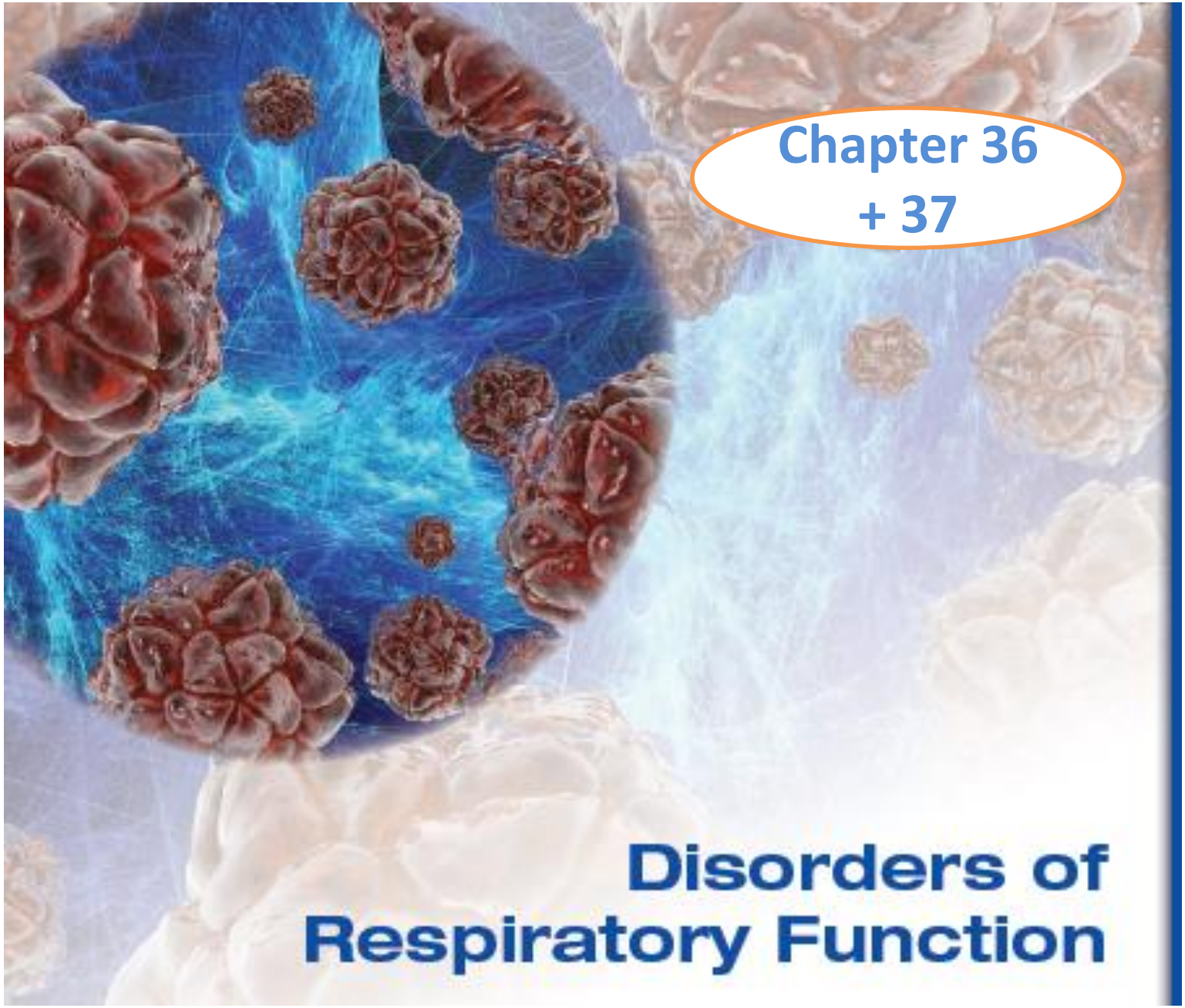

Chapter 36
+ 37
Disorders of
Respiratory Function

Respiratory diseases

1. *Pulmonary infections:*

- Respiratory tract infections can occur in the upper or lower respiratory tract, or both.
- Upper infections of respiratory tract include common cold and influenza.
- Lower infections of respiratory tract include pneumonia and tuberculosis

2. *Obstructive pulmonary* disorders:

- There are obstructions in the airflow into and out of the lungs
- They include asthma and chronic obstructive pulmonary diseases (such as bronchitis and emphysema).

3. *Restrictive disorders:*

- They limit the normal expansion of the lungs
- Of these disorders is pneumothorax.

