

Cough-variant asthma typically responds well to inhaled glucocorticoids and intermittent use of inhaled  $\beta$ -agonist bronchodilators.

Patients who fail to respond to treatment targeting the common causes of chronic cough or who have had these causes excluded by appropriate diagnostic testing should 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.

### SYMPTOM-BASED TREATMENT OF COUGH

*Chronic idiopathic cough*, also called *cough hypersensitivity syndrome*, is distressingly common. It is often experienced as a tickle or sensitivity in the throat, occurs more often in women, and is typically “dry” or at most productive of scant amounts of mucoid sputum. It can be exhausting, interfere with work, and cause social embarrassment. Once serious underlying cardiopulmonary pathology has been excluded, an attempt at cough suppression is appropriate. Most effective are narcotic cough suppressants, such as codeine or hydrocodone, 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. *Benzonate* 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. Case series have reported benefit from off-label use of *gabapentin* or *amitriptyline* for chronic idiopathic cough. Novel cough suppressants without the limitations of currently available agents are greatly needed. Approaches that are being explored include the development of neurokinin receptor antagonists, type 1 vanilloid receptor antagonists, and novel opioid and opioid-like receptor agonists.

### HEMOPTYSIS

*Hemoptysis*, the expectoration of blood from the respiratory tract, can arise at any location from the alveoli to the glottis. It is important to distinguish hemoptysis from *epistaxis* (bleeding from the nasopharynx) and *hematemesis* (bleeding from the upper gastrointestinal tract). Hemoptysis can range from the expectoration of blood-tinged sputum to that of life-threatening large volumes of bright red blood. For most patients, any degree of hemoptysis can cause anxiety and often prompts medical evaluation.

While precise epidemiologic data are lacking, the most common etiology of hemoptysis is infection of the medium-sized airways. In the United States, the cause is usually viral or bacterial bronchitis. Hemoptysis can arise in the setting of acute bronchitis or during an exacerbation of chronic bronchitis. Worldwide, the most common cause of hemoptysis is infection with *Mycobacterium tuberculosis*, presumably because of the high prevalence of tuberculosis and its predilection for cavity formation. While these are the most common causes, the differential diagnosis for hemoptysis is extensive, and a step-wise approach to evaluation is appropriate.

### ETIOLOGY

One way to approach the source of hemoptysis is to search systematically for potential sites of bleeding from the alveolus to the mouth. Diffuse bleeding in the alveolar space, often referred to as *diffuse alveolar hemorrhage* (DAH), may present as hemoptysis. Causes of DAH can be inflammatory or noninflammatory. Inflammatory DAH is due to small-vessel vasculitis/capillaritis from a variety of diseases, including granulomatosis with polyangiitis and microscopic polyangiitis. Similarly,

systemic autoimmune diseases such as systemic lupus erythematosus can manifest as pulmonary capillaritis. Antibodies to the alveolar basement membrane, as are seen in Goodpasture’s disease, can also result in alveolar hemorrhage. In the early period after bone marrow transplantation, patients can develop a form of inflammatory DAH that can be catastrophic and life-threatening. The exact pathophysiology of this process is not well understood, but DAH should be suspected in patients with sudden-onset dyspnea and hypoxemia in the first 100 days after bone marrow transplantation.

Alveoli can also bleed due to direct inhalational injury, including thermal injury from fires, inhalation of illicit substances (e.g., cocaine), and inhalation of toxic chemicals. If alveoli are irritated from any process, patients with thrombocytopenia, coagulopathy, or antiplatelet or anticoagulant use will be at increased risk of hemoptysis.

Bleeding in hemoptysis most commonly arises from the small- to medium-sized airways. Irritation and injury of the bronchial mucosa can lead to small-volume bleeding. More significant hemoptysis can result from the proximity of the bronchial artery and vein to the airway, with these vessels and the bronchus running together in what is often referred to as the *bronchovascular bundle*. In the smaller airways, these blood vessels are close to the airspace, and lesser degrees of inflammation or injury can therefore result in their rupture into the airways. While alveolar hemorrhage arises from capillaries that are part of the low-pressure pulmonary circulation, bronchial bleeding generally originates from bronchial arteries, which are under systemic pressure and thus are predisposed to larger-volume bleeding.

Any infection of the airways can result in hemoptysis, although acute bronchitis is most commonly caused by viral infection. In patients with a history of chronic bronchitis, bacterial superinfection with organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis* can also result in hemoptysis. Patients with bronchiectasis (a permanent dilation of the airways with loss of mucosal integrity) are particularly prone to hemoptysis due to chronic inflammation and anatomic abnormalities that bring the bronchial arteries closer to the mucosal surface. One common presentation of patients with advanced cystic fibrosis—the prototypical bronchiectatic lung disease—is hemoptysis, which can be life-threatening.

Pneumonias of any sort can cause hemoptysis. Tuberculous infection, which can lead to bronchiectasis or cavity pneumonia, is a very common cause of hemoptysis worldwide. Patients may present with a chronic cough productive of blood-streaked sputum or with larger-volume bleeding. *Rasmussen’s aneurysm* (the dilation of a pulmonary artery in a cavity formed by previous tuberculous infection) remains a source of massive, life-threatening hemoptysis in the developing world. Community-acquired pneumonia and lung abscess can also result in bleeding. Once again, if the infection results in cavitation, there is a greater likelihood of bleeding due to erosion into blood vessels. Infections with *Staphylococcus aureus* and gram-negative rods (e.g., *Klebsiella pneumoniae*) are especially likely to cause necrotizing lung infections and thus to be associated with hemoptysis.



While not common in North America, pulmonary paragonimiasis (i.e., infection with the lung fluke *Paragonimus westermani*) often presents as fever, cough, and hemoptysis. This infection is a public health issue in Southeast Asia and China and is frequently confused with active tuberculosis, in which the clinical picture can be similar. Paragonimiasis should be considered in recent immigrants from endemic areas who have new or recurrent hemoptysis. In addition, pulmonary paragonimiasis has been reported secondary to ingestion of crayfish or small crabs in the United States.

Other causes of airway irritation resulting in hemoptysis include inhalation of toxic chemicals, thermal injury, and direct trauma from suctioning of the airways (particularly in intubated patients). All of these etiologies should be considered in light of the individual patient’s history and exposures.

Perhaps the most feared cause of hemoptysis is bronchogenic lung cancer, although hemoptysis is a presenting symptom in only ~10% of patients. Cancers arising in the proximal airways are much more likely to cause hemoptysis, but any malignancy in the chest can do so. Because both squamous cell carcinomas and small-cell carcinomas are