

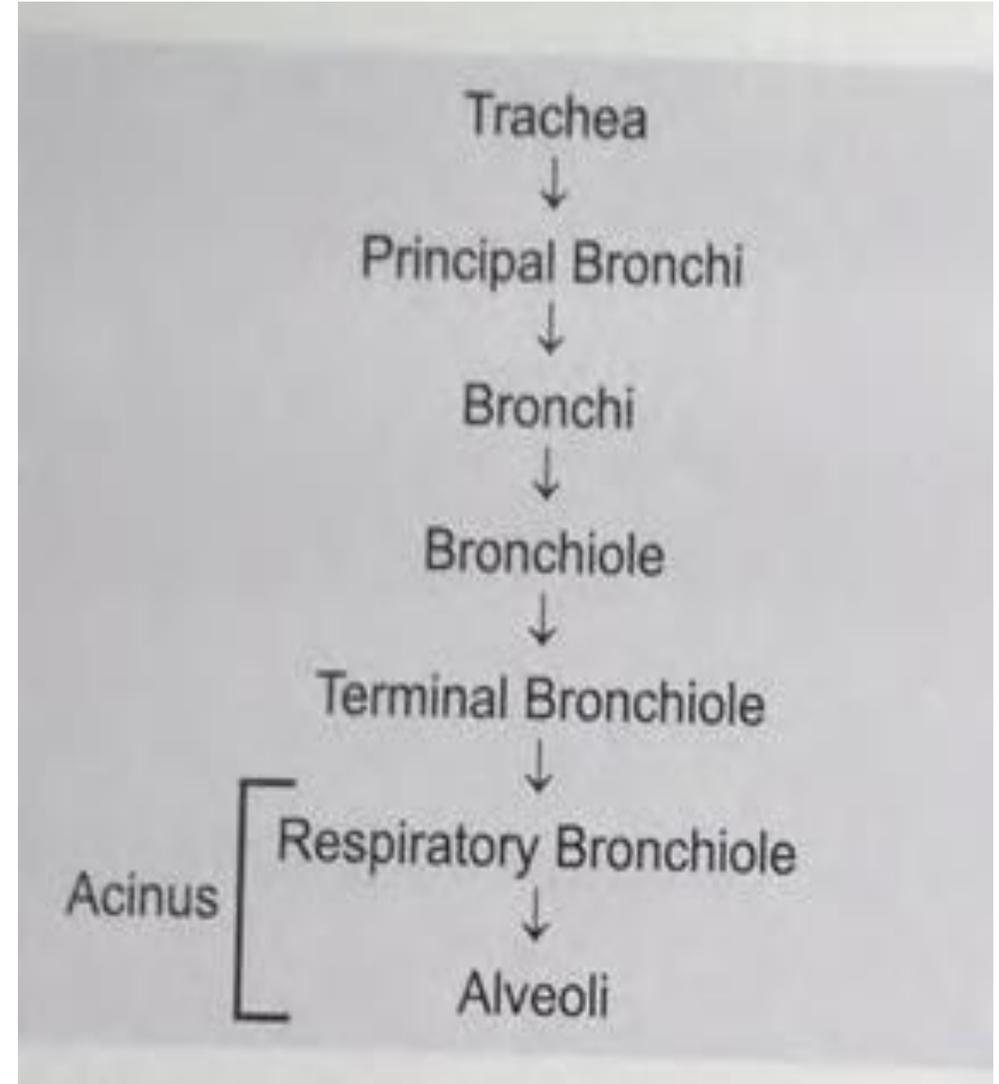
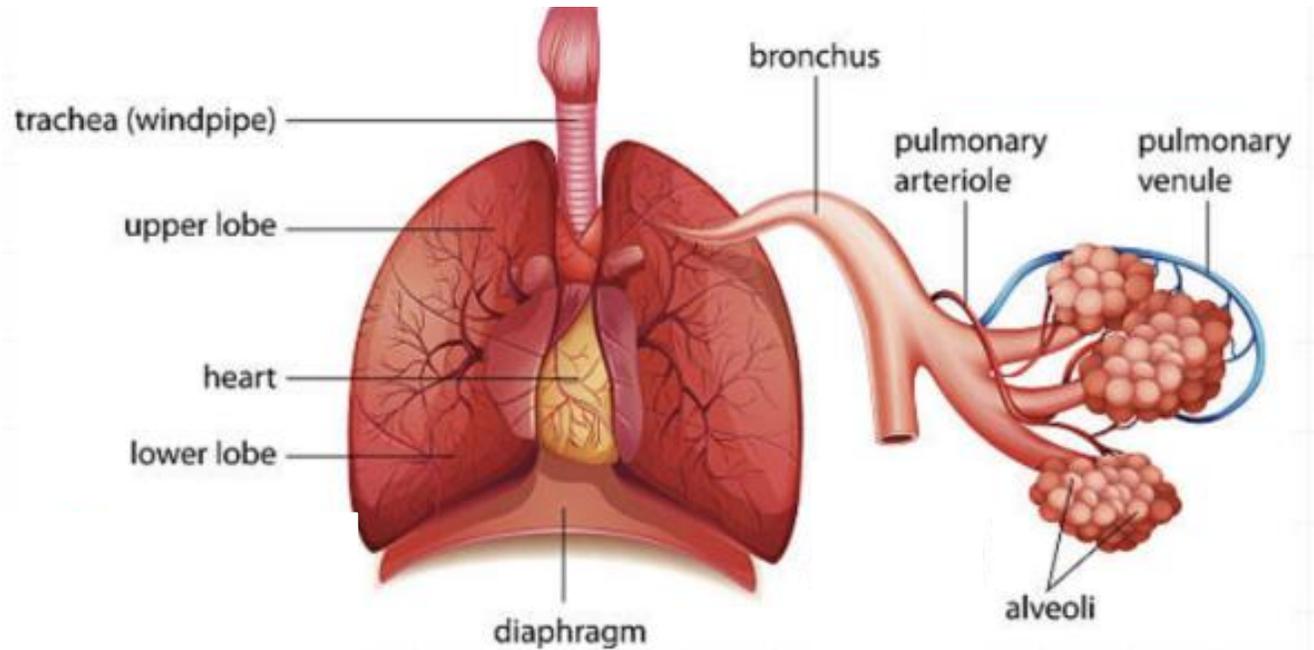
Respiratory system (RS)

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Main diseases of lung discussed in this lecture:

- 1) Infective lung disease
- 2) Obstructive lung diseases
- 3) Restrictive lung disease
- 4) Vascular lung disease
- 5) Neoplastic lung disease



Infective lung disease:

Pneumonia

❖ Infection of the lung parenchyma.

❖ Classification according to:

- **Pathogens:** bacterial, viral, fungal
- **Clinical setting:** community acquired pneumonia (CAP), hospital acquired pneumonia (HAP), ventilator associated pneumonia (VAP)
- **Extent:**
 - Lobar pneumonia: involvement of the entire lung lobe
 - Bronchopneumonia: patchy involvement of the lung parenchyma, originating from the airway

• Community acquired pneumonia (CAP):

- Lung infection that is acquired from the normal environment

• Hospital acquired pneumonia (HAP):

- Pneumonia not incubating at the time of hospital admission and occurring > 48 hours after admission

• Ventilator associated pneumonia (VAP):

- Pneumonia occurring > 48 hours after endotracheal intubation



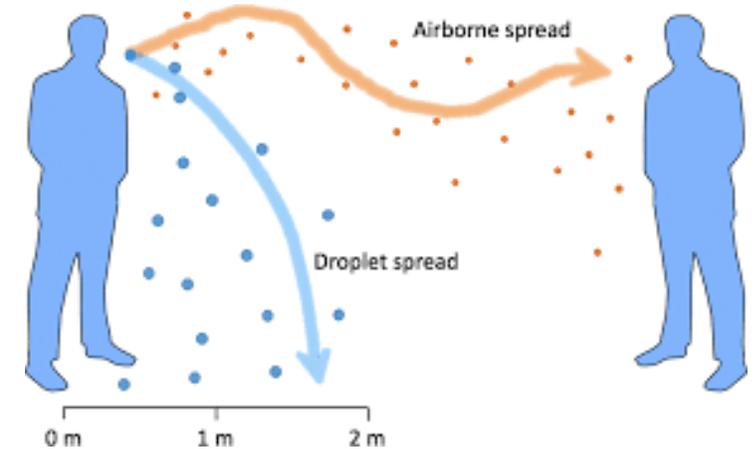
➤ Modes of transmission of Bacteria to the lungs:

- 1) Airborne/ droplet spread
- 2) Microaspiration of pathogens that have colonized the oropharynx is a common mechanism in bronchopneumonia
- 3) Spread to the lungs via the pulmonary or systemic blood supply

