CURRENT
Medical Diagnosis & Treatment

UPDATED ANNUALLY

2025

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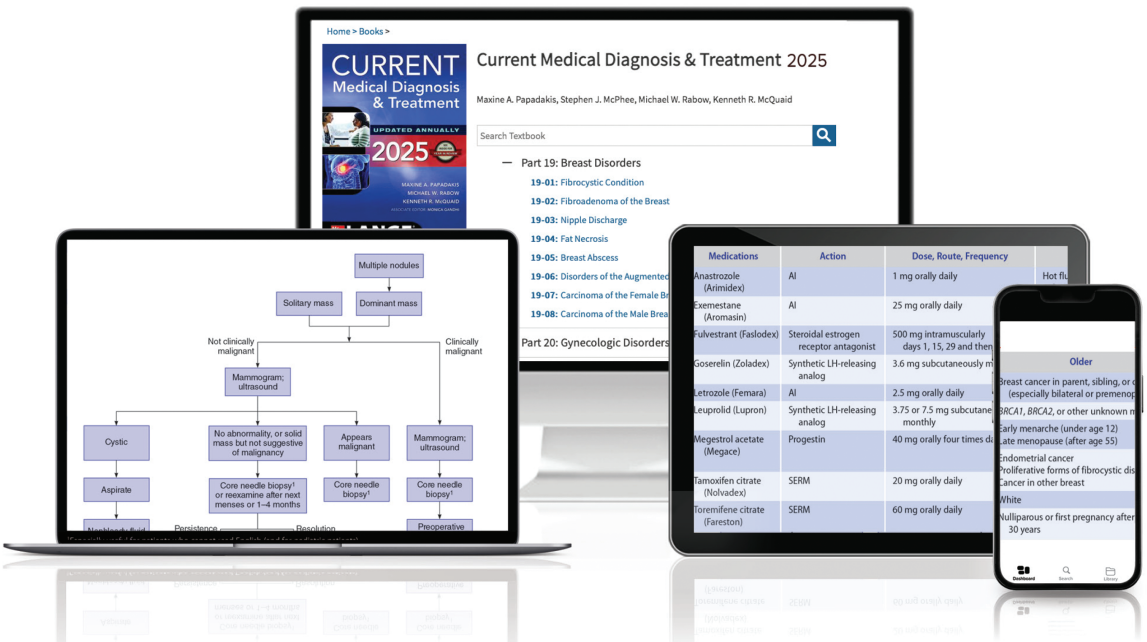

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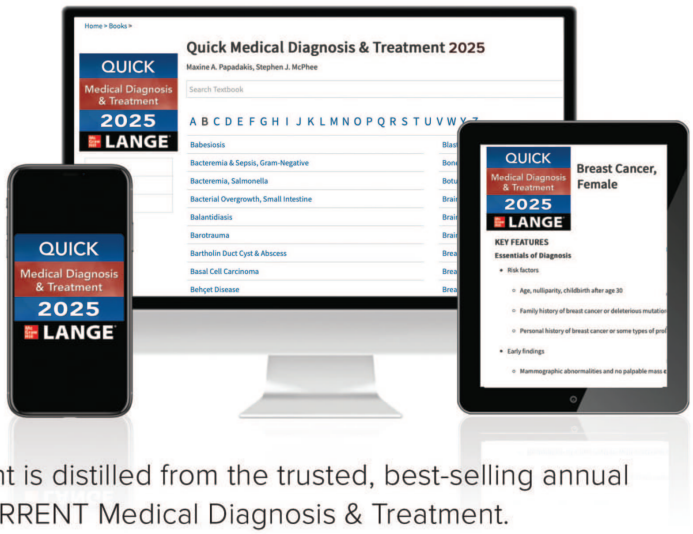

Quick Medical Diagnosis & Treatment is distilled from the trusted, best-selling annual guide to adult internal medicine–CURRENT Medical Diagnosis & Treatment.

Organized alphabetically, topics are bulleted for concise and at-a-glance use in a busy clinical setting.

Each disease is structured to highlight:

- Essentials of diagnosis
- Symptoms, signs, and differential diagnosis
- Laboratory tests, imaging studies, and diagnostic procedures
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2025 CURRENT Medical Diagnosis & Treatment

SIXTY-FOURTH EDITION

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The following chapters are available online without subscription at www.accessmedicine.com/CMDT

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Preface

CURRENT Medical Diagnosis & Treatment 2025 (CMDT 2025) is the 64th edition of this single-source reference for practitioners of adult medicine in both hospital and ambulatory settings. The book emphasizes the practical features of clinical diagnosis and patient management in all fields of internal medicine and in specialties of interest to primary care practitioners and to subspecialists who provide general care.

With a growing recognition of systemic racism and other biases in institutions across our societies, including the institution of medicine (https://www.mdcalc.com/race), the editors of *CMDT*, with humility, have committed to a thorough examination of our content to remove biased language, research, and recommendations. Since 2020, we have been pursuing an ongoing, formal process of review and revision in an effort to recognize and correct biases and to promote equity in our book and thus in the practice of medicine. While we, the editors, take this on as our responsibility, we also invite readers to share with us any *CMDT* content that they find problematic or biased. Please email comments to CMDT@mheducation.com.

We have tried to describe populations used in the studies that form the basis of the information in *CMDT* and use appropriate language where we can (eg, persons of sub-Sahara African descent, rather than African Americans). We continue, however, to use terms from original sources when study populations are broad.

INTENDED AUDIENCE FOR *CMDT*

House officers, medical students, and all other health professions learners will find the descriptions of diagnostic and therapeutic modalities, with citations to the current literature, of everyday usefulness in patient care.

Internists, family physicians, hospitalists, nurse practitioners, physician associates, and all primary care providers of adult medicine will appreciate *CMDT* as a ready reference and refresher text. Physicians in other specialties, pharmacists, and dentists will find the book a useful basic medical reference text. Nurses, nurse practitioners, and physician associates will welcome the format and scope of the book as a means of quickly referencing medical diagnosis and treatment modalities.

Patients and their family members who seek information about the nature of specific diseases and their diagnosis and treatment may also find this book to be a valuable resource.

NEW IN THIS EDITION OF *CMDT*

The **"Year in Review: Key Clinical Updates in *CMDT 2025*"** highlights what the editors consider to be the most significant clinical changes over the last year, providing page numbers and reference citations for easy access. This tool is meant to get users "current" quickly but does not reflect all the changes since the last edition.

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- Medical advances up to time of annual publication
- Detailed presentation of internal medicine disciplines, plus key primary care topics
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Six ***e-chapters*** listed in the Table of Contents can be accessed at **www.AccessMedicine.com/CMDT.** These online-only chapters (available without the need for subscription) include

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- Podiatric Disorders
- Women's Health Issues
- Appendix: Therapeutic Drug Monitoring, Laboratory Reference Intervals, & Commonly Used Blood Specimen Collection Tubes

SPECIAL RECOGNITION: PHILIP TISO, MFA

With this edition of *CMDT*, we say goodbye to Phil Tiso, our extraordinary Principal Editor at the University of California, San Francisco, and we offer our gratitude for his 22 years of work on *CMDT*.

Phil received his undergraduate degree from UC San Diego and earned an MFA from UC Riverside. Prior to working at UCSF, he served in the United States Coast Guard, maintaining aids to navigation on the Mississippi River and helping coordinate search and rescue operations in the Puget Sound. He began work with us in 2000 as an editorial assistant to McGraw Hill author and editor Dr. Stephen McPhee with many grants and publications. Phil worked on annual editions of *CMDT*, from the 2001 through the 2024 edition.

In addition to his responsibilities on *CMDT*, Phil worked closely with Dr. McPhee on other McGraw Hill textbooks: *Pathophysiology of Disease* 4th through 8th editions; [*Pocket*] *Guide to Diagnostic Tests* 6th and 7th editions; and the McGraw Hill/JAMA Evidence textbook, *Care at the Close of Life: Evidence and Experience*. In recognition of his extraordinary service to these texts as well as to Dr. McPhee's grants and manuscripts, Phil was promoted to a Principal Editor at UCSF.

We have admired and appreciated Phil's enthusiasm, cheerful presence, and reliable calm in the face of mounting pressure as deadlines approached. He kept *CMDT* on schedule without fail.

Our entire editorial team will greatly miss their daily interactions with Phil. For all of us, he has been a truly special partner!

ACKNOWLEDGMENTS

We wish to thank our authors for participating once again in the annual updating of this important book. We are especially grateful to Bryn A. Boslett, MD, Rachel Bystritsky, MD, Steven Z. Pantilat, MD, Jonathan A. Waitman, MD, and Thomas J. Walsh, MD, who are passing the baton this year. We have all benefited from their clinical wisdom and commitment.

Many students and physicians have contributed useful suggestions to this and previous editions, and we are grateful. We continue to welcome comments and recommendations for future editions via email at CMDT@mheducation.com.

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Dedication

Dr. Stephen J. McPhee

After completing 35 years as a title page editor of *CURRENT Medical Diagnosis & Treatment* (*CMDT*) and with the publication of *CMDT* 2024, Dr. Stephen J. McPhee retired from his illustrious editing career. As a highly respected academician (with nearly 200 peer-reviewed publications) and a consummate clinician (everyone wanted Steve to be their doctor!), Steve brought his superb writing and keen eye to his editorial work. His contributions have been immeasurable and included expanding the topics covered in *CMDT*, recruiting many talented authors, and bringing his unfailing commitment to deliver the most current evidence-based information to clinicians throughout the world.

In 1980, Steve came to University of California San Francisco (UCSF) as an Assistant Professor in the new Division of General Internal Medicine. He quickly became known as an expert diagnostician, teacher, clinician, and writer. A working-class kid who went to Yale University, Steve majored in philosophy and graduated *summa cum laude* while cleaning rugs in Yale's rare book library and cleaning glassware in its science labs to support himself. As a medical student at the Johns Hopkins School of Medicine, Steve was immersed in the Osler tradition, which prized expert diagnosis and treatment choices and constantly tested trainees' acumen in Saturday morning Grand Rounds and daily ward rounds. He finished his required coursework in 3 years before beginning his Hopkins medicine internship. After finishing his Hopkins residency, Steve was selected to be Hopkins' first General Internal Medicine fellow by the famed diagnostician and teacher of medicine, Dr. Philip Tumulty. Steve was then appointed to be an Osler Chiefs of Service, serving as the physician of record for one-fourth of the patients on the Osler Service each night.

While at UCSF, Steve served as the primary care residency program director in the early 1980s. Following the unexpected death of his hospitalized toddler son, David, in 1986, Steve taught about medical mistakes and with Dr. Steven Pantilat founded the Palliative Care Service at UCSF. Steve edited the monthly "Care at the Close of Life" section in *JAMA* and this *JAMA* section was later turned into a book.

After writing and annually updating the "Disease Prevention and Health Promotion" chapter in *CMDT* with his mentor and co-author Dr. Steven Schroeder, Steve became a title page editor beginning with *CMDT* 1989. Over the years, with Steve's vision and contributions, *CMDT* expanded from 34 chapters in 1989 to 50 chapters in 2024. Today, *CMDT* is one of the most utilized resources on McGraw Hill's AccessMedicine platform and is often ranked number one in key medical categories on Amazon.com. Steve and Dr. Maxine Papadakis developed the related *Quick Medical Diagnosis & Treatment* as a digital teaching tool for medical and other health professional students. Then, working with UCSF Laboratory Medicine and Radiology faculty, Steve and his colleagues developed the first edition of the *[Pocket] Guide to Diagnostic Tests*, which has subsequently been published six more times. Finally, Steve went on to prepare the first chapters of *Pathophysiology of Disease: An Introduction to Clinical Medicine* and remained as its editor for eight subsequent editions.

Steve's dedication to *CMDT*'s legacy is remarkable. He generously donated his collection of 35 annual editions of *CMDT* (1989 to 2024) to the McGovern Historical Center at the University of Texas Medical Center Library in Houston. It is a resource for researchers studying changes in the practice of medicine. In addition, by enlisting bright physician trainees to participate in literature searches for topics in each new edition, Steve provided a great educational opportunity for the next generation and ensured that *CMDT* was indeed *current*.

Steve has our gratitude for his leadership, his prolific contributions to the science and art of medicine, and for his friendship. We wish him our heartfelt congratulations on a most extraordinary career.

YEAR IN REVIEW: KEY CLINICAL UPDATES IN *CMDT* 2025

Entries presented in the Year in Review are curated by the editors as being extremely impactful to daily clinical practice. These highlighted entries are only a fraction of all the updates included across this edition of *CMDT*.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
CHAPTER 1: DISEASE PREVENTION & HEALTH PROMOTION		
Cancer Prevention	12	• The USPSTF recommends offering annual lung cancer screening with low-dose CT to current smokers aged 50 to 80 years and at least a 20-pack-year smoking history and to smokers who quit within the past 15 years. Updated American Cancer Society recommendations remove the restriction on the number of years since quitting. *Wolf AMD. CA Cancer J Clin. [PMID: 37909877]*
CHAPTER 3: PREOPERATIVE EVALUATION & PERIOPERATIVE MANAGEMENT		
Perioperative Hematologic Evaluation	48	• The AABB (formerly American Association of Blood Banks) states that a transition threshold of 7.5 g/dL (75 g/L) could be considered for hospitalized patients undergoing cardiac surgery, and 8 g/dL (80 g/L) could be considered for hospitalized patients undergoing orthopedic surgery or who have underlying CVD. *Carson JL et al. JAMA. [PMID: 37824153]*
CHAPTER 4: GERIATRIC DISORDERS		
Dementia	56	• Patients living with Alzheimer disease who are chosen for treatment with monoclonal antibodies (aducanumab or lecanemab) require regular monitoring for amyloid-related imaging abnormalities (ARIA) using MRI. *Cummings J et al. J Prev Alzheimers Dis. [PMID: 37357276]* *Van Dyck CH et al. N Engl J Med. [PMID: 36449413]*
CHAPTER 6: DERMATOLOGIC DISORDERS		
Psoriasis	136	• The IL-36 receptor antibody spesolimab is the first therapy approved specifically for generalized pustular psoriasis. *Raharia A et al. Clin Med (Long). [PMID: 34001566]* *Lee H et al. Int J Mol Sci. [PMID: 37686119]*
Scabies	128	• For treatment-resistant patients, 0.9% spinosad suspension, applied once over a greater than 6-hour time period, can be considered, though efficacy is lower than that for ivermectin or permethrin. *Richards RN. J Cutan Med Surg. [PMID: 32998532]* *Widaty S et al. J Infect Dev Ctries. [PMID: 35298417]*
CHAPTER 9: PULMONARY DISORDERS		
Chronic Obstructive Pulmonary Disease	259	• For stable COPD management, if the patient has significant dyspnea and airflow obstruction, the 2023 GOLD update recommends early initiation of treatment with long-acting muscarinic antagonists (LAMA) plus long-acting beta-2-agonist (LABA), rather than LAMA alone. • The GOLD 2023 guidelines do not encourage use of inhaled corticosteroid (ICS) in early stages of COPD and call for more judicious use of ICS in patients with more severe COPD with frequent exacerbations, those with blood eosinophilia of 300 cells per mcL or more, concomitant asthma, or history of hospitalizations due to COPD exacerbations. *Venkatesan P et al. Lancet Respir Med. [PMID: 36462509]*

*See chapter for further details and references.

(continued on following page)

Topic	Page Number	Key New Advances Affecting Clinical Practice*
Pneumonia	270	• Two classes of pneumococcal vaccines for adults are available and approved for use in the United States: one containing capsular polysaccharide antigens to 23 common strains of *Streptococcus pneumoniae* (PPSV23) and several other polyconjugate vaccines, including 13-valent (PCV13), 15-valent (PCV15), and 20-valent (PCV20). *Kobayashi M et al. MMWR Recomm Rep. [PMID: 37669242]*
	270	• Vaccination is recommended for all adults aged 65 and over, and adults aged 19-64 with certain medical comorbidities (diabetes, chronic lung disease, chronic liver disease); increased risk of meningitis (CSF leak, cochlear implant); or immunocompromising condition, including asplenia. *Kobayashi M et al. MMWR Recomm Rep. [PMID: 37669242]*
Pulmonary Tuberculosis	281	• In 2023, a regimen was approved using a longer course of pretomanid, bedaquiline, and linezolid for multidrug-resistant tuberculosis (MDR-TB) resistant to fluoroquinolone. *Bateson A et al. N Engl J Med. [PMID: 36053506]*
CHAPTER 10: CORONARY ARTERY DISEASE, VALVULAR DISEASE, & OTHER KEY TOPICS IN CARDIOLOGY		
Acute MI with ST-Segment Elevation	369	• For a typical patient, it is reasonable to use a DOAC and clopidogrel and to discontinue aspirin at the time of hospital discharge or 1–4 weeks after stenting. *Writing Committee Members, Lawton JS et al. J Am Coll Cardiol. [PMID: 34895950]*
Coronary Heart Disease	349	• Treatment with bempedoic acid, an ATP citrate lyase inhibitor, resulted in reduction in the composite primary end-point of cardiovascular death/nonfatal MI/nonfatal stroke/or coronary revascularization procedure. *Nissen SE et al. N Engl J Med. [PMID: 36876740]*
	350	• The SELECT RCT showed a statistically significant decrease in the composite primary end-point of cardiovascular death/nonfatal MI/or nonfatal stroke in the group treated with semaglutide. *Lincoff AM et al. N Engl J Med. [PMID: 37952131]*
	350–351	• Colchicine 0.5 mg daily resulted in a 23% reduction in major adverse cardiac events in patients after MI and 31% in patients with stable CAD. *Nelson K et al. J Am Coll Cardiol. [PMID: 37558377]*
Tricuspid Regurgitation	344	• Transcatheter edge-to-edge repair was safe and effective at reducing the degree of tricuspid regurgitation and improving quality of life in patients with severe functional tricuspid regurgitation randomized to treatment with the TriClip device versus medical therapy. *Sorajja P et al. N Engl J Med. [PMID: 36876753]*
CHAPTER 11: HEART FAILURE & CARDIOMYOPATHY		
Heart Failure	397	• Resynchronization therapy is indicated for patients with class II to III HF, EF of 35% or less, sinus rhythm, and left bundle branch block pattern with QRS duration of 150 msec or more. *Heidenreich PA et al. J Am Coll Cardiol. [PMID: 35379503]*
	398	• Both empagliflozin and dapagliflozin have been shown to decrease cardiovascular mortality and HF hospitalization or worsening of HF in patients with HFpEF. *Kosiborod MN et al. N Engl J Med. [PMID: 37622681]*
Restrictive Cardiomyopathy	409	• Tafamidis, the only FDA-approved medication available for all ATTR cardiomyopathy, reduced the composite of all-cause mortality and cardiovascular hospitalizations in trials. *Writing Committee: Kittleson MM et al. J Am Coll Cardiol. [PMID: 36697326]*

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
CHAPTER 12: DISORDERS OF CARDIAC RHYTHM		
Atrial Fibrillation	420	• In patients with atrial fibrillation and no clinical risk factors (CHA_2DS_2-VASc score 0), there is no indication for anticoagulant or antithrombotic therapy. In general, unless there is an indication for antiplatelet therapy (CHD, peripheral vascular disease), patients with atrial fibrillation should not be prescribed aspirin for stroke prevention.
	422	• In patients with atrial fibrillation duration of greater than 48 hours (or unknown), a minimum of 3 weeks of anticoagulation or exclusion of left atrial thrombus by TEE pre-cardioversion is required. Anticoagulation should be continued for at least 4 weeks following cardioversion to prevent thromboembolism. • In patients with prior left atrial appendage occlusion, TEE is recommended to exclude device-related thrombus or peri-device leak which may prompt anticoagulant initiation. *Joglar J et al. Circulation. [PMID: 38033089]*
Syncope	429	• Cardioneuroablation in patients with vasovagal syncope with significant cardioinhibitory response significantly decreased recurrent syncope compared to medical therapy in a small RCT. *Piotrowski R et al. JACC Clin Electrophysiol. [PMID: 36114133]*
CHAPTER 13: SYSTEMIC HYPERTENSION		
Drug Therapy: Current Antihypertensive Agents	452	• "Polypills" combining multiple drugs in a single pill are effective and well tolerated in initial treatment of hypertension. *O'Hagan ET et al. Heart. [PMID: 36810213]*
	452	• Cardiovascular and renal outcomes in type 2 diabetes are improved with GLP-1 agonists despite modest reductions in blood pressure. • SGLT-2 inhibitors increase the risk of diabetic ketoacidosis in type 1 diabetes. *Tonelli M et al. Circulation. [PMID: 36409780]* *Neuen BL et al. Circulation. [PMID: 37952217]*
CHAPTER 15: BLOOD DISORDERS		
Chronic Lymphocytic Leukemia	519	• Caution should be exercised when a Bruton's Tyrosine Kinase inhibitor (BTKi) is used in conjunction with anticoagulants (DOACs) and in the pre- and postoperative setting. *Chirino A et al. Genes (Basel). [PMID: 38137005]*
Cold Agglutinin Disease	504	• Complement blockade of the C1s protein with sutimlimab (a monoclonal protein) is now FDA-approved for cold agglutinin hemolysis. *Röth A et al. Engl J Med. [PMID: 33826820]*
Hairy Cell Leukemia	521	• Vemurafenib in combination with an anti-CD20 antibody can be used as initial therapy for patients who are frail or have active infections. The next generation BRAF inhibitor, dabrafenib, in combination with trametinib, can be used for patients refractory to initial nucleoside analogue–based therapy. *Kreitman R et al. Blood. [PMID: 36108341]*
Non-Hodgkin Lymphomas	523	• The CD20:CD3 bispecific antibodies epcoritamab and glofitamab have shown clinical activity in patients who have progressed after two lines of therapy.
Primary Myelofibrosis	512	• The newer JAK2 inhibitor pacritinib is an option for patients with a platelet count less than 50,000/mcL (50×10^9/L). • RAS/CBL mutations predict resistance to ruxolitinib therapy. *Tefferi A. Am J Hematol. [PMID: 36680511]*

*See chapter for further details and references.

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Topic	Page Number	Key New Advances Affecting Clinical Practice*
Sickle Cell Anemia & Related Syndromes	501	• Two genetically engineered stem cell products used with autologous transplantation, lovotibeglogene autotemcel and exagamglogene autotemcel, are approved in the United States for patients 12 years or older with severe disease and offer the potential for long-term disease control. *Kanter J et al. N Engl J Med. [PMID: 34898139]*
CHAPTER 16: DISORDERS OF HEMOSTASIS, THROMBOSIS, & ANTITHROMBOTIC THERAPY		
Antithrombotic Therapy	562–563	• The American Society of Hematology suggests consideration of thrombophilia testing in patients with VTE provoked by a non-surgical transient risk factor, in patients who had VTE associated with pregnancy or the post-partum period, and in patients with VTE associated with oral contraceptives, when negative results might lead to consideration of stopping treatment. *Middeldorp S et al. Blood Adv. [PMID: 37195076]*
CHAPTER 17: GASTROINTESTINAL DISORDERS		
Benign Esophageal Lesions	605	• The Baveno VII international consensus group favors carvedilol over other nonselective beta-blockers due to its anti-alpha-adrenergic effects, which promote vasodilation and a greater reduction in portal pressures. It is initiated at a dose of 6.25 mg orally once daily and increased, as tolerated, to a maximum of 12.5 mg once daily provided the systolic blood pressure remains greater than 90 mm Hg. Carvedilol is not recommended for patients with decompensated cirrhosis. *De Franchis R et al. J Hepatol. [PMID: 35120736]* *Pierre-Emmanuel R et al. Clin Gastroenterol Hepatol. [PMID: 37121529]* *Tapper EB et al. JAMA. [PMID: 37159031]*
Gastroesophageal Reflux Disease	599	• Vonoprazan (20 mg orally once daily) may be considered in patients with erosive esophagitis or persistent nocturnal heartburn that is unresponsive to PPI therapy. *Laine L et al. Gastroenterology. [PMID: 36228734]*
Inflammatory Bowel Disease	638	• FDA has issued a black box warning for tofacitinib and upadacitinib about an increased risk of thrombosis, including MI, stroke, arterial thrombosis, DVT, PE, and death.
	639	• In 2023, a new subcutaneous formulation of infliximab became available. *Buisson A et al. Clin Gastroenterol Hepatol. [PMID: 35987302]*
	639	• Vedolizumab is approved for administration as both an intravenous and subcutaneous formulation. *Lim SH et al. Inflamm Bowel Dis. [PMID: 37603730]*
Crohn Disease	645	• In a 2023 head-to-head controlled trial, patients with Crohn disease who had not responded to prior anti-TNF therapies were randomized to induction and maintenance therapy with either risankizumab (360 mg subcutaneously every 8 weeks) or ustekinumab (90 mg subcutaneously every 8 weeks). After 48 weeks, clinical remission (61% versus 40%) and endoscopic remission (32% versus 16%) were significantly higher with risankizumab than ustekinumab, suggesting risankizumab may be the preferred anti-IL agent.
	645	• In a 2023 network meta-analysis of biologic and small molecule therapies, risankizumab ranked first in efficacy for patients with Crohn disease who had or had not received prior biologic therapies. *Barberio B et al. Gut. [PMID: 35907636]*
	645	• For patients who have not responded or lost response to anti-TNF agents, vedolizumab appears to be less effective than anti-IL agents (risankizumab or ustekinumab).

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
Crohn Disease (*cont.*)	645	• In 2023, the oral JAK inhibitor upadacitinib was approved for induction and maintenance therapy for Crohn disease. • Network meta-analyses suggest upadacitinib may be equivalent to biologic agents in the treatment of Crohn disease and offers the convenience of oral therapy. However, in light of the uncertain risks of JAK inhibitors for serious complications (including thrombosis, cardiovascular events, and malignancy), upadacitinib should be reserved for patients who have failed biologic therapies. *Barberio B et al. Gut. [PMID: 35907636]* *Loftus EV et al. N Engl J Med. [PMID: 37224198]*
Ulcerative Colitis	651	• Subcutaneous formulations of vedolizumab and infliximab are available for maintenance therapy but are not approved for induction therapy.
	651	• Despite the convenience and rapid symptom response of oral small molecules, the injectable IL antagonists (mirikizumab and ustekinumab) offer a superior safety profile, especially in patients who are older or have an increased risk of cardiovascular or thrombosis events. *D'Haens G et al. N Engl J Med. [PMID: 37611136]*
	640	• Mirikizumab was approved in 2023 for the treatment of patients with moderate to severe ulcerative colitis; it, along with another IL antibody, ustekinumab, is available as intravenous formulation for induction therapy and as a subcutaneous formulation for maintenance therapy. *D'Haens G et al. N Engl J Med. [PMID: 37611136]*
	651	• The small model JAK inhibitors (upadacitinib and tofacitinib) offer the convenience of oral administration and rapid symptom improvement within 3 days. Furthermore, network meta-analyses suggest these agents are highly effective in achieving disease remission in patients who have failed therapy with biologic agents.
	651	• The small molecule S1P receptor modulator and once-daily oral agent etrasimod was approved by the FDA in 2023 for the treatment of moderate to severe ulcerative colitis. *Sandborn WJ et al. Lancet. [PMID: 36871574]*
CHAPTER 18: LIVER, BILIARY TRACT, & PANCREAS DISORDERS		
Acute Pancreatitis	720	• Statin use may reduce the risk of diabetes. *Thiruvengadam NR et al. Clin Gastroenterol Hepatol. [PMID: 35750248]*
Benign Liver Neoplasms	708	• Focal nodular hyperplasia is not caused by contraceptives. *Demory A et al. Hepatology. [PMID: 35980227]*
Metabolic Dysfunction–Associated Liver Disease	690	• In 2024, the FDA granted accelerated approval to resmetirom, a thyroid hormone receptor-beta-agonist, for patients with MASH and fibrosis. *Harrison SA et al. N Engl J Med. [PMID: 38324483]*
CHAPTER 19: BREAST DISORDERS		
Carcinoma of the Female Breast	730–731	• Low-dose tamoxifen (5 mg daily for 3 years) is an effective risk-reducing strategy in women with proliferative atypia or carcinoma in situ. *Lazzeroni M et al. J Clin Oncol. [PMID: 36917758]*
	731	• The USPSTF recommends screening mammography every other year beginning at age 40 years. (https://www.uspreventiveservicestaskforce.org/uspstf/draft-recommendation/breast-cancer-screening-adults#bcei-recommendation-title-area)

*See chapter for further details and references.

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Topic	Page Number	Key New Advances Affecting Clinical Practice*
Carcinoma of the Female Breast (*cont.*)	739	• It may be appropriate to treat multiple tumors or even recurrent tumors in the same breast with breast-conserving therapy. *Mota BS et al. Cochrane Database Syst Rev. [PMID: 36972145]* *Youn S et al. Ann Surg Oncol. [PMID: 37620525]*
	739	• One phase 3 study showed that omission of lymph node sampling is noninferior to sentinel node biopsy in patients with T1 tumors and negative axillary ultrasound, thus supporting further surgical de-escalation in select cases. *Gentilini OD et al. JAMA Oncol. [PMID: 37733364]*
	740	• Recent studies suggest that even younger women with favorable lesions may avoid post-lumpectomy radiation. *Civil YA et al. Ann Surg Oncol. [PMID: 36869253]* *Whelan TJ et al. N Engl J Med. [PMID: 37585627]*
	741	• Adding an immune checkpoint inhibitor to chemotherapy improves the pCR rate in high-grade hormone-receptor–positive cancers. *Cardoso F et al. Presented at ESMO Conference 2023. Abstract LBA21.* *Loi S et al. Presented at ESMO Conference 2023. Abstract LBA20.*
	746	• The oral AKT inhibitor capivasertib is FDA approved for patients with HR-positive metastatic breast cancer and a tumor with a *PIK3CA*, *AKT1* or *PTEN* alteration. *Turner NC et al. N Engl J Med. [PMID: 37256976]*
CHAPTER 20: GYNECOLOGIC DISORDERS		
Carcinoma of the Endometrium	780	• Molecular subtyping may inform treatment decisions. *Karpel HC et al. Curr Opin Obstet Gynecol. [PMID: 36943683]*
Pelvic Inflammatory Disease	775	• Procedural intervention is reserved for cases of large tubo-ovarian abscess (TOA) (> 8 cm), TOA rupture, or cases with a poor response to antibiotics. Interventional radiology drainage may be considered after TOA antibiotic failure or for large (> 8 cm) TOA. *Frock-Welnak DN et al. Obstet Gynecol Clin North Am. [PMID: 36122985]*
CHAPTER 25: UROLOGIC DISORDERS		
Benign Prostatic Hyperplasia	956	• A 5-year multi-center clinical trial of aquablation shows significant and sustained improvements in urinary flow rate, postvoid residual volume, and quality of life. *Zorn KC et al. BJUI Compass. [PMID: 35474721]*
	957	• A double-blind, randomized, sham-controlled study of the Optilume BPH catheter system showed improvement in flow rate, post-void residual, and patient satisfaction scores that were sustained at 1 year. Treatment was limited to prostates ranging in size from 20 mL to 80 mL and long-term benefit has yet to be proven. *Kaplan SA et al. J Urol. [PMID: 37555604]*
CHAPTER 26: NERVOUS SYSTEM DISORDERS		
Dementia	1004	• Lecanemab (10 mg/kg intravenously every 2 weeks) modestly slowed cognitive decline in patients with early Alzheimer disease and reduced brain amyloid burden measured by amyloid PET compared with placebo. *Van Dyck CH et al. N Engl J Med. [PMID: 36449413]*

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
Multiple Sclerosis	1012	• Patients without a typical clinical attack may be diagnosed with *radiologically isolated syndrome* if a brain MRI incidentally demonstrates findings consistent with multiple sclerosis. Teriflunomide and dimethyl fumarate were shown to delay time to first clinical attack compared to placebo in such patients. *Lebrun-Frénay C et al. JAMA Neurol. [PMID: 37603328]* *Okuda DT et al. Ann Neurol. [PMID: 36401339]*
Myopathic Disorders	1033	• Patients who weigh ≥ 40 kg and are not improving on initial enzyme replacement therapy [for acid maltase deficiency or Pompe disease] are eligible for treatment with the combination of cipaglucosidase alfa-atga and miglustat, which demonstrated similar efficacy to alglucosidase alfa in a randomized trial. *Schoser B et al. J Neurol. [PMID: 38418563]*
Parkinson Disease	996	• A continuous subcutaneous infusion of foslevodopa-foscarbidopa also reduces "off" time and improves the amount of "on" time without troublesome dyskinesias. *Jankovic J et al. J Neurol Neurosurg Psychiatry. [PMID: 32576618]*
Polyneuropathies & Mononeuritis Multiplex	1019	• An implanted 10 kHz spinal cord stimulator combined with medical management reduced pain by an average of 80% in a RCT in patients with painful diabetic neuropathy, a result that was sustained for 24 months and was also associated with neurologic improvement in most patients. *Petersen E et al. Diabetes Res Clin Prac. [PMID: 37536514]*
Stupor & Coma	1008	• An electroencephalogram, even when combined with brainstem auditory and somatosensory evoked potentials, does not fully evaluate brainstem function and should *not* be used to make a formal determination of brain death. *Greer DM et al. Neurology. [PMID: 37821233]*
CHAPTER 27: PSYCHIATRIC DISORDERS		
Alcohol Use Disorder	1075	• Phenobarbital and, most recently, ketamine, have not demonstrated superiority to benzodiazepines in the treatment of alcohol withdrawal. *Kelson M et al. Cureus. [PMID: 37273364]* *Malone D et al. Neuropsychopharmacol Rep. [PMID: 37368937]*
Anxiety	1040	• Virtual reality therapy has similar efficacy to other established therapies. *Schröder D et al. J Behav Ther Exp Psychiatry. [PMID: 37453405]*
CHAPTER 28: ENDOCRINE DISORDERS		
Hyperthyroidism (Thyrotoxicosis)	1111–1112	• Digoxin is a second-line agent for ventricular rate control in thyrotoxicosis-induced atrial fibrillation. It is reduced as hyperthyroidism is corrected. Serum digoxin levels should be kept below 1.2 ng/mL, since higher levels are associated with increased mortality.
Osteoporosis	1133	• Patients with severe osteoporosis (DXA T-score below –2.5 with a fragility fracture) should be considered for anabolic therapy with PTH, PTHrP, or romosozumab. *Händel MN et al. BMJ. [PMID: 37130601]*
	1135	• In 2024, the FDA issued a black box warning about the risk of severe hypocalcemia with denosumab in patients with advanced CKD, especially those with related mineral bone disorder. *Bird ST et al. JAMA. [PMID: 38241060]*

*See chapter for further details and references.

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Topic	Page Number	Key New Advances Affecting Clinical Practice*
Thyroid Cancer	1119	• Levothyroxine is no longer prescribed for euthyroid patients with low-risk differentiated thyroid cancer (DTC) who have had a unilateral thyroid lobectomy. *Gigliotti BJ et al. Endocrine. [PMID: 37824045]*
	1119	• For patients with low-risk differentiated thyroid carcinoma (DTC), radioiodine is no longer recommended either for thyroid remnant ablation or as adjuvant therapy following total or near-total thyroidectomy. *Ullmann TM et al. J Clin Endocrinol Metab. [PMID: 36327392]*
Thyroid Nodules & Multinodular Goiter	1115	• When cytopathology is indeterminate for malignancy, molecular testing reduces the need for surgery by about 50%. *Alzahrani AS. J Clin Endocrinol Metab. [PMID: 37200449]*
CHAPTER 29: DIABETES MELLITUS & HYPOGLYCEMIA		
Diabetes Mellitus	1199	• Insulin delivery systems (eg, MiniMed 7870 G, Tandem Control-IQ, Omnipod 5) should be considered for all patients with type 1 diabetes who are no longer in partial clinical remission. Patients with other types of diabetes who have labile glucose levels and are on intensive insulin therapy are also candidates (eg, after total pancreatectomy).
	1199	• V-go (MannKind) is a mechanical patch pump designed specifically for patients with type 2 diabetes who use a basal/bolus insulin regimen. CeQur Simplicity (CeQur) is a 3-day mechanical patch device that holds 200 units of rapid-acting insulin and delivers two units per press of a button to cover meals and to lower high-glucose excursions.
CHAPTER 30: LIPID DISORDERS		
Screening & Treatment in Patients with HIV	1228	• The striking results of the REPRIEVE cardiovascular outcomes trial, in which baseline LDL was just 108 mg/dL, argues for routine statin therapy for nearly all patients with HIV who have no contraindications. Treatments with pitavastatin may have less drug-drug interactions than certain other statins (ie, simvastatin). *Grinspoon SK et al. N Engl J Med. [PMID: 37486775]* *Kalra DK et al. J Am Coll Cardiol. [PMID: 37407116]*
CHAPTER 31: NUTRITION, NUTRITIONAL DISORDERS, & OBESITY		
Obesity	1238	• In the 2023 SELECT cardiovascular outcomes trial, semaglutide 2.4 mg reduced the risk of major adverse cardiovascular events (MACE) by 20% in adults aged 45 and older with preexisting cardiovascular disease who were overweight (BMI greater than 27) but who did not have type 2 diabetes. This is the first AOM to demonstrate reduced incidence of MACE in patients without diabetes. *Lincoff AM et al. N Engl J Med. [PMID: 37952131]* *Wilding JPH et al. N Engl J Med. [PMID: 33567185]*
	1238, 1242	• In the SURMOUNT-1 trial, tirzepatide 15 mg weekly produced a 20.9% total body weight loss compared to 3.1% with placebo. Tirzepatide is associated with the same contraindications, adverse events, and boxed warnings as liraglutide and semaglutide but is typically better tolerated. *Aronne LJ et al. JAMA. [PMID: 38078870]* *Jastreboff AM et al. N Engl J Med. [PMID: 35658024]*
CHAPTER 33: HIV INFECTION & AIDS		
Choosing an Antiretroviral Treatment Regimen	1335	• Demonstration projects are examining long-acting cabotegravir and rilpivirine as injectables in people challenged by adherence or viremi, with high virologic suppression achieved in one demonstration project in San Francisco, with 97.5% virologic suppression projected. *Gandhi M et al. Ann Intern Med. [PMID: 37399555]*

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
Prevention	**1320**	• Studies demonstrating the efficacy of doxycycline post-exposure prophylaxis (DoxyPEP) among MSM and transgender women with and without HIV (single 200 mg dose after sex up to 72 hours) have shown it effective in preventing chlamydia and syphilis, and in one study, gonorrhea. The study among HIV-negative cisgender women did not show efficacy, although adherence was low in this study. *Luetkemeyer AF. N Engl J Med. [PMID: 37018493]*
CHAPTER 34: VIRAL & RICKETTSIAL DISEASES		
Dengue	**1382**	• TAK-003 has efficacy against all four dengue serotypes in children 4-16 years old living in endemic countries who are seropositive at baseline and against serotypes 1 and 2 in children who are seronegative at baseline. *Patel SS et al. Clin Infect Dis. [PMID: 35639602]*
Herpes Zoster	**1346–1347**	• Available evidence suggests that vaccination with the recombinant zoster vaccine significantly reduces the duration of herpes zoster-related pain. *Wang Y et al. Eur J Dermatol. [PMID: 37823492]*
Human T-Cell Lymphotropic Virus (HTLV)	**1375**	• Combination therapy with zidovudine and interferon-alpha may be helpful. *Shafiee A et al. Virol J. [PMID 37287047]*
	1376	• A Japanese trial showed that l-arginine may improve motor function. *Nozuma S et al. Ann Clin Transl Neurol. [PMID: 36547017]*
Kawasaki Disease	**1427**	• In a Cochrane review IVIG was most effective in controlling fever but also in reducing coronary artery aneurysm incidence at 30 days. *Broderick C et al. Cochrane Database Syst Rev. [PMID: 36695415]*
	1428	• Exercise stress echocardiograms are especially sensitive in assessing myocardial dysfunction. *Tedla BA et al. Pediatr Cardiol. [PMID: 36383234]*
Measles	**1356**	• Data on febrile convulsions after vaccination show a slightly increased risk associated with MMRV over MMR vaccination separate from vaccinia vaccination but with the statistical weakness of the association, experts recommend that the two be separated only when there is an indication such as a family history of convulsions. *Casabona G et al. Expert Rev Vaccines. [PMID: 37642012]*
Mumps	**1358**	• A new live attenuated mumps vaccine is reported from China, and it appears to be safe and effective. *Hu W et al. PLoS One. [PMID: 37733724]*
Q Fever	**1425**	• For children under age 8 years, ciprofloxacin-based therapy is preferred, combined with rifampin or trimethoprim/sulfamethoxazole. • Because of adverse reactions among recipients with a prior exposure to *C burnetii*, the Q fever vaccine should never be used as a booster. *Peng M et al. Microbes Infect. [PMID: 37499790]* *Redden P et al. Future Microbiol. [PMID: 37850346]*
Respiratory Syncytial Virus (RSV) & Other Paramyxoviruses	**1398**	• In 2023, major advances in combatting RSV occurred, with two RSV vaccines being approved for individuals 60 years and older (Arexvy) and for pregnant women between 32- and 36-weeks' gestation (Abrysvo) to protect the neonate. • A monoclonal antibody for RSV (nirsevimab) was also approved for infants and young children for severe disease. Nirsevimab is currently available in the United States, Europe, and the United Kingdom for prevention of RSV in neonates during their first season at risk (and extended in the United States through their second at-risk season). Physicians have the option of providing Abrysvo to the mother and relying on passively transmitted antibody to protect infants, or using nirsevimab for infants. *Centers for Disease Control: Update on RSV and new vaccine recommendations. 2023 Sept 23.* *Keam SJ. Drugs. [PMID: 36577878]* *Papi A et al. N Engl J Med. [PMID: 36791160]* *Walsh EE et al. N Engl J Med. [PMID: 37018468]*

*See chapter for further details and references.