4. *Cancers*

General Manifestations of Respiratory Diseases

1. **Hypoxia**: decreased level of oxygen in the tissues.
2. **Hypoxemia**: decreased levels of oxygen in the arterial blood.
3. **Hypercapnia**: increased levels of CO_2 in the blood.
4. **Hypocapnia**: decreased levels of CO_2 in the blood.
5. **Dyspnea**: difficulty breathing
6. **Tachypnea**: rapid and shallow (i.e., shortness) breathing.
7. **Cyanosis**: bluish discoloration of skin and mucous membranes due to poor oxygenation of the blood.
8. **Hemoptysis**: blood in the sputum.

Defenses Vs. Predisposing Factors

- Defenses of the Respiratory System
  - Mucus-covered surfaces — Trap particles and organisms
  - Cell surface – IgA, lysosomes
  - Ciliated epithelium — Clears trapped particles and organisms from airway passages
  - Cough reflex and epiglottis — Prevents aspiration of particles and irritants into lower airways
  - Pulmonary macrophages — Phagocytize foreign particles and organisms in the alveolar spaces
- Predisposing factors
  - loss or decrease of cough reflex leading to aspiration .
  - Injury to mucociliary apparatus (smoking cigarettes)
  - Decreased function of alveolar macrophages (AIDS)
  - Congestion, edema (heart diseases)
  - Accumulation of secretions (allergic reactions)

Pneumonia

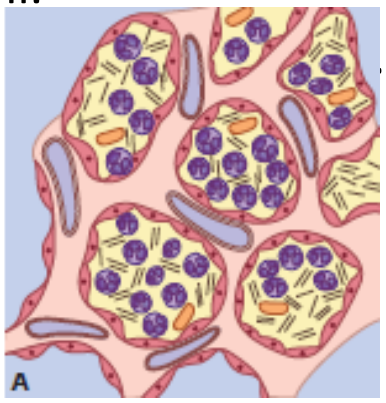
- **Pneumonia**: is a condition that involves inflammation of lower lung structures such as the alveoli or interstitial spaces and bronchioles. It may be caused by bacteria, viruses or parasites such as *pneumocystis carinii* (infection of the lower respiratory track results in inflammation of that part).
- Pneumonias can be classified according to the type of agent causing the infection into:

1. Typical pneumonia.
2. Atypical pneumonia

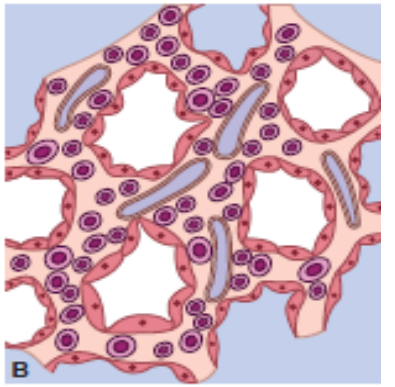
Typical pneumonia

- Usually **bacterial** in origin.
- Organisms replicate in the **spaces of the alveoli**.
- *Manifestations:*

1. Inflammation and fluid accumulation are seen in the alveoli.
2. White cell infiltration and **exudation** that can be seen on c
3. High fever, chest pain, chills, and malaise.
4. Purulent sputum is present.
5. Some degree of hypoxemia is present.



Atypical pneumonia



- Usually **viral** in origin.
- Organisms replicate in the spaces **around the alveoli**.
- *Manifestations*

1. Milder symptoms than typical pneumonia.
2. Lack of white cell infiltration in alveoli (and subsequent formation of purulent sputum).
3. Lack of fluid accumulation in the alveoli (alveolar exudate).
4. Not usually evident on radiographs.
5. May make the patient susceptible to bacterial pneumonia.

Treatment of pneumonia

- Antibiotics if bacterial in origin. The health-care provider should consider the possibility that antibiotic-resistant organisms are present.
- Oxygen therapy for hypoxemia.
- A vaccine for *pneumococcal* pneumonia is currently available and highly effective. This vaccine should be **considered in high-risk individuals**.

Individuals most at risk for pneumonia

1. Elderly.
2. Those with viral infection.
3. Chronically ill.
4. AIDS or immunosuppressed patients.
5. **SMOKERS**
6. Patients with chronic respiratory disease.

Tuberculosis (TB)

- Tuberculosis is an infectious disease caused by the organism *Mycobacterium tuberculosis,* which is primarily transmitted via the airborne route (coughing, sneezing, and talking all create respiratory droplets. These droplets evaporate and leave organisms (droplet nuclei), which remain suspended in the air and are circulated by air currents)
- There are two types of TB:

1. **Primary tuberculosis**: is a form of disease that develops in a previously unexposed and therefore unsensitised person.
2. **Secondary tuberculosis**: is the pattern of disease that arises in previously sensitized or infected host.

