Respiratory block
2016

Restrictive Lung Disease

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Restrictive Lung Disease

- Are a category of diseases that restrict lung expansion, resulting in a decreased total lung capacity (lung volume), increased work of breathing, and inadequate ventilation and/or oxygenation (decreased lung compliance).
- Both forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) are reduced with normal to high FEV1/VC and decreased Tco. The expiratory flow rate is near normal.
- have similar clinical and radiologic presentations.
- Their clinical features vary from mildly to severely symptomatic.
- The reduced lung volume is either because of an alteration in lung parenchyma or because of a disease of the pleura, chest wall, or neuromuscular apparatus.
- Stiff Lung

Restrictive Lung Disease

The restrictive lung diseases can be caused by or are divided into:

1. **Intrinsic lung diseases/ diseases of the lung parenchyma/primary interstitial lung disease:**

The diseases cause inflammation or scarring of the lung tissue (interstitial lung disease) or result in filling of the air spaces with exudate and debris (pneumonitis). They are characterized by inflammatory infiltrates in the interstitial space and the interstitium becomes thickened and therefore there is decreased oxygen-diffusing capacity. They are acute or chronic.

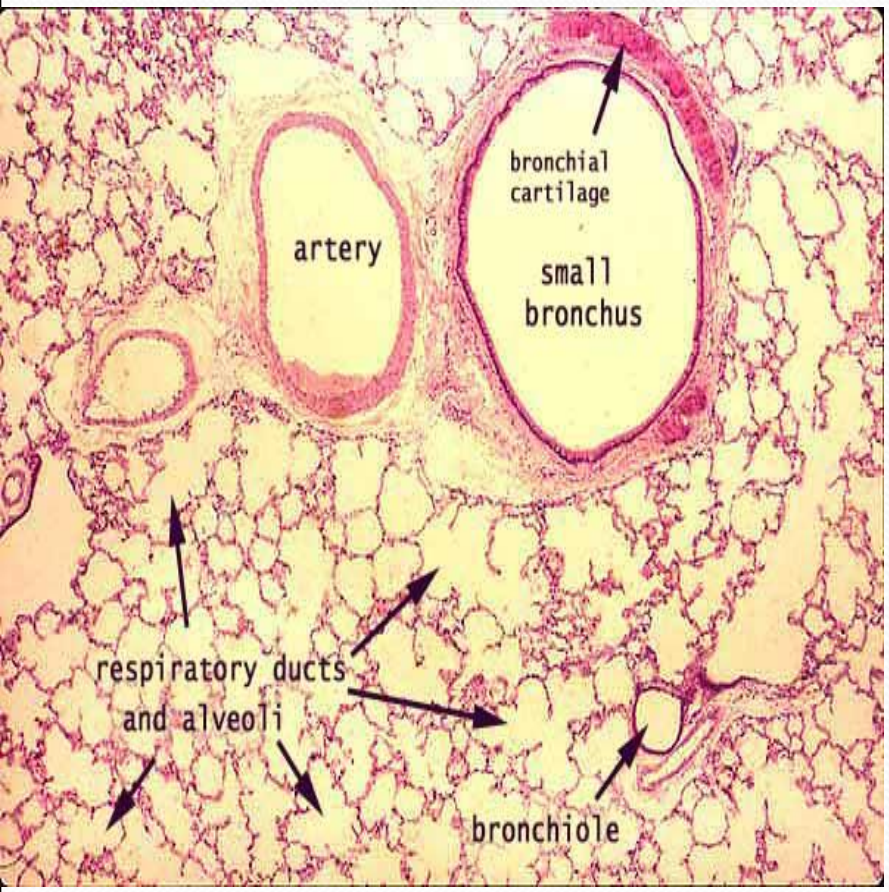
2. **Extrinsic disorders or extraparenchymal diseases:**

