Obstructive Pulmonary Disease

Intended Learning Objectives (ILOs)

- Define bronchial asthma and describe its pathophysiology, morphology and pathological consequences.
- Discuss chronic bronchitis.
- Define emphysema and enumerate its types; distinguish between its two main types with particular reference to the underlying pathogenesis of each.
- Define bronchiectasis, outline its main causes, pathogenesis, morphological changes and complications.

Definition of Obstructive Pulmonary Disease

Chronic, noninfectious, diffuse pulmonary disease characterized by increased resistance to airflow, at any level from trachea to alveoli.

General consideration:

- The relevant entities: emphysema, chronic bronchitis, asthma, and bronchiectasis

- Emphysema and chronic bronchitis are typically grouped together as *chronic obstructive pulmonary disease* (COPD) as many patients have overlapping features and smoking is often a common denominator.

I- Bronchial asthma

Definition: Chronic inflammatory relapsing disorder characterized by hyperreactive airways when triggered by certain stimuli, which undergo episodic bronchospasm leading to dyspnea and chest wheeze.

Types of asthma:

a. Atopic (Extrinsic or Immune) asthma

- is mediated by a **type I hypersensitivity response** involving IgE bound to mast cells.
- Disease begins in **childhood,** usually in patients with a **family history of allergy**.

b. Non-Atopic (Intrinsic or Non-immune) asthma

- includes asthma associated with **chronic bronchitis,** as well as **other asthma variants** such as **exercise- or cold-induced asthma.** It usually begins in **adult life** and is **not associated with a history of allergy**.

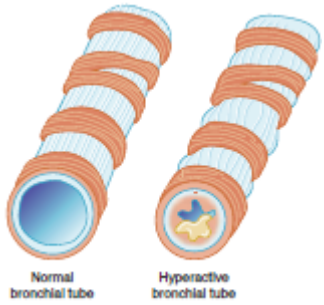
c- Drug-induced asthma affects about 10% of adults with a diagnosis of asthma. Aspirin is a key example of a precipitating drug.

d- Occupational asthma is caused by workplace triggers including fumes and dusts.

Clinical presentation:

- Classic attacks last up to several hours
- **Symptoms:** There is marked episodic **dyspnea** and **wheezing expiration** caused by narrowing of the airways.
- In severe acute episodes (status asthmaticus), symptoms persist for days to weeks, and significant airflow obstruction can cause cyanosis and even death.

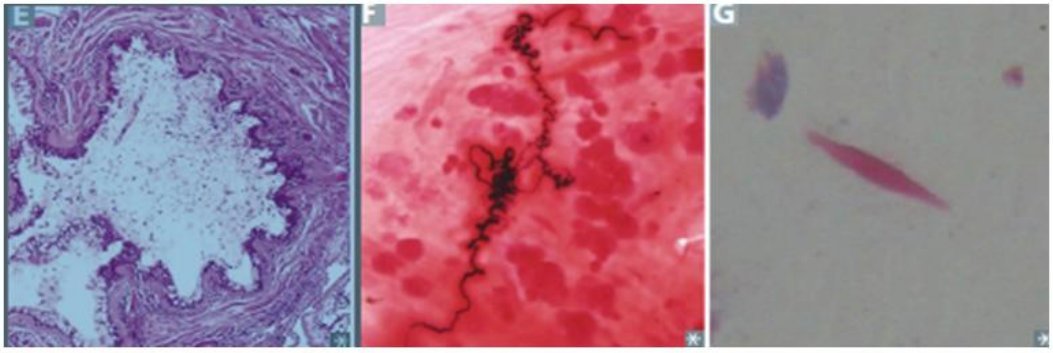
Pathology:



Gross: Lungs are overinflated with patchy atelectasis and mucus plugging of airways.

Microscopically

- Bronchial smooth muscle hypertrophy
- Hyperplasia of goblet cells,
- Thickening and hyalinization of basement membranes,
- Oedema and inflammatory infiltrate including **numerous eosinophils**, and
- Intrabronchial mucous plugs containing whorl-like accumulations of epithelial cells (Curschmann spirals) and crystalloids of eosinophil derived proteins (Charcot-Leyden crystals).