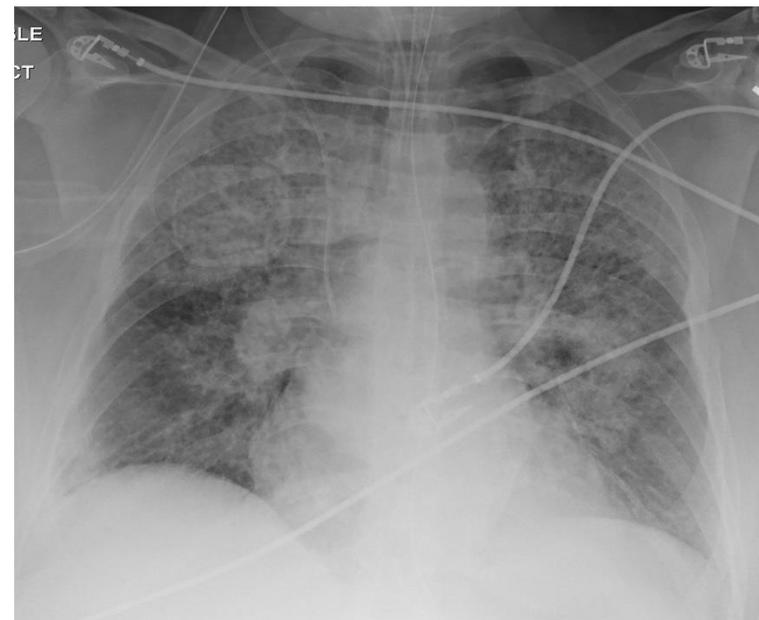
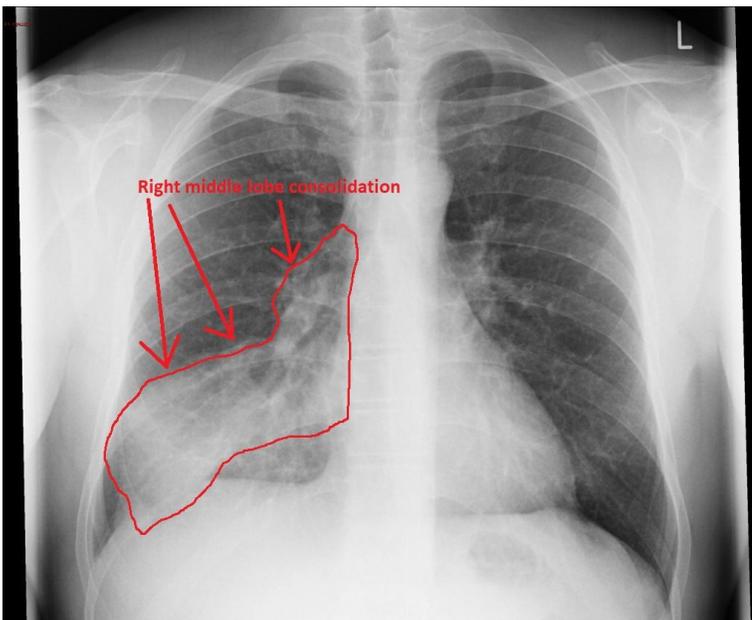
➤ Most common pathogens:

- Community – Acquired pneumonia: streptococcus pneumonia
- Hospital acquired pneumonia (HAP): Staphylococcus aureus

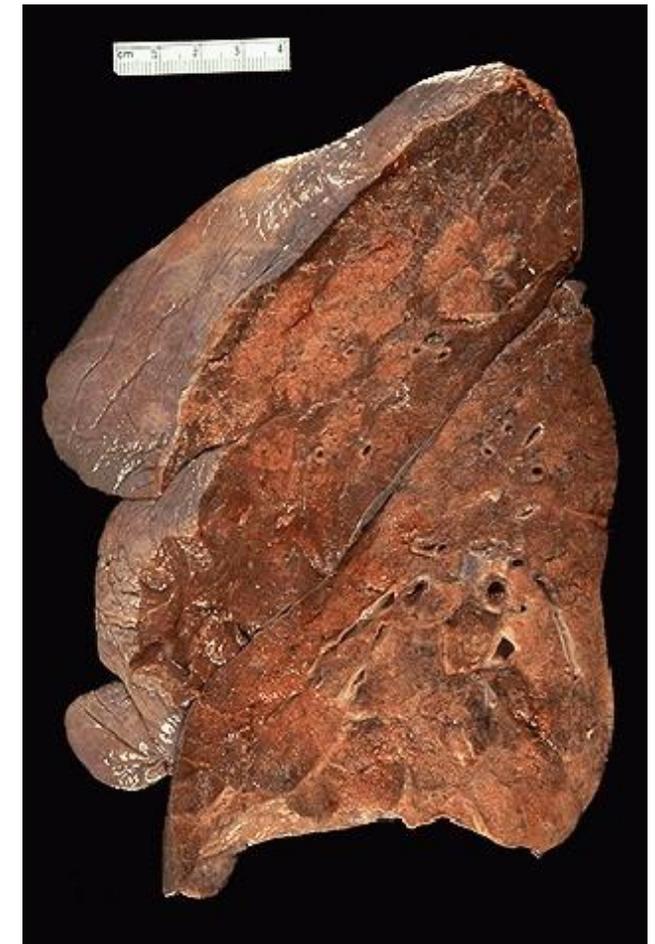
➤ Clinically : Characterized by fever, purulent sputum, leukocytosis and decline in oxygenation



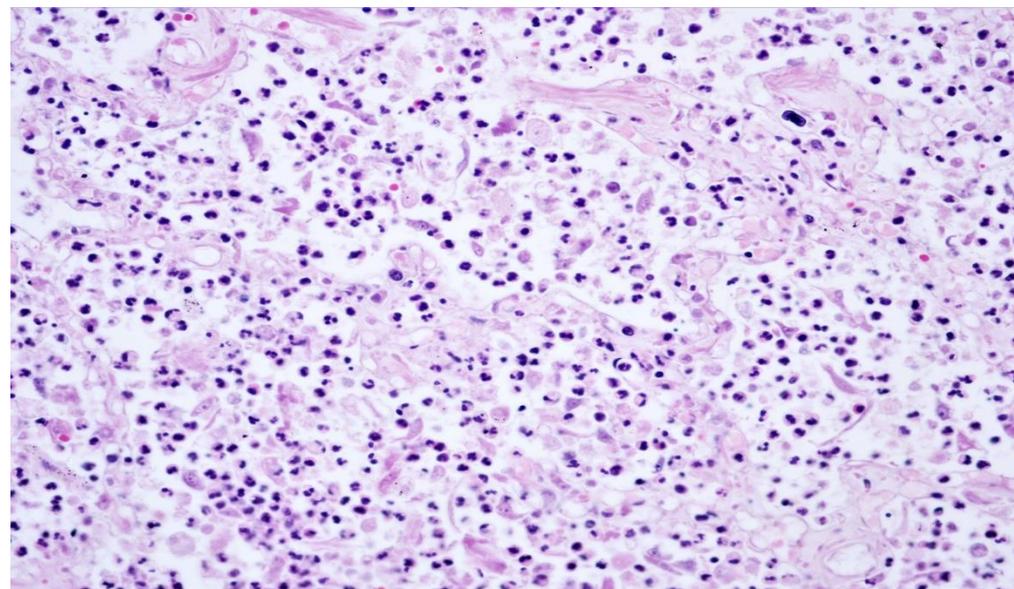
| Typical pneumonia | Atypical pneumonia |
|--|--|
| Bacterial pathogens, most commonly <i>Strep. pneumoniae</i> , <i>Staph. aureus</i> , and <i>Haemophiles influenzae</i> | Atypical bacteria (like <i>Mycoplasma pneumoniae</i> , <i>Chlamydophila pneumoniae</i> , <i>Legionella pneumophila</i>) or viruses. |
| Sudden onset | More gradual, often preceded by upper respiratory symptoms |
| Symptoms: High fever, chills, sudden onset of a productive cough, and pleuritic chest pain. | Often milder, with symptoms like headache, low-grade fever, malaise, and an unproductive cough |
| X-ray: Shows a dense, lobar consolidation (a whole lobe of the lung is affected) | Shows patchy or diffuse shadows, known as ground-glass opacities |



| Lobar pneumonia | Bronchopneumonia |
|---|---|
| | Most common pattern of pulmonary infection |
| Uniform inflammatory infiltrate, the changes are at the same stage throughout the entire lobe | Different stages in the different areas |
| Progression stages: vascular congestion then intra-alveolar exudate rich in neutrophils then fibromyxoid masses rich in macrophages and fibroblasts last resolve with fibrosis | Patchy intra-alveolar fibrinopurulent exudate with neutrophils - Mostly affect lower lobes |



The lighter areas that appear to be raised on cut surface from the surrounding lung are the areas of consolidation of the lung.



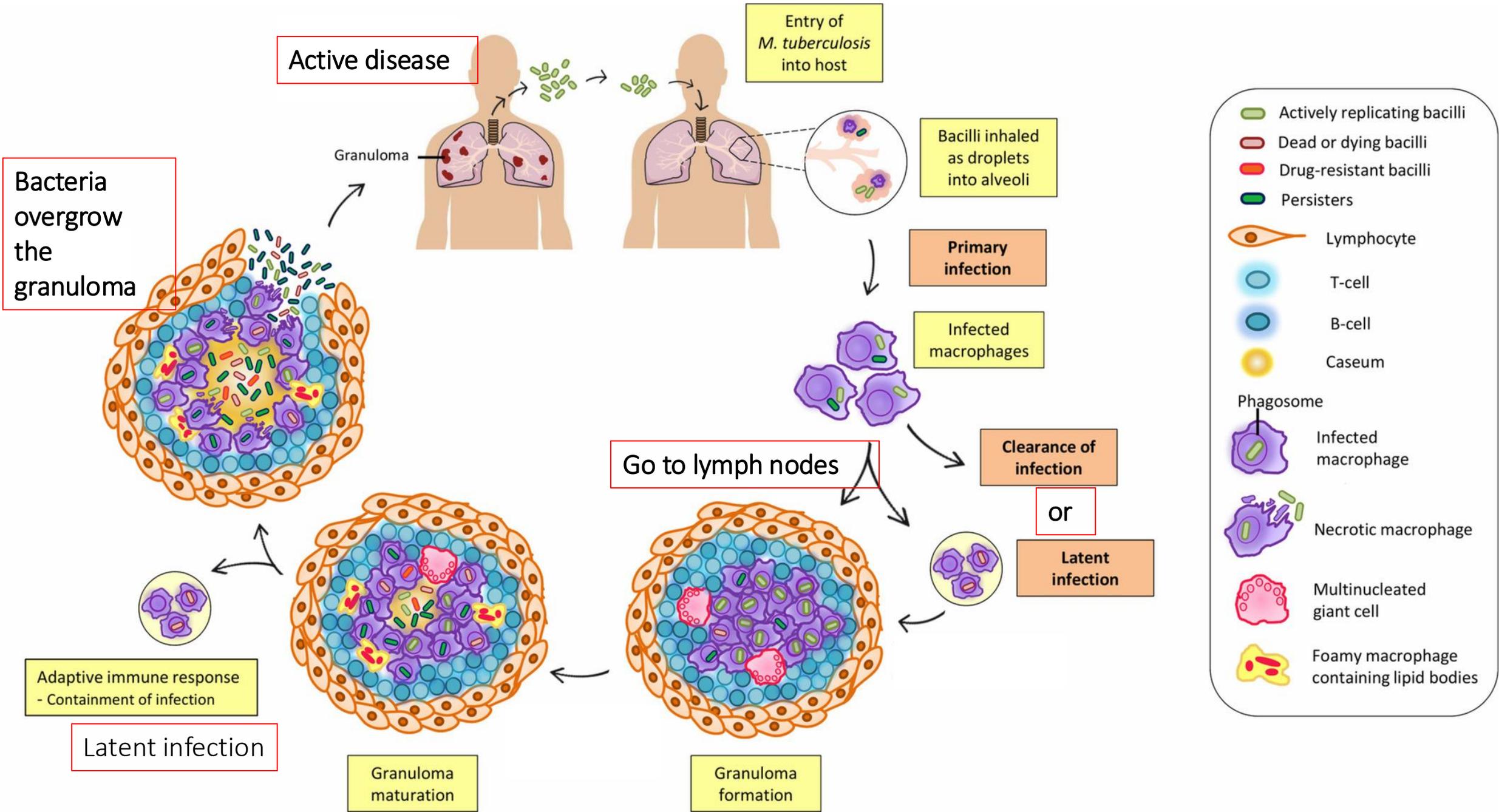
Intra alveolar neutrophils

Tuberculosis :