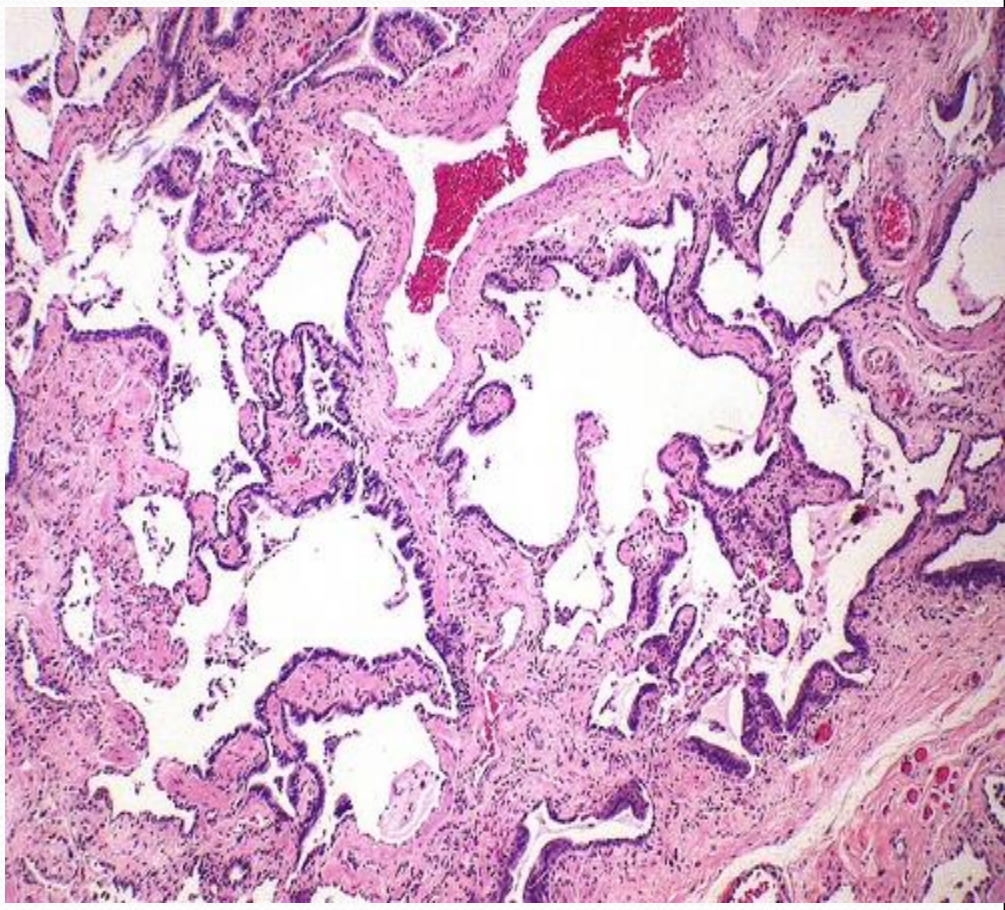
The chest wall, pleura, and respiratory muscles are the components of the respiratory pump, and they need to function normally for effective ventilation. Abnormalities of the chest wall include:

- bony abnormalities (kyphosis or kypho-scoliosis)
- massive pleural effusion,
- morbid obesity
- neuromuscular disease of respiratoy muscles results in respiratory muscle weakness and respiratory failure e.g. myopathy or myositis, quadriplegia, or phrenic neuropathy from infectious or metabolic causes

Intrinsic type of Restrictive lung diseases

- Characterized by reduced compliance of the lung.
- Important signs and symptoms:
  - Dyspnea.
  - Hypoxia.
  - In advanced cases of restrictive lung disease there severe hypoxia, hypercapnia and cyanosis respiratory failure and cor pulmonale.
- The final stage of all restrictive lung disease is extensive fibrosis with honeycomb lung. The lung becomes more solid.
- Honeycomb lung indicates end stage disease. In it both alveoli and bronchioles coalescence to form cysts lined with cuboidal or columnar epithelium and seperated by inflammatory fibrous tissue.
- It can be:
  - Acute.
  - Chronic.


bronchial
cartilage
artery
small
bronchus
respiratory ducts
and alveoli
bronchiole



Acute restrictive lung diseases (INTRINSIC TYPE)

1. **Adult respiratory distress syndromes**
2. **Neonatal respiratory distress syndromes**

Adult Respiratory Distress Syndrome

- ARDS is a severe form of acute lung injury with diffuse alveolar injury.
- It is also known as shock lung/ diffuse alveolar damage/ adult respiratory failure/acute alveolar injury/ traumatic wet lung
- It is:
  - rapid acute onset progressive severe life threatening respiratory insufficiency, cyanosis, severe arterial hypoxia
  - decreased arterial oxygen pressure
  - refractory to oxygen therapy and that may progress to multiorgan failure
  - bilateral pulmonary infiltrates (edema)
  - absence of evidence of left sided heart failure
- It is the most common cause of non- cardiogenic pulmonary edema

Adult respiratory distress syndromes (ARDS)

Can be caused by many conditions:

Direct injury to lung:

- Pneumonia,
- aspiration of gastric contents,
- pulmonary contusion/trauma,
- fat embolism
- near drowning
- toxic inhalation injury (irritants such as chlorine, oxygen toxicity)
- post lung transplant,
- severe acute respiratory syndrome (SARS). The SARS virus is a coronavirus that destroys the type II pneumocytes and causes diffuse alveolar damage.