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Topic	Page Number	Key New Advances Affecting Clinical Practice*
Rubella	1359	• Vaccination outside the recommended age range (greater than age 7) is effective. *Pawaskar M et al. Hum Vaccin Immunother. [PMID: 34128759]*
Scrub Typhus	1419	• A RCT comparing doxycycline, azithromycin and both for severe scrub typhus showed no difference between doxycycline and azithromycin but noted lower incidence of primary outcome (composite 28-day mortality, complications at day 7 and persistent fever at day 5) with combination therapy. *Varghese GM et al. N Engl J Med. [PMID: 36856615]*
Seasonal Influenza	1401	• The new recommendation for those with egg allergy is that only those with urticarial reactions should be observed closely, but all vaccinated patients should be followed for possible reactions regardless of egg allergy history. *Grohskopf LA et al. MMWR Recomm Rep. [PMID: 36006864]*
Severe Acute Respiratory Syndrome—Coronavirus 2019 (SARS-CoV-2)	1393	• Treatment with nirmatrelvir/ritonavir does not reduce the incidence of long-COVID in a small study, although the RECOVER-VITAL trial is studying whether a longer course of the medication will reduce long-COVID symptoms. *Durstenfeld MS et al. J Med Virol. [PMID: 38175151]*
	1393	• Nirmatrelvir/ritonavir had no benefit in two trials (EPIC-SR and EPIC-PEP). In one study of elderly patients from Massachusetts and New Hampshire, however, the medication reduced hospitalization and death among outpatients by one-half. • A low rate of recurrent viremia is reported after nirmatrelvir/ritonavir is stopped, most likely from the immune response. Delaying the medication for 2 days after symptom onset will likely reduce the risk of rebound. *Dryden-Peterson S et al. Ann Intern Med. [PMID: 36508742]* *Edelstein GE et al. medRxiv [Preprint]. Update in Ann Intern Med. [PMID: 37425934]*
	1394	• In one VA study molnupiravir showed a benefit for mortality at both 30 and 30-180 days but not for hospitalization (unlike nirmatrelvir/ritonavir which did show a 30-day benefit for hospitalization). *Bajema KL et al. Ann Intern Med. [PMID: 37276589]*
	1394	• On March 1, 2024, the CDC updated their isolation guidance again to recommend people with COVID stay home when sick or until symptoms have resolved for 24 hours.
	1394–1395	• Population-level masking probably made little or no difference to the outcome of laboratory-confirmed influenza or SARS-CoV-2 compared to not wearing masks (RR 1.01, 95% CI 0.72 to 1.42; 6 trials, 13,919 participants; moderate-certainty evidence). However, compliance to mask wearing varied across randomized trials and an individual-level benefit of face masks could certainly still be present. *Jefferson T et al. Cochrane Database Syst Rev. [PMID: 36715243]*
	1395	• The WHO and most countries recommend ongoing boosters for older and immunosuppressed groups given their continued vulnerability to severe disease and death if infected.
	1396	• In general, the neurologic safety profile of COVID-19 vaccinations is high. *Guo M et al. Autoimmun Rev. [PMID: 37075917]*
Viruses & Gastroenteritis	1411	• A meta-analysis of 15 randomized controlled studies shows no statistically significant increase in intussusception with rotavirus vaccination. *Wang G et al. Front Pediatr. [PMID: 37583623]*

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
CHAPTER 35: BACTERIAL & CHLAMYDIAL INFECTIONS		
Infective Endocarditis	1445	• The 2023 Duke-International Society for Cardiovascular Infectious Disease (ISCVID) criteria establish a diagnosis of endocarditis by pathologic criteria in the context of clinical signs of endocarditis. *Fowler VG et al. Clin Infect Dis. [PMID: 37138445]*
Mycoplasma Genitalium	1460	• Routine screening for *M genitalium* is not recommended, but testing should be pursued in individuals with symptoms of persistent or recurrent urethritis/cervicitis. • Antibiotic resistance is common, and treatment requires two different antibiotics used in sequential order. When *M genitalium* resistance testing is not available, the recommended treatment consists of doxycycline 100 mg orally twice per day for 7 days (to reduce *M genitalium* bacterial load), followed by moxifloxacin 400 mg daily by mouth for another 7 days. If resistance testing is available and the organism retains macrolide sensitivity, treatment can instead be with doxycycline 100 mg orally twice daily for 7 days followed by azithromycin (1 g orally on day 1, followed by 500 mg orally once per day for 3 more days). • Sex partners of patients with confirmed *M genitalium* infections should be tested for *M genitalium* and provided treatment if their test results are positive. • Neither doxycycline nor moxifloxacin are recommended for use in pregnant people, so *M genitalium* treatment decisions in pregnancy are made on a case-by-case basis, considering symptom severity, patient preferences, and risk/benefit discussions. *Workowski KA et al. MMWR Recomm Rep. [PMID: 34292926]*
Plague	1457	• Combination therapy with two different classes of antimicrobials is recommended for the initial treatment of patients with severe pneumonic or septicemic plague. *Centers for Disease Control and Prevention. Resources for clinicians: plague. Available at: https://www.cdc.gov/plague/healthcare/clinicians.html. Accessed 10 Dec 2023.*
CHAPTER 36: SPIROCHETAL INFECTIONS		
Lyme Disease	1484	• The Infectious Diseases Society of America guidelines recommend 10 days of doxycycline treatment while a European study demonstrated efficacy with 7 days of treatment. *Stupica D et al. Lancet Infect Dis. [PMID: 36209759]*
CHAPTER 37: PROTOZOAL & HELMINTHIC INFECTIONS		
African Trypanosomiasis	1488	• Acoziborole has demonstrated effective and simpler single dose oral therapy for West African disease and may soon be available. *Kumeso VKB et al. Lancet Infect Dis. [PMID: 36460027]*
Leishmaniasis	1492	• In East Africa, paromomycin plus miltefosine, a simpler regimen than sodium stibogluconate plus paromomycin, has demonstrated equivalent efficacy. Liposomal amphotericin B may be considered in older adults or pregnant women due to toxicity concerns. *Musa AM. Clin Infect Dis. [PMID: 36164254]*
	1492	• In Brazil, the use of intralesional meglumine antimoniate for cutaneous leishmaniasis was as effective and better tolerated than systemic therapy with the drug. *Lyra MR et al. Clin Infect Dis. [PMID: 37100061]*
Onchocerciasis	1522	• As with lymphatic filariasis, combination drug therapy with ivermectin, diethylcarbamazine, and albendazole offers improved long-term clearance of parasites. *Opoku NO et al. PLoS Negl Trop Dis. [PMID: 37205721]*

*See chapter for further details and references.

(continued on following page)

Topic	Page Number	Key New Advances Affecting Clinical Practice*
CHAPTER 41: CANCER		
Bladder Cancer	**1631**	• Nadofaragene firadenovec-vncg was FDA-approved this year for patients with high-risk BCG unresponsive non–muscle-invasive bladder cancer. This is the first approved gene therapy for bladder cancer.
	1632	• The recently reported EV302 trial showed dramatically improved survival rates with combination enfortumab vedotin and pembroluzamab over chemotherapy alone and may become the new standard of care in this setting. *Powles T et al. N Engl J Med. [PMID: 38446675]*
Bronchogenic Carcinoma	**1595**	• A phase 3 trial published in 2023 has shown that sublobar resection for patients with solitary primary tumors smaller than 2 cm achieves similar overall survival and disease-free survival compared to lobectomy. *Altorki N et al. N Engl J Med. [PMID: 36780674]*
	1595	• Atezolizumab or pembrolizumab (checkpoint inhibitors) can be given for 1 year post–adjuvant chemotherapy to patients with resected stage IB to IIIA NSCLC based on phase 3 trials showing improvement in disease-free survival compared with adjuvant chemotherapy without a checkpoint inhibitor. *Wakelee H et al. N Engl J Med. [PMID: 37272513]*
Carcinoma of the Biliary Tract	**1603**	• The combination of cisplatin and gemcitabine (now given with durvalumab) or capecitabine and gemcitabine prolongs survival in patients with locally advanced or metastatic cholangiocarcinoma. Second-line therapy is with FOLFOX (folinic acid, fluorouracil, and oxaliplatin). *Merters J et al. J Hepatol. [PMID: 36400328]*
Gastric Adenocarcinoma	**1610**	• A 2023 retrospective study of 716,567 patients with *H pylori* in a community-based population found a significant reduction after 8 years in the risk of gastric adenocarcinoma in those who were treated for *H pylori* versus those who were untreated (HR 0.37). *Li D et al. Gastroenterology. [PMID: 37142201]*
Hepatocellular Carcinoma	**1600**	• "Abbreviated" MRI, in which the number of sequences acquired is limited, is under study as a time- and cost-effective screening approach. *Ronot M et al. Hepatology. [PMID: 36896975]*
Prostate Cancer	**1626**	• The 2023 AUA/SUO guidelines on early detection of prostate cancer advise clinicians to engage in shared decision-making with men whom prostate cancer screening would be appropriate, incorporating the patient's values and preferences. This update provides important information for clinicians on deciding when to start screening men and how often. (See https://www.auanet.org/guidelines-and-quality/guidelines/early-detection-of-prostate-cancer-guidelines.) *Wei JT et al. J Urol. [PMID: 37096582]*
	1628	• The EMBARK clinical trial demonstrated improved metastasis-free survival with enzalutamide with or without ADT over ADT alone for men with PSA-recurrent, non-metastatic prostate cancer after primary therapy (radiation or prostatectomy) and rapid PSA doubling time of less than 9 months. *Freedland SJ et al. N Engl J Med. [PMID: 37851874]*
	1630	• Guidelines recommend genomics testing for all men with metastatic prostate as men who are found to have specific germline or somatic pathogenic variants may benefit from personalized treatment strategies. *Tuffaha H et al. Prostate Cancer Prostatic Dis. [PMID: 37202470]*

*See chapter for further details and references.

Topic	Page Number	Key New Advances Affecting Clinical Practice*
Renal Cell Carcinoma	1635	• Most recently, cabozantinib in combination with nivolumab and ipilimumab showed improved progression-free survival in patients with intermediate and poor prognostic risk advanced renal cell carcinoma over nivolumab or ipilimumab alone. Combination therapy with two or three agents is considered standard first-line treatment for metastatic RCC. *Choueiri TK et al. N Engl J Med. [PMID: 37163623]*
CHAPTER 43: ORTHOPEDIC DISORDERS & SPORTS MEDICINE		
Hip Fractures	1677	• Cemented total hip arthroplasty has clinically small to large improvements in health-related quality of life and lower mortality at 1 year compared to other hip replacement options. *Lewis SR et al. Cochrane Database Syst Rev. [PMID: 35156192]*
Lumbar Disc Herniation	1670	• A systematic review of 14 moderate quality studies suggests that percutaneous endoscopic discectomy and open microdiscectomy have similar results and complications. Patient-related risk factors for recurrent pain after percutaneous endoscopic discectomy, include age 50 years or older, Modic changes, obesity, no college education, diabetes, inappropriate manual labor, cigarette smoking, the protrusion type of lumbar disc herniation, and a factor related to the surgical experience of spinal surgeons. *Gadjradj PS et al. Spine (Phila Pa 1976). [PMID: 33290374]*
Neck Pain	1672	• Cervical branch radiofrequency ablation is a second-line treatment for chronic neck pain. *Hurley RW et al. Reg Anesth Pain Med. [PMID: 34764220]*
Spinal Stenosis	1669	• Minimally invasive lumbar decompression does not leave hardware in the spine and patients typically resume unrestricted normal activity within 24 hours. Percutaneous image-guided lumbar decompression uses minimally invasive techniques with instrumentation and image guidance to debulk thickened ligamentum flavum. *Deer TR et al. J Pain Res. [PMID: 35546905]* *Pryzbylkowski P et al. Pain Manag. [PMID: 34344197]*
Spine Problems	1667–1668	• Cognitive-behavioral therapy and other psychological interventions of even less than 10 hours' duration produce better outcomes than active physical treatment alone, with post-treatment improvements in pain intensity in the short term and in the long term. *Hochheim M et al. Pain Pract. [PMID: 36565010]*

*See chapter for further details and references.

COMMONLY USED ACRONYMS & ABBREVIATIONS

AAA	Abdominal aortic aneurysm
ABG	Arterial blood gas
ACE	Angiotensin-converting enzyme
ACS	Acute coronary syndrome
ACTH	Adrenocorticotropic hormone
AKI	Acute kidney injury
ALT	Alanine aminotransferase
ANA	Antinuclear antibodies
ARB	Angiotensin receptor blocker
AST	Aspartate aminotransferase
ATN	Acute tubular necrosis
BMI	Body mass index
BNP	B-type natriuretic peptide
BPH	Benign prostatic hypertrophy
BUN	Blood urea nitrogen
CAD	Coronary artery disease
CBC	Complete blood count
CDC	Centers for Disease Control and Prevention
CHD	Coronary heart disease
CI	Confidence interval
CKD	Chronic kidney disease
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computed tomography or computed tomographic
CVD	Cardiovascular disease
CVP	Central venous pressure
CXR	Chest radiograph
D_{LCO}	Diffusing capacity for carbon monoxide
DOAC	Direct-acting oral anticoagulant
DSM-5	*Diagnostic Statistical Manual*, 5e
DVT	Deep venous thrombosis
ECG	Electrocardiogram; electrocardiography
EF	Ejection fraction
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
ESKD	End-stage kidney disease
ESR	Erythrocyte sedimentation rate
FEV_1	Forced expiratory volume in 1 second
FSH	Follicle-stimulating hormone
FVC	Forced vital capacity
GERD	Gastroesophageal reflux disease
GFR	Glomerular filtration rate
GI	Gastrointestinal
GLP-1	Glucagon-like peptide-1
HCC	Hepatocellular carcinoma
HDL	High-density lipoprotein
HF	Heart failure
HPV	Human papillomavirus
HRCT	High-resolution computed tomography
IBD	Inflammatory bowel disease
ICD-11	International Classification of Diseases, 11e
ICU	Intensive care unit
INR	International normalized ratio
IUD	Intrauterine device
LD	Lactate dehydrogenase
LDL	Low-density lipoprotein
LH	Luteinizing hormone
LR	Likelihood ratio
LV	Left ventricle or left ventricular
LVEDP	Left ventricular end-diastolic pressure
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
MAO	Monoamine oxidase inhibitor
MI	Myocardial infarction
MMR	Measles, mumps, rubella
MRI	Magnetic resonance imaging
NIH	National Institutes of Health
NSAIDs	Nonsteroidal anti-inflammatory drugs
nSTEMI	Non–ST-segment elevation myocardial infarction
OCD	Obsessive-compulsive disorder
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PEF	Peak expiratory flow
PET	Positron emission tomography
PFTs	Pulmonary function tests
PPI	Proton pump inhibitor
PSA	Prostate-specific antigen
RBC	Red blood cell
RCT	Randomized controlled trial
RSV	Respiratory syncytial virus
RV	Right ventricle or right ventricular
RVH	Right ventricular hypertrophy
SGLT-2	Sodium-glucose cotransporter-2
SIADH	Syndrome of inappropriate antidiuretic hormone
SLE	Systemic lupus erythematosus
SSRI	Selective serotonin reuptake inhibitor
STEMI	ST-segment elevation myocardial infarction
STI	Sexually transmitted infection
TLC	Total lung capacity
TNF	Tumor necrosis factor
TSH	Thyroid-stimulating hormone
UA	Urinalysis
US FDA	United States Food and Drug Administration
USPSTF	United States Preventive Services Task Force
UTI	Urinary tract infection
VTE	Venous thromboembolism
WBC	White blood cell
WHO	World Health Organization

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Disease Prevention & Health Promotion

1

Michael Pignone, MD, MPH[1]

GENERAL APPROACH TO THE PATIENT

The medical interview serves several functions. It is used to collect information to assist in diagnosis (the "history" of the present illness), to understand patient values and goals, to assess and communicate prognosis, to establish a therapeutic relationship, and to reach agreement with the patient about further diagnostic procedures and therapeutic options. It also serves as an opportunity to influence patient behavior, such as in motivational discussions about smoking cessation or medication adherence. Interviewing techniques that promote shared decision making increase patient involvement and satisfaction. Effective clinician-patient communication and increased patient involvement can improve health outcomes.

Patient Adherence

For many illnesses, successful prevention and treatment depend on difficult fundamental behavioral changes, including altering diet, taking up exercise, giving up smoking, cutting down drinking, wearing masks to prevent infection, and adhering to complex medication regimens. *Adherence* is a common problem; up to 50% of patients fail to achieve full adherence, and one-third never take their medicines. Many patients with medical problems, even those with access to care, do not seek appropriate care or may drop out of care prematurely. Adherence rates for short-term, self-administered therapies are higher than for long-term therapies and are inversely correlated with the number of interventions, their complexity and cost, and the patient's perception of overmedication.

As an example, in persons with HIV, adherence to antiretroviral therapy is a crucial determinant of treatment success. Studies have unequivocally demonstrated a close relationship between patient adherence and plasma HIV RNA levels, CD4 cell counts, and mortality. High adherence levels are needed to maintain virologic suppression. However, studies show that adherence varies over time, and inconsistent adherence is associated with incomplete viral suppression.

Patient reasons for suboptimal adherence include simple forgetfulness, being away from home, being busy, and changing daily routine. Other reasons include psychiatric disorders (depression or substance misuse), uncertainty about the effectiveness of treatment, lack of knowledge about the consequences of poor adherence, regimen complexity, and treatment side effects. The rising costs of medications, including generic medications, and the increase in patient cost-sharing burden have made adherence even more difficult, particularly for patients with lower incomes.

Patients seem better able to take prescribed medications than to adhere to recommendations to change their diet, exercise habits, or alcohol intake or to perform various self-care activities (such as monitoring blood glucose levels at home). For short-term regimens, adherence to medications can be improved by giving clear instructions. Writing out advice to patients, including changes in medication, may be helpful. Because low functional health literacy is common (almost half of English-speaking US patients are unable to read and understand standard health education materials), other forms of communication—such as illustrated simple text, videotapes, or oral instructions—may be more effective. Clinicians and health care delivery systems should provide culturally and linguistically appropriate health services.

To help improve adherence to long-term regimens, clinicians can work with patients to reach agreement on the goals for therapy, provide clear, concise information about the regimen, ensure understanding by using the "teach-back" method, counsel about the importance of adherence and how to organize medication-taking, reinforce self-monitoring, provide more convenient care, prescribe a simple dosage regimen for all medications (preferably no more than one or two doses daily), suggest ways to help in remembering to take doses (time of day, mealtime, alarms) and to keep appointments, prescribe lower-cost generic medications when available, and provide ways to simplify dosing (medication boxes). Single-unit doses supplied in foil wrappers can increase adherence but should be avoided for patients who have difficulty opening them. Medication

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boxes with compartments (eg, Medisets) that are filled weekly are useful. Devices can provide feedback to show patients whether they have taken doses as scheduled or to notify patients (or others) within a day if doses are skipped. Reminders, including cell phone text messages, are another effective means of encouraging adherence. The clinician can also enlist social support from family and friends, recruit an adherence monitor, provide a more convenient care environment with fewer barriers, and provide rewards and recognition for the patient's efforts to follow the regimen. Collaborative programs in which pharmacists help ensure adherence are also effective. Motivational interviewing techniques can be helpful when patients are ambivalent about their therapy.

Adherence is also improved when a trusting clinician-patient relationship has been established and when patients actively participate in their care. Clinicians can improve patient adherence by inquiring about specific behaviors and barriers in a nonjudgmental manner. When asked, many patients admit to incomplete adherence with medication regimens, plans for giving up cigarette smoking, or engaging only in "safer sex" practices. Although difficult, sufficient time must be made available for communication of health messages.

Medication adherence can be assessed generally with a single question: "In the past month, how often did you take your medications as your clinician prescribed?" Other ways of assessing medication adherence include pill counts and refill records; monitoring serum, urine, or saliva levels of medications or metabolites; watching for appointment nonattendance and treatment nonresponse; and assessing predictable medication effects, such as weight changes with diuretics or bradycardia from beta-blockers. In some conditions, even partial adherence, as with medication treatment of hypertension and diabetes mellitus, improves outcomes compared with nonadherence; in other cases, such as HIV antiretroviral therapy or tuberculosis treatment, partial adherence actually may be *worse* than complete nonadherence.

Guiding Principles of Care

Ethical practices are called for in medical care at both the "micro" level of the individual patient-clinician relationship and the "macro" level of allocation of resources or the adoption of infection-reducing public health interventions. Ethical principles that guide the successful approach to diagnosis and treatment are honesty, beneficence, justice, avoidance of conflict of interest, and the pledge to do no harm. Increasingly, Western medicine involves partnership with patients in important decisions about medical care, eg, which colorectal screening test to obtain or which modality of therapy for breast cancer or how far to proceed with treatment attempts for patients who have end-stage illnesses (see Chapter 5).

The clinician's role does not end with diagnosis and treatment. The importance of the empathic clinician in helping patients and their families face serious illness and death cannot be overemphasized. *"To cure sometimes, to relieve often, and to comfort always"* is a French saying as apt today as it was five centuries ago—as is Francis Peabody's admonition: *"The secret of the care of the patient is in caring for the patient."* Training to improve mindfulness and enhance patient-centered communication increases patient satisfaction and may also improve clinician satisfaction.

Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. HIV Surveillance Supplemental Report. 2021;26(No. 2). https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published May 2021. Accessed November 21, 2023.

Chan AHY et al. Effect of electronic adherence monitoring on adherence and outcomes in chronic conditions: a systematic review and meta-analysis. PLoS One. 2022;17:e0265715. [PMID: 35312704]

Daliri S et al. Medication-related interventions delivered both in hospital and following discharge: a systematic review and meta-analysis. BMJ Qual Saf. 2021;30:146. [PMID: 32434936]

Foley L et al. Prevalence and predictors of medication non-adherence among people living with multimorbidity: a systematic review and meta-analysis. BMJ Open. 2021;11:e044987. [PMID: 34475141]

Peh KQE et al. An adaptable framework for factors contributing to medication adherence: results from a systematic review of 102 conceptual frameworks. J Gen Intern Med. 2021;36:2784. [PMID: 33660211]

HEALTH MAINTENANCE & DISEASE PREVENTION

Preventive medicine can be categorized as primary, secondary, or tertiary. *Primary prevention* aims to remove or reduce disease risk factors (eg, immunization, giving up or not starting smoking). *Secondary prevention* techniques promote early detection of disease or precursor states (eg, routine cervical Papanicolaou screening to detect carcinoma or dysplasia). *Tertiary prevention* measures are aimed at limiting the impact of established disease (eg, partial mastectomy combined with radiation therapy to remove and control localized breast cancer).

Tables 1–1 and 1–2 show leading causes of death in the United States for 2022 and recent estimates of deaths from preventable causes from 2019. The 2022 data continue to demonstrate the large, though declining, impact of COVID-19 on mortality in the United States: over 244,000 COVID-associated deaths, of which over 186,000 deaths were attributed to COVID-19 as the principal cause.

Overall mortality rates remained high, generally driven by the effects of COVID-19 as well as increases in deaths from heart disease, unintentional injuries (including overdoses), and liver disease. Recent increases in mortality and decreased life expectancy have been larger in the United States than in Western European countries; this discrepancy has been driven partially by differences in COVID-19 mortality as well as ongoing trends in other midlife preventable mortality.

Many effective preventive services are underutilized, and few adults receive all of the most strongly recommended services. Several methods, including the use of provider or patient reminder systems (including interactive patient health records), reorganization of care

Table 1–1. Leading causes of death in the United States, 2022.

Category	Estimate
All causes	**3,273,705**
1. Heart disease	702,996
2. Cancer	608,340
3. Unintentional injuries	227,404
4. COVID-19	186,547
5. Stroke	165,389
6. Chronic lower respiratory diseases	147,362
7. Alzheimer disease	120,110
8. Diabetes mellitus	101,194
9. Kidney disease	57,931
10. Chronic liver disease and cirrhosis	54,815
11. Suicide	49,491
12. Influenza and pneumonia	47,040

Data from National Center for Health Statistics, 2023 (provisional).

environments to reduce barriers, and possibly provision of financial incentives to clinicians (though this remains controversial), can increase utilization of preventive services, but such methods have not been widely adopted.

Ahmad FB et al. COVID-19 mortality update—United States, 2022. MMWR Morb Mortal Wkly Rep. 2023;72:493. [PMID: 37141157]
Ahmad FB et al. Provisional mortality data—United States, 2022. MMWR Morb Mortal Wkly Rep. 2023;72:488. [PMID: 37141156]
Schöley J et al. Life expectancy changes since COVID-19. Nat Hum Behav. 2022;6:1649. [PMID: 36253520]

Table 1–2. Leading preventable causes of death in the United States, 2019.

Category	Estimate
Tobacco use	546,401
High blood pressure	495,201
High fasting plasma glucose	439,212
Dietary risks	418,350
High BMI	392,352
High LDL cholesterol	226,343
Impaired kidney function	214,740
Alcohol use	136,866
Non-optimal temperature	126,623
Drug use	104,141

Data from the US Burden of Disease Collaborators, 2021.

PREVENTION OF INFECTIOUS DISEASES

Much of the historic decline in the incidence and fatality rates of infectious diseases is attributable to public health measures—especially immunization, improved sanitation, nonpharmacologic interventions (eg, mask-wearing to prevent respiratory-transmissible conditions, improvements in indoor air quality), and better nutrition. This observation has been reinforced by the experience during the global COVID-19 pandemic.

Immunization remains the best means of preventing many infectious diseases. Recommended immunization schedules for children and adolescents can be found online at https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html, and the schedule for adults is at https://www.cdc.gov/vaccines/schedules/hcp/adult.html (see also Chapters 32 and 34). In addition to the severe toll in morbidity and mortality from COVID-19, substantial morbidity and mortality continue to occur from vaccine-preventable diseases, such as hepatitis A, hepatitis B, influenza, and pneumococcal infections. *The high incidence and mortality rates from COVID-19 and other recent outbreaks of vaccine-preventable diseases in the United States highlight the need to better understand vaccine hesitancy or refusal and methods for mitigating it.*

The Advisory Committee on Immunization Practices recommendations for the following vaccines appear in Table 1–3: influenza; MMR; 23-valent pneumococcal polysaccharide vaccine; tetanus, diphtheria, and acellular pertussis; hepatitis B; HPV; and the newly available RSV vaccine. Updated guidance for COVID-19 vaccination also is provided.

Persons traveling to countries where infections are endemic should take the precautions described in Chapter 32 and at https://wwwnc.cdc.gov/travel/destinations/list. Immunization registries—confidential, population-based, computerized information systems that collect vaccination data about all residents of a geographic area—can be used to increase and sustain high vaccination coverage.

Globally, COVID-19 has resulted in more than 6.9 million deaths through November 2023, including over 1.1 million in the United States. In addition to its tremendous overall health impact, the COVID-19 pandemic has revealed and exacerbated profound inequities in health and health care. In the United States, the COVID-19 mortality rates are higher in Black, Latina/Latino, and American Indian patients compared with White patients. Currently, the CDC recommends that everyone aged 6 months and older stay up to date with COVID-19 vaccination (through receiving a primary series and appropriate boosters) to help protect against COVID-19 (see Chapter 34 and Table 1–3) using one of the CDC-approved vaccines.

The USPSTF recommends **behavioral counseling** for adolescents and adults who are sexually active and at increased risk for STIs. Sexually active women aged 24 years or younger and older women who are at increased risk for infection should be **screened for chlamydia and gonorrhea**. Screening HIV-positive men or men who have sex with men for syphilis every 3 months is associated with improved syphilis detection.

Table 1–3. Advisory Committee on Adult Immunization Practices vaccine recommendations, 2023.

Vaccine	Recommendation	Comment
Influenza	Routine vaccination for all persons aged 6 months and older, including all adults. An alternative high-dose inactivated vaccine is available for adults aged 65 years and older.	When vaccine supply is limited, certain groups should be given priority, such as adults aged 50 years and older, individuals with chronic illness or immunosuppression, and pregnant women
COVID-19	Routine vaccination for all persons 19 and older. For previously unvaccinated persons: • 1 dose of updated (2023–2024 Formula) Moderna or Pfizer-BioNTech vaccine • 2-dose series of updated (2023–2024 Formula) Novavax at 0, 3–8 weeks For previously vaccinated with one or more doses of any COVID-19 vaccine: one dose of any updated (2023–2024 Formula) COVID-19 vaccine administered at least 8 weeks after the most recent COVID-19 vaccine dose.	
MMR	Two doses for adults at high risk for exposure and transmission (eg, college students, health care workers); otherwise, one dose for adults aged 18 years and older.	Physician documentation of disease is not acceptable evidence of MMR immunity
Pneumococcal vaccination	One dose of PCV15 followed by PPSV23 *or* One dose of PCV20 For all adults aged 65 years and older plus those aged 19–64 years who are at increased risk.	
Tdap	Routine use of a single dose of Tdap for adults aged 19–64 years.	Replaces next booster dose of Td vaccine
Hepatitis B	Two-, three-, or four-dose primary series recommended for all adults aged 19–59 years who have not been previously vaccinated or infected. Recommended for patients aged 60 years and over who are at increased risk or who wish to be vaccinated.	Prevents chronic hepatitis B and cirrhosis and their predispositions to HCC
HPV VLP	Routine HPV vaccination for children and adults aged 9–26 years. Shared decision making is recommended for unvaccinated individuals between 27 and 45 years of age (vaccine is not licensed for adults older than 45 years).	Prevents persistent HPV infections effectively and thus may impact rate of CIN II–III
RSV	Routine RSV vaccination (one dose) for pregnant persons at 32 weeks 0 days through 36 weeks 6 days gestation from September through January in most of the continental United States. Shared decision making for adults aged 60 and older. Those who are immunocompromised or who have chronic conditions are most likely to benefit.	

CIN, cervical intraepithelial neoplasia; HPV VLP, human papillomavirus virus-like particle; PCV15, 15-valent pneumococcal conjugate; PCV20, 20-valent pneumococcal conjugate; PPSV23, 23-valent pneumococcal polysaccharide; Td, tetanus and diphtheria toxoids; Tdap, tetanus, diphtheria, and five-component acellular pertussis.

The CDC recommends universal **HIV screening** of all patients aged 13–64, and the USPSTF recommends that clinicians screen adolescents and adults aged 15–65 years. Clinicians should integrate biomedical and behavioral approaches for HIV prevention. In addition to reducing sexual transmission of HIV, initiation of antiretroviral therapy reduces the risk for AIDS-defining events and death among patients with less immunologically advanced disease.

Daily **preexposure prophylaxis (PrEP)** with the fixed-dose combination of tenofovir disoproxil 300 mg and emtricitabine 200 mg (Truvada) should be considered for persons who are HIV-negative but at substantial risk for HIV infection. Studies of men who have sex with men suggest that PrEP is very effective in reducing the risk of contracting HIV. Patients taking PrEP should be encouraged to use other prevention strategies, such as consistent condom use, to maximally reduce their risk. **Postexposure prophylaxis (PEP)** with combinations of antiretroviral medications is widely used after occupational and nonoccupational contact and may reduce the risk of transmission by approximately 80%. PEP should be initiated within 72 hours of exposure.

Herpes zoster, caused by reactivation from previous varicella zoster virus infection, affects many older adults and persons with immune system dysfunction. The Advisory Committee on Immunization Practices recommends that the **herpes zoster subunit vaccine** (HZ/su; Shingrix) be used for the prevention of herpes zoster and related complications in immunocompetent adults aged 50 and older and in individuals who previously received Zostavax.

Centers for Disease Control and Prevention (CDC). https://covid.cdc.gov/covid-data-tracker/#datatracker-home
Centers for Disease Control and Prevention (CDC). HIV PrEP (preexposure prophylaxis), 2022. https://www.cdc.gov/hiv/basics/prep.html
Centers for Disease Control and Prevention (CDC). Pneumococcal vaccination, 2022. https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html
Centers for Disease Control and Prevention (CDC). Recommended adult immunization schedule for ages 19 years or older, United States, 2024. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf
Centers for Disease Control and Prevention (CDC). Shingrix recommendations, 2022. https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html
Centers for Disease Control and Prevention (CDC). Use of COVID-19 vaccines in the U.S., 2022. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html
Melgar M et al. Use of respiratory syncytial virus vaccines in older adults: recommendations of the Advisory Committee on Immunization Practices—United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793. [PMID: 37471262]
Oshman LD et al. Human papillomavirus vaccination for adults: updated recommendations of the Advisory Committee on Immunization Practices (ACIP). JAMA. 2020;323:468. [PMID: 31930397]
Patel R et al. A comprehensive review of SARS-CoV-2 vaccines: Pfizer, Moderna & Johnson & Johnson. Hum Vaccin Immunother. 2022;18:2002083. [PMID: 35130825]

PREVENTION OF CARDIOVASCULAR DISEASE

Cardiovascular disease, including CHD and stroke, is the leading cause of death globally, with over 20 million deaths in 2021, nearly one-third of all deaths. Over three-quarters of all cardiovascular deaths occur in low- and middle-income countries; however, CHD and stroke remain top causes of death in the United States as well. Several risk factors increase the risk for coronary disease and stroke. These risk factors can be divided into those that are modifiable (eg, lipid disorders, hypertension, cigarette smoking) and those that are not (eg, age, sex, family history of early coronary disease). Impressive declines in age-specific mortality rates from heart disease and stroke were achieved in all age groups in North America from 1980 to 2015, in large part through improvement of modifiable risk factors: reductions in cigarette smoking, improvements in lipid levels, and more aggressive detection and treatment of hypertension. However, the past several years have seen a disturbing increase in cardiovascular deaths in the United States and a plateau in the reduction in cardiovascular mortality rates. This section considers the role of screening for cardiovascular risk and the use of effective therapies to reduce such risk. Key USPSTF recommendations for cardiovascular prevention are shown in Table 1–4. Guidelines encourage regular assessment of global cardiovascular risk in adults 40–79 years of age without known CVD using standard cardiovascular risk factors and in younger adults at increased risk. The role of nontraditional risk factors for improving risk estimation and therapeutic decision making remains unclear. However, current guidance recommends considering cardiovascular risk prevention within the context of cardiovascular-kidney-metabolic health.

Khan SS et al; American Heart Association. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. Circulation. 2023;148:1982. [PMID: 37947094]
Roth GA et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76:2982. [PMID: 33309175]
World Heart Report 2023: Confronting the World's Number One Killer. Geneva, Switzerland. World Heart Federation. 2023. https://world-heart-federation.org/resource/world-heart-report-2023/

Abdominal Aortic Aneurysm

One-time screening for AAA by ultrasonography is recommended by the USPSTF (B recommendation) in men aged 65–75 years who have ever smoked. One-time screening for AAA is associated with a relative reduction in odds of AAA-related mortality over 12–15 years and a similar reduction in AAA-related ruptures (OR, 0.62 [95% CI 0.55–0.70]). Women who have never smoked and who have no family history of AAA do not appear to benefit from such screening (D recommendation); the current evidence for women who have ever smoked or who have a family history of AAA is insufficient to assess the balance of risks versus benefits (I recommendation) (Table 1–4).

US Preventive Services Task Force, Owens DK et al. Screening for abdominal aortic aneurysm: US Preventive Services Task Force Recommendation Statement. JAMA. 2019;322:2211. [PMID: 31821437]

Cigarette Smoking

Cigarette smoking remains the most important cause of preventable morbidity and early mortality. In 2019, there were an estimated 7.69 million deaths in the world attributable to smoking and tobacco use (13.6% of all deaths worldwide); smoking is the second leading cause of disability-adjusted life-years lost overall and the leading cause among men. Cigarettes are responsible for one in every five deaths in the United States, or over 480,000 deaths annually. The most frequent causes of smoking-related deaths are cancer, CVD, and respiratory disease (COPD). The annual cost of smoking-related health care is approximately $240 billion in the United States, with another $372 billion in productivity losses. Fortunately, US smoking rates have been declining; in 2015, 15.1% of US adults were smokers, and by 2020, 12.5% were smokers. Global direct health care costs from smoking in 2012 were estimated at $422 billion, with total costs of more than $1.4 trillion.

Over 1.3 million deaths worldwide were attributed to secondhand smoke in 2019.

Although tobacco use constitutes one of the most serious common medical problems, it is undertreated. Almost 40% of smokers attempt to quit each year, but only 4% are successful. Persons whose clinicians advise them to quit are

Table 1–4. Expert recommendations for cardiovascular risk prevention methods: USPSTF.[1]

Prevention Method	Recommendation/[Year Issued]
Screening for AAA	Recommends one-time screening for AAA by ultrasonography in men aged 65–75 years who have ever smoked. (B) Selectively offer screening for AAA in men aged 65–75 years who have never smoked. (C) Current evidence is insufficient to assess the balance of benefits and harms of screening for AAA in women aged 65–75 years who have ever smoked or have a family history of AAA. (I) Recommends against routine screening for AAA in women who have never smoked and have no family history of AAA. (D) [2019]
Aspirin use	The decision to initiate low-dose aspirin use for the primary prevention of CVD in adults aged 40–59 years who have a 10% or greater 10-year CVD risk should be an individual one. Evidence indicates that the net benefit of aspirin use in this group is small. Persons who are not at increased risk for bleeding and are willing to take low-dose aspirin daily are more likely to benefit. [C] Recommends against initiating low-dose aspirin use for primary prevention of CVD in adults aged 60 years or older. [D] [2022]
Blood pressure screening	Recommends screening for hypertension in adults aged 18 years or older with office blood pressure measurement. Recommends obtaining blood pressure measurements outside of the clinical setting for diagnostic confirmation before starting treatment. (A) [2021]
Serum lipid screening and use of statins for prevention	Recommends that clinicians prescribe a statin for primary prevention of CVD for adults aged 40–75 years who have one or more CVD risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year risk of a cardiovascular event of 10% or greater. [B] Recommends that clinicians selectively offer a statin for primary prevention of CVD for adults aged 40–75 years who have one or more CVD risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year risk of a cardiovascular event of 7.5% to less than 10%. The likelihood of benefit is smaller in this group than in persons with a 10-year risk of 10% or greater. [C] Current evidence is insufficient to assess the balance of benefits and harms of initiating a statin for the primary prevention of CVD events and mortality in adults aged 76 years or older. [I] [2022]
Counseling about healthful diet and physical activity for CVD prevention	Recommends offering or referring adults with CVD risk factors to behavioral counseling interventions to promote a healthy diet and physical activity. (B) [2020] Recommends that primary care professionals individualize the decision to offer or refer adults without CVD risk factors to behavioral counseling interventions to promote a healthy diet and physical activity. (C) [2022]
Screening for diabetes mellitus	Recommends screening for prediabetes and type 2 diabetes in adults aged 35–70 years who have overweight or obesity. Clinicians should offer or refer patients with prediabetes to effective preventive interventions. (B) [2021]
Screening for smoking and counseling to promote cessation	Recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, provide those who use tobacco behavioral interventions, and prescribe US FDA–approved pharmacotherapy to nonpregnant adults. (A) [2021]

USPSTF recommendations available at http://www.uspreventiveservicestaskforce.org/BrowseRec/Index/browse-recommendations.
Recommendation A: The USPSTF strongly recommends that clinicians routinely provide the service to eligible patients. (The USPSTF found good evidence that the service improves important health outcomes and concludes that benefits substantially outweigh harms.)
Recommendation B: The USPSTF recommends that clinicians routinely provide the service to eligible patients. (The USPSTF found at least fair evidence that the service improves important health outcomes and concludes that benefits substantially outweigh harms.)
Recommendation C: The USPSTF makes no recommendation for or against routine provision of the service.
Recommendation D: The USPSTF recommends against routinely providing the service to asymptomatic patients. (The USPSTF found at least fair evidence that the service is ineffective or that harms outweigh benefits.)
Recommendation I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing the service.

1.6 times as likely to attempt quitting. Over 70% of smokers see a physician each year, but only 20% of them receive any medical quitting advice or assistance.

Factors associated with successful cessation include having a rule against smoking in the home, being older, and having greater education. Several effective clinical interventions are available to promote smoking cessation, including counseling, pharmacotherapy, and combinations of the two.

Helpful counseling strategies are shown in Table 1–5. Additionally, a system should be implemented to identify smokers, and advice to quit should be tailored to the patient's level of readiness to change. *All patients trying to quit should be offered pharmacotherapy (*Table 1–6*) except*

Table 1–5. Inquiries to help in support of smoking cessation.

Component	Helpful Clinician Statements and Inquiries
Communicate your caring and concern	"I am concerned about the effects of smoking on your health… • and want you to know that I am willing to help you quit." • and so how do you feel about quitting?" • do you have any fears or ambivalent feelings about quitting?"
Encourage the patient to talk about the quitting process	"Tell me… • why do you want to quit smoking?" • when you tried quitting smoking in the past, what sort of difficulties did you encounter?" • were you able to succeed at all, even for a while?" • what concerns or worries do you have about quitting now?"
Provide basic information about smoking (eg, its addictive nature) and successful quitting (eg, nature and time course of withdrawal)	"Did you know that… • the nicotine in cigarette smoke is highly addictive?" • within a day of stopping, you will notice nicotine withdrawal symptoms, such as irritability and craving?" • after you quit, any smoking (even a single puff) makes it likely that you will fully relapse into smoking again?"
Encourage the patient to make a quit attempt	"I want to reassure you that… • as your clinician, I believe you are going to be able to quit." • many effective smoking cessation treatments are now available." • more than half the people who have *ever* smoked have now successfully quit."

Table 1–6. Medications for tobacco dependence and smoking cessation (categories listed in order of frequency of use).

Drug	Some Formulations	Usual Adult Dosage[1,2]
Nicotine Replacement Therapies (NRTs)		
Nicotine transdermal patch[3] – generic (NicoDerm CQ)	7, 14, 21 mg/24-h patches	1 patch/day
Nicotine polacrilex gum[3] – generic (Nicorette gum)	2, 4 mg/pieces	8–24 pieces/day[4,5]
Nicotine polacrilex lozenge[3,6] – generic (Nicorette lozenge)	2, 4 mg/lozenges	8–20 lozenges/day[4,7]
Nicotine oral inhaler – Nicotrol	10 mg cartridges[8]	4–16 cartridges/day
Nicotine nasal spray – Nicotrol NS	200 sprays/10 mL bottles (0.5 mg/spray)	2 sprays 8–40×/day (max 10 sprays/h)[3]
Dopaminergic-Noradrenergic Reuptake Inhibitor		
Bupropion SR – generic	100, 150, 200 mg SR tablets[9]	150 mg orally once daily × 3 days, then 150 mg orally twice daily
Nicotinic Receptor Partial Agonist		
Varenicline tartrate – Chantix	0.5, 1 mg tablets	0.5 mg orally once daily × 3 days, then 0.5 mg twice daily on days 4–7, then 1 mg twice daily

SR, sustained-release.
[1]Dosage reductions may be needed for liver or kidney impairment.
[2]Patients should receive a minimum of 3–6 months of effective therapy. In general, the dosage of NRTs can be tapered at the end of treatment; bupropion SR and varenicline can usually be stopped without a gradual dosage reduction, but some clinicians recommend a taper.
[3]Available over the counter for persons ≥ 18 years old.
[4]Avoid eating or drinking within 15 minutes of using a gum or lozenge.
[5]A second piece of gum can be used within 1 hour. Continuously chewing one piece after another is not recommended.
[6]Also available in a mini-lozenge.
[7]Maximum of 5 lozenges in 6 hours or 20 lozenges/day. Use of more than 1 lozenge at a time or continuously using one after another is not recommended.
[8]Each cartridge delivers 4 mg of nicotine.
[9]Only the generic 150-mg SR tablets are FDA-approved as a smoking cessation aid.
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those with medical contraindications, women who are pregnant or breastfeeding, and adolescents. Weight gain occurs in most patients (80%) following smoking cessation. Average weight gain is 2 kg, but for some (10–15%), major weight gain—over 13 kg—may occur. Planning for the possibility of weight gain, and means of mitigating it, may help with maintenance of cessation.