- ❖ Infectious disease caused by *Mycobacterium tuberculosis*
- ❖ **Hallmark** is necrotizing granulomatous inflammation, composed of central necrotic zone surrounded by epithelioid histiocytes and Langhans type giant cells
- ❖ **Risk factors:**
 - 1) Immunosuppression, including HIV / AIDS and chronic immunosuppressive therapy.
 - 2) Occupational: mining, construction work, pneumoconiosis (silicosis)
- ❖ **Clinically:** Chronic and persistent cough (often productive), weight loss, fever, night sweats and hemoptysis

| Latent disease | Active disease |
|--|---|
| Controlled bacteria within granuloma | Uncontrolled bacteria and multiplying |
| No symptoms | Symptoms |
| Non contagious | Contagious |
| Can become active later, especially with weakened immunity | Requires multiple drugs for months to cure and prevent spread |





Active disease

Entry of *M. tuberculosis* into host

Bacilli inhaled as droplets into alveoli

Primary infection

Infected macrophages

Go to lymph nodes

Clearance of infection

or

Latent infection

Granuloma maturation

Granuloma formation

Bacteria overgrow the granuloma

Adaptive immune response - Containment of infection

Latent infection

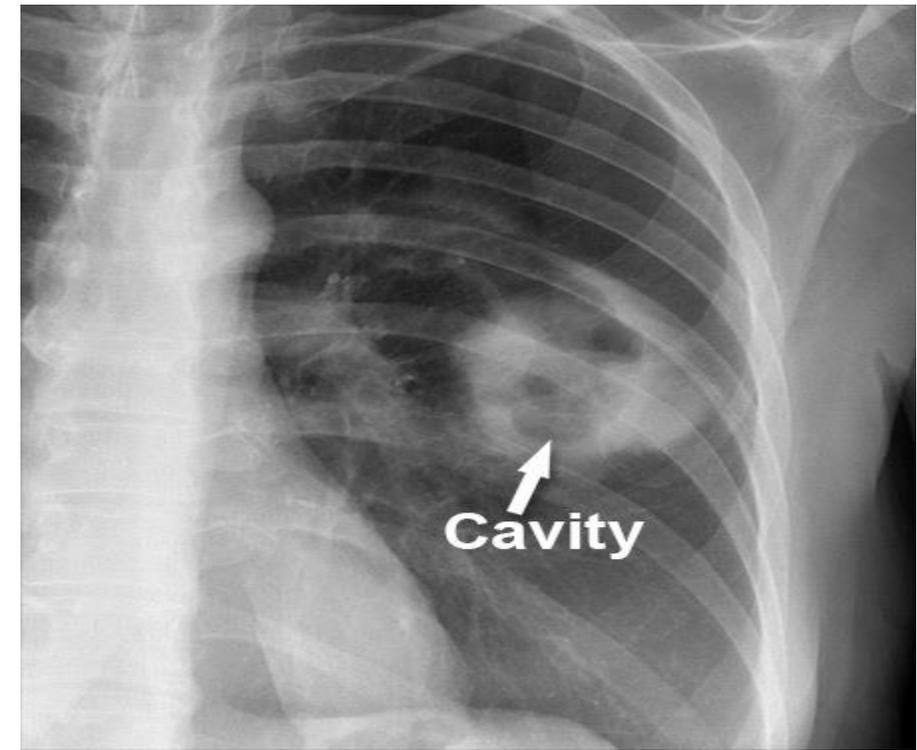
Granuloma

- Actively replicating bacilli
- Dead or dying bacilli
- Drug-resistant bacilli
- Persisters
- Lymphocyte
- T-cell
- B-cell
- Caseum
- Phagosome
- Infected macrophage
- Necrotic macrophage
- Multinucleated giant cell
- Foamy macrophage containing lipid bodies

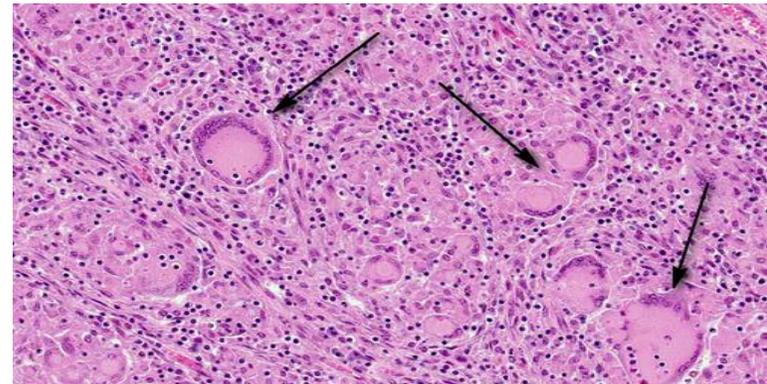
❖ Laboratory investigations:

- **Active TB disease**
 - Imaging techniques (chest X-rays and PET CT)
 - Sputum smears (AFB or Ziehl-Neelsen staining)
 - Cultures
- **Latent TB infection**
 - Tuberculin skin testing (Mantoux test with purified protein derivative [PPD])

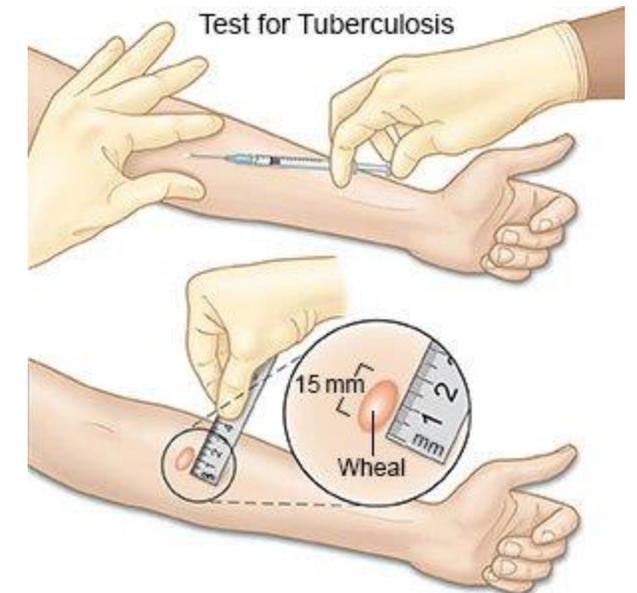
❖ On radiology: **Commonly presents as cavitary lesion in upper lobe in infected immunocompetent hosts**



Acid Fast bacilli stain

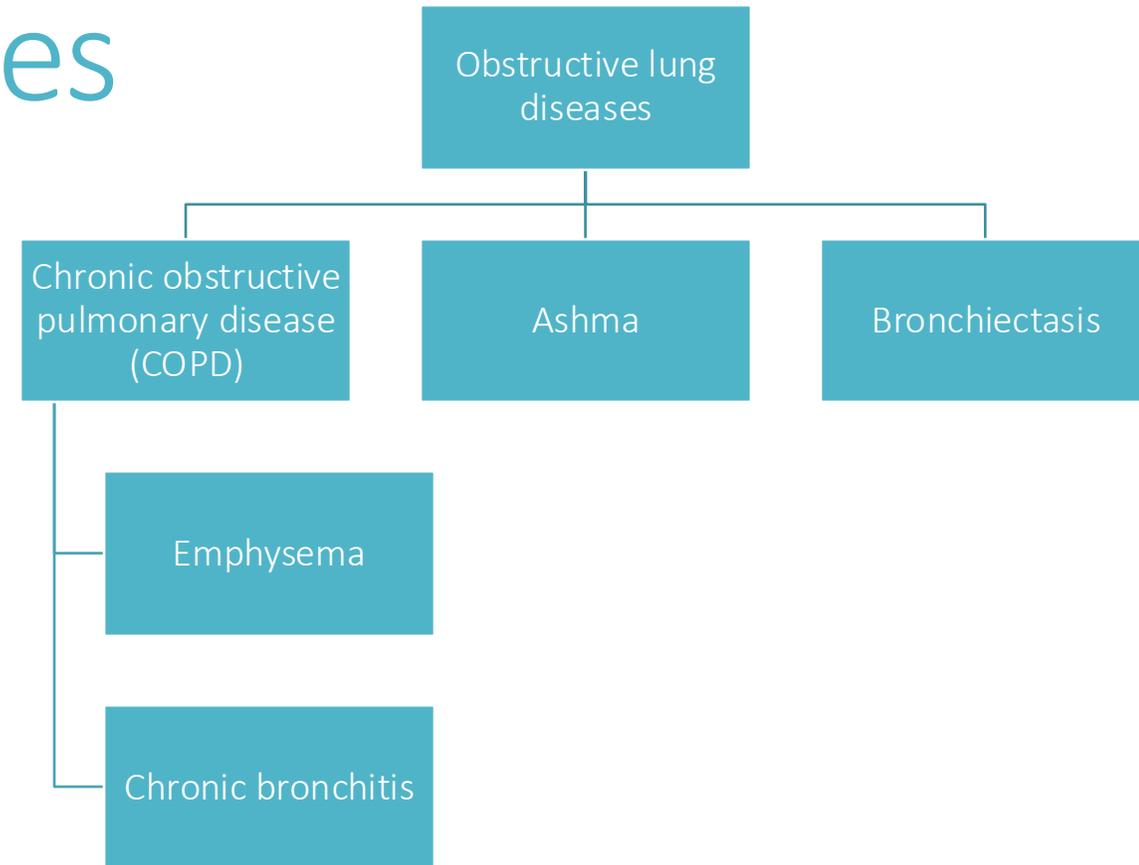


Langhan giant cells



Obstructive lung diseases

- ❖ Increased resistance to airflow due to airway obstruction
- ❖ Airways become narrowed or blocked, making it hard to breathe out, causing symptoms like shortness of breath, cough (often with mucus), wheezing, and chest tightness
- ❖ pulmonary function tests show decreased maximal airflow rates during forced expiration,