Mucous plugging | **Curschmann spirals** | **Charcot-Leyden crystals (eosinophilic, hexagonal, double-pointed crystals formed from breakdown of eosinophils in sputum)**

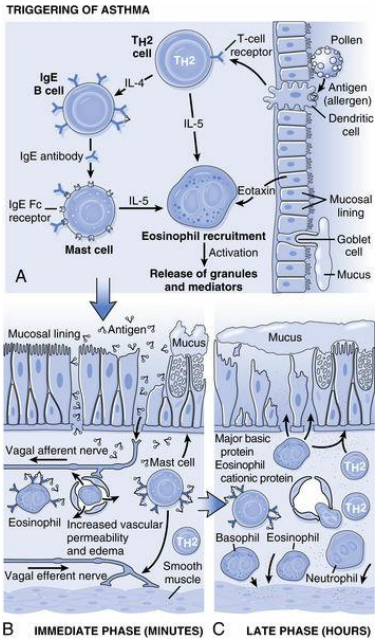
Pathogenesis of Asthma:

Genetic susceptibility interact with environmental factors to produce asthma

A. Inhaled allergens (antigen) induce **IgE production and eosinophil recruitment.**
B. On re-exposure to antigen (Ag), the immediate reaction is triggered by Ag **binding of IgE attached to mast cells (Acute phase)**
C. Mast cells then release preformed mediators (acute phase mediators) that directly and via neuronal reflexes induce **bronchospasm, increased vascular permeability, mucus production, and recruitment of leukocytes.**
D. Leukocytes recruited to the site of reaction (neutrophils, eosinophils, and basophils; lymphocytes and monocytes) release **additional mediators that initiate the late phase of asthma**. Late phase characterized by persistent bronchospasm and edema, leukocytic infiltration, and epithelial damage and loss.

Unlike COPD, the process in **asthma is generally reversible**, so between attacks, most asthmatics have relatively normal physiology.

Repeated bouts cause **airway remodeling** with bronchial smooth muscle and mucus gland hypertrophy and hyperplasia, increased vascularity, and increased deposition of subepithelial collagen.



Pathogenesis of asthma (Robbins and Cotran pathologic basis of diseases)

Complications of asthma:

- **Superimposed infection**
- **Chronic bronchitis,** and **pulmonary emphysema.**
- Bronchial asthma may lead to **status asthmaticus,** a prolonged bout of bronchial asthma that can last form days and that responds poorly to therapy. **Death** can result.

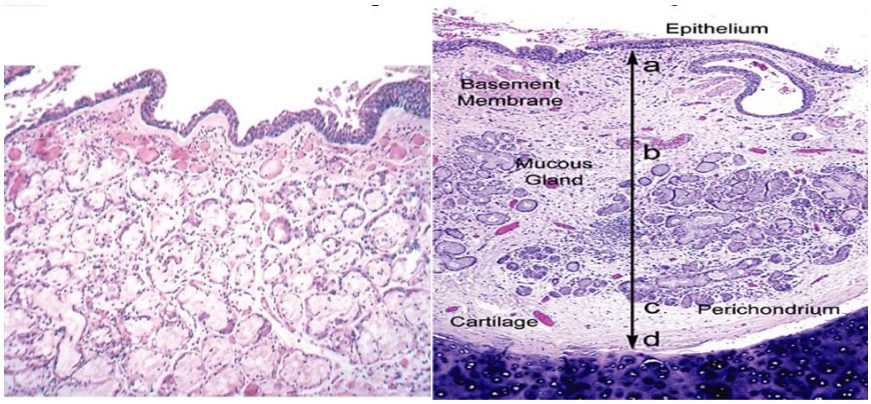
II- Chronic bronchitis

Clinical definition:
A productive cough that occurs during at least three consecutive months over at least two consecutive years.

Pathogenesis:
Chronic irritation of the airways by inhaled substances.
Chronic bronchitis is clearly linked to **cigarette smoking**
and is **also** associated with air pollution, infection, and genetic factors.