Several pharmacologic therapies shown to be effective in promoting cessation are summarized in Table 1–6. Nicotine replacement therapy doubles the chance of successful quitting. The nicotine patch, gum, and lozenges are available over the counter, and nicotine nasal spray and inhalers are available by prescription. The sustained-release antidepressant drug bupropion (150–300 mg/day orally) is an effective smoking cessation agent and is associated with minimal weight gain, although seizures are a contraindication. It acts by boosting brain levels of dopamine and norepinephrine, mimicking the effect of nicotine. Varenicline, a partial nicotinic acetylcholine-receptor agonist, also has been shown to improve cessation rates; however, its adverse effects, particularly its effects on mood, are not completely understood and warrant careful consideration, although recent safety data have provided reassurance. A head-to-head trial found varenicline to be more effective than other pharmacologic therapies and all pharmacologic therapies to be more effective than placebo. Combination therapy is more effective than a single pharmacologic modality. The efficacy of e-cigarettes in smoking cessation has not been well evaluated, and some users may find them addictive. Reports of "e-cigarette or vaping use–associated lung injury" (EVALI) should prompt additional caution in the use of unregulated nicotine delivery devices for smoking cessation (see Chapter 9).

Clinicians should not show disapproval of patients who fail to stop smoking or who are not ready to make a quit attempt. Thoughtful advice that emphasizes the benefits of cessation and recognizes common barriers to success can increase motivation to quit and quit rates. An upcoming medical procedure or intercurrent illness or hospitalization may motivate even the most addicted smoker to quit.

Individualized or group counseling is very cost-effective, even more so than treating hypertension. Smoking cessation counseling by telephone ("quitlines") and text messaging have both proved effective. An additional strategy is to recommend that any smoking take place outdoors to limit the effects of passive smoke on housemates and coworkers. This can lead to smoking reduction and quitting.

Public policies, including higher cigarette taxes and more restrictive public smoking laws, have also been shown to encourage cessation, as have financial incentives directed to patients.

Black N et al. Behaviour change techniques associated with smoking cessation in intervention and comparator groups of randomized controlled trials: a systematic review and meta-regression. Addiction. 2020;115:2008. [PMID: 32196796]

Centers for Disease Control and Prevention (CDC). Burden of cigarette use in the U.S., 2022. https://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html

GBD 2019 Tobacco Collaborators. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet. 2021;397:2337. [PMID: 34051883]

Rigotti NA et al. Treatment of tobacco smoking: a review. JAMA. 2022;327:566. [PMID: 35133411]

US Preventive Services Task Force; Krist AH et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325:265. [PMID: 33464343]

Lipid Disorders

Higher LDL cholesterol concentrations and lower HDL levels are associated with an increased risk of CHD (see Chapter 30). Measurement of total and HDL cholesterol levels can help assess the degree of CHD risk. The best age to start screening is controversial, as is its frequency. Cholesterol-lowering therapy reduces the relative risk of CHD events, with the degree of reduction proportional to the reduction in LDL cholesterol achieved, at least at initial LDL levels greater than 100 mg/dL. The absolute benefits of screening for—and treating—abnormal lipid levels depend on the presence and level of other cardiovascular risk factors, including hypertension, diabetes mellitus, smoking, age, and sex (see Chapter 30). If other risk factors are present, atherosclerotic CVD risk is higher and the potential benefits of therapy are greater. Patients with known CVD are at higher risk and have larger benefits from reduction in LDL cholesterol. The optimal risk threshold for initiating statins for primary prevention remains somewhat controversial, although most guidelines now suggest statin therapy when 10-year atherosclerotic cardiovascular risk is greater than 10%. Use of a cardiovascular risk calculator can help inform decision making for primary prevention.

Evidence for the effectiveness of statin-type medications is better than for the other classes of lipid-lowering agents or dietary changes specifically for improving lipid levels. Multiple large, randomized, placebo-controlled trials have demonstrated important reductions in total mortality, major coronary events, and strokes with lowering levels of LDL cholesterol by statin therapy for patients with known CVD. Statins also reduce cardiovascular events for patients with diabetes mellitus. For patients with no previous history of cardiovascular events, meta-analyses have shown important reductions of cardiovascular events and all-cause mortality.

Newer antilipidemic monoclonal antibody agents (eg, evolocumab and alirocumab) lower LDL cholesterol by 50–60% by binding proprotein convertase subtilisin kexin type 9 (PCSK9), which decreases the degradation of LDL receptors. PCSK9 inhibitors also decrease Lp(a) levels. These medications are very expensive and so are often used mainly in high-risk patients when statin therapy does not reduce LDL cholesterol sufficiently at maximally tolerated doses or when patients are intolerant of statins. Few side effects have been reported with PCSK9 inhibitor use.

Guidelines for statin and PCSK9 therapy are discussed in Chapter 30.

Chou R et al. Statin use for the primary prevention of cardiovascular disease in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2022;328:754. [PMID: 35997724]
Khan SS et al; American Heart Association. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement =from the American Heart Association. Circulation. 2023;148:1982. [PMID: 37947094]
US Preventive Services Task Force; Mangione CM et al. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2022;328:746. [PMID: 35997723]

Hypertension

According to the American Heart Association, over 133 million US adults have hypertension, of which approximately 83 million are eligible for pharmacologic treatment. Of these 83 million, hypertension is treated in only about 66% and well controlled in only about 30% (see Chapter 13). In every adult age group, higher values of systolic and diastolic blood pressure carry greater risks of stroke and HF. Systolic blood pressure is a better predictor of morbid events than diastolic blood pressure. Home monitoring is better correlated with target organ damage than clinic-based values. Clinicians can apply specific blood pressure criteria, such as those of the Joint National Committee or American Heart Association guidelines, along with consideration of the patient's cardiovascular risk and personal values, to decide at what levels treatment should be considered in individual cases.

Primary prevention of hypertension can be accomplished by strategies aimed at both the general population and special high-risk populations. The latter include persons with high-normal blood pressure or a family history of hypertension; Black persons; and individuals with various behavioral risk factors, such as physical inactivity; excessive consumption of salt, alcohol, or calories; and deficient intake of potassium. Effective interventions for primary prevention of hypertension include reduced sodium and alcohol consumption, weight loss, and regular exercise. Diets high in fresh fruits and vegetables and low in saturated fat and sugar-containing beverages are associated with lower blood pressure.

Improved identification and treatment of hypertension has been a major cause of the decline in stroke deaths as well as the reduction in incidence of HF-related hospitalizations; more recently, stalled progress in control of hypertension has led to slowing of improvements in cardiovascular outcomes. *Because hypertension is usually asymptomatic, screening is strongly recommended to identify patients for treatment.* Elevated office readings should be confirmed with repeated measurements, ideally from ambulatory monitoring or home measurements. Despite strong recommendations in favor of screening and treatment, hypertension control remains suboptimal. Several types of interventions, including telehealth applications, have been shown to be effective in increasing adherence and blood pressure control. An intervention that included both patient and provider education was more effective than provider education alone in achieving control of hypertension, suggesting the benefits of patient participation; another trial found that home monitoring combined with telephone-based nurse support was more effective than home monitoring alone for blood pressure control. Pharmacologic management of hypertension is discussed in Chapter 13.

Centers for Disease Control and Prevention (CDC). Million Hearts 2022: estimated hypertension prevalence, treatment, and control among U.S. adults. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html
Mikulski BS et al. Mobile health applications and medication adherence of patients with hypertension: a systematic review and meta-analysis. Am J Prev Med. 2022;62:626. [PMID: 34963562]
Muntner P et al. Trends in blood pressure control among US adults with hypertension, 1999–2000 to 2017–2018. JAMA. 2020;324:1190. [PMID: 32902588]
US Preventive Services Task Force; Krist AH et al. Screening for hypertension in adults: US Preventive Services Task Force Reaffirmation Recommendation Statement. JAMA. 2021;325:1650. [PMID: 33904861]

Chemoprevention

Regular use of low-dose aspirin (81–325 mg) can reduce cardiovascular events but increases GI bleeding and hemorrhagic stroke. The potential benefits of aspirin may exceed the possible adverse effects among middle-aged adults who are at increased cardiovascular risk, which can be defined as a 10-year risk of greater than 10%, and who do not have an increased risk of bleeding. However, a large trial in older healthy adults did not find clear benefit from aspirin for reduction of cardiovascular events and saw an increase in all-cause mortality with aspirin. Therefore, aspirin should *not* be routinely initiated in healthy adults over age 70.

NSAIDs may reduce the incidence of colorectal adenomas and polyps but may also increase heart disease and GI bleeding and thus are *not* recommended for colon cancer prevention in average-risk patients.

Antioxidant vitamin (vitamin E, vitamin C, and beta-carotene) supplementation produced no significant reductions in the 5-year incidence of—or mortality from—vascular disease, cancer, or other major outcomes in high-risk individuals with CAD, other occlusive arterial disease, or diabetes mellitus.

US Preventive Services Task Force; Davidson KW et al. Aspirin use to prevent cardiovascular disease: US Preventive Services Task Force Recommendation Statement. JAMA. 2022;327:1577. [PMID: 35471505]

PREVENTION OF OSTEOPOROSIS

See Chapter 28.

Osteoporosis, characterized by low bone mineral density, is common and associated with an increased risk of fracture. The lifetime risk of an osteoporotic fracture is approximately 50% for women and 30% for men. Osteoporotic fractures can cause significant pain and disability.

As such, research has focused on means of preventing osteoporosis and related fractures. Primary prevention strategies include calcium supplementation, vitamin D supplementation, and exercise programs. The effectiveness of calcium and vitamin D for fracture prevention remains controversial, particularly in noninstitutionalized individuals.

Screening for osteoporosis on the basis of low bone mineral density is recommended for women over age 65, based on indirect evidence that screening can identify women with low bone mineral density and that treatment of women with low bone density with bisphosphonates is effective in reducing fractures. However, real-world adherence to pharmacologic therapy for osteoporosis is low: one-third to one-half of patients do not take their medication as directed. Screening for osteoporosis is also recommended in younger women who are at increased risk. The effectiveness of screening in men has not been established. Bisphosphonates may increase the risk of certain uncommon, atypical types of femoral fractures and rare osteonecrosis of the jaw and are associated with some nonserious GI symptoms. As such, consideration of the benefits and risks of therapy, as well as the importance of consistent adherence, is important when deciding about screening.

Anam AK et al. Update on osteoporosis screening and management. Med Clin North Am. 2021;105:1117. [PMID: 34688418]
Calikyan A et al. Osteoporosis screening disparities among ethnic and racial minorities: a systematic review. J Osteoporos. 2023;2023:1277319. [PMID: 37138642]
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PREVENTION OF PHYSICAL INACTIVITY

Lack of sufficient physical activity is the second most important contributor to preventable deaths, trailing only tobacco use. The US Department of Health and Human Services and the CDC recommend that adults (including older adults) engage in 150 minutes of moderate-intensity (such as brisk walking) or 75 minutes of vigorous-intensity (such as jogging or running) aerobic activity or an equivalent mix of moderate- and vigorous-intensity aerobic activity each week. In addition to activity recommendations, the CDC recommends activities to strengthen all major muscle groups (abdomen, arms, back, chest, hips, legs, and shoulders) at least twice a week.

Patients who engage in regular moderate to vigorous exercise have a lower risk of MI, stroke, hypertension, hyperlipidemia, type 2 diabetes mellitus, diverticular disease, and osteoporosis. Regular exercise may also have a positive effect on executive function in older adults.

In longitudinal cohort studies, individuals who report higher levels of leisure-time physical activity are less likely to gain weight. Conversely, individuals who are overweight are less likely to stay active. However, at least 60 minutes of daily moderate-intensity physical activity may be necessary to maximize weight loss and prevent significant weight regain. Moreover, adequate levels of physical activity appear to be important for the prevention of weight gain and the development of obesity.

Systematic reviews have consistently found that more intensive counseling interventions are more effective than brief interventions.

Several factors influence physical activity behavior, including personal, social (eg, family and work), and environmental (eg, access to exercise facilities and well-lit parks) factors.

Patnode CD et al. Behavioral counseling interventions to promote a healthy diet and physical activity for cardiovascular disease prevention in adults without known cardiovascular disease risk factors: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2022;328:375. [PMID: 35881116]
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PREVENTION OF OVERWEIGHT & OBESITY

Obesity is a true epidemic and public health crisis that both clinicians and patients must face. Obesity is associated with type 2 diabetes mellitus, hypertension, hyperlipidemia, cancer, osteoarthritis, CVD, obstructive sleep apnea, asthma, and (for more severe obesity) increased all-cause mortality. Risk assessment for overweight and obesity begins with determination of BMI, waist circumference for patients with a BMI of 35 or less, presence of comorbid conditions, and a fasting blood glucose and lipid panel. Normal body weight is defined as a BMI of less than 25, overweight is defined as a BMI of 25.0–29.9, and obesity is defined as a BMI greater than 30. Persons with a BMI of 40 or higher have death rates from cancers that are 52% higher for men and 62% higher for women than the rates in men and women of normal weight.

Primary, secondary, and tertiary prevention of overweight and obesity involves both increasing physical activity and dietary modification to reduce caloric intake. Adequate levels of physical activity appear to be important for the prevention of weight gain and the development of obesity. Physical activity programs consistent with public health recommendations may promote modest weight loss (~2 kg); however, the amount of weight loss for any one individual is highly variable.

Clinicians can help prevent and treat obesity by intensive, multicomponent interventions, often best delivered by a trained nutritionist. Patients engaged in such interventions learn to develop personalized eating plans to reduce energy intake, particularly by recognizing the contributions of unhealthy fats, concentrated carbohydrates, and large portion sizes (see Chapter 31). Patients typically

underestimate caloric content, especially when consuming food away from home. Providing patients with caloric and nutritional information may help limit caloric intake as part of a multicomponent intervention.

Other treatment options for obesity include pharmacotherapy and surgery (see Chapter 31). Recent evidence has demonstrated the effectiveness of GLP-1 agonists in producing sustained weight loss. However, the high cost of these medications has limited their access, especially for patients with low incomes and limited or no health insurance coverage.

Weight loss strategies using dietary, physical activity, or behavioral interventions can produce significant improvements in weight among persons with prediabetes and a significant decrease in diabetes incidence. Intensive lifestyle interventions including diet combined with physical activity are effective in achieving weight loss and reducing cardiometabolic risk factors among patients with severe obesity.

Bariatric surgical procedures, eg, adjustable gastric band, sleeve gastrectomy, and Roux-en-Y gastric bypass, are reserved for patients with severe obesity in whom BMI exceeds 40 or for patients with less severe obesity (with BMIs between 35 and 40) and high-risk comorbid conditions, such as life-threatening cardiopulmonary problems (eg, sleep apnea, obesity-hypoventilation syndrome, and obesity-related HF) or diabetes mellitus. In selected patients, surgery can produce substantial weight loss (10–159 kg) over 1–5 years, with rare, but sometimes serious, complications. Surgery also appears to be successful in improving glycemic control and reducing diabetes. Nutritional deficiencies are one complication of bariatric surgical procedures and close monitoring of a patient's metabolic and nutritional status is essential. Further research is needed to best elucidate the optimal use of bariatric surgery in the era of effective GLP-1 agonists.

Finally, clinicians seem to share a general perception that almost no one succeeds in long-term maintenance of weight loss. However, research demonstrates that approximately 20% of overweight individuals are successful at long-term weight loss (defined as losing 10% or more of initial body weight and maintaining the loss for 1 year or longer).

Liu Y et al. The weight-loss effect of GLP-1RAs glucagon-like peptide-1 receptor agonists in non-diabetic individuals with overweight or obesity: a systematic review with meta-analysis and trial sequential analysis of randomized controlled trials. Am J Clin Nutr. 2023;118:614. [PMID: 37661106]

Martin JC et al. Preventing weight gain in adults: a systematic review and meta-analysis of randomized controlled trials. Obes Rev. 2021;22:e13280. [PMID: 34028958]

CANCER PREVENTION

Primary Prevention

Cancer mortality rates continue to decrease in the United States. Part of this decrease results from reductions in tobacco use, since cigarette smoking is the most important preventable cause of cancer; cancer incidence is also lower in persons with higher levels of physical activity and lower levels of obesity and alcohol use. Persons who engage in regular physical exercise, limit alcohol use, and avoid obesity have lower rates of breast and colon cancer.

Chemoprevention has been widely studied for primary cancer prevention without clear evidence of benefits (see earlier Chemoprevention section and Chapter 41). Use of tamoxifen, raloxifene, and aromatase inhibitors for breast cancer prevention is discussed in Chapters 19 and 41. Hepatitis B vaccination can prevent HCC. Screening and treatment of hepatitis C is another strategy to prevent HCC (see Chapter 18); new recommendations have extended the population eligible for screening. HPV virus-like particle (VLP) vaccine is recommended to prevent cervical cancer (Table 1–3). HPV vaccines may also have a role in the prevention of HPV-related head and neck and possibly anal cancers. The USPSTF recommends genetic counseling and, if indicated after counseling, genetic testing for women whose family or personal history is associated with an increased risk of harmful mutations in the *BRCA1/2* gene.

Athanasiou A et al. HPV vaccination and cancer prevention. Best Pract Res Clin Obstet Gynaecol. 2020;65:109. [PMID: 32284298]

Screening & Early Detection

Screening prevents death from cancers of the breast, colon, lung, and cervix. Current cancer screening recommendations from the USPSTF are available online at https://www.uspreventiveservicestaskforce.org/BrowseRec/Index/browse-recommendations.

Most guidelines are based on trial evidence from middle-aged adults, mostly of European ancestry. Cancer screening in adults over the age of 75 requires an individualized approach that considers differences in disease risk, differences in risk of adverse effects of diagnostic procedures and treatments and competing health issues.

Despite an increase in rates of screening for breast, cervical, lung, and colon cancer over the last decade, overall screening for these cancers is suboptimal. Interventions effective in promoting recommended cancer screening include group education, one-on-one education, patient reminders, reduction of structural barriers, reduction of out-of-pocket costs, and provider assessment and feedback. Multicomponent interventions are generally more effective than single-component ones.

Though breast cancer mortality is reduced with mammography screening, this screening has both benefits and downsides, including overdiagnosis (detecting cancers that would have never progressed to become clinically meaningful). Clinicians should discuss the risks and benefits with each patient and consider individual patient preferences when deciding when to begin screening (see Chapter 19).

Prostate cancer screening remains controversial: completed trials have not fully answered the question of whether early detection and treatment after screen detection produce sufficient benefits (in terms of cancer-specific mortality reduction) to outweigh harms of treatment and overdiagnosis. For men between the ages of 55 and 69, the decision to screen should be individualized and include a

discussion of its risks and benefits with a clinician. The USPSTF recommends *against* PSA-based prostate cancer screening for men older than age 70 years (grade D recommendation).

The USPSTF recommends colorectal cancer screening for adults aged 45–75 years and selectively screening adults aged 76–85 years (considering the patient's preferences, overall health, and prior screening history). Choice of screening test is based on patient preferences. Screening colonoscopy every 10 years is one recommended screening option. Annual or biennial fecal occult blood testing reduces mortality from colorectal cancer and is also recommended, with fecal immunochemical tests (FIT) used most commonly. CT colonography (virtual colonoscopy) is a noninvasive option in screening for colorectal cancer. It has been shown to have a high safety profile and performance similar to colonoscopy for large polyps and cancers.

The American Cancer Society recommends screening for persons aged 25–65 years with primary HPV testing every 5 years based on trial evidence showing it to be superior to other options. The USPSTF recommends screening for cervical cancer in women aged 21–65 years with a Papanicolaou smear (cytology) every 3 years or, for women aged 30–65 years who desire longer intervals, screening with cytology and HPV testing every 5 years, but its recommendation is being revised. The USPSTF recommends against screening in women younger than 21 years of age and average-risk women over 65 with adequate negative prior screenings. Receipt of HPV vaccination does not yet affect screening intervals, although it may have an effect in the future, as a greater proportion of persons are vaccinated.

The USPSTF recommends offering annual lung cancer screening with low-dose CT to current smokers aged 50 to 80 years and at least a 20-pack-year smoking history and to smokers who quit within the past 15 years. Updated American Cancer Society recommendations remove the restriction on the number of years since quitting. A person should stop screening when health problem that limits life expectancy to less than 5 years has developed or if the person cannot safely undergo treatment if lung cancer is detected. Screening should not be viewed as an alternative to smoking cessation but rather as a complementary approach.

Fontham ETH et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin. 2020;70:321. [PMID: 32729638]

Jonas DE et al. Screening for lung cancer with low-dose computed tomography: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2021;325:971. [PMID: 33687468]

US Preventive Services Task Force; Davidson KW et al. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325:1965. [PMID: 34003218]

US Preventive Services Task Force; Krist AH et al. Screening for lung cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325:962. [PMID: 33687470]

Wolf AMD et al. Screening for lung cancer: 2023 guideline update from the American Cancer Society. CA Cancer J Clin. 2024;74:50. [PMID: 37909877]

PREVENTION OF INJURIES & VIOLENCE

Injuries are an important cause of morbidity and mortality, particularly before age 65. Homicide and motor vehicle collisions are a major cause of injury-related deaths among young and middle-aged adults, and accidental falls are the most common cause of injury-related death in older adults. Although motor vehicle collision deaths per miles driven have declined in the United States over many years, there was an increase in 2020–2021, and the United States has not achieved reductions in motor vehicle collision deaths comparable with other high-income countries.

Men, particularly those aged 16–35, are at especially high risk for serious injury and death from firearm-related violence, with Black men at greatest risk and Latino and American Indian men also at increased risk. Firearm suicide rates are highest for White men but have been increasing for other racial/ethnic groups. *Deaths from firearms have reached epidemic levels in the United States.* Having a gun in the home increases the likelihood of homicide nearly threefold and of suicide fivefold. Educating clinicians to recognize and treat depression, assess suicide risk, and restrict access to lethal methods in persons at risk has been found to reduce suicide rates.

Clinicians have a critical role in the detection, prevention, and management of intimate partner violence (IPV). The USPSTF recommends screening women of reproductive age for IPV and providing or referring women to intervention services when needed. Inclusion of a single question in the medical history—"At any time, has a partner ever hit you, kicked you, or otherwise physically hurt you?"—can increase identification of this common problem. Assessment for abuse and offering referrals to community resources create the potential to interrupt and prevent recurrence of IPV and associated trauma (and even mortality). Clinicians should take an active role in following up with patients whenever possible, since IPV screening with passive referrals to services may not be adequate to prevent recurrence and escalation.

Physical and psychological abuse, exploitation, and neglect of older adults are serious, underrecognized problems; they may occur in up to 10% of older adults. Risk factors for elder abuse include a culture of violence in the family; a demented, debilitated, or depressed and socially isolated victim; and a perpetrator profile of mental illness, alcohol or drug abuse, or emotional or financial dependence (or both) on the victim. Clues to elder mistreatment include the patient's ill-kempt appearance, recurrent urgent-care visits, missed appointments, suspicious physical findings, and implausible explanations for injuries.

Cimino-Fiallos N et al. Elder abuse—a guide to diagnosis and management in the emergency department. Emerg Med Clin North Am. 2021;39:405. [PMID: 33863468]

Curtin SC et al. Suicide rates for the three leading methods by race and ethnicity, 2000–2020. NCHS Data Brief, no 450. Hyattsville, MD: National Center for Health Statistics. 2022. [PMID: 36409535]

Kirk L et al. What barriers prevent health professionals screening women for domestic abuse? A literature review. Br J Nurs. 2020;29:754. [PMID: 32649247]

QuickStats: Age-adjusted rates of firearm-related homicide, by race, Hispanic origin, and sex — National Vital Statistics System, United States, 2021. MMWR Morb Mortal Wkly Rep. 2023;72:737. [PMID: 37384572]

PREVENTION OF SUBSTANCE USE DISORDERS: ALCOHOL & ILLICIT DRUGS

A. Alcohol

Unhealthy alcohol use is a major public health problem in the United States. The spectrum of alcohol use disorders includes alcohol dependence; harmful pattern use of alcohol; and entities such as alcohol intoxication, alcohol withdrawal, and several alcohol-induced mental disorders. The *ICD-11* includes a new category: *hazardous alcohol use*. Categorized as a risk factor, hazardous alcohol use is a pattern of alcohol use that appreciably increases the risk of harmful physical or mental health consequences to the user.

Underdiagnosis and undertreatment of alcohol misuse are substantial. As with cigarette use, clinician identification and counseling about unhealthy alcohol use are essential. The USPSTF recommends screening adults aged 18 years and older for unhealthy alcohol use. The National Institute on Alcohol Abuse and Alcoholism recommends the following single-question screening test (validated in primary care settings): "How many times in the past year have you had X or more drinks in a day?" ("X" is 5 for men and 4 for women, and a response of more than 1 time is considered a positive screen.)

Persons who screen positive on the single-item questionnaire should complete the Alcohol Use Disorder Identification Test (AUDIT), which consists of questions on the quantity and frequency of alcohol consumption, on alcohol dependence symptoms, and on alcohol-related problems (Table 1–7).

Clinicians should provide persons who screen positive for hazardous or risky drinking with brief behavioral counseling interventions to reduce alcohol misuse. Use of screening procedures and brief intervention methods (see Chapter 27) can produce a 10–30% reduction in long-term alcohol use and alcohol-related problems. Those whose AUDIT scores suggest alcohol use disorder (AUDIT > 12) should undergo more extensive evaluation and potential referral for treatment. Naltrexone and acamprosate are effective for treating alcohol use disorder. However, less than 9% of eligible patients receive these effective medications.

Table 1–7. Screening for alcohol abuse using the Alcohol Use Disorder Identification Test (AUDIT).

(Scores for response categories are given in parentheses. Added together, Total Scores range from 0 to 40, with scores of 1 to 7 suggesting low-risk drinking; 8 to 14, hazardous or harmful drinking; and > 15, alcohol dependence.)				
1. How often do you have a drink containing alcohol?				
(0) Never	(1) Monthly or less	(2) Two to four times a month	(3) Two or three times a week	(4) Four or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?				
(0) 1 or 2	(1) 3 or 4	(2) 5 or 6	(3) 7 to 9	(4) 10 or more
3. How often do you have six or more drinks on one occasion?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
4. How often during the past year have you found that you were not able to stop drinking once you had started?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
5. How often during the past year have you failed to do what was normally expected of you because of drinking?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
6. How often during the past year have you needed a first drink in the morning to get yourself going after a heavy drinking session?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
7. How often during the past year have you had a feeling of guilt or remorse after drinking?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
8. How often during the past year have you been unable to remember what happened the night before because you had been drinking?				
(0) Never	(1) Less than monthly	(2) Monthly	(3) Weekly	(4) Daily or almost daily
9. Have you or has someone else been injured as a result of your drinking?				
(0) No		(2) Yes, but not in the past year		(4) Yes, during the past year
10. Has a relative or friend or a doctor or other health worker been concerned about your drinking or suggested you cut down?				
(0) No		(2) Yes, but not in the past year		(4) Yes, during the past year

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B. Opioids

Deaths due to opioid overdose have dramatically increased. Opioid risk mitigation strategies include use of risk assessment tools, treatment agreements (contracts), and urine drug testing to limit diversion of prescription opiates. Additional strategies include establishing and strengthening prescription drug monitoring programs, regulating pain management facilities, and establishing dosage thresholds requiring consultation with pain specialists. More recently, non-prescription opioid use has become predominant as a cause of opioid-related mortality. Harm reduction interventions are important, including strategies to prevent or treat overdose and strategies to reduce infectious complications of injection drug use. The US FDA supports greater access to naloxone and is exploring options to make naloxone more available to treat opioid overdose (see Chapters 5 and 45).

Medication-assisted treatment, the use of medications with counseling and behavioral therapy, is effective in the prevention of opioid overdose and substance abuse disorders. Methadone, buprenorphine, and naltrexone are FDA approved for use in medication-assisted treatment. Buprenorphine has potential as a medication to ameliorate the symptoms and signs of withdrawal from opioids and is effective in reducing concomitant cocaine and opioid abuse.

Use of non-opioid drugs—including cocaine, methamphetamine, and so-called designer drugs—either sporadically or episodically remains an important problem with or without concomitant use of opioids.

Clinical aspects of substance abuse are discussed in Chapters 27 and 45.

McPheeters M et al. Pharmacotherapy for alcohol use disorder: a systematic review and meta-analysis. JAMA. 2023;330:1653. [PMID: 37934220]

Mekonen T et al. Treatment rates for alcohol use disorders: a systematic review and meta-analysis. Addiction. 2021;116:2617. [PMID: 33245581]

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Common Symptoms

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2

COUGH

ESSENTIAL INQUIRIES

- Age, duration of cough, occupational history, environmental exposures, and risk of infection with SARS-CoV-2.
- Use of tobacco, cannabis, e-cigarettes (vaping).
- Dyspnea (at rest or with exertion).
- Vital signs (heart rate, respiratory rate, body temperature); pulse oximetry.
- Chest examination.
- CXR, especially when unexplained cough lasts > 3–6 weeks.

General Considerations

Cough is the most common symptom for which patients seek medical attention. Cough results from stimulation of mechanical or chemical afferent nerve receptors in the bronchial tree. Effective cough depends on an intact afferent–efferent reflex arc, adequate expiratory and chest wall muscle strength, and normal mucociliary production and clearance.

Clinical Findings

A. Symptoms

Distinguishing **acute** (less than 3 weeks), **persistent** (3–8 weeks), and **chronic** (more than 8 weeks) cough illness syndromes is a useful first step in evaluation. Postinfectious cough lasting 3–8 weeks is referred to as **subacute** cough to distinguish this common, distinct clinical entity from acute and chronic cough.

1. Acute cough—In healthy adults, most acute cough syndromes are due to viral respiratory tract infections. Additional features of infection such as fever, nasal congestion, and sore throat help confirm this diagnosis. Dyspnea (at rest or with exertion) may reflect a more serious condition, and further evaluation should include assessment of oxygenation (pulse oximetry or ABG measurement), airflow (peak flow or spirometry), and pulmonary parenchymal disease (CXR). The timing and character of the cough are not useful in establishing the cause of acute cough syndromes, although cough-variant asthma should be considered when there is prominent nocturnal cough. Loss of smell or taste accompanying a new cough illness is specific but not sensitive for COVID-19 infection. The presence of posttussive emesis or inspiratory whoop in adults modestly increases the likelihood of pertussis, and the absence of paroxysmal cough and the presence of fever decrease its likelihood. Uncommon causes of acute cough should be suspected in those with HF or hay fever (allergic rhinitis) and those with occupational risk factors (such as farmworkers).

2. Persistent and chronic cough—Cough due to acute respiratory tract infection resolves within 3 weeks in more than 90% of patients. Pertussis should be considered in adolescents and adults who have persistent or severe cough lasting more than 3 weeks, who have not been adequately boosted with Tdap, and who have been exposed to a person with confirmed pertussis. It should also be considered in geographic areas where the prevalence of pertussis approaches 20% (although the prevalence is difficult to ascertain due to the limited sensitivity of diagnostic tests).

When ACE inhibitor use, acute respiratory tract infection, and chest radiographic abnormalities are absent, most cases of persistent and chronic cough are related to postnasal drip (upper airway cough syndrome), cough-variant asthma, or GERD, or some combination of these three entities. Approximately 10% of cases are caused by nonasthmatic eosinophilic bronchitis. A history of nasal or sinus congestion, wheezing, or heartburn should direct subsequent evaluation and treatment, though these conditions frequently cause persistent cough in the absence of typical symptoms. Dyspnea at rest or with exertion is not commonly reported with persistent cough; dyspnea requires assessment for chronic lung disease, HF, anemia, PE, or pulmonary hypertension.

Bronchogenic carcinoma is suspected when cough is accompanied by unexplained weight loss, hemoptysis, and fevers with night sweats, particularly in persons with significant tobacco or occupational exposures (asbestos, radon, diesel exhaust, and metals). Second-hand smoke is a risk factor for small airways dysfunction in patients with

chronic cough who do not smoke cigarettes. Persistent and chronic cough with excessive phlegm increases the likelihood of COPD, particularly if there is a history of cigarette smoking, or of bronchiectasis if accompanied by recurrent or complicated pneumonia; CXRs are helpful in diagnosis. Chronic cough with dry eyes may represent Sjögren syndrome. A chronic dry cough may be the first symptom of idiopathic pulmonary fibrosis.

B. Physical Examination

Pneumonia is suspected when acute cough is accompanied by vital sign abnormalities (tachycardia, tachypnea, fever). Findings suggestive of airspace consolidation (crackles, decreased breath sounds, fremitus, egophony) are specific predictors of community-acquired pneumonia but are present in a minority of cases. Purulent sputum is associated with bacterial infections in patients with structural lung disease (eg, COPD, cystic fibrosis), but it is a poor predictor of pneumonia in the otherwise healthy adult. Wheezing and rhonchi are frequent findings with acute bronchitis and do not indicate consolidation or adult-onset asthma in most cases.

Examination of patients with persistent cough should include a search for chronic sinusitis, which may contribute to postnasal drip syndrome or to asthma. Physical examination may help distinguish COPD from HF. In patients with cough and dyspnea, a normal match test (ability to blow out a match from 25 cm away) and maximum laryngeal height greater than 4 cm (measured from the sternal notch to the cricoid cartilage at end expiration) substantially decrease the likelihood of COPD. Similarly, normal jugular venous pressure and no hepatojugular reflux decrease the likelihood of biventricular HF.

C. Diagnostic Studies

1. Acute cough—CXR should be considered for any adult with acute cough whose vital signs are abnormal or whose chest examination suggests pneumonia. The relationship between specific clinical findings and the probability of pneumonia is shown in Table 2–1. A large, multicenter randomized study found that elevated serum CRP (greater than 30 mg/dL) improves diagnostic accuracy of clinical prediction rules for pneumonia in adults with acute cough; serum procalcitonin had only marginal utility in outpatient management (in contrast with severe pneumonia requiring hospital care). A meta-analysis found that lung ultrasonography had better accuracy than CXR for the diagnosis of adult community-acquired pneumonia. In patients with dyspnea, pulse oximetry and peak flow help exclude hypoxemia or obstructive airway disease. However, a normal pulse oximetry value (eg, greater than 93%) does not rule out a significant alveolar–arterial (A–a) gradient when patients have effective respiratory compensation.

2. Persistent and chronic cough—CXR is indicated when ACE inhibitor therapy–related and postinfectious cough are excluded. If pertussis is suspected, PCR testing should be performed on a nasopharyngeal swab or nasal wash specimen—although the ability to detect pertussis decreases as the duration of cough increases. When the chest film is normal, postnasal drip, asthma, or GERD are the most likely causes. The presence of typical symptoms of these conditions directs further evaluation or empiric therapy, though typical symptoms are often absent. Definitive tests for determining the presence of each are available (Table 2–2). However, empiric treatment with a

Table 2–1. Positive and negative LRs of history, physical examination, and laboratory findings in the diagnosis of pneumonia.

Finding	Positive LR	Negative LR
Medical history		
Fever	1.7–2.1	0.6–0.7
Chills	1.3–1.7	0.7–0.9
Physical examination		
Tachypnea (respiratory rate > 25 breaths/min)	1.5–3.4	0.8
Tachycardia (> 100 beats/min in two studies or > 120 beats/min in one study)	1.6–2.3	0.5–0.7
Hyperthermia (> 37.8°C)	1.4–4.4	0.6–0.8
Chest examination		
Dullness to percussion	2.2–4.3	0.8–0.9
Decreased breath sounds	2.3–2.5	0.6–0.8
Crackles	1.6–2.7	0.6–0.9
Rhonchi	1.4–1.5	0.8–0.9
Egophony	2.0–8.6	0.8–1.0
Laboratory findings		
Leukocytosis (> 11,000/mcL [11 × 10^9/L] in one study or ≥ 10,400/mcL [10.4 × 10^9/L] in another study)	1.9–3.7	0.3–0.6
CRP > 20 mg/mL	3.8 (2.3–5.9)	0.5 (0.4–0.6)
Procalcitonin > 0.25 ng/mL	7.6 (3.3–15.1)	0.9 (0.8–0.9)

Table 2–2. Empiric therapy or definitive testing for persistent cough.

Suspected Condition	Step 1 (Empiric Therapy)	Step 2 (Definitive Testing)
Postnasal drip	Therapy for allergy or chronic sinusitis	Sinus CT scan; otolaryngologic referral
Asthma	Beta-2-agonist	Spirometry; consider methacholine challenge if normal
GERD	Lifestyle and diet modifications with or without PPIs	Esophageal pH monitoring

maximum-strength regimen for postnasal drip, asthma, or GERD for 2–4 weeks is one recommended approach since the presence of postnasal drip, asthma, or GERD does not mean they are the cause of the cough. Alternative approaches to identifying corticosteroid-responsive cough due to asthma include examining induced sputum for increased eosinophil counts (greater than 3%) or providing an empiric trial of prednisone, 30 mg daily orally for 2 weeks.

Nonasthmatic eosinophilic bronchitis can be diagnosed by finding eosinophils with induced sputum analysis after the exclusion of other causes for chronic cough by clinical, radiologic, and lung function assessment. The cough usually responds well to inhaled corticosteroids.

Spirometry may help measure large airway obstruction (eg, foreign body or cancer) in patients who have persistent cough and wheezing and who are not responding to asthma treatment. When empiric treatment trials are not successful, additional evaluation with pH manometry, endoscopy, barium swallow, sinus CT, or HRCT of the chest may identify the cause.

Differential Diagnosis

A. Acute Cough

Acute cough may be a symptom of acute respiratory tract infection, COVID-19, asthma, allergic rhinitis, HF, and ACE inhibitor therapy, as well as less common causes.

When community influenza-like illness activity levels are high, clinical diagnosis of influenza (cough, fever, chills with or without sweats, myalgias, and acute onset) has a positive predictive value of approximately 70%; this usually obviates the need for rapid diagnostic tests to guide isolation and empiric treatment decisions. The CDC's FluView displays weekly updates of influenza surveillance data (https://www.cdc.gov/flu/weekly/index.htm).

B. Persistent and Chronic Cough

Causes of persistent cough include environmental exposures (cigarette smoke, air pollution), occupational exposures, pertussis, postnasal drip, asthma (including cough-variant asthma), GERD, COPD, chronic aspiration, bronchiectasis, nonasthmatic eosinophilic bronchitis, tuberculosis or other chronic infection, interstitial lung disease, and bronchogenic carcinoma. The prevalence of cough 1 year after hospitalization for COVID-19 is 2.5%. COPD is a common cause of persistent cough among patients older than 50 years who have smoked cigarettes. Persistent cough may also be due to somatic cough syndrome or tic cough, or vocal fold dysfunction. When empiric treatment trials fail, consider other causes of chronic cough such as obstructive sleep apnea, tonsillar or uvular enlargement, and environmental fungi (see Chapter 38).

C. Cough in the Immunocompromised Patient

The evaluation of cough in immunocompromised patients is the same as in immunocompetent patients but with an increased concern for tuberculosis (regardless of radiographic findings), fungi, cytomegalovirus, varicella, herpesvirus, and *Pneumocystis jirovecii*.

Treatment

A. Acute Cough

Treatment of acute cough should target the underlying etiology of the illness, the cough reflex, and any additional factors that exacerbate the cough. Cough duration is typically 1–3 weeks, yet patients frequently expect cough to last fewer than 10 days. An open randomized trial of adults with uncomplicated acute bronchitis (symptoms less than 3 weeks) found no benefit compared to usual care with dextromethorphan 15 mg three times a day, ipratropium bromide inhaler 20 mcg 2 puffs three times a day, or 30 mg of honey three times a day for up to 14 days.

When influenza is diagnosed, oral oseltamivir or zanamivir or intravenous peramivir are equally effective (1 less day of illness) when initiated within 30–48 hours of illness onset; treatment is recommended regardless of illness duration when patients have severe, complicated, or progressive influenza and in patients requiring hospitalization. In *Chlamydophila*- or *Mycoplasma*-documented infection or outbreaks, first-line antibiotics include erythromycin or doxycycline; antibiotics do not otherwise improve cough severity or duration in patients with uncomplicated acute bronchitis. In patients with bronchitis and wheezing, inhaled beta-2-agonists reduce severity and duration of cough. In patients with acute cough, treating the accompanying postnasal drip (with antihistamines, decongestants, saline nasal irrigation, or nasal corticosteroids) can be helpful. Two studies found codeine to be no more effective than placebo in reducing acute cough symptoms.

B. Persistent and Chronic Cough

Evaluation and management of persistent cough often require multiple visits and therapeutic trials, which frequently lead to frustration, anger, and anxiety. When pertussis infection is suspected early in its course, treatment with a macrolide antibiotic (see Chapter 35) is appropriate to reduce organism shedding and transmission. When pertussis has lasted more than 7–10 days, antibiotic treatment does not affect the duration of cough, which can last up to 6 months. Early identification, revaccination with Tdap, and treatment are encouraged for adult patients who work or live with persons at high risk for complications from pertussis (pregnant women, infants [particularly younger than 1 year], and immunosuppressed individuals).

Table 2–2 outlines empiric treatments for persistent cough. There is no evidence to guide how long to continue treatment for persistent cough due to postnasal drip, asthma, or GERD. Studies have not found a consistent benefit of inhaled corticosteroid therapy in adults with persistent cough.

There is insufficient evidence to recommend routine pharmacologic treatments (antibiotics, bronchodilators, mucolytics) to relieve chronic cough due to stable chronic bronchitis.