Chronic Obstructive Pulmonary disease (COPD):

- **Definition:** common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities caused by exposure to noxious particles or gases.

➤ 1) Chronic bronchitis:

➤ **Diagnosis:** persistent cough with sputum for 3 months in 2 consecutive years without other apparent explanation.

➤ The most important causing agent: Smoking

➤ Pathogenesis:

➤ **Inflammation:** tobacco interferes with ciliary action, directly damages airway epithelium and inhibits ability of white blood cells to clear bacteria

➤ **Mucus hypersecretion.** The earliest feature of chronic bronchitis is hypersecretion of mucus in the large airways, With time, there is also a **marked increase in goblet cells in small airways** (small bronchi and bronchioles) accompanied with enlargement of submucosal glands

➤ Clinically:

- **Blue bloaters:** Their cardinal symptom is a persistent cough productive of sputum, coupled with hypercapnia, hypoxemia, and mild cyanosis.

➤ 2) Emphysema:

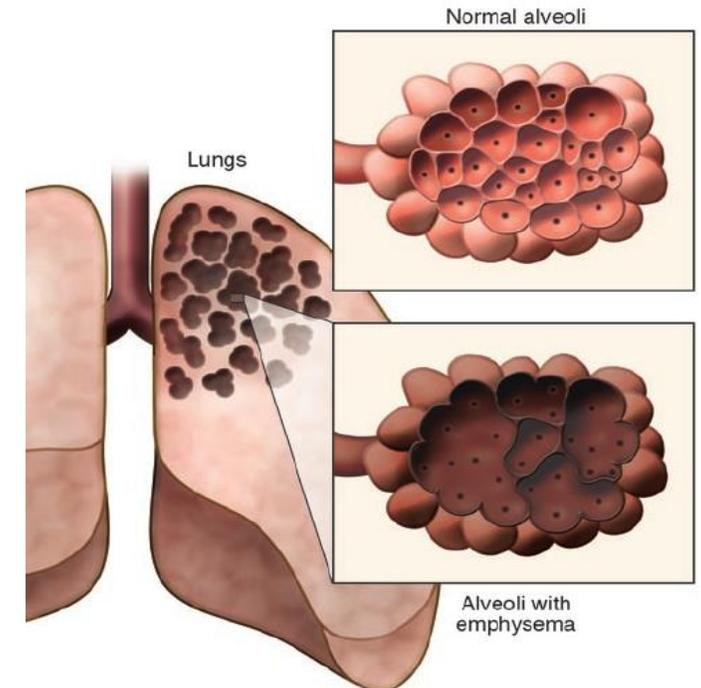
- **Definition:** irreversible enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls
- The most common causing agents: smoking and patients with α 1-antitrypsin deficiency.
- **Pathogenesis:** Normally, the pulmonary tissue destruction by elastase is prevented by the presence of anti-elastase activity (α 1-antitrypsin and α 1-macroglobulin). So any increase in neutrophils (usually in smokers) or α 1-antitrypsin deficiency would contribute to development of emphysema.

➤ Morphological progression:

- 1) Increase in size and number of small fenestrae in alveolar walls (pores of Kohn), which leads to loss of elastic recoil.
- 2) Breakdown and merging of fibrovascular trabeculae (framework)
- 3) Remodeling of acini results in airspace enlargement

➤ Clinically:

- Pink Puffers: Skinny/ Take short, fast breaths and use their accessory muscles to exhale/ pursed-lip breathing/ Cheeks and face may appear temporarily pink due to the fast, labored breathing/ barrel-chested due to trapped air.