Indirect injury to lung:

- Sepsis,
- severe trauma (e.g. bone fractures, head injury, burns, radiation)
- shock,
- cardiopulmonary bypass,
- acute pancreatitis
- transfusion, uremia
- overdose with street drugs such as heroin, therapeutic drugs such as bleomycin
- Hematologic conditions e.g multiple transfusion, coagulation disorders

Pneumonia and sepsis are the most common causes

Adult Respiratory Distress Syndrome

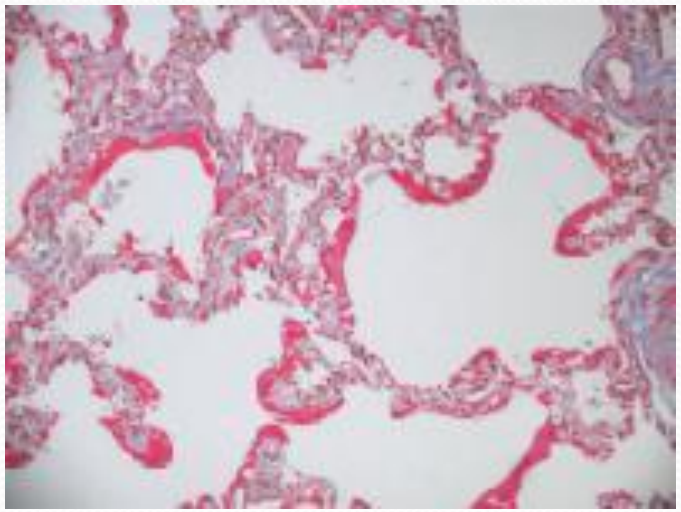
Pathophysiology

- ARDS is associated with diffuse alveolar damage.
- It is initiated by injury to
  - alveolar capillary endothelium a with resultant increase in alveolar capillary permeability and
  - alveolar epithelium,
- The injury is induced by the:

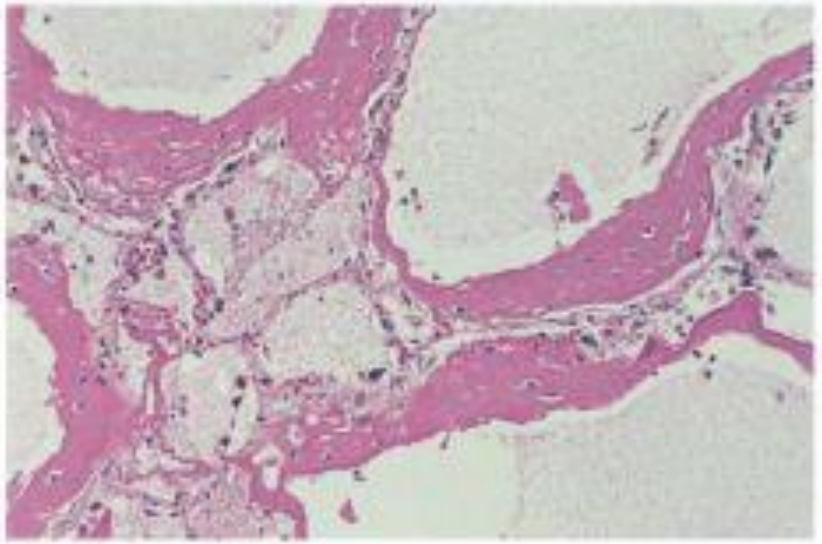
(a) Neutrophils releasing substances toxic to the alveolar wall.

(b) Activation of the coagulation cascade.

