in either codon 609, 618, or 620 of exon 10 of the *RET* proto-oncogene. MTC generally occurs earlier than pheochromocytoma or hyperparathyroidism. Nonetheless, biochemical testing to exclude pheochromocytoma is mandatory in all MEN-2 and MTC patients prior to any elective surgical operation. Pheochromocytoma in children as young as age 8 has been reported (*J Surg Oncol.* 2013;108:203–206).

b. MEN-2B. MTC develops in all patients with MEN-2B and is particularly aggressive. MTC may be present at birth in these patients and invasive disease with lymph node metastasis occurs at an early age. Pheochromocytoma penetrance is variable. Patients also develop ganglioneuromatosis and a characteristic physical appearance, with hypergnathism of the midface, marfanoid body habitus, and multiple mucosal neuromas. MEN-2B patients may also demonstrate multiple gastrointestinal symptoms and megacolon.

ACKNOWLEDGMENTS

The authors would like to dedicate this chapter to the memory of Dr. Jeffrey Moley who was the Chief of Endocrine and Oncologic Surgery at Washington University for over two decades and who was senior author on the prior editions of this chapter.

CHAPTER 33: ADRENAL, PITUITARY, AND HEREDITARY ENDOCRINE SYNDROMES

Multiple Choice Questions

1. **A 6-month-old female whose father has multiple endocrine neoplasia (MEN)-2B has tested positive for the RET proto-oncogene mutation. The patient should:**

   a. Have calcitonin levels closely monitored and undergo total thyroidectomy when calcitonin levels are greater than 20.
   b. Undergo total thyroidectomy at age 5.
   c. Undergo total thyroidectomy within the next several months.
   d. Wait to undergo total thyroidectomy until over 1 year old to prevent permanent damage to the parathyroid glands.
   e. Undergo total thyroidectomy at age 20.

2. **A 40-year-old male presents to the emergency department with a blood pressure of 200/120 and complains of intermittent bouts of headache, heart palpitations, and diaphoresis. CT of the abdomen and pelvis shows a 3-cm left adrenal mass. Appropriate biochemical workup is performed and confirms the suspected diagnosis. Preoperative planning should include:**

   a. Cardiac stress test
   b. PET scan to rule out metastatic disease
   c. β-Blocker therapy alone
   d. α-Blocker therapy
   e. Potassium supplementation

3. **A 32-year-old male is incidentally found to have a 3.5-cm left adrenal mass on a CT scan performed following a motor vehicle accident. He is otherwise healthy and normotensive. He undergoes a dexamethasone suppression test with normal suppression of cortisol levels. Plasma metanephrines and normetanephrines are within normal limits. On review of the CT scan, the appearance is consistent with an adenoma. What is the next step in the patient's management?**

a. Undergo plasma aldosterone level testing.
b. Repeat CT scan in 6 months.
c. Perform laparoscopic left adrenalectomy.
d. Undergo MRI to further evaluate mass.
e. Undergo RET proto-oncogene testing to rule out multiple endocrine neoplasia type 2.

4. **A 50-year-old male with persistent hypertension despite antihypertensive combination therapy with a β-blocker, calcium channel blocker, and ACE inhibitor presents with hypokalemia and elevations in plasma aldosterone levels. CT and MRI imaging demonstrate a 1-cm left-sided adrenal nodule and a 6-mm right-sided adrenal nodule, both benign appearing. Dexamethasone suppression testing and plasma metanephrines are normal. The next step in management is:**

a. Right adrenalectomy
b. Medical management alone with addition of spironolactone
c. Repeat imaging in 6 months
d. Bilateral adrenal vein sampling
e. Bilateral adrenalectomy

5. **A 65-year-old female with hypertension and coronary artery disease status post placement of a drug eluting stent 3 weeks ago presents with an 8-cm right adrenal mass with macroscopic fat found incidentally on CT done for other reasons. Biochemical evaluation reveals a normal dexamethasone suppression test, normal plasma metanephrines, normal aldosterone/renin ratio, and a normal metabolic panel. Appropriate management of this patient includes:**

a. Repeat CT imaging at 12 months
b. PET scan to exclude metastatic disease
c. Immediate right adrenalectomy with patient on Plavix
d. Right adrenalectomy 1 year after coronary stent placement with patient off Plavix
e. No further imaging or intervention

34

Thyroid and Parathyroid Glands

Jesse T. Davidson IV and William E. Gillanders

I. THYROID

A. Embryology, Anatomy, and Physiology

1. **Embryology.** The thyroid gland develops from the **endoderm of the primitive foregut** and arises in the ventral pharynx near the base of the tongue, which ultimately becomes the foramen cecum. The thyroid then descends in the midline of the neck anterior to the hyoid bone and laryngeal cartilages. Congenital anomalies such as ectopic thyroid tissue or thyroglossal duct cysts are directly related to variations in this process. The **parafollicular cells**, or **C cells**, are derived from the neural crest and migrate to the thyroid to produce calcitonin.
2. **Anatomy.** The adult thyroid is a bilobar structure connected by an **isthmus** that lies anterior to the trachea. The thyroid gland's blood supply arises mainly from the **superior and inferior thyroid arteries**, which are branches of the external carotid artery and thyrocervical trunk, respectively. Important structures in close proximity to the thyroid include parathyroid glands, trachea, esophagus, external branch of the **superior laryngeal nerve** (SLN, **located near the superior pole of the thyroid**), and the **recurrent laryngeal nerve** (RLN, **located just anterior or posterior to the inferior thyroid artery in the tracheoesophageal groove**).
3. **Physiology. Thyrotropin-releasing hormone** (TRH) secreted by the **hypothalamus** stimulates **thyroid-stimulating hormone** (TSH) secretion by the **anterior pituitary gland**. TSH then stimulates thyroid hormone secretion by the thyroid gland. The process of

thyroid hormone synthesis begins when dietary iodide is ingested, actively transported into the thyroid, and oxidized by **thyroid peroxidase** (TPO) into iodine. Iodination of tyrosine residues in **thyroglobulin** creates monoiodotyrosine and diiodotyrosine. Coupling reactions of monoiodotyrosine and diiodotyrosine result in the formation of **triiodothyronine (T3) and thyroxine (T4)**, both of which are bound to thyroglobulin and stored in thyroid follicles. When released into plasma, more than 99% of T_3 and T_4 are bound to carrier proteins, including **thyroxine-binding globulin** (TBG), thyroxine-binding prealbumin, and albumin. Only the unbound or "free" hormones are active (i.e., available to tissues), and T_4 is converted to T_3 by deiodinases in the peripheral tissues. Compared to T_3, T_4 has a 20-fold higher circulating concentration but is three to five times less potent. The half-life of T_4 (7 days) is significantly longer than the half-life of T_3 (1 day). Assessment of thyroid function requires biochemical evaluation and interpretation in the context of clinical findings. Measurement of **TSH** (0.3 to 4.12 mIU/L) **is the most useful biochemical test in the assessment of thyroid function**. In most patients without hypothalamic or pituitary disease (rare), TSH and free T_4 (FT_4) vary inversely around a euthyroid state: Increased TSH and low FT_4 signify hypothyroidism, while suppressed TSH and high FT_4 suggest hyperthyroidism. Assessment of FT_4 (0.8 to 1.8 ng/dL) supports identified abnormalities in TSH and provides an index of severity of thyroid dysfunction.

B. Benign Thyroid Disease

1. **Thyroid nodule.** A **solitary thyroid nodule** is defined as a discrete lesion that is distinct from the surrounding thyroid parenchyma.
   a. **Epidemiology.** Thyroid nodules are common with 4% to 7% of all adults having palpable thyroid nodules and a higher prevalence (19% to 68%) on ultrasound (US). Although commonly benign, up to 15% of thyroid nodules may harbor malignancy depending on patient factors such as age, sex, and history of radiation exposure. Thus, diagnostic testing is recommended to separate patients with malignancy from the larger population with benign nodules. Management guidelines from the ATA Guidelines Task

Force for the evaluation and treatment of thyroid nodules were recently revised (*Thyroid.* 2016;26(1):1–133).

b. Clinical evaluation of thyroid nodules includes a thorough history and physical examination. Risk of malignancy is higher at the extremes of age (especially in older men) and in those with a personal history of ionizing radiation exposure, a positive family history of thyroid malignancy, familial adenomatous polyposis (FAP), or other endocrine diseases. Rapid nodule growth, pain, compressive symptoms, or hoarseness is nonspecific but increases the likelihood of malignancy. Physical findings of a solitary nodule with firm or irregular texture, fixation to surrounding structures, or associated enlarged cervical lymph nodes may also suggest malignancy. Generally, only nodules >1 cm should undergo further investigation as these have a greater potential of being clinically significant cancers. Figure 34-1 illustrates the algorithm for workup of a newly diagnosed thyroid nodule.

c. Biochemical evaluation. For patients with nodules >1 cm in size, a serum TSH level will determine the subsequent diagnostic pathway. In patients with suppressed TSH, an iofetamine (^{123}I) radionuclide scan should be performed. Malignancy is uncommon in hyperfunctioning nodules (i.e., those that take up more ^{123}I than surrounding normal thyroid), and no further workup is necessary in these lesions. However, patients with hypofunctioning nodules or with normal or high serum TSH should undergo diagnostic US.

d. Diagnostic imaging

(1) Thyroid US. All patients with known or suspected thyroid nodules should undergo diagnostic US. Multiple sonogram-based risk-stratification systems have been validated to guide nodule management, but use is often practice dependent. In order to improve consistency across institutions, the American College of Radiology (ACR) implemented a standardized US reporting system in 2017 known as TI-RADS (Thyroid Imaging, Reporting and Data System, Fig. 34-2), to help identify which nodules warrant fine-needle aspiration (FNA), follow-up US examination, or no further action (*J Am Coll Radiol.* 2017;15(5):587–595). In general, nodules with a low risk of malignancy are cystic and anechoic with smooth

margins and either no echogenic foci or those with large comet-tail artifact. Nodules with an elevated risk of malignancy are solid, hypoechoic, taller than wide, with irregular margins and small punctate echogenic foci. TI-RADS criteria do not encompass evaluation of regional lymph nodes, but the ATA Guidelines recommend FNA of suspicious lymph nodes and any associated thyroid nodule regardless of nodule size. In a retrospective comparison to other risk-stratification systems, TI-RADS offered a meaningful reduction in the number of thyroid nodules recommended for biopsy and a significant improvement in the accuracy of recommendations for nodule management (*Radiology.* 2018;285(1):185–193).

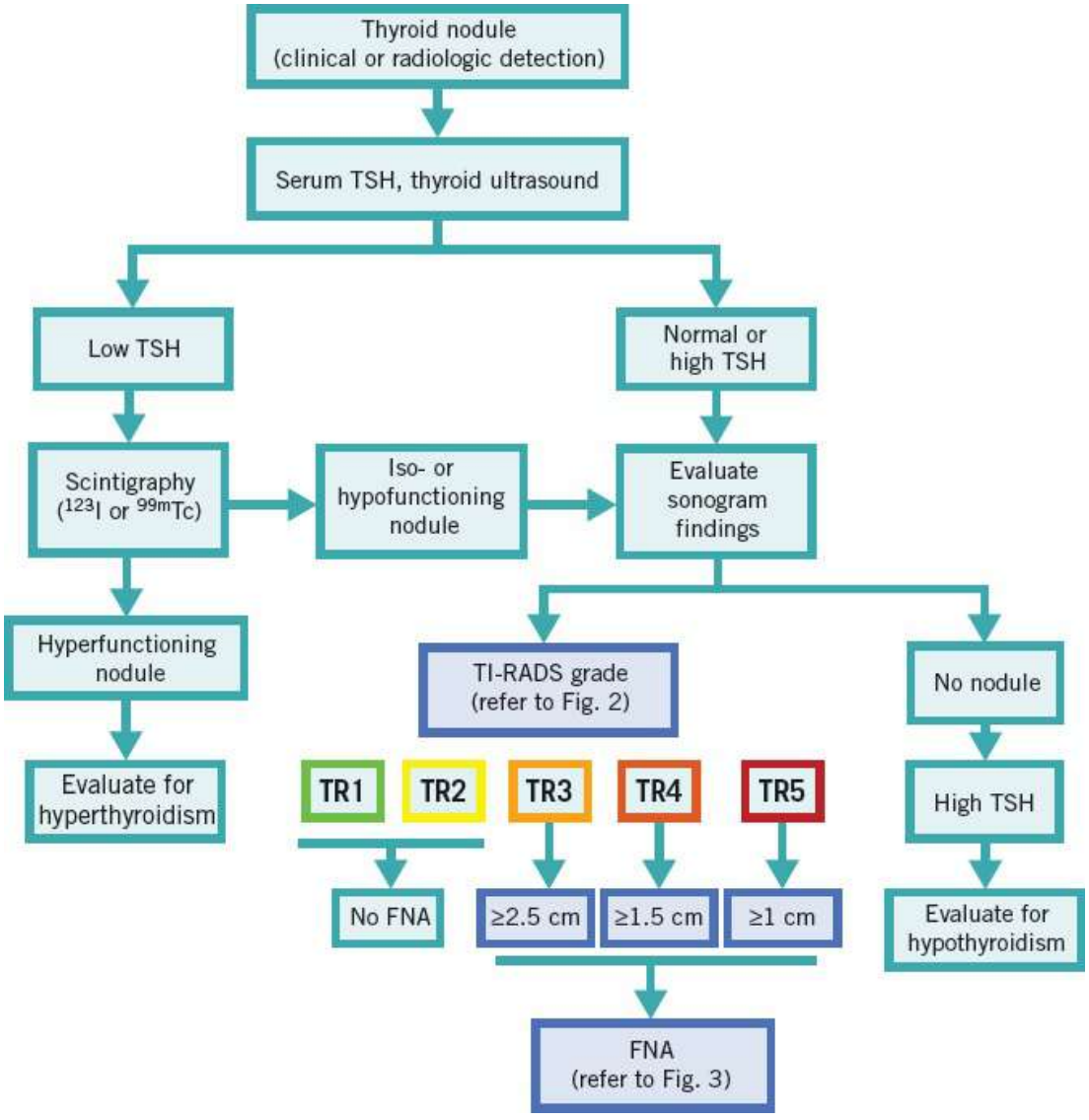


FIGURE 34-1 Thyroid nodule initial evaluation algorithm.

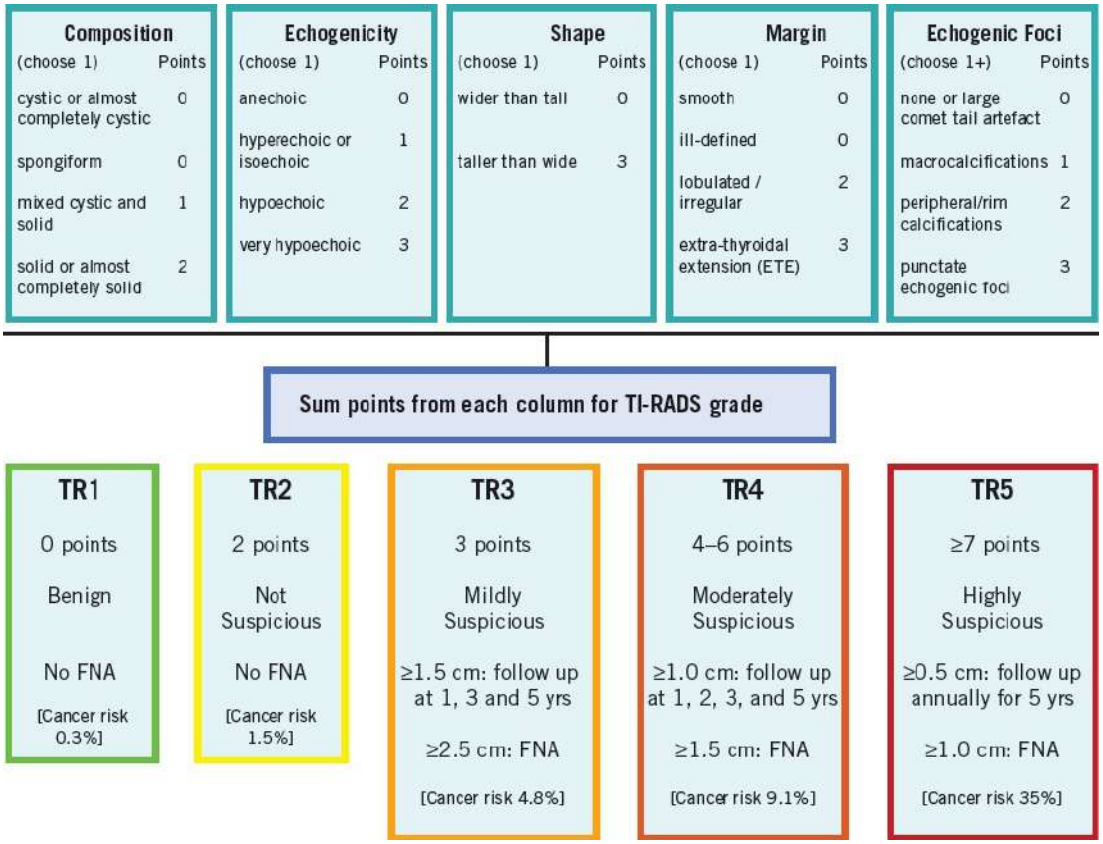


FIGURE 34-2 ACR Thyroid Imaging, Reporting and Data System (TI-RADS, 2017).

(2) Thyroid scan. Thyroid scans cannot differentiate benign from malignant lesions and are generally not recommended in the initial workup of a thyroid nodule. Following US, technetium (^{99m}Tc) pertechnetate or ^{123}I thyroid scanning can help distinguish solitary functioning nodules from multinodular goiter or Graves disease. Hypofunctioning areas (cyst, neoplasm, or suppressed tissue adjacent to autonomous nodules) are "cold," whereas areas of increased uptake are "hot." Cold nodules are more likely to be malignant than hot nodules. Nevertheless, most cold nodules are still benign. Whole-body scanning at 4 to 24 hours after administration of ^{123}I or iodine-131 (^{131}I) is useful for identifying metastatic differentiated thyroid tumors or predicting a response to ^{131}I radioablation.

(3) Other imaging studies. CT and MRI of the thyroid are

generally reserved for assessing substernal or retrosternal masses, for staging known malignancy, or for evaluating local invasion that may change the operative approach (*Radiol Clin North Am.* 2015;53(1):145–161). Routine use of preoperative fluorodeoxyglucose-positron emission tomography (FDG-PET) scan is not recommended.

e. FNA biopsy +/- molecular testing. FNA is an accurate and cost-effective diagnostic modality for evaluating thyroid nodules. The revised 2017 **Bethesda System for Reporting Thyroid Cytopathology** (BSRTC) continues to classify FNA results into six categories (*Thyroid.* 2017;27(11):1341–1346). Figure 34-3 delineates the appropriate management for each type. As shown in Table 34-1, the risk of malignancy for categories III to VI has decreased with the recent exclusion of **follicular variant of papillary thyroid cancer** (FVPTC) as a carcinoma, and its reclassification to noninvasive follicular thyroid **neoplasm with papillary-like nuclear features** (NIFTP). This shift in terminology was intended to reduce overtreatment of these indolent tumors. In addition, **molecular testing** (e.g., ThyroSeq® Genomic Classifier, UPMC, Pittsburgh, PA), designed to detect somatic mutations, is now commercially available and has substantially improved diagnostic accuracy in cases of indeterminate cytology. It may allow surgery to be avoided in ∼60% of Bethesda III/VI nodules. The most recent version (ThyroSeq®v3.0) tests for mutations in 112 genes, including *BRAF, RAS, RET, PAX8/PPARγ,* and *TERT* (*Cancer.* 2018;124(8):1682–1690).

(1) (I) Nondiagnostic cytology. Nondiagnostic cytology fails to meet the criteria for an adequate specimen, and repeat FNA should be performed under US guidance. Nodules that continue to yield nondiagnostic specimens require either close observation or surgical excision, particularly for lesions with high-suspicion US patterns, growth during surveillance, or clinical risk factors for malignancy.

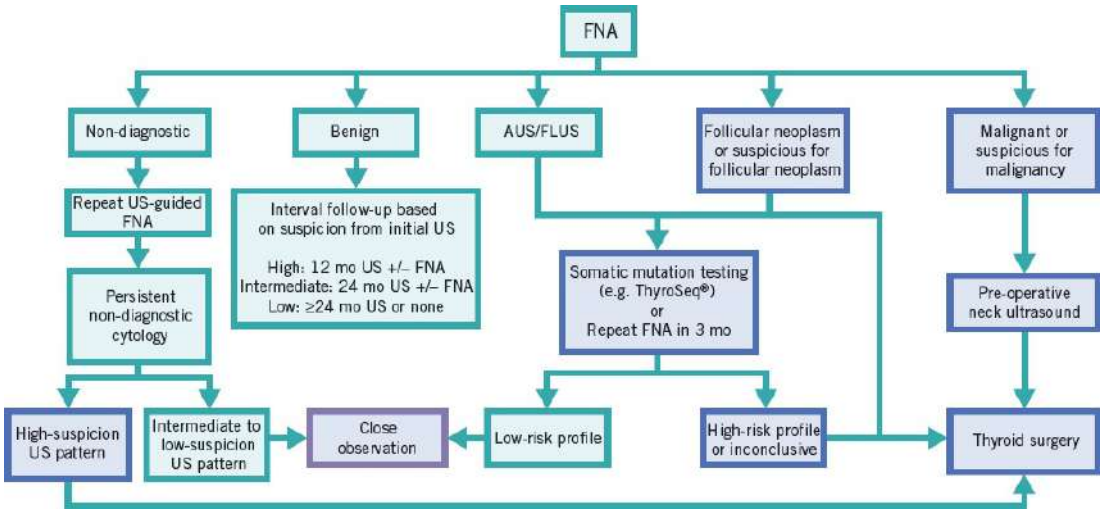


FIGURE 34-3 Thyroid nodule management following fine-needle aspiration (FNA) biopsy.

TABLE 34-1 Bethesda System for Reporting Thyroid Cytopathology

Diagnostic Category	Risk for Malignancy (%)[a]	Recommendation
(I) Nondiagnostic or unsatisfactory	5–10	Repeat FNA with US guidance
(II) Benign	0–3	Clinical follow-up, repeat US (12–24 mo)
(III) Atypia of undetermined significance (AUS) Follicular lesion of undetermined significance (FLUS)	6–18	Molecular testing, repeat FNA (3 mo), or lobectomy
(IV) Follicular neoplasm Suspicious for follicular neoplasm	10–40	Molecular testing or lobectomy

(V) Suspicious for malignancy	45–60	Near-total thyroidectomy or lobectomy
(VI) Malignant	94–96	Near-total thyroidectomy or lobectomy

[a]NIFTP is no longer considered malignancy.

US, ultrasound; FNA, fine-needle aspiration; NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features.

Adapted from Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *Thyroid.* 2017;27(11):1341–1346.

(2) **(II) Benign cytology.** Benign cytology has a low risk of malignancy and requires no further diagnostic testing. Patients can be followed clinically with a repeat US at 6 to 18 months.

(3) **(III) Atypia or Follicular lesion of undetermined significance (AUS or FLUS).** Cytology noting AUS or FLUS is synonymous and carries a 6% to 18% risk of malignancy. Molecular testing is preferred, though repeat FNA, lobectomy, or surveillance can be pursued based on risk factors, imaging, and patient preference.

(4) **(IV) Suspicious for a follicular neoplasm.** Lesions reported as "suspicious for follicular neoplasm" or either "follicular neoplasm" or "Hürthle cell neoplasm" (also referred to as "**indeterminate**") carry a 10% to 40% risk of malignancy. Molecular testing may be used in this setting for additional diagnostic information. Otherwise, these lesions are **typically treated with surgical excision (thyroid lobectomy**). **If final pathology reveals thyroid cancer, completion thyroidectomy should be considered.**

(5) **(V) Suspicious for malignancy or (VI) Malignant.** "Suspicious for malignancy" confers a cancer risk greater than 45% while "malignant" is greater than 94%. Both should be **treated with near-total thyroidectomy or lobectomy**. Preoperative neck US of central and lateral neck lymph nodes

is often indicated.

2. **Toxic adenoma and multinodular goiter.** Multinodular goiter is a common condition, and each individual nodule needs to be evaluated for possible biopsy. Indications for surgery include suspicious cytology as detailed above, nodule size, and compressive symptoms. Toxic adenoma and toxic multinodular goiter (**Plummer disease**) are most often secondary to autonomous function in one or several thyroid nodules which produce thyroid hormone independent of TSH stimulation. A radioactive ^{131}I scan is diagnostic with one or more "hot" areas and suppression of the rest of the gland. Either **radioactive iodine (RAI) ablation** or surgical excision (lobectomy or subtotal thyroidectomy) can be implemented, though surgery is indicated for multiple large nodules, obstructive symptoms, thyrotoxicosis, or failure of RAI therapy.
3. **Graves disease**
   a. **Epidemiology.** Autoimmune diffuse toxic goiter (**Graves disease**) is the most common cause (60% to 80%) of hyperthyroidism, presenting up to seven times more frequently in women and usually in the second to fourth decade.
   b. **Pathophysiology.** Hyperthyroidism results from excess circulating levels of thyroid hormones and a resultant increase in catabolism and sympathetic activity. In Graves disease, this is due to **constitutive activation of the TSH receptor by stimulating immunoglobulins** thereby leading to increased hormone production. Diagnosis is made by history and physical examination, depressed TSH levels, and detection of **anti–TSH-R antibodies**, which are present in more than 90% of patients.
   c. **Clinical manifestations.** Symptoms of hyperthyroidism include weight loss despite normal or increased appetite, heat intolerance, excessive perspiration, anxiety, irritability, palpitations, fatigue, and oligomenorrhea. Signs include goiter, sinus tachycardia or atrial fibrillation, tremor, hyperreflexia, fine or thinning hair, eyelid lag or retraction, thyroid bruit, muscle wasting, and proximal muscle weakness. Unique features of Graves disease include **infiltrative ophthalmopathy and pretibial myxedema**.
   d. **Medical therapy.** Thioamide drugs, such as **propylthiouracil (PTU)** or **methimazole**, are used for antithyroid drug therapy and

mainly prevent synthesis of thyroid hormones. However, long-term remission is achieved in less than 20% to 30% of patients. Methimazole is commonly recommended to prepare thyrotoxic patients for surgery or ablative therapy.

e. RAI ablation therapy is the treatment of choice for most patients with Graves disease. Given orally, the initial dose is approximately 75% effective after 8 to 12 weeks. A second dose at the same or higher dose is given in the 25% of patients who have persistent thyrotoxicosis 6 to 12 months later. **Cure rates approach 90%** by 1 year, and hypothyroidism will eventually develop in the majority of treated patients. Contraindications to radiotherapy include pregnancy or lactation, newborns, patient refusal to comply with radiation safety guidelines, suspicion for or known thyroid cancer, and low RAI uptake (<20%).

f. Surgery. Thyroidectomy for Graves disease may be indicated for patients who refuse or have a contraindication to RAI or who have an obstructive goiter or exophthalmos. **Near-total or total thyroidectomy is recommended** due to high recurrence rates in patients treated with subtotal thyroidectomy (8% to 15%) and a relatively high risk of occult malignancy (5% to 20%). Patients undergoing thyroidectomy as primary therapy should be treated at a high-volume thyroid surgery center with preoperative antithyroid drug therapy to render them euthyroid. Patients with recurrent hyperthyroidism after thyroidectomy should be considered for RAI treatment due to higher reoperative complication rates.

4. **Nontoxic goiter.** Multinodular nonfunctioning goiter, typically **secondary to iodine deficiency**, can result in tracheal compression due to size or retrosternal extension. Subtotal or total thyroidectomy can be performed for compressive symptoms, suspicion of malignancy, or cosmesis.

5. **Thyroiditis.** Thyroiditis encompasses several autoimmune and inflammatory disorders characterized by inflammatory cell infiltration and subsequent fibrosis of the gland.

a. Hashimoto thyroiditis is a chronic autoimmune disorder involving destructive lymphocytic infiltration of the thyroid and is the **most common cause of hypothyroidism in the United States**. Up to

10 times more common in women, more than 90% of affected patients have circulating **anti-TPO and antithyroglobulin antibodies**. Hypothyroidism generally has an insidious onset, and patients may initially be euthyroid and asymptomatic. Clinical features of hypothyroidism include cold intolerance, weight gain, constipation, edema, dry skin, weakness, bradycardia, somnolence, and menorrhagia. Diagnosis is made by an increased serum TSH level and decreased FT_4 levels. Thyroid hormone is the preferred replacement therapy for hypothyroid patients, and thyroidectomy is indicated for persistent compressive symptoms, a dominant nodule suspicious for malignancy, or cosmesis.

b. Other causes of thyroiditis are rare and include **acute suppurative thyroiditis, subacute (de Quervain) thyroiditis, and Riedel thyroiditis**. Acute suppurative thyroiditis is caused by pyogenic *Streptococcus* or *Staphylococcus* infection and requires antibiotic therapy with possible surgical drainage of abscesses. Subacute thyroiditis occurs more commonly in young women, often after a viral upper respiratory tract infection, and almost always remits spontaneously within a few weeks. Symptoms of fatigue, weakness, or jaw/ear pain from thyroid enlargement may be treated with nonsteroidal anti-inflammatory drugs or steroids. Finally, Riedel thyroiditis is an idiopathic progressive inflammatory condition that causes fibrosis of the entire thyroid gland, strap muscles, and other neck structures. Surgical excision may be required to exclude malignancy or relieve compressive symptoms.

C. Thyroid Cancer. Differentiated thyroid cancers (papillary, follicular, and Hürthle cell) are relatively indolent cancers arising from follicular epithelial cells and are the most common types of thyroid malignancy. Overall, these cancers are rare in children, more common in females (2.5:1), and have a peak incidence in the fourth decade. Exposure to ionizing radiation is the best documented environmental factor. The majority of patients (85% to 90%) fall into a low-risk category with favorable prognosis. The ATA Guidelines Task Force has issued the revised management guidelines for the workup and treatment of differentiated thyroid cancers (*Thyroid.* 2016;26(1):1–133). Table 34-2 reviews the major categories of thyroid malignancies with clinical

features and management recommendations for each type.

1. Papillary thyroid cancer

a. Epidemiology. Papillary thyroid carcinoma (PTC) represents 85% of thyroid carcinomas, is often multifocal, and frequently metastasizes to cervical lymph nodes. Occult, clinically insignificant foci of microscopic PTC are found in 5% to 30% of autopsies or in thyroidectomy specimens for benign diseases. **High-risk features associated with worse prognosis** include male gender, primary tumor size >4 cm, gross local invasion and extrathyroidal extension, age >45 years, certain histologic subtypes (specifically tall cell, follicular, insular, columnar, diffuse sclerosing, or hobnail variant), lymphovascular invasion (LVI), or known metastatic disease.

b. Staging. Despite being an indolent cancer, cervical lymph node metastases are found in 20% to 50% of patients at the time of diagnosis. Therefore, it is reasonable to consider preoperative neck US with FNA of suspicious nodes >8 to 10 mm prior to surgical intervention. Alternatively, US on the day of surgery can be used to mark suspicious nodes which are sent intraoperatively for frozen section, followed by compartmental resection if malignancy is detected.

c. Operative strategies

(1) Total thyroidectomy is recommended in several conditions: Tumors >4 cm, presence of bilateral nodules, regional or metastatic disease, personal history of head/neck radiation exposure, or first-degree relatives with PTC.

(2) Thyroid lobectomy is appropriate for low-risk patients with small (<1 cm), intrathyroidal, unifocal tumors without evidence of regional or metastatic disease. For similar patients with tumor size 1 to 4 cm, either thyroid lobectomy or total thyroidectomy can be considered.

(3) Lymph node dissection (LND) of the central neck (level VI) and/or the ipsilateral lateral neck (levels II, III, IV) should be performed as **therapeutic** in all patients with nodal disease as determined by biopsy, imaging, or clinical examination. **Prophylactic LND** of the central compartment should be

considered for high-risk patients (e.g., T3/T4 tumors, radiation exposure, clinically involved lateral nodes), but currently there is **no role for prophylactic lateral neck dissection**.

TABLE 34-2 Categories of Thyroid Malignancies

Category	Percent of All Thyroid Malignancies	Clinical Features	Management
Papillary carcinoma	70–80	Indolent, often multifocal Frequently metastatic to cervical lymph nodes	Surgery ± RAI ablation therapy ± thyroid hormone suppression therapy Follow-up: Serum thyroglobulin, neck ultrasound
Follicular carcinoma	10–15	More common in women, age ≥30 yr Hematogenous spread to bone, lung, liver	Surgery ± RAI ablation therapy ± thyroid hormone suppression therapy Follow-up: Serum thyroglobulin, neck ultrasound
Medullary carcinoma	5–10	Sporadic (75%) vs. familial (25%) Familial forms: MEN syndromes type 2A and 2B Frequent early nodal metastasis	Genetic testing (*RET* proto-oncogene) for all patients Screening for pheochromocytoma Total thyroidectomy + lymph node dissection

		Elevated calcitonin and CEA levels	
Anaplastic carcinoma	1–2	Frequently presents at advanced stage May be highly symptomatic with local invasion Nearly 100% disease-specific mortality	Palliative surgery Chemotherapy ± external beam radiation
Lymphoma	2–8	Often non-Hodgkin type Associated with Hashimoto thyroiditis	External beam radiation vs. chemotherapy

MEN, multiple endocrine neoplasia; RAI, radioactive iodine.

d. Complications

(1) Hemorrhage is a rare but serious complication (0.3% to 1%) of thyroidectomy that usually occurs within 6 hours of operation. Management typically requires airway control by endotracheal intubation but may necessitate immediate opening of the incision and/or an emergent surgical airway before return to the operating room for wound irrigation and control of bleeding.

(2) Hypocalcemia may occur 24 to 48 hours after total or near-total thyroidectomy and is usually transient. We start patients routinely on oral calcium carbonate (1 g TID) for 2 weeks after total thyroidectomy. If symptoms occur, additional oral calcium

and calcitriol (0.25 μg/day) can be implemented, or if severe, IV replacement is achieved using six ampules of 10% calcium gluconate (93-mg elemental calcium in 10 mL) mixed in 500 mL of 5% dextrose in water (D5W) at a goal infusion of elemental calcium at 0.5 to 1.5 mg/kg/hr. Permanent hypoparathyroidism is uncommon after total thyroidectomy. Normal parathyroid tissue removed or devascularized during surgery should be minced into 1-mm fragments and **autotransplanted** into individual muscle pockets in the sternocleidomastoid muscle to minimize risk of postoperative hypoparathyroidism (*Ann Surg.* 1996;223(5):472–478).

(3) RLN injury is a significant complication of thyroidectomy that should rarely occur (<1%). **Unilateral RLN injury** causes hoarseness, which often presents immediately but may appear days to weeks after surgery, and **bilateral injury** compromises the airway, usually manifesting immediately postoperatively and potentially requiring tracheostomy. Reoperative neck surgery or thyroidectomy for extensive goiter; Graves disease; or fixed, locally invasive cancers carries additional risk of RLN injury. Intentional (as with locally invasive cancer) or inadvertent RLN transection can be repaired primarily or with a nerve graft, and primary repair has been associated with improved phonation in small studies. **Transient RLN injury** can also occur following thyroidectomy but usually resolves over a period of 1 to 6 weeks. If a permanent injury develops, a cord medialization procedure should be considered.

e. RAI ablation therapy is recommended for all patients with primary tumor size >4 cm, gross local invasion, and for selected patients with tumor size 1 to 4 cm and high-risk features such as age >45 years, certain histologic subtypes, extrathyroidal extension, LVI, or known metastatic disease. Ablation is performed with 30 to 150 mCi of ^{131}I approximately 2 to 4 weeks after total thyroidectomy once the patient is hypothyroid (i.e., TSH >30 mU/mL on no replacement of T_4) and may be repeated at 6 to 12 months if residual disease is detected on follow-up surveillance.

f. Thyroid hormone suppression therapy should be considered after

total or near-total thyroidectomy or RAI ablation and functions to suppress TSH levels by negative feedback mechanisms. Thyroid hormone suppression therapy with initial TSH suppression below 0.1 mU/L and lifelong TSH suppression at or below the lower limit of normal (0.1 to 0.5 mU/L) decreases recurrences and may improve survival. Oral levothyroxine is started at a dose of 1.4 μg/kg/day. Adequacy of thyroid hormone replacement is assessed by measuring TSH and FT_4 6 to 12 weeks after initiating therapy. Dose adjustments should be conservative (12.5- to 25-μg increments) and not more frequent than monthly in the absence of symptoms.

g. Follow-up long-term for differentiated thyroid cancer requires **monitoring of serum thyroglobulin levels** every 6 to 12 months and **periodic neck US** in patients who underwent less than total thyroidectomy or did not undergo RAI ablation. For low- and intermediate-risk patients undergoing RAI ablation, if post-therapy RAI whole-body scans (WBS) do not reveal uptake outside the thyroid bed, subsequent WBS are not indicated in the setting of undetectable thyroglobulin levels and negative cervical US. Diagnostic WBS should be used in patients at increased risk of persistent disease.

2. Follicular thyroid cancer (FTC, 10% of thyroid carcinomas) is rare before age 30 years, is three times more common in women than in men, and has a slightly worse prognosis than PTC. Unlike PTC, FTC tends to spread hematogenously to bone, lung, or liver. Small (<1 cm), unilateral lesions with limited invasion of the tumor capsule may be treated with thyroid lobectomy, whereas tumors >1 cm, multicentric tumors, and tumors with more extensive capsular and vascular invasion or distant metastases are treated with total thyroidectomy. **RAI ablation is indicated after total thyroidectomy, followed by lifelong TSH suppression with thyroid hormone suppression therapy**.

3. Medullary thyroid cancer

a. Epidemiology, pathophysiology, and clinical manifestations. Medullary thyroid carcinoma (MTC) arises from the thyroid parafollicular C cells and accounts for 5% to 10% of all thyroid cancers in the United States. MTC may occur sporadically (75%)

or may be associated with a familial syndrome, either alone or as a component of **multiple endocrine neoplasia (MEN) syndromes type 2A or 2B** (25%). Sporadic MTC generally presents as a firm, palpable, unilateral nodule with or without involved cervical lymph nodes, whereas hereditary MTC more often develops as bilateral, multifocal tumors with diagnosis on the basis of genetic or biochemical screening. MTC spreads early to cervical lymph nodes and may metastasize to liver, lungs, or bone. **All patients with MTC should undergo genetic testing for germline mutations in the *RET* proto-oncogene to exclude familial medullary thyroid carcinoma (FMTC) or MEN2 syndromes**. Similar to other thyroid malignancies, diagnosis is made by FNA of suspicious thyroid nodules. More than 50% of patients presenting with a palpable primary tumor will already have nodal metastases and elevated basal serum calcitonin levels (>20 to 100 pg/mL). **Calcitonin and CEA levels are important tumor markers for MTC** and correlate strongly with extent of disease. Preoperative neck US is critical for identification of regional metastases and surgical planning, and **screening for pheochromocytoma** with serum or urine metanephrines and catecholamines should be considered in all patients undergoing surgery for MTC. (For more information on MEN, see Chapter 33.) The ATA Guidelines Task Force has issued the revised management guidelines for the workup and treatment of MTC (*Thyroid.* 2015;25(6):567–610).

b. Operative strategies. Total thyroidectomy alone is only indicated for MEN2 patients who have thyroid nodules <5 mm and calcitonin levels <40 pg/mL. Otherwise, treatment of both hereditary and sporadic MTC requires at least **total thyroidectomy with central neck compartment (level VI) LND**, and additional dissection of **ipsilateral lateral compartment nodes** should be performed in patients with palpable primary tumors. Surgical management of residual or recurrent disease remains the standard of care based upon patient clinical factors.

c. Medical therapy. MTC does not concentrate RAI, and thus postoperative RAI treatment is not used. In patients with significant tumor burden and progressive metastatic disease,

treatment with tyrosine kinase inhibitors (TKIs) of *RET* and *VEGF* receptors (e.g., **vandetanib and cabozantinib**) should be considered. Adjuvant radiation therapy and systemic chemotherapy have not shown significant benefit.

4. **Anaplastic or undifferentiated thyroid carcinoma** (1% to 2% of thyroid cancers) carries an extremely **poor prognosis** with nearly 100% disease-specific mortality. Disease usually presents as a fixed, sometimes painful goiter in patients older than 50 years, and over 90% of patients have regional or distant disease at the time of diagnosis. Invasion of local structures can preclude resection, and local symptoms such as dysphagia, respiratory compromise, or hoarseness may occur due to RLN involvement. External beam radiation or chemotherapy may provide limited palliation.
5. **Primary Thyroid Lymphoma.** Primary malignant lymphoma of the thyroid is usually non-Hodgkin type and is frequently associated with Hashimoto thyroiditis. Surgical resection is usually not indicated following diagnosis, and radiation or chemotherapy regimens are effective.

II. PARATHYROID

A. Embryology, Anatomy, and Physiology

1. **Embryology.** The inferior and superior parathyroid glands are derived from the **endoderm of the third and fourth pharyngeal pouches**, respectively. The inferior parathyroids are intimately associated with the thymus, which also develops from the third pharyngeal pouch, and ectopic inferior glands can be found anywhere along the tract of descent by the thymus into the chest that becomes the thyrothymic ligament. The superior glands have a limited descent from the neck and are much less variable in position.
2. **Anatomy.** Typically, the inferior parathyroid glands are found inferior to the inferior thyroid artery and anterior to the RLN. The superior glands are usually found at the posterolateral aspect of the superior thyroid lobe, posterior to the RLN, and superior to the **inferior thyroid artery**, which is the main blood supply for all of the parathyroids. Because the embryologic path of descent of the inferior parathyroid crosses that of the superior glands, the glands can rarely be found at the same level, above, or below the crossing of the

inferior thyroid artery and RLN.

3. **Physiology.** Serum calcium levels are maintained within normal range (8.2 to 10.2 mg/dL) by the interplay of **parathyroid hormone (PTH) and vitamin D**. Upon stimulation, **chief cells** of the parathyroid glands secrete PTH that (1) stimulates calcium and phosphate release from bone, (2) increases calcium and inhibits phosphate reabsorption in the kidneys, and (3) enhances intestinal absorption of calcium through increased renal activation of vitamin D. Vitamin D is initially absorbed through the small intestine, undergoes hydroxylation in the liver to $25(OH)D_3$, and then undergoes a second hydroxylation in the kidney under the influence of PTH to its active form, $1,25(OH)D_3$. While vitamin D stimulates bone and intestinal calcium resorption, **calcitonin antagonizes the effect of PTH** in the bones and kidneys.

B. Benign Parathyroid Disease

1. Primary hyperparathyroidism

a. **Epidemiology.** Primary hyperparathyroidism (HPT) has an incidence of 0.25 to 1 per 1,000 in the United States and is especially common in postmenopausal women. It most often occurs sporadically but can be inherited alone or as a component of familial endocrinopathies, including MEN types 1 and 2A.

b. **Clinical manifestations** associated with HPT include nephrolithiasis, osteoporosis, hypertension, and emotional disturbances. Patients may also have subtle symptoms such as muscle weakness, polyuria, anorexia, fatigue, bone/joint pain, poor sleep, reflux, and nausea.

c. **Biochemical evaluation.** Diagnosis of primary HPT typically requires documentation of **hypercalcemia** (serum calcium >10.5 mg/dL) **and an elevated PTH level**. The assay of choice for PTH is the highly sensitive and specific intact PTH immunoassay, and ionized calcium is a more sensitive test of physiologically active calcium. In addition, multiple biochemical abnormalities may be present concurrently with hypercalcemia. Hyperchloremia, metabolic acidosis, and hypophosphatemia are more commonly associated with primary HPT due to increased urinary excretion of bicarbonate and phosphate. Hypomagnesemia can occur in 5% to

10% of patients with primary HPT. Serum alkaline phosphatase levels may be elevated due to an increase in osteoclastic bone resorption.

d. Differential diagnosis. Hypercalcemia can be due to a variety of causes (e.g., malignancy, Paget disease, sarcoidosis, milk-alkali syndrome), which are typically associated with normal PTH levels. Familial hypocalciuric hypercalcemia (FHH) commonly presents with mild hypercalcemia and low urine calcium, with elevated PTH in 15% to 20% of patients. Caused by loss-of-function mutations in renal and parathyroid calcium-sensing receptors, FHH patients have loss of feedback inhibition of PTH secretion and inadequate clearance of calcium in the urine. FHH can be distinguished from HPT by a 24-hour measurement of urine calcium or by measuring the renal calcium/creatinine clearance ratio. A ratio less than 0.01 suggests FHH while the ratio seen in HPT is usually much higher. Parathyroidectomy is ineffective for FHH.

e. Preoperative localization studies. Parathyroid imaging has no role in the diagnosis of HPT but is critical in operative planning to facilitate limited neck exploration. **Technetium-99m sestamibi scintigraphy** has historically been utilized to localize hyperfunctioning parathyroid tissue, though newer modalities of scintigraphy in combination with **single-photon emission computed tomography** (SPECT), SPECT with computed tomography (SPECT/CT), and four-dimensional (4D) CT have demonstrated higher sensitivity and positive predictive values (*J Nucl Med.* 2007;48(7):1084–1089). US with color Doppler examination complements the sestamibi scan and can assist in precise localization of adenomas, assessment of concomitant thyroid pathology, or FNA of equivocal lesions.

f. Indications for surgery. Parathyroidectomy is indicated for patients with classic symptoms of primary HPT (e.g., nephrolithiasis, pathologic fracture, neuromuscular disturbances, hypercalcemic crisis). Management of asymptomatic patients is more controversial, but recent guidelines from an expert consensus panel recommend parathyroidectomy for those meeting one of the following criteria: (1) Age less than 50 years, (2)

unable to participate in appropriate follow-up, (3) serum calcium level >1 mg/dL above normal range, (4) urine calcium >400 mg per 24 hours, (5) creatinine clearance <60 mL/min, or (6) complications of primary HPT (*J Clin Endocrinol Metab.* 2014;99(10):3561–3569). If patients do not meet one of these criteria, surgery is not required, but remains an option. Many patients choose surgery if they have significant nonspecific symptoms. Nephrolithiasis, bone disease, and neuromuscular symptoms are improved following surgery more often than renal insufficiency, hypertension, and psychiatric manifestations.

g. Operative strategies

(1) Minimally invasive parathyroidectomy. Preoperative localization studies used with rapid intraoperative PTH measurement now enable several minimally invasive techniques, including open, radio-guided, video-assisted, and endoscopic methods. Since the majority (>85%) of patients with primary HPT have a **single parathyroid adenoma**, successful preoperative localization allows for directed unilateral neck exploration while normal parathyroids do not need to be identified. The rapid intraoperative PTH assay allows surgeons to verify the adequacy of resection: following adenoma removal, a **50% decrease in PTH levels at 10 minutes is highly indicative of cure**.

(2) Conventional neck exploration. Historically, bilateral neck exploration and identification of all four parathyroids have been the cornerstone of surgical management in HPT, with resultant normocalcemia in more than 95% of patients. If an abnormally enlarged parathyroid or all four parathyroids cannot be found, exploration for **ectopic or supernumerary glands** should be performed. Ectopic **superior glands** may be found **posterior and deep to the thyroid**, in the **tracheoesophageal groove**, or **between the carotid artery and the esophagus**. Ectopic **inferior glands** are most likely found **embedded in the thymus** in the anterior mediastinum. Occasionally, multiple parathyroid adenomas are found and should be removed, leaving at least one normal parathyroid behind. Four-gland parathyroid hyperplasia is rare, and acceptable

management options include total parathyroidectomy with parathyroid autotransplantation or 3.5-gland parathyroidectomy.

(3) Parathyroid autotransplantation. Total parathyroidectomy with heterotopic parathyroid autotransplantation should be considered in patients with renal failure and secondary HPT, four-gland parathyroid hyperplasia, and those undergoing neck reexploration in which the adenoma is the only remaining parathyroid gland. The sternocleidomastoid or the brachioradialis muscles of the patient's nondominant forearm are **common sites for autotransplantation**. Parathyroid autotransplantation into the forearm is advantageous if recurrent HPT is a possibility (e.g., MEN type 1 or 2A) because the transplanted hyperfunctioning parathyroid tissue can easily be localized and excised. To autotransplant, the freshly removed parathyroid tissue is finely minced (approximately 1 × 1 × 2 mm) and placed in sterile iced saline. Separate intramuscular beds are created by spreading the fibers of the brachioradialis or the sternocleidomastoid with a fine forceps. Four to five pieces of parathyroid tissue are placed in each site for a total transplant volume of approximately 100 mg. Nonabsorbable suture is used to close the beds and to mark the site of transplanted tissue. Transplanted parathyroid tissue begins to function within 14 to 21 days of surgery. Cryopreservation of parathyroid glands is performed in all patients who are at risk for permanent hypoparathyroidism after repeat exploration. Approximately 200 mg of minced parathyroid tissue is frozen in vials containing autologous serum, dimethyl sulfoxide, and cell culture media. Cryopreserved tissue can be used for autotransplantation in patients with failure of the initial graft. Viable cryopreservation and subsequent thawing must be performed in an FDA-approved facility.

h. Management of postoperative hypocalcemia

(1) Clinical manifestations. Transient hypocalcemia commonly occurs after total thyroidectomy or parathyroidectomy and requires treatment if it is severe (total serum calcium <7.5

mg/dL) or if the patient is symptomatic. Symptoms may involve numbness/paresthesias in the distal extremities, perioral numbness, or hyperactive tendon reflexes. **Chvostek sign** (twitching of the facial muscles with tapping over the facial nerve anterior to the ear) indicates relative hypocalcemia, but it is present in up to 15% of the normal population and does not necessarily require calcium replacement.

(2) Oral calcium supplementation. Hypocalcemic patients may require postoperative supplementation for 6 to 8 weeks and are given oral calcium carbonate (500 to 1,000 mg TID) and calcitriol (0.25 μg/day).

(3) IV calcium supplementation of calcium gluconate or calcium chloride may be necessary in persistently symptomatic patients or in emergent situations such as **hypocalcemic tetany**. Ten to 20 mL of 10% calcium gluconate are given IV over 10 minutes and may be repeated every 15 to 20 minutes as required until symptom resolution. Subsequently, a continuous infusion of calcium gluconate in D5W is initiated at 0.5 to 1.5 mg/kg/hr with correction of any concurrent hypomagnesemia.

2. Secondary and tertiary hyperparathyroidism

a. Biochemical evaluation. Most commonly due to chronic renal failure, secondary HPT manifests as increased PTH levels in response to hypocalcemia. Decreased serum calcium levels are a terminal feature of kidney dysfunction, which becomes evident through phosphate retention, decreased vitamin D activation, and poor calcium absorption. Intestinal malabsorption of calcium or vitamin D can also result in elevated PTH levels and secondary HPT. Thus, patients with secondary HPT have high PTH levels and low calcium levels. **Tertiary HPT** can be seen in patients who have undergone a kidney transplant for renal failure. Typically, parathyroid gland function returns to normal within 1 year after kidney transplant, but in patients with tertiary HPT, the parathyroid glands fail to respond to normal signals for PTH secretion and regulation of calcium homeostasis. In these patients, **both the PTH and calcium levels are high**.

b. Medical management. Hypercalcemia from secondary and tertiary HPT is treated initially with dietary phosphate restriction,

phosphate binders, and vitamin D supplementation. **Cinacalcet**, a calcimimetic, is also commonly used. Although it does not impact mortality, it may decrease the need for parathyroidectomy.

c. Operative strategies. Patients with medically unresponsive, symptomatic HPT (e.g., bone pain, osteopenia, ectopic calcification, pruritus) may undergo total parathyroidectomy with autotransplantation or subtotal parathyroidectomy. Controversy exists regarding type of surgery and appropriate postoperative PTH level to prevent adynamic bone disease.

3. Recurrent or persistent hyperparathyroidism

a. Biochemical evaluation. In all cases of **persistent hypercalcemia**, the diagnosis of HPT should be confirmed. In addition to calcium and intact PTH levels, a 24-hour urine calcium should be obtained to rule out FHH. Factors associated with recurrent or persistent disease include failed preoperative localization studies, multiple gland disease, ectopic or supernumerary glands, malignancy, and surgeon inexperience.

b. Preoperative localization is mandatory in patients being considered for reoperative parathyroidectomy and may include ^{99m}Tc-sestamibi scintigraphy with SPECT/CT, US with FNA, or 4D CT scan. Approximately 70% to 80% of patients undergoing reexploration have a missed gland that is accessible through a cervical incision. Noninvasive imaging is successful in gland localization in 25% to 75% of cases. For patients with negative or discordant noninvasive studies, selective venous sampling with rapid PTH assessment can be considered.

c. Operative strategy. The goal of reexploration is to perform an orderly search based on information from the initial operation and from preoperative localization studies. Reoperative parathyroid surgery carries a substantially **higher risk of RLN injury and of hypocalcemia** due to postoperative scarring and disruption of normal tissue planes.

(1) Missed parathyroid glands can be found in either normal anatomic location or in ectopic sites. They may occasionally be intrathyroidal (especially in patients with multinodular goiter), and thyroid lobectomy can be performed if an exhaustive search fails to identify a parathyroid adenoma. If four normal

glands have been located, a supernumerary gland is likely responsible. Intraoperative US and/or **venous sampling** from the right and left internal jugular veins can sometimes be useful in localizing adenomas.

(2) Mediastinal adenomas within the thymus are managed by resecting the cranial portion via gentle traction on the thyrothymic ligament or by a complete transcervical thymectomy using a specialized substernal retractor (*Ann Surg.* 1991;214:555). Median sternotomy is associated with higher morbidity and increased postoperative pain, and the possibility that this procedure may be required should be discussed with the patient preoperatively.

C. Parathyroid Cancer

1. **Clinical manifestations.** Parathyroid cancer is a rare disease, accounting for <1% of patients with primary HPT. **Most (>90%) of parathyroid carcinomas are biochemically functional**. Approximately 50% of patients have a palpable neck mass, and serum calcium levels may exceed 15 mg/dL. In addition, PTH levels are often five times the upper limit of normal (300 pg/mL or more). US and ^{99m}Tc sestamibi imaging can help localize disease, but diagnosis depends on histologic findings of vascular or capsular invasion, metastases, or gross invasion of local structures.
2. **Medical management of hypercalcemic crisis.** Patients with parathyroid cancer and some patients with benign HPT may develop hypercalcemic crisis with serum calcium levels of 16 to 20 mg/dL and azotemia. Symptoms of this acute, sometimes fatal illness, include profound muscular weakness, nausea and vomiting, drowsiness, and confusion. Ultimate **treatment is surgery**, but volume and electrolyte abnormalities should be addressed first. First-line therapy involves IV infusion of 0.9% sodium chloride at 300 to 500 mL/hr to restore intravascular volume and to promote renal excretion of calcium. After urinary output exceeds 100 mL/hr, **furosemide** (80 to 100 mg intravenously every 2 to 6 hours) may be given to promote further renal sodium and calcium excretion, though consequent hypokalemia and hypomagnesemia should be corrected. **Thiazide diuretics** impair calcium excretion and **should be avoided**. If diuresis alone is unsuccessful in lowering the serum calcium, other

agents may be used, including the **bisphosphonates pamidronate and etidronate, mithramycin, and salmon calcitonin**. **Orthophosphate, gallium nitrate, and glucocorticoids also have calcium-lowering effects**. Both **cinacalcet**, an activator of calcium-sensing receptor, and **denosumab**, a monoclonal antibody to RANKL, may be used to manage hypercalcemia associated with unresectable disease.

3. **Operative strategy.** Surgical treatment of parathyroid cancer can be curative, and entails **radical local excision of the tumor en bloc with surrounding soft tissue, lymph nodes, and ipsilateral thyroid lobe**. Reoperation should be considered for local and distant recurrences to control malignant hypercalcemia.

CHAPTER 34: THYROID AND PARATHYROID GLANDS

Multiple Choice Questions

1. **A 56-year-old man presents to clinic for evaluation of a small anterior right neck mass at the level of the thyroid. He has no significant past medical history and denies any history of smoking. The mass has been slowly enlarging over the last 2 years but is not painful. The patient is normotensive with a negative review of systems, and he denies any dyspnea, choking sensations, or hoarseness. What is the first diagnostic study that should be performed in the workup of this mass?**

   a. Ultrasonography of the thyroid
   b. Serum thyroid-stimulating hormone (TSH) level
   c. Fine-needle aspiration (FNA)
   d. Computed tomography (CT) scan of the neck and chest
   e. Thyroid scintigraphy

2. **A 64-year-old woman presents to the emergency department with vague abdominal pain, nausea, confusion, and muscle weakness. An ECG shows a short QT interval. A serum calcium level is 15.2 mg/dL. What etiology does this suggest?**

   a. Thiazide use
   b. Secondary hyperparathyroidism
   c. Parathyroid carcinoma
   d. Single parathyroid adenoma
   e. Factitious hypercalcemia

3. **Following total thyroidectomy, a 50-year-old male presents for his 1-year follow-up visit. He is currently on daily levothyroxine therapy. The best method to monitor the adequacy of replacement therapy is:**

   a. Radioactive iodine (RAI) uptake
   b. Thyroglobulin
   c. Triiodothyronine resin uptake (RT_3U)

d. Serum TSH level
e. Total thyroxine level (total T_4)

4. A 72-year-old woman with recently diagnosed primary hyperparathyroidism presents for surgical evaluation. Her serum calcium level is found to be 13.6 mg/dL. Other biochemical abnormalities that may accompany hypercalcemia in patients with primary hyperparathyroidism include which of the following?

a. Metabolic alkalosis
b. Hyperphosphatemia
c. Hypochloremia
d. Hypermagnesemia
e. Elevated alkaline phosphatase

5. A 63-year-old patient with primary hyperparathyroidism and nonlocalizing studies undergoes neck exploration. He is found to have normal right and left superior parathyroids and a normal left inferior parathyroid gland. Of the following, which is the most likely location for the missing right inferior parathyroid?

a. Tracheoesophageal groove
b. Right thyroid lobe
c. Superior thymus
d. Posterior mediastinum
e. Pharyngeal mucosa

6. Which of the following patients with thyroid gland enlargement is LEAST likely to have a diagnosis of thyroid cancer?

a. A 5-year-old boy with two family members with medullary thyroid carcinoma
b. A 75-year-old man with a solitary nodule and hoarseness
c. A 56-year-old woman with a solitary nodule and a history of radiation therapy to the neck
d. A 43-year-old woman with a diffuse goiter and tremor
e. A 14-year-old girl with an asymptomatic solitary nodule

7. A 47-year-old woman presents to clinic for evaluation of weight gain, thinning hair, constant fatigue, constipation, and muscle weakness over the past year. She denies any prior history of thyroid disorders and currently takes no medications. Serum TSH level is elevated at greater than 30 mIU/L. What is the most likely cause of the patient's symptoms?

a. Thyroid adenoma
b. Self-administration of thyroid hormone
c. Papillary thyroid carcinoma
d. Radioactive iodine administration
e. Hashimoto thyroiditis

8. A 75-year-old female is taken to the operating room for surgical excision of a 4- × 5-cm papillary thyroid cancer of the right lobe. Which of the following would be an indication for a right lateral compartment lymph node dissection?

a. Tumor size
b. History of radiation exposure
c. Positive central node on frozen section
d. Patient's age
e. None of the above

9. A 43-year-old female presents with a 2.5-cm thyroid nodule. Her serum TSH level is normal and FNA cytology is consistent with atypia of undetermined significance (AUS). Molecular testing reveals a somatic *BRAF V600E* mutation. What is the appropriate next step?

a. Germline genetic testing
b. Repeat fine-needle aspiration
c. Initiate vemurafenib therapy
d. Total or near-total thyroidectomy
e. Complete dermatologic examination to search for a melanoma primary

10. A 16-year-old female presents with early satiety, postprandial vomiting, and epigastric distension for 3 weeks. She has presented to

the ED multiple times. She endorses nervousness, difficulty sleeping, and unintentional weight loss for 3 months. CT of the abdomen and pelvis reveals a proximal small bowel obstruction with transition point at the third portion of the duodenum. What other findings is she most likely to have?

a. Cold sensitivity and bradycardia
b. Diffuse goiter and exophthalmos
c. Low serum iodine level
d. Increased urinary phosphate
e. Kidney stones and constipation

35 Lung and Mediastinal Diseases

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I. PNEUMOTHORAX

A. Pneumothorax is the presence of air in the pleural cavity, leading to separation of the visceral and parietal pleura. This interferes with pulmonary mechanics and may progress to tension pneumothorax, which causes cardiac compromise and is a true emergency. Pneumothoraces may be spontaneous, iatrogenic, or due to trauma.

1. **Spontaneous** pneumothoraces typically occur when an apical bleb ruptures. The typical patients are tall young males who present with acute shortness of breath and chest pain on the side of occurrence. Older patients usually have significant parenchymal disease, such as emphysema. These patients present with a ruptured bulla and tend to have a more dramatic presentation, including tachypnea, cyanosis, and hypoxia. Other etiologies of spontaneous pneumothorax include cystic fibrosis (CF), tuberculosis, and rarely, lung cancer. The risk of ipsilateral recurrence of a spontaneous pneumothorax is 50%, 62%, and 80% after the first, second, and third episodes, respectively, if managed conservatively without surgery.
2. **Iatrogenic** pneumothoraces are usually the result of pleural injury during central venous access attempts, pacemaker placement, transthoracic biopsy, or transbronchial lung biopsy.
3. **Traumatic** pneumothoraces are discussed in Chapter 11.

B. Physical examination demonstrates decreased breath sounds on the involved side with hyperresonance to percussion. Examination for signs of tension pneumothorax looking for tracheal deviation to the contralateral side, distended neck veins, respiratory distress, and hypotension, should be performed. An upright chest x-ray (CXR) can

establish the diagnosis of pneumothorax (Fig. 35-1); however, confirming the diagnosis of tension pneumothorax with a radiograph is unnecessary and leads to dangerous delays. Smaller pneumothoraces may only be evident on expiratory CXR or CT scan.

C. Management options include observation, aspiration, needle thoracostomy, chest tube placement with or without pleurodesis, and surgery.

1. **Observation** is an option in a healthy, asymptomatic patient with a small or occult pneumothorax. Supplemental oxygen may help to reabsorb the pneumothorax by affecting the gradient of nitrogen in the pneumothorax. Interval CXR may be obtained to reassess for expansion of the pneumothorax that may be amenable to intervention or if symptoms develop.

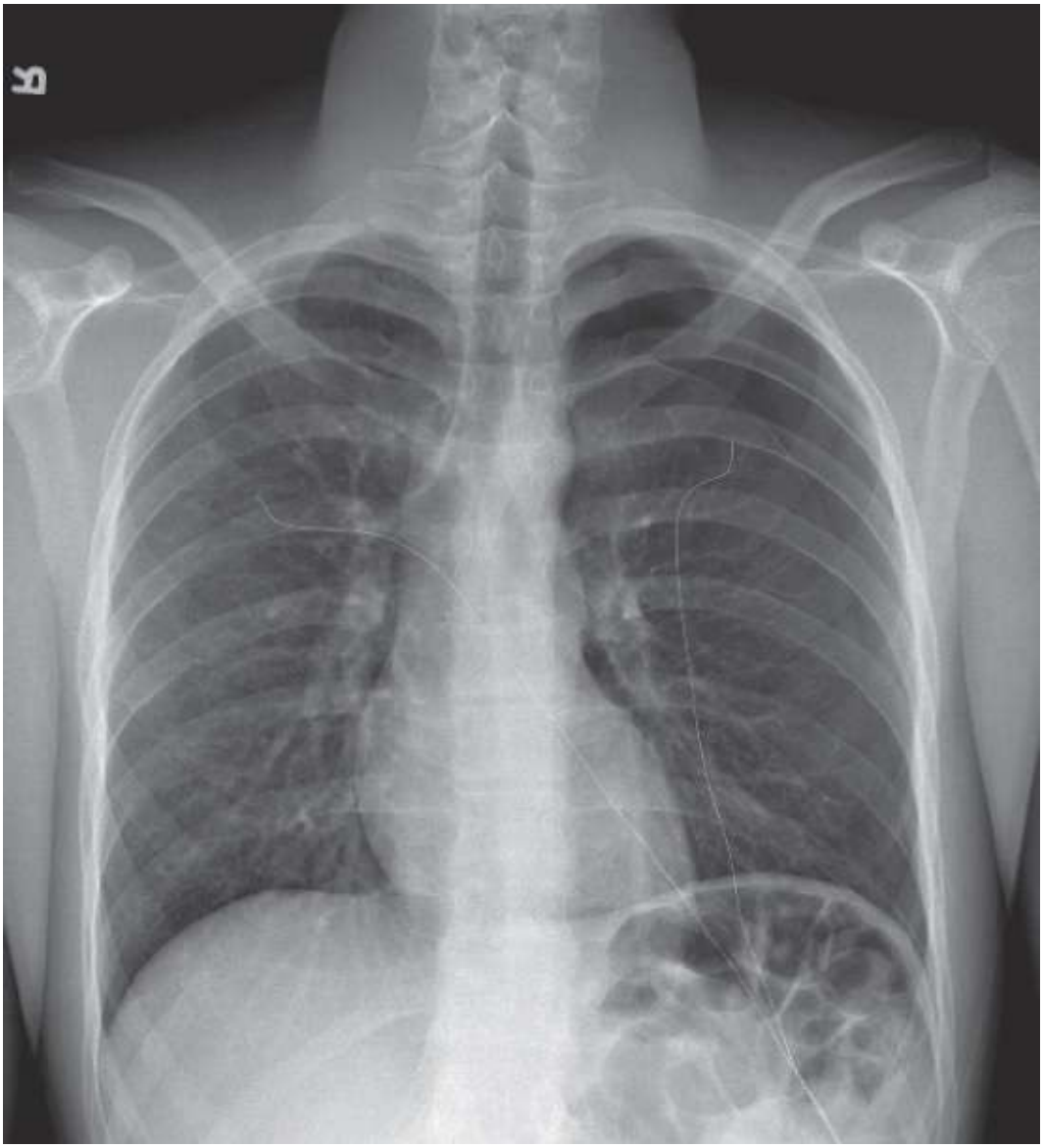

FIGURE 35-1 Spontaneous left-sided pneumothorax.

2. **Aspiration** of the pneumothorax may be performed using a small catheter attached to a three-way stopcock. This should be reserved for small to moderate pneumothoraces with low suspicion of an ongoing air leak.
3. **Needle thoracostomy** should be performed for suspected tension pneumothorax in the setting of hemodynamic compromise. A large-bore IV catheter (14 to 16 gauge) is placed in the second intercostal space in the midclavicular line, with the needle advanced into the pleural space until air is freely aspirated into a syringe. The needle is then removed and the catheter is kept open and in place until a formal

chest tube is expeditiously placed.

4. **Percutaneous catheters** are mini chest tubes that may be placed using Seldinger technique for moderate pneumothoraces. Multiple commercial kits exist and allow for the catheter to be placed to a water seal or suction. The catheters are of small caliber, therefore limiting their use to situations of simple pneumothorax. If there is concern for lung adhesions, bedside percutaneous catheters should be avoided to decrease the risk of intraparenchymal insertion.
5. **Tube thoracostomy** remains the gold standard for large pneumothoraces, associated effusion, when there is an expected need for pleurodesis, or when there is expected adhesions from previous intrathoracic operations. Chest tubes may be connected to a Heimlich one-way valve, a simple underwater-seal system, or to vacuum suction (typically 20 cm H_2O). If the water-seal chamber bubbles with expiration or with coughing, it is indicative of a persistent air leak. In most cases, the tube stays in while the air leak persists. Typically, chest tube bore should not exceed 24 Fr for pneumothorax.
6. **Bedside pleurodesis.** In cases of persistent pneumothoraces that have failed conservative management with tube thoracostomy, pleurodesis may be performed via administration of sclerosing agents through the chest tube to induce fusion of the parietal and visceral pleural surfaces. Doxycycline, bleomycin, and talc have all been described. Chemical pleurodesis can be associated with an inflammatory pneumonitis in the lung on the treated side. In patients with limited pulmonary reserve, this may present as clinically significant hypoxia. Pleurodesis can be associated with pain and requires adequate analgesia. Talc is the most commonly used agent and induces less pain.
7. **Surgery** is performed using a video-assisted thoracoscopic surgery (VATS) or rarely via thoracotomy.
   a. **Indications for operation** for pneumothorax include:
      (1) Recurrent spontaneous ipsilateral pneumothoraces
      (2) Bilateral pneumothoraces
      (3) Persistent air leaks on chest tube suction (usually >3 to 5 days)
      (4) First spontaneous pneumothorax in patients with high-risk occupations (e.g., pilots and divers) or who live at a great

distance from medical facilities

(5) Clear anatomic target such as blebs with initial presenting episode of pneumothorax

b. Operative management consists of stapled wedge resection of blebs or bullae, usually found in the apex of the upper lobe or superior segment of the lower lobe. Pleural abrasion (mechanical pleurodesis) should be performed to promote formation of adhesions between visceral and parietal pleurae. In older patients, intraoperative talc insufflation in the pleural space provides reliable pleurodesis.

II. PLEURAL EFFUSION

A. Pleural effusions are buildup of fluid in the pleural space and may result from a wide spectrum of benign, malignant, and inflammatory conditions. They are broadly categorized as either **transudative** (protein-poor fluid from increased intravascular pressure) or **exudative** (protein- or cell-rich fluid resulting from increased vascular permeability).

B. Presenting symptoms of pleural effusions can include dyspnea, cough, or pleuritic chest pain, as well as a variety of symptoms specific to the underlying etiology. Small pleural effusions are often asymptomatic.

C. Diagnosis

1. Most pleural effusions are first diagnosed on upright **CXRs** which demonstrate blunting of the costophrenic angle with or without a concave meniscus depending on the amount of fluid accumulated (Fig. 35-2). **CT scan** and **ultrasound** can be helpful if history suggests a more chronic organizing process such as empyema.

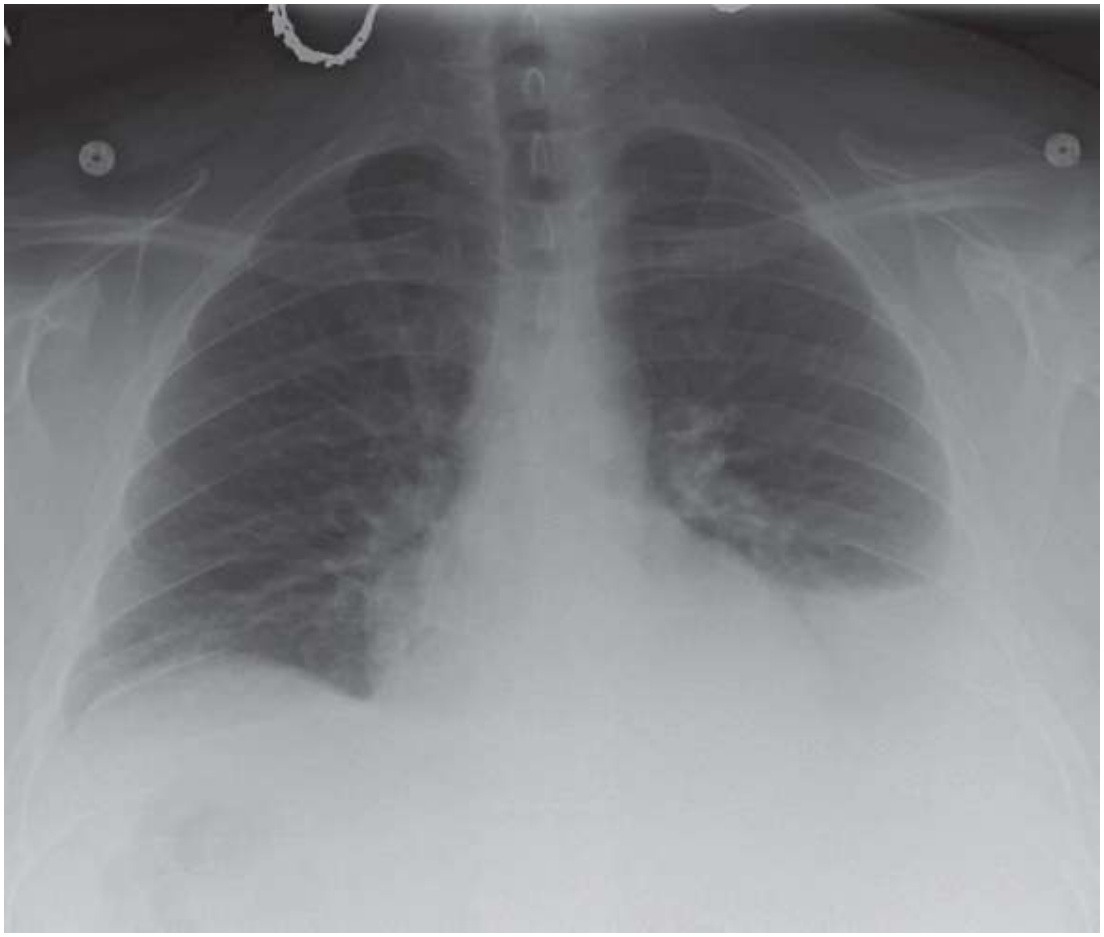

FIGURE 35-2 Left-sided moderate pleural effusion.

2. **Thoracentesis** can serve as a diagnostic or therapeutic tool for large, recurrent, or symptomatic pleural effusions. The fluid should be sent for pH, glucose, amylase, lactate dehydrogenase (LDH), protein levels, culture and Gram stain, a differential cell count, and cytology, to aid in diagnosis (Fig. 35-3). Appearance of the fluid often indicates etiology: Thin yellow or clear fluid is common with transudative effusions; cloudy, foul-smelling fluid usually signals infection; milky white fluid suggests chylothorax.

D. Management

1. **Transudative pleural effusions** are considered a secondary diagnosis; therefore, therapy should be directed at the underlying problem (e.g., congestive heart failure, cirrhosis, or nephrotic syndrome). Intermittent therapeutic thoracentesis can be used for drainage of recurrent symptomatic effusions (Fig. 35-4).
2. **Exudative pleural effusions** satisfy at least one of Light's criteria:

(1) Ratio of pleural fluid protein to serum protein greater than 0.5; (2) Ratio of pleural fluid LDH to serum LDH greater than 0.6; (3) Pleural fluid LDH greater than two-thirds the upper normal limit of serum LDH. They may be broadly classified based on whether the cause is benign or malignant:

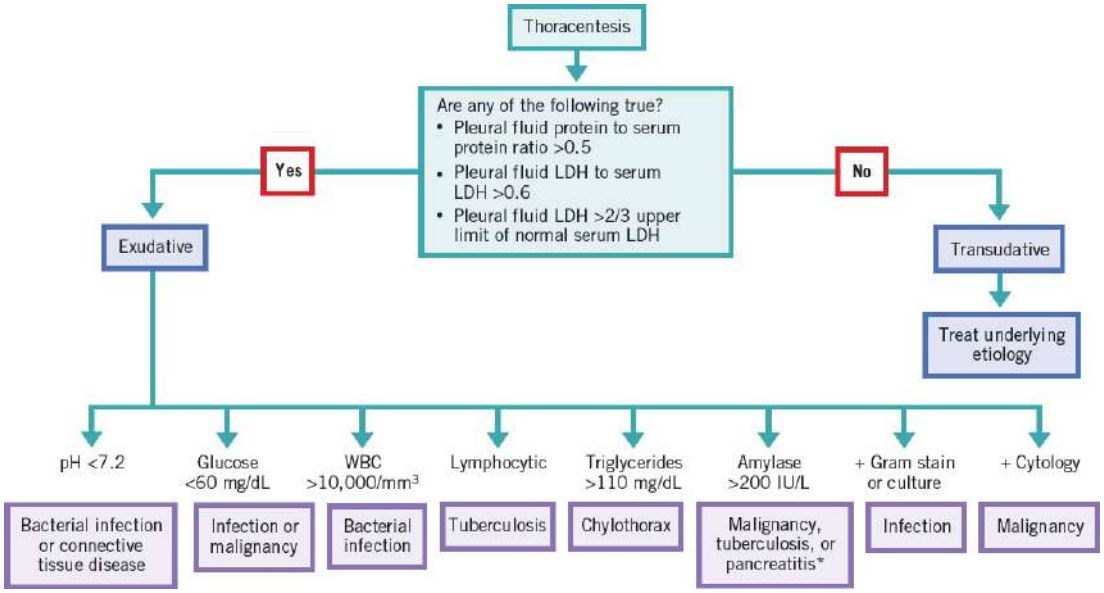

FIGURE 35-3 Interpreting laboratory results from a thoracentesis. *(Modified from Villena V, Pérez V, Pozo F, et al. Amylase levels in pleural effusions: a consecutive unselected series of 841 patients. *Chest*. 2002:121:470–474.)

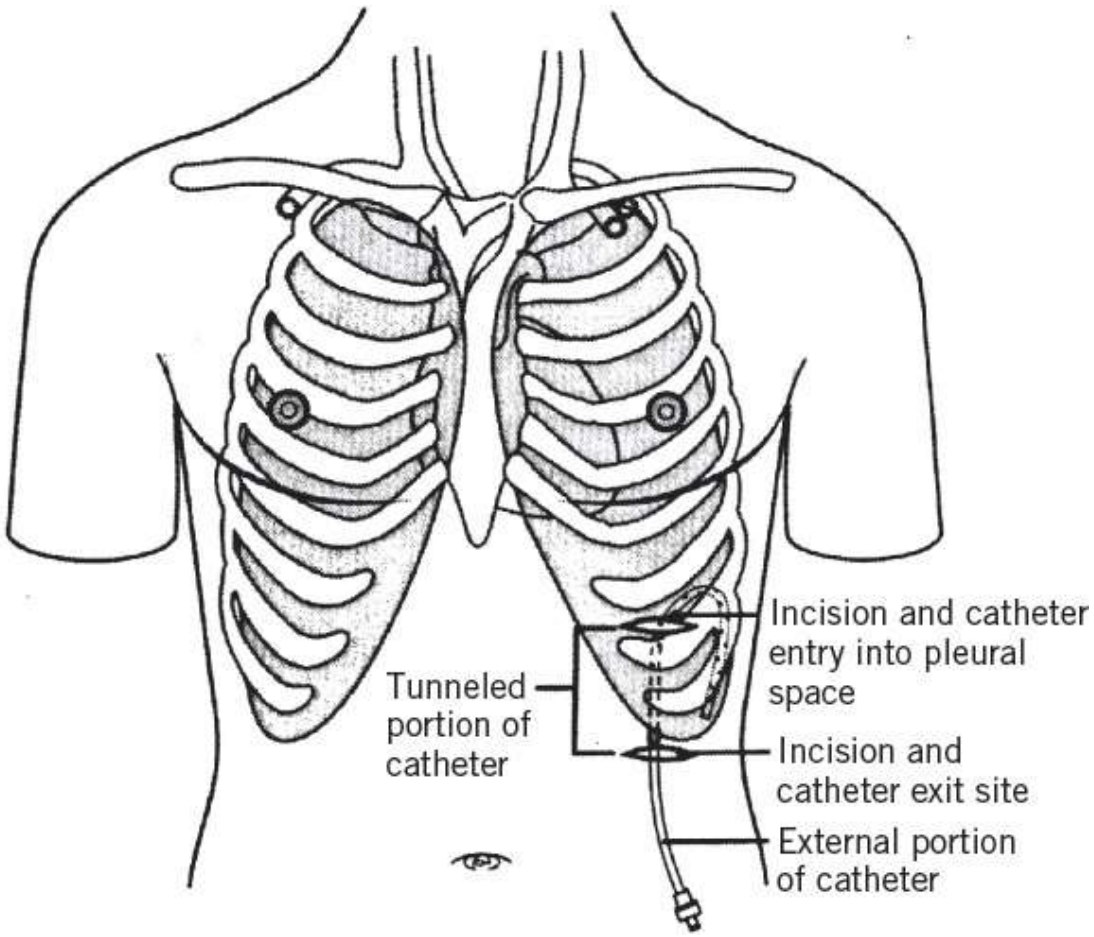

FIGURE 35-4 PleurX catheter.

a. Benign exudative effusions are often a result of pneumonia (parapneumonic). They can also be a true empyema (see next section), tuberculous, chylous, or pancreatic reactive effusions. Treatment of parapneumonic and tuberculous effusions is adequate pleural drainage and appropriate antibiotics. Chylothorax can be controlled with diet changes and drainage, somatostatin analog (octreotide), pleurodesis, thoracic duct embolization, or thoracic duct ligation. A pancreatic reactive effusion usually disappears with resolution of the pancreatitis.

b. Malignant effusions are most often associated with cancers of the breast, lung, and ovary and with lymphoma. Diagnosis is often made by cytology. In the event that cytology is not diagnostic, pleural biopsy may be indicated. Given the overall poor prognosis in these patients, **therapy offered by the thoracic surgeon is generally palliative.**

(1) **Intermittent drainage** of effusion to alleviate dyspnea and improve pulmonary mechanics by reexpanding the lung is performed with an indwelling pleural catheter (PleurX).

(2) **Pleurodesis**, usually with talc, can prevent reaccumulation of the effusion.

III. EMPYEMA

A. Empyema is a purulent collection in the pleural space. Fifty percent of empyemas are complications of pneumonia; 25% are complications of esophageal, pulmonary, or mediastinal surgery; and 10% are extensions from subphrenic abscesses. Among pathogens causing empyema, common gram-positive bacteria are *Staphylococcus aureus* and *Streptococci;* gram-negative bacteria are *Escherichia coli, Pseudomonas,* and *Klebsiella;* and anaerobic bacteria are *Bacteroides* species.

B. Presentation of empyema ranges from chronic loculated effusion in a patient with fatigue to systemic sepsis requiring emergent care. Other symptoms include pleuritic chest pain, fever, cough, and dyspnea. Empyemas are diagnosed via thoracentesis and better evaluated by CT scan with intravenous contrast. Pleural fluid analysis demonstrates abundant WBCs, decrease in glucose, pH less than 7.2, positive Gram stain and bacterial culture.

C. Management includes control of the infection by appropriate antibiotics, drainage of the pleural space, and obliteration of the empyema space. Evolution of empyema involves three main phases:

1. **Early or exudative phase (1 to 5 days)** is associated with simple infected fluid which can be adequately treated with antibiotics and simple chest tube drainage.
2. **Fibropurulent or fibroproliferative phase (5 to 10 days)** has loculated fluid composed of fibrin and may be amenable to tube drainage alone or may require thoracoscopic drainage in addition to antibiotics.
3. **Advanced or organizing phase (10 to 14 days)** has thicker fluid and a fibrous peel encases and traps the lung, thus limiting its expansion. Thoracotomy may be necessary to free the entrapped lung.
4. If a patient has a persistent fluid collection with an adequately placed tube as evidenced by chest CT, intrapleural fibrinolytic therapy with

tissue plasminogen activator (TPA) with DNase may be useful to break down thin adhesions. Failure of intrapleural fibrinolytics usually requires operative intervention.

5. A **postpneumonectomy empyema** can result from a bronchial stump dehiscence with contamination of the pneumonectomy space. Increasing air in the pneumonectomy space on CXR is often diagnostic. Bronchopleural fistula has a high mortality rate and is managed via drainage of the space, antibiotics, and surgical repair of the fistula. **Great caution should be taken in inserting chest tubes into postpneumonectomy empyemas.** Chest tube is best placed with patient positioned with the affected side down in order to avoid contamination of the contralateral lung. Surgical repair involves primary closure of the bronchial stump buttressed with vascularized muscle flaps. The residual pleural cavity can be obliterated by a muscle transposition, thoracoplasty, or delayed Clagett procedure/Eloesser flap which permits a means for irrigation, debridement, and drainage of the infected pleural space.

IV. LUNG ABSCESS

A. Lung abscess is commonly associated with aspiration superimposed with infection or with necrotizing pneumonia. Common bacterial culprits are similar to those that cause empyema. Main symptoms include fever, productive cough with foul-smelling sputum, weight loss, malaise, chest pain, and dyspnea.

B. Diagnosis is made radiographically with CXR or CT scan which may demonstrate an air–fluid level within the abscess cavity.

C. Treatment is mainly medical with antibiotics and pulmonary hygiene. Most patients respond to medical treatment. An external drain should not be directly inserted into a lung abscess to prevent the risk of developing a chronic bronchopleural fistula. Surgical therapy is indicated for failure of long-term medical treatment, sepsis, and to exclude malignancy. Surgical therapy involves resection of involved lung parenchyma.

V. HEMOPTYSIS

A. Hemoptysis is the expectoration of blood and can originate from a number of causes, including infectious, malignant, and cardiac disorders

(e.g., bronchitis or tuberculosis, bronchogenic carcinoma, and mitral stenosis, respectively).

B. Workup of hemoptysis includes a focused history and physical examination to assess for symptoms that suggest infection or systemic disease, in conjunction with a radiographic study such as CXR or CT scan.

1. In the setting of a negative CXR and hemoptysis that is likely due to acute bronchitis, observation can be appropriate.
2. If the CXR is abnormal, further workup and management are indicated.
3. For negative CXR and recurrent hemoptysis, a CT scan with intravenous contrast is warranted to further assess the underlying etiology, and can be used as an adjunct to bronchoscopy to localize the source of bleeding.

C. Massive hemoptysis is defined as more than 600 mL of blood loss from the lung in 24 hours. It is a surgical emergency as delay in intervention can lead to a fatal asphyxiation. Therefore, the first steps are to assess the patient and secure the airway. An urgent CXR may localize the side of the source of bleeding.

1. **Bronchoscopy** can identify the bleeding side and allow for prompt protection of the remaining lung parenchyma, either by controlling the area of bleeding or selective ventilation. Bleeding can be controlled by topical or injected vasoconstrictors or by placement of a balloon-tipped catheter in the lobar orifice. Selective ventilation can be achieved with a double-lumen tube or by direct intubation of the contralateral mainstem bronchus.
2. If unable to identify the site of bleeding or after temporizing the bleed, **angiographic embolization** of a bronchial arterial source may allow for lung salvage without the need for resection. The bronchial circulation is almost always the source of hemoptysis. Bleeding from the pulmonary circulation is seen only in patients with pulmonary hypertension or some lung cancers.
3. **Definitive therapy** may require thoracotomy with lobar resection or, rarely, pneumonectomy. Rarely, emergent surgical resection is necessary to control the hemoptysis. The etiology of the bleeding and the pulmonary reserve of the patient are important because many

patients are not candidates for surgical resection.

VI. LUNG CANCER

A. Lung cancer is the second most common nonskin malignancy following prostate cancer in men and breast cancer in women. It is the leading cause of cancer death. An estimated 234,030 cases will be diagnosed and 154,050 patients will die of the disease in 2018 (www.cancer.org). Cigarette smoking is the leading risk factor for the development of lung cancer. Increasing age, asbestos and radiation exposure increase the risk of development of lung cancer. The American Cancer Society (ACS) recommends annual screening for lung cancer with low-dose CT scan in adults aged 55 to 74, in fairly good health, and who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

B. Pathology. The two main classes of lung cancer are small cell lung carcinoma (SCLC) and non–small cell lung carcinoma (NSCLC):

1. **Small cell carcinoma** accounts for approximately 15% of all lung cancers. It is an aggressive tumor, usually occurs centrally near the hilum, is almost exclusive to smokers, and rarely is amenable to surgery because of wide dissemination by the time of diagnosis. These cancers initially respond to chemotherapy, but overall 5-year survival remains less than 10%.
2. **Non–small cell carcinomas** account for 85% of all lung cancers and make up the vast majority of those treated by surgery as they are less aggressive and can be diagnosed at an earlier stage. The three main subtypes are **adenocarcinoma** (30% to 50% of cases), **squamous cell** (20% to 35%), and **large cell** (4% to 15%). **Bronchioloalveolar carcinoma** is a variant of adenocarcinoma, produces mucin, and can be multifocal. Recently, important subgroups of bronchogenic neuroendocrine carcinoma have been appreciated. These include typical carcinoid tumors (grade I neuroendocrine carcinoma), atypical carcinoid tumors (grade II neuroendocrine carcinoma), and large cell carcinoma. This may explain the more aggressive behavior of large cell carcinoma relative to other non–small cell cancers.

C. Radiographic presentation may occur during a diagnostic evaluation for symptoms or as an incidental finding.

1. **Solitary pulmonary nodules (SPN)** are circumscribed lung lesions

in an asymptomatic individual, with lesions greater than 3-cm labeled masses. The first step in evaluation of SPN is to compare current radiographic images with previous images if available (Fig. 35-5).

2. **Radiographic imaging by CT** is used to follow lesions and predict outcome. Factors favoring a benign lesion include stable size over a 2-year period, lesion diameter <6 mm, and certain patterns of calcification such as diffuse, centrally located, laminar, or popcorn-like calcifications. Malignancy is favored with intravenous contrast enhancement, irregular borders, lobulations, and eccentric or stippled calcifications (Fig. 35-6).

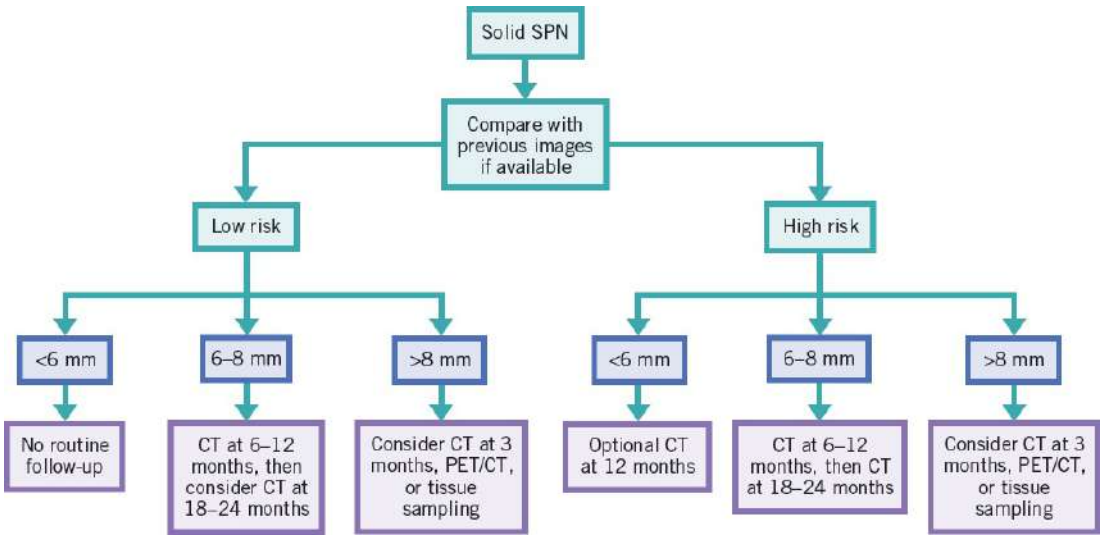

FIGURE 35-5 Management of solid solitary pulmonary nodule (SPN) based on Fleischner Society 2017 Guidelines. High risk is defined by age greater than 55 years old and smoking history of 30 pack-years or more. Low risk is defined by age lesser than 50 years old or smoking history of <20 pack-years.

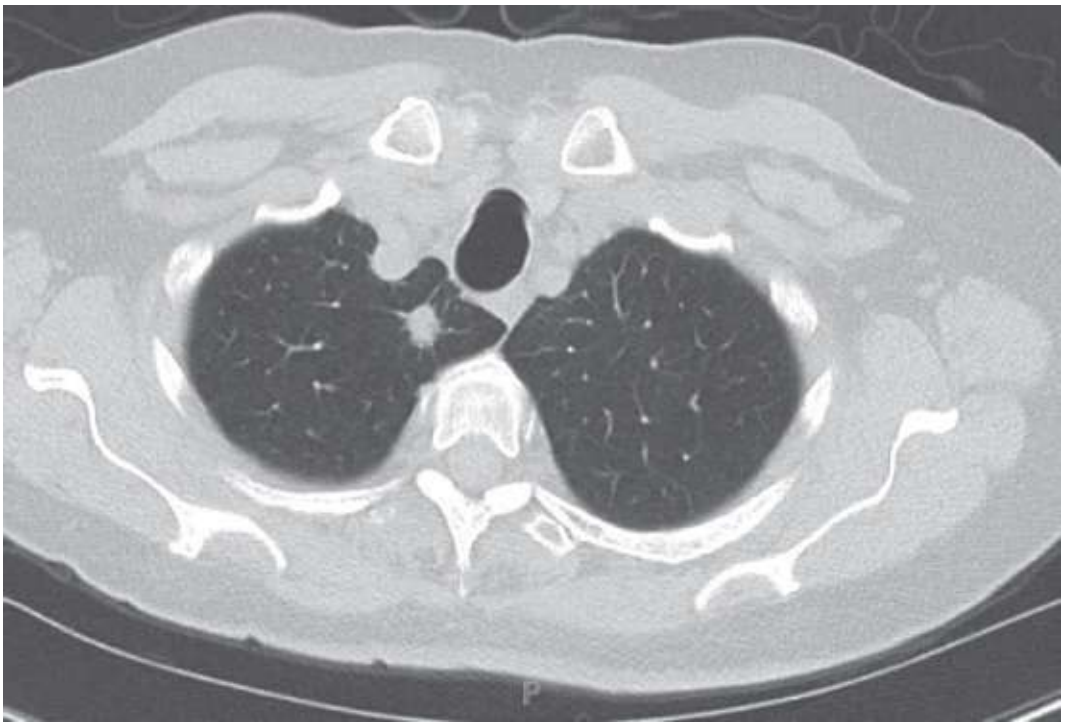

FIGURE 35-6 Solitary pulmonary nodule in right upper lobe.

3. **Positron emission tomography (PET) scanning** is 95% sensitive and 80% specific in characterizing nodules. However, bronchoalveolar carcinoma and carcinoid tumor can be falsely negative, and inflammatory and infectious processes can be falsely positive. The patient's overall risk factor profile must also be considered. In the setting of low risk (e.g., young age, nonsmoker, favorable CT finding), a negative PET scan has a high negative predictive value, but the same result in an elderly smoker is considered discordant, and further evaluation is warranted.
4. **Tissue biopsy** is the gold standard for diagnosis. Tissue may be obtained by bronchoscopy in patients with central lung lesions or by CT-guided biopsy for peripheral lesions. An advanced form of bronchoscopy called radial endobronchial ultrasound (EBUS) can also access peripheral lesions. Surgical biopsy via video thoracoscopy can provide a definitive diagnosis, often as a prelude to therapeutic resection at the same operation.

D. Symptomatic presentation of lung cancer implies a more advanced stage and is associated with an overall lower rate of survival:

1. **Bronchopulmonary features** include cough or a change in a

previously stable smoker's cough, increased sputum production, dyspnea, and wheezing. Minor hemoptysis should be investigated with bronchoscopy in patients with a history of smoking who are 40 years of age or older. Lung cancer may also present with postobstructive pneumonia.

2. **Extrapulmonary thoracic symptoms** include chest wall pain secondary to local tumor invasion, hoarseness from invasion of the left recurrent laryngeal nerve near the aorta and left main pulmonary artery, shortness of breath secondary to malignant pleural effusion or phrenic nerve invasion, and superior vena cava syndrome causing facial, neck, and upper extremity swelling. A Pancoast tumor (superior sulcus tumor) can lead to invasion of the brachial plexus or the cervical sympathetic ganglia, causing an ipsilateral Horner syndrome (ptosis, miosis, and anhidrosis). Rarely, lung cancer can present as dysphagia from compression or invasion of the esophagus by mediastinal nodes or the primary tumor.
3. The most frequent **sites of distant metastases** include the liver, bone, brain, adrenal glands, and the contralateral lung. Symptoms may include pathologic fractures from bony involvement. Brain metastasis may cause headache, cranial neuropathies, or changes in mental status. Adrenal involvement infrequently presents with Addison disease. Lung cancer is the most common tumor causing adrenal dysfunction.
4. **Paraneoplastic syndromes** are frequent and occur due to release of endocrine substances by tumor cells. They include Cushing syndrome (ACTH, SIADH secretion, and Lambert–Eaton syndrome in small cell carcinoma), hypercalcemia (PTH-related protein secreted by squamous cell carcinomas), hypertrophic pulmonary osteoarthropathy (clubbed fingers, joint stiffness, and periosteal thickening on XR in adenocarcinoma), and gynecomastia in large cell carcinoma.

E. Accurate clinical and pathologic staging is critical in the management of patients with non–small cell carcinoma. Surgery is the primary therapy for many stage I and II patients and selected stage III patients. The essential elements of staging include evaluation for lymph node involvement and distant metastasis. The staging system was most recently modified in 2017 (*AJCC Cancer Staging Manual 8th edition*; Table 35-1).

1. **Chest CT to include the upper abdomen** assesses the size, location, and local invasion of tumor, identifies mediastinal lymphadenopathy, and evaluates for liver or adrenal metastasis. The sensitivity for identifying metastatic lymph nodes by CT is 65% to 80% and the specificity is only 65%.
2. **PET imaging** is often used to stage patients with NSCLC, but its accuracy for detecting primary tumors and metastatic disease may be limited by the presence of inflammation and ongoing infection. In regions endemic for inflammatory processes such as granulomatous diseases, the usefulness of PET imaging for investigating mediastinal lymph nodes is limited. However, it can be useful for identifying occult distant metastatic disease to the liver, adrenals, and bone.
3. **Lymph node staging** of the mediastinum is done using either **EBUS**-guided fine-needle aspiration or **mediastinoscopy** in patients with localized disease to determine resectability. The pretracheal, paratracheal, and subcarinal lymph nodes can be easily accessed by these techniques. Aortopulmonary nodes can be sampled via endoscopic (transesophageal) ultrasound (EUS), VATS, or, less commonly, anterior mediastinoscopy (Chamberlain procedure). Routine use of either of these techniques in the staging of patients with NSCLC should be favored, with the exception of select patients with clinical stage I lung cancer staged by CT and PET with no abnormal lymphadenopathy (*J Thorac Cardiovasc Surg*. 2006;131:822–829). The timing of mediastinoscopy, whether before or during a planned resection, depends on surgeon preference and the availability of accurate pathologic evaluation of mediastinal lymph node frozen sections.

