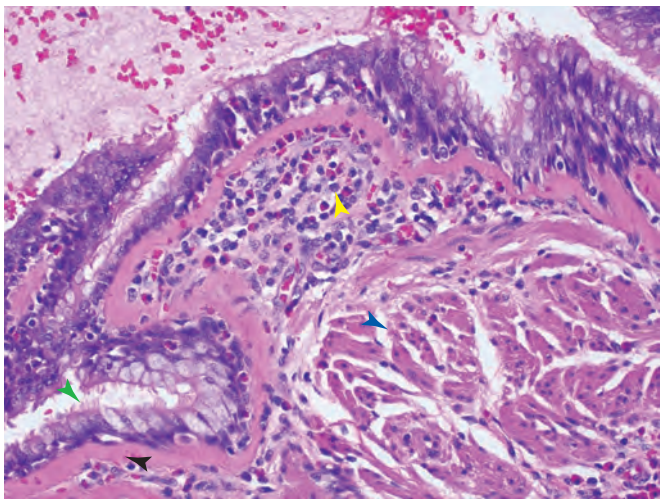

Figure 15-11 Bronchus from an asthmatic patient showing goblet cell hyperplasia *(green arrowhead)*, subbasement membrane fibrosis *(black arrowhead)*, eosinophilic inflammation *(yellow arrowhead)*, and muscle hypertrophy *(blue arrowhead)*.

reactions. The T_H2 cytokines IL-4, IL-5, and IL13 are important mediators. IL17 and IL9 are also being shown to be important in some asthmatics.

- Triggers for nonatopic asthma are less clear but include viral infections and inhaled air pollutants, which can also trigger atopic asthma.
- Eosinophils are key inflammatory cells found in almost all subtypes of asthma; other inflammatory cells include mast cells, neutrophils and T lymphocytes.
- Airway remodeling (sub-basement membrane fibrosis, hypertrophy of bronchial glands, and smooth muscle hyperplasia) adds an irreversible component to the obstructive disease.

Bronchiectasis

Bronchiectasis is a disorder in which destruction of smooth muscle and elastic tissue by chronic necrotizing infections leads to permanent dilation of bronchi and bronchioles. Because of better control of lung infections, bronchiectasis is now uncommon. It may still develop in association with a variety of conditions, including the following:

- *Congenital or hereditary conditions*, including cystic fibrosis, intralobar sequestration of the lung, immunodeficiency states, and primary ciliary dyskinesia and Kartagener syndromes
- *Infections*, including necrotizing pneumonia caused by bacteria, viruses, or fungi; this may be a single severe episode or recurrent infections
- *Bronchial obstruction*, due to tumor, foreign bodies, or mucus impaction; in each instance the bronchiectasis is localized to the obstructed lung segment
- Other conditions, including rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, COPD, and posttransplantation (chronic lung rejection, and chronic graft-versus-host disease after bone marrow transplantation)
- One fourth to one half of cases are *idiopathic*, lacking the aforementioned associations.

Pathogenesis. Obstruction and infection are the major conditions associated with bronchiectasis, and it is likely that both are necessary for the development of full-fledged lesions. After bronchial obstruction, normal clearing mechanisms are impaired, resulting in pooling of secretions distal to the obstruction and secondary infection and inflammation. Conversely, severe infections of the bronchi lead to inflammation, often with necrosis, fibrosis, and eventually dilation of airways.

Both mechanisms are readily apparent in a severe form of bronchiectasis that is associated with cystic fibrosis (Chapter 10). In cystic fibrosis the primary defect in ion transport leads to defective mucociliary action and airway obstruction by thick viscous secretions. This sets the stage for chronic bacterial infections, which cause widespread damage to airway walls. With destruction of supporting smooth muscle and elastic tissue, the bronchi become markedly dilated, while smaller bronchioles are progressively obliterated as a result of fibrosis (bronchiolitis obliterans).

In *primary ciliary dyskinesia*, an autosomal recessive syndrome with a frequency of 1 in 15,000 to 40,000 births, ciliary dysfunction due to defects in ciliary motor proteins (e.g., mutations involving dynein) contributes to the retention of secretions and recurrent infections that in turn lead to bronchiectasis. Ciliary function is necessary during development to ensure proper rotation of the developing organs in the chest and abdomen; it is absence, their location becomes a matter of chance. As a result, approximately half of the patients with primary ciliary dyskinesia have *Kartagener syndrome*, marked by situs inversus or a partial lateralizing abnormality associated with bronchiectasis and sinusitis. The lack of ciliary activity interferes with bacterial clearance, predisposes the sinuses and bronchi to infection, and affects cell motility during embryogenesis, resulting in the situs inversus. Males with this condition tend to be infertile, as a result of sperm dysmotility.

Allergic bronchopulmonary aspergillosis occurs in patients with asthma and cystic fibrosis who develop periods of exacerbation and remission that may lead to proximal bronchiectasis and fibrotic lung disease. It is a condition that results from a hypersensitivity reaction to the fungus *Aspergillus fumigatus*. Sensitization to *Aspergillus* in the allergic host leads to activation of T_H2 helper T cells, which play a key role in recruiting eosinophils and other leukocytes. Characteristically, there are high serum IgE levels, serum antibodies to *Aspergillus*, intense airway inflammation with eosinophils, and the formation of mucus plugs, which play a primary role in its pathogenesis.

MORPHOLOGY

Bronchiectasis usually affects the lower lobes bilaterally, particularly air passages that are vertical, and is most severe in the more distal bronchi and bronchioles. When tumors or aspiration of foreign bodies lead to bronchiectasis, the involvement may be localized to a single lung segment. **The airways are dilated, sometimes up to four times normal size.** Characteristically, the bronchi and bronchioles are so dilated that they can be