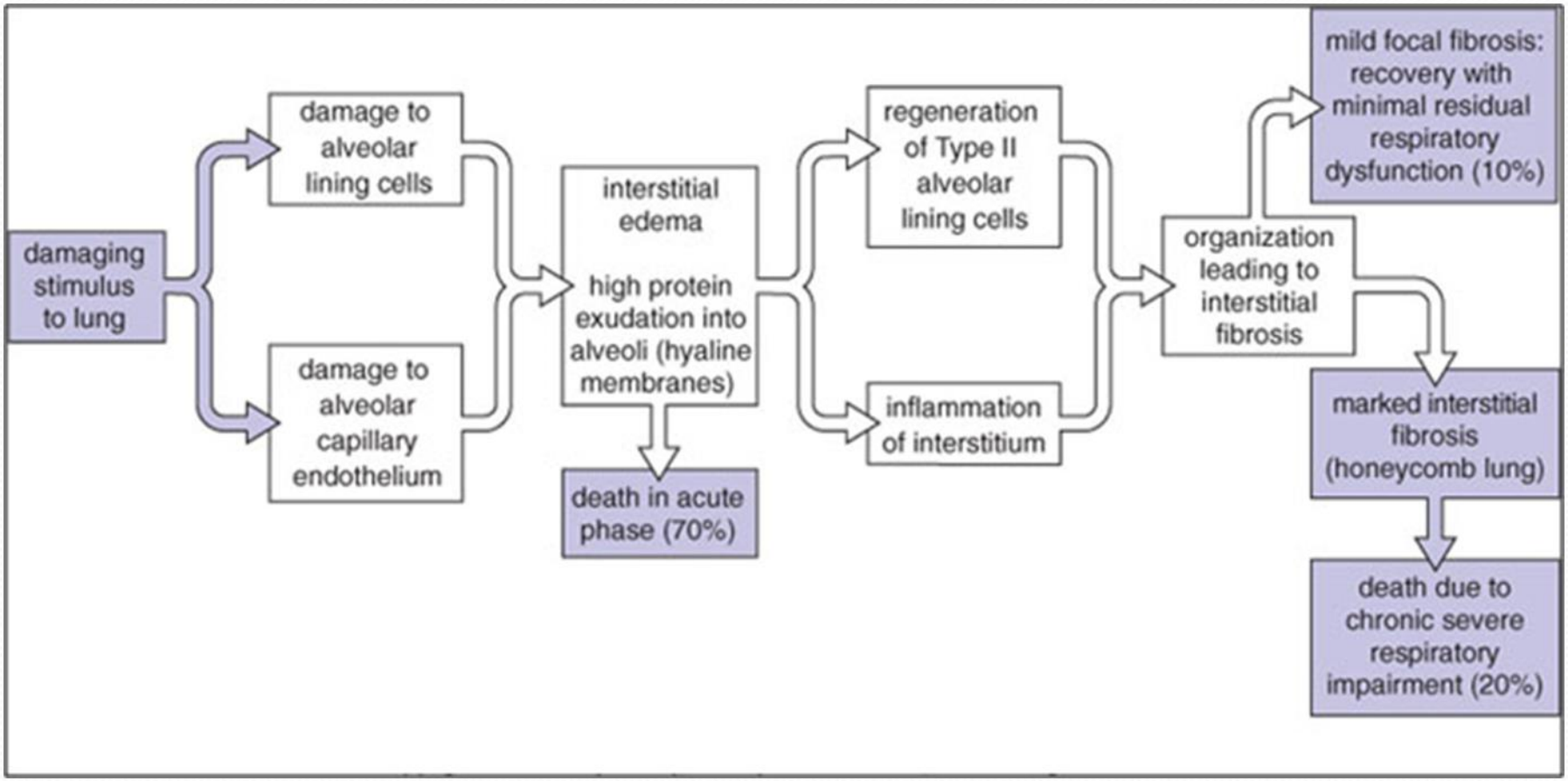
(c) Oxygen toxicity (due to formation of free radicals).



- this causes leakage of protein-rich fluid into alveoli, formation of characteristic alveolar hyaline membrane lining the inner surface of alveoli, the membrane is composed of fibrin and cellular debris.
- the lungs become remarkably heavy and stiff due to inflammation and odema and eventually there is interstitial fibrosis.