Pathology:
Typical histologic characteristics include:

- **Marked hyperplasia of mucus-secreting submucosal glands** → hypersecretion of mucus**.**
- **Reid index increased** (Reid index equals the submucosal gland thickness divided by the bronchial wall thickness between the pseudostratified columnar epithelium and the perichondrium; normal ratio is <0.4).
- Goblet cell metaplasia in bronchiolar epithelium contributes to the mucus production and small airway obstruction.
- Inflammation , both acute and chronic
- Fibrosis in long standing inflammation.
- Squmous metaplasia and dysplasia of bronchiolar epithelium may occur.



Clinical presentation:

- Cough and sputum production (defining symptoms).
- Dyspnea on exertion
- Cyanosis (hypoxemia), C02 retention (hypercapnia) that may lead to secondary polycythemia.

Complications:

- **Recurrent infections** (may cause death)
- Secondary **pulmonary hypertension** leading to **right heart failure (cor pulmonale**)
- **Lung cancer**

III- Emphysema

Definition:

Emphysema is abnormal persistent dilatation of air spaces distal to terminal bronchioles, often associated with destruction of elastic tissue in their walls.
- The result is loss of elastic recoil, **increased lung compliance,** dilation of the terminal air spaces, and air trapping.
- The disease is strongly associated with **cigarette smoking.**

Pathogenesis:

Loss of alveolar elastic tissue reduces radial traction and causes respiratory bronchiole collapse during expiration, resulting in functional obstruction.

1- Protease / antiprotease imbalance

Emphysema may result from the action of proteolytic enzymes (e.g. elastase) on the alveolar wall. **Elastase** can induce destruction of elastin unless neutralized by the anti-elastase activities of ***alpha-1*** **antitrypsin**.

a. Cigarette smoking

- attracts neutrophils and macrophages, which are sources of elastase.
- It also inactivates *alpha-1* antitrypsin.

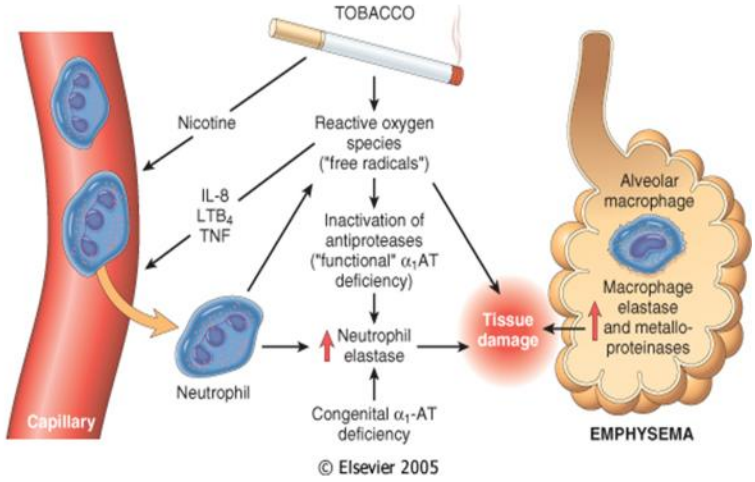
b. Hereditary

- **Alpha-1 antitrypsin deficiency** accounts for a small subgroup of cases of **panacinar emphysema.**

2- Inflammatory mediators and leukocytes, are released by resident epithelial cells and macrophages; these recruit inflammatory cells, amplify the inflammatory process, and induce structural changes.

3- Oxidative stress (from tobacco smoke, alveolar damage, and inflammatory cells) also drives tissue damage and inflammation.

4- Infection: Although infection does not initiate tissue destruction, bacterial and/or viral infections can exacerbate the associated inflammation.