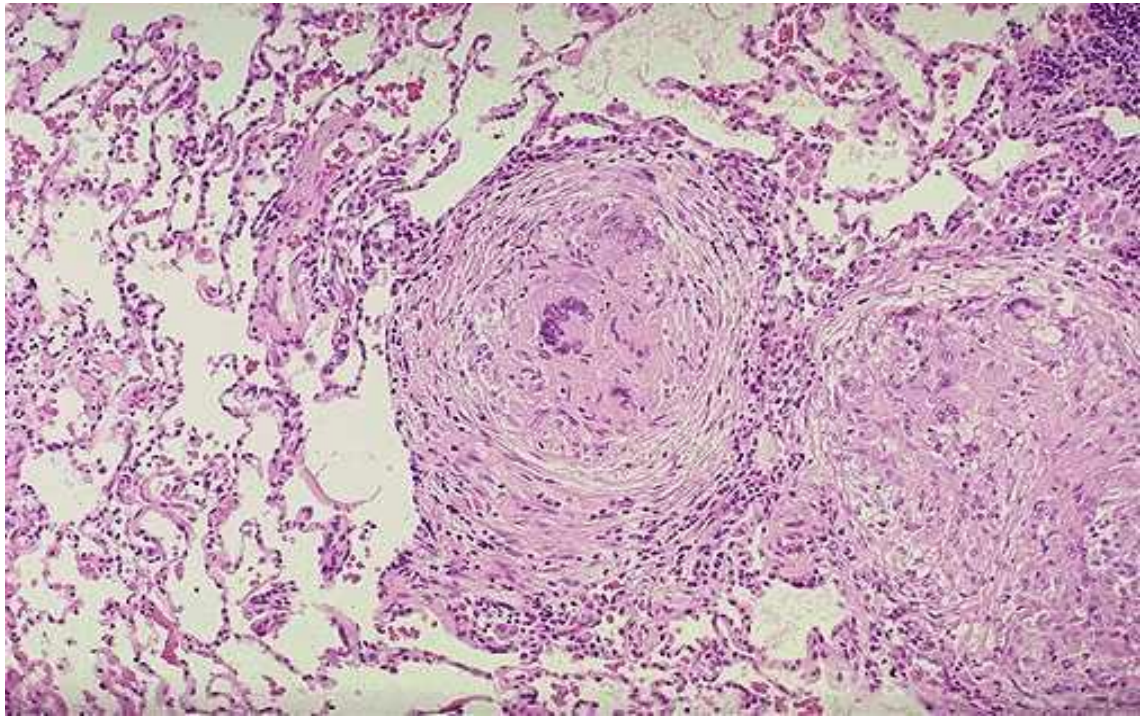
Primary tuberculosis

- Soon after entering the lung and **reaching alveoli**, the bacilli are **phagocytosed by alveolar macrophages but resist killing**. **Although the macrophages that first ingest *M. tuberculosis* *cannot kill the organisms, they initiate a cell-mediated*** **immune response that eventually contains the infection**.
- The cell-mediated immune response results in the development of a granulomatous lesion (gray-white), called **a *Ghon focus* (primary lesion/local infection)*, that contains the tubercle bacilli, modified macrophages,*** **and other immune cells.** It is usually located in the **subpleural area** of the upper segments of the lower lobes or in the lower segments of the upper lobe.
- **The lytic enzymes released from macropahges also damage lung tissue**. The destructive features of the disease, **such as caseating necrosis and cavitation.**

- During the same period, **tubercle bacilli, free or inside macrophages, drain along the lymph channels to the lymph nodes of the affected lung**, and there evoke **the formation of caseous granulomas. The combination of the primary lung lesion and lymph node granulomas is called a *Ghon complex.*** *The Ghon complex eventually* undergoes scarring, and **calcification, the latter visible radiographically**.
- People with **latent tuberculosis** do **NOT** have **active disease and cannot transmit the organism to others**.

Tuberculosis Granuloma

1. Rounded tight collection of chronic inflammatory cells.
2. Central Caseous necrosis (Necrosis of infected lung tissues may result in a cheesy appearance to the tissue due to liquefaction of the necrotic lesions).
3. Active macrophages – epithelioid cells.
4. Langhans giant cells – joined epithelioid cells.
5. Outer layer of lymphocytes & fibroblasts.



Manifestations of primary tuberculosis

1. Productive and prolonged cough with *hemoptysis.*
2. Chest pain.
3. Chill with fever and night sweats.
4. Anorexia with subsequent weight loss.

Secondary tuberculosis

- It is active infection in a **previously sensitized** individual (previous exposure to the bacteria).
- It is either the result of **reactivation of dormant bacilli** from primary infection when host resistance is weakened or following **exogenous re-infection.**
- It is characterized by a focus of infection and subsequent granuloma formation usually in **the apex of the lung**.
- Cavitation is characteristic.

