Airway cooling appears to be responsible for exercise-induced bronchoconstriction as well as some wintertime asthma attacks.

Asthma is associated with airway wall remodeling, which is characterized by hyperplasia and hypertrophy of smooth muscle cells (E-Fig. 16-12), edema, inflammatory infiltration, angiogenesis, and increased deposition of connective tissue components such as type I and type III collagen. This last effect leads not only to a thickening of the subepithelial lamina reticularis (E-Fig. 16-13) but also to an expansion of the entire airway wall. Airway remodeling may begin fairly early in the course of the disease. Whether inflammation leads to remodeling or whether these processes represent two independent manifestations of the disease is unknown. Pulmonary function does seem to decline at an accelerated rate over time in patients with asthma, and airway wall remodeling may play a role in this functional loss. Over time, airway wall remodeling may lead to irreversible airflow limitation, which can worsen the disease by rendering bronchodilator drugs less effective. In this way, airway wall remodeling may make the clinical distinction between asthma and COPD difficult.

The cause of asthma is unknown, but it is likely to be a polygenic disease influenced by environmental factors. Atopy is strongly linked to asthma. Asthma is associated with an allergic-type activation of the immune system, typified by a T_H2-predominant T-cell response to inhaled antigens with consequent IgE production and allergic airway inflammation. Exposure to indoor allergens such as dust mites, cockroaches, furry pets, and fungi is a significant factor; outdoor pollution and other irritants, including cigarette smoke, are also important.

Current concepts of asthma pathogenesis include a focus on impairment of the shift from a T_H2-predominant immunity to a T_H1 immune response early in life. Paradoxically, in the developed world, the perpetuation of T_H2 immune responses and the development of inappropriate allergic responses may be related to a relative lack of exposure of the immune system to appropriate infectious antigenic stimuli in childhood, the so-called hygiene hypothesis. Farming, for example, appears to be protective against the development of asthma and allergic disease, possibly in part because of the increased exposure to microbial antigens eliciting a T_H1 response. Increased exposure to other children (as in daycare settings) and less frequent use of antibiotics may also decrease asthma risk, supporting this hypothesis. On the other hand, asthma is common in poor urban settings in which there is heavy exposure to allergic antigens from dust mites and cockroaches. The timing and roles of particular environmental exposures in utero and in early life in the pathogenesis of asthma and allergic diseases remain to be fully elucidated, and there is no current theory that completely explains asthma pathogenesis or the recent increased incidence of asthma. The interplay of other aspects of modern life, such as changes in the microbiome, with regard to asthma propensity continues to be explored.

Several genetic polymorphisms have been associated with asthma, including variations in the β-adrenergic receptor leading to diminished responsiveness to β-agonists. Identification of other genetic polymorphisms that are important in asthma is a subject of ongoing research. Although asthma is more common in male children than in female children, the prevalence of asthma changes after puberty, and it is more common in adult women than in men. These facts, along with evidence of variation in asthma symptoms during the menstrual cycle and during pregnancy, suggest possible hormonal influences on asthma pathogenesis.

Asthma can be induced by workplace exposures in persons having no previous history of asthma (occupational asthma). Certain substances, such as isocyanates (used in spray paints) and Western red cedar wood dust, are strongly provocative agents for the development of occupational asthma. Obesity has been linked to a higher incidence of asthma. The mechanisms by which obesity may influence asthma development are unclear. Certain infectious agents and other conditions can cause acute bronchospasm even in patients without the diagnosis of asthma. Examples include viral infections, gastroesophageal reflux disease (GERD), and exposure to gases or fumes. These disorders may play a role in the development or control of some cases of asthma.

Clinical Presentation

Major symptoms of asthma are wheezing, episodic dyspnea, chest tightness, and cough. The clinical manifestations vary widely, from mild intermittent symptoms to catastrophic attacks resulting in asphyxiation and death. Although wheezing is not a pathognomonic feature of asthma, in the setting of a compatible clinical picture, asthma is the most common diagnosis. Often symptoms worsen at night or during the early hours of the morning. Other associated symptoms are sputum production and chest pain or tightness. Patients may exhibit only one or a combination of symptoms, such as chronic cough only (cough-variant asthma). Wheezing may occur several minutes after exercise (exercise-induced bronchoconstriction). Physical examination typically shows evidence of wheezing, although findings may be normal in between symptomatic periods. Rhinitis or nasal polyps may be present. In the case of an acute episode of bronchospasm or an exacerbation, the clinician may find that the patient has difficulty talking, is using accessory muscles of inspiration, has pulsus paradoxus, is diaphoretic, and has mental status changes ranging from agitation to somnolence. In patients with these findings, treatment should be immediate and aggressive.

Diagnosis and Differential Diagnosis

A diagnosis of asthma requires documentation of bronchial hyperreactivity and reversible airway obstruction. The history may provide sufficient documentation because most patients complain of characteristic periodic episodes of wheezing and other symptoms that respond to use of a bronchodilator. However, spirometry is recommended to assess formally for expiratory flow limitation, and reversibility is demonstrated by repeat spirometry after bronchodilator administration. At least 12% and 200 mL improvement in FEV_1 after bronchodilator use indicates reversibility. Because asthma is episodic, airflow limitation is variable and patients may exhibit symptoms at a time when spirometry cannot be performed. Peak expiratory flow measurements can be performed at home and may be helpful in establishing evidence of variability in expiratory flow.

Depending on the circumstances, formal testing for airway hyperactivity by bronchoprovocation challenge may be necessary. A stimulant with bronchoconstrictor activity, most