The small percentage of patients with idiopathic chronic cough should be managed in consultation with an otolaryngologist or a pulmonologist; consider an HRCT scan of the lungs. Treatment options include lidocaine throat spray, nebulized lidocaine therapy, and morphine sulfate, 5–10 mg orally twice daily. Sensory dysfunction of the laryngeal branches of the vagus nerve may contribute to persistent cough syndromes and may explain the effectiveness of gabapentin and baclofen in patients with chronic cough.

Speech pathology therapy combined with pregabalin has some benefit in chronic refractory cough. In patients with cough hypersensitivity syndrome, therapy aimed at shifting the patient's attentional focus from internal stimuli to external focal points can be helpful. PPIs are not effective when used in isolation for treating chronic cough due to gastroesophageal reflux; most benefit appears to come from lifestyle modifications and weight reduction.

When to Refer

- Failure to control persistent or chronic cough following empiric treatment trials.
- Patients with recurrent symptoms should be referred to an otolaryngologist, pulmonologist, or gastroenterologist.

When to Admit

- Patients at high risk for tuberculosis for whom adherence to respiratory precautions is uncertain.
- Need for urgent bronchoscopy, such as suspected foreign body.
- Smoke or toxic fume inhalational injury.
- Gas exchange is impaired by cough.
- Patients at high risk for barotrauma (eg, recent pneumothorax).

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DYSPNEA

ESSENTIAL INQUIRIES

- Fever, cough, risk of COVID-19 infection, and chest pain.
- Vital sign measurements; pulse oximetry.
- Cardiac and chest examination.
- CXR and ABG measurement in selected patients.

General Considerations

Dyspnea is a subjective experience or perception of uncomfortable breathing. The relationship between the level of dyspnea and the severity of underlying disease varies widely. Dyspnea can result from conditions that increase the mechanical effort of breathing (eg, asthma, COPD, respiratory muscle weakness, pneumothorax, and pleural effusion [which impact gas exchange, as well]), alveolar lung disease (pulmonary edema, pneumonia, alveolar proteinosis), conditions that produce compensatory tachypnea (eg, hypoxemia, acidosis), primary pulmonary vasculopathy (pulmonary hypertension), or psychogenic conditions.

Clinical Findings

A. Symptoms

The duration, severity, and periodicity of dyspnea influence the tempo of the clinical evaluation. Rapid onset or severe dyspnea in the absence of other clinical features should raise concern for PE, increased LVEDP, or pneumothorax.

PE should always be suspected when a patient with new dyspnea reports a recent history (previous 4 weeks) of prolonged immobilization or surgery, estrogen therapy, or other risk factors for DVT (eg, previous history of thromboembolism, cancer, obesity, lower extremity trauma), but also when the cause of dyspnea is not apparent. Silent MI, which occurs more frequently in women and persons with diabetes, can result in increased LVEDP, acute HF, and dyspnea. Spontaneous pneumothorax is usually accompanied by chest pain and occurs most often in thin, young men and in those with underlying lung disease.

Accompanying symptoms provide clues to causes of dyspnea. When cough and fever are present, pulmonary disease (particularly infection) is the primary concern; myocarditis, pericarditis, and septic emboli can also present in this manner. Chest pain should be further characterized as acute or chronic, pleuritic or exertional. Although acute pleuritic chest pain is the rule in acute pericarditis and pneumothorax, most patients with pleuritic chest pain in the outpatient clinic have pleurisy due to acute viral respiratory tract infection. Periodic chest pain that precedes the onset of dyspnea suggests myocardial ischemia or PE. Most cases of dyspnea associated with wheezing are due to acute bronchitis; however, other causes include new-onset asthma, foreign body, and vocal fold dysfunction. Interstitial lung disease and pulmonary hypertension

should be considered in patients with symptoms (or history) of connective tissue disease. Pulmonary lymphangitic carcinomatosis should be considered if a patient has a malignancy, especially breast, lung, or gastric cancer.

When a patient reports prominent dyspnea with mild or no accompanying features, consider chronic PE and noncardiopulmonary causes of impaired oxygen delivery (anemia, methemoglobinemia, cyanide ingestion, carbon monoxide poisoning), metabolic acidosis, panic disorder, and neuromuscular disorders.

The diagnosis of HFpEF as the cause of dyspnea is challenging in the absence of overt congestion; the diagnosis may be made by echocardiography.

Patients who recover from their initial COVID-19 infection may have persistent dyspnea as part of the "long COVID" syndrome. Platypnea-orthodeoxia syndrome is characterized by dyspnea and hypoxemia on sitting or standing that improves in the recumbent position. Hyperthyroidism can cause dyspnea from increased ventilatory drive, respiratory muscle weakness, or pulmonary hypertension.

B. Physical Examination

A focused physical examination should include evaluation of the head and neck, chest, heart, and lower extremities. Visual inspection of the patient can suggest obstructive airway disease (pursed-lip breathing, use of accessory respiratory muscles, barrel-shaped chest), pneumothorax (asymmetric excursion), or metabolic acidosis (Kussmaul respirations). Patients with impending upper airway obstruction (eg, epiglottitis, foreign body) or severe asthma sometimes assume a tripod position. Focal wheezing suggests a foreign body or other bronchial obstruction.

Maximum laryngeal height (the distance between the top of the thyroid cartilage and the suprasternal notch at end expiration) is a measure of hyperinflation. Obstructive airway disease is virtually nonexistent when a nonsmoking patient younger than age 45 years has a maximum laryngeal height greater than 4 cm; factors increasing the likelihood of obstructive airway disease (in patients without known obstructive airway disease) include patient history of more than 40 pack-years smoking (adjusted LR+ 11.6; LR– 0.9), patient age 45 years or older (LR+ 1.4; LR– 0.5), and maximum laryngeal height less than or equal to 4 cm (LR+ 3.6; LR– 0.7). With all three of these factors present, the LR+ rises to 58.5 and the LR– falls to 0.3.

Absent breath sounds suggest a pneumothorax. An accentuated pulmonic component of the second heart sound (loud P_2) is a sign of pulmonary hypertension and PE.

Clinical predictors of increased LVEDP in dyspneic patients with no prior history of HF include tachycardia, systolic hypotension, jugular venous distention, hepatojugular reflux, bibasilar crackles, third heart sound, lower extremity edema, and chest film findings of pulmonary vascular redistribution or cardiomegaly. When none is present, there is a low probability (less than 10%) of increased LVEDP, but when two or more are present, there is a high probability (greater than 90%) of increased LVEDP.

C. Diagnostic Studies

Causes of dyspnea that can be managed without CXR are few: anemia, carbon monoxide poisoning, and ingestions causing lactic acidosis and methemoglobinemia.

1. Chest radiography—The diagnosis of pneumonia should be confirmed by CXR in most patients, and elevated blood levels of procalcitonin or CRP can support the diagnosis of pneumonia in equivocal cases or in the presence of interstitial lung disease. Conversely, a low procalcitonin can help exclude pneumonia in dyspneic patients presenting with HF. (See Table 2–1 for other diagnostic findings in pneumonia.)

CXR has a moderate sensitivity (53–75%) and a high specificity (86–96%) for new-onset HF (represented by redistribution of pulmonary venous circulation) and can help guide treatment of patients with other cardiac diseases. NT-proBNP can assist in the diagnosis of HF (see below). End-expiratory CXR enhances detection of small pneumothoraces. A normal CXR has substantial diagnostic value. When there is no physical examination evidence of COPD or HF and the CXR and ECG are normal, the major remaining causes of dyspnea include PE, *P jirovecii* infection (the initial radiograph may be normal in up to 25%), upper airway obstruction, foreign body, anemia, and metabolic acidosis. If a patient has tachycardia or hypoxemia but a normal CXR and ECG, then tests to exclude pulmonary emboli, anemia, or metabolic acidosis are warranted.

2. Point-of-care ultrasonography (POCUS)—When added to a standard diagnostic pathway, studies have confirmed that the use of POCUS leads to statistically significantly more correct diagnoses in patients with acute dyspnea than the standard diagnostic pathway alone. POCUS consistently improves the sensitivities and specificities of standard diagnostic pathways to detect HF, pneumonia, PE, pleural effusion, or pneumothorax.

3. High-resolution chest CT—This test is particularly useful in the evaluation of interstitial and alveolar lung disease. Helical ("spiral") CT is useful to diagnose PE since the images are high resolution and require only one breath hold by the patient. To minimize unnecessary testing and radiation exposure, however, the clinician should first employ a clinical decision rule for ruling out acute PE, such as the PERC (Pulmonary Embolism Rule-Out Criteria), the Wells score, the revised Geneva scores with fixed or adapted D-dimer thresholds, or the YEARS algorithm. It is appropriate to forego CT scanning in patients with low probability of pulmonary embolus when other causes of dyspnea are more likely (see Chapter 9).

4. Pulmonary function testing with diffusing capacity of the lungs for carbon monoxide—A low DLCO is associated with interstitial lung disease, emphysema, pulmonary vascular disease, chronic HF, and drug toxicity. A DLCO above the upper limit of normal (uncommon) may occur in individuals with asthma, obesity, or increased blood volume or hemoglobin (polycythemia, left-to-right cardiac shunt, pregnancy, pulmonary hemorrhage).

5. Cardiopulmonary exercise testing—A maximal exercise test with a gas exchange analysis that determines minute ventilation, heart rate, oxygen uptake, and carbon dioxide output may help determine the cause of exertional dyspnea, exercise intolerance, or exercise-induced hypoxemia.

6. Serum BNP and cardiac troponin—Laboratory findings suggesting increased LVEDP include elevated serum BNP or NT-proBNP levels. Acute decompensated HF is unlikely if NT-proBNP is less than300 pg/mL or BNP is less than 100 pg/mL, and ECG is normal. High-sensitivity cardiac troponin T (hs-CTnT) may be a marker of HFpEF causing dyspnea.

7. Arterial blood gas—ABG measurement may be considered if clinical examination and routine diagnostic testing are equivocal. With two notable exceptions (carbon monoxide poisoning and cyanide toxicity), ABG measurement distinguishes increased mechanical effort causes of dyspnea (respiratory acidosis with or without hypoxemia) from compensatory tachypnea (respiratory alkalosis with or without hypoxemia or metabolic acidosis) and from psychogenic dyspnea (respiratory alkalosis). Carbon monoxide and cyanide impair oxygen delivery with minimal alterations in Po_2; percent carboxyhemoglobin identifies carbon monoxide toxicity. Cyanide poisoning should be considered when profound lactic acidosis follows exposure to burning vinyl (such as a theater fire or industrial accident). Suspected carbon monoxide poisoning or methemoglobinemia can also be confirmed with venous carboxyhemoglobin or methemoglobin levels. Venous blood gas testing is also an option for assessing acid-base and respiratory status by measuring venous pH and Pco_2 but is unable to provide information on oxygenation. To correlate with ABG values, venous pH is typically 0.03–0.05 units lower, and venous Pco_2 is typically 4–5 mm Hg higher than arterial samples.

8. Pulse oximetry—Because ABG testing is impractical in most outpatient settings, pulse oximetry is useful in the office evaluation of dyspnea. Oxygen saturation values above 96% almost always correspond with a Po_2 greater than 70 mm Hg, whereas values less than 94% may represent clinically significant hypoxemia. Important exceptions to this rule include carbon monoxide toxicity, which leads to normal oxygen and methemoglobinemia, which results in an oxygen saturation of about 85% that fails to increase with supplemental oxygen. Pulse oximetry to detect occult hypoxia is less accurate in Black patients (OR, 2.57) compared to White patients. A delirious or obtunded patient with obstructive lung disease warrants immediate measurement of ABGs to exclude hypercapnia and the need for intubation, regardless of the oxygen saturation. If a patient reports dyspnea with exertion, but resting oximetry is normal, assessment of desaturation with ambulation (eg, a brisk walk around the clinic) can be useful for confirming impaired gas exchange. Persons with COVID-19 may have low oxygen saturation with minimal dyspnea and profound desaturation with minimal exertion.

For patients without known cardiac or pulmonary disease reporting dyspnea on exertion, spirometry, NT-proBNP, and CT imaging are the most informative tests.

Episodic dyspnea can be challenging if an evaluation cannot be performed during symptoms. Life-threatening causes include recurrent PE, myocardial ischemia, and reactive airway disease. When dyspnea follows an emotionally or physically stressful event, Takotsubo cardiomyopathy (stress cardiomyopathy or broken heart syndrome) should be considered. When associated with audible wheezing, vocal fold dysfunction should be considered, particularly in a young woman who does not respond to asthma therapy. Spirometry is helpful in further classifying patients with obstructive airway disease but is rarely needed in the initial or emergent evaluation of patients with acute dyspnea.

Differential Diagnosis

Urgent and emergent conditions causing acute dyspnea include pneumonia, COPD, asthma, pneumothorax, PE, cardiac disease (eg, HF, acute MI, valvular dysfunction, arrhythmia, intracardiac shunt), pleural effusion, COVID-19, diffuse alveolar hemorrhage, metabolic acidosis, cyanide toxicity, methemoglobinemia, and carbon monoxide poisoning. Chronic dyspnea may be caused by interstitial lung disease, pulmonary hypertension, or pulmonary alveolar proteinosis.

Treatment

Pending diagnosis, patients with hypoxemia should immediately be provided supplemental oxygen unless significant hypercapnia is strongly suspected pending ABG measurement. In the management of acute respiratory failure, high-flow nasal oxygen may reduce all-cause mortality, rates of intubation, and hospital-acquired pneumonia compared to noninvasive ventilation. Dyspnea frequently occurs in patients nearing the end of life. Opioid therapy, anxiolytics, and corticosteroids can provide substantial relief independent of the severity of hypoxemia. Inhaled opioids are not effective.

Oxygen therapy is most beneficial to patients with significant hypoxemia (Pao_2 less than 55 mm Hg) (see Chapter 5). In patients with severe COPD and hypoxemia, oxygen therapy improves exercise performance and mortality. Pulmonary rehabilitation programs are another therapeutic option for patients with moderate to severe COPD or interstitial pulmonary fibrosis. Noninvasive ventilation may be considered for patients with dyspnea caused by an acute COPD exacerbation.

When to Refer

- Following acute stabilization, patients with advanced COPD should be referred to a pulmonologist, and patients with HF or valvular heart disease should be referred to a cardiologist.
- Cyanide toxicity or carbon monoxide poisoning should be managed in conjunction with a toxicologist.
- Lung transplantation can be considered for patients with advanced interstitial lung disease.

When to Admit

- Impaired gas exchange from any cause or high risk of PE pending definitive diagnosis.
- Suspected cyanide toxicity or carbon monoxide poisoning.

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HEMOPTYSIS

ESSENTIAL INQUIRIES

- Fever, cough, and other symptoms of lower respiratory tract infection.
- Smoking history.
- Nasopharyngeal or GI bleeding.
- CXR and CBC (and, in some cases, INR).

General Considerations

Hemoptysis is the expectoration of blood that originates below the vocal folds. It is commonly classified as trivial, mild, or massive—the latter defined as more than 200–600 mL (about 1–2 cups) in 24 hours. Massive hemoptysis can be usefully defined as any amount that is hemodynamically significant or threatens ventilation. Its in-hospital mortality was 6.5% in one study. The initial goal of management of massive hemoptysis is therapeutic, not diagnostic.

The causes of hemoptysis can be classified anatomically.

Blood in the **upper airway** may come from malignant invasion or foreign body.

Hemoptysis from **lower airways** may arise from COPD, bronchiectasis, bronchial Dieulafoy disease, or bronchogenic carcinoma.

Pulmonary vasculature can be the source of hemoptysis in LV failure, mitral stenosis, PE, pulmonary arterial hypertension, telangiectasias, arteriovenous malformations, and multiple pulmonary artery aneurysms. Diffuse alveolar hemorrhage—manifested by alveolar infiltrates on CXR—is due to small vessel bleeding usually caused by autoimmune or hemostatic disorders, or rarely precipitated by hypertensive emergency, anticoagulant therapy and infection.

Systemic circulation can be the source of hemoptysis when there is intralobar pulmonary sequestration or aortobronchial fistula.

Pulmonary parenchyma diseases due to pneumonia, fungal infections, inhalation of crack cocaine, granulomatosis with polyangiitis, or Takayasu arteritis with pulmonary arteritis can cause hemoptysis. Hemoptysis can also be caused by the parasitic diseases paragonimiasis (most common cause worldwide) and human echinococcosis (also called hydatid disease).

Most cases of hemoptysis presenting in the outpatient setting are due to infection (eg, acute or chronic bronchitis, pneumonia, tuberculosis, infection with *Mycobacterium avium* complex, aspergillosis). Hemoptysis due to lung cancer increases with age, causing up to 20% of cases among older adults. Pulmonary venous hypertension (eg, mitral stenosis, PE) causes hemoptysis in less than 10% of cases. Most cases of hemoptysis that have no visible cause on CT scan or bronchoscopy will resolve within 6 months without treatment, with the notable exception of patients at high risk for lung cancer (patients who smoke cigarettes and are older than 40 years). Iatrogenic hemorrhage may follow transbronchial lung biopsies, anticoagulation, or pulmonary artery rupture due to distal placement of a balloon-tipped catheter. Obstructive sleep apnea with elevated pulmonary arterial pressure may be a risk factor for hemoptysis. Amyloidosis of the lung can cause hemoptysis, as can endometriosis. No cause is identified in up to 15–30% of cases.

Clinical Findings

A. Symptoms

Blood-tinged sputum in the setting of an upper respiratory tract infection in an otherwise healthy, young (age under 40 years) nonsmoker does not warrant an extensive diagnostic evaluation if the hemoptysis subsides with resolution of the infection. However, hemoptysis is frequently a sign of serious disease, especially in patients with a high prior probability of underlying pulmonary pathology. Hemoptysis is the only symptom found to be a specific predictor of lung cancer. It portends a high risk of mortality in COVID-19 infection. There is no value in distinguishing blood-streaked sputum and cough productive of blood during evaluation; the goal of the history is to identify patients at risk for one of the disorders listed earlier. Pertinent features include duration of symptoms, presence of respiratory infection, and past or current tobacco use. Nonpulmonary sources of hemorrhage—from the sinuses or the GI tract—must be excluded.

B. Physical Examination

Elevated pulse, hypotension, and decreased oxygen saturation suggest large-volume hemorrhage that warrants emergent evaluation and stabilization. The nares and oropharynx should be carefully inspected to identify a potential upper airway source of bleeding. Chest and cardiac examination may reveal evidence of HF or mitral stenosis.

C. Diagnostic Studies

Diagnostic evaluation should include a CXR and CBC. Kidney function tests, UA, and coagulation studies are appropriate in specific circumstances. Hematuria that accompanies hemoptysis may be a clue to anti-glomerular basement membrane antibody disease or vasculitis. Flexible bronchoscopy reveals endobronchial cancer in 3–6% of patients with hemoptysis who have a normal (nonlateralizing) CXR. Nearly all these patients are cigarette smokers over the age of 40, and most will have had symptoms for more than 1 week. HRCT of the chest complements bronchoscopy; it can visualize unsuspected bronchiectasis and arteriovenous malformations and will show central endobronchial cancers in many cases. It is the test of choice for suspected small peripheral malignancies. Helical pulmonary CT angiography is the initial test of choice for evaluating patients with suspected PE, although caution should be taken to avoid large contrast loads with even mild CKD (serum creatinine greater than 2.0 g/dL or rapidly rising creatinine in normal range). Helical CT scanning can be avoided in patients who are at "unlikely" risk for PE using the Wells score or PERC (Pulmonary Embolism Rule-Out Criteria) rule for PE and the sensitive D-dimer test (see Chapter 9). Echocardiography may reveal evidence of HF or mitral stenosis. Multidetector CT angiography is the study of choice to determine the location, etiology, and mechanism of the bleeding.

Treatment

Mild hemoptysis management consists of identifying and treating the specific cause. One double-blind RCT compared treatment with inhalations of tranexamic acid (an antifibrinolytic drug) versus placebo (normal saline) in patients hospitalized with mild hemoptysis (less than 200 mL of expectorated blood per 24 hours). The study findings included faster resolution of bleeding, shorter length of hospital stay, and fewer invasive procedures with tranexamic acid treatment. Decreased in-hospital mortality was observed in a separate randomized trial (11.5% mortality rate in control group versus 9.0% in patients who received tranexamic acid).

Massive hemoptysis is life-threatening. The airway should be protected with endotracheal intubation, ventilation ensured, and effective circulation maintained. If the location of the bleeding site is known, the patient should be placed in the decubitus position with the involved lung dependent. Uncontrollable hemorrhage warrants rigid bronchoscopy and surgical consultation. In stable patients, flexible bronchoscopy may localize the site of bleeding, and angiography can embolize the involved bronchial arteries. Embolization is effective initially in 85% of cases, although rebleeding may occur in up to 20% of patients during the following year. The anterior spinal artery arises from the bronchial artery in up to 5% of people, and paraplegia may result if it is inadvertently cannulated and embolized.

When to Refer

- Refer to a pulmonologist when bronchoscopy of the lower respiratory tract is needed.
- Refer to an otolaryngologist when an upper respiratory tract bleeding source is identified.
- Refer to a hematologist when severe coagulopathy complicates management.

When to Admit

- To stabilize bleeding in patients at risk for or experiencing massive hemoptysis.
- To correct disordered coagulation (using clotting factors or platelets, or both) or to reverse anticoagulation.
- To stabilize gas exchange.

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CHEST PAIN

ESSENTIAL INQUIRIES

- Pain onset, character, location/size, duration, periodicity, and exacerbators; shortness of breath.
- Vital signs; chest and cardiac examinations.
- ECG and biomarkers of myocardial necrosis in selected patients.

General Considerations

Chest pain (or chest discomfort) can occur as a result of cardiovascular, pulmonary, pleural, or musculoskeletal disease; esophageal or other GI disorders; herpes zoster; cocaine use; or anxiety states. The frequency and distribution of life-threatening causes of chest pain, such as ACS, pericarditis, aortic dissection, vasospastic angina, PE, pneumonia, and esophageal perforation, vary substantially between clinical settings.

SLE, rheumatoid arthritis, reduced eGFR, and HIV infection are conditions that confer a strong risk of CAD. Precocious ACS (occurring in patients aged 35 years or younger) may represent acute thrombosis independent of underlying atherosclerotic disease. Risk factors for

precocious ACS are obesity, familial hypercholesterolemia, and cigarette use.

Although ACS presents with a broader range of symptoms in women than men, typical chest pain characteristics of acute MI do not differ in frequency or strength between men and women.

Because PE can present with a variety of symptoms, consideration of the diagnosis and rigorous risk factor assessment for VTE is critical. VTE risk factors include cancer, trauma, recent surgery, prolonged immobilization, pregnancy, oral contraceptives, family history, HF, COPD, and prior history of VTE. Sickle cell anemia can cause acute chest syndrome, often with chest pain, fever, and cough.

Clinical Findings

A. Symptoms

Myocardial ischemia is usually described as a dull, aching sensation of "pressure," "tightness," "squeezing," or "gas," rather than as sharp or spasmodic. Chest discomfort at rest is the most common presenting symptom of ACS, reported by 79% of men and 74% of women. Pain reaching maximum intensity in seconds is uncommon. Ischemic symptoms usually subside within 5–20 minutes but may last longer. Progressive symptoms or symptoms at rest may represent unstable angina. Up to one-third of patients with acute MI do not report chest pain. In patients who have a STEMI, chest pain is present in more than 90% of persons under age 65 but in only 57% of those over age 85.

Continuous chest pain lasting 24 hours or longer is unlikely to be due to an acute MI (LR, 0.15). However, chest pain lasting 1 minute or less does not exclude MI (LR, 0.95). When present, pain due to myocardial ischemia is commonly accompanied by a sense of anxiety or uneasiness. The location is usually retrosternal or left precordial. Because the heart lacks somatic innervation, precise localization of pain due to cardiac ischemia is difficult; the pain is commonly referred to the throat, lower jaw, shoulders, inner arms, upper abdomen, or back. Ischemic pain may be precipitated or exacerbated by exertion, cold temperature, meals, stress, or combinations of these factors and is usually relieved by rest. However, many episodes do not conform to these patterns, and a broader range of symptoms of ACS are more common in women, older adults, and persons with diabetes mellitus. Other symptoms that are associated with ACS include shortness of breath; dizziness; a feeling of impending doom; and vagal symptoms, such as nausea and diaphoresis. In older persons, unusual or unexplained fatigue is a common presenting complaint of ACS.

The presenting symptoms of acute MI in patients aged 18–55 (average age 47) are different in men and women. The VIRGO study of this younger cohort hospitalized for MI found that women are more likely than men to present with three or more associated symptoms (eg, epigastric symptoms; palpitations; and pain or discomfort in the jaw, neck, arms, or between the shoulder blades; 61.9% for women versus 54.8% for men). In adjusted analyses, women with an acute STEMI were more likely than men to present without chest pain (OR, 1.51). In comparison with men, women were more likely to perceive symptoms as stress/anxiety (20.9% versus 11.8%) but less likely to attribute symptoms to muscle pain (15.4% versus 21.2%).

One analysis found the following clinical features to be associated with acute MI: chest pain that radiates to the left, right, or both arms (LR, 2.3); diaphoresis (LR, 2.0); nausea and vomiting (LR, 1.9); third heart sound (LR, 3.2); systolic blood pressure less than or equal to 80 mm Hg (LR, 3.1); pulmonary crackles (LR, 2.1); any ST-segment elevation greater than or equal to 1 mm (LR, 11.2); any ST depression (LR, 3.2); any Q wave (LR, 3.9); any conduction defect (LR, 2.7); and new conduction defect (LR, 6.3).

A meta-analysis reported the clinical features and risk factors with highest positive LRs for ACS were prior abnormal stress test (specificity, 96%; LR, 3.1), peripheral arterial disease (specificity, 97%; LR, 2.7), and pain radiation to both arms (specificity, 96%; LR, 2.6), as well as the following ECG findings: ST-segment depression (specificity, 95%; LR, 5.3) and any evidence of ischemia (specificity, 91%; LR, 3.6). Risk scores derived from both the HEART trial (https://www.mdcalc.com/heart-score-major-cardiac-events) and TIMI trial (https://www.mdcalc.com/timi-risk-score-ua-nstemi#use-cases) performed well in detecting ACS (LR, 13 for HEART score of 7–10, and LR, 6.8 for TIMI score of 5–7).

Hypertrophy of either ventricle or aortic stenosis may give rise to chest pain with less typical features. Pericarditis produces pain that may be greater when supine than upright and increases with breathing, coughing, or swallowing. Pleuritic chest pain is usually not ischemic, and pain on palpation may indicate a musculoskeletal cause. Aortic dissection classically produces an abrupt onset of tearing pain of great intensity that often radiates to the back; however, this classic presentation occurs in a small proportion of cases. Anterior aortic dissection can also lead to myocardial or cerebrovascular ischemia.

In PE, chest pain is present in about 75% of cases. The chief objective in evaluating patients with suspected PE is to assess the clinical risk for VTE based on medical history and associated symptoms and signs (see above and Chapter 9). Rupture of the thoracic esophagus iatrogenically or from vomiting is another cause of chest pain.

B. Physical Examination

Findings on physical examination can occasionally yield important clues to the underlying cause of chest pain; however, a normal physical examination should never be used as the sole basis for ruling out most causes of chest pain, particularly ACS and aortic dissection. Vital signs (including pulse oximetry) and cardiopulmonary examination are the first steps for assessing the urgency and tempo of the subsequent examination and diagnostic workup. Although chest pain that is reproducible or worsened with palpation strongly suggests a musculoskeletal cause, up to 15% of patients with ACS will have reproducible chest wall tenderness. In one study, reproducible chest pain had a negative predictive value of 98%. A prominent xyphoid process painful to palpation may indicate xiphodynia. Slipping rib syndrome should be suspected if the chest pain is reproduced by the examiner pulling superiorly and anteriorly

under the costal margin with their fingers. Pointing to the location of the pain with one finger has been shown to be highly correlated with nonischemic chest pain.

Aortic dissection can result in differential blood pressures between arms (greater than 20 mm Hg), pulse amplitude deficits, and new diastolic murmurs. Although hypertension is considered the rule in patients with aortic dissection, systolic blood pressure less than 100 mm Hg is present in up to 25% of patients.

A cardiac friction rub represents pericarditis until proven otherwise. It can best be heard with the patient sitting forward at end-expiration. Tamponade should be excluded in all patients with a clinical diagnosis of pericarditis by assessing pulsus paradoxus (a decrease in systolic blood pressure greater than 10 mm Hg during inspiration) and inspection of jugular venous pulsations. Subcutaneous emphysema is common following cervical esophageal perforation but present in only about one-third of thoracic perforations (ie, those most commonly presenting with chest pain).

The absence of abnormal physical examination findings in patients with suspected PE usually serves to *increase* its likelihood, although a normal physical examination is also compatible with the more common conditions of panic/anxiety disorder and musculoskeletal disease.

C. Diagnostic Studies

1. ECG—Unless a competing diagnosis can be confirmed, an ECG is warranted in the initial evaluation of most patients with acute chest pain to help exclude ACS. When compared with White patients, Black patients who came to the emergency department with chest pain were less likely to have an ECG ordered (adjusted OR = 0.82). In a study of 11 emergency departments in Italy, 67% of patients with confirmed ACS had new-onset alterations of the ECG (compared with only 6.2% among non-ACS patients). ST-segment elevation is the ECG finding that is the strongest predictor of acute MI; however, up to 20% of patients with ACS can have a normal ECG.

In the emergency department, patients with suspected ACS can be safely removed from cardiac monitoring if they are pain-free at initial clinician assessment and have a normal or nonspecific ECG. This decision rule had 100% sensitivity for serious arrhythmia. Clinically stable patients with CVD risk factors, normal ECG, normal cardiac biomarkers, and no alternative diagnoses (such as typical GERD or costochondritis) should be followed up with a timely exercise stress test that includes perfusion imaging. However, more than 25% of patients with stable chest pain referred for noninvasive testing will have normal coronary arteries and no long-term clinical events. The ECG can also provide evidence for alternative diagnoses, such as pericarditis and PE.

2. Troponins—Diagnostic protocols using a single high-sensitivity troponin assay combined with a standardized clinical assessment are an efficient strategy to rapidly determine whether patients with chest pain are at low risk and may be discharged from the emergency department. A study of the modified HEART score using a single blood draw had a sensitivity of 100% for 30-day major adverse cardiac events if the results exceeded the threshold of either high-sensitivity troponin (3.9 ng/L), high-sensitivity troponin I (0.9 ng/L), or conventional troponin I (0.0 ng/L) at presentation.

Point-of-care troponin testing for acute MI during ambulance transport to the emergency department has good specificity and positive predictive value (99.2% and 85.7%) but poor sensitivity (26.5%).

3. Risk scores—Six established risk scores for predicting acute MI are (1) the revised Goldman Risk Score, (2) TIMI Risk Score, (3) Global Registry of Acute Cardiac Events Risk Score, (4) HEART Risk Score, (5) Vancouver Chest Pain Rule, and (6) the European Society of Cardiology (ESC) 0/1, 0/2, 0/3-h algorithm. A study comparing these risk scores (not including the ESC algorithm) for predicting acute MI within 30 days reported a sensitivity of 98% (which correlates with a negative predictive value of greater than or equal to 99.5%) if patients had a TIMI score of 1 or less with normal high-sensitivity troponin T, modified Goldman score of 1 or less with normal high-sensitivity troponin T, TIMI score of 0 with normal high-sensitivity troponin T, or HEART score of 3 or less with normal high-sensitivity troponin I. In Black patients with average cardiovascular risk, HEART score is a better predictive tool for 6-week major adverse cardiac events when compared to TIMI score. Six-week major adverse cardiac events among patients with a low-risk HEART score (0–3) was 0.9–1.7%. However, the HEART score performs poorly in stratifying risk from cocaine-associated chest pain and does not eliminate the potential for gender bias. A study found that female patients with high HEART scores were admitted to the hospital from the emergency room at much lower rates than male patients with similar HEART scores.

4. Chest radiography—CXR is often useful in the evaluation of chest pain and is always indicated when cough or shortness of breath accompanies chest pain. Findings of pneumomediastinum or new pleural effusion are consistent with esophageal perforation.

5. Stress echocardiography—Stress echocardiography is useful in risk stratifying patients with chest pain, even among those with significant obesity. Patients who arrive at the emergency department with chest pain of intermediate probability for ACS without electrocardiographic or biomarker evidence of an MI can be safely discharged from an observation unit after stress echocardiography.

6. Coronary CT angiography—Sixty-four–slice coronary CT angiography is an alternative to stress testing in the emergency department for detecting ACS among patients with normal or nonspecific ECG and normal biomarkers. A meta-analysis of nine studies found CT angiography had an estimated sensitivity of 95% for ACS and specificity of 87%, yielding a negative LR of 0.06 and a positive LR of 7.4.

7. Functional testing—Exercise ECG, nuclear stress testing or stress echocardiography appear to be the best initial noninvasive tests in symptomatic patients with suspected CAD.

A minimal-risk model for discharging patients with suspected ACS for whom noninvasive testing may be deferred was developed by the PROMISE investigators, and

includes 10 clinical variables that correlate with normal coronary CT angiography results and no clinical events: (1) younger age (mean 57.5); (2) female sex; (3) racial or ethnic minority; (4–6) no history of hypertension, diabetes, or dyslipidemia; (7) no family history of premature CAD; (8) never smoked cigarettes; (9) symptoms unrelated to physical or mental stress; and (10) higher HDL cholesterol level.

In the PROMISE trial, women had higher rates of normal noninvasive testing compared with men, but women with abnormalities on such testing were less likely to be referred for catheterization or to receive statin therapy.

In the evaluation of PE as the cause of chest pain, diagnostic test decisions and results must be interpreted in the context of the clinical likelihood of VTE. A negative D-dimer test is helpful for excluding PE in patients with low clinical probability of VTE (3-month incidence = 0.5%); however, the 3-month risk of VTE among patients with intermediate and high risk of VTE is sufficiently high in the setting of a negative D-dimer test (3.5% and 21.4%, respectively) to warrant further imaging given the life-threatening nature of an untreated PE. CT angiography has replaced ventilation-perfusion scanning as the preferred initial diagnostic test, having approximately 90–95% sensitivity and 95% specificity for detecting PE (compared with pulmonary angiography). However, for patients with high clinical probability of VTE, lower extremity ultrasound or pulmonary angiogram may be indicated even with a normal helical CT.

Panic disorder is a common cause of chest pain, accounting for up to 25% of cases that present to emergency departments and a higher proportion of cases presenting in primary care office practices. Features that correlate with an increased likelihood of panic disorder include absence of CAD, atypical quality of chest pain, female sex, younger age, and a high level of self-reported anxiety. Depression is associated with recurrent chest pain with or without CAD (OR, 2.11).

Treatment

Treatment of chest pain should be guided by the underlying etiology. The term "noncardiac chest pain" is used when a diagnosis remains elusive after an extensive workup. Almost half of patients with noncardiac chest pain reported symptom improvement with high-dose PPI therapy. Relief of constipation may be therapeutic in PPI refractory noncardiac chest pain. A meta-analysis of 15 trials suggested modest to moderate benefit for psychological (especially cognitive-behavioral) interventions. It is unclear whether tricyclic or SSRI antidepressants have benefit in noncardiac chest pain. Hypnotherapy may offer some benefit.

When to Refer

- Refer patients with angina that is poorly controlled using maximal medical therapy to a cardiologist.
- Refer patients with poorly controlled, noncardiac chest pain to a pain specialist.
- Refer patients with sickle cell anemia to a hematologist.

When to Admit

- Failure to adequately exclude life-threatening causes of chest pain, particularly MI, dissecting aortic aneurysm, PE, and esophageal rupture.
- Patients with high-risk of complications from PE, or when PE is likely despite negative spiral CT.
- TIMI score of 1 or more, HEART score greater than 3, abnormal ECG, and abnormal 0- and 2-hour troponin tests.
- Pain control for rib fracture that impairs gas exchange.

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PALPITATIONS

ESSENTIAL INQUIRIES

- Forceful, rapid, or irregular beating of the heart.
- Rate, duration, and degree of regularity of heartbeat; age at first episode.
- Factors that precipitate or terminate episodes.
- Light-headedness or syncope; neck pounding.
- Chest pain; history of MI or structural heart disease.

General Considerations

Palpitations are defined as an unpleasant awareness of the forceful, rapid, or irregular beating of the heart. They are the primary symptom for approximately 16% of patients presenting to an outpatient clinic with a cardiac complaint. Palpitations are experienced in 3.3% to 11.5% of pregnancies. Palpitations represent 5.8 of every 1000 emergency department visits, with an admission rate of 24.6%. While palpitations are usually benign, they are occasionally the symptom of a life-threatening arrhythmia. To avoid missing a dangerous cause of the patient's symptom, clinicians sometimes pursue costly and invasive testing when a conservative diagnostic evaluation is sufficient. The converse is also true. Table 2–3 lists history, physical examination, and ECG findings suggesting a cardiovascular cause for the palpitations.

When assessing palpitations in an acute care setting, the clinician must ascertain whether the symptoms represent (1) significant CVD, (2) a cardiac manifestation of a systemic disease such as thyrotoxicosis, (3) an arrhythmia that is minor and transient, or (4) a benign somatic symptom that is amplified by the patient's underlying psychological state.

Etiology

Patients with palpitations who come to an emergency department instead of a medical clinic are more likely to have a cardiac cause (47% versus 21%), whereas psychogenic causes are more common among those who seek care in office practices (45% versus 27%). In a study of patients who went to a university medical clinic with the chief complaint of palpitations, causes were cardiac in 43%, psychogenic in 31%, and miscellaneous in 10%.

Cardiac arrhythmias that can manifest as palpitations include sinus bradycardia; atrial fibrillation or flutter; sinus, supraventricular, and ventricular tachycardia; premature ventricular and atrial contractions; sick sinus syndrome; and advanced atrioventricular block.

Structural cardiac conditions that lead to palpitations due to cardiac arrhythmias include valvular heart diseases, such as aortic regurgitation or stenosis, atrial or ventricular septal defect, cardiomyopathy, congenital heart disease, pericarditis, arrhythmogenic RV cardiomyopathy, atrial myxoma, and rarely, left atrial appendage aneurysm. Mitral valve prolapse is not associated with arrhythmic events, but ventricular arrhythmias are frequent in mitral annulus disjunction.

Pericardial or myocardial infection with SARS-CoV-2 and other viruses, tuberculosis, and *Trypanosoma cruzi* (Chagas disease) can cause palpitations.

The most common psychogenic causes of palpitations are anxiety and panic disorder. The release of catecholamines during a significant stress or panic attack can trigger an arrhythmia. Asking a single question, "Have you experienced brief periods, for seconds or minutes, of an overwhelming panic or terror that was accompanied by racing heartbeats, shortness of breath, or dizziness?" can help identify patients with panic disorder.

Other causes of palpitations include fever, dehydration, hypoglycemia, hyperkalemia, anemia, thyrotoxicosis, mastocytosis, postural orthostatic tachycardia syndrome and pheochromocytoma. Drugs (such as cocaine, alcohol, caffeine, pseudoephedrine, cannabis, and illicit ephedra), prescription medications and drugs that prolong the QT interval (eg, digoxin, amitriptyline, erythromycin, methylphenidate), class 1 antiarrhythmics, dihydropyridine calcium channel blockers, acetylcholinesterase inhibitors, phenothiazines, theophylline, chemotherapeutic agents, and beta-agonists can precipitate palpitations.

Table 2–3. Palpitations: Patients at high risk for a cardiovascular cause.

Historical risk factors
Family history of significant arrhythmias
Personal or family history of syncope or resuscitated from sudden death
History of MI
Palpitations that occur during sleep
Anatomic abnormalities
Structural heart disease such as dilated or hypertrophic cardiomyopathies
Valvular disease (stenotic or regurgitant)
ECG findings
Long QT syndrome
Bradycardia
Second- or third-degree heart block
Sustained ventricular arrhythmias

Clinical Findings

A. Symptoms

Guiding the patient through a careful description of their palpitations may indicate a mechanism and narrow the differential diagnosis. Pertinent questions include the age at first episode; precipitants; and rate, duration, and degree of regularity of the heartbeat during the subjective palpitations. Palpitations lasting less than 5 minutes and a family history of panic disorder reduce the likelihood of an arrhythmic cause (LR+ = 0.38 and LR+ = 0.26, respectively). To better understand the symptom, ask patients to "tap out" the rhythm with their fingers. The circumstances associated with onset and termination can also be helpful in determining the cause. Palpitations that start and stop abruptly suggest supraventricular or ventricular tachycardias. Termination of palpitations using vagal maneuvers (eg, Valsalva maneuver or forced coughing) suggests supraventricular tachycardia.

Three common descriptions of palpitations are (1) "flip-flopping" (or "stop and start"), often caused by premature contraction of the atrium or ventricle, with the perceived "stop" from the pause following the contraction, and the "start" from the subsequent forceful contraction; (2) rapid "fluttering in the chest," with regular "fluttering" suggesting supraventricular or ventricular arrhythmias (including sinus tachycardia) and irregular "fluttering" suggesting atrial fibrillation, atrial flutter, or tachycardia with variable block; and (3) "pounding in the neck" or neck pulsations, often due to "cannon" A waves in the jugular venous pulsations that occur when the right atrium contracts against a

closed tricuspid valve (common with premature ventricular contractions and atrial ventricular dissociation).

Palpitations associated with chest pain suggest ischemic heart disease, or if the chest pain is relieved by leaning forward, pericardial disease. Palpitations with light-headedness, presyncope, or syncope suggest hypotension and may signify a life-threatening cardiac arrhythmia. Palpitations that occur regularly with exertion suggest silent ischemia, a rate-dependent bypass tract, or hypertrophic cardiomyopathy. If a benign etiology cannot be ascertained at the initial visit, ambulatory monitoring or prolonged inpatient cardiac monitoring might be warranted.

Noncardiac symptoms should be elicited since palpitations may be caused by a normal heart responding to a metabolic or inflammatory condition. Weight loss suggests hyperthyroidism. Palpitations can be precipitated by vomiting or diarrhea causing electrolyte disorders and hypovolemia. Hyperventilation, hand tingling, and nervousness are common when anxiety or panic disorder is the cause of the palpitations. Palpitations associated with flushing, episodic hypertension, headaches, anxiety, and diaphoresis may be caused by a pheochromocytoma or paraganglioma.

A family history of palpitations or sudden death suggests an inherited etiology such as long QT syndrome or Brugada syndrome. Chagas disease may cause palpitations and acute myocarditis. Younger patients should be asked about consumption of "energy drinks." Dual use of cigarettes and e-cigarettes may cause palpitations.