TABLE 35-1 American Joint Committee on Cancer Staging System of Lung Cancer 8th Edition

Tumor Status (T)	
T1a	≤1 cm
T1b	>1–2 cm
T1c	>2–3 cm
	No invasion of visceral pleura or more proximal than lobar

	bronchus
T2a	>3–4 cm
T2b	>4–5 cm Involvement of bronchus without carina involvement Invasion of visceral pleura Associated atelectasis or obstructive pneumonitis extending to the hilum, either involving part of the lung or the entire lung
T3	>5–7 cm or tumor with any of the following characteristics: Invasion of chest wall (parietal pleura or superior sulcus), phrenic nerve, or parietal pericardium Separate tumor nodule(s) in the same lobe
T4	>7 cm or tumor with any of the following characteristics: Invasion of mediastinum, heart, great vessels, carina, trachea, diaphragm, esophagus, recurrent laryngeal nerve, or vertebral body Separate tumor nodule(s) in a different lobe of ipsilateral lung

Nodal Involvement (N)

N0	None
N1	Ipsilateral hilar, intrapulmonary, or peribronchial lymph nodes
N2	Ipsilateral mediastinal lymph nodes or subcarinal lymph nodes
N3	Contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph nodes

Distant Metastases (M)

M0	None
M1a M1b	Separate tumor nodule(s) in a contralateral lung, pleural or pericardial nodule, malignant pleural or pericardial effusion
M1c	Single extrathoracic metastasis Multiple extrathoracic metastasis in one or several organs

Stage	TNM	5-yr Survival (%)
IA1	T1a N0 M0	92
IA2	T1b N0 M0	83

IA3	T1c N0 M0	77
IB	T2a N0 M0	68
IIA	T2b N0 M0	60
IIB	T1a,b,c N1 M0 T2a,b N1 M0 T3 N0 M0	53
IIIA	T1a,b,c N2 M0 T2a,b N2 M0 T3/4 N1 M0 T4 N0 M0	36
IIIB	T1a,b,c N3 M0 T2a,b N3 M0 T3/4 N2 M0	26
IIIC	T3/4 N3 M0	13
IVA	Any T, any N, M1a,b	10
IVB	Any T, any N, M1c	<1

4. **CT or magnetic resonance (MR) imaging of the brain** to identify brain metastases is mandatory in the patient with neurologic symptoms, stage III and IV cancer, those with SCLC, or superior sulcus tumors because these patients may have a higher probability for occult brain metastasis.
5. **Fiberoptic bronchoscopy** is important in diagnosing and assessing the extent of the endobronchial lesion. Although peripheral cancers rarely can be seen with bronchoscopy, preoperative bronchoscopy is important for excluding synchronous lung cancers (found in approximately 1% of patients) prior to resection and can help rule out suspicious mediastinal nodal metastasis.

F. Management of lung cancer includes a combination of surgery, chemotherapy, and radiation.

1. Stage I disease is generally treated with surgical resection alone. Stage II cancers are also treated with surgery, but chemotherapy increases 5-year survival and is recommended in patients with stage II and stage III disease. Adjuvant radiation therapy is considered in patients with close surgical margins or central lymph node metastasis. Certain patients with stage IIIA disease appear to benefit from surgical resection alone (T3N1M0). Selected patients with mediastinal lymph node metastasis (N2 disease) may be candidates for surgical resection after neoadjuvant chemoradiation therapy with good clinical response. Patients with bulky, diffuse mediastinal lymphadenopathy or stage IIIB tumors are typically treated using definitive chemoradiation. Stage IV tumors have distant metastases and are considered unresectable, though some patients with node-negative lung cancer and a solitary brain metastasis have achieved long-term survival with combined resection.
2. **Operative principles.** In the patient able to tolerate any resection, the minimum extent of resection is usually an anatomic lobectomy. Even in stage I disease, a wedge resection results in a threefold higher local recurrence rate and a decreased overall and disease-free survival. Patients with limited pulmonary reserve may be treated by segmental or wedge resection. Most centers report operative mortality of less than 2% with lobectomy and 6% with pneumonectomy. VATS has become a widespread technique for lung resections. Thoracotomy can be performed when there is local invasion that requires en bloc resection.
3. **Stereotactic body radiation therapy (SBRT)** is external beam radiation therapy that precisely delivers high-dose radiation to a target in the body over one or more treatments. SBRT has been shown to be effective for early-stage lung cancer in patients that are poor candidates for surgical resection.

G. Five-year survival rates are summarized in Table 35-1.

VII. TUMORS OF THE PLEURA

A. The most common tumor of the pleura is mesothelioma. Malignant mesothelioma is a rare and aggressive cancer that has been linked to asbestos exposure with a latency period of decades. They are classified into different subtypes: epithelioid (50%), sarcomatoid (20%), mixed,

and desmoplastic.

1. **Patient presentation** varies, but can include chest pain, malaise, cough, weakness, weight loss, and shortness of breath with pleural effusions. One-third of patients report paraneoplastic symptoms of osteoarthropathy, hypoglycemia, and fever.
2. **Diagnosis** is made via cytology of pleural fluid, needle biopsy of the pleura, or biopsy of suspicious pleural nodules via thoracoscopy. CT scans can differentiate pleural from parenchymal disease. Routine use of MRI is not recommended, while PET scan is used to identify distant metastatic disease (*J Thorac Cardiovasc Surg.* 2003;126:11–15).
3. **Treatment** consists of multimodal therapy comprising surgery, chemotherapy, and radiation. Surgical options include extrapleural pneumonectomy (EPP) or pleurectomy/decortication. For early-stage cases, EPP may offer the best chance of cure. The best reported 5-year survival following completion of the multimodal therapy in patients without nodal metastasis is 53% but survival is typically lower than that (*J Clin Oncol.* 2009;27:1413–1418). Median survival of patients with untreated malignant mesothelioma is 8 to 10 months. Not all patients with mesothelioma are candidates for surgery.

B. Less common tumors of the pleura include lipomas, angiomas, soft tissue sarcomas, and fibrous histiocytomas.

VIII. TUMORS OF THE MEDIASTINUM. The location of a mass in relation to the heart helps the surgeon to form a differential diagnosis (Table 35-2). On the lateral CXR, the mediastinum is divided into thirds, with the heart comprising the middle segment, with the anterior and posterior mediastinum comprising their respective thirds. Overall, lymphoma is the most common mediastinal tumor. Neurogenic tumors are more likely in children.

A. Presentation of mediastinal tumors vary, and symptoms are only present in one-third of patients. Symptoms are often nonspecific and include dyspnea, cough, hoarseness, weight loss, vague chest pain, and fever.

B. Radiographic evaluation includes CXR, which should be followed by a CT scan to further delineate the anatomy. Malignant germ cell tumors are further evaluated with abdominal CT and scrotal ultrasound.

C. Anterior mediastinal masses are represented by the "Four Ts": Thymoma, teratomas/germ cell tumors, "terrible" lymphoma, or thyroid tumors.

1. **Thymomas** are malignant in 15% of cases, and are staged by the Masaoka system (Table 35-3). The presence of capsular invasion decreases survival. Approximately 50% of patients with a thymoma have paraneoplastic syndromes, including myasthenia gravis (MG), hypogammaglobulinemia, and red cell aplasia.
   a. The thymus gland plays a role in **MG** by generating autoreactive antibodies against the acetylcholinesterase receptor. Roughly 15% of MG patients have a thymoma, though 80% of cases demonstrate complete or partial response to thymectomy.
   b. **Preoperative preparation** for patients with MG includes decreasing corticosteroids and weaning of anticholinesterases. Plasmapheresis can be performed preoperatively to aid in this. Muscle relaxants and atropine should be avoided during anesthesia.

TABLE 35-2 Differential Diagnosis of Tumors Located in the Mediastinum

Anterior		Middle	Posterior
Thymoma	Lymphoma	Congenital enteric cyst	Neurogenic
Germ cell	Parathyroid	Lymphoma	Lymphoma
Teratoma	Lipoma	Primary cardiac cyst	Mesenchymal
Seminoma	Fibroma	Neural crest	
Nonseminoma	Lymphangioma	Bronchogenic cyst	
Aberrant thyroid			

Modified from Young RM, Kernstine KH, Corson JD. Miscellaneous cardiopulmonary conditions. In: Corson JD, Williamson RCN, eds. *Surgery*. Philadelphia, PA: Mosby; 2001.

TABLE 35-3 Masaoka Staging System of Thymomas and 5-Year Survival

Stage		5-yr Survival (%)
Stage I	Macroscopic complete encapsulation and no microscopic capsular invasion	100
Stage II	II-A Microscopic invasion into surrounding fatty tissue or mediastinal pleura	98.4
	II-B Macroscopic invasion into the capsule	
Stage III	Macroscopic invasion into neighboring organs	88.7
Stage IV	IV-A Pleural or pericardial implants	70.6
	IV-B Lymphogenous or hematogenous metastasis	52.8

Adapted from Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. *Ann Thorac Surg*. 2003;76(3):878–884.

   c. **Operative approach** involves en bloc resection via transcervical thymectomy, median sternotomy, VATS resection, and robotic resection. For more advanced stages of thymoma, neoadjuvant chemotherapy may be indicated.

2. **Germ cell tumors** should be biochemically evaluated with β-human chorionic gonadotropin (β-HCG) and α-fetoprotein (AFP).
   a. **Teratomas** are usually benign and often contain ectodermal components such as hair, teeth, and bone. Elevation of both β-HCG and AFP is very rare, and suggests a malignant teratoma. Treatment is surgical resection.

b. Seminomas do not have elevated AFP, and fewer than 10% present have elevated β-HCG. Their treatment is primarily nonsurgical (radiation and chemotherapy), except in the case of localized disease. CT scan of the abdomen and pelvis should be obtained to rule out advanced disease.

TABLE 35-4 Ideal Lung Donor Selection Criteria

1. Age <55 years old
2. No history of pulmonary disease
3. PaO_2 >300 mm Hg, FiO_2 = 1.0, PEEP = 5 cm H_2O
4. Negative serologic screening for hepatitis B and HIV
5. Normal CXR
6. Normal bronchoscopic examination
7. ABO compatibility
8. Size matching

c. Nonseminomatous germ cell tumors present with an elevation of both tumor markers. The treatment is with platinum-based chemotherapy, with resection of residual masses after definitive chemotherapy.

3. Lymphoma often presents as irregular masses on CT scan. They are best diagnosed with tissue biopsy which helps guide treatment. This involves cervical lymph node biopsy, CT-guided biopsy, or mediastinoscopy with biopsy. Treatment is primarily nonsurgical.

D. Middle mediastinal masses include bronchogenic and enteric cysts. They should be resected if they are symptomatic, enlarging, or the diagnosis is unclear.

E. Posterior mediastinal masses present as paravertebral masses. Catecholamine levels should be measured to rule out **pheochromocytomas**.

Esophageal diseases and management are discussed in Chapter 17.

IX. LUNG TRANSPLANTATION

A. Lung transplantation has been increasing steadily over the last decade, with the leading indications for lung transplant being chronic

obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), and CF. Other indications include α_1-antitrypsin deficiency (alpha-1) and pulmonary arterial hypertension (PAH).

B. COPD is a long-term consequence of smoking and is the result of nonuniform destruction of lung parenchyma. As lung tissue loses its elastic recoil, the areas of destruction expand. This expansion of diseased areas, in combination with inflammation, leads to poor ventilation of relatively normal lung.

1. Typical findings on CXR include **hyperexpanded lungs** due to chronic air trapping. Other findings include flattened diaphragms, widened intercostal spaces, and horizontal ribs. On pulmonary function testing (PFT), patients present with increased residual volumes and decreased forced expiratory volume in 1 second (FEV_1). Surgical treatment is generally reserved for the symptomatic patient who has failed maximal medical treatment.
2. The **goals of resectional surgery** for COPD are to remove diseased areas of lung and allow improved function of the remaining healthy lung tissue. Previously, bullectomy or lung volume reduction surgery (LVRS) was more commonly offered; however, currently lung transplantation is the most common surgical approach. LVRS is reserved for symptomatic patients who have predominantly apical disease and FEV_1 >20%.

C. Both single lung and bilateral lung transplants are options. Nationally, the number of single lung transplants is steady, while the number of double lung transplants is increasing annually. Single lung transplants offer greater use of donor organs, shorter ischemic time, and allow for the ability to replace the other native lung if rejection develops. Bilateral lung transplants allow for more pulmonary reserve and the ability to use more marginal donor lungs. Our institution favors bilateral lung transplant as patients have improved long-term survival (Fig. 35-7). The only absolute indication for bilateral lung transplantation is CF because single lung transplantation would leave a chronically infected native lung in an immunocompromised patient.

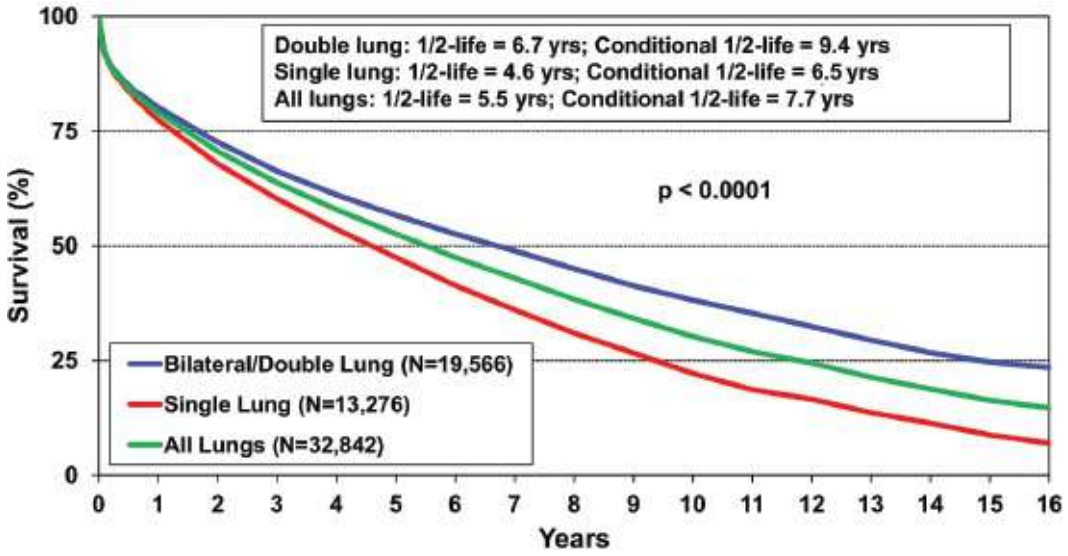

FIGURE 35-7 Chart showing lung transplant graft survival of bilateral, single, and all lung transplants from January 1994 to June 2010 and by diagnosis from January 1990 to June 2010. Conditional half-life is the 50% survival time for recipients who were alive 1 year after lung transplants. (From Stehlik J, Edwards LB, Kucheryavaya AY, et al.; International Society of Heart and Lung Transplantation. The Registry of the International Society for Heart and Lung Transplantation: 29th official adult heart transplant report—2012. *J Heart Lung Transplant*. 2012;31(10):1052–1064, with permission.)

D. Ex vivo lung perfusion (EVLP) is one of the most recent development in the area of lung transplantation. It is a preservation technique that enables the use of marginally suitable donor lungs for transplantation. In EVLP, the donor lungs are ventilated externally via a ventilator, kept warm at normal room temperature, flushed off donor blood which contain inflammatory cells, and finally perfused with antibiotics and anti-inflammatory agents. EVLP is a valuable tool that could increase potential pool of organs available.

E. Current problems with lung transplantation include donor shortage, technical/anastomosis problems, infectious complications, primary graft dysfunction, and acute and chronic rejection. Long-term, chronic allograft dysfunction in the form of bronchiolitis obliterans occurs in 50% of patients. Ideal lung donor selection criteria can be found in Table 35-4.

X. MANAGEMENT OF THORACIC SURGICAL PATIENTS

A. Preoperative assessment of pulmonary function and estimation of postoperative pulmonary reserve is the most critical factor in planning lung resection.

1. **PFTs,** which include **FEV**1, diffusing capacity of the lungs for carbon monoxide (DLCO), and **arterial blood gas (ABG),** are used to assess risk of postoperative pulmonary failure (Fig. 35-8). **Quantitative ventilation–perfusion lung scan** and **cardiopulmonary exercise testing (CPET)** are indicated in patients with marginal function for accurate assessment of postoperative function. In general, average risk for pulmonary resection is associated with a 1% to 2% mortality.

   Preoperative resting hypercapnia (arterial carbon dioxide tension >45 mm Hg) and preoperative resting hypoxemia (arterial oxygen tension <60 mm Hg) may preclude resection.

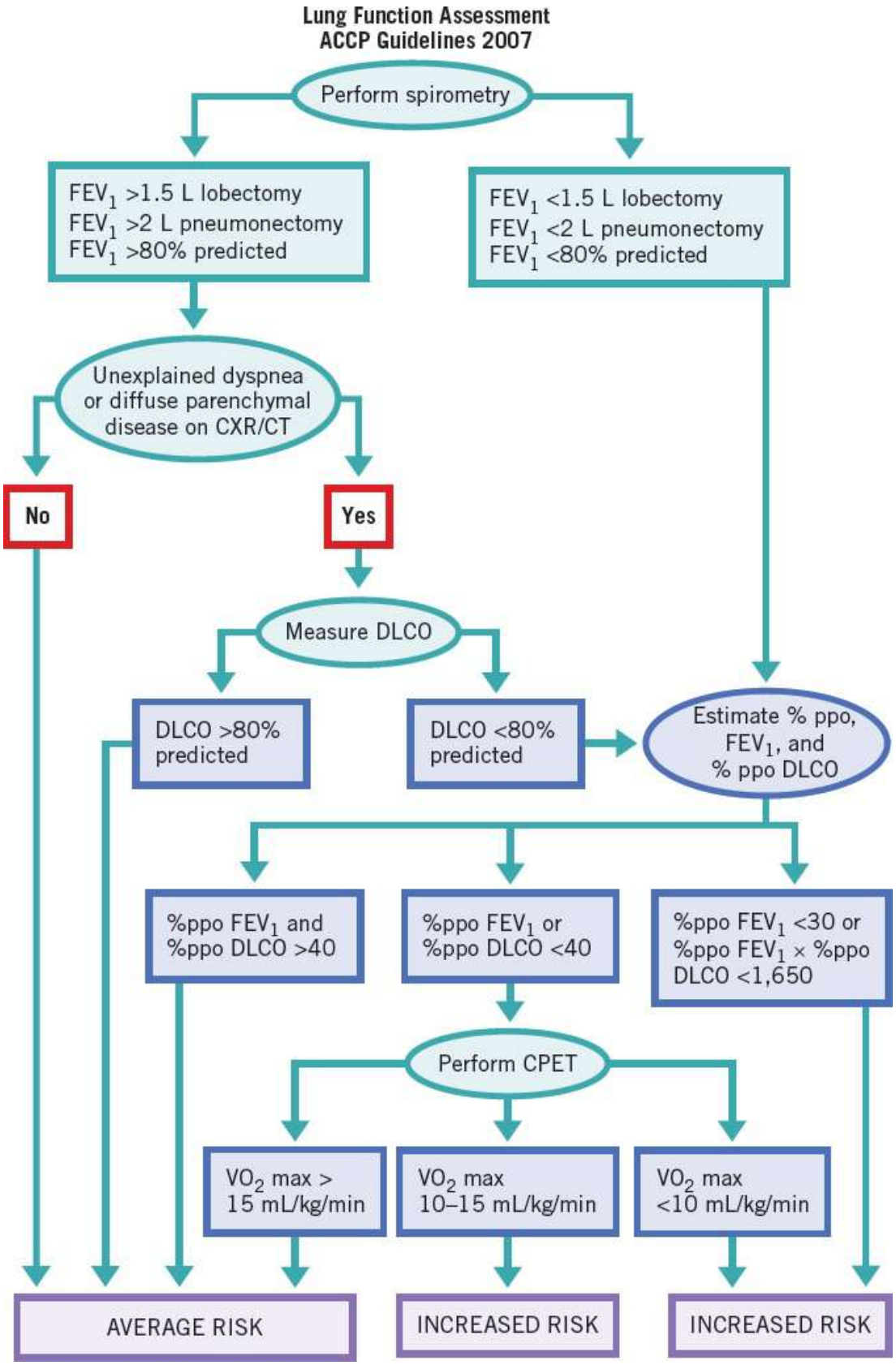

FIGURE 35-8 Preoperative lung function assessment algorithm. (From Colice GL, Shafazand

S, Griffin JP, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines (2nd edition). *Chest*. 2007;132(3 Suppl):161S–177S, with permission.)

2. **Evaluation of cardiac disease** starts with a detailed history and physical examination to elicit symptoms of ischemia and a baseline ECG. Abnormal findings should be pursued with stress tests or coronary catheterization.
3. **Smoking cessation** preoperatively for as little as 2 weeks can aid in the regeneration of the mucociliary function and has been associated with fewer postoperative respiratory complications.

B. Postoperative care of the thoracic surgery patient focuses on pain control, fluid management, maintenance of pulmonary function, and cardiovascular monitoring.

1. The **thoracotomy incision is one of the most painful and debilitating** in surgery. Inadequate pain control contributes heavily to postoperative complications. Chest wall splinting contributes to atelectasis and poor pulmonary toilet. Pain increases sympathetic tone and myocardial oxygen demand, provoking arrhythmias and cardiac ischemic episodes. The routine use of epidural catheter anesthesia during the early recovery period significantly improves pain management. Other effective analgesic maneuvers include intercostal blocks with long-acting local anesthetic before closure of the chest and subpleural administration of local anesthetic via catheters placed adjacent to intercostal nerves at the time of thoracotomy or thoracoscopy.
2. **Perioperative fluid management** of thoracic surgery patients differs from that of patients after abdominal surgery. Pulmonary surgery does not induce large fluid shifts, while collapse and reexpansion of lungs during surgery can lead to pulmonary edema. Judicious fluid management to avoid fluid overload and pulmonary edema is critical in patients with limited pulmonary reserve. Discussions regarding intraoperative fluid management should be held with the anesthesiologist before surgery. Physicians may need to accept transiently decreased urine output and increased serum creatinine. Mild hypotension may be treated with intravenous α-agonists such as phenylephrine. Cardiac dysfunction may also be the source of

postoperative oliguria, pulmonary edema, and hypotension and should always be considered in patients who are not responding normally. Echocardiography or placement of a Swan–Ganz catheter may guide treatment. Pulmonary edema should be treated with aggressive diuresis.

3. **Maintenance of good bronchial hygiene** is often the most difficult challenge facing the postthoracotomy patient. A lengthy smoking history, decreased ciliary function, chronic bronchitis, and significant postoperative pain all contribute to the ineffective clearance of pulmonary secretions. Adequate analgesia along with aggressive pulmonary toilet, incentive spirometry, and chest physiotherapy delivered by the respiratory therapist are essential. Occasionally, saline instillation with nasotracheal suctioning or bedside flexible bronchoscopy can be indicated to clear thick airway secretions.
4. **Cardiovascular complications** are more common than after abdominal cancer surgery because the population that develops lung cancer is at higher risk for heart disease. The three most common sources of cardiac morbidity are arrhythmias, myocardial infarctions, and congestive heart failure. Although a thorough preoperative cardiac evaluation and optimization is necessary, a negative preoperative cardiac evaluation does not exclude the risk of developing postoperative cardiac complications.
   a. **Cardiac arrhythmias** occur in up to 30% of patients undergoing pulmonary surgery. The most common arrhythmia is atrial fibrillation. The highest incidence occurs in elderly patients undergoing pneumonectomy or intrapericardial pulmonary artery ligation.
   b. **Treatment** of any rhythm disturbance begins with an assessment of the patient’s hemodynamic status. Manifestations of these arrhythmias vary in acuity from palpitations to hemodynamic collapse. If the patient is hemodynamically unstable, the advanced cardiac life support protocol should be followed. After the patient has been examined and hemodynamic stability confirmed, an ECG, ABG sample, and serum electrolyte panel should be obtained. Frequently, rate control agents such as β-blockers or calcium channel blockers, supplementary oxygen, and aggressive potassium and magnesium replenishment are the only treatments

necessary. Occasionally, chemical cardioversion with antiarrhythmic agents such as amiodarone may be necessary if atrial fibrillation persists despite rate control agent in order to achieve normal sinus rhythm.

5. **Chest tube management** after lung resection surgery involves daily evaluation for air leak, drain output, and reviewing CXR. The purpose of the chest tube placement after lung resection is to allow drainage of air and fluid from the pleural space and ensure reexpansion of the remaining lung. Chest tubes are removed after air leak has resolved and fluid drain output has decreased to about <100 mL over 8 hours.

CHAPTER 35: LUNG AND MEDIASTINAL DISEASES

Multiple Choice Questions

1. **Which of the following patients can be initially managed by observation:**

   a. A 45-year-old pilot with a small pneumothorax on room air
   b. A 62-year-old teacher with a small pneumothorax on room air
   c. An 18-year-old college student with a recurrent small pneumothorax on room air
   d. A 31-year-old police officer with a small pneumothorax and shortness of breath on room air

2. **A patient with COPD has acute respiratory failure from pneumonia and is intubated in the ICU. The nurse calls you to inform that the patient's oxygen requirement has increased, in addition to his blood pressure slowly trending down, with his MAP going from 70 to 60 over the last hour. On physical examination, you notice significantly decreased breath sounds on the right. The next step is:**

   a. Obtain a CXR
   b. Needle decompression
   c. Percutaneous catheter placement
   d. Chest tube placement

3. **A 50-year-old female with hepatitis C cirrhosis has a recurrent right-sided pleural effusion that is being managed with drainage from a PleurX catheter. Her serum lab results are protein 6.8, LDH 100, amylase 20, WBC 9,000. Which of the following laboratory results would be expected in this effusion?**

   a. Pleural fluid protein is 2.0
   b. Pleural fluid LDH is 75
   c. Pleural amylase is 250
   d. Pleural WBC is 12,000

4. **A 35-year-old male presents with an incidentally found**

mediastinal mass on CXR. Further workup with a CT scan demonstrates an anterior mediastinal mass. AFP and β-HCG are both elevated. Treatment of this mass is:

a. Observation as he is asymptomatic
b. Radiation and chemotherapy without surgery
c. Surgical resection
d. Chemotherapy followed by surgery

5. **A 70-year-old patient presents to the ER after a motor vehicle collision. In the ER, he undergoes a chest CT that demonstrates an incidentally found 3-cm peripheral mass in the RUL. What is the next step in management?**

a. Observation with repeat CT in 6 to 12 months
b. PET scan
c. Navigational bronchoscopy
d. Wedge resection

6. **A 65-year-old patient had a chronic cough with a 40 pack-year smoking history. CXR demonstrated an RLL mass with staging by PET/CT concerning for a T1, N2, M0 lesion. A percutaneous biopsy indicates that the patient has lung adenocarcinoma. What is the appropriate management?**

a. Mediastinoscopy or EBUS
b. Surgical resection alone
c. Surgical resection followed by chemotherapy
d. Neoadjuvant chemotherapy

36 Cardiac Surgery

Timothy S. Lancaster and Spencer J. Melby

INTRODUCTION

This chapter focuses on the preoperative evaluation, surgical indications, procedures, and postoperative management of adult cardiac surgery patients. Surgical management of coronary artery disease, valvular heart disease, atrial fibrillation (AF), and heart failure are discussed. Aortic pathology, including aneurysm and dissection, are referenced in Chapter 38.

ANATOMY

In normal cardiac anatomy, oxygenated pulmonary venous blood drains to the left atrium, flows through the (bicuspid) **mitral valve** to the left ventricle, and is then pumped through the **aortic valve** and into the systemic circulation. Deoxygenated systemic venous blood returns through the superior and inferior vena cavae to the right atrium, flows through the **tricuspid valve** to the right ventricle, and is pumped through the **pulmonic valve** to the pulmonary circulation. The coronary arteries arise from the **sinuses of Valsalva** just above the left and right coronary cusps of the aortic valve. The **left main coronary artery** gives rise to two main branches, the **left anterior descending artery (LAD)** and the **left circumflex artery (LCx)**. The **right coronary artery (RCA)** descends in the atrioventricular (AV) groove and terminates as the **posterior descending artery (PDA)** in **right dominant coronary circulation** (80% to 85% of cases). The PDA arises from the LCx in a **left dominant coronary circulation** (10% to 15%) (Fig. 36-1).

Clinical correlation: Dominance is important in selecting targets during coronary artery bypass grafting (CABG) and in predicting location of culprit vessels in post-myocardial infarction (MI) ventricular septal defect (VSD).

Clinical correlation: Because of its anterior location, intracardiac air preferentially enters the orifice of the RCA when weaning from cardiopulmonary bypass (CPB), resulting in right ventricular dysfunction.

Electrical activation of the heart begins in the **sinoatrial (SA) node** (located at the junction of the anteromedial aspect of the superior vena cava and the right atrium) and travels to the **AV node**. The AV node is located in the triangle of Koch (defined by the coronary sinus, tendon of Todaro, and the septal leaflet of the tricuspid valve; Fig. 36-2) and protects the ventricle from atrial tachyarrhythmias. From the AV node, conduction travels to the right and left **bundles of His.**

PREOPERATIVE EVALUATION

Many complications encountered during cardiac surgery may be avoided by careful preoperative assessment and planning. This assessment is also extremely important in communicating operative risk and possible alternatives to the patient. Several preoperative assessment tools are available to provide an objective evaluation of operative risk. These tools include the Society of Thoracic Surgeons (STS) Risk Score and the *Euro*SCORE (STS score at http://riskcalc.sts.org; *Euro*SCORE at http://www.euroscore.org).

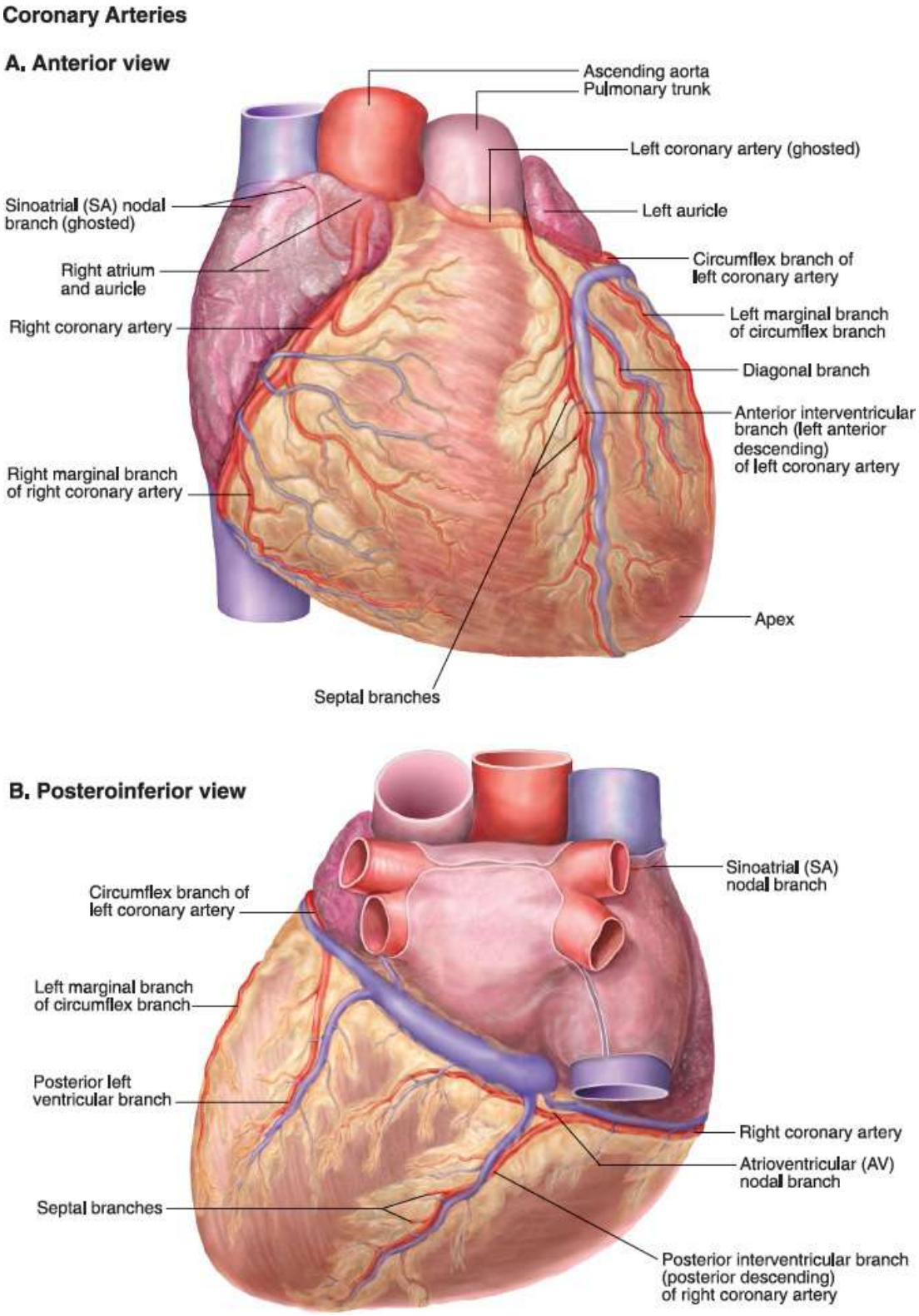

FIGURE 36-1 Coronary artery anatomy. (Reprinted with permission from Tank PW, Gest TR. Phiadelphia, PA: *Lippincott Williams & Wilkins Atlas of Anatomy*. 1st ed. 2008.)

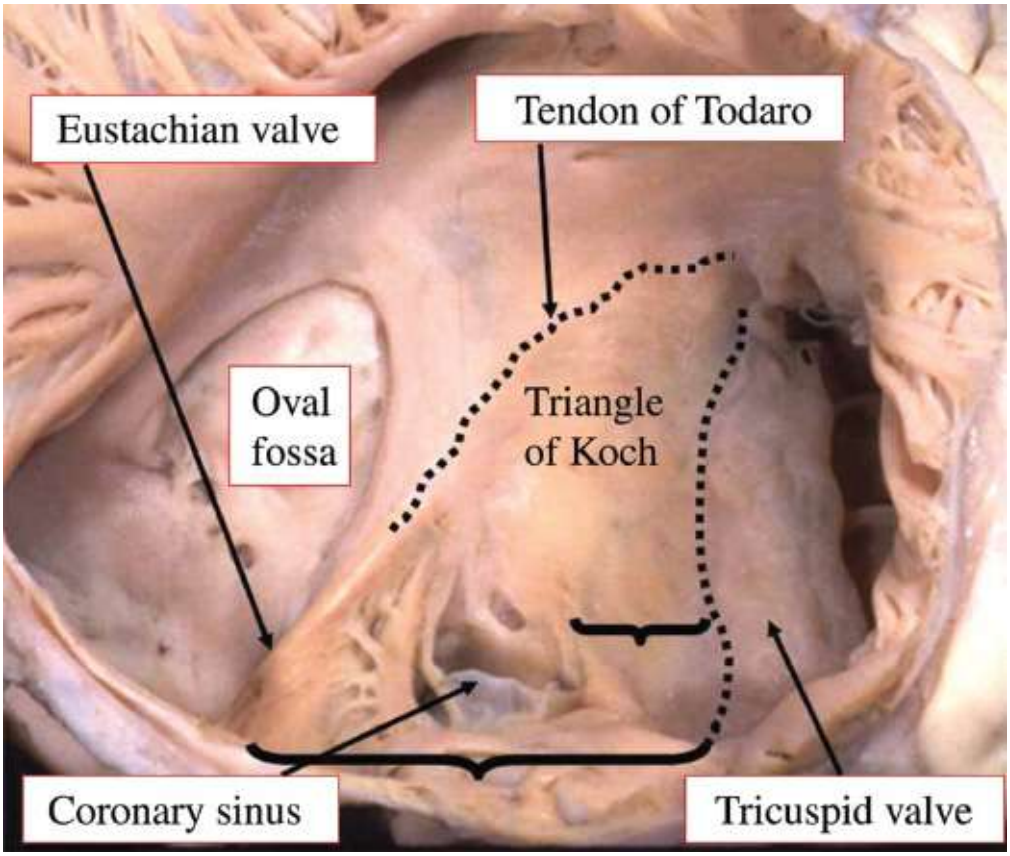

FIGURE 36-2 Triangle of Koch viewed from the inside of the right atrium. Patient head at top and feet at bottom of page. (Reprinted with permission from Anderson RH, Cook AC. The structure and components of the atrial chambers. *Europace*. 2007;9(Suppl 6):vi3–vi9.)

History and Physical Examination

Table 36-1 highlights key historical and physical findings that may prompt additional evaluation and alert one to the possibility of future complications.

Chest Radiography

A careful review of the *chest x-ray* will alert the surgeon to aortic calcification (Fig. 36-3), significant lung disease, and mediastinal pathology. A *computerized tomography scan* of the chest and abdomen may provide further information regarding calcification of the aorta (Fig. 36-4), the extent of adhesions between the heart and the sternum prior to redo surgery, lung pathology, and unexpected findings in other organs. Significant aortic calcification increases the risk of embolization and stroke, and indicates a potential need for alternate cannulation sites or even inoperability. Select patients, such as those undergoing a redo sternotomy, benefit from this study so that the surgeon may avoid injury upon reentry and while performing dissection of the heart and great vessels.

Cardiac Catheterization

Nearly all adult patients evaluated for cardiac surgery undergo *cardiac catheterization* to determine the presence of coronary artery disease and to delineate coronary anatomy for bypass planning. Prior to contrast injection, calcified valve annuli and coronary arteries may be visualized. Significantly stenotic coronary arteries must be of sufficient size and have a patent, anatomically accessible target in order to accept a bypass graft. Intramyocardial vessels may be anticipated by viewing the injection through the cine cycle. The left ventricular injection is particularly valuable as it provides an estimation of wall motion and ejection fraction (EF) as well as the size of the ascending aorta and a visual estimation of mitral valve competence.

TABLE 36-1 Preoperative Risk Assessment

History	Potential Complication and Evaluation
DM Immunosuppression Abnormal BMI	Increased risk of infection and poor wound healing
Poorly controlled DM Increased age Gender (female)	Increased mortality
Hypertension	Increased risk of CVA
Recent cath	Increased risk of renal failure
Home oxygen use Lung disease Tobacco use Previous tracheostomy	Increased risk of prolonged ventilation; consider PFTs
Liver disease Recent antiplatelet agent use (Plavix, IIb–IIIa inhibitors, thrombin inhibitors)	Increased risk of bleeding, consider hematology or hepatology consults

Thrombocytopenia	
Previous sternotomy Chest wall XRT Pericarditis	Anticipate difficult dissection
Poor social support Neurologic dysfunction	Difficult rehabilitation
Exercise tolerance	Good indicator of outcome
Pulsatile abdominal mass	Abdominal ultrasound
Carotid bruit History of carotid endarterectomy TIA symptoms History of stroke	Carotid Doppler
Poor dental hygiene	Panorex prior to valve procedure

BMI, body mass index; DM, diabetes mellitus; XRT, radiation therapy; CVA, cerebrovascular accident; PFT, pulmonary function test; TIA, transient ischemic attack.

Adapted from Lawton JS, Gay WA. On-pump coronary artery bypass grafting. In: Little AG, Merrill WH, eds. *Complications in Cardiothoracic Surgery: Avoidance and Treatment*. Oxford, UK: Blackwell Publishing; 2010:334–335.

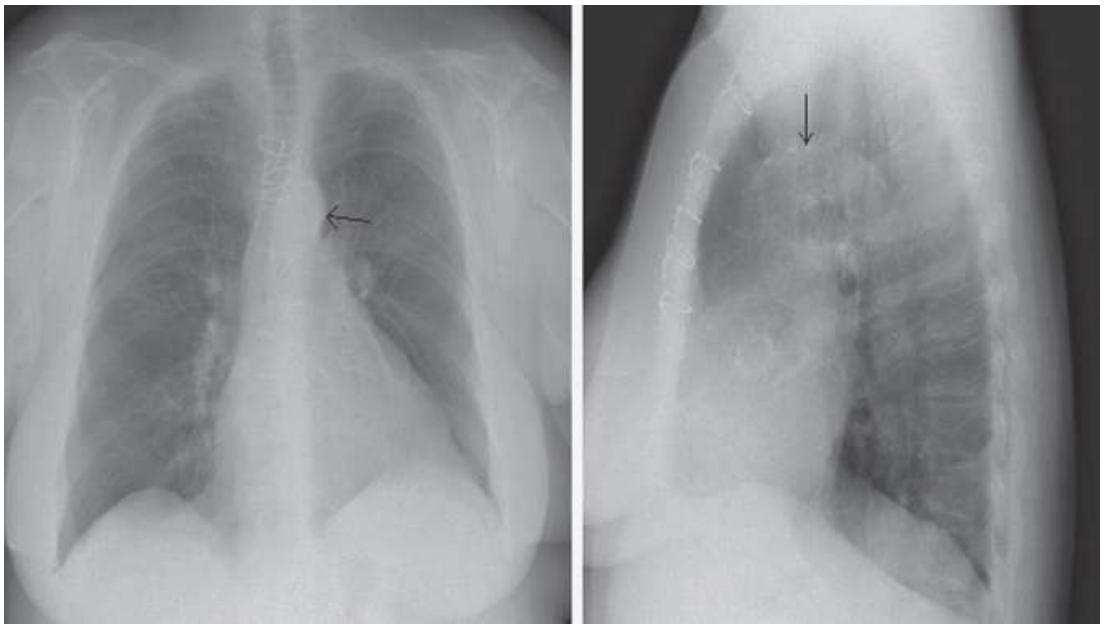

FIGURE 36-3 AP (**left**) and lateral (**right**) chest x-ray demonstrating a calcified aorta (*black arrows*).

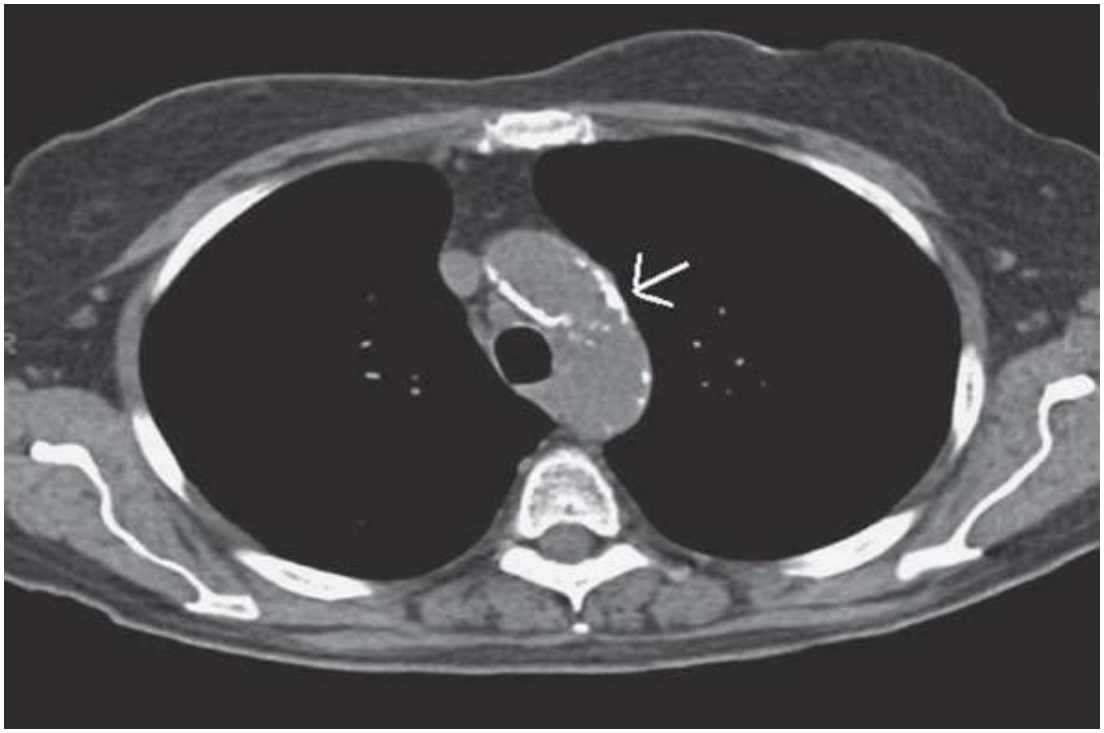

FIGURE 36-4 CT scan demonstrating a calcified aorta (*white arrow*).

Transthoracic or Transesophageal Echocardiogram

Transthoracic or *transesophageal echocardiogram* (TTE, TEE) provides assessment of ventricular function and valvular pathology. Because of the posterior position of the mitral valve, the superior imaging obtained by TEE is especially important in the planning of mitral valve surgery.

Viability Study

If a significantly reduced EF is noted, then an assessment of *myocardial viability* should be considered. Several types of viability studies are available, including dobutamine stress echocardiography, single-photon emission computed tomography (SPECT), positron emission tomography (PET), and magnetic resonance imaging (MRI) techniques. Territories of nonviable or infarcted myocardium indicate low utility of revascularization and should alert the surgeon to heavily weigh the risk of surgery.

Conduit Selection for Coronary Artery Bypass Grafting

Common conduits used for CABG include single or bilateral internal mammary arteries, radial artery, and saphenous vein. In appropriately selected patients, preference for more arterial grafting has been supported by greater long-term patency rates and improved long-term survival as compared to saphenous vein grafts. Use of the **left internal mammary artery (LIMA)** provides patency of 94% at 10 years and prolongs patient survival (*J Thorac Cardiovasc Surg.* 1999;117:855), and its use is considered a quality metric in Medicare and STS outcomes reports. Additionally, **the use of bilateral internal mammary arteries prolonged survival compared with one internal mammary artery in select patients** (*Ann Thorac Surg.* 2004;78:2005). Patency of radial artery grafts is approximately 80% at 10 years while that of saphenous vein grafts is approximately 50% to 60% (*Ann Thor Surg.* 2004;77:93; *J Thorac Cardiovasc Surg.* 2010;140:73). **The use of a radial artery has also been documented to prolong survival in propensity matched studies** (*Circulation.* 2003;108:1350–1354).

In real-world practice, conduit selection may be influenced by several factors, including patient age, comorbidities, and quantity and quality of vein available. The use of one or two internal mammary arteries may be influenced by patient obesity, presence of diabetes mellitus, subclavian artery stenosis, prior chest wall radiation, and emergency surgery. Use of the radial artery may be influenced by the degree of coronary artery stenosis, Allen testing, anticipated patient life span, severe diabetes or peripheral vascular disease, emergency surgery, and patient preference. Preoperative *venous mapping* may be obtained to determine the presence and size of bilateral greater and lesser saphenous veins.

CARDIOPULMONARY BYPASS

Extracorporeal circulation, in the form of CPB, allows for the performance of cardiothoracic surgery in a quiet, bloodless field. Although technologic advances have made the routine use of CPB safer and readily available, its use carries some detrimental consequences including the need for systemic anticoagulation, blood exposure to nonendothelialized surfaces and provocation of a systemic inflammatory response, nonpulsatile flow that can precipitate renal hypoperfusion, risk of air and particulate embolism to cerebral and systemic circulations, and the potential for pump malfunction. It may be difficult to ascertain what portion of observed complications are attributed to CPB alone; however, it is clear that prolonged CPB time (e.g., >3 hours) is a significant risk

factor for all postoperative complications.

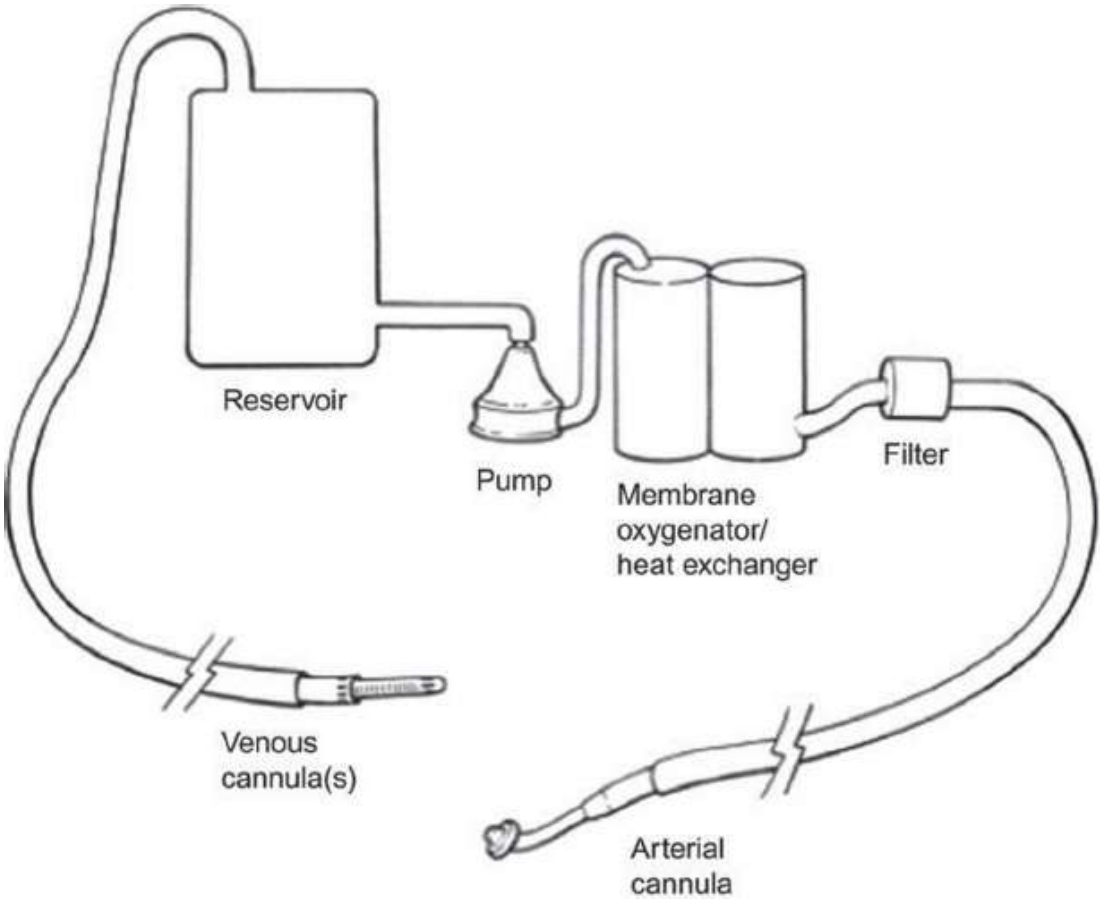

FIGURE 36-5 Cardiopulmonary bypass circuit. (Reprinted with permission from Punjabi PP, Taylor KM. The science and practice of cardiopulmonary bypass: From cross circulation to ECMO and SIRS. *Glob Cardiol Sci Pract*. 2013;2013(3):249–260.)

The CPB circuit consists of a venous cannula, a venous line (tubing), a reservoir, a heat exchanger, a membrane oxygenator, an air vent, an arterial line (tubing), and the arterial cannula. The **venous reservoir** stores the blood volume that drains by gravity and allows for the escape of air via the reservoir. All pump suction devices also drain to this reservoir. A **membrane oxygenator** performs gas exchange. A **heat exchanger** regulates the blood temperature. The **arterial pump** serves to return the warmed, oxygenated blood back to the patient via the arterial cannula (Fig. 36-5).

CARDIAC SURGICAL PROCEDURES

I. CORONARY ARTERY BYPASS GRAFTING

A. Background. Coronary artery disease (CAD) is the leading cause of death in men and women in the United States and in most developed countries. Patients may present with angina pectoris, MI, or several other sequelae of CAD, as described here.

Angina pectoris, or chest pain, occurs when reversible myocardial ischemia is present without cellular necrosis. Angina may manifest as a pain or pressure that often radiates to the left shoulder and down the left arm or into the neck. An anginal equivalent may manifest as epigastric discomfort or shortness of breath. Angina occurs during times of increased myocardial oxygen demand (exercise) and typically resolves with rest or the administration of nitrates. Unstable angina refers to chest pain that occurs at rest or with increasing frequency, duration, or severity.

MI results when there is a lack of myocardial oxygen supply with irreversible muscle injury and cell death. Increases in cardiac-specific enzymes and ECG changes (ST-segment elevation, T-wave inversions, and new Q waves) are observed. Early and late sequelae of MI can include arrhythmias, congestive heart failure (CHF), VSD, papillary muscle rupture, left ventricular aneurysm, and ischemic cardiomyopathy.

Clinical correlation: Continued angina following MI warrants consideration for urgent or emergent revascularization. Medical optimization includes nitrates, intravenous heparin, and placement of an intra-aortic balloon pump (IABP).

Arrhythmias (potentially fatal ventricular arrhythmias, AF, atrial flutter, heart block, or junctional rhythm) are common during the first 24 hours after acute MI.

CHF may result when a large portion of the left ventricle is infarcted. The extent to which the patient's activity is limited can be graded according to the New York Heart Association (NYHA) classification: Class I, no symptoms; class II, symptoms with heavy exertion; class III, symptoms with mild exertion; class IV, symptoms at rest.

VSD occurs in approximately 2% of patients after MI (anterior wall in 60%, inferior wall in 40%). An acute VSD occurs in the anterior or posterior septum depending upon the location of the coronary artery occlusion and coronary artery dominance (right or left) between 5 days and 2 weeks or more after an acute MI.

Clinical correlation: The onset of a new postinfarction VSD is

noted when a new holosystolic murmur is found on physical examination with hemodynamic deterioration (differential diagnosis also includes papillary muscle rupture as noted below). Diagnosis is made by cardiac cath (oxygen step up in the right heart and left to right shunt noted on left ventriculogram) and by TEE. Treatment is IABP placement and emergent surgery.

Papillary muscle rupture with severe mitral regurgitation (MR) results when MI involves a papillary muscle and often the adjacent myocardial wall.

Clinical correlation: Acute papillary muscle rupture is noted when a new holosystolic murmur is found on physical examination with hemodynamic deterioration. Diagnosis is made by echocardiography and treatment includes IABP and emergent surgery.

Left ventricular aneurysm occurs late following MI. A well-defined fibrous scar that is dyskinetic develops in 5% to 10% of patients in the infarcted territory. Large dyskinetic left ventricular aneurysms reduce left ventricular EF, result in symptoms of CHF, serve as the substrate for ischemic reentrant ventricular arrhythmias, and create an area of stagnant blood that may lead to thrombus and peripheral emboli.

Clinical correlation: Left ventricular aneurysmectomy (Dor procedure) may be indicated in appropriate patients who may benefit from restoration of ventricular geometry.

Ischemic cardiomyopathy may develop after multiple MIs and is associated with signs and symptoms of heart failure. Treatment is optimal medical management, placement of an automatic implantable cardioverter defibrillator for prevention of sudden cardiac death in patients with significantly reduced EF, and consideration of other support (see section on heart failure).

B. Indications for CABG. Myocardial revascularization may be accomplished via percutaneous coronary intervention (PCI) or CABG. Goals are to relieve angina, prevent repeat revascularization and MI, and to prolong survival. The American Heart Association (AHA) and American College of Cardiology (ACC) have established *guidelines for CABG and PCI* (*Circulation.* 2011;124:e652). Current guidelines recommend that CABG be performed to improve survival in patients with significant (≥50% stenosis) left main coronary artery stenosis, in patients with significant (>70%) stenosis in three major coronary

arteries or in the proximal LAD plus one other major artery, in patients with significant stenosis in two major coronary arteries with severe or extensive myocardial ischemia or target vessels supplying a large area of viable myocardium, in patients with LV dysfunction (EF 35% to 50%) and significant stenosis when viable myocardium in the area of intended revascularization, in patients with significant stenosis in the proximal LAD and evidence of extensive ischemia, in patients with complex three-vessel CAD with or without involvement of the LAD who are good candidates for surgery, and in patients with multivessel CAD with diabetes mellitus.

C. CABG Versus Medical Therapy. CABG offers symptom relief, reduced risk of MI, survival advantage, and improvement in functional status over medical therapy in patients with LMCA disease, multivessel disease, and those with left ventricular dysfunction (*Circulation.* 1979;60:888; *Lancet.* 1982;2:1173; *Circulation.* 1983;68:939; *N Engl J Med.* 1984;311:1333; *N Engl J Med.* 1988;319:332; *Circulation.* 1990;82:1629; *J Am Coll Cardiol.* 2004;43:1743).

D. CABG Versus PCI. The SYNTAX trial, the largest, prospective randomized controlled trial, compared CABG to PCI (with drug-eluting stents) in patients with untreated left main or three-vessel CAD. At 1 year, PCI was associated with higher rates of major adverse cardiac or cerebrovascular events (MACCE) (17.8% PCI vs. 12.4% CABG, $p = 0.002$) and higher rates of repeat revascularization (13.5% PCI vs. 5.9% CABG, $p < 0.001$), but CABG was associated with higher rates of stroke. By 3 years, there were no statistically significant differences in stroke rates between groups (2.9% CABG vs. 2.6% PCI, $p = 0.64$). The 5-year results demonstrated persistent divergence in all event rates except stroke in patients with three-vessel CAD (MACCE 37.5% PCI vs. 24.2% CABG, $p < 001$; all-cause death 14.6% PCI vs. 9.2% CABG, $p = 0.006$; MI 10.6% PCI vs. 3.3% CABG, $p < 0.001$; repeat revascularization 25.4% PCI vs. 12.6% CABG, $p < 0.001$; and stroke 3.0% PCI vs. 3.4% CABG, $p = 0.66$) (*Eur Heart J.* 2014;35:2821).

E. Minimally Invasive CABG. Minimally invasive approaches for CABG surgery include off-pump (OPCAB), robotic, or endoscopic CABG, hybrid CABG (includes CABG to LAD and DES placed to other vessels), and CABG through only a left anterior thoracotomy for bypass of the LAD. Despite its theoretical promise to minimize the deleterious

effects of CPB, off-pump CABG has fallen out of widespread practice after data showing fewer grafts performed, diminished long-term graft patency, increased coronary reintervention rates, and increased long-term mortality (*Innovations.* 2015;10:219). OPCAB may still be applicable in very select patients with prohibitive risk for CPB or with porcelain aorta in whom a "no-touch" aortic technique is planned.

II. VALVULAR HEART DISEASE. An excellent summary of valve pathology and indications for surgery in adult patients is provided in the 2014 aha/acc guidelines for the management of patients with valvular heart disease (*j thorac cardiovasc surg*. 2014;64:1763).

A. Aortic Valve Disease

1. **Aortic stenosis (AS)** may result from senile degeneration and calcification of a normal valve, a congenitally bicuspid aortic valve, or an abnormal valve (rheumatic disease). The degree of valvular stenosis is graded using echocardiography from mild to severe. AS places a pressure overload on the left ventricle, resulting in left ventricular hypertrophy. Symptoms include chest pain or angina, shortness of breath or CHF, and syncope.

   Clinical correlation: Physical examination findings include a loud systolic murmur across the precordium and a murmur audible in the carotid arteries.

   Aortic valve replacement (AVR) provides relief of symptoms as well as a survival benefit in patients with symptomatic severe (AVA <1 cm^2) AS compared to medical management alone (*Circulation.* 1982;66:1105). AVR is also indicated in asymptomatic patients with severe AS undergoing CABG or other cardiac surgery and in patients with severe AS and left ventricular systolic dysfunction (EF <50%).

   Clinical correlation: Patients who undergo surgical AVR often have significant left ventricular hypertrophy. Because of this, treatment of hypotension should first include volume resuscitation rather than vasoconstrictor agents.

2. **Aortic insufficiency (AI)** is often the result of valve leaflet pathology resulting in thickening, calcification and fixation (rheumatic heart disease or combined with AS), leaflet redundancy or destruction (myxomatous degeneration), poor coaptation (aortic root dilatation, aortic dissection), inflammatory disease (ankylosing spondylitis),

trauma (blunt chest injury, balloon dilatation, or transaortic valve implantation), or destruction (endocarditis). Chronic AI results in volume overload of the left ventricle, causing chamber enlargement and wall thickening and pulmonary congestion. Severity of insufficiency is graded from mild to severe by echocardiography. Acute AI is not well tolerated and often results in fulminant pulmonary edema, myocardial ischemia, and cardiovascular collapse.

Clinical correlation: IABP is contraindicated with severe AI as the balloon inflates during diastole, resulting in increased AI.

Indications for surgery in symptomatic patients include severe AI, chronic moderate to severe AI and left ventricular dysfunction (EF < 50%), and patients with chronic severe AI who are undergoing other cardiac surgery. Surgery is reasonable in patients without symptoms and normal left ventricular function but who have severe left ventricular dilatation (left ventricular end-systolic dimension >50 mm or indexed left ventricular end-systolic dimension >25 mm/m^2).

Surgical treatment of aortic valve disease may include open valve repair or replacement or alternative access approaches depending upon the pathology, leaflet quality, and patient comorbidities. One alternative access approach is **transcatheter aortic valve replacement (TAVR)**, which is the replacement of the aortic valve through a transfemoral, transaortic, subclavian, transapical, or other approach. TAVR is now in widespread clinical use throughout the United States for patients with elevated risk for standard surgical AVR (STS mortality risk >3%), and clinical trials are underway for patients with low surgical risk. The long-term durability, infectious risk, and potential complications of TAVR valves remain to be seen, especially in the younger and lower-risk group of patients.

B. Mitral Valve Disease

1. **Mitral stenosis (MS)** is caused by valve leaflet thickening and calcification due to rheumatic fever or senile calcification, collagen vascular diseases, amyloidosis, congenital stenosis, or mitral inflow obstruction (tumors or masses). MS places a pressure overload on the left atrium, with relative sparing of ventricular function. Left atrial dilation to more than 45 mm is associated with a high incidence of AF and subsequent thromboembolism. Critical MS occurs when the valve area is 1.5 cm^2 or less.

Clinical correlation: Physical examination findings include an apical diastolic murmur and a loud S1.

Symptoms usually develop late and reflect pulmonary congestion (dyspnea), reduced left ventricular preload (low cardiac output syndrome), or AF (thromboembolism). Surgery is indicated in patients with severe MS and severe symptoms, patients with moderate MS undergoing cardiac surgery for other indications, or in patients who have had recurrent embolic events while receiving adequate anticoagulation and excision of the left atrial appendage may be considered. Percutaneous mitral balloon valvuloplasty is indicated in symptomatic patients with severe mitral rheumatic stenosis who have favorable valve morphology in the absence of contraindications.

2. **MR** may be categorized as primary (degenerative) or chronic secondary (functional). Primary causes include those that involve the leaflets (mitral valve prolapse, fibroelastic deficiency, connective tissue disorders, rheumatic heart disease, cleft mitral valve, radiation injury, trauma following mitral valvuloplasty, or endocarditis), the chordae tendineae (rupture [endocarditis or MI], fusion, or elongation), or the papillary muscles (ischemic papillary muscle dysfunction or rupture secondary to MI). Chronic secondary MR is due to either chronic ischemic cardiomyopathy or idiopathic myocardial disease causing secondary dilation of the annulus itself.

   Clinical correlation: Physical examination findings include loud systolic murmur loudest at the apex.

   MR places a volume overload on the left ventricle and atrium, causing chamber enlargement and wall thickening and pulmonary congestion. AF often develops due to left atrial dilation. Acute severe MR results in pulmonary congestion and low cardiac output.

   Clinical correlation: In acute, severe MR, IABP is beneficial as it decreases afterload, thereby increasing forward flow and decreasing regurgitant volume.

   Mitral valve repair or replacement is recommended for symptomatic patients with chronic severe MR and left ventricular EF greater than 30%, and is recommended in asymptomatic patients with chronic severe primary MR and left ventricular dysfunction (EF 30% to 60%). Specific indications and recommendations for repair of the mitral valve continue to evolve. Mitral surgery in patients with

chronic ischemic MR is challenging and is associated with increased operative risk. In a recent randomized trial, mitral valve replacement provided more durable freedom from MR compared to mitral repair in patients with severe ischemic MR (*N Engl J Med.* 2014;370:1).

C. Tricuspid Valve Disease

1. **Tricuspid stenosis (TS)** is most commonly secondary to rheumatic disease. TS may be associated with regurgitation and may not be detectable on bedside examination. Tricuspid valve surgery is recommended in patients with severe TS at the time of operation for left-sided valve disease and in isolated symptomatic severe TS. Tricuspid balloon commissurotomy might be considered in patients with isolated severe TS without TR.
2. **Tricuspid regurgitation (TR)** most often results from a secondary (functional) dilation of the valve annulus caused by pulmonary hypertension, caused by intrinsic mitral or aortic valve disease. Causes of primary TR include rheumatic heart disease, bacterial endocarditis (often in IV drug users), carcinoid tumors, Ebstein anomaly, and blunt trauma. Mild-to-moderate TR usually is well tolerated. Tricuspid repair is indicated in the case of moderate to severe TR at the time of surgery for other cardiac anomalies. The majority of tricuspid valves can be repaired with annuloplasty techniques rather than replacement.

   Clinical correlation: TR may be associated with a systolic murmur, a prominent jugular venous pulse, and a pulsatile liver.

   Clinical correlation: The AV node is of particular importance during tricuspid valve surgery because it may be injured resulting in heart block. Tricuspid valve repair techniques involve incomplete rings to avoid injury to the conduction system and sutures in the annulus at the time of valve replacement are preferentially placed in the leaflet tissue only (Fig. 36-2).

D. Pulmonic Valve Disease

1. **Pulmonic insufficiency (PI)** that is mild to moderate does not require intervention if asymptomatic and if associated with normal right ventricular function and size. PI in adults more commonly requires treatment in patients following childhood repair of tetralogy of Fallot. The pulmonic valve may be affected by endocarditis, tumors (carcinoid, papillary fibroelastoma), or radiation injury.

2. Pulmonic stenosis (PS) is mostly seen as a congenital disorder and is rarely seen in adults.

E. Infective Endocarditis. Endocarditis may involve infection or native valves or prosthetic valves and originates with an episode of bacteremia (sources can include dental infections or procedures, intravenous drug abuse [IVDA], nosocomial infection, indwelling intravenous catheters or dialysis). Surgical treatment is associated with increased survival compared to antibiotic therapy alone and should be aggressive in order to eradicate all infected tissues (*Heart.* 2001;89:269; *Heart.* 2001;88:61). The risk of embolization is reduced significantly following the initiation of appropriate antibiotics. Indications for surgery due to endocarditis include hemodynamic instability, CHF, embolism, large foci of disease (>1 cm), aggressive bacterial organisms or fungal organisms, prosthetic valve endocarditis, aortic root abscess, and persistent evidence of infection despite appropriate antibiotic therapy (persistent fever, recurrent septic emboli, persistent positive blood cultures). The risk for reoperation for recurrent infective endocarditis is about 17% for IV drug users and 5% for non-IV drug users (*Ann Thorac Surg.* 2007;83:30).

Clinical correlation: Aortic root abscess is an indication for urgent surgery. Daily ECGs should be monitored for signs of heart block that may occur with destruction of the AV node between the right and noncoronary cusps of the aortic annulus.

F. Prosthetic Valve Selection. *Tissue bioprostheses* include porcine aortic valves or valves constructed with bovine pericardium. These prostheses are associated with a low rate of thromboembolism, even without long-term anticoagulation (daily aspirin is recommended). They are less durable than mechanical valves (mean time to failure is approximately 10 to 15 years), although this may potentially be prolonged in newer valves due to modern preservation methods. Bioprostheses are often the preferred valves for patients >65 years or patients with a contraindication to anticoagulation.

Mechanical valves have excellent long-term durability; however, the rate of thromboembolic complications (0.5% to 3% per year) is cumulative and these valves require lifelong anticoagulation.

Homograft and autograft valved conduits are useful in special circumstances, such as endocarditis or for the Ross procedure (*J Heart*

Valve Dis. 1994;3:377).

G. New Valve Technology. Following the introduction of TAVR, the treatment of valvular heart disease continues to rapidly evolve. Transcatheter therapies for the mitral valve are gaining wider use that allow for mitral valve repair via a transfemoral approach by clipping the two leaflets of the mitral valve (MitraClip, Abbott Laboratories, Abbott Park, IL) and for transcatheter mitral valve replacement (TMVR). The MitraClip procedure has been shown to give a survival advantage in patients with advanced heart failure on optimal medical management (*N Engl J Med.* 2018;379:2307). Additional advances in surgical aortic valve design include stent-mounted, sutureless valves designed for rapid surgical deployment, surgical valves on expandable annulus rings designed to accommodate future transcatheter valve-in-valve replacement, and mechanical valves with less thrombotic risk that have lower anticoagulation requirements. The trend toward minimally invasive procedures and the combination of transcatheter and surgical techniques have mandated a multidisciplinary approach to the treatment of valvular disease.

III. HYPERTROPHIC CARDIOMYOPATHY. Hypertrophic cardiomyopathy (HCM) is characterized by asymmetric hypertrophy and fibrosis of the myocardium, causing obstruction of the left ventricular outflow tract. Medical therapy with β-blockade or calcium channel blockade is the preferred first-line treatment. Nifedipine, nitroglycerin, angiotensin-converting enzyme inhibitors, and angiotensin II blockers are all generally contraindicated due to their vasodilatory properties, which can exacerbate the outflow tract obstruction. Surgical treatment of HCM is septal myectomy, with a postoperative mortality of 1% or less (*Ann Thorac Surg.* 2000;69:1732). By convention, surgery is recommended for symptomatic patients who have failed medical therapy or septal ablation with a documented at-rest outflow tract gradient of at least 30 mm Hg.

IV. ATRIAL FIBRILLATION. AF affects 1% to 2% of the general population and it affects nearly 10% of individuals >80 years of age. Morbidity includes patient discomfort, hemodynamic compromise, and thromboembolism. Indications for surgery include symptomatic AF in patients undergoing other cardiac procedures, selected asymptomatic AF

patients undergoing cardiac surgery in whom ablation can be performed with minimal risk, and symptomatic AF patients who prefer a surgical approach, have failed one or more attempts at catheter ablation, or are not candidates for catheter ablation (*Heart Rhythm.* 2007;4:816). The Cox-maze procedure is the gold standard for surgical AF ablation and its current iteration, the cox-maze IV, utilizes a combination of cryoablation and bipolar radiofrequency ablation. This procedure has provided postoperative freedom from AF of 93% at 1 year and 78% at 5 years, substantially higher than that achieved by catheter ablation (*J Thorac Cardiovasc Surg*. 2015;150:1168).

V. SURGICAL TREATMENT OF HEART FAILURE. Approximately 250,000 people suffer from advanced heart failure in the United States (*Curr Heart Fail Rep.* 2010;7:140). For patients failing maximal medical management, surgical care of advanced heart failure involves the use of mechanical circulatory support (MCS) devices either as destination therapy or as a bridge to heart transplant. Several types of MCS are available, and device selection depends on the acuity of need, planned amount and duration of support needed, and specific patient physiology.

A. Mechanical Circulatory Support. The *IABP* is the first-line mechanical device to provide circulatory support in *acute* heart failure. Indications include preoperative low cardiac output states, preoperative unstable angina refractory to medical therapy, difficulty weaning from CPB, and postoperative low cardiac output states. An IABP is a catheter-mounted balloon that is positioned in the descending thoracic aorta and functions by counterpulsation, inflating during diastole and rapidly deflating during systole. The physiologic effects of counterpulsation include augmentation of coronary perfusion (which occurs primarily during diastole) and afterload reduction, thereby providing an additional 500 mL/min of cardiac output. Potential complications include abdominal organ malperfusion, perforation of the aorta, femoral artery injury, and lower extremity ischemia.

Clinical correlation: Contraindications for IABP include AI, aortic dissection, and severe peripheral vascular disease.

Extracorporeal membrane oxygenation (ECMO) is similar to a simplified CPB circuit, although it does not include a venous reservoir and therefore cannot decompress the LV unless a specific LV vent is

used. ECMO can provide full support of the cardiac output up to about 7 L/min, and multiple configurations are possible to provide cardiac, pulmonary, or cardiopulmonary support. Indications include postoperative myocardial dysfunction (stunning), acute heart failure as bridge to recovery or bridge to a durable device, or respiratory failure of various etiologies.

Temporary ventricular assist devices are small, catheter-mounted mechanical support devices such as the Impella (Abiomed, Danvers, MA) and the TandemHeart (TandemLife, Pittsburgh, PA). They can be used for short-term support in acute heart failure, and provide from 1 to 5 L/min of flow. Placement is via the peripheral vasculature (femoral, axillary) and may be percutaneous for the smallest devices or via surgical cutdown.

Durable ventricular assist devices are mechanical heart pumps used for long-term left ventricular support either as destination therapy or as a bridge to heart transplant. In adults, these devices are approved only as left ventricular assist devices (LVADs), although patients may require temporary use of a nondurable right ventricular assist device (RVAD) during the postoperative period. Modern LVADs can provide up to 7 L/min of flow and require long-term anticoagulation. The newest generation of LVADs includes the HVAD (HeartWare, Framingham, MA) and the HeartMate 3 (Abbott, Abbott Park, IL).

B. Heart Transplant. *Cardiac transplantation* can be considered in patients with end-stage cardiomyopathy refractory to maximal medical therapy, and has an associated survival of 84.5% at 1 year and 72.5% at 5 years (*J Heart Lung Transplant.* 2014;33:996–1008). *Contraindications* to transplantation include age older than 65 years, irreversible pulmonary hypertension, active infection or malignancy, recent pulmonary embolus, and excessive comorbidity (renal dysfunction, hepatic dysfunction, systemic disease such as amyloidosis, significant peripheral vascular disease, active peptic ulcer disease, uncontrolled diabetes mellitus, morbid obesity, mental illness, active substance abuse, inadequate social support, or psychosocial instability) (*Mayo Clin Proc.* 2014;89:662).

Complications of heart transplant include acute and chronic rejection that may be diagnosed by endomyocardial biopsy or echocardiography. Coronary artery vasculopathy (CAV) is the manifestation of chronic

vascular rejection, and is the major long-term source of morbidity after cardiac transplantation, being responsible for 30% of deaths in after 5 years (*J Heart Lung Transplant.* 2007;26:769). CAV is usually not amenable to conventional revascularization owing to the diffuse small-vessel nature of disease, and may require retransplantation.

VI. POSTOPERATIVE MANAGEMENT AND COMPLICATIONS

A. Monitoring and Management. Early extubation following cardiac surgery is preferred if the patient is hemodynamically stable and bleeding is minor. Neurologic assessment is obtained as soon as possible. Normal hemodynamic values obtained from a Swan–Ganz catheter are listed in Table 36-2. A *cardiac index* of 2 L/min/m^2 is generally a minimum acceptable value. A *mixed-venous oxygen saturation* of less than 60% suggests inadequate peripheral tissue perfusion and increased peripheral oxygen extraction. Etiologies of low cardiac output must be aggressively corrected by manipulation of factors affecting cardiac output (heart rate, preload, afterload, and contractility). Myocardial stunning is common following heart surgery and requires additional support (pharmacologic and/or mechanical). Stunning is defined as a transient postischemic myocardial dysfunction that persists despite adequate reperfusion and in the absence of irreversible damage. One of the easiest methods to increase cardiac output is to increase the heart rate. This may be accomplished by using the temporary epicardial pacing electrodes (placed at the time of operation) at 80 to 100 beats/min. **Optimal pacing always involves maintaining AV synchrony.**

B. Complications of Cardiac Surgery. *Arrhythmias* are common following cardiac surgery. *Supraventricular arrhythmias* (AF, atrial flutter, atrial tachycardia) are most common, with postoperative AF occurring in 30% of patients at a peak incidence on postoperative day 2 (*J Thorac Cardiovasc Surg*. 2015;149:886). Supraventricular arrhythmias with hemodynamic compromise can be rapidly treated with electrical cardioversion. For patients with hemodynamic stability and atrial flutter, overdrive pacing may be used to terminate the arrhythmia. For AF and flutter, ventricular rate control may be facilitated with β-blockade and amiodarone. For AF or flutter that persists beyond 12 hours, anticoagulation should be considered to reduce stroke risk.

Sustained *ventricular arrhythmias* other than premature ventricular contractions suggest an underlying ischemic pathology and should be investigated.

TABLE 36-2 Normal Hemodynamic Parameters

Parameter	Normal Value	Unit
Central venous pressure	2–8	mm Hg
Right ventricular pressure (syst/diast)	15–30/2–8	mm Hg
Pulmonary artery pressure (syst/diast)	15–30/4–12	mm Hg
Pulmonary capillary wedge pressure	2–15	mm Hg
Left ventricular pressure (syst/diast)	100–140/3–12	mm Hg
Cardiac output	3.5–5.5	L/min
Cardiac index	2–4	L/min/m^2 BSA
Pulmonary vascular resistance	20–130	dynes sec/cm^5
Systemic vascular resistance	700–1,600	dynes sec/cm^5
Mixed-venous oxygen saturation	65–75	Percent

BSA, body surface area; diast, diastolic; syst, systolic.

Respiratory failure may occur following cardiac surgery. Prolonged postoperative mechanical ventilation beyond 24 hours after surgery is

associated with increased rates of pneumonia and other morbidity.

Postoperative bleeding is relatively common after cardiac surgery and necessitates reexploration in up to 5% of patients. A treatment algorithm for the management of postoperative bleeding is represented in Figure 36-6.

Low cardiac output state represents postoperative shock and has many potential causes, including myocardial stunning, myocardial ischemia, and cardiac tamponade. A treatment algorithm for the management of low cardiac output is represented in Figure 36-7.

Cardiac tamponade is a potentially lethal cause of low cardiac output with associated narrowed pulse pressure, increased jugular venous distention, rising CVP, muffled heart sounds, pulsus paradoxus, widened mediastinal silhouette on chest radiograph, and decreased urine output. Diagnosis is clinical and may be confirmed by echocardiography. Treatment is emergent drainage. *Delayed tamponade* occurs after the acute postoperative period and may be extremely difficult to diagnose. A high index of suspicion for this diagnosis must be maintained. A decline in renal or liver function, poor urine output, or an elevated coagulation profile may be the initial clue. An echocardiogram is helpful in making the diagnosis. This complication must also be treated with reexploration of the chest and evacuation of mediastinal fluid.

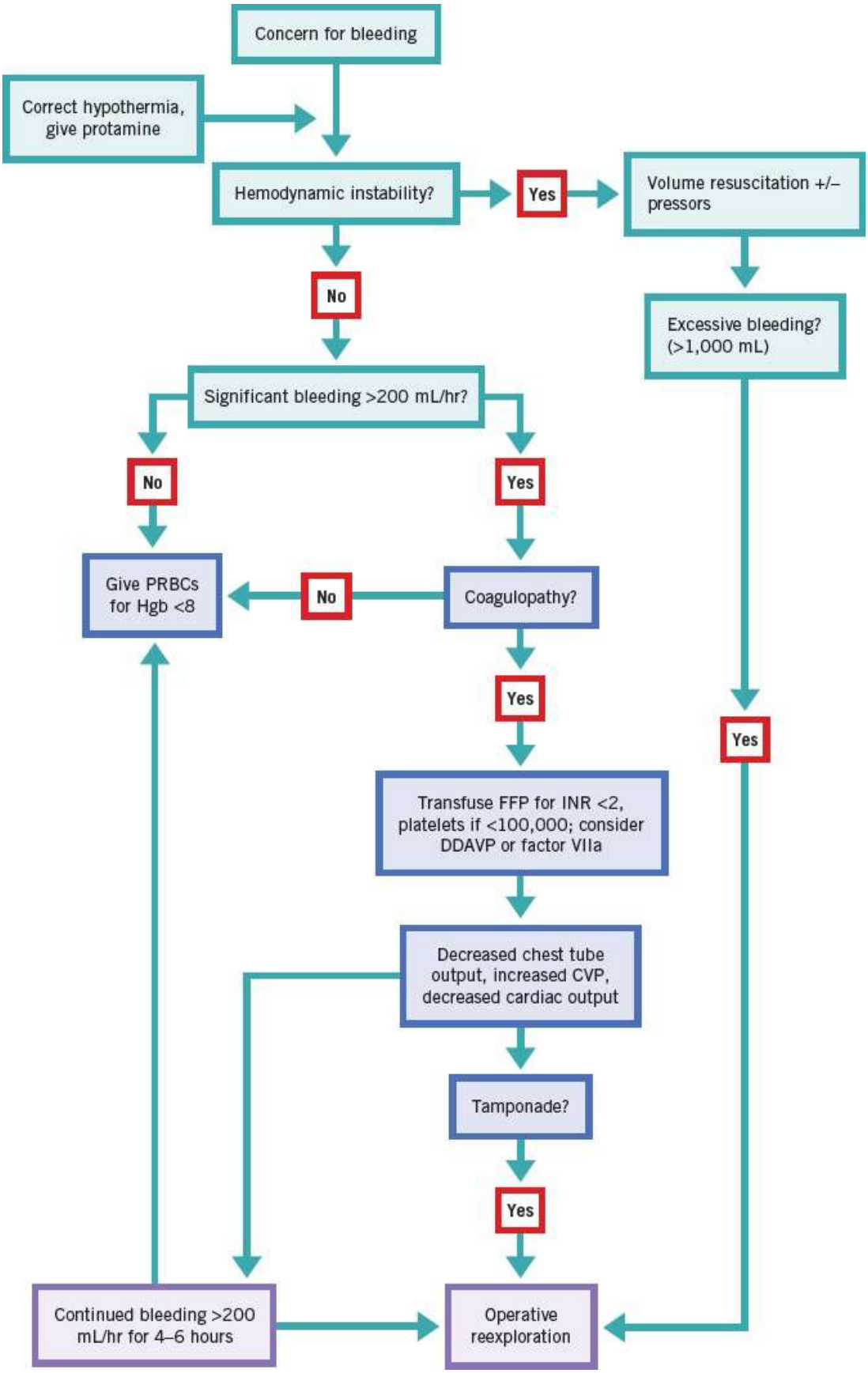
Concern for bleeding
Correct hypothermia, give protamine
Hemodynamic instability?
Yes
Volume resuscitation +/– pressors
Excessive bleeding? (>1,000 mL)
No
Significant bleeding >200 mL/hr?
No
Yes
Give PRBCs for Hgb <8
No
Coagulopathy?
Yes
Yes
Transfuse FFP for INR <2, platelets if <100,000; consider DDAVP or factor VIIa
Decreased chest tube output, increased CVP, decreased cardiac output
Tamponade?
Yes
Continued bleeding >200 mL/hr for 4–6 hours
Operative reexploration

FIGURE 36-6 Postoperative bleeding algorithm.

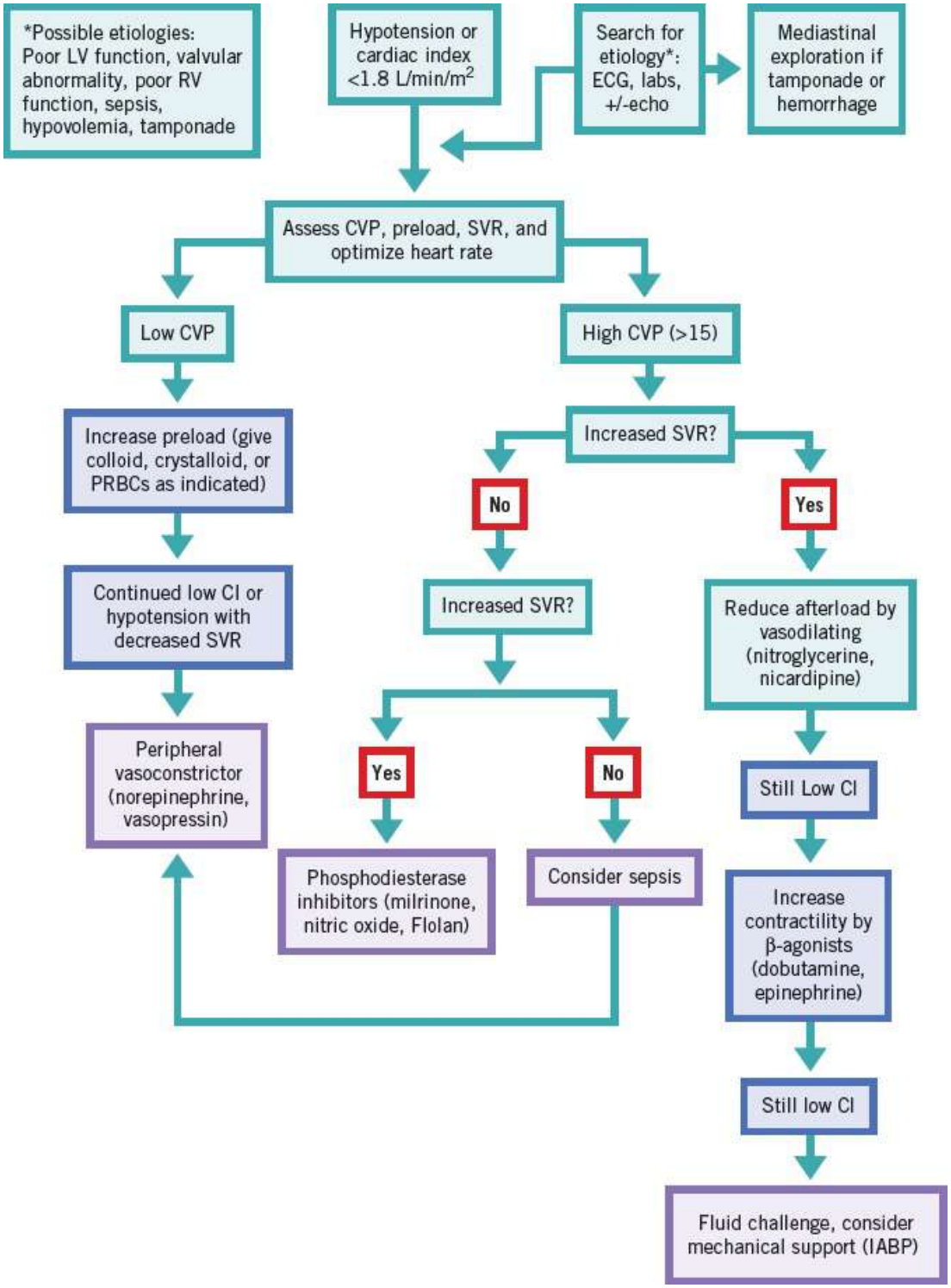

FIGURE 36-7 Postoperative evaluation and treatment of low cardiac output state. (Adapted from Cohn LH, Dody DB, McElvein RB. Decision making in cardiothoracic. *Surgery*. 1993;2:83.)

Perioperative MI occurs in approximately 1% to 2% of patients and can be diagnosed by chest pain, ventricular arrhythmias, ECG changes, elevated cardiac enzymes, or new changes on echocardiography. Newly constructed bypass grafts can be occluded due to thrombosis or spasm. Cardiac catheterization can delineate appropriate treatment, which may include return to the operating room or stenting for myocardial revascularization.

Renal dysfunction in the postoperative period significantly increases mortality. To limit renal injury, adequate cardiac index and mean arterial pressure must be maintained. Nephrotoxic agents should be avoided or limited, and any renally excreted medications should have dose adjustment.

Cerebrovascular accident (CVA) can be the most devastating of neurologic complications following cardiac surgery. Neurologic complications may be manifested by a wide range of signs and symptoms from delirium and confusion to permanent stroke and may be related to intraoperative (aortic atherosclerotic or air emboli) or perioperative events.

Postoperative infection may be clinically significant in the sternal wound, urinary tract, conduit harvest sites, or lungs. Perioperative intravenous antibiotics and aggressive blood sugar management are utilized to limit the occurrence of sternal wound infection. Deep sternal infections require operative debridement of devitalized sternal and soft tissue, administration of broad-spectrum IV antibiotics, and sometimes muscle flap closure of the soft tissue defects.

CHAPTER 36: CARDIAC SURGERY

Multiple Choice Questions

1. **A 75-year-old female underwent coronary bypass grafting with LIMA to the LAD and two vein grafts, and returns to the ICU in stable condition with normal ventricular function. Overnight, the patient's cardiac index falls to 1.5 L/min/m^2 and does not improve with volume resuscitation. ECG shows ST elevations in the anterior leads and bedside echocardiography shows hypokinesis of the anterior wall despite normal preoperative LVEF. The cardiac index improves to 1.9 with initiation of epinephrine. What is the best next step in management?**

   a. Transfuse blood
   b. Start norepinephrine infusion
   c. Return to the operating room for exploration
   d. Cardiac catheterization
   e. Check troponin level

2. **A 60-year-old male returns to the ICU after redo aortic valve replacement. Mediastinal chest tube output appears sanguineous and 200 mL per hour for the first 2 hours. In the third hour, chest tube output drops to 25 mL and the patient becomes hypotensive, develops JVD, muffled heart sounds, and cardiac index falls to 1.4 L/min/m^2. CVP is 22 mm Hg. What is the best next step in management?**

   a. Obtain echocardiogram
   b. Chest reexploration
   c. Transfuse platelets
   d. Place an intra-aortic balloon pump
   e. Transfuse FFP

3. **A 55-year-old male comes to the emergency room with severe chest pain and is diagnosed with an ST-elevation myocardial infarction. He becomes hypoxic and has to be intubated. He undergoes left heart catheterization and is found to have 95% left**

main and 99% RCA lesions, as well as an EF of 15% on ventriculogram. An intra-aortic balloon pump is placed and cardiac surgery is consulted for CABG. Which of the following is true about the intra-aortic balloon pump?

a. It inflates during systole.
b. It increases afterload.
c. It is positioned in the ascending aorta.
d. It inflates during diastole.
e. It reduces coronary blood flow.

4. **A 65-year-old female undergoes uncomplicated mitral valve repair for severe mitral regurgitation. On postoperative day 2, she develops new-onset atrial fibrillation with rapid ventricular response. Soon after onset of the atrial fibrillation, her heart rate is 165 and blood pressure falls to 72/40. She reports lightheadedness, palpitations, and shortness of breath. What is the best management?**

a. Anticoagulate with heparin infusion.
b. Perform electrical cardioversion.
c. Administer 1 L of saline.
d. Initiate amiodarone infusion.
e. Initiate epinephrine infusion.

5. **A 72-year-old male with exertional angina and three-vessel coronary artery disease is referred for CABG evaluation. He is nondiabetic, has normal weight, has normal Allen test bilaterally, no history of varicose veins or lower extremity vein procedures, and equal arm blood pressures. No aortic calcification is seen on chest x-ray or the catheterization films. Which conduit should always be used for bypass grafting unless a specific contraindication exists?**

a. Left internal mammary artery.
b. Right internal mammary artery.
c. Radial artery.
d. Greater saphenous vein.
e. a and b.

37 Cerebrovascular Disease

Thomas J. Desmarais and Jeffrey Jim

INTRODUCTION

Atherosclerotic occlusive disease of the extracranial carotid artery is a major risk factor for stroke, the primary cause of disability, and the fifth most common cause of death in the United States. **Nearly 800,000 new strokes occur annually**, with an estimated total cost of more than $40 billion. The initial mortality from stroke is approximately 30%. Among those who survive the initial stroke event, 60% suffer long-term disability, and 40% recover with mild or no deficits.

I. PRESENTATION. **Presentation** of patients with symptomatic occlusive disease is a **neurologic deficit**. However, many patients have an asymptomatic carotid artery stenosis that is identified by a health care provider based on auscultation of a carotid bruit or screening duplex ultrasound (US). **Lateralizing ischemic events** can result in aphasia (expressive or receptive), combined sensory and motor deficits, and various visual disturbances. Deficits such as these are usually associated with the anterior cerebral circulation (i.e., **the internal carotid artery** [ICA] and its branches).

A. Transient ischemic attacks (TIAs) are defined as neurologic deficits that may last from several seconds to hours, but no longer than 24 hours. TIAs that occur in rapid succession, interspersed with complete recovery, but with progressively shorter intervals between attacks, are termed **crescendo TIAs**, and carry a high risk of progression to a permanent neurologic deficit.

B. Stroke. If the neurologic deficit persists beyond 24 hours, it is considered a **stroke**. In addition, some patients may present with a

neurologic deficit that fluctuates, gradually worsening over a period of hours or days. This is termed a **stroke in evolution**. Unlike crescendo TIAs, symptoms of stroke in evolution do not return to baseline.

C. Amaurosis fugax (temporary monocular blindness), often described as a "shade coming down over one eye," results from **atheroemboli lodging in the ophthalmic artery**. Funduscopic examination may reveal **Hollenhorst plaques**.

D. Global ischemic events are manifested by symptoms such as vertigo, dizziness, perioral numbness, ataxia, or drop attacks. These are **rarely associated with carotid disease** unless there is severe bilateral stenosis. Instead, they are associated with an interruption of the posterior circulation supplying the brain stem (i.e., the vertebrobasilar system) or global hypoperfusion (e.g., cardiac arrhythmia).

II. PATHOPHYSIOLOGY. Atherosclerotic disease of the carotid artery can cause stroke or TIA by three mechanisms: (1) **atheroembolization** of debris originating from the carotid artery plaque and traveling to the brain, (2) **acute thrombotic occlusion of a severe stenosis**, (3) **global cerebral hypoperfusion (rare).** The most common site of atherosclerotic plaque formation is at the carotid bulb, which can be attributed to dynamic flow changes and wall stress. A **"vulnerable" plaque** refers to an unstable plaque that is prone to embolization, thrombosis, and subsequent stroke. **Carotid duplex US features predictive of a vulnerable plaque include hypoechoic and heterogeneous plaques and increased plaque area.** These plaque morphologic features may confer an increased risk of stroke.

III. DIAGNOSTIC EVALUATION. Diagnostic evaluation of a patient suspect of having carotid artery disease. A careful history and physical examination is performed before obtaining any diagnostic studies.

A. History. The patient or patient advocate is asked to describe the presence of, acuity, and duration of symptoms. Risk factors for TIA and stroke should be sought, including age greater than 55 years, male gender, African American or Hispanic race, presence of hypertension, diabetes, atrial fibrillation, hypercholesterolemia, morbid obesity, renal insufficiency, family history of stroke, and tobacco use.

B. Physical examination of the patient should begin with a review of the

patient's vital signs, with particular attention on the blood pressure, heart rate, and rhythm (arrhythmias). A focused neurologic assessment should be conducted, with observation of the patient's alertness and orientation, analysis of any speech quality/deficits (e.g., dysarthria, aphasia), detection of facial asymmetry, and assessment of cranial nerves. Motor and sensory deficits should be tested for, as should any visual field deficits. Auscultation should be done to document the presence or absence of a carotid bruit. **The absence of a bruit does not exclude the presence of carotid stenosis.**

C. Diagnostic Studies. Any patient with neurologic symptoms suggestive of acute stroke or TIA requires brain imaging. Noncontrast **brain computed tomography** (CT) can be obtained quickly and is often adequate to rule out cerebral hemorrhage. **Magnetic resonance imaging (MRI) is a much more sensitive study for confirming acute stroke**. Further imaging of the carotid arterial system can be employed to classify the degree of stenosis. Because of methodologic differences in calculating the percentage of stenosis encountered with different imaging modalities, there is some disagreement about exact cutoff percentages. However, **four levels of stenosis are typically described: mild (<50%), moderate (50% to 79%), severe (80% to 99%), and occluded (100%).** For consideration of optimal treatment strategies, a variety of noninvasive and invasive diagnostic studies are available:

1. **Color-flow duplex scanning** uses real-time B-mode US and color-enhanced pulsed Doppler flow measurements to determine the extent of the carotid stenosis and is the initial screening test for carotid disease. When performed by an accredited vascular laboratory, **carotid revascularization can be undertaken on the basis of US duplex scanning alone**. However, the vascular laboratory must have clear and validated criteria for measuring carotid stenosis, well-trained technologists, and must provide information about plaque morphology and the extent of distal ICA involvement. It should be noted that assessment for **intracranial disease cannot be obtained with US alone**. Furthermore, findings of complete occlusion and/or contralateral high-grade occlusion on US are best confirmed by an alternate imaging technique.
2. **CT angiography (CTA)** and **MRI angiography (MRA)** are additional imaging modalities to assess carotid disease. They have the

advantage of being noninvasive and allow for the evaluation of the entire extra- and intracranial vascular anatomy. However, these studies are more expensive than US, often require the use of contrast (adding risk of contrast-induced nephropathy), and may expose the patient to radiation. CTA has the advantage of being fast, is inexpensive compared to MRA, and offers exceptional spatial resolution and visualization of soft tissues, bone, and vessels. MRA can be done without radiation exposure but can be limited by poor sensitivity and specificity for diagnosing moderate stenoses, the presence of flow-related artifacts, and a tendency to overestimate stenosis severity.

3. **Conventional catheter angiography** remains the "gold standard" for imaging the extra- and intracranial circulation in cerebrovascular disease. However, angiography is an invasive procedure with inherent risks, such as contrast allergy, renal toxicity, access complications, and even procedure-related stroke (<1% of patients). Because of these risks, and improvements in alternative techniques, carotid angiography is generally reserved for patients with technically inadequate studies or with discordant noninvasive study findings.

IV. MANAGEMENT

A. Best medical therapy is focused on modifying risk factors to prevent progression of carotid occlusive disease. Control of hypertension and hyperglycemia, cessation of smoking, management of lipid disorders, attainment of ideal body weight, and regular exercise should be undertaken and are the cornerstones of medical therapy. The components of best medical therapy are summarized in Table 37-1. Medical management in **all patients** is focused primarily on the use of **antiplatelet agents**, specifically aspirin, with low doses (81 mg/day) as efficacious as higher dose (325 mg/day). The additional role of **clopidogrel** is less clear as data suggest it to be slightly more efficacious compared to aspirin alone but no clear benefit with dual therapy. At the current time, secondary prophylaxis with either aspirin or clopidogrel is reasonable.