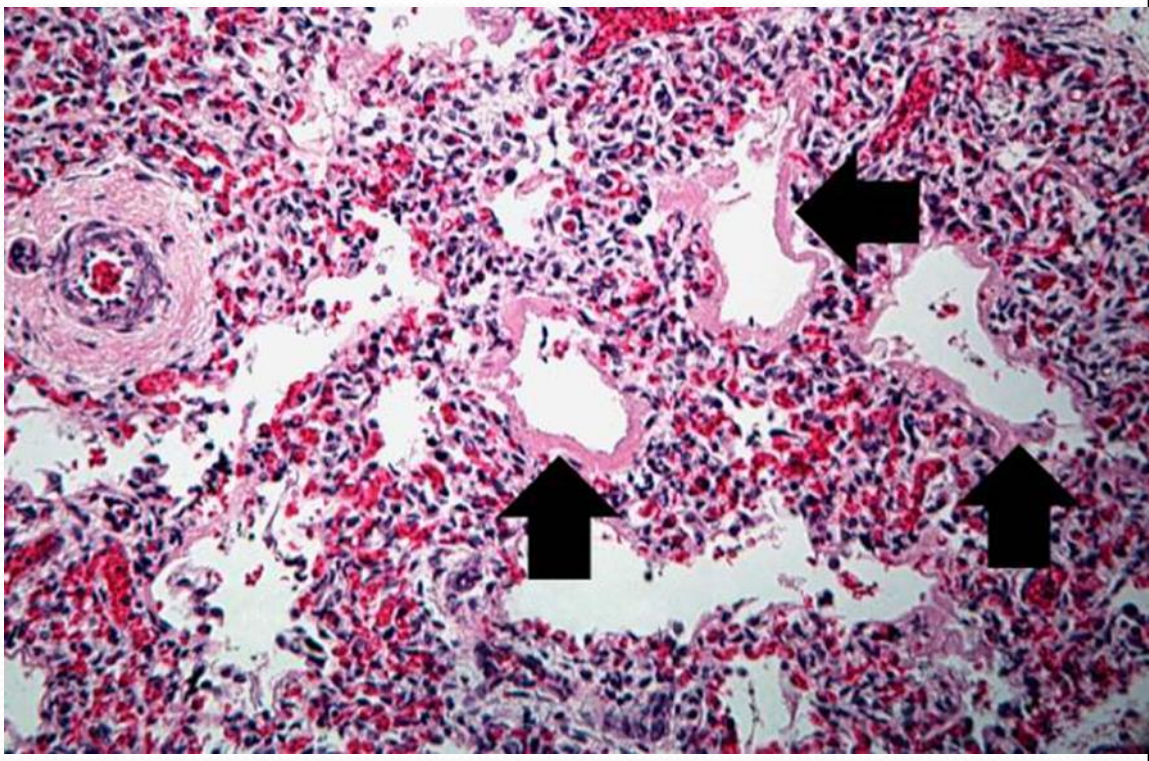
The picture below depicts the main events and outcomes of ARDS



- Mortality was 100%
- Now 30 -40% with good ICU support
- Poor prognosis: old age, multisystem failure, high level of IL-1

Neonatal Respiratory Distress Syndrome/Hyaline membrane disease

- It is the most common cause of respiratory failure in the newborn and is the most common cause of death in premature infants.
- It is the same as ARDS except that it is caused by a deficiency of pulmonary surfactants in new borns, most often as a result of immaturity.
- It too results in diffuse alveolar damage with the development of a hyaline membrane lining the alveoli.
- This syndrome is marked by dyspnea, cyanosis and tachypnea shortly after birth.

