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undergo chest CT. Diseases causing cough that may be missed on chest x-ray include tumors, early interstitial lung disease, bronchiectasis, and atypical mycobacterial pulmonary infection. On the other hand, patients with chronic cough who have normal findings on chest examination, lung function testing, oxygenation assessment, and chest CT can be reassured as to the absence of serious pulmonary pathology.

■ ■GLOBAL CONSIDERATIONS Regular exposure to air pollution can cause chronic cough and throat clearing, as well as lower respiratory tract disease. Smoke from cooking and heating fuels in poorly ventilated homes; toxic exposures in work settings lacking implementation of occupational safety standards; and ambient chemicals and particulates in highly polluted outdoor air are all forms of air pollution causing cough. Limited therapeutic options are available; treatment focuses on improving environmental air quality (e.g., use of a stove chimney in the home), removal from the exposure, and use of an appropriate face mask.

PART 2 Cardinal Manifestations and Presentation of Diseases In areas of the world where tuberculosis is endemic, chronic cough conjures the possibility of active pulmonary tuberculosis and mandates appropriate evaluation, including chest imaging and sputum analysis.

■ ■SYMPTOM-BASED TREATMENT OF COUGH Empiric treatment of chronic idiopathic cough with inhaled corticosteroids, inhaled anticholinergic bronchodilators, and macrolide antibiotics has been tried without consistent success. Currently available cough suppressants are only modestly effective. Most potent are narcotic cough suppressants, such as codeine, hydrocodone, or morphine, which are thought to act in the “cough center” in the brainstem. The tendency of narcotic cough suppressants to cause drowsiness and constipation and their potential for addictive dependence limit their appeal for long-term use. Dextromethorphan is an over-the-counter, centrally acting cough suppressant with fewer side effects and less efficacy than the narcotic cough suppressants. Dextromethorphan is thought to have a different site of action than narcotic cough suppressants and can be used in combination with them if necessary. Benzonatate is thought to inhibit neural activity of sensory nerves in the cough-reflex pathway. It is generally free of side effects; however, its effectiveness in suppressing cough is variable and unpredictable. Inhaled lidocaine, an inhibitor of voltage-gated sodium channels, provides transient cough suppression, but because of associated oropharyngeal anesthesia, it poses an increased risk of aspiration. Attempts to treat cough hypersensitivity syndrome have focused on inhibition of neural pathways. Small case series and randomized clinical trials have indicated benefit from off-label use of gabapentin, pregabalin, or amitriptyline. Recent studies suggest a role for behavioral modification using specialized speech therapy techniques, but widespread application of this modality is currently not practical. Novel cough suppressants without the limitations of currently available agents are greatly needed. Approaches that are being explored include the development of neurokinin-1 receptor antagonists, transient receptor protein

vanilloid-1 (TRPV1) channel antagonists, P2X3 channel antagonists, and novel opioid and opioid-like receptor agonists. Acknowledgment Christopher H. Fanta contributed to this chapter in the 21st edition and some material from that chapter has been retained here. ■ ■ FURTHER READING Brightling CE et al: Eosinophilic bronchitis as an important cause of chronic cough. *Am J Respir Crit Care Med* 160:406, 1999. Carroll TL (ed): *Chronic Cough*. San Diego, Plural Publishing, Inc., 2019. Gibson P et al: Treatment of unexplained chronic cough: CHEST guideline and expert panel report. *Chest* 149:27, 2016. Kahrilas PJ et al: Chronic cough due to gastroesophageal reflux in adults: CHEST Guideline and Expert Panel Report. *Chest* 150:1381, 2016. Mazzone SB et al: Chronic cough and cough hypersensitivity: From mechanistic insights to novel antitussives. *Lancet Respir Med* 10:1113, 2022. Morice AH et al: ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J* 55:1901136, 2020. Smith JA, Woodcock A: Chronic cough. *N Engl J Med* 375:1544, 2016.

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Hemoptysis Hemoptysis is the expectoration of blood originating from the lower respiratory tract. It can be confused initially with bleeding from the gastrointestinal tract (hematemesis) or nasal cavities (epistaxis). The amount of blood that is being expectorated (volume and frequency) is the most important information to gather as massive or life-threatening hemoptysis (variable definitions but commonly expectorating >150 mL in 24 h or a bleeding rate of ≥ 100 mL/h) requires emergent intervention. This chapter focuses on non-life-threatening hemoptysis, which is more common.