B. Carotid endarterectomy (CEA) had been considered the gold-standard revascularization procedure and has been documented to reduce stroke rates in patients with carotid artery disease. Indications for CEA have

been extensively studied in both asymptomatic and symptomatic patients, comparing surgical treatment to best medical therapy. Table 37-2 provides results of four randomized controlled trials comparing CEA and best medical therapy. Among these trials, the two United States trials include the **Asymptomatic Carotid Atherosclerosis Study (ACAS)** and the **North American Symptomatic Carotid Endarterectomy Trial (NASCET)**. In the ACAS trial, the ipsilateral **5-year** stroke rate in asymptomatic patients with at least 60% stenosis was **5.1% in patients undergoing a CEA versus 11% receiving best medical therapy**. For symptomatic patients with at least 70% stenosis in the NASCET, the 2-year ipsilateral stroke rate was **9% with CEA versus 26% with best medical therapy alone**. Based largely on these two definitive trials, current **indications for CEA include the following**:

TABLE 37-1 Summary of Effect of Best Medical Therapy

Best Medical Therapy for Prevention of Stroke and Cardiovascular Events

Treatment	Target	Evidence
Antiplatelet therapy	1. Either single or dual antiplatelet therapy acceptable 2. Aspirin 81–325 mg/day is recommended 3. Plavix 75 mg equivalent to aspirin 4. Ticlopidine 250 mg twice daily similar to aspirin in effectiveness	Reduces both stroke risk and overall cardiovascular morbidity
Antihypertensive therapy	Variable depending on age and comorbidities	Reduces stroke recurrence—wait at least 24 hrs after acute

		stroke to implement regimen No definitive benefit of one class of antihypertensive agents over another
Diabetes mellitus	Target HgbA1c <7	Reduce overall stroke rate No definitive benefit of tight control (i.e., HgbA1c ≤6)
Smoking cessation	Total abstinence	Reduces risk of stroke and major adverse cardiovascular events
Statin therapy	1. Reduce LDL by 50% 2. Target LD <70 mg/dL	Reduces risk of stroke and major adverse cardiovascular events, particularly among patients with a history of cardiovascular disease
Alcohol	Avoid excessive consumption	

TABLE 37-2 **Summary of Randomized Trials Comparing CEA and Best Medical Therapy**

Results of Randomized Trials of CEA Versus BMT

Study	Population	Stroke Rate for BMT	Stroke Rate for CEA + BMT	Conclusions
NASCET[a]	Symptomatic patients with carotid stenosis ≥70%	26% (2 yr)	9% (2 yr)	CEA is beneficial for symptomatic patients with ≥70% stenosis ($p < 0.001$)
NASCET[b]	Symptomatic patients with carotid stenosis 50–69%	22% (2 yr)	15% (5 yr)	CEA is beneficial for symptomatic patients with ≥50% stenosis ($p = 0.045$)
ECST[c]	Symptomatic patients with carotid stenosis 80–99% (60–99% by NASCET criteria)	20% (3 yr)	7% (3 yr)	CEA is beneficial for symptomatic patients with ≥60% stenosis by NASCET criteria ($p < 0.001$)
ACAS[d]	Asymptomatic patients with carotid stenosis ≥60%	11% (5 yr)	5% (5 yr)	CEA is beneficial for asymptomatic patients with ≥60% carotid stenosis ($p = 0.004$)
ACST[e]	Asymptomatic patients with carotid stenosis ≥60%	12% (5 yr)	6% (5 yr)	CEA is beneficial for asymptomatic patients with ≥60% carotid stenosis ($p < 0.001$)

[a]NASCET, North American Symptomatic Carotid Endarterectomy Trial. *N Engl J Med*. 1991;325:445–453.

[b]NASCET, North American Symptomatic Carotid Endarterectomy Trial. *N Engl J Med*. 1998;339:1415–1425.

[c]ECST, European Carotid Surgery Trial. *Lancet*. 1998;351:1379–1387.

[d]ACAS, Asymptomatic Carotid Atherosclerosis Study. *JAMA*. 1995;273:1421–1428.

[e]ACST, Asymptomatic Carotid Surgery Trial. *Lancet*. 2004;363:1491–1502.

- **Asymptomatic patients with greater than 60% stenosis.** It should be noted that while this recommendation remains, there have been some notable improvements in best medical therapy (e.g., introduction of statin medications) since performance of the ACAS trial 30 years ago. Given that the rates of stroke have decreased in the recent decades likely due to improvement in medical therapy, **physicians may choose to withhold surgical intervention until a greater degree of stenosis (e.g., >80%) is present**. Furthermore, there has to be an evaluation of a patient's comorbidities and periprocedural risks along with expected life expectancy (e.g., 3 to 5 years) before considering a revascularization procedure in an asymptomatic patient for future stroke risk reduction.
- **Symptomatic patients with greater than 50% stenosis.** Surgery should be performed as soon as within reason. **For patients with a stroke, surgery should be performed within 2 weeks in order to decrease the rate of recurrent stroke**. There is evidence to suggest that operating within 48 hours confers increased operative risk. Furthermore, there is a risk of hemorrhagic conversion in patients with a recent stroke and an assessment of the volume of brain involved in the stroke should be undertaken. The NASCET did not include patients with disabling stroke, and while these patients may

benefit from surgical intervention, the decision to proceed and the timing of intervention in these patients should be individualized. Surgery is rarely performed on patients with **completely occluded carotid arteries.** Candidates for surgery may include those who had: (1) recent endarterectomy with immediate postoperative thrombosis, (2) recent occlusion with fluctuating or progressive symptoms, and (3) new ICA occlusion that can be operated on within 2 to 4 hours of the onset of symptoms. **There is no role for surgical revascularization in patients with *asymptomatic* ICA occlusion.** Best practice guidelines merit that CEA should be performed with perioperative adverse event rates (stroke and death) below 3% for asymptomatic patients and 6% for symptomatic patients. Anyone performing this procedure must achieve similar (or better) perioperative outcomes.

1. **Procedural detail**
    a. **Preoperative considerations. Anesthesia** for CEA consists of general endotracheal anesthesia, regional cervical block, or local anesthesia, depending on a patient factors and surgeon expertise. No single method of anesthesia has demonstrated superiority. The successful completion of a CEA relies on meticulous technique and a thorough understanding of the cervical anatomy. **Prophylactic antibiotics** should be administered. An arterial line is placed for continuous blood pressure monitoring and vasoactive agents should be readily available to avoid extremes of blood pressure.
    b. **Positioning.** After induction, the patient is placed in the semi-Fowler position, with the head of the table slightly elevated in the reverse Trendelenburg position and the knees slightly flexed. A towel or sandbag is placed between the shoulders to extend the neck, and the arms are tucked to the sides. The head is turned away from the side that is being operated, and the endotracheal tube is secured opposite the surgical field.
    c. **Initial dissection.** An incision centered over the carotid bifurcation is made along the anterior border of the **sternocleidomastoid muscle**, or a transverse incision in the skin crease can be used. The skin, subcutaneous tissues, and platysma muscle are divided, and the deep cervical fascia is

then divided and a self-retaining retractor is placed in the incision to reflect the sternocleidomastoid muscle posteriorly. The **common facial vein** is ligated and divided to expose the underlying carotid sheath. The carotid sheath is opened and the common carotid artery (CCA) and both the ICA and external carotid artery (ECA) are exposed. The **hypoglossal and vagus nerves** are identified and preserved. The **ansa cervicalis** can usually be found anterior to the internal jugular vein and may be divided if necessary to facilitate exposure, and it can also be followed cephalad to help identify the hypoglossal nerve. This should all be done with minimal manipulation of the **carotid bulb** to prevent embolization from the atherosclerotic plaque. The **carotid sinus** can be infiltrated with 1% lidocaine to prevent hypotension and bradycardia. Vessel loops are carefully passed around the CCA, ICA, and ECA. **Systemic heparinization** is established with an IV bolus of heparin (80 units per kg). The ICA, CCA, and ECA are clamped sequentially in that order to avoid embolization to the intracranial circulation.

d. Endarterectomy and closure. A longitudinal arteriotomy is made on the anterior wall of the CCA from a segment just proximal to the plaque and extended into the ICA to a point a few millimeters distal to the plaque. The use of a shunt is described below. If used, **the shunt is first inserted into the ICA**, and blood is allowed to backflow to fill the shunt. The proximal end of the shunt is then placed into the CCA, and cerebral blood flow restored. Endarterectomy begins with the plaque being separated in an appropriate plane with a spatula. The proximal extent of the plaque is transected with fine scissors, and the endarterectomy is continued distally. The plaque is first dissected from the ECA using an eversion technique and the use of a fine hemostat clamp. In the ICA, the plaque typically feathers to the end. If intimal flaps are present, they are carefully tacked down with U-shaped 6-0 polypropylene monofilament sutures. The artery is then flushed with heparinized saline, and the artery is typically closed with a patch using a running 5-0 suture. **Common patch materials**

include bovine pericardium, Dacron, polytetrafluoroethylene (Gore-Tex), or autogenous vein. Just before the suture line is completed, the shunt is removed and vascular clamps are replaced. After appropriate flushing maneuvers, the patch angioplasty is completed and **the clamps are then removed sequentially to allow for flushing of any potential debris away from the intracranial circulation**. The clamps are first removed from the ECA, then the CCA, and finally the ICA. Blood flow is confirmed with a Doppler probe or US. **Protamine sulfate** can be administered to reverse heparinization if needed (typically 0.5 to 1 mg of protamine per 100 units of heparin). Closure of the incision begins by reapproximating the sternocleidomastoid muscle and cervical fascia with interrupted 3-0 absorbable sutures. Through a separate stab incision, a surgical drain may be placed below the platysma prior to final wound closure.

e. Shunting during CEA may prevent cerebral ischemia during carotid clamping but can also lead to distal embolization or arterial injury during placement. There is varying data to support and discourage the use of intravascular shunt during CEA, and physician practices vary depending on surgeon preference and expertise. Several large series have demonstrated excellent results of CEA without the use of shunts while others advocate routine shunt placement for all CEAs. Another option is to use shunts selectively in patients who are at high risk for ischemic stroke. For this approach, there are different modalities available to assist in the decision to shunt or not. Adequate cerebral perfusion without shunting occurs in 85% to 90% of patients. For awake patients receiving local/regional anesthesia, a direct assessment of neurologic function is the most sensitive and specific method of determining the need for shunt placement. This can be done by having the patient squeeze a noise toy in the contralateral hand and answering simple questions after carotid occlusion. **Patients who develop weakness or changes in mental status should be shunted**. For patients under general anesthesia, the **decision to shunt can be aided by measurement of carotid**

stump pressure, intraoperative neurologic monitoring with EEG or somatosensory evoked potentials, measurement of middle cerebral artery flow by transcranial Doppler US, and monitoring with cerebral oximetry. A stump pressure lower than 40 mm Hg has been found to correlate with cerebral ischemia by EEG criteria, suggesting the need for shunt placement in these patients.

2. **Postoperative care.** Immediately after CEA, neurologic function and blood pressure alterations should be carefully monitored. Hypertension and hypotension are common after endarterectomy and may cause neurologic complications. The extremes of blood pressure should be treated with IV nitrates or phenylephrine to keep the systolic blood pressure within 20% of preoperative levels. The wound should be examined for hematoma formation. **Aspirin** is maintained throughout the perioperative period.
3. **Patient follow-up.** The Society of Vascular Surgery (SVS) Practice Guidelines recommend a baseline duplex US within 3 months of surgery, then every 6 months for the first 2 years, and annually thereafter. Patients should continue with best medical therapy including the use of an antiplatelet agent.
4. **Complications**
   - **a.** Stroke/death rates must be low (3% for asymptomatic patients; 6% for symptomatic) in order to consider carotid revascularization for future stroke risk reduction.
   - **b. Myocardial infarction (MI) remains the most common cause of death** in the early postoperative period. It is important to ask about activity level and symptoms of coronary disease preoperatively, obtain a preoperative workup if necessary, and optimize medical management.
   - **c. Cranial nerve injuries** (CNI) can occur in over 5% of patients who undergo CEA. The most commonly injured nerve is the hypoglossal, followed by the facial, vagus, and glossopharyngeal nerves. The vast majority CNI are transient with <1% persisting at follow-up.
   - **d. Recurrent carotid stenosis** has been reported to occur in 5% to 10% of cases, although symptoms are present in fewer than

3%. Recurrent stenoses are more common among women, patients who continue to smoke, and in those who have hyperlipidemia, diabetes, or hypertension. Early recurrent stenosis typically develops **within 2 years of CEA** and results from **neointimal hyperplasia**. Lesions that develop **more than 2 to 3 years after CEA** generally result from **progressive atherosclerotic disease**. **The presence of symptoms is an indication for treatment of a recurrent lesion**. Frequently, these lesions do not lend themselves to endarterectomy and are **best treated by carotid stent placement**.

e. **Cerebral hyperperfusion syndrome** is a feared complication that usually occurs several days after CEA. The incidence is 0.5% to 5% in published reports. **It is often associated with severe hypertension, and patients initially complain of a severe headache.** Intracranial hemorrhage is the most devastating consequence of this phenomenon. Patients suspected of having cerebral hyperperfusion syndrome should undergo noncontrast brain CT to rule out cerebral hemorrhage. They should be admitted for strict blood pressure control, and administration of antiseizure medications should be considered for select patients.

C. Transfemoral Carotid Artery Stenting (CAS) was introduced in the 1990s and presented as an alternative for patients who are considered as "high risk" for CEA. These can include physiologic or anatomic criteria as described below. The **indications for CAS are the same as those for a CEA**. **Relative contraindications to CAS** include severe tortuosity of the CCA and ICA, complex aortic arch anatomy (leading to higher risk of embolization/stroke with vessel manipulation during the procedure), severe calcification or extensive thrombus formation, or near-complete or complete ICA occlusion. Several studies have been completed or are underway to examine the efficacy of CAS compared to CEA, particularly in high-risk patients. Outcomes have varied, especially as device technology and operator experience have improved. The **Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)** study randomly assigned patients with symptomatic or asymptomatic carotid stenosis to undergo CAS or CEA. This trial showed that the rate of composite stroke, MI, or death did not differ significantly. During the

periprocedural period, there was a higher risk of stroke with CAS and a higher risk of MI (defined as elevation in troponin) with CEA. On follow-up, the patients who suffered a stroke were more affected than those who had an MI. **As CEA is well tolerated with low risk of complications, CAS is commonly reserved for high-risk patients**, including (but not limited to) patients with the following "high-risk" criteria:

- Severe cardiac disease, including NYHA class III or IV congestive heart failure, left ventricular ejection fraction <30%, recent unstable angina, or MI
- Prior ipsilateral neck surgery
- Prior neck radiation
- Contralateral vocal cord paralysis or recurrent laryngeal nerve injury
- Surgically inaccessible lesion (e.g., C2 or higher based on appropriate imaging)

1. **Procedural detail.** The procedure is usually done with IV sedation and local anesthesia. Careful catheter and wire manipulation minimize risk of distal embolization and reduce the incidence of stroke. Retrograde femoral access is obtained under US guidance, and alternative arterial access sites (e.g., transcervical or brachial artery) have also been described. A sheath is placed with the distal tip in the distal CCA. Carotid arteriogram is performed to delineate the anatomy and the stenosis is crossed and an embolic protection device (EPD) is deployed into the ICA. A typical distal EPD is a filter-like device that is advanced across the lesion and then opened in the distal ICA prior to angioplasty and stent deployment. Alternatively, "proximal" protection devices using balloon occlusion can also be utilized. After deployment of the protection device, predilatation of the stenosis is performed followed by placement of a self-expanding stent at the site of the stenosis. The stent is then postdilated as necessary. The available stents come in a variety of diameters (6 to 10 mm), lengths (3 to 4 cm), and configurations (straight or tapered).
2. **Patient follow-up.** Similar to CEA, the SVS Practice Guidelines recommend a baseline duplex US within 3 months of surgery, then every 6 months for the first 2 years, and annually thereafter.

Patients should continue with best medical therapy and **dual antiplatelet therapy with aspirin and clopidogrel** should be maintained **for a minimum of 1 month**.

3. **Complications**

   a. Embolic stroke is the most common complication of transfemoral CAS. Risk factors include lack of EPD use, long or multiple lesions, and patient age above 80 years. Thrombolysis may be a successful treatment option, especially if the source of emboli is an acute thrombus. When an embolus is composed of atheroma or chronic thrombus, however, mechanical removal of emboli may become necessary to restore flow.

   b. Hemodynamic instability may occur during manipulation and angioplasty of the carotid bifurcation. **Bradycardia should be anticipated** and pretreated with **atropine or glycopyrrolate** prior to dilation of the carotid bifurcation. Postoperatively, as with CEA, patients should be monitored to avoid extremes of blood pressure.

   c. Restenosis occurs at rates similar to CEA, occurring in approximately 5% of patients at 12 to 24 months and is typically secondary to intimal hyperplasia. These lesions are often amenable to repeat endovascular intervention.

D. Transcarotid artery revascularization (TCAR) is a novel hybrid technique that combines surgical exposure of the CCA for carotid stent delivery and use of flow reversal for embolic protection. The procedure received approval from the FDA in 2015. The **ROADSTER Trial** is a multicenter clinical study that evaluated the efficacy of TCAR in asymptomatic and symptomatic patients at high risk for standard CEA. The results of the trial showed a 30-day composite death, stroke, and MI rate of 3.5%. The stroke rate of 1.4% represented the lowest stroke rate for stenting in “high-risk” patients and compared favorably to results of “standard-risk” patients in the CEA arm of CREST. **More recent data from the TCAR Surveillance Project demonstrated stroke rates comparable and lower than those reported with standard CEA**.

1. **Procedural detail.** TCAR can be performed under general anesthesia or with sedation/local anesthesia. Direct carotid access is obtained through a small 2- to 3-cm incision just above the clavicle at the base

of the neck. A sheath is placed directly into the CCA with care not to engage the stenotic lesion. A second venous sheath is placed into a common femoral vein and a “flow controller” is connected between the two sheaths. Distal embolic protection is obtained with occlusion of the CCA proximal to the sheath. The differential in pressure between the arterial sheath and venous sheath will lead to a “flow reversal” of blood from the carotid circulation away from the brain into the venous sheath. The lesion is then crossed with a wire and generously predilated prior to stent placement. Any potential debris is diverted through an inline filter in the flow controller.

2. **Complications.** Access site complications (e.g., dissection) can be minimized with attention to meticulous technique and careful patient selection. Distal embolization is less frequent than transfemoral CAS. The postoperative management should be similar to those patients undergoing CEA, with blood pressure monitoring and surgical site surveillance. **Patients should be continued on dual antiplatelet therapy as well as statin**.

CHAPTER 37: CEREBROVASCULAR DISEASE

Multiple Choice Questions

1. **Which one of the following is not considered a risk factor for stroke and TIA?**

   a. Age greater than 55 years
   b. African American or Hispanic race
   c. Female gender
   d. Hypertension
   e. Smoking

2. **A 67-year-old male is referred to your clinic by his primary care physician after a routine checkup revealed a right carotid bruit. A subsequent duplex ultrasound revealed 50% stenosis of his right carotid artery. According to the ACAS trial, carotid endarterectomy for asymptomatic patients is indicated for stenoses defined by which of the following?**

   a. ≥90%
   b. ≥80%
   c. ≥70%
   d. ≥60%
   e. ≥50%

3. **According to the NASCET, what is the approximate reduction in stroke rate over 2 years if CEA is completed for a symptomatic patient with 70% stenosis of her left carotid artery?**

   a. 6% absolute risk reduction (i.e., 11% control vs. 5% CEA)
   b. 7% absolute risk reduction (i.e., 22% control vs. 15% CEA)
   c. 13% absolute risk reduction (i.e., 20% control vs. 7% CEA)
   d. 17% absolute risk reduction (i.e., 26% control vs. 9% CEA)
   e. 20% absolute risk reduction (i.e., 25% control vs. 5% CEA)

4. **Which of the following represents the major cranial nerve most commonly injured during carotid endarterectomy?**

a. Vagus nerve
b. Hypoglossal nerve
c. Glossopharyngeal nerve
d. Facial nerve
e. Recurrent laryngeal nerve

5. Which of the following veins is commonly ligated during carotid endarterectomy?

a. Facial vein
b. Internal jugular vein
c. Superior thyroid vein
d. Anterior jugular vein
e. Subclavian vein

6. The first extracranial branch of the internal carotid artery is:

a. Superior thyroid artery
b. Inferior thyroid artery
c. Lingual artery
d. Ophthalmic artery
e. None of the above

7. The first branch of the external carotid artery is:

a. Superior thyroid artery
b. Inferior thyroid artery
c. Lingual artery
d. Ophthalmic artery
e. None of the above

8. A 72-year-old female with a history of TIAs is found to have 80% stenosis of the left carotid artery on duplex ultrasound. The most appropriate next step in management is:

a. Repeat ultrasound in 6 months
b. Start aspirin and clopidogrel
c. Start aspirin only
d. Recommend carotid revascularization
e. Defer management until permanent development of stroke

9. **The following, by themselves, are all acceptable indications for carotid artery stenting, except:**

   a. Surgically inaccessible lesion
   b. Severe high-grade stenosis
   c. Contralateral vocal cord paralysis
   d. Prior ipsilateral neck surgery
   e. Prior neck radiation

10. **While undergoing carotid stenting, a patient develops bradycardia and hypotension, during predilatation of a stenotic region. This is most likely due to which process?**

    a. Global cerebral hypoperfusion
    b. Myocardial infarction
    c. Stimulation of the carotid body
    d. Stimulation of the hypoglossal nerve
    e. Distal embolization of atheroemboli

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Thoracoabdominal Vascular Disease

Jason R. Cook, J. Westley Ohman, and Luis A. Sanchez

INTRODUCTION

The majority of vascular diseases are secondary to atherosclerotic changes of the arterial wall, which are multifactorial and are influenced by a combination of genetic predisposition, age, and environmental factors such as diet, smoking, and exercise. The **arterial wall** consists of the **intima** (lined by endothelium), the **media** (comprised of smooth muscle cells and extracellular matrix [ECM]) proteins, and the **adventitia** (which includes loose connective tissue and fibroblasts). A true **aneurysm is a permanent localized dilation of all three layers >50% of the normal** or adjacent vessel diameter or **>3 cm for the abdominal aorta**. Aortic dilation is a degenerative process that characteristically involves macrophage and lymphocytic infiltration of the intima, smooth muscle cell loss, and matrix-metalloproteinase–associated lysis of elastin and collagen of the medial and adventitial layers (*J Vasc Surg*. 2003;38(3):584–588).

I. ABDOMINAL AORTIC ANEURYSMS (AAAS). They are the most common type of aneurysm disease of the aorta, occurring in 3% to 9% of people >50 years of age in the Western world (*Br J Surg*. 1998;85(2):155–162). In the United States, ruptured AAAs are the 13th leading cause of death overall and the 10th leading cause of death in men >55 years, a rate that has held steady for the past two decades despite improvements in operative technique and perioperative management (*Cardiovasc Diagn Ther*. 2017;8(1):S191–S199).

A. Pathophysiology. Ninety percent AAAs are degenerative in origin, 5% are inflammatory, and the remainder are idiopathic (*J Vasc Surg*. 2003;38(3):584–588). Eighty-five percent AAAs are infrarenal, 25%

involve the iliac arteries, and 2% involve the renal or other visceral arteries (*Exp Clin Cardiol.* 2011;16(1):11–15). Importantly, 14% of patients with AAA have associated peripheral (e.g., femoral or popliteal) aneurysms (*J Vasc Surg.* 2000;31(5):863–869). The presence of a peripheral aneurysm mandates screening for AAA as 62% of patients with popliteal aneurysms and 82% with femoral aneurysms have an associated AAA. The most accepted predictor of AAA rupture is maximal diameter, and the major risk factors for aortic dilation are hypertension and smoking. Several trials (**UKSAT** [*Lancet.* 1998;352(9141):1649–1655] and **ADAM** *[Ann Intern Med.* 1997;126(6):441–449]) have established the risk of AAA rupture at 0.6% to 1% per year, with the risk rising to 10% at 6 cm, 20% at 6.5 cm, and 30% at 7.5 cm.

B. Diagnosis

1. **Clinical manifestations.** Seventy-five percent AAAs are asymptomatic and are found incidentally on physical examination or imaging such as computed tomography (CT) scans or screening ultrasound (US). Aneurysm expansion or rupture may cause severe back, flank, or abdominal pain and varying degrees of shock. Distal embolization of mural thrombus, thrombosis of the aorta, or local expansion can lead to compression on neighboring structures such as the duodenum or ureter. Half of AAAs are identifiable on physical examination as a pulsatile mass at or above the umbilicus. AAA rupture may mimic renal colic, peritonitis, duodenal perforation, pancreatitis, degenerative spine disease, acute disk herniation, or myocardial infarction.
2. **Radiologic evaluation**
   a. **US** is an accepted screening study with sensitivity of 87% and specificity nearing 100%, but for patients nearing size criteria for repair, the study of choice is CT angiography (CTA) (*J Vasc Surg.* 2018;67(1):2–77.e2).
   b. **Magnetic resonance (MR) scan** is comparable to CT but avoids radiation exposure and is useful in patients with intravenous (IV) contrast contraindications such as chronic kidney disease.
   c. **Aortography** is not sensitive for the diagnosis of AAA because the study is a luminogram and will underestimate the total aortic size due to the presence of mural thrombus.

C. Elective Management of AAA. Aortic diameter has long been considered the best quantifiable variable to determine for risk of AAA rupture (*J Vasc Surg*. 2018;67(1):2–77.e2; *Ann Vasc Surg*. 2000;14(2):152–157; *J Vasc Surg.* 2002;36(3):589–597). Advances in imaging now allow for the quantification of AAA wall stress, stiffness, and wall tension, though long additional work is needed before such modalities become the gold standard for presurgical evaluation.

1. **Medical management.** Patients with small aneurysms (<4.5 cm in diameter) without risk factors for rupture can be followed using US or CT scan yearly, with larger ones being followed more frequently. Smoking cessation, exercise, control of hypertension, and treatment of chronic obstructive pulmonary disease (COPD) are critical (*J Vasc Surg.* 2010;52(3):539–548).
2. **Elective surgical treatment.** Operative mortality ranges from 1% to 4% for uncomplicated AAA to greater than 18% to 32% for ruptured AAA (*J Vasc Surg.* 2007;46(4):669–675; *J Vasc Surg*. 2007;45(3):443–450). Five-year survival after elective repair is no different from that for age-matched patients without AAA. Associated cardiovascular disease, hypertension, decreased renal function, COPD, and morbid obesity increase operative risk (*J Vasc Surg*. 2018;67(1):2–77.e2). Indications for **surgical management** include (*J Vasc Surg.* 2003;37(5):1106–1117):
   a. Symptomatic aneurysms of any size.
   b. Aneurysms exceeding 5.5 cm diameter in men, 5 cm in women.
   c. Increase in diameter by more than 0.5 cm/6 months or 1 cm/yr.
   d. Saccular aneurysms.
3. **Relative contraindications** to elective repair include recent myocardial infarction, intractable congestive heart failure, unreconstructable coronary artery disease, life expectancy of less than 2 years, and incapacitating neurologic deficits after a stroke.
4. **Open operative technique.** The two open surgical approaches are the transabdominal and retroperitoneal approaches. In the transabdominal repair, the aneurysm is approached through a midline laparotomy and the aorta exposed by shifting the small bowel and mobilizing the left colon before incising the retroperitoneum. The duodenum and left renal vein are mobilized from the anterior portion of the aorta prior to

administration of systemic heparin and confirming activated clotting time (ACT) greater than 250. The aorta is then clamped proximally and distally and any associated side branches controlled before an aortotomy is made and extended longitudinally through the aneurysm neck. At this point, the proximal extent of the aortotomy is fashioned in a T to facilitate the proximal anastomosis. Mural thrombus is removed from the inside of the aneurysm sac and lumbar arteries are oversewn from within the sac. The proximal anastomosis is performed to nonaneurysmal aorta using a conduit, either Dacron graft or CryoArtery, or possibly a vein composite, depending on the indication. After completion of the proximal anastomosis, the graft is flushed and the proximal clamp can be moved down to facilitate perfusion to any visceral segment that was clamped during the anastomosis. The distal anastomosis is completed at the aortic bifurcation (**tube graft**) or at the iliac or femoral arteries (**bifurcated graft**), as the extent of the aneurysmal disease dictates. At the completion of the case, the aneurysm sac is trimmed and then used to close over the graft to reduce the risk of fistulizations to the graft. An alternative approach is through a left retroperitoneal incision. This approach is advantageous in obese patients, those with COPD, patients with previous intra-abdominal surgery, and is the preferred approach at our institution. The anterior-lateral aspect of the aorta is exposed with the retroperitoneal approach, which facilitates suprarenal and supraceliac control though **complicates control of the right renal artery**, which must be controlled from within the aneurysm sac.

D. Management of Ruptured AAA

1. **Preoperative management.** Unstable patients with a presumed diagnosis of a ruptured aneurysm (hypotension, abdominal or back pain, and a pulsatile abdominal mass or history of aneurysmal disease) are gently resuscitated (crystalloid, colloid, or blood) to maintain organ perfusion while avoiding overresuscitation with the associated diluting of clotting factors, destabilization of thrombus, and hemorrhage (so-called "**permissive hypotension**"). Unstable patients are transferred immediately to the operating room for exploration, whereas those who are stable should undergo emergent CT scanning to confirm the diagnosis.

2. **Operative management** is aimed at rapidly controlling the aorta. **Anesthetic induction is delayed until moments before incision**. Through a midline incision, the supraceliac aorta is controlled at the diaphragmatic hiatus by dividing the pars flaccida, mobilizing the left lateral segment of the liver toward the patient's right, and isolating the aorta from the adjacent esophagus and attaining vascular control with an aortic clamp, or direct pressure against the spine. The retroperitoneal hematoma is opened, and the proximal neck of the aneurysm is identified and cross-clamped. Distal vessel dissection continues, and management is similar to repair of an elective AAA. The use of bifurcated grafts should be avoided in favor of the more expeditious tube graft reconstruction. Heparin should also be avoided in these patients who are likely to be already coagulopathic due to the high risk of intra- and postoperative bleeding. However, in centers with endovascular capabilities, this less invasive approach has become the preference for initial treatment of ruptured AAA in patients with favorable anatomy.
3. **Complications** from open AAA repair
   a. **Arrhythmia, myocardial ischemia/infarction.**
   b. **Intraoperative hemorrhage** can be reduced by clamping the aorta proximal to the aneurysm and the iliac arteries distally. Once the aneurysm is opened, retrograde bleeding from lumbar arteries must be controlled rapidly with transfixing ligatures. Blood should be salvaged in the operating room and autotransfused to the patient.
   c. Management of resuscitation, electrolytes, and pressors is critically important during aortic unclamping due to **sudden hypotension** from a decrease in systemic vascular resistance and introduction of previously sequestered metabolites.
   d. **Renal insufficiency** may be related to the use of IV contrast, inadequate hydration, hypotension, renal ischemia from a period of aortic clamping above the renal arteries, or embolization to the renal arteries. Elective situations allow for the use of cold perfusate to be delivered to the renal arteries with the use of Pruitt catheters.
   e. **Lower extremity ischemia** may result from embolism or thrombosis, especially in emergency operations for which heparin

might not be used. This can be prevented by minimizing manipulation of the aneurysm prior to clamping. Use of **Fogarty balloon catheters** to remove distal emboli from lower extremity vessels is indicated when leg ischemia is identified in the operating room.

f. Microemboli arising from atherosclerotic debris can cause cutaneous ischemia ("**trash foot**"), which is usually treated expectantly as long as the major vessels are patent. Amputation may be required if significant necrosis results.

g. Gastrointestinal complications consist of prolonged paralytic ileus, anorexia, periodic constipation, or diarrhea, which is reduced with the retroperitoneal approach. **Ischemic colitis of the left colon** can occur with ligation of the inferior mesenteric artery (IMA) in the absence of adequate collateral circulation, especially in patients with prior colonic resection. Symptoms include leukocytosis, significant fluid requirement in the first 8 to 12 hours postoperatively, fever, and peritonitis. Diagnosis is confirmed by flexible sigmoidoscopy to 20 cm above the anal verge. **Necrosis limited to the mucosa may be treated expectantly with IV antibiotics and bowel rest**. Necrosis of the muscularis causes segmental strictures, which may require delayed segmental resection. **Transmural necrosis requires immediate resection of necrotic colon and construction of an end colostomy**.

h. Paraplegia, a rare complication of infrarenal aneurysm surgery, may occur after repair of a ruptured AAA due to **spinal cord ischemia**. Supraceliac cross-clamping, prolonged hypotension, and obliteration or embolization of important collateral flow to the spinal artery (internal iliac arteries or an abnormally low origin of the accessory spinal artery [**artery of Adamkiewicz**]) increase the risk.

i. Sexual dysfunction and **retrograde ejaculation** result from damage to the sympathetic plexus ("**Nervi erigentes**") during dissection near the proximal left common iliac artery.

E. Endovascular management of AAAs has dramatically decreased the acute morbidity of aneurysm surgery. The indications are equivalent to those for traditional open repair, although it is essential to consider the

anatomic configuration of the aneurysm when determining candidacy for endoluminal repair.

1. The most important **selection criterion** for endovascular treatment of an AAA is appropriate aortoiliac anatomy. Further advances in fenestrated and branched devices are allowing treatment of pararenal and other more complex AAAs. Preoperative CT assessment should include the following factors:

a. Current devices require at least 15 mm of healthy infrarenal aorta.

b. Evaluation for angulation between the neck and body of the aneurysm.

c. Intraluminal thrombus in the proximal neck represents a relative contraindication for endovascular treatment.

d. A cone-shaped neck or reverse taper (i.e., widens more distally) may preclude adequate apposition of the endograft to the aortic wall.

e. Iliac artery tortuosity, calcification, and luminal narrowing are critical factors for endograft delivery and deployment.

f. Patent aortic branches may influence the decision as to whether to proceed with endovascular repair. Large accessory renal arteries or the presence of a horseshoe kidney with multiple renal arteries is often a contraindication for endograft placement. Patent lumbar arteries arising from the aneurysm do not preclude endograft placement. A large patent IMA suggests abnormal mesenteric blood supply and risk of large-bowel ischemia with endograft coverage of the IMA orifice.

2. Technique. Endovascular devices are introduced retrograde through open or percutaneous femoral arterial access. Most commonly utilized devices are bifurcated and modular in design. Appropriate oversizing of stent grafts (by 20%) is based on preoperative assessment of arterial diameter to ensure adequate graft apposition to the aortic wall. Device length can be tailored by overlapping extension segments. The distal end of the iliac limbs is typically positioned proximal to the hypogastric orifices to maintain pelvic perfusion.

3. Complications of endograft repairs of AAAs

a. Branch occlusion, distal embolization, graft thrombosis or

fracture, and arterial injury (especially iliac artery avulsion at the iliac bifurcation).

b. Arterial dissection may occur during placement of large endografts. Dissection flaps not covered by the device and seen on completion angiogram can be treated with additional stents as needed.

c. Bowel ischemia may occur postoperatively secondary to embolization or hypoperfusion, but this is rare compared to open surgical repair.

d. Renal dysfunction may occur because of the nephrotoxicity of the contrast agent used for intraoperative angiography or due to embolization or renal artery occlusion from wire manipulation.

e. Graft migration occurs in 1% to 6% of patients and is associated with challenging arterial anatomy, poor graft placement, or changes in the aneurysm sac over time. When found on follow-up CT scans, patients can usually be treated with secondary endovascular procedures.

f. Endoleak is defined as failure to fully exclude the aneurysmal sac from arterial blood flow, potentially predisposing to rupture (*J Endovasc Ther*. 1997;4(2):152–168). Management strategies for endoleaks discovered on follow-up imaging studies are evolving and outlined below. Intervention is warranted for any endoleak that is associated with persistent aneurysm sac enlargement. Endoleaks are usually corrected by endovascular means but may require conversion to open surgical repair.

(1) In general, endoleaks from the proximal or distal attachment sites **(type I)** warrant intervention because of continued direct flow into the AAA. Treatment options include conversion to open or placement of a more proximal stent. **Type Ia endoleaks are leaks from the neck of the aneurysm, whereas type Ib endoleaks are from the distal landing zone**.

(2) Type II endoleaks are **due to collateral flow** (e.g., IMA, lumbar arteries) and may be closely observed in the absence of aneurysm expansion. Type II endoleaks may be treated with transarterial embolization through collateral vessels, translumbar embolization, or a transcaval approach, though

long-term outcomes are equivocal (*Cardiovasc Diagn Ther.* 2017;8(1):S131–S137; *J Vasc Surg.* 2012;55(5):1263–1267).

(3) Type III endoleaks are caused by **inadequate seal between graft components**. They should be corrected as soon as they are diagnosed as they too result in direct flow into the aneurysm sac. These are typically identified at placement of the device, though over time components can move and lead to separation.

(4) Type IV endoleaks are due to **porosity of the graft material**. Although rare with new generation grafts, increased graft porosity can lead to aneurysm expansion and should be treated with relining the graft with a new endograft. Treatment may be isolated to the limb or body component, or may involve the flow divider requiring a new bifurcated endograft.

4. **Results.** Relative to open surgical repair, endovascular treatment of AAA is associated with a reduction in perioperative morbidity, shorter duration of hospitalization (*J Vasc Surg.* 2003;37(2):262–271), and reduction in perioperative mortality (EVAR 1 [*Lancet.* 2004;364(9437):843–848]; DREAM [*N Engl J Med.* 2005;352(23):2398–2405]). However, studies of long-term outcome comparing open versus endovascular repair have demonstrated **similar rates of survival after 4 years** (DREAM [*N Engl J Med.* 2005;352(23):2398–2405]; UK EVAR [*N Engl J Med.* 2010;362(20):1863–1871]). Close follow-up with CT scanning every 6 months for 1 year, and then yearly, is essential to maintaining long-term clinical success using this technique.

II. THORACIC AORTIC ANEURYSMS.

Thoracic aortic aneurysms (TAAS) are primarily a disease of the elderly, with an estimated incidence of 10.4 per 100,000 person-years (*JAMA.* 1998;280(22):1926–1929). Ascending aortic aneurysms are most common (~60%) followed by aneurysms of the descending aorta (~35%) and of the transverse aortic arch (<10%). Most descending taas begin just distal to the orifice of left subclavian artery.

A. Pathophysiology.

TAAs are divided into five main types: **ascending, transverse, descending, thoracoabdominal, and traumatic**. Ascending aortic aneurysms are secondary to medial degeneration,

whereas transverse, descending, and thoracoabdominal aortic aneurysms are degenerative changes secondary to progressive atherosclerosis and hypertension. Traumatic aneurysms are usually due to blunt injury to the chest.

B. Diagnosis

1. **Clinical manifestations** are infrequently identified as most TAAs are detected as incidental findings on chest imaging obtained for other purposes. A minority of patients may present with chest discomfort or pain that intensifies with aneurysm expansion or rupture, aortic valvular regurgitation, congestive heart failure, compression of adjacent structures (e.g., recurrent laryngeal nerve, left mainstem bronchus, esophagus, superior vena cava), erosion into adjacent structures (e.g., esophagus, lung, airway), or distal embolization.
2. **Radiologic evaluation**
   a. **Chest x-ray** may reveal a widened mediastinum or an enlarged calcific aortic shadow. Traumatic aneurysms may be associated with skeletal fractures.
   b. **MR or CT imaging** with IV contrast provides axial imaging of the size and extent of aneurysms, which is necessary to plan for surgical intervention with either open or endovascular repair.
   c. **Echocardiography** with transesophageal imaging may be useful in evaluating aneurysms involving the aortic arch.
   d. **Aortography** demonstrates the proximal and distal extent of the aneurysm and its relationship with aortic branch vessels arising from it.

C. Surgical management varies by underlying etiology and location of the TAA. Repair of proximal arch aneurysms requires cardiopulmonary bypass and circulatory arrest. Preclotted woven polyethylene terephthalate **(Dacron)** is the graft of choice. Ascending and transverse arch repairs are completed through a median sternotomy. Descending and thoracoabdominal aneurysms are approached from a left posterolateral thoracotomy or thoracoabdominal incision. Intraoperative management of patients undergoing thoracotomy is facilitated by selective ventilation of the right lung using a double-lumen endobronchial tube. Several adjuncts for limiting postoperative paraplegia following surgery for descending and thoracoabdominal

aneurysms are employed, including cerebrospinal fluid drainage and retrograde perfusion.

1. Ascending aortic aneurysms and arch aneurysms

a. Indications for surgical repair include symptomatic or rapidly expanding aneurysms, aneurysms ≥6 cm in diameter, ascending (**type A**) aortic dissections, mycotic aneurysms, and asymptomatic aneurysms ≥5.5 cm in diameter in patients with **Marfan syndrome** (*Coron Artery Dis.* 2002;13(2):85–92).

b. Operative management. An aneurysm in the ascending aorta arising distal to the coronary ostia is traditionally replaced with an interposition graft. Recent advances in endovascular technology are altering the management of ascending and arch aneurysms. A branched thoracic aortic graft is now on trial in the United States with ascending aortic to descending aortic coverage that is preconfigured for innominate and left carotid artery branches to negate the need for total arch debranching. An aneurysm resulting in aortic valve annulus dilation and valve incompetence is replaced with a composite valved conduit **(Bentall procedure)** or a supracoronary graft with separate aortic valve replacement. All ascending arch aneurysms that are due to connective tissue disorders should undergo open aortic repair through replacement with a Dacron graft and reimplantation of the coronary arteries.

2. Transverse aortic arch aneurysms

a. Indications for repair include aneurysms ≥6 cm in diameter, aortic arch dissections, and ascending arch aneurysms that extend into the transverse arch.

b. Operative management. After opening the aorta under hypothermic circulatory arrest, the distal anastomosis is performed using a beveled graft, followed by anastomosis of a patch that incorporates the orifices of the brachiocephalic vessels to the superior aspect of the graft. The proximal anastomosis is sewn to the supracoronary aorta (if the aortic valve is not involved) or to a segment of the composite valved conduit interposed to complete the arch reconstruction. Involvement of the transverse arch and its branch vessels requires interposition grafting to the involved vessels. As described above, newer endografts have been designed to accommodate the aortic arch

with a fenestration to allow for retrograde placement of innominate artery and left carotid artery stents to preserve cerebral blood flow. Such patients require bilateral neck incisions with a left carotid–subclavian artery bypass.

3. Descending TAAs

a. Indications for repair include asymptomatic aneurysms ≥6 cm in diameter and any symptomatic aneurysms.

b. Operative management. Descending TAAs can be managed with either open or endovascular repair depending on the anatomy. In an open repair, a posterior-lateral thoracotomy incision is made with mobilization of the aorta to facilitate clamping and sewing. After the distal clamp is applied, a proximal clamp is placed just distal to the left subclavian artery or between the left common carotid and left subclavian arteries. Selected intercostal branches can be reimplanted into the aortic interposition graft. **Left heart (atriofemoral) bypass** is often used to protect the heart from overdistention and to provide distal blood flow to the intra-abdominal aorta while the distal thoracic aorta is clamped. Cerebrospinal fluid drainage is used as an adjunct to decrease the incidence of postoperative paraplegia. Endovascular treatment with stent graft placement requires specific anatomic criteria including an adequate proximal landing zone length (2 cm) and aortic diameter measuring up to 42 mm, absence of significant mural thrombus within the sealing zones, and aortic and iliofemoral anatomy amenable to device introduction. In situations in which the proximal neck length is too short, coverage of the left subclavian artery can be performed with or without an adjunctive left carotid–left subclavian transposition or bypass. Placement of an **Amplatzer plug** into the proximal subclavian is used to reduce the risk of a type II endoleak from the subclavian artery. Endovascular repair requires groin access, either open or percutaneous, to facilitate a diagnostic catheter (pigtail) for an aortogram and placement of a thoracic stent graft.

4. Thoracoabdominal aneurysms

a. Indications for repair include asymptomatic aneurysms ≥6 cm in diameter and any symptomatic aneurysms.

b. Operative management consists of tube graft replacement along

with anastomosis of the major visceral branches to the graft. Aneurysms involving the thoracic and proximal abdominal aortic segments may be approached through a left posterolateral thoracotomy extended to the umbilicus. Use of left heart (atriofemoral) bypass is a valuable adjunct to allow for both cerebral perfusion and visceral perfusion off the bypass circuit via a femoral cannula. The thoracic aorta is clamped and opened to perform the proximal anastomosis. The aorta is clamped distally opening the remaining aneurysm. The orifices of all major aortic branches are occluded with balloon catheters or vascular clamps. Temporary perfusion can be maintained to those branches during aneurysm repair by using balloon catheters connected to the atriofemoral bypass. The anastomoses of significant aortic branches to the graft are performed as a patch or with separate bypasses. The clamp is moved to the graft below the renal arteries to reperfuse all visceral vessels in an antegrade fashion. The distal anastomosis is made either to the uninvolved aorta or to the iliac arteries. A hybrid approach or full endovascular repair can be employed for patients who cannot tolerate an open repair, especially elderly patients (*J Vis Surg.* 2018;4:61). In a hybrid approach, the thoracic component of a thoracoabdominal aneurysm can be treated with a straight tube endograft landing just proximal to the celiac artery, thereby converting a type II thoracoabdominal aortic aneurysm into a type IV. After this conversion, the viscera can either be debranched from a transabdominal approach with extension of the tube graft, or a traditional open AAA repair with reimplantation of the visceral arteries can be performed. More recently, abdominal endografts with fenestrations for the visceral segments have been used as an extension of the thoracic endograft. Coverage of the descending thoracic aorta to aortic bifurcation with endograft substantially increases the risk of spinal cord ischemia and is therefore used with caution and preservation, when possible, of the left subclavian and bilateral hypogastric arteries.

5. Traumatic aortic aneurysms

a. Indications. Urgent repair is indicated, except when precluded by more compelling life-threatening injuries or major central nervous

system trauma.

b. Classification. Traumatic aortic injuries have the following categories:

(1) Grade I: Intimal tear

(2) Grade II: Intramural hematoma

(3) Grade III: Pseudoaneurysm

(4) Grade IV: Rupture

c. Management. Historically, these aneurysms were repaired by primary aortorrhaphy, aneurysmectomy, and end-to-end reanastomosis or by interposition grafting. In current practice, grade I injuries may be observed on serial imaging and grade II to IV injuries should undergo prompt endovascular repair, if amenable. Age should not disqualify from endovascular repair (*J Vasc Surg*. 2011;53(1): 187–192).

D. Complications of thoracic aortic surgery are similar to those for abdominal aortic surgery. The incidence of paraplegia may be as high as 30% with some types of TAAs (*Ann Thorac Surg*. 2007;83(2):S856–S861). This risk has been reduced to less than 2% by multimodal therapies used to minimize spinal cord ischemia including distal aortic perfusion, intercostal and lumbar artery reimplantation, pre- or intraoperative localization of spinal cord blood supply, hypothermia, cerebrospinal fluid drainage, and pharmacotherapy (*World J Surg*. 2008;32(3):355–360).

III. OTHER ARTERIAL ANEURYSMS

A. Infected aneurysms have risen in incidence with the increased prevalence of immunocompromised patients and invasive transarterial procedures.

1. Pathophysiology. Infected aneurysms can be divided into four types: **mycotic aneurysm, microbial arteritis with aneurysm, infection of pre-existing aneurysm, and posttraumatic infected false aneurysm**. ***Staphylococcus aureus*** is the most common pathogen, although *Salmonella* species (arteritis), *Streptococcus* species, and *Staphylococcus epidermidis* (pre-existing aneurysms) also may occur (*Ann Vasc Surg*. 2018;51:306–313). **Gram-negative infections have the highest risk of rupture**.

2. Diagnosis

a. Clinical manifestations may be absent or include fever, tenderness, or sepsis. Physical examination may demonstrate a **tender, warm, palpable mass** in an infected peripheral aneurysm. Laboratory tests may reveal leukocytosis. Aerobic and anaerobic blood cultures should be obtained but are positive in only 50% of patients.

b. MRI or CTA can be employed to evaluate the cross-sectional size and qualitative aspects of the aneurysm and surrounding tissue. **Angiography** can also be used to evaluate characteristics of the aneurysm but does not provide axial slices provided by CT scan. Aneurysms that are saccular, multilobed, or eccentric with a narrow neck are more likely a result of infection.

B. Management

1. **Preoperative.** Broad-spectrum IV antibiotics should be administered after aerobic and anaerobic blood cultures have been obtained.
2. **Intraoperative.** Goals of surgery include (1) controlling hemorrhage; (2) obtaining arterial specimens for Gram stain, aerobic and anaerobic cultures, and drug sensitivities; (3) resecting the aneurysm with wide debridement and drainage; and (4) reconstructing major arteries through uninfected tissue planes. Extra-anatomic bypass may be necessary to avoid contamination of the graft. Inline reconstructions with antibiotic-impregnated grafts, cryopreserved homografts, or native veins are alternatives that can be used for arterial reconstructions depending on the location of the aneurysm and the extent of the infection.
3. **Postoperative.** Adequate drainage of the aneurysm cavity and long-term antibiotic therapy for at least 6 weeks are typically required.

IV. ACUTE AORTIC SYNDROMES

A. Aortic dissection is a tear in the intima allowing blood to travel between the intima and the media resulting in the creation of two flow channels named the “true lumen” and the “false lumen.” Aortic dissection occurs at an incidence of 6 in 100,000 patients, and the natural history is notable for a mortality rate as high as 1% per hour for the first 24 hours for ascending aortic dissection (*Circulation.* 2013;127(20):2031–2037; *Am J Cardiol.* 1972;30(3):263–273).

Dissections are classified according to the **Stanford classification system** based on involvement of the ascending arch, which simplified the previously used **DeBakey classification**.

1. Diagnosis

a. Clinical manifestations include the hallmark sudden-onset, ripping chest/abdominal pain, radiating to the back. There may be an associated blood pressure discrepancy between the upper extremities, new-onset heart murmur, and, less commonly, paraplegia or paresthesias.

b. Risk factors include long-standing uncontrolled hypertension, tobacco abuse, family history, and **collagen vascular diseases** such as Marfan syndrome.

c. Radiographic tests

(1) CTA remains the gold standard for diagnosis in the acute setting with modern techniques having a sensitivity and specificity of 100% and gives accurate information regarding the location of the intimal injury and any associated involvement of branch vessels (*Radiology.* 1996;199(2):347–352).

(2) MR angiography has been supplanted by CTA in the acute setting but is used in long-term follow-up.

2. Type A dissections involve the proximal ascending aorta and are treated as surgical emergencies. These are the most common type of dissection, accounting for approximately 60% of all dissections. The high mortality rate is due to progression of retrograde dissection, hemopericardium, and cardiac tamponade.

a. Management nearly universally involves emergent surgery with replacement of the proximal ascending arch with or without valve replacement.

3. Type B dissections are those isolated to the descending thoracic aorta distal to the left subclavian. The clinical presentation is described based on association between symptom onset and dissection, thus subdivided into the **hyperacute** (within 24 hours), **acute** (2 to 7 days), **subacute** (8 to 30 days), and **chronic** (>30 days) (*Am J Med.* 2013;126(8):730.e19–e24). Furthermore, type B dissections are subdivided into uncomplicated or complicated based on evidence of

end-organ dysfunction, including but not limited to refractory pain, visceral malperfusion, or spinal cord ischemia.

a. **Management** of complicated type B dissections is aimed at revascularization of the affected segment through whatever means is most expedient, utilizing both endovascular and open options.

b. **Management** of uncomplicated type B dissections includes strict blood pressure monitoring with a goal systolic blood pressure of 100 to 120 mm Hg. Despite optimal control with adequate blood pressure management, uncomplicated type B dissections may progress to become complicated, and up to 25% require intervention within 4 years (ADSORB trial [*Eur J Vasc Endovasc Surg*. 2014;48(3):285–291]).

c. **Surgical management** may include interposition of the affected segment with graft through an open thoracotomy, removal of the flap via aortotomy, or endovascular fenestration with or without stenting. The goal of surgical management is to restore perfusion of the true lumen and reduce the extent of malperfused visceral organs and the lower extremities.

d. **Endovascular coverage** of the intimal tear in **uncomplicated type B dissections** has become the **standard of treatment**. In the chronic setting, this has been shown to promote favorable aortic remodeling with improved mortality at 5 years (INSTEAD-XL, [*Circ Cardiovasc Interv.* 2013;6(4):407–416]). Trials are ongoing in the acute setting and also demonstrate favorable aortic remodeling (ADSORB trial [*Eur J Vasc Endovasc Surg*. 2014;48(3):285–291]).

B. Intramural hematomas are a focal hemorrhage in the wall of the aorta between the intima and media layer due to the rupture of the vasa vasorum without evidence of an intimal tear or dissection flap due to iatrogenic injuries, trauma, or hypertension. These are classified similar to dissections, with those involving the ascending aorta being corrected surgically, and the remainder being medically managed unless the hematoma is >1 cm thick (9-fold higher progression), aortic diameter >40 mm (30-fold higher risk of progression), progression on serial imaging, or persistent substernal or radiating back pain despite maximal antihypertensive management (*J Vasc Surg.* 2002;35(6):1179–1183).

C. Penetrating aortic ulcer is a projection into an intramural hematoma

that is associated with higher rates of disease progression. These are associated with smoking and atherosclerotic disease. These are classified and treated similar to intramural hematomas.

V. RENOVASCULAR DISEASE. Stenosis or occlusion of the renal arteries may result in hypertension, ischemic nephropathy, or both. **Renovascular hypertension is the most common form of surgically correctable secondary hypertension.**

A. There are several clinical features that may be used to identify patients with potential renovascular hypertension:

1. The onset of hypertension before the age of 18 or after the age of 55

2. Accelerated, resistant, or malignant hypertension

3. Unexplained impairment of renal function

4. Refractory to appropriate multidrug therapy

5. Hypertension in a patient with extensive coronary disease, cerebral vascular disease, or peripheral vascular disease

B. The majority have a normal physical examination. However, an epigastric, subcostal, or flank bruit, or findings of a unilateral small kidney on any imaging study, are possible indicators of the disease.

C. Pathophysiology

1. Renal arterial stenosis (RAS) leads to activation of the **renin–angiotensin–aldosterone system** by the ipsilateral kidney and results in volume expansion and peripheral vasoconstriction. **Even in the absence of hypertension, RAS may lead to renal failure**.

a. Acute renal failure may result from a subclinical RAS in a patient with an otherwise unrevealing workup or in a patient recently started on an **angiotensin-converting enzyme (ACE) inhibitor**, or another antihypertensive, or on a diuretic.

b. RAS may account for up to 20% of **unexplained chronic renal failure** in patients >50 years of age.

c. Isolated **unilateral RAS** generally does not cause a rise in serum creatinine due to compensation from the contralateral kidney.

2. Atherosclerosis accounts for nearly 90% of cases of renovascular hypertension and usually affects the ostia and proximal renal artery.

3. The second most common renovascular lesion is **fibromuscular dysplasia**, most commonly medial fibroplasia. These lesions are

multifocal, have a **string-of-beads** appearance on angiography, and typically occur in young women.

D. Diagnosis. Testing for clinically significant renal artery disease must evaluate both the **anatomic and physiologic changes** related to the condition.

1. **Arteriography** remains the "gold standard" for the diagnosis of anatomic RAS. However, the usual risks of arteriography, especially the nephrotoxic effects of the contrast agent, are important caveats to consider.
2. **Duplex scanning** is the preferred method for screening in patients with indicators of renovascular hypertension.
3. **MR angiography** is useful for evaluating kidney and main renal artery morphology without the use of nephrotoxic agents.
4. Two rarely used tests to determine the functional significance of a renal artery lesion are **captopril renal scintigraphy** and **selective renal vein renin measurement** when other workup is unrevealing.

E. Management of Fibromuscular Disease. While this rarely causes renal failure, it is **treated with endovascular balloon angioplasty** with 75% of patients free from hypertension and 95% free from reduction in renal function at 5 years after treatment (*J Vasc Surg.* 2012;55(2):421–427). For failure of endovascular treatment (see Section F.3), surgical correction may be required.

F. Management of atherosclerotic disease aims to control target organ damage from hypertension and avoid progressive ischemic renal failure. Response to therapy is difficult to predict because a patient's hypertension may be primarily essential in origin and their renal failure may due to hypertensive glomerulosclerosis rather atherosclerotic disease, *per se*.

1. **Medical therapy** is often successful in the management of patients with renovascular hypertension and remains the cornerstone of treatment. A combination of β-blockers and a calcium channel blocker, an ACE inhibitor, or an angiotensin II-receptor inhibitor is commonly used as first-line therapy.
2. **Surgical therapy**
   a. Surgical revascularization is a durable option for patients with long segment disease and declining renal function (*Ann Surg.*

1999;230(4):524–530). In patients undergoing aortic surgery for aneurysmal or occlusive disease with concomitant renal stenoses, consideration should be given to renal revascularization through concomitant renal artery reconstruction, although this may be associated with higher overall complication rates (*J Vasc Surg.* 2017;66(4):1149–1156).

b. Procedures

(1) Aortorenal bypass is the classic treatment of renal revascularization, using saphenous vein, autologous hypogastric artery (in children), or prosthetic graft.

(2) Renal endarterectomy is another option and often used for bilateral orificial lesions through a transverse arteriotomy over both orifices.

(3) Alternative bypass procedures can be employed in patients with unfavorable anatomy. Bypass grafts from the supraceliac aorta or the superior mesenteric, common hepatic, gastroduodenal, splenic, or iliac arteries can be transposed onto the renal arteries. Results are comparable to direct aortic reconstruction with less morbidity and mortality.

(4) Nephrectomy may be required in patients who have unreconstructable disease or a normal contralateral kidney and who are high-risk surgical candidates without an endovascular option.

c. Postoperative care

(1) Immediately after operation, patients should be hydrated to maintain adequate urine output. Concern about the patency of the reconstruction may be addressed by a renal or duplex scan.

(2) Patient follow-up should consist of blood pressure monitoring, a renal scan, and creatinine determination at 3 months, 12 months, and then yearly. Any recurrence of hypertension or deterioration in renal function should prompt diagnostic imaging including renal artery duplex.

d. Complications of surgery include persistent hypertension, acute renal failure, renal artery restenosis, thrombosis, aneurysm formation, and/or distal embolization.

3. Endovascular management of RAS

a. Indications for angioplasty of RAS include failure of medical management of renovascular hypertension. Renal artery stents are used for restenosis after previous angioplasty, procedural complications (e.g., dissection), and atherosclerotic ostial lesions.

b. Results. Technical success for renal artery angioplasty is defined as a less than 30% residual stenosis and a pressure gradient less than 10 mm Hg. For patients with atherosclerotic RAS, large studies (ASTRAL [*N Engl J Med.* 2009;361(20):1953–1962] and CORAL [*N Engl J Med.* 2013;370(1):13–22]) have shown no impact on renal function or major adverse renal and cardiovascular events compared to medical management.

VI. MESENTERIC ISCHEMIA.

This can be a difficult diagnosis to make because most patients are asymptomatic until late in the disease process. Although considerable advances have been made in the perioperative care as well as the diagnosis and treatment of intestinal ischemia, mortality remains 60% TO 80% (*Langenbecks Arch Surg.* 2008;393(2):163–171).

A. Acute Mesenteric Ischemia (AMI)

1. **Pathophysiology.** The most common cause is embolization to the SMA, although other causes include thrombosis of the SMA or portomesenteric venous thrombosis. Patients often have multiple **risk factors**, including significant cardiovascular disease, atrial fibrillation and severe atherosclerotic disease of nonmesenteric vessels, and/or may have a history consistent with chronic intestinal ischemia.

   a. Abdominal pain is sudden in onset and intermittent at first, progressing to continuous severe pain. Patients often describe **pain out of proportion to examination** and bloody diarrhea.

   b. Mesenteric venous thrombosis presents with varying manifestations from the asymptomatic patient to a patient in profound shock on multiple vasopressors. Patients usually complain of prolonged, generalized abdominal pain, constipation, early satiety, or nausea that develops somewhat less rapidly than with acute mesenteric arterial occlusion. These patients may have occult gastrointestinal bleeding but no frank hemorrhage.

2. **Diagnosis**

   a. Angiography of the mesenteric circulation, including lateral views of the celiac axis and SMA, remains the gold standard. However,

most centers use **CTA** especially for the diagnosis of AMI. Abdominal plain radiographs are of limited utility for evaluation of the vasculature though can be of help to evaluate for signs of intestinal ischemia including pneumatosis.

b. Other laboratory findings can include elevated white blood cell count with a left shift, persistent metabolic acidosis, and lactic acidosis in more advanced cases, but they are insensitive and nonspecific for the diagnosis of mesenteric ischemia (*Langenbecks Arch Surg.* 2011;396(1):3–11).

3. Surgical therapy

a. Patients with AMI frequently require intestinal resection, and therefore laparotomy with open revascularization is the preferred method of treatment.

(1) Assessment of bowel viability is accomplished by either diagnostic laparotomy or laparoscopy based on the gross characteristics of the bowel. The bowel is likely viable if it appears pink and if arterial pulsations are present in the adjacent mesenteric arcades. Other techniques have been described, including the use of fluorescein dye, Doppler studies, indocyanine green (with appropriate fluorescent camera), and tissue oximetry, but these are not substitutes for experienced clinical judgment.

(2) Second-look procedures within 24 to 72 hours are prudent when bowel viability is questionable. This is especially important in patients who have extensive bowel involvement and in whom resection of all questionable areas could result in short-bowel syndrome.

b. For **venous occlusion**, surgical intervention or lytic therapy rarely is helpful. Systemic anticoagulation should begin at the time of diagnosis to limit progression of the thrombotic process and be combined with bowel rest to minimize stress on the intestines.

c. Nonocclusive mesenteric ischemia (NOMI) is intestinal ischemia in the absence of thromboembolic occlusion. It occurs in patients with a low–cardiac-output state and chronic intestinal angina and is commonly identified in severely ill patients in the ICU on multiple vasopressors. Mortality is high and treatment is directed

toward improving circulatory support and increasing cardiac output. In cases in which cardiac recovery is expected, intra-arterial infusions of vasodilators (e.g., papaverine, prostaglandin E_1, nitroglycerin) have been attempted without clear benefit.

4. **Perioperative care** usually requires maximal medical support as AMI patients are frequently hemodynamically unstable and develop multiple organ system failure. Admission to the ICU, prolonged endotracheal intubation, parenteral nutrition, and broad-spectrum antibiotic therapy are typically required.

B. Chronic Mesenteric Ischemia (CMI)

1. Patients present with **intestinal angina**, which is pain usually beginning within an hour after eating and abating within 4 hours (**postprandial pain**). Such patients typically endorse significant weight loss related to the decreased intake secondary to recurrent pain ("**food fear**") and the diagnosis is suspected after a thorough history because physical findings are usually nonspecific.
2. **Surgical therapy** should be reserved for symptomatic patients. Surgical revascularization via bypass or endarterectomy remains the treatment of choice. Studies comparing surgery and endovascular approaches show higher patency in the surgical group, with no significant difference in 2-year mortality, recurrence of symptoms or imaging findings, or reintervention (*J Vasc Surg.* 2007;45(6):1162–1171).
3. **Perioperative care** is vital as food aversion can lead to severe malnutrition, and patients may require parenteral nutrition for 1 to 2 weeks before surgery as well as in the immediate postoperative period. Some patients develop a revascularization syndrome consisting of abdominal pain, tachycardia, leukocytosis, and intestinal edema. Concern about the adequacy of revascularization should prompt diagnostic imaging.
4. **Complications** include intestinal infarction, perforation, prolonged multisystem organ failure, and need for dialysis.

CHAPTER 38: THORACOABDOMINAL VASCULAR DISEASE

Multiple Choice Questions

1. **Which of the following is not associated with development of an abdominal aortic aneurysm (AAA)?**

   a. Diabetes mellitus
   b. Hypertension
   c. Hyperlipidemia
   d. Smoking
   e. Family history of AAA

2. **Which of the following is not a useful diagnostic modality for AAA?**

   a. Computed tomography (CT)
   b. Ultrasound
   c. Magnetic resonance imaging (MRI)
   d. Aortography
   e. Computed tomography angiography (CTA)

3. **Which of the following patients with AAA can be medically managed at this point in time?**

   a. A 75-year-old male with a 6.3-cm AAA
   b. A 68-year-old female with an AAA that has grown from 4.9 to 5.3 cm in the last year
   c. A 72-year-old male with a known 4.8-cm AAA and intractable pain
   d. A 70-year-old male with an AAA that has grown from 4.8 to 5.1 cm in the last year
   e. A 68-year-old female with a ruptured AAA

4. **24 hours after undergoing elective AAA repair, the ICU nurse notices purple-blackish discoloration to the toes on both feet of the patient. He has palpable pedal pulses, what is the next step in management?**

a. CT angiogram
b. Operative reexploration
c. Angioplasty
d. Expectant management
e. Guillotine amputation

5. **10 hours after undergoing elective AAA, the patient becomes tachycardic, febrile to 39°C, has required 5 L of IV fluid to maintain his blood pressure goals, and develops diarrhea. His abdomen is diffusely tender and sigmoidoscopy reveals severe necrosis of the mucosa. What is the next step?**

a. IV hydration, antibiotics, and bowel rest
b. Delayed segmental resection
c. Emergent resection of the involved segment with colostomy
d. Oral vancomycin and fecal transplant
e. Repeat sigmoidoscopy in 12 to 24 hours

6. **During elective endovascular procedure, both hypogastric arteries are inadvertently covered by the graft. All of the following are potential consequences of acute hypogastric artery occlusion EXCEPT:**

a. Buttock claudication
b. Paraplegia
c. Small bowel ischemia
d. Rectal ischemia
e. Perineal skin necrosis

7. **Following endovascular repair of a ruptured AAA in which the patient received 12 units of blood, 2 units of platelets, and 10 units of plasma, he remains anuric, with peak airway pressures of 50 mm Hg leading to difficulty with adequate oxygenation, and his abdomen is distended. What is the next step?**

a. Emergent laparotomy and decompression
b. Observation in ICU
c. Place the patient in prone positioning for oxygenation
d. Flush, and if necessary replace, the Foley catheter

e. Hypertonic saline and hyperventilation

8. **Which of the following is true regarding the structure of the aorta?**

   a. The intima is composed of smooth muscle and extracellular matrix proteins.
   b. The media is the layer most involved with atherosclerotic changes.
   c. The adventitia is composed of loose connective tissue and fibroblasts.
   d. An aneurysm is dilation of the intima and the media, but not the adventitia.
   e. The majority of degeneration in an aneurysm develops in the adventitia.

9. **All of the following are contraindications to endovascular repair of AAA EXCEPT:**

   a. A patient with 4 mm of healthy tissue between the renal arteries and the aneurysm
   b. A patient with significant thrombus at the proximal landing zone
   c. A patient with an occluded left hypogastric artery
   d. A patient with a large IMA with a meandering mesenteric artery
   e. A patient with a horseshoe kidney

10. **Which of the following is true with regard to endoleaks?**

    a. Type I endoleaks are via collateral circulation, and must be treated.
    b. Type II endoleaks are due to leaks at proximal or distal components, and may be observed.
    c. Type III endoleaks are due to inadequate seal of the graft components.
    d. Type IV endoleaks are due to neovascularization of the AAA sac.
    e. Type V endoleaks are due to porosity of the graft material.

11. **Large-scale studies comparing endovascular to open AAA repair have shown reduction in all of the following with endovascular repair EXCEPT:**

    a. Perioperative morbidity

b. Duration of hospitalization
c. Perioperative mortality
d. 4-year survival rates
e. Incisional hernia rates

12. A 78-year-old male is found to have a widened mediastinum on routine chest x-ray. A CT scan shows a 5-cm aortic aneurysm beginning distal to the left subclavian artery. Which of the following is true?

a. This aneurysm should be repaired immediately
b. Open repair is accomplished via a median sternotomy
c. Repair requires hypothermic circulatory arrest
d. In the absence of symptoms, this can safely be watched until 6 cm
e. There is no role for endovascular treatment of this aneurysm

13. A 68-year-old male presents to the ED with sudden-onset ripping chest pain radiating to his back with a systolic blood pressure of 210. He has no ECG changes, but CT angiogram shows an intimal flap beginning in the ascending aortic segment. Which is the next step in management?

a. Transesophageal echocardiography to confirm location of flap
b. Emergent open repair with conduit replacement
c. Admission to ICU with anti-impulse control
d. Endovascular coverage of intimal flap
e. Observation, as this is a uniformly fatal diagnosis

14. A 56-year-old male presents to the ED with a worsening of ripping chest pain radiating to his back. He reports the pain began 3 weeks ago, but has progressed this morning. His systolic blood pressure is 205. A CT angiogram shows an intimal flap beginning distal to the left subclavian artery. He is admitted to the ICU and his pain improves with blood pressure control. Which of the following is true?

a. This patient should be evaluated for endovascular coverage of the intimal tear
b. This patient has an acute type B dissection

c. No further intervention is warranted, as this has a low long-term mortality rate
d. This is a complicated type B dissection
e. β-Blockers should never be used in the care of this disease

15. All of the following are clinical features of patients that may be used to identify potential renovascular hypertension EXCEPT:

a. Onset in a young adult
b. Refractory to multidrug therapy
c. Accelerated onset
d. Unexplained renal impairment
e. Onset at the age of 45

16. You are called to see a 72-year-old female patient in the MICU with "abdominal pain out of proportion to examination" who is now passing bloody stools. She has heart failure due to viral myocarditis requiring significant inotropic and vasopressor agents. Due to acute kidney injury, a noncontrast CT is obtained, that shows minimal calcification of the aorta or any of the visceral branches. Which of the following is true?

a. This condition has a low mortality rate
b. These patients are best assessed with diagnostic laparoscopy and resection of viable bowel
c. Initial treatment is directed at increasing cardiac output and circulatory support
d. Open revascularization is the preferred therapy
e. Early initiation of enteral nutrition is indicated

39

Peripheral Arterial Disease

Gayan S. De Silva and Patrick J. Geraghty

INTRODUCTION

Peripheral arterial disease (PAD) is a chronic, occlusive, and inflammatory condition predominantly affecting the lower extremity. Currently affecting over 150 million people worldwide, PAD **equally affects men and women** in the developed world. The predominant etiology of occlusive disease of the lower extremities is **atherosclerotic change of the arterial intima and media**. Major risk factors for developing atherosclerosis include cigarette smoking, diabetes mellitus, dyslipidemia, hypertension, and hyperhomocysteinemia. The prevalence of PAD is generally higher in patients of age ≥70, ages 50 to 69 with a history of smoking or diabetes, ages 40 to 49 with diabetes and at least one other above-mentioned risk factor, or patients with leg symptoms suggestive of claudication either with exertion or at rest. Atherosclerotic disease is a systemic illness, and although symptomatic disease may predominate in one organ, subclinical disease, particularly of the coronary arteries, is generally present. In fact, 50% of the mortality associated with peripheral arterial reconstructions for atherosclerotic disease is cardiac in nature. Other, less common causes of occlusive disease include fibromuscular dysplasia, radiation-induced vascular injury, and the vasculitides (e.g., **Takayasu arteritis and Buerger disease**).

CLINICAL PRESENTATION

The clinical presentation of PAD is variable and dependent on the degree of atheroocclusive disease affecting the involved arteries, as well as the location of involvement. Often, patients with PAD have no complaints in the early stages of disease, but as ongoing tissue demand for oxygen and nutrients exceeds the

delivery capacity of the involved vessels, symptoms begin to develop. Most commonly, symptoms include pain related to activity (**intermittent claudication**), which resolves with rest, and advancing into **rest pain**, nonhealing wounds, and tissue loss. These latter entities encompass the severe end of the PAD spectrum known as **critical limb ischemia (CLI) or chronic limb-threatening ischemia (CLTI)**.

ACUTE ARTERIAL OCCLUSION OF THE EXTREMITY

PAD, though generally thought of as a chronic occlusive disease, can also present with symptoms of acute arterial insufficiency, which occur abruptly. The presentation generally includes the **six Ps of acute ischemia: pain, pallor, pulselessness, paresthesias, poikilothermy (cold extremity), and paralysis**. The level of occlusion may be localized by the absence of pulses and the proximal extent of coolness and sensorimotor changes. If adequate collateral circulation is not present, **irreversible changes may appear as early as 4 to 6 hours after onset**. Therefore, priority must be given to prompt restoration of blood flow.

I. ETIOLOGY

A. The most common cause of acute arterial insufficiency is embolization.

1. **Cardiac sources** account for >70% of emboli and are usually the result of mural thrombi that develop due to **cardiac aneurysms following myocardial infarction or arrhythmias** such as atrial fibrillation. Other cardiac sources of emboli include valvular heart disease, prosthetic heart valves, bacterial endocarditis, and atrial myxoma.
2. **Arterial–arterial emboli** can result from ulcerated atheroma or aneurysms, although embolization from abdominal aortic aneurysms is distinctly rare. The **blue toe syndrome** occurs in patients with microemboli from unstable proximal arterial plaques and is characterized by intact pulses and painful ischemic lesions in the distal lower extremity. Atheroemboli in the lower extremity can also occur secondary to plaque disruption by catheter-based intervention. A severely diseased distal aorta in some of these patients is evident on computed tomography (CT) scan and arteriography, and has been termed **shaggy aorta**. Upper extremity ischemia/gangrene can occur

due to emboli arising from subclavian stenosis and/or poststenotic aneurysmal dilation in **arterial thoracic outlet syndrome**. In these patients, **first rib/anomalous cervical rib** or band causes compression of subclavian artery with subsequent poststenotic dilation and mural thrombus formation.

3. **Venous–arterial emboli** (**paradoxical emboli**) can result from an **intracardiac shunt** (e.g., patent foramen ovale) or **intrapulmonary arteriovenous malformations** (e.g., Osler–Weber–Rendu syndrome).

   Occasionally, it is difficult to discern whether a patient with advanced atherosclerotic disease developed symptoms due to an acute embolus, or if the presentation is secondary to an already compromised vessel having developed acute thrombosis. This is particularly true in patients without arrhythmias or prior myocardial infarction. In this clinical scenario, the presence of contralateral pulses and the absence of a history of claudication direct suspicion toward an embolic source.

B. Direct arterial trauma is frequently obvious but may initially be occult. Arterial stenosis or occlusion may occur in a delayed fashion, after progression of an intimal flap or arterial wall hematoma. Arterial compromise can also occur in the setting of compression by **joint dislocations** (e.g., popliteal artery due to posterior knee dislocation), bone fragments (e.g., tibial plateau fracture), or compartment syndrome.

C. Other causes of acute ischemia include arterial thrombosis, aortic dissection, venous outflow occlusion, and low-flow state.

II. DIAGNOSIS AND EVALUATION

A. See Table 39-1 for the Rutherford classification of clinical categories of acute limb ischemia. If history and physical examination demonstrate clear evidence and location of embolization, **definitive therapy** can be undertaken after rapid **CT angiography (CTA)** or with intraprocedural angiography to verify clearance of emboli. If the occlusive process is thrombotic, or of an unclear etiology, then arterial imaging is indicated for procedural planning. CTA provides a wealth of anatomic detail, although delayed sequences are often needed to visualize arteries beyond the level of occlusion. Radiographically, embolic occlusions can be distinguished from thrombotic occlusions by their occurrence at

vascular bifurcations and by the **concave shadow** formed at the interface with the contrast. In general, patients with acute ischemia unrelated to trauma should be considered to have **coexistent cardiac disease**, unless proven otherwise. All patients should have an electrocardiogram and chest x-ray performed. After limb revascularization, a transesophageal echocardiogram can be useful in diagnosing a cardiac source. In patients who present with embolism, systemic anticoagulation and postoperative hypercoagulable workup are recommended (Table 39-1).

TABLE 39-1 Clinical Categories of Acute Limb Ischemia

		Clinical Findings		Doppler Signals	
Category	Prognosis	Sensory Loss	Muscle Weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
b. Immediately	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	Inaudible	Audible
III. Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

Adapted from Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg.* 1997;26(3):517–538.

B. Patients who present with penetrating trauma, long bone fractures, or joint dislocations may have vascular injuries. Duplex scan of the injured area can be useful in the diagnosis of intimal flap, pseudoaneurysm, and arterial or venous thrombi. Patients with penetrating injuries who display "hard" signs of arterial injury need urgent surgical intervention without preoperative angiography. **Hard signs** of arterial injury include the following:

1. Diminished or absent pulses distal to an injury

2. Ischemia distal to an injury

3. Visible arterial bleeding from a wound

4. A bruit at or distal to the site of injury

5. Large, expanding, or pulsatile hematomas

Soft signs of injury include the anatomic proximity of a wound to a major vessel, injury to an anatomically related nerve, unexplained hemorrhagic shock, or a moderately sized, nonexpanding hematoma.

In those with only soft signs, a careful documentation of pulses by clinical examination, and Doppler signals and pressure distal to the injury should be undertaken, along with comparison with the contralateral (uninjured) limb. A **difference of >10% to 20% in the ankle–brachial indices (ABIs) suggests the need for arterial imaging or exploration.**

III. MANAGEMENT

A. Once a diagnosis of acute arterial ischemia due to emboli or thrombi is made, heparin should be administered immediately. An IV bolus of 80 units/kg followed by an IV infusion of 18 units/kg/hr is usually sufficient to maintain a goal partial thromboplastin time (PTT) between 60 and 80 seconds.

1. **Surgical therapy,** such as embolectomy, should be performed urgently in patients with evidence of embolic acute ischemia. Once the artery is isolated, a **Fogarty catheter** is passed proximally and distally to extract the embolus and associated thrombus. In some cases, **intraoperative thrombolysis** may be necessary as distal vessels may be thrombosed beyond the reach of the Fogarty catheter. Distal patency can be documented with an **intraoperative arteriogram**. If adequate distal perfusion is not established and an angiogram demonstrates distal thrombus, the distal popliteal artery and tibial arteries may be explored via angiographic or open surgical approach. In addition, it is not uncommon for **vasospasm** to occur **following embolectomy** and direct intra-arterial infusion of 50 to 100 μg of **nitroglycerin** may resolve it. In conjunction with steerable guidewires, over-the-wire Fogarty catheters can be used to select the tibial arteries to retrieve distal thrombus. When angiographic approaches fail, popliteal artery cutdown can allow direct access to these vessels. Patch angioplasty or bypass grafting may be required if significant pre-existing arterial disease in the affected segment is discovered. Experience is gradually accumulating in the use of aspiration devices (such as the Penumbra catheter, see below) to achieve percutaneous clearance of embolic occlusions, and these tools may also be used to augment surgical embolectomy by providing a less invasive means of restoring flow to distal arterial branches.

2. **Thrombolytic therapy** and **pharmacomechanical thrombectomy** may be useful in patients with clearly viable extremities, where thrombosis is the likely underlying cause of the acute ischemia. Thrombolytic agents work best on acute processes, as opposed to chronic thrombi. Thrombolysis and follow-up angiography frequently can identify an underlying stenosis that may be treated by balloon angioplasty/stent or by surgical intervention. Commonly used thrombolytic agents, such as **alteplase or reteplase**, are instilled through an intra-arterial perfusion catheter positioned within the thrombosed vessel. These agents are also commonly used in conjunction with percutaneous mechanical thrombectomy for large clot burdens. There are several devices available, each utilizing different strategies for thrombus removal. The AngioJet thrombectomy system (Boston Scientific, MA) uses a high-pressure saline jet flow to aspirate softened thrombus, and may also be used to disperse lytic agent into the thrombus to hasten clot dissolution. The EkoSonic catheter (EKOS Corporation, WA) delivers high-frequency, low-energy ultrasound (US) in a radial fashion to enhance the penetration of lytic agents by exposing plasminogen receptor sites. This mechanism probably has less hemolytic effect than with saline pressure thrombectomy and less endothelial damage than with rotational thrombectomy, but it requires multiple sessions. Additionally, the Penumbra Indigo System (Penumbra, Alameda, CA) is a continuous aspiration mechanical thrombectomy device, which can also be used to remove emboli and thrombi from the peripheral arterial system.

B. In the setting of trauma, operative exploration should be performed in any limb that is ischemic or if arteriography demonstrates a significant intimal flap or other pathology. In the presence of coexistent neurologic or orthopedic injuries, it is prudent to reestablish arterial flow first, whether by direct repair, bypass grafting, or temporary shunting. If the decision is made to temporarily shunt, shunt patency should be assessed by handheld Doppler examination throughout the case. At the conclusion of the orthopedic repair, the arterial repair should be reexamined to ensure that it has not been disrupted and has been correctly fashioned to the final bone length. In cases of joint dislocation, reduction of the dislocation should be accomplished first because this

may alleviate the need for arterial reconstruction, though frequent vascular examinations should be performed within the first 24 hours.

1. It is essential to **obtain proximal and distal control** of the injured artery before exploring the hematoma or wound. When feasible, an end-to-end anastomosis is preferable. Often, a few centimeters of the proximal and distal artery can be mobilized proximally and distally to accomplish reapproximation. However, the uninjured leg or other potential vein harvest site should be prepared in case a conduit is required, as an **autologous graft has superior outcomes** to both PTFE and CryoVein. In the setting of significant vasospasm causing diminished or absent distal pulses or inadequate Doppler signal, a completion angiogram can assist in documenting distal flow.
2. In general, injuries to the subclavian, axillary, brachial, femoral, superficial femoral, profunda femoral, and popliteal arteries should be repaired. The radial or ulnar artery may be ligated if the other vessel is intact and the hand is well perfused. Similarly, isolated injuries to a solitary tibial artery may be ligated if one or more of the tibial arteries remain intact and the foot is well perfused through clinical examination with either palpable pulses or adequate Doppler signals.

IV. COMPLICATIONS

A. Reperfusion injury results from the formation of oxygen-free radicals that directly damage the tissue and cause white blood cell accumulation and sequestration in the microcirculation. This process prolongs the ischemic interval because it impairs adequate nutrient flow to the tissue, despite the restoration of axial blood flow. This is particularly detrimental in the case of lower extremity revascularization, if **fasciotomies** are not performed during the index intervention. If fasciotomies are not performed, and there is concern for reperfusion injury and compartment syndrome, there should be a low threshold for reoperative examination and fasciotomies to prevent muscle death and irreversible tissue damage.

B. Rhabdomyolysis following reperfusion releases the by-products of ischemic muscle, including potassium, lactic acid, myoglobin, and creatine phosphokinase. The electrolyte and pH changes that occur can trigger dangerous arrhythmias and precipitation of **myoglobin in the**

renal tubules can cause pigment nephropathy and acute renal failure. The likelihood that a patient will develop these complications relates to the duration of ischemia and the muscle mass at risk. **Aggressive hydration, diuresis, and IV infusion of bicarbonate to alkalinize the urine** are accepted methods of mitigating renal impairment secondary to rhabdomyolysis.

C. Compartment syndrome results when prolonged ischemia and delayed reperfusion cause cell membrane damage and leakage of fluid into the interstitium. Additional muscle and nerve necrosis occurs when the intracompartmental pressures exceed capillary perfusion pressure (generally >30 mm Hg). A **four-compartment fasciotomy** should be performed when there is concern about the **possibility** of developing lower leg compartment syndrome. Less commonly, thigh compartment fasciotomies may be indicated. In the upper extremity, fasciotomies of the forearm and hand may be needed to prevent development of compartment syndrome after emergent revascularization. **Fasciotomy should be routinely considered in any patient with >6 hours of acute extremity ischemia, or in the presence of combined arterial and venous injuries**.

D. Follow-up care is usually directed at treating the underlying cause of the obstruction. Patients with mural thrombi or arrhythmias require long-term anticoagulation. The in-hospital mortality rate associated with embolectomy is as high as 30%.

CHRONIC ARTERIAL AND ATHEROOCCLUSIVE DISEASE

The lower extremities are most frequently affected by chronic occlusive disease, although upper extremity disease can occur. The principal early symptom of arterial occlusive disease is **claudication**, usually described as a cramping pain or heaviness in the affected extremity that occurs after physical exertion. Claudication is relieved by rest but recurs predictably with exercise. Lower extremity occlusive disease may be subdivided into three anatomic sections on the basis of symptoms and treatment options. **Aortoiliac occlusive disease**, or "inflow disease," affects the infrarenal aorta and the common and external iliac arteries. **Femoral–popliteal occlusive disease**, or "outflow disease," affects the common femoral, superficial femoral, and popliteal arteries. Finally, **tibial–peroneal disease,** or "runoff disease," affects the vessels distal to the popliteal

artery. An algorithm for the clinical approach to claudication is shown in Figure 39-1.

I. CLINICAL PRESENTATION

A. Aortoiliac disease presents with symptoms of lower extremity claudication, usually of the hip, thigh, or buttock. It may coexist with femoral–popliteal disease, contributing to more distal symptoms as well. The symptoms usually develop gradually, although sudden worsening suggests acute thrombosis of a diseased vessel. Patients ultimately develop incapacitating claudication but not rest pain unless distal disease is also present. **Leriche syndrome (sexual impotence, buttock and leg claudication, leg musculature atrophy, trophic changes of the feet, and leg pallor)** is a constellation of symptoms that results from the gradual occlusion of the terminal aorta.

B. Patients with femoral–popliteal and tibial–peroneal disease present with claudication of the lower extremity, usually most prominent in the calves. More severe impairment of arterial flow can present as rest pain. **Rest pain** is a burning pain in the distal foot, calf, or thigh, **exacerbated by limb elevation,** and often relieved by placing the leg in a dependent position. Examination findings of the chronically ischemic extremity include the following:

1. Decreased or absent distal pulses

2. Dependent rubor

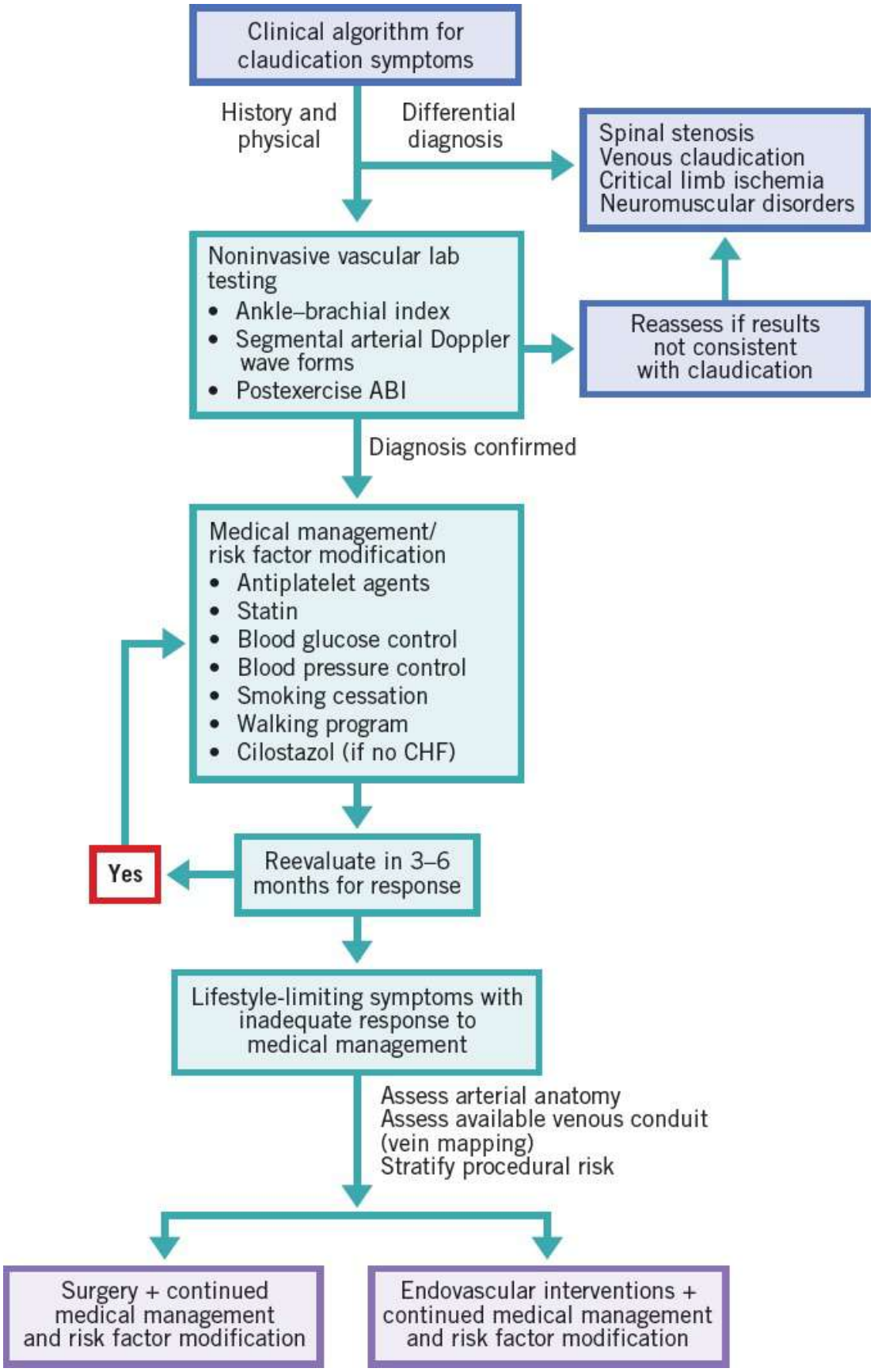
Clinical algorithm for claudication symptoms
History and physical
Differential diagnosis
Spinal stenosis
Venous claudication
Critical limb ischemia
Neuromuscular disorders
Noninvasive vascular lab testing
• Ankle–brachial index
• Segmental arterial Doppler wave forms
• Postexercise ABI
Reassess if results not consistent with claudication
Diagnosis confirmed
Medical management/ risk factor modification
• Antiplatelet agents
• Statin
• Blood glucose control
• Blood pressure control
• Smoking cessation
• Walking program
• Cilostazol (if no CHF)
Yes
Reevaluate in 3–6 months for response
Lifestyle-limiting symptoms with inadequate response to medical management
Assess arterial anatomy
Assess available venous conduit (vein mapping)
Stratify procedural risk
Surgery + continued medical management and risk factor modification
Endovascular interventions + continued medical management and risk factor modification

FIGURE 39-1 Clinical approach to claudication.

3. Trophic changes that include thickening of the nails, loss of leg hair, shiny skin, and ulceration at the tips of the toes

C. Symptomatic arterial occlusive disease of the **upper extremity** is relatively rare, but does occur in the clinical circumstances detailed below:

1. The **proximal subclavian artery is most commonly affected by atherosclerotic disease,** followed by axillary and brachial arteries. These patients typically present with arm claudication or finger–hand ischemia or necrosis. Occasionally, ulcerated plaques of the innominate or subclavian arteries can be a source of embolization to the hand.
2. Although many patients with proximal subclavian lesions are asymptomatic, **subclavian steal** can result when an occlusive subclavian artery lesion is located proximal to the origin of the vertebral artery. With exercise of the affected limb, the arm's demand for blood is supplied by retrograde flow in the ipsilateral vertebral artery, shunting blood from the **posterior cerebral circulation** and resulting in **drop attacks, ataxia, sensory loss, or diplopia**.

II. DIAGNOSIS.

Diagnosis of chronic arterial occlusive disease is concerned with determining the presence of **significant flow-limiting lesions** and distinguishing the disease from other conditions that may mimic it.

A. For patients presenting with lower extremity symptoms, it is essential to examine the femoral and distal pulses at rest and after exercise. The **absence of femoral pulses is indicative of aortoiliac disease,** although some patients with aortoiliac stenoses have palpable pulses at rest that are lost after exercise. Bruits may also be appreciated over the lower abdomen or femoral vessels. It is also important to differentiate ulcers that arise from arterial insufficiency versus those generated by venous insufficiency and neuropathy.

1. **Arterial insufficiency ulcers** are **usually painful** and have a pale appearance.
2. **Neuropathic ulcers** are **painless** and usually occur over bony prominences, particularly the plantar aspect of the metatarsophalangeal joints.

3. **Venous stasis ulcers** are located on the **distal calves and perimalleolar region (“gaiter” distribution**) and are dark and irregular in shape.

B. Segmental arterial Doppler readings with waveforms should be performed in all patients with suspected symptomatic arterial disease. **ABI,** the ratio of the systolic blood pressure in the leg to that in the arm, allows quantification of the degree of peripheral arterial flow. **In general, patients without vascular disease have an ABI of 1.0 or greater, patients with claudication have an ABI of less than 0.8, and patients with rest pain and severe ischemia have an ABI of less than 0.4**. Waveform changes help to localize the level of disease, and the severity of obstruction. Patients with history of claudication and normal resting waveforms require postexercise ABI measurements. In patients with diabetes and renal insufficiency, **calcified vessels can result in a falsely elevated ABI measurement**. Digit pressures are less affected by calcification and thus often provide a more accurate representation of arterial perfusion.

C. Digital subtraction arteriography is the gold standard for evaluating the arterial tree before planned revascularization. Typical digital subtraction arteriography of the lower extremities extends from the proximal abdomen to the toes. Noninvasive angiography using imaging modalities such as CTA and magnetic resonance angiography (MRA) has also gained widespread use. CTA produces high-resolution images of the vascular tree. However, diffuse calcifications may make interpretation of CTA images difficult. In addition, CTA does require iodinated contrast, which may adversely affect patients with renal insufficiency. **MRA** is an excellent imaging modality for assessing PAD and is useful for selecting patients who are endoluminal candidates. However, MRA may overestimate the degree of stenosis and may be inaccurate in stented arteries. Following the linkage of **nephrogenic systemic fibrosis** (NSF) to gadolinium administration in renal failure patients, alternative noncontrast MRA techniques have emerged (e.g., time-of-flight), which are being used more readily in high-volume vascular centers.

III. MANAGEMENT

A. Society for Vascular Surgery practice guidelines for atherosclerotic

occlusive disease of the lower extremities (*J Vasc Surg*. 2015;61[3 Suppl]:2S–41S) offer detailed recommendations for management of patients with PAD. With adequate control of risk factors, intermittent claudication follows a benign course in most patients. In patients presenting with claudication alone, 70% to 80% remain stable or improve and 10% to 20% worsen over the ensuing 5-year period. Only 5% to 10% of patients develop gangrene and are at risk for limb loss. Therefore, **first-line treatment for patients with claudication should emphasize risk factor modification and structured exercise therapy.**

Despite this appropriate focus on medical optimization of the claudicant, **incapacitating claudication** that jeopardizes a patient's livelihood, daily activities, or severely influences his or her quality of life may be considered for revascularization after failure of risk factor modification and exercise therapy. **CLI** is characterized by severely diminished arterial flow (**ABI <0.4, and toe pressures <50 mm Hg), ischemic rest pain, and the development of ischemic ulceration or pedal gangrene**. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System WIfI classification uses the severity of limb ischemia, wound complexity, and foot infection to estimate the likelihood of limb salvage in CLI patients (*J Vasc Surg*. 2014;59:220–234). In addition to maximal medical therapy, revascularization is indicated for symptom relief and limb preservation.

B. Medical Therapy

1. **Risk factor modification** is the most important intervention for reducing the impact of advanced atherosclerotic disease. Control of hypertension and serum glucose, cessation of smoking, management of lipid disorders, attainment of ideal body weight, and regular exercise should be the goals (*J Vasc Surg.* 2015;61[3 Suppl]:2S–41S).
2. **Lipid reduction** is imperative in patients with PAD because the majority of the morbidity associated with PAD is related to cardiac events. On the basis of the Heart Protection Study involving statins, it is recommended to keep the low-density lipoprotein level of patients with PAD <100 mg/dL, and <70 mg/dL for patients with disease in two vascular beds, to reduce the likelihood of morbidity associated with cardiac events (*J Vasc Surg*. 2007;45:645). Additional recent data suggest that all patients with symptomatic PAD should receive high-intensity **statin therapy** (*J Am Heart Assoc*.

2017;6(7):e005699).

3. **Antihypertensives** should be administered to normalize blood pressure. The Intersociety Consensus for the Management of peripheral arterial disease (TASC II, *Eur J Vasc Endovasc Surg*. 2007;33:S1–75) recommends blood pressure control to <140/90 mm Hg in all patients or <130/80 mm Hg if they also have diabetes or renal insufficiency.
4. Because many of these patients have concomitant coronary artery or cerebrovascular disease, daily **aspirin** therapy (81 or 325 mg) is indicated to reduce the risk of myocardial infarction or stroke.
   a. **Clopidogrel** is an **antiplatelet agent** that has been shown to reduce cardiac and cerebral events in patients with systemic atherosclerosis. Although rigorous proof of its utility following peripheral arterial interventions is lacking, clopidogrel is frequently prescribed following these procedures.
   b. **Cilostazol** is a **type III phosphodiesterase inhibitor** and available for treatment of claudication. Cilostazol inhibits platelet aggregation and causes vasodilation. Given at 50 or 100 mg twice daily, it increases walking distances when compared with placebo and pentoxifylline. Early studies suggest that the drug is safe in most patients, although **its use is contraindicated in those with class III or IV heart failure** due to the **toxicity of phosphodiesterase inhibitors** in these patients.

C. Preoperative care of patients with PAD includes complete arterial imaging and procedural risk stratification. Myocardial complications account for the majority of early and late deaths. The American College of Cardiology/American Heart Association Guidelines on Perioperative Cardiovascular Evaluation and Management (*Circulation*. 2014;130(24):2215–2245) offer a structured approach to the assessment and subsequent treatment of concomitant coronary artery disease.

D. Open Surgical Therapy

1. **Aortoiliac occlusive disease**
   a. **Aortobifemoral grafting** is the treatment of choice in low-risk patients with diffuse aortoiliac stenoses and occlusions. Aortobifemoral bypass may be performed via transperitoneal or retroperitoneal approach. Distal endarterectomy and/or

profundaplasty may be performed in conjunction with a bypass to improve outflow. Results are excellent, with reported patency rates of up to 95% at 5 years.

b. Femorofemoral bypass is an alternative in high-risk patients with **unilateral iliac disease**. The patency rates are lower than those achieved with aortobifemoral grafts, but may be better suited to patients who would otherwise not tolerate an extended procedure.

c. Axillobifemoral bypass provides a **less invasive option** for high-risk patients who need revascularization, or in the setting of an **infected field,** where an extra-anatomic bypass is required. This bypass avoids an intra-abdominal procedure and the need for aortic cross-clamping. Patency rates are poorer than those achieved with aortobifemoral bypass.

d. Aortoiliac endarterectomy may be considered for patients who have disease localized to the distal aorta and common iliac vessels, although its use is now uncommon. **Advantages** include the avoidance of prosthetic material and preservation of antegrade flow into the hypogastric arteries.