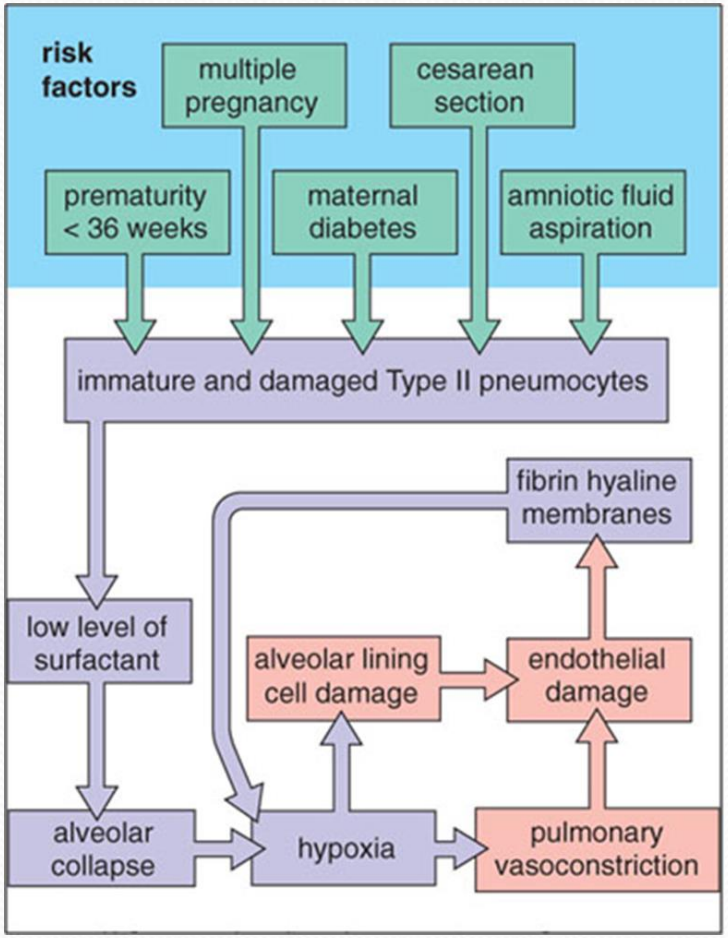


Neonatal respiratory distress syndromes

(HYALINE MEMBRANE DISEASE)

Predisposing Risk factors:

- **Prematurity.**
- **Maternal diabetes mellitus**
- **delivery by cesarean section.**
- **Amniotic fluid aspiration**
- **multiple birth**



Pathogenesis of NRDS.

Chronic restrictive lung disease

(INTRINSIC TYPE)

Chronic restrictive lung disease (INTRINSIC TYPE)

Definition

- Are a heterogenous group of diseases.
- Many entities are of unknown cause and pathogenesis.
- They have similar clinical signs, symptoms, radiographic alterations and pathophysiologic changes.
- Account for about 15% of non-infectious lung diseases.
- End-stage: diffuse interstitial pulmonary fibrosis