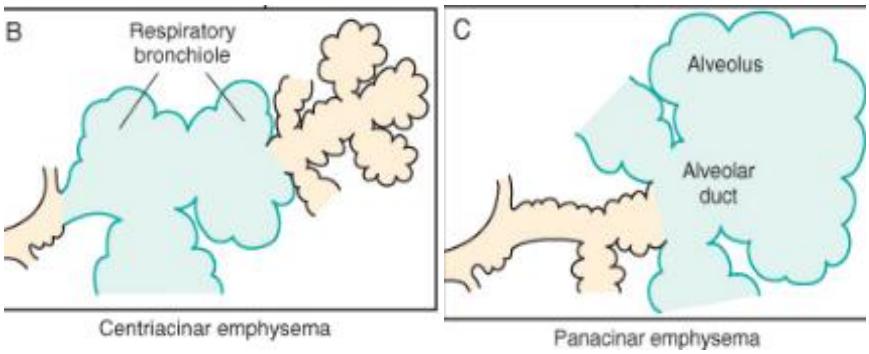
Types of emphysema:

a. Centriacinar emphysema.

- Dilation of the respiratory bronchioles (proximal portion of acinus)
- most often localized to the upper part of the pulmonary lobes.
- It is strongly associated with cigarette smoking.

b. Panacinar emphysema

- Dilation of the entire acinus, including the alveoli, alveolar ducts and respiratory bronchioles.
- most often distributed uniformly throughout the lung.
- It is associated with loss of elasticity and sometimes with genetically determined **deficiency of *alpha 1* antitrypsin** (protease inhibitor).



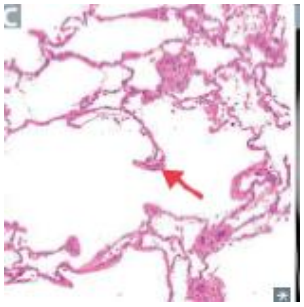
Centriacinar (Centrilobular)	Panacinar (Panlobular)
Proximal respiratory bronchioles involved, distal alveoli spared	Entire acinus involved
Most common type (95%)	
Associated with smoking, air pollution	α-1-antitrypsin deficiency
Distribution: worse in apical segments of upper lobes	Distribution: entire lung; worse in bases of lower lobes

c. Distal acinar emphysema (Para-septal emphysema)
- Dilation involves mainly the distal part of the acinus, including the alveoli and, to a lesser extent, the alveolar ducts. It tends to localize subjacent to the pleura and interlobar septa.
- It is associated occasionally with large subpleural bullae, or blebs, which can predispose to pneumothorax.

d. Irregular emphysema
- Irregular involvement of the acinus with scarring within the walls of enlarged air spaces.
- Usually a complication of various inflammatory processes (post inflammatory scarring).

Pathology:

- **On gross examination**, the lungs are overinflated and enlarged, and have enlarged, grossly visible air spaces, surface indentation marks of ribs and surface bullae
- **Microscopically**
  - Alveolar spaces are enlarged, dilated and separated by thin septa;
  - Septal capillaries are compressed and bloodless.
  - Alveolar wall rupture can produce very large airspaces (blebs and bullae) with alveolar spurs.
  - Elastic tissue decrease in the alveolar walls.



Clinical presentation:
- Progressive dyspnea, pursing of lips and use of accessory respiratory muscles to breathe,
- Obvious prolonged expiration; **spirometry is a key diagnostic tool**.
- Classically patients overventilate to compensate for loss of parenchyma and are typically well oxygenated at rest, so-called pink puffers.
- Weight loss

- Chest X-Ray: increased anteroposterior diameter of the chest (Barrel shaped chest), flattened diaphragm, and increased lung field lucency.
- Emphysema is often complicated by, or coexistent with, **chronic bronchitis.**
- Hypoxia and cyanosis.

Complications of emphysema:

- Development of pulmonary hypertension and right sided heart failure (cor pulmonale): poor prognosis
- Respiratory acidosis
- Massive pneumothorax : due to rupture of surface blebs
- Interstitial emphysema, in which air escapes into the interstitial tissues of the chest from a tear in the airways.

IV- Bronchiectasis

Definition: **permanent abnormal bronchial dilation** caused by chronic infection, with inflammation and necrosis of the bronchial wall.