2. Femoral, popliteal, and tibial occlusive disease

a. In patients with **superficial femoral artery** (SFA) occlusion, a **femoral–above-knee popliteal bypass may be constructed**. In patients who have **disease below the knee, a distal bypass may be performed to the below-knee popliteal, posterior tibial, anterior tibial, or peroneal arteries**. If all tibial vessels are occluded, pedal vessels may serve as suitable outflow vessels. These grafts usually originate from the **common femoral artery** (CFA), although a more distal vessel may be used if the inflow into that vessel is unobstructed.

b. The best results are obtained with the use of **autologous vein**. Single-segment greater saphenous vein is the conduit of choice, but the lesser saphenous vein or the arm veins provide suitable alternatives. These autologous grafts can be used either in situ or reversed orientation. The advantages of the **in situ bypass** are that (1) the vein's nutrient supply is left intact and (2) the vein orientation allows for a better size match (the large end of the vein is sewn to the large CFA, and the small end is sewn to the distal vessel). The advantage of the **reversed vein bypass** is that

endothelial trauma is minimized because valve lysis is not necessary.

c. When autologous vein is not available, **polytetrafluoroethylene (PTFE) grafts** and **cryopreserved vein grafts** can be used. Patency rates for PTFE above-knee grafts approach those achieved with venous conduit, but use of PTFE for more distal bypass (below the knee) procedures is associated with substantially lower patency and is reserved for patients with CLI who lack venous conduit. An alternative technique when performing PTFE bypass is the use of a small cuff of vein (**Miller cuff**) or patch angioplasty (**Taylor patch**) at the distal anastomosis. These modifications appear to **improve prosthetic graft patency** by improving compliance match at the distal anastomosis. Cryopreserved vein graft patency also fares poorly in comparison to autologous conduit, but may prove useful when bypass is required in an infected field.

d. Endarterectomy is most commonly used to address severe stenosis or occlusion of the CFA and profunda femoris artery.

e. Amputation is reserved for patients with gangrene or persistent painful ischemia not amenable to vascular reconstruction. These patients often have severe coexistent vascular and cardiovascular disease, and the **survival rate for patients undergoing major amputations is approximately 50% at 3 years and 30% at 5 years**.

(1) The level of amputation is determined clinically. Important factors include the necessity of removing all the infected tissue and the adequacy of the blood supply to heal the amputation. A general principle is to preserve as much length of the extremity as safely possible, as this improves the patient's opportunity for rehabilitation.

(2) Digital amputations are performed for isolated gangrene and/or recalcitrant osteomyelitis.

(3) Transmetatarsal amputations (TMA) are usually performed when several toes are involved in the ischemic process or after previous single-digit amputations.

(4) Below-knee amputation (BKA) is the most common type of

amputation performed for patients with severe occlusive disease.

(5) **Above-knee amputation** (AKA) heals more easily than BKA and is useful in older patients who do not ambulate.

(6) **Hip disarticulation** is rarely performed for vascular disease.

3. **Upper extremity occlusive disease**

   a. For **proximal subclavian disease,** the choice of bypass procedure depends primarily on the patency of the ipsilateral common carotid artery.

   b. If the ipsilateral common carotid artery is patent, **carotid–subclavian bypass** is performed through a supraclavicular approach using a prosthetic graft (vein grafts are to be avoided). **Subclavian artery transposition** to ipsilateral carotid artery is an excellent alternative if anatomically feasible.

   c. If the ipsilateral carotid artery is occluded, **subclavian–subclavian bypass** may be performed. This extra-anatomic approach uses a longer-segment prosthetic graft, with reduced patency.

4. **Intraoperative anticoagulation** is employed during most vascular reconstructions. Generally, unfractionated heparin (80 to 100 units/kg) is administered IV shortly before cross-clamping and supplemented as necessary until the cross-clamps are removed. Anticoagulation can be monitored intraoperatively by following **activated clotting time (ACT) levels,** with a goal of >250 seconds. The anticoagulant effect of heparin can be reversed with protamine administration. For patients with **heparin-induced thrombocytopenia,** direct thrombin inhibitors such as **bivalirudin** are preferred.

E. Postoperative Care

1. Open aortic procedures are initially managed in the intensive care unit, due to the need for continuous monitoring and rapid intervention. Assessment of distal pulses should be done regularly. Early ambulation is encouraged.
2. For distal bypass grafts, **pulses should be assessed frequently.** Antibiotics are continued for 24 hours, or longer if infected ulcers warrant additional treatment. Early ambulation is encouraged in patients without tissue necrosis. In patients who are unable to

ambulate immediately, physical therapy can help to increase strength in the limb and prevent contracture. Sitting with the hips flexed to 90 degrees is discouraged in any patient with a femoral anastomosis. Patients should be instructed to elevate their legs while resting because this will mitigate the edema that develops in the revascularized extremity.

3. **Perioperative antithrombotic therapy** should include **aspirin** (81 to 325 mg/day) for all infrainguinal reconstructions. In patients intolerant of aspirin, clopidogrel (75 mg/day) may be substituted.
4. Postoperative oral anticoagulation has a more limited role. Owing in part to the increased risk of hemorrhage, anticoagulation with **warfarin** (INR 2 to 3) is generally limited to grafts considered to be at a high risk for thrombosis.
5. Following major amputations, weightbearing is delayed for 4 to 6 weeks. Some advocate the use of compressive wraps to aid in the maturation of the stump. In all cases, early consultation with a physical therapist and prosthetist is recommended.
6. **Surveillance of distal bypass grafts** consists of serial evaluations of vein graft patency by clinical examination and duplex US. Less frequent follow-up is necessary for aortoiliac bypasses. Detection of severe stenosis predicts impending graft failure, and such grafts should undergo arteriography and correction. Repair or revision of stenosed grafts results in higher long-term patency than repairing or replacing occluded grafts.

F. Complications

1. Early complications occur in approximately 5% to 10% of patients after aortic surgery and frequently relate to preoperative comorbid disease. Myocardial infarction, congestive heart failure, pulmonary insufficiency, and renal insufficiency are most common. Complications related directly to the aortic reconstruction include hemorrhage, embolization or thrombosis of the distal arterial tree, microembolization, ischemic colitis, ureteral injuries, impotence, paraplegia, and wound infection. Late complications include anastomotic pseudoaneurysm or graft dilation, graft limb occlusion, aortoenteric erosion or fistula, and graft infections.
2. In distal revascularizations, most of the early complications are also

related to comorbid conditions. Early graft thrombosis (within 30 days of surgery) most often results from technical errors, hypercoagulability, inadequate distal runoff, and postoperative hypotension. **Technical errors** include graft kinks, retained valve leaflets, valvulotome trauma, intimal flaps, significant residual arteriovenous fistulas, and the use of a poor-quality conduit.

G. Endovascular Options

1. Aortoiliac occlusive disease

a. Indications. Balloon angioplasty and intravascular stent placement for aortoiliac occlusive lesions produce excellent results. These procedures are indicated for symptomatic stenotic or occlusive lesions. Short-segment stenoses (less than 3 cm in length) of the common and external iliac arteries display excellent long-term patency rates when treated with angioplasty alone, or with stent placement. Angioplasty failure (defined as residual stenosis of ≥30%, residual mean translesional pressure gradient of ≥10 mm Hg, or flow-limiting dissection) is an indication for stent deployment.

b. Technique. Access for iliac artery angioplasty and stenting is generally via a femoral arterial approach. When the occlusive lesion is in the distal aorta or ostial common iliac artery, angioplasty should be performed using two balloons, one in each iliac artery and both partially projecting into the distal aorta ("**kissing balloons**"). The rationale for this technique is that lesions in proximity to the aortic bifurcation typically involve the distal aorta and both common iliac arteries. Unilateral balloon dilation may cause plaque shifting with compromise of the contralateral iliac artery lumen. Stenting may produce a more favorable result if postangioplasty dissection or lesion recoil is noted. Balloon-expandable and self-expanding stents are generally oversized 10% to 15% relative to the adjacent normal artery to ensure satisfactory stent apposition to the vessel wall. If stent deployment is required in proximity to the aortic bifurcation, "**kissing stents**" are utilized in a fashion similar to that described above.

c. Complications. Procedural complications of iliac angioplasty and stenting include arterial dissection, vessel occlusion, arterial

rupture, and distal embolization, which may result in the need for surgical intervention or amputation, as well as complications due to the puncture site, including hematoma, pseudoaneurysm, or retroperitoneal bleed.

d. Results. Immediate balloon angioplasty failure can result from elastic recoil of atherosclerotic plaque or arterial wall dissection. These complications are potentially amenable to stent placement. **Early failure is usually due to intimal hyperplasia, whereas late failure may also be caused by progressive atherosclerosis**. Iliac artery balloon angioplasty 2-year patency rates between 60% and 70% have been reported. Reports of iliac artery stenting demonstrate 4-year patency rates as high as 85%. In general, the results of angioplasty and stenting are better for common iliac artery lesions than for external iliac artery lesions, and are better for short-segment disease than for long-segment disease.

2. Infrainguinal occlusive disease

a. Indications. Balloon angioplasty and stenting of infrainguinal occlusive lesions has been widely applied for the treatment of claudication and CLI. See Figures 39-2 to 39-4 for an example of angiographic intervention for SFA occlusion. Aggressive modification of risk factors, institution of antiplatelet and statin medications, and a trial of exercise therapy are recommended prior to intervention, particularly in the setting of claudication. The Trans-Atlantic Inter-Society Consensus (TASC II) group has provided recommendations regarding the characteristics of femoropopliteal and infrapopliteal lesions that are best addressed by either endovascular or surgical therapy (Table 39-2). Short, focal stenoses (TASC A) are felt to be amenable to endovascular therapy, whereas long-segment occlusions (TASC D) are best addressed by surgical bypass.

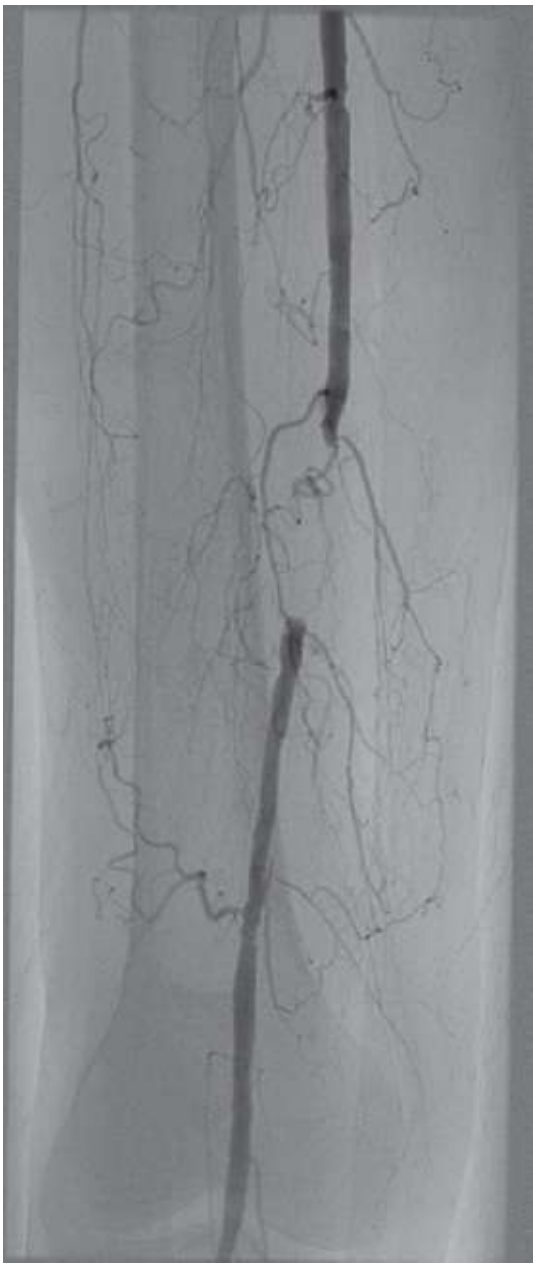

FIGURE 39-2 Superficial femoral artery occlusion prior to treatment.

b. Technique. Arterial access for infrainguinal intervention is usually accomplished via retrograde contralateral femoral artery approach or ipsilateral antegrade femoral artery approach. Retrograde tibial/pedal access is also being studied as an alternate access option. The most frequent cause of treatment failure is the inability to negotiate across the stenosis or occlusion and into the distal outflow target vessel. In general, once guidewire access to the distal target vessel has been established, technical success

rates are excellent. Hydrophilic guidewires and catheters, occlusion crossing devices, lumen reentry devices, and specialized sheaths have been developed to facilitate this process.

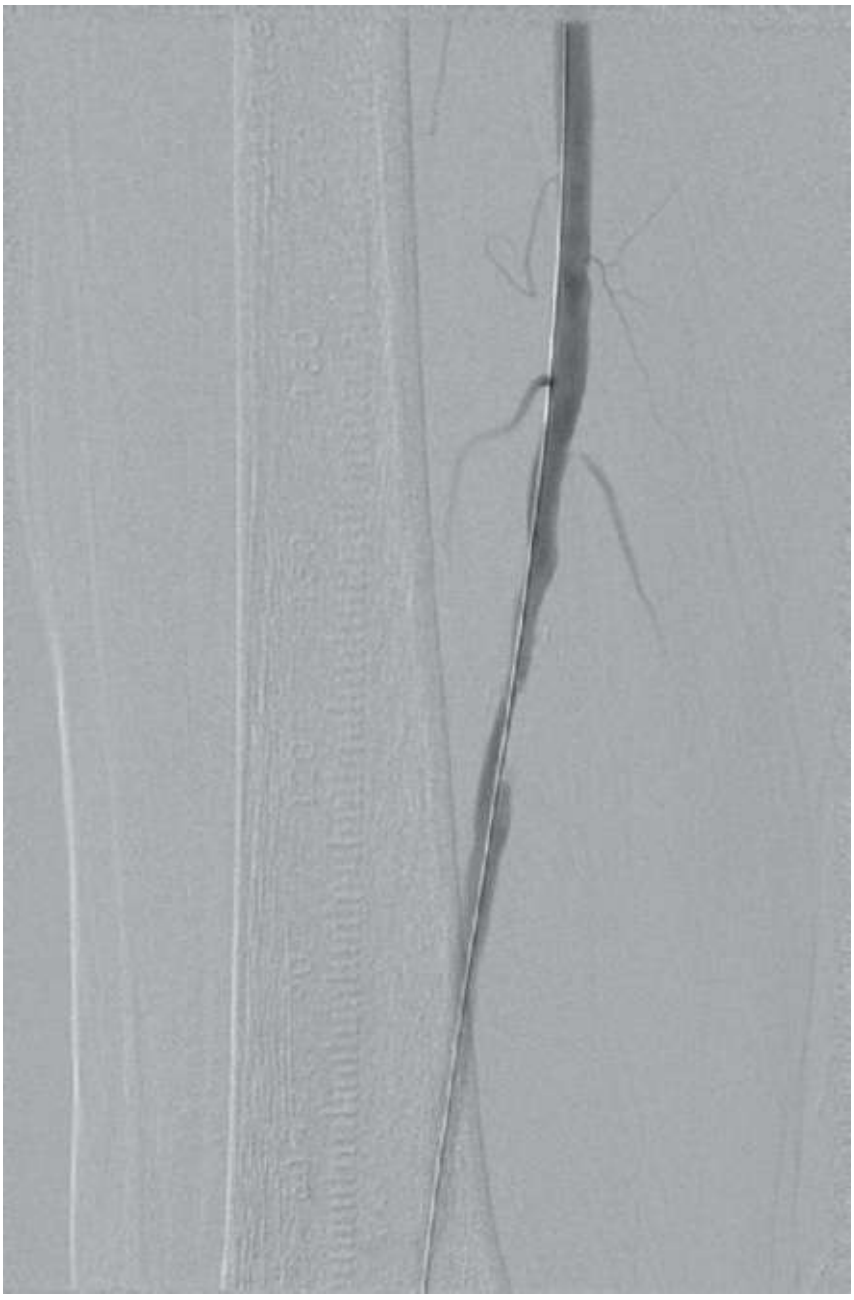

FIGURE 39-3 Recoil following balloon angioplasty.

c. Complications of infrainguinal endovascular intervention include bleeding, arterial thrombosis, vessel perforation, flow-limiting dissection, arteriovenous fistula formation, and distal

embolization. Severe complications may require surgical intervention or, rarely, amputation.

d. Results. For moderate severity lesions of the femoropopliteal distribution, the ABSOLUTE trial demonstrated that primary nitinol stenting may provide a patency advantage over plain balloon angioplasty, and that this may be sustained through 2 years of follow-up (*NEJM*. 2006;354:1879–1888). Biologic modification of the intimal hyperplastic response to endovascular intervention appears to also hold promise. The ZILVER PTX randomized controlled trial of paclitaxel-eluting nitinol stents for femoropopliteal disease has shown superior 5-year patency rates compared to angioplasty alone or bare metal stent deployment (*Circulation*. 2016;133(15):1472–1483). More recently, paclitaxel-eluting balloon angioplasty has been shown to increase 1- and 2-year patency rates for SFA intervention (*JACC Cardiovasc Interv*. 2016;9(13):1386–1392). Perhaps the most compelling data regarding endovascular versus surgical intervention have been derived from the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial from the United Kingdom (*J Vasc Surg*. 2010;51:52S–68S). Although the initial results reported from the trial were widely interpreted as demonstrating equivalency between angioplasty and bypass surgery for this patient cohort, longer-term follow-up has shown an advantage in both overall survival and amputation-free survival in those patients who underwent bypass surgery and survived beyond 2 years. Interestingly, the BASIL investigators noted that outcomes were worse for patients who underwent angioplasty followed by salvage bypass surgery, rather than a bypass-first approach. Good surgical candidates with complex anatomic lesions—in particular, those possessing good venous conduit—should be considered for surgical reconstruction. **Endovascular intervention is the preferred approach for the medically compromised patient, particularly those lacking autologous venous conduit**. Finally, hybrid open surgical/endovascular procedures are frequently utilized in the treatment of CLI. Vascular surgeons who are skilled in both open surgical reconstruction and endovascular interventions will therefore tailor

their therapeutic approach based on each patient's unique risk factors and arterial anatomy.

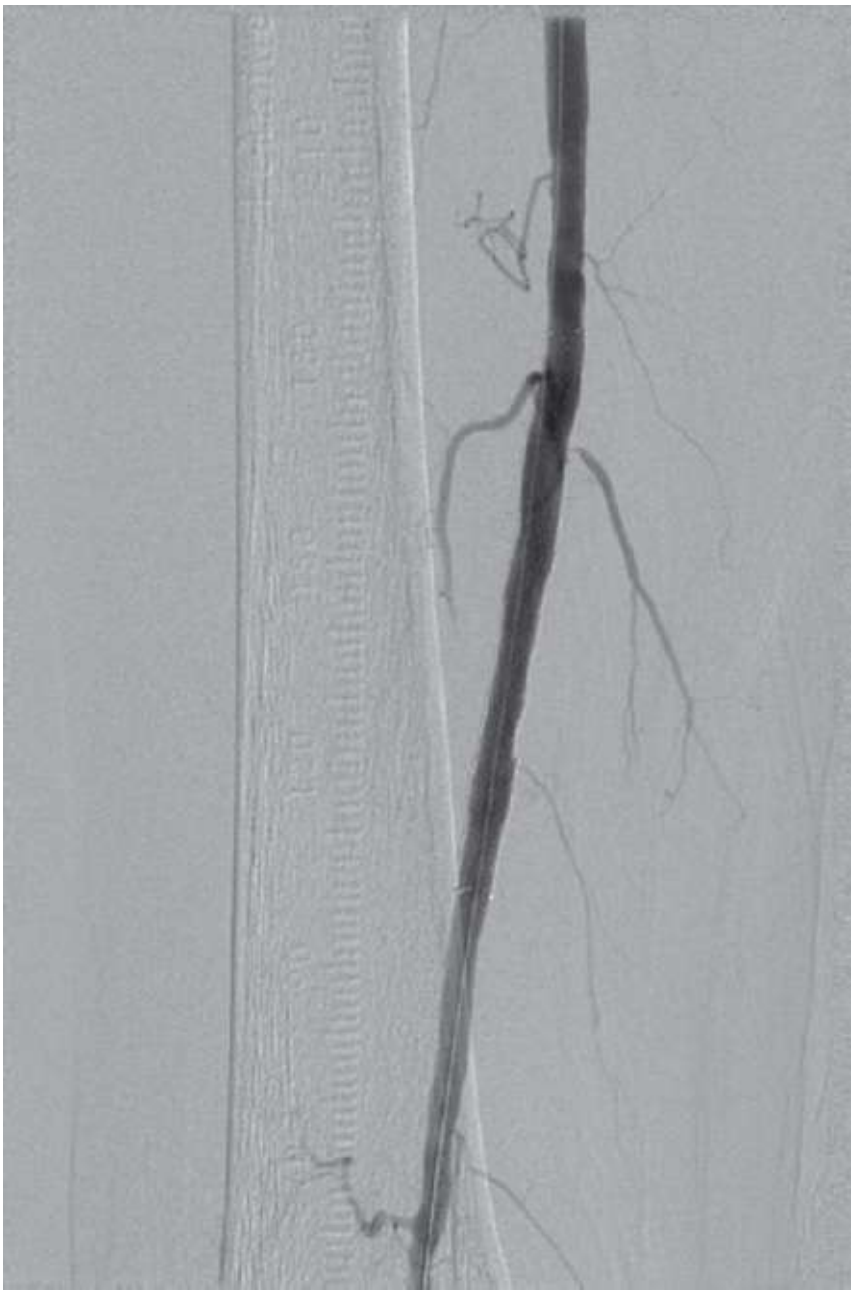

FIGURE 39-4 Completion angiogram following balloon angioplasty and stenting.

TABLE 39-2 TASC II Classification

TASC Classification	Lesion Characteristics

A	Single stenosis <10 cm Single occlusion <5 cm
B	Multiple lesions <5 cm Single or multiple lesions in the absence of continuous tibial vessels Single stenosis/occlusion <15 cm Heavily calcified occlusion <5 cm Single popliteal stenosis
C	Multiple stenoses/occlusions totaling >15 cm Recurrent stenoses/occlusions needing intervention after two prior interventions
D	Chronic total occlusions of CFA or SFA Chronic total occlusion of popliteal and proximal trifurcation vessels

CFA, common femoral artery; SFA, superficial femoral artery; TASC, The Trans-Atlantic Inter-Society Consensus.

CHAPTER 39: PERIPHERAL ARTERIAL DISEASE

Multiple Choice Questions

1. **A 47-year-old male with medical history of smoking, diabetes, hypertension, and hyperlipidemia presents to your office with right calf claudication at six blocks of ambulation. He works as a lawyer and states that the symptoms do not hinder his desired activities. ABIs are R = 0.6, L = 1.1. What is the appropriate initial management of this patient?**

   a. Begin anticoagulation with Lovenox
   b. Risk factor modification and structured exercise
   c. Schedule angiography and stent placement in the interventional suite
   d. Schedule CT angiography, and book OR for right femoral–popliteal bypass grafting
   e. Prescribe 20- to 30-mm Hg graded compression stockings

2. **You have completed a femoral embolectomy on a patient in atrial fibrillation who presented with an 18-hour history of acute-onset left leg pain accompanied by calf muscle weakness and loss of sensation. The pedal pulses are now palpable, but the calf muscle is tense. You should:**

   a. Apply Nitropaste to the foot
   b. Administer systemic thrombolytics
   c. Perform four-compartment calf fasciotomies
   d. Recommend early ambulation
   e. Begin cilostazol

3. **A 51-year-old male smoker with past medical history of type 1 diabetes mellitus, hypertension, congestive heart failure, COPD presents to you with intermittent bilateral calf claudication for 6 months and upon further evaluation his ABIs are consistent with his symptoms (0.7 bilaterally). You counsel him regarding smoking cessation, blood pressure control, and glucose control. Which of the following medications should be added to his**

management first?

a. Statin
b. Cilostazol
c. Pentoxifylline
d. Coumadin
e. Clopidogrel

4. **A 19-year-old male restrained front seat passenger is brought by EMS following a head-on motor vehicle collision. During an initial primary and secondary survey, no pulse can be felt in his left foot and there appears to be a deformity of his left knee. He is complaining of severe pain in his left knee and down to his foot. There is no obvious hematoma in the vicinity of left popliteal fossa. X-rays of the left knee are performed and reveal a posterior dislocation. What is the next step in management?**

a. Perform a CT angiogram of left lower extremity
b. Perform an angiogram of left lower extremity in the operating room
c. Perform a reduction of left knee dislocation with sedation in the ER, followed by CTA
d. Exploration of left popliteal fossa in the operating room
e. Perform formal ABIs in the vascular laboratory

40

Venous and Lymphatic Disease

Brandon D. Downing and Nanette R. Reed

I. VENOUS ANATOMY. Lower extremity venous anatomy is divided into three compartments: superficial, perforating, and deep. In general, blood flows from the superficial to the deep veins through the perforating system. In the lower extremity, the major superficial veins are the **greater saphenous vein (GSV),** formed from the union of the dorsal vein of the great toe and the dorsal venous arch; the **small saphenous vein,** formed from the joining of the dorsal vein of the fifth toe and the dorsal venous arch; and the **posterior arch vein,** also called *Leonardo vein*, beginning in the medial ankle and joining the GSV below the knee. The deep veins in the leg are named according to their paired arteries. The deep veins of the calf are typically duplicated as **venae comitantes** with numerous communicating branches. The posterior tibial and peroneal veins also communicate with the **soleal sinusoids**. In the thigh, the deep venous system includes the femoral and deep femoral veins that join approximately 4 cm below the inguinal ligament to form the **common femoral vein.** Perforating veins connect the superficial and deep systems through both direct and indirect mechanisms. Venous return from the lower extremities depends largely on compression of the deep veins by the muscles during ambulation. Flow is unidirectional due to a series of one-way valves, which prevent reflux. Failure of these valves to close leads to pooling, stasis, and congestion of veins in the lower extremities.

II. CHRONIC VENOUS INSUFFICIENCY. Chronic venous insufficiency (CVI) is a spectrum of pathology, which includes telangiectasias, varicose veins, venous ulceration, and venous claudication.

A. Pathophysiology

1. **Etiology** includes congenital, primary (i.e., cause undetermined), secondary (e.g., postthrombotic, posttraumatic).
2. **Risk factors** include obesity, tobacco use, multiparity, genetics, hormone therapy, obstruction (e.g., from adenopathy, compression, pregnancy), and history of deep venous thrombosis (DVT). DVT accounts for most secondary cases and may be responsible for a significant number of other cases because many DVTs are asymptomatic.
3. Reflux from **venous valvular incompetence** accounts for most (>80%) of chronic venous disease.
   - **a.** Valve malfunction can be inherited or acquired through sclerosis, elongation of valve cusps, or dilation of the valve annulus despite normal valve cusps.
   - **b. Varicose veins** may represent superficial venous insufficiency in the presence of competent deep and perforator systems or may be a manifestation of perforator or deep venous disease. Valvular disease below the knee appears to be more critical in the pathophysiology of severe venous disease versus disease above the knee. Incompetent perforator veins are frequently implicated when **venous ulcers** exist, but any component of the venous system, either alone or in combination, may be incompetent.

B. Differential Diagnosis

1. **Arterial disease:** present with ulcers with discrete edges and pale bases and generally at the tips of the toe, poor or absent pulses on examination, dependent rubor, pallor with elevation, and/or claudication.
2. **Lymphedema** presents with pitting edema without pigmentation and ulceration, typically involving the top of the foot, less responsive to elevation and usually requires several days to improve.
3. **Squamous cell carcinoma** can occur in patients with chronic wounds or de novo, and biopsy is required.
4. **Others:** trauma, arteriovenous malformation (AVM), orthostatic edema.

C. Nomenclature

1. **CEAP classification,** the standardized nomenclature of chronic venous disease (*J Vasc Surg*. 2004;40:1248; *Eur J Vasc Endovasc*

Surg. 1996;12:487), is based on **C**linical signs, **E**tiology, **A**natomic distribution, and **P**athophysiology (Table 40-1).

2. **Venous Clinical Severity Score (VCSS).** Developed in 2000, revised in 2010, this assesses ongoing response to therapy through 10 descriptors: pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number of active ulcers, duration of active ulceration, size of ulcer, and compressive therapy use.

D. Diagnosis is based on personal history of DVT or trauma and family history of varicose veins or CVI with complaint of lower extremity edema, aching, skin irritation, or varicose veins. Leg pain is described as a dull ache, worsening at the end of the day, and often relieved with exercise or elevation. In rare instances, individuals can experience acute, bursting pain with ambulation (**venous claudication**). Prolonged rest and leg elevation (20 minutes) are needed to obtain relief.

1. **Physical examination** findings include ankle edema, subcutaneous fibrosis, hyperpigmentation (brownish discoloration secondary to hemosiderin deposition), lipodermatosclerosis (painful inflammation of the fat layer leading to fibrosis and thickening of the skin), venous eczema, subcutaneous vein dilation (including telangiectasias [0.1 to 1 mm], reticular veins [1 to 4 mm], and varicose veins [>4 mm]), and/or ulcers (typically proximal to the medial malleolus in the **gaiter distribution).** Signs of infection should be noted, and pulse examination should be performed.

2. **Noninvasive studies**

   a. **Duplex scanning.** B-mode ultrasound (US) imaging combined with Doppler frequency shift display is used to assess venous valvular competence, obstruction, and presence of acute or chronic DVT.

TABLE 40-1 Classification of Chronic Lower Extremity Venous Disease

Classification	Definition
C	Clinical classification C_0: No visible or palpable signs of venous disease

	C_1: Telangiectasias or reticular veins C_2: Varicose veins; distinguished from reticular veins by a diameter of 3 mm or more C_3: Edema C_4: Changes in skin and subcutaneous tissue secondary to CVD C_{4a}: Pigmentation or eczema C_{4b}: Lipodermatosclerosis or atrophie blanche C_5: Healed venous ulcer C_6: Active venous ulcer *S: Symptomatic (includes aching, pain, tightness, skin irritation, heaviness, muscle cramps, and other complaints attributable to venous dysfunction)* *A: Asymptomatic*
E	Etiologic classification E_c: Congenital E_p: Primary E_s: Secondary (i.e., postthrombotic) E_n: No venous cause identified
A	Anatomic distribution A_s: Superficial veins involved A_p: Perforator veins involved A_d: Deep veins involved A_n: No venous location identified
P	Pathophysiologic dysfunction P_r: Reflux P_o: Obstruction $P_{r,o}$: Reflux and obstruction P_n: No venous pathophysiology identified

CVD, chronic venous disease.

(1) With the leg in a dependent position, cuffs are placed on the thigh, calf, and foot and inflated; the cuffs are then rapidly deflated in an attempt to create retrograde venous blood flow in segments of valvular incompetence. Competent valves generally take 0.5 to 1 second to close.

(2) Detailed mapping of valve competence of each segment of the venous system is possible with a positive predictive value of 77% for diagnosing reflux leading to severe symptoms.

b. Trendelenburg test has been largely replaced by the much more accurate duplex imaging studies.

(1) Patient's leg is elevated to drain venous blood, an elastic tourniquet is applied at the saphenofemoral junction, and the patient then stands.

(2) Rapid filling (<30 seconds) of the saphenous system from the deep system indicates perforator valve incompetence.

(3) When the tourniquet is released, additional filling of the saphenous system occurs if the saphenofemoral valve is also incompetent.

E. Nonsurgical Treatment

1. **Infected ulcers** require treatment of the infection first, usually with local wound care (topical antiseptics should be avoided, see below), damp-to-dry dressings, and oral antibiotics (severe infections require IV antibiotics). *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Pseudomonas* species are responsible for most infections.
2. Leg elevation can temporarily decrease edema and should be done before a patient is fitted for stockings or boots.
3. **Compression therapy**

a. Elastic compression stockings fitted to provide a compression gradient from **30 to 40 mm Hg** with the greatest compression at the ankle.

b. Should be worn from awakening and removed at bedtime.

c. Effective in healing ulcers but *can take months* to obtain good results. Study of 113 patients treated with initial bed rest, local wound care, and elastic compression stockings demonstrated a 93% ulcer healing rate in a mean of 5.3 months with a total recurrence of 16% for compliant patients at a mean follow-up of

30 months (*Surgery*. 1991;109:575).

d. Stockings do not correct the abnormal venous hemodynamics and must be worn after the ulcer has healed to prevent recurrence.

e. Patient compliance is the principal limiting factor.

4. Unna boots are indicated when there is skin ulceration, combining compression therapy with a zinc oxide paste to assist in wound healing and prevent further skin breakdown and are changed once or twice a week.

5. Pneumatic compression devices provide dynamic sequential compression and are used primarily in the prevention of DVT in hospitalized patients but can be used successfully to treat venous insufficiency.

6. Topical medications

a. Directed at absorbing wound drainage and avoiding desiccation of the wound, they are largely ineffective as a stand-alone therapy for venous stasis ulcers.

b. Antiseptics can be counterproductive. Hydrogen peroxide, povidone-iodine, acetic acid, and sodium hypochlorite are toxic to cultured fibroblasts and should be used for the shortest duration necessary, if at all, to control ulcer infection.

F. Surgical therapy is indicated for severe disease refractory to medical treatment and for patients who cannot comply with the lifelong regimen of compression therapy.

1. Sclerotherapy is effective in treating telangiectasias, reticular varicosities, and small varicose veins, but if saphenous reflux is present, it should be corrected first. Contraindications include arterial occlusive disease, immobility, acute thrombophlebitis, and hypersensitivity to sclerosing agents.

a. Sclerosing agents: sodium tetradecyl sulfate, sodium morrhuate, hypertonic saline, polidocanol

b. Technique

(1) Varices are marked while the patient is standing. A 25-gauge needle is used to inject 0.25 to 0.50 mL of sclerosant slowly into the lumen of larger veins. A 30-gauge needle is used for sclerosing reticular veins and telangiectasias in supine patients.

(2) Compression stockings are applied at the end of the procedure

and are worn for several days to 6 weeks. Patients should walk for 30 minutes after the procedure.

(3) Complications include cutaneous necrosis, hyperpigmentation, telangiectatic matting (new, fine, red telangiectasias), thrombophlebitis, anaphylaxis/allergic reaction, visual disturbances, and venous thromboembolism (VTE) (*J Vasc Surg*. 2010;52:939; *Dermatol Surg*. 1995;21:19).

2. Endovenous ablation of the saphenous vein

a. Effectively treats saphenous reflux and associated varicose veins with less morbidity than saphenectomy (*J Vasc Surg*. 2003;38:207), and has replaced **saphenous vein stripping,** once the gold standard for superficial venous surgery.

b. Technique. A probe is inserted into the GSV under US guidance, emitting either laser or radiofrequency energy, which coagulates and coapts the vein walls and causes complete obliteration of the lumen. Outcomes are comparable to saphenectomy (*Ann Vasc Surg*. 2010;24:360; *J Vasc Interv Radiol*. 2009;20:752; *J Vasc Surg*. 2008;47:151). Incomplete obliteration and recanalization occur in a small percentage of patients.

c. Contraindicated if saphenous vein thrombosis present.

d. Complications include skin burns, DVT, pulmonary thromboembolism, vein perforation and hematoma, paresthesias, phlebitis.

3. Subfascial endoscopic perforating vein surgery (SEPS) is associated with decreased morbidity as compared to vein stripping and has gained recognition as an alternative treatment option.

a. Technique. Small port incisions made in unaffected skin in the calf and fascia of the posterior superficial compartment. Various types of endoscopes (laparoscopic, arthroplastic, or bronchoscopic) can be used. Carbon dioxide insufflation in the subfascial space may or may not be used. A balloon expander can expand the subfascial space to improve visualization. Typically, 3 to 14 perforators are identified and ligated.

b. Most patients are discharged within 24 hours.

4. Varicose vein stab avulsion

a. Preoperatively, the patient’s varicose veins are carefully marked

with indelible ink while the patient is standing.

b. Two- to 3-mm incisions are made next to the markings. The vein is elevated from the incision with a small vein hook, divided, and avulsed from the subcutaneous tissue. This process can be repeated many times to remove large clusters of veins. The small incisions are closed with Steri-Strips and the leg is wrapped with a compression stocking for several days to weeks. This technique is often used in conjunction with other modalities to provide optimal results.

III. VENOUS THROMBOEMBOLISM

A. Epidemiology. VTE represents a significant problem, with 250,000 hospitalizations for DVT/pulmonary embolus (PE) annually. Approximately 50% to 60% of DVT episodes are asymptomatic. Of those patients with DVTs, 30% will have a symptomatic PE with a mortality of 17.5% if untreated. DVT and PE can occur in approximately 10% to 40% of general surgical patients without perioperative prophylaxis, and 40% to 60% following major orthopedic operation (*Chest*. 2008;133(6 Suppl):381S–453S; *Chest*. 2016;149:315–352).

B. Pathophysiology. DVT starts as a platelet nidus, usually on the venous valves of the calf. The thrombogenic nature of the nidus activates the clotting cascade, leading to platelet and fibrin accumulation. The fibrinolytic system is subsequently activated, with thrombus propagation if thrombogenesis predominates over thrombolysis. A thrombus can detach from the endothelium and migrate into the pulmonary system, becoming a PE. Alternatively, it can also organize and grow into the endothelium, resulting in venous incompetency and phlebitis. Thrombi localized to the calf have lesser tendency to embolize than thrombi that extend to the thigh veins (*Am Rev Respir Dis*. 1990;141:1). Approximately 20% of cases of calf DVT propagate to the thigh, and 50% of cases of thigh or proximal DVT embolize.

C. Risk factors are identified in 80% of VTE patients and include personal or family history of VTE, advanced age, malignancy and cancer therapy, pregnancy and postpartum state, endothelial injury, venous stasis, and perioperative status, as well as:

1. Oral contraceptives (OCPs) or hormonal therapy increases the odds

of DVT three to five times when compared to non–OCP-using patients. Smoking and increased age increase the risk of DVT formation for patients taking OCPs.

2. **Hypercoagulable states** occur in 25% of VTE patients. Primary hypercoagulable states are inherited conditions that can lead to abnormal endothelial cell thromboregulation. Secondary hypercoagulable states are acquired disorders in which endothelial activation by cytokines leads to an inflammatory, thrombogenic vessel wall.

D. Diagnosis of DVT

1. Diagnosis is made based on risk factors assessment, clinical presentation, and examination findings (e.g., presence of extremity pain, increased calf circumference compared to the contralateral extremity, dilation of superficial veins of the suspected extremity only, and/or calf pain on dorsiflexion of the ankle).
   a. **Phlegmasia alba dolens** represents a more severe manifestation of DVT in which the deep venous channels of the extremity are affected while sparing collateral veins and therefore maintaining some degree of venous return. Patients present with edema, pain, and white appearance (alba). Commonly seen in pregnancy or just after birth secondary to compression of left common iliac vein.
   b. **Phlegmasia cerulea dolens** occurs with extension of thrombus into the collateral venous system, resulting in limb pain and swelling, accompanied by cyanosis, a sign of arterial ischemia.
2. **Duplex US** of the femoral, popliteal, and calf trifurcation veins is highly sensitive (>90%) in detecting thrombosis of the proximal veins (femoral and popliteal) but less sensitive in detecting calf vein thrombosis.
   a. Less invasive than the reference standard of venography and more sensitive than impedance plethysmography.
   b. Approximately 2% of patients with initial normal US results have positive results on repeat tests performed 7 days later. Delayed detection rate is attributed to extension of calf vein thrombi or small, nonocclusive proximal vein thrombi. Therefore, if calf vein DVT is noted, a repeat duplex US should be obtained in 1 to 2 weeks to screen for propagation.

E. Diagnosis of PE

1. Contrast-enhanced spiral chest computed tomography (CT) is preferable to pulmonary angiography and has sensitivity of 70% to 90%.
2. Chest CT can be combined with CT angiography of pelvic and deep thigh veins to detect DVT as well as PE.
3. Radionucleotide ventilation and perfusion lung imaging (V/Q scan) has been replaced by chest CT as the initial imaging test for suspected PE. V/Q scanning is used in situations in which CT is not feasible. A V/Q scan result of "high probability" strongly suggests the presence of PE. However, more than 50% of patients have "intermediate probability" results. Because approximately 25% of these patients have PE, further evaluation or initiation of empiric treatment must be considered.
4. Pulmonary angiography, the reference test, is reserved for patients in whom diagnosis is still uncertain.

F. Prevention of Venous Thromboembolism. For anticoagulation treatments following specific procedures, please see the recent Chest Guideline for Antithrombotic Therapy for VTE Disease (*Chest*. 2016;149(2): 315–352).

1. **Low-dose unfractionated heparin (LDUH)**
   - **a.** Standard dose is 5,000 units administered subcutaneously 1 to 2 hours preoperatively and every 8 or 12 hours postoperatively (*N Engl J Med*. 1988;318:1162–1173).
   - **b.** Reduces the risk of VTE by 50% to 70% (*N Engl J Med*. 1988;318:1162–1173) and does not require laboratory monitoring. It should not be used for patients undergoing cerebral, ocular, or spinal surgery given the potential for minor bleeding.
2. **Low–molecular-weight heparin (LMWH)**
   - **a.** Enoxaparin (Lovenox) is a commonly used LMWH typically dosed at 40 mg subcutaneously daily, but some patient groups require specialized dosing.
3. Other medications such as **direct thrombin inhibitors** and **fondaparinux** represent a possible alternative to LDUH and LMWH in the prevention of VTE.
4. **Graduated compression stockings** reduce venous stasis, are

relatively inexpensive, and should be considered for all high-risk patients, even when other forms of prophylaxis are used.

a. Augments protective benefit of LDUH by nearly 75%, and is significantly more effective than LDUH alone, with DVT rates of 4% versus 15% (*Cochrane Database Syst Rev*. 2000;1:CD001484; *Br J Surg*. 1985;72:7).

b. Early use of either over-the-counter or custom-fit stockings following diagnosis of DVT results in a reduction of the incidence of postthrombotic syndromes (*Lancet*. 1997;349:759; *Ann Intern Med*. 2004;141:249).

5. Intermittent pneumatic compression of the extremities

a. Enhances blood flow in the deep veins and increases blood fibrinolytic activity through upregulation of thrombomodulin, fibrinolysin, tPA, and endothelial nitric oxide synthase expression (*Acta Anaesthesiol Scand*. 2005;49:660).

b. For patients with significant bleeding risk with anticoagulation, pneumatic compression is an effective alternative.

c. Compression devices should not be placed on an extremity with known DVT. In the case of known bilateral lower extremity DVT, devices can be placed on the upper extremity, as the upregulated agents have systemic effects.

G. Treatment of DVT

1. Lower extremity DVT

a. Acute distal lower extremity DVT (limited to calf veins such as anterior tibial, posterior tibial, or peroneal veins) does not require therapeutic anticoagulation but prophylactic anticoagulation or ambulation should be continued, and repeat duplex US performed in 7 to 10 days to screen for proximal propagation. If proximal progression into the popliteal vein or higher occurs, the patient is systemically treated with anticoagulation.

b. Acute proximal lower extremity DVT should be treated with therapeutic anticoagulation. In large randomized trials of patients with DVT, outpatient treatment with LMWH was as safe and effective as inpatient treatment with IV heparin (*J Thromb Thrombolysis*. 2005;19(3):173–181).

c. Length of treatment

(1) First provoked or unprovoked proximal lower extremity DVT: 3 months of therapeutic anticoagulation is recommended.

(2) Second unprovoked proximal lower extremity DVT and high bleeding risk: 3 months of therapeutic anticoagulation is recommended.

(3) Second unprovoked proximal lower extremity DVT and low bleeding risk: extended anticoagulant therapy is recommended (*Chest*. 2016;149(2):315–352).

d. Phlegmasia cerulea dolens and phlegmasia alba dolens require therapeutic anticoagulation but may require more aggressive treatment if the limb is threatened such as systemic thrombolytic therapy or invasive strategies including mechanical thrombectomy, angioplasty +/− stenting, catheter-directed thrombolysis, or venous bypass (*Vasc Endovasc Surg*. 2010;45:5–14).

e. Catheter-directed thrombolysis of acute DVT with or without mechanical thrombectomy has been advocated to avoid adverse sequelae of iliofemoral DVT with the goal to restore venous flow, preserve venous valve function, and eliminate the possibility of VTE.

(1) The ATTRACT trial (multicenter randomized controlled trial [RCT] comparing anticoagulation alone to pharmacomechanical thrombolysis in patients with proximal acute DVT) showed no difference in the incidence of postthrombotic syndrome between patients treated with thrombolysis and those treated with anticoagulation alone. Those treated with thrombolysis had higher risk of major bleeding (*NEJM*. 2017;377(23):2240–2252).

(2) In patients with migration of DVT resulting in severe PE and hemodynamic instability, potentially life-saving thrombolytics should be considered (*Curr Opin Anaes*. 2006;19:52; *Chest*. 2016;149(2):315–352).

2. Upper extremity DVT

If DVT involves axillary or more proximal veins, anticoagulation therapy is recommended. If the DVT is associated with a catheter, it does not need to be removed if it is functional and necessary; rather,

anticoagulation is started and continued for 3 months after removal of the catheter (*Chest*. 2016;149(2):315–352).

H. Inferior Vena Cava (IVC) Filter

1. IVC filter placement is recommended only in those patients with proven VTE with a contraindication for anticoagulation, a complication of anticoagulation, or recurrent VTE despite adequate anticoagulation.
2. No RCTs have examined the prophylactic use of IVC filters in any patient population, and several meta-analyses found no difference in the rates of PE among patients with and without prophylactic IVC filters (*J Trauma*. 2000;49:140; *J Am Coll Surg*. 1999;189:314).

TABLE 40-2 Use of Inferior Vena Cava Filters

Absolute indications (*strongly* recommended according to evidence-based guidelines)
Proven VTE with contraindication for anticoagulation.
Proven VTE with complication of anticoagulation treatment.
Recurrent VTE despite anticoagulation treatment (“failure of anticoagulation”).
Relative indications (*expanded* use; not guideline recommended)
Recurrent PE complicated by pulmonary hypertension.
Patients with DVT and limited cardiopulmonary reserve or chronic obstructive pulmonary disease.
Patients with large, free-floating iliofemoral thrombus.
Following thrombectomy, embolectomy, or thrombolysis of DVT.
High-risk trauma patients (head and spinal cord injury, pelvic or lower extremity fractures) with a contraindication for anticoagulation.
Patients with DVT who have cancer or burns, or are pregnant.
Contraindications for filter placement
Chronically thrombosed IVC.
Anatomical abnormalities preventing access to the IVC for filter placement.

VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep venous thrombosis; IVC, inferior vena cava.

3. Absolute and relative indications for caval interruption are listed in Table 40-2 (*Chest*. 2016;149(2):315–352; *Am J Med*. 2007;120:S13; *Prog Cardiovasc Dis*. 2006;49:98; *J Am Coll Surg*. 2005;201:957; *J Vasc Interv Radiol*. 2003;14:425; *Blood*. 2000;95:3669).

4. Complications related to IVC filter occur in 4% to 11% of patients. The most common complications are thrombotic in nature: insertion site thrombosis (2% to 28%); IVC thrombosis (3% to 11%); and recurrent DVT (6% to 35%). Other complications include filter migration, penetration of the IVC, filter fracture, vena caval obstruction, and guidewire entrapment. The specific types of retrievable and permanent filters are beyond the scope of this chapter, but the use of retrievable filters can reduce the incidence of thrombotic complications (*Am J Med*. 2007;120:S13).

IV. LYMPHEDEMA

A. Pathophysiology

1. Primary lymphedema

a. From congenital aplasia, hypoplasia, or hyperplasia of lymphatic vessels and nodes that causes the accumulation of a protein-rich fluid in the interstitial space. Swelling of the patient's leg initially produces pitting edema, which progresses to a nonpitting form and may lead to dermal fibrosis and disfigurement.

b. Classified according to age at presentation:

(1) Congenital primary lymphedema (present at birth) represents 10% to 15% of all cases, which can be hereditary (**Milroy disease**) or nonhereditary.

(2) Praecox (early in life) or **Meige disease** represents 70% to 80% of cases. Eighty percent to 90% of patients are female, and a single lower extremity is affected in 70% of patients. Presents during second and third decades of life, typically with localized swelling of the foot and ankle and is worsened by prolonged standing.

(3) Tarda (late in life) primary lymphedema represents 10% to 15% of cases and is seen equally in men and women and presents after the third or fourth decade of life.

2. **Secondary lymphedema** results from impaired lymphatic drainage secondary to a known cause and is the most common cause of lymphedema in the United States. Surgical or traumatic interruption of lymphatic vessels (often from an axillary or groin lymph node dissection), carcinoma, infection, VTE, and radiation are causes of secondary lymphedema. Secondary lymphedema in the context of filariasis, caused by the parasite *Wuchereria bancrofti*, represents the most common worldwide etiology of the disease.

B. Diagnosis and Clinical Presentation

1. **Symptoms.** Early lymphedema is characterized by unilateral or bilateral arm or pedal swelling that resolves overnight. With disease progression, the swelling increases and extends up the extremity, producing discomfort and thickened skin. With more advanced disease, swelling is not relieved with elevation. Significant pain is unusual. Patients with secondary lymphedema commonly present with repeated episodes of cellulitis secondary to high interstitial protein content.
2. **Physical examination.** When a lower extremity is involved, the *toes are often spared*. With advanced disease, the extremity becomes tense with **nonpitting edema,** dermal fibrosis results in skin thickening, hair loss, and generalized keratosis.
3. **Imaging studies**
   a. **Lymphoscintigraphy** is the injection of radiolabeled (technetium-99m) colloid into the web space between the patient's second and third toes or fingers. The patient's limb is exercised periodically, and images are taken of the involved extremity and the whole body. Lymphedema is seen as an abnormal accumulation of tracer or as slow tracer clearance along with the presence of lymphatic collaterals. The study has a sensitivity and specificity of 92% and 100%, respectively, in the diagnosis of lymphedema (*J Vasc Surg*. 1989;9:683).
   b. CT and MR scan are able to exclude any mass obstructing the lymphatic system. MR scan has been able to differentiate lymphedema from chronic venous edema and lipedema (excessive subcutaneous fat and fluid).
   c. Lymphangiography involves catheter placement and injection of

radiopaque dye directly into lymphatic channels; it has largely been replaced by lymphoscintigraphy and CT.

C. Differential diagnosis includes all other causes of a swollen extremity: trauma, infection, arterial disease, CVI, lipedema, neoplasm, radiation effects, and systemic diseases (e.g., right ventricular failure, myxedema, nephrosis, nephritis, protein deficiency).

D. Medical Treatment

1. Limited by the physiologic and anatomic nature of the disease. Diuretics are ineffective because of the high interstitial protein concentration. Development of fibrosis and irreversible changes in the subcutaneous tissue further limit options. The objectives of conservative treatment are to control edema, maintain healthy skin, and avoid cellulitis and lymphangitis.
2. Combination of physical therapies (CPT), consisting of a two-stage treatment program of skin care followed by the application of compression bandages, is the primary approach recommended (*Lymphology*. 2009;42:51–60; *Lymphology*. 2013;46:1–11). Sequential pneumatic compression has been shown to improve lymphedema.
3. Skin care and good hygiene are important. Topical hydrocortisone cream may be needed for eczema.
4. Cellulitis and lymphangitis should be suspected when sudden onset of pain, swelling, or erythema of the leg occurs, and IV antibiotics to cover staphylococci and beta-hemolytic streptococci as well as limb elevation and immobilization should be initiated. Warm compresses can be used for symptomatic relief. Topical antifungal cream may be needed for chronic infections.

E. Surgical Options. Only 10% of patients with lymphedema are surgical candidates, and surgery is directed at reducing limb size. Indications for operation are related to function because cosmetic deformities persist postoperatively. Results are best when performed for severely impaired movement and recurrent cellulitis. Operative management is aimed at physiologic and reductive techniques.

1. **Lymphatic transposition** includes direct (e.g., lymphovenous bypass, lymphatic grafting) and indirect (e.g., mesenteric bridge, omental flap) procedures. Lymphatic grafting is performed for upper

extremity or unilateral lower extremity lymphedema. Good results have been reported in 80% of patients (*Plast Reconstr Surg*. 1990;85:64).

2. Reductive techniques involve surgical resection of the skin and subcutaneous tissues with potential closure by a split- or full-thickness skin graft from the resected specimen or a split-thickness skin graft from an involved site. Liposuction may also be attempted.

CHAPTER 40: VENOUS AND LYMPHATIC DISEASE

Multiple Choice Questions

1. **A 72-year-old woman presents to your clinic with 3 days of right leg swelling. After completing a thorough history and physical examination you determine that a venous duplex is indicated. The results confirm your suspicion of proximal DVT. Which of the following statements is true regarding DVT?**

   a. The diagnosis of DVT is easily made by clinical examination.
   b. Only half of patients with DVT have even one identifiable risk factor.
   c. IVC filters are indicated in all patients with iliofemoral DVT.
   d. Female gender is an independent risk factor for DVT.
   e. DVT is a common complication of orthopedic surgery.

2. **A 65-year-old female returns to your wound clinic for routine follow-up of her venous ulcer. She had a venous duplex showing reflux at her saphenofemoral junction and you performed a radiofrequency ablation of her left GSV 1 year ago. Today you observe that her ulcer is well healed. What is the CEAP classification of her venous disease?**

   a. $C_5\ E_s\ A_s\ P_r$
   b. $C_5\ E_s\ A_d\ P_r$
   c. $C_{4b}\ E_s\ A_d\ P_r$
   d. $C_5\ E_p\ A_s\ P_r$
   e. $C_5\ E_p\ A_s\ P_p$

3. **You are part of a hospital task force dedicated to reducing the incidence of DVT. As part of your presentation you recommend giving all patients low-dose subcutaneous heparin TID. A hospital administrator asks you how effective this treatment is for preventing DVT as this proposal is projected to cost the hospital a million dollars/year. Low-dose unfractionated heparin reduces the risk of DVT by how much?**

a. 10% to 30%
b. 30% to 50%
c. 50% to 70%
d. 70% to 90%
e. 90% to 100%

4. **You are serving as the vascular surgery consult resident. You are called by the neurosurgery service to place an IVC filter on a patient prior to spine surgery, there is no evidence of DVT on the duplex but the patient will be nonambulatory for 7 days postop. Which of the following are complications of IVC filter placement?**

a. Filter fracture
b. Filter embolus
c. DVT
d. Hematoma
e. All of the above

5. **A 43-year-old female presents to your vascular surgery clinic for a newly diagnosed peroneal vein DVT. Patient has no symptoms associated with this DVT. What is the correct recommendation for treatment?**

a. IVC filter placement
b. Lovenox for 2 weeks with a repeat ultrasound
c. Repeat ultrasound in 7 to 10 days
d. Lovenox with bridge to Coumadin for 3 months
e. Lovenox with bridge to Coumadin for 6 months

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Vascular Access

Ali J. Khiabani and Surendra Shenoy

INTRODUCTION

Hemodialysis (HD) is the most common renal replacement therapy used to prolong survival in patients with end-stage renal disease (ESRD). As per the most recent United States Renal Data System (USRDS), on December 31, 2016, there were 726,331 ESRD patients in the United States. Approximately 63.1% of all prevalent ESRD patients were receiving HD therapy, 7.0% were treated with peritoneal dialysis (PD), and 29.6% had a functional kidney transplant (USRDS, 2018 at https://www.usrds.org/adr.aspx). HD, based on body mass and the type of dialysis prescription (intermittent, daily, nocturnal, etc.), requires **200 to 500 mL/min** of patient's blood circulation through the dialyzer. "Vascular access" (VA) is a port or site in the body capable of supporting the blood flow required for dialysis. Adequacy of HD, responsible for the well-being of the ESRD patient, is directly dependent on the function of the dialysis access.

I. INDICATIONS FOR DIALYSIS

A. Short-term HD (temporary) may be urgently indicated in patients with acute renal failure in clinical situations such as severe fluid overload; refractory hypertension; symptomatic hyperkalemia; uremia-induced gastrointestinal symptoms or bleeding, encephalopathy, seizures, or pericarditis; and intractable metabolic acidosis. Occasionally, HD may also be necessary in medication overdose or intoxication.

B. Long-term HD (permanent) is initiated in patients with stage 5 chronic kidney disease (CKD) presenting with intractable fluid overload, electrolyte imbalance, hypertension, and/or uremia.

II. TYPES OF ACCESS

A. VA. Short-term or urgent HD needs are met by placing HD catheters temporarily in the central veins. Long-term dialysis requires surgical creation of subcutaneous conduits with high-volume blood flow that can be accessed with needles to circulate blood through the dialyzer and back to the body.

B. PD Access. PD uses a silicone (Tenckhoff) catheter or polyurethane catheter, inserted with its tip placed in the most dependent part of the peritoneal cavity, the pelvis, that allows free in- and outflow of dialysate. The peritoneal membrane acts as a blood filter to exchange electrolytes and uremic toxins retained from renal failure.

III. DIALYSIS ACCESS CATHETERS

A. HD Catheters. HD catheters are large (approximately 10F to 15F) double-lumen tubes (polyurethane, silicone, or copolymers) available in varying lengths (11 to 55 cm) intended to provide immediate VA for HD. The arterial lumen (marked with a red Luer Lock) draws blood to the dialyzer, and the venous lumen (marked with a blue Luer Lock) returns blood to the body circulation. HD catheter placement should be performed under sterile conditions, using ultrasound (US) guidance. The preferred site is the right internal jugular vein because it enters the superior vena cava and the right atrium in a straight path (*Tech Vasc Interv Radiol*. 2008;11:181–185).

1. **HD catheter indications and types.** Multiple HD catheters are currently available (Tesio, DuraMax, NextStep, UltraStream, HemoSplit, Palindrome, Mahurkar, ProGuide, Vaxcel, CentrosFLO, etc.), differing in their luminal and tip design for providing uninterrupted blood flow and proper mixing of dialyzed blood with circulating blood to minimize recirculation during HD (*Tech Vasc Interven Radio*. 2008;11:186–191). They are classified as nontunneled and tunneled dialysis catheters (TDCs). Table 41-1 compares the two types.

2. **HD catheter complications**

   a. **Insertion complications** result from inadvertent injury to adjacent structures (vessels, nerves, and muscles) during needle puncture, guidewire/catheter introduction, or their misplacement. Complications are less common with the use of US guidance (*Semin Interv Radiol*. 2008;25:432–446).

b. Catheter dysfunction. Early dysfunction of HD catheters is usually due to a luminal thrombus, subtle kinks in the catheter, or malpositioning of the tip. Late dysfunctions are usually secondary to fibrin sheath formation around the catheter, tip migration, or luminal thrombosis.

TABLE 41-1 Differences Between Tunneled and Nontunneled Dialysis Catheters

Dialysis Catheter Type	Nontunneled	Tunneled
Location for placement	Bedside, dialysis unit imaging guidance optional, US is preferred	Setup with surgical sterility imaging guidance with US and/or fluroscopy
Site of skin and vein puncture	Close to each other	Separated by a subcutaneous tunnel
Cuff as infection barrier and securing point	No cuff on the catheter	Often present
Duration of use	Short term (7–21 days)	Intermediate term (months)
Management of exit site infections	Often needs catheter removal and antibiotics	Often treated with antibiotics and no catheter removal
Blood flow rates	Stiff material, smaller internal diameter, and support lower flows	Soft material, larger internal diameter, and may support higher flows

c. Catheter infection is a major cause of morbidity and mortality. HD using a TDC has a 10 times higher relative risk of infection when

compared to an arteriovenous fistula (AVF) (*Am J Infect Control*. 2004;32:155). Catheters may present with exit site or systemic infection. While most exit site infections in TDC may respond to antibiotics; cuff, tunnel, and systemic infections usually need catheter exchange or removal based on severity of symptoms during hospitalization, response to IV antibiotics, and the etiology of infection. Catheter-related bacteremia has a high rate (20% to 35%) of systemic infection that can lead to death.

d. **Central vein stenosis or thrombosis.** Catheter-related acute venous thrombosis often requires systemic anticoagulation therapy. The incidence of catheter-induced central vein stenosis varies (5% to 50%) based on site, type, and duration of access, but may be precipitated by a single-catheter insertion. Despite treatment, they frequently result in loss of VA in the ipsilateral extremity.

e. **Mortality.** Catheter-based HD has double the relative risk of mortality compared with AVF. Hence, attempts should be made to either avoid catheter usage or remove them as early as possible. Catheters should be limited to ESRD patients either awaiting permanent VA (AVF or arteriovenous graft [AVG]), with living donors awaiting transplant, or suffering acute failure of AVF, AVG, or PD catheter. They may be indicated for long-term access in patients with limited life expectancy (e.g., metastatic tumors) or when all other permanent access modalities have failed.

B. PD Catheters

1. **PD catheter indications and types.** PD catheters are used in acute (short-term) or chronic (long-term) renal failure. PD catheter designs vary in cuff, body, and tip configuration (e.g., straight with disc, weight balloon and fluting, or coiled with similar variations, swan neck presternal catheters, etc.). None have shown convincing superiority in function or complication rates (*Perit Dial Int*. 2007;27:S119–S125). Surgeons, nephrologists, or interventional radiologists (based on expertise available) can place single-cuff Tenckhoff catheters for short-term immediate use at the bedside. Long-term PD catheters (usually two cuffs) are placed surgically with or without the use of radiologic imaging, peritoneoscopy, or laparoscopy. PD is the preferred technique for children. Some relative

surgical contraindications for PD catheter placement include recent abdominal surgery, ascites, peritoneal infections, adhesions, abdominal wall hernia, significant gastroesophageal reflux, and diaphragmatic hernia.

2. PD catheter complications

a. Early complications

(1) Injury to intraperitoneal structures resulting in intestinal perforation, peritonitis, and bleeding.

(2) Dialysate infusion resulting in perineal pain, hydrothorax, exacerbation of hernia, scrotal swelling, and abdominal wall edema.

(3) Catheter dysfunction due to malposition or kink, fibrin sheath or coagulum, or constipation.

b. Late complications

(1) Catheter related: Leakage from fractures, intra-abdominal bleeding from tugging, intestinal obstruction, and intestinal perforations from erosions.

(2) Dialysate-related problems (listed above) can occasionally manifest late.

c. Infections

(1) Exit site infection or cuff extrusion can be treated with antibiotics and cuff removal in double-cuff catheters.

(2) Peritonitis is a major cause of hospitalization, PD failure, and mortality (35 deaths per 1,000 years at risk). Infections can include gram-positive bacteria, gram-negative bacteria including *Pseudomonas,* fungal infections, or tuberculous infections. First cultures should be obtained, and then empiric intraperitoneal therapy should be initiated with vancomycin or a cephalosporin to cover gram-positive bacteria and a third-generation cephalosporin or an aminoglycoside to cover gram-negative bacteria. Once cultures and sensitivities are reported, the regimen should be targeted to the specific microbe (*Perit Dial Int*. 2010;30:393). Severe, recurrent, or resistant infections require catheter removal.

IV. ARTERIOVENOUS ACCESS. An **arteriovenous access** (AVA) is a

subcutaneous conduit that can consistently deliver blood flow required to provide adequate dialysis. The increased conduit flow is a physiologic response to the permanent arteriovenous communication (anastomosis) created between a peripheral artery and a vein. Functionally, it is a complete circuit starting at the left ventricle and ending on the right atrium. The important functional components include the **inflow, needle access segment (NAS) or conduit, and outflow**. Based on the conduit used, AVA is classified as AVF or AVG.

A. Inflow. A normal (without atherosclerosis or calcification) radial artery with a diameter over **2 mm** is the most common vessel used to obtain inflow to a VA. Due to the narrow caliber, VA with distal (at the wrist) or proximal (at the elbow) radial artery inflow has lower blood flows and low risk of flow-induced distal ischemic complications (**steal syndrome**). Larger arteries such as brachial or axillary artery are also used as inflow for AVA. Any stenosis in the inflow beyond the heart up to 3 to 4 cm beyond the anastomosis (juxta-anastomotic) can lead to low VA flow. The most common site to encounter flow-limiting stenosis is the juxta-anastomotic area.

B. Conduit. For easy placement of two needles during dialysis, the NAS should be 6 mm in diameter, less than 5-mm deep from the skin surface, and have a 10-cm long straight segment. This allows two 2.6-cm needles (one to draw blood to the dialyzer and one to return blood to body circulation) to be placed 4- to 5-cm apart for proper mixing and to prevent recirculation of dialyzed blood inside the conduit. Inadequate conduits often cause needle access problems during dialysis. With the increased flow, superficial veins (usually cephalic) in the forearm or upper arm dilate in 4 to 6 weeks and serve as a good NAS. An AVA constructed by anastomosing a native vein (to develop as conduit and outflow) to a native artery (inflow) is termed an **arteriovenous fistula (AVF)** or **autogenous fistula.** When veins are not available, or fail to develop or mature as good conduits, tubes made of biocompatible materials are used as NAS. Such AVA is termed **arteriovenous graft (AVG)** or **nonautogenous access.** Expanded polytetrafluoroethylene (ePTFE) is the most common material used for AVG. Composite grafts coated with ePTFE, biologic tissue such as formaldehyde-fixed bovine arteries and veins, and cryopreserved human veins are also available.

C. Outflow. Veins beyond the NAS carrying blood flow back to the heart

are termed as the outflow for an AVA. Flow restriction caused by stenosis developing in the peripheral aspect of the outflow results in increased pressure (pulsatile access) within the NAS and causes aneurysmal dilation and/or prolonged bleeding from needle holes following dialysis. When the stenosis develops more centrally (within the chest or abdominal cavity), due to paucity of collaterals, the increased pressure is reflected in the entire venous system of the ipsilateral limb with AVA resulting in symptoms of venous hypertension. Arm swelling (edema) is the most common symptom of central venous stenosis.

D. Timing. All CKD patients likely to need dialysis should have a conscious attempt at vein preservation or "save the vein" (identify and preserve veins by minimizing venipuncture and central vein instrumentation) for VA. VA evaluation and planning requires approximately 6 months. Planning renal replacement when the patient reaches **CKD stage 4** (GFR <30 mL/min) should provide ample opportunity for VA referral and placement.

V. PREOPERATIVE EVALUATION

A. History. Assess CKD stage and the urgency of need for dialysis. Obtain demographics, previous VA attempts, and details related to arterial disease (e.g., claudication, rest pain, limb/digit loss, neuropathy), venous problems (e.g., venipunctures, catheter placements, percutaneously introduced central catheters [PICC], cardiac implantable electronic device [CIED]), and lymphatics problems (e.g., prior chest wall radiation or axillary node dissection). Evaluate comorbidities such as smoking, diabetes, cardiac problems, peripheral neuropathy, and/or thrombophilia that may contribute to VA failure.

B. Physical Examination

1. **Arterial (inflow) evaluation.** Palpate and compare strength of pulse and quality of arterial wall (radial, brachial, and axillary) bilaterally. When indicated, the femoral, popliteal, and pedal arteries should be evaluated. Bilateral blood pressures should be measured (difference >20 mm Hg is significant for proximal stenosis). The role of the **Allen test,** intended to assess the integrity of palmar circulation, is not certain for end-to-side VA placement. Scars from previous surgery and catheters should be noted.

2. **Venous (outflow) evaluation.** Using vein dilation techniques (e.g., tourniquets, warmth, tapping, use of gravity) is critical for peripheral vein evaluation. Presence of edema, unequal extremities, and/or chest and shoulder collaterals may suggest central venous stenosis. Patency and continuity of the vein can be assessed by eliciting fluid thrill.

C. Color Doppler duplex ultrasound scanning (CDDUS) should always complement clinical examination. Best results from US vessel mapping are obtained when the operating surgeon evaluates the scan in real time. CDDUS provides both functional (distensibility, flow pattern, and volumes) and structural evaluation of the peripheral arteries and veins (superficial and deep). It is not very reliable in evaluation of central veins.

D. Diagnostic Imaging

1. **Contrast venography** is the gold standard for determining the patency (luminal dimension) and adequacy of central venous anatomy. Peripheral vein visualization is limited to downstream tributaries receiving contrast from the distal peripheral vein injection site.
2. **Arteriography** remains the gold standard for the evaluation of a suspected arterial inflow stenosis or occlusion.
3. **Magnetic resonance angiography (MRA)** or **computed tomography arteriography (CTA)** may be used to evaluate larger veins and arterial run-off.

E. Laboratory Studies. Hyperkalemia and acidosis are the most common electrolyte abnormalities seen in ESRD patients. Testing (on the day of surgery) should include hemoglobin, serum potassium, and glucose levels to avoid possible procedural or anesthesia-related complications.

VI. ARTERIOVENOUS FISTULAS. AVF is the preferred access, as once it is functional, it has superior longevity, patency, and resistance to infections requiring minimum interventions. Disadvantages of AVF include wide variation in maturation failure (13% to 58%), duration for maturation (4 weeks to 4 months), and need for additional procedures to help maturation (∼40%). The National Kidney Foundation, Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) suggests a goal of 65% fistula prevalence. In the United States, following the initiation of “fistula first” initiative, the

prevalence of AVF has steadily increased to 63.5%.

A. AVF Locations and Planning. There are multiple established locations (Fig. 41-1) in the upper limb where the anatomy may lend itself to AV anastomosis. When suitable, the nondominant limb is used first. Using distal sites has less risk of ischemic complication, and allows proximal veins to dilate for future use as secondary options. Using isolated segments of superficial veins preserves proximal veins for future use.

B. Surgical Procedure. All AVF procedures are generally performed on an outpatient basis, using conscious sedation and local anesthetics or regional blocks. The end of a superficial vein is anastomosed to the side of the artery using conventional or piggyback straight line onlay technique (pSLOT) (*J Vasc Surg*. 2012;55:274–280) that provides an opportunity to tailor anastomotic length. Anastomotic length in conventional techniques is often dictated by the size of the vessels used and need for spatulation. Computational modeling suggests that a **diameter of 3 mm** is sufficient to provide flows necessary for AVF. Larger anastomotic diameters in larger-inflow arteries (e.g., brachial) have a higher propensity for high flow-related distal ischemia (steal syndrome). **Endovascular fistula creation:** Two available devices provide an opportunity to create fistulous communication between the proximal radial or ulnar artery and their venae comitantes. To direct the blood to the superficial venous system, the procedure requires simultaneous or subsequent procedures such as angioplasty coil embolization of multiple superficial and deep veins. Long-term outcome of such interventions at the elbow location is uncertain. The role of this procedure in AVF planning algorithm is currently uncertain.

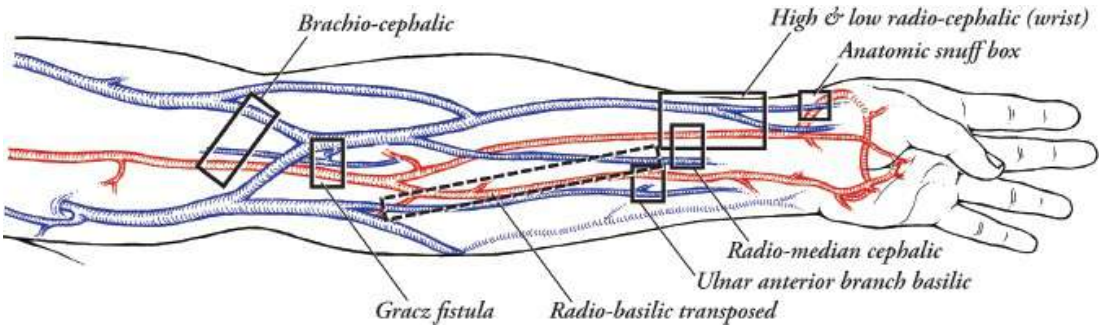


FIGURE 41-1 Possible sites of arteriovenous anastomosis in the upper extremity. (Reprinted from Shenoy S. Surgical anatomy of upper arm: what is needed for AVF planning. *J Vasc Access*. 2009;10(4):223–232, with permission of the publisher.)

C. Postoperative Evaluation. Early assessment (7 to 10 days) is necessary to evaluate the surgical wound and fistula patency, and detect any distal vascular or neurologic problems. It also provides an opportunity to further evaluate early postoperative problems that may interfere with maturation. A **maturation evaluation** (assess inflow, conduit, and outflow) should be performed between 4 and 6 weeks postoperatively using clinical evaluation and CDDUS. Any problems detected should be further evaluated. AVF meeting maturation criteria can then be accessed. Fistulae that have good inflow but deep and not accessible outflow veins need superficialization (Vascular access: Principle and Practice, 5th ed. Williams & Wilkins. 2010:1996–2005). Occasionally, fistulae may need a few additional weeks to mature.

VII. ARTERIOVENOUS GRAFTS.

AVGs are conduits (anastomosed to an artery to obtain inflow and a vein for outflow) placed in a subdermal location to provide NAS for dialysis. Based on the configuration of the conduit, they are termed loop or straight grafts. The graft segment receiving arterial inflow, termed arterial limb, provides blood to the dialysis circuit. The graft segment delivering dialyzed blood into the outflow vein is termed the venous limb.

A. AVG Locations and Planning. The proximal radial, brachial, and axillary arteries usually provide graft inflow. Since patients requiring AVG often lack sufficient superficial venous anatomy for AVF, the venae comitantes or the deep veins of the upper arm (basilic, brachial, or axillary) provide the outflow for AVG. Distal ischemia becomes more of an issue when larger vessels are used for inflow in AVG. They can also be placed in the thigh using femoral artery and femoral or saphenous veins, but lower extremity grafts have higher infection risk.

B. Surgical Procedure. AVGs are placed under local anesthesia with conscious sedation. Prophylactic antibiotics (e.g., second-generation cephalosporins) are commonly administered immediately prior to the surgery.

C. Postoperative Evaluation. While conventional AVGs need good tissue incorporation prior to cannulation (3 to 6 weeks), newer composite graft materials permit early cannulation when indicated. A standard 6-mm caliber graft, placed in a subdermal location, and with rigid walls make graft cannulation easier than many AVF. Once placed, AVG are more

predictably available for dialysis; however, they are prone to repeated thrombosis requiring a significantly higher number of interventions and have poor longevity relative to a well-matured AVF.

VIII. ARTERIOVENOUS ACCESS PLANNING. The goal of clinical evaluation is to plan a sequence of options to provide VA throughout the life span of the ESRD patient. Access planning should take into consideration the life expectancy of the esrd patient, renal function at the time of referral (CKD 4 or 5 or already on HD), and the available access options based on clinical and US evaluation. Based on these factors, the surgeon should plan to create a VA that has the longest durability, needing the least interventions, in a timely fashion, without jeopardizing future access options (*J Vasc Access*. 2014;15:S1–S5). When the anatomy is suitable, AVF is the preferred access. AVG should be considered when AVF is not an option or is not able to provide a timely access.

IX. COMPLICATIONS OF ARTERIOVENOUS ACCESS. VA dysfunction is a major cause of morbidity and mortality in ESRD. Stenosis (responsible for over 90% of VA dysfunctions) can present as thrombosis, infection, and aneurysm. NKF-KDOQI guidelines recommend prospective monitoring and surveillance using physical examination, US evaluation of flow, and assessment of dialysis adequacy to help detect access dysfunction. Interventions guided by CDDUS, angiography imaging, and/or surgical procedures are used to prolong access patency.

A. Stenosis. The functional impact of stenoses depend on their location, diameter relative to the inflow volume, and pressure (*J Vasc Acc*. 2014;15: 409–414). Development of venous neointimal hyperplasia (VNH), the cause for luminal narrowing, is common in areas of outflow (e.g., graft vein anastomosis of AVG and juxta-anastomotic venous stenosis of AVF) experiencing hemodynamic stress resulting from blood flow increase. Balloon angioplasty, using CDDUS or contrast angiography, prior to development of thrombosis, helps improve access patency and delay failure. Surgical venoplasty and vascular stents are also used based on indications or when angioplasty fails.

B. Thrombosis. Seen early after AVA placement, this is attributed to flow interruption due to technical factors, inflammatory narrowing of outflow veins, pre-existing vein occlusions, or kinked grafts. Occasionally,

patient-related factors such as thrombophilia and hypotension may be responsible. Early thrombosis of AVF often results in loss of the access site. AVG with early thrombosis may be salvaged by surgical or radiologic image-guided thrombectomy. Late thrombosis both in AVG and AVF is mostly due to development of stenosis in the circuit. They are salvaged by thrombectomy and dilation of stenotic lesions using surgical or interventional means.

C. Infection. Infections in AVA are caused by cutaneous flora (commonly *Staphylococcus* species) contamination, mostly through the needle access sites, presenting as skin ulceration, infections in chronic thrombi within aneurysms, or seeding of graft material. Management of infection depends on severity and presentation. Most graft infections result in removal of the graft and loss of the access site. Focal infections may be salvaged with resection of the infected portion and reconstruction with a bypass graft. Most AVF infections are treated with antibiotics, with or without surgical intervention.

D. Aneurysms and Pseudoaneurysms. These develop secondary to loss of AVG integrity, repeated needle puncture, and extravasation of blood which is walled off by surrounding tissue (pseudoaneurysms). AVF aneurysms are often true dilations of the vein developing over time due to stretch on the healing puncture site from the pressure within. Aneurysms can develop chronic thrombi resulting in access difficulty. They may also be at risk of rupture and bleeding due to thinning of the overlying skin. In such situations, both AVG and AVF aneurysms can be electively repaired.

E. "Steal" Syndrome. Increased blood flow in all AV accesses divert or "steal" a fraction of blood from the distal circulation which is usually well tolerated by the distal extremity. In 1% to 4% of patients (mainly diabetics, those with underlying neuropathy, and vascular disease) this may precipitate ischemic pain, worsening neuropathy, ulceration, or gangrene (*Ann Vasc Surg*. 2000;14(2):138–144). Mild symptoms such as subjective coolness and paresthesias without sensory or motor loss may be managed expectantly with increasing exercise tolerance. Failure to improve or worsening symptoms require further evaluation. Reduction of AVA flow may improve symptoms due to high VA flows. Symptomatic patients with low AVA flows may benefit from procedures that enhance distal perfusion. Severe ischemia requires immediate

evaluation and management including access ligation to avoid irreversible nerve injury.

F. Venous Hypertension. Venous hypertension caused by central vein stenosis manifests as edema, skin discoloration, and/or hyperpigmentation in the affected limb. Management options include venoplasty of the stenosis, stent graft repair, or surgical provision of improved outflow drainage.

G. Congestive Heart Failure (CHF). High-volume flow, often resulting from large artery-based AVA, can occasionally precipitate CHF. This is more common in patients with underlying heart problems or pre-existing fluid overload. Based on the situation, this may necessitate flow reduction or access ligation.

CHAPTER 41: VASCULAR ACCESS

Multiple Choice Questions

1. **A 43-year-old male underwent brachiocephalic AVF creation 4 months ago. What is the minimum flow rate for adequate hemodialysis?**

   a. 100 to 200 mL/min
   b. 200 to 500 mL/min
   c. 500 to 700 mL/min
   d. 800 to 1,000 mL/min
   e. 1,000 to 1,200 mL/min

2. **A 56-year-old female underwent left upper extremity AVG placement 3 years ago. She now presents to your office stating that the dialysis nurses have been having "issue with the flow." What is the most common cause of AVG dysfunction?**

   a. Infection
   b. Thrombosis
   c. Stenosis
   d. Maturation failure
   e. Pseudoaneurysm

3. **A 35-year-old male with ESRD and no prior abdominal surgery is inquiring about peritoneal dialysis. What is the most common reason for abandoning peritoneal dialysis for hemodialysis?**

   a. Inconvenience
   b. Hydrothorax
   c. Bleeding
   d. Peritonitis
   e. Surgical site infection

4. **A 48-year-old male with ESRD has been on peritoneal dialysis for the past 2 years. He now presents with abdominal pain and fever. On examination, his HR is 120, temperature 102.3°F, and abdomen is diffusely tender. What is an acceptable initial empiric**

antibiotic regimen?

a. Oral vancomycin and ceftriaxone
b. Intraperitoneal cefazolin and gentamicin
c. Intraperitoneal vancomycin and metronidazole
d. Intraperitoneal cefazolin and vancomycin
e. Oral metronidazole

5. **A 63-year-old male underwent left upper extremity arteriovenous graft placement 7 months ago. He now presents to your office stating that the dialysis nurses have been having “issue with the flow.” What is the most common site of flow-limiting stenosis in AV fistulae?**

a. Central vein
b. Proximal artery
c. Juxta-anastomotic area
d. Previous central line site
e. Midportion of the fistula

42 Pediatric Surgery

Elisabeth K. Wynne and Brad W. Warner

INTRODUCTION

Care of pediatric surgical patients presents unique challenges for the general surgeon. A thorough understanding of pre- and postnatal development, nutritional needs, and pathophysiology is essential for successfully managing such patients.

I. FLUIDS AND NUTRITION

A. Fluid Requirements. Normal daily fluid requirements of children are higher than those of adults per unit of body weight due to greater insensible and urinary losses. Infants have a particularly high ratio of body surface area to volume and a limited ability to concentrate urine due to immature renal function. In addition, total body water is a higher percentage of body weight (75% in children vs. 60% in adults). Postoperative fluid replacement can be calculated using the "4-2-1" rule and should be adjusted to support hemodynamic stability and urine output between 1 and 2 mL/kg/hr (Table 42-1).

1. Total body weight is a surrogate for total blood volume, which is approximately 80 mL/kg. Isotonic fluid boluses should be in a volume of 10 to 20 mL/kg.

2. Initial transfusion of packed red blood cells is typically 10 mL/kg.

B. Nutrition. Nutritional intake for infants and children must carefully account for the needs for both growth and maintenance. Calculations of daily nutritional needs are usually based on calories per kilogram body weight.

1. Parenteral nutrition. Several surgical conditions, particularly neonatal gastrointestinal anomalies, require the surgeon to possess a

basic understanding of nutritional values and titration of TPN (Table 42-2).

a. Common nutritional values in pediatric surgery:

(1) Newborn enteral caloric requirements are 100 to 120 kcal/kg/day, while parenteral are 90 to 100 kcal/kg/day.

(2) Daily caloric needs decrease throughout childhood to adult values of roughly 25 to 30 kcal/kg/day (Table 42-3).

(3) A newborn is expected to gain weight at about 15 to 30 g/day.

(4) Most enteral infant formulas and breast milk contain ~20 kcal/oz.

II. NEONATAL SURGICAL CONDITIONS

A. Tracheoesophageal Malformations. Tracheoesophageal malformations describe a spectrum of anomalies including esophageal atresia (EA) alone or as a component of a tracheoesophageal fistula (TEF) (Fig. 42-1). The incidence of these disorders is 3 in 10,000 births, with a slight male predominance.

TABLE 42-1 Postoperative Fluid Replacement

Weight (kg)	Fluids (mL/kg/hr)
0–10	+4
11–20	+2
>20	+1

1. Diagnosis

a. Clinical examination. Suspicion should be raised for EA/TEF in the neonatal patient with difficulty clearing secretions, regurgitation of saliva, or respiratory difficulty during feeds. The classic clinical finding in EA/TEF is inability to pass an oro- or nasogastric tube.

b. Imaging. Visualization of a coiled orogastric tube in the upper chest on plain radiograph implies EA (Fig. 42-2), and associated presence of gas in the GI tract confirms a distal communication

between the respiratory and GI systems (TEF). Plain imaging should also be reviewed with concern for aspiration of feeds and secretions. Contrast studies are rarely necessary to visualize the level of EA and/or TEF, and are associated with risk for aspiration.

TABLE 42-2 Components of Parenteral Nutrition and Titration in Neonates[a,b]

	Caloric Density (kcal/g)	Daily Calories (%)	Starting Value	Daily Titration	Goal
Carbohydrate	3.4	60	5.5 mg/kg/min	2–3 mg/kg/min	12–14 mg/kg/min
Fat	4	30	1 g/kg/day	1 g/kg/day	3 g/kg/day
Protein	9	10	2.5 g/kg/day	0.5–1 g/kg/day	Term infant: 3 g/kg/day Preterm infant: 3.4–4 g/kg/day

[a]Please note that starter TPN is indicated when neonates are <1,500 g or <32 weeks. This helps promote an anabolic state after withdrawal of placental nutrients and protein and aids in glucose utilization, overall improving neurodevelopment.

[b]Addition of insulin is not routine in pediatric TPN infusions, as exogenous insulin-naive cells are particularly sensitive to its effects and risk hypoglycemia. However, blood glucose should be monitored to prevent seizures and impaired neurodevelopment from hypoglycemia and osmotic diuresis with possible resultant intraventricular hemorrhage in the setting from hyperglycemia.

TABLE 42-3 Daily Caloric Needs in Children

Age (yrs)	REE (kcal/kg/day)	Average (kcal/kg/day)
<36 wks	63	120

0–0.5	53	108
0.5–1	56	98
1–3	57	102
4–6	48	90
7–10	40	70
11–14	32	55
15–18	27	45

REE, resting energy expenditure.

2. **Workup.** Up to two-thirds of EA/TEF patients have associated anomalies. Physical examination and imaging (plain film/ultrasound) should be used to search for VACTERL anomalies (*V*ertebral, *A*norectal, *C*ardiac, *T*racheal, *E*sophageal, *R*enal, and *L*imb).
3. **Management**
   a. **Preoperative management** should include decompression of the proximal esophageal pouch along with elevation of the head of the bed to 30 degrees to reduce the risk of aspiration from reflux of gastric contents through the TEF. Ventilation may prove challenging in the presence of a TEF, as positive pressure can be directed through the TEF into the GI system, resulting in increased abdominal distention and pressure. Passage of an endotracheal tube beyond the fistula, right mainstem intubation, or high-frequency oscillatory ventilation may be necessary to appropriately ventilate the patient.
   b. **Operative approach** is typically determined by the side of the aortic arch. A TEF with a normal left-sided aortic arch is approached through a right fourth intercostal space, retropleural thoracotomy. The fistula is ligated, and the proximal esophageal stump is mobilized in an attempt to create a tension-free primary anastomosis. Pure EA without TEF is typically associated with a long gap, and a gastrostomy is the usual first procedure. Later, long-gap EA can be reconstructed with a variety of techniques

including lengthening myotomy, colonic interposition, gastric pull-up, or delayed repair after a period of growth or traction (the Foker process). An isolated TEF without EA is often more proximal and can be approached via a cervical incision.

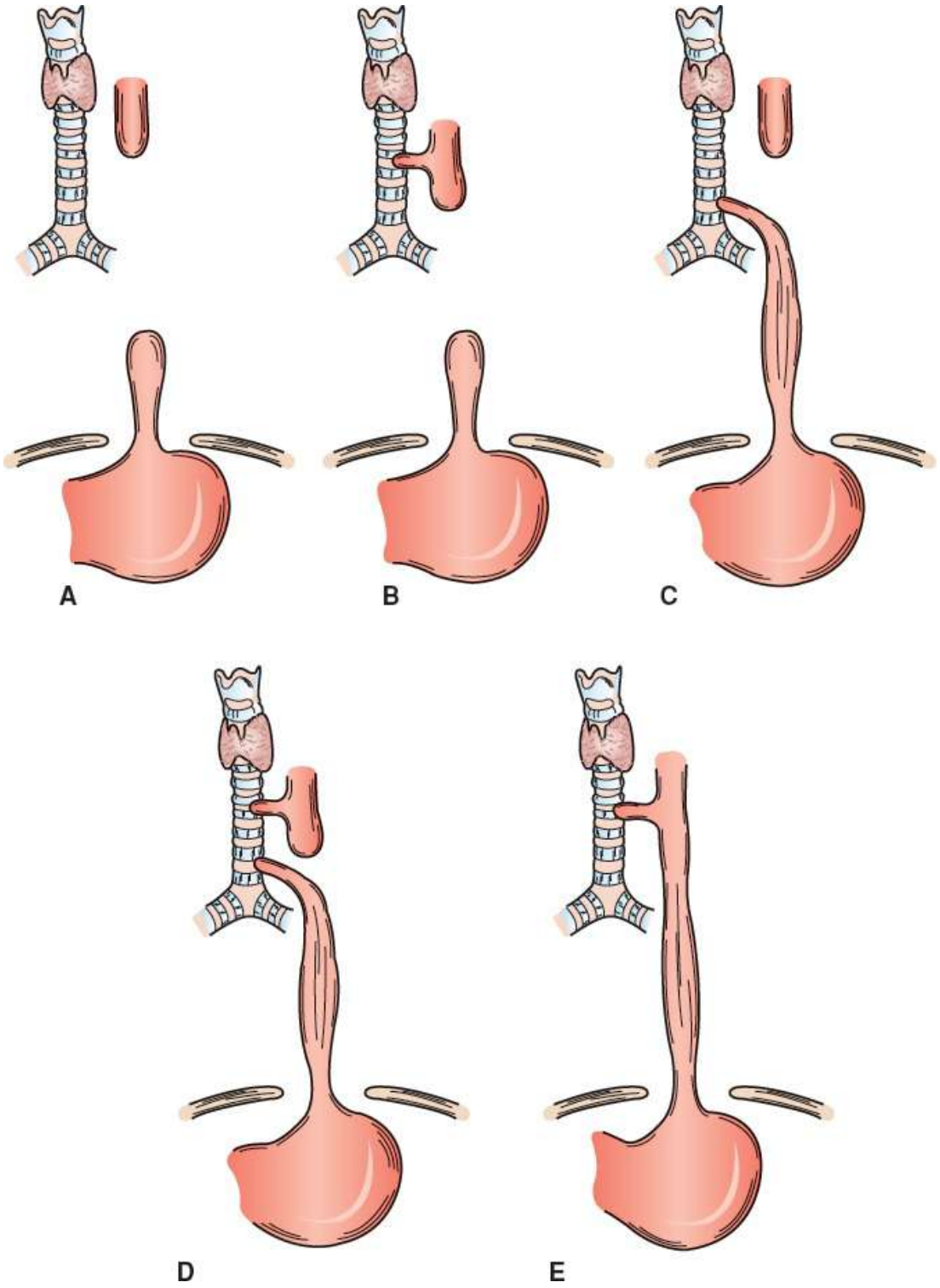


FIGURE 42-1 Variants of TEF. **A:** Pure esophageal atresia without fistula (5% to 7% of cases). **B:** Proximal fistula and distal pouch (<1% of cases). **C:** Proximal pouch with distal fistula (85% to 90% of cases). **D:** Atresia with proximal and distal fistulas (<1% of cases). **E:** Fistula without atresia ("H type") (2% to 6% occurrence).

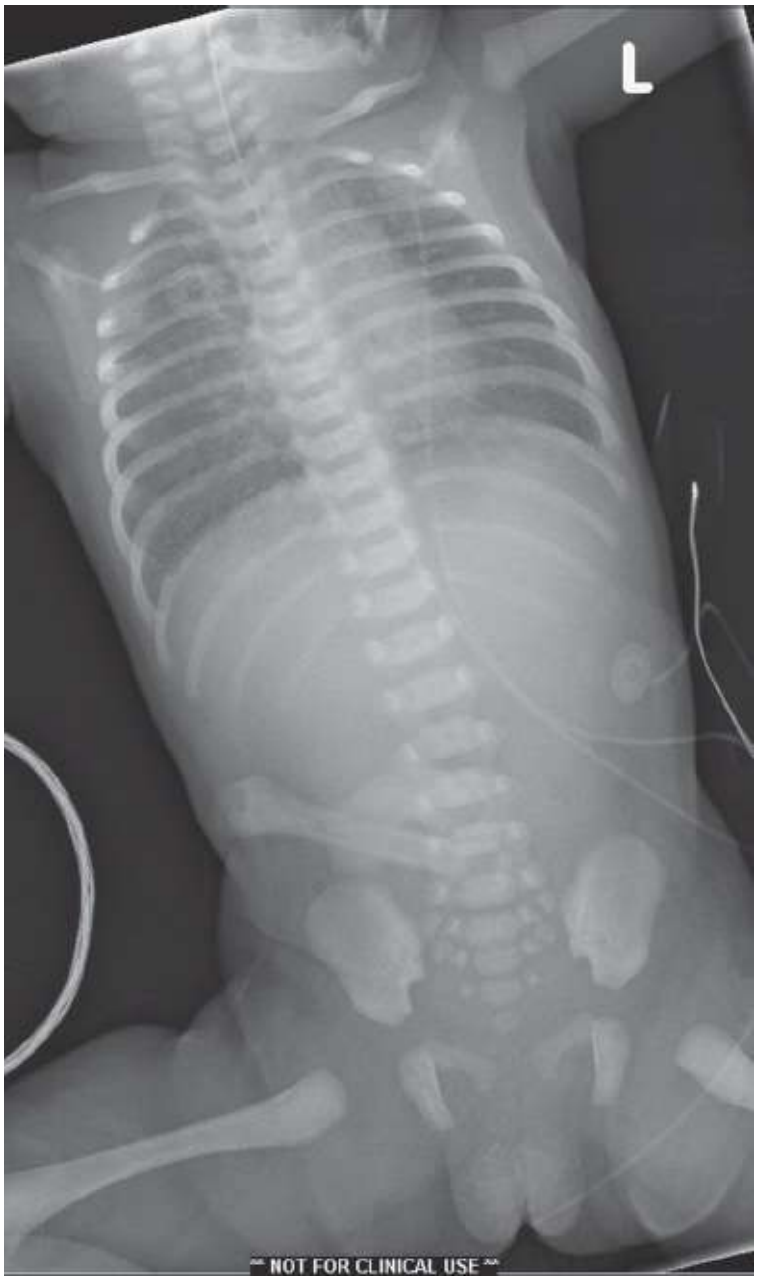


FIGURE 42-2 Radiographic findings of esophageal atresia. Note the orogastric tube ending in upper chest and the absence of bowel gas, suggesting pure esophageal atresia without any communication between the airway and gastrointestinal tract.

B. Congenital Diaphragmatic Hernia (CDH). CDH has an incidence of 1 in every 3,000 live births and an equal male to female distribution.

CDH develops as a result of incomplete diaphragm development at 8 weeks of gestation. Abdominal contents herniate into the chest, resulting in lung compression and subsequent hypoplasia. The pulmonary vasculature develops increased tone in the muscular arterioles, which predisposes to pulmonary hypertension and vasospasm. The majority (80% to 90%) of hernias are posterolateral (Bochdalek), with the remainder presenting anteriorly (Morgagni). Approximately 90% of hernias occur on the left.

1. **Diagnosis** of CDH is frequently made during routine prenatal screening ultrasounds. Prenatal diagnosis should set in motion a team of critical care neonatologists and surgeons available for respiratory management at the time of birth. For patients not diagnosed prenatally, significant respiratory distress including tachypnea, cyanosis, and retractions should raise immediate concern. Asymmetric chest wall diameter and a scaphoid abdomen as a result of abdominal contents herniating into the chest are additional clinical clues. A second set of patients will present after an initial "honeymoon" phase of several hours that can occur before signs of pulmonary hypertension and hypoxemia present. Finally, less than 20% of cases present after the first 24 hours of life with respiratory distress, pneumonia, and feeding intolerance or intestinal obstructions. In all patients, a plain chest radiograph demonstrating bowel gas patterns in the chest is sufficient for diagnosis (Fig. 42-3). Major negative predictors of outcome for prenatally diagnosed CDH include an intrathoracic liver, presence of major congenital heart disease, and other associated anomalies.

2. **Management**

   a. Immediate postnatal care must focus on cardiopulmonary stabilization. Endotracheal intubation is often required, as is oro- or nasogastric tube decompression to reduce gastric distension. Conventional ventilation with low positive-pressure, permissive hypercapnia and stable hypoxemia (tolerance of preductal oxygen saturations above 80%) has been shown to improve survival (*J Pediatr Surg*. 2002;37:357–366). Complex cases may require further cardiopulmonary stabilizing measures such as high-frequency oscillator ventilation, inhaled pulmonary vasodilators such as nitric oxide, epoprostenol, or sildenafil, and extracorporeal

membrane oxygenation. Between 20% and 40% of CDH neonates will require extracorporeal membrane oxygenation (ECMO) (*J Pediatr Surg*. 2013;48(6):1172–1176).

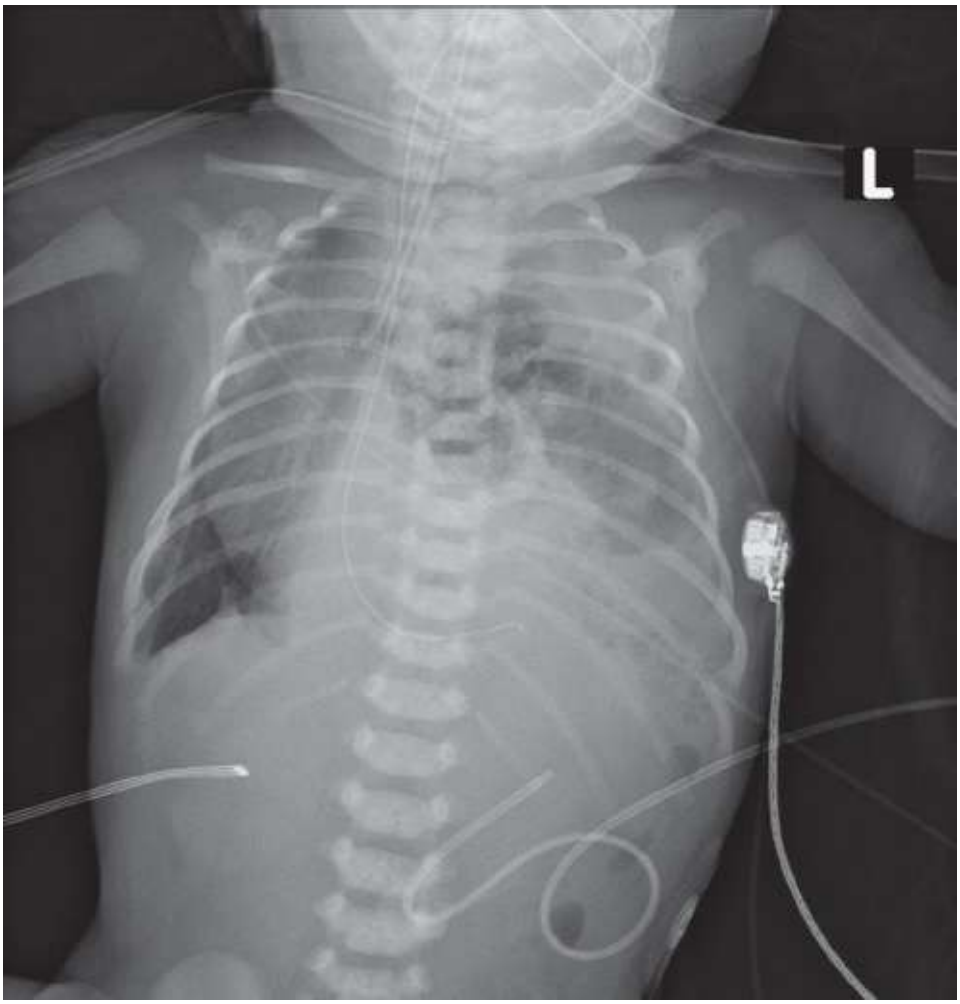


FIGURE 42-3 A case of congenital diaphragmatic hernia showing bowel filling the left chest.