ANATOMY AND PHYSIOLOGY OF HEMOPTYSIS Hemoptysis originates in the lower respiratory tract, anywhere from the glottis to the alveolus. The bleeding most commonly arises from the bronchi or medium-sized airways, but a thorough evaluation of the entire respiratory tree is important. The blood supply to the lungs is from both the pulmonary and bronchial circulations. The pulmonary circulation is a low-pressure system that is essential for gas exchange at the alveoli; in contrast, the bronchial circulation originates from the aorta and, thus, is a higher-pressure system. The bronchial arteries supply the airways and can neovascularize tumors, dilated airways in bronchiectasis, and cavitory lesions. Most hemoptysis originates from the bronchial circulation, the higher-pressure system, which can make it difficult to control.

ETIOLOGY Infection, malignancy, and vascular disease are some of the common causes of hemoptysis, but the differential is quite broad. In the United States, the most common causes remain viral bronchitis, bronchiectasis, or malignancy. In other parts of the world, infections such as tuberculosis are the most common causes. ■ ■ **INFECTIONS** Although most small-volume hemoptysis cases are due to viral bronchitis, patients with chronic bronchitis are at risk for bacterial superinfection. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are the more common bacteria involved, and these infections can increase airway inflammation that leads to bleeding. Similarly, patients with bronchiectasis, including those with cystic fibrosis, can have hemoptysis during exacerbations. Due to recurrent bacterial infection, bronchiectatic airways are dilated, inflamed, and highly vascular, supplied by the bronchial circulation. This can cause bronchiectasis to also be a significant cause of massive hemoptysis and subsequent death. Tuberculosis used to be the most common cause of hemoptysis worldwide, but in industrialized countries, bronchitis and bronchiectasis are more common. In patients with tuberculosis, development of cavitory disease is frequently the source of bleeding, but rarer complications such as erosion of a pulmonary artery aneurysm into a preexisting cavity (i.e., Rasmussen's aneurysm) can also be the source. Other infectious agents such as endemic fungi, *Nocardia*, and non

tuberculous mycobacteria can present as cavitary lung disease complicated by hemoptysis. In addition, *Aspergillus* species can develop into mycetomas within preexisting cavities, with neovascularization to these inflamed spaces leading to bleeding. Pulmonary abscesses and necrotizing pneumonia can cause bleeding by devitalizing lung parenchyma. Common responsible organisms include *Staphylococcus aureus*, *Klebsiella pneumoniae*, and oral anaerobes. Paragonimiasis can mimic tuberculosis and is another significant cause of hemoptysis seen globally; it is common in Southeast Asia and China, although cases have been reported in North America from raw

crayfish ingestion. It should be considered as a cause of hemoptysis in recent immigrants from endemic areas. ■ ■VASCULAR Hemoptysis from a vascular cause can be associated with cardiac disease, pulmonary embolism, arteriovenous malformation, or diffuse alveolar hemorrhage (DAH). While the classic description of the sputum expectorated in pulmonary edema (from elevated left end-diastolic pressure) is “pink and frothy,” a spectrum of hemoptysis including frank blood can be seen. This observation is particularly true now with the more widespread use of anticoagulants and antiplatelet medications. Pulmonary embolism with parenchymal infarction can present with hemoptysis, but pulmonary emboli do not commonly cause hemoptysis. An ectatic vessel in an airway or a pulmonary arteriovenous malformation can be a source of bleeding. A rare vascular cause of hemoptysis is the rupture of an aortobronchial fistula; these fistulae arise in the setting of aortic pathology such as aneurysm or pseudoaneurysm and can cause small bleeding episodes that result in massive hemoptysis. DAH causes significant bleeding into the lung parenchyma but, interestingly, is not often associated with hemoptysis. DAH typically presents with diffuse ground-glass opacities on chest imaging. A range of insults cause DAH, including immune-mediated capillaritis from diseases such as systemic lupus erythematosus, toxicity from cocaine and other inhalants, and stem cell transplantation. The so-called