Diagnosis of TB

1. Mantoux test– intradermal test for reaction against the tuberculin purified protein derivative standard (PPDS). The reaction is read by measuring the diameter of induration (localised swelling) across the forearm in millimeters.
2. Acid-fast staining of sputum cultures to visualise M. tuberculosis
3. Chest radiograph to identify Ghon's complex.

TB treatments

1. Administrating antitubercular agents (Isoniazid, Rifampicin and Ethambutol). Use more than one of these drugs to overcome the drug resistance.
2. Determining the factors that affect immune function such as proper nutrition
3. Management of other diseases are also essential for successful treatment of tuberculosis.

II. Obstructive respiratory disorders

1. *Chronic Obstructive Pulmonary Diseases (COPD)*

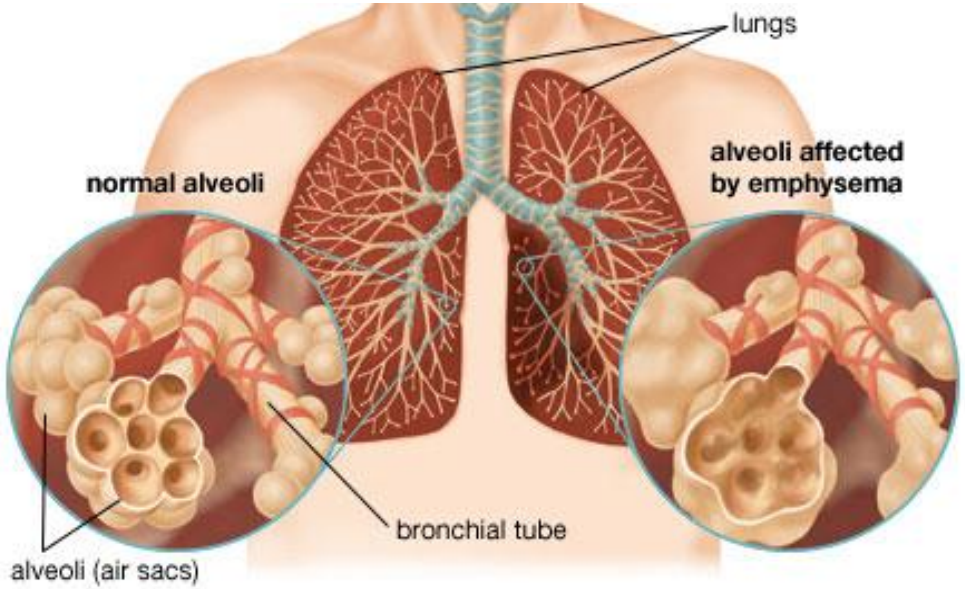
- It is a chronic inflammatory lung disease that causes obstructed airflow in/out the lungs. They are characterized by increased resistance to airflow because of chronic or recurring expiratory obstruction.
- They are characterized by decrease of forced expiratory volume 1 (FEV1).
- They include **(a) pulmonary emphysema** and **(b) chronic bronchitis**.

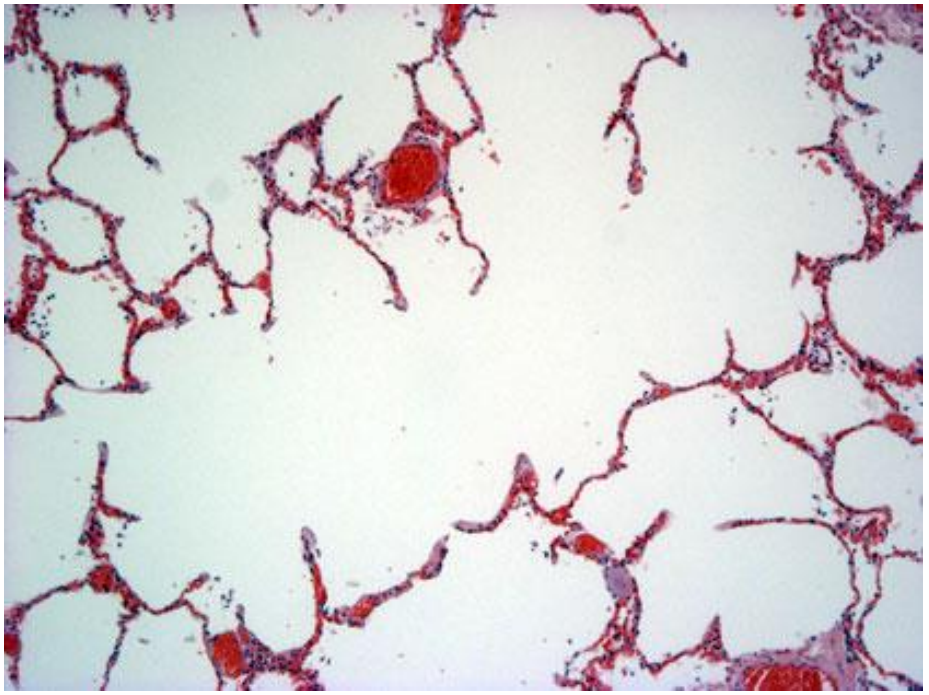
(a) Emphysema

- It is characterized by abnormal enlargement of alveolar spaces with **destruction of their walls and capillary beds as well as loss of lung elasticity**.
- **Pathogenesis:**