Predisposing factors:

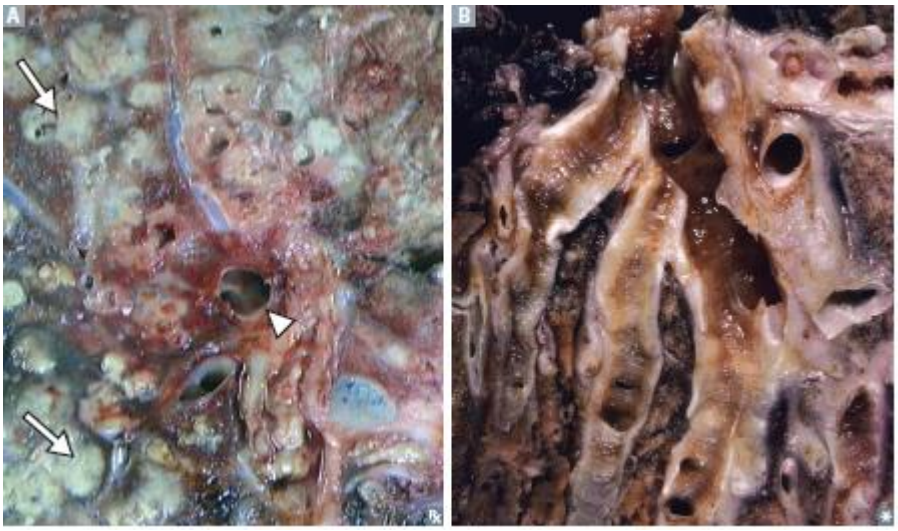
- **Congenital or hereditary conditions:**
  - **Kartagener syndrome:** It is an autosomal recessive condition caused by immotile cilia (**primary ciliary dyskinesia** i.e. a defect in the motility of respiratory, auditory, and sperm cilia).
    It is characterized clinically by bronchiectasis, chronic sinusitis, and situs inversus (a congenital condition where the major visceral organs are anatomically reversed compared with their normal anatomical positions), sometimes with hearing loss and male sterility.
  - C**ystic fibrosis** develop bronchiectasis due to the production of thick secretions that are difficult to clear as well as chronic infection with multiple pathogens.
  - Pulmonary sequestration
- **Bronchial obstruction** by foreign body, mucus or by tumor.
- **Chronic sinusitis** accompanied by postnasal drip.
- **Necrotizing pneumonia**

-Other chronic inflammatory states (e.g., rheumatoid arthritis, chronic graft-versus-host disease, or allergic bronchopulmonary aspergillosis)

-Idiopathic bronchiectasis is diagnosed when the other causes are excluded; it accounts for 25% to 50% of cases.

Pathology:

Bronchiectasis most often involves the lower lobes of both lungs.
On gross examination, bronchiectasis shows dilated bronchi and bronchioles extending out to the pleura.
Marked dilation of the airways in one of three patterns: cylindrical, varicose, or saccular. Increased secretions are also seen.
The arteries also enlarge and proliferate. New anastomoses may form, leading to hemoptysis.



Bronchiectasis: A) Fibrotic lung parenchyma with numerous areas of pneumonia (arrows) and thick inspissated secretions in areas of bronchiectasis (arrowhead) in a patient with cystic fibrosis. **B)** Permanently dilated airways.

Clinical presentation:

- Production of **copious purulent sputum**
- Hemoptysis
- Recurrent pulmonary infection that may lead to **lung abscess.**

Disorder	Pathologic Findings
Bronchial asthma	Bronchial smooth muscle hypertrophy Hyperplasia of bronchial submucosal glands and goblet cells Airways plugged by viscid mucus containing Curschmann spirals, eosinophils, and Charcot-Leyden crystals
Chronic bronchitis	Hyperplasia of bronchial submucosal glands, leading to increased Reid index, ratio of the thickness of the gland layer to that of the bronchial wall
Pulmonary emphysema	Abnormal dilation of air spaces with destruction of alveolar walls Reduced lung elasticity
Bronchiectasis	Abnormally dilated bronchi filled with mucus and neutrophils Inflammation and necrosis of bronchial walls and alveolar fibrosis