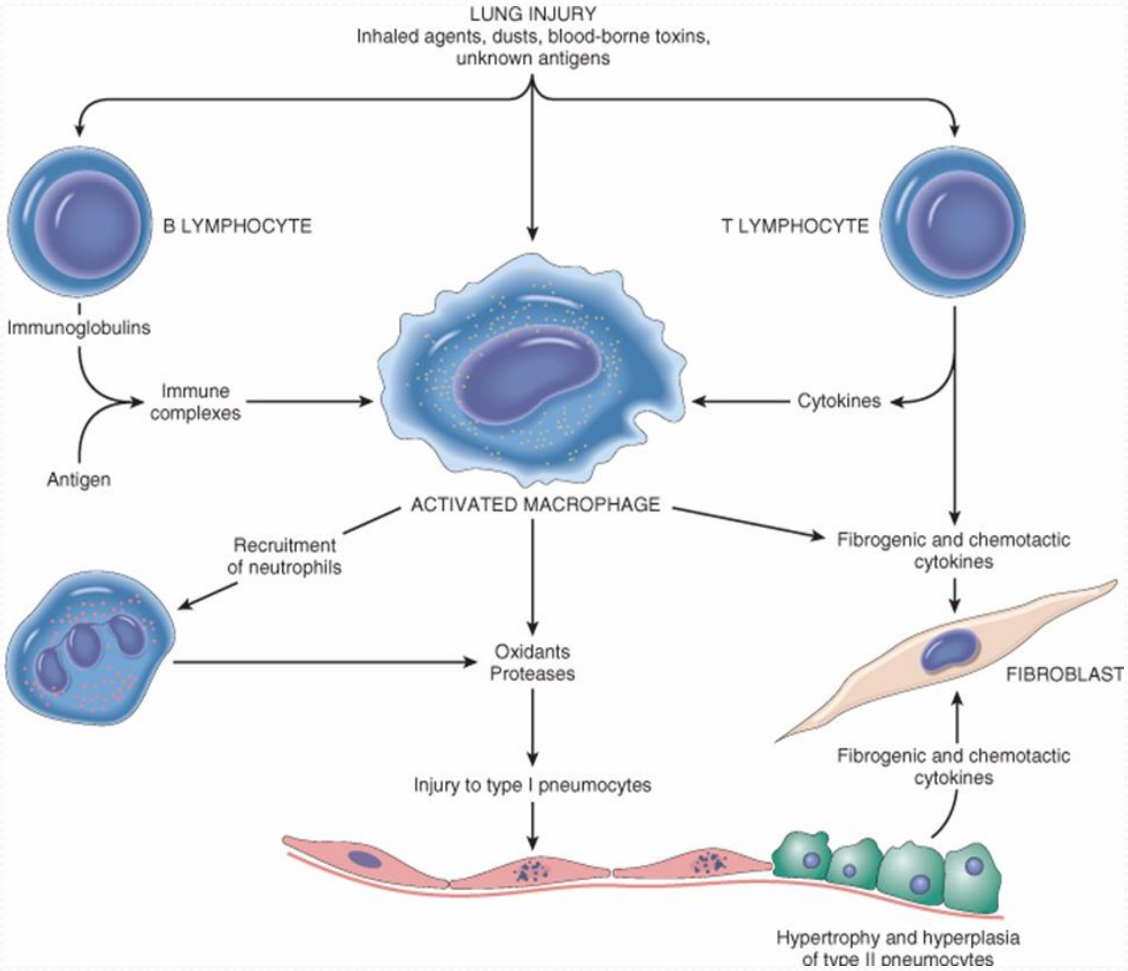
Chronic restrictive lung disease

Major Categories of Chronic Interstitial Lung Disease

- Occupational: **Pneumoconiosis**
  - **anthracosis and coal worker's pneumoconiosis,**
  - **silicosis**
  - **asbestosis**
- Fibrosing:
  - **Usual interstitial pneumonia (idiopathic pulmonary fibrosis)**
- Immune diseases:
  - **Sarcoidosis**
  - **Goodpasture syndrome**
  - **Hypersensitibity pneumonitis(extrinsic allergic alveolitis)**
  - systemic lupus erythematosus
  - systemic sclerosis (scleroderma)
  - Wegener granulomatosis
- Drug: Chemotherapy, methotrexate, bleomyxin toxicity
- Radiation Reactions
- Smoking related:
  - **Eosinophilic granuloma**
  - Desquamative interstitial pneumonia
  - Respiratory bronchiolitis-associated interstitial lung disease

Pathogenesis of intrinsic chronic interstitial lung diseases

- Influx of inflammatory cells into the alveoli and alveolar walls
- Distortion of the normal structure of alveoli
- Release of chemical mediators
- Promotion of fibrosis



Pneumoconiosis

- Pneumoconiosis is a group of pulmonary diseases caused by chronic exposure to inorganic mineral dust inhalation and this leads to lung damage.
- More than 40 inhaled minerals can cause lung problems.
- They include **carbon dust, silica, asbestos**, beryllium etc.
- Pathophysiology:
  - Alveolar macrophages ingest the particles, become activated, and release cytokines and chemotactic factors that recruit other inflammatory cells.
  - The ensuing inflammation damages lung cells and also damages the interstitium of the lung by degrading the extracellular matrix glycoproteins.
  - The inhaled particles also stimulate the fibroblasts to proliferate and produce collagen; fibrosis results.
  - As the disease progresses the blood vessels become compromised, and ischemic necrosis ensues.

Pneumoconiosis

The development of pneumoconiosis is dependent on:

- The amount of dust retained in the lung and airways.
    a. Concentration of the dust in the ambient air.
    b. Duration of the exposure.
    c. Effectiveness of the clearance mechanisms.
- The size (1-5μ) shape.
- Their solubility and physiochemical activity.
- The possible additional effects of other irritants, tobacco smoking.

Coal Worker's Pneumoconiosis

- Coal worker's pneumoconiosis (CWP) can be defined as the accumulation of coal dust in the lungs and the tissue's reaction to its presence.
- The disease is divided into 2 categories:

1. simple coal worker’s pneumoconiosis
2. complicated coal worker’s pneumoconiosis (CCWP), or pulmonary massive fibrosis (PMF), depending on the extent of the disease.

- Pulmonary massive fibrosis in association with rheumatoid arthritis is known as Caplan syndrome.