➢ Destruction of alveolar walls by **elastase** either due to hereditary **deficiency of anti-trypsin** (which functions as a protective enzyme to the lungs against elastase's actions involved in the damage of healthy lung tissues) or due to **smoking.**

Emphysema





Manifestations of emphysema

1. Dyspnea that may be severe.
2. Dry or no cough.
3. Cyanosis rare.
4. Infrequent infections.

Treatment of emphysema

1. Bronchodilator Medications.
2. Steroids.
3. Oxygen Therapy.
4. Protein Therapy.

Chronic Obstructive Pulmonary Diseases (COPD)

(b) Chronic bronchitis

- Chronic bronchitis is a chronic obstructive pulmonary disease (COPD) that is most frequently associated with **cigarette smoking** (approximately 90% of cases). It may also be caused by prolonged exposure to inhaled particulates such as coal dust or other **pollutants**.

- **Pathogenicity**

- Submucosal hypertrophy
- Excess mucus production in the lower respiratory tract.
- Impaired function of the ciliated epithelium
- prevention the clearing of debris and organisms
- repeated bouts of respiratory infection

Manifestations of chronic bronchitis

1. Productive, chronic cough.
2. Production of purulent sputum.
3. Frequent respiratory infections.
4. Dyspnea.
5. Hypoxia, cyanosis.
6. Fluid accumulation in later stages (pulmonary edema).

Treatment of chronic bronchitis

1. **Cessation** of smoking or exposure to irritants.
2. **Bronchodilators** to open **airway passages.**
3. **Expectorants** to loosen mucus.
4. **Anti-inflammatories** to relieve airway inflammation and reduce mucus secretion.
5. **Prophylactic antibiotics** for respiratory infections.
6. **Oxygen therapy**.

II. Obstructive respiratory disorders

2. Bronchial Asthma

- Asthma is a condition characterised by reversible **bronchospasm**, **non-specific bronchial hyperreactivity** and **chronic inflammation of airway passages**.
- Exposure to certain "triggers" can induce marked **bronchospasm** and **airway inflammation** in susceptible patients. They appear to produce **large amounts of the antibody IgE** that attach to the *mast cells* present in many tissues. For example, exposure to a trigger such as *pollen* (see next slide) will result in the allergen-binding mast cell-bound IgE, which in turn causes the release of inflammatory mediators such as *Histamine, Leukotrienes a*nd *Eosinophilic Chemotactic Factor.*
- The response of a patient with asthma to these triggers can be divided into an "early phase" and a "late phase."

Some Potential Asthma Triggers

1. Allergens — Pollen, pet dander, fungi and dust mites (العث)
2. Cold air.
3. Pollutants.
4. Cigarette smoke.
5. Exercise.
6. Respiratory tract infections.

Early phase of asthma

- The primary or initial-phase response is mediated by acute mast cell degranulation and the release of preformed and/or enzymatically activated mediators. These mediators include histamine, acetylcholine, chemotactic mediators, and neutral proteases that lead to generation of kinins (e.g., bradykinin).
- These mediators produce vasodilation and increased in vascular permeability, and causes bronchial constriction, resulting in:
  - ✓ Marked constriction of bronchial airways rather than inflammation.
  - ✓ Edema of the airways.
  - ✓ Production of excess mucus.

Late phase of asthma

- The secondary or late phase of the type I hypersensitivity response **occurs 2 to 8 hours after resolution of the initial phase** and can last for several days. In some cases, the late phase may be significantly prolonged or only partially resolved as in the case of uncontrolled bronchial asthma.

- **It results from** the action of **lipid mediators and cytokines** released from immune cells. **The lipid mediators,** which are **derived from phospholipids found in mast cell** membranes, are broken down to form arachidonic acid during the process of mast cell degranulation. Arachidonic acid is then utilised in the synthesis of **leukotrienes and prostaglandins, which produce end-organ effects similar to histamine and acetylcholine**, **except that they have a longer onset and prolonged duration of action.** Mast cells also produce cytokines that promote migration of eosinophils and leukocytes to the site of allergen exposure, contributing to late-phase responses, which include:

✓ Epithelial injury and edema

✓ Changes in mucociliary function

✓ Reduced clearance of respiratory tract secretions

✓ Increased airway responsiveness

- **Manifestations of asthma:**

1. Coughing, wheezing.
2. Dyspnea.
3. Tachypnea.
4. Increased respiratory rate.
5. Excess mucus production.
6. Barrel chest (a rounded, bulging chest that resemble the shape of a barrel). It occurs due to trapping of air in the lungs, so the rib cage stays overinflated with air, making the breath less efficient.
7. Significant anxiety.