(1) ECMO is frequently employed in cases of respiratory failure, with the greatest experience reported being in neonatal patients (*Semin Perinatol*. 2005;29:24–33). Frequent indications for ECMO in addition to CDH include meconium aspiration, respiratory distress syndrome, pulmonary hypertension, and sepsis. Selection criteria commonly include patients with a reversible cardiopulmonary process, greater than 2-kg body weight, and greater than 34 weeks of gestation. Exclusion criteria include irreversible cardiopulmonary congenital

anomalies and contraindications to anticoagulation, such as the presence of greater than grade 1 intracranial hemorrhage.

The ECMO circuit is intended to remove carbon dioxide and provide oxygenated blood while supporting or temporarily replacing the normal function of the lungs (veno-veno "V-V" ECMO) or both the lungs and heart (veno-arterial "V-A" ECMO). Venoarterial bypass is used most commonly, and the right internal jugular vein and common carotid artery are typically chosen for cannulation because of their large size, accessibility, and adequate collateral circulation. Systemic anticoagulation is required, necessitating serial coagulation monitoring, platelet and hematocrit trends, and daily head ultrasounds to screen for intracranial hemorrhage.

Once the patient has achieved acceptable arterial blood gas measurements on circuit, ECMO circuit flow rates are maintained until there are signs of pulmonary improvement (increased pO_2 levels, clearing chest radiographs, and improved lung compliance). At this point, ECMO flow rates can be weaned slowly. Survival rates on ECMO with appropriate patient selection are greater than 80%. Morbidity is highest in patients of low birth weight and gestational age less than 35 weeks and includes sequelae of bleeding, exposure to blood products, neurologic deficits or seizures, renal failure, infection, and risk of mechanical failure of the circuit.

b. Operative intervention. Once the patient has shown stability on lower ventilator settings, operative fixation of the hernia should be undertaken. A subcostal incision or thoracotomy is made on the affected side. Herniated abdominal contents are dissected free and reduced into the abdomen. The defect is repaired primarily or with a synthetic patch as needed.

3. Outcomes. Mortality of CDH is difficult to assess, as the outcome of cases presenting with profound respiratory distress at birth contrast greatly with patients presenting greater than 24 hours after birth. Overall survival rates greater than 70% are frequently reported (*J Pediatr Surg*. 2004;39:657–660). Significant respiratory disease at birth can result in neurologic deficits, including developmental delay and seizures. Patients must be followed to observe for respiratory

symptoms, gastroesophageal reflux, management of chronic lung disease, surveillance for hernia recurrence, and the possibility of reoperation if a patch was used in the initial operation.

C. Abdominal Wall Defects. During normal development of the human embryo, the midgut herniates outward through the umbilical ring and continues to grow. By the 11th week of gestation, the midgut returns back into the abdominal cavity and undergoes counterclockwise rotation and fixation, along with closure of the umbilical ring. **Omphalocele** is the failure of the abdominal contents to reduce back into the abdomen, resulting in a large hernia covered by a peritoneal sac. In contrast, **gastroschisis** is believed to be the result of an isolated intrauterine vascular insult resulting in an abdominal wall defect to the right of the umbilical cord. The bowel herniates through the defect but is not covered by a sac. Gastroschisis defects tend to be smaller than those of an omphalocele. Although there is a small incidence of associated anomalies with gastroschisis (10% rate of associated intestinal atresias), omphalocele is more typically associated with congenital anomalies, with 50% of cases having an associated genetic and/or cardiac anomaly that often has a major impact on the prognosis of the infant.

1. **Diagnosis** is often made at the time of prenatal ultrasound after 13 weeks of gestation or simply by clinical examination at the time of birth.
2. **Management.** Naso- or orogastric tube decompression and broad-spectrum prophylactic antibiotics should be initiated. Heat and fluid losses from exposed viscera should be corrected with intravenous fluids and warming while covering the exposed organs and lower body in a clear plastic bag. Do not cover the bowel with gauze and pour warm saline on the infant as the gauze prevents visualization of the bowel prior to surgery, and the warm saline ultimately drops to room temperature, thereby cooling the infant. In cases of gastroschisis, the bowel may be placed within a silastic silo at the bedside, with gradual gravity-based reduction into the abdomen while carefully monitoring for abdominal compartment syndrome and respiratory compromise (*J Pediatr Surg*. 2009;44(11):2126–2129). In cases of omphalocele, the sac serves as sufficient coverage until operative closure is undertaken.

   a. Operative repair. Once the herniated abdominal contents can be

reduced into the abdomen, the abdominal wall defect may be closed primarily. In omphalocele, the sac should be excised with care to dissect out and ligate the umbilical vessels. Repair of gastroschisis should involve careful examination of the length of the bowel for atresias, which may be managed primarily or with diversion and subsequent repair. In the case of large abdominal wall defects that cannot be closed primarily, the skin can be closed over the bowel or, if this is not possible, the exposed bowel can be allowed to granulate. Either management method requires operative repair of the fascial defect at a later date.

D. Necrotizing Enterocolitis (NEC). NEC is the most common neonatal gastrointestinal emergency. It is characterized by an acute inflammatory disease of the intestine associated with ulceration and necrosis of the gastrointestinal tract most frequently affecting the small bowel. The pathogenesis is believed to be multifactorial involving prematurity, an immature gut barrier defense, bacteria, enteral feeding, and hypoxia/ischemia or low-flow states. The incidence of NEC is 1 to 3 per 1,000 live births, with prematurity being the single most prominent risk factor.

1. **Diagnosis** requires a high clinical suspicion. NEC is unusual within the first few days of life, but approximately 80% of cases occur within the first month of life. Clinical examination may demonstrate a lethargic or irritable patient with abdominal distention, feeding intolerance, or passage of bloody stools. Advanced cases may show signs of peritonitis including erythema of the abdominal wall. Temperature instability is common, as well as increasing incidence of apneic or bradycardic episodes. Laboratory studies may reveal increasing leukocytosis or leukopenia as well as metabolic acidosis and thrombocytopenia. Plain radiographs often reveal dilated loops of bowel with evidence of ischemia including pneumatosis intestinalis (Fig. 42-4), portal venous gas, or pneumoperitoneum. Based on clinical examination and laboratory and imaging data, patients and their expectant management can be guided by Bell staging (*Ann Surg*. 1978;187(1):1–7).
2. **Initial management** of the hemodynamically stable patient should focus on bowel rest, nasogastric decompression, parenteral nutrition, and broad-spectrum antibiotics. Antibiotic regimen historically was a

combination of ampicillin, gentamicin, and clindamycin (*J Pediatr Surg*. 1980;15(4):569–573), but studies have failed to show any single superior regimen (*Cochrane Database Syst Rev*. 2012;8:CD007448). Serial abdominal examinations, laboratory studies including CBC and blood gas, and plain radiographs are valuable studies to determine the success of nonoperative management (Fig. 42-5). Fifty percent patients will experience improvement and resolution of signs of NEC with nonoperative management.

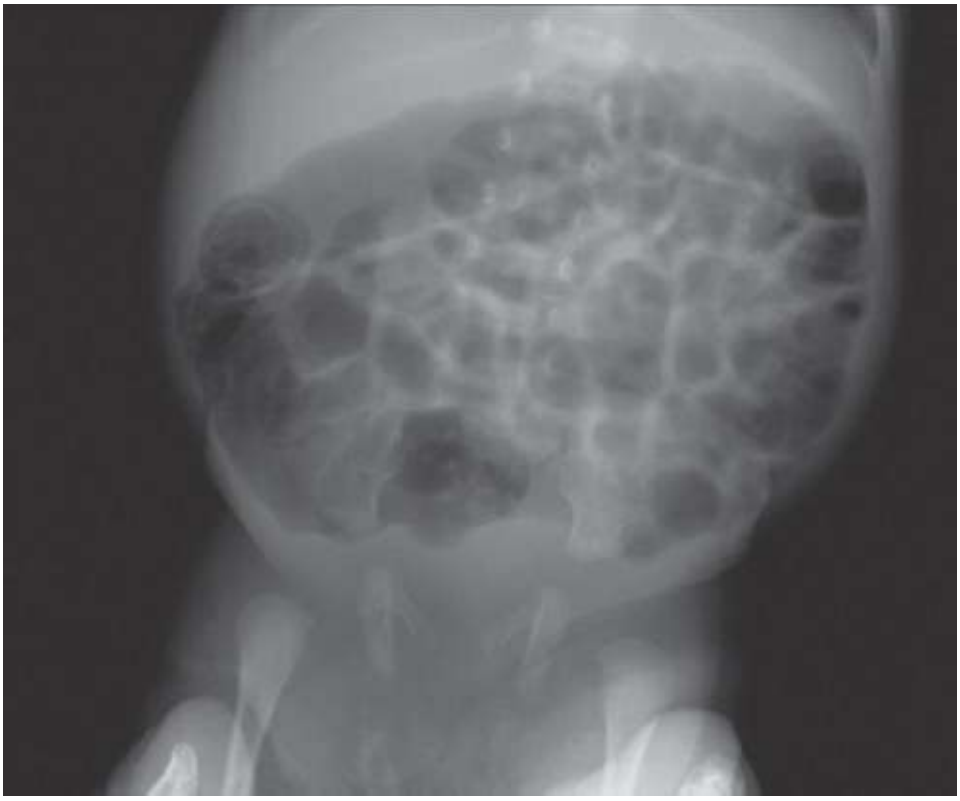


FIGURE 42-4 Radiographic findings of necrotizing enterocolitis. Pneumatosis intestinalis is visualized in the right upper quadrant.

3. **Operative management** is indicated for intestinal perforation, as indicated by free air on abdominal radiograph. Relative indications for operative management include overall clinical deterioration, abdominal wall cellulitis, worsening acidosis, falling white blood cell or platelet count, a palpable abdominal mass, or a persistent fixed loop on repeated abdominal radiographs. Improvement of clinical status can be achieved with laparotomy, including resection of

nonviable bowel and anastomoses or stomas as necessary, or with peritoneal drainage, a bedside procedure performed under local anesthesia that has shown comparable outcomes to laparotomy in select patients (*N Engl J Med*. 2006;354(21):2225–2234).

E. Meconium Syndromes, Malrotation, and Intestinal Atresias. Meconium plug or failure to pass meconium within the first 24 hours of life can be associated with a range of diagnoses including cystic fibrosis (CF) and Hirschsprung disease. Unrecognized surgical causes of obstruction can quickly progress to enterocolitis, sepsis, and perforation. Water-soluble contrast enemas can be both therapeutic and diagnostic. Testing for CF and Hirschsprung disease is often recommended even in the setting of simple and resolved meconium plug.

1. **Meconium ileus** represents the earliest manifestation of CF. Plain radiographs will demonstrate dilated loops of small bowel filled with meconium, resulting in an absence of air–fluid levels. Relief of the obstructed bowel, frequently located in the distal ileum, may require laparotomy, in which case an enterotomy is made to remove and irrigate inspissated meconium using saline or *N*-acetylcysteine. Postoperative confirmation of CF diagnosis by sweat testing or genetic analysis is then performed.
2. **Malrotation** results when the intestine fails to complete its normal 270 degrees of counterclockwise rotation about the superior mesenteric artery from the 4th to 10th weeks of gestation. Patients may present later in life but often exhibit bilious emesis and abdominal distention in the neonatal period. Plain abdominal radiographs can show dilated or normal bowel patterns, but an upper GI contrast study demonstrating failure of the duodenojejunal junction to cross midline with jejunum in the right side of the abdomen is consistent with malrotation. Volvulus may appear as a classic “bird’s beak” or corkscrew appearance of the intestine. Mesenteric attachments (Ladd bands) can result in mechanical obstruction.
   a. **Surgical treatment** for malrotation is the Ladd procedure, during which the bowel is untwisted in a counterclockwise manner (“turn back the hands of time”). Ladd bands are then divided between the duodenum and colon, which allows for broadening of the mesenteric base and reducing the risk for volvulus. There is no

benefit of pexying the duodenum or cecum. The small bowel is placed on the right side of the abdomen and the colon is placed on the left side of the abdomen. An appendectomy is performed to prevent future diagnostic uncertainty since the cecum is ultimately located in an aberrant location.

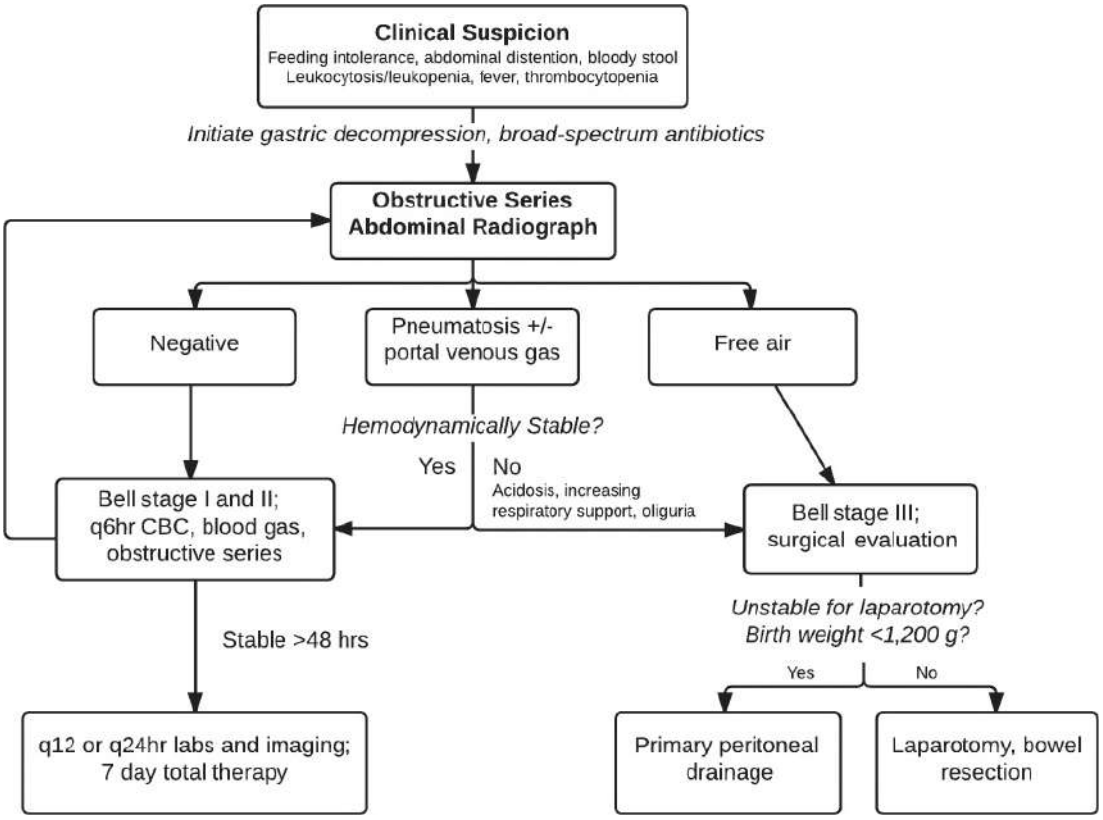


FIGURE 42-5 Algorithm for management of patients with suspected necrotizing enterocolitis.

3. **Intestinal atresias,** believed to be the result of an intrauterine vascular insult, present as either distal obstructive symptoms such as failure to pass meconium or proximal symptoms including feeding intolerance and bilious emesis. The most common location is the distal small bowel. Prenatal ultrasound may demonstrate polyhydramnios and postnatal imaging with plain abdominal radiograph will show dilated proximal loops with absence of air distally. Upper gastrointestinal contrast studies are helpful in identifying the suspected level of the atresia and ruling out volvulus, which is a surgical emergency.

a. Duodenal atresia results after failure of recanalization of the duodenal lumen. Plain radiographs demonstrate the "double bubble" sign caused by air within both the stomach and duodenum. Duodenal atresia has a much higher association with other conditions than jejunoileal atresias, including prematurity, Down syndrome, maternal polyhydramnios, malrotation, annular pancreas, and biliary atresia. Operative repair may be through duodenoduodenostomy with or without duodenoplasty to account for proximal dilatation of the bowel.

(1) Duodenal web represents a subcategory of duodenal atresia that can present later in life and can be repaired with simple transduodenal excision.

b. Anorectal malformations include a variety of congenital defects of development that can result in intestinal obstruction. These anomalies are often associated with other congenital defects as part of the VACTERL syndromes. Lesions are characterized by their level—low or high—and that distinction determines whether or not repair can be done in the newborn period without the need for a colostomy. Low lesions are typically indicated by an anocutaneous fistula (meconium noted at the perineum) and are often amenable to perineal anoplasty in the newborn period. Management follows an algorithmic approach in the majority of cases (Fig. 42-6).

4. Hirschsprung disease occurs in 1 out of every 5,000 live births and is characterized by absent ganglion cells in the myenteric (Auerbach) and submucosal (Meissner) plexuses starting in the rectum and extending proximally. This neurogenic abnormality is associated with nerve hypertrophy and muscular spasm of the distal colon and internal anal sphincter resulting in a functional obstruction. There is a predisposition for patients with affected family members as well as those with trisomy 21.

a. Diagnosis. The most common presentation is abdominal distention and failure to pass meconium within 24 hours. Older patients may present with chronic constipation. Plain radiographs demonstrate absence or paucity of air distal to the obstruction and contrast enema reveals a transition zone between proximally dilated and distally decompressed pathologically abnormal bowel (inversion

of rectosigmoid ratio). Rectal biopsy, which can be performed transanally with a suction device or on the seromuscular surface of the bowel, is required for pathologic confirmation of the diagnosis.

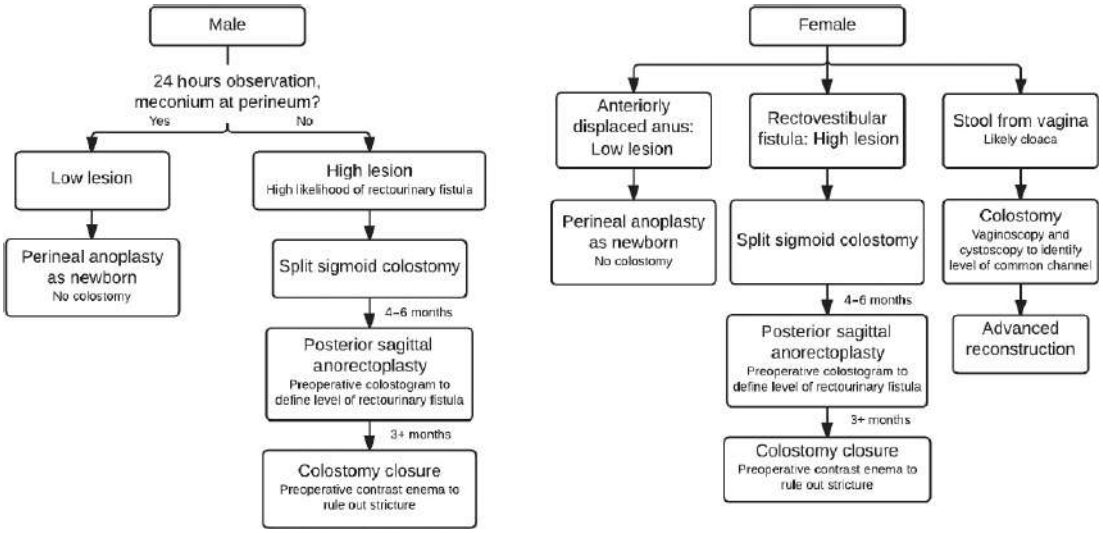


FIGURE 42-6 Algorithm for management of neonatal anorectal anomalies.

b. Management. Preoperative management includes decompression and saline colonic irrigations to evacuate impacted stool. Operative technique is aimed at identifying the transition zone ("leveling") with serial biopsies, then bringing ganglionated bowel down to the anus while preserving sphincter function. The definitive management of Hirschsprung disease involves variations among three main procedures. In the **Swenson procedure,** the aganglionic bowel is removed down to the level of the internal sphincters and a coloanal anastomosis is performed on the perineum. In the **Duhamel procedure,** the aganglionic rectal stump is left in place and the ganglionated, normal colon is pulled behind and anastomosed to this stump. Finally, the **Soave procedure** involves an endorectal mucosal dissection within the aganglionic distal rectum. The normally ganglionated colon is then pulled through the remnant muscular cuff and a coloanal anastomosis performed. Transanal procedures involving an endorectal pull-through are associated with fewer complications and fewer episodes of enterocolitis without higher rates of incontinence when compared to transabdominal approaches (*J*

Pediatr Surg. 2010;45(6):1213–1220).

III. THORACIC PATHOLOGY

A. Congenital Airway Malformations

1. **Pulmonary sequestrations** are lung malformations with an aberrant blood supply and no bronchial communication.
   a. **Intralobar** sequestrations are contained within lung parenchyma, commonly in the medial and posterior segments of the lower lobe. Two-thirds of these sequestrations are found on the left side, and 85% receive anomalous arterial supply from the infradiaphragmatic aorta via the inferior pulmonary ligament. Indications for surgery include risk of hemorrhage or infection. CT and MRI are useful preoperative imaging studies to elucidate the vascular supply.
   b. **Extralobar** sequestrations are surrounded by a separate pleural layer and are a predominantly male disease (3:1). Extralobar sequestrations are associated with other anomalies in 40% of cases, including diaphragmatic hernia, chest wall deformities, and congenital heart disease. Extralobar lesions present less of an infection risk, allowing for a period of observation if the patient is asymptomatic.
2. **Congenital pulmonary airway malformations (CPAMs)** describe multicystic lesions of bronchial tissue with relatively little alveoli. These typically do not have normal bronchial communication. CPAMs are classified by size, with type I considered macrocystic (>2 cm), type II describing epithelial-lined cysts (<1 cm) (frequently associated with other anomalies including CDH or cardiac malformations), and type III being microcystic and having a poor prognosis. Pulmonary resection in the newborn period should be performed due the potential for increase in size, infection, or malignancy.
3. **Bronchogenic cysts** are lined by ciliated cuboidal or columnar epithelium and mucus glands. Two-thirds of cysts are within lung parenchyma and the remainder are within the mediastinum. These should be resected due to symptoms and concern for malignant potential.
4. **Congenital lobar emphysema (CLE),** which occurs most commonly

in the left upper lobe, is the result of overdistention of one or more lobes within a histologically normal lung due to abnormal cartilaginous support of the feeding bronchus. Bronchial collapse creates a one-way valve promoting air trapping. Although many patients are asymptomatic, acute cases of respiratory distress with radiographic imaging mimicking tension pneumothorax may actually be the result of CLE. Placement of a chest tube in these instances would be detrimental and, instead, emergent lobar resection may be needed.

B. Chest Wall Deformities. The two major types of chest wall deformities are **pectus excavatum** and **pectus carinatum.** Pectus excavatum, also referred to as sunken chest, has an incidence roughly five times higher than carinatum and is found in a 3:1 male to female ratio. The etiology of these conditions is believed to be related to abnormal and asymmetric costal cartilage development.

1. **Preoperative evaluation** must include examination for scoliosis, which is present in 15% of cases, as well as any cardiorespiratory abnormalities. Chest radiograph is considered a standard component of the preoperative assessment. Additional workup may require an echocardiogram and an ophthalmologic examination if concern for cardiac abnormalities or Marfan syndrome exists. Pulmonary function tests should be obtained if there is concern for the condition causing pulmonary impairment. CT scan allows evaluation of the Haller index, the transverse chest diameter divided by the anterior–posterior diameter, to document the severity of the defect, but it has little bearing on operative consideration—normal <2, mild 2 to 3.2, moderate 3.2 to 3.5, severe >3.5.
2. **Indications for surgery** are largely cosmetic, as the condition becomes exaggerated both physically and psychosocially in the pubescent years. Correction is generally performed after 8 years of age in order to prevent restrictive chest wall deformities. Two standard techniques, the **Ravitch and Nuss (minimally invasive)** offer effective approaches, with both requiring subsequent surgery to remove hardware. Carinatum defects can be similarly repaired with cartilage resection and fixation or more frequently with external chest compression (*J Pediatr Surg*. 2006;41:40–45).

IV. ABDOMINAL PATHOLOGY

A. Acquired Alimentary Obstruction

1. **Hypertrophic pyloric stenosis (HPS)** is the most common surgical cause of nonbilious vomiting, occurring in 1 of every 400 births, commonly between 2 and 8 weeks of age and with a male to female ratio of 4:1. Infants of Northern European descent are most commonly affected and there appears to be an increased incidence for children of parents with HPS. Pyloric stenosis has no known causative factor and is characterized by hypertrophy of the circular muscle of the pylorus resulting in gastric outlet obstruction leading to nonbilious projectile emesis.

   a. Presentation. History of an appropriately aged infant presenting with projectile nonbilious emesis (+/− coffee ground) associated with feeding, persistent fussiness, or presumed hunger are all characteristics. Parents may initially present to a pediatrician for evaluation of their child and can be given more common diagnoses such as reflux or intolerance of feeds requiring a change in formula.

   b. Diagnosis. Patients must be evaluated for dehydration by sufficient urine production and electrolyte abnormalities. Hypokalemic, hypochloremic metabolic alkalosis is the most common electrolyte abnormality due to a loss of hydrochloric acid from gastric secretions and potassium from the kidney in attempt to compensate for hypovolemia. **Physical examination** may reveal the “olive sign,” the palpable pylorus to the right of and superior to the umbilicus. **Abdominal ultrasound** is used for diagnosis, with criteria including a pyloric channel length greater than 14 mm and single-wall muscular thickness of 4 mm or greater. These criteria have 99.5% sensitivity and 100% specificity for identifying HPS (*J Pediatr Surg*. 2007;16(1):27–33).

   c. Management includes evaluation and treatment of dehydration and electrolyte abnormalities. Patients are made NPO to prevent further episodes of emesis and are administered intravenous fluids titrated to urine output greater than 1 mL/kg/hr. Addition of potassium into fluids should be withheld until urine output has been restored. Surgical timing is largely decided by the severity of

electrolyte abnormalities, particularly the HCO_3, which, if significantly elevated, results in a compensatory respiratory acidosis that may result in apnea, a devastating consequence particularly exaggerated by postanesthetic respiratory depression.

d. Pyloromyotomy, separation of the external muscular layers down to the level of mucosa, is performed either through right upper quadrant or periumbilical incision, or with laparoscopy.

e. Postoperative feeding protocols typically start with an electrolyte solution with gradual advancement over the first 24 hours postoperatively to formula or breast milk volumes that are appropriate for age. Vomiting is a common postoperative issue, but, rarely, may be an indicator of incomplete myotomy. Additional complications include perforation of the mucosa, which is treated by mucosal repair and nasogastric drainage.

2. Intussusception is another common acquired cause of intestinal obstruction, resulting from invagination or telescoping of the proximal intestine into the distal bowel. This is most common in infants 3 months to 3 years of age and most frequently originates at the ileocecal junction. Although a lead point (pathologic or anatomic source) is most commonly not present, definitive identification of a contributing structure may occur in up to 12% of patients, most frequently either a Meckel diverticulum (remnant of the omphalomesenteric duct), intestinal polyp, or tumor. Affected infants present with periods of intense crying during which they retract their legs up in pain; these “attacks” subside within a few minutes. Recent gastrointestinal or upper respiratory illness may also be part of the patient’s history. Obstruction may result in ischemia, which produces stool with a mix of blood and mucous (i.e., “currant jelly” stools).

a. Diagnosis. Plain abdominal radiographs may be sufficient for diagnosis in as many as 50% of cases, revealing abnormal gas patterns concerning for a mass with subsequent paucity of gas in the right lower abdomen. Ultrasound may identify a “target” lesion representing a transverse view of the intussuscepted layers of bowel.

b. Nonoperative management of active intussusception is performed by contrast or air enema. This is successful in 80% of cases, with

recurrence rates of approximately 10% within the first 24 hours. Management of recurrence is usually again attempted nonoperatively, but failure or a second recurrence are indications for surgery, as is peritonitis or concern for bowel ischemia at any stage of presentation.

c. Operative management can be approached via either open or laparoscopic techniques. With open surgery, reduction is achieved with retrograde (distal to proximal) squeezing or milking of the intussusceptum until reduced. During laparoscopy, the bowel is pulled apart. The affected bowel should be examined closely for signs of ischemia. Lymphoid tissue is often noted to be hypertrophic, but it is unclear if this is causative or reactive. If manual reduction is unsuccessful, the involved bowel is resected. Incidental appendectomy may also be performed.

B. Hepatopancreatobiliary. Although jaundice may be a normal physiologic condition of the newborn, it should only be transient. Any infant with direct, conjugated hyperbilirubinemia (greater than 2 mg/dL) beyond 2 weeks of age should undergo further workup. Unconjugated hyperbilirubinemia is often caused by nonsurgical conditions, including physiologic jaundice of the newborn, hemolytic conditions, and breastmilk jaundice. Conjugated hyperbilirubinemia may be caused by hepatitis or biliary obstruction. There are two common obstructive surgical conditions.

1. Choledochal cysts are a spectrum of abnormalities characterized by cystic dilatation of the biliary system of uncertain etiology. Fifty percent of affected children present within the first 10 years of life. Jaundice in the setting of abdominal pain and a right upper quadrant mass are highly suspicious. Pancreatitis or cholangitis may also occur.

a. Diagnosis is frequently made using ultrasound, which can demonstrate biliary dilatation in one of five types.

b. Surgical repair is undertaken for either resolution of symptoms or due to the potential for malignant degeneration, and the procedure is specific to the type of cyst (see Chapter 22).

2. Biliary atresia is the result of progressive obliteration of the extrahepatic bile ducts. There is no causative factor. The incidence is estimated to be 1 in 15,000 births. Patients typically present with

jaundice, acholic stools, dark urine, and/or hepatomegaly.

a. Diagnosis is frequently made with ultrasound, which demonstrates a shrunken or absent gallbladder and incomplete or nonvisualized extrahepatic bile ducts. Percutaneous liver biopsy is then performed to confirm the diagnosis (bile duct plugs, biliary epithelial proliferation). Technetium-99m hepatobiliary iminodiacetic acid (HIDA) scan aids in differentiating liver parenchymal disease and biliary obstructive disease. In biliary atresia, the liver readily takes up the tracer molecule, but no excretion into the extrahepatic biliary system or duodenum is seen. Cholangiography may also be performed.

b. Kasai hepatoportoenterostomy is the only surgical management for biliary atresia. The distal bile duct and gallbladder remnant are excised and a Roux-en-Y limb of jejunum is anastomosed to the divided portal plate (the scarred remnant of the biliary tract).

c. Outcomes are best for patients if surgical correction takes place within the first 60 days of life with 30% of these patients requiring no further surgical intervention (*J Pediatr Gastroenterol Nutr*. 2006;42:93–99). The remainder of patients inevitably progress to fibrosis, portal hypertension, and cholestasis and will require liver transplantation. Older patients or those with significant fibrosis at initial presentation may require immediate transplantation.

V. HEAD AND NECK MASSES

A. Branchial Cleft Cyst. Head and neck structures are embryologically derived from six pairs of branchial arches and the corresponding external clefts and internal pouches. Congenital cysts, sinuses, or fistulae result from failure of appropriate migration or regression of these structures. Branchial remnants are present at the time of birth but may not become clinically evident until later in life. In children, fistulas are more common than external sinuses, which are more frequent than cysts. Patients present with a spectrum of symptoms including visible or palpable lesions, mucoid drainage, or development of cystic masses that may become infected.

1. First branchial remnants are typically located in the front or back of the ear, or in the upper neck in the region of the mandible and may involve the parotid gland, facial nerve, or external auditory canal.

2. **Second branchial cleft remnants** are the most common. These are usually located along the anterior border of the sternocleidomastoid muscle, invade the platysma, ascend along the carotid sheath to the level of the hyoid bone, and extend medially between the carotid artery bifurcation. The fistula then courses behind the posterior belly of the digastric and stylohyoid muscles to end in the tonsillar fossa.
3. **Third branchial cleft remnants** usually do not have associated sinuses or fistulae. These most often contain cartilage, are located in the suprasternal notch or clavicular region, and present as a firm mass or as a subcutaneous abscess.

B. Thyroglossal duct cysts are common lesions in the midline of the neck and frequently present in preschool-aged children. These cysts represent incomplete thyroid gland formation and, as such, are located along the normal course of thyroid migration: from the foramen cecum to the anatomically normal site of the pyramidal lobe of the thyroid gland. Frequently the tongue or hyoid bone is involved.

1. **Indications for surgery** include increasing size, infection or risk for infection, and risk for carcinoma (1% to 2%). Preoperative ultrasound can aid significantly in identifying involved structures including the site of normal thyroid tissue, which should be preserved if possible. Standard surgery, the **Sistrunk procedure,** involves excision of the central portion of the hyoid bone in addition to the cyst in continuity with its tract.

C. Cystic hygroma is a lymphatic malformation resulting from abnormal development of a lymphatic network that fails to drain into the venous system. Seventy-five percent of these lesions involve the lymphatic jugular sacks, presenting as a posterior neck mass. The majority of cystic hygromas present at birth (50% to 65%), with most becoming apparent by the second year of life.

1. **Indications for resection** are largely cosmetic, although expansion that threatens compression of the airway, infection, or pain, possibly due to hemorrhage, are also acceptable indications for treatment. Complete surgical excision is preferred. Preoperative magnetic resonance imaging can assist in determining the extent of the lesion and any neurovascular involvement. Postoperative morbidity includes recurrence, lymphatic leak, infection, and neurovascular injury. Additional therapeutic modalities include injection of sclerosing

agents such as bleomycin.

D. Cervical lymphadenopathy is a frequent diagnosis for referral to a pediatric surgeon. Infectious etiologies are the overwhelming majority of diagnoses, including cat-scratch fever as a result of Bartonella, which contributes to approximately 3% of lymphadenopathy cases. Lymph nodes that are unilateral, firm, fixed, or greater than 2 cm should prompt additional workup, including a chest radiograph to evaluate for mediastinal lymphadenopathy or masses.

VI. TUMORS AND NEOPLASMS

A. Neuroblastoma is the most common neoplasm of childhood, accounting for 6% to 10% of all childhood cancers with an incidence of 1 in 10,000 cases annually and a median age of diagnosis of 2 years. Only 25% of patients present with isolated disease, often found incidentally on examination or imaging, for which surgical therapy is standard of care. The remainder present with metastatic disease and have a poor prognosis. These neoplasms are of neural crest origin and are thus found along the sympathetic nervous system, with 75% in the abdomen or pelvis and half of these within the adrenal medulla.

1. **Preoperative evaluation** should include routine laboratory work such as CBC and CMP. Blood pressure should be checked to investigate the potential for hypertension, and urine should be tested for catecholamine metabolites. CT and MRI assist in preoperative planning, particularly as neuroblastoma is capable of invading into adjacent vascular structures. They are also useful for metastatic workup, with frequent sites of metastases being bone and lung. Radiolabeled metaiodobenzylguanidine (MIBG) is a high-yield study to document the presence of metastatic disease. Bone marrow aspirate and biopsy complete the staging evaluation. Staging and survival are determined by burden of disease as well as genetic markers including N-*myc* overexpression and chromosomal deletions, which portend a worse prognosis. Young patients with early disease and favorable pathology have >90% survival, while older patients with unfavorable pathology or metastatic disease can have survival as low as 10%.
2. **Surgical management** is reserved for anatomically resectable cases of early nonmetastatic disease or can be undertaken after neoadjuvant

therapies.

B. Wilms tumor accounts for 6% of all malignancies in children and is the most common renal malignancy in children. Approximately 500 cases are diagnosed annually in the United States, with an average age of diagnosis of 3 or 4 years. There is no gender predominance, and 5% of cases are bilateral. Although there are heritable forms of Wilms tumor including an association with Beckwith–Wiedemann syndrome, most cases are sporadic and present as incidental abdominal masses. Patients may have hypertension or hematuria.

1. **Preoperative evaluation** includes ultrasound to confirm renal origin of the mass and to evaluate for any potential intravascular extension. CT or MRI may further assist in differentiating Wilms tumor from neuroblastoma, as will urine catecholamines. Chest imaging via CT scan is needed for complete staging.
2. **Surgical intervention** requires radial nephroureterectomy and lymph node sampling. Intraoperative spillage of tumor contents must be carefully avoided, as it upstages the patient's disease (Table 42-4). For resectable disease, surgery and chemotherapy together result in a greater than 90% cure rate.

TABLE 42-4 Wilms Tumor Staging System

Stage	Characteristics
I	Tumor confined to the kidney and completely excised intact
II	Tumor extends through the renal capsule into adjacent tissues (fat, vessels, etc.), but all affected tissue is completely excised intact. Stage II also includes cases in which the kidney is biopsied preoperatively or localized spillage occurs during resection

III	Tumor without hematogenous or extra-abdominal spread. Includes cases of positive lymph nodes, positive resection margins, or peritoneal implants
IV	Hematogenous metastases
V	Bilateral renal involvement

C. Hepatic tumors make up fewer than 5% of all intra-abdominal pediatric malignancies but are malignant in up to 70% of cases.

1. **Hepatoblastoma** typically presents before 3 years of age and is often unifocal. Chemotherapy is somewhat effective and overall survival is dictated primarily as to whether the tumor is resectable or not.
2. **Hepatocellular carcinoma** is often multifocal, with an overall survival of 25%. Surgical resection or liver transplantation can be curative.

D. Teratomas are tumors containing tissue from more than one of the three embryonic germ cell layers (endoderm, ectoderm, mesoderm). A frequent presentation is as a **sacrococcygeal teratoma** in the neonatal period, which has a 4:1 female to male ratio. Ultrasound and rectal examination should be performed preoperatively to rule out pelvic or presacral extension. The majority of these are benign and are removed along with the sacrum to prevent recurrence.

E. Soft tissue sarcomas account for 6% of childhood malignancies, with half of these being rhabdomyosarcomas. Wide local excision depending on the anatomic location with or without chemotherapy and lymph node sampling should be performed.

VII. PEDIATRIC GENERAL SURGICAL CONDITIONS

A. Appendicitis is one of the most common pediatric surgical conditions. Patients typically present with abdominal pain followed by nausea and have physical examination findings of tenderness at McBurney point (one-third the distance between right anterior iliac spine and umbilicus) and obturator, iliopsoas, and Rovsing signs (palpation of left lower quadrant causes pain in right lower quadrant). Scoring systems

incorporating history, physical, and laboratory values such as the Alvarado score (*Ann Emerg Med*. 1986;15(5):557–564) can aid in objectively risk-stratifying patients.

Ultrasound is routinely the first imaging modality of choice in the pediatric population. A positive study should result in surgical management, whereas a negative study or one in which the appendix was nonvisualized should prompt either observation, evaluation of other diagnoses, or consideration for obtaining a CT scan, particularly in patients showing signs of advanced illness. Management is with antibiotics and laparoscopic appendectomy, though some institutions are beginning to utilize nonoperative management.

B. Indirect inguinal hernias affect approximately 1% to 5% of children, with a predominance in males (8:1) and an increased rate in premature infants (7% to 30%). Bilateral hernias are present in 10% to 40% and occur more frequently in premature infants and girls. Due to an increased risk of recurrence and postanesthesia apnea in premature patients, neonatal inguinal hernias are frequently repaired prior to the patient leaving the hospital or at 50 weeks post conception (*J Pediatr Surg*. 1996;31:1166–1169).

C. Hydroceles are fluid collections within the processus vaginalis that envelop the testicles. They occur in approximately 6% of full-term male newborns.

1. **Communicating hydroceles** allow the free flow of peritoneal fluid down to the scrotum through a patent processus vaginalis. This must be regarded as a hernia and repaired as such.
2. **Noncommunicating hydroceles** contain fluid confined to the scrotum due to an obliterated processus vaginalis. This is usually a self-limiting process that resolves in 6 to 12 months.

D. Umbilical hernia is common in children due to a persistence of the umbilical ring. In the vast majority of cases, these close spontaneously by age 4 to 5. If the hernia has not closed by age 5, or if it is exceptionally large (>2 cm), or if the patient has had incarceration of bowel within the hernia it will require operative primary closure.

E. Trauma

1. **Imaging.** Limiting radiation exposure and unnecessary testing is important in children. However, the inability to obtain reliable

examinations in this population, particularly in trauma settings, complicates the decision to obtain imaging. Diffuse abdominal pain, a seatbelt sign, or distracting injuries can be indications for computed tomography scan. In addition, elevated serum glutamic-oxaloacetic transaminase (SGOT) or serum glutamic-pyruvic transaminase (SGPT) levels higher than 200 or 100 IU/L, respectively, are accepted thresholds for obtaining a CT scan in the setting of blunt trauma.

2. **Treatment of injury.** Indications for exploratory laparoscopy or laparotomy are similar to those utilized in adults and include hemodynamic instability with either visible or suspected organ or vascular injury, penetrating abdominal injury, imaging findings consistent with bowel injury, or the presence of pelvic free fluid after blunt trauma without solid organ injury, suggestive of small bowel injury.
   a. **Conservative or nonoperative management of isolated solid organ injury** is covered by the guidelines of the Liver/Spleen Trauma Study Group of the American Pediatric Surgical Association (Table 42-5). Regardless of the injury grade and in the absence of specific indications, follow-up imaging either at the time of discharge or prior to resumption of normal activities is not indicated.

TABLE 42-5 Nonoperative Management of Pediatric Blunt Traumatic Isolated Spleen or Liver Injury

	CT Grade			
	I	II	III	IV
ICU stay (days)	–	–	–	1
Hospital stay (days)	2	3	4	5
Return to age-appropriate activity (wks)	3	4	5	6

CHAPTER 42: PEDIATRIC SURGERY

Multiple Choice Questions

1. **A 10-year-old, 35-kg girl presents to your emergency room after being in a highway-speed motor vehicle crash. She was a restrained back seat passenger and airbags did deploy. She is tachycardic, hypotensive, and has diffuse abdominal pain with a positive seatbelt sign. Focused Assessment with Sonography in Trauma (FAST) is positive for intra-abdominal fluid. Her hypotension has not improved after two boluses of isotonic fluid. You next ask for rapid transfusion of blood as you prepare to take her to the operating room. What blood volume should you initially transfuse?**

   a. 100 mL
   b. 175 mL
   c. 250 mL
   d. 350 mL
   e. 475 mL

2. **You receive a call from a primary care physician who is working up a 4-year-old female for chronic abdominal pain, distention, and jaundice. The physician describes a CT scan finding of a cystic structure arising from the common bile duct that is separate from the gallbladder. You suspect choledochal cyst as a possible diagnosis. This imaging is consistent with what type of choledochal cyst?**

   a. Type I
   b. Type II
   c. Type III
   d. Type IV
   e. Type V

3. **You are asked to see a patient in the neonatal intensive care unit. The infant was born just hours ago and has progressed into significant respiratory distress. The intensivists have intubated**

the patient but are unsuccessful in passing an orogastric tube due to resistance. Your attempts also fail. What additional workup would you request to make a diagnosis?

a. CT chest
b. Spinal ultrasound
c. Plain chest/abdominal x-ray
d. CT abdomen and pelvis
e. Upper GI study with contrast

4. **Hirschsprung disease results from a failure of neural crest cell development in the Meissner and Auerbach plexi. In what layers of the bowel wall are these plexi contained?**

Choice	Meissner	Auerbach
a	Mucosal	Mucosal
b	Submucosal	Mucosal
c	Muscular	Submucosal
d	Submucosal	Muscular
e	Serosal	Muscular

5. **A young patient presents to you with <12 hours of severe abdominal pain, diffuse tenderness on examination, and bilious emesis. You are concerned about malrotation and, while awaiting imaging, plan your operative approach. Which step is not a common component of Ladd procedure?**

a. Reduction of volvulus by counterclockwise rotation
b. Division of Ladd bands
c. Appendectomy
d. Pexying the cecum to the peritoneal sidewall

43 Otolaryngology for the General Surgeon

Heidi E. L'Esperance and John S. Schneider

I. THE NECK

A. Anatomy and Physiology

1. The cervical fascia provides planes for passage of infection, hemorrhage, and surgical dissection (Fig. 43-1).
2. The lymphatic system of the neck is divided into six levels. Level I contains the submental and submandibular lymph nodes, level II through IV parallel the jugular vein, level V consists of the posterior triangle, and level VI is the central compartment. These levels are important for predicting spread of cancer from the head and neck, as well as determining the extent of surgery necessary during a neck dissection (Fig. 43-2).

B. Neck Masses. History for a neck mass should focus on duration, location, and symptoms (e.g., pain, fevers, weight loss, dysphagia, voice changes, otalgia), past medical history, and social history (including tobacco and alcohol use, travel history, animal exposures, sick contacts). Differential diagnosis is strongly influenced by age. **Neck masses in adults are presumed malignant until proven otherwise**. In contrast, **neck masses in children are usually inflammatory or congenital,** and neoplasms are rare.

1. **Adult neck masses** are commonly metastatic squamous cell carcinoma (SCC) from a primary tumor of the oral cavity, pharynx, or larynx. See Figure 43-3 for an algorithm describing workup of a neck mass in an adult.
2. **Pediatric neck masses.** Children often have palpable lymph nodes, but children with a large or persistent neck mass should undergo an

ultrasound (US), as this is safe and noninvasive. CT should be reserved for deep neck space infections. Additional studies include white blood cell count (WBC) with differential and specific serologic tests for infectious etiologies. See Figure 43-4 for an algorithm describing workup of a neck mass in children.

C. Congenital Neck Lesions. Congenital masses may swell during an upper respiratory infection (URI). The acute infection should be treated with antibiotics. If necessary, needle aspiration may be performed for decompression.

1. **Branchial cleft anomalies.** These congenital masses may result in cysts, sinuses, or fistulae. The most common anomaly is of the second branchial cleft (∼95%), which presents as a nontender, fluctuant mass anterior to the sternocleidomastoid muscle (SCM) with a deep tract that travels between the internal and external carotid arteries to the tonsillar fossa. **First branchial cleft anomalies** present near the angle of the mandible or around the ear and may be associated with the facial nerve. **Third branchial cleft anomalies** track posterior to the SCM to the pyriform sinus and often present as a fluctuant mass or abscess in the posterior triangle. **Fourth branchial cleft anomalies** track anterior to the SCM to the pyriform fossa and often present as a recurrent anterior neck abscess or recurrent acute left superior thyroiditis.

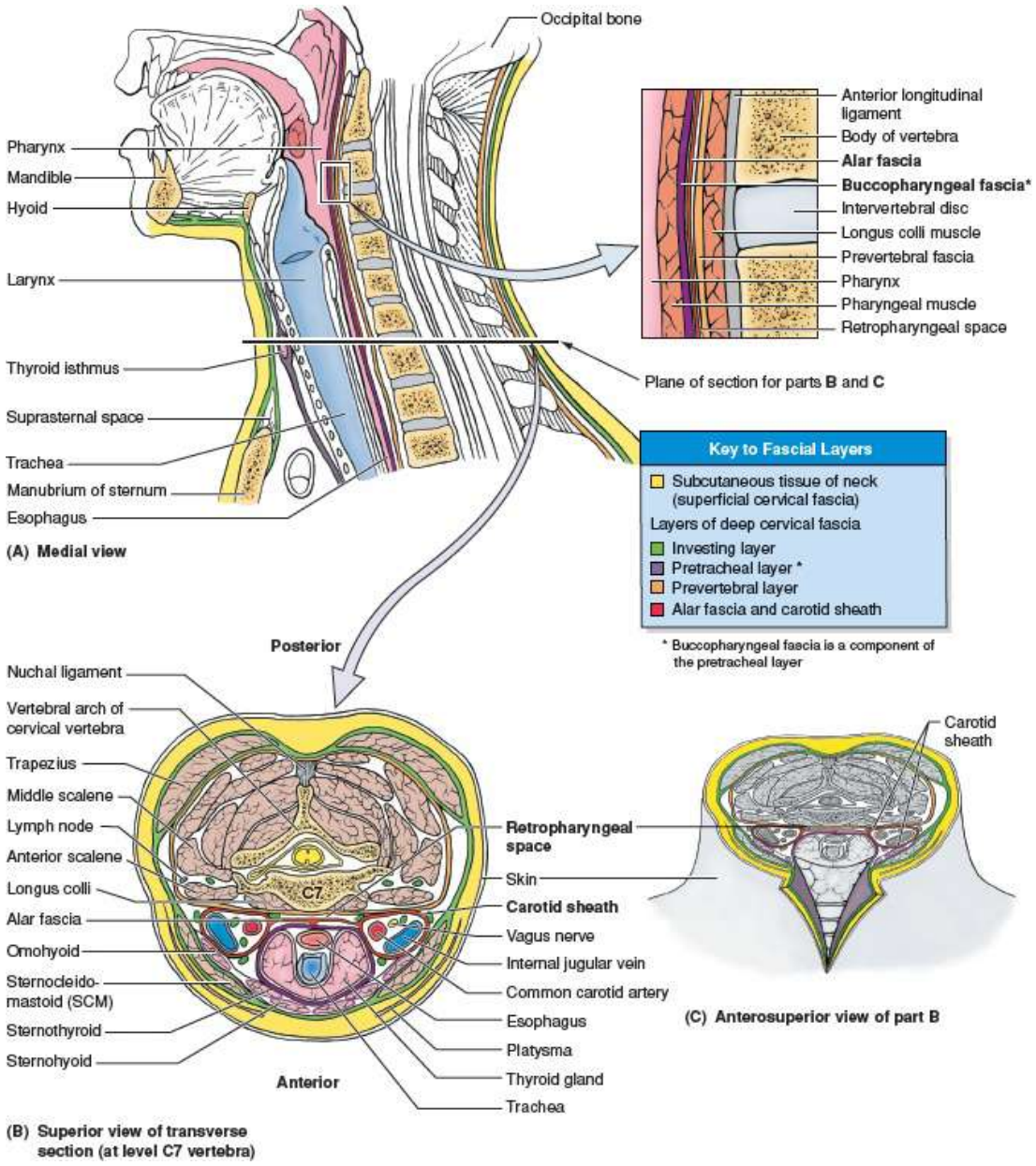


FIGURE 43-1 Fascial layers of the neck. (From Moore KL, Dalley AF, Agur AM. *Clinically Oriented Anatomy.* 6th ed. Baltimore, MD: Wolters Kluwer Health; 2010.)

2. **Thyroglossal duct cysts (TGDC).** During embryologic development, the thyroid descends from the base of the tongue to its position low in the neck along the thyroglossal duct. TGDCs are due to persistence of this duct, and on examination these midline masses will move with tongue protrusion. Before surgery, a US should be performed to evaluate if thyroid tissue exists outside of the TGDC. The definitive treatment is the **Sistrunk procedure,** which involves removal of the

cyst, tract, and the central portion of the **hyoid**.

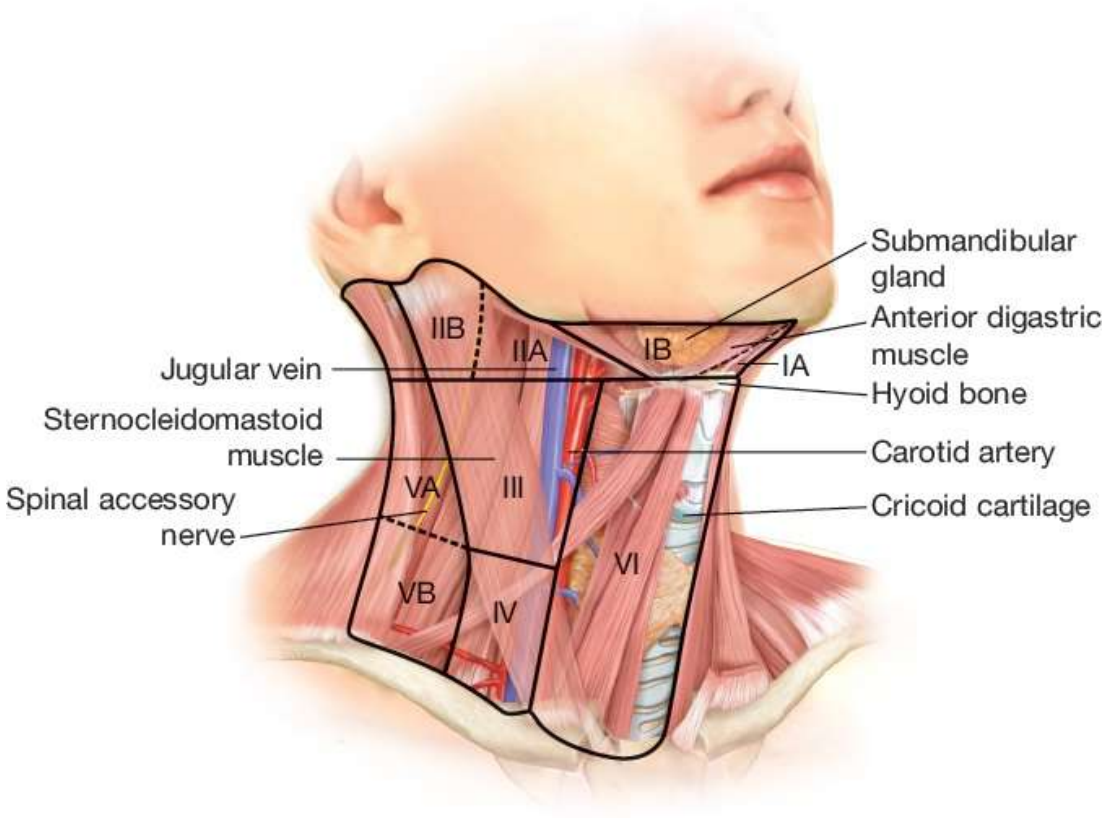


FIGURE 43-2 Neck node levels. IA: submental, IB: submandibular, II: upper jugular, III: middle jugular, IV: lower jugular, V: posterior triangle, VI: anterior compartment. (From Mulholland MW, ed. *Operative Techniques in Surgery*. Philadelphia, PA: Wolters Kluwer Health; 2015.)

3. **Hemangioma.** This lesion presents as a reddish-bluish compressible mass in infancy, which rapidly grows during the first year of life, then slowly involutes. The majority do not require treatment. Treatment is reserved for cervicofacial hemangiomas that interfere with vision, cause disfiguration, or involve the airway. Treatment options include propranolol, steroids, laser therapy, and surgical resection.
4. **Lymphatic malformations.** These lesions are soft, doughy, compressible lesions. Treatment includes sclerotherapy and resection.
5. Other congenital masses include laryngoceles, dermoid cysts, teratomas, plunging ranulas, and thymic cysts.

D. Infectious/Inflammatory Disorders

1. **Suppurative bacterial lymphadenitis.** This condition is common in children and is often due to *Staphylococcus aureus* or group A

streptococcal infections. Treatment includes intravenous (IV) antibiotics and incision and drainage (I&D) if an abscess forms.

2. **Acute mononucleosis.** Mononucleosis is caused by Epstein–Barr virus (EBV) infection and commonly causes lymphadenopathy, fevers, tonsillitis, and hepatosplenomegaly. Treatment is supportive.
3. **Kawasaki disease.** An acute vasculitis with sudden onset of symptoms including cervical lymphadenopathy, conjunctivitis, high fevers >5 days, “strawberry tongue,” and rash. This is associated with development of coronary aneurysms in 20% to 25%, and risk of myocardial infarction. Treatment includes IVIG and aspirin.

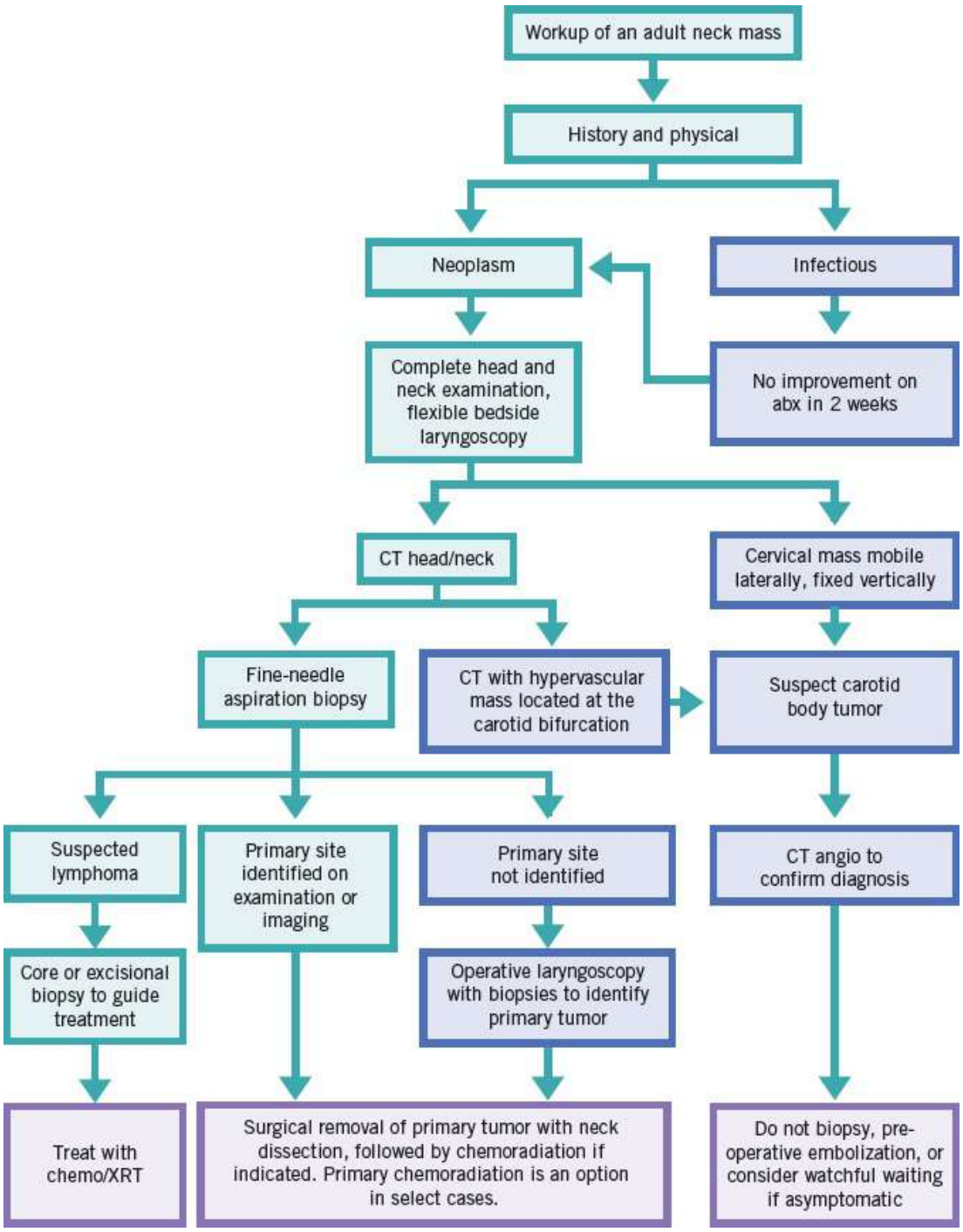


FIGURE 43-3 Workup of adult neck mass.

4. **Deep neck space infections.** Neck infections present with fevers, tender neck swelling, and local symptoms. Pathogen sources include odontogenic, tonsils, trauma, and instrumentation, among other etiologies. Treatment includes IV antibiotics and I&D. Outside of local space-named infections, additional deep neck infections

include:

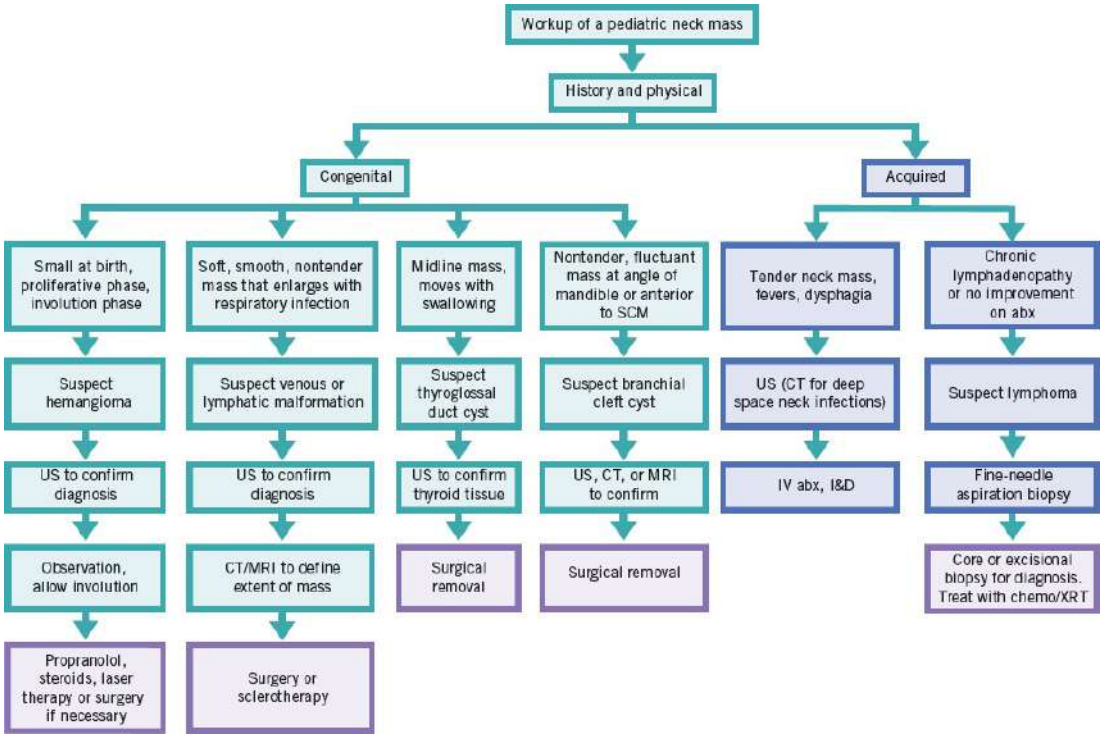


FIGURE 43-4 Workup of pediatric neck mass.

a. Necrotizing fasciitis. It is characterized by rapidly progressive infection of skin and soft tissues resulting in crepitus and air in deep neck spaces. These patients are often septic at the time of presentation. This is associated with a high mortality rate. Treatment includes aggressive surgical debridement of involved skin and soft tissue, ICU admission, IV antibiotics, and control of underlying comorbidities (e.g., diabetes, HIV) that may have contributed to the severity of this infection.

b. Ludwig angina is characterized by bilateral cellulitis of submandibular, sublingual, and submental regions, which causes elevation in the floor of the mouth, swelling of the tongue, and may rapidly progress to complete upper airway obstruction and subsequent respiratory failure. Treatment includes control of the airway through emergent tracheostomy or awake fiberoptic intubation, ICU admission, IV antibiotics, and I&D.

c. Retropharyngeal abscess. While this is a local space infection, it deserves particular mention as this space communicates with the

mediastinum and thus has risk of acute mediastinitis. At time of presentation, patients will often have high fevers, a “hot potato” voice, and will resist rotating their neck. Treatment includes IV antibiotics, I&D, and inpatient hospitalization.

E. Neoplasms

1. Benign

a. Paragangliomas arise from paraganglionic cells of the autonomic nervous system. These can be familial, and 40% of patients have a genetic mutation (*Nat Rev Endocrinol*. 2015;11:101–111). These tumors may be secreting or nonsecreting, and prior to resection, patients should have a workup including plasma and urine metanephrines and CT abdomen/pelvis to rule out concomitant pheochromocytoma. The most common paragangliomas are carotid body tumors. These tumors can be monitored with serial imaging if asymptomatic or be treated with surgical resection and/or radiotherapy.

2. Malignant. The most common malignant neck mass in adults is metastatic SCC. The most common malignant neck mass in children is lymphoma. Location of the mass is suggestive of primary site, based on patterns of lymphatic drainage.

a. SCC of aerodigestive mucosa often metastasizes to the neck. Unknown primary SCC with cervical metastases represents a diagnostic dilemma. PET/CT imaging may also help identify the primary lesion. Tumor histologic staining +p16 is associated with an oropharyngeal primary, and +EBV is associated with a nasopharynx primary. In the event a primary source cannot be located, operative palatine and/or lingual tonsillectomy and panendoscopy should be considered.

(1) Complications of neck dissection include the following: chyle leak, injury to major vessels of the neck including the carotid artery and internal jugular vein, and temporary or permanent injury to the following nerves: marginal mandibular branch of cranial nerve VII; cranial nerves X, XI, and XII; multiple rootlets; as well as the sympathetic trunk. Patients are counseled preoperatively regarding risk of injury to these structures and resultant effects.

b. Thyroid carcinoma (see Chapter 34 for more in-depth discussion of thyroid malignancy).

c. Lymphoma. The majority of head and neck lymphomas are present in cervical lymph nodes. Patients may have **B symptoms** (fevers, night sweats, weight loss). Surgical interventions are not curative. FNA biopsy provides cytologic material, but tissue samples obtained from core or excisional biopsy are often required for architectural detail, flow cytometry, and immunophenotyping. Treatment is chemotherapy and radiation.

II. THE LARYNX

A. Anatomy and Physiology

1. The larynx is divided into the supraglottis (which includes the epiglottis, arytenoid cartilages, false vocal cords/folds, and ventricles), the glottis (true vocal cords/folds), and subglottis (extending from the true vocal cords inferiorly to the cricoid cartilage). See Figure 43-5 for more detailed laryngeal anatomy.
2. The recurrent laryngeal nerve (branch of cranial nerve [CN] X) provides sensory innervation to most of the laryngeal mucosa and motor innervation to all of the intrinsic laryngeal muscles, except for the cricothyroid muscle, which is innervated by the superior laryngeal nerve (also a branch of CN X). Most importantly, the recurrent laryngeal nerves provide innervation to the vocal cords, allowing for movement during speech and swallowing.

B. Infectious/Inflammatory Disorders

1. **Viral croup.** Viral laryngotracheitis is glottic and subglottic inflammation from parainfluenza virus. Patients present with a barking cough, hoarseness, and inspiratory stridor. Lateral airway x-ray may show the **steeple sign** from subglottic edema. Treatment includes humidified air, glucocorticoids for moderate to severe croup, racemic epinephrine, and heliox.
2. **Epiglottitis** is usually caused by *Haemophilus influenzae* type B. Patients present with fever, muffled voice, drooling, and stridor. Treatment is urgent airway management and IV antibiotics.

C. Neuromuscular Disorders

1. **Vocal cord paralysis.** Etiology of this may be due to iatrogenic

injury, neoplasm, or trauma to the neck or thorax.

a. Unilateral nerve paralysis often results in dysphonia and/or dysphagia, including possible aspiration. Treatment depends upon the underlying etiology of the vocal cord paralysis, symptom severity, and if recovery is anticipated. Treatment options include speech therapy and observation, temporary vocal cord medialization via injectable material to prevent aspiration and improve voice, permanent vocal cord medialization thyroplasty, or reinnervation procedures.

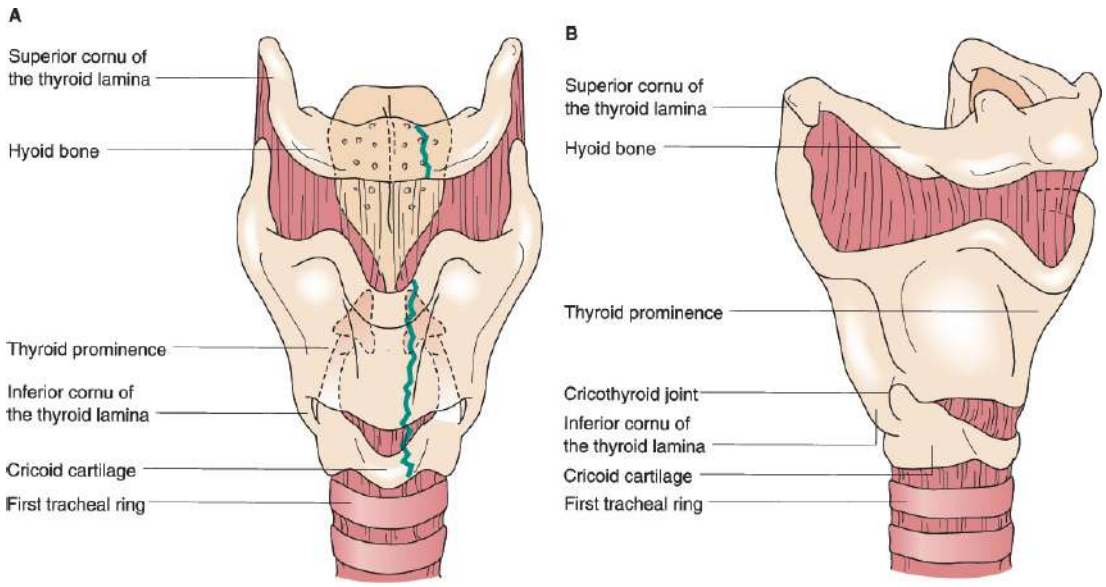


FIGURE 43-5 **A, B:** External larynx anatomy. (From Mulholland MW, Lillemoe KD, Doherty GM, Maier RV, Simeone DM, Upchurch GR Jr, eds. *Greenfield's Surgery: Scientific Principles and Practice*. Philadelphia, PA: Wolters Kluwer Health; 2011.)

b. Bilateral nerve paralysis leads to bilateral vocal cord paralysis (in a variety of configurations), which results in respiratory difficulty requiring prompt treatment. Bilateral paralysis in the median or paramedian position may result in complete airway occlusion, requiring urgent treatment such as temporary suture lateralization, cordotomy, arytenoidectomy, and/or tracheostomy. Bilateral paralysis in the intermediate or "cadaveric" position often presents with aphonia and ongoing aspiration leading to pneumonia and may require treatments as noted above.

D. Neoplasms

1. **Benign.** Recurrent respiratory papillomatosis (RRP) is characterized

by bulky papillomas, caused by human papilloma virus (HPV) 6 and 11 on the larynx and tracheobronchial tree, causing hoarseness and airway obstruction. Treatment is repeated excision.

2. **Malignant.** SCC is the most common laryngeal malignancy. Patients present with hoarseness, dyspnea, stridor, dysphagia, and neck mass (from metastases). Treatment is complex and is based on stage and location of tumor, as well as patient preferences.

E. Trauma/Injury

1. Blunt neck trauma

a. Symptoms: crepitus, pain, bruising of neck, voice changes

b. Evaluation: flexible laryngoscopy, CT neck to look for fractures, and chest x-ray. CT angiogram (CTA) if concerned for vascular injury. *Cervical spine injuries must be ruled out in all cases of laryngeal trauma.*

c. Schaefer classification of laryngeal trauma

(1) Minimal airway compromise, minor endolaryngeal hematoma, no fractures

(a) Management: Medical management (steroids, antibiotics, antireflux medications, humidification, head of bed elevation, voice rest), observation with pulse oximetry

(2) Moderate edema or hematoma with airway compromise, minor mucosal disruption without cartilage exposure, or nondisplaced fracture

(a) Management: Direct laryngoscopy and esophagoscopy in the operating room to better assess injury severity, consider intubation and/or tracheostomy versus observation with serial scope examinations, medical management as above

(3) Massive edema with airway obstruction *or* mucosal tears with exposed cartilage *or* displaced fracture *or* immobile true vocal cord(s) *or* arytenoid dislocation

(a) Management: Intubation to stabilize airway. Direct laryngoscopy and esophagoscopy should be performed in operating room +/− surgical exploration and repair of injury, tracheostomy

(4) Same as group III, but more severe and disruption of anterior larynx, unstable fractures, 2+ fracture lines, or severe mucosal

injuries

(a) Management: Direct laryngoscopy, esophagoscopy, and tracheostomy. Surgical repair of injured larynx +/− stent placement

(5) Laryngotracheal separation

(a) Management: Tracheostomy or cervical airway is often required to secure airway initially, which may be quite challenging. The patient will require complex laryngotracheal repair in the operating room

2. **Penetrating neck trauma.** Considered a penetrating injury only if the platysma is violated. Anterior and lateral neck regions contain vital structures, whereas posterior neck contains primarily nonvital vessels and muscles and thus injuries to the posterior neck is less likely to be catastrophic.

a. Mandatory neck exploration is required in any case presenting with expanding hematoma, nonexpanding hematoma with hemodynamic instability, or hypovolemic shock

b. Zones of penetrating neck trauma

(1) Zone 1 (cricoid cartilage to clavicle): Contains common carotid, subclavian and vertebral arteries, subclavian and jugular veins, recurrent laryngeal and vagus nerves, lymphatic ducts, trachea, and esophagus

(2) Zone 2 (between cricoid and angle of mandible): Contains internal and external carotid arteries, jugular and vertebral veins, pharynx, larynx, thyroid, parathyroids, marginal mandibular branch of facial nerve, recurrent laryngeal nerve, vagus nerve, phrenic nerve, submandibular gland, and spinal cord

(3) Zone 3 (angle of mandible to skull base): Contains internal and external carotid arteries, jugular veins, glossopharyngeal nerve, vagus nerve, spinal accessory nerve, hypoglossal nerve, sympathetic trunk, portion of parotid gland, and spinal cord.

c. Management

(1) Symptomatic: Operating room for neck exploration. If patient is stable and injury involves zone 1 or 3, a preoperative CTA may be helpful in deciding surgical approach. Patients with

injury to zone 1 or 2 require endoscopy (preferred) and/or swallow studies to rule out an occult esophageal injury.

(2) Asymptomatic: Workup including CTA, panendoscopy +/− swallow studies to rule out injuries to vital structures. If workup identifies an occult injury, the patient should be brought to the operating room for neck exploration. If no injury is identified on workup then patient should be admitted and observed.

F. Airway Management

1. **Difficult intubation adjuncts.** In situations where the patient is unable to be adequately ventilated with bag-mask ventilation, consider laryngeal mask airway (LMA) or endotracheal intubation. In event of difficult intubation, consider attempting one or more of the following adjuncts before proceeding with invasive airway attempts: different laryngoscope blades, intubation through LMA, use of intubating bronchoscope, intubating stylet or light wand, alternative type or size of endotracheal tube, and use of bougie or tube exchange catheter.
2. **Emergent cricothyrotomy**
   - **a.** Indications for establishing a cervical airway: inability to ventilate or intubate
   - **b.** Steps:
     - **(1)** Palpate airway anatomy. If the neck is thick and the airway not readily palpable, there is often a prominent crease over the cricothyroid membrane.
     - **(2)** Prep neck with Betadine.
     - **(3)** Incise skin with either a horizontal or vertical incision.
     - **(4)** Palpate anatomy again—once the cricothyroid membrane is located, make a horizontal incision through this membrane and place tracheostomy appliance or endotracheal tube through this incision into the airway.
     - **(5)** Following this procedure, patient should undergo formal tracheostomy placement within 24 to 72 hours due to risk of subglottic stenosis formation and infection risks with cricothyrotomy.
3. **Tracheostomy.** Multiple methods to form a tracheostomy exist, and

the decision to perform this via an open versus percutaneous approach is based on provider preference as well as patient factors (open approach in general is preferred in cases of altered patient anatomy or high-riding innominate vessel).

a. Indications: Persistent need for mechanical ventilation (of note, there is some evidence to support early tracheostomy in patients requiring mechanical ventilation), upper airway obstruction (e.g., tumor, severe obstructive sleep apnea [OSA] not amenable to noninvasive measures, etc.).

b. Complications

(1) Tracheitis, pneumonia

(2) Tracheal obstruction—most often due to mucus plugging. Prevent with good trach care including gentle suctioning and secretion management, replacement of trach and/or inner cannula on both a scheduled and as-needed basis.

(3) Bleeding

(a) Local oozing or trauma (e.g., from thyroid edges, skin edges, suction trauma causing bleeding).

(b) **Tracheoinnominate fistulae** (TIF) are rare (<1% to 2% patients who undergo tracheostomy placement) and may be preceded by **sentinel bleed**. Greater than 50% of bleeding that occur >48 hours after tracheostomy placement are due to TIF, and 75% of TIF present within the first 3 to 4 weeks after tracheostomy placement. TIF are fatal in a majority of cases. TIF are prevented by performing the tracheostomy above the third tracheal ring, monitoring cuff pressures to prevent erosion through the tracheal wall, and observing tube for pulsation (if this is noted, use a shorter tube). If TIF occur, place a cuffed endotracheal tube in the trach site and inflate the cuff, and place direct pressure on the artery with a finger against the sternum.

(4) False passage into soft tissues of the neck. Risk factors include percutaneous tracheostomy placement, morbid obesity, or new tracheostomy site. False passage needs to be promptly identified and rectified to prevent catastrophic consequences including death from airway loss. It is critical to verify the

position of all tracheostomies after tube changes with the use of either end-tidal CO_2 monitoring or fiberoptic laryngoscopy, as well as assessing the ability to suction beyond the end of the tube after placement.

(5) Pneumothorax noted on postplacement chest x-ray, treated based on size and symptomatology, but unlikely to require tube thoracostomy.

(6) Tracheoesophageal fistulae (TEF) are rare (<1% tracheostomy procedures), but are usually fatal. TEF may be an acute complication due to injury of the esophagus at the time of the procedure, or a long-term complication of tracheostomy placement due to pressure on the airway wall and subsequent erosion. TEF are prevented by keeping cuff pressures low if a cuffed tracheostomy is in place.

(7) Tracheal stenosis is a long-term complication of tracheostomy placement, prevented by minimizing trauma to the tracheal wall (i.e., gentle suctioning, keeping balloon pressures low). In children, decreased incidence is noted with the use of vertical tracheostomy incisions. Depending on the severity, tracheal stenosis may require repeat operative interventions for management or even a tracheal resection.

4. **Total laryngectomy.** A total laryngectomy involves removal of the entire larynx such that the trachea is sewn directly to the neck skin and the remaining pharyngeal tissues are sutured together to create a neopharynx. These patients can never be intubated orally following this procedure. This is different from a tracheostomy, where a hole has been made in the airway but the airway remains intact.

III. ORAL CAVITY AND PHARYNX

A. Anatomy and Physiology. The oral cavity extends from the vermillion border of the lips anteriorly to the circumvallate papillae and junction of the hard and soft palate posteriorly. The pharynx is divided into the nasopharynx, oropharynx, and hypopharynx.

B. Malignant Neoplasms. SCC is the most common neoplasm of the head and neck, and SCC can arise in the oral cavity or pharynx and metastasize to the neck, as noted above. Risk factors for oropharyngeal SCC include the following: tobacco, alcohol use, HPV genotypes 16 and

18. Treatment of SCC is complex and based on location and extent of disease.

C. Trauma. Mandible fractures occur most commonly at the angle and parasymphysis, as well as at the condylar neck. Fractures present with dental malocclusion, halitosis, and pain with crepitus while chewing or on manipulation. Panorex radiographs are often sufficient to diagnose these fractures, however high-resolution maxillofacial CT may be more sensitive. Treatment varies depending upon fracture location, dentition status, and age of patient, but may include conservative management with soft diet and antibiotics, or operative intervention including closed reduction and external fixation ("wiring the jaw shut") and/or open reduction and internal fixation. Complications include wound infection, malocclusion, nonunion, tooth loss, temporomandibular joint ankylosis, and paresthesias.

IV. THE SALIVARY GLANDS

A. Anatomy and Physiology. There are three pairs of major salivary glands (parotid, submandibular, and sublingual) and many minor salivary glands in the mucosa of the oral cavity, oropharynx, and nasopharynx.

1. The **parotid gland** lies over the masseter muscle and is the largest salivary gland. The **facial nerve** travels through this gland, dividing it into superficial and deep lobes. CN IX provides parasympathetic innervation, which helps to regulate saliva flow.
2. The **submandibular gland** is inferomedial to the mandible and the **sublingual gland** lies beneath the floor of the mouth mucosa. Secretomotor innervation to these glands is provided by the chorda tympani nerve (CN VII).

B. Inflammatory Diseases. Acute sialadenitis is an infectious process usually involving the parotid gland, presenting as a tender, preauricular swelling with purulence expressible from the parotid duct (**Stensen duct**). Treatment is hydration, warm compresses, massage, antibiotics, and sialogogues to stimulate saliva flow.

C. Neoplasms. Salivary neoplasms are most frequent in the parotid gland (70%), but most parotid tumors are benign. A larger percentage of submandibular tumors are malignant (50% malignant), and sublingual tumors have a high likelihood of malignancy (*Sem Rad Oncol*.

2012;22:245–253).

1. **Benign.** The most common neoplasm is **pleomorphic adenoma,** followed by **Warthin tumor.** These tumors grow slowly, are painless, and usually occur in the parotid gland. Treatment is excision with a cuff of normal parotid tissue and facial nerve preservation.
2. **Malignant.** The most common malignancy is **mucoepidermoid carcinoma,** followed by **adenoid cystic carcinoma.** Other types include acinic cell carcinoma, adenocarcinoma, and primary SCC. Treatment is parotidectomy, with facial nerve sacrifice if involved in tumor, possible neck dissection, and possible adjuvant radiation therapy.

V. THE EAR AND TEMPORAL BONE

A. Anatomy and Physiology

1. The **temporal bone** lies on the lateral aspect of the head, posterior to the mandible and anterior to the occiput. The external ear lies lateral to the temporal bone. Medial to the temporal bone lies the brain and its associated meninges.
   - **a. External ear.** The auricle (pinna) is composed of elastic cartilage and channels sound waves to the external auditory canal.
   - **b.** The **middle ear** is a mucosa-lined sinus in the temporal bone and lies medial to the tympanic membrane. The middle ear contains the ossicular chain, which consists of the malleus, incus, and stapes.
   - **c.** The **inner ear** contains cochlea and the vestibular system surrounded by thick bone, the otic capsule. The vestibular system consists of three semicircular canals, which sense angular acceleration, and the saccule and utricle, which sense linear acceleration. The vestibulocochlear nerve receives sensory input from these structures.
   - **d.** The **facial nerve** (CN VII) travels a complex path through the temporal bone, where it is vulnerable to trauma. It innervates the facial musculature and stapedius muscle, and it provides taste sensation for the anterior two-thirds of the tongue via the chorda tympani. It then exits the skull base at the stylomastoid foramen to enter the parotid gland and innervate the muscles of facial expression.

e. Important vessels housed within the temporal bone include internal carotid artery, jugular vein, and sigmoid sinus.

B. Trauma

1. Temporal bone fractures

a. Examination. Cranial nerve examination concentrating on CN VII and CN VIII function, assess Weber and Rinne with tuning fork, look for clear rhinorrhea/otorrhea, "**Battle" sign**: ecchymosis over mastoid.

(1) If clear otorrhea/rhinorrhea, send beta2 transferrin to rule out CSF leak.

(2) If CT shows involvement of carotids or vascular structure, obtain CTA and neurosurgery consult.

(3) Facial nerve injuries—assess time course as delayed-onset nerve injuries are most often from contusion and recover with time.

b. Management

(1) Nonoperative measures: no nose blowing, open mouth sneezing, no straining with bowel movements, bowel regimen to prevent constipation.

(2) Audiogram when able.

(3) Steroids if cranial nerve involvement (e.g., sensorineural or mixed hearing loss, facial nerve weakness) or otic capsule involvement.

(4) Systemic antibiotics to prevent meningitis +/− short course of ofloxacin otic drops, and neurosurgery consult for possible lumbar drain placement if concerned for CSF otorrhea.

(5) Facial nerve paralysis is generally treated conservatively with steroids and eye care (moisture chamber, eye taping at night, artificial tears or Refresh ophthalmic drops while awake, Lacri-lube at night). Serial electroneuronography (ENoG) should be performed in cases of complete facial nerve palsy.

(6) Surgical management is rare and occurs in a planned, delayed fashion. Indications for surgical procedures include the following: persistent conductive hearing loss, persistent/nonhealing tympanic membrane perforation, severe facial nerve injury, CSF otorrhea or rhinorrhea that persists

despite conservative measures, severe comminuted fractures requiring debridement, or ear canal stenosis.

VI. THE NOSE AND PARANASAL SINUSES

A. Anatomy and Physiology

1. The nose and septum are composed of bone superiorly and posteriorly and cartilage anteriorly. The **turbinates** are mucosa-covered bony prominences from the lateral nasal cavity that humidify, warm, and filter inhaled air. The nasopharynx contains the eustachian tube orifices bilaterally and the adenoid pad centrally, which involutes in late childhood.

2. The **paranasal sinuses** are pneumatized cavities in the skull named for the bone in which they lie (frontal, sphenoid, ethmoid, or maxillary). They reduce the weight of the skull, contribute to the resonance of a person's voice, and cushion the cranial contents against trauma. They are lined with ciliated respiratory epithelium.

B. Epistaxis. Nose bleeds are common and can be caused by trauma, neoplasm, environmental irritants, rhinitis, coagulopathies, and granulomatous diseases.

1. Differential diagnosis should include **juvenile nasopharyngeal angiofibromas**. These vascular tumors usually present in adolescent boys as nasal obstruction and recurrent epistaxis. Treatment is surgical excision (either open or endoscopic), with preoperative embolization to reduce blood loss. Bleeding and recurrence are both complications to be discussed with patients (*Laryngoscope*. 2013;123:859–869).

2. Preventive measures. High-humidity face tent in lieu of nasal cannula, humidification, saline spray, nasal emollients (e.g., Ayr nasal gel, Ponaris nasal emollient), discontinuation of offending agent.

3. Management:

a. Correct underlying etiologies

b. Self-care (pinching anterior cartilaginous nose to provide pressure over septum +/− oxymetazoline). Topical decongestants (e.g., oxymetazoline) aid in symptomatic relief, but use *should not exceed 3 days*, as it may result in rebound congestion (rhinitis medicamentosa)

c. Bedside interventions:

(1) Silver nitrate cauterization if discrete bleeding vessel visualized

(2) Floseal or HemaDerm if nasal oozing, patient with hereditary hemorrhagic telangiectasia (HHT), or patient on therapeutic anticoagulation

(3) Nasal packing with product (e.g., Rapid Rhino, Rhino Rocket, Surgicel, Gelfoam)

(a) Strongly consider antibiotics while nasal packing in place to prevent toxic shock

(b) Ensure patient follow-up for removal of packing material (usually 3 to 5 days after it is placed)

d. Operative and procedural interventions

(1) Sphenopalatine artery ligation is performed by a surgeon familiar with sinonasal anatomy

(2) Internal maxillary artery embolization is performed by interventional radiologist

(3) Lateral canthotomy and anterior ethmoid artery ligation in case of anterior ethmoid artery bleeds (rare) is performed by surgeon familiar with sinonasal anatomy or ophthalmologist

CHAPTER 43: OTOLARYNGOLOGY FOR THE GENERAL SURGEON

Multiple Choice Questions

1. **A 60-year-old male comes into the emergency department following a motor vehicle accident. He has a well-formed cervical stoma, and no device is in place. Although he nods to questions, he is not able to vocalize his responses. He denies any difficulty breathing at this time. His pulse ox is noted to be 89%. What type of airway does this patient most likely have and what management should be initiated?**

   a. Tracheostomy site—site should be covered with an occlusive dressing and patient should press on dressing in order to talk, and oxygen via nasal cannula should be initiated since his oxygen is moderately low
   b. Tracheostomy site—a new tracheostomy tube should be placed in the stoma to prevent premature closure of the site and patient should be suctioned
   c. Total laryngectomy site—high-humidity trach collar should be placed around neck
   d. Total laryngectomy site—oxygen via nasal cannula should be delivered to patient
   e. The cervical stoma is not part of the patient's airway. If respiratory distress worsens, he should be intubated orally.

2. **A 72-year-old male currently 2 days out from wedge resection of his lung, is noted to have epistaxis. Nothing has been tried at this time. What is the next step?**

   a. Stop nasal cannula and start high-humidity face tent
   b. Spray nose with oxymetazoline, and have patient hold on the bony bridge of his nose
   c. Spray nose with oxymetazoline, and have patient pinch the nasal ala to the septum
   d. Roll 4 × 4 gauze and insert into nasal cavity
   e. Call ENT to come see this patient as he likely needs to go to the

operating room for an intervention

3. **A 5-year-old, otherwise healthy male presents to clinic with a neck mass that appears to move vertically when he swallows. The mass is nontender and midline. What important diagnostic test/study should be performed before surgical intervention?**

   a. MRI of the head and neck
   b. CT of the neck and chest
   c. EBV testing for mononucleosis
   d. Fine-needle aspiration for cytology to diagnosis this mass
   e. Ultrasound of the neck

4. **A 45-year-old woman is found to have papillary thyroid cancer and undergoes a total thyroidectomy. Immediately following surgery in PACU, the patient complains of difficulty breathing. On examination, she is noted to have stridor and desaturations. An awake scope examination is performed in PACU, and it appears that both vocal cords are paralyzed. Which of the following options below would provide the best care for this patient?**

   a. Medialization thyroplasty
   b. Tracheostomy
   c. Speech therapy
   d. Temporary vocal cord injection laryngoplasty
   e. Oxygen via nasal cannula

5. **A 50-year-old male with a history of intermittent smoking over the past 10 years and arthritis presents to clinic with a right-sided neck mass. Examination reveals asymmetry of his tonsils with bulkiness of the right tonsil. You suspect squamous cell carcinoma, as you know this commonly metastasizes to the neck. What is the next best step in management?**

   a. Removal of right tonsil and right neck dissection
   b. 14-day course of antibiotic therapy as this might be reactive lymphadenitis
   c. Core or open biopsy to confirm diagnosis

d. Chemoradiation
e. FNA biopsy of right neck node

6. **A 25-year-old female presents with a slowly growing deep neck mass. She reports that she has been having episodes of lightheadedness with fainting and she remembers a family member having neck surgery in the past. She is healthy outside of history of anxiety. The radiologist reviews her CT and notifies you that the mass appears to be splaying the internal and external carotid arteries, and you are considering a diagnosis of carotid body tumor. What is your next step in management?**

a. Preoperative embolization followed by surgical resection
b. Testing for urine and serum metanephrines, CT abdomen
c. Open or core biopsy for diagnosis
d. Surgical resection
e. FNA biopsy of neck mass

7. **A 12-year-old female with a history of asthma presents to clinic with large bulky persistent cervical lymph nodes, despite a 2-week course of antibiotics. A fine-needle aspiration (FNA) biopsy is suspicious for lymphoma. What is the next best step in management and treatment for this patient?**

a. Bilateral radical neck dissection
b. Selective neck dissection of affected nodes
c. Radiation without chemotherapy
d. Core or excisional biopsy for flow cytometry, to direct further treatment
e. Fine-needle aspiration of a second lymph node to verify diagnosis

44 Plastic, Reconstructive, and Hand Surgery

Elspeth J.R. Hill and Kamlesh B. Patel

INTRODUCTION

Plastic surgery focuses on restoration of form and function, and is built on principles and techniques rather than specific procedures. In this chapter, we discuss topics pertinent to the general surgeon.

BASIC TECHNIQUES AND PRINCIPLES

I. **The Reconstructive Ladder.** When planning reconstruction, the simplest approach is often the best, but it is critical to know when a more complex solution is appropriate.

A. Healing by secondary intention. Maintain a clean protected wound with dressings. Contraindications include exposed critical structures, prolonged anticipated period of healing (>3 weeks), undesirable aesthetic consequences. **Negative-pressure wound therapy (NPWT)** can be used to accelerate the healing; contraindications include malignancy, ischemic wounds, infected wounds, or inadequately debrided tissue beds.

B. Primary closure will often have best aesthetic result. Avoid tension to prevent tissue ischemia, dehiscence, hypertrophic scar formation, and displacement of neighboring structures (e.g., lower eyelid).

C. Random pattern flaps rely on subdermal plexus perfusion for local tissue rearrangement.

D. Skin grafting requires a healthy, vascularized, uninfected wound bed, and an available donor site. Bare tendon, desiccated bone or cartilage,

radiation-damaged tissue, or infected wounds will not support skin graft survival. **NPWT** may be used to promote granulation tissue and create a graft-able wound.

E. Tissue expansion involves slowly stretching existing tissue to cover a defect in a staged manner, such as expanding scalp tissue to provide hair-bearing coverage of a scalp defect.

F. Local tissue transfers and flaps are based on an axial named vessel, which acts as a vascular pedicle.

G. Free tissue transfer requires microvascular anastomosis but may allow single-stage wound closure and often an acceptable aesthetic outcome.

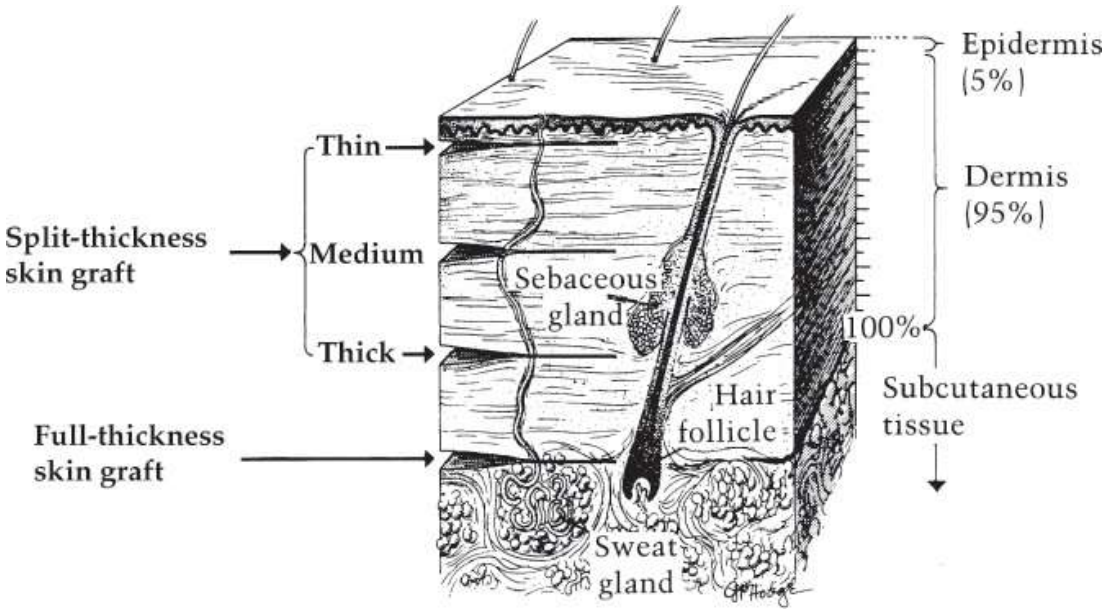


FIGURE 44-1 Skin graft thickness. (From Thorne CH, Chung KC, Gosain AK, et al., eds. *Grabb and Smith's Plastic Surgery*. 7th ed. Philadelphia, PA: Wolters Kluwer Health; 2014.)

II. TYPES OF GRAFTS

A. Skin Grafts (Fig. 44-1)

1. **Split-thickness grafts (STSGs)** include epidermis and a portion of dermis
   - **a.** A 20% primary contracture, 40% secondary contracture (thicker grafts will have reduced contracture)
   - **b.** Donor sites: Thigh, buttock, abdomen, and scalp
   - **c.** Heals by secondary intention
   - **d.** Use a moist occlusive dressing to reduce pain and facilitate healing

e. Meshing can be used to increase coverage surface area and reduce risk of fluid accumulation (a ratio of 1.5:1 is commonly used)

f. Relative contraindications: Joint coverage, aesthetically demanding location

2. Full-thickness grafts include epidermis and dermis

a. >40% primary contraction, ~0% secondary contraction

b. Donor sites: Groin, postauricular, supraclavicular, abdomen

c. Graft failures are most commonly the result of hematoma, seroma, infection, or shearing.

3. Stages of skin graft healing

a. Days 1 and 2: Imbibition (diffusion of nutrients from the wound bed)

b. Days 3 and 5: Inosculation (graft and wound bed capillaries begin to align)

c. Day 4: Graft well anchored by collagen (earliest time at which bolster should be removed)

d. >5 days: Graft revascularized by capillary ingrowth

e. 6 weeks: Ninety percent of maximal tensile strength

B. Other Graft Sources

1. Tendon grafts: Palmaris longus, plantaris tendons.

2. Bone grafts:

a. Cancellous: Iliac crest.

b. Cortical: Ribs, outer table of cranium, fibula.

3. Cartilage grafts: Costal cartilage, concha of ear, nasal septum.

4. Nerve grafts: Sural nerve, lateral or medial antebrachial cutaneous nerves. Cadaveric allograft also available.

5. Fat grafts: Liposuction of abdomen, thigh, buttocks.

III. TYPES OF FLAPS.

A flap is any tissue that is transferred to another site with its native blood supply intact.

A. Classification Based on Blood Supply

1. Random cutaneous flaps are used to cover adjacent defects.

a. Blood supply from the dermal and subdermal plexus.

b. Length-to-width ratio (usually 3:1), varies by anatomic region (e.g., the face has a ratio of up to 5:1).

c. Flaps that rotate about a pivot point include **rotation flaps** (Fig. 44-2) and **transposition flaps** (Fig. 44-3).

(1) The effective length shortens through the arc of rotation

(2) The further from the base of the flap, the greater the risk of necrosis

(3) More complex rotation flaps: **Bilobed flaps** (Fig. 44-4) and **rhomboid flaps** (Fig. 44-5)

d. Advancement of skin directly into a defect without rotation.

(1) Simple advancement

(2) V-Y advancement (Fig. 44-6)

(3) Bipedicle advancement flap

2. Axial cutaneous flaps contain a single dominant arteriovenous system, allowing for a potentially greater length-to-width ratio.

a. Peninsular flap. Skin and vessels are moved together as a unit.

b. Island flaps. Skin is divided from surrounding tissue and maintained on an isolated, intact vascular pedicle.

c. Free flaps. Vascular pedicle is isolated and divided, then reanastomed at a new anatomic site.

B. Specialized Flaps

1. Fascial/fasciocutaneous flaps are used when thin, well-vascularized coverage is needed (e.g., dorsum of the hand or foot).

a. Fascia: Temporoparietal fascia.