Blue lips



inflamed airway



increased sputum

Barrel chest

minimal or absent cough



Pursed lip breathing

Crackles & wheezing

excess fluid

BLUE BLOATER

Chronic Bronchitis VS

PINK PUFFER Emphysema

cyanosis
obese



Anxious



Speaks in short sentences

exertional dyspnea



Pulmonary HTN

can lead to R sided heart failure



cor pulmonale or enlarged R ventricle



Secondary polycythemia vera

edema



lean forward to breath

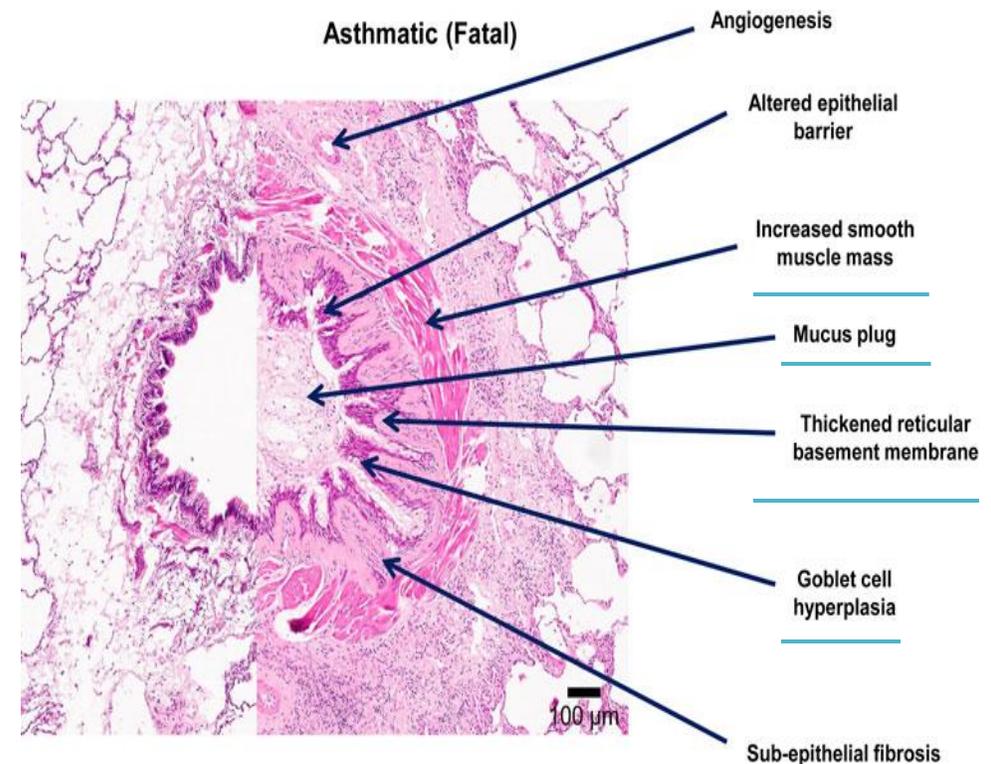


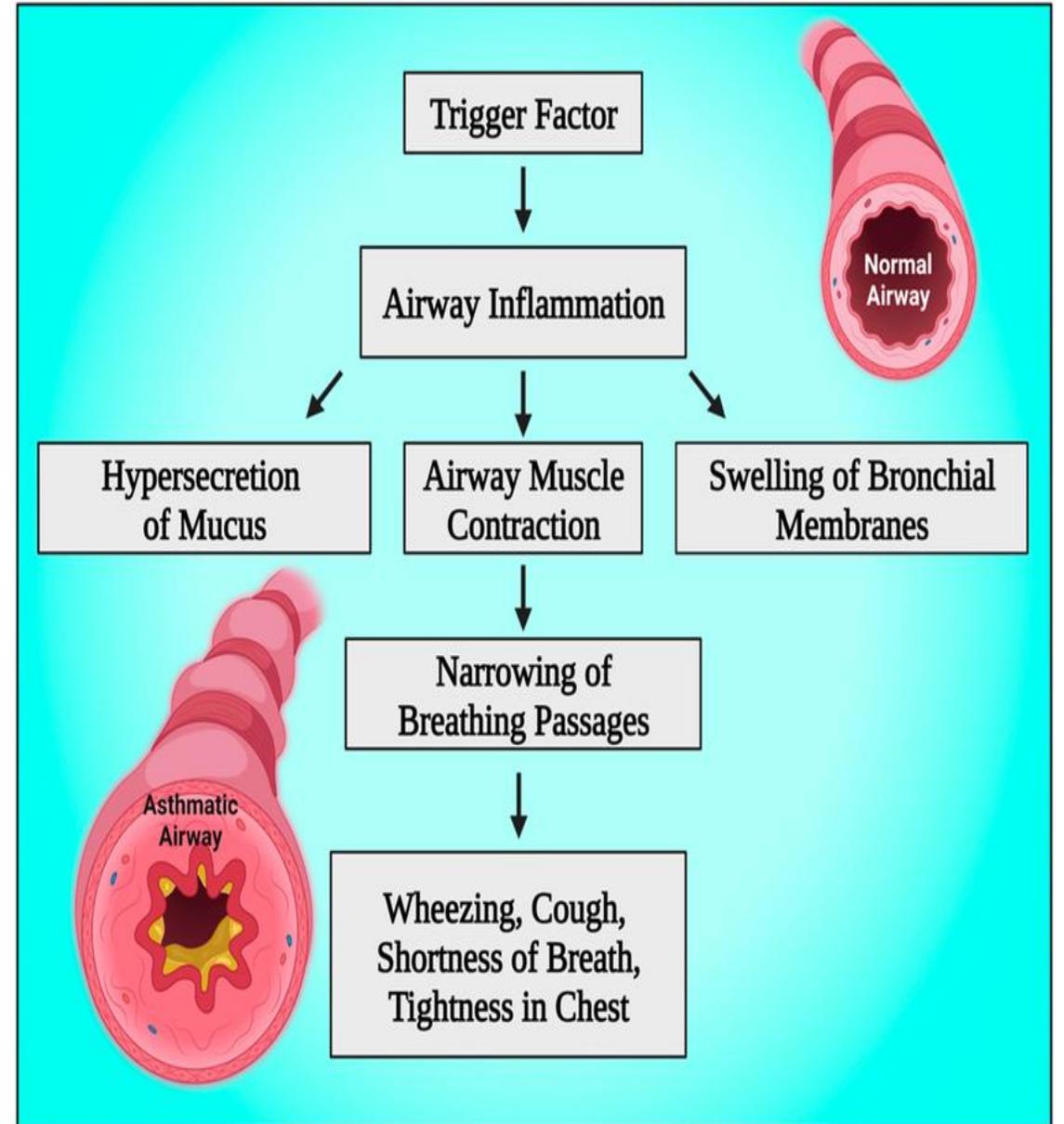
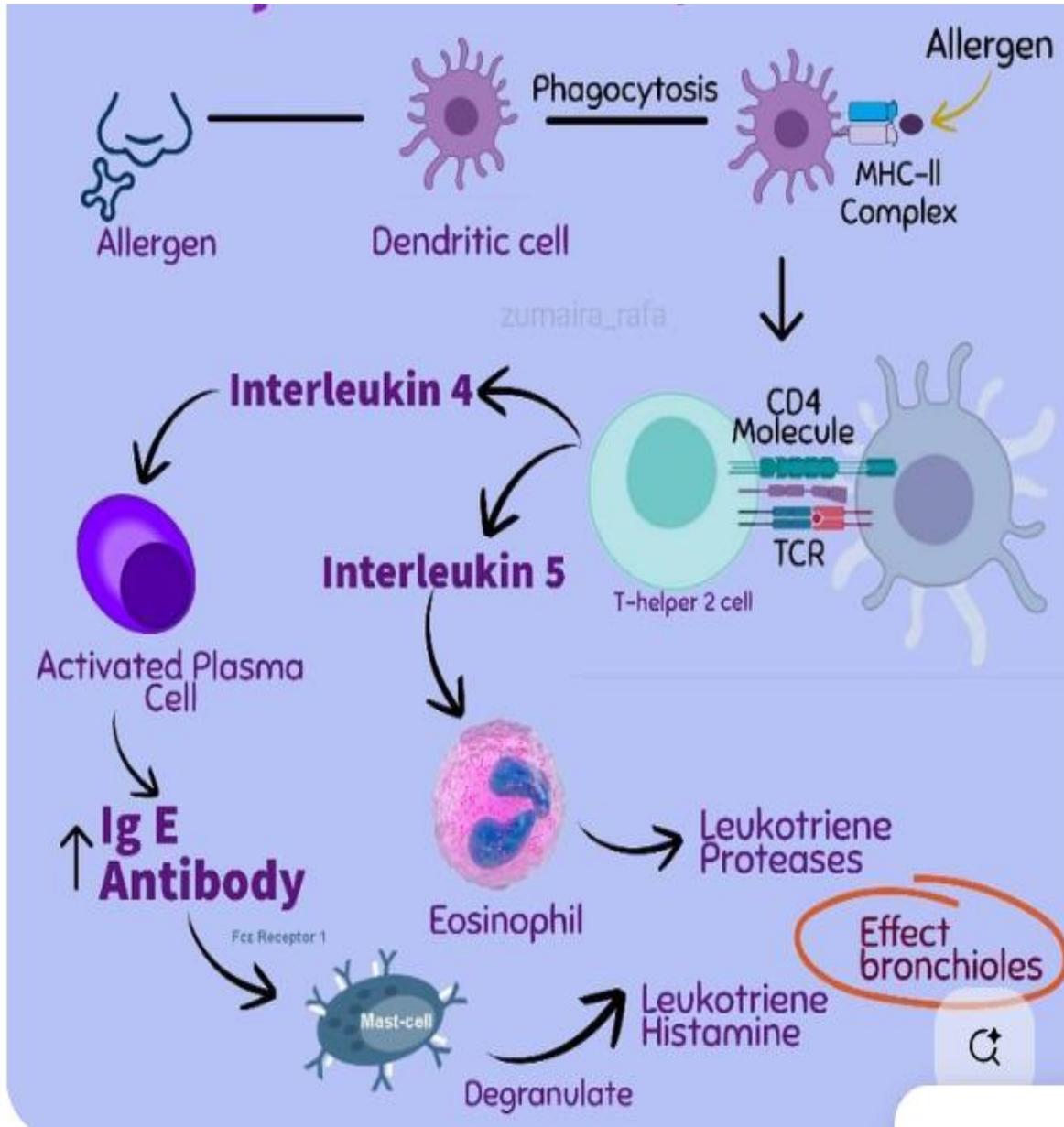
Uses accessory muscles to breath



Asthma:

- - **Definition:** characterized by hyperactivity of the airway resulting in **reversible bronchoconstriction and airflow obstruction on exposure to some external stimuli.**
- **Clinically:**
 - **wheezing, shortness of breath, chest tightness, and cough**, which vary over time and in intensity.
 - **symptomatic episodes usually at night or in the early morning.**
- **Pathogenesis:**
 - Atopic asthma, the most common form of the disease, is caused by a **Th2-mediated IgE response** to environmental allergens in genetically predisposed individuals.
- **Morphology:** increased mucosal goblet cells and submucosal glands, thickened basement membrane, bronchial smooth muscle hypertrophy, airway wall edema.





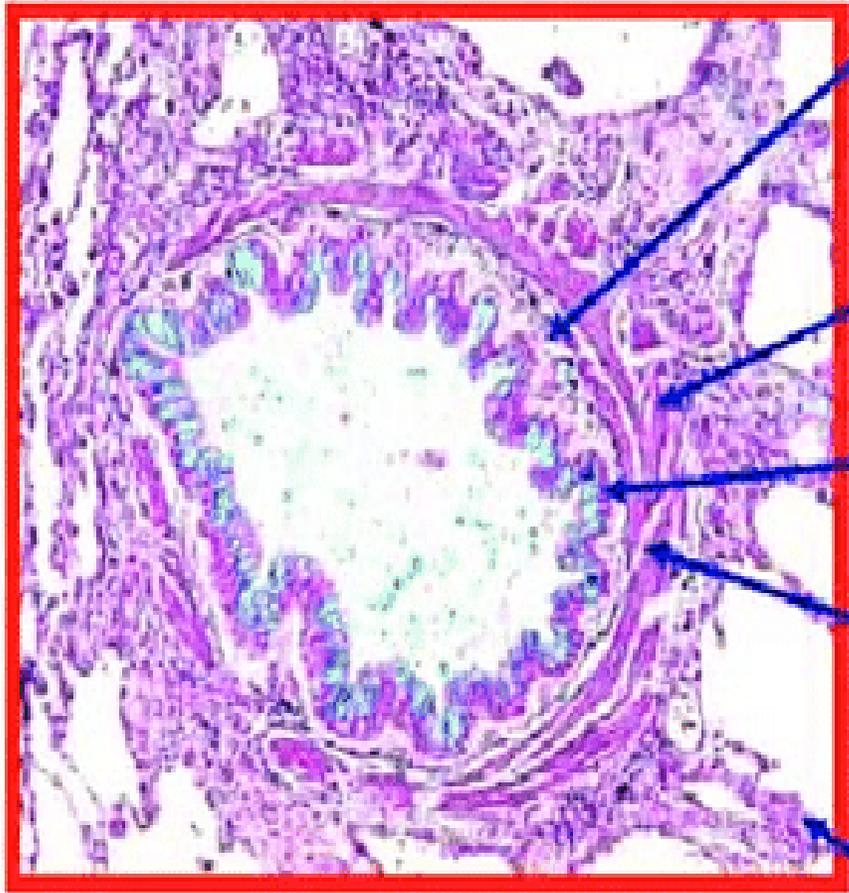
❖ Subtypes of asthma:

| Features | Extrinsic asthma | Intrinsic asthma |
|---|---|--|
| Pathogenesis | Type 1 hypersensitivity reaction to extrinsic antigen | Initiated by non-immune mechanisms with intrinsic body stimuli |
| Age of presentation | Child | Adult |
| Family history | Present | Absent |
| Prior allergic reaction/ allergen exposure | Positive history of rhinitis, urticaria, eczema | Absent |
| Serum IgE level | Increased | Normal |
| Skin test | Positive | Negative |
| Examples | Atopic asthma, occupational asthma | Drug (aspirin), viral infection, cold, exercise |



❖ Status asthmaticus: unremitting attacks due to exposure to previously sensitized antigen; may be fatal, usually in patients with a long history of asthma