- **Complications of asthma:**

1. *Status asthmaticus:* is a life-threatening condition of prolonged bronchospasm that is often not responsive to drug therapy.
2. *Pneumothorax* i.e., increasing the lung pressure which results from the extreme difficulty in expiration during a prolonged asthma attack. Marked hypoxemia and acidosis might also occur and can result in overall respiratory failure.

Clinical Classification of Asthma

- **Mild** *intermittent* — Attacks occur 2 times per week or less.
- **Mild** *persistent* — Attacks occur more than 2 times per week.
- **Moderate** *persistent* — Attacks occur daily or almost daily and are severe enough to affect activity.
- **Severe** *persistent* — Attacks are very frequent and persist for a long period of time; attacks severely limit activity.

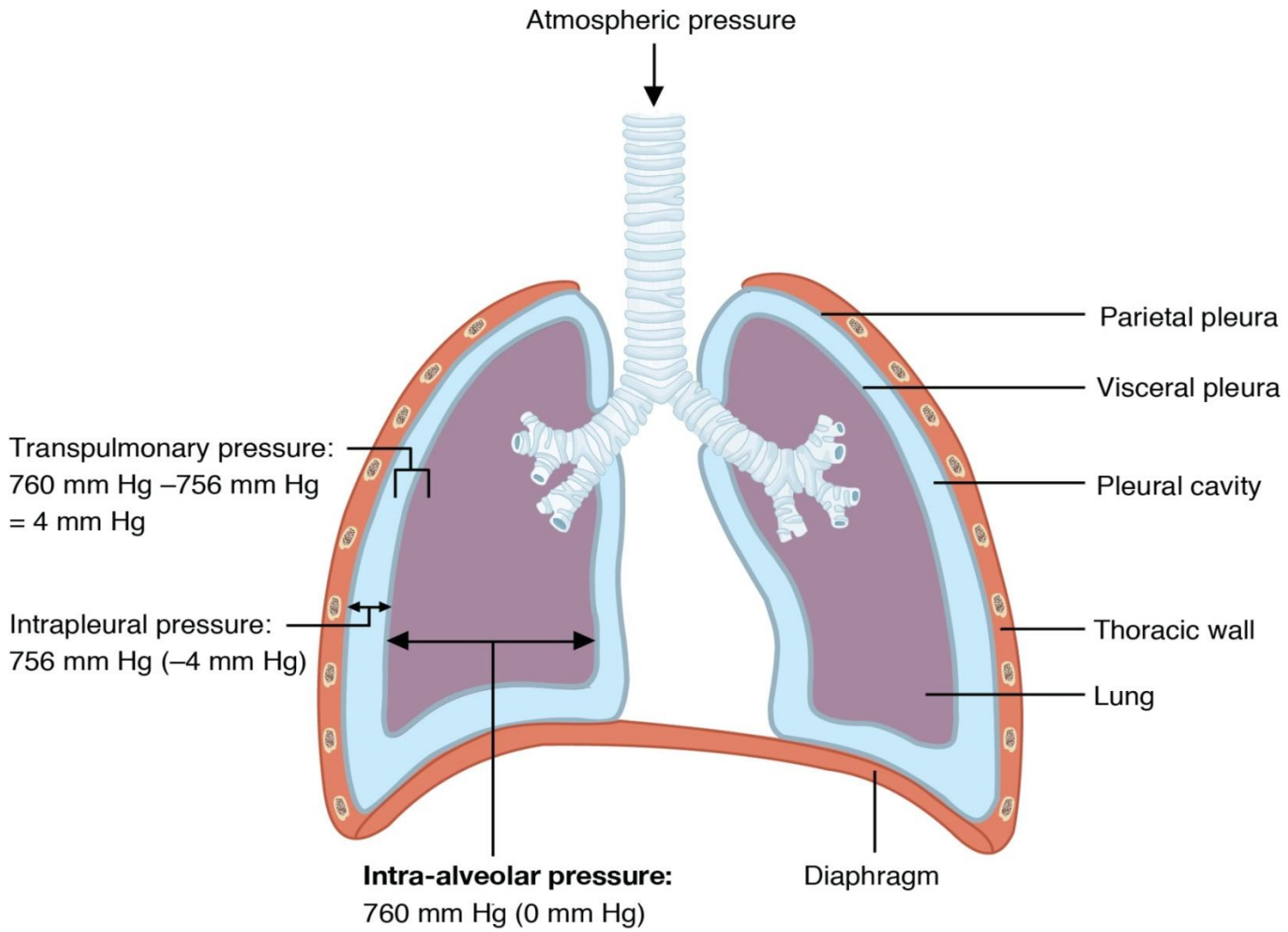
Treatment of Asthma

1. *Avoidance of triggers and allergens. Improved ventilation of the living spaces*.
2. *Bronchodilators* (examples: **albuterol**, which is a short acting β-*adrenergic* receptor activators).
3. *Xanthine drugs* (example: **theophylline**) — Cause bronchodilation but may also inhibit the late phase of asthma.
4. *Anti-inflammatory drugs* (example: **corticosteroids**) — Used orally or by inhalation to blunt the inflammatory response of asthma.
