

Pathogenesis: From immunology lecture

Subtypes:

Atopic Asthma

This is the most common type of asthma and is a classic example of type I IgE-mediated hypersensitivity reaction. It usually begins in childhood. A positive family history of atopy and/or asthma is common, and the onset of asthmatic attacks is often preceded by allergic rhinitis, urticaria, or eczema. Attacks may be triggered by allergens in dust, pollen, animal dander, or food, or by infections. A skin test with the offending antigen results in an immediate wheal-and-flare reaction. Atopic asthma also can be diagnosed based on serum radioallergosorbent tests (RASTs) that identify the presence of IgEs that recognize specific allergens.

Non-Atopic Asthma

Patients with nonatopic forms of asthma do not have evidence of allergen sensitization, and skin test results usually are negative. A positive family history of asthma is less common. Respiratory infections due to viruses (e.g., rhinovirus, parainfluenza virus) and inhaled air pollutants (e.g., sulfur dioxide, ozone, nitrogen dioxide) are common triggers. It is thought that virus-induced inflammation of the respiratory mucosa lowers the threshold of the subepithelial vagal receptors to irritants. Although the connections are not well understood, the ultimate humoral and cellular mediators of airway obstruction (e.g., eosinophils) are common to both atopic and nonatopic variants of asthma, so they are treated in a similar way.

Drug-Induced Asthma

Several pharmacologic agents provoke asthma, aspirin being the most striking example. Patients with aspirin sensitivity present with recurrent rhinitis, nasal polyps, urticaria, and bronchospasm. The precise pathogenesis is unknown but is likely to involve some abnormality in prostaglandin metabolism stemming from inhibition of cyclooxygenase by aspirin.

Occupational Asthma

Occupational asthma may be triggered by fumes (epoxy resins, plastics), organic and chemical dusts (wood, cotton, platinum), gases

(toluene), and other chemicals. Asthma attacks usually develop after repeated exposure to the inciting antigen(s).

Morphology

The morphologic changes in asthma have been described in individuals who die of prolonged severe attacks (status asthmaticus) and in mucosal biopsy specimens of individuals challenged with allergens. In fatal cases, the lungs are distended due to air trapping (overinflation), and there may be small areas of atelectasis. The most striking finding is occlusion of bronchi and bronchioles by thick, tenacious mucous plugs containing whorls of shed epithelium (Curschmann spirals). Numerous eosinophils and Charcot-Leyden crystals (crystalloids made up of the eosinophil protein galectin-10) also are present. Other characteristic morphologic changes in asthma, collectively called airway remodeling, include

- Thickening of airway wall
- Sub-basement membrane fibrosis
- Increased submucosal vascularity
- An increase in size of the submucosal glands and goblet cell metaplasia of the airway epithelium
- Hypertrophy and/or hyperplasia of the bronchial muscle

Clinical Features

An attack of asthma is characterized by severe dyspnea and wheezing due to bronchoconstriction and mucus plugging, which leads to trapping of air in distal airspaces and progressive hyperinflation of the lungs. In the usual case, attacks last from 1 to several hours and subside either spontaneously or with therapy. Intervals between attacks are characteristically free from overt respiratory difficulties, but persistent, subtle deficits can be detected by pulmonary function tests. Occasionally a severe paroxysm occurs that does not respond to therapy and persists for days and even weeks (*status asthmaticus*). The associated hypercapnia, acidosis, and severe hypoxia may be fatal, although in most cases the condition is more disabling than lethal.