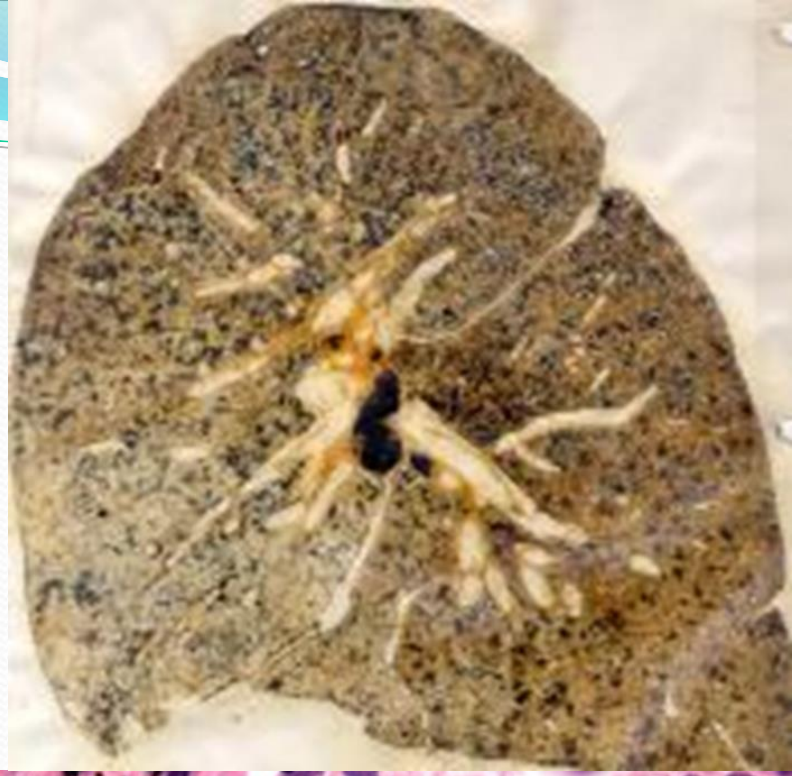
Simple Coal worker pneumoconiosis

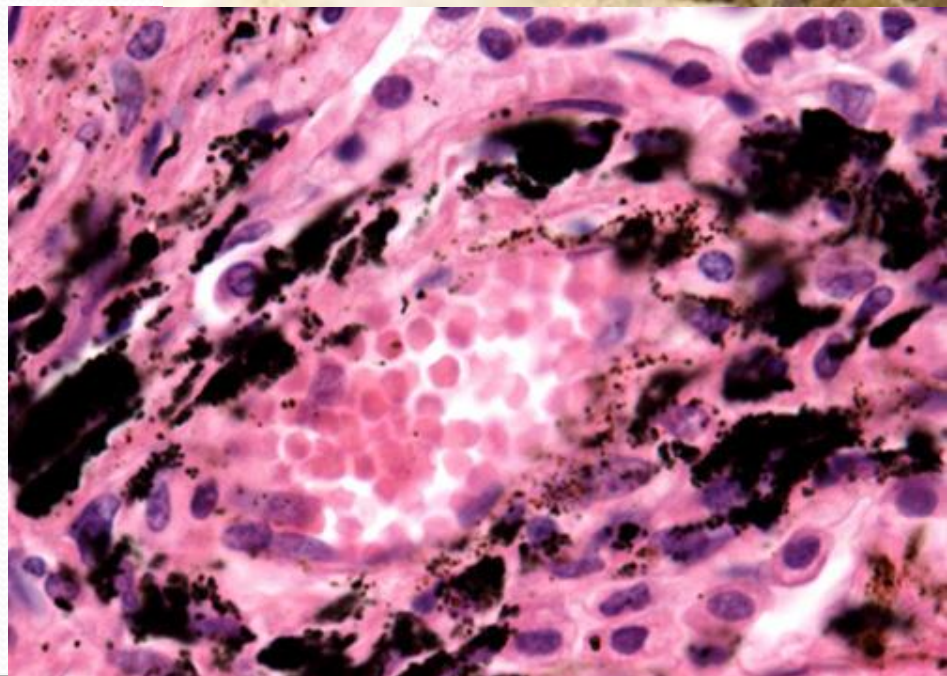
Morphology:

-Focal aggregations of black coal dust-laden macrophages (coal macules)1 to 5 mm are scattered through the lung.

- Mostly in the upper zones of the lower and upper lobes of the lungs.

-Patients have slight cough and blackish sputum