5. ***Cromolyn sodium*** — Anti-inflammatory agent that blocks both the early and late phase of asthma.
6. *Leukotriene modifiers* (example: **Zafirlukast**) — New class of agents that blocks the synthesis of the key inflammatory mediators, **leukotrienes**.

Restrictive pulmonary disorders

- *Pneumothorax*

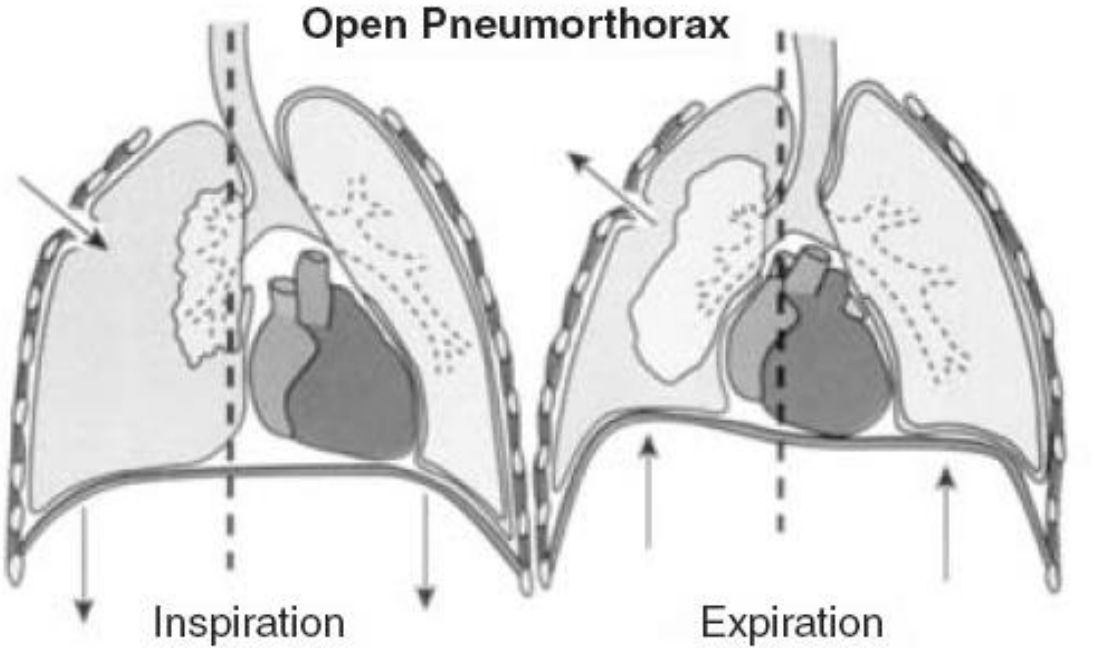
- Is an abnormal collection of air in the pleural space between the lung and the chest wall.
- In order for normal lung expansion to occur, there must be a negative pressure within the pleural cavity with respect to atmospheric pressure outside the pleural cavity.
- When air enters the pleural cavity the negative pressure is lost (i.e., equal or exceed the atmospheric pressure) and the lungs consequently collapse.
- Because each lung sits in a separate pleural cavity, pneumothorax of one plural cavity **will not** cause collapse of the other lung.


Atmospheric pressure
Parietal pleura
Visceral pleura
Transpulmonary pressure:
760 mm Hg –756 mm Hg
= 4 mm Hg
Pleural cavity
Intrapleural pressure:
756 mm Hg (–4 mm Hg)
Thoracic wall
Lung
Intra-alveolar pressure:
760 mm Hg (0 mm Hg)
Diaphragm

Types of pneumothorax

1) Open or communicating pneumothorax

- Usually involves a traumatic chest wound.
- Air enters the pleural cavity from the atmosphere.
- The lung collapses due to equilibration of pressure within the pleural cavity with atmospheric pressure.