B. Physical Examination

Cardiovascular examination can find abnormalities that increase the likelihood of specific cardiac arrhythmias. The midsystolic click of mitral valve prolapse suggests the diagnosis of a supraventricular arrhythmia. The harsh holosystolic murmur of hypertrophic cardiomyopathy, which occurs along the left sternal border and increases with the Valsalva maneuver, suggests atrial fibrillation or ventricular tachycardia. A crescendo mid-diastolic murmur may be caused by an atrial myxoma. The presence of dilated cardiomyopathy, suggested by a displaced and enlarged cardiac point-of-maximal impulse, increases the likelihood of ventricular tachycardia and atrial fibrillation. In patients with chronic atrial fibrillation, in-office exercise (eg, a brisk walk in the hallway) may reveal an intermittent accelerated ventricular response. The clinician should look for signs of hyperthyroidism (eg, tremulousness, brisk deep tendon reflexes, or fine hand tremor) or signs of stimulant drug use (eg, dilated pupils or skin or nasal septal perforations). Visible neck pulsations (LR+, 2.68) in association with palpitations increase the likelihood of atrioventricular nodal reentry tachycardia.

C. Diagnostic Studies

1. ECG—A 12-lead ECG should be performed on all patients reporting palpitations; although, in most instances, a specific arrhythmia will not be detected. Evidence of prior MI on ECG (eg, Q waves) increases the patient's risk of nonsustained or sustained ventricular tachycardia. Ventricular preexcitation (Wolff-Parkinson-White syndrome) is suggested by a short PR interval (less than 0.20 ms) and delta waves (upsloping PR segments). Left atrial enlargement (a terminal P-wave force in V1 more negative than 0.04 ms and notching in lead II) reflects an increased risk of atrial fibrillation. A prolonged QT interval and abnormal T-wave morphology suggest the long QT syndrome and an increased risk of ventricular tachycardia.

2. Monitoring devices—For high-risk patients (Table 2–3), further diagnostic studies are warranted. A stepwise approach has been suggested—starting with ambulatory monitoring devices (ambulatory ECG monitoring if the palpitations are expected to occur within the subsequent 72-hour period, event monitoring [see Zio Patch, below] if less frequent). An implantable loop recorder can be used for extended monitoring if clinical suspicion is high and symptom to rhythm correlation cannot be otherwise established. Although the use of an implantable loop recorder has traditionally been reserved for patients experiencing syncope, the diagnostic yield of this device may be cost-effective for a broader range of patients. In patients with recurrent unexplained palpitations, a single-lead, lightweight, continuously recording ambulatory adhesive patch monitor (Zio Patch) worn for 14–21 days increases diagnostic yield while reducing the cost of diagnosis. Inpatient continuous monitoring is indicated if serious arrhythmias are strongly suspected despite normal findings on the ambulatory monitoring; invasive electrophysiologic testing should be done if the ambulatory or inpatient monitor records a worrisome arrhythmia.

An ambulatory cardiac monitoring or a signal-averaged ECG is an appropriate next step to help exclude ventricular tachycardia in patients with a prior MI. ECG exercise testing is appropriate in patients with suspected CAD and in patients who have palpitations with physical exertion. Echocardiography is useful when physical examination or ECG suggests structural abnormalities or decreased ventricular function.

Treatment

After ambulatory monitoring, most patients with palpitations are found to have benign atrial or ventricular ectopy or nonsustained ventricular tachycardia. In patients with structurally normal hearts, these arrhythmias are not associated with adverse outcomes. Abstention from caffeine and tobacco may help. Often, reassurance suffices. If not, or in symptomatic patients, a trial of a beta-blocker may be prescribed. A three-session course of cognitive-behavioral therapy that includes some physical activity has proven effective for patients with benign palpitations with or without chest pain. For treatment of specific atrial or ventricular arrhythmias, see Chapter 12.

When to Refer

- For electrophysiologic studies.
- For advice regarding treatment of atrial or ventricular arrhythmias.

When to Admit

- Palpitations associated with syncope or near-syncope, particularly when the patient is aged 75 years or older and has an abnormal ECG, hematocrit less than 30%, shortness of breath, respiratory rate higher than 24/min, or a history of HF.
- Patients with risk factors for a serious arrhythmia.

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LOWER EXTREMITY EDEMA

ESSENTIAL INQUIRIES

- History of VTE.
- Symmetry of swelling.
- Pain.
- Change with dependence.
- Hyperpigmentation, stasis dermatitis, lipodermatosclerosis, ulceration.

General Considerations

Acute and chronic lower extremity edema present important diagnostic and treatment challenges.

Chronic venous insufficiency is by far the most common cause, affecting up to 2% of the population, and the incidence of venous insufficiency has not changed over the past 25 years. Venous insufficiency is a common complication of DVT; however, only a small number of patients with chronic venous insufficiency report a history of this disorder. Venous ulceration commonly affects patients with chronic venous insufficiency, and its management is labor-intensive and expensive. Normal lower extremity venous pressure (in the erect position: 80 mm Hg in deep veins, 20–30 mm Hg in superficial veins) and cephalad venous blood flow require competent bicuspid venous valves, effective muscle contractions, normal ankle range of motion, and normal respirations. When one or more of these components fail, venous hypertension may result. The risk of cellulitis increases as the stage of chronic edema increases. Adults with unilateral or bilateral chronic edema have a 37–47% lifetime prevalence of cellulitis.

Clinical Findings

A. Symptoms and Signs

1. Unilateral lower extremity edema—Among common causes of unilateral lower extremity swelling, DVT is the most life-threatening. Clues suggesting DVT include a history of cancer, recent limb immobilization, or confinement to bed for at least 3 days following major surgery within the past month (Table 2–4). Adults with varicose veins have a significantly increased risk of DVT. Lower extremity swelling and inflammation in a limb recently affected by DVT could represent anticoagulation failure and thrombus recurrence but more often are caused by **postphlebitic syndrome** with valvular incompetence. Other causes of a painful, swollen calf include cellulitis, musculoskeletal disorders (Baker cyst rupture ["pseudothrombophlebitis"]), gastrocnemius tear or rupture, calf strain or trauma, and left common iliac vein compression (May-Thurner syndrome), complex regional pain syndrome, diabetic myonecrosis, as well as other sites of nonthrombotic venous outflow obstruction, such as the inguinal ligament, iliac bifurcation, and popliteal fossa.

2. Bilateral lower extremity edema—Bilateral involvement and significant improvement upon awakening favor systemic causes (eg, venous insufficiency) and can be presenting symptoms of volume overload (HF, cirrhosis, kidney disease [eg, nephrotic syndrome]). The most frequent

Table 2–4. Risk stratification of adults referred for ultrasound to rule out DVT.

Step 1:		
Score 1 point for each		
Active cancer (treatment within previous 6 months or current palliative care)		
Paralysis, paresis, or recent plaster immobilization of the lower extremities		
Recently bedridden for ≥ 3 days, or major surgery within previous 12 weeks		
Localized tenderness along distribution of deep venous system		
Entire leg swelling		
Swelling of one calf ≥ 3 cm more than the other (measured 10 cm below tibial tuberosity)		
Ipsilateral pitting edema		
Collateral superficial (nonvaricose) veins		
Previously documented DVT		
Step 2:		
Subtract 2 points if alternative diagnosis has equal or greater likelihood than DVT		
Step 3:		
Obtain sensitive D-dimer for score ≥ 0		
Score	**D-Dimer Positive[1]**	**D-Dimer Negative**
0–1	Obtain ultrasound	Ultrasound not required
≥ 2	Obtain ultrasound	

[1]"Positive" is above local laboratory threshold based on specific test and patient age.
Based on Wells PS et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med. 2003;349:1227. [PMID: 14507948]

symptom of chronic venous insufficiency is the sensation of "heavy legs," followed by itching. Chronic exposure to elevated venous pressure accounts for the brawny, fibrotic skin changes observed in patients with chronic venous insufficiency as well as the predisposition toward skin ulceration, particularly in the medial malleolar area. Pain, particularly if severe, is uncommon in uncomplicated venous insufficiency.

Lower extremity swelling is a familiar complication of therapy with calcium channel blockers (particularly felodipine and amlodipine), pioglitazone, gabapentin, and minoxidil. Prolonged airline flights (longer than 10 hours) are associated with edema even in the absence of DVT.

B. Physical Examination

Physical examination should include assessment of the heart, lungs, and abdomen for evidence of pulmonary hypertension (primary or secondary to chronic lung disease), HF, or cirrhosis. The skin findings related to chronic venous insufficiency depend on the severity and chronicity of the disease, ranging from hyperpigmentation and stasis dermatitis to abnormalities highly specific for chronic venous insufficiency: lipodermatosclerosis (thick, brawny skin; in advanced cases, the lower leg resembles an inverted champagne bottle) and atrophie blanche (small, depigmented macules within areas of heavy pigmentation). The size of both calves should be measured 10 cm below the tibial tuberosity and pitting and tenderness elicited. Swelling of the entire leg or of one leg 3 cm more than the other suggests deep venous obstruction. The left calf is normally slightly larger than the right as a result of the left common iliac vein coursing under the aorta.

A shallow, large, modestly painful ulcer located over the *medial* malleolus is a hallmark of chronic venous insufficiency, whereas small, deep, and more painful ulcers over the *lateral* malleolus are more apt to be due to arterial insufficiency, vasculitis, or infection. Diabetic vascular ulcers, however, may be painless. When an ulcer is on the foot or above the mid-calf, causes other than venous insufficiency should be considered.

The physical examination is usually inadequate to distinguish lymphedema from venous insufficiency. Only the Kaposi-Stemmer sign (inability to pinch a fold of skin at the base of the second toe because of its thickness) is a significant predictor of lymphedema (OR, 7.9).

C. Diagnostic Studies

Patients without an obvious cause of acute unilateral lower extremity swelling (eg, calf strain) should have an ultrasound performed, since DVT is difficult to exclude on clinical grounds. A prediction rule allows a clinician to exclude a lower extremity DVT in patients without an ultrasound if the patient has low pretest probability for DVT and a negative sensitive D-dimer test (the "Wells prediction rule") (https://www.mdcalc.com/wells-criteria-pulmonary-embolism) (Chapter 9). Previously unidentified lower extremity thrombi may be discovered in 21% of patients incompletely studied during the initial evaluation.

The diagnostic study of choice to detect chronic venous insufficiency due to venous incompetence is duplex ultrasonography. Assessment of the ankle-brachial pressure index is important in the management of chronic venous insufficiency since peripheral arterial disease may be exacerbated by compression therapy (see Chronic Venous Insufficiency, Chapter 14). Caution is required in interpreting the results of ankle-brachial pressure index in older patients and patients with diabetes due to the decreased compressibility of their arteries. A urine dipstick test that is strongly positive for protein can suggest nephrotic syndrome, and a serum creatinine can estimate kidney function. Measuring serum albumin can further assess for nephrotic syndrome or chronic liver disease. Lymphoscintigraphy can be used to confirm a clinical suspicion of lymphedema.

Treatment

See relevant chapters for treatment of edema in patients with HF (Chapter 11), nephrosis (Chapter 24), cirrhosis (Chapter 18), and lymphedema and venous stasis ulcers (Chapter 14). Edema resulting from calcium channel blocker therapy may respond to concomitant therapy with ACE inhibitors or ARBs.

In patients with chronic venous insufficiency without comorbid volume overload (eg, HF), it is best to avoid diuretic therapy since intravascular volume is relatively decreased. Instead, the most effective treatment involves (1) leg elevation, above the level of the heart, for 30 minutes three to four times daily, and during sleep; (2) compression therapy; and (3) ambulatory exercise to increase venous return through calf muscle contractions.

A wide variety of stockings and devices are effective in decreasing swelling, preventing and healing venous leg ulcers, treating stasis dermatitis, and reducing the risk of cellulitis. They should be put on with awakening before hydrostatic forces result in edema. To control mild edema, 20–30 mm Hg compression is usually sufficient, whereas 30–40 mm Hg compression is usually required to control moderate to severe edema associated with ulcer formation. To maintain improvement, consider switching from an elastic stocking to one made of inelastic grosgrain material. Patients with decreased ankle-brachial pressure index should be managed in concert with a vascular surgeon. Compression stockings (12–18 mm Hg at the ankle) are effective in preventing edema and asymptomatic thrombosis associated with long airline flights in low- to medium-risk persons, and compression therapy decreases recurrence of cellulitis among patients with chronic venous insufficiency. Support stockings are recommended for pregnant women during air travel. For lymphedema, bandaging systems applied twice weekly can be effective. Multi-component compression bandaging may offer additional benefit. Short-term manual lymphatic drainage treatment may improve chronic venous insufficiency severity, symptoms, and quality of life. For patients with reduced mobility and leg edema, intermittent pneumatic compression treatment can reduce edema and improve ankle range of motion.

Liposuction, suction-assisted lipectomy, and subcutaneous drainage may have treatment benefit if conservative measures fail in treatment of lymphedema.

When to Refer

- Refer patients with chronic lower extremity ulcerations to wound care specialist.
- Refer patients with coexisting severe arterial insufficiency (claudication) that would complicate treatment with compression stockings to a vascular surgeon.

When to Admit

- Pending definitive diagnosis in patients at high risk for DVT despite normal lower extremity ultrasound.
- Severe, acute swelling raising concern for an impending compartment syndrome.
- Severe edema that impairs ability to ambulate or perform activities of daily living.

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FEVER & HYPERTHERMIA

ESSENTIAL INQUIRIES

- Age; injection substance use.
- Localizing symptoms of infection; weight loss; joint pain.
- Immunosuppression or neutropenia; history of cancer.
- Medications.
- Travel.

General Considerations

The average normal oral body temperature taken in midmorning is 36.7°C (range 36–37.4°C). This range includes a mean and two standard deviations, thus encompassing 95% of a normal population (normal diurnal temperature variation is 0.5–1°C).

The normal rectal or vaginal temperature is 0.5°C higher than the oral temperature, and the axillary temperature is 0.5°C lower. However, a normal body temperature based on a peripheral thermometer (tympanic membrane, temporal artery, axillary, oral) does not always exclude the presence of a fever. To exclude a fever, a rectal temperature is more reliable than an oral temperature (particularly in patients who breathe through their mouth, who are tachypneic, or who are in an ICU setting where a rectal temperature probe can be placed to detect fever).

Fever is a regulated rise to a new "set point" of body temperature in the hypothalamus induced by pyrogenic cytokines. These cytokines include IL-1, TNF, interferon-gamma, and IL-6. The elevation in temperature results from either increased heat production (eg, shivering) or decreased heat loss (eg, peripheral vasoconstriction). **Hyperthermia**—not mediated by cytokines—occurs when body metabolic heat production (as in thyroid storm) or environmental heat load exceeds normal heat loss capacity or when there is impaired heat loss (eg, heat stroke). *Body temperature in cytokine-induced fever seldom exceeds 41.1°C unless there is structural damage to hypothalamic regulatory centers; body temperature in hyperthermia may rise to levels (more than 41.1°C) capable of producing irreversible protein denaturation and resultant brain damage; no diurnal variation is observed.*

Clinical Findings

A. Fever

Fever as a symptom provides important information about the presence of illness—particularly infections—and about changes in the clinical status of the patient. Fever may be more predictive of bacteremia in older patients. The fever pattern, however, is of marginal value for most specific diagnoses except for the relapsing fever of malaria, borreliosis, and occasional cases of lymphoma, especially Hodgkin disease. The degree of temperature elevation does not necessarily correspond to the severity of the illness. Fever with rash and eosinophilia defines the **d**rug **r**eaction with **e**osinophilia and **s**ystemic **s**ymptoms (DRESS) syndrome.

In general, the febrile response tends to be greater in children than in adults. In older persons, neonates, and persons receiving certain medications (eg, NSAIDs, corticosteroids), rather than a fever, a normal temperature or even hypothermia may be observed. Markedly elevated body temperature may result in profound metabolic disturbances. Febrile patients admitted to a hospital with a body temperature above 39.5°C had higher mortality and AKI events compared to patients with less fever (38.0–38.1°C). High temperature during the first trimester of pregnancy may cause birth defects, such as anencephaly. Fever increases insulin requirements and alters the metabolism and disposition of drugs used for the treatment of the diverse diseases associated with fever.

The source of fever varies by population and setting. In a study of 92 patients who underwent shoulder arthroplasty and developed fever, an infectious cause was found in only 6 patients. In the neurologic ICU, fever can occur directly from brain injury ("central fever"). One model predicted "central fever" with 90% probability if a patient met all of the following criteria: (1) less than 72 hours of neurologic ICU admission; (2) presence of subarachnoid hemorrhage, intraventricular hemorrhage, or brain tumor; (3) absence of infiltrate on CXR; and (4) negative cultures. For patients in the ICU, elevated procalcitonin and CRP levels favor infection, rather than central fever, as the cause of fever.

Spinal cord injury may cause fever by the loss of supraspinal control of the sympathetic nervous system and

defective thermoregulation due to loss of sensation. Fever may also be more common in patients with other forms of trauma. In a study of 268 patients, including patients with multiple injuries (n = 59), isolated head injuries (n = 97), isolated body injuries (n = 100), and minor trauma (n = 12), the incidence of fever was similar in all groups irrespective of injury (11–24%). In all groups, there was a significant association between the presence of early fever and death in the hospital (6–18% versus 0–3%), as well as longer median ICU stays (3–7 days versus 2–3 days).

Among pregnant women, the prevalence of intrapartum fever of 38°C or greater in pregnancies of 36 weeks' gestation or more is 6.8% (1 in 15 women in labor), but the neonatal sepsis rate among affected mothers is 0.24% (less than 1 in 400 babies). This finding calls into question the need for universal laboratory work, cultures, and antibiotic treatment pending culture results for this newborn population.

Contrary to classical teaching, postoperative atelectasis probably does not cause fever. Febrile nonhemolytic transfusion reaction is common, occurring in about 1% of transfusion episodes, and is mediated by proinflammatory cytokines elaborated by donor leukocytes during storage.

B. Hyperthermia

Malignant catatonia consists of catatonic symptoms, hyperthermia, autonomic instability, and altered mental status.

Neuroleptic malignant syndrome is a variant of malignant catatonia that is a rare and potentially lethal idiosyncratic reaction to neuroleptic medications, particularly haloperidol and fluphenazine. It has also been reported with the atypical neuroleptics (such as olanzapine or risperidone) (see Chapter 27).

Serotonin syndrome resembles neuroleptic malignant syndrome but occurs within hours of ingestion of agents that increase levels of serotonin in the CNS, including SSRIs, MAOIs, tricyclic antidepressants, meperidine, dextromethorphan, bromocriptine, tramadol, lithium, and psychostimulants (such as cocaine, methamphetamine, and MDMA) (see Chapter 40).

Clonus and hyperreflexia are more common in serotonin syndrome, whereas "lead pipe" rigidity is more common in neuroleptic malignant syndrome. Neuroleptic malignant and serotonin syndromes share common clinical and pathophysiologic features with **malignant hyperthermia of anesthesia** (see Chapter 40).

C. Fever of Undetermined Origin

See Fever of Unknown Origin, Chapter 32.

Treatment

Most fever is well tolerated. When the temperature is less than 40°C, symptomatic treatment only is required. The treatment of fever with antipyretics does not appear to affect mortality of critically ill patients or affect the number of ICU-free days. A temperature greater than 41°C is likely to be hyperthermia rather than cytokine-mediated fever, and *emergent management is indicated*. (See Heat Stroke, Chapter 39.)

A. General Measures for Removal of Heat

Regardless of the cause of the fever, alcohol sponges, cold sponges, ice bags, ice-water enemas, and ice baths will lower body temperature (see Chapter 39). They are more useful in hyperthermia since patients with cytokine-related fever will attempt to override these therapies.

B. Pharmacologic Treatment of Fever

1. Antipyretic drugs—Antipyretic therapy is only needed for patients with marginal hemodynamic status. It can, however, be used for symptomatic relief. Aspirin or acetaminophen, 325–650 mg orally every 4 hours, is effective in reducing fever. Early administration of acetaminophen to treat fever due to probable infection does not affect the number of ICU-free days. These drugs are best administered around the clock, rather than as needed, since "as needed" dosing results in periodic chills and sweats due to fluctuations in temperature caused by varying levels of drug.

2. Prophylactic antimicrobial therapy—Antibacterial and antifungal prophylactic regimens are recommended only for patients expected to have less than 100 neutrophils/mcL for more than 7 days, unless other factors increase risks for complications or mortality.

3. Empiric antimicrobial therapy—Empiric antibiotic therapy is sometimes warranted. Even before infection can be documented, prompt broad-spectrum antimicrobials are indicated for febrile patients who have hemodynamic instability, severe neutropenia (neutrophils less than 500/mcL [0.5×10^9/L]), asplenia (surgical or from sickle cell disease), or immunosuppression (from HIV infection [see Chapter 33] or from medications such as systemic corticosteroids, azathioprine, cyclosporine) (Tables 32–1 and 32–5). Febrile neutropenic patients should receive initial doses of empiric antibacterial therapy within an hour of triage and should either be monitored for at least 4 hours to determine suitability for outpatient management or be admitted to the hospital (see Infections in the Immunocompromised Patient, Chapter 32). It is standard to admit patients to the hospital with febrile neutropenic episodes, although carefully selected patients may be managed as outpatients after systematic assessment beginning with a validated risk index (eg, Multinational Association for Supportive Care in Cancer [MASCC] score or Talcott rules). In the MASCC index calculation, low-risk factors include the following: age under 60 years (2 points), burden of illness (5 points for no or mild symptoms and 3 points for moderate symptoms), outpatient status (3 points), solid tumor or hematologic malignancy with no previous fungal infection (4 points), no COPD (4 points), no dehydration requiring parenteral fluids (3 points), and systolic blood pressure greater than 90 mm Hg (5 points). Patients with MASCC scores of 21 or higher or in Talcott group 4 (presentation as an outpatient without significant comorbidity or uncontrolled cancer), and without other risk factors, can be managed safely as outpatients.

The carefully selected outpatients determined to be at low risk by MASCC score (particularly in combination

with a normal serum CRP level) or by Talcott rules can be managed with an oral fluoroquinolone plus amoxicillin/clavulanate (or clindamycin, if penicillin allergic), unless fluoroquinolone prophylaxis was used before fever developed. For treatment of fever during neutropenia following chemotherapy, outpatient parenteral antimicrobial therapy can be provided effectively and safely in low-risk patients with a single agent such as cefepime, piperacillin/tazobactam, imipenem, meropenem, or doripenem. High-risk patients should be referred for inpatient management with combination parenteral antimicrobial therapy based on specific risk factors such as pneumonia-causing pathogens or central line–associated bloodstream infections (see Infections in the Immunocompromised Patient and Table 32–1 in Chapter 32 and see Infections in Chapter 41).

If a fungal infection is suspected in patients with prolonged fever and neutropenia, fluconazole is equally effective as amphotericin B but less toxic.

C. Treatment of Hyperthermia

Discontinuation of the offending agent is mandatory. Treatment of neuroleptic malignant syndrome includes dantrolene in combination with bromocriptine or levodopa (see Chapter 27). Treatment of serotonin syndrome includes a central serotonin receptor antagonist—cyproheptadine or chlorpromazine—alone or in combination with a benzodiazepine (see Chapter 40). In patients for whom it is difficult to distinguish which syndrome is present, treatment with a benzodiazepine may be the safest therapeutic option.

When to Admit

- For vital sign abnormalities or evidence of end-organ dysfunction in clinical cases when early sepsis is suspected.
- Patients with febrile neutropenia at high risk for clinical decompensation.
- For measures to control a temperature higher than 41°C or when fever is associated with seizure or other mental status changes.
- Heat stroke (see Chapter 39).
- Malignant catatonia; neuroleptic malignant syndrome; serotonin syndrome; malignant hyperthermia of anesthesia.

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INVOLUNTARY WEIGHT LOSS

ESSENTIAL INQUIRIES

- Age; caloric intake; secondary confirmation (eg, changes in clothing size).
- Fever; change in bowel habits.
- Substance use.
- Age-appropriate cancer screening history.

General Considerations

Body weight is determined by a person's caloric intake, absorptive capacity, metabolic rate, and energy losses. Body weight normally peaks by the fifth or sixth decade and then gradually declines at a rate of 1–2 kg per decade. In NHANES II, a national survey of community-dwelling older adults (aged 50–80 years), recent involuntary weight loss (IWL) (more than 5% usual body weight) was reported by 7% of respondents, and this was associated with a 24% higher mortality. In postmenopausal women, unintentional weight loss was associated with increased rates of hip and vertebral fractures.

Etiology

IWL is regarded as clinically significant when it exceeds 5% or more of usual body weight over a 6- to 12-month period. While it often indicates serious physical or psychological illness, nonmalignant diseases more commonly cause unintentional weight loss than malignant causes. Physical causes are usually evident during the initial evaluation, but an easily identifiable cause is not found in 6–28% of cases. The most common causes are cancer (about 30%), GI disorders (about 15%), and dementia or depression (about 15%). At a university hospital in Thailand, the three most common causes of IWL were reduced appetite (20.1%), dementia (13.7%), and medications (11.0%). Nearly half of patients with Parkinson disease have weight loss associated with disease progression. When an adequately nourished–appearing patient reports weight loss, inquiry should be made about exact weight changes (with approximate dates) and about changes in clothing size. Family members can provide confirmation of weight loss, as can old documents such as photographs from driver's licenses. A mild, gradual weight loss occurs in some older individuals because of

decreased energy requirements. However, rapid IWL is predictive of morbidity and mortality.

In addition to various disease states, causes in older individuals include loss of teeth and consequent difficulty with chewing, medications interfering with taste or causing nausea, alcohol use disorder, and social isolation. Among Black persons at an adult day health center, 65% had a significant nutritional disorder: 48.5% reported involuntary weight loss or gain, 21% ate fewer than two meals daily, and 41.2% had tooth loss or mouth pain.

Clinical Findings

Once the weight loss is established, the history, medication profile, physical examination, and conventional laboratory and radiologic investigations (eg, CBC, liver biochemical tests, kidney panel, serologic tests including HIV, TSH level, UA, fecal occult blood test, and CXR) usually reveal the cause. Age-appropriate cancer screening should be completed as recommended by guidelines (eg, Papanicolaou smear, mammography, fecal occult blood test/screening colonoscopy/flexible sigmoidoscopy, possibly PSA) (Chapter 1). Whole-body CT imaging is increasingly used for diagnosis; one study found its diagnostic yield to be 33.5%. Another study found a low yield from CT scanning with contrast of the abdomen and pelvis for malignancy (2.3%) in patients whose only symptom was weight loss. When these tests are normal, a more definitive GI investigation (eg, tests for malabsorption, endoscopy) should be considered. However, one prospective case study in patients with IWL showed that colonoscopy did not find colorectal cancer if weight loss was the sole indication for the test. A low spot urinary creatinine may be a marker of muscle wasting in patients with new-onset or worsening HF as a cause of IWL.

If the initial evaluation is unrevealing, follow-up is preferable to further diagnostic testing. Death at 2-year follow-up was not nearly as common in patients with unexplained IWL (8%) as in those with weight loss due to malignant (79%) and established nonmalignant diseases (19%). Psychiatric consultation should be considered when there is evidence of depression, dementia, anorexia nervosa, or other emotional problems. Ultimately, in approximately 15–25% of cases, no cause for the weight loss can be found.

Differential Diagnosis

Malignancy, GI disorders (poorly fitting dentures, cavities, swallowing or malabsorption disorders, pancreatic insufficiency), HF, HIV, tuberculosis, psychological problems (dementia, depression, paranoia), endocrine disorders (hyper-, hypothyroidism, hyperparathyroidism, hypoadrenalism), Whipple disease, eating problems (dietary restrictions, lack of money for food, teeth problems), social problems (alcohol use disorder, social isolation), and medication side effects are all established causes.

Treatment

Weight stabilization occurs in most surviving patients with both established and unknown causes of weight loss through treatment of the underlying disorder and caloric supplementation. Nutrient intake goals are established in relation to the severity of weight loss, in general ranging from 30–40 kcal/kg/day. In order of preference, route of administration options include oral, temporary nasojejunal tube, or percutaneous gastric or jejunal tube. Parenteral nutrition is reserved for patients with serious associated problems. A variety of pharmacologic agents have been proposed for the treatment of weight loss. These can be categorized into appetite stimulants (corticosteroids, progestational agents, cannabinoids, and serotonin antagonists); anabolic agents (growth hormone, ghrelin, and testosterone derivatives); and anticatabolic agents (omega-3 fatty acids, pentoxifylline, hydrazine sulfate, and thalidomide). There is no evidence that appetite stimulants decrease mortality, and they may have severe adverse side effects. The anabolic agent nandrolone decanoate reversed weight and lean tissue loss in women with HIV, and human growth hormone temporarily increased weight and walking speed in undernourished older patients. However, studies have not consistently shown mortality benefit.

Exercise training may prevent or even reverse the process of muscle wasting in HF ("cardiac cachexia"). Protein or creatine supplementation combined with resistance exercise training and aerobic activity may prevent aging-related attenuation of muscle mass and functional performance. Some patients with cancer-associated weight loss may benefit from nutritional assessment and intervention as decreased food intake may be playing a role. The effectiveness, acceptability, and safety of exercise training for adults with cancer cachexia has not been established.

When to Refer

- Weight loss caused by malabsorption.
- Persistent nutritional deficiencies despite adequate supplementation.
- Weight loss as a result of anorexia or bulimia.

When to Admit

- Severe protein-energy malnutrition, including the syndromes of kwashiorkor and marasmus.
- Vitamin deficiency syndromes.
- Cachexia with anticipated progressive weight loss secondary to unmanageable psychiatric disease.
- Careful electrolyte and fluid replacement in protein-energy malnutrition and avoidance of "re-feeding syndrome."

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FATIGUE & SYSTEMIC EXERTION INTOLERANCE DISEASE (Chronic Fatigue Syndrome)

ESSENTIAL INQUIRIES

- Weight loss; fever.
- Sleep-disordered breathing.
- Medications; substance use.

General Considerations

Fatigue, as an isolated symptom, accounts for 1–3% of visits to generalists. Fatigue or lassitude and the closely related complaints of weakness, tiredness, and lethargy are often attributed to overexertion, poor physical conditioning, sleep disturbance, obesity, undernutrition, and emotional problems. A history of the patient's daily living and working habits may obviate the need for extensive and unproductive diagnostic studies.

Fatigue in older adults increases the risk of developing negative health outcomes (mortality OR, 2.14), the development of disabilities in basic activities of daily living (OR, 3.22), or the occurrence of physical decline (OR, 1.42).

Systemic exertion intolerance disease (SEID) (chronic fatigue syndrome) is not a homogeneous abnormality, there is no single pathogenic mechanism, and no physical finding or laboratory test can be used to confirm the diagnosis. Other conditions identified as causing chronic fatigue include myalgic encephalitis and neurasthenia, each with specific diagnostic criteria creating inconsistent diagnoses and treatment plans.

Clinical Findings

A. Fatigue

Clinically relevant fatigue is composed of three major components: generalized weakness (difficulty in initiating activities); easy fatigability (difficulty in completing activities); and mental fatigue (difficulty with concentration and memory). Important diseases that can cause fatigue include hyper- and hypothyroidism, hyperparathyroidism, HF, infections (endocarditis, hepatitis), COPD, asthma, interstitial lung disease, ESKD, sleep apnea, anemia, autoimmune disorders, multiple sclerosis, IBD, irritable bowel syndrome, Parkinson disease, cerebral vascular accident, and cancer.

Alcohol use disorder, vitamin C deficiency (scurvy), side effects from medications (eg, sedatives and beta-blockers), and psychological conditions (eg, insomnia, depression, anxiety, panic attacks, dysthymia, and somatic symptom disorder may be the cause. Common outpatient infectious causes include mononucleosis and sinusitis. These conditions are usually associated with other characteristic signs, but patients may emphasize fatigue and not discuss their other symptoms unless directly asked. The lifetime prevalence of significant fatigue (present for at least 2 weeks) is about 25%. Fatigue of unknown cause or related to psychiatric illness exceeds that due to physical illness, injury, alcohol, or medications.

Although frequently associated with Lyme disease, severe fatigue as a long-term sequela is rare. Posttraumatic brain injury fatigue and sleep disturbance may respond to a light box and in-home dynamic light therapy.

B. Systemic Exertion Intolerance Disease (Chronic Fatigue Syndrome)

Diagnosis of SEID requires the presence of all three of the following symptoms:

1. Substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest.
2. Postexertional malaise.
3. Unrefreshing sleep.

In addition, the patient must have at least one of the following two manifestations: (1) cognitive impairment or (2) orthostatic intolerance (lightheadedness, dizziness, and headache that worsen with upright posture and improve with recumbency).

The evaluation of SEID includes a history and physical examination as well as CBC; ESR; kidney function; serum electrolytes, glucose, creatinine, calcium; liver biochemical tests and thyroid function tests; UA; tuberculin skin test; and screening questionnaires for psychiatric disorders. Other tests to be performed as clinically indicated are serum cortisol, ANA, rheumatoid factor, immunoglobulin levels, Lyme serology in endemic areas (although rarely a long-term complication of this infection), and HIV antibody. More extensive testing is usually unhelpful, including antibody to Epstein-Barr virus. There may be an abnormally high rate of postural hypotension.

Treatment

A. Fatigue

Resistance training and aerobic exercise lessens fatigue and improves performance for a number of chronic conditions associated with a high prevalence of fatigue, including HF, COPD, arthritis, and cancer. Continuous positive airway pressure is an effective treatment for obstructive sleep apnea. Pitolisant, a selective histamine H_3-receptor antagonist with wake-promoting effect, may reduce daytime sleepiness in patients with moderate to severe obstructive sleep apnea who decline continuous positive airway pressure treatment.

Psychostimulants such as methylphenidate have shown inconsistent results in randomized trials of treatment of cancer-related fatigue. Methylphenidate and cognitive-behavioral therapy may improve mental fatigue and cognitive function in patients with traumatic brain injury. Modafinil and armodafinil appear to be effective, well-tolerated agents in patients who have HIV with fatigue and as adjunctive agents in patients who have depression or bipolar disorder with fatigue. Testosterone

replacement in hypoandrogenic men over age 65 had no significant benefits for walking distance or vitality, as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue scale. However, men receiving testosterone reported slightly better mood and lower severity of depressive symptoms than those receiving placebo. Vitamin D treatment significantly improved fatigue in kidney transplantation patients as well as in otherwise healthy persons with vitamin D deficiency. Solution-focused therapy has a significant initial beneficial effect on the severity of fatigue and quality of life in patients with quiescent IBD. Internet-based cognitive-behavioral therapy is effective in reducing severe fatigue in those who have experienced breast cancer. Therapeutic Care (a complementary medicine modality that uses acupressure) reduces fatigue in some patients with breast cancer receiving chemotherapy, while moderate-intensity exercise did not. Six weeks of Swedish massage therapy reduced fatigue in females who have experienced breast cancer and who had surgery plus radiation, chemotherapy/chemoprevention, or both. There is limited and preliminary evidence that rasagiline, modafinil, and doxepin are associated with improvement of fatigue in Parkinson disease. Amantadine, modafinil, and methylphenidate were not found to be superior to placebo in improving fatigue associated with multiple sclerosis and caused more frequent adverse events.

The treatment of subclinical hypothyroidism is unlikely to benefit symptoms of fatigue. Oral melatonin does not improve fatigue in patients with advanced cancer. Exceeding the RDA for protein intake does not increase muscle or physical function, nor augment anabolic response to testosterone in older men, nor reduce muscle soreness or fatigue after prolonged moderate-intensity walking exercise.

B. Systemic Exertion Intolerance Disease

A variety of agents and modalities have been tried for the treatment of SEID without improvement in symptoms.

Some patients with postural hypotension report response to increases in dietary sodium as well as fludrocortisone, 0.1 mg orally daily. The immunomodulator rintatolimod improved some measures of exercise performance compared with placebo in two trials (with low strength of evidence). Low-dose naltrexone is being used off-label with anecdotal reports of benefit. There is limited evidence that dietary modification is beneficial.

Patients with SEID have benefited from a comprehensive multidisciplinary intervention, including optimal medical management, treating any ongoing affective or anxiety disorder pharmacologically, and implementing a comprehensive cognitive-behavioral treatment program. At present, cognitive-behavioral therapy and graded exercise are the treatments of choice for patients with SEID.

When to Refer

- Infections not responsive to standard treatment.
- Difficult-to-control hyper- or hypothyroidism.
- Severe psychological illness.
- Malignancy.

When to Admit

- Failure to thrive.
- Fatigue severe enough to impair activities of daily living.

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ACUTE HEADACHE

ESSENTIAL INQUIRIES

- Age > 40 years.
- Rapid onset and severe intensity (ie, "thunderclap" headache), trauma, onset during exertion.
- Fever, vision changes, neck stiffness.
- HIV infection.
- Current or past history of hypertension.
- Neurologic findings (mental status changes, motor or sensory deficits, loss of consciousness).

General Considerations

Approximately 90% of people in the United States experience a headache in their lifetime. A broad range of disorders can cause headache (see Chapter 26). This section deals only with acute nontraumatic headache in adults and adolescents; migraine headache is covered in Chapter 26. The challenge in the initial evaluation of acute headache is to identify which patients are presenting with an uncommon but life-threatening condition; approximately 1% of patients seeking care in emergency department settings and considerably less in office practice settings fall into this category.

Diminution of headache in response to typical migraine therapies (such as serotonin receptor antagonists or ketorolac) does not rule out critical conditions such as subarachnoid hemorrhage or meningitis as the underlying cause. A "sentinel headache" before a subarachnoid hemorrhage is a sudden, intense, persistent headache different from previous headaches; it precedes subarachnoid hemorrhage by days or weeks and occurs in 15–60% of patients with spontaneous subarachnoid hemorrhage.

Clinical Findings

A. Symptoms

A careful history and physical examination should aim to identify causes of acute headache that require immediate treatment. These causes can be broadly classified as (1) imminent or completed vascular events (intracranial hemorrhage, thrombosis, cavernous sinus thrombosis, vasculitis, malignant hypertension, arterial dissection, cerebral venous thrombosis, reversible cerebral vasoconstriction syndrome, transient ischemic attack, or aneurysm); (2) infections (abscess, encephalitis, or meningitis), intracranial masses causing intracranial hypertension, preeclampsia; and (3) carbon monoxide poisoning and methemoglobinemia. Having the patient carefully describe the onset of headache can help diagnose a serious cause.

Report of a sudden-onset headache that reaches maximal and severe intensity within seconds or a few minutes is the classic description of a "thunderclap" headache; it should precipitate workup for subarachnoid hemorrhage, since the estimated prevalence of subarachnoid hemorrhage in patients with thunderclap headache is 43%.

Thunderclap headache during the postpartum period precipitated by the Valsalva maneuver or recumbent positioning may indicate reversible cerebral vasoconstriction syndrome or irreversible cerebral venous sinus thrombosis. Venous-specific imaging sequences may be needed for diagnosis. Other historical features that raise the need for diagnostic testing include headache brought on by cough, exertion, or sexual activity.

The medical history can guide the need for additional workup. Under most circumstances (including a normal neurologic examination), new headache in a patient older than 50 years or with HIV infection warrants immediate neuroimaging (Table 2–5). When the patient has a history of hypertension—particularly uncontrolled hypertension—a complete search for other features of "malignant hypertension" is appropriate to determine the urgency of control of hypertension (see Chapter 13). Headache and hypertension associated with pregnancy may be due to preeclampsia. Episodic headache associated with the triad of hypertension, palpitations, and sweats is suggestive of pheochromocytoma. In the absence of thunderclap headache, advanced age, and HIV infection, a careful physical examination and detailed neurologic examination will usually determine acuity of the workup and need for further diagnostic testing. A history consistent with hypercoagulability is associated with an increased risk of cerebral venous thrombosis.

Findings in migraine headache are discussed in Chapter 26. A systematic list called the SNNOOP10 has been developed as a screening method for secondary causes of headache (Table 2–6).

B. Physical Examination

Critical components of the physical examination of a patient with acute headache include vital signs, neurologic examination, and vision testing with funduscopic examination. The finding of fever with acute headache warrants additional maneuvers to elicit evidence of meningeal inflammation, such as a Kernig sign (a supine patient with hips flexed to 90 degrees who displays resistance or reports pain with passive extension of the knees) and Brudzinski sign (supine patient who reflexively flexes the hip and knees after the examiner passively flexes the neck). The absence of jolt accentuation of headache cannot accurately rule out meningitis. Patients older than 60 years should be examined for scalp or temporal artery tenderness.

Careful assessment of visual acuity, ocular gaze, visual fields, pupillary defects, optic disks, and retinal vein pulsations is crucial. Diminished visual acuity is suggestive of glaucoma, temporal arteritis, or optic neuritis. Ophthalmoplegia or visual field defects may be signs of venous sinus thrombosis, tumor, or aneurysm. Afferent pupillary defects can be due to intracranial masses or optic neuritis. In the setting of headache and hypertension, retinal cotton wool spots, flame hemorrhages, and disk swelling indicate acute severe hypertensive retinopathy. Ipsilateral ptosis and miosis suggest Horner syndrome and in conjunction with acute headache may signify carotid artery dissection. Finally, papilledema or absent retinal venous pulsations are signs of elevated intracranial pressure—findings that should be followed by neuroimaging prior to performing lumbar puncture (Table 2–5). On nonmydriatic fundoscopy, up to 8.5% of patients who arrive at the emergency department reporting headache had abnormalities; although few had other significant physical examination findings, 59% of them had abnormal neuroimaging studies.

Complete neurologic evaluations should include assessment of mental status, motor and sensory systems, reflexes, gait, cerebellar function, and pronator drift. Any abnormality on neurologic evaluation (especially mental status) warrants emergent neuroimaging (Table 2–5).

Table 2–5. Clinical features associated with acute headache that warrant urgent or emergent neuroimaging.

Indications for neuroimaging prior to lumbar puncture
Abnormal neurologic examination (particularly focal neurologic deficits)
Abnormal mental status
Abnormal funduscopic examination (papilledema; loss of venous pulsations)
Meningeal signs
Indications for emergent neuroimaging completed prior to leaving office or emergency department
Abnormal neurologic examination
Abnormal mental status
"Thunderclap" headache
Patients with HIV with new type of headache[1]
Indications for urgent neuroimaging scheduled prior to leaving office or emergency department
Age > 50 years (normal neurologic examination) with new type of headache

[1]Use CT with or without contrast or MRI if positive for HIV.