Asthma death



+++Inflammation+++

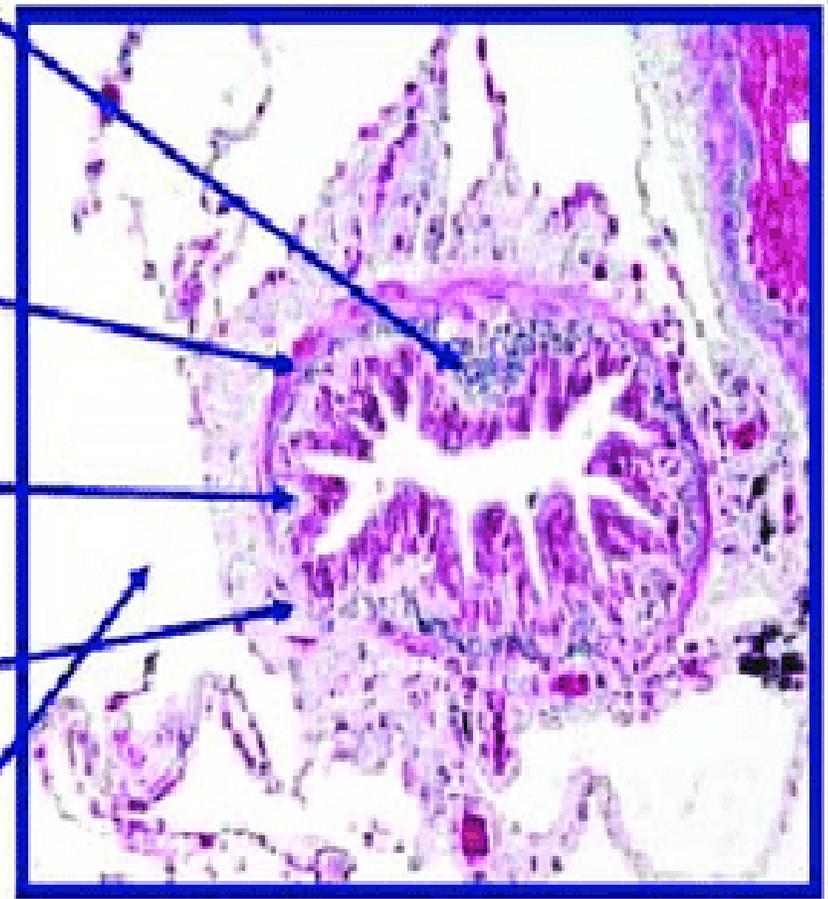
+++ASM+++

+++BM-

+Fibrosis+++

Alveolar
-disruption+++

Severe COPD



Restrictive lung disease

- ❖ Reduced lung compliance due to lung tissue stiffness (parenchymal) or chest wall issues (extra parenchymal), leading to decreased lung volumes, especially total lung capacity (TLC).
- ❖ Category according to pathogenic mechanism:

Pulmonary Parenchymal Diseases (Intrinsic Causes)

- Caused by intrapulmonary restriction due to inflammatory processes within the lung tissue such as:

- Idiopathic pulmonary fibrosis (IPF)
- Pneumoconiosis: silicosis, Asbestosis.
- Sarcoidosis
- Pulmonary alveolar proteinosis
- Others

Extrinsic or Extrapulmonary Diseases

- They can be a result of diseases of the chest wall, such as:

- Kyphoscoliosis
- Pleural conditions such as effusions, pleural scarring, chronic empyema
- Obesity
- Neuromuscular disorders like muscular dystrophy, phrenic neuropathies.
- Ascites

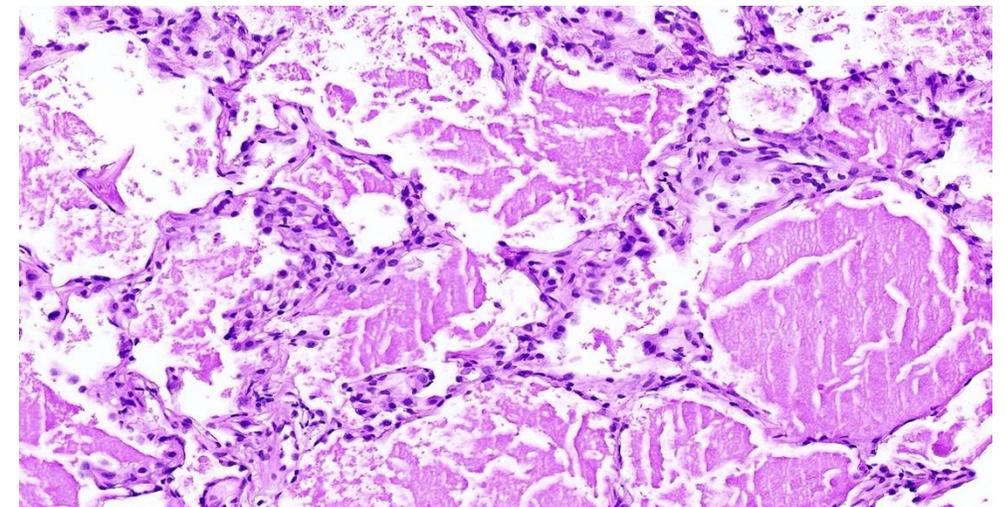
Idiopathic pulmonary fibrosis (IPF)

- Risk factors: Genetic, smoking, Gastroesophageal reflux disease.
- Clinically: Chronic dyspnea, Dry cough, Fatigue, Digital clubbing
- **Poor prognosis, Median survival is 2 to 3 years**
- Pathogenesis: by fibroblast proliferation, collagen deposition,
- CT scan: **honeycombing cysts** and reticular septal thickening with subpleural and posterior basal predominance



Pulmonary alveolar proteinosis

- Pathogenesis: **Abnormal accumulation of acellular alveolar surfactant due to impaired surfactant clearance or abnormal surfactant production**
- Morphology: Histology will show **acellular and coarsely granular eosinophilic material in the alveoli** with absent to mild associated fibrosis and minimal inflammation
- Risk factors: Genetic, exposure to toxins, HIV, malignancy.

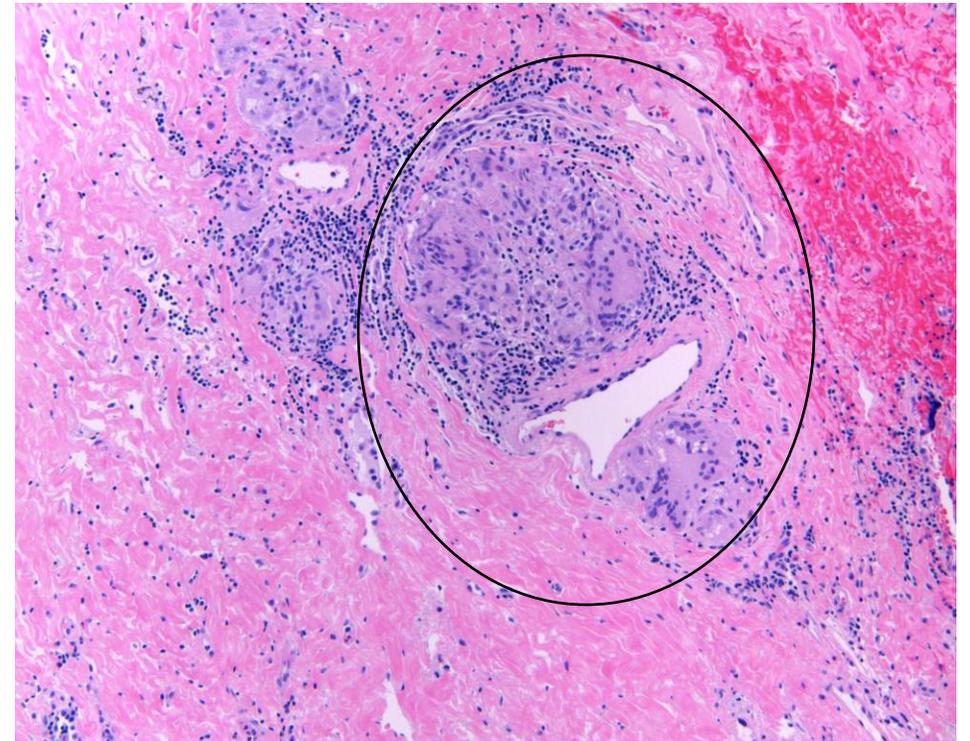


Pneumoconiosis:

- Inhalation of mineral dust causes chronic inflammation, scarring (fibrosis), and potentially asbestos bodies or silica nodules, disrupting normal lung structure.
- Subtypes: Silicosis, Asbestosis.
- **Silicosis:** Most prevalent chronic occupational disease in the world, due to sandblasting work, stone cutting and coal mining
- **Asbestosis:** if person worked in an industry such as building or construction, particularly from the 1950s to the 1990s.

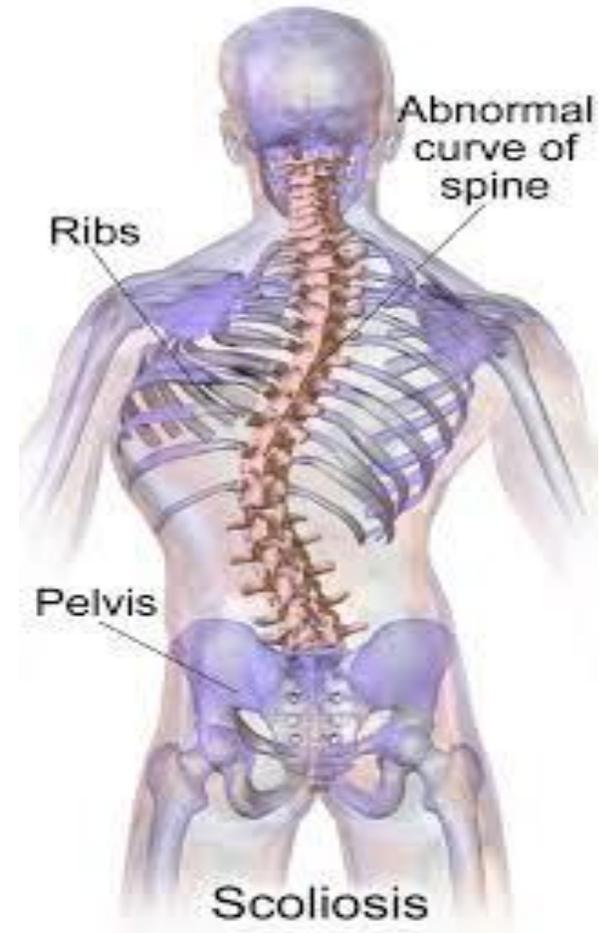
Sarcoidosis:

- Systemic disease characterized by non-ecrotizing granulomatous inflammation, with 90% of overall cases showing involvement of the lungs and hilar lymph nodes
- Sarcoidosis occurs more frequently in those with chronic inhalational exposures of silica and metal particulates





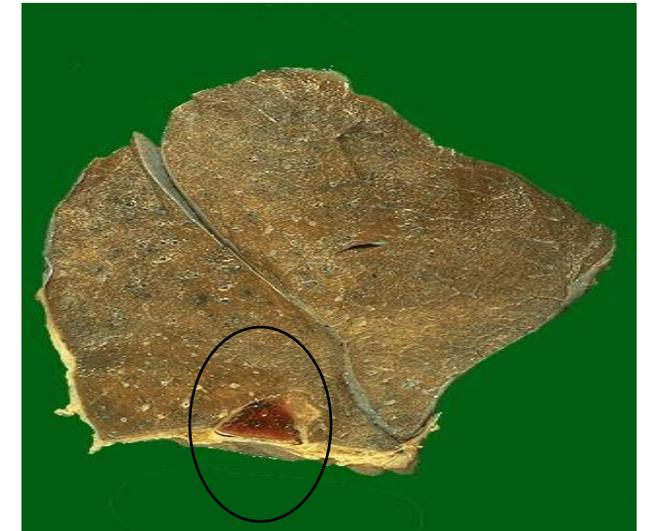
Digital clubbing



Vascular lung disease

Pulmonary emboli and Pulmonary infarction

- **Definition:** Pulmonary embolus (PE) is a blockage of the pulmonary artery or one of its branches due to material (solid, gaseous or liquid) that has traveled through the circulation from elsewhere in the body
- Risk factors can be divided into genetic versus acquired:
 - Genetic factors include hypercoagulable conditions, such as factor V Leiden mutation, protein C and S deficiency, prothrombin mutations, antiphospholipid syndrome, etc.
 - Acquired risk factors include but are not limited to pregnancy, hospitalization, obesity, oral contraceptive use, malignancy, long bone fracture.
- 90-95% of pulmonary emboli arise for Deep Vein Thrombosis (DVT) in the leg.
- Only 10% of emboli cause infarction.
- Complication of emboli: pulmonary hypertension, cor pulmonale, pulmonary abscess and sudden death.
- Morphology of infarction: wedge shaped hemorrhagic infarction.



Pulmonary hypertension

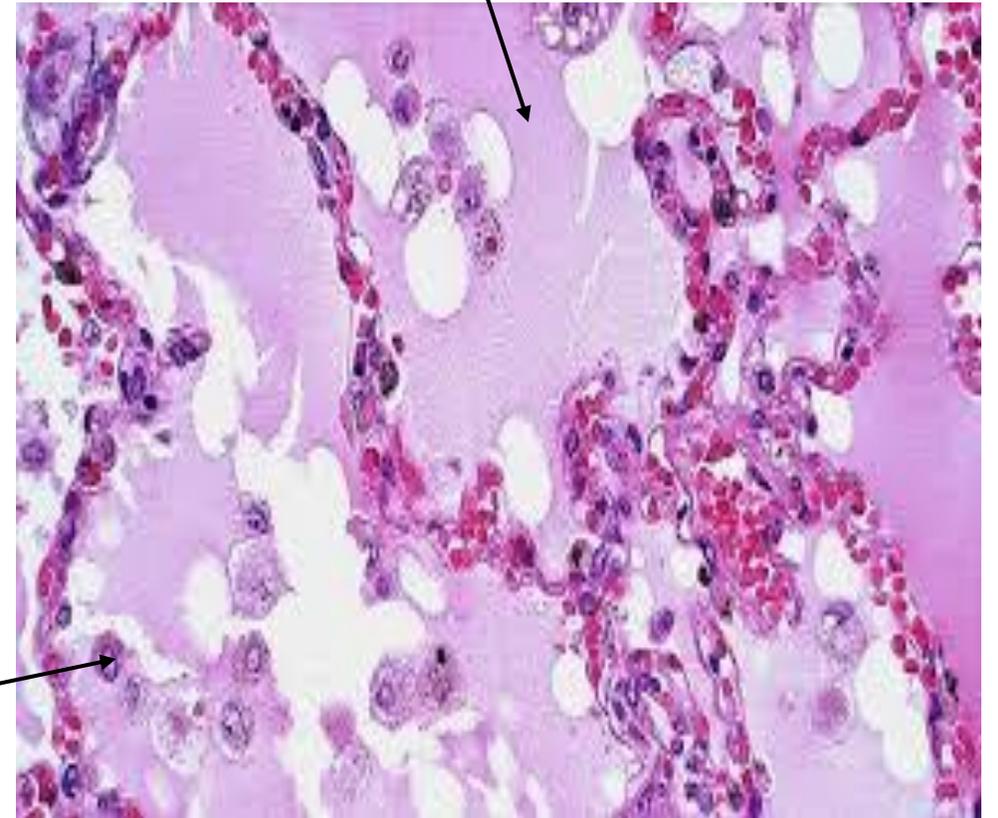
- Definition: increased pulmonary artery pressure > 20 mm Hg
- Pulmonary blood pressure is the pressure that the heart uses to pump blood from the heart through the arteries of the lungs. Normally pulmonary artery pressure is 11-20 mm Hg at rest.
- Common causes:
 - Left-Sided Heart Disease: High blood pressure (hypertension) or coronary artery disease affecting the heart's left side.
 - Lung Diseases/Low Oxygen: COPD, interstitial lung disease, emphysema, sleep apnea, or living at high altitudes.
 - Blood Clots: Chronic or acute blood clots in the pulmonary arteries (pulmonary embolism).
 - Connective Tissue Diseases: Conditions like scleroderma, lupus, or rheumatoid arthritis.
 - Liver Disease: Cirrhosis.
 - Congenital Heart Defects: Heart problems present from birth

Pulmonary edema

- ❖ **Definition:** fluid accumulation within the lungs usually due to hemodynamic disturbances (cardiogenic) or local microvascular injury
- ❖ **Causes:**
 - Cardiogenic: Left sided heart failure
 - Local microvascular injury: infections, drug ,radiation.
- ❖ **Morphology:**
 - Lungs are wet and heavy, fluid initially at base of lower lobes because hydrostatic pressure is greater here
 - Congestion, fluid and hemosiderin laden macrophages (heart failure cells) are present

Heart failure cells

Fluid ... pink material



Neoplastic lung disease

Carcinomas

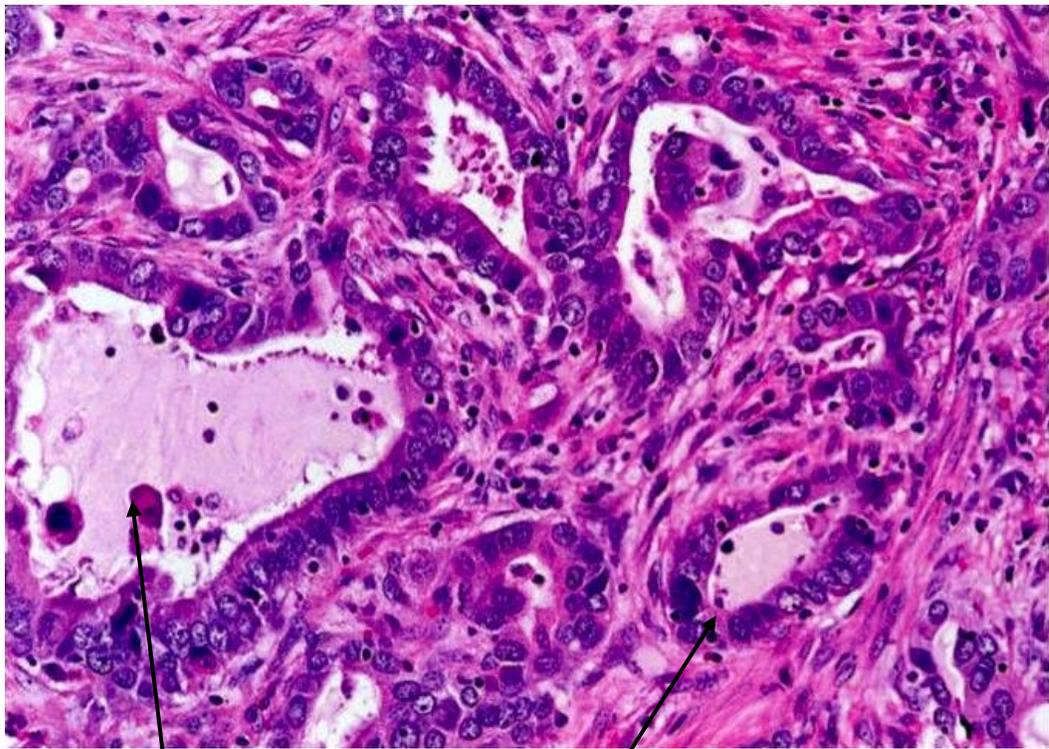
- Lung cancer is currently the most frequently diagnosed major cancer and the most common cause of cancer mortality worldwide.
- **Tobacco Smoking.** About 80% of lung cancers occur in active smokers or those who stopped recently, and there is a nearly linear correlation between the frequency of lung cancer and pack-years of cigarette smoking
- **Adenocarcinoma:**
 - ✓ the most common type of lung cancer
 - ✓ the most common type of non-smokers and females
 - ✓ Usually peripheral location
 - ✓ Morphology: glandular pattern of growth of tumor cells.