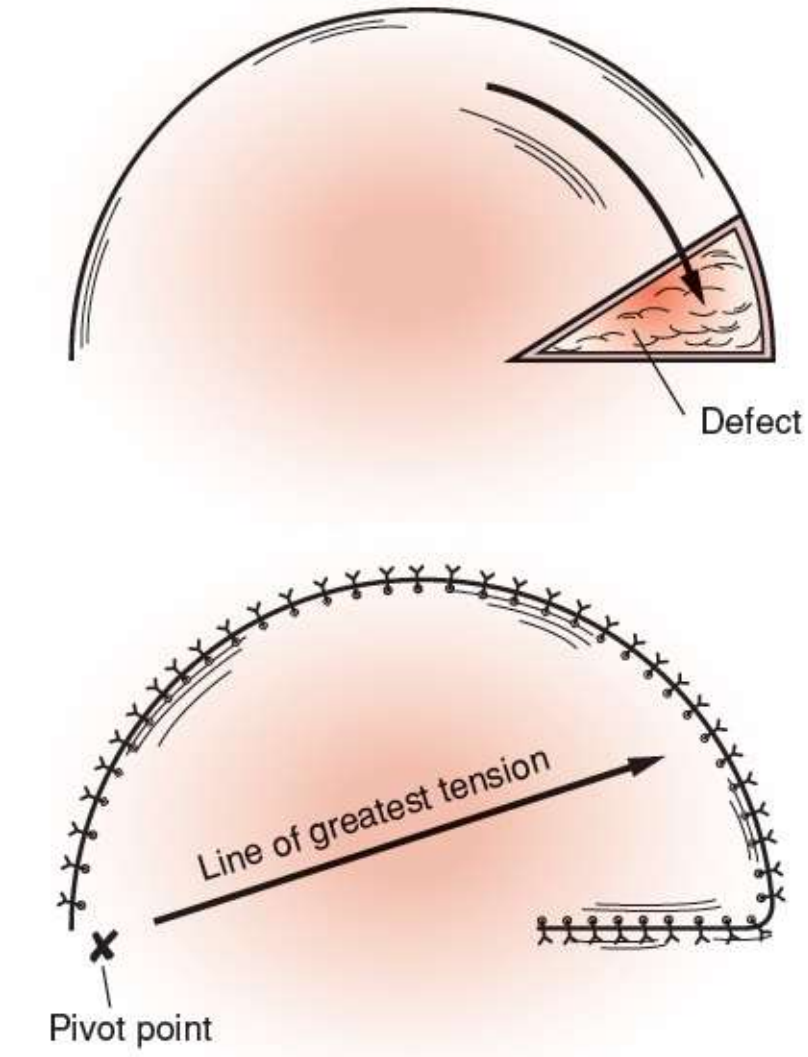
b. Fasciocutaneous flaps: Radial forearm, anterolateral thigh, lateral arm, and groin flaps.

2. Muscle or musculocutaneous flaps are used when muscle is needed for bulk, to obliterate dead space, or robust well-vascularized coverage is needed.

a. Muscle: Sartorius, rectus femoris, gracilis muscle for groin coverage.

b. Musculocutaneous: Latissimus dorsi or pectoralis major for chest, or rectus abdominis or gracilis for perineal coverage.

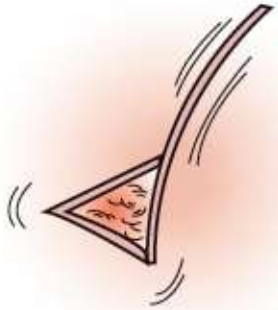
3. Vascularized bone flaps are used for critical bony defects >8 cm.


Defect
Line of greatest tension
Pivot point

A


Backcut

B


Burow triangle

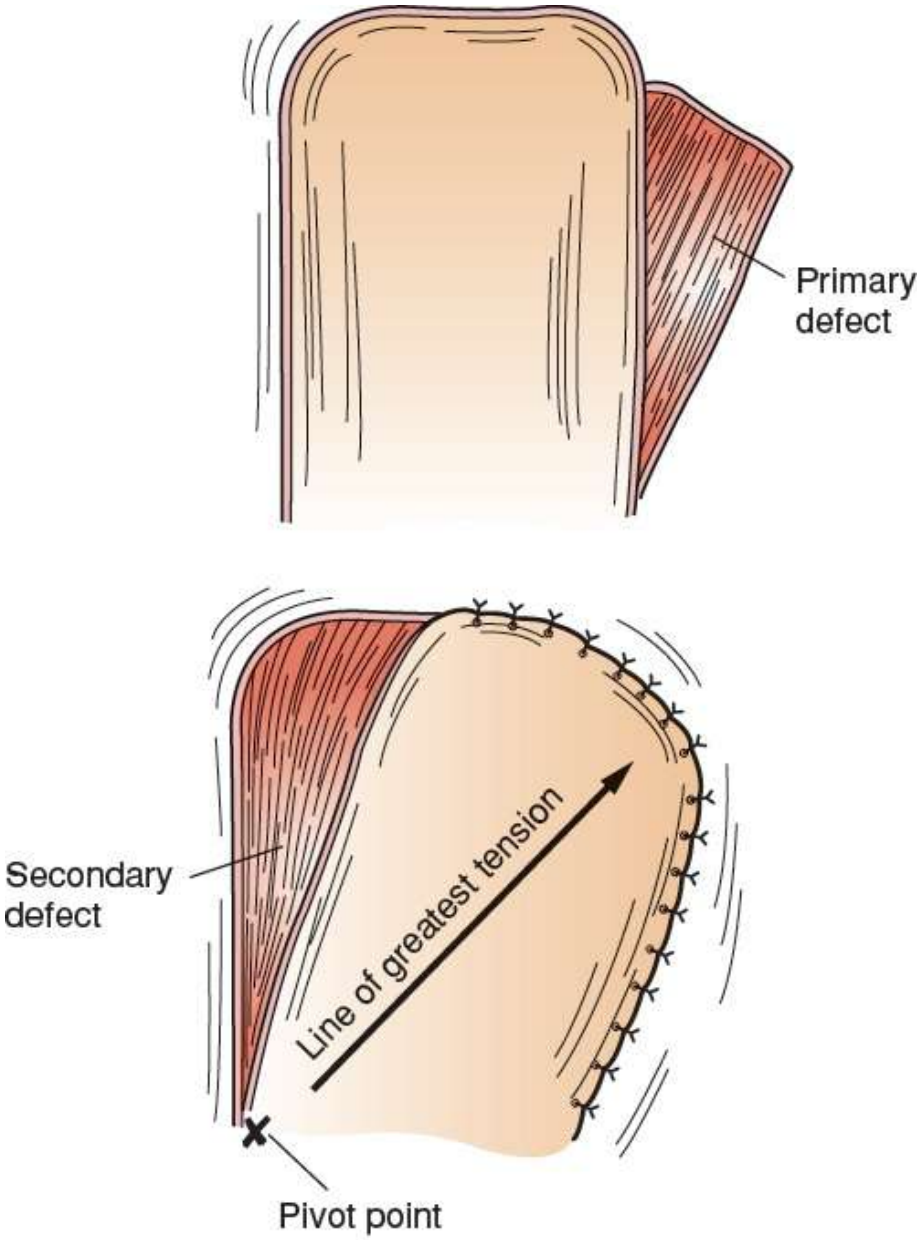
C

FIGURE 44-2 Rotation flap. **A:** The edge of the flap is four to five times the length of the base of the defect triangle. **B, C:** A backcut or Burow triangle can be useful if the flap is under tension.

   a. **Donors:** Fibula, scapular spine, iliac (with overlying internal oblique muscle), and rib (with pectoralis major or intercostal muscle).

4. **Functional muscle** may be transferred with its accompanying dominant nerve.

   a. **Donors:** Gracilis, latissimus dorsi.


Primary
defect
Secondary
defect
Line of greatest tension
Pivot point

A

Backcut

B

FIGURE 44-3 **A:** Transposition flap (more complex rotation flap that creates a defect that must be closed). The secondary defect is typically covered with a skin graft. **B:** A backcut may be added to reduce tension at the pivot point.

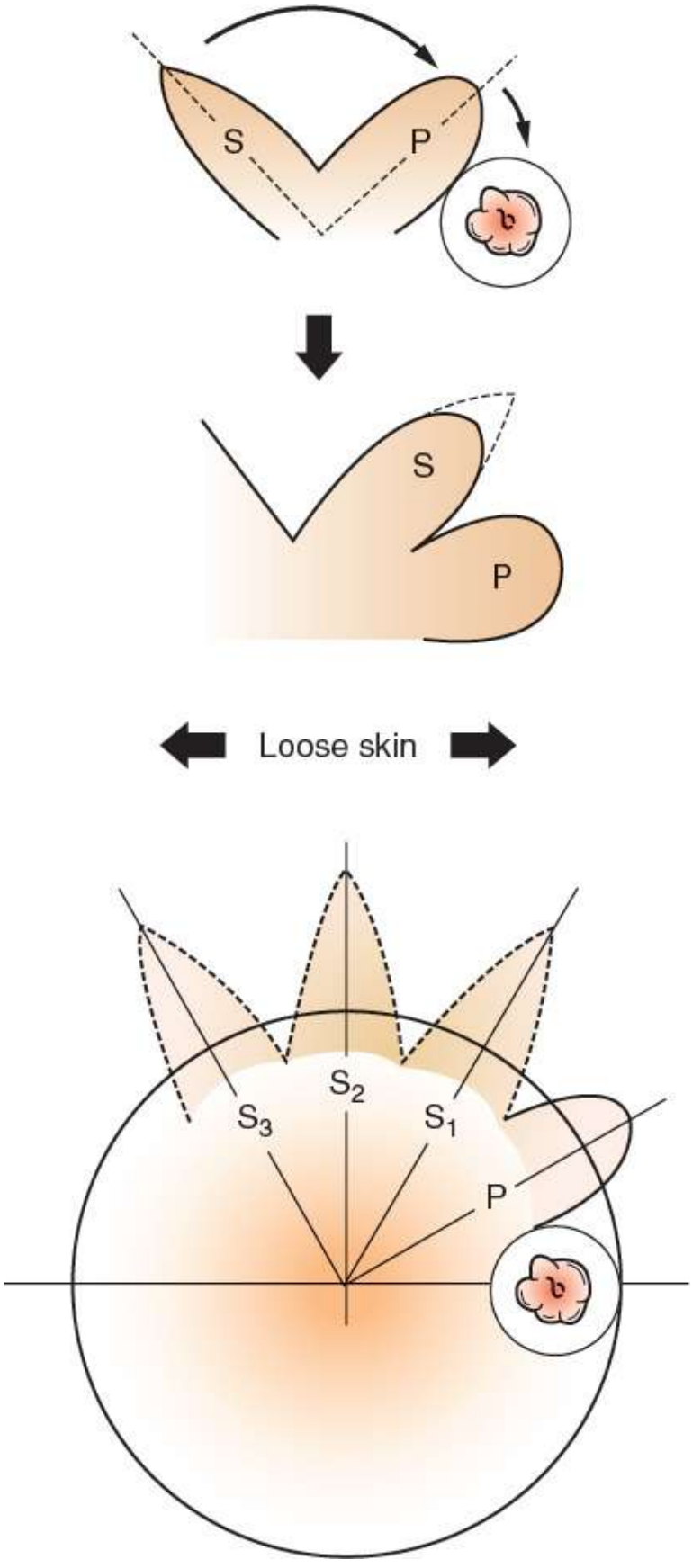

S
P
S
P
Loose skin
S_2
S_3
S_1
P

FIGURE 44-4 Bilobed flap. After the lesion is excised, the primary flap (*P*) is transposed into the initial defect, and the secondary flap (*S*) is moved to the site vacated by the primary flap. The bed of the secondary flap is then closed primarily. The primary flap is slightly narrower than the initial defect, whereas the secondary flap is half the width of the primary flap. To be effective, this must be planned in an area where loose skin surrounds the secondary flap site. Three choices for the secondary flap are shown (S_1, S_2, S_3).

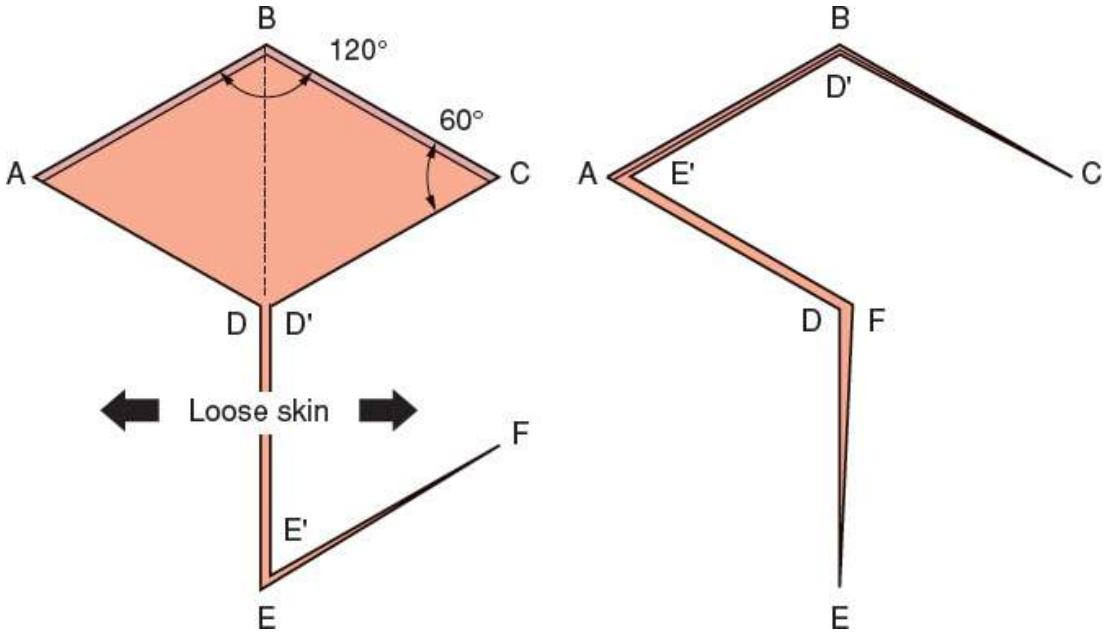


FIGURE 44-5 Rhomboid or Limberg flap. The rhomboid defect must have 60- and 120-degree angles so that the length of the short diagonal is the same as the length of the sides. The short diagonal is extended by its own length to point *E*. The line *EF* is parallel to *CD*, and they are equal in length. The greatest tension will be between points *F* and *D*. Four possible Limberg flaps exist for any rhomboid defect; the flap should be planned in an area where loose skin is available to close the donor defect primarily and hide scars.

IV. Tissue Expansion. Tissue expansion uses an inflatable silicone balloon to serially expand surrounding skin. During expansion, the dermis thins, collagen realigns, and the epidermis thickens. The expansion phase begins 2 to 3 weeks after expander placement. Inflate weekly/biweekly using saline. Common indications include burn alopecia, congenital nevi, and postmastectomy breast reconstruction.

A. Advantages. Low donor-site morbidity, provision of donor tissue of similar color, texture, thickness, and sensation to the recipient tissue (like for like).

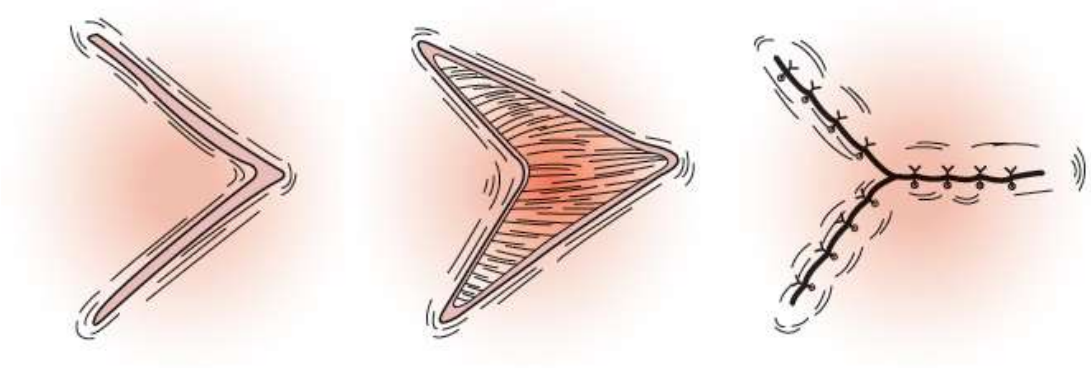


FIGURE 44-6 V-Y advancement. The skin to the sides of the V is advanced.

B. Disadvantages. Staged technique, there is a visible deformity during the period of expansion, frequent visits for expansion, and a relatively high rate of complications (infection, extrusion).

ACUTE INJURIES

I. FACIAL TRAUMA

A. Examination Pearls

1. **Cervical spine.** Ten percent of facial trauma patients have associated C-spine injury.
2. **Oral examination.** Malocclusion or limited mouth opening can indicate fractures; assess for loose teeth that are at risk for aspiration.
3. **Facial nerve.** Assess the five branches: Brow raise (temporal), squeeze eyes shut (zygomatic), puff out cheeks (buccal), smile and grimace to depress lower lip (marginal mandibular), flex platysma (cervical), noting any paresis or asymmetry. Facial nerve injuries located lateral to the pupil should be explored and repaired within 72 hours; more medial injuries can be managed expectantly as the facial nerve is highly arborized in the medial face.
4. **Ocular examination**
   - **a.** Assess extraocular movements; limited movement may **indicate muscle entrapment** in an orbital fracture (acute indication for surgery).
   - **b.** **Orbital compartment syndrome** results from retrobulbar hematoma and requires emergent lateral cantholysis. Look for proptosis, acute vision loss, and severe eye pain.

5. **Nasal examination.** Examine the nasal septum with an otoscope to assess for septal hematoma. Acute evacuation of the hematoma will prevent permanent deformity.

B. Imaging

1. **Maxillofacial CT** is a fast, sensitive, and specific means of determining the location and orientation of facial fractures. No imaging needed for isolated nasal fractures.
2. **Panorex** radiograph is useful in the setting of isolated mandible fractures or dental injuries.

C. Facial Hemorrhage. Nasal hemorrhage will generally cease with packing. Massive hemorrhage refractory to packing is likely a branch of the external carotid and will require embolization.

D. Soft Tissue Repair

1. Local anesthesia may be used to block facial nerve branches. Copiously irrigate, debride devitalized tissue.
2. Align anatomic structures such as vermillion border, or rhytids/creases to prevent aesthetic distortion.
3. For deep dermal closure use interrupted resorbable suture. For epidermal closure use absorbable fast gut or permanent monofilament if removed in timely fashion. For mucosal closure use interrupted or locking longer-lasting absorbable suture (chromic).

E. Fractures

1. Most can be repaired electively within 1 to 2 weeks
2. Exceptions: Airway compromise, ocular muscle entrapment
3. Indications for fixation
   a. **Mandible:** Malocclusion
   b. **Orbital:** Persistent diplopia, enophthalmos, extraocular muscle entrapment, hypoglobus
   c. **Midface:** Cosmetic deformity, trismus/malocclusion
   d. **Nasal fracture:** Cosmetic deformity, airway obstruction

II. HAND TRAUMA

A. Assessment Pearls

1. **History.** Hand dominance, patient occupation, hobbies, smoking status.
2. **Vascular assessment.** Color, temperature, capillary refill, and the

presence of pulses at the wrist and individual digits (palpable or Doppler).

a. Allen test. Verifies integrity of the palmar arches, identifies radial or ulnar artery transection or occlusion.

b. Control bleeding with direct pressure. Tourniquets should be reserved for life-threatening exsanguinations only and should be placed as distally as possible.

3. **Motor examination.** Examine extension and flexion of digits.
4. **Sensory testing** includes gross examination of the ulnar, radial, and median nerves (Table 44-1).
   a. Two-point discrimination. Test fingertips, normal is distinguishing two points ≤5 mm apart.
   b. 10–10 test. Note light-touch sensation from 0 to 10 (0 = no sensation, 10 = normal sensation) compared to an uninjured area.
5. **Diagnostic radiology.** If **fracture/dislocation** suspected, obtain at least three views (posteroanterior, lateral, oblique) including the joint above and below the suspected fracture/dislocation. For penetrating trauma or abscess, use plain films to assess for retained foreign bodies such as needles or teeth.

TABLE 44-1 Unambiguous Tests of Hand Nerve Function

Test	Radial Nerve	Median Nerve	Ulnar Nerve
Sensory	Dorsum first web	Index fingertip	Small fingertip
Extrinsic motor	Extend wrist	FDP index	FDP small
Intrinsic motor	None	Abduct thumb perpendicular to palm	Cross long finger over index (interossei)

FDP, flexor digitorum profundus.

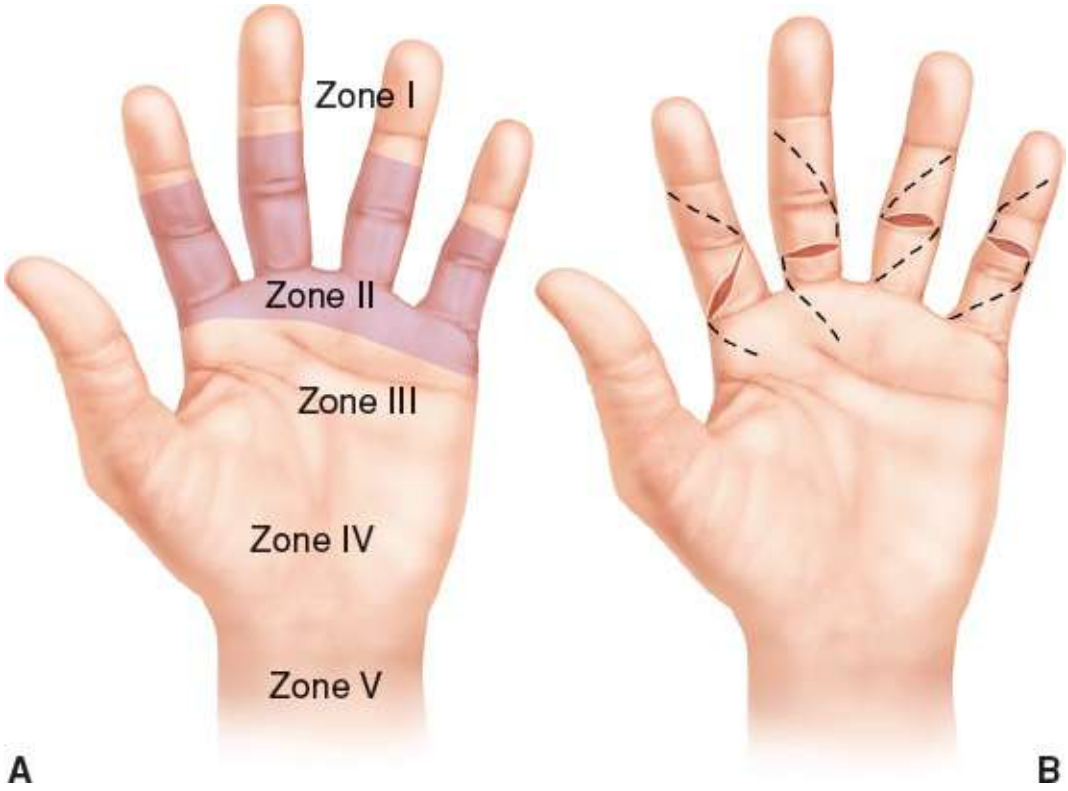


FIGURE 44-7 Zones of flexor tendon injury. **A:** Zone I. At the DIP level, distal to the FDS insertion; Zone II. From proximal A1 pulley (MCP joint) to FDS insertion. Injuries in this zone may affect both FDS and FDP; Zone III. From distal transverse carpal ligament (carpal tunnel) to A1 pulley. Look for associated palmar arch or median/ulnar nerve injury; Zone IV. Within the carpal tunnel, look for median nerve injury; Zone V. Proximal to the carpal tunnel. In general, flexor tendons repaired in zones I, III, IV, and V have a better prognosis than those in zone II, known as "no man's land." **B:** Brunner zigzag extensions to optimize exposure of the proximal and distal ends of the flexor tendon. (From Thorne CH, Chung KC, Gosain AK, et al., eds. *Grabb and Smith's Plastic Surgery*. 7th ed. Philadelphia, PA: Wolters Kluwer Health; 2014.)

6. **Wound closure.** After thorough irrigation, primary closure with absorbable (4-0 chromic or similar) or nonabsorbable (3-0 or 4-0 nylon) interrupted suture is appropriate. **Glabrous skin** on palm or fingers should be closed in single layer with eversion of skin edges to prevent epidermal inclusion cysts. Horizontal mattress or interrupted simple sutures achieve this well.

B. Fractures—refer to Chapter 13 for management of hand fractures.

C. Tendon Injuries

1. **Flexor tendons** are frequently lacerated during everyday activities **(flexor tendon zones**, Fig. 44-7).

   a. Acute management. Wound should be irrigated and closed. Dorsal

blocking splint with wrist in 20- to 30-degree flexion, MCPs in 90-degree flexion, and IP joints in gentle flexion minimizes retraction of cut tendon ends. Repair early (within 10 days) to avoid the need for tendon grafting.

b. Definitive repair involves a core, locking suture and an epitendinous repair. Injuries in zones II to IV have a worse prognosis because of scarring and reduced tendon glide within the sheath.

2. Extensor tendon injuries result from lacerations and closed axial loading of the digits.

a. Rupture of the terminal tendon over the DIP joint secondary to forced flexion results in **Mallet finger**, or inability to extend the DIP.

b. Injury over PIP joint may injure central slip and/or lateral bands. If untreated results in **boutonnière deformity** (PIP flexion and DIP hyperextension).

c. Injury over **MCP joint should be explored** to assess for sagittal band injury at this level as this must be repaired to prevent tendon subluxation. These injuries can occur secondary to delivering a punch to the mouth.

d. Management. Can be repaired acutely. Quality of repair less critical than flexor tendons as less force transmitted through extensors, and not required to glide through a tendon sheath. Mallet injuries can be treated in a closed fashion with extension splinting of the DIP for 6 weeks.

D. Local Infections

1. Most finger infections heal well if all the purulence is drained and the wound is irrigated two to three times daily with soapy water and allowed to heal from the inside out. Splinting for comfort and elevation to reduce edema are important adjuncts. Always obtain plain films prior to exploration to assess for foreign bodies (i.e., needles).

a. Paronychia is a localized infection of the skin and lateral nail fold, often due to nail biting or foreign body penetration, such as a needlestick injury. Treatment requires incision and drainage (I&D), with removal of the nail when the infection extends deep

to the nail plate. **Chronic paronychia** is sometimes associated with underlying osteomyelitis or fungal organisms (Fig. 44-8).

b. Felon is a local infection of the finger pulp commonly due to a puncture wound. Adequate drainage requires dividing all involved septae.

c. Cellulitis in the hand usually arises secondary to a laceration, abrasion, or other soft tissue injury. Management involves draining an abscess, if present, and treating with antibiotics.

d. In **animal bites**, the wound must be thoroughly irrigated to decrease the bacterial load and to remove any foreign body, such as a tooth. Bite wounds should be treated with oral antibiotics prophylactically and with intravenous (IV) antibiotics when an established infection is present.

e. Human bites/fight bites are most commonly associated with a punch to the mouth. If overlying the MCP aggressive wound exploration, generally in the operating room, must be undertaken as the skin will retract proximally and cover a deeper wound; 75% of fight bites result in bone/tendon/cartilage injury. Treat with IV antibiotics acutely. May require multiple washouts.

E. Surgical Emergencies

1. **Compartment syndrome** in the hand and forearm results from increased pressure within an osseofascial space, leading to decreased perfusion pressure. Left untreated, it will result in muscle and nerve ischemia and necrosis. Refer to Chapter 13 for complete workup and management of compartment syndrome.

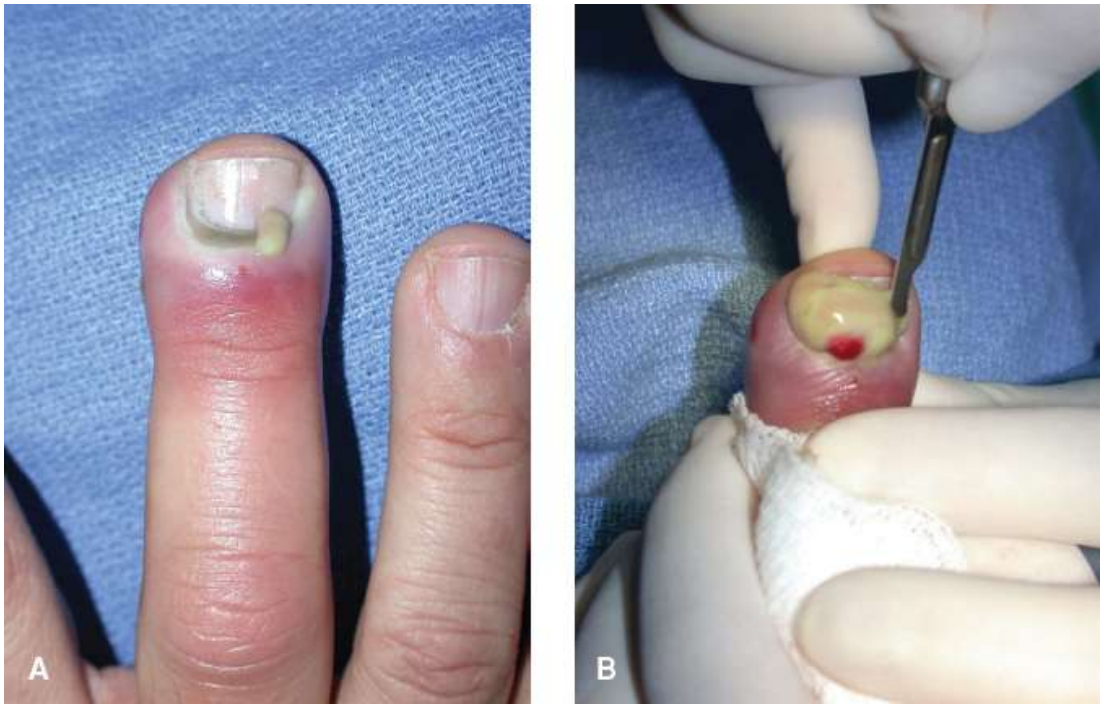


FIGURE 44-8 Acute paronychia. **A:** As seen in the emergency room. **B:** Incision is made through the most fluctuant region. (From Thorne CH, Chung KC, Gosain AK, et al., eds. *Grabb and Smith's Plastic Surgery*. 7th ed. Philadelphia, PA: Wolters Kluwer Health; 2014.)

2. **Suppurative tenosynovitis** is infection of the flexor tendon sheath, usually due to a puncture wound to the volar aspect of the digit or palm.
   a. **Diagnosis: Cardinal signs of Kanavel**
      (1) Finger held in flexion
      (2) Fusiform swelling of the finger
      (3) Tenderness along the tendon sheath
      (4) Pain on passive extension
   b. **Management** involves urgent I&D in the operating room and IV antibiotics
3. **Palmar abscess** is usually associated with a puncture wound. The fascia divides the palm into thenar, midpalmar, and hypothenar spaces; each involved space must be incised and drained.
4. **Necrotizing infections** threaten both limb and life. Aggressive and repeated surgical debridement, broad-spectrum antibiotics, and supportive management are the mainstays of treatment.

F. Local Anesthesia in Hand Surgery

1. **Local anesthetic.** Highly effective, may avoid general anesthetic, and reduce narcotic use.
2. **Local field blocks** ideal for I&D or laceration repairs.
3. **Digital blocks.** Dorsal approach to lateral bases of digit minimizes pain. Injection into flexor tendon sheath from volar approach over metacarpal head requires single injection but is more painful. Safe to use epinephrine in digits unless they are vascularly compromised.
4. **Pre- and postoperative US-guided blocks.** Available from anesthesia team and highly effective. Avoid if critical sensation or motor examination needed postoperatively.
5. **Bier block.** Involves injection of IV local anesthesia into extremity once exsanguinated and tourniquet inflated; useful in conjunction with sedation. Tourniquet pain limits duration of cases.

GENERAL RECONSTRUCTIVE PLASTIC SURGERY

I. SCALP, CALVARIAL, AND FOREHEAD RECONSTRUCTION

A. Scalp Layers. Skin, subcutaneous tissue, galea aponeurotica, loose areolar tissue, and pericranium.

B. Scalp Lacerations

1. Often associated with blunt head trauma: Assess for associated skull, cervical spine, or intracranial injuries.
2. Rich blood supply results in significant blood loss; expedient management is critical. Hemostasis is achieved with closure of the galea and skin following thorough irrigation and debridement of devitalized tissue. Stapled closure of the hair-bearing scalp is expedient and results in reduced trauma to hair follicles compared to sutures.

C. Partial-thickness scalp loss from avulsion usually occurs at the subaponeurotic layer. Large avulsions may be skin grafted acutely. Definitive management often requires tissue expander placement to replace hair-bearing scalp.

D. Full-thickness scalp loss can occur from trauma or tumor extirpation. The optimal treatment varies depending on the size of the defect.

1. **Small defects** (<3 cm) can often be closed primarily after undermining of flaps.

2. **Medium-sized defects** (3 to 10 cm) can be covered with a skin graft or skin substitute (e.g., Integra) by burring the bone down to the vascular diploic space or using a scalp flap combined with skin grafting of the donor pericranium. Tissue expansion can later be used to replace hair-bearing scalp.
3. **Large defects** (>10 cm) often require free tissue transfer with omentum or latissimus dorsi.

II. TRUNK

A. Breast

1. **Reconstruction after mastectomy** is an important part of recovery for many women and can lead to a significant improvement in body image (*J Natl Cancer Inst*. 2000;92:1422–1429). **The aims of reconstruction** are to recreate a breast mound, and if desired, a new nipple–areola complex. Extensive preoperative consultation is required to allow women to explore their options. Any approach to breast reconstruction usually requires multiple operations, and extensive clinic visits, and the reconstructed breast will never completely replicate the original.
2. **Autologous tissue** involves using the patient's own tissue to recreate a breast. Pedicled options include rectus abdominis and latissimus dorsi myocutaneous flaps. Free options include deep inferior epigastric perforator (DIEP) muscle-sparing abdominal flap and transverse upper gracilis (TUG) myocutaneous inner thigh flaps.
   a. Advantages: A more natural appearance and feel, minimizes future procedures and clinic visits, and fewer complications with subsequent radiation.
   b. Disadvantages: Longer initial procedure, additional scars, and potential donor-site morbidity.
3. **Implant-based reconstruction** is the most common form of breast reconstruction. Tissue expansion is often required because the mastectomy flaps are insufficient for the desired size of the breast. A **tissue expander** is placed at the time of mastectomy and serial expansions performed in clinic until the desired size is reached. The expander is then replaced with a silicone gel or saline-filled permanent implant.
   a. Advantages: Minimal additional operative time at mastectomy,

fewer additional scars, and a shorter recovery.

b. Disadvantages: The risks of permanent implants (rupture, infection, capsular contracture) and the inability to reproduce certain natural contours. Implants are not lifetime devices and may need replacement.

4. **Breast implant–associated anaplastic large cell lymphoma** (BIA-ALCL) has emerged as a rare lymphoma associated with capsule formation around textured implants. It classically presents as a late seroma, and diagnosis is via radiologic aspiration. Treatment with complete capsulectomy and implant removal, and possible systemic treatment if often curative. Lifetime risk after textured implants varies from 1:1,000 to 1:30,000 and research is ongoing.
5. **Radiation** challenges any reconstruction secondary to adverse wound healing, increased necrosis and infection, capsular contracture around implants, and overall fibrosis of tissue. To reduce complications if radiation is planned: Irradiate a tissue expander before placing permanent implants; irradiate before definitive autologous reconstruction (tissue expander can act as space saver in interim) (Fig. 44-9).
6. **Role of prophylactic contralateral mastectomy** is controversial. Bilateral reconstruction achieves better symmetry with both autologous and implant-based reconstruction, but has higher chances of complications.
7. **Reconstruction of the nipple–areola complex** is most commonly done via local flaps with areola tattoo, or 3D tattoo alone.
8. **Symmetry procedures** may be performed concomitantly or subsequently, and include contralateral reduction or mastopexy, fat grafting, modification of the inframammary fold, removal of dog ears, and revision or liposuction of flaps.
9. **Reconstruction after breast conservation** therapy can be challenging given radiation damage, and falls into two main approaches:

a. Volume replacement with fat grafting or local tissue rearrangement

b. Contralateral balancing reduction or mastopexy

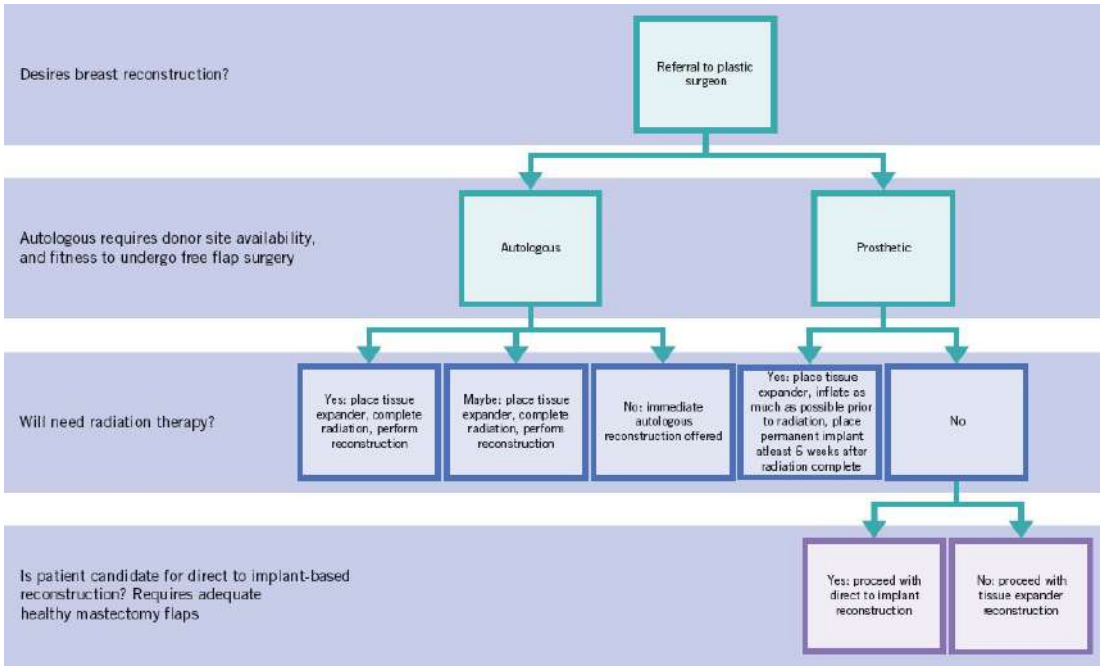


FIGURE 44-9 Breast reconstruction algorithm.

B. Chest Wall Reconstruction

1. Indications

a. Obliteration of dead space (e.g., closure of Clagett window, sternotomy dehiscence, obliteration of pocket from left ventricular assist device [LVAD])

b. Provision of vascularized tissue around an intrathoracic anastomosis

c. Restore chest wall integrity

2. Preoperative assessment

a. Available vascular pedicles must be assessed. Prior use of the internal mammary artery for a bypass precludes using an ipsilateral rectus abdominis flap or pectoralis turnover flap.

b. The chest wall defect must be completely clear of neoplasm, radiation damage, and infected tissue/hardware (i.e., sternotomy wires). NPWT can be used to bridge to definitive coverage.

3. Wound location determines flap options; flaps must be able to cover wound without tension while remaining attached to their vascular pedicle (Fig. 44-10).

4. Skeletal stabilization is required if more than four rib segments or 5 cm of chest wall are missing. This can be achieved using autologous

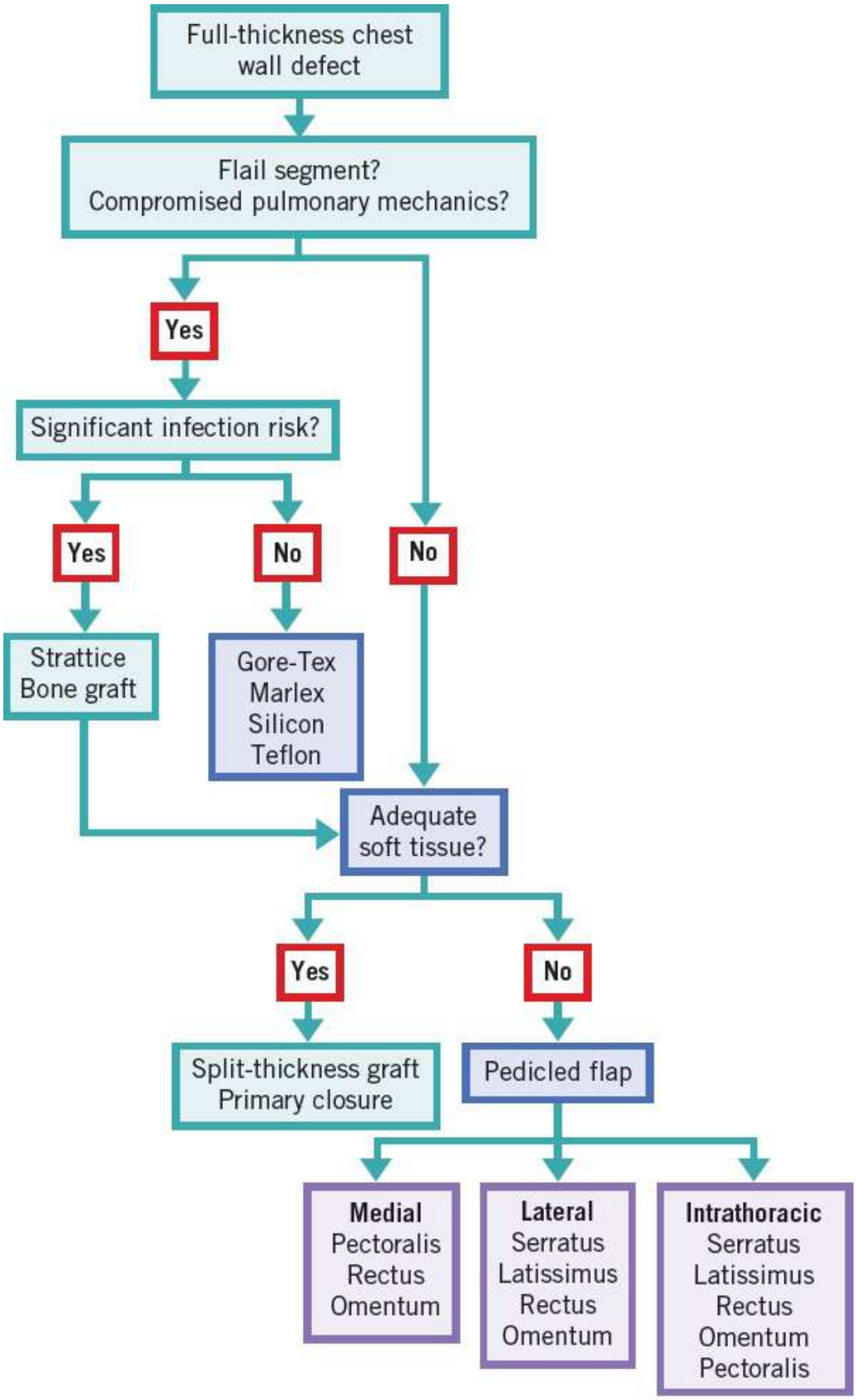
or prosthetic material.

C. Abdominal Wall Reconstruction

1. **Goals:** Fascial and cutaneous coverage to recreate a competent abdominal wall.
2. **Primary closure of fascial defects** represents the best approach and can be assisted by sliding myofascial advancement flaps. Lateral release of the external oblique fascia, or "**component separation**," is ideal for midline musculofascial defects >3 cm. Using bilateral relaxing incisions and release, a total of 10, 18, and 6 to 10 cm of advancement may be obtained in the upper, middle, and lower thirds of the abdomen, respectively (*Plast Recon Surg*. 1990;86:519). The anterior sheath of one or both rectus muscles can be divided and turned over to provide additional fascia for closure.
3. **Mesh reinforcement/bridging** can be used to strengthen a fascial closure or provide closure when component separation is inadequate. Synthetic meshes have the advantage of being resistant to stretch and are generally associated with lower recurrence rates. Biologic meshes should be considered in the case of contaminated abdominal closure because they will revascularize. However, most available biologic meshes stretch significantly.
4. **Skin coverage.** STSGs can be used over vascularized tissue. Coverage of synthetic mesh can be achieved using abdominal advancement flaps or grafting of muscle flaps.
5. More challenging cases may require myofascial or myocutaneous flaps harvested from the anterolateral thigh, tensor fascia lata, or rectus femoris.

D. Pressure Sores

1. The **etiology and staging criteria** of pressure ulcers are described in Chapter 15. Stage I/II ulcers can generally be managed with wound care, while stage III/IV ulcers ***may*** benefit from definitive coverage.



If flap failure or unavailable pedicle → free flap

FIGURE 44-10 Chest wall reconstruction algorithm.

2. A pressure sore is considered ready for definitive coverage when it is clean and infection free, all devitalized tissue has been debrided, and associated osteomyelitis has been treated. **Diverting colostomy**, as part of the treatment strategy is controversial; in select patients, laparoscopic colostomy has been shown to reduce recurrence (*Dis Colon Rectum.* 2003;46:1525).
3. **Commonly utilized flaps.** Gluteus maximus, tensor fascia lata, hamstring, or gracilis-based rotation or advancement flaps.

III. LOWER EXTREMITY. Soft tissue defects from trauma to the lower extremity are common. A multidisciplinary approach involving orthopedic, vascular, and plastic surgeons provides optimal care.

A. Soft tissue defects of the thigh are usually closed by primary closure, skin grafts, or local flaps. The thick muscular layers ensure adequate local tissue for coverage of bone and vessels and adequate vascular supply to any fracture sites.

B. Open tibia fractures frequently involve degloving of the thin layer of soft tissue covering the anterior tibial surface. The distal tibia is a watershed zone, and fracture with loss of periosteum or soft tissue leads to increased rates of infection and nonunion.

1. Open tibial fractures are classified according to the scheme of **Gustilo** (Table 44-2).
2. **Gustilo types IIIb and IIIc** frequently require flap coverage of exposed bone, most commonly with a pedicled gastrocnemius or soleus flap; for more distal wounds, consider a perforator or free flap.

TABLE 44-2 Gustilo Open Fracture Classification

Classification	Characteristics
I	Clean wound <1 cm long
II	Laceration >1 cm long with extensive soft tissue damage

III	Extensive soft tissue laceration, damage, or loss; open segmental fracture; or traumatic amputation
IIIa	Adequate periosteal cover of the bone despite extensive soft tissue damage; high-energy trauma with small wound or crushing component
IIIb	Extensive soft tissue loss with periosteal stripping and bone exposure requiring soft tissue flap closure; usually associated with massive contamination
IIIc	Vascular injury requiring repair

Adapted from Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analysis. *J Bone Joint Surg Am*. 1976;58:453–458.

C. Limb salvage reconstruction for neoplasm may require replacement of large segments of bone, nerve, or vessels. **Skeletal replacement** can be accomplished using an endoprosthesis, allogenic bone transplant, or vascularized free bone (fibula) transfer.

D. Foot wound coverage may be necessary due to trauma, neoplasm, or ulceration. The etiology of ulcers (e.g., arterial insufficiency requiring extremity revascularization in the case of ischemic ulcers) should be addressed prior to coverage.

1. **Plantar surface.** Optimally provides a durable, sensate coverage; options include dermal substitutes, rotation of instep tissue for small wounds, or free flaps.
2. **Dorsal foot.** Optimally provides thin pliable coverage to allow for standard footwear. If paratenon present then skin grafting may be used; otherwise, consider a dermal substitute or thin fascial free flaps (temporoparietal, parascapular, or radial forearm) covered by skin graft.

IV. PERIPHERAL NERVE

A. Clinical assessment of neuropathy requires evaluation of both motor and sensory function as well as electrodiagnostic evaluation of nerve conduction and muscle innervation.

1. Evaluation of motor nerve function is standardized (Table 44-3).

2. **Diagnostic studies** include nerve conduction studies (NCS) and electromyography.
3. Nerve injuries are classified according to severity (Table 44-4).

B. Management of Acute Injuries

1. **Sharp transection (trauma, iatrogenic).** Nerve should be repaired within 72 hours when intraoperative electrical stimulation will allow differentiation between motor and sensory fascicles. Debride injured nerve to healthy fascicles. If possible, a tension-free primary repair should be performed. If gap is too large for tension-free repair, consider grafting.

TABLE 44-3 Classification of Motor Function

Grade	Motor Function
M0	No contraction
M1	Perceptible contraction in proximal muscles
M2	Perceptible contraction in proximal and distal muscles
M3	All important muscles powerful enough to act against gravity
M4	Muscles act against strong resistance; some independent movement possible
M5	Normal strength and function

Adapted from Mackinnon SE, Dellon AL. *Surgery of the Peripheral Nerve*. New York: Thieme; 1988:118.

TABLE 44-4 Classification of Nerve Injuries

Sunderland[a]	Seddon[b]	Structure Injured	Prognosis
First degree	Neurapraxia	Schwann cell (demyelination)	Complete recovery

			within 3 months
Second degree	Axonotmesis	Axon (wallerian degeneration)	Complete recovery, regeneration 1 mm/day
Third degree		Endoneurium	Incomplete recovery
Fourth degree		Perineurium	No recovery
Fifth degree	Neurotmesis	Epineurium	No recovery
Sixth degree		Mixed injury, neuroma in continuity[c]	Unpredictable recovery

[a]Sunderland S. A classification of peripheral nerve injuries producing loss of function. *Brain*. 1951;74:491.

[b]Seddon HJ. Three types of nerve injury. *Brain*. 1943;66:237.

[c]Mackinnon SE. New direction in peripheral nerve surgery. *Ann Plast Surg*. 1989;22(3):257–273.

2. **Acute postoperative nerve deficit unrelated to location of surgery.** Commonly **due to patient positioning or traction**, especially at anatomically restrictive sites (e.g., the ulnar nerve at the elbow or the common peroneal nerve at the knee).
   - **a.** Usually a first-, second-, or third-degree injury, and full recovery can be expected in most cases.
   - **b.** If no improvement by 6 weeks, obtain baseline NCS and EMG. If there is no evidence of return of function at 3 months, obtain repeat studies.
3. **Loss of nerve function after gunshot or open blunt trauma** is usually the result of first- or second-degree injury.
   - **a.** Treat as a closed injury, observing for improvement and obtaining EMG and NCS at 6 weeks and 3 months, as needed.
   - **b.** If the nerve is visible or the wound is explored for other reasons (e.g., vascular repair), the nerve is explored. If the nerve is in

continuity, manage as one would for a closed injury. If the nerve is not in continuity, it is usually best to tag the ends of the nerve for ease of identification and delay definitive repair until the zone of injury to the nerve is clearer (generally by 3 weeks).

4. **Nerve deficit from compartment syndrome** is treated by emergent fasciotomy. If decompressed early (within 6 hours), there is usually a rapid return of function.

AESTHETIC SURGERY PEARLS FOR THE GENERAL SURGEON

I. AUGMENTATION MAMMOPLASTY

A. Implants

1. **Placement.** Subglandular, submuscular, or a combination (*dual plane*) via periareolar, transaxillary, or inframammary fold incisions.
2. **Monitoring**
   a. **Cancer screening.** Use **standard mammography plus Eklund views** (pushes implant against the chest wall and breast tissue is pulled forward).
   b. **Rupture.** Saline implant rupture presents as a deflated breast. Silicone implants must be **monitored by MRI** with an initial study 3 years after placement and every 2 years thereafter.

B. Fat transfer may be used in large volume to recreate a whole breast or to fill the upper pole following implant placement, most commonly in the case of postmastectomy reconstruction.

C. Reduction Mammoplasty

1. Indications: Include upper back and neck pain, rashes and infections in the inframammary fold, shoulder strap grooving, and functional limitations to daily activities such as exercising.
2. The breast volume is decreased and excess skin excised to reduce volume of the breast while maintaining blood supply to the nipple. In extreme cases the nipple must be removed and grafted. Reduction mammoplasty has the highest patient satisfaction of any plastic surgery procedure due to symptomatic improvement and quality of life.
3. Complications:

a. Acute—bleeding, nipple ischemia, infection

b. Medium term—infection, epidermolysis or wound healing problems along incision

c. Late—decreased nipple sensation, poor scarring, asymmetry, poor cosmesis

II. ABDOMINOPLASTY

A. Involves elevation of large subcutaneous flaps extending from umbilicus to xiphoid, transposition of the umbilicus, with or without rectus plication. Blood supply to the flaps comes from lateral intercostals, subcostals, and lumbar vessels. Large abdominal scars (e.g., subcostal incision after open cholecystectomy) can result in flap necrosis.

B. Risk of pulmonary embolism is between 1/300 and 1/1,000, with the highest risk period being the first postoperative week. Accordingly, patients are commonly discharged on 5 to 10 days of anticoagulation therapy.

III. POSTBARIATRIC BODY CONTOURING

A. Timing. Weight should be stable for at least 3 to 4 months; generally, this occurs 12 to 18 months after a bariatric operation. Lower BMI equates to lower complications and better cosmesis.

B. Patients must be nutritionally optimized to avoid healing complications: Preoperative iron, cyanocobalamin (vitamin B_{12}), calcium, folate, and albumin testing is recommended.

CHAPTER 44: PLASTIC, RECONSTRUCTIVE, AND HAND SURGERY

Multiple Choice Questions

1. **An 83-year-old man undergoes excision of a basal cell carcinoma of the cheek. The defect is 3 × 3 cm with subcutaneous fat exposed at the base. Reconstruction with skin grafting is planned. Which of the following will minimize long-term graft contracture?**

   a. Split-thickness skin grafting with meshing
   b. Split-thickness skin grafting without meshing
   c. Full-thickness skin grafting
   d. Cultured epidermal autografting
   e. A skin graft is inappropriate in this situation

2. **A 46-year-old female is brought to the emergency room 3 days after abdominoplasty at an ambulatory surgery center. The patient appears lethargic. On examination, she is hypotensive, tachycardic and pulse oximetry on room air is 98%. Her abdomen is tender, incisions are intact, and dressings are clean. Her drains contain serosanguineous fluid and a few clots. The husband is not sure when the drains were last emptied. Following initial resuscitation and stabilization, which of the following studies is most appropriate?**

   a. Spiral CT of the chest
   b. Type and cross
   c. Lower extremity duplex ultrasound
   d. Chest x-ray
   e. Urine drug screen

3. **A 76-year-old male underwent coronary artery bypass surgery using the left internal mammary artery and left saphenous vein for grafts. His course was complicated by mediastinitis and sternal dehiscence with a resultant 3 X 7 cm central chest defect with exposed sternum. Following multiple debridements and**

negative-pressure wound therapy, wound cultures are negative. Which of the following is most appropriate for coverage?

a. Skin graft
b. Left pedicled rectus abdominis flap with skin graft
c. Left turnover pectoralis flap with skin graft
d. Pedicled omentum with skin graft
e. Free anterolateral thigh flap

4. **A 20-year-old suffered multiple gunshot wounds to the chest, abdomen, and right arm. He is stabilized and able to participate in an upper extremity examination 1 week following presentation. On examination, he is unable to extend his wrist, fingers, and thumb. What is the most appropriate management of this patient?**

a. Obtain electromyography and nerve conduction studies, explore nerve if evidence of denervation
b. Obtain baseline electromyography and nerve conduction studies at 6 weeks, repeat at 3 months, and explore nerve if no evidence of recovery
c. Observation, explore nerve if no recovery at 6 months
d. Explore and graft nerve injury as soon as patient is stable for surgery
e. Immediate tendon transfers for elbow and wrist extension

5. **A 33-year-old paraplegic woman in an assisted living facility is found to have a stage IV ischial pressure ulcer. There is a hydrocolloid dressing in place, the wound base appears clean, and the surrounding skin is clean and intact. Which of the following is a contraindication to flap coverage?**

a. Osteomyelitis of the ischium
b. Fecal incontinence
c. Negative-pressure wound therapy
d. Low serum Fe
e. Baclofen treatment for spasticity

45 Urology

Jonathan R. Weese and Alana C. Desai

INTRODUCTION

The discipline of **urologic surgery** encompasses the management of benign and malignant conditions of the genitourinary system including the kidneys, ureters, bladder, urethra, and the male reproductive system.

I. HEMATURIA. Hematuria, or blood in the urine, warrants a complete urologic workup. **Gross hematuria** is visibly bloody urine, whereas **microscopic hematuria** is defined as *three or more* red blood cells per high-power field. Common etiologies include urinary tract infection (UTI), stones, benign prostatic hyperplasia (BPH), malignancy, and recent trauma or instrumentation.

A. Evaluation for hematuria (gross or microscopic) consists of the following:

1. **Urinalysis** (UA) and **urine culture** from a *freshly voided* midstream specimen.
2. **Urine cytology.**
3. **Computed tomography (CT) urogram:** A three-phase CT of the abdomen/pelvis without contrast, with contrast, and with delayed images postcontrast is the preferred imaging modality. However, *magnetic resonance (MR) urogram* and *renal ultrasound (US) with retrograde pyelograms* may be performed for patients with poor renal function or renal transplant recipients to evaluate native kidneys and ureters.
4. **Cystoscopy** is required for a complete assessment of the urethra and bladder to evaluate for small lesions not seen on imaging, other anatomic abnormalities (e.g., strictures); allows for biopsies of any

lesions, and is typically performed in the outpatient setting.

5. If the etiology of hematuria remains unclear, repeat UA in 1 year.
   a. For recurrent *gross* hematuria: At least an annual complete workup is warranted, with severity and duration of episodes dictating further evaluation and management.
   b. For recurrent *microscopic* hematuria, repeat workup at least every 3 to 5 years, with more frequent evaluation for those with significant risk factors such as history of smoking or carcinogen exposure.

B. Treatment of Symptomatic Gross Hematuria

1. Patients in **urinary retention due to clots** require urgent urologic consultation. If the patient has an indwelling catheter, it should be manually irrigated and aspirated with sterile saline or water until the bladder is free of clots. Smaller-caliber catheters may not allow for aspiration of larger clots, and placement of a large-bore catheter may be required for complete irrigation and aspiration. Placement of a three-way catheter (22F to 24F) for **persistent bleeding** may be indicated for **continuous bladder irrigation** (CBI) and *should not be initiated* until all clots have been aspirated from the bladder. CBI should be used with caution in patients with recent urinary reconstruction (e.g., recent renal transplantation or bladder reconstruction/repair) as bladder perforation may occur.
2. **Persistent gross hematuria** from a lower urinary tract source (bladder, prostate, urethra) despite conservative measures requires operative management via **cystoscopy and fulguration** of the bleeding source.
3. Persistent hematuria from an upper urinary tract source (kidney, ureter) may be due to **malignant lesions, angiomyolipoma, arteriovenous fistula, or renal trauma.** These patients may require surgical intervention by urology or angiography ± embolization by interventional radiology.

II. DISEASES OF THE KIDNEY

A. Renal cysts

occur in approximately 50% of persons older than 50 years, and the vast majority is benign. Renal cysts can be diagnosed with CT, MRI, or US (Table 45-1).

TABLE 45-1 **Bosniak Classification System of Renal Cystic Masses**

Bosniak Category	Characteristics	Risk of Malignancy (%)	Management
I	Simple cyst. Thin wall, no septa. Low attenuation, no enhancement	0	None
II	Few thin septa or fine calcifications. Can be high attenuation (if <3 cm) but no enhancement	5–18.5[a]	None
IIF	Multiple thin septa, minimal wall thickening or thick calcifications. Can be high attenuation (>3 cm) but no enhancement	15–25	Surveillance imaging q6–12mo
III	Walls or septa with measurable enhancement	33+	Resection/ablation
IV	Contains enhancing soft tissue components	92.5	Resection/ablation

[a]There is limited data on category II cysts as most studies combine II and IIF cysts. Category II cysts (excluding IIF) are thought to be essentially benign.

Adapted from Whelan TF. Guidelines on the management of renal cyst disease. *Can Urol Assoc J*. 2010;4(2):98–99.

B. The majority (80%) of solid renal masses are malignant. The classic triad of **flank pain, hematuria, and flank mass** occurs uncommonly. **Renal cell carcinoma** is the most common malignant solid renal mass. The differential diagnosis for other renal masses includes urothelial carcinoma (UC), oncocytoma (usually benign), lymphoma, and metastatic tumors (lung, breast, gastrointestinal, prostate, pancreas, and melanoma).

1. Evaluation of a renal mass:

a. Laboratory tests. Complete blood count, renal panel, liver function tests, and UA. Lactate dehydrogenase (LDH) may be prognostic in metastatic disease.

b. Abdominal imaging with both noncontrast and contrast phases (*renal protocol CT/MR*) is indicated to **assess for enhancement. US** can determine whether a mass is cystic or solid.

c. Chest x-ray (CXR) should be obtained to rule out metastases (consider chest CT for high suspicion of chest metastases or when CXR is positive).

d. Bone scan is indicated in patients with elevated alkaline phosphatase or bone-related complaints. **Head CT** is warranted in patients with neurologic symptoms.

e. The role of percutaneous **renal mass biopsy** is expanding. Diagnostic accuracy is typically greater than 90%, while the complication rate is less than 5% (*J Urol*. 2008;179:20–27). Due to the possibility of false negatives, presence of tumor heterogeneity, and possible nondiagnostic biopsy, the decision to recommend biopsy is nuanced.

2. Paraneoplastic syndromes occur in 10% to 40% of renal cell carcinomas.

a. Renin overproduction can present as hypertension.

b. Stauffer syndrome is benign elevation of liver enzymes, which

usually resolves after tumor removal.

c. Hypercalcemia can be caused by the production of **parathyroid hormone–like protein** produced by the tumor.

d. Erythrocytosis may result from overproduction of erythropoietin.

C. Management of Renal Masses

1. The **management of solid renal masses depends on the tumor stage** (Table 45-2).
   - **a. T1 and T2 lesions.** Nephron-sparing surgery via **partial nephrectomy is preferred** whenever possible for lesions <7 cm; otherwise, **radical nephrectomy is considered the standard of care.** The role of minimally invasive techniques (e.g., cryoablation) is expanding for small lesions.
   - **b. T3 and T4 lesions mandate radical nephrectomy.**
2. **Metastatic renal cell carcinoma is resistant to radiation and chemotherapy.** Radiation may be used for palliation of brain or bone metastases. The role of cytoreductive nephrectomy in the modern era of targeted therapy is diminishing and only indicated in carefully selected patients (*N Engl J Med*. 2018;379:417–427). Targeted therapy with ***tyrosine kinase inhibitors*, mTOR inhibitors, VEGF inhibitors**, or **checkpoint inhibitors** may be utilized (*Eur Urol*. 2018;74(3):309–321). Cytokine therapy is rarely utilized in the modern era.

TABLE 45-2 AJCC 2017 TNM Staging for Renal Cell Carcinoma

Primary Tumor (T)	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7 cm or less in greatest dimension, limited to kidney
T1a	Tumor 4 cm or less in greatest dimension, limited to kidney
T1b	Tumor greater than 4 cm but not larger than 7 cm and limited to kidney
T2	Tumor greater than 7 cm in greatest dimension and limited to kidney
T2a	Tumor greater than 7 cm but not larger than 10 cm and limited to

	kidney
T2b	Tumor greater than 10 cm and limited to kidney
T3	Tumor extends into the major veins or perinephric tissues but not into the ipsilateral adrenal or beyond Gerota fascia
T3a	Tumor grossly extends into the renal vein or its segmental branches, or invades the pelvicalyceal system, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the IVC
T4	Tumor invades beyond Gerota fascia
Regional Lymph Nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional node(s)
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

III. DISEASES OF THE URETER

A. Hydronephrosis is commonly caused by ureteral obstruction, which can be intrinsic or extrinsic in origin.

1. Common ***intrinsic*** causes include stones, ureteropelvic junction obstruction (UPJO), stricture, and UC. Common ***extrinsic*** causes include compression from abdominal/pelvic masses, crossing blood vessels, pregnancy, or retroperitoneal fibrosis.
2. Short-term management includes placement of a **ureteral stent** or **percutaneous nephrostomy tube** to relieve obstruction. Long-term management is based on etiology of obstruction.

3. The best **imaging** modality depends on the suspected etiology. US and noncontrast CT are best to evaluate urolithiasis (see below). Intrinsic compression is best defined by CT/MR urogram. CT/MR with contrast can distinguish most forms of extrinsic compression.
4. To determine the functional significance of chronic obstruction, **diuretic renal scintigraphy** (**furosemide renal scan**) may be performed. This study can estimate the relative function and excretion of each kidney.

B. Urolithiasis (ureteral calculi) typically presents as the acute onset of severe, intermittent flank pain often associated with nausea and vomiting. Patients may present with hematuria; however, this is nonspecific. Patients should always be assessed for signs of infection, including history of fever, as UTI with obstructive uropathy can quickly progress to sepsis, which may be life threatening and requires urgent intervention.

1. **Epidemiology.** Stone formation commonly occurs between the **third and fifth decades of life** and tends to have a **male** predominance, although recent trends show females approaching similar prevalence.
2. There are numerous **risk factors** for stone formation. Common modifiable factors include **low fluid intake** and diets that **contain high animal protein, sodium, or oxalate**. Medical conditions such as **obesity**, **diabetes, inflammatory bowel disease, gout, hyperparathyroidism**, and **type I renal tubular acidosis (RTA)** increase urolithiasis risk. Various medications and high doses of vitamins C or D can also favor stone formation (*Lancet*. 1997;349:1294–1295).
3. **Evaluation** of urolithiasis
   - **a.** In the acute setting, obtain **UA, urine culture,** and **a renal panel**.
   - **b. Noncontrast CT** is the most accurate study for urolithiasis. Though CT has superior sensitivity to US (88+% vs. 57%), recent data have shown that US may be a reasonable and safe option as an initial diagnostic study, providing lower cost and radiation exposure without significantly affecting clinical outcome (*N Engl J Med*. 2014;371:1100–1110).
   - **c. Abdominal x-ray (KUB)** is useful to monitor for stone passage of radiopaque stones and to assess whether the stone is amenable to

extracorporeal shock wave therapy or **lithotripsy (ESWL),** a noninvasive means to fragment the calculi.

4. **Management.** Many patients can be managed as an outpatient with close urologic follow-up. Patients with intractable pain, nausea, or emesis not adequately controlled by oral medication require hospital admission. Urgent **surgical intervention** is indicated if there are signs of infection, significant acute kidney injury, an obstructed solitary kidney, or bilateral obstruction.
   a. **Medical expulsive therapy.** Over **70% of stones <5 mm and up to 40% of stones <10 mm will pass spontaneously.** Stone passage can be aided with **narcotics** and **daily α-blocker therapy (e.g., tamsulosin)**, which has been shown to improve stone passage rates by up to 20%, in some studies. Urine should be strained for stones. Spontaneous stone passage may take up to 3 to 4 weeks (*J Urol.* 1997;178:2418–2434).
   b. **Surgical treatment.** In the acute setting, patients meeting surgical criteria can be managed by **ureteral stenting or percutaneous nephrostomy tube placement**. If patients remain symptomatic, have failure of stone passage within 4 to 6 weeks, or have large stones, surgical options include **ESWL**, **ureteroscopy ± laser lithotripsy**, and **percutaneous nephrolithotomy.**

C. Ureteropelvic Junction Obstruction (UPJO)

1. **UPJO etiologies** include a congenital aperistaltic or stenotic segment of proximal ureter, extrinsic compression from crossing vessels, benign polyps, and scarring.
2. Patients may present at any age. Common symptoms are **flank pain** (which may be intermittent), nausea/vomiting, and pyelonephritis.
3. CT/MR with contrast and **diuretic renal scintigraphy** help to determine the site and functional significance of the obstruction.
4. **Treatment** is based on severity of symptoms and renal function of the affected side and may consist of **observation, endopyelotomy** of the strictured segment via ureteroscopy, or **pyeloplasty** (surgical reconstruction of the affected segment).

IV. DISEASES OF THE URINARY BLADDER

A. Bladder cancer is found in up to 5% of patients with microscopic

hematuria.

1. UC accounts for more than 90% of bladder tumors in the United States; squamous cell carcinoma and adenocarcinoma are rare. Bladder tumors are linked strongly to **smoking**, as well as to **textile dyes, cyclophosphamide, chronic indwelling catheters, chronic parasitic infection (*Schistosoma haematobium*), and radiation exposure**.
2. **UC is categorized as superficial or invasive.** Staging is outlined in Table 45-3. Evaluation for UC requires upper tract imaging via CT/MR urogram, cystoscopy, and urine cytology. In patients unable to undergo CT/MR urogram, renal US combined with bilateral retrograde pyelograms is sufficient for evaluation. Metastatic evaluation includes **CXR/CT, CT urogram, and liver function tests**.
   a. **Superficial tumors** (CIS, Ta, T1) do not invade the muscular bladder wall. These tumors can be staged and treated with **transurethral resection (TUR)** and possibly **intravesical therapy (bacillus Calmette–Guérin** [BCG] or **mitomycin C**). Between 40% and 80% of superficial tumors recur within 1 year; thus, diligent follow-up with cystoscopy is necessary. Recurrent tumors are treated with TUR and intravesical therapy.
   b. The gold standard therapy for **muscle-invasive UC** (stage ≥ T2) is radical cystectomy, bilateral pelvic lymph node dissection, and urinary diversion. This involves **radical cystoprostatectomy** (removal of bladder, prostate, and possibly urethra) in males and **anterior exenteration** (removal of bladder, uterus, cervix, and vaginal anterior wall) in females. Radical cystectomy may be performed via an open or robotic surgical approach. **Urinary diversion** (Table 45-4) typically consists of a reservoir made from detubularized ileum or colon; stomach is rarely used. Diversion may be *continent* (requiring Valsalva or catheterization to empty) or *incontinent* (drains continuously). Common chronic derangements from the use of intestine include metabolic acidosis, B_{12} deficiency, and bone loss. The 90-day postoperative complication rate is 60% to 70% (*Eur Urol*. 2015;67(3):376–401). Locally advanced or metastatic bladder cancer is treated with **chemotherapy**. Neoadjuvant and adjuvant chemotherapy have

been shown to benefit patients with invasive UC who undergo surgery. **Trimodal therapy** with TUR, chemotherapy, and radiation may be utilized for locally advanced UC, but only in select older patients as it is associated with a lower long-term overall survival than radical cystectomy (*Eur Urol*. 2017;72(4):483–487). Despite aggressive management, 5-year survival ranges from 5% to 70% based on stage (*National Cancer Institute SEER database, https://seer.cancer.gov/*).

TABLE 45-3 AJCC 2017 TNM Staging for Urothelial Carcinoma

Primary Tumor (T)	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Carcinoma in situ; “flat tumor”
T1	Tumor invades the subepithelial connective tissue (lamina propria)
T2	Tumor invades the muscularis propria
pT2a	Tumor invades superficial muscularis propria
pT2b	Tumor invades deep muscularis propria
T3	Tumor invades perivesical tissue
pT3a	Microscopic invasion
pT3b	Macroscopic invasion
T4	Tumor invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic/abdominal wall
Regional Lymph Nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single regional lymph node in the true pelvis
N2	Multiple regional lymph nodes in the true pelvis
N3	Lymph node metastasis to the common iliac lymph nodes
Distant Metastasis (M)	

M0	No distant metastasis
M1	Distant metastasis
M1a	Distant metastasis limited to lymph nodes beyond the common iliacs
M1b	Non–lymph node distant metastases

TABLE 45-4 Common Types of Urinary Diversion

Type	Name	Outlet
Noncontinent	Ileal conduit	Abdominal stoma empties into urostomy bag
Continent	Indiana/Miami pouch	Continent catheterizable channel made of the ileocecal valve and terminal ileum
	Neobladder	Orthotopic anastomosis to the native urethra

V. DISEASES OF THE PROSTATE

A. Prostate cancer is the most common malignancy in United States' men and the third leading cause of cancer death. Prostate cancer rarely causes symptoms until it becomes locally advanced or metastatic. Risk factors for prostate cancer include African-American race, family history of prostate cancer, and advanced age.

1. Screening includes measurement of **serum prostate-specific antigen (PSA)**. The use of **digital rectal examination (DRE)**, or other biomarkers, is not useful for primary prostate cancer screening.

a. Abnormalities in PSA should be evaluated by a urologist for consideration of a **transrectal ultrasound (TRUS) with needle biopsy of the prostate**. DRE, biomarkers other than PSA, and imaging may inform the decision to undergo prostate biopsy, but

they should not be utilized for initial screening.

b. PSA screening garnered controversy after seemingly contradictory conclusions from two large, prospective randomized trials (*N Engl J Med*. 2009;360:1310–1319; *N Engl J Med*. 2009;360:1320–1328). Current American Urological Association (AUA) guidelines (2018) and USPSTF recommendations (2018) recommend discussion with patients about the risks and benefits of screening, including the detection of indolent cancer. **If elected, screening should begin at age 55 and occur every 1 or 2 years until age 70** (AUA. [2018]. Early Detection of Prostate Cancer; U.S. Preventative Services Task Force. [2018]. Prostate Cancer: Screening).

2. Staging of prostate cancer (Table 45-5) is performed for those men with higher risk of the disease and consists of an **abdomen/pelvis CT/MRI** and a **bone scan**.

3. **Treatment options** for men with organ-confined prostate cancer include active **surveillance, radical prostatectomy**, and **radiation therapy. Recurrent** or **metastatic disease** is treated with **androgen deprivation therapy**, medications that inhibit testosterone precursors or receptors, and/or chemotherapy.

TABLE 45-5 AJCC 2017 TNM Staging for Prostate Carcinoma

Primary Tumor (T)—Clinical	
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor that is not palpable
T1a	Tumor incidental histologic finding in 5% or less of tissue resected
T1b	Tumor incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy, but not palpable
T2	Tumor palpable and confined within the prostate
T2a	Tumor involves one-half of one side or less
T2b	Tumor involves more than one-half of one side, but not

	both sides
T2c	Tumor involves both sides
T3	Extraprostatic tumor that is not fixed or does not invade adjacent structures
T3a	Extraprostatic extension
T3b	Seminal vesicle invasion
T4	Tumor is fixed or invades adjacent structures other than the SVs, such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall
Regional Lymph Nodes (N)	
Nx	Regional lymph nodes were not assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional node(s)
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease

B. Acute bacterial prostatitis presents with signs and symptoms of acute illness and UTI. Many patients have fevers, malaise, and significant voiding complaints. Prostate examination will reveal a **tender, enlarged prostate.** Prostatic massage should not be performed to avoid urosepsis/bacteremia. Empiric antibiotics should be started immediately. If no improvement, pelvic imaging should be obtained to rule out abscess. Other forms of prostatitis include chronic bacterial prostatitis, chronic pelvic pain syndrome, and asymptomatic prostatitis.

C. Benign prostatic hyperplasia (BPH) can manifest with both irritative and obstructive lower urinary tract symptoms (LUTS) including weak

stream, frequency/urgency, incontinence, bladder outlet obstruction, and nocturia.

1. Objective evidence of **bladder outlet obstruction** includes decreased urinary flow rate, increased postvoid residual, and urinary retention. Bladder stones, hematuria, recurrent UTI, and renal failure can also occur.

a. Postobstructive diuresis (polyuria and natriuresis) can occur after chronic urinary obstruction is acutely relieved via catheterization. Rarely, this can last >48 hours and cause severe electrolyte abnormalities. Patients should be monitored closely with vital signs, serial laboratory tests, and fluid replacement as needed.

2. Treatment

a. Observation is best suited for minimally symptomatic patients.

b. Medical treatment includes long-acting **selective α-blockers** (e.g., tamsulosin) or **5α-reductase inhibitors** (e.g., finasteride). Combination therapy with an α-blocker + 5α-reductase inhibitor is used for moderate to severe BPH.

c. Surgical therapy is indicated in patients who have failed medical therapy or have severe symptoms. The gold standard for surgical treatment of BPH is **transurethral resection of the prostate (TURP)**, but other options such as prostatic urethral lift, water vapor thermal therapy, transurethral photoselective vaporization of the prostate, or laser enucleation of the prostate may be considered based on patient characteristics, preference, and surgeon experience (AUA. [2018]. Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia).

VI. DISEASES OF THE PENIS

A. Priapism is a persistent penile erection that continues beyond, or is unrelated to, sexual stimulation. **Ischemic priapism** lasting >4 hours is an emergency (Table 45-6).

1. Treatment

a. First-line treatment involves **corporal irrigation and aspiration** of old blood via a 14- to 18-gauge needle.

TABLE 45-6	Ischemic versus Nonischemic Forms of Priapism	
	Ischemic Priapism	**Nonischemic Priapism**
Emergency?	**YES**	No
Pain	Painful	Nonpainful
Rigidity	Rigid corpora, flaccid glans	Partially rigid phallus
Pathogenesis	Decreased venous outflow	Increased arterial inflow
Etiologies	i. Hematologic abnormalities, such as **sickle cell disease;** ii. **Drugs,** particularly trazodone, cocaine, and erectile dysfunction medications; iii. Invasive neoplasm	i. Arterial fistula related to perineal/genital trauma; ii. Neurogenic
First-line treatment	Irrigation, aspiration, phenylephrine	None, most resolve with observation
Prognosis	**Erectile dysfunction** from fibrosis/scarring of the corpora can occur without prompt treatment	Good, but selective arterial embolization can be used for refractory/recurrent cases

b. Intracorporal injection of an **α-adrenergic agent** (phenylephrine, 100 to 500 μg/mL) administered every 2 to 5 minutes until detumescence is achieved. Patients should be monitored for hypertension and reflex bradycardia during treatment.

c. For patients with **sickle cell disease**, treatment involves aggressive hydration, supplemental oxygen, and blood transfusion if anemic.

d. Surgical cavernosal-venous shunting should be considered if the above methods fail. If there is no prospect of regaining erectile

function due to prolonged ischemia, a penile prosthesis may be placed at the same time, if desired.

B. Paraphimosis is a urologic emergency in which the foreskin becomes constricted below the glans, resulting in progressive penile edema, pain, and potentially penile necrosis. It may occur following Foley catheter placement in an uncircumcised patient if the foreskin is not returned to its anatomical position.

1. Immediate **manual reduction** should be performed. Edema is reduced by applying a firm grip to the distal penis, squeezing for several minutes and the glans pushed down, within the foreskin. If this is unsuccessful, a urology consult should be obtained urgently.

C. Phimosis is typically a benign condition where the foreskin is unable to be fully retracted over the glans. Many patients are asymptomatic but phimosis can result in glans/foreskin infections or urinary retention (rare).

VII. DISEASES OF THE SCROTUM AND TESTICLES

A. Testicular torsion is the rotation of the testicle on its vascular pedicle, resulting in ischemia. This is a true **emergency** because testicular viability depends on detorsion within a few hours.

1. **History.** Acute onset of severe testicular pain and swelling often associated with abdominal pain, nausea, and/or vomiting.
2. **Examination** reveals an extremely tender, swollen testicle which may be high-riding in the scrotum with a transverse lie. The cremasteric reflex is usually absent on the affected side. Normal UA and the absence of leukocytosis may help to rule out epididymitis.
3. Testicular torsion is a clinical diagnosis, and treatment should not be delayed to obtain imaging. However, *Doppler US* can help to confirm or exclude the diagnosis with reported sensitivity and specificity >95%.
4. Immediate **scrotal exploration and bilateral orchiopexy** is required if torsion is suspected. Manual detorsion of the testicle may be attempted; however, **bilateral orchiopexy** is still necessary, even if detorsion is successful, to prevent future episodes of torsion.

B. Torsion of testicular/epididymal appendage (appendix testis) presents with mild to moderate testicular pain and gradual onset over 12

to 24 hours without abdominal symptoms. On examination, the testicle has a normal position but tenderness in the superior testicle and/or epididymis. The testicle may be mildly swollen due to reactive inflammation. There may be a palpable "pea-like" nodule on the superior testicle or epididymis, which can sometimes be visible through the scrotal skin (**"blue dot" sign**). Diagnosis can be confirmed with US. Treatment consists of **NSAIDs, light physical activity**, and **scrotal support** until resolution over 7 to 14 days.

C. Epididymitis usually presents with a 1- to 2-day onset of unilateral testicular pain and swelling, sometimes associated with dysuria, urethral discharge, or LUTS.

1. Findings include a painful, indurated epididymis, and pyuria. UA, urine culture, and CBC are obtained. When clinically indicated, tests for gonococci and chlamydiae are performed.
2. If sexually transmitted infection (STI) is less likely (e.g., if >35 years old), treat empirically with an **oral fluoroquinolone,** then a **culture-specific antibiotic** for 2 weeks. NSAIDs can reduce inflammation and provide symptomatic relief. For moderate to severe cases with fever and/or leukocytosis, US can be useful to rule out abscess formation and assess testicular perfusion. Broad-spectrum antibiotics may be required.

D. Fournier gangrene is a severe necrotizing fasciitis involving the subcutaneous tissue of the genitals and perineum. This is an emergency as mortality ranges from 20% to 30% in most series. Diabetic, alcoholic, and other immunocompromised patients are more susceptible to this condition.

1. Examination reveals **painful edema and erythema** of the perineal skin (including the scrotum and phallus in men). This may progress rapidly to frank necrosis with crepitus and malodor.
2. **Evaluation** should include CBC, electrolytes, UA, urine, and blood cultures. **CT scan** may be obtained to evaluate for extension of infection and **presence of subcutaneous gas** but should never delay operative treatment.
3. **Broad-spectrum antibiotics** that are active against mixed organisms (aerobic and anaerobic, gram-positive and -negative) should be started immediately.

4. **Wide surgical debridement** is urgently required, with aggressive postoperative support. *Orchiectomy is rarely indicated* because the testicles are usually uninvolved. The wound should be left open and initially managed with wet-to-dry dressing changes, and multiple debridements may be necessary. Wound vacuum may be utilized to expedite wound healing after the infection and necrosis is controlled. Wound closure often is an extensive process and may require skin grafting.

E. Nonacute Scrotal Masses

1. **Hydroceles** are fluid collections around the testicle that can **transilluminate** and are usually asymptomatic. US is recommended to rule out testicular malignancy or other scrotal pathology. If hydroceles do become symptomatic, they can be surgically repaired. **Reducible hydroceles** indicate an open peritoneal communication.
2. **Varicoceles** are abnormally dilated testicular veins. On examination, they feel like a "bag of worms" and increase in severity with Valsalva. **Right-sided varicoceles are rare and should be evaluated with retroperitoneal imaging to rule out malignancy**. Varicoceles are the **most common surgically correctable cause of male infertility**; nevertheless, most men with varicoceles remain fertile, asymptomatic, and never require treatment. Varicocele repair results in improved semen quality in approximately 70% of patients.

F. Testicular tumors are the most common solid tumors in males aged 15 to 35 years. The estimated lifetime risk for testicular malignancy is <1 in 300. Owing to improved multimodal therapy, overall 5-year survival for testis cancer is 97%. Risk factors associated with testicular tumors include cryptorchidism, HIV infection, gonadal dysgenesis, and infertility.

1. The typical clinical finding is a **painless testicular mass,** although one-third of patients may present with pain. Scrotal US is mandatory. α-Fetoprotein (**AFP**), β-human chorionic gonadotropin (**β-hCG**), and **LDH** are serum tumor markers that help to identify and stage the tumor, monitor the effectiveness of therapy, and screen for recurrence.
2. **Testicular tumor staging** (Table 45-7) consists of a CXR and CT/MRI of the abdomen/pelvis.

3. Initial therapy for all testicular tumors is **radical inguinal orchiectomy**.
   a. **Seminomas** constitute 60% to 65% of germ cell tumors, are sensitive to chemotherapy and radiation, and have the best prognosis. Low-stage seminomas are often closely observed after orchiectomy. Advanced disease is usually treated with chemotherapy.

TABLE 45-7 AJCC 2017 TNM Staging for Testes Carcinoma

Primary Tumor (T)—Pathologic	
pTx	Primary tumor cannot be assessed
pT0	No evidence of primary tumor
pTis	Germ cell neoplasia in situ
pT1	Tumor limited to testis (including rete testis invasion) without lymphovascular invasion
pT2	Tumor limited to testis with lymphovascular invasion OR tumor invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of the tunica albuginea with or without lymphovascular invasion
pT3	Tumor invades the spermatic cord with or without lymphovascular invasion
pT4	Tumor invades the scrotum with or without lymphovascular invasion
Regional Lymph Nodes (N)–Pathologic	
pNx	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension, or multiple nodes (less than or equal to five), none greater than 2 cm in greatest dimension
pN2	Lymph node mass >2 cm but <5 cm or multiple nodes (more than five) with one mass >2 cm, but none >5 cm or with extranodal extension of tumor
pN3	Lymph node mass >5 cm in greatest dimension

Distant Metastasis (M)	
M0	No distant metastases
M1	Distant metastases
M1a	Nonretroperitoneal nodal or pulmonary metastases
M1b	Nonpulmonary visceral metastases

Serum Tumor Markers (S)	
S0	Marker study levels within normal limits
S1	LDH <1.5 × normal and hCG <5,000 and AFP <1,000
S2	LDH 1.5–10 × normal or hCG 5,000–50,000 or AFP 1,000–10,000
S3	LDH >10 × normal or hCG >50,000, or AFP >10,000
Sx	Marker studies not available or not performed

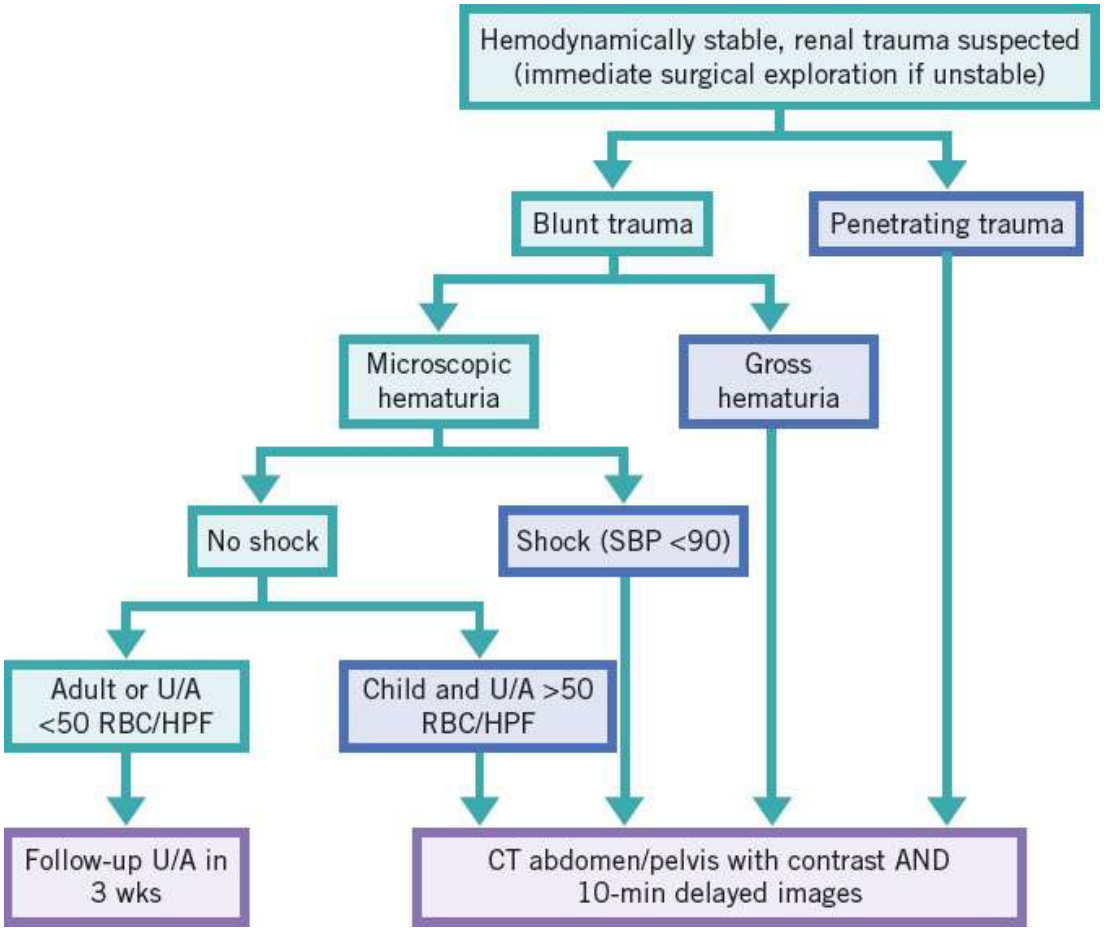


FIGURE 45-1 Algorithm for the management of suspected renal trauma. (Adapted from Wieder JA. *Pocket Guide to Urology*. 5th ed. Oakland, CA: J Wieder Medical; 2014.)

b. Nonseminomatous germ cell tumors include embryonal carcinoma, teratoma, choriocarcinoma, and yolk sac elements. These are more likely to present with advanced disease. Patients may require **chemotherapy** and/or **retroperitoneal lymph node dissection**.

c. Nongerm cell tumors are rare and include **Leydig** and **Sertoli cell tumors** (90% benign) and lymphoma (common in men >50 years).

VIII. GENITOURINARY TRAUMA

A. Renal Trauma

1. Evaluation. See Figure 45-1

2. Grading of renal injury. See Figure 45-2 and Table 45-8

3. Management:

a. Grade I to IV injuries can usually be **observed** with serial CBCs, bedrest until hematuria resolves, and repeat imaging in 36 to 72 hours **(grade IV and V injuries**) to assess for delayed collecting system injury, and long-term blood pressure checks.

b. Vascular grade IV or **V injuries** may require **renal embolization** or **exploration with possible nephrectomy**. Ureteral stenting may be required when there is persistent urinary extravasation.

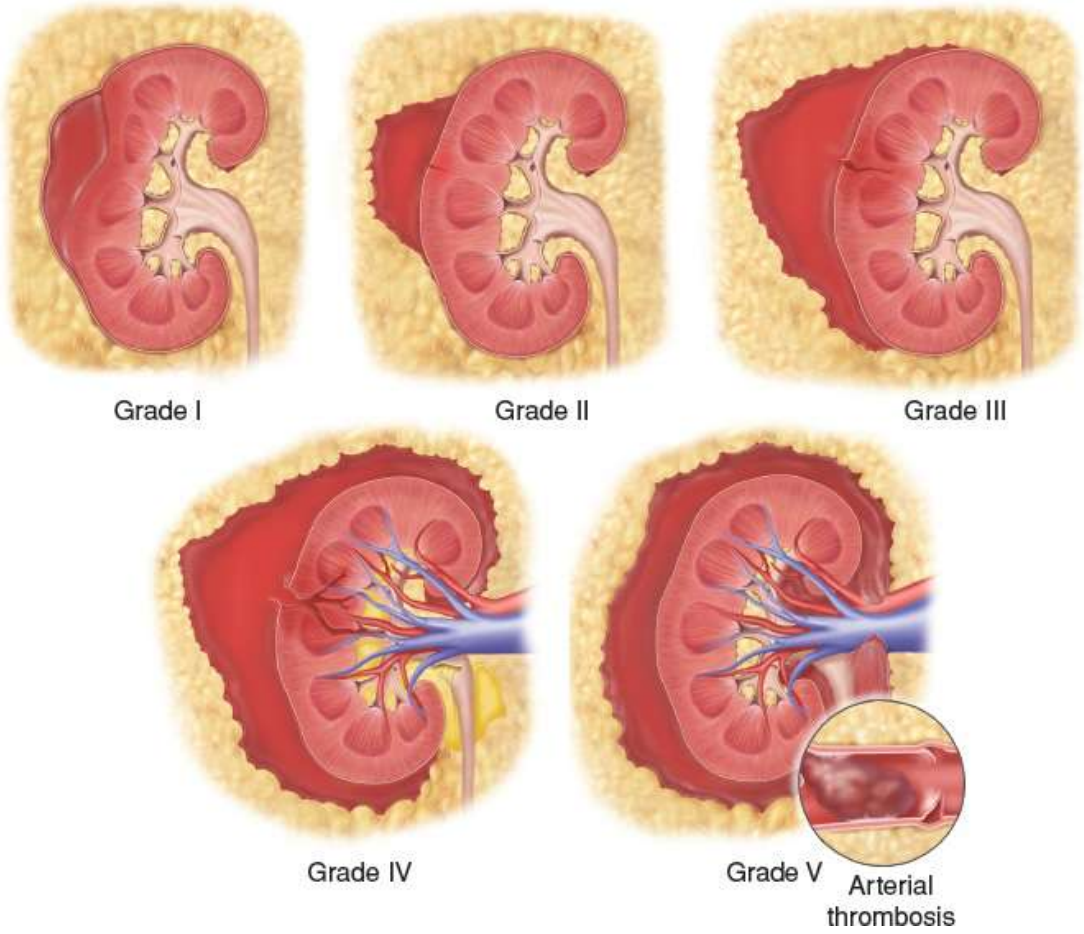


FIGURE 45-2 American Association for the Surgery of Trauma grading. (From Britt LD, Peitzman AB, Barie PS, Jurkovich GJ, eds. *Acute Care Surgery*. Philadelphia, PA: Wolters Kluwer Health; 2012.)

c. Absolute indications for intervention include hemodynamic instability, persistent hemorrhage from renal injury, expanding or pulsatile perirenal mass, or renal pedicle avulsion.

B. Ureteral injuries are associated with penetrating and multiorgan trauma. A high index of suspicion is often necessary to make the

diagnosis, and many ureteral injuries have a delayed presentation. Up to 30% of patients do not have hematuria.

1. Radiographic findings include **extravasation**, lack of contrast in the distal ureter, proximal dilation, and deviation of the ureter. *Delayed CT images* are necessary to assess ureteral integrity.
2. **Adequately visualizing the ureter during laparotomy** is important for diagnosing ureteral injury; **IV injection of indigo carmine or methylene blue**, which are excreted in the urine, may help find the injury location by noting blue urine extravasating.
3. Most ureteral injuries (minor extravasation or ureteral damage without extravasation) can be managed with **ureteral stent placement**.
4. Management of more severe injuries may require **ureteroureterostomy** or **ureteral reimplantation**, depending on location.

TABLE 45-8 **American Association for the Surgery of Trauma Grading**

Grade	Type	Description
I	Contusion	No laceration
	Hematoma	Subcapsular, nonexpanding
II	Hematoma	Nonexpanding perirenal hematoma
	Laceration	<1-cm parenchymal depth of renal cortex without urinary extravasation
III	Laceration	>1-cm parenchymal depth of renal cortex without collecting system rupture or urinary extravasation
IV	Laceration	Parenchymal laceration extending through renal cortex, medulla, and collecting system
	Vascular	Main renal artery or vein injury with contained hemorrhage

V	Laceration	Completely shattered kidney
	Vascular	Avulsion of renal hilum, devascularizing the kidney

C. Bladder Injuries

1. The majority of bladder injuries present with gross hematuria. CT cystogram is necessary in any patient with gross hematuria and pelvic fracture and should be considered for (i) patients with recent pelvic trauma and hematuria or suprapubic pain or (ii) pelvic fracture without hematuria.
2. **CT cystogram** is the most sensitive imaging modality for bladder injury. The bladder should be filled retrograde by gravity via a catheter as bladder filling with excreted contrast alone does not constitute an adequate study.
3. **Treatment**
   - **a.** Patients with **intraperitoneal extravasation** of contrast require **surgical exploration and repair** of the bladder.
   - **b.** Patients with **extraperitoneal extravasation** of contrast can be managed nonoperatively initially with **catheter drainage** for 10 to 14 days. A cystogram should be performed prior to catheter removal and must include postdrainage films to assess for posterior bladder injury.

D. Urethral Injuries

1. **Evaluation.** See Figure 45-3.
2. **Posterior urethral injuries** involve the **prostatic and membranous urethra** (from the bladder neck to the external sphincter).
   - **a.** Acute management involves urologic consultation with careful urethral catheterization. **Blood at the urethral meatus** after pelvic trauma should prompt consideration of **retrograde urethrography**.
   - **b.** If catheterization is unsuccessful, suprapubic catheter placement is recommended and endoscopic primary realignment may be attempted.

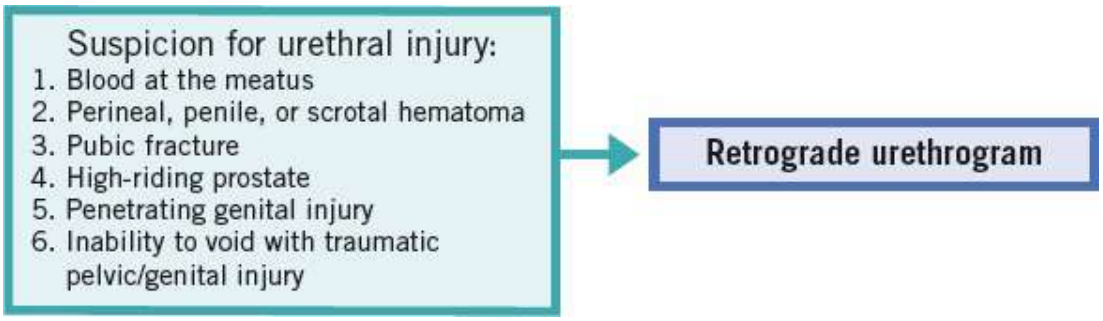


FIGURE 45-3 Workup for suspected urethral injury. (Adapted from Wieder JA. *Pocket Guide to Urology*. 5th ed. Oakland, CA: J Wieder Medical; 2014.)

c. Surgical repair of a posterior urethral injury is *not recommended* in the acute setting as it is complicated by higher rates of impotence, incontinence, and stricture (*Urol Clin North Am*. 2006;33:87–95).

d. Delayed repair in 3 to 6 months is recommended.

3. **Anterior urethral injuries** include those sustained in the bulbous and penile urethra distal to the external sphincter. Examination may show diffuse penile ecchymosis or a "**butterfly" pattern of perineal ecchymosis**. Prompt urinary drainage must be established in patients with urethral injury. The AUA Urotrauma Guidelines recommend **immediate surgical repair** for penetrating anterior injuries unless the patient is unstable or there is concern about tissue viability (AUA. [2017]. Urotrauma).

E. Penile Trauma

1. **Penile fracture** occurs when excessive bending force is applied to the erect penis resulting in a tear of the tunica albuginea. Patients describe an auditory "pop" heard during intercourse followed by rapid detumescence and swelling of the penis/scrotum. Inability to void or blood at the meatus indicates concomitant urethral injury (20% of cases).

a. Examination demonstrates edema and ecchymosis/hematoma of the penis ("eggplant deformity") and/or perineum.

b. Imaging is not indicated unless urethral injury is suspected.

c. Early surgical exploration (<36 to 48 hours) with repair is the standard of care and is associated with better outcomes than delayed repair. Penile fracture with associated urethral injury warrants more urgent exploration.