“pulmonary-renal” syndromes, including granulomatosis with polyangiitis and anti-glomerular basement membrane (anti-GBM) disease, may lead to both hemoptysis and hematuria (though one manifestation may be present without the other). A recently identified cause of hemoptysis and DAH is vaping-induced lung injury. ■ ■MALIGNANCY Bronchogenic carcinoma of any histology is a common cause of hemoptysis (both massive and nonmassive). Hemoptysis can indicate airway involvement of the tumor and can be a presenting symptom of carcinoid tumors, vascular lesions that frequently arise in the proximal airways. Small-cell and squamous cell carcinomas are frequently central in nature and more likely to erode into major pulmonary vessels, resulting in massive hemoptysis. Pulmonary metastases from distant tumors (e.g., melanoma, sarcoma, adenocarcinomas of the breast and colon) can also cause bleeding. Kaposi’s sarcoma, seen in advanced acquired immunodeficiency syndrome, is very vascular and can develop anywhere along the respiratory tract, from the bronchi to the oral cavity. Rule out other sources: -Oropharynx - Gastrointestinal tract Nonmassive No risk factors Risk factors ■ ■MECHANICAL AND OTHER CAUSES In addition to infection, vascular disease, and malignancy, other insults to the pulmonary system can cause hemoptysis. Pulmonary endometriosis causes cyclical bleeding known as catamenial hemoptysis. Foreign body aspiration can lead to airway irritation and bleeding. Diagnostic and therapeutic procedures are also potential offenders: pulmonary vein stenosis can result from left atrial procedures, such as pulmonary vein isolation, and pulmonary artery catheters can lead to rupture of the pulmonary artery if the distal balloon is kept inflated. Finally, in the setting of thrombocytopenia, Treat underlying disease (usually infection) Persistent bleeding

FIGURE 41-1 Approach to the management of hemoptysis. CBC, complete blood count; CT, computed tomography; CXR, chest x-ray; UA, urinalysis.

coagulopathy, anticoagulation, or antiplatelet therapy, even minor insults can cause hemoptysis.

EVALUATION AND MANAGEMENT

HISTORY The initial history should be directed at assessing the pattern, severity, and quantity of hemoptysis. An approach to management of hemoptysis is outlined in Fig. 41-1. A patient's description of the sputum (e.g., flecks of blood, pink-tinged, frank blood or clot) is helpful if you cannot examine it. Quantification is often challenging for patients, so using references like cups (one U.S. cup is 236 mL) can be helpful. Life-threatening hemoptysis is defined by the presence of significantly abnormal gas exchange, hemodynamic compromise, or threat for airway obstruction. Patients rarely die of exsanguination but, rather, are at risk of death due to asphyxiation from blood filling the airways and airspaces. This can occur with blood loss of >400 mL within 24 h or >150 mL at one time. Fortunately, life-threatening hemoptysis only accounts for 5–15% of cases of hemoptysis.

CHAPTER 41 Further history may help define the etiology of hemoptysis. Smoking history and/or unintentional weight loss may point to possible malignancy. Preceding fevers, cough, and/or sputum production may suggest infection. A history of prior diagnosed chronic lung conditions, especially cystic fibrosis or other chronic bronchiectatic diseases, is important to note. Screening for causes of pseudohemoptysis (i.e., other upper airway or gastrointestinal) is also helpful.

PHYSICAL EXAMINATION Patients should initially be assessed for signs of life-threatening hemoptysis including hypoxemia, tachycardia, and hemodynamic instability. Examination should include possible sites of extrapulmonary bleeding such as the nasal and oral cavities. Auscultation of the lungs may suggest a laterality. Other relevant physical findings may suggest other etiologies of the hemoptysis and include clubbing, signs of a bleeding diathesis (e.g., skin or mucosal ecchymoses and petechiae), telangiectasias, or skin rash.

Patient with hemoptysis

History and physical examination

Quantify amount of bleeding

Massive Protect airway

CXR, CBC, UA, creatinine, coagulation studies

Bleeding stops

Bleeding continues Embolization or resection

CT scan

Bronchoscopy

Treat underlying disease

Persistent bleeding

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