MORPHOLOGY

Grossly, there is hyperemia, swelling, and edema of the mucous membranes, frequently accompanied by excessive mucinous or mucopurulent secretions. Sometimes, heavy casts of secretions and pus fill the bronchi and bronchioles. The characteristic features are mild chronic inflammation of the airways (predominantly lymphocytes) and enlargement of the mucus-secreting glands of the trachea and bronchi. Although the numbers of goblet cells increase slightly, the **major change is in the size of mucous glands (hyperplasia)**. This increase can be assessed by the ratio of the thickness of the mucous gland layer to the thickness of the wall between the epithelium and the cartilage (**Reid index**). The Reid index (normally 0.4) is increased in chronic bronchitis, usually in proportion to the severity and duration of the disease. The bronchial epithelium may exhibit squamous metaplasia and dysplasia. There is marked narrowing of bronchioles caused by mucus plugging, inflammation, and fibrosis. In the most severe cases, there may be obliteration of lumen due to fibrosis (**bronchiolitis obliterans**).

Clinical Features. The cardinal symptom of chronic bronchitis is a persistent cough productive of sparse sputum. For many years no other respiratory functional impairment is present, but eventually dyspnea on exertion develops. With the passage of time, and usually with continued smoking, other elements of COPD may appear, including hypercapnia, hypoxemia, and mild cyanosis *("blue bloaters")*. Differentiation of pure chronic bronchitis from that associated with emphysema can be made in the classic case (Table 15-4), but, as has been mentioned, many patients with COPD have both conditions. Long-standing severe chronic bronchitis commonly leads to cor pulmonale and cardiac failure. Death may also result from further impairment of respiratory function due to superimposed acute infections.

KEY CONCEPTS

Chronic Bronchitis

- Chronic bronchitis is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years.
- Cigarette smoking is the most important risk factor; air pollutants also contribute.
- The dominant pathologic features are mucus hypersecretion and persistent inflammation.
- Histologic examination demonstrates enlargement of mucous-secreting glands, goblet cell hyperplasia, chronic inflammation, and bronchiolar wall fibrosis.

Asthma

Asthma is a chronic disorder of the conducting airways, usually caused by an immunological reaction, which is marked by episodic bronchoconstriction due to increased airway sensitivity to a variety of stimuli; inflammation of the bronchial walls; and increased mucus secretion. The disease is manifested by recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and/or in the early morning. These symptoms are usually associated with widespread but variable bronchoconstriction and airflow limitation that is at least partly reversible, either spontaneously or with treatment. Some of the stimuli that trigger attacks in patients would have little or no effect in subjects with normal airways. Rarely, a state of unremitting attacks, called acute severe asthma (formerly known as *status asthmaticus*), may prove fatal; usually, such patients have had a long history of asthma. Between the attacks, patients may be virtually asymptomatic. Of note, there has been a significant increase in the incidence of asthma in the Western world over the past 40 to 50 years, which may be reaching a plateau now. More recently, although treatment for asthma has improved substantially, the prevalence of asthma continues to increase in low and middle income countries and in some ethnic groups in which prevalence was previously low.

Asthma may be categorized as *atopic* (evidence of allergen sensitization and immune activation, often in a patient with allergic rhinitis or eczema) or *non-atopic* (no evidence of allergen sensitization). In either type, episodes of bronchospasm can have diverse triggers, such as respiratory infections (especially viral infections), exposure to irritants (e.g., smoke, fumes), cold air, stress, and exercise. There is some evidence that sub-classifying asthma according to its clinical features and underlying biology is clinically useful. One example is early-onset allergic asthma associated with T_H2 helper T cell inflammation, a feature seen in about half of the patients. This form of asthma responds well to corticosteroids. However, there is no current consensus as to definitions and diagnostic criteria. Asthma may also be classified according to the agents or events that trigger bronchoconstriction. These include seasonal, exercise-induced, drug-induced (e.g., aspirin), and occupational asthma, and asthmatic bronchitis in smokers.

Atopic Asthma. This most common type of asthma is a **classic example of IgE-mediated (type I) hypersensitivity reaction**, discussed in detail in Chapter 6. The disease usually begins in childhood and is triggered by environmental allergens, such as dusts, pollens, cockroach or animal dander, and foods, which most frequently act in synergy with other proinflammatory environmental cofactors, most notable respiratory viral infections. A positive family history of asthma is common, and a skin test with the offending antigen in these patients results in an immediate wheal-and-flare reaction. Atopic asthma may also be diagnosed based on high total serum IgE levels or evidence of allergen sensitization by serum radioallergosorbent tests (called RAST), which can detect the presence of IgE antibodies that are specific for individual allergens.

Non-Atopic Asthma. Individuals with non-atopic asthma do not have evidence of allergen sensitization and skin test results are usually negative. A positive family history of asthma is less common in these patients. Respiratory infections due to viruses (e.g., rhinovirus, parainfluenza virus and respiratory syncytial virus) are common triggers in non-atopic asthma. Inhaled air pollutants, such as smoking, sulfur dioxide, ozone, and nitrogen dioxide, may also contribute to the chronic airway inflammation and hyperreactivity in some cases. As already mentioned, in some instances attacks may be triggered by seemingly innocuous events, such as exposure to cold and even exercise.