2. **Serious blunt or penetrating trauma** with injury to the corpus cavernosum requires surgical exploration and repair. It is necessary to rule out urethral injury.

F. Testicular Injury

1. **Surgical exploration** is required for all penetrating scrotal trauma deep to the dartos fascia or if there is concern for **testicular rupture**.
2. US can help to diagnose traumatic testicular injury with a 100% sensitivity and 93.5% specificity (*J Urol.* 2006;175:175–178).
3. Traumatic testicular repair consists of **hematoma evacuation, debridement of the necrotic tubules**, and **closure of the tunica albuginea.** Orchiectomy is rarely indicated.

G. Scrotal avulsion with skin loss should be copiously irrigated and debrided. Clean wounds may be closed in layers, whereas grossly contaminated wounds should be left open to heal by secondary intention.

CHAPTER 45: UROLOGY

Multiple Choice Questions

1. **A 72-year-old male presents to you with a complaint of mild right lower back pain and one episode of blood in his urine 2 weeks ago. He denies voiding symptoms. He quit smoking 5 years ago. His creatinine is 0.8. What are the next step(s) in management?**

   a. Urine culture, noncontrast (stone protocol) CT abdomen/pelvis
   b. Urine culture, urine cytology, renal/bladder ultrasound
   c. Renal/bladder ultrasound, cystoscopy with bilateral retrograde pyelograms
   d. Urine culture, urine cytology, CT urogram, cystoscopy
   e. No workup needed unless he has another episode of hematuria

2. **A 45-year-old woman with a history of diverticulitis comes to the emergency room (ER) with a 2-day history of left lower quadrant pain and vomiting. She has mild leukocytosis with a white blood cell count of 15. Her creatinine is mildly elevated to 1.3, consistent with dehydration. In the ER, she develops a fever of 38.5°C. Urinalysis shows positive leukocyte esterase but no nitrites. A CT scan reveals a 6-mm left ureteral stone with mild to moderate hydronephrosis. What are the next best step(s) in management?**

   a. Urine culture, antibiotics, IV fluids
   b. Urine culture and urgent urology consult for left ureteral stent placement
   c. Bowel rest (make NPO) and IV fluids
   d. Urine culture, antibiotics, and urology consult for a possible left ureteroscopy
   e. Discharge home with oral antibiotics and follow-up with urology

3. **A 62-year-old male presents with urinary retention and perirectal pain. He has had recent low-grade fevers, urinary urgency, and increasing difficulties voiding until he was unable to void at all this morning. Digital rectal examination reveals a swollen, boggy**

prostate that is tender on examination. What is the likely diagnosis?

a. Benign prostatic hyperplasia (BPH)
b. Urinary tract infection
c. Bacterial prostatitis
d. Prostatic abscess
e. Prostate cancer

4. **Which of the following statements about priapism management is FALSE?**

a. Any form of priapism constitutes a urologic emergency
b. First-line treatment for priapism caused by sickle cell disease is supplemental oxygen and hydration
c. Delay in treatment of ischemic priapism may result in permanent erectile dysfunction
d. Ischemic priapism is treated with intracavernosal injections of phenylephrine
e. Ischemic priapism is typically caused by medications or illegal drug use

5. **A 35-year-old obese male presents to the emergency room with concern for perirectal abscess. He recently developed increasing perianal pain with fevers. He has had perianal abscesses before which required incision and drainage. On examination he has a 1.5-cm palpable perianal fluctuant collection consistent with an abscess. The fluid appears to track up the perineum. The perineum and inferior scrotum are moist, erythematous, and edematous. His WBC is 18.5. A CT of the abdomen/pelvis shows a perianal abscess tracking to the perineum with a few flecks of gas and edema of the scrotal wall. What is the most appropriate management at this time?**

a. IV antibiotics and admission for observation
b. Bedside I&D of the perirectal abscess with packing
c. Bedside I&D of the perirectal abscess with antibiotics for scrotal cellulitis
d. Admission with IV antibiotics and abscess I&D in the OR in the

morning

e. Immediate surgical exploration and debridement

6. **TRUE or FALSE: Most traumatic renal injuries do not require any surgical intervention.**

7. **A 25-year-old male was in an ATV accident and presents with a shattered pelvis with bruising extending to his perineum. In the ER, he is unable to void. There is no blood at the meatus. What are the appropriate next steps in management?**

   a. Carefully place a Foley catheter. If there is hematuria, obtain a CT urogram.
   b. Obtain a retrograde urethrogram and CT urogram.
   c. Obtain a retrograde urethrogram; if negative, place a Foley and obtain a CT cystogram.
   d. Place a suprapubic tube and obtain a cystogram.
   e. Place bilateral percutaneous nephrostomies.

46 Obstetrics and Gynecology for the General Surgeon

Kelli Kreher and Andrea R. Hagemann

I. OBSTETRIC AND GYNECOLOGIC DISORDERS. Vaginal Bleeding

(Fig. 46-1, Table 46-1). Gather a thorough history including pattern and intensity of bleeding and date of last menstrual period. Obtain urine beta-human chorionic gonadotropin (β-hCG) level, complete blood count (CBC), coagulation studies, and blood type. Physical examination should include a speculum and bimanual pelvic examination. Pelvic and transvaginal ultrasound (US) is the most sensitive imaging modality for pelvic organs in the pregnant and nonpregnant patient.

A. Obstetric Etiologies.

Forty percent of all pregnancies are associated with vaginal bleeding and approximately half of these result in spontaneous abortions (SABs).

First trimester: SABs, postcoital bleeding, ectopic pregnancy (see Section IIA, Nonobstetric surgery in the pregnant patient, Perioperative considerations), lower genital tract lesions/lacerations, and expulsion of a molar pregnancy.

Third trimester: Placenta previa, placental abruption, vasa previa, preterm labor, and lower genital tract lesions/lacerations.

1. Terminology

a. Threatened abortion: Any vaginal bleeding <20 weeks of gestation without expulsion of products of contraception (POCs); cervix closed

b. Missed abortion: Nonviable gestation <20 weeks with retention of POCs; cervix closed

c. Inevitable abortion: Cervical dilation with or without ruptured

membranes

d. Incomplete abortion: Partial passage of POCs; cervix open

e. Complete abortion: Expulsion of all POCs; cervix closed

f. Septic abortion: Retained infected POC

2. Transvaginal ultrasound

a. Intrauterine gestation seen with β-hCG >2,000 mIU/mL

b. Cardiac activity seen with β-hCG >10,000 mIU/mL

3. Treatment

a. Threatened abortion

(1) Viable: Expectant management.

(2) Indeterminate viability: Repeat US in 7 days, repeat β-hCG in 48 hours.

b. Missed/inevitable/incomplete abortion. Expectant management, surgical management (dilation and curettage [D&C], manual vacuum aspiration [MVA]), or medical therapy (misoprostol 800 µg vaginally) is acceptable. After medical therapy, ensure follow-up within 1 to 2 weeks to confirm completion. Give bleeding precautions (return to emergency room [ER] or call a physician for bleeding or soaking one pad/hour) and infection precautions (return to ER or call a physician for temperature of 101°F).

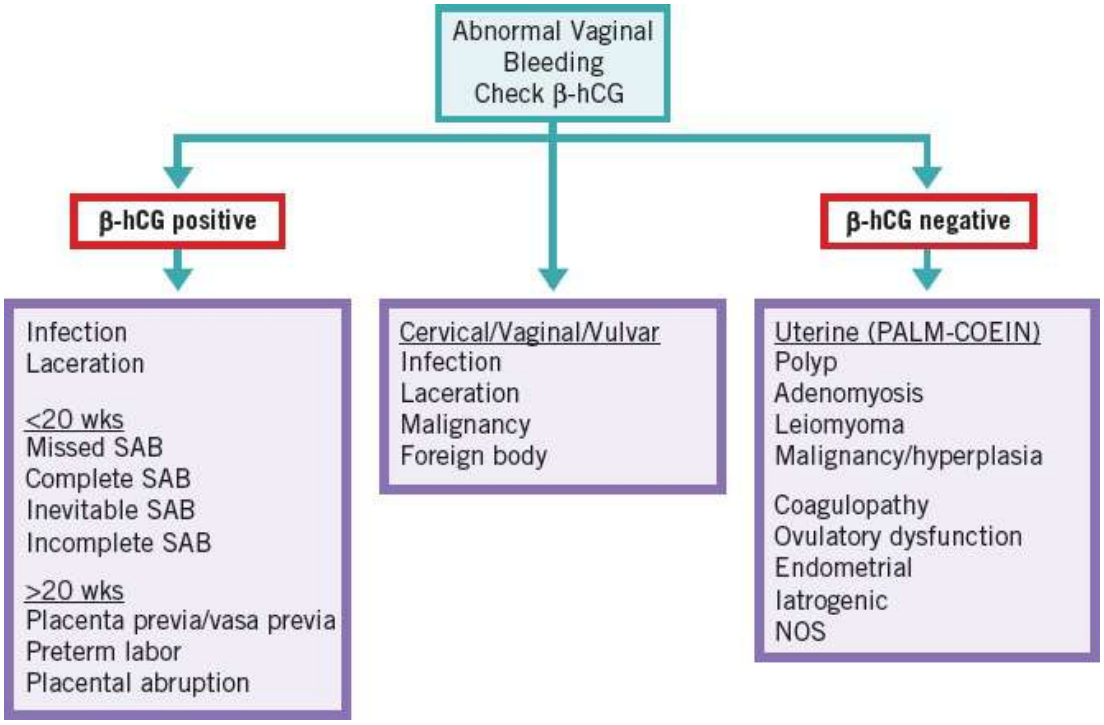


FIGURE 46-1 Management of vaginal bleeding.

c. Complete abortion. If hemodynamically stable, expectant management is appropriate.

d. RhoGAM (50 µg intramuscular [IM]) to any pregnant patient with vaginal bleeding who is Rh negative with a negative antibody screen.

B. Nonobstetric Etiologies of Vaginal Bleeding. See Figure 46-1 for diagnostic workup and Table 46-1 for treatment options.

C. Risks and Complications of D&C

1. **Uterine perforation.** US guidance is recommended to prevent risk of uterine perforation. Perform laparoscopy/cystoscopy if concerned for bowel/bladder injury or if suction was utilized at time of perforation. Manage expectantly if hemodynamically stable and no injury to surrounding organs.
2. **Endometritis.** If unrelated to gonorrhea/chlamydia, doxycycline 100 mg BID × 7 days. If high level of suspicion for gonorrhea/chlamydia infection, use pelvic inflammatory disease (PID) treatment regimen.

II. NONOBSTETRIC SURGERY IN THE PREGNANT PATIENT. If Nonemergent, it is **safest to proceed with surgery in the second trimester**. There is conflicting data regarding the risks of anesthesia and pregnancy loss, with the greatest risk being in the first trimester. maternal exposure to anesthesia in very early pregnancy (within 17 days from LMP) seems to have an all or nothing effect, but weeks 2 to 8 fall in the period of organogenesis; after 9 weeks there is risk to impaired fetal physiology and growth restriction.

TABLE 46-1 Nonobstetric Causes of Vaginal Bleeding

Differential Diagnosis	Laboratory Data	Signs and Symptoms	Treatment
Menses	CBC count, urine hCG	Cyclic bleeding every 21–35 days	Iron therapy if indicated

Abnormal uterine bleeding	CBC count, urine hCG, endometrial biopsy if >45 years old, or any age with risk factors	Noncyclic bleeding; may have associated dysmenorrhea, fatigue, or dizziness	Hormonal therapy if patient is hemodynamically stable; if unstable, transfuse as needed, IV estrogen or high-dose OCPs
Gonorrhea/ *Chlamydia* cervicitis	Cervical culture, wet prep	Purulent vaginal discharge, possible spotting	Ceftriaxone, 250 mg IM × 1; azithromycin, 1 g PO × 1
Trichomonas vaginitis	Wet prep	Yellow-green frothy vaginal discharge, possible spotting	Metronidazole, 500 mg PO BID × 7 days or 2 g PO × 1 (if pregnant, defer until second trimester)
Sexual trauma	Rape kit	Vaginal bleeding and/or discharge	Emergency contraception, prophylactic treatment for STDs; if laceration, pack vagina, possible surgical repair

BID, twice daily; CBC, complete blood cell; hCG, human chorionic gonadotropin; OCPs, oral contraceptive pills; STDs, sexually transmitted diseases; IM, intramuscular; IV, intravenous; PO, oral.

Between 13 and 23 weeks, the uterus is less responsive to stimulating effects from surgery and if preterm labor develops, given previable GA, would not attempt heroic measures for neonatal resuscitation.

After 24 weeks, there is increased risk of fetal hypoxia and preterm labor. Fetal hypoxia can occur in setting of severe prolonged supine hypotension as the gravid uterus compresses the great vessels. Surgery in the third trimester carries a risk of inducing preterm labor and injury to the enlarging uterus.

Risk of pregnancy interruption (any trimester) from nonobstetric surgery in the pregnant patient is approximately 3% to 11%. Pregnancy is not a contraindication to indicated/emergent surgery (*Clin Obstet Gynecol*. 2009;52:586–596). Once the need for surgery has been identified, communication with the obstetrics and anesthesia teams is critical. The age and weight threshold for viability is controversial and may differ between institutions. Traditionally, 24 weeks or 500 g is used as the cutoff for fetal viability. However, some institutions are offering interventions after 23 weeks or 400 g.

A. Perioperative Considerations

1. **Increased risk for aspiration** results from upward displacement of the stomach and the inhibitory effects of progesterone on gastrointestinal motility during pregnancy. Nonparticulate antacids should be given prior to induction of anesthesia (*J Clin Anesth*. 2006;18:60–66).
2. **Increased risk for difficult airway** due to laryngeal and upper airway edema.
3. **Vena cava compression.** Maintain left lateral positioning in third trimester to decrease IVC compression and maintain adequate maternal circulation and placental blood supply (*J Clin Anesth*. 2006;18:60–66). The uterine–placental interface is a low-resistance state that is directly reflective of maternal MAPs.
4. **Avoid maternal hypoxia** (goal >95% SpO_2), which can cause vasoconstriction and decreased uterine artery perfusion and therefore inadequate blood flow to the developing fetus.
5. **Fetal monitoring.** If previable (<23 weeks, <400 g), Doptone maternal abdomen prior to and following the procedure. If pregnancy is viable, intraoperative continuous fetal monitoring and uterine contraction monitoring are recommended if the following conditions are met: (1) Monitoring is compatible with patient position and planned procedure, (2) there are appropriate staff in the operating

room (OR) to interpret fetal monitoring, and (3) there are appropriate staff immediately available to perform an emergency cesarean section. Expect minimal variability on fetal monitoring in the setting of general anesthesia; avoid intervening for delivery unless a significant prolonged fetal bradycardia or deceleration occurs. If intraoperative continuous monitoring is not feasible, monitor fetal heart rate and uterine contractions pre- and postoperatively (ACOG Committee Opinion Number 474; *Clin Obstet Gynecol*. 2009;52:586–596).

6. **Antenatal steroids.** If gestation is between 23 and 34 weeks, start antenatal steroids (betamethasone 12 mg IM q24h × two doses) prior to proceeding to OR to decrease risk of respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, neonatal infection, and neonatal mortality (*NIH Consensus Statement*. 1994;12:1–24).
7. **Maternal hematologic changes.** Pregnancy is a relative hypercoagulable state with increased hepatic production of coagulation factors, decreased fibrinolysis [in second/third trimesters] and venous stasis.

B. Laparoscopy in Pregnancy. Based on the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) Guidelines for laparoscopic surgery during pregnancy (*Surg Endosc*. 1998;12:189), laparoscopy is safe and has similar advantages over open surgery as in the nonpregnant patient. Initial trocar placement is best accomplished by an open Hasson technique and/or left upper quadrant entry as after ~16 weeks of gestation, the uterus becomes an extrapelvic organ. Avoid Veress needle entry. Carbon dioxide pneumoperitoneum up to 15 mm Hg is safe and is unlikely to result in fetal hypoxia or acidosis. Avoid cervical or uterine manipulation.

III. GYNECOLOGIC SURGICAL ANATOMY

A. Uterus and Cervix. The primary blood supply to the uterus and cervix comes from the uterine branch of the hypogastric artery. After passing through the cardinal ligament the uterine artery has ascending and descending branches (Fig. 46-2). The uterine suspensory ligaments include the uterosacral ligaments, cardinal ligaments, round ligaments, and utero-ovarian ligaments. The ureter travels through the cardinal

ligament passing under the uterine artery and vein within the ureteric tunnel. Hypogastric or uterine artery ligation either surgically or by interventional radiology (IR) can be used to treat uncontrolled uterine hemorrhage. The uterus can be amputated from the cervix and the cervix can be left in situ, for instance, in a supracervical hysterectomy, or the cervix can be removed with the uterus in the case of a total abdominal hysterectomy.

B. Ovary. The ovary receives its primary blood supply from the gonadal arteries, which branch off the aorta inferior to the celiac plexus and renal vessels and superior to the inferior mesenteric artery. The left ovarian vein drains into the left renal vein. The right ovarian vein empties into the vena cava. The gonadal vessels travel retroperitoneally within the infundibulopelvic ligament. The infundibulopelvic ligament and gonadal vessels pass over the ureter approximately at the bifurcation of the iliac vessel into external and internal branches as the ureter crosses the pelvic brim and descends into the pelvis. The ovary attaches to the uterus via the utero-ovarian ligament.

C. Bladder. In order to safely perform a hysterectomy, the bladder must be dissected off the uterus and cervix. This is done by incising the vesicouterine peritoneum down to the pubocervical fascia and opening the vesicovaginal space. Fat and vascular tissue stays with the bladder during this dissection. If the plane is obscured by prior cesarean section, the plane can often be established distally and then developed in a retrograde manner to avoid bladder injury.

D. Rectum. The posterior cul-de-sac can be obliterated by adhesion, inflammatory diseases, and malignancy. In these circumstances, the rectovaginal septum can be developed by incising the posterior uterus just caudad to the attachment of the uterosacral ligament to the uterus. The plane can be dissected bluntly, thus dropping the rectum away from the uterus, cervix, and vagina to isolate the structures.

E. Pelvic Avascular Spaces. Developing the avascular spaces allows for identification of the major vessels and ureter, palpation of the parametrial tissue (an important step in evaluation of pelvic masses and gynecologic malignancies), and separation of pelvic organs.

1. **Prevesical** (also called **space of Retzius**). Lies between posterior pubic bone and anterior wall of the bladder.
2. **Vesicovaginal space.** Lies between vagina posteriorly and bladder

anteriorly. Laterally defined by bladder pillars.

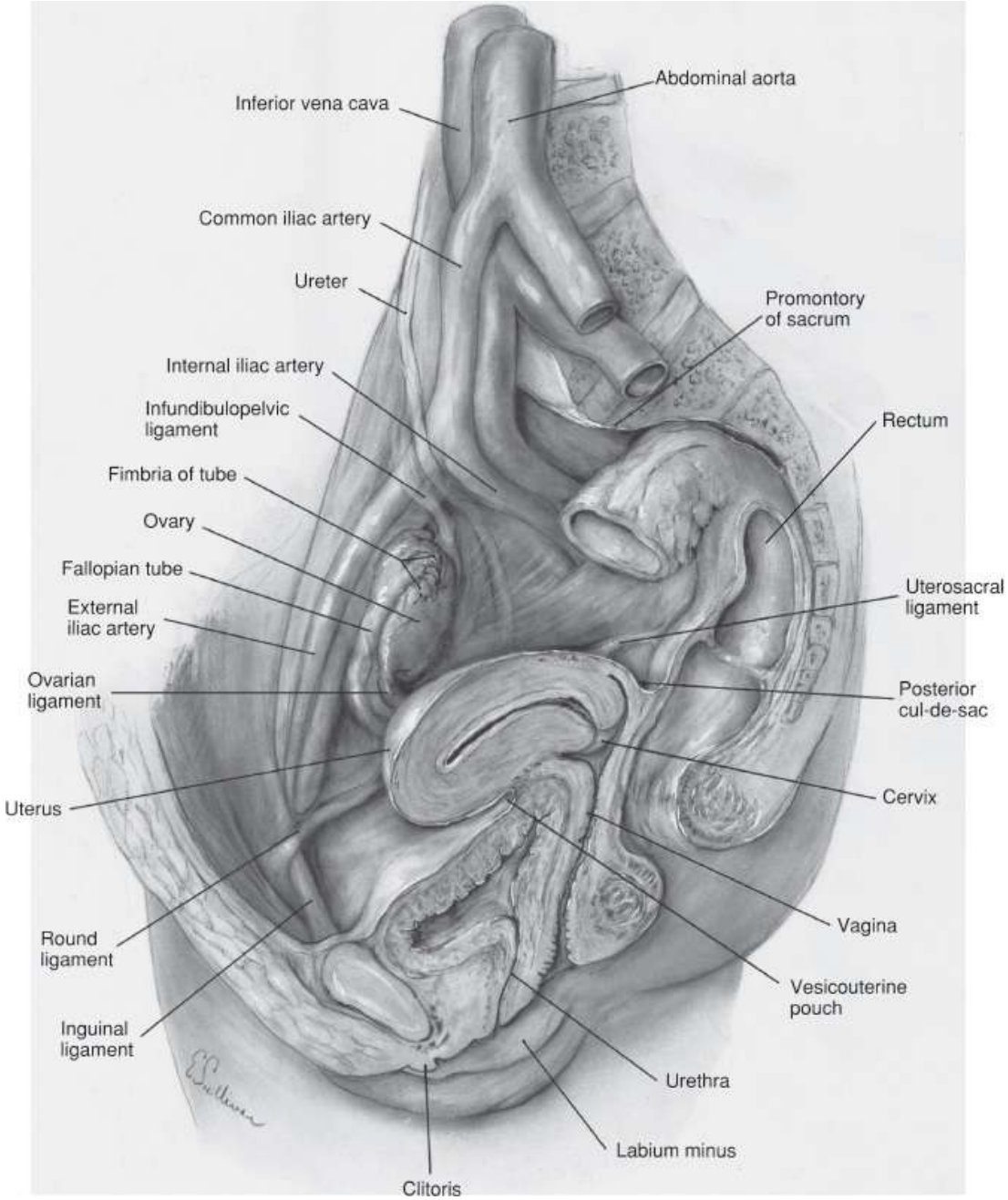


FIGURE 46-2 Pelvic viscera. (From Rock JA, Jones HW, eds. *Te Linde's Operative Gynecology*. 10th ed. Philadelphia, PA: Wolters Kluwer Health; 2008.)

3. **Paravesical space.** Bordered by bladder pillars medially and pelvic sidewall/obturator internus laterally.
4. **Pararectal space.** Identified between the ureter and the hypogastric artery.

5. **Rectovaginal space.** Potential space between the rectum and vagina. Laterally defined by the rectal pillars/uterosacral ligaments.

IV. GYNECOLOGIC MALIGNANCIES.

over 110,000 new cases of gynecologic malignancy were diagnosed in the united states in 2018 (*CA Cancer J Clin*. 2018;68:7–30). A brief overview of vulvar, cervical, endometrial, and ovarian cancers is presented with emphasis on diagnosis and initial management. If a gynecologic malignancy is suspected, all effort should be made to obtain an intraoperative consult with a gynecologic oncologist.

A. Vulvar Carcinoma

1. **Epidemiology.** There were an estimated 6,190 new cases and 1,200 deaths in the United States in 2018. The mean age at diagnosis is 68 years old. Vulvar cancer is associated with HPV in 60% of cases. Other risk factors for vulvar cancer include cigarette smoking, vulvar and cervical dysplasia, vulvar dystrophy, and immunodeficiency.
2. **Presentation and clinical features.** The most common symptom is itching, but lesions can be pruritic, painful, or asymptomatic. Vulvar examination typically yields an ulcerated, hyper- or hypopigmented, or exophytic lesion. A biopsy should be taken any time such a lesion is noted on the vulva.
3. **Standard of care.** Vulvar cancer is staged using both clinical and surgical assessment. Size of the lesion and regional or distant metastasis must be assessed. Radical vulvectomy is defined as complete resection of the lesion with at least 1-cm margins and deep excision to the inferior fascia of the urogenital diaphragm (coplanar with the fascia lata and fascia over the pubic symphysis). Adjuvant radiation is reserved for cancers confined to the vulva at high risk for recurrence or tumors that metastasize to the inguinofemoral lymph nodes.
4. **What to do if a lesion is identified pre- or intraoperatively.** As above, it is essential to obtain a biopsy for pathologic diagnosis. A 3- to 5-mm Keyes punch biopsy is usually adequate.

B. Cervical Carcinoma

1. **Epidemiology.** There were an estimated 13,240 new cases and 4,170 deaths in the United States in 2018. The mean age of diagnosis is 48

years old. HPV is detected in over 99% of cervical cancer cases. Other risk factors for cervical cancer include cigarette smoking, immunosuppression, history of multiple sexual partners, early sexual debut (i.e., onset of sexual activity), history of sexually transmitted infections (STIs), and vulvar or vaginal dysplasia.

2. **Presentation and clinical features.** Irregular or postcoital vaginal bleeding and malodorous, watery discharge are the most common symptoms. Advanced stage disease may present with leg pain (sciatic nerve involvement), flank pain (ureteral obstruction), renal failure, or rectal bleeding from a pelvic mass.
3. **Standard of care.** See Table 46-2 for treatment by stage. **Cervical cancer is clinically, not surgically, staged**. The World Health Organization (WHO) recognizes a standard worldwide staging system for cervical cancer that includes a pelvic examination, x-ray, intravenous pyelogram, endoscopy (hysteroscopy, cystoscopy, proctoscopy), and cervical biopsy. Rectovaginal examination is essential to characterize parametrial involvement. In the United States, a positron emission tomography (PET) scan, magnetic resonance imaging (MRI), or computerized tomography (CT) is typically performed to assess for pelvic or para-aortic lymphadenopathy and guide treatment planning, but this does not change clinical stage as it is not available worldwide.

TABLE 46-2 Cervical Cancer Staging

TNM	FIGO	Definition	Treatment
T1	I	Cervical carcinoma confined to the cervix (disregard extension to the corpus)	
T1a	IA	Preclinical invasive carcinoma, diagnosed by microscopy only. Deepest invasions ≤5 mm and largest extension ≥7 mm	

T1a1	IA1	Microscopic stromal invasion ≤3 mm in depth and extension ≤7 mm	Simple hysterectomy LEEP or cone biopsy (margins negative) if fertility desired
T1a2	IA2	Tumor with stromal invasion between 3 and 5 mm in depth and extension <7 mm	Radical hysterectomy and pelvic lymphadenectomy
T1b	IB	Clinically visible tumor confined to the cervix but larger than IA2, >5 mm in depth	
T1b1	IB1	Clinical lesions ≤2 cm in greatest dimension	Radical hysterectomy and pelvic lymphadenectomy or primary radiation
T1b2	IB2	Clinical lesions >2 and <4 cm in size	Stage 1B2–IIA primary radiation with sensitizing cisplatin or radical hysterectomy with pelvic lymphadenectomy
T1b3	IB3	Clinical lesions >4 cm in greatest dimension	
T2	II	Invades beyond the cervix but not to the pelvic side wall or the lower one-third of the vagina	

T2a	IIA	Tumor without parametrial involvement	
T2a1	IIA1	Tumor ≤4 cm	
T2a2	IIA2	Tumor >4 cm	
T2b	IIB	Tumor with parametrial involvement	Stage IIB–IVA primary radiation with sensitizing cisplatin
T3	III	Extends to the pelvic side wall and/or involves the lower one-third of the vagina and/or causes hydronephrosis or nonfunctioning kidney	
T3a	IIIA	Invades lower one-third of the vagina with no extension to the pelvic side wall	
T3b	IIIB	Extends to the pelvic side wall and/or causes hydronephrosis or a nonfunctioning kidney	
T4	IVA	Invades mucosa of the bladder/rectum and/or extends beyond the true pelvis	
M1	IVB	Distant metastasis	Taxane, platinum, bevacizumab with or without pelvic radiation for symptom control

FIGO, International Federation of Gynecology and Obstetrics; TNM, tumor, node, metastasis.

Early-stage cervical cancers (stage IA1–IB1) can often be cured by surgical management alone. For patients with early-stage disease desiring fertility, a *loop electrosurgical excision procedure* (LEEP) or cone biopsy with negative margins (stage IA1) or a radical cervicectomy (also known as trachelectomy; stage IB1) may be recommended. While surgery is an option for bulkier early-stage cancers (stage IB2–IIA), the benefits must be weighed against the potential risks of vesicovaginal or rectovaginal fistula formation from subsequent radiation; chemoradiation without surgery is often a reasonable option. Locally advanced cervical cancers (stage IIB–IVA) should be treated with radiation and cisplatin. Cervical cancers with distant spread can be treated with combination taxane and platinum chemotherapy in combination with anti–VEGF-A monoclonal antibody bevacizumab. In the case of distant spread, radiation is used for palliation of bleeding or potentially for isolated supraclavicular lymphadenopathy. Pelvic exenteration with removal of the bladder and rectum is reserved for recurrent cervical cancer localized to the pelvis.

4. **What to do if suspected pre- or intraoperatively.** Obtain a biopsy. Perform a speculum examination and use a Tischler biopsy forceps to obtain a biopsy of cervix or malignant-appearing tissue. Do not attempt to resect bulky cervical cancer.
5. **Uncontrolled vaginal bleeding.** Heavy vaginal bleeding from cervical cancer can occasionally be encountered in the emergency department. Place a tight vaginal packing and a transurethral Foley catheter. Acetone-soaked gauze is the most effective packing for vessel sclerosis and control of hemorrhage from necrotic tumor. If ineffective at controlling bleeding, IR embolization may be necessary. Prompt consultation with radiation oncology is also indicated once a biopsy has confirmed invasive cancer.

C. Endometrial Cancers

1. **Epidemiology.** Endometrial carcinoma is the most common gynecologic cancer in the United States with 63,230 new cases and 11,350 deaths in 2018. The average age of diagnosis is 61 years old. Risk factors include excess/unopposed estrogen (as seen with obesity, medication, anovulation, early menarche, and late menopause), age, and Lynch syndrome. Over 80% of endometrial cancers are **endometrioid adenocarcinomas**, and they are subdivided into grades 1, 2, and 3 based on the degree of glandular formation. Less common histologies include *clear cell*, *serous*, and *poorly differentiated*. More recently, endometrial cancers have been divided into "type 1" and "type 2" cancers. **Type 1 cancers** are thought to be related to excess estrogen and typically have endometrioid histology with a grade of 1 and 2. **Type 2 cancers** include grade 3 endometrioid, clear cell, serous, or poorly differentiated adenocarcinomas, all of which are high grade and more aggressive and less related to excess estrogen than their more common type 1 counterparts. **Uterine carcinosarcomas** also arise from the endometrium and are considered a poorly differentiated endometrial carcinoma. They are aggressive, having features of endometrial carcinoma as well as sarcomatous overgrowth, and are also known as malignant mixed müllerian tumors (MMMT). **Sarcomas** are malignancies that arise in the connective tissue/stroma (**stromal sarcomas**) or myometrium (**leiomyosarcomas**) of the uterus. They make up 4% of all uterine malignancies and are staged separately from endometrial cancers. These tumors are managed surgically, with or without adjuvant therapy.
2. **Presentation and clinical features.** The most common symptom is abnormal vaginal bleeding, often in a postmenopausal patient.
3. **Standard of care.** Endometrial cancers are staged surgically with a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic and para-aortic lymphadenectomy. Omental biopsy should be performed for high-grade cancers. The role of lymphadenectomy is evolving, especially for lower-grade and earlier-stage cancers. Adjuvant or postoperative treatment recommendations are outlined in Table 46-3 by stage.

TABLE 46-3 Endometrial Cancer Staging

TNM	FIGO	Definition	Adjuvant Treatment
T1	I	Tumor confined to the corpus uteri	
T1a	IA	Invades one-half or less of the myometrium	Observation for most type 1 carcinomas Consider chemotherapy (platinum + taxane) with radiation for type 2 carcinomas
T1b	IB	Invades more than one-half of the myometrium	Vaginal brachytherapy or pelvic radiation Consider chemotherapy (platinum + taxane) with radiation for type 2 carcinomas
T2	II	Invades cervical stroma but does not extend beyond the uterus	Pelvic radiation Platinum and taxane chemotherapy with radiation for type 2 carcinomas
T3	III	Local and/or regional spread as specified	Radiation of involved field (pelvic +/− para-aortic) and chemotherapy (platinum + taxane)
T3a	IIIA	Involves the serosa and/or adnexa	
T3b	IIIB	Vaginal and/or parametrial involvement	

N1	IIIC	Metastasis to the pelvic and/or para-aortic lymph nodes	
	IIIC1	Positive pelvic nodes	
	IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes	
T4	IVA	Invades the bladder and/or bowel mucosa	Chemotherapy (platinum + taxane) with radiation depending on pattern of spread
M1	IVB	Distant metastasis including intra-abdominal and/or inguinal lymph nodes	Chemotherapy (platinum + taxane)

FIGO, International Federation of Gynecology and Obstetrics; TNM, tumor, node, metastasis.

4. **What to do if suspected pre- or intraoperatively.** If suspected preoperatively, obtain an endometrial biopsy using either a curette or a biopsy Pipelle. Endometrial biopsy should be performed in any woman with postmenopausal vaginal bleeding, any woman >45 years old with abnormal uterine bleeding, or women of any age with abnormal bleeding and risk factors such as obesity, polycystic ovarian syndrome, or unopposed estrogen. If suspected intraoperatively because of uterine surface disease, obtain a biopsy and send for

frozen pathology. If positive for adenocarcinoma of müllerian origin, consult a gynecologic oncologist if available. If unavailable, proceed with total abdominal hysterectomy, bilateral salpingo-oophorectomy, and staging lymphadenectomy or close the abdomen and promptly refer to a gynecologic oncologist.

D. Ovarian Carcinoma

1. **Epidemiology.** Ovarian cancer is the most deadly gynecologic malignancy in the United States with 22,240 new cases and 14,070 deaths in 2018. The average age at diagnosis is 63 years old. Risk factors include age, *BRCA1* or *BRCA2* mutation, early menarche, late menopause, nulliparity, endometriosis, and infertility. Efforts to decrease lifetime ovulation (birth control or pregnancy) decrease the risk for ovarian cancer.
2. **Presentation and clinical features.** Early-stage disease is generally asymptomatic. Patients experience pelvic pain or pressure, nausea, early satiety, weight loss, and bloating with increasing tumor burden (*Cancer*. 2011;117:4414–4423).
3. **Standard of care.** Ovarian cancer is surgically staged with a total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, peritoneal biopsies, and omental biopsy. If bulky disease is identified outside of the pelvis, the goal of the surgery is maximal cytoreduction of all gross disease. This can require bowel resection, diaphragm resection, liver resection, splenectomy, peritoneal stripping, and ablation or coagulation of tumor deposits using argon beam or plasma jet. Adjuvant treatment is listed by stage in Table 46-4. **Fallopian tube and peritoneal carcinomas** are staged and treated similarly to ovarian carcinoma. Neoadjuvant chemotherapy can be given to reduce tumor bulk, followed by interval cytoreduction and continued chemotherapy.

   Treatment of **sex cord stromal tumors** and **germ cell tumors of the ovary** are outside of the scope of this chapter.
4. **What to do if suspected pre- or intraoperatively.** If suspected preoperatively, obtain pelvic US and serum CA-125 level. If US is suspicious, a CT scan of the abdomen/pelvis is indicated to assess disease spread, along with a CXR or chest CT to evaluate the lungs. Consult a gynecologic oncologist if possible. Do not proceed with

nonemergent surgery until this consultation is complete if suspicion for ovarian malignancy is high. If detected intraoperatively, obtain a tissue biopsy and send for frozen section. If positive for müllerian malignancy, obtain an intraoperative gynecologic oncology consult. If unavailable, bilateral salpingo-oophorectomy in a postmenopausal patient with or without hysterectomy is reasonable if within the operating surgeon's scope of practice.

TABLE 46-4 Ovarian Cancer Staging

TNM	FIGO	Definition	Adjuvant Treatment
T1	I	Tumor limited to one or both ovaries	
T1a	IA	Limited to one ovary; capsule intact, no tumor on ovarian surface, no malignant cells in ascites or peritoneal washings	Carboplatin and paclitaxel for high-grade or clear cell carcinomas
T1b	IB	Limited to both ovaries; capsule intact, no tumor on ovarian surface, no malignant cells in ascites or peritoneal washings	Carboplatin and paclitaxel for high-grade or clear cell carcinomas
T1c	IC	Limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings	Carboplatin and paclitaxel
T2	II	Tumor involves one or both ovaries with pelvic	Combination intravenous and

		extension	intraperitoneal platinum and taxane chemotherapy
T2a	IIA	Extension and/or implants on uterus and/or tubes; no malignant cells in ascites or peritoneal washings	
T2b	IIB	Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings	
T2c	IIC	Pelvic extension with malignant cells in ascites or peritoneal washings	
T3	III	Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis and/or regional lymph node metastasis	Combination intravenous and intraperitoneal platinum and taxane chemotherapy
T3a	IIIA	Microscopic peritoneal metastasis beyond the pelvis	
T3b	IIIB	Macroscopic peritoneal metastasis beyond the pelvis ≤2 cm	
T3c	IIIC	Peritoneal metastasis beyond the pelvis >2 cm and/or regional lymph	

		node involvement	
M1	IV	Distant metastasis (excludes peritoneal metastasis)	Carboplatin and paclitaxel

FIGO, International Federation of Gynecology and Obstetrics; TNM, tumor, node, metastasis.

CHAPTER 46: OBSTETRICS AND GYNECOLOGY FOR THE GENERAL SURGEON

Multiple Choice Questions

1. **Which of the following procedures is included in an ovarian cancer staging procedure?**

   a. Small-bowel resection
   b. Splenectomy
   c. Diaphragm stripping
   d. Omentectomy

2. **What is the most appropriate next step in an asymptomatic 52-year-old woman with a suspected adnexal mass on clinical examination?**

   a. CT chest/abdomen/pelvis
   b. Pelvic and transvaginal ultrasound
   c. Observation
   d. Exploratory laparotomy

3. **Which of the following genetic syndromes is most associated with endometrial cancer?**

   a. Lynch syndrome
   b. BRCA1
   c. BRCA2
   d. Multiple endocrine neoplasia 1 (MEN1)

4. **If feasible, what is ideal positioning for a gravid patient undergoing surgery?**

   a. Supine with a left lateral tilt
   b. Dorsal lithotomy
   c. Prone
   d. Supine in Trendelenburg

5. **Which of the following is the most appropriate treatment for**

stage IIIB cervical cancer with no distant metastatic disease?

a. Radical surgical resection
b. Simple hysterectomy followed by radiation
c. Radiation with sensitizing cisplatin
d. Chemotherapy with cisplatin, taxane, and bevacizumab

47 Radiology

Cathleen M. Courtney and Vincent Mellnick

INTRODUCTION

Radiologic evaluation is often a critical component of a diagnostic workup in the surgical patient. Ultrasonography, conventional radiography (plain film), computed tomography (CT), and magnetic resonance imaging (MRI) are nearly universally available in most modern facilities. However, all imaging modalities come with limitations, risks, and costs. Therefore, it is important that studies be performed selectively by practitioners.

I. IMAGING MODALITIES

A. Ultrasound (US) uses sound waves to image internal structures with more echogenic structures—like calcium—appearing brighter and less echogenic structures—like fluid—appearing black. Advantages of US include portability, low cost, and lack of radiation exposure. However, potential limitations include operator dependency, patient body habitus, and attenuation of the sound beam by gas, making evaluation of, or through, the GI tract often difficult. US serves as a first-line modality for evaluating the biliary tract, gallbladder, ovarian/testicular pathology, thyroid/parathyroid disease, and peripheral vascular abnormalities. Doppler examination can also assess blood flow into and out of the solid organs. Focused assessment for sonography in trauma (FAST) can be used for rapid detection of free fluid at the bedside in trauma patients. However, small quantities of free fluid may be missed, as can organ injuries that have not resulted in intraperitoneal bleeding. Lastly, US can be used as a guide to percutaneous procedures, including biopsies, fluid drainage, and central vascular access.

B. Conventional radiography (plain film) is often the initial radiologic

evaluation as it is readily available, fast, and inexpensive. Limitations include 2D-viewing capabilities and poor characterization of soft tissues. Radiographs can be especially useful for evaluating highly dense structures such as bones, urinary stones, and calcifications. For the general surgeon, x-ray plays an important role in both the trauma patient and the workup of abdominal pain and distention by evaluating the bowel gas pattern.

1. **Trauma.** Chest radiographs (CXRs) and pelvis radiographs remain recommended by Advanced Trauma Life Support as a routine in the evaluation of blunt trauma (*J Trauma Acute Care Surg*. 2013;74:1363–1366). A single-view anteroposterior CXR may show a life-threatening injury such as pneumothorax or hemothorax. In the trauma setting, CXR can also identify pulmonary contusion/aspiration, abnormal mediastinal width or contour (potentially indicating traumatic aortic injury), abnormal diaphragm contour, rib fractures, retained bullets or other objects, and extrathoracic injuries. CXRs are also used commonly to document the appropriate positioning of support lines and tubes.
2. **Acute abdominal pain.** For patients with acute abdominal pain, an abdominal series may be performed, which consists of at least two views: a supine view and a dependent—either an upright or a left lateral decubitus—view. The supine view is insensitive for free intraperitoneal gas, a sign of hollow viscous perforation. The supine or left lateral decubitus view improves conspicuity of free gas by allowing the gas to antidependently collect next to the liver surface. Dilated small or large bowel may also be demonstrated on radiographs and may allow the diagnosis of obstruction. The most common indication for abdominal radiography is to confirm appropriate positioning of enteric tubes, however.

C. Computer tomography (CT) consists of a rotating x-ray beam with multiple detectors surrounding the patient on a moving table. Computer reconstruction of the detected x-rays allows for viewing the internal structures in “slices” in different planes as well as three-dimensional reconstructions. Structures on CT are displayed in grayscale with shades dependent upon their attenuation, measured in Hounsfield units. Dense structures—like bone—are white due to their stopping more x-rays. Gas does not stop x-rays well and is displayed as black. CT can also

distinguish between fat, fluid, and blood, allowing detection of many acute processes. This and the ability to view structures like the brain that were previously primarily visible surgically have led to a marked increase in use of this technology. Accordingly, the number of ED visits that included a CT examination from 1995 to 2007 increased from 2.7 million to 16.3 million (*Radiology*. 2011;258:164–173). It has become a standard part of the evaluation of stable—and in some studies, unstable-–patients with blunt and penetrating trauma, allowing for triage of patients who do and do not need immediate surgery for life-threatening injuries (*Injury*. 2015;46:29–34; *Am J Surg*. 2015;209:834–840). Although in certain instances contrast is not needed, such as detecting intracranial hemorrhage, fractures, or renal stones, the addition of iodinated intravenous contrast media helps to better delineate normal structures such as the soft tissues, blood vessels, and organs. Similarly, pathologic processes such as tumors, active bleeding, and vascular abnormalities, are also often only identified with intravenous contrast. However, acute renal failure and contrast allergies are relative contraindications for iodinated contrast. Enteric contrast agents may be administered prior to an abdominal CT to delineate the contrast-filled GI tract from other abdominal structures. The potential benefits of enteric contrast must be weighed against the time and discomfort for the patient, however.

II. Ionizing Radiation CONSIDERATIONS. With the increased usage of CT, the amount of ionizing radiation that patients are exposed to has become increasingly important. Table 47-1 describes the typical organ radiation doses from various radiologic studies. The radiation energy absorbed by tissue is measured in rad or Gray (1 rad = 0.01 Gy). The biologic effect of the energy is called effective dose and is measured in rem, sieverts, or millisieverts (1 rem [roentgen equivalent man] = 0.01 Sv = 10 mSv). Effective dose is the theoretic sum of all biologic effects of radiation, accounting for intrinsic tissue sensitivity and mass (*Surg Clin North Am*. 2017;97:1175–1183). There is evidence extrapolated from epidemiologic studies that the organ doses corresponding to common CT studies result in an, albeit small, increased risk of cancer (*N Engl J Med*. 2007;357:2277–2284). Therefore, physicians should be judicious in the number and types of radiology examinations that are ordered.

TABLE 47-1 Typical Organ Radiation Doses From Various Radiologic Studies

Study Type	Relevant Organ	Relevant Organ Dose (mSv)[a]
Dental radiography	Brain	0.005
Chest radiography	Lung	0.1
Mammography	Breast	0.4
Barium enema	Colon	8
Adult abdominal CT	Stomach	10
Neonatal abdominal CT	Stomach	20

[a]The scientific unit of measurement for whole-body radiation dose, called "effective dose," is the millisievert (mSv).

Adapted from https://www.radiologyinfo.org/en/info.cfm?pg=safety-xray.

A. **MRI utilizes** external magnetic fields and radiofrequency waves to multiplanar imaging—similar to CT—without exposure to ionizing radiation. It is typically costlier and acquisition takes longer than CT and US, and the patient must be able to lie supine and still for a prolonged period of time within the tunnel-like bore of the machine. Imaging of the torso also requires repeated breath holds, which may be difficult for acutely ill patients. Due to the examination length of MRI and the relatively tight confines of the MRI bore, it may be difficult for patients with claustrophobia. In addition, patients must be screened for medical devices—such as pacemakers—or other metal objects within their bodies that may make MRI unsafe for them. Despite these limitations, the lack of ionizing radiation makes MRI advantageous for use in the pediatric and pregnant populations. MRI's exquisite contrast resolution is also far above that attainable by other imaging modalities for looking at soft tissues, particularly the brain, spinal cord, and joints

(*Magn Reson Imaging*. 1985;3:345–352). In addition, this soft tissue contrast makes MRI useful in assessing the biliary tree, bowel wall pathology in patients with known or suspected Crohn disease, and for local staging of tumors in locations such as the rectum and prostate. In many instances, the addition of intravenous, gadolinium-based contrast improves the ability of MRI to detect disease.

III. SPECIAL POPULATIONS

A. Pregnant Patients. According to the American College of Obstetrics and Gynecology (ACOG), the impact of ionizing radiation is most detrimental between weeks 2 and 15 of gestation (*Obstet Gynecol.* 2016;127:75–80). Therefore, US and MRI are the imaging techniques of choice for pregnant patients. However, if techniques using ionization radiation, including CT scan, are necessary—such as in acute trauma—then they should not be withheld since the dose of radiation exposure from CT is likely much lower than the exposure associated with known fetal harm. Iodinated contrast for CT has also not been demonstrated to be harmful during pregnancy. However, MRI contrast is contraindicated during pregnancy.

B. Pediatric Patients. The effective dose for radiologic studies varies inversely and strongly with age: Children's tissues are more intrinsically radiosensitive, and children have longer latency before detrimental effects manifest (*Surg Clin North Am*. 2017;97:1175–1183). Therefore, an effort should always be made to keep the radiation dose low with adherence to the acronym ALARA (as low as reasonably achievable). Ordering physicians are encouraged to critically evaluate the number and type of studies performed and to minimize the effective dose of studies. Modalities such as US and MRI should be preferentially utilized in this population. Smaller children may require sedation to achieve a diagnostic MRI examination due to the necessity to lie still.

C. Contrast Allergies. Allergic-type reactions may occur after administration of iodinated contrast media and range from minor (e.g., hives) to anaphylaxis. Predisposing risk factors for immediate allergic-type reactions include a previous adverse reaction, atopy, asthma, dehydration, heart disease, existing renal disease, hematologic disease (e.g., sickle cell anemia), age less than 1 year or more than 65 years, and use of β-blockers or nonsteroidal anti-inflammatory drugs (*CMAJ*.

2010;182(12):1328). In patients who have had a previous allergic-type reaction to iodinated contrast media, premedication with a combination of prednisone and diphenhydramine prior to contrast injection is advised (*J Allergy Clin Immunol*. 1991;87(4):867–872). Depending upon the indication and the severity of the reaction, it may be advisable to pursue imaging with another modality such as MRI.

D. Renal Failure. Patients with renal failure are at increased risk for contrast-induced nephrotoxicity after iodinated contrast material. Therefore it is a relative contraindication in this patient population. However, anuric patients on hemodialysis can receive iodinated contrast material without the need for urgent dialysis due to the widespread use of low-osmolality contrast agents. Both acute renal failure and advanced chronic kidney disease are relative contraindications for gadolinium-based contrast agents used in MRI due to the risk of nephrogenic systemic fibrosis. The acuity of the renal failure, glomerular filtration rate, and the indication for the examination should all be assessed with an analysis of the potential risks and benefits.

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Biostatistics for the General Surgeon

Melanie P. Subramanian and Graham A. Colditz

INTRODUCTION

Evidence-based medicine aims to use information gleaned from the existing and ever-expanding body of published research to inform clinical practice. Whether contributing to the literature via the conduct and publication of original research, critically evaluating existing data to incorporate changes into day-to-day health care delivery, or evaluating practice patterns to improve patient outcomes at a systems level, a basic knowledge of biostatistics is essential for the general surgeon.

I. Study Design. Study design can be stratified into two separate categories based on the aims of inquiry: observational and experimental. In an **observational study**, participants are not assigned to treatment or control groups. Inferences are made by surveillance of a group of participants. Observational studies can determine associations between exposures and outcomes, but causation cannot be established. In contrast, in **experimental studies**, investigators assign participants to treatment and nontreatment groups and observe a specified effect. In a properly crafted prospective randomized trial, experimental studies can establish a causal relationship between exposure and outcome (Fig. 48-1).

A. Observational Studies

1. **Case-control study.** In this study design, **participants are selected based on the presence or absence of the outcome of interest**. In order to determine the relationship of exposure to outcome, a group of individuals with the disease (cases) are compared to a group of individuals without the disease (controls). Evaluation of exposures in

both cases and controls is conducted to determine systematic differences between the groups. A case-control study can be a quick and relatively inexpensive first step in evaluating whether an exposure is associated with a given disease. Additionally, this study design is useful for investigation of rare diseases. This approach can also be used to sample cases and controls from a much larger randomized trial or cohort study in which biomarkers or other expensive laboratory measures are being considered for additional analysis (Fig. 48-2).

2. **Cohort study.** In cohort studies, **individuals are divided into groups based on exposure and followed over time to document incidence of disease or the development of the outcome of interest**. At the outset of the study, the study participants must be free of the outcome of interest or disease process. As such, cohort studies require that the study population be followed for a long period of time in order to evaluate whether the outcome has developed. Cohort studies can be retrospective or prospective (Fig. 48-3).

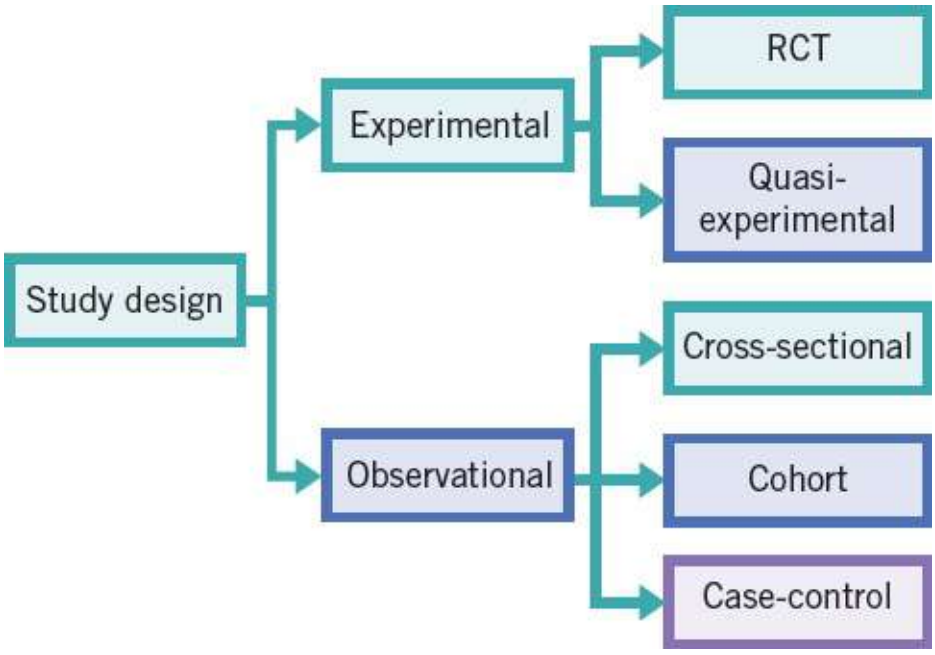

FIGURE 48-1 Summary of study designs.

a. In a **prospective** cohort design, the study population is identified at the outset of the study, data are collected, and participants followed for a period of time sufficient for the outcome of interest

to develop in a portion of the population. This is not an ideal study design for projects studying outcomes that are rare events, as a large number of patients must be enrolled and followed for a prolonged period of time for the specified outcome or disease process to occur.

b. In a **retrospective** cohort design, historical data are assembled and used to compare exposed and nonexposed individuals. The outcome of interest is evaluated at the study's onset, and historical data from a pre-existing population are used to evaluate exposure status. This methodology allows for quicker completion of studies but is limited by the post hoc definition of exposure and by having to rely on the quality of the historical database.

3. Cross-sectional studies provide information on a population during a single period of observation. **Exposure and outcomes are measured simultaneously in a defined study population**. The benefit of this method of study is that it is easy to conduct, low cost, and a large volume of information can be obtained quickly. This study method is useful for describing populations, identifying risk factors, quantifying the magnitude of health problems, and generating hypotheses about exposures and disease outcomes.

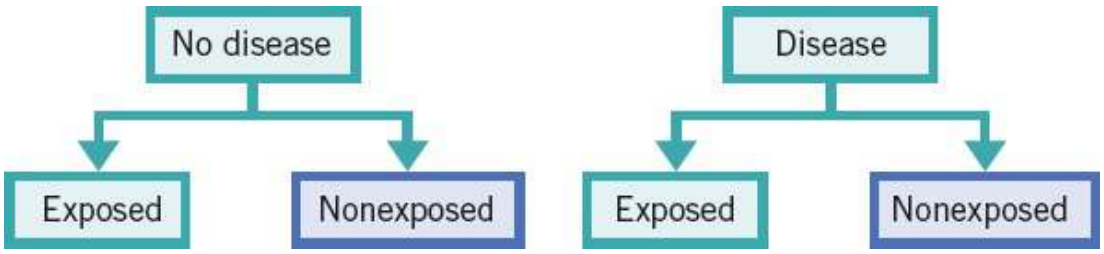

FIGURE 48-2 Design of a case-control study.

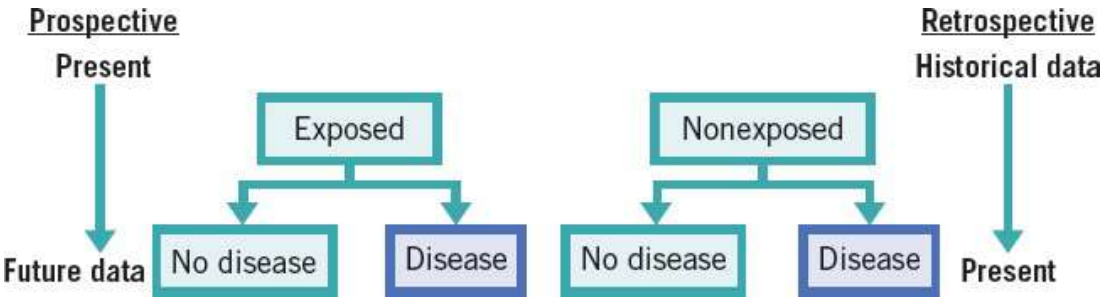

FIGURE 48-3 Design of prospective and retrospective cohort studies.

4. **Case series** are conducted and published on a small group of participants. **These studies document the natural course of a disease and the associated treatment and outcome**. These reports are typically used to document rare disease processes or outcomes and are **hypothesis generating** in nature. Including all cases treated in a defined period is necessary to reduce bias.

B. Experimental Studies

1. **Randomized controlled trials (RCTs).** In an RCT, patients are randomly assigned to **intervention** and **control** groups or "arms." This trial design is the **gold standard for clinical research.**
   a. **Randomization** is a key element in this study design. The random allocation of participants facilitates unbiased distribution to the study arms of both known/measured and unknown/unmeasured participant **covariates,** that is, observed, immutable characteristics that may or may not be associated with the outcome of interest and that may bias an observer's interpretation of the relationship between the intervention being studied and the outcome to be observed.
   b. **Blinding** is the concealment of participant allocation to treatment and control groups. It can be utilized by the trial researchers with respect to both the investigators and the participants. From the trial participant perspective, blinding means that participants do not know if they are in the treatment or control group. Investigators can also be blinded so they are not aware of patient assignment. When neither investigators nor participants are informed of participants' allocation status, an experiment is considered **double blinded.**
2. **Pragmatic trials.** RCTs are often limited in their generalizability due to strict inclusion/exclusion criteria and testing under artificial conditions. In addition to limited generalizability, RCTs may experience challenges in patient recruitment due to strict inclusion/exclusion criteria. Pragmatic trials have developed in response to these limitations. Pragmatic clinical trials are designed for the primary purpose of performing **comparative effectiveness research between interventions as they are experienced in the "real world."** According to one commonly cited definition by Califf and Sugarman (*Clin Trials*. 2015;12(5):436–441), pragmatic trials

share three common traits:

a. Pragmatic trials intend to inform decision makers from multiple backgrounds (patients, clinicians, policy makers) rather than characterize a biologic or social mechanism.

b. Pragmatic trials enroll patients that are representative of the populations and settings for whom the study in question is relevant.

c. Pragmatic trials aim to streamline study procedures and data collection to increase the chances of performing an adequately powered study that can inform clinical/policy decisions or measure an expansive range of outcomes.

Pragmatic clinical trials have several advantages. They maximize external validity and generalizability, and they are generally easier to obtain sufficient power due to less restrictive inclusion criteria. Additionally, they test treatments as they occur in usual patient care, which may translate easier into real world clinical practice. However, given these characteristics, the data can be more complicated and can suffer more from confounding.

Agencies tasked with promoting patient-centered comparative effectiveness research, including the National Institutes of Health and the Patient-Centered Outcomes Research Institute, have given increased attention and funding to pragmatic trials. One method for evaluating pragmatic trials that has been commonly used is the **Pragmatic Explanatory Continuum Indicator Summary** (**PRECIS-2**). This tool evaluates pragmatic trials in nine domains (eligibility criteria, recruitment, setting, organization, flexibility delivery, flexibility adherence, follow-up, primary outcome, primary analysis) to help researchers carefully consider the impact that their intended study would have on applicability (*BMJ*. 2015;350:h2147).

C. Systematic review and meta-analysis are methods to critically appraise existing published literature and develop a consensus among the data. The terms are often used interchangeably, but they are distinct entities. A **systematic review** is a qualitative literature review. It is conducted by establishing a clear clinical question, completing an exhaustive search of published data, identifying relevant studies, and analyzing the data. Analysis is largely qualitative but may have

quantitative components. A quantitative statistical analysis of results gleaned from a literature search of published data is referred to as a **meta-analysis.** Furthermore, if individual patient data are abstracted from these results, they can be analyzed in a **pooled analysis,** which reduces heterogeneity among studies by using a more uniform classification of participant covariates.

II. DATA ANALYSIS

A. Basic Statistical Principles

1. The **null hypothesis** (H_0) is the premise that there is **no difference between the control group and the treatment group**. In the simplest terms, the aim of the typical study is to reject the null hypothesis and demonstrate a statistically significant difference between the control and treatment groups.
2. ***p*-value** (*p)* is defined as the **probability of rejecting the null when the null hypothesis is in fact true**. In the typical clinical study, authors refer to a finding as statistically significant when $p < 0.05$.
3. A **confidence interval (CI) indicates the precision of a study measure**. It is expressed as a lower limit (A) and an upper limit (B) bounded by parentheses (A,B). When the *p*-value is set at 0.05, the CI is 95%, indicating that if a study were repeated multiple times, the true sample parameter or measure would fall between A and B (within the CI) 95% of the time.

B. Measures of Effect

1. **Prevalence** is the proportion of individuals in a given population with a specific disease process or risk factor at a particular point in time.
2. **Incidence** is the number of *new cases* developing in a population over a discrete period of time.
3. **Absolute measures**
   - **a. Absolute risk** (AR): The number of events in treated or control groups, divided by the number of people in that group.
     - **(1)** Absolute risk, treated (ART): The absolute risk in the treatment group
     - **(2)** Absolute risk, control (ARC): The absolute risk in the control group
   - **b. Absolute risk reduction** (ARR): The excess risk among

individuals exposed to a risk factor that can be attributed to the risk factor. This is the difference between ART and ARC.

c. Number needed to treat/number needed to harm (NNT/NNH): This represents the number of people that would need to receive a particular treatment/intervention for one person to benefit or be harmed by that treatment/intervention. This does not provide information about the degree of benefit or harm that the individual will experience. This is the **inverse of the ARR**.

4. Relative risk (RR) is the **measure of association for *cohort studies.*** It is calculated by evaluating the incidence of a disease in those who were exposed to a certain risk factor and comparing it to the incidence of that disease in those who were not exposed to the same risk factor.

a. Interpreting RR

(1) If **RR = 1,** the risk of developing the outcome is the same for individuals with and without the risk factor, that is, exposed and unexposed individuals.

(2) If **RR >1,** the risk of developing the outcome is greater among the exposed individuals.

(3) If **RR <1,** the risk of developing the outcome is less in the exposed group.

5. Odds ratio (OR) is the **measure of association for *case-control studies.*** This ratio compares the likelihood that people with the outcome of interest might have been exposed to a particular risk factor to the likelihood that people who did NOT have the outcome of interest were exposed. The OR represents a snapshot of cases and controls and does not evaluate the incidence of disease over time as seen in a cohort study.

TABLE 48-1 Sample 2 × 2 Table

	Outcome (Disease)	No Outcome (No Disease)
Exposed	A	B
Unexposed	C	D

a. Interpreting ORs

(1) If **OR = 1,** there is no difference in exposure between cases and controls.

(2) If **OR >1,** those with disease are more likely to have been exposed.

(3) If **OR <1,** those with disease are less likely to have been exposed.

6. Using contingency tables (2 × 2 tables) to calculate RR and ORs

a. A **contingency table** organizes data according to outcome and exposure status (Table 48-1)

b. Calculating RR (cohort studies)

$$RR = \frac{\textit{Incidence of disease in an exposed population}}{\textit{Incidence of disease in an unexposed population}}$$

$$= \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

c. Calculating OR (case-control studies)

$$OR = \frac{\textit{Odds that a case was exposed}}{\textit{Odds that a control was exposed}}$$

$$\frac{\frac{a}{c}}{\frac{b}{d}} = \frac{a \times d}{b \times c}$$

d. Calculating ARR is the difference in risk between the unexposed and exposed groups

$$\frac{c}{c+d} - \frac{a}{a+b}$$

e. Calculating NNT is the number of patients that must be treated over a given period of time to prevent one adverse outcome

$$1/ARR$$

C. Evaluating screening and **diagnostic tests. Sensitivity** and **specificity** evaluate the accuracy of a screening or diagnostic tool from the perspective of the *disease status.* The **predictive value** of a tool describes its performance from the perspective of the *test result.*

1. **Sensitivity** (i.e., the **true-positive rate**) is the ability of a test to correctly identify those with disease. This is the probability of having a positive test result provided that the disease is present. **A high sensitivity means that there will be a low "false-negative" rate**.
2. **Specificity** (i.e., the **true-negative rate**) is the ability to correctly identify individuals without disease. In other words, this is the probability of having a negative test result if disease is not present. **A high specificity means that there will be a low "false-positive" rate.**
3. **Positive predictive value (PPV)** is the probability of having a disease given a test result is positive.
4. **Negative predictive value (NPV)** is the probability of not having a disease given a negative test result.
5. It is worth noting that while sensitivity and specificity are not affected by the prevalence of disease, the **predictive value of a test is related to the prevalence of a disease process**. As the prevalence of a disease process decreases, the PPV also decreases and the NPV increases (Table 48-2).

D. Commonly Used Statistical Tests and Analytic Approaches

1. **t-tests** allow for comparison of a **continuous, normally distributed variable** of interest **in *two* groups**. For example, a t-test could be used to compare hospital lengths of stay after laparoscopic versus open colectomy.
2. **Analysis of variance (ANOVA)** allows for comparison of a **continuous, normally distributed variable** of interest **in *more than two* groups**. Thus, ANOVA could be used to compare hospital lengths of stay after laparoscopic versus open versus robotic

colectomy.

3. The **chi-square test** is used to **analyze categorical data and contingency tables.**
4. **Survival analyses** allow for modeling and comparison of differences in *time-to-event* between groups. Time-to-event is the duration of time between entry into a study or diagnosis of disease and a specified end point, which in medicine is often death or recurrence of disease. A patient is **censored** if the time-to-event is unknown either because the patient or the patient's information cannot be accounted for (e.g., the patient becomes lost to follow-up) or because the study ends before the patient experiences the event.

TABLE 48-2 Calculating Sensitivity, Specificity, PPV, and NPV Using a 2 × 2 Table

	Disease Present	Disease Absent	
Positive test	True positive (A)	False positive (B)	PPV = A/(A + B)
Negative test	False negative (C)	True negative (D)	NPV = D/(C + D)
	Sensitivity = A/(A + C)	Specificity = D/(B + D)	

PPV, positive predictive value; NPV, negative predictive value.

   a. The **Kaplan–Meier** method involves comparing the survival curves of two or more populations.
   b. **Cox proportional hazards regression** allows for the comparison of the effect of several covariates on survival in a given population. It assumes the relationships between the covariates and the effects of the covariates upon survival do not vary over time.

E. Propensity Scores and Observational Data. Observational data is

subject to treatment selection bias, which can occur via the following mechanisms:

1. **Confounding by indication.** Patients with certain characteristics are more likely to receive a specific treatment (e.g., a patient has certain comorbidities/illnesses that are likely to qualify them for treatment).
2. **Confounding by contraindication.** Patients who possess certain characteristics are less likely to be candidates for a specific treatment (e.g., a patient might be too ill to qualify for a treatment).
3. **Survivor treatment selection bias.** Patients who live longer are likely to receive a treatment.

These modes of selection bias can create patient populations that are dissimilar, and thus not ideal for accurate comparison. **Propensity scores have been increasingly utilized to address treatment selection bias in observational research by minimizing confounding by indication and contraindication.** Broadly speaking, propensity score matching attempts to approximate RCTs in observational research by creating similar study cohort populations.

Propensity scores quantify the likelihood that a patient with a certain set of covariates will receive a specific treatment. Typically, patient-level propensity scores are created using logistic regression, with the treatment assignment as the dependent variable. **Independent variables** include covariates based on clinical knowledge and literature search that are considered to be strongly linked to receipt of treatment as well as outcome. Often, these covariates are imbalanced in the original data set between groups. The observational data set is used as the study sample. There are multiples ways for assigning matches, including **nearest neighbor** and **caliper distance matches**. Regardless of technique, it is **important to check for balance of baseline covariates** between study cohorts after creating the model. Methods for checking balance include assessing propensity score distributions and covariate standardized mean differences (SMDs) between cohorts. SMD represents the mean difference of the pooled standard deviations of the two cohorts. Ideally, propensity score distributions will have significant overlap and SMDs will be minimized after matching.

There are multiple methods for using propensity scores, with propensity score matching and inverse probability of treatment

weighting being the two most common techniques. While it is not within the scope of this chapter to go in-depth into the details of propensity score methods, it is vital that the reader understands that subsequent data analysis should involve the use of **matched-pair statistical methods**.

III. ASSESSING STUDY QUALITY.

Study quality is assessed based on self-reported design details. Guidelines such as consort for randomized trials, strobe for observational studies, and coreq for qualitative research have improved the consistency of reporting.

A. Internal Validity

1. **Power** is defined as the **probability of rejecting a null hypothesis that is false**. In other words, it is the ability of a statistical test to correctly detect a difference between the experimental and control groups. Power is affected by the significance level of the test, or *p*-value (typically set at 0.05), and the sample size.
2. A **type I error** is also known as a "**false positive.**" This occurs when the null hypothesis is true but is falsely rejected.
3. A **type II error** is known as a "**false negative.**" In this scenario, the null hypothesis is false but is incorrectly accepted. In other words, a difference between the experimental and control groups is not detected even though the difference actually exists. It is important to note that as type I error decreases, type II error increases and conversely, as type II error decreases, type I error increases. In order to minimize both error types, sample size must be increased (Table 48-3).
4. **Bias** is the existence of systematic differences between experimental groups that affect the observed causal relationship between exposure and disease.
   a. **Selection bias** occurs when there are systematic differences in participants' and nonparticipants' covariates, often as a result of procedures or criteria used to include or exclude participants.
   b. **Measurement or misclassification bias** occurs when there is an error in how the exposure status of participants or the recording of outcomes is coded. Measurement error may be introduced through variation in laboratory assays or recall of exposure in epidemiologic studies.

c. Recall bias is an error that results from the incomplete or inaccurate recollection of past events by study participants in a way that is systematically different between participants in different arms of a study.

d. Interviewer bias occurs when interviewers are not blinded to exposure or disease status and frame questions and record responses differently based on participant status.

TABLE 48-3 Assessing Internal Validity: Power and Error

		Null Hypothesis	
		True	**False**
Decision	***Accept***	Correct decision $1-\alpha$	Type II error (β)
	Reject	Type I error (α)	Correct decision Power = $1-\beta$

e. The **Hawthorne effect** occurs when individuals modify their behavior because they are aware they are under observation.

f. Attrition bias results when participants are lost to follow-up. These individuals may be systematically different from those that continue to participate in a trial.

g. Lead-time bias occurs when a disease is detected earlier due to the implementation of screening protocols in one group. This early detection falsely lengthens survival or time-to-event.

5. **Confounding** may occur when a factor (i.e., covariate) is associated with both the exposure and outcome. This covariate, also known as a **confounder,** interferes with or drives the relationship between the exposure and outcome. This factor or covariate must be addressed with randomization or statistical analysis to prevent erroneous or inaccurate conclusions.

B. External validity refers to the ability to generalize the results of a study to the greater population. In order to improve the external validity or generalizability of the data, the experimental population must be similar

to the reference population from which the study population was extracted. More extensive reporting of patient selection processes, study participants' demographic information, and providers' professional and personal characteristics assists with the extrapolation of study conclusions to other clinical settings and patient populations.

IV. CLINICAL PRACTICE GUIDELINES. With the wealth of published data, evaluating the integrity of research findings and determining best practices to implement can be challenging for the clinician. Researchers have developed a hierarchical grading system to assess the quality of data and clinical recommendations. While there are many published grading systems, the **United States Preventive Services Task Force** (USPSTF) has developed one of the most widely accepted systems (see Tables 48-4 and 48-5).

TABLE 48-4 USPSTF Quality of Data Classification

Level of Evidence	Source of Evidence
I	Evidence from systematic review of randomized controlled trials
IIa	Evidence from controlled trials without randomization
IIb	Evidence from cohort or case-control studies
IIc	Evidence from multiple time series or historic controls
III	Expert opinion based on clinical experience

USPSTF, United States Preventive Services Task Force.

TABLE 48-5 USPSTF Clinical Practice Recommendations

Grade of Evidence	Recommendations for Practice

A	High certainty that the net benefit is substantial. Offer or provide this service.
B	High certainty that the net benefit is moderate to substantial. Offer or provide this service.
C	Moderate certainty that the net benefit is small. Provide this service based on individual patient preference and professional judgment.
D	Moderate to high certainty that this service has no benefit or the harms outweigh the benefit. Discourage use of this service.
I	Insufficient evidence to assess benefits and harms of service.

USPSTF, United States Preventive Services Task Force.

These systems for synthesis of evidence have now been more formally accepted by many professional societies. The Institute of Medicine has published a set of guiding principles addressing the methods for developing these types of practice guidelines in order to bring a more consistent approach to their development across the overlapping sectors in health care delivery.

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WEBSITES

The equator site maintains the reporting guidelines accepted across many biomedical journals for clinical studies: **http://www.equator-network.org/toolkits/authors/**

CHAPTER 48: BIOSTATISTICS FOR THE GENERAL SURGEON

Multiple Choice Questions

1. **A study was conducted to determine the impact of sodium bicarbonate preprocedural hydration on the incidence of contrast-induced nephropathy. Which of the following analytic techniques would be best suited to analyze this data?**

   a. ANOVA
   b. Cox proportional hazards analysis
   c. Chi-square test
   d. t-test
   e. Kaplan–Meier

2. **A colorectal surgeon wants to investigate the role of alvimopan (Entereg), a peripherally acting μ-opioid antagonist, on the number of days until return of bowel function after open colectomy. Which of the following statistical methods would be used to evaluate the impact of this drug?**

   a. Wilcoxon rank sum test
   b. t-test
   c. ANOVA
   d. Chi-square test
   e. Cox proportional hazards analysis

3. **As the prevalence of a disease increases, which of the following is true?**

   a. Positive predictive value decreases
   b. Positive predictive value does not change
   c. Sensitivity increases
   d. Sensitivity does not change
   e. Specificity increases

4. **Pseudomyxoma peritonei is a form of cancer that produces mucinous ascites and is most commonly secondary to a primary**

tumor of the appendix. Researchers are interested in conducting a study to determine factors associated with the development of pseudomyxoma peritonei in patients with appendiceal cancer. Which of the following study designs is most appropriate to investigate this clinical question?

a. Case-control study
b. Cohort study
c. Randomized controlled trial
d. Cross-sectional study
e. Pragmatic trial

The following scenario applies to questions 5 to 7:

Researchers are developing a new diagnostic test to identify patients with lung cancer. A total of 150 patients with lung cancer are tested and 300 patients without lung cancer are included for study. A total of 125 of the patients with lung cancer and 20 without lung cancer receive positive test results.

5. **What is the sensitivity and specificity of the diagnostic test, respectively?**

a. 93% and 83%
b. 86% and 83%
c. 83% and 93%
d. 92% and 86%

6. **What are the positive predictive value and the appropriate interpretation of the result?**

a. Given a positive test result, the likelihood of having lung cancer is 86%.
b. Given a positive test result, the likelihood of having lung cancer is 83%.
c. In patients with lung cancer, the probability of a positive test is 86%.
d. In patients with lung cancer, the probability of a positive test is 83%.

7. What is the false-positive rate?

a. 17%
b. 13%
c. 7%
d. 8%

8. A randomized placebo controlled trial was carried out among patients with atherosclerosis to prevent myocardial infarction (MI). Among 100 subjects allocated to receive active treatment, there was one MI. Among 100 subjects allocated to receive placebo, there were two MIs. What is the number needed to treat (NNT) to prevent a single MI under the conditions of this trial?

a. 0.01
b. 0.02
c. 10
d. 100
e. 200

49

Patient Safety and Quality Improvement

David G. Brauer, Bruce L. Hall, and Jacqueline M. Saito

I. PATIENT SAFETY

A. Introduction. The modern era of patient safety can be traced to the landmark **Institute of Medicine** (IOM) report, *To Err is Human: Building a Safer Health System* (National Academy Press, 2000). This report, part of the Quality of Health Care in America Project, highlighted the impact of medical errors and brought shocking statistics into the public eye:

1. As many as 98,000 Americans die annually as the result of medical errors
2. The societal expense of preventable medical adverse events could be as high as $29 billion

B. Safety. Importantly, the IOM report emphasized that the "focus must shift from blaming individuals for past errors to a focus on preventing future errors by designing safety into the system" and set forth the following definitions:

1. **Safety:** freedom from accidental injury
2. **Error:** failure of a planned action to be completed as intended (an **error of execution**) or the use of a wrong plan to achieve an aim (an **error of planning**) (Reason J. *Human Error*. Cambridge: Cambridge University Press; 1990)
   - **a. Error of commission:** doing the wrong thing
   - **b. Error of omission:** not doing the right thing; difficult to detect and perhaps more common
3. **Adverse event:** an injury resulting from a medical intervention, specifically not due to the underlying condition of the patient

C. How to Achieve Safety. The IOM suggests that, within health care organizations, safety can be achieved through a combination of strong leadership for safety, an organizational culture that encourages recognition and learning from errors, and an effective patient safety program.

1. **Organizational culture.** To promote reporting of adverse events or near misses without fear of retaliation or discipline, numerous health care organizations have adopted a "**just culture.**" In this environment, addressing errors has transitioned from a **person approach,** in which individuals are blamed for adverse events due to acts such as forgetfulness or negligence, to a **systems approach,** in which human error is expected and the focus is placed on barriers and safeguards to prevent adverse events (Marx D. *Patient Safety and the "Just Culture": A Primer for Health Care Executives.* New York: Columbia University; 2001).

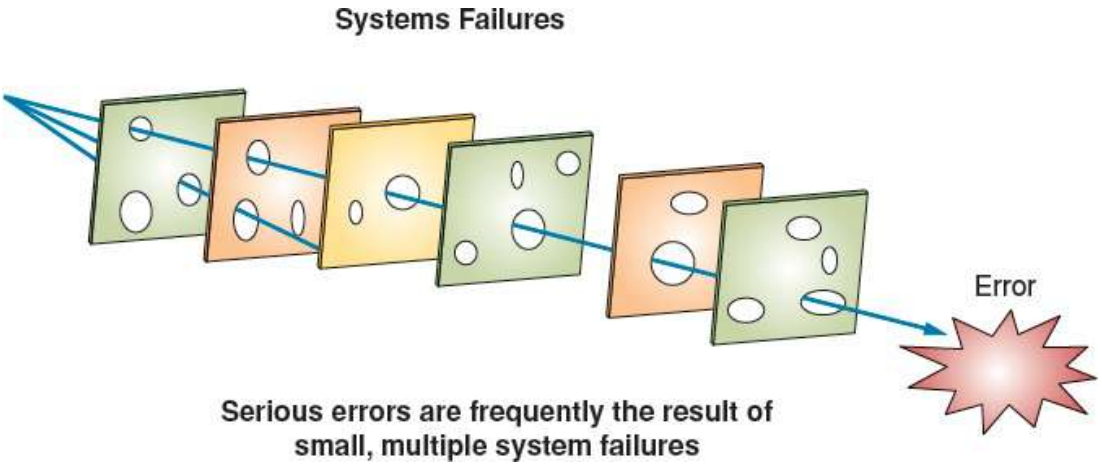

FIGURE 49-1 The Swiss cheese model demonstrating how defenses, barriers, and safeguards may be penetrated by a specific trajectory, leading to an adverse event. (From Reason JT, Carthey J, de Leval MR. Diagnosing "vulnerable system syndrome": an essential prerequisite to effective risk management. *Qual Health Care*. 2001;10(s2):ii21–ii25.)

   a. From this systems approach arose the **Swiss cheese model of accident causation** (Fig. 49-1; *Qual Health Care.* 2001;10(s2):ii21–ii25). A number of specific acts leading to an outcome may have many potential sources of error ("holes"), but the presence of these holes in a single "slice" does not normally cause a bad outcome thanks to downstream defensive layers. When holes in many layers line up, a trajectory of "accident

opportunity" develops. Holes arise for two reasons:

(1) **Active failures:** unsafe acts committed by people in direct contact with the patient or system (e.g., mistakes, violations of protocols, etc.)

(2) **Latent conditions:** existing structures within an organization that can translate into error under the right circumstances (e.g., understaffing, inadequate equipment, inexperience, etc.)

2. Additional organizational concepts:

a. High-reliability organization: an organization operating in a complex, high-hazard domain for extended periods that experiences fewer accidents or failures than would be anticipated due to specific organizational characteristics. For more information, see *Additional Resources: Patient Safety Network.*

b. Stop the line: representative of a culture empowering care team members **at any level** to report behaviors, actions, or inactions that might jeopardize patient safety.

c. Human factors engineering: designing systems and workplace environments to account for human strengths and weaknesses.

d. Normalization of deviance: violations of standard of practice may inadvertently become normalized over time at the risk of patient safety (*Bus Horiz.* 2010;53(2):139).

e. Second victim: although patients and families typically receive support in the setting of an adverse event, physicians involved in the event can be negatively affected ("second victim"; *BMJ.* 2000;320(7237):726–727). Lack of confidence, anxiety about future errors, sleep difficulties, reduced job satisfaction, and increases in job-related stress have all been reported by second victims (*Jt Comm J Qual Patient Saf.* 2007;33(8):467–476). Organizations should ensure adequate resources are available to support physicians in these circumstances.

3. Reporting systems offer organizations the opportunity to collect, review, and learn from patient safety events. Through analysis of events, practices to limit or prevent similar events may be identified and implemented. **Near misses,** events in which an error occurs but does not result in an adverse event or harm, should also be reported, as these are opportunities from which to learn and take action to

prevent recurrence or future harm. Many organizations have internal and anonymous reporting systems and participate in external system-wide, state-wide, or national reporting efforts.

4. **Patient safety processes**

   a. **Root cause analyses (RCAs)** are used by institutional risk management and patient safety representatives to retrospectively review adverse events or near misses systematically. Using a systems approach, a multidisciplinary team maps out the actions and processes that contributed to an outcome, identifies one or multiple critical actions, and develops and implements strategies to prevent future harm. Specific tools for completing RCAs include process-mapping contributing factors onto a **fishbone diagram** (also known as cause-and-effect diagram or an **Ishikawa diagram,** named after Kaoru Ishikawa, a Japanese quality management researcher) and using the "**five why's**" technique. For more information, see *Additional Resources: Patient Safety Network* and *Guidance for Performing Root Cause Analysis (RCA) with Performance Improvement Projects (PIPs).*

   b. **Communication and transitions of care** are particularly important in surgery, as a patient can experience a number of different venues of care. If conducted improperly, handoffs can lead to increased adverse events, worse patient outcomes, longer hospital stays, and increased admissions to the intensive care unit (*Am J Med.* 2012;125(1):104–110). A number of standardized communication tools have been developed and validated, including I-PASS (*Pediatrics*. 2012;129(2):201–204) and SBAR (*Jt Comm J Qual Patient Saf.* 2006;32(3):167–175).

II. QUALITY IMPROVEMENT

A. Introduction. As with patient safety, an IOM report has been pivotal in establishing new thresholds for quality improvement. *Crossing the Quality Chasm: A New Health System for the 21st Century* issued a challenge to improve quality through drastic redesign of care coordination (National Academy Press, 2001). The report recommended a constant focus on **six aims: care should be safe, effective, patient centered** (person centered), **timely, efficient, and equitable.**

B. Tracking Quality. A number of groups, including government agencies

(Agency for Healthcare Research and Quality [AHRQ]), national organizations (National Quality Forum), and surgical societies (American College of Surgeons National Surgical Quality Improvement Program [ACS-NSQIP]) have established **quality measures,** defined by the Institute for Healthcare Improvement as tools to track or quantify a health care outcome or event. Specific categories of these measures include:

1. **Outcome measures** track how a particular practice or a health care system affects patient well-being. Examples include 30-day mortality, 30-day readmission rates, or specific postoperative complications such as surgical site infection or pneumonia.
2. **Process measures** track how well the steps in a process are being followed or how well they are performing. Examples include time to intervention or the percentage of cases adhering to a protocol.
3. **Balancing measures** track whether changes in one metric cause problems in another metric. An example is whether decreased hospital length of stay is resulting in increased readmissions or emergency room visits.

C. Achieving Quality Improvement. A number of models have been applied to tracking and improving outcomes in medicine.

1. The **Model for Improvement** (Fig. 49-2) poses three fundamental questions:
   - **a. Set an aim:** What are we trying to accomplish? This aim should ideally follow the **SMART objectives** of being **Specific, Measurable, Achievable, Realistic, and Time-bound** (*Manag Rev.* 1981;70:35–36).
   - **b. Establish measures:** How will we know that change is an improvement?
   - **c. Identify changes:** What change can we make that will result in improvement?

     Then, changes are tested on a small scale using the **PDSA cycle** (**Plan, Do, Study, Act**), a common framework used in the field of **implementation science**. Finally, changes are implemented on a larger scale while tracking compliance (using **audit** and **feedback**) and preventing drift (gradual movement away from an established protocol). For more information, see *Additional Resources: How to*

Improve.

2. Other quality improvement frameworks include "**Lean,"** the process of improving value through reduction of waste of time and resources, and "**Six Sigma**," which aims to reduce variations or defects using the **DMAIC** objectives: **Define, Measure, Analyze** how variations or defects occur, **Improve**, and **Control** results by determining the steps for maintaining performance (*Surgeon.* 2015;13(2):91–100).
3. Visualizing quality improvement
   a. **Run chart:** graphical depiction of outcome over time to determine if interventions have led to intended changes (Fig. 49-3).
   b. **Pareto chart:** based on the Pareto Principle using the concept of disproportion ("80% of the effect will come from just 20% of the causes"), contributors to an outcome are displayed according to their relative contribution. Teams can focus attention on the major factors while maintaining awareness of lesser contributors. For additional information, see *Additional Resources: Quality Improvement Essentials Toolkit.*

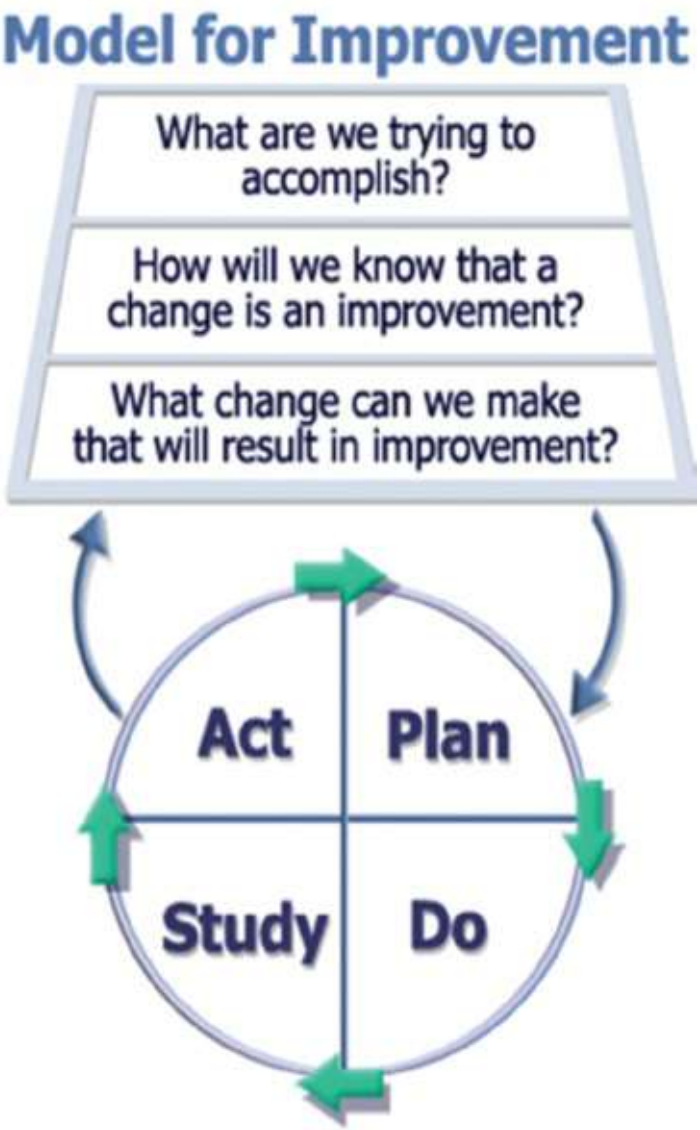

FIGURE 49-2 The Model for Improvement. (From Associates in Process Improvement. Available at http://www.apiweb.org)

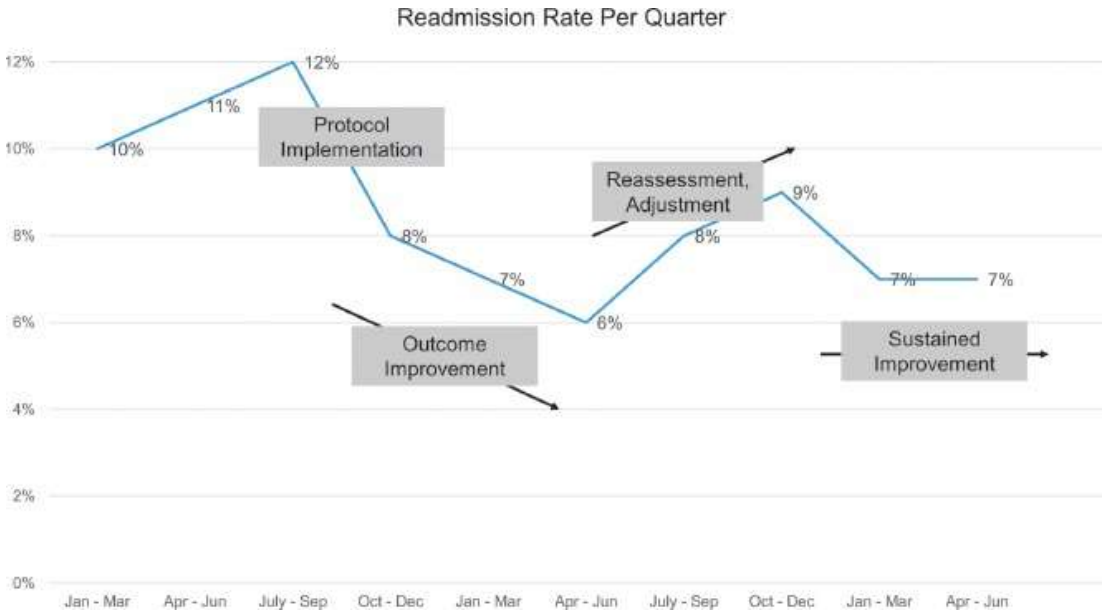

FIGURE 49-3 Fictional run chart. Postoperative readmissions are graphed over time. Implementing a new protocol reduced the readmission rate. After a period of success, the run chart demonstrated that progress had been lost as the readmission rate increased, leading to reassessment and adjustments in the protocol to again improve the readmission rate.

D. Additional Concepts

1. **Checklists** such as the World Health Organization Surgical Safety Checklist (available at http://www.who.int/patientsafety/safesurgery/ss_checklist/en/) have been shown to improve medical team communication and reduce complications through process standardization (*N Engl J Med.* 2009;360(5):491–499).
2. **Morbidity and mortality conference** is a well-established forum for surgeons to address patient safety and explore quality improvement opportunities. This conference is used by training programs to fulfill the practice-based learning competency set forth by the Accreditation Council for Graduate Medical Education (ACGME) and the American Board of Surgery (ABS). These conferences are meant to be iterative such that errors or gaps in care can be identified that should lead to quality improvement initiatives that can then be carried out and followed up on at subsequent sessions.
3. Multidisciplinary **peer review conferences** are used across many specialties and shift the quality improvement focus from a single-patient encounter or event to the system of care delivery. Many of

these are used to fulfill requirements of accreditation programs including the ACS Children's Surgery Verification or trauma center designations.

4. **Patient-reported outcomes** are a rapidly expanding area of quality monitoring and research. These have been used as stand-alone quality measures or to track other measures. Patient satisfaction must be carefully monitored by hospitals and providers as satisfaction, measured by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), is now tied into specific reimbursement incentives or penalties through the Centers for Medicare and Medicaid Services.

ADDITIONAL RESOURCES

Efforts of the ACS, including:

NSQIP

Quality In-Training Initiative. Available at **https://qiti.acsnsqip.org/ACS_NSQIP_2017_QITI_Curriculum.pdf.**

Surgical Risk Calculator. Available at: **https://riskcalculator.facs.org/RiskCalculator/.**

Optimal Resources for Surgical Quality and Safety. Available at **https://www.facs.org/quality-programs/about/optimal-resources-manual.**

Guidance for Performing Root Cause Analysis (RCA) with Performance Improvement Projects (PIPs). Centers for Medicare & Medicaid Services. Quality Assurance and Performance Improvement (QAPI). Available at **https://www.cms.gov/medicare/provider-enrollment-and-certification/qapi/downloads/guidanceforrca.pdf.**

How to Improve. Institute for Healthcare Improvement. Available at **http://www.ihi.org/resources/Pages/HowtoImprove/default.aspx.**

Open School. Institute for Healthcare Improvement. Available at **http://www.ihi.org/education/IHIOpenSchool/Pages/default.aspx.**

Patient Safety Network. Agency for Healthcare Research and Quality. Available at **https://psnet.ahrq.gov/Primers.**

Quality Improvement Essentials Toolkit. Institute for Healthcare Improvement.

Available at **http://www.ihi.org/resources/Pages/Tools/Quality-Improvement-Essentials-Toolkit.aspx.**

CHAPTER 49: PATIENT SAFETY AND QUALITY IMPROVEMENT

Multiple Choice Questions

1. **You are leading a root cause analysis to determine how a patient was administered an incorrect medication. During process mapping, you identify that understaffing was a major contributor to this error. Understaffing would be described as what type of error or condition?**

   a. Error of omission
   b. Error of commission
   c. Active error
   d. Latent condition
   e. System error

2. **Over time, protocols designed to enhance patient safety may become underutilized or entirely forgotten. Sometimes, specific violations of practice standards may inadvertently become a new standard of care and pose a risk to patient safety. What is the term for this occurrence?**

   a. Errors of omission
   b. Normalization of deviance
   c. Latent errors
   d. System error
   e. Individual error

3. **Iterative small-scale testing and improvement of a quality improvement project defines what implementation framework?**

   a. Lean
   b. Six Sigma
   c. High-reliability organization
   d. Swiss cheese model of accident causation
   e. PDSA (Plan-Do-Study-Act) cycle

4. **The general surgery service in your hospital recently**

implemented a quality improvement protocol to decrease length of stay following routine elective surgeries. A few weeks later, you believe there has been an increase in the number of calls from patients to the surgical clinic and a greater number of patients being readmitted through the emergency room. You propose to monitor these events by defining a measure. Your measure should be what type?

a. Outcome measure
b. Process measure
c. Balancing measure
d. Clinical measure
e. Readmission measure

5. **Which of the following tools is a visual aid used to track an outcome over time to determine if a quality improvement intervention has had its intended effect?**

a. Fishbone diagram
b. Flowchart
c. Histogram
d. Run chart
e. Pareto chart

Answer Key

Chapter 1

1. **Answer: c.** Per Table 1-1, patients with a history of TIA are at elevated risk for MACE. Patients with diabetes controlled with oral agents, mild renal insufficiency, and controlled hypertension are not in this elevated risk group.
2. **Answer: b.** Please see Table 1-2 for details regarding assessment of functional status.
3. **Answer: d.** Please see Table 1-3. To reduce SSI risk, hair removal should be performed with clippers. Glucose control goal should be <180 mg/dL. Core body temperature should be kept above 36 degrees.
4. **Answer: c.** Please see Figure 1-1. The patient in scenario C has several risk factors and has claudication that limits the ability to perform exercise stress testing. The patient in A requires emergent surgery. The patients in B and D, despite risk factors, have no functional impairment requiring testing.
5. **Answer: b.** The patient in B is anuric with fluid overload that appears to be leading to a requirement of mechanical ventilatory support. This is an indication for hemodialysis to remove fluid and improve pulmonary function. Mild to moderate metabolic derangements such as in A and C can be treated with measures less invasive than hemodialysis. Creatinine level (D) is not an indication for hemodialysis per se.
6. **Answer: b.** Foley catheters should be removed on postoperative day 1 unless there is concern for urinary retention, urinary tract injury, or renal insufficiency/oliguria.
7. **Answer: d.** Frailty screening is recommended in those over age 65 undergoing intermediate or high-risk surgery.

Chapter 2

1. **Answer: b.** The use of briefings and time-outs has been shown in a multicenter prospective study to reduce postoperative mortality by 47%. Neither placement of drains nor technique of fascial closure following laparotomy has been shown to impact mortality, although they may impact morbidity.
2. **Answer: a.** It is important to recall that while others may assist in assessing a patient's risk for surgery (anesthesiologist, cardiologist, etc.), it is the surgeon who bears final responsibility and must therefore work deliberately to optimize patient selection and procedure choice.
3. **Answer: d.** Throughout the operative procedure, the operative plan should be examined and reassessed to ascertain that optimal outcomes can be achieved.
4. **Answer: a.** There are instances where resection will not be in the patient's best interest (i.e., tumor invasive to adjacent organs); other phases of the operation are constants in the conduct of a procedure.
5. **Answer: b.** Paramedian incisions have fallen out of favor due to the risk of hernia and potential loss of nervous supply to the rectus muscle.

Chapter 3

1. **Answer: e.** Oliguria and tachycardia in the early postoperative period is a red flag for possible bleeding. This patient is in stage II shock with oliguria and mild tachycardia. The *initial* workup and treatment are to restore intravascular volume with a bolus of crystalloid and check a hematocrit to assess for bleeding. This patient may need transfer to the intensive care unit, but the first step is to give the fluid bolus and assess for bleeding. Prior to returning to the operating room, the patient should receive resuscitation and the cause of his oliguria need to be established. Although he could be bleeding, he may also be underresuscitated.
2. **Answer: d.** The Surgical Care Improvement Project recommends a maximum of 24 hours of perioperative antibiotic coverage for routine general surgery procedures.
3. **Answer: d.** The first step in evaluating this agitated patient is to check her vital signs and pulse oximetry. It is more likely a deficit in executive function than a focal neural deficit, therefore a to c should be considered after the vital signs, but at this time e is not indicated.
4. **Answer: e.** While a cause for hypovolemia, sepsis typically is not on the differential until after postoperative day 2, unless the patient has recently been operated on, or was septic prior to the operation.
5. **Answer: d.** Patients with inability to void after 6 hours, especially after a hernia repair, should undergo a bladder scan. If there is significant volume they can be straight catheterized or have a Foley inserted. If there is no volume in the bladder, a Foley can be inserted to monitor urinary output, or a fluid challenge and brief waiting period can be tried, knowing that if the patient fails the fluid challenge they will need a Foley catheter.
6. **Answer: d.** The patient's low normal urinary output and his FeNa less than 1% both indicate prerenal failure. The next step would be a fluid challenge and close monitoring.

