clubbing may be present. Periodic exacerbations due to infection with bacterial pathogens, including *H. influenzae* and *P. aeruginosa*, are common. Nontuberculous mycobacterial colonization or infection may also occur. Pulmonary function tests typically show mild to moderate obstruction. Evidence of bronchial hyperresponsiveness is not infrequent.

Diagnosis and Differential Diagnosis

Chest radiographs may be normal or may show increased interstitial markings. The classic finding is parallel lines in peripheral lung fields, described as "tram tracks," which represent thickened bronchial walls that do not taper from proximal to distal sites. However, HRCT is more sensitive for the detection of dilated airways and is the diagnostic test of choice in the evaluation of suspected bronchiectasis. Bronchiectasis on HRCT is diagnosed by demonstration of lack of airway tapering, airways that are larger in diameter than their accompanying blood vessel, and the presence of visible bronchi at the lung periphery (outer 1 to 2 cm of the lung). Bronchoscopy may be indicated in localized bronchiectasis to assess for endobronchial abnormalities or foreign body. Sputum can be cultured to assess for fungal or mycobacterial organisms that may be causative or for identification of specific bacterial pathogens during exacerbations. Once the diagnosis of bronchiectasis is established, investigation to determine the underlying cause, such as assessment of immunoglobulin levels to rule out combined variable immunodeficiency, is indicated.

The differential diagnosis includes chronic bronchitis and COPD, asthma, and, in the setting of hemoptysis and clubbing, lung cancer.

Treatment

Treatment of the underlying cause of the bronchiectasis should be undertaken if possible. An anatomic obstruction, such as from a foreign body or benign tumor, should be relieved. Atypical mycobacterial infection should be treated with an appropriate multidrug regimen in symptomatic patients after confirmation of the diagnosis with multiple smears and cultures. Allergic bronchopulmonary aspergillosis is typically treated with corticosteroids; addition of azole antifungals may also be beneficial (level 3 evidence). Bacterial exacerbations of bronchiectasis should be treated with a broad-spectrum antibiotic that is effective against the likely pathogens, such as amoxicillin or, in patients known to be colonized or infected by *Pseudomonas*, a fluoroquinolone (level 2). Aerosolized antibiotics are of benefit to suppress bacterial growth in bronchiectasis associated with CF and may be beneficial in non-CF bronchiectasis if *Pseudomonas* infection is present or if frequent exacerbations occur (level 3). Chronic administration of macrolide antibiotics has been shown to reduce inflammation and exacerbations in bronchiectasis but may also promote development of macrolide-resistant bacteria (level 2).

Immunoglobulin supplementation may aid in the host defense against bacterial infection in individuals with hypogammaglobulinemia. Airway clearance and postural drainage are frequently employed in bronchiectasis. Bronchodilators may provide symptomatic relief. Massive hemoptysis should be managed with airway protection and identification of the bleeding site; bronchial artery angiography with embolization of the causative bleeding vessels can be life-saving (level 3). The role of surgery is mainly in resection of obstructing lesions that are causing distal bronchiectasis, in removal of a badly damaged isolated segment of bronchiectatic lung, and, on occasion, as a salvage therapy in resection of a site with uncontrolled hemorrhage (level 3).

Prognosis

The prognosis of patients with bronchiectasis is generally thought to be favorable, although deterioration of lung function over time has been shown to occur. Quality of life may be affected adversely, for example by chronic production of copious sputum or frequent exacerbations. Massive hemoptysis is an emergency situation that requires intensive management and may be fatal.

CYSTIC FIBROSIS

Definition and Epidemiology

CF is an autosomal recessive genetic disorder that results from mutations in the *CFTR* gene. CF affects about 30,000 children and adults in the United States. This disorder affects many organs, including the lungs, pancreas, and reproductive organs, although most mortality related to CF is due to lung disease. It is the most common lethal genetic disorder in the white population, with a carrier frequency of about 1 in 29, affecting 1 in 3300 live births. About 1000 new cases of CF are diagnosed each year. Although most patients are diagnosed in infancy and childhood, some are not diagnosed until adulthood. About 45% of the population with CF in the United States is older than 18 years of age, but before 1940, infants with CF rarely lived to their first birthday. Currently, the median predicted life span for a person with CF is about 37 years.

Pathology

CF results from pathogenic mutations in both alleles of a single gene, *CTFR*, which encodes the cystic fibrosis transmembrane conductance regulator (CFTR), a cAMP-regulated chloride channel that is present on the apical surface of epithelial cells (E-Fig. 16-10). The most common mutation is the ΔF508 mutation, a three-base-pair deletion that results in absence of the phenylalanine residue at the 508 position of the protein. However, more than 1600 mutations in CFTR have been identified to date.

The abnormal CFTR protein results in defective chloride transport and increased sodium reabsorption in airway and ductal epithelia; this leads to abnormally thick and viscous secretions in the respiratory, hepatobiliary, gastrointestinal, and reproductive tracts. The thick secretions do not easily clear from the airways, resulting in respiratory symptoms, and they cause luminal obstruction and destruction of exocrine ducts in other organs, leading to exocrine organ fibrosis and dysfunction, including pancreatic damage.

In patients with CF, the airways become colonized initially with *S. aureus* or *H. influenzae,* followed by *P. aeruginosa* in ensuing years. Persistent inflammation and infection cause bronchial wall destruction and bronchiectasis. Mucus plugging of small airways results in postobstructive cystic airway dilation and parenchymal destruction; progressive airflow obstruction and eventually hypoxemia ensue. The course of CF may additionally be complicated by the development of allergic bronchopulmonary aspergillosis or by nontuberculous mycobacterial infection.