2) **Closed or spontaneous pneumothorax**

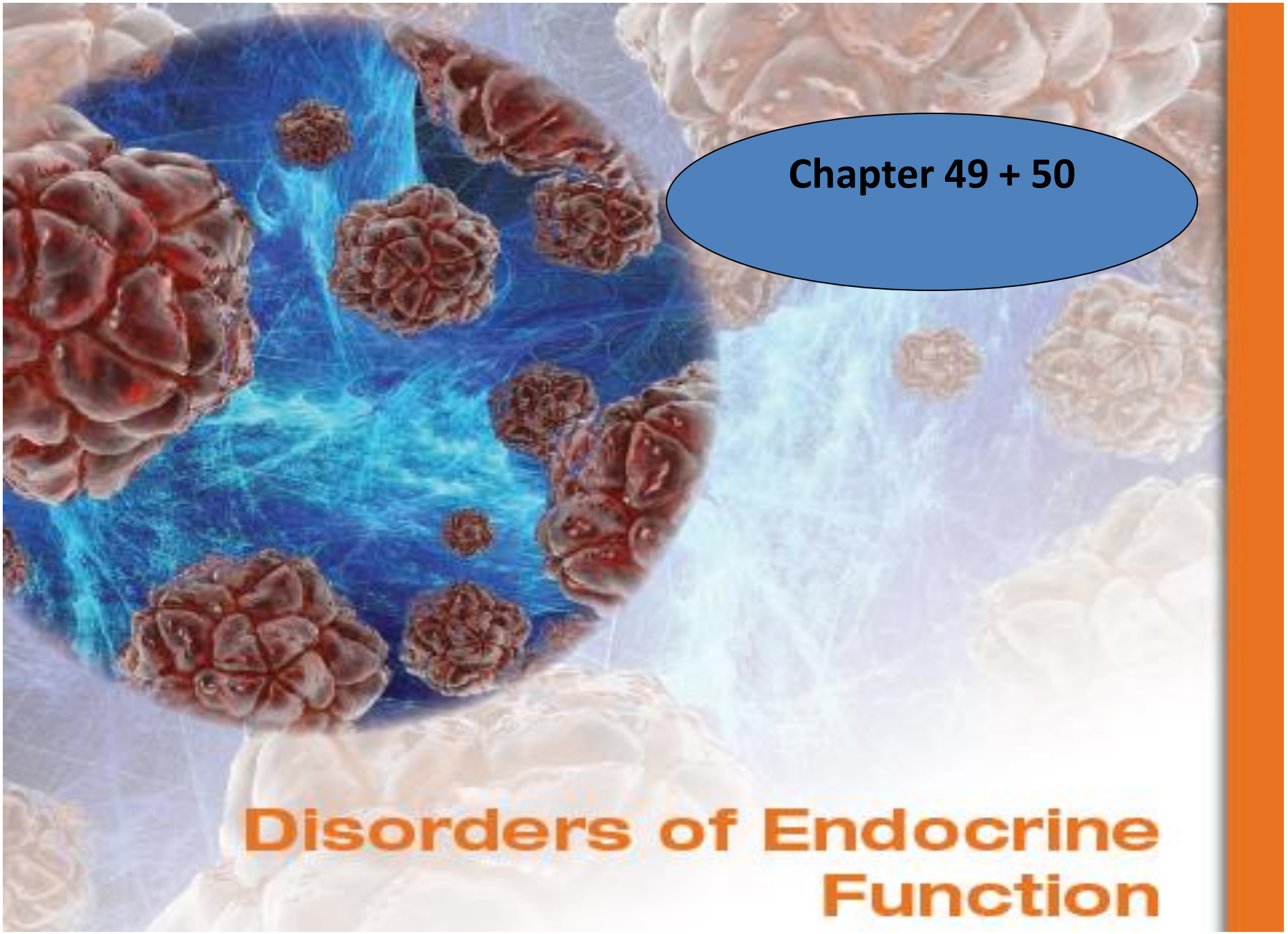
- Occurs when air “leaks” from the lungs into the pleural cavity.
- May be caused by lung cancer, rupture, pulmonary disease.
- The increased plural pressure prevents lung expansion during inspiration and the lung remains collapsed.

Manifestations of pneumothorax

1. Tachypnea.
2. Dyspnea.
3. Chest pain.
4. Possible compression of thoracic blood vessels and heart, especially with tension pneumothorax.

Treatment of pneumothorax

1. Removal of air from the pleural cavity with a needle or chest tube.
2. Repair of trauma and closure of opening into pleural cavity.


Chapter 49 + 50
Disorders of Endocrine Function