Chapter 4

1. **Answer: d**
2. **Answer: a**
3. **Answer: b**
4. **Answer: c**
5. **Answer: e**

Chapter 5

1. **Answer: e.** There is no proven clinical benefit to resuscitation with hypertonic saline. Although it is commonly used for intracranial hypertension, it should not for initial resuscitation in those patients.
2. **Answer: c.** In a septic patient requiring high volume fluid resuscitation, albumin should be administered if the patient continues to have a low MAP after large volume crystalloid administration.
3. **Answer: b.** This patient has hypervolemic hyponatremia associated with congestive heart failure. Initial management includes fluid restriction to 1 L of free water per day.
4. **Answer: a.** Diabetes insipidus is characterized by polydipsia, polyuria, and hypotonic urine. A urine specific gravity less than 1.005 is diagnostic of diabetes insipidus. A basic metabolic profile in addition to urine electrolytes can also be used to make this diagnosis.
5. **Answer: b.** Hyperkalemia should first prompt an ECG to look for peaked T waves, followed by a confirmatory whole-blood level. Calcium is given to stabilize cardiomyocytes, followed by administration of insulin and glucose to transiently lower potassium levels. Dialysis is last in the algorithm for refractory hyperkalemia.
6. **Answer: d.** The most common clinical manifestation of hypomagnesemia is QT prolongation and associated ventricular arrhythmias.
7. **Answer: e.** The most common causes of metabolic alkalosis in postsurgical patients are dehydration from inadequate fluid resuscitation, followed by acid losses from nasogastric suction.
8. **Answer: b.** Bicarbonate therapy is indicated as treatment for refractory acidemia when underlying causes of acidosis have been addressed.
9. **Answer: c.** This patient has severe hypocalcemia. Immediate

intravenous calcium therapy is indicated because of the severity of her symptoms.

10. **Answer: b.** Rapid correction of free water deficit can lead to cerebral edema. In order to avoid this complication, half of the free water deficit should be corrected in the first 24 hours, and the remaining deficit should be corrected in the next 2 to 3 days.

Chapter 6

1. **Answer: c.** The patient has developed HIT type II. HIT type II is a severe immune-mediated syndrome caused by heparin-dependent antiplatelet antibodies and develops 5 to 10 days following heparin exposure. The patient needs anticoagulation because of the atrial fibrillation and new DVT; however, this should be achieved with a nonheparin anticoagulant such as bivalirudin. Transfusion of platelets is contraindicated since it will actually worsen the thrombosis.
2. **Answer: d.** DIC is often marked by low levels of fibrinogen. Patients present with prolonged INRs and PTTs, along with decreased fibrinogen levels. Cryoprecipitate is often used to help correct fibrinogen deficiency in DIC or as second-line therapy in vWD. Transfusions of all other products are inappropriate in this case.
3. **Answer: c.** Antifactor VIII antibodies may develop in hemophiliacs in response to prior factor VIII infusion. Hemophilia A rarely presents with spontaneous bleeding. Since hemophilia A is characterized by decreased factor VIII levels, there is no need for transfusion of factor IX prior to surgery. Hemophilia A is an X-linked recessive disorder and is therefore found mostly in males. Platelet membrane receptors are normal.
4. **Answer: e.** Active menses in females is not considered an absolute contraindication. All other options are. For a list of both absolute and relative contraindications, see Table 6-3.
5. **Answer: e.** von Willebrand disease is the most common inherited bleeding disorder. It is characterized by low levels of vWF (type 1) or dysfunctional vWF (types 2 and 3). Type 1 is treated with administration of DDAVP which causes endothelial release of vWF, increasing intravascular levels. Types 2 and 3 require exogenous functional vWF which can be found in cryoprecipitate.
6. **Answer: b.** Factor XIIIa is involved in the cross-linking of fibrin which helps to stabilize newly formed clots. It has no role in the

activation of platelets. Christmas disease, otherwise known as hemophilia B, is marked by a deficiency in factor IX, not XIIIa. The prothrombinase assembly involves factors Va, Xa, and calcium.

7. **Answer: a.** Prekallikrein is involved in the intrinsic clotting cascade and its deficiency causes an elevation in the PTT but does not actually cause a hypercoagulability. Protein C, protein S, plasminogen, and antithrombin III are all natural anticoagulants, and deficiencies in these cause hypercoagulable states.
8. **Answer: a.** Antithrombin III is a major inhibitor of thrombin and Xa. Heparin, an anticoagulant, binds to antithrombin III and increases its activity. Argatroban is a direct thrombin inhibitor while fondaparinux is an indirect factor Xa inhibitor. Antithrombin III is secreted by the liver, and its synthesis is not inhibited by warfarin.
9. **Answer: a.** The prothrombinase complex is composed of factor Xa and factor Va bound to a negatively charged phospholipid membrane with calcium. Heparin, an inhibitor of factor Xa and thrombin, works by activating antithrombin III. Therefore the prothrombinase complex is inhibited by heparin. Argatroban directly inhibits thrombin which is not involved. Ionized calcium is required for phospholipid binding. Clopidogrel and aspirin both decrease platelet binding by binding to the ADP receptor and inhibiting cyclooxygenase, respectively.
10. **Answer: e.** Cryoprecipitate contains factors VIII, XII, and vWF. It is used in patients with DIC, dysfunctional vWF, and hemophilia A. FFP contains factors II, V, VII, IX, X, and XI.

Chapter 7

1. **Answer: d.** This patient has signs of local anesthetic systemic toxicity (LAST) from accidental intravascular injection of local anesthetic. The priorities for LAST management include airway management, seizure suppression, management of cardiac arrhythmias, and lipid emulsion therapy. Benzodiazepines are the preferred antiseizure medications in LAST, as propofol is a cardiovascular depressant that may exacerbate hemodynamic instability and its lipid content is too low to provide benefit (a). Hypotension and cardiovascular collapse should be treated with modified ACLS protocols, including the avoidance of vasopressin (b) and the use of smaller doses of epinephrine (<1 mcg/kg) (c). High doses of epinephrine can impair resuscitation in LAST and reduce the efficacy of lipid rescue. 20% lipid emulsion therapy is the preferred antidote for local anesthetic toxicity and, although the timing of infusion is controversial, it should be implemented when the clinical severity and rate of progression of symptoms suggest a high likelihood of progression to severe toxicity and cardiovascular compromise (d). Prolonged monitoring for >12 hours after any signs of LAST is recommended, since cardiovascular depression can persist or recur after treatment (e). (Refers to Section II.B.3. Treatment of local anesthetic systemic toxicity; see American Society of Regional Anesthesia Checklist for Treatment of LAST, *Reg Anesth Pain Med*. 2012;37(1):16–18.)
2. **Answer: d.** Cervical blockade is used to achieve anesthesia of the neck and was historically used primarily for carotid endarterectomy, although its use is now falling out of favor (a). Interscalene (b), supraclavicular (c), and infraclavicular (d) blockade will all provide anesthesia of the upper arm and are acceptable techniques for humerus fixation. However, of these the infraclavicular approach carries the lowest risk of ipsilateral phrenic nerve palsy and is therefore preferred to minimize the risk of pulmonary complications in patients with COPD. Axillary blockade (e) provides reliable

anesthesia only for procedures below the elbow. (Refers to Section III.C.1. Brachial plexus blockade.)

3. **Answer: b.** The diaphragm (b) exhibits the most rapid recovery from neuromuscular blockade. Recovery of upper airway, pharyngeal, and flexor hallucis muscles generally parallels that of the adductor pollicis, which can be used for twitch monitoring as an indicator of extubating conditions. Both the muscles of respiration and those that protect the airway must recover to extubate the patient safely. (Refers to Section V.C. Neuromuscular blockade.)
4. **Answer: c.** The patient shows signs concerning for malignant hyperthermia (MH)—most often triggered by the administration of volatile anesthetics or succinylcholine and characterized by hyperthermia, tachycardia, tachypnea, hypertension, acidosis, and skeletal muscle rigidity. The first step in MH event management is immediate cessation of triggering agents (c). Steps that should be rapidly performed include calling for an MH cart, dantrolene 1 to 2.5 mg/kg IV administration (a), and hyperventilation with 100% oxygen to flush volatile anesthetics and lower end-tidal CO_2 (b). Monitoring for hyperkalemia and associated electrocardiogram changes is important (d). Family history (e) of MH increases the risk of an MH event and this history should be sought during preoperative evaluation with anesthetic plan tailored accordingly. (Refers to Section V.G.3. Malignant hyperthermia, see *Emergency treatment of an acute MH event*, Malignant Hyperthermia Association of the United States [www.mhaus.org].)
5. **Answer: a.** Intraoperative awareness is unintended consciousness and recall of intraoperative events, which may result in long-term psychological sequelae. Risk factors for awareness include use of neuromuscular blockade (a), total intravenous anesthesia (vs. inhalational anesthetics [b]), and inadequate anesthetic dosing because of technical, surgical, or patient-related factors. Patient-related factors that increase resistance to anesthetics and thus risk of awareness include pyrexia, hyperthyroidism (e), obesity, anxiety,

younger age (c), emergency surgery (d), and chronic exposure to tobacco, alcohol, recreational drugs, or anesthetic agents. (Refers to Section V.G.1. Intraoperative awareness.)

6. **Answer: b.** Contraindications to succinylcholine for neuromuscular blockade include severe burns (a), muscular dystrophy (c), hyperkalemia (d), and family or personal history of malignant hyperthermia (e). Succinylcholine has a more rapid onset of action (30 to 60 seconds) than any of the nondepolarizing neuromuscular blocking agents (90 seconds for high-dose rocuronium), thus is preferred for rapid sequence (b) and emergent intubation in absence of contraindications. The short duration of action of succinylcholine (5 to 10 minutes) is beneficial with blunt head injury or elective surgeries when the ability to complete a neurologic examination soon after induction is desired (see Section V.C. Neuromuscular blockade).
7. **Answer: c.** The maximum dose of lidocaine with epinephrine is 7 mg/kg. 1% lidocaine has 10 mg/mL. So for a 70-kg male, 70 mg × 7 mg/kg = 490 mg/10 mg/mL = 49 mL. Answer a would be the maximum dose for lidocaine without epinephrine and b would be for bupivacaine with epinephrine.

Chapter 8

1. **Answer: d.** This patient likely had a PA rupture due to balloon inflation. This patient should have the side of the PA catheter in the dependent position and an urgent thoracic surgical consult should be obtained.
2. **Answer: b.** The sedating medication and sedation goal should be decided upon and communicated to the bedside nurse who will titrate the sedative to reach the desired goal. Sedation should be minimal to keep the patient comfortable and interrupted for a daily sedation vacation. A BIS of 40 to 60 is the goal for a patient receiving a neuromuscular blockade. Propofol leads to hypotension due to increased venous capacitance and decreased preload. Ketamine is often used in patients with depressed cardiac function due to its lack of cardiac depression.
3. **Answer: a.** This patient has a TI fistula with a “herald bleed” the day prior. The treatment is as described, and must be done urgently if the patient is to survive.
4. **Answer: d.** APRV or BiLevel is an advanced ventilatory mode. It uses an inverse I:E ratio so that there is more time spent at the pressure high to increase the mean airway pressure without increasing the peak. Ventilation occurs during spontaneous breathing over the pressure high and during the pressure release to pressure low.
5. **Answer: c.** In a patient with a poorly developed tract after tracheostomy placement, if it is inadvertently removed, the patient should be intubated from above. Once an airway is secured, the tracheostomy can be replaced in a more controlled setting. The blind replacement of a tracheostomy tube can result in placement in the pretracheal space and potentially the patient’s demise.
6. **Answer: e.** The findings listed above are consistent with cardiogenic shock.
7. **Answer: e.** The current guidelines suggest that steroids should be

given to septic patients who do not respond to volume or vasoactive medications. A cortisol level does not need to be checked, they should be given hydrocortisone 50 mg IV q6h. The data seem to show a quicker duration of sepsis; however the impact on survival is less clear.

8. **Answer: b.** This patient most likely has a tension pneumothorax and should be treated with needle decompression and tube thoracostomy.
9. **Answer: a.** Stress ulcer prophylaxis should be administered selectively in the ICU to patients with a high risk because its use does increase the risk of *C. difficile* infection.
10. **Answer: c.** Information from the TRICC trial illustrates the futility of blood transfusion when unnecessary. A restrictive transfusion protocol would necessitate transfusion only if the hemoglobin is <7 mg/dL, unless the patient has had a recent cardiac event.

Chapter 9

1. **Answer: a.** The combination of progressive hypertension associated with bradycardia and decreased respiratory rate is called the Cushing response. These symptoms strongly suggest a rise in intracranial pressure due to a mass effect, such as an acute subdural hematoma.
2. **Answer: a.** Class 2 hemorrhagic shock is defined as loss of 750 to 1,500 mL of blood, tachycardia, decreased pulse pressure, and normal blood pressure. Class 2 hemorrhagic shock should be treated with crystalloid solutions such as normal saline or lactated Ringer.
3. **Answer: c.** With a negative FAST exam (likely ruling out intra-abdominal hemorrhage) and a deformed limb, the patient is likely bleeding into his thigh. Patients can lose an extensive amount of blood into their thighs secondary to fractures.
4. **Answer: c.** Calculating the Glasgow Coma Score for this patient, you find that he is moaning (verbal—2), opens eyes to pain (eyes—2), and withdraws his right leg to pain (motor—5). Motor is counted by the highest score if there are different scores between limbs.
5. **Answer: c.** Based on EAST guidelines, penetrating trauma to the chest with signs of life is the strongest recommendation for an ED thoracotomy.

Chapter 10

1. **Answer: a.** Hemodynamically stable patients with penetrating trauma should undergo CTA to determine the trajectory prior to possible operative management. See section on penetrating neck injury.
2. **Answer: c.** Based on his age, this patient meets Canadian Head CT guidelines for obtaining a CT head. Based on Canadian C-spine criteria, he is high risk both for his age and dangerous mechanism (high speed MVC).
3. **Answer: d.** Idarucizumab directly reverses dabigatran, a factor II inhibitor. If idarucizumab is unavailable, prothrombin complex concentrates (PCC) can be used.
4. **Answer: b.** The patient is intoxicated and thus his C-spine cannot be reliably cleared. He is at risk for C-spine injury due to the mechanism. He should be placed in a cervical collar until he can be reliably examined.
5. **Answer: d.** This patient is not stable enough to undergo diagnostic imaging. An airway should be secured and an attempt made to tamponade bleeding prior to emergent neck exploration. See section on penetrating neck injury.

Chapter 11

1. **Answer: d.** The patient is suffering from a tension pneumothorax. This is a life-threatening condition which leads to obstructive shock. Signs and symptoms include absent breath sounds on the affected side, tracheal deviation to the contralateral side, hypotension, tachycardia, hypoxia, and mediastinal shift to the opposite side. Tension pneumothorax should be diagnosed clinically. Initial emergent treatment is needle decompression with a 14-gauge angiocatheter placed in the second intercostal space in the midclavicular line. Thoracostomy tube placement follows initial emergent needle decompression.
2. **Answer: b.** While the majority of hemopneumothorax in trauma can be managed by simple thoracostomy tube placement, according to trauma.org, emergent thoracotomy in the operating room following thoracic trauma should be undertaken if initial chest tube output is 1,500 mL or 200 mL/hr of blood is evacuated over the following few hours.
3. **Answer: c.** Resuscitative thoracotomy is performed in the emergency department in certain instances of thoracic trauma. The steps include left-sided thoracotomy in the fifth intercostal space, dissection and division of the inferior pulmonary ligament, incision in the anterior pericardium with subsequent evacuation of clot and blood, repair of any cardiac injury, and (in some cases) cross-clamp of the thoracic aorta.
4. **Answer: a.** According to the EAST guidelines, the initial diagnostic test to evaluate for BCI is an ECG. See Table 11-2 for EAST recommendations.
5. **Answer: c.** Aerodigestive injury can be difficult to diagnose, but can represent significant morbidity in thoracic trauma. A high index of suspicion for injury to the trachea or esophagus is essential for prompt diagnosis and management. Initial testing includes bronchoscopy and esophagoscopy or esophagography. While CXR

is usually performed early in any trauma workup and can reveal mediastinal gas or pleural fluid, sensitivity for aerodigestive injury is low and direct evaluation of the trachea and esophagus is required to make the diagnosis.

6. **Answer: d.** Tension pneumothorax, cardiac tamponade, and pulmonary embolism are all capable of causing obstructive shock. While the etiologies and treatments of these potentially life-threatening conditions are often quite different, each can potentially cause obstruction of cardiac outflow with subsequent hemodynamic collapse. Because of this, these three disorders have been lumped into their own separate category of shock.

Chapter 12

1. **Answer: b.** This patient has an extraperitoneal rectal injury. Although older studies advocated diversion, distal rectal washout, and presacral drainage (the so-called “3 D’s”), further research demonstrated this resulted in overall worse outcomes and no improvement in the rate of pelvic sepsis. However, diversion is still mandatory.
2. **Answer: c.** This patient has a duodenal hematoma and cannot tolerate oral intake. Given the self-limited nature of most duodenal hematomas, generally nonoperative management with nasogastric drainage (if needed) and TPN is recommended, awaiting resolution of the hematoma.
3. **Answer: a.** This patient is in severe shock. As all trauma patients are assumed to be in hemorrhagic shock until proven otherwise, you must find the source of bleeding causing his shock. Given that he has no obvious signs of external bleeding, his chest and pelvic x-rays are normal, and he has no obvious extremity fractures, the most likely source of bleeding is in his abdomen. The patient is too unstable for transport to the CT scanner, thus FAST is the best choice. DPL would be a reasonable option if FAST was not available or the FAST was negative.
4. **Answer: d.** This patient suffered a flank GSW and is hemodynamically normal without peritonitis. Given that the majority of flank GSWs do not penetrate the peritoneal cavity, the next best step is to obtain a CT scan to delineate the bullet’s trajectory. If the bullet clearly did not violate the peritoneum, he can be safely discharged. Thus, neither immediate laparotomy nor serial abdominal examinations are indicated.
5. **Answer: b.** This patient has a grade IV blunt liver injury. Most blunt hepatic trauma can be managed nonoperatively. In fact, operating on hemodynamically normal patients can result in disruption of the clot around the liver and the release of the natural tamponade of a

closed abdomen, worsening the degree of hemorrhage. However given the severity of injury on imaging, the patient should be admitted to the ICU for close observation. Evidence of contrast extravasation (i.e., a “blush”) should trigger referral to IR for angiography and possible embolization. Ongoing transfusion requirements or the development of hemodynamic instability of peritonitis is an indication for immediate laparotomy.

6. **Answer: d.** Given the patient’s profound hypothermia, acidosis, and coagulability, and that the bleeding is temporarily controlled, the operation should be aborted and the patient taken to the ICU for further resuscitation. More formal attempts at controlling bleeding at this time are likely to be futile.
7. **Answer: a.** This patient is in hemorrhagic shock and needs to be given blood products as soon as possible. Given that she is a female of child-bearing age, she should be given uncrossmatched type O negative blood until crossmatched blood is available in order to prevent the development of Rh sensitization.
8. **Answer: b.** After splenectomy, patients are susceptible to infections by encapsulated organisms, thus b is correct.
9. **Answer: c.** This patient is hypotensive and has an open-book pelvic fracture. Placing a binder will help stop bleeding from the pelvic fracture. The other options may be necessary later, but a binder should be the first step.
10. **Answer: e.** This patient has a <50% circumferential injury to the colon with minimal contamination and is hemodynamically normal. Closure of the defect alone is sufficient.

Chapter 13

1. **Answer: b.** Using pressure measurements for diagnosis of compartment syndrome has been done for decades, but benchmark pressures were challenged by a group in Scotland establishing the “delta 30” criteria, by which the compartment pressure is compared to the current diastolic blood pressure. A difference of less than 30 mm Hg is diagnostic, and follow-up studies confirmed no sequelae of missed compartment syndrome of the leg in patients with tibia fracture.
2. **Answer: c.** Initial volume containment of the retroperitoneum can be accomplished very quickly with a sheet or binder following evaluation of the abdomen. A study of practice guidelines in Australia demonstrated a decrease in mortality comparing pre- and postimplementation, with a goal of abdominal “clearance” and noninvasive pelvic binding within 15 minutes.
3. **Answer: d.** Polytrauma patients with femur fractures, especially those with thoracic injury, are predisposed to a second-hit phenomenon that can result in ARDS following intramedullary nail fixation of the femur in an underresuscitated state. To accomplish the goal of femur fracture stabilization within 24 hours of injury, in the setting of ongoing resuscitation requirements, external fixation (“damage control orthopedics”) has been recommended to control pain, allow for comfortable positioning changes, decrease the risk of fat embolism, and avoid the complications associated with instrumenting the medullary canal.
4. **Answer: c.** Reduction and stabilization of femur fractures decreases the risk of malunion, fat embolism, blood loss at the fracture, and nonunion. Stabilization of these fractures within 24 hours was demonstrated to decrease ICU length of stay, and possibly the complication of ARDS. However, more recent publications have demonstrated an increased risk of ARDS for “borderline” patients who are underresuscitated prior to intramedullary fixation of femur fractures.

5. **Answer: c.** Loss of wrist and digit extension due to an injury to the radial nerve is commonly associated with humerus shaft fractures. While radial nerve palsy is common with humerus shaft fractures, neurapraxia (stretch but no transection of the nerve) is the most common nerve injury. Most neurapraxia will recover. Transection of the nerve that would benefit from early surgical intervention is, most commonly, the result of a high-energy injury resulting in an open fracture or a direct laceration of the nerve from a stab wound.

Chapter 14

1. **Answer: b.** Burn-Specific Secondary Survey, Table 14-1. First-degree burns are red but have no blisters. Second-degree burns have blisters and are painful. Third- and fourth-degree burns are insensate.
2. **Answer: b.** The “rule of nines” helps determine the percent body surface area. The anterior surface of each leg is 9%, and the anterior torso is 18%. Note, children have a different percentage distribution.
3. **Answer: e.** Pseudomonas and fungi are the most common causes of burn wound sepsis.
4. **Answer: a.** Mafenide acetate can lead to a metabolic acidosis due to carbonic anhydrate inhibition.
5. **Answer: b.** Patients with electrical burns are at risk for renal failure due to rhabdomyolysis. The release of myoglobin from injured cells can lead to precipitation in the renal tubules.

Chapter 15

1. **Answer: e.** Even well-healed wounds never reach the original strength of uninjured tissue.
2. **Answer: a.** Wounds that are not infected do not require antibiotics. It is important to establish if there is any arterial insufficiency that is impeding adequate healing. This patient is showing signs of rest pain and tissue loss, suggestive of an arterial inflow problem that must be addressed before debridement in the setting of a noninfected wound.
3. **Answer: b.** In a noninfected wound, there is no reason to use Dakin or hydrogen peroxide as they impede wound healing. The patient is at high risk for recurrence due to being bedridden and should not get a musculocutaneous flap. Normal saline damp-to-dry dressing changes continue to debride tissue with every dressing change.
4. **Answer: c.** This wound will heal by secondary intention. The wound is left open and will heal by contraction and epithelialization.
5. **Answer: e.** NPWT have multiple benefits and increases wound healing by decreasing edema and increasing capillary growth, thereby increasing granulation tissue. The VAC also protects the wound from any external contaminants.

Chapter 16

1. **Answer: b.** Abdominal pain followed by loss of consciousness suggests an intra-abdominal catastrophe with associated sepsis and/or shock. The first step is resuscitation, basic labs, and a quick abdominal film to rule out a perforated viscus. Induction of anesthesia of an unresponsive patient with sepsis or shock will often precipitate cardiovascular collapse.
2. **Answer: e.** The first next step in the management of sigmoid volvulus without evidence of necrotic bowel is endoscopic reduction followed by elective sigmoidectomy after bowel preparation.
3. **Answer: a.** This patient likely has an acute abdomen with peritonitis. A radiographic abdominal obstructive series with a chest x-ray is a fast way to determine if the patient has a perforated viscus, and should be the first diagnostic test. If there is intraperitoneal free air, the patient needs an urgent operation.
4. **Answer: c.** This patient has a ruptured abdominal aortic aneurysm, which carries an extremely high mortality. Time is of the essence. Given that the patient is hypotensive and acidotic, urgent repair is indicated. There is no time for imaging.

Chapter 17

1. **Answer: c.** Frequently with type III hiatal hernias the esophagus is shortened since the GE junction and the greater curvature of the stomach have herniated into the chest. In order to perform the repair, it may be necessary to perform a lengthening procedure so that the repair may sit in the abdominal cavity without tension.
2. **Answer: e.** The Toupet fundoplication is the preferred posterior fundoplication for GERD patients with abnormal esophageal motility due to a lower incidence of postoperative dysphagia.
3. **Answer: e.** While all of the options are potential symptoms of achalasia, virtually all patients will experience progressive dysphagia.
4. **Answer: c.** Nutcracker esophagus is characterized manometrically by prolonged, high-amplitude peristaltic waves associated with chest pain that may mimic cardiac symptoms. Treatment with calcium-channel blockers and long-acting nitrates has been helpful.
5. **Answer: b.** Intramural tumors, like leiomyomas, are typically asymptomatic, but can produce dysphagia or chest pain if large enough. Intramural tumors usually can be enucleated from the esophageal muscular wall without entering the mucosa. Intraluminal tumors, like polyps, cause esophageal obstruction, and patients present with dysphagia, vomiting, and aspiration. Intraluminal tumors can usually be removed endoscopically.

Chapter 18

1. **Answer: d.** Patients with significant gastric losses, such as with prolonged vomiting or nasogastric tube suction, experience hypochloremic, hypokalemic metabolic alkalosis.
2. **Answer: e.** Low-grade mucosal-associated lymphoid tissue lymphomas of the stomach are thought to arise as a result of *H. pylori* infection. First-line treatment of this disease begins with *H. pylori* eradication, which often results in a cure.
3. **Answer: b.** Bleeding duodenal ulcers are usually located on the posterior wall. In the hemodynamically unstable patient, unable to tolerate endoscopy, duodenotomy with three-point ligation is the treatment of choice. Vagotomy has largely been abandoned due to the added morbidity with the high efficacy of proton-pump inhibitors.
4. **Answer: c.** Imatinib is first-line therapy for metastatic or recurrent gastrointestinal tumors.
5. **Answer: d.** A minimum of 15 lymph nodes should be resected during gastric cancer lymphadenectomy for adequate staging and possibly therapeutic control.

Chapter 19

1. **Answer: b.** Indications for bariatric surgery include BMI of 40 or greater, BMI of 35 or greater with one or more weight-related comorbidities, or SMI of 30 to 34.9 with poorly controlled diabetes or metabolic syndrome.
2. **Answer: a.** Intravenous fluid resuscitation and prompt surgical intervention is warranted in an unstable patient with imaging evidence of obstruction. Observation is inappropriate in this patient. Further imaging is unnecessary and will likely delay delivery of appropriate care.
3. **Answer: e.** Persistent nausea, vomiting following gastric banding should be treated with immediate removal of the fluid from the adjustable band as these symptoms suggest that the band is too tight. Imaging can be used to assess band positioning including abdominal x-rays and esophagram with Gastrografin.
4. **Answer: d.** In asymptomatic incisional hernias, repair should be deferred until weight loss has stabilized (typically around 12 to 18 months postoperatively) and nutritional status is optimized. If a patient is symptomatic or presents with evidence of incarceration or strangulation, prompt surgical management is warranted.
5. **Answer: e.** The patient has a marginal ulcer, a complication noted in approximately 16% of patients undergoing RYGB. Medical therapy with proton pump inhibitors and sucralfate is employed. Surgical therapy is rarely necessary as medical therapy is usually effective.

Chapter 20

1. **Answer: c.** The most common cause of SBO in a patient who has had a prior abdominal operation is adhesions.
2. **Answer: b.** This patient is presenting with unstable vital signs (fever, tachycardia, and hypotension) as well as peritonitis on physical examination. Patients who are unstable or have diffuse peritonitis should be taken emergently to the operating room and are not candidates for nonoperative management.
3. **Answer: a.** This patient presents with a small bowel obstruction secondary to an inguinal hernia. The timing and lack of skin changes suggest this is an incarcerated but not strangulated hernia. Initial management should include attempts to reduce the hernia in the emergency room. Often this requires pain medicine and sedation as reduction can be quite painful. If the hernia is successfully reduced, the patient should be admitted for observation to ensure the hernia was not strangulated and undergo an inguinal hernia repair in a semielective fashion. If the hernia is unable to be reduced, the patient should undergo urgent hernia repair and evaluation of the bowel contained in the hernia for strangulation.
4. **Answer: a.** C-kit mutation suggests that the tumor was a SI GIST. Traditional chemo/radiation therapy is not effective treatment for GIST. However, the tyrosine kinase inhibitor *imatinib mesylate (Gleevec)* effectively inhibits the overactive tyrosine receptor c-kit found on all GIST cells. Adjuvant imatinib therapy improves recurrence-free survival in high risk GIST.
5. **Answer: c.** This patient is presenting with carcinoid syndrome. The somatostatin analog octreotide offers excellent palliation of carcinoid syndrome symptoms in patients with unresectable disease.
6. **Answer: b.** Central venous catheter-related complications are common in patients who are on long-term TPN. The main long-term complications of central venous catheters include blood stream infections, catheter-induced venous thrombosis, and catheter-related

venous stenosis.

Chapter 21

1. **Answer: d.** Hepatic adenoma is commonly identified incidentally in young women due to an association with estrogen and progesterone exposure. It is characteristically a heterogeneous mass that does not retain gadoxetate disodium contrast on hepatobiliary phase imaging, as this lesion does not contain bile ductules. Alternatively, focal nodular hyperplasia does retain this contrast and is more homogeneous. Hemangioma and biliary cysts would appear hyperintense on T2-weighted imaging. Imaging-based descriptions of hepatocellular carcinoma should include commentary on arterial phase enhancement, capsular enhancement, and the pattern of washout.
2. **Answer: e.** This clinical scenario is a classic description of an amebic abscess caused by *Entamoeba histolytica*. Treatment is with metronidazole and supportive care. Drainage or operative management would be necessary only in particularly unique or complex cases. Aspiration, cyst injection, and albendazole are all appropriate treatments for echinococcal cysts.
3. **Answer: a.** This clinical scenario demonstrates the myriad options for the management of multiple hepatic metastases with colorectal cancer. A is the only incorrect answer, as the patient would be left with a future liver remnant under 20%, which is commonly accepted as too low to support necessary physiologic hepatic function. Any of the other options could be reasonable depending on the preferences or capabilities of an institution and the wishes of the patient.
4. **Answer: b.** This patient is showing signs of hepatic toxicity from chemotherapy. Proceeding with surgery should not be performed until her hepatic function has been assessed for any injury from systemic chemotherapy, including with a liver biopsy. Her future liver remnant after a two-stage procedure was going to be low (under 20%) and was reliant on hypertrophy after the first stage. Now, with possible worsened hepatic function, her FLR may need to be higher, around 30%, to consider offering her a resection. Portal vein

embolization would be inappropriate at this time, as she has already undergone unilateral hepatic resection. Cessation of chemotherapy would be an appropriate alternative answer but, in a patient who might be a surgical candidate, additional workup including liver biopsy can enhance an informed discussion of the risks and benefits of further treatment.

5. **Answer: c.** Bilirubin, INR, creatinine, and sodium are combined into a complex equation to determine a score for the Model for End-Stage Liver Disease (MELD). Choice A reflects the lab values that are part of the Child–Pugh score, which also requires an assessment of the severity of ascites and hepatic encephalopathy.

Chapter 22

1. **Answer: a.** The patient appears to have cholecystitis; an ultrasound would help establish the diagnosis. Ultrasound is much more sensitive for cholecystitis than CT and can better assess for gallstones. A HIDA scan may be useful in some cases of equivocal cholecystitis, but an ultrasound should always be ordered first. Antibiotics and IV fluids are reasonable steps, but a clear diagnosis is needed first. While this patient may indeed need cholecystectomy, the diagnosis must be confirmed and there is no need to operate emergently. There are no apparent contraindications to operation in this otherwise healthy patient, so a percutaneous cholecystostomy tube may not be appropriate.
2. **Answer: d.** This woman likely has choledocholithiasis and has passed a gallstone. In a nontoxic patient with a mildly elevated bilirubin, laparoscopic cholecystectomy with intraoperative cholangiography is reasonable to perform. An ERCP is probably not immediately necessary because she is nontoxic, her bilirubin is only mildly elevated, and no choledocholithiasis was seen on ultrasound. An MRCP would not be therapeutic though it might provide a little more information. Open cholecystectomy is not necessary and laparoscopic removal should be attempted. Generally, patients with choledocholithiasis should undergo cholecystectomy during the index admission to prevent additional admissions for choledocholithiasis and minimize the chance for gallstone pancreatitis or biliary obstruction and cholangitis.
3. **Answer: e.** This patient has acalculous cholecystitis. Decompression of the gallbladder is necessary and probably best accomplished with cholecystostomy tube rather than LC in this very ill patient. Biliary drainage via percutaneous drainage or ERCP is not indicated in the absence of cholangitis, and a relatively low bilirubin and lack of ductal dilation make cholangitis less likely. This patient may not tolerate a general anesthetic very well, so laparoscopic cholecystectomy is not the best choice in this patient. MRCP may

provide some additional information, but without any other markers for choledocholithiasis, the utility is limited.

4. **Answer: e.** This patient has a T1 gallbladder cancer isolated to the mucosa. Cholecystectomy alone is sufficient in this case, but the cystic duct margin should be evaluated because of the risk of spread down the biliary system, though unlikely. Additional imaging, including serial ultrasounds or MRCP are unnecessary. CA19-9 or CEA may be useful for following a patient with a high risk of recurrence, but that risk is low in this patient.
5. **Answer: a.** Patients with a biliary injury should be managed by a hepatobiliary specialist, hence d and e are incorrect answers. Attempt to complete the cholecystectomy risks additional injury and outpatient referral is inappropriate. Cholangiogram could be performed, but in this setting, is probably best performed by the hepatobiliary specialist.
6. **Answer: c.** Gallbladder polyps greater than 1 cm should be removed via cholecystectomy due to increased risk for underlying malignancy. There is no role for radical cholecystectomy in the absence of a gallbladder cancer. Biopsy is not indicated, and observation is not appropriate because of malignant risk. PET scan would not be helpful in the absence of suspected malignancy and would not be sensitive for detecting underlying cancer.

Chapter 23

1. **Answer: d.** Serous cystadenoma (SCA) is most commonly discovered incidentally in women in the fifth to sixth decades of life. Imaging characteristics include a microcystic “honeycomb” appearance with central scar present in 30%. SCA is a benign lesion and asymptomatic patients do not require resection or additional surveillance imaging.
2. **Answer: b.** RUQ ultrasound is the most sensitive means to establish the likely etiology of gallstones as the source of pancreatitis, thus impacting consideration of cholecystectomy prior to discharge. Gallstone disease is one of the most common etiologies of pancreatitis. In medically fit patients, cholecystectomy on index admission is associated with reduced risk of recurrent pancreatitis and readmission rates (*Pancreas.* 2018;47(8):996–1002).
3. **Answer: c.** Side branch IPMN management per current consensus guidelines recommends resection in patients with lesions >3 cm, mural nodules, cytology concerning for malignancy, or in symptomatic patients. In patients without these concerning features, routine surveillance imaging is recommended.
4. **Answer: a.** Main duct IPMNs have a high incidence of associated malignancy or high-grade dysplasia (70%) and oncologic resection is recommended in medically fit patients. Intraoperative frozen section is useful to confirm the resection margin is free of high-grade dysplasia or malignancy.
5. **Answer: c.** Pseudoaneurysm, most commonly of the GDA stump, is a relatively rare, but potentially fatal complication following pancreatectomy. Patients may present with an initial “herald” bleed, followed by postoperative hemorrhage. Initial diagnosis with angiography allows for simultaneous treatment via embolization or stent placement.
6. **Answer: b.** Patients with suspicious pancreatic mass consistent with adenocarcinoma should undergo pancreatectomy if resectable at

time of diagnosis. Pathologic confirmation with tissue biopsy may confirm the diagnosis, but is not required in patients with a resectable lesion. While several studies have shown adjuvant chemotherapy to provide a survival benefit, neoadjuvant therapy remains controversial and is reserved for patients with borderline resectable disease.

Chapter 24

1. **Answer: a.** The most common organism involved in postsplenectomy sepsis syndrome is *Streptococcus pneumoniae*. Patients who undergo splenectomy for thalassemia major are specifically at high risk for OPSI. The highest risk for OPSI is in patients with Wiskott–Aldrich syndrome.
2. **Answer: c.** Vaccinations should be administered 2 weeks before (preferred) or 2 weeks after splenectomy (trauma splenectomy) and should include coverage against encapsulated organisms and influenza.
3. **Answer: a.** Splenic abscess is most commonly due to hematogenous spread or endocarditis. If multilocular abscesses are found on imaging, splenectomy is indicated. For simple abscesses, these can be treated with antibiotics and percutaneous drainage.
4. **Answer: b.** Postsplenectomy changes include an increase in RBCs, WBCs, and platelets. Howell–Jolly bodies, Heinz and Pappenheimer bodies and presence of spur cells and target cells may also appear on peripheral smear.
5. **Answer: d.** Adult patients with normal immune system undergoing splenectomy for trauma are at lowest risk for developing postsplenectomy sepsis.
6. **Answer: d.** The first-line therapy for TTP is plasmapheresis. Plasmapheresis has improved initial response (47% vs. 25%) and 6-month survival (78% vs. 63%) compared with plasma infusion (*N Eng J Med.* 1991:325:393–397). Second-line medical therapy includes rituximab, cyclosporin, and increased frequency of plasmapheresis. Splenectomy in patients who do not respond to medical management has limited utility and has only shown benefit in the setting of continued plasmapheresis. ADAMTS-13, a von Willebrand factor cleaving protein, is often severely deficient and levels have been shown to increase following splenectomy.
7. **Answer: d.** ITP is the most common reason for elective

splenectomy followed by hereditary spherocytosis, hemolytic anemia, and TTP. Trauma is the most common reason for splenectomy overall. Previously splenectomy for staging of Hodgkin lymphoma had been a common reason for elective splenectomy.

8. **Answer: e.** Splenic artery aneurysms are usually found incidentally. In a woman of child-bearing age, splenic aneurysm >2 cm should be addressed due to the high maternal and fetal mortality associated with rupture during gestation. For aneurysms in the proximal and middle third of the splenic artery exclusion by proximal and distal ligation may be performed. Splenic perfusion occurs through collaterals in the short gastrics. For distal aneurysms resection with splenectomy is the curative.
9. **Answer: b.** Patients undergoing splenectomy are at increased risk for thrombotic complications, particularly portal vein thrombosis. The etiology is a multifactorial combination of thrombocytosis, alterations in platelet function, and decreased velocity in the splenic vein remnant. Symptoms include low-grade fever, abdominal pain, leukocytosis, and thrombocytosis. CT of the abdomen with contrast is the diagnostic modality of choice, followed by prompt treatment with systemic anticoagulation. Splenomegaly >30 cm and myeloproliferative disorders are the two main risk factors for portal vein thrombosis.
10. **Answer: e.** Approximately 80% of accessory spleens are found in the splenic hilum. Other locations include the gastrocolic ligament, tail of the pancreas, omentum, stomach, and mesentery. Identification of an accessory spleen is critical, particularly in the setting of hematologic indications, as retained accessory spleen is associated with recurrence.

Chapter 25

1. **Answer: e.** The evaluation of potential living donors includes assessment of their overall health, comorbid conditions, and psychosocial influences. Compatibility with their intended recipient is determined though ABO blood typing and HLA histocompatibility. Donors who are not compatible with their intended recipient may still donate through paired exchange and ABO-incompatible protocols.
2. **Answer: c.** Hepatic artery thrombosis in the early posttransplantation period may lead to fever, hemodynamic instability, and rapid deterioration, with a marked elevation of the transaminases. An associated bile leak may be noted soon after liver transplantation due to the loss of the bile ducts' main vascular supply. Acute thrombosis may be treated by attempted thrombectomy; however, this is usually unsuccessful and retransplantation is needed. The gold standard treatment is to relist this patient for a new liver allograft.
3. **Answer: b.** Transplantation for hepatic malignancy. Cirrhosis is a risk factor for hepatocellular carcinoma (HCC). Given that most patients who develop HCC die from their underlying cirrhosis rather than from metastatic disease, it was reasoned that transplantation may be a potentially curative approach to the primary tumor as well as the underlying pathology. The Milan Criteria are outcome driven and establish guidelines for considering OLT in patients who present with early stage I or II HCC and underlying cirrhosis. Given the concern for HCC progression while awaiting transplantation, candidates receive MELD exception points beyond what is calculated from their cirrhosis.
4. **Answer: b.** Most patients are type I diabetics with concomitant nephropathy who are evaluated for a pancreas transplant in conjunction with kidney transplantation. Ninety-five percent of all pancreas transplants are performed in conjunction with a kidney transplant. Long-term survival of an SPK recipient is similar to that of a diabetic with ESRD receiving a living donor kidney transplant.

Whole organ pancreas transplantation represents the only therapeutic option for long-term insulin independence.

5. **Answer: d.** The peak levels of serum alanine transaminase and serum aspartate transaminase usually are less than 2,000 units/L, and should decrease rapidly over the first 24 to 48 hours postoperatively. Persistent transaminitis should prompt a liver ultrasound to assess vessel patency and flow.
6. **Answer: b.** Urine leak. The etiology is usually anastomotic leak or ureteral sloughing secondary to ureteral blood supply disruption. Urine leaks present with pain, rising creatinine, and possibly urine draining from the wound. A renal scan demonstrates radioisotope outside the urinary tract. Urine leaks are treated by placing a bladder catheter to reduce intravesical pressure and subsequent surgical exploration.
7. **Answer: e.** Approved indications for intestinal transplant include the life-threatening complications associated with PN therapy.
8. **Answer: d.** Panel reactive antibodies (PRA) help to predict the likelihood of a positive cross-match. It is determined by testing the potential recipient's serum against a panel of cells of various HLA specificities in a manner similar to the cross-match. The percentage of specificities in the panel with which the patient's sera react is the PRA. Patients who have been exposed to other HLAs via blood transfusion, pregnancy, or prior transplantation will have higher PRAs.

Chapter 26

1. **Answer: e.** When the appendix first becomes inflamed, the visceral pain response is stimulated and the patient experiences pain referred to the umbilicus. As the appendix enlarges, it will irritate the parietal peritoneum overlying it, causing localized RLQ tenderness.
2. **Answer: c.** Computerized tomography (CT) imaging has become the most common imaging modality to diagnose acute appendicitis. However, CT imaging is relatively contraindicated in patient populations in which ionizing radiation can be especially harmful. This includes pregnant women and young children. In these populations, ultrasound (US) and magnetic resonance imaging (MRI) are the imaging modalities of choice. US is preferred given its low cost. However, it has a few key disadvantages: it is technician dependent and it may not visualize the appendix in obese patients. MRI can be used to clarify equivocal US results.
3. **Answer: a.** Acute appendicitis is the most common nongynecologic surgical problem in pregnant women. All women of childbearing age who present with acute abdominal pain should have a pregnancy test. Pregnant women may present with different symptoms and will undergo a different diagnostic algorithm than other adults with appendicitis. However, treatment is relatively the same. All pregnant women with nonperforated appendicitis should undergo appendectomy, unless otherwise contraindicated. Tocolytic therapy is not widely used in pregnant women undergoing abdominal surgery as there is little evidence to indicate it protects against premature labor or fetal demise (*Obstet Gynceol Clin North Am.* 2007;34(3):389–402).
4. **Answer: c.** As acute appendicitis progresses, the appendiceal wall becomes inflamed and increasingly fragile, leading to perforation. Perforated appendicitis can develop into a phlegmon and/or intra-abdominal abscess. As with any other infection, source control is key. If technically feasible, the least invasive procedure should be pursued. Percutaneous drainage can provide adequate source

control in most cases. The duration of antibiotic therapy depends on whether adequate source control has been achieved.

5. **Answer: b.** Rarely, a patient may present with classic signs of acute appendicitis but actually have an alternative diagnosis. These cases are much scarcer now that imaging has been widely adopted. However, the general surgeon may still encounter this scenario and must use his or her clinical judgment to determine the next step. In this scenario, severe inflammation of the cecum and terminal ileum suggest this patient may have a new diagnosis of Crohn disease. Given that the cecum is inflamed, appendectomy is contraindicated as it has a high risk of leak. Similarly, biopsying inflamed tissue can be more harmful than beneficial. The general surgeon must recognize this diagnosis and refer the patient to gastroenterology for definitive diagnosis and medical management.
6. **Answer: b.** The most common appendiceal neoplasm is carcinoid tumor. These tumors can cause luminal obstruction and often present as acute appendicitis; they are then diagnosed incidentally on pathology. The most important prognostic indicator of appendiceal carcinoid tumors is size. Tumors smaller than 1 cm and not located at the appendiceal base can be excised with an appendectomy. Tumors larger than 2 cm have a higher risk of lymph node metastases and require a right colectomy. The management of tumors between 1 cm and 2 cm are influenced by location and the histopathologic characteristics.

Chapter 27

1. **Answer: a.** The Rome criteria for the diagnosis of constipation are as follows:

1. Straining during at least 25% of defecations.
2. Lumpy or hard stools in at least 25% of defecations.
3. Sensation of incomplete evacuation for at least 25% of defecations.
4. Sensation of anorectal obstruction/blockage for at least 25% of defecations.
5. Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor).
6. Fewer than three defecations per week.

2. **Answer: c.** Neostigmine has potent cholinergic properties that can lead to bradyarrhythmias requiring atropine.
3. **Answer: b.** It is imperative to ensure the patient is adequately resuscitated or continues to receive appropriate resuscitation as the workup for a source is undertaken.
4. **Answer: d.** The initial treatment of sigmoid volvulus is endoscopic decompression; however, the risk of recurrence is 40% and mortality of emergent sigmoidectomy is much higher than elective sigmoidectomy, so all patients should undergo sigmoidectomy if medically able to decrease risk of mortality.
5. **Answer: e.** Diverticulosis is the most common cause of LGIB in the United States.
6. **Answer: d.** Hinchey IV diverticulitis is characterized by fecal peritonitis.
7. **Answer: c.** Distinguishing between ulcerative colitis and Crohn colitis can be difficult. Ulcerative colitis is characterized by mucosal disease that always begins in the rectum and extends proximally without skip lesions. Crohn colitis or disease causes full thickness disease, can involve any part of the GI tract and commonly has “skip” lesions or areas of disease interspersed between normal areas. Crohn disease also commonly causes fistulae and includes

perianal disease which distinguish Crohn's from ulcerative colitis. Pyoderma gangrenosum or other systemic manifestations of IBD can be associated with either Crohn disease or ulcerative colitis.

8. **Answer: b.** Total abdominal colectomy with end ileostomy or total proctocolectomy are required for the treatment of ulcerative colitis as leaving any colon in situ involves risking recurrence of disease and potential for dysplasia or malignancy. Segmental colectomy has been shown to be associated with poor outcomes.
9. **Answer: a.** It is important to remember that the IMA is ligated in an open AAA repair and covered by the endograft in an EVAAR, so in this patient your primary concern should be ischemic colitis. To confirm this diagnosis, the patient should undergo flexible sigmoidoscopy to diagnose and characterize the extent of disease. CT scan may show colitis, but does not definitively diagnose ischemic colitis. Barium enema is contraindicated.
10. **Answer: d.** Hyperplastic polyps are 10 times more common than adenomatous polyps and are benign. Large polyps (>1 cm) or right side hyperplastic polyps may be a marker of increased risk for adenomatous polyps; however, so it is important to consider this when performing endoscopy.
11. **Answer: d.** The Kudo classification SM3 is an independent risk factor for lymph node metastasis in malignant polyps and therefore patients require surgical resection for treatment.
12. **Answer: d.** The current recommendations state that screening colonoscopy should be initiated 10 years prior to the earliest age relative with colon cancer, so the age of the patient's father at time of diagnosis is the most important factor to consider.
13. **Answer: b.** While it is true that patients with stage II disease receive only marginal benefit from receiving adjuvant therapy, this patient did not receive an adequate lymph node harvest, so there is the potential for inappropriate downstaging. Giving this information, the patient should be counseled that adjuvant chemotherapy may be beneficial given his or her inadequate staging. The current recommendations are that all patients with stage III disease receive chemotherapy.

14. **Answer: a.** To adequately stage rectal cancer a chest x-ray or CT is obtained to confirm the lack of lung metastasis, abdominal CT to confirm lack of liver metastasis and pelvic MRI or transrectal ultrasound (TRUS) to assess lymph nodes and the level of tumor invasion as this will determine whether the patient is a candidate for transanal resection, surgery alone or if there is need for preoperative chemoradiation therapy.
15. **Answer: b.** The two most important principles of resection for rectal cancer limiting recurrence are to ensure a complete and intact total mesorectal excision and high ligation of the arterial pedicle (IMA) to perform a complete lymphadenectomy. Resection of Denonvilliers fascia is not necessary, resection of the hypogastric nerves could cause issues with continence and sexual function, and as long as a 1 cm distal margin is insured, patients can undergo low anterior resection with coloproctostomy or coloanal anastomosis.

Chapter 28

1. **Answer: d.** This patient presents with stage IV internal hemorrhoids and undergoes surgical excision. While each of the listed answers are potential complications of excisional hemorrhoidectomy, urinary retention is the most common, occurring in up to 20% of patients in some series. Limiting IV fluid administration has been shown to decrease this risk most effectively (*Int J Colorectal Dis.* 2006;21(7): 676–682).
2. **Answer: b.** This patient presents with a transsphincteric fistula and abscess that is partially open and draining. First, control of the inherent infection must be gained; this is achieved by incision of the internal sphincter to drain the abscess. Then, definitive therapy should be pursued with seton placement to allow wound to granulate and heal, although future intervention may be needed. Complex sphincterotomy of the internal and external sphincters simultaneously should not be performed during first stage of transsphincteric fistula excision due to high rates of residual incontinence. While advancement flap may be required in the future, it would not be indicated with an abscess present.
3. **Answer: b.** Anal sphincteric function requires synchronized function of the puborectalis, internal anal sphincter, and external anal sphincter. The internal anal sphincter, innervated by the sympathetic and parasympathetic fibers of the autonomic nervous system, is responsible for 80% of the resting pressure of the complex. The external sphincter, under somatic nerve control, contributes most to voluntary contraction. The external sphincter can become damaged during perineal trauma such as complications of vaginal deliveries.
4. **Answer: c.** For anal squamous cancers under 5 cm in size, chemoradiation under the Nigro protocol is the first-line treatment.
5. **Answer: e.** Extramammary Paget disease is cutaneous adenocarcinoma in situ. It most commonly occurs in white men during the sixth decade of life. When diagnosed, it is often

associated with additional digestive tract malignancy; therefore, further investigation of potential malignancy is warranted. For noninvasive disease, wide local excision is treatment of choice. However, radical resection with APR is indicated when disease is invasive.

6. **Answer: c.** Anal fissures are commonly located in the posterior midline and overwhelmingly respond to medical therapies. The “anal triad” classically includes a deep ulcer, sentinel pile, and enlarged anal papillae superior to the ulcer. Fissurectomy is rare, and lateral sphincterotomy is highly effective but accompanied by the potential for morbidity and incontinence.

Chapter 29

1. **Answer: d.** Inguinal hernias are more common in men. They are frequently bilateral. Indirect inguinal hernias are more common than direct inguinal hernias. Recurrence rates vary widely depending on type of repair: mesh-based repairs have lower rates of recurrence than tissue-based repairs except for potentially the Shouldice repair (in the correct patient populations). It has been reported that direct inguinal hernias are more likely to recur than indirect inguinal hernias. The exact mechanism is unclear, though posited reasons include: inadequate mesh overlap on the pubic tubercle or differences in local collagen composition. Interestingly, there is a correlation between the primary subtype and recurrent subtype of hernia; that is, indirect inguinal hernias were correlated with finding a recurrent indirect inguinal hernia at reoperation and direct inguinal hernias were correlated with finding recurrent direct inguinal hernias (*Surgery*. 2014;155(1):173–177).
2. **Answer: d.** Obturator hernias frequently occur in elderly, thin female patients. They have a high incidence of incarceration and small bowel obstruction may be the initial presentation. Pain with medial thigh rotation is the Howship–Romberg sign.
3. **Answer: c.** Though this patient is presenting with an incarcerated inguinal hernia requiring operative intervention, she is tachycardic and febrile and will require resuscitation. Obtaining a CT scan may be appropriate prior to operative repair. In the emergent setting, laparoscopic repair is typically not attempted and most patients with similar presentations will undergo open operations.
4. **Answer: d.** The patient's defect is relatively small and he is a good candidate for laparoscopic repair, which is associated with less postoperative pain and a shorter hospital length of stay. Because the mesh will be placed as an intraperitoneal onlay (IPOM), only barrier-coated meshes should be used, to prevent adhesion and erosion into bowel.

5. **Answer: d.** The patient's prior prostatectomy will make laparoscopic repair difficult. Of the answer choices, open repair without mesh (a) is incorrect, as it will unnecessarily subject the patient to higher chances of hernia recurrence. Choice e is incorrect, because the patient's right side is symptomatic. Open repair of the right side is appropriate, and if the patient elects for watchful waiting of the asymptomatic left side, he should be counseled that there is a high crossover rate from watchful waiting to operative repair secondary to repair, especially in elderly men.

Chapter 30

1. **Answer: d.** The other options may be relative contraindications (SBO, peritonitis, hypothermia), if at all (obesity), but coagulopathy would preclude a laparoscopic approach.
2. **Answer: c.** Most surgeons aim for 12 to 15 mm Hg to achieve adequate visualization and minimize the physiologic consequences of the pneumoperitoneum. The 2 and 6 mm Hg are likely too low to allow for any visualization and 18 and 25 mm Hg cause increased physiologic impacts.
3. **Answer: a.** Keeping the trocar in place during conversion to open may allow for a tamponading effect of the trocar until the vascular injury can be identified and controlled. Laparoscopic approach or radiologic approach to the injury will be unlikely to identify and control the source of bleeding prior to exsanguination or severe shock or physiologic compromise occurs. Manual pressure with be inexact and will not definitively control the bleeding source.
4. **Answer: b.** Ergonomic advantages of robotic surgery to the operating surgeon have been shown subjectively and objectively. In general, operative time, blood loss, and visualization are comparable to conventional laparoscopy. Haptic feedback with current robotic systems is decreased when compared to conventional laparoscopic instruments.
5. **Answer: e.** Pneumoperitoneum leads to a number of physiologic alterations, including decreased venous return, metabolic acidosis (from the CO_2), decreased pulmonary compliance, and increased intracranial pressure.

Chapter 31

1. **Answer: c.** Radiation therapy is contraindicated in patients who have received past chest wall radiation (a) or in patients in the second or third trimester of pregnancy (d). Radiation therapy is of minimal utility in the management of a small focus of DCIS in an elderly woman (b). However, a woman in the late stages of pregnancy with a small tumor and possible lymph node involvement could receive and would benefit from postpartum radiation therapy both as part of breast conservation treatment (BCT) and axillary treatment without undue delay.
2. **Answer: a.** Radiation therapy is NOT associated with improved overall or breast-cancer-specific survival and increases the risk of lymphedema after ALND.
3. **Answer: d.** Topical nonsteroidal anti-inflammatory drugs are considered first-line therapy for mastalgia once more concerning etiologies are ruled out.
4. **Answer: b.** First-line treatment for likely lactation mastitis is antibiotics and increased frequency of breastfeeding. If her symptoms fail to resolve, inflammatory breast cancer must be excluded.
5. **Answer: a.** *BRCA2* mutations are associated with approximately 4% to 6% of male breast cancers. Eighty-five percent of malignancies are infiltrating ductal carcinoma. MRM was traditionally the surgical procedure of choice; however, SLNB has been shown to be effective in men. Thus, total (simple) mastectomy with SLNB is a valid option in men. Adjuvant hormonal, chemotherapy, and radiation treatment criteria are the same as in women. Overall survival per stage is comparable to that observed in women, although men tend to present at later stages.
6. **Answer: c.** While malignancy is the underlying cause of pathologic nipple discharge in 10% of patients, the most likely etiologies are benign intraductal papilloma, duct ectasia, and fibrocystic changes.

7. **Answer: e.** The patient likely has a combination of senescent and drug-related gynecomastia. Renal failure may also be contributing to the problem. The treating physician should contact his PCP to discuss potential changes to his medications.
8. **Answer: b.** Follow-up for BIRADS 3 lesions is 4 to 6 months with repeat imaging.
9. **Answer: e.** Depending on patient preferences and characteristics, as well as the LCIS characteristics, any of the presented options are acceptable options for LCIS treatment.
10. **Answer: c.** Pertuzumab was approved for use in the United States by the Food and Drug Administration (FDA) in 2011. When administered with trastuzumab (another anti-Her2 monoclonal antibody) and docetaxel (a taxane), pertuzumab has been associated with progression-free survival in patients with metastatic HER2+ breast cancer.

Chapter 32

1. **Answer: e.** Melanomas less than 0.75 mm regardless of histology do not require SLNB (choice a), nor does melanoma in situ (choice b). Regional spread (choice c) warrants lymph node dissection while SLNB has no role in metastatic disease (choice d).
2. **Answer: d.** Mohs microsurgery may be appropriate, but not until after diagnosis (choice a). Excisional biopsy is not indicated on cosmetically sensitive areas such as the face (choice b). FNA is reserved for soft tissue masses, not cutaneous lesions (choice c). Shave biopsy is not the preferred method since depth of the lesion is difficult to assess and leads to an inferior cosmetic result (choice e).
3. **Answer: e.** This patient has a chronic nonhealing wound that is concerning for the development of cancer—likely a Marjolin ulcer. There are no signs or symptoms of infection so topical antibiotics are not indicated (choice a). The patient's diabetes is well controlled and his smoking is minimal, so they are likely not contributing significantly to his failure to heal (choices b and c). Ankle–brachial indices are likely to be unhelpful in this young patient with palpable pulses (choice d).
4. **Answer: d.** 1-cm margins are insufficient for melanomas >1 mm in thickness (choices a and c). SLNB is indicated for all lesions >1 mm in thickness in the absence of metastases or clinical adenopathy, hence choice b is incorrect. Axillary lymph node dissection is not indicated at this juncture as he does not have documented adenopathy (choice e).
5. **Answer: d.** Observation (choice a) is not appropriate as new nevi after 40 years of age must be considered potentially malignant until proven otherwise. Shave biopsy is suboptimal due to difficulty in assessing depth (choice b). Margins should be dictated by pathology instead of arbitrarily chosen (choice c). A diagnosis is needed before topical therapy can be instituted (choice e).
6. **Answer: a.** This lesion is small and has benign characteristics

including mobility, soft texture, and perhaps most importantly, the lesion has not grown over time. This presentation is most consistent with lipoma. Given these characteristics and the fact that the patient is asymptomatic, this can be safely observed.

7. **Answer: a.** The patient has unresectable metastatic melanoma. Treatment includes systemic therapy, extracranial intralesional injection of T-VEC, and palliative resection. Systemic first-line treatment includes targeted BRAF therapy and immunotherapy. The patient does not have a *BRAF* mutation, thus BRAF therapy is not indicated. Indicated immunotherapy would be anti-PD-1 monotherapy (pembrolizumab, nivolumab) or combination therapy (nivolumab/ipilimumab).
8. **Answer: b.** The patient's presentation is concerning for soft tissue sarcoma with likely neurovascular involvement. MRI is the preferred imaging modality for primary disease while CT chest is indicated for staging. A diagnosis must be made prior to intervention (choices a and d). While biopsy will be needed, the preferred method is core tissue biopsy; hence choices c and e are incorrect.
9. **Answer: a.** This patient has adenopathy of unknown origin, most consistent with occult or regressed melanoma given normal mammograms. PET scan will not reveal a diagnosis which is what this patient needs (choice b). Core needle biopsy is warranted to obtain a diagnosis. Observation is not appropriate in a patient with likely malignancy (choice c). The presentation is not consistent with an infectious etiology (choice d) and a diagnosis is needed before treatment can be considered (choice e).
10. **Answer: e.** Grade has been found to be the most important prognostic factor in soft tissue sarcoma.
11. **Answer: c.** Patients with soft tissue sarcoma should be staged before undergoing therapy (choices a, b, d, e).
12. **Answer: d.** En bloc resection of a soft tissue sarcoma with involved organs greatly enhances survival. This patient has no history of renal failure and has a normal creatinine, so en bloc resection is indicated.

Chemotherapy is relatively ineffective and gross positive margins worsen survival; hence answers a, b, c, and e are incorrect.

Chapter 33

1. **Answer: c.** Patients with MEN-2B tend to have aggressive MTC that can develop and metastasize within the first year of life. Thus, these patients should undergo thyroidectomy within the first months to year of life. Calcitonin levels are often very high in the first months of life and are of limited value in determining the timing of thyroidectomy in these patients (*Thyroid.* 2015;25(6):567–610).
2. **Answer: d.** This patient presents with the characteristic symptoms of pheochromocytoma with paroxysmal catecholamine release. These patients should undergo preoperative α-blockade to prevent intraoperative hypertensive emergency. β-Blocker therapy may be added after full α-blockade in some cases but should never be used alone as it can precipitate acute pulmonary edema and, in some cases, can further raise blood pressure by blocking peripheral β-vasodilatory effects. PET scanning may be used in select cases to identify occult pheochromocytomas or in patients at high risk of metastatic disease such as those with large tumors or paragangliomas.
3. **Answer: b.** Nonfunctioning adrenal tumors <4 cm in size should be observed and followed for 2 years with periodic imaging. In this case, the benign appearance and lack of evidence of hypersecretory function, the appropriate management is to follow the patient with a repeat CT scan in 6 months. More workup may be required before resection in patients with bilateral adrenal tumors or those where the mass is a suspected metastatic lesion from another primary tumor (*Horm Res.* 1997;47(4-6):279–283).
4. **Answer: d.** Primary hyperaldosteronism can be due to either an aldosterone-producing adenoma (APA) or idiopathic hyperaldosteronism (IHA) from bilateral cortical hyperplasia. In the case of bilateral adrenal lesions, adrenal vein sampling is recommended to determine if there is a unilateral source of increased aldosterone. IHA is typically treated medically. In this patient, the presence of bilateral small nodules should be evaluated

next with adrenal vein sampling for cortisol and aldosterone to distinguish these possibilities (*J Clin Endocrinol Metab.* 2014;99(8):2712–2719).

5. **Answer: a.** This patient has the characteristic imaging appearance of a myelolipoma. These lesions are benign and should only be resected in the case of symptoms due to mass-effect or hemorrhage. Given the size of the lesion, follow-up imaging in 1 year is appropriate (*J Surg Oncol.* 2012;106(5):557–564).

Chapter 34

1. **Answer: b.** TSH level is the first study performed on an asymptomatic patient with a thyroid nodule >1 cm. Imaging is the next diagnostic step. See Figure 34-1.
2. **Answer: c.** Although exceedingly rare, parathyroid carcinoma should be suspected in patients with extreme elevations in serum calcium (>15 mg/dL) and/or PTH levels (5× the upper limit of normal). The hypercalcemic crisis must be managed before taking the patient to the operating room. See “Medical management” in Parathyroid Cancer.
3. **Answer: d.** Adequacy of thyroid hormone replacement is assessed 6 to 12 weeks after therapy initiation by measuring TSH and free T_4. See “Thyroid suppression therapy” in Thyroid Cancer.
4. **Answer: e.** Elevated PTH limits renal reabsorption of phosphate, magnesium, and bicarbonate. Bicarbonate losses lead to a hyperchloremic metabolic acidosis. Elevated serum alkaline phosphatase reflects bone destruction by osteoclasts. See “Biochemical evaluation” in Primary Hyperparathyroidism.
5. **Answer: c.** Ectopic inferior glands are most likely found embedded in the thymus in the anterior mediastinum. Ectopic superior glands may be found posterior and deep to the thyroid, in the tracheoesophageal groove, or between the carotid artery and the esophagus. See “Conventional neck exploration” in Primary Hyperparathyroidism.
6. **Answer: d.** Strong risk factors for thyroid cancer include radiation exposure and family history. Thyroid cancer may manifest as hoarseness due to local nerve invasion. In the pediatric population, the risk of cancer in a thyroid nodule ≥1 cm is 22% to 26% compared to 5% to 10% in adults. Adolescents have a 10-fold greater incidence of thyroid cancer than younger children, with a 5:1 female-to-male preponderance (*Thyroid.* 2015;25(7):716–759). Thyroid cancer arising in the setting of Graves disease is uncommon (2% or less;

Thyroid. 2016;26(10):1343–1421).

7. **Answer: e.** The clinical scenario classically describes the symptoms and biochemical findings of hypothyroidism. In the areas of the world with sufficient dietary iodine, the most common cause is Hashimoto thyroiditis. See “Hashimoto thyroiditis” in Nontoxic Goiter.
8. **Answer: e.** There is currently no role for lateral compartment lymph node dissection (LND) in papillary thyroid cancer if the nodes are not involved by imaging, biopsy, or clinical examination, that is, prophylactic LND. Prophylactic *central* compartment LND should be considered, however, in patients with high-risk features. See “Operative strategies” in Papillary Thyroid Cancer.
9. **Answer: d.** For indeterminant cytology on FNA (Bethesda categories III to V), molecular testing can add significant diagnostic value. In one series, 100% of thyroid FNA samples with either a *BRAF V600E*, *RET/PTC*, or *PAX8/PPAR*γ mutation were malignant by postoperative histology; those with RAS mutations harbored malignancy in 85% of cases. These findings support total or near-total thyroidectomy in patients with Bethesda categories III to V cytology and a positive somatic mutation (*J Clin Endocrinol Metab.* 2011;96(11):3390–3397).
10. **Answer: b.** The CT findings described above are consistent with superior mesenteric artery syndrome, an uncommon disorder typically caused by abrupt weight loss, thinning of mesenteric fat, and subsequent compression of the duodenum at the aortomesenteric angle. In the majority of patients, particularly children and adolescents, a metabolic or behavioral cause should be sought. The catabolic state of Graves thyrotoxicosis can lead to such rapid involuntary weight loss. Most cases are treated by correcting the underlying disorder. Surgery is rarely indicated, but laparoscopic duodenojejunostomy is the operation of choice (*Ann R Coll Surg Engl.* 2017;99(6):472–475).

Chapter 35

1. **Answer: b.** The patient has no respiratory distress, has a job that is not high risk, is a first time pneumothorax, and is small. See Section I.C.
2. **Answer: b.** This patient is developing a tension pneumothorax, likely from a ruptured bleb in the setting of positive pressure ventilation. The immediate next step is needle decompression, followed by further evaluation and chest tube placement. See Section I.C.3.
3. **Answer: a.** This patient has a transudative effusion, so his pleural fluid should have <0.5 pleural protein to serum protein, <0.6 pleural LDH to serum LDH, and pleural LDH <2/3 upper limit of normal (upper limit is 200–300). See Figure 35.3.
4. **Answer: d.** This anterior mediastinal mass is likely a nonseminomatous germ cell tumor, with elevation of both AFP and β-HCG. Treatment is with platinum-based chemotherapy followed by resection of the remaining masses. See Section VII.C.2.c.
5. **Answer: b.** Given the size, it is concerning for malignancy. Thus further workup with PET scan is indicated to help determine malignant nature and any regional or distant spread. Navigational bronchoscopy can be challenging to reach and biopsy peripheral lesions. A biopsy in this scenario may be obtained by a CT-guided biopsy or a wedge followed by a lobectomy if cancerous, depending on institutional preferences. Section V.C.3.
6. **Answer: a.** The patient needs a mediastinoscopy or EBUS to confirm N2 disease. If the N2 level nodes are positive, then the patient has Stage IIIA cancer, which should be managed initially with neoadjuvant therapy. See Section V.E.3.

Chapter 36

1. **Answer: d.** Regional ventricular dysfunction and correlating ECG changes of ischemia or arrhythmias after coronary artery bypass grafting should raise concern for bypass graft thrombosis. Emergent cardiac catheterization provides both diagnostic assessment and the opportunity for intervention.
2. **Answer: b.** This patient initially has findings of postoperative hemorrhage, followed by an acute cessation of chest tube output due to clotting of the drainage tubes. This is accompanied by signs of cardiac tamponade (decreased cardiac output, hypotension, elevated CVP, JVD, and muffled heart sounds). Emergent reexploration and evacuation of the hemopericardium is the appropriate treatment, which can be undertaken either in the OR or bedside in the ICU depending on patient stability. If treatment is delayed, the likely outcome is cardiac arrest, which would necessitate emergent bedside chest reexploration in the ICU.
3. **Answer: d.** The intra-aortic balloon pump is positioned in the descending thoracic aorta and functions by counterpulsation, inflating during diastole and deflating during systole. This provides for increased coronary blood flow and decreased afterload.
4. **Answer: b.** In a patient with rapid atrial fibrillation and hemodynamic instability, electrical cardioversion is the appropriate first step in management. Anticoagulation is generally not initiated unless atrial fibrillation has persisted for at least 12 to 24 hours. Amiodarone may be useful in this patient, but cardioversion should be the first priority in an unstable patient. Adrenergic agonists (epinephrine) tend to exacerbate atrial arrhythmias.
5. **Answer: a.** Use of the left internal mammary artery (LIMA) is expected in all patients undergoing CABG because of its superior long-term patency and survival benefit, especially when used to bypass the LAD territory. Its use is reported as a quality metric to Medicare and the Society of Thoracic Surgeons. Specific, valid

reasons why the LIMA may not be used include significant left subclavian artery stenosis, prior chest radiation with prohibitive scarring, injury to the artery during harvest, or emergency surgery.

Chapter 37

1. **Answer: c.** In general, ischemic strokes are more prevalent among men than among women, although women tend to account for a higher percentage of stroke deaths. This is likely attributed to their greater longevity, compared to men. The risk of stroke increases with advancing age. Atherosclerosis increases with age, subsequently increasing the risk of myocardial infarction and ischemic stroke. For each decade after age 55 years, the risk of stroke approximately doubles. For individuals greater than 80 years of age the prevalence of stroke is 27%; for those 60 to 79 years of age, the prevalence is 13%. Population studies estimate that the incidence of stroke is nearly three times higher among African American individuals, and nearly two times higher among Hispanic individuals. The relationship between hypertension and stroke is well established. Observational studies indicate that the risk of stroke death doubles with each 20-mm Hg incremental increase above a systolic blood pressure of 115 mm Hg. Smoking similarly increases the risk of stroke, and overall has a relative risk of 1.9 among all smokers. Interestingly, former smokers continue to have an increased risk of stroke despite cessation, and second-hand smoke exposure nearly doubles the risk of stroke.
2. **Answer: d.** In 1995, the Asymptomatic Carotid Atherosclerosis Study (ACAS) demonstrated that asymptomatic patients with at least 60% carotid stenosis, whose general health is suitable for elective surgery, have a significantly lower 5-year risk of ipsilateral stroke if carotid endarterectomy can be performed with less than 3% perioperative morbidity.
3. **Answer: d.** In 1991, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) demonstrated that symptomatic patients with at least 70% carotid stenosis have a significantly lower 2-year risk of ipsilateral stroke if carotid endarterectomy is performed. The absolute risk reduction is 17%, when compared to patients that received medical therapy. The Asymptomatic Carotid

Atherosclerosis Study (ACAS) demonstrated that the absolute risk reduction in stroke is 6% over 5 years among asymptomatic patients if carotid endarterectomy is performed. The European Carotid Study Trial (ECST) revealed that among symptomatic patients with 80% to 99% stenosis (equivalent to 60% to 99% by NASCET criteria), the 3-year absolute risk reduction for stroke is approximately 13% after carotid endarterectomy (20% among controls and 7% among CEA patients).

4. **Answer: b.** Cranial nerve dysfunction is the most common neurologic complication of carotid endarterectomy, and exceeds the risk of perioperative stroke. The incidence of postoperative cranial nerve dysfunction ranges from 5% to 20% in most respective series, and was 4.7% among patients that underwent carotid endarterectomy during the CREST study. The majority of these cranial injuries had no significant impact on patients, and seldom represented permanent nerve injuries. Most cranial nerve injuries are transient and resolve within a few weeks to months after carotid endarterectomy. There is considerable variability in the reported incidence of cranial nerve injury, and discrepancy as to which nerve is most commonly injured. Many series, however, suggest that the hypoglossal nerve is the most commonly injured nerve. It is important to identify this nerve during carotid exposure, particularly before clamping the internal carotid artery. The position of the hypoglossal nerve is quite variable; a safe approach is to follow the ansa cervicalis cephalad to its junction with the hypoglossal nerve, and to avoid dissecting tissue along the anterior border of the ansa until the hypoglossal is first identified. The reported incidence of hypoglossal nerve injury ranges from 4% to 17%.
5. **Answer: a.** During carotid exposure, the facial vein is identified coursing medially from the internal jugular vein. The vein is ligated and divided to facilitate exposure of the underlying carotid sheath and the bifurcation of the artery. Frequently, the vein has multiple branches that need to be ligated. The superior thyroid artery (rather than the vein) is identified medially at the carotid bifurcation or

proximal external carotid artery. This vessel is controlled with a tie or vessel loop, and should not be ligated. The anterior jugular and subclavian veins are not often encountered during carotid exposure.

6. **Answer: e.** The internal carotid artery (ICA) has *no* extracranial branches. The ophthalmic artery represents the first branch of the ICA, and branches just after the ICA emerges from the cavernous sinus. This artery is of particular importance when it becomes temporarily occluded, giving rise to the syndrome of amaurosis fugax (i.e., transient monocular vision loss). The superior thyroid and lingual arteries are branches of the external carotid artery. The inferior thyroid artery is a branch of the subclavian artery, and not often encountered during carotid exposure.
7. **Answer: a.** Among the responses above, only the superior thyroid and lingual arteries are branches off the external carotid artery. If the surgeon were to dissect cephalad along the external carotid artery, the following arterial branches would be encountered (in order): Superior thyroid, ascending pharyngeal, lingual, facial, occipital, posterior auricular, maxillary, and superficial temporal. The superior thyroid artery is identified medially at the carotid bifurcation or proximal external carotid artery. This vessel may be controlled with a tie or vessel loop, and should be preserved during carotid exposure.
8. **Answer: d.** According to the North American Symptomatic Carotid Endarterectomy Trial (NASCET), a symptomatic patient with at least 70% carotid stenosis has a significantly lower 2-year risk of ipsilateral stroke after carotid endarterectomy (CEA). Long-term follow-up data from NASCET demonstrated that symptomatic patients with 50% to 69% carotid stenosis also have a significantly lower 5-year risk of ipsilateral stroke after CEA, although the absolute risk reduction is only 7%. The patient above should be offered CEA if she is a suitable candidate for elective surgery, and if the specialist or surgeon performing the carotid endarterectomy has perioperative stroke and death rates below 6%.
9. **Answer: b.** Carotid stenting is reserved for high-risk patients, with

severe cardiac disease, or adverse neck conditions that increase the complexity of carotid endarterectomy. The latter includes a history of prior ipsilateral neck surgery or neck radiation, contralateral vocal cord paralysis, or a surgically inaccessible lesion that extends caudally near the clavicle or cephalad to the C2 vertebral body. There are conflicting data in the literature demonstrating an increased risk of stroke in patients with contralateral carotid occlusion. Current observational studies do not support contralateral carotid occlusion in the absence of other criteria as an absolute indication for carotid stenting.

10. **Answer: c.** Bradycardia and hypotension can manifest during carotid stenting, and frequently occur during predilatation or after stent deployment. The mechanism is due to stretching of the carotid bulb and carotid sinus, which can cause vagal stimulation, resulting in severe bradycardia and hypotension. Preventive measures consist of fluid administration in the preoperative holding area, intraprocedural atropine administration, and infusion of vasopressors. Temporary pacemakers are indicated only in the presence of pre-existing dysrhythmias. It is also critical that the interventionist or surgeon inform the anesthesia provider when balloon dilatation and stent deployment are performed.

Chapter 38

1. **Answer: a.** Of the listed risk factors, only DM has not been associated with development or enlargement of AAA.
2. **Answer: d.** Aortography is not sensitive for the diagnosis of AAA because it may underestimate the aneurysm size or fail to reveal the aneurysm owing to the presence of mural thrombus.
3. **Answer: d.** Asymptomatic AAAs <5.5 cm in males and <5.0 cm in females can safely be observed.
4. **Answer: d.** Cutaneous ischemia following AAA repair can be observed in the setting of adequate perfusion.
5. **Answer: c.** Transmural necrosis of the sigmoid colon is a feared complication of AAA repair, and requires emergent resection of the involved segment to prevent perforation and peritoneal contamination.
6. **Answer: c.** All of the above are supplied by branches of the hypogastrics with the exception of small bowel.
7. **Answer: a.** Surgical repair of ruptured AAAs can be marked by massive fluid resuscitation. In some instances, abdominal compartment syndrome (ACS) may develop with the triad of distended abdomen, high peak airway pressures/elevated bladder pressures, and abdominal distention. These patients require decompression via laparotomy in the operating room or the ICU.
8. **Answer: c.** The aorta is composed of three layers: the intima (lined with endothelium), the adventia (composed of smooth muscle and ECM proteins), and the adventitia (composed of loose connective tissue and fibroblasts). All three layers are involved in aneurysmal degeneration, with the majority occurring in the media.
9. **Answer: c.** Of the above, only an occluded left hypogastric artery does not preclude endograft placement.
10. **Answer: c.** Type I endoleaks are due to inadequate seal of the proximal or distal components, and are usually treated as soon as

identified. Type II endoleaks are due to collateral circulation and may be watched if there is no sac expansion. Type III endoleaks are due to inadequate seal between components, including fractures. Type IV is due to graft porosity. There is no type IV endoleak.

11. **Answer: d.** The EVAR1 and DREAM (EVAR1: *Lancet.* 2004;364:843–848; DREAM: *NEJM.* 2005;352:2398–2405) studies demonstrated short-term reductions in perioperative morbidity and mortality, and duration of hospitalization. However, DREAM and UK EVAR (DREAM: *NEJM.* 2010;362:1881–1889; UK EVAR: *NEJM.* 2010;362:1863–1871) did not show a reduction in long-term mortality on long-term follow-up.
12. **Answer: d.** An asymptomatic TAA can be watched if less than 6 cm. Open repair is done via a left thoracotomy, often with use of aortofemoral bypass. Thoracic endovascular repair of aortic aneurysm (TEVAR) is a viable option, and this patient should be evaluated for candidacy.
13. **Answer: b.** Rapid surgical repair of type A dissections has significantly decreased the mortality of this condition. At this time there are no endovascular options for treatment of this condition.
14. **Answer: a.** This patient has an uncomplicated, chronic (greater than 14 days duration) type B dissection. β-Blockade forms the basis of blood pressure management in these patients. The INSTEAD-XL trial (INSTEAD-XL: *Circ Cardiovasc Interv*. 2013;6:407–416) showed improved mortality at 5 years in those patients treated with endovascular coverage of the intimal tear.
15. **Answer: e.** Renovascular HTN should be distinguished from other forms of HTN prior to surgical intervention. Of the above, age of onset in the middle ages (25 to 55) suggests some other underlying cause.
16. **Answer: c.** Nonocclusive mesenteric ischemia (NOMI) is characterized by intestinal ischemia in the absence of thromboembolic occlusion. The patients are marked by a low-output cardiac state, and imaging often reveals minimally diseased vessels. The mortality rate is high, and patients benefit from optimization of

their hemodynamics rather than surgical intervention.

Chapter 39

1. **Answer: b.** In patients presenting with claudication, without evidence of rest pain, or tissue loss, or a threatened limb, the first step in expectant management is risk factor modification and a structured exercise program. In this particular patient, smoking cessation, better medical management of his hypertension, diabetes, and hyperlipidemia (if not already optimized) are warranted prior to any other therapies. Please refer to the Management section of Chronic Arterial and Atheroocclusive Disease.
2. **Answer: c.** In a patient at risk of reperfusion injury, especially with such a long onset of diminished blood flow, a four-compartment fasciotomy is the standard of care to prevent compartment syndrome and reperfusion injury. Please refer to the Compartment Syndrome section of Acute Arterial Occlusion of the Extremity.
3. **Answer: a.** Patients with a likely long-standing history of PAD are more likely to present secondary to atheroocclusive disease and should be started on a statin immediately. Please refer to the Medical Therapy section of Chronic Arterial and Atheroocclusive Disease for further explanation.
4. **Answer: c.** In the case of acute trauma with posterior knee dislocation, the most commonly injured vessel is the popliteal artery. Attention should be placed on reducing the knee dislocation as urgently as possible to restore flow through the vessel. Care should be taken to document return of pedal pulses following reduction of the knee. ABIs can be performed in the ED following reduction, and if any question exists, CT angiogram can be performed in an urgent fashion to highlight any further injury.

Chapter 40

1. **Answer: e.** The diagnosis of DVT based on physical findings is inaccurate; rather a high index of suspicion along with risk factor identification results in appropriate referral for venous duplex. In fact, 80% of patients with a DVT have at least one identifiable risk factor. IVC filters may be indicated in certain patients with contraindications to anticoagulation but are certainly not indicated in all patients with a DVT. Finally, female gender is a not an independent risk factor for DVT.
2. **Answer: a.** This patient has C_5 E_s A_s P_r classification of her lower extremity venous disease. Her ulcer is healed, which is C_5. It is secondary to venous reflux diagnosed on the duplex. Her GSV was involved which is a superficial lower extremity vein. Finally, the pathology as stated in the body of the text is reflux; no mention was made of obstructive pathology.
3. **Answer: c.** Low-dose unfractionated heparin in perioperative patients has been shown to reduce DVTs by 50% to 70% (*N Engl J Med*. 1988;318(18):1162–1173).
4. **Answer: e.** All of the above are risk factors associated with IVC filter placement.
5. **Answer: c.** Distal DVTs including those in the anterior tibial, posterior tibial, and peroneal veins do not require anticoagulation due to low risk of embolization; however, there is a risk of propagation to the proximal DVTs and patient should have repeat ultrasound duplex in 7 to 10 days.

Chapter 41

1. **Answer: b.** 200 to 500 mL/min is necessary for adequate hemodialysis.
2. **Answer: c.** Pseudointimal hyperplasia in a graft or neointimal hyperplasia in a native fistula is the most common cause of dysfunction. Hemodynamically significant stenoses can lead to thrombosis. Evaluation with Duplex ultrasound and fistulogram aid in diagnosis, and intervention with angioplasty or surgery may be required.
3. **Answer: d.** Catheter-associated peritonitis is a serious complication of PD requiring removal of the catheter if antibiotic therapy is unsuccessful.
4. **Answer: b.** Initial empiric antibiotics for catheter-associated peritonitis should cover gram-positive and gram-negative bacteria. Therefore, vancomycin or a first-generation cephalosporin and a third-generation cephalosporin or aminoglycoside would be indicated. Of the choices offer, b. offers appropriate coverage via an appropriate route.
5. **Answer: c.** Juxta-anastomotic stenosis occurs secondary to shear stress on the vessel walls adjacent to the anastomosis (between 2 and 4 cm) proximal on the arterial inflow side of the anastomosis and 2 to 4 cm distal on the venous outflow side of the anastomosis.

Chapter 42

1. **Answer: d.** Initial blood transfusion should be in the volume of 10 mL/kg. Her initial fluid boluses should also have been in a volume of 10 mL/kg, with up to 20 mL/kg up to two times acceptable.
2. **Answer: b.** Type II choledochal cyst is an isolated cyst arising from the common bile duct and is typically repaired via hepaticojejunostomy.
3. **Answer: c.** Plain abdominal films can aid in the diagnosis of tracheoesophageal fistula. Coiling of the orogastric tube in the upper chest is sufficient for a presumptive diagnosis of esophageal atresia. Plain abdominal film could aid in the determination of whether or not there is an associated tracheoesophageal fistula. The presence of air within the bowel would suggest that there is a communication between the trachea and the distal esophagus.
4. **Answer: d.** Meissner plexus resides in the submucosal plane, while the Auerbach plexus is between the longitudinal and circular muscular layers.
5. **Answer: d.** Pexying the cecum does not have any benefit in a Ladd procedure. Appendectomy is performed to eliminate any future appendicitis from arising in a nonanatomical position.

Chapter 43

1. **Answer: c.** In patients who present to the ED with well-formed cervical stomas and without respiratory distress, you should have a high suspicion that this represents a total laryngectomy site and NOT a tracheostomy site. As this is the patient's only airway, do NOT occlude the airway, do NOT use oxygen via nose or mouth, and do NOT try to ventilate the patient through the mouth or nose. In this setting, the upper airway has been permanently disconnected from the patient's respiratory tract. Instead, high-humidity trach collar alone is generally the most comfortable form of supplemental oxygen for these patients. If the patient requires higher level of intervention, a tracheostomy tube or endotracheal tube may be placed through the stoma. Of note, as the trachea is sutured to the skin for a total laryngectomy site, the carina is often quite close, and it is important to insert the endotracheal tube until the cuff is just visualized inferior to the stoma to avoid mainstem intubation.
2. **Answer: c.** First step to managing most epistaxis is firm continued pressure to bilateral nasal ala for several minutes without peeking +/− use of oxymetazoline spray (or other vasoconstrictive agent)—this management will control most epistaxis. Pinching the bony bridge of the nose will not provide pressure to the septum as the bony bridge is immobile. A 4 × 4 gauze rolled and inserted into the nasal cavity often debrides the septum and makes the epistaxis worse. Until the patient has failed conservative management and other measures, going to the operating room for intervention for simple epistaxis would be overkill. While use of high-humidity face tent in lieu of nasal cannula will help prevent epistaxis by avoiding nasal trauma, other measures must be tried to help control acute bleeding.
3. **Answer: e.** This is the classic description of a thyroglossal duct cyst. The most important measure before proceeding to operating room to remove this mass (via a Sistrunk procedure) is obtaining an ultrasound of neck to ensure that other thyroid tissue exists in the neck. If no other thyroid tissue exists, surgery may still be indicated

but a conversation with the parents must be had about need for lifelong thyroid supplementation if all thyroid tissue is removed. MRI would also accomplish this evaluation; however, it is more costly and may also require that the child be sedated for procedure (and is therefore more risky). CT would also accomplish this evaluation; however, it requires radiation exposure, which should be avoided (if possible) in a young child. Mononucleosis would not generally present in this fashion. Cytology is not necessary for diagnosis of this lesion.

4. **Answer: b.** This patient has most likely suffered from bilateral recurrent laryngeal nerve injury as a result of her procedure. While more conservative measures could be trialed (e.g., oxygen via nasal cannula, positive pressure ventilation, steroids) and/or reintubation in the urgent setting, a suture lateralization thyroplasty and/or tracheostomy would be likely the best options to secure her airway in the longer term until the extent of injury is known. Speech therapy will not fix bilateral cord palsy. Temporary cord injection laryngoplasty and medialization thyroplasty are options for unilateral vocal cord palsy. These procedures medialize the affected vocal cord, allowing it to contact the unaffected vocal cord and thus prevent aspiration and improve vocalization. However, in the setting of bilateral cord palsy where both vocal cords are in the paramedian position, as in this case, these interventions would only serve to worsen her airway obstruction.
5. **Answer: e.** Unilateral neck mass in an adult is most likely cancer and thus needs to be worked up as such. The least morbid option for diagnosis of malignancy is FNA of right neck lymph node. If this cannot be reliably performed, a biopsy could be considered from the suspected tonsil; however this may result in a false-negative result (as squamous cell carcinoma of oropharynx may metastasize to the neck when the primary is quite small). Antibiotics are not likely to be effective, and trials of these are frequently associated with delay in diagnosis. Chemoradiation and/or surgical intervention prior to diagnosis and staging is not appropriate for clinical care of patients.

6. **Answer: b.** This patient most likely has a carotid body tumor, a type of paraganglioma. It is important to know if this is a secreting or nonsecreting tumor before proceeding with any intervention; and thus testing for urine and serum metanephrines, and performing a CT abdomen (to look for possible pheochromocytoma, which can accompany paragangliomas) before proceeding with surgical intervention is the next step. FNA or biopsy of mass is not required as these lesions have a characteristic appearance on imaging, and biopsy would place individual at significant risk of bleeding.
7. **Answer: d.** In this case, the patient is diagnosed with an unknown subtype of lymphoma and additional FNA would not add any additional information. It is important to have enough tissue to perform flow cytometry and/or for additional studies in order to direct future treatments and thus a core or excisional biopsy is required. Additionally, the patient would require imaging to stage his cancer prior to treatment with chemotherapy and/or radiation therapy depending on the subtype of lymphoma. Surgical resection is not used to treat lymphoma; so performing a neck dissection puts the child at significant risk of morbidity including possible cranial nerve deficits and would not add much beyond what information could be gleaned with a smaller core or excisional biopsy.

Chapter 44

1. **Answer: c.** A full-thickness skin graft includes both the epidermis and dermis. As such, the elastin fibers in the dermis recoil, resulting in up to 40% contracture immediately following harvest from the donor site. However, there is minimal contracture once the graft is inset. Split-thickness skin grafts, regardless of meshing, do not contract greatly initially, but contract up to 40% during the healing process, likely due to the action of myofibroblasts.
2. **Answer: b.** There is a large volume of dead space beneath the abdominoplasty flaps, allowing for a large volume of hemorrhage. Although the index of suspicion for pulmonary embolism following abdominoplasty should always be high, this presentation is more consistent with hemorrhage.
3. **Answer: d.** The critical component of this scenario is recognizing that the left internal mammary artery is the vascular pedicle for options (b) and (c). A skin graft would not take over exposed sternum and a free flap is rarely necessary in the chest. Other reasonable options would be a right pedicled rectus flap (right internal mammary artery), pectoralis advancement flap (based on thoracoacromial pedicle), or right turnover pectoralis flap (right internal mammary artery).
4. **Answer: b.** Nerve palsies secondary to gunshot wounds, in the absence of vascular injury or observation of the nerve in the wound, should be treated as closed injuries. There are no useful findings on electromyography and nerve conduction studies in the acute period, so it is best to wait until 6 weeks to obtain baseline studies and follow-up in 3 months.
5. **Answer: a.** Osteomyelitis must be treated prior to definitive coverage; a bone biopsy showing more than 10 organisms per gram of tissue is predictive of flap failure. As long as surrounding skin is clean and the wound can be adequately protected, fecal incontinence is not a contraindication. Negative-pressure wound

therapy can be adequate treatment for stage I/II ulcers, but is unlikely to result in full healing of a stage IV ulcer. Secondary to a chronic inflammatory state, serum iron is low in most patients with pressure sores and cannot be reversed with supplementation. Untreated spasticity would be a contraindication for flap coverage; baclofen is a standard therapy.

Chapter 45

1. **Answer: d.** A complete hematuria workup should be performed with any history of hematuria, even if it has resolved. A noncontrast CT or renal/bladder ultrasound would be appropriate imaging modalities for a patient with confirmed kidney stones, but are inadequate for diagnostic hematuria workup. Patients with renal failure or an IV contrast allergy require renal ultrasound, cystoscopy, and retrograde pyelograms (performed in the OR) as well as a urine culture and cytology
2. **Answer: b.** A patient with an obstructing stone and any signs of infection (fevers, chills, leukocytosis, urinalysis concerning for urinary tract infection [UTI]) is at high risk for developing urosepsis and needs an urgent urology consult for either a ureteral stent or percutaneous nephrostomy tube to relieve the obstruction. Any patient with an obstructing stone should have a urinalysis with microscopic analysis and a urine culture sent immediately before starting antibiotics. In a patient with a stone and fever, it is appropriate to start an empiric antibiotic, usually a fluoroquinolone or third- or fourth-generation cephalosporin, but this does not replace obtaining an urgent consult.
3. **Answer: c.** Urinary retention can be caused by any of the above. BPH alone does not present with systemic symptoms like fevers. The prostatic examination is typically normal with a urinary tract infection. Prostatic abscess typically presents with high fevers, leukocytosis, and significant pain. A periprostatic fluid collection may be palpable. While this clinical scenario does not rule out a prostatic abscess, the most likely diagnosis is bacterial prostatitis which is treated with empiric antibiotics.
4. **Answer: a.** Ischemic priapism is a urologic emergency and can result in permanent erectile dysfunction, if untreated. Nonischemic or “high-flow” priapism is usually caused by increased arterial flow due to a traumatic fistula; it is not painful, and the penis is only semirigid on examination. Ischemic priapism is treated initially with irrigation

with normal saline, aspiration, and intracavernosal phenylephrine injections. It is most commonly caused by medications (including trazodone and treatments for erectile dysfunction) or use of illegal drugs (e.g., cocaine) that affect vascular contractility.

5. **Answer: e.** Fournier gangrene is a necrotizing groin infection which initially presents with erythema and edema of the penis, scrotum, and/or perineum. It may originate from a scrotal, perineal, or perianal abscess. If left untreated, it progresses rapidly to frank necrosis with significant morbidity and mortality risk. It is a clinical diagnosis, but the presence of gas/free air in the subcutaneous groin tissues along with the above examination findings should prompt immediate exploration with debridement. Patients often also have fevers and leukocytosis
6. **Answer: TRUE.** All grade I to III renal injuries and most grade IV renal injuries may be safely observed with serial CBCs, bedrest until hematuria resolves, and repeat imaging in 48 to 72 hours. Exploration with possible nephrectomy is required when there is hemodynamic instability, an injury to the major renal vessels, and/or persistent hemorrhage. Urinary diversion, usually via a ureteral stent, is required if there is significant injury to the renal pelvis and/or proximal ureter with disruption of contrast excretion down the ureter.
7. **Answer: c.** Suspect bladder and/or urethral injury in any patient with pelvic or pubic fractures, particularly if they have urinary retention, hematuria, perineal or penile bruising. Blood at the meatus is a sensitive sign for urethral injury, but its absence does not rule it out. Catheterization should never be attempted without a retrograde urethrogram if there is any concern for urethral injury. If the RUG is negative, a Foley catheter can be safely placed. CT cystogram is the most sensitive test for bladder injury. Passive bladder filling via a CT urogram is not adequate and a standard fluoroscopic cystogram may miss subtle or posterior injuries. Placing a suprapubic tube may be appropriate if there is significant urethral injury but is unnecessarily morbid as initial management.

Chapter 46

1. **Answer: d.** Surgical staging for ovarian cancer involves collecting pelvic washings, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, peritoneal biopsies, and omentectomy. If bulky disease is present in the intraperitoneal cavity, it should be removed to accomplish a debulking surgery to a point of no gross residual disease. This can require splenectomy, bowel or bowel mesentery resection, diaphragm and peritoneal resection or stripping, and argon beam or plasma jet coagulation of tumor deposits. These procedures are not standard staging procedures.
2. **Answer: b.** Ultrasound is the best first-line imaging to evaluate the pelvic anatomy and differentiate physiologic adnexal structures from abnormal or potentially malignant masses. CT and MRI can be helpful in further classifying pelvic masses once the presence of a mass is established with ultrasound.
3. **Answer: a.** Women with Lynch syndrome have a 15% to 66% lifetime risk of endometrial cancer depending on the mutation. There is some preliminary data to suggest that women with *BRCA* mutations may be at increased risk for endometrial cancer but not to the degree of women with Lynch syndrome.
4. **Answer: a.** The gravid uterus can compress the inferior vena cava resulting in decreased blood return to the mother and poor placental perfusion resulting in maternal hypotension and fetal hypoxia.
5. **Answer: c.** The standard of care for stage IIIB cervical cancer is radiation therapy with sensitizing cisplatin. Stage IIIB cervical cancer by definition extends to the sidewall or obstructs ureteral flow and is therefore not resectable without significant morbidity.

Chapter 48

1. **Answer: c.** Chi-square test is used for categorical or nominal data. In this instance, patients either received prehydration with sodium bicarbonate or they did not. The outcome represents the presence or absence of contrast-induced nephropathy. This data can be summarized in a 2 × 2 contingency table.
2. **Answer: b.** A t-test allows for comparison of means between two separate treatment groups. If more than two treatment groups were compared, ANOVA would be the statistical test of choice. In order to use a t-test, data must be normally distributed.
3. **Answer: d.** While positive and negative predictive values are affected by the prevalence of a disease, sensitivity and specificity are not. As the prevalence of a disease increases, the positive predictive value increases and negative predictive value decreases.
4. **Answer: a.** Case-control studies are useful for rare diseases, as is the case with appendiceal cancer and pseudomyxoma peritonei. In the above question, the cases would be presented by patients with pseudomyxoma peritonei from appendiceal cancer and the controls would be patients with appendiceal cancer alone. Exposures in both groups could be evaluated to determine factors associated with the development of pseudomyxoma peritonei.

5–7. Answers: The correct answer for no. **5** is **c**, for no. **6** is **a**, and for no. **7** is **c**. The false-positive rate is equal to the false positives divided by the sum of the false-positive patients and the true-negative patients.

8. **Answer: d.** The number needed to treat is the number of patients that must receive active treatment to prevent one MI. It is the inverse of the attributable risk percent.

$$ARR = \frac{\textit{events}}{\textit{placebo group}} - \frac{\textit{events}}{\textit{active treatment group}}$$

$$ARR = \frac{2}{100} - \frac{1}{100} = 0.01$$

$$NNT = \frac{2}{ARR} = \frac{1}{0.01} = 100$$

Chapter 49

1. **Answer: d.** Latent conditions are organizational issues beyond the role of a single person that can lead to patient safety events under certain conditions. In this instance, we assume the care team was too busy to perform safety checks or follow protocols due to understaffing, which was a contributor to a patient safety event.
2. **Answer: b.** Normalization of deviance is an inadvertent and often unexpected transition away from standard practices to unsafe practices. This can frequently pose a hazard to patients and compromise patient safety initiatives over time. Ongoing observation monitoring adherence to protocols should be undertaken to prevent regression and adverse events.
3. **Answer: e.** The Plan-Do-Study-Act (PDSA) cycle involves constructing and implementing a quality improvement project while tracking adherence and outcomes on a small scale. Shortcomings, challenges, or other errors are then adjusted and trialed again before rolling a project out full scale.
4. **Answer: c.** Balancing measures are measures used to track the effect of one measure or intervention on another measure or outcome. Although tracking readmissions or phone calls could be considered an outcome measure, relating these to what you believe to be the underlying cause will aid in constructing resultant quality improvement efforts.
5. **Answer: d.** Run charts are one of many tools used to guide or track quality improvement initiatives. The primary purpose of a run chart is to track a single outcome and observe for trends in this outcome as quality improvement initiatives are implemented. Improvements can be observed, as can deviation from protocols that should lead to continued investigations.

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