Data from American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of patients presenting to the emergency department with acute headache. Ann Emerg Med. 2008;52:407.

Table 2–6. SNNOOP10 list of "red" flags for secondary causes of headache.

Sign or Symptom	Related Secondary Headaches
Systemic symptoms[1]	Headache attributed to infection, nonvascular intracranial disorders, carcinoid, or pheochromocytoma
Neoplasm in history	Neoplasms of the brain; metastasis
Neurologic deficit/dysfunction	Headaches attributed to vascular, nonvascular intracranial disorders; brain abscess and other infections
Onset of headache is sudden or abrupt	Subarachnoid hemorrhage and other headache attributed to cranial or cervical vascular disorders
Older age (> 50 years)	Giant cell arteritis and other headache attributed to cranial or cervical vascular disorders; neoplasms and other nonvascular intracranial disorders
Pattern change or recent onset of headache	Neoplasms, headaches attributed to vascular, nonvascular intracranial disorders
Positional headache	Intracranial hypertension or hypotension
Precipitated by sneezing, coughing, or exercise	Posterior fossa malformations; Chiari malformation
Papilledema	Neoplasms and other nonvascular intracranial disorders; intracranial hypertension
Progressive headache and atypical presentations	Neoplasms and other nonvascular intracranial disorders
Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders; postdural puncture headache; hypertension-related disorders (eg, preeclampsia); cerebral sinus thrombosis; hypothyroidism; anemia; diabetes mellitus
Painful eye with autonomic features	Pathology in posterior fossa, pituitary region, or cavernous sinus; Tolosa-Hunt syndrome (severe, unilateral headaches with orbital pain and ophthalmoplegia due to extraocular palsies); other ophthalmic causes
Posttraumatic onset of headache	Acute and chronic posttraumatic headache; subdural hematoma and other headache attributed to vascular disorders
Immunosuppression, eg, HIV, immunosuppressive medications	Opportunistic infections
Painkiller overuse or new drug at onset of headache	Medication overuse headache; drug incompatibility

[1]"Orange" flag for isolated fever alone.

Reproduced with permission from Do TP et al. Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Neurology. 2019;92(3):134–144. https://n.neurology.org/content/92/3/134.long.

C. Diagnostic Studies

1. Neuroimaging indications—Indications for neuroimaging are listed in Table 2–5. Under most circumstances, a noncontrast head CT is sufficient to exclude intracranial hypertension with impending herniation, intracranial hemorrhage, and many types of intracranial masses (notable exceptions include lymphoma and toxoplasmosis in patients with HIV, herpes simplex encephalitis, and brain abscess). When needed, a contrast study can be ordered to follow a normal noncontrast study. A normal neuroimaging study does not exclude subarachnoid hemorrhage and should be followed by lumbar puncture. One study supported a change of practice wherein a lumbar puncture can be withheld when a head CT scan was performed less than 6 hours after headache onset and showed no evidence of subarachnoid hemorrhage (negative predictive value 99.9%).

In a prospective study of 1536 emergency department patients, the yield for acute findings on head CT differed based on the indications for imaging and were 27% for seizures, 20% for confusion, 19% for syncope, 16% for focal neurologic deficit, 15% for head injury, 12% for headache, and 8% for dizziness.

In patients for whom there is a high level of suspicion for subarachnoid hemorrhage or aneurysm, a normal CT and lumbar puncture should be followed by angiography within the next few days (provided the patient is medically stable).

2. Lumbar puncture—This test is indicated to exclude infectious causes of acute headache, particularly in patients with fever or meningeal signs. CSF tests should routinely include Gram stain, WBC count with differential, RBC count, glucose, total protein, and bacterial culture. In appropriate patients, also consider testing CSF for Venereal Disease Research Laboratory (syphilis), cryptococcal antigen (patients with HIV), acid-fast bacillus stain and culture, and complement fixation and culture for coccidioidomycosis. Storage of an extra tube with 5 mL of CSF is prudent for conducting unanticipated tests in the immediate future. PCR tests for specific infectious pathogens (eg, herpes simplex 2) should be considered in patients with evidence of CNS infection but no identifiable pathogen.

The Ottawa subarachnoid hemorrhage clinical decision rule had 100% sensitivity (and 13–15% specificity in different studies) in predicting subarachnoid hemorrhage. According to it, patients who seek medical attention in an emergency department describing an acute nontraumatic headache should be evaluated for subarachnoid hemorrhage if they have one or more of the following factors: age 40 years or older, neck pain or stiffness, witnessed loss of consciousness, onset during exertion, thunderclap headache (instantly peaking pain), or limited neck flexion on examination.

In addition to neuroimaging and lumbar puncture, additional diagnostic tests for exclusion of life-threatening causes of acute headache include ESR (temporal arteritis; endocarditis), UA (malignant hypertension; preeclampsia), and sinus CT (bacterial sinusitis, independently or as a cause of venous sinus thrombosis).

Treatment

The treatment of migraine headaches is discussed in Chapter 26. Severe benign headache treated in the emergency department responds to haloperidol (2.5 mg intravenously).

Galcanezumab is an approved treatment for episodic cluster headache. High-flow oxygen therapy may provide effective treatment for all headache types in the emergency department setting (eg, benefitting older patients with cluster headaches).

A study found that metoclopramide plus diphenhydramine was more effective than placebo for acute posttraumatic headache (with 43% of the patients who received metoclopramide reporting adverse events).

When to Admit

- Need for repeated doses of parenteral pain medication.
- To facilitate an expedited workup requiring a sequence of neuroimaging and procedures.
- To monitor for progression of symptoms and to obtain neurologic consultation when the initial emergency department workup is inconclusive.
- Pain severe enough to impair activities of daily living or impede follow-up appointments or consultations.
- Patients with subarachnoid hemorrhage, intracranial mass, or meningitis.

Bilello LA et al. Retrospective review of pregnant patients presenting for evaluation of acute neurologic complaints. Ann Emerg Med. 2021;77:210. [PMID: 32418678]
Claassen J et al. Spontaneous subarachnoid haemorrhage. Lancet. 2022;400:846. [PMID: 35985353]
Lebedeva ER. Diagnostic criteria for acute headache attributed to ischemic stroke and for sentinel headache before ischemic stroke. J Headache Pain. 2022;23:11. [PMID: 35057731]
Robbins MS. Diagnosis and management of headache: a review. JAMA. 2021;325:1874. [PMID: 33974014]
Viera AJ et al. Acute headache in adults: a diagnostic approach. Am Fam Physician. 2022;106:260. [PMID: 36126007]
Wu WT et al. The Ottawa subarachnoid hemorrhage clinical decision rule for classifying emergency department headache patients. Am J Emerg Med. 2020;38:198. [PMID: 30765279]

DYSURIA

ESSENTIAL INQUIRIES

- Fever; new back or flank pain; nausea or vomiting.
- Vaginal discharge.
- Pregnancy risk.
- Structural abnormalities.
- Instrumentation of urethra or bladder.

General Considerations

Dysuria (painful urination) is a common reason for adults and adolescents to seek urgent medical attention.

An inflammatory process (eg, bacterial UTI, herpes simplex, autoimmune disorder) underlies most causes of dysuria. In women, cystitis is diagnosed in up to 50–60% of cases. Cystitis has an incidence of 0.5–0.7% per year in sexually active young women. The key objective in evaluating women with dysuria is to exclude serious upper urinary tract disease, such as acute pyelonephritis, and STIs. In older men, dysuria may be a symptom of prostatitis; in younger men, urethritis accounts for most cases of dysuria. Male cyclists have no worse sexual or urinary functions than swimmers or runners, but cyclists are more prone to urethral stricture.

Clinical Findings

A. Symptoms

Well-designed cohort studies have shown that some cases of uncomplicated cystitis can be reliably diagnosed without a physical examination or UA, and RCTs show that telephone management of uncomplicated cystitis is safe and effective. An increased likelihood of UTI is present when women report multiple irritative voiding symptoms (dysuria, urgency, frequency), fever, or back pain (positive LRs = 1.6–2.0). A cohort study found that the symptom of dysuria most reliably predicted a culture-positive UTI. Older patients with cognitive impairment may not have local urinary tract symptoms. A history of recurrent UTI is associated with a positive urine culture (recurrent UTI adjusted OR 2.45). Inquiring about symptoms of vulvovaginitis is imperative. When women report dysuria and urinary frequency and deny vaginal discharge and irritation, the LR for culture-confirmed cystitis is 24.5. In contrast, when vaginal discharge or irritation is present, as well as dysuria or urinary frequency, the LR is 0.7. Gross hematuria in women with voiding symptoms usually represents hemorrhagic cystitis but can be a sign of bladder cancer (particularly in older patients) or upper tract disease. Failure of hematuria to resolve with antibiotic treatment should prompt further evaluation of the bladder and kidneys. Chlamydial infection should be strongly considered among women aged 25 years or younger who are sexually active and seeking medical attention for a suspected UTI for the first time or who have a new sexual partner.

Fever, back pain, nausea, and vomiting are clinical criteria for acute pyelonephritis. Women with these symptoms should usually be examined before initiation of treatment to exclude coexistent urosepsis, hydronephrosis, or nephrolithiasis that would affect management decisions. Risk factors for acute pyelonephritis among women aged 18–49 years relate to sexual behaviors (frequent sexual intercourse [three times per week or more], new sexual partner in the previous year, recent spermicide use), as well as diabetes mellitus and recent UTI or incontinence.

Pregnancy, underlying structural factors (polycystic kidney disease, nephrolithiasis, neurogenic bladder), immunosuppression, diabetes mellitus, and a history of recent bladder or urethral instrumentation usually alter the treatment regimen (antibiotic choice or duration of treatment, or both) for cystitis. Presence of UTI during pregnancy is strongly associated with preeclampsia (particularly UTI during the third trimester).

B. Physical Examination

Fever, tachycardia, or hypotension suggests urosepsis and potential need for hospitalization. In uncomplicated circumstances, a focused examination in women can be limited to ascertainment of costovertebral angle tenderness as a finding for pyelonephritis and to a lower abdominal and pelvic examination if the history suggests vulvovaginitis or cervicitis.

C. Diagnostic Studies

1. Urinalysis—UA is probably overutilized in the evaluation of dysuria. The probability of culture-confirmed UTI among women with a history and physical examination compatible with uncomplicated cystitis is about 70–90%. UA is most helpful in atypical presentations of cystitis. Dipstick detection (greater than trace) of leukocytes, nitrites, or blood supports a diagnosis of cystitis. When both leukocyte and nitrite tests are positive, the LR is 4.2, and when both are negative, the LR is 0.3.

The negative predictive value of UA is not sufficient to exclude culture-confirmed UTI in women with multiple typical symptoms, and randomized trial evidence shows that antibiotic treatment is beneficial to women with typical symptoms and negative UA dipstick tests. Microscopy of unspun urine may also be helpful in diagnosis and reduces unnecessary use of antibiotics. The combination of urgency, dysuria, and pyuria assessed with the high-power (40×) objective for leukocytes (more than 1 leukocyte/7 high-power fields) had a positive predictive value of 71 and LR of 2.97. Urine samples produced at home rarely meet diagnostic standards.

2. Urine culture—Urine culture should be considered for all women with upper urinary tract symptoms (prior to initiating antibiotic therapy), as well as those with dysuria and a negative urine dipstick test. In symptomatic women, a clean-catch urine culture is considered positive when 10^2–10^3 colony-forming U/mL of a uropathogenic organism are detected. Urine culture sensitivity decreases rapidly after empiric antibiotic administration (75% of cultures were negative 9 hours after antibiotic treatment). Multiplex PCR analysis is as beneficial as a urine culture.

3. Renal imaging—When severe flank or back pain is present, the possibility of complicated kidney infection (perinephric abscess, nephrolithiasis) or of hydronephrosis should be considered. Renal ultrasound or CT scanning should be done to rule out abscess and hydronephrosis. To exclude nephrolithiasis, noncontrast helical CT scanning is more accurate than renal ultrasound and is the diagnostic test of choice. In a meta-analysis, the positive and negative LRs of helical CT scanning for diagnosis of nephrolithiasis were 23.2 and 0.05, respectively.

Differential Diagnosis

The differential diagnosis of dysuria in women includes acute cystitis, acute pyelonephritis, vaginitis (*Candida*, bacterial vaginosis, *Trichomonas*, herpes simplex), urethritis/cervicitis (*Chlamydia*, gonorrhea), and interstitial cystitis/painful bladder syndrome. Pelvic congestion syndrome (dilated and refluxing pelvic veins) may also cause dysuria and pelvic pain.

Nucleic acid amplification tests from first-void urine or vaginal swab specimens are highly sensitive for detecting chlamydial infection in men and women. Other infectious pathogens associated with dysuria and urethritis in men include *Mycoplasma genitalium* and Enterobacteriaceae.

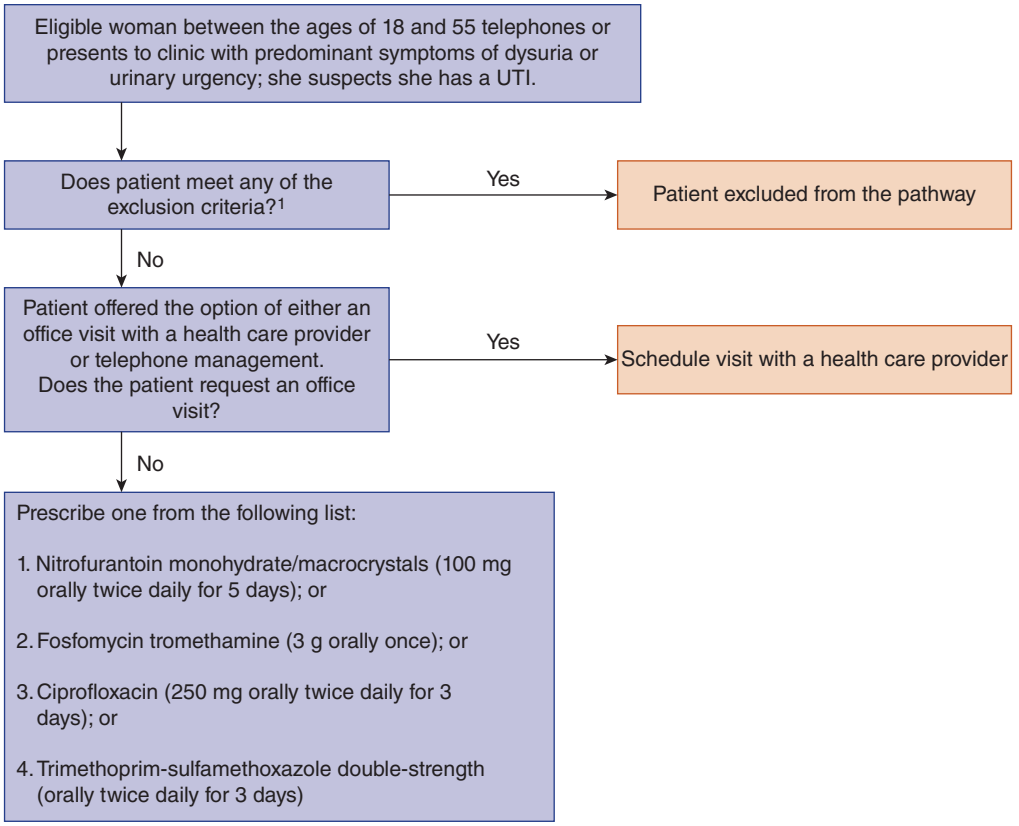
Treatment

An evidence-informed algorithm for managing suspected UTI in women is shown in Figure 2–1. This algorithm supports antibiotic treatment of most women with multiple and typical symptoms of UTI without performing UA or urine culture. Telemedicine may be an appropriate technology to assess and manage uncomplicated UTI for average-risk patients who can self-diagnose. Antibiotic selection should be guided by local resistance patterns and expert-panel clinical practice guidelines; major options for uncomplicated cystitis include nitrofurantoin, fosfomycin, ciprofloxacin, and trimethoprim-sulfamethoxazole. Five days of nitrofurantoin results in a significantly greater likelihood of clinical and microbiologic resolution than single-dose fosfomycin.

According to the American Academy of Pediatrics' Committee on Drugs, antibiotics that are usually acceptable when treating women who are breastfeeding include trimethoprim-sulfamethoxazole (unless G6PD deficiency is present), amoxicillin, nitrofurantoin, ciprofloxacin, and ofloxacin. Plazomicin, a novel neoglycoside, is FDA approved for the treatment of adults with complicated UTIs who have limited or no alternative treatment options.

In men, prolonged treatment of UTIs (more than 7 days) out of concern for delayed clearance of infection within the prostate does not appear to reduce early or late recurrences. A 5-day course of fluoroquinolones for outpatient men with UTI is as effective as a 10-day course. Among afebrile men with symptoms of UTI, treatment with ciprofloxacin or trimethoprim/sulfamethoxazole for 7 days was noninferior to 14 days regarding resolution of UTI symptoms.

Symptomatic relief can be provided with phenazopyridine, a urinary analgesic that is available over the counter; it is used in combination with antibiotic therapy (when a



[1]Primary exclusion criteria include documented fever 38°C or greater; symptoms of dysuria or urgency ≥ 7 days; symptoms of vaginitis are present; abdominal pain, nausea, or vomiting; gross hematuria in patients older than 50 years; immunosuppression (eg, current use of chemotherapeutic agents); diabetes mellitus; known pregnancy; chronic renal or urologic abnormalities, other than stress urinary incontinence (eg, polycystic kidney disease, neurogenic bladder, renal failure); recent or persistent urinary stones; urinary catheterization or other urologic procedure ≤ 2 wk ago; discharge from hospital or nursing home ≤ 2 wk ago; treatment for UTI ≤ 2 wk ago; recurrent symptomatic UTI.

▲ **Figure 2–1. Proposed algorithm for evaluating women with symptoms of acute UTI.** (Data from Gupta K et al; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52:e103.)

UTI has been confirmed) but for no more than 2 days. Patients should be informed that phenazopyridine will cause orange/red discoloration of their urine and other body fluids (eg, some contact lens wearers have reported discoloration of their lenses). Rare cases of methemoglobinemia and hemolytic anemia have been reported, usually with overdoses or underlying kidney dysfunction. NSAIDs have also been shown to be of symptomatic benefit, but less effective than antibiotic therapy. Although some women recover from uncomplicated UTI when treated with NSAIDs alone (53% in a Norwegian study), the rate of progression to pyelonephritis was substantial. Delayed antibiotic therapy in older patients with UTI leads to a substantially higher rate of urosepsis and all-cause mortality. If a broad-spectrum antibiotic was initially prescribed empirically for UTI and urine culture results return establishing efficacy of a narrow-spectrum antibiotic, treatment should be "de-escalated" to the narrow-spectrum antimicrobial. Among premenopausal women with recurrent UTIs, the group with increased daily water consumption (1500 mL per day) had a lower mean number of cystitis episodes over a 12-month period of 1.7 compared with 3.2 in the control group and reduced number of antibiotic prescriptions (1.9 and 3.6, respectively). A systematic review and meta-analysis found D-mannose protective against recurrent UTIs, but there are few high-quality RCTs testing this therapy. In patients with asymptomatic renal calculi and recurrent UTIs, stone extraction eliminated infections in 50% of women. Vaginal estrogen effectively relieves urinary urgency and frequency as well as recurrent UTIs related to vulvovaginal atrophy of menopause (also known as genitourinary syndrome of menopause).

In cases of interstitial cystitis/painful bladder syndrome (see Chapter 25), patients will often respond to a multimodal approach that may include urethral/vesicular dilation, biofeedback, cognitive-behavioral therapy,

antidepressants, dietary changes, vaginal emollients, and other supportive measures.

Asymptomatic bacteriuria—The incidence of asymptomatic bacteriuria increases with age and may be more than 15% in women older than age 80 (50% for those who reside in long-term care facilities). A meta-analysis found that antibiotic treatment for most people with asymptomatic bacteriuria is not beneficial and may be harmful. Antibiotic treatment benefits pregnant women with asymptomatic bacteriuria as well as persons about to undergo urologic surgery. The USPSTF recommends screening pregnant patients for asymptomatic bacteriuria by obtaining a urine culture (B recommendation). The USPSTF recommends against screening for asymptomatic bacteriuria in nonpregnant adults (D recommendation). Urine WBC count greater than 25 cells/high-power field was associated with a 53.8% rate of bacteriuria in a study of 46,127 adult inpatients and is suggested to be the optimal "cutoff" value.

There were no differences in the prevalence of postoperative UTI in women who had mixed flora on preoperative urine cultures compared to those with no growth on preoperative urine cultures.

When to Refer

- Anatomic abnormalities leading to repeated urinary infections.
- Infections associated with nephrolithiasis.
- Persistent interstitial cystitis/painful bladder syndrome.

When to Admit

- Severe pain requiring parenteral medication or impairing ambulation or urination (such as severe primary herpes simplex genitalis).
- Dysuria associated with urinary retention or obstruction.
- Pyelonephritis with ureteral obstruction.
- Symptoms and signs suggesting urosepsis.

Aslam S et al. Recurrent urinary tract infections in adult women. JAMA. 2020;323:658. [PMID: 31995139]

Chernaya A et al. Validity of the urinary dipstick test in the diagnosis of urinary tract infections in adults. Dan Med J. 2021;69: A07210607. [PMID: 34913433]

Hoffmann TC et al. Uncomplicated urinary tract infection in women. BMJ. 2021;372:n725. [PMID: 33785479]

Luu T et al. Asymptomatic bacteriuria: prevalence, diagnosis, management, and current antimicrobial stewardship implementations. Am J Med. 2022;135:e236. [PMID: 35367448]

Maki DG. USPSTF recommends screening for asymptomatic bacteriuria in pregnant women but not nonpregnant adults. Ann Intern Med. 2020;172:JC14. [PMID: 32066147]

Woods R et al. Just the facts: diagnosis and treatment of urinary tract infections in older adults. CJEM. 2021;23:593. [PMID: 33881765]

3 Preoperative Evaluation & Perioperative Management

Hugo Q. Cheng, MD

EVALUATION OF THE ASYMPTOMATIC PATIENT

Patients without significant medical problems—especially those under age 50—are at very low risk for perioperative complications. Their preoperative evaluation should include a history and physical examination; emphasis should be on a pharmacologic history and assessment of functional status, exercise tolerance, and cardiopulmonary status to look for unrecognized disease that may require further evaluation prior to surgery. In addition, a directed bleeding history (Table 3–1) should be taken to uncover coagulopathy that could contribute to excessive surgical blood loss. Routine preoperative laboratory tests in asymptomatic healthy patients under age 50 have *not* been found to help predict or prevent complications. Even older patients undergoing minor or minimally invasive procedures (such as cataract surgery) are unlikely to benefit from preoperative screening tests.

Harris AHS et al. Frequency and costs of low-value preoperative tests for patients undergoing low-risk procedures in the Veterans Health Administration. Perioper Med (Lond). 2022;13:33. [PMID: 36096937]

CARDIAC RISK ASSESSMENT & REDUCTION IN NONCARDIAC SURGERY

The most important perioperative cardiac complications are MI and cardiac death. Other complications include HF, arrhythmias, and need for urgent revascularization.

Table 3–1. Directed bleeding history: Findings suggestive of a bleeding disorder.

Unprovoked bruising on the trunk of > 5 cm in diameter
Frequent unprovoked epistaxis or gingival bleeding
Menorrhagia with iron deficiency
Hemarthrosis with mild trauma
Prior excessive surgical blood loss or reoperation for bleeding
Family history of abnormal bleeding
Presence of severe kidney or liver disease
Use of medications that impair coagulation, including nutritional supplements and herbal remedies

The principal patient-specific risk factor for cardiac complications is the presence of end-organ CVD. This includes not only CAD and HF but also CKD and cerebrovascular disease. Diabetes mellitus, especially if treated with insulin, is considered a CVD equivalent that increases the risk of cardiac complications. Major abdominal, thoracic, and vascular surgical procedures (especially AAA repair) carry a higher risk of postoperative cardiac complications. These six risk factors comprise the Revised Cardiac Risk Index (RCRI), a validated, multifactorial risk prediction tool (Table 3–2). Another prediction tool is from the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP). This risk prediction tool uses patient age, the type of operation, serum creatinine greater than 1.5 mg/dL (132.6 mcmol/L), dependency in activities of daily living, and the patient's American Society of Anesthesiologists physical status classification as predictors for postoperative MI or cardiac arrest. A risk calculator using the NSQIP tool can be found at https://qxmd.com/calculate/calculator_245/gupta-perioperative-cardiac-risk. The American College of Cardiology and American Heart Association endorse both prediction tools. Patients with two or more RCRI predictors or a risk of perioperative MI or cardiac arrest in excess of 1% as calculated by the NSQIP prediction tool are at elevated risk for cardiac complications.

Limited exercise capacity (eg, inability to walk for two blocks at a normal pace or climb a flight of stairs without resting) also predicts higher cardiac risk. Emergency operations have greater cardiac risk but should not be delayed for extensive cardiac evaluation. Instead, patients facing emergency surgery should be medically optimized for surgery and closely monitored for cardiac complications during the perioperative period.

Role of Preoperative Noninvasive Ischemia Testing

History and physical examination are sufficient to risk stratify most patients. A resting ECG should be obtained in patients with at least one RCRI predictor before major surgery but generally omitted in asymptomatic patients undergoing minor operations. Additional noninvasive ischemia testing rarely improves risk stratification or

Table 3–2. Revised Cardiac Risk Index (RCRI).

Independent Predictors of Postoperative Cardiac Complications	
Intrathoracic, intraperitoneal, or suprainguinal vascular surgery	
History of ischemic heart disease	
History of HF	
Insulin treatment for diabetes mellitus	
Serum creatinine level > 2 mg/dL (> 176.8 mcmol/L)	
History of cerebrovascular disease	
Scoring (Number of Predictors Present)	**Risk of Major Cardiac Complications[1]**
None	0.4%
One	1%
Two	2.4%
More than two	5.4%

[1]Cardiac death, MI, or nonfatal cardiac arrest.
Data from Devereaux PJ et al. Perioperative cardiac events in patients undergoing noncardiac surgery: a review of the magnitude of the problem, the pathophysiology of the events and methods to estimate and communicate risk. CMAJ. 2005; 173:627.

management, especially in patients without CVD undergoing minor operations, or who have at least fair functional capacity. Stress testing has more utility in patients with elevated risk scores on prediction tools, especially if they have poor functional status. In these patients, the absence of ischemia on dipyridamole scintigraphy or dobutamine stress echocardiography is reassuring; in contrast, extensive inducible ischemia predicts a high risk of cardiac complications, particularly with vascular surgery, which may not be modifiable by either medical management or coronary revascularization. The predictive value of an abnormal stress test result for nonvascular surgery patients is less well established. An approach to perioperative cardiac risk assessment and management in patients with known or suspected stable CAD is shown in Figure 3–1.

Role of Cardiac Biomarkers

Preoperative BNP or N-terminal fragment of proBNP (NT-proBNP) levels directly correlate with the risk for perioperative cardiac complications, and their measurement may improve risk assessment. A meta-analysis of 2179 patients found that BNP of 92 mg/L or higher or NT-proBNP of 300 ng/L or higher before noncardiac surgery were associated with a fourfold increase in 30-day mortality and MI. American cardiology societies' guidelines are equivocal about the use of biomarkers to enhance risk prediction; the Canadian Cardiovascular Society and European Society of Cardiology, however, recommend measuring BNP or NT-proBNP levels prior to major noncardiac surgery in patients older than 65 years and those with CVD or CVD risk factors.

Perioperative Management of Patients with Coronary Artery Disease

Patients with acute coronary syndromes require immediate management of their cardiac disease prior to any preoperative evaluation (see Chapter 10).

A. Medications

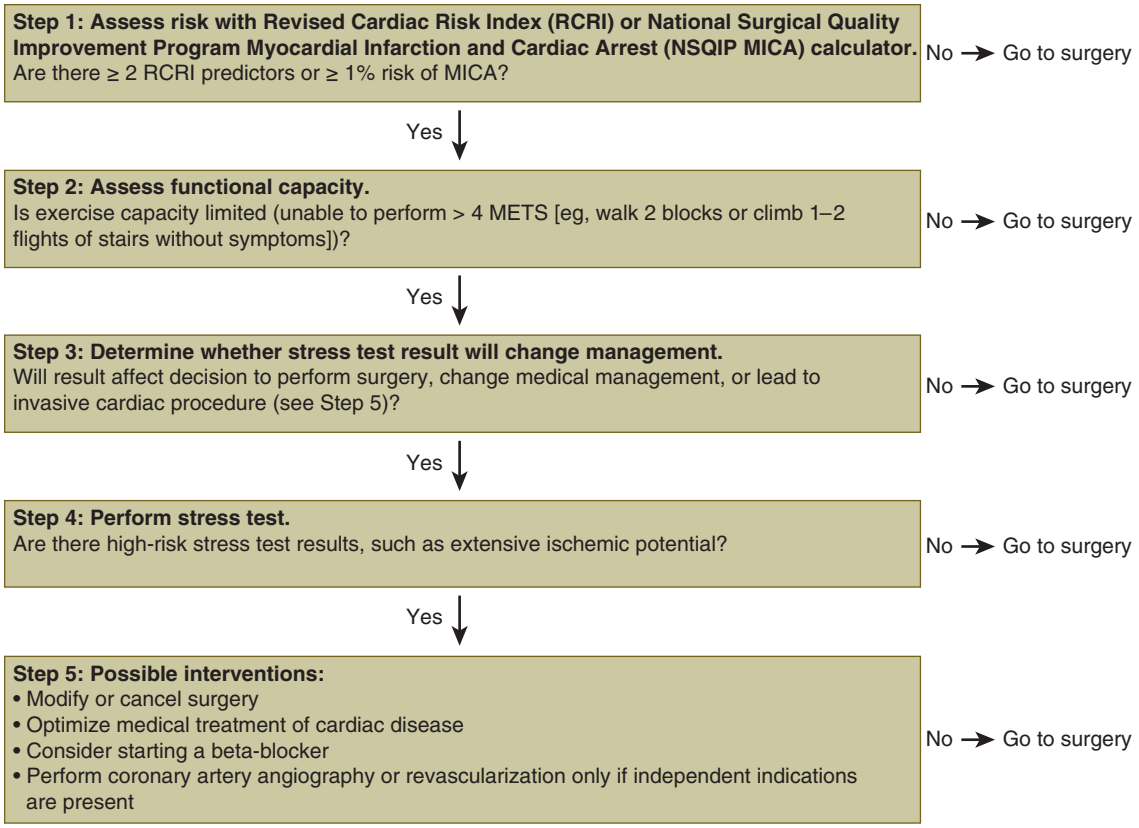
1. Antianginal medications—Preoperative antianginal medications, including beta-blockers, calcium channel blockers, and nitrates, should be continued throughout the perioperative period. Several trials have shown that initiation of beta-blockers before major noncardiac surgery reduces the risk of nonfatal MI. However, in the largest trial, a high, fixed dose of metoprolol succinate *increased* total mortality and the risk of stroke. Because of the uncertain benefit-to-risk ratio, initiation of perioperative beta-blockade should be considered only in patients with a high risk of cardiac complications. Possible indications for prophylactic beta-blockade are presented in Table 3–3. If used, beta-blockers should be started at a low dose (atenolol 25 mg orally daily, bisoprolol 2.5 mg orally daily, or metoprolol *tartrate* 25 mg orally twice daily) well in advance of surgery. They should not be started on the day of surgery. The dose of beta-blocker should be carefully titrated to keep the heart rate below 70 beats per minute and the systolic blood pressure above 100 mm Hg. Beta-blockers, if started, should be continued for at least 3–7 days after surgery.

2. Statins—Several randomized trials found that HMG-CoA reductase inhibitors (statins) prevent MI in patients undergoing noncardiac surgery. Safety concerns, such as liver injury or rhabdomyolysis, have not materialized in these studies. Based on treatment protocols used in clinical trials, at least a moderate statin dose (eg, atorvastatin 20 mg or fluvastatin 80 mg orally daily) should be considered in all patients undergoing vascular surgery and other patients deemed to be at high risk for cardiac complications, regardless of lipid levels, and initiated at least 30 days before surgery if possible. Patients already taking statins should continue these agents during the perioperative period.

3. Aspirin—In patients without coronary stents, initiation of aspirin therapy before noncardiac surgery is not recommended because it did not reduce cardiac risk and caused increased bleeding in a large, randomized trial. Holding long-term prophylactic aspirin therapy in such patients does not increase cardiac risk.

B. Coronary Revascularization

A trial that randomized over 500 patients with angiographically proven CAD to either coronary revascularization (with either coronary artery bypass grafting [CABG] or percutaneous coronary interventions [PCI]) or medical management alone before vascular surgery found no difference in postoperative MI, 30-day mortality, and long-term mortality. Thus, **preoperative CABG or PCI should be performed only when patients have guideline-concordant indications independent of the planned noncardiac operation.** In addition, surgical patients who have



Notes:

Step 2: Reasonable to avoid stress test in patients with excellent functional capacity (> 10 METs) and may avoid stress test in patients with moderate or good functional capacity (4–10 METs); patients with unknown functional capacity should be considered unable to perform 4 METs.

Step 3: Regardless of decision to perform stress test, patients should receive optimal guideline-concordant medical therapy.

Step 4: Pharmacologic stress test preferred due to assumption of poor exercise capacity.

Step 5: Possible indications for beta-blockers include ≥ 3 RCRI predictors, ischemia on stress test, or indications independent of surgery.

▲ **Figure 3–1.** Approach to cardiac evaluation in stable patients undergoing major elective surgery. METs, metabolic equivalents.

undergone recent coronary stenting are at high risk for stent thrombosis, especially if antiplatelet therapy is stopped prematurely. **Therefore, elective surgery should be deferred for at least 30 days after placement of a bare-metal stent and ideally for 6 months after placement of a drug-eluting stent.** If this delay poses significant risks, such as in patients undergoing an operation for cancer, surgery could be considered 3 months after drug-eluting stent implantation. Antiplatelet agents should be continued perioperatively if possible or resumed as soon as possible after surgery. The patient, surgeon, anesthesiologist, and cardiologist should discuss risks and benefits of delaying surgery and management options for dual antiplatelet therapy.

Table 3–3. Indications for prophylactic perioperative beta-blockade.[1]

Strong indications	Patient already taking beta-blocker to treat ischemia, arrhythmia, or hypertension
Possible indications	Patient with myocardial ischemia detected on preoperative stress testing Patient has ≥ 3 Revised Cardiac Risk Index predictors (see Table 3–2)

[1]See dosages in the text.

Postoperative MI

In a large cohort study, postoperative MI (defined by a combination of ECG abnormality and cardiac enzyme elevation) typically occurred within 3 days of surgery and was asymptomatic in most cases. Clinical findings that should prompt its consideration include unexplained hypotension, hypoxemia, and delirium. Postoperative MI is associated

with increased mortality, even when asymptomatic. Elevated postoperative troponin levels correlate directly with mortality risk, even in patients without ECG abnormalities or other findings of MI. The Canadian Cardiovascular Society and European Society of Cardiology advocate routine postoperative screening of high-risk patients with troponin levels, while American guidelines remain equivocal. It is unclear how asymptomatic postoperative MI or troponin elevation should be managed, but optimizing secondary cardiac risk reduction strategies is reasonable.

Heart Failure & LV Dysfunction

Elective surgery should be postponed until decompensated HF (manifested by an elevated jugular venous pressure, an audible third heart sound, or evidence of pulmonary edema) has been brought under control. In patients with compensated HF, the risk of perioperative cardiac complications is similar in patients with ischemic or nonischemic cardiomyopathy. HF with reduced EF likely confers more risk than HF with preserved EF. Guidelines recommend preoperative echocardiography to evaluate LV function in patients without known HF who have unexplained dyspnea and in patients with known HF with clinical deterioration.

Patients receiving diuretics should have serum electrolytes measured prior to surgery because abnormalities in these levels may increase the risk of perioperative arrhythmias. Clinicians must be cautious not to give too much diuretic since the volume-depleted patient will be much more susceptible to intraoperative hypotension. The surgeon and anesthesiologist should be made aware of the presence and severity of LV dysfunction so that appropriate decisions can be made regarding perioperative fluid management and intraoperative monitoring.

Valvular Heart Disease

If the nature or severity of valvular lesions is unknown, or if there has been a recent change in clinical status, echocardiography should be performed prior to noncardiac surgery. In addition, patients with known or suspected stenotic or regurgitant valvular disease that is moderately severe or worse should undergo echocardiography within 1 year before surgery. Candidates for valvular intervention independent of elective noncardiac surgery should have the valve correction procedure performed first. Patients with uncorrected critical or symptomatic aortic stenosis are at particular risk for cardiac complications. They should undergo surgery only after consultation with a cardiologist and anesthesiologist. Patients with asymptomatic moderate or severe aortic stenosis appeared to be at lower risk than patients with symptomatic aortic stenosis and may be reasonable candidates for major noncardiac surgery with appropriate intraoperative and postoperative monitoring at centers with experience operating on such patients. Patients with mitral stenosis require heart rate control to prolong diastolic filling time. Regurgitant valvular lesions are generally less problematic during surgery because the vasodilatory effect of anesthetics promotes forward flow. Patients with aortic or mitral regurgitation likely benefit from afterload reduction and careful attention to volume status; negative chronotropes may worsen the regurgitant volume and should be avoided.

Arrhythmias

The finding of a rhythm disturbance on preoperative evaluation should prompt consideration of further cardiac evaluation, particularly when the finding of structural heart disease would alter perioperative management. **Patients with adequately controlled rhythm disturbance without evidence of underlying heart disease are at low risk for perioperative cardiac complications.** While long-term antiarrhythmic medications should be continued perioperatively, there is no evidence that the use of medications to suppress an asymptomatic arrhythmia alters perioperative risk.

Patients with symptomatic arrhythmias should not undergo elective surgery until their cardiac condition has been addressed. Adequate rate control of atrial fibrillation or other supraventricular arrhythmias should be established prior to surgery. Symptomatic ventricular tachycardia must be thoroughly evaluated and controlled prior to surgery. Patients who have independent indications for a permanent pacemaker or implanted defibrillator should have it placed prior to noncardiac surgery. The anesthesiologist must be notified that a patient has a cardiac implantable electronic device to prevent device malfunction from intraoperative electrocautery.

After major surgery, previously undiagnosed atrial fibrillation develops in approximately 1% of patients. Although most episodes resolve spontaneously within hours to days, postoperative atrial fibrillation is associated with increased long-term risk of atrial fibrillation stroke. Whether the same criteria for anticoagulation therapy should be used for patients undergoing surgery as for patients not undergoing surgery is unclear.

Hypertension

No evidence supports delaying surgery in order to better control mild to moderate hypertension (systolic blood pressure below 180 mm Hg and diastolic blood pressure below 110 mm Hg). Severe hypertension (systolic pressure greater than 180 mm Hg or a diastolic pressure greater than 110 mm Hg) appears to be an independent predictor of perioperative cardiac complications, including MI and HF. It is reasonable to consider delaying elective surgery in patients with such severe hypertension until blood pressure can be controlled, although it is not known whether the risk of cardiac complications is reduced with this approach.

Most medications for chronic hypertension should be continued up to and including the day of surgery. Cardiology societies' guidelines differ in their recommendation on whether to continue or hold ACE inhibitors and ARBs on the day of surgery. Continuation increases the risk of intraoperative and postoperative hypotension, whereas holding these agents increases postoperative hypertension. Diuretic agents are frequently held on the day of surgery to prevent

hypovolemia and electrolyte disorders if they are not needed to control HF; however, the benefit of this practice is uncertain.

Patients without chronic hypertension may manifest hypertension after surgery, and patients being treated for hypertension often experience decreased control of their blood pressure. Potential causes include elevated sympathetic tone due to injury or pain, volume overload from intravenous fluids, hypercarbia, urine retention, and withholding long-term antihypertensive medications. Before initiating postoperative medical management of hypertension, reversible contributors should be addressed.

Chyou JY et al. Atrial fibrillation occurring during acute hospitalization: a scientific statement from the American Heart Association. Circulation. 2023;147:e676. [PMID: 36912134]
Halvorsen S et al. 2022 ESC guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery: developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J. 2022;43:3826. [PMID: 36017553]
Sahai SK et al. Preoperative management of medications: a Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement. Mayo Clin Proc. 2022;97:1734. [PMID: 36058586]

PULMONARY EVALUATION IN NON–LUNG RESECTION SURGERY

Pneumonia and respiratory failure requiring prolonged mechanical ventilation are the most important postoperative pulmonary complications. The occurrence of these complications has been associated with a significant increase in mortality and hospital length of stay. Pulmonary thromboembolism is another serious complication; prophylaxis against venous thromboembolic disease is detailed in Table 16–14.

Risk Factors for the Development of Postoperative Pulmonary Complications

Procedure-related risk factors for postoperative pulmonary complications include location of surgery (highest rates occur in cardiac, thoracic, and upper abdominal cases), prolonged anesthesia, and emergency cases. Operations not requiring general anesthesia tend to have lower rates of postoperative pulmonary complications; laparoscopic procedures tend to have lower risk than comparable open procedures.

A summary of patient-specific risk factors for pulmonary complications is presented in Table 3–4. The presence and severity of systemic disease of any type is associated with pulmonary complications. In particular, patients with COPD or HF have at least twice the risk of postoperative pulmonary complications compared with patients without these conditions. Advanced age, physical debility, malnutrition, and poor functional capacity also predict higher risk of postoperative pulmonary complications. A NSQIP risk calculator for predicting postoperative respiratory failure is available (https://qxmd.com/calculate/calculator_261/postoperative-respiratory-failure-risk-calculator).

Table 3–4. Clinical risk factors for postoperative pulmonary complications.

Upper abdominal or cardiothoracic surgery
Prolonged anesthesia time (> 4 hours)
Emergency surgery
Age > 60 years
COPD
HF
Severe systemic disease
Tobacco use (> 20 pack-years)
Impaired cognition or sensorium
Functional dependency or prior stroke
Preoperative sepsis
Low serum albumin level
Obstructive sleep apnea

Pulmonary Function Testing & Laboratory Studies

The main role for preoperative pulmonary function testing (PFT) is to identify pulmonary disease in patients with unexplained symptoms prior to major abdominal or cardiothoracic surgery. In patients with diagnosed lung disease, PFT usually adds little information above clinical assessment. CXRs in unselected patients also rarely add clinically useful information. The benefit of polysomnography to diagnose obstructive sleep apnea prior to bariatric surgery is unproven. ABG measurement is not routinely recommended except in patients with known lung disease and suspected hypoxemia or hypercapnia.