➤ Squamous cell carcinoma:

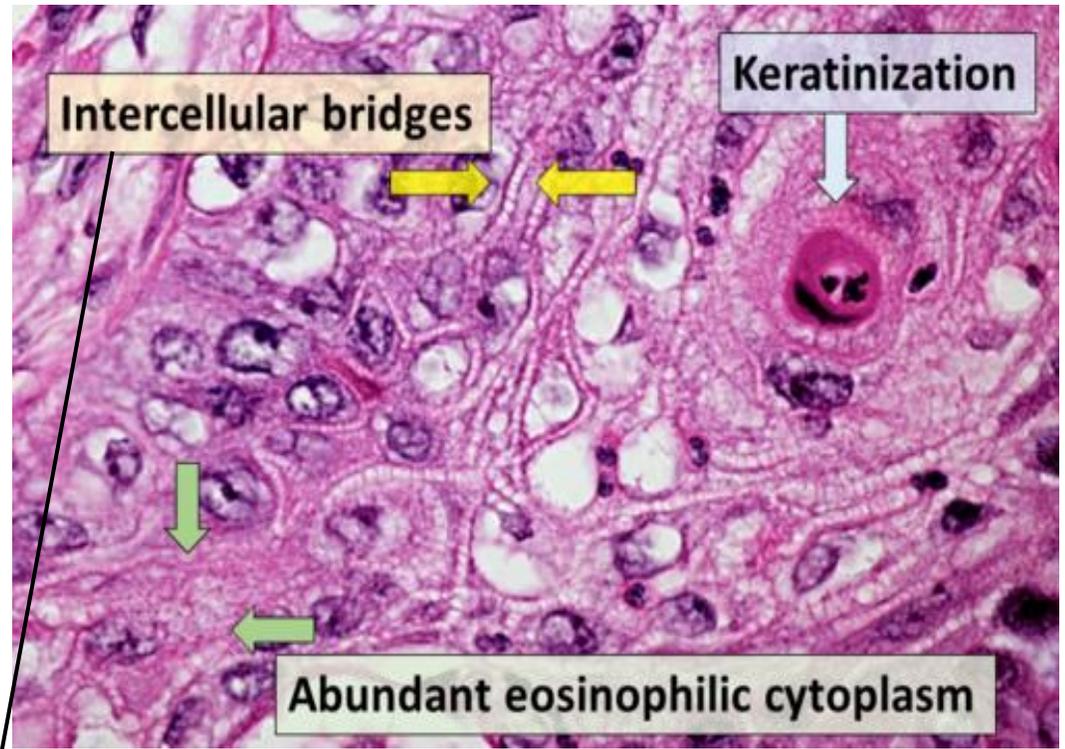
- ✓ The most common type of lung cancer in smokers.
- ✓ Most common type in males
- ✓ Usually central in location
- ✓ Has the best prognosis
- ✓ Morphology: presence of keratinization and intercellular bridges

➤ Small cell cancer

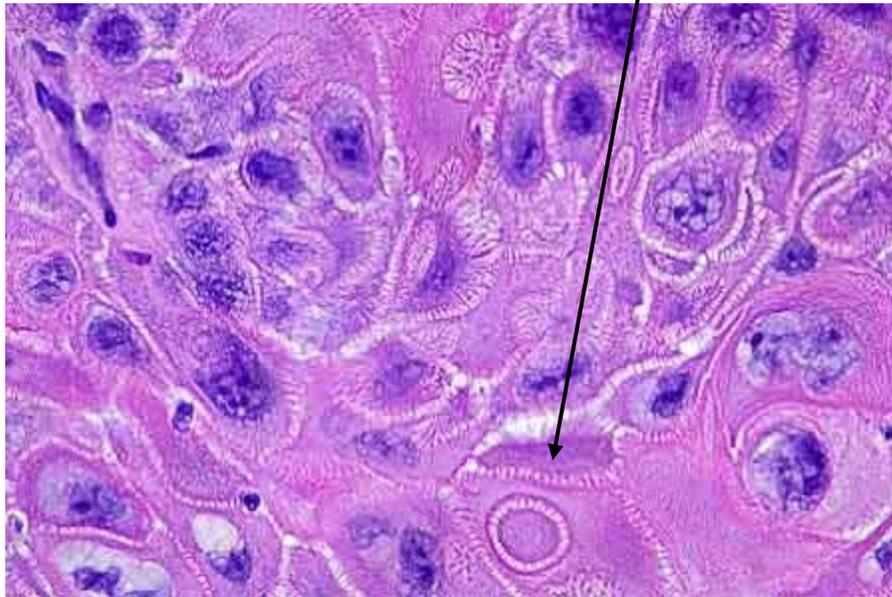
- ✓ Associated with smoking
- ✓ Central in location
- ✓ Morphology: Salt and pepper nucleus.
- ✓ Has the worst prognosis

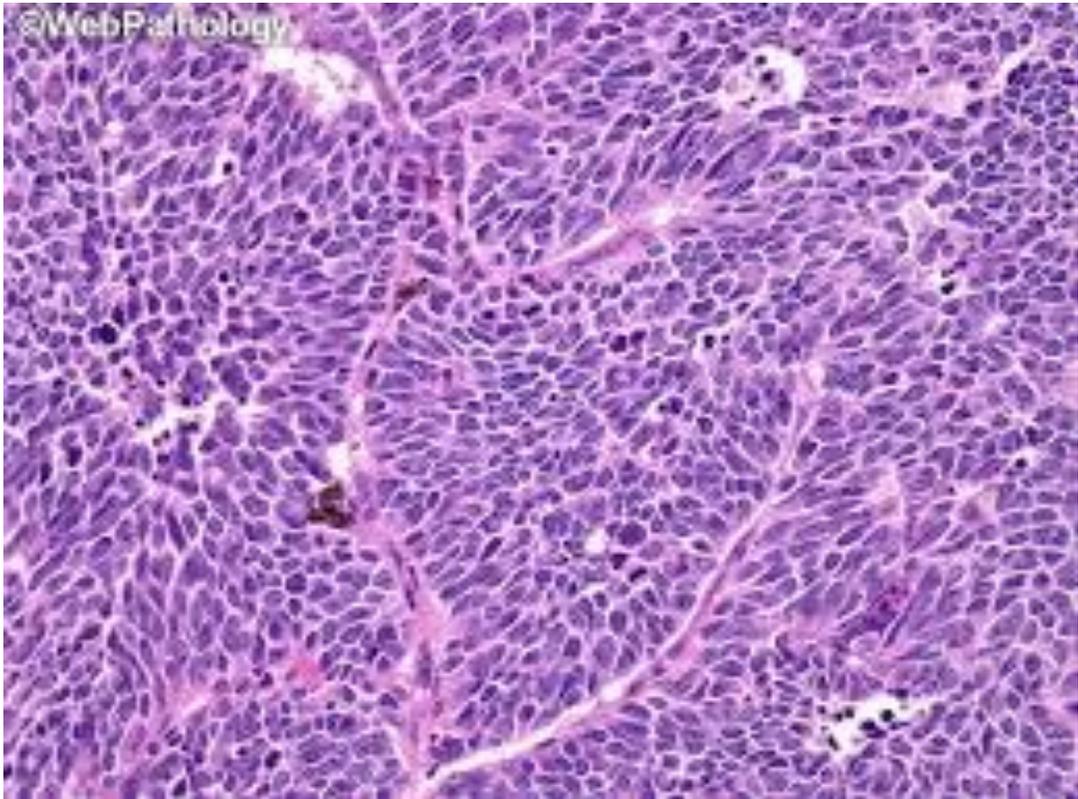


Adenocarcinoma
Malignant glands

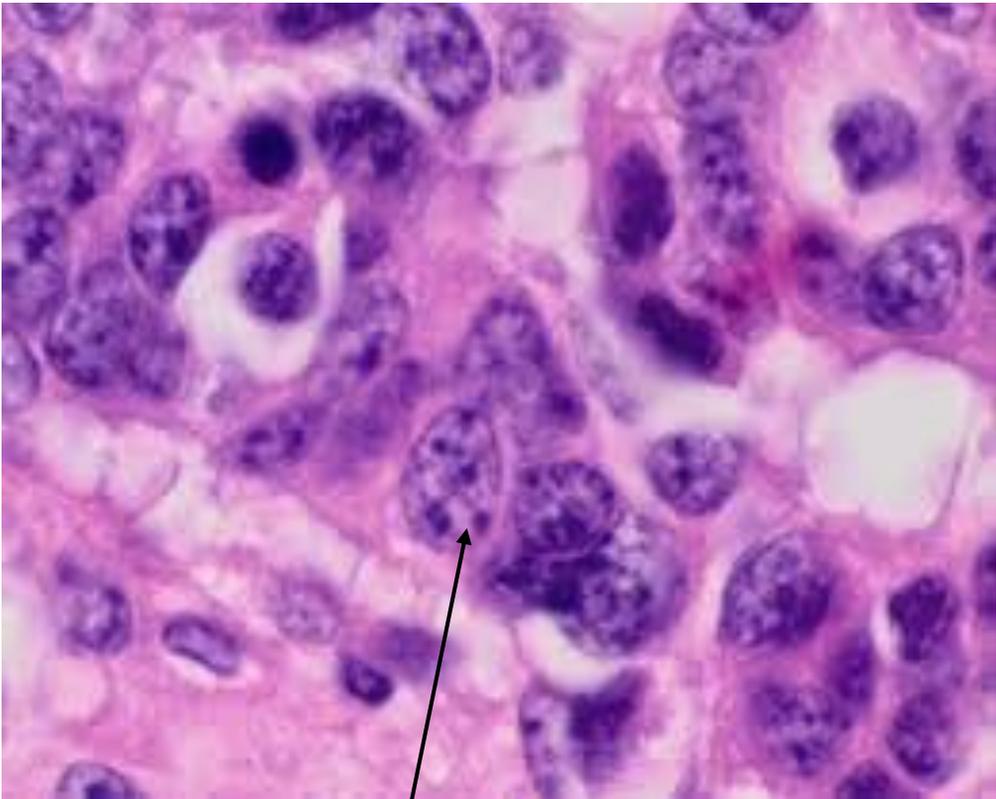


Squamous cell carcinoma





Small cell carcinoma



Salt and pepper nucleus

Thank
you.

