

Table 9-1 Disorders Associated with Airflow Obstruction: The Spectrum of Chronic Obstructive Pulmonary Disease

Clinical form	Acronym (s)	Major Pathologic Changes	Smoking	Emphysema
Chronic bronchitis	Bronchitis	Mucous gland hyperplasia/hypersecretion	Major cause, as pathogen	Cough, sputum production
Bronchospasm	Bronchitis	Airways dilator and relaxing	Percent of cases reflects inheritance in individual cases	Cough, bronchospasm, later hyperinflation, cough, dyspnea
Asthma	Bronchitis	Small airway hyperplasia, eosinophilic inflammation	Major cause	Dyspnea
Emphysema	Asthma	Alveolar septa destroyed with emphysema	Major cause, as pathogen	Cough, dyspnea
Small airway disease* "Bronchiolitis"	Bronchiolitis	Inflammatory bronchiolitis	Major cause, as pathogen	

*Asthma is a chronic inflammatory disease.

Distal Acinar (Paraseptal) Emphysema (p. 719)

- Involves mostly the distal acinus
- Typically near the pleura and adjacent to fibrous or scars
- Represents the underlying lesion in spontaneous pneumothorax

Alveolar Enlargement with Fibrosis
(Irregular Emphysema) (p. 719)

Alveolar enlargement with fibrosis refers to irregular acinar enlargement and is associated with scarring. It is usually symptomatic. Other related entities are *bullous emphysema* (blebs in bullae > 1 cm) and *interstitial emphysema* (infiltration of air into lung connective tissue, mediastinum, or subcutaneous tissue).

Pathogenesis

The *protease-antiprotease hypothesis* holds that alveolar wall destruction in emphysema results from imbalances between proteolytic proteases and their inhibitors.

- Individuals with hereditary deficiency of the major protease inhibitor, α_1 -antitrypsin, inevitably develop emphysema, and it develops at a younger age if they smoke.
- Experimental pulmonary instillation of proteolytic enzymes, including streptokinase, causes emphysema.

Tobacco smoking contributes to emphysema by:

- Attracting alveolar macrophages that, in turn, recruit neutrophils into the lung.
- Enhancing neutrophil and macrophage elastase activity.
- Increasing α_1 -antitrypsin (via oxidants in tobacco smoke) for release released by activated neutrophils.

Acute particle impaction in small bronchioles leads to inflammatory cell recruitment, increased elastase, and increased α_1 -antitrypsin, resulting in the characteristic pattern of emphysema seen in smokers.

Histopathology

With diffuse disease, lungs can become voluminous and weigh the least. Microscopically, alveolar spaces are enlarged, separated by thin septa; septal capillaries are compressed and bloodless. Alveolar wall rupture can produce very large cysts (blebs and bullae).

Chronic Bronchitis (p. 722)

Chronic bronchitis is clinically defined as persistent cough and sputum production for at least 3 months in at least 2 consecutive years.

Pathogenesis

Chronic irritation of the airways by inhaled substances—especially tobacco smoke—is the dominant pathogenic mechanism. The irritants cause:

- Mucus hypersecretion with mucous gland hypertrophy
- Ciliated-cell metaplasia to bronchiolar epithelium
- Bronchiolitis

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