Preoperative Risk Reduction

Retrospective studies have shown that smoking cessation reduced the incidence of pulmonary complications, but only if it was initiated at least 1–2 months before surgery. A meta-analysis of randomized trials found that preoperative smoking cessation programs reduced both pulmonary and surgical wound complications, especially if smoking cessation was initiated at least 4 weeks prior to surgery. **The preoperative period may be an optimal time to initiate smoking cessation efforts.** A systematic review found that smoking cessation programs started in a preoperative evaluation clinic increased the odds of abstinence at 3–6 months by nearly 60%.

Increased surgical mortality was observed for up to 7 weeks after SARS-CoV-2 infection. Elective surgery should not be scheduled within 2 weeks of SARS-CoV-2 infection, and risks and benefits should be assessed when infection occurred 2–7 weeks prior to scheduled surgery.

Postoperative Risk Reduction

Postoperative risk reduction strategies have centered on promoting lung expansion through the use of incentive spirometry, deep breathing exercises, and in selected populations, continuous positive airway pressure (CPAP) or intermittent positive-pressure breathing (IPPB). Although trial results have been mixed, all these techniques reduce the incidence of postoperative atelectasis and, in a few studies, reduce the incidence of other postoperative

pulmonary complications. In most comparative trials, these methods were equally effective. Given the higher cost of CPAP and IPPB, **incentive spirometry and deep breathing exercises are the preferred methods for most patients.** Multi-component respiratory care programs may be particularly beneficial. One program termed "I COUGH"—an acronym for *I*ncentive spirometry, *C*oughing and deep breathing, *O*ral care, *U*nderstanding (patient education), *G*et out of bed (early ambulation), and *H*ead of bed elevation—reduced the rates of pneumonia and unplanned intubation after general and vascular surgery.

Iida H et al. A practical guide for perioperative smoking cessation. J Anesth. 2022;36:583. [PMID: 35913572]
Muhammad S et al. Preoperative pulmonary evaluation. Respir Care. 2021;66:1150. [PMID: 34210743]

EVALUATION OF THE PATIENT WITH LIVER DISEASE

Risk Assessment in Surgical Patients with Liver Disease

Screening unselected patients with liver biochemical tests has a low yield and is not recommended. Patients with suspected or known liver disease based on history or physical examination, however, should have measurement of liver enzyme levels as well as tests of hepatic synthetic function performed prior to surgery.

Elective surgery in patients with acute viral or alcoholic hepatitis should be delayed until the acute episode has resolved. In three small series of patients with acute viral hepatitis who underwent abdominal surgery, the mortality rate was roughly 10%. Similarly, patients with undiagnosed alcoholic hepatitis had high mortality rates when undergoing abdominal surgery. In the absence of cirrhosis or synthetic dysfunction, chronic viral hepatitis is unlikely to increase risk significantly. Similarly, nonalcoholic fatty liver disease without cirrhosis probably does not pose a serious risk in surgical patients.

In patients with cirrhosis, postoperative complication rates correlate with the severity of liver dysfunction, and decompensated cirrhosis is associated with an extremely high perioperative mortality. Traditionally, severity of dysfunction has been assessed with the Child-Pugh score (see Chapter 18). A conservative approach would be to avoid elective surgery in patients with Child-Pugh class C cirrhosis and pursue it with great caution in class B patients. The Model for End-stage Liver Disease (MELD) score, based on serum bilirubin and creatinine levels, and the prothrombin time expressed as the INR, also predicted surgical mortality and outperformed the Child-Pugh classification in some studies. Generally, a MELD score less than 10 predicts low risk, whereas a score greater than 16 portends high mortality after elective surgery. The VOCAL-Penn score also predicted mortality and risk of hepatic decompensation in surgical patients with cirrhosis and performed better than MELD-based prediction tools in an external validation study.

Ascites, encephalopathy, and coagulopathy should be controlled preoperatively. Ascites is a particular problem in abdominal operations, where it can lead to wound dehiscence and hernias. Great care should be taken when using analgesics and sedatives, since these can worsen hepatic encephalopathy; in general, short-acting agents and lower doses should be used. Postoperative constipation should be aggressively treated because it can precipitate encephalopathy. Kidney function and volume status need to be closely monitored to prevent AKI and volume overload, which are common complications in these patients. Patients with coagulopathy should receive vitamin K and may need fresh frozen plasma transfusion at the time of surgery; however, transfusing to a specific INR target for cirrhosis is discouraged.

Canilas L et al. Clinical guideline on perioperative management of patients with advanced chronic liver disease. Life (Basel). 2023;13:132. [PMID: 36676081]
Endale SA et al. Perioperative management of patients with liver disease for non-hepatic surgery: a systematic review. Ann Med Surg (Lond). 2022;75:103397. [PMID: 35242334]
Mahmud N et al. External validation of the VOCAL-Penn cirrhosis surgical risk score in 2 large, independent health systems. Liver Transpl. 2021;27:961. [PMID: 33788365]

PERIOPERATIVE HEMATOLOGIC EVALUATION

Three of the more common clinical situations faced by the medical consultant are anemia, assessment of bleeding risk, and the perioperative management of long-term anticoagulation.

The main goals of the preoperative evaluation of patients with anemia are to determine the need for preoperative diagnostic evaluation and the need for transfusion. **When feasible, the diagnostic evaluation of the patient with previously unrecognized anemia should be done prior to surgery because certain types of anemia (particularly those due to sickle cell disease, hemolysis, and acute blood loss) have implications for perioperative management.** These types of anemia are typically associated with an elevated reticulocyte count. Given the prevalence of iron deficiency, excluding it as the cause of anemia is reasonable. However, the practice of administering intravenous iron to unselected patients with anemia before elective surgery has not been proven beneficial. Preoperative anemia is associated with higher perioperative morbidity and mortality. Whether raising preoperative hemoglobin level to specific targets will improve postoperative outcomes is unknown. The clinician determining the need for preoperative transfusion in a patient must consider factors other than the absolute hemoglobin level, including the presence of cardiopulmonary disease, the type of surgery, and the likely severity of surgical blood loss. For most hemodynamically stable hospitalized patients, the AABB (formerly American Association of Blood Banks) recommends transfusion for a hemoglobin level less than 7 g/dL (70 g/L). However, a meta-analysis of trials comparing transfusion strategies suggests that a trigger of 8 g/dL (80 g/L) was associated with lower mortality than more

Table 3–5. Recommendations for perioperative management of DOACs.

Drug and Kidney Function	Last Dose Before Procedure	Resume Medication
Dabigatran with normal creatinine clearance (> 50 mL/min [0.83 mL/s]); rivaroxaban, apixaban, edoxaban	2 days before procedure with low risk of bleeding or 3 days before procedure with high risk of bleeding	If hemostasis is adequate, resume 24 hours after procedure with low risk of bleeding or 48–72 hours after procedure with high risk of bleeding
Dabigatran with reduced creatinine clearance (30–50 mL/min [0.5–0.83 mL/s])	3 days before procedure with low risk of bleeding or 5 days before procedure with high risk of bleeding	

restrictive thresholds in surgical patients. Furthermore, many transfusion trials in surgical patients used a slightly higher threshold of 7.5–8 g/dL (75–80 g/L) in their restrictive transfusion arm. Thus, the AABB states that a threshold of 7.5 g/dL (75 g/L) could be considered for hospitalized patients undergoing cardiac surgery, and 8 g/dL (80 g/L) could be considered for hospitalized patients undergoing orthopedic surgery or who have underlying CVD.

The most important component of the bleeding risk assessment is a directed bleeding history (see Table 3–1). Patients who provide a reliable history of no abnormal bleeding and have no suggestion of abnormal bleeding on physical examination are at very low risk for having an occult bleeding disorder. Laboratory tests of hemostatic parameters in these patients are generally not needed. When the directed bleeding history is unreliable or incomplete, or when abnormal bleeding is suggested, a formal evaluation of hemostasis should be done prior to surgery and should include measurement of the prothrombin time, activated partial thromboplastin time, and platelet count (see Chapter 14).

Patients receiving long-term oral anticoagulation are at risk for thromboembolic complications when an operation requires interruption of this therapy. However, "bridging anticoagulation," where unfractionated or low-molecular-weight heparin is administered parenterally while oral anticoagulants are held, has not been shown to be beneficial and can increase bleeding. A cohort study found that DOACs could be safely held without bridging by using a protocol based on the patient's kidney function; the DOACs are withheld several days prior to surgery and restarted 24–48 hours after surgery if hemostasis appears adequate (Table 3–5). A randomized trial of bridging anticoagulation in surgical patients taking warfarin for atrial fibrillation demonstrated no difference in thromboembolism between those with and without bridging. Bleeding complications, however, were twice as common in patients who received bridging anticoagulation. A trial of postoperative bridging anticoagulation that included patients with atrial fibrillation or mechanical prosthetic heart valves also found no benefit for stroke prevention. **Most experts recommend bridging therapy only in patients at high risk for thromboembolism.** An approach to perioperative anticoagulation management with warfarin is shown in Table 3–6, but the recommendations must be considered in the context of patient preference and hemorrhagic risk.

Table 3–6. Recommendations for management of perioperative anticoagulation with warfarin.

Thromboembolic Risk without Anticoagulation	Recommendation
Low Risk (eg, atrial fibrillation with CHA_2DS_2VASc score 0–6,[1] mechanical bileaflet aortic valve prosthesis, or single VTE > 3 months ago without hypercoagulability condition[2])	Stop warfarin 5 days before surgery Measure INR the day before surgery to confirm that it is acceptable (< 1.6 for most operations) Resume warfarin when hemostasis permits No bridging with parenteral anticoagulants before or after surgery
High Risk (eg, either atrial fibrillation or mechanical heart valve with stroke < 3 months prior, atrial fibrillation with CHA_2DS_2VASc score 7–9,[1] mechanical mitral valve prosthesis, caged-ball or tilting disk valve prosthesis, or venous thrombosis < 3 months ago or associated with hypercoagulability condition[2])	Stop warfarin 5 days before surgery Begin bridging with therapeutic dose UFH infusion or LMWH 2 days after stopping oral anticoagulation Administer last dose of LMWH 24 hours before surgery; discontinue UFH 4–6 hours before surgery Measure INR the day before surgery to confirm that it is acceptable (< 1.6 for most operations) Resume warfarin when hemostasis permits If hemostasis permits, consider bridging with therapeutic dose UFH infusion or LMWH beginning 48–72 hours after surgery and continuing until the INR is therapeutic

[1]See Table 12–2.
[2]Patients should receive VTE prophylaxis after surgery (see Chapter 16).
LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

Carson JL et al. Red blood cell transfusion: 2023 AABB international guidelines. JAMA. 2023;330:1892. [PMID: 37824153]
Douketis JD et al. Perioperative management of antithrombotic therapy: an American College of Chest Physicians clinical practice guideline. Chest. 2022;162:e207. [PMID: 35964704]

NEUROLOGIC EVALUATION

Delirium can occur after any major operation but is particularly common after hip fracture repair and cardiovascular surgery, where the incidence is 30–60%. Postoperative delirium has been associated with higher rates of major postoperative cardiac and pulmonary complications, poor functional recovery, increased length of hospital stay, increased risk of subsequent dementia and functional decline, and increased mortality. The American Geriatrics Society recommends screening preoperative patients for these delirium risk factors: age greater than 65 years, chronic cognitive impairment or dementia, severe illness, poor vision or hearing, and the presence of infection. Patients with any of these risk factors should be enrolled in a multicomponent, nonpharmacologic delirium prevention program after surgery, which includes interventions such as reorientation, sleep hygiene, bowel and bladder care, mobilization and physical therapy, and the elimination of unnecessary medications. Moderate-quality evidence supports the use of these nonpharmacologic interventions.

Only a minority of patients with postoperative delirium will have a single, reversible etiology for their condition (see Delirium, Chapter 4). Evaluation of delirious patients should exclude electrolyte derangements, occult UTI, and adverse effects from psychotropic medications such as opioids, sedatives, anticholinergic agents, and antispasmodics. Conservative management includes reassuring and reorienting the patient; eliminating unneeded medications, intravenous lines, and urinary catheters; and keeping the patient active during the day while allowing uninterrupted sleep at night. Use of multimodal postoperative analgesic strategies can reduce or avoid the need for opioids. Scheduled administration of non-opiate analgesics such as acetaminophen or NSAID in the absence of contraindications often forms the core of these techniques. The analgesic effect of both opioid and non-opioid analgesics can be augmented by medications, such as gabapentin, which targets neuropathic pain; local or regional anesthetic agents; and nonpharmacologic approaches such as cognitive-behavioral therapy. When agitation jeopardizes patient or provider safety, neuroleptic agents given at the lowest effective dose for the shortest duration needed are preferred over the use of benzodiazepines or physical restraints (Table 27–1).

Stroke complicates less than 1% of all surgical procedures but may occur in 1–6% of patients undergoing cardiac or carotid artery surgery. Most of the strokes in cardiac surgery patients are embolic in origin, and about half occur within the first postoperative day. Patients who had previously suffered a stroke had a high risk of MI, recurrent stroke, or cardiac death if they underwent noncardiac surgery within 3 months of the stroke. One retrospective study found that this risk declined over time and reached a nadir 9 months after the stroke, while another study found little additional risk reduction after 3 months. American cardiology and neurology societies suggest delaying elective surgery for 6–9 months after a stroke.

Symptomatic carotid artery stenosis is associated with a high risk of stroke in patients undergoing cardiac surgery. In general, patients with independent indications for correction of carotid stenosis should have the procedure done prior to elective surgery. In contrast, most studies suggest that asymptomatic carotid bruits and asymptomatic carotid stenosis are associated with little or no increased risk of stroke in surgical patients.

Benesch C et al. Perioperative neurological evaluation and management to lower the risk of acute stroke in patients undergoing noncardiac, nonneurological surgery: a scientific statement from the American Heart Association/American Stroke Association. Circulation. 2021;143:e923. [PMID: 33827230]
Swarbrick CJ et al. Evidence-based strategies to reduce the incidence of postoperative delirium: a narrative review. Anaesthesia. 2022;77 Suppl 1:92. [PMID: 35001376]

MANAGEMENT OF ENDOCRINE DISEASES

Diabetes Mellitus

The goal of management for all patients with diabetes is the prevention of severe hyper- or hypoglycemia in the perioperative period. In addition, patients with type 1 diabetes are at risk for developing ketoacidosis. Increased secretion of cortisol, epinephrine, glucagon, and growth hormone during and after surgery causes insulin resistance and hyperglycemia in patients with diabetes. Conversely, reduced caloric intake after surgery and frequent, unpredictable periods of fasting increase the risk for hypoglycemia. Thus, all surgical patients with diabetes require frequent blood glucose monitoring. Ideally, such patients should undergo surgery early in the morning. The specific pharmacologic management of diabetes during the perioperative period depends on the type of diabetes (insulin-dependent or not), the level of glycemic control, and the type and length of surgery.

Poor preoperative glycemic control, sometimes defined as a hemoglobin A_{1c} level above 8%, is associated with a greater risk of surgical complications, particularly infections. However, a strategy of delaying surgery until glycemic control improves has not been rigorously studied. The ideal postoperative blood glucose target is also unknown. Based on trials that showed increased mortality in hospitalized patients randomized to tight control, the American College of Physicians recommends maintaining serum glucose between 140 mg/dL and 200 mg/dL (7.8–11.1 mmol/L), whereas the British National Health Service guidelines recommend a range of 108–180 mg/dL (6–10 mmol/L).

A. Diabetes Controlled by Diet

For people with diabetes controlled with diet alone, no special precautions must be taken unless diabetic control is markedly disturbed by the procedure. If this occurs, small doses of short-acting insulin as needed will correct the hyperglycemia.

B. Diabetes Treated with Oral Hypoglycemic Agents

Most oral hypoglycemic agents should be held on the day of surgery. However, the SGLT-2 inhibitors (eg, canagliflozin) should be discontinued for 3–4 days before surgery due to their long half-life and associated risk of ketoacidosis. Oral hypoglycemic agents should not be restarted after surgery until patients are clinically stable and oral intake is adequate and unlikely to be interrupted. A possible exception are dipeptidyl peptidase-4 inhibitors which have a low risk of causing hypoglycemia and might be continued perioperatively. Patients who experience significant hyperglycemia when oral agents are held should be treated in the same way as patients with type 2 diabetes who require insulin, as described below. Postoperative kidney function should be checked with a serum creatinine level prior to restarting metformin.

C. Diabetes Treated with Insulin

The protocol used to control glucose depends on (1) the kind of diabetes (type 1 or type 2); (2) whether it is minor surgery (lasting less than 2 hours and patient able to eat afterward) or major surgery (lasting more than 2 hours, with invasion of a body cavity, and patient not able to eat afterward); and (3) the preoperative insulin regimen (basal bolus or premixed insulin twice a day or premeal bolus only or regular insulin before meals and NPH at bedtime).

1. Preoperative insulin regimen—For patients with either type 1 or type 2 diabetes who are receiving insulin, a common practice is to reduce the last preoperative dose of long-acting, basal insulin (used to control fasting glucose levels) by 30–50% and hold rapid-onset, short-acting nutritional insulin (used to prevent hyperglycemia following meals).

2. Perioperative insulin regimen—Patients with type 1 diabetes must receive basal insulin to prevent the development of diabetic ketoacidosis. **Consultation with an endocrinologist or hospitalist should be strongly considered when a patient with type 1 diabetes mellitus undergoes major surgery.** Major surgical procedures in patients with type 1 diabetes lasting more than 2 hours usually require an insulin infusion. Some patients with type 2 diabetes who are taking insulin will also need insulin infusion to maintain adequate glycemic control. An insulin infusion is a complex procedure for a high-risk medication and involves extensive monitoring, dose titrations, and contingency plans. There are a number of algorithms available for insulin infusions (http://ucsfinpatientdiabetes.pbworks.com).

3. Postoperative insulin regimen—After surgery, when a patient with either type 1 or type 2 diabetes has resumed adequate oral intake, subcutaneous administration of insulin can be restarted. Intravenous administration of insulin and dextrose can be stopped 30 minutes after the first subcutaneous dose of long-acting insulin. Insulin needs may vary in the first several days after surgery because of continuing postoperative stresses and because of variable caloric intake. In this situation, multiple doses of short-acting insulin plus some long-acting basal insulin, guided by blood glucose determinations, can keep the patient in acceptable metabolic control. Use of correctional insulin only (without basal or nutritional insulin) after surgery is discouraged. A trial comparing correctional insulin with basal-bolus dosing found that the latter strategy led to fewer postoperative complications.

Glucocorticoid Replacement

Hypotension or shock resulting from primary or secondary adrenocortical insufficiency is rare, and the practice of administering supraphysiologic "stress-dose" glucocorticoid perioperatively is inadequately studied. A guideline from rheumatology and orthopedic surgery societies recommends that patients taking glucocorticoids continue their regimen when undergoing arthroplasty and not receive "stress-dose" glucocorticoids. Another approach is to administer stress-dose glucocorticoids to patients who have received the equivalent of at least 7.5 mg of prednisone daily for 3 weeks within the past year when they undergo major surgery. A commonly used stress-dose regimen is hydrocortisone 100 mg intravenously daily, divided every 8 hours, beginning before induction of anesthesia and stopped after 24 hours without tapering. Patients who have been taking less than 5 mg of prednisone daily and those receiving alternate-day glucocorticoid dosing are unlikely to require supplemental coverage.

Thyroid Disease

Severe symptomatic hypothyroidism has been associated with perioperative complications, including intraoperative hypotension, HF, cardiac arrest, and death. Elective surgery should be delayed in patients with severe hypothyroidism until adequate thyroid hormone replacement can be achieved. Patients with symptomatic hyperthyroidism are at risk for perioperative thyroid storm and should not undergo elective surgery until their thyrotoxicosis is controlled; an endocrinologist should be consulted if emergency surgery is needed. Patients with mild hypothyroidism (median TSH level 8.6 mIU/L) tolerate surgery well, with only a slight increase in the incidence of intraoperative hypotension; surgery need not be delayed for the month or more required to ensure adequate thyroid hormone replacement.

American Diabetes Association Professional Practice Committee. 16. Diabetes care in the hospital: standards of medical care in diabetes—2022. Diabetes Care. 2022;45(Suppl 1):S244. [PMID: 34964884]

Chen Cardenas SM et al. Perioperative evaluation and management of patients on glucocorticoids. J Endocr Soc. 2022;7:bvac185. [PMID: 36545644]

Pfeifer KJ et al. Preoperative management of endocrine, hormonal, and urologic medications: Society for Perioperative Assessment and Quality Improvement (SPAQI) consensus statement. Mayo Clin Proc. 2021;96:1655. [PMID: 33714600]

KIDNEY DISEASE

The development of AKI in patients undergoing general surgery is an independent predictor of mortality, even if mild or if kidney dysfunction resolves. The mortality

Table 3–7. Risk factors for the development of AKI after non-cardiac surgery.[1]

Age > 50 years
CKD
HF
Hepatic failure
Diabetes mellitus
Sepsis
Volume depletion
Crush injury
Volume depletion

[1]Adapted from Acute Disease Quality Initiative 24, www.ADQI.org, CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/).
Prowle JR et al. Postoperative acute kidney injury in adult non-cardiac surgery: joint consensus report of the Acute Disease Quality Initiative and PeriOperative Quality Initiative. Nat Rev Nephrol. 2021;17:605.

associated with the development of perioperative AKI that requires dialysis exceeds 50%. Risk factors associated with postoperative deterioration in kidney function are shown in Table 3–7. Several medications, including "renal-dose" dopamine, mannitol, *N*-acetylcysteine, and clonidine, failed to preserve kidney function during the perioperative period in clinical trials and should not be used for this indication. **Maintenance of adequate intravascular volume is likely to be the most effective method to reduce the risk of perioperative deterioration in kidney function.** Exposure to renal-toxic agents, such as NSAIDs and intravenous contrast, should be minimized or avoided. ACE inhibitors and ARBs reduce renal perfusion and may increase the risk of perioperative AKI. Although firm evidence is lacking, it may be useful to temporarily discontinue these medications in patients at risk for perioperative AKI.

Although the mortality rate for elective major surgery is low (1–4%) in patients with dialysis-dependent ESRD, the risk for perioperative complications, including postoperative hyperkalemia, pneumonia, fluid overload, and bleeding, is substantially increased. Patients should undergo dialysis preoperatively within 24 hours before surgery, and their serum electrolyte levels should be measured just prior to surgery and monitored closely during the postoperative period.

Fielding-Singh V et al. Association between preoperative hemodialysis timing and postoperative mortality in patients with end-stage kidney disease. JAMA. 2022;328:1837. [PMID: 36326747]
Prowle JR et al. Postoperative acute kidney injury in adult non-cardiac surgery: joint consensus report of the Acute Disease Quality Initiative and PeriOperative Quality Initiative. Nat Rev Nephrol. 2021;17:605. [PMID: 33976395]

ANTIBIOTIC PROPHYLAXIS OF SURGICAL SITE INFECTIONS

Surgical site infection is estimated to occur in roughly 4% of general or vascular operations. Although the type of procedure is the main factor determining the risk of developing a surgical site infection, certain patient factors are associated with increased risk, including diabetes mellitus, older age, obesity, cigarette smoking, heavy alcohol consumption, admission from a long-term care facility, and multiple medical comorbidities. **For most major procedures, the use of prophylactic antibiotics has been demonstrated to reduce the incidence of surgical site infections.** Substantial evidence suggests that a single dose of an appropriate intravenous antibiotic—or combination of antibiotics—administered 30–60 minutes prior to skin incision is as effective as multiple-dose regimens that extend into the postoperative period. For most procedures, a first-generation cephalosporin (eg, cefazolin 2 g intravenously) is as effective as later-generation agents.

Guidelines for antibiotic prophylaxis against infective endocarditis in patients undergoing invasive procedures are presented in Chapter 35. Given the lack of evidence for antibiotic prophylaxis before dental procedures to prevent prosthetic joint infection, guidelines from the American Academy of Orthopedic Surgeons and the American Dental Association recommend against this practice.

Fields AC et al. Preventing surgical site infections: looking beyond the current guidelines. JAMA. 2020;323:1087. [PMID: 32083641]

4 Geriatric Disorders

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GENERAL PRINCIPLES OF GERIATRIC CARE

The following principles help guide the care of older adults:

1. Many disorders are multifactorial in origin and are best managed by multifactorial interventions.
2. Diseases often present atypically or with nonspecific symptoms (eg, confusion, functional decline).
3. Not all abnormalities require evaluation and treatment.
4. Multiple chronic conditions and geriatric syndromes often coexist and should be managed in concert with one another.

The Geriatric 5Ms is a framework for optimizing care for the older adult, addressing Mind, Mobility, Medications, Multicomplexity, and what Matters Most. This framework represents a practical and easy-to-remember summary of core geriatric principles. "Mind" relates to dementia, delirium, and depression. "Mobility" relates to immobility, falls, and gait disorders. "Medications" includes pharmacotherapy and polypharmacy. What "Matters Most" assesses patient values and goals of care. "Multicomplexity" is evaluated (for example, in a comprehensive geriatric assessment) to guide treatment decision-making, incorporating the interplay of disease burden, comorbidities, functional status, prognosis, and patient preferences.

COMPREHENSIVE ASSESSMENT OF THE OLDER ADULT

The comprehensive geriatric assessment incorporates an evaluation of the Geriatric 5M "multicomplexity," which (1) expands upon the conventional assessment of symptoms, diseases, and medications; (2) considers the biopsychosocial situation; and (3) includes an analysis of prognosis, values and preferences, and ability to function independently.

Assessment of Prognosis

When an older person's life expectancy is longer than 10 years (ie, 50% of similar persons live longer than 10 years), it is reasonable to consider effective tests and treatments such as they are considered in younger persons. When life expectancy is less than 10 years (and especially when it is much less), choices of tests and treatments should be made based on their ability to affect *a clinical outcome that is valued by the patient* in the context of their estimated life expectancy (Figure 4–1). The relative benefits and harms of tests and treatments often change as prognosis worsens and net benefit (benefits minus harms) diminishes.

Social determinants of health are important factors that impact health outcomes and prognosis. As part of the comprehensive assessment, asking about socioeconomic status, food security, access to healthcare, education, support system, and neighborhoods can impart significant insight into the management of chronic diseases, outcomes after acute hospitalizations, or medical decisions.

Assessment of Values & Preferences

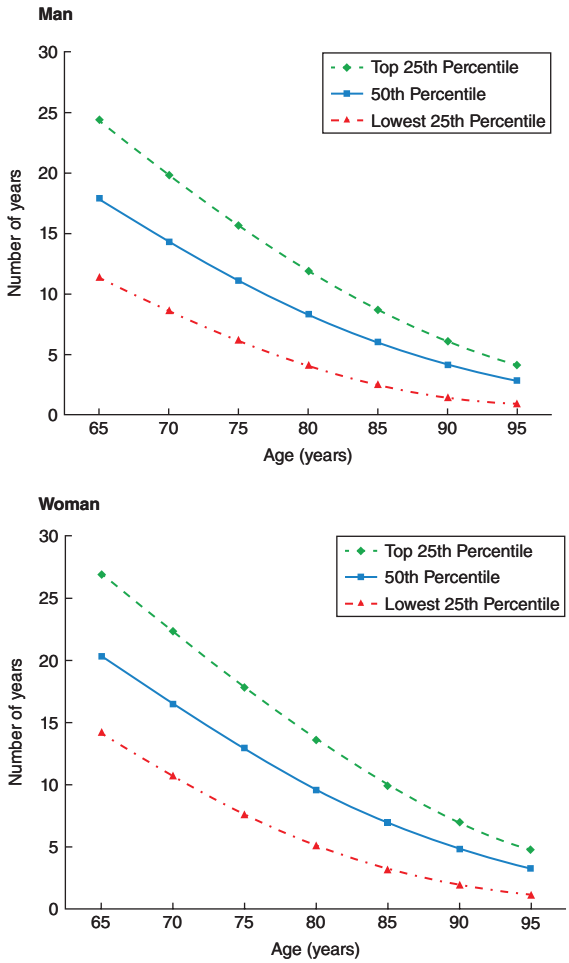
Although patients vary in their values and preferences, many frail older adults prioritize maintaining their *independence* over prolonging survival. Values and preferences, described by the Geriatric 5M what "Matters Most," are determined by speaking directly with a patient or, when the patient cannot express preferences reliably, with the patient's surrogate.

In assessing values and preferences, it is important to keep in mind the following:

1. Patients are experts about their preferences for outcomes and experiences; however, they may not have adequate information to make and express informed preferences for specific tests or treatments.
2. Patients' preferences often change over time. For example, some patients find living with a disability more acceptable than they thought before experiencing it.

Assessment of Function

People often lose function in multiple domains as they age, and as a result, they may not be able to do some activities as quickly or capably and may need assistance. Assessment of function improves prognostic estimates. *Assessment of function, which is described by the Geriatric 5M "Mobility," is essential to determine an individual's needs in the context of his or her values and preferences and the possible effects of recommended treatment.*



▲ **Figure 4–1.** Median life expectancy of older men and women. (Data derived from Arias E. United States Life Tables, 2011. Natl Vital Stat Rep. 2015;64(11):1–63.)

About one-fourth of patients over age 65 and half of persons older than 85 need help performing their **basic activities of daily living (ADLs)**, such as bathing, dressing, eating, transferring from bed to chair, continence, and toileting; or **instrumental activities of daily living (IADLs)**, such as transportation, shopping, cooking, using the telephone, managing money, taking medications, housecleaning, or laundry.

Functional screening should include assessment of ADLs and IADLs and questions to detect weight loss, falls, incontinence, depressed mood, self-neglect, fear for personal safety, and common serious impairments (eg, hearing, vision, cognition, and mobility). One technique for these patients is to identify and ask about a target routine activity, such as bowling or gardening. Difficulty with or discontinuation of the activity may indicate new or worsening impairment.

Frailty

Frailty is a syndrome characterized by loss of physiologic reserve and dysregulation across multiple systems, ultimately resulting in greater risk of poor health outcomes. Estimates of its prevalence in community-dwelling older adults range from 4.0% to 59.1%. Elements of frailty include **weakness (diminished grip strength), slow gait speed, decreased physical activity, weight loss,** and **exhaustion or low energy.** While there is not one universally agreed upon definition or assessment tool for frailty, generally an individual is defined as frail when three or more of the above features are present. Persons with frailty are at increased risk for falls, hospitalization, functional decline, poorer outcomes associated with medical interventions (eg, surgery, dialysis), and death. *Exercise, particularly strength and resistance training, can increase walking speed and improve function.* There is evidence that optimal nutrition, especially higher levels of protein intake, may be associated with reduced incidence of frailty. However, once frailty is established, the treatment is largely supportive, multifactorial, and individualized based on patient goals, life expectancy, and chronic conditions. Sometimes, transitioning a patient to a comfort-focused or hospice approach is the most appropriate clinical intervention when irreversible complications from frailty develop.

Briggs R et al. Comprehensive geriatric assessment for community-dwelling, high-risk, frail, older people. Cochrane Database Syst Rev. 2022;5:CD012705. [PMID: 35521829]
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MANAGEMENT OF COMMON GERIATRIC PROBLEMS

1. Dementia

ESSENTIALS OF DIAGNOSIS

- Progressive decline of mental processes.
- Acquired cognitive deficits severe enough to impair function.
- Not due to delirium or another mental disorder.

General Considerations

Dementia, also called major neurocognitive disorder, is an acquired, persistent, and progressive impairment in mental processes, with compromise of one or more cognitive domains. The *DSM-5* identifies these domains (with example deficits) as: (1) **complex attention** (easily distracted, difficulty performing calculations), (2) **executive function** (poor abstraction, mental flexibility, planning, and judgment), (3) **learning and memory** (difficulty recalling items from a list, forgetting recent events), (4) **language** (word finding and object naming difficulty), (5) **perceptual-motor function** (difficulty navigating in known environments, copying a drawing), and (6) **social cognition** (change in personality, trouble reading social cues). The

diagnosis of dementia requires a significant decline in function that is *severe enough to result in the loss of independence in IADLs.*

While dementia prevalence doubles every 5 years in the older population, reaching 30–50% at age 85, the prevalence among US adults 65 years or older has been declining. This improvement has been attributed to higher education levels and better control of cardiovascular risk factors. Alzheimer disease accounts for roughly two-thirds of dementia cases in the United States, with vascular dementia (either alone or combined with Alzheimer disease) and Lewy body dementia accounting for much of the rest.

Depression and delirium are also common in older adults, may coexist with dementia, and may also present with cognitive impairment. Major depressive disorder may occur in up to 20–50% of patients with dementia, and because they share common features, distinguishing the two can prove difficult. Delirium, characterized by acute confusion, occurs much more commonly in patients with underlying dementia.

Clinical Findings

A. Screening

1. Cognitive impairment—According to the USPSTF, there is insufficient evidence to recommend for or against screening all older adults for cognitive impairment. While there is logic in the argument that early detection may improve future planning and patient outcomes, empiric evidence that demonstrates a clear benefit for either patients or caregivers is lacking. Because new therapies are emerging for early Alzheimer disease, if clinical benefits can be confirmed, this recommendation will need reevaluation. For primary care clinicians, the Medicare Annual Wellness Visit mandates that clinicians assess patients for cognitive impairment based on the clinician's observations and reports from others.

At-home genetic testing for the Alzheimer disease susceptibility gene APOE-e4 is US FDA-approved and available to consumers. Although APOE-e4 carrier status influences the risk for developing Alzheimer disease, not all carriers will develop the dementia syndrome. Therefore, routine testing for screening purposes is *not* recommended, and for individuals who are considering it, genetic counselling is encouraged.

When there is suspicion of cognitive impairment, several cognitive tests have been validated for clinical use. The **mini-cog** is a combination of a three-item word recall with a clock drawing task, and it can be completed in 3 minutes. When a patient fails this simple test, further cognitive evaluation with a standardized instrument is warranted. The **Montreal Cognitive Assessment (MoCA©)** is a 30-point test that takes about 10 minutes to administer and examines several areas of cognitive function. A score below 26 has a sensitivity of 0.94 or more and a specificity of 0.60 or less. Free downloadable versions in multiple languages are available at https://www.mocatest.org. Completion of a training and certification program or signing a disclaimer if you choose not to take the training is required to gain access to the test.

2. Decision-making capacity—Older adults with cognitive impairment commonly face serious medical decisions, and the clinicians involved in their care must ascertain whether the capacity exists to make medical decisions. To make a determination of capacity, the clinician should interview the patient using open-ended questions to assess the following four abilities: (1) **understanding** relevant information about the patient's condition, including the risks and benefits of the proposed intervention and the alternatives (including no intervention); (2) **expressing** a choice; (3) **appreciating** the relevant facts and how they relate to the patient's own situation; and (4) **reasoning** as demonstrated by comparing the consequences of the potential decisions.

Sensitivity must be used in applying these four components to people of various cultural backgrounds. Decision-making capacity varies over time. Furthermore, *the capacity to make a decision is a function of the decision in question.*

B. Symptoms and Signs

Most patients with dementia can be identified by a primary care clinician after completion of a history (often requiring collateral information), a physical examination, and cognitive testing. The clinician can gather additional information about the type of dementia by asking about (1) the rate of progression of the deficits as well as their nature (including any personality or behavioral change); (2) the presence of other neurologic and psychiatric symptoms, particularly motor problems and psychotic symptoms; (3) risk factors for HIV; (4) family history of dementia; and (5) medications, with particular attention to recent changes.

Workup is directed at identifying any potentially *reversible* causes of dementia. However, such cases are rare. For a detailed description of the symptoms and signs of different forms of dementia, see Chapter 26.

C. Physical Examination

The neurologic examination emphasizes assessment of mental status but should also include evaluation for sensory deficits, previous strokes, parkinsonism, gait impairment, and peripheral neuropathy. The examination should focus on identifying comorbid conditions that may aggravate the individual's disability. For a detailed description of the neuropsychological assessment, see Chapter 26.

D. Laboratory Findings

Laboratory studies should include a CBC and serum electrolytes, calcium, creatinine, glucose, TSH, and vitamin B_{12} levels. While hypothyroidism or vitamin B_{12} deficiency may contribute to the cognitive impairment, treating these conditions typically does *not* reverse the dementia. HIV and rapid plasma reagin (RPR) tests, a heavy metal screen, and liver biochemical tests may be informative in selected patients but are not part of routine testing. For a detailed description of laboratory findings, see Chapter 26.

E. Imaging

The American Academy of Neurology recommends neuroimaging (noncontrast head CT or MRI) in all patients

with dementia while other experts limit routine use of neuroimaging to those patients more likely to have a structural cause of dementia (eg, subdural hematoma, tumor, previous stroke, or hydrocephalus). Those who are younger; those who have focal neurologic symptoms or signs, seizures, or gait abnormalities; and those with an acute or subacute onset are most likely to have positive findings and most likely to benefit from MRI scanning. In older patients with a more classic picture of Alzheimer disease for whom neuroimaging is considered, a noncontrast CT scan is sufficient. For a detailed description of imaging, see Chapter 26.

Differential Diagnosis

Older individuals experience occasional difficulty retrieving items from memory (usually word-finding difficulty) and experience a slowing in their rate of information processing. In the amnestic type of **mild cognitive impairment (MCI),** a patient describes memory problems, demonstrates mild deficits (most commonly in short-term memory) on formal testing, but the impairment does not significantly impact function. Annual dementia conversion rates vary from less than 5% to 15%. *No medications have been demonstrated to delay the progression of MCI to Alzheimer disease.* An older patient with intact cognition but with severe impairments in vision or hearing may become confused in an unfamiliar medical setting and consequently may be falsely labeled as having dementia.

Delirium can be distinguished from dementia by its acute onset, fluctuating course, and deficits in attention rather than memory. Many medications have been associated with delirium and other types of cognitive impairment in older patients. Anticholinergic agents, hypnotics, neuroleptics, opioids, NSAIDs, antihistamines (both H_1- and H_2-antagonists), and corticosteroids are just some of the medications that have been associated with cognitive impairment in elders.

Treatment

Patients and families should be made aware of the Alzheimer's Association (http://www.alz.org) as well as the wealth of helpful community and online resources and publications available. Caregiver support, education, and counseling may prevent or delay nursing home placement. Education should include the manifestations and natural history of dementia as well as the availability of local support services, such as respite care. Exercise should be a component of treatment since evidence suggests physical activity may have beneficial effects on cognition and physical function, while limited evidence has found that intellectual engagement through a variety of nonpharmacologic interventions may have a modest positive impact on cognitive function.

A. Cognitive Impairment

1. Acetylcholinesterase inhibitors—Donepezil, galantamine, and rivastigmine are acetylcholinesterase inhibitors approved for the treatment of Alzheimer disease. These medications produce a modest improvement in cognitive function that is *not* likely to be detected in routine clinical encounters, and they have *not* convincingly been shown to delay functional decline or institutionalization. There is insufficient evidence to recommend their use in MCI to slow the progression toward dementia.

Starting (and maximum) doses are donepezil, 5 mg orally once daily (maximum 10 mg once daily); galantamine, 4 mg orally twice daily (maximum 12 mg twice daily); extended-release galantamine, 8 mg orally once daily (maximum 24 mg once daily); rivastigmine, 1.5 mg orally twice daily (maximum 6 mg twice daily); and rivastigmine transdermal patch, 4.6 mg/24 h (maximum 13.3 mg/24 h for severe disease). Dosages are increased as tolerated at no less than 4-week intervals. Donepezil is also available in a 23-mg tablet, but this higher dose is associated with greater frequency of side effects without appreciable increase in benefit. The most bothersome side effects of acetylcholinesterase inhibitors include diarrhea, nausea, anorexia, weight loss, and syncope. As dementia progresses, some patients with moderate to severe cognitive impairment may continue to experience subjective benefits from acetylcholinesterase inhibitors, but the medication should be discontinued in those patients who have had no apparent benefit, who experience side effects, or for whom the financial outlay is a burden. While there are no published guidelines that describe what constitutes an adequate treatment trial, evaluation after 2 months at the highest tolerated dose is reasonable.

2. Memantine—In clinical trials, patients with moderate to severe Alzheimer disease have been shown to have statistical benefit from the use of memantine (5 mg orally daily to 10 mg twice daily), an *N*-methyl-D-aspartate (NMDA) antagonist. Long-term and meaningful functional outcomes have yet to be demonstrated, and evidence suggests *there is no clinically meaningful benefit to giving memantine in combination with an acetylcholinesterase inhibitor.* Evidence does not support the use of memantine in other forms of dementia.

3. Immunotherapy targeting amyloid-beta—In 2021, aducanumab became the first FDA-approved monoclonal antibody for the treatment of MCI and mild dementia due to Alzheimer disease by targeting amyloid-beta protein and promoting its clearance from the brain. In 2023, lecanemab, another anti-amyloid antibody, received FDA approval for the same indications. Both medications received approval based on the results of industry-sponsored clinical trials that showed statistically significant differences on an intermediate marker, the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB), between the treatment groups and the placebo groups at 18 months. While these differences suggest that these medications may modestly slow the progression of the disease, uncertainty remains as to whether either medication will lead to meaningful clinical benefits. Other anti-amyloid antibodies are under clinical investigation. (See Table 4–1.)

Amyloid-related imaging abnormalities (ARIA), subclassified as edema (ARIA-E), hemorrhage (ARIA-H), or both, are known class effects of these medications and occur commonly. In the two aducanumab trials, roughly 40% of patients who received high-dose aducanumab

Table 4–1. Anti-amyloid-beta antibodies for Alzheimer disease (listed in alphabetical order).

Medication	Relevant Clinical Trial Names	Dosing	Target Population	Primary Endpoint[1]	Outcomes	MRI Monitoring for ARIA[2]
Aducanumab[3]	EMERGE ENGAGE	10 mg/kg intravenously every 4 weeks after 6-month dose titration	Patients with MCI or mild dementia due to AD	Change in CDR-SB from baseline at 18 months	Slower decline in CDR-SB compared to placebo	Within 1 year prior to initiation of treatment; prior to fifth, seventh, ninth, and twelfth infusions
Donanemab[4]	TRAILBLAZER-ALZ 2	700 mg intravenously every 4 weeks for three doses, then 1400 mg intravenously every 4 weeks	Patients with MCI or mild dementia due to AD	Change in the iADRS from baseline at 76 weeks	Slower decline in iADRS compared to placebo	Prior to initiation of treatment; at weeks 4, 12, 24, 52, and 76
Lecanemab[5]	Clarity AD	10 mg/kg intravenously every 2 weeks	Patients with MCI or mild dementia due to AD	Change in CDR-SB from baseline at 18 months	Slower decline in CDR-SB compared to placebo	Within 1 year prior to initiation of treatment; prior to fifth, seventh, and fourteenth infusions
Remternetug[6]	TRAILRUNNER-ALZ 1	Intravenous and subcutaneous formulations are being studied	Patients with MCI or mild dementia due to AD	Amyloid plaque clearance at 52 weeks	Study results expected in 2025	Not available

AD, Alzheimer disease; ARIA, amyloid-related imaging abnormalities; CDR-SB, Clinical Dementia Rating Scale-Sum of Boxes; iADRS, integrated Alzheimer Disease Scale; MCI, mild cognitive impairment.
[1]For industry-sponsored clinical trials.
[2]APOE-e4 homozygotes have a higher incidence of ARIA.
[3]Approved under the FDA accelerated approval pathway.
[4]Denied accelerated pathway approval; full approval awaiting FDA decision.
[5]Converted from accelerated to traditional FDA approval in July 2023.
[6]Undergoing phase 3 clinical trials.

experienced ARIA. While most cases were asymptomatic, about 25% experienced symptoms, such as headaches, confusion, or dizziness; these symptoms usually resolved with dose reduction or stopping the medication. The overall discontinuation rate in the high-dose group was 6.2% compared to 0.6% in the placebo group. Lecanemab had fewer reports of ARIA (21.5%) in the treatment arm, of which 3.5% developed symptoms compared to 0.2% in the placebo group. Discontinuation due to all adverse events occurred in 6.9% of the treatment group and 2.9% in the placebo group.

Because of the lack of racial and ethnic diversity and limited data on the oldest old in clinical trials for both aducanumab and lecanemab, questions remain about generalizability of the results to more diverse populations. Any patient living with Alzheimer disease under consideration for monoclonal antibody treatment requires a thorough evaluation to assess eligibility including confirming amyloid presence on a PET scan or CSF biomarker evidence and should be counseled about the known benefits and risks. Those that are chosen for treatment require regular monitoring for ARIA using MRI.

B. Behavioral Problems

1. Nonpharmacologic approaches—Behavioral problems in patients with dementia are often best managed nonpharmacologically. Initially, it should be established that the problem is not unrecognized delirium, pain, urinary obstruction, fecal impaction, or other intercurrent illness. Determining whether the caregiver or institutional staff can tolerate the behavior is also helpful, since *it is often easier to find ways to accommodate to the behavior than to modify it.* If not, the caregiver should keep a brief log in which the behavior is described along with antecedent events and consequences. This may uncover patterns that delineate precipitants of the behavior or perhaps that the behavior is somehow being rewarded. Caregivers are taught to use simple language when communicating with the patient, to break down activities into simple component tasks, and to use a "distract, not confront" approach when the patient seems disturbed by a troublesome issue. Additional steps to address behavioral problems include providing structure and routine, discontinuing all medications except those considered necessary, and correcting, if possible, sensory deficits.

2. Pharmacologic approaches—There is no clear consensus about pharmacologic approaches to the treatment of behavioral problems in patients who have not benefited from nonpharmacologic therapies. Pharmacologic treatment should be reserved for those patients who pose an imminent danger to others or themselves or when symptoms are substantially distressing to the patient.

Despite evidence of harm and recommendations against their use, antipsychotic medications have remained a mainstay for the treatment of behavioral disturbances, particularly agitation and aggression, largely because of the lack of alternatives. The atypical antipsychotic agents (eg, risperidone, olanzapine, quetiapine, aripiprazole, brexpiprazole) are usually the first choice because of an overall better side-effect profile compared to typical agents (eg, haloperidol) but should be used with caution in patients with vascular risk factors due to an increased risk of stroke; they can also cause weight gain, are associated with hyperglycemia in patients with diabetes, and are considerably more expensive. Both typical and atypical antipsychotics increase the risk of mortality compared with placebo when used to treat older patients with dementia and behavioral disturbances. Starting and target dosages should be much lower than those used in schizophrenia (eg, haloperidol, 0.5–2 mg orally; risperidone, 0.25–2 mg orally).

Citalopram at a dose of 30 mg daily may improve symptoms of agitation; however, the maximum recommended dose is 20 mg daily for patients older than 60 years because of the risk of QT prolongation and associated dysrhythmia. Thus, while citalopram may be used to treat agitation, safe and effective dosing for patients older than age 60 has not been established. In the specific instance of patients with Lewy body dementia, treatment with acetylcholinesterase inhibitors has been shown to improve behavioral symptoms. Valproate medications have been used in the treatment of agitated and physically aggressive behavior, but studies demonstrate no identifiable benefit.

C. Driving

Although drivers with dementia are at an increased risk for motor vehicle accidents, many patients continue to drive safely well beyond the time of initial diagnosis, making the timing of when to recommend that a patient stop driving challenging.

There is no clear-cut evidence to suggest a single best approach to determining an individual patient's capability, and there is no accepted gold-standard test. The result is that clinicians must consider several factors upon which to base their judgment. For example, determining the severity of dementia can be useful. Patients with very mild or mild dementia according to the Clinical Dementia Rating Scale were able to pass formal road tests at rates of 88% and 69%, respectively. Experts agree that patients with moderately severe or more advanced dementia should be counseled to stop driving. Although not well studied, clinicians should also consider the effects of comorbid conditions and medications and the role each may play in contributing to the risk of driving by a patient with dementia. Assessment of the ability to carry out IADLs may also assist in the determination of risk. Finally, in some cases of mild dementia, referral may be needed to a driver rehabilitation specialist for evaluation. Although not standardized, this evaluation often consists of both off- and on-road testing. Experts recommend such an evaluation for patients with mild dementia, for those with dementia whose driving skills are newly impaired, and for those with significant deficits in cognitive domains (such as attention, executive function, and visuospatial skills).

Clinicians must also be aware of the reporting requirements in their individual jurisdictions. When a clinician has made the decision to report an unsafe driver to the Department of Motor Vehicles, he or she must consider the impact of a potential breach in confidentiality and must weigh and address, in advance, when possible, the consequences of the loss of driving independence.

D. Advance Financial Planning

Difficulty in managing financial affairs often develops early in dementia. Although expertise is not expected, clinicians should have some proficiency to address financial concerns. Just as clinicians counsel patients and families about advance care planning, the same should be done to educate about the need for advance financial planning and to recommend that patients complete a **durable power of attorney for finance matters (DPOAF)** while the capacity to do so still exists.

No gold-standard test is available to identify when a patient with dementia no longer has financial capacity. However, the clinician should be on the lookout for signs that a patient is either at risk for or experiencing financial incapacity. Because financial impairment can occur when dementia is mild, making that diagnosis should alone be enough to warrant further investigation. Questioning patients and caregivers about late, missed, or repeated bill payments, unusual or uncharacteristic purchases or gifts, overdrawn bank accounts, or reports of missing funds can provide evidence of suspected financial impairment. *Patients with dementia are also at increased risk for becoming victims of financial abuse*, and some answers to these same questions might also be signs of potential exploitation. When financial abuse is suspected, clinicians should be aware of the reporting requirements in their local jurisdictions.

Prognosis

Life expectancy after a diagnosis of Alzheimer disease is typically 3–12 years; it may be shorter than previously reported. Other neurodegenerative dementias, such as Lewy body dementia, show more rapid decline. Hospice care is often appropriate for patients with end-stage dementia.

When to Refer

Referral for neuropsychological testing may be helpful to distinguish dementia from depression, to diagnose dementia in persons of poor education or high premorbid intellect, and to aid diagnosis when impairment is mild. For

patients under consideration for treatment with novel anti-amyloid antibody therapy, clinicians should consult with a dementia specialist.

Budd Haeberlein S et al. Two randomized phase 3 studies of aducanumab in early Alzheimer's disease. J Prev Alzheimers Dis. 2022;9:197. [PMID: 35542991]
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2. Depression

ESSENTIALS OF DIAGNOSIS

- May manifest in older adults as physical symptoms (eg, fatigue, anhedonia) rather than symptoms of depressed mood.
- *Often undertreated in older adults.* Approximately one-third of those treated with an antidepressant will achieve remission, and two-thirds will need additional treatment.

General Considerations

Major depressive disorder has prevalence rates of approximately 2% among community-dwelling adults aged 55 years and older. Prevalence rises with increasing age as well as conditions such as chronic illness, multimorbidity, cognitive impairment, functional impairment, social isolation, and loneliness. *Major depressive disorder is less common in older adults than in younger adults, but depressive symptoms (not meeting criteria for major depressive disorder) are common and present in up to 15% of older adults.* Depression is more common among hospitalized and institutionalized elders. Older single men have the highest rate of completed suicides of any demographic group.

New incidence of depressive symptoms may be an early sign of cognitive impairment in older adults; therefore, evaluation of depression should include cognitive assessment. Older patients with depression and depressive symptoms who have comorbid conditions (eg, HF) are at higher risk for hospitalization, tend to have longer hospital stays, and have worse outcomes than patients without depression.

Clinical Findings

The **Patient Health Questionnaire-2 (PHQ-2)** is highly sensitive for detecting major depression in persons over age 65. Positive responses should be followed up with more comprehensive questionnaires, such as the PHQ-9.

Evaluation of depression should include a careful review of substances that can contribute to depressive symptoms, such as medications (eg, benzodiazepines) and alcohol/illicit drugs. A thorough review of the medical history is critical, since many medical problems can cause fatigue, lethargy, or hypoactive delirium, all of which may be mistaken for depression.

Treatment

First-line treatment is the same for older adults as it is for younger adults; psychotherapy and SSRI medications are the mainstays of treatment. Adjunctive treatment may include psychosocial interventions, increased physical activity, reduction of substance use (eg, alcohol), reduction of potentially contributing medications, or electroconvulsive therapy. In older patients with depressive symptoms who do not meet criteria for major depressive disorder, nonpharmacologic treatments are indicated. Among those with MCI or dementia, cognitive behavioral therapy (CBT) added to usual care probably increases depression remission and slightly reduces depression symptoms, based on a 2022 Cochrane review. Telehealth for mental health support is an important innovation in the field.

Choice of antidepressant agent is usually based on side-effect profile, cost, and patient-specific factors, such as presenting symptoms and comorbidities. SSRIs are used as first-line agents because they are relatively well-tolerated and have good evidence to support efficacy (see Table 27–6). Older adults are more susceptible to SSRI-induced hyponatremia, falls, and osteoporosis. SNRIs (eg, duloxetine and venlafaxine) lead to more adverse events versus placebo than do SSRIs. Regardless of the medication chosen, many experts recommend starting elders at a relatively low dose, titrating to full dose slowly, and continuing for a longer trial (at least 8 weeks) before trying a different medication. Titration to full dose is critical to achieve efficacy of treatment. Of note, the maximum citalopram dose for adults older than 60 years is 20 mg orally daily, due to dose-dependent QT prolongation.

One-third of older adults achieve remission after adequate treatment with first-line SSRI treatment. For the remainder, referral to a mental health specialist is indicated. For those who do not achieve remission, augmentation therapy (eg, with lithium, methylphenidate, or aripiprazole) can enhance clinical response. Esketamine, the S-enantiomer of ketamine, is approved for treatment-resistant depression, but studies of its safety and efficacy did not include adults older than age 65. For patients with severe or catatonic depression, electroconvulsive therapy has high rates of efficacy (60–80%) and should be considered.

Pharmacologic treatment for the first episode of depression should continue for 1 year after remission. Clinicians and patients should share in decision-making regarding maintenance therapy for depression since risk of major depressive disorder recurrence is high. This decision should weigh how long-term pharmacotherapy may contribute to polypharmacy and adverse effects in the landscape of a patient's comorbidities and medication regimen.

When to Refer

- Any patient who might be considered for electroconvulsive therapy should be referred for psychiatric evaluation.
- Consider referral for patients who have mania, psychosis, catatonia, or treatment-resistant depression.

When to Admit

Recommend urgent psychiatric evaluation and admission for patients who have psychosis, suicidality, homicidality, catatonia, grave disability, or self-neglect.

Choi NG et al. Effect of telehealth treatment by lay counselors vs by clinicians on depressive symptoms among older adults who are homebound: a randomized clinical trial. JAMA Network Open. 2020;3:e2015648. [PMID: 32865577]
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3. Delirium

ESSENTIALS OF DIAGNOSIS

- Rapid onset and fluctuating course.
- Primary deficit in attention rather than memory.
- May be hypo- or hyperactive.
- Dementia frequently coexists.

General Considerations

Delirium is described in the *DSM*-5 as a disturbance in attention and awareness of the environment that usually occurs acutely over a short period of time, represents a change from baseline, tends to fluctuate, and is accompanied by a change in cognition (see also Chapter 27). It is often the pathophysiologic consequence of an underlying general medical condition (eg, infection, coronary ischemia, hypoxemia, metabolic derangement) or the adverse effect of a medication. Delirium occurs in 29–64% of hospitalized older adults, persists in 25% or more, and is associated with worse clinical outcomes (higher in-hospital and post-discharge mortality, longer lengths of stay, delayed and limited recovery of physical function, greater probability of placement in a nursing facility).

The acutely agitated older patient often comes to mind when imagining delirium. However, such **hyperactive delirium** occurs less frequently than **hypoactive delirium** in hospitalized older adults and may be suspected only if the clinician notices new cognitive slowing or inattention.

Cognitive impairment is an important risk factor for delirium. Other risk factors include advanced age, functional impairment, severe illness, polypharmacy, use of psychoactive medications, sensory impairment, depression, volume depletion, and alcohol use disorder.

Clinical Findings

Several bedside instruments are available for the assessment of delirium. The **confusion assessment method (CAM)** requires (1) acute onset and fluctuating course and (2) inattention and *either* (3) disorganized thinking *or* (4) altered level of consciousness (https://oxfordmedicaleducation.com/geriatrics/cam/). The 3D CAM (3-minute diagnostic CAM) is useful for clinical assessment of delirium in general medical and surgical patients (http://eddelirium.org/delirium-assessment/3d-cam/).

A key component of a delirium workup is review of medications because polypharmacy, the addition of a new medication, an increase in dose of a medication, or the discontinuation of a medication known to cause withdrawal symptoms are all associated with the development of delirium. Medications that are likely to increase the risk of delirium include sedative/hypnotics, anticholinergics, opioids, benzodiazepines, and H_1- and H_2-antihistamines.

Evaluation of most patients should include a CBC; BUN; serum electrolytes, creatinine, glucose, calcium, and liver biochemical tests; UA; and ECG. In selected cases, serum magnesium, medication levels, ABG measurements, blood cultures, CXR, urinary toxin screen, and lumbar puncture may be helpful. When delirium develops during a hospitalization in the absence of trauma or new localizing neurologic signs, a head CT is rarely revealing.

Prevention

The best evidence for prevention comes from nonpharmacologic multicomponent interventions. These components include improving cognition (frequent reorientation, activities, socialization with family and friends when possible), sleep (massage, noise reduction, minimizing interruptions at night), mobility (early initiation of rehabilitation services as appropriate), vision (visual aids and adaptive equipment), hearing (portable amplifiers or hearing aids, cerumen disimpaction), and hydration status (volume repletion). No medications have been consistently shown to prevent delirium or improve outcomes such as length of stay or mortality should delirium develop.

Treatment

Management of established episodes of delirium combines the elements of preventive interventions with reassurance and reorientation, treatment of underlying causes, eliminating unnecessary medications, and avoidance of indwelling catheters and restraints. *Antipsychotics offer little to no proven benefit and can cause harm.* For example, haloperidol and second-generation antipsychotics have not been

found to reduce delirium severity or duration, hospital length of stay, or mortality when compared to placebo. QT interval prolongation can occur and is a potential risk for serious dysrhythmias. Benzodiazepines should be avoided except in the circumstance of alcohol or benzodiazepine withdrawal. In ventilated patients in the ICU setting, dexmedetomidine or propofol (or both) may also be useful alternatives to antipsychotic therapy in patients with delirium.

Most episodes of delirium clear in a matter of days after correction of the precipitant, but some patients suffer episodes of much longer duration, and a significant percentage never return to their former baseline level of functioning.

When to Refer

If an initial evaluation does not reveal the cause of delirium or if entities other than delirium are in the differential diagnosis, referral to a geriatrician, neuropsychologist, neurologist, or geropsychiatrist should be considered.

When to Admit

Patients with delirium of unknown cause should be admitted for an expedited workup if consistent with the patient's goals of care.

Burton JK et al. Non-pharmacological interventions for preventing delirium in hospitalised non-ICU patients. Cochrane Database Syst Rev. 2021;11:CD013307. [PMID: 34826144]
Inouye SK. The importance of delirium and delirium prevention in older adults during lockdowns. JAMA. 2021;325:1779. [PMID: 33720288]
LaHue SC et al. Approach to altered mental status and inpatient delirium. Neurol Clin. 2022;40:45. [PMID: 34798974]
Ormseth CH et al. Predisposing and precipitating factors associated with delirium: a systematic review. JAMA Netw Open. 2023;6:e2249950. [PMID: 36607634]
Pereira JV et al. Delirium in older adults is associated with development of new dementia: a systematic review and meta-analysis. Int J Geriatr Psychiatry. 2021;36:993. [PMID: 33638566]

4. Immobility

Mobility limitations are common in older adults and are associated with increased rates of morbidity, hospitalization, disability, and mortality. Hospital-associated bed rest is a common precipitant of immobility and functional decline. Among hospitalized medical patients over age 70, about 10% experience a decline in function, and those who experience critical illness are particularly at high risk.

The hazards of bed rest in older adults are multiple, serious, quick to develop, and slow to reverse. Within days of being confined to bed, deconditioning of the cardiovascular system occurs. This deconditioning causes fluid shifts, decreased cardiac output, decreased peak oxygen uptake, increased resting heart rate, and postural hypotension. More striking changes occur in skeletal muscle, resulting in loss of strength and function. Pressure injuries, VTE, and falls are additional serious outcomes of immobility and deconditioning.

Prevention & Treatment

Physical activity should be encouraged for all older adults, *including during hospitalizations*. Physical activity is associated with a myriad of health benefits in older adults. Structured physical activity programs may help reduce mobility-related disability among community-dwelling elders.

When immobilization cannot be avoided, several measures can be used to minimize its consequences. Avoiding restraints and discontinuing intravenous lines and urinary catheters will increase opportunities for early mobility. Graduated ambulation should begin as soon as it is feasible. Among hospitalized older adults, exercise protocols can improve functional outcomes. Prior to discharge, physical therapists can recommend appropriate exercises and assistive devices; after discharge, they can recommend home safety modifications and maintenance exercises. Severe functional disability impeding the patient's ability for independent self-care often leads to discharge to an acute or subacute rehabilitation facility. Recovery from illness-related deconditioning takes weeks to months, and in many cases, full recovery to the pre-illness physical condition does not occur. Evidence supports widespread implementation of **Acute Care for Elders units,** which protocolize delivery of the above preventive measures to prevent hospital-associated disability; however, there are only 43 such units in the United States.

Loyd C et al. Prevalence of hospital-associated disability in older adults: a meta-analysis. J Am Med Dir Assoc. 2020;21:455. [PMID: 31734122]
Pahor M et al. Impact and lessons from the Lifestyle Interventions and Independence for Elders (LIFE) clinical trials of physical activity to prevent mobility disability. J Am Geriatr Soc. 2020;68:872. [PMID: 32105353]
Rogers SE et al. The current landscape of Acute Care for Elders units in the United States. J Am Geriatr Soc. 2022;70:3012. [PMID: 35666631]

5. Falls & Gait Disorders

Annually, about one-third of people over age 65 fall, and the frequency of falls increases markedly with advancing age. About 10% of falls result in serious injuries. *Complications from falls (eg, hip fracture, subdural hematoma) are the leading cause of death from injury in persons over age 65, and fall-associated mortality is increasing.*

Every older person should be asked about falls. Assessment of patients who fall should include measurement of postural blood pressure and pulse; cardiac examination; evaluations of strength, range of motion, cognition, and proprioception; and examination of feet and footwear. A thorough gait assessment should be performed in all older people. Gait and balance can be readily assessed by the **"Timed Up and Go Test,"** in which the patient is asked to stand up from a sitting position without use of hands, walk 10 feet/3 meters, turn around, walk back, and sit down. An older adult who takes 12.5 seconds or greater is considered at increased risk for falling. The ability to recognize common patterns of gait disorders is an extremely useful clinical skill to develop.

Table 4–2. Fall risk factors, targeted interventions, and best evidence for fall prevention (listed in alphabetical order).

To Consider for All Patients	
Exercise or physical therapy	Tai chi, gait training, balance training, strength training
Multifactorial intervention	Home safety assessment, medication review, review of specific conditions (below), advice on appropriate footwear, vision check, adaptive aids as appropriate, physical therapy or exercise as appropriate
Condition	**Targeted Intervention**
Environmental hazards	Removal or mitigation of hazards; installation of safety equipment (eg, grab bars)
Gait impairment	Gait training, assistive devices, balance or strengthening exercises
High-risk footwear	Education on appropriate footwear (eg, avoid slippers, high heels)
Impairment in leg or arm muscle strength or limb range of motion	Exercise with resistance bands or putty, with graduated increases in resistance
Impairment in transfer or balance	Balance exercises, training in transfers, environmental alterations (eg, grab bars)
Inability to get up after a fall	Medical alert system, physical therapy training for fall-prevention strategies
Osteoporosis	Bisphosphonate treatment to prevent first or recurrent fractures
Postural hypotension (> 20 mm Hg drop in systolic blood pressure, or systolic blood pressure < 90 mm Hg)	Behavioral recommendations, such as hand clenching, elevation of head of bed; discontinuation or substitution of high-risk medications
Use of benzodiazepine or sedative/hypnotic agent	Education about sleep hygiene; discontinuation or substitution of medications
Use of multiple prescription medications	Review of medications with a focus on discontinuation (deprescribing)
Vision impairment	Cataract surgery or other interventions as appropriate (eg, corrective lenses)

Causes of Falls

Balance and ambulation require a complex interplay of cognitive, neuromuscular, and cardiovascular function. With age, balance mechanisms can become compromised, reaction time slows, and postural sway increases. These changes predispose the older person to a fall when challenged by an additional insult to any of these systems.

Falls in older people are rarely due to a single cause, and effective intervention entails a comprehensive assessment of the patient's intrinsic deficits (eg, diseases and medications), the activity engaged in at the time of the fall, and environmental obstacles (Table 4–2).

Medication use is one of the most common, significant, and reversible causes of falling. A meta-analysis found that sedative/hypnotics, antidepressants, and benzodiazepines were the classes of medications most likely to be associated with falling. Polypharmacy has also been associated with increased fall risk. Other often overlooked but treatable contributors include postural hypotension (including postprandial, which peaks 30–60 minutes after a meal), insomnia, use of multifocal lenses, and urinary urgency.

Since most falls occur in or around the home, a **home safety evaluation** by a visiting nurse, physical therapist, or health care provider may be beneficial in identifying environmental obstacles.

Complications of Falls

The most common fall-related fractures are of the wrist, hip, and vertebrae. Osteoporosis significantly increases fracture risk and is vastly undertreated in older adults. Following hip fracture, older women experience a high mortality rate (approximately 20% in 1 year), particularly if they were debilitated prior to the time of the fracture. Fear of falling again is a common, serious, but treatable factor in the older person's loss of confidence and independence.

Chronic subdural hematoma is an easily overlooked complication of falls that must be considered in any older patient presenting with new neurologic symptoms or signs, including evidence of new cognitive impairment. Headache and known history of trauma may both be absent.

Prevention & Management

Exercise is the intervention that is most consistently reported to reduce the risk of falls. Balance focused exercises (eg, Tai Chi), gait, and strength training appear to be more effective for fall prevention than general exercise programs (Table 4–2). **Physical therapy** for gait training can help restore an individual's confidence and independence in ambulation, which can help prevent (and treat) falls.

Multifactorial interventions appear to have a small benefit in preventing falls. These interventions include an assessment of potentially modifiable risk factors and tailored interventions to reduce risk. Emphasis is placed on treating all contributory medical conditions, minimizing environmental hazards, and eliminating medications where the harms may outweigh the benefits (eg, sedative-hypnotics).

The USPSTF recommends *against* vitamin D supplementation to prevent falls in community-dwelling adults. Vitamin D supplementation might be considered for high-risk individuals (eg, institutionalized elders) on a case-by-case basis.

Osteoporosis treatment (both preventive and post-fracture) is essential to prevent first and recurrent fracture. First-line treatment with bisphosphonates is effective; for example, alendronate significantly reduces the risk of hip, vertebral and nonvertebral fracture in people with osteoporosis. Unfortunately, less than 20% of people who sustain a fragility fracture receive osteoporosis treatment (this treatment failure is called the "osteoporosis care gap"; see Chapter 28 for more information).

Assistive devices, such as canes and walkers, are useful for many older adults but often are used incorrectly. Canes should be used on the "good" side. The height of walkers and canes should generally be at about the level of the wrist. Physical therapists are invaluable in assessing the need for an assistive device, selecting the best device, and training a patient in its correct use.

Eyeglasses, particularly bifocal or graduated lenses, may increase the risk of falls, especially in the early weeks of use. Patients should be counseled about the need to take extra care when new eyeglasses are being used.

Patients with repeated falls are often reassured by the availability of telephones at floor level, a mobile telephone on their person, a personalized fall detection system (eg, watch), or a lightweight radio call system.

When to Refer

Patients with a recent history of falls should be referred for physical therapy, eye examination, and home safety evaluation.

When to Admit

Consider hospitalization for patients with new falls that are unexplained, particularly in combination with a change in the physical examination (eg, neurologic status) or with an injury/fracture requiring surgery.

Dautzenberg L et al. Interventions for preventing falls and fall-related fractures in community-dwelling older adults: a systematic review and network meta-analysis. J Am Geriatr Soc. 2021;69:2973. [PMID: 34318929]

Ganz DA et al. Prevention of falls in community-dwelling older adults. N Engl J Med. 2020;382:734. [PMID: 32074420]

Reid IR et al. Drug therapy for osteoporosis in older adults. Lancet. 2022;399:1080. [PMID: 35279261]

Silverstein WK et al. Closing the osteoporosis care gap: a teachable moment. JAMA Intern Med. 2021;181:1635. [PMID: 34661618]

6. Urinary Incontinence

ESSENTIALS OF DIAGNOSIS

- Involuntary loss of urine.
- **Stress incontinence:** leakage of urine upon coughing, sneezing, or standing.
- **Urge incontinence:** urgency and inability to delay urination.
- **Overflow incontinence:** variable presentation.

General Considerations

Urinary incontinence in older adults is common, and interventions can greatly improve patients' quality of life. Many do not voluntarily disclose their experiences with urinary incontinence to their health care providers, possibly due to embarrassment or the belief that it is a normal part of aging. A simple question about involuntary leakage of urine is a reasonable annual screen: "Do you have a problem with urine leaks or accidents?"

Classification

A. Transient Causes

The mnemonic "DIAPPERS" represents categories of "transient" urinary incontinence.

1. Delirium—A clouded sensorium impedes recognition of both the need to void and the location of the nearest toilet. Delirium is the most common cause of incontinence in hospitalized patients.

2. Infection—Symptomatic UTI can cause or contribute to urgency and incontinence. Asymptomatic bacteriuria does not.

3. Atrophic urethritis and vaginitis—Atrophic urethritis and vaginitis can usually be diagnosed by the presence of vaginal mucosal telangiectasia, petechiae, erosions, erythema, or friability.

4. Pharmaceuticals—Medications are one of the most common causes of transient incontinence. Typical offending agents include diuretics, anticholinergics, psychotropics, opioid analgesics, alpha-blockers (in women), alpha-agonists (in men), and calcium channel blockers.

5. Psychological factors—Severe depression with psychomotor retardation may impede the ability or motivation to reach a toilet.

6. Excess urinary output—Excess urinary output may overwhelm the ability of an older person to reach a toilet in time. In addition to diuretics, common causes include excess fluid intake; metabolic abnormalities (eg, hyperglycemia, hypercalcemia, diabetes insipidus); and peripheral edema.

7. Restricted mobility—(See Immobility, above.) If mobility cannot be improved, access to a urinal or commode (eg, at the bedside) may improve continence.

8. Stool impaction—This is a common cause of urinary incontinence in hospitalized or immobile patients. A clinical clue to its presence is the onset of both urinary and fecal incontinence.

B. Established Causes

Causes of "established" incontinence should be addressed after any "transient" causes have been managed appropriately.

1. Detrusor overactivity (urge incontinence)—Detrusor overactivity refers to uninhibited bladder contractions that

cause leakage. It is the most common cause of established incontinence in older adults, accounting for two-thirds of cases. Women will report leakage associated with a strong and sudden urge to urinate that cannot be forestalled. In men, the symptoms are similar, but detrusor overactivity commonly coexists with urethral obstruction from benign prostatic hyperplasia. Because detrusor overactivity also may be due to bladder stones or tumor, the abrupt onset of unexplained urge incontinence should be investigated by urine cytology and cytoscopy.

2. Urethral incompetence (stress incontinence)— Urethral incompetence is the second most common cause of established urinary incontinence in older women. In men, it commonly occurs after radical prostatectomy. Stress incontinence is characterized by instantaneous leakage of urine in response to an increase in intra-abdominal pressure. It can coexist with detrusor overactivity causing "mixed" incontinence. Typically, urinary loss occurs with laughing, coughing, or lifting heavy objects. To test for stress incontinence, have the patient relax the perineum and cough vigorously (a single cough) while standing with a full bladder. Instantaneous leakage indicates stress incontinence.

3. Overflow incontinence—Urethral obstruction (due to prostatic enlargement, urethral stricture, bladder neck contracture, or prostatic cancer) is a common cause of established incontinence in older men but is rare in older women. It can present as dribbling incontinence after voiding, urge incontinence due to detrusor overactivity, or overflow incontinence due to urinary retention. Detrusor underactivity is less common but can also cause overflow incontinence. It may be idiopathic or have an identifiable cause including medications and sacral lower motor nerve dysfunction. When it causes incontinence, detrusor underactivity is associated with urinary frequency, nocturia, and frequent leakage of small volumes.

Treatment

A. Transient Causes

Each identified transient cause should be treated regardless of whether an established cause coexists.

B. Established Causes

1. Detrusor overactivity—The cornerstone of treatment is **bladder training.** Patients start by voiding on a schedule based on the shortest interval recorded on a bladder record. They then gradually lengthen the interval between voids by 30 minutes each week using relaxation techniques to postpone the urge to void. Lifestyle modifications, including weight loss and caffeine reduction, may also improve incontinence symptoms. **Pelvic floor muscle ("Kegel") exercises** can reduce the frequency of incontinence episodes when performed correctly and sustained. For cognitively impaired patients and nursing home residents who are unable to manage on their own, **timed and prompted voiding** initiated by caregivers is effective.

If behavioral approaches prove insufficient, pharmacotherapy with beta-3-agonists or antimuscarinic agents can be considered. Efficiency and safety profiles are comparable in both groups, with fewer anticholinergic adverse drug effects reported in patients taking beta-3-agonists. Mirabegron, at 20–50 mg by mouth daily, and vibegron, at 75 mg by mouth daily, are FDA-approved beta-3-agonists for overactive bladder symptoms.

FDA-approved antimuscarinic agents include short-acting tolterodine, 1–2 mg orally twice daily; long-acting tolterodine, 2–4 mg orally daily; short-acting oxybutynin, 2.5–5 mg orally two or three times daily; long-acting oxybutynin, 5–15 mg orally daily; oxybutynin transdermal patch, 3.9 mg/day applied twice weekly; oxybutynin 10% transdermal gel, 100 mg applied daily; fesoterodine, 4–8 mg orally once daily; trospium chloride, 20 mg orally once or twice daily; long-acting trospium chloride, 60 mg orally daily; darifenacin, 7.5–15 mg orally daily; and solifenacin, 5–10 mg orally daily. They are commonly available, have low-cost generic options, come in short-acting and long-acting formulations, and can be combined with beta-3-agonists for synergistic effects. Potential adverse drug effects to consider include cognitive impairment, dry mouth, constipation, and urinary retention.

Women who have persistent symptoms despite an adequate trial of initial treatment, or who are unable to tolerate pharmacotherapy options, may be referred to urologists or urogynecologists for alternative options. Other possible treatment approaches include percutaneous or transcutaneous tibial nerve stimulation and botulinum toxin type A injection into the detrusor muscle. Symptom relief from botulinum toxin injections has been reported to last 6–12 months; possible adverse effects include urinary retention and the need for self-catheterization.

In men with both benign prostatic hyperplasia and detrusor overactivity and with postvoid residual of 150 mL or less, an antimuscarinic agent added to an alpha-blocker may provide additional relief of lower urinary tract symptoms.

2. Urethral incompetence (stress incontinence)— **Lifestyle modifications** include limiting caffeine and fluid intake and may be helpful for those with mixed stress/urge incontinence; strong evidence supports weight loss in women with BMI of 30 or more. **Pelvic floor therapy** is effective for women with mild to moderate stress incontinence. Instruct the patient to pull in the pelvic floor muscles and hold for 6–10 seconds and to perform three sets of 8–12 contractions daily. Benefits may not be seen for 6 weeks. **Pessaries** or **vaginal cones** may be helpful in some women but should be prescribed only by providers who are experienced with using these modalities. No medications are approved for the treatment of stress incontinence, and a clinical practice guideline from the American College of Physicians recommends against pharmacologic treatment. Patients experiencing symptoms despite initial approaches should be evaluated for **surgical treatments.** Midurethral sling procedures, with their rapid recovery times, high cure rates, and low risk of complications, have become the standard surgeries for stress incontinence in older women.

3. Overflow incontinence—Most men with overflow incontinence from obstructive uropathy will first undergo bladder decompression with intermittent or indwelling

catheterization followed by initiation of alpha-blocking agents (eg, terazosin, 1–10 mg orally daily; prazosin, 1–5 mg orally twice daily; or tamsulosin, 0.4–0.8 mg orally daily taken 30 minutes after a meal). Finasteride, 5 mg orally daily, can provide additional benefit in men with an enlarged prostate. If medical therapy fails to allow for adequate bladder emptying, surgical decompression can be an option. A variety of nonsurgical techniques make decompression feasible even for frail patients. For the nonoperative candidate with urinary retention, intermittent or indwelling catheterization are options. For the patient with a poorly contractile bladder, augmented voiding techniques (eg, double voiding, suprapubic pressure) can prove effective. If further emptying is needed, intermittent or indwelling catheterization is the only option. Antibiotics should be used only for symptomatic UTI or as prophylaxis against recurrent symptomatic infections in a patient using intermittent catheterization; they should not be used as prophylaxis in a patient with an indwelling catheter.

When to Refer

- Men with urinary obstruction who do not respond to medical therapy should be referred to a urologist.
- Women who do not respond to pelvic floor therapy, medical treatment, or both should be referred to a urogynecologist or urologist.

Funada S et al. Bladder training for treating overactive bladder in adults. Cochrane Database Syst Rev. 2023;10:CD013571. [PMID: 37811598]
Olagundoye O et al. A scoping review of risk factors for urinary incontinence in older men. BMC Geriatr. 2023;23:534. [PMID: 37660036]
Vaughan CP et al. Urinary incontinence in women. Ann Intern Med. 2020;172:ITC17. [PMID: 32016335]

7. Involuntary Weight Loss

General Considerations

Aging, even in the absence of disease, is associated with reduced appetite. Involuntary weight loss affects substantial numbers of older adults. Most studies of involuntary weight loss in community-dwelling older adults define it as loss of 5% of body weight in 6 months or 10% of body weight in 1 year.

Clinical Findings

The many potential causes of involuntary weight loss include **medical conditions** (60–70%; eg, cancer cachexia, chronic HF) and **psychiatric conditions** (10–20%; eg, depression), but in up to 25%, the cause of weight loss cannot be identified. **Social factors,** such as lack of access to food and poor dental health, should be investigated. The clinical evaluation should search for symptoms and signs that could point to a potential cause (eg, abdominal pain to peptic ulcer disease; tachycardia to hyperthyroidism). When the history, physical examination, and basic laboratory studies do not suggest a possible diagnosis, additional evaluation (eg, total body CT scan) is usually low yield.

Treatment

Initial treatment should focus on identifying medical causes of involuntary weight loss while also addressing and improving social barriers, such as social isolation and lack of access to food. Social meals can improve intake and nutrition. Oral nutritional supplements of 200–1000 kcal/day can increase weight and improve outcomes in malnourished hospitalized older adults but have *not* been shown to have benefits in community-dwelling older adults. Sodium-containing flavor enhancers (eg, iodized salt) can improve food intake without adverse health effects when there is no contraindication to their use. Megestrol acetate as an appetite stimulant has *not* been shown to increase lean body mass or lengthen life among elders and has significant side effects. For those patients with advanced dementia, percutaneous liquid artificial nutrition ("tube feeding") is *not* recommended, but rather assiduous hand feeding may allow maintenance of weight and provide more comfort.

Gaddey HL et al. Unintentional weight loss in older adults. Am Fam Physician. 2021;104:34. [PMID: 34264616]

8. Pressure Injury

ESSENTIALS OF DIAGNOSIS

- Examine at-risk patients on admission to the hospital and daily thereafter.
- Pressure injury is classified into one of six categories:
  - Stage 1: Non-blanchable erythema of intact skin
  - Stage 2: Partial-thickness skin loss with exposed dermis
  - Stage 3: Full-thickness skin loss
  - Stage 4: Full-thickness skin and tissue loss
  - Unstageable: Obscured full-thickness skin and tissue loss
  - Deep tissue: Persistent non-blanchable, deep red, maroon, or purple discoloration of intact skin

General Considerations

The National Pressure Injury Advisory Panel defines pressure injuries as damage to the skin and underlying tissue from pressure in combination with shear and friction forces, usually over a bony prominence or related to a medical device. The term "pressure ulcer" was changed to "pressure injury" to more accurately reflect that the skin is intact in stage 1 and deep tissue injury, since the word "ulcer" implies that the skin has opened. Deep tissue and unstageable pressure injuries are included in the

six pressure injury stages. An area of purple or maroon discolored intact skin or blood-filled blister is characteristic of deep tissue injury, sometimes preceded by tissue that is painful, firm, mushy, boggy, warmer, or cooler compared with adjacent tissue. Ulcers in which the base is covered by slough (yellow, tan, gray, green, or brown) or eschar (tan, brown, or black) are considered unstageable. Most pressure injuries develop during an acute illness. The primary risk factor for pressure injuries is immobility. Other contributing risk factors include reduced tissue perfusion, reduced sensory perception, moisture (urinary and fecal incontinence), and poor nutritional status.

Older adults admitted to hospitals and nursing homes should be assessed for their risk of developing pressure injuries, utilizing risk assessment instruments such as the Braden Scale and the Norton score. These tools should be used in conjunction with clinical judgment since each may cover a limited range of risk factors and each depends on the skills of the examiner.

Prevention

Using specialized support surfaces (including mattresses, beds, and cushions), patient repositioning, optimizing nutritional status, reducing shear and friction forces, and being mindful of skin integrity are strategies that have been shown to reduce pressure injury. In general, advanced supportive surfaces are superior to standard hospital beds in preventing and managing pressure injuries, but there is no clear advantage of one support surface over another.

Evaluation

Evaluation of pressure injuries should include the patient's risk factors and goals of care; injury stage, size, and depth; absence or presence (and type) of exudate; appearance of the wound bed and possible surrounding infection; and any sinus tracking, undermining, or tunneling.

Treatment

High-quality evidence that rigorously examines the effectiveness of various treatments remains limited. Clinicians should therefore focus on the principles of wound care, including pressure reduction, removing necrotic debris, and maintaining a moist wound bed to promote formation of granulation tissue and healing. The type of dressing recommended depends on the location and depth of the wound, whether necrotic tissue or dead space is present, and the amount of exudate (Table 4–3). Pressure-reducing devices (eg, air-fluid beds and low-air-loss beds) are associated with improved healing rates. Although poor nutritional status is a risk factor for the development of pressure injury, the evidence that nutritional supplementation helps correct pressure injury is limited.

Institutions should designate a wound care expert or team to select a streamlined wound care product line with simple guidelines. In a patient with end-stage disease who is receiving end-of-life care, appropriate treatment might be directed toward palliation only (including minimizing dressing changes and odors) rather than efforts directed at healing.

Table 4–3. Pressure injury dressings and other measures.

Injury Type	Dressing Type and Considerations
Stage 1	Barrier ointment Polyurethane film
Stage 2	Hydrocolloid dressings Semipermeable foam dressing Polyurethane film Hydrogel
Stages 3 and 4	For highly exudative wounds, use highly absorptive dressing or packing, such as calcium alginate; negative pressure wound therapy or vacuum-assisted wound closure also can be considered Wounds with necrotic debris should be debrided Debridement can be autolytic, enzymatic, mechanical, or surgical Shallow, clean wounds can be dressed with hydrocolloid wafers, semipermeable foam, hydrogels, or polyurethane film Deep wounds can be packed with gauze; if the wound is deep and highly exudative, an absorptive packing should be used
Heel injury	Do not remove eschar on heel pressure injury because it can help promote healing (eschar in other locations should be debrided)
Unstageable	Debride if appropriate before deciding on further therapy
Deep tissue injury	Offload pressure to the affected area

Complications

Bacteria contaminate all chronic pressure injuries with skin loss, but it can be difficult to identify those wounds that are infected. Suspicion for infection should rise if there is pain, increased or foul-smelling wound drainage, erythema of the skin around the wound, or if the wound will not heal. Fever and leukocytosis are other indicators of systemic infection but are not always present. Culture from a superficial swab adds little valuable diagnostic information. For nonhealing infected wounds without evidence of systemic involvement, topical antiseptics (eg, silver sulfadiazine) are recommended and may need to be accompanied by debridement of necrotic tissue. When systemic infections such as cellulitis and osteomyelitis are present, oral or parenteral antibiotics are warranted and medication choice should be guided by tissue culture, but obtaining this can be painful and it is not always readily available.

When to Refer

- Pressure injuries that are large or nonhealing should be referred to a plastic or general surgeon or dermatologist for biopsy, debridement, and possible skin grafting.
- For hospitalized patients or residents of skilled nursing facilities in whom pressure injuries develop, early involvement of a wound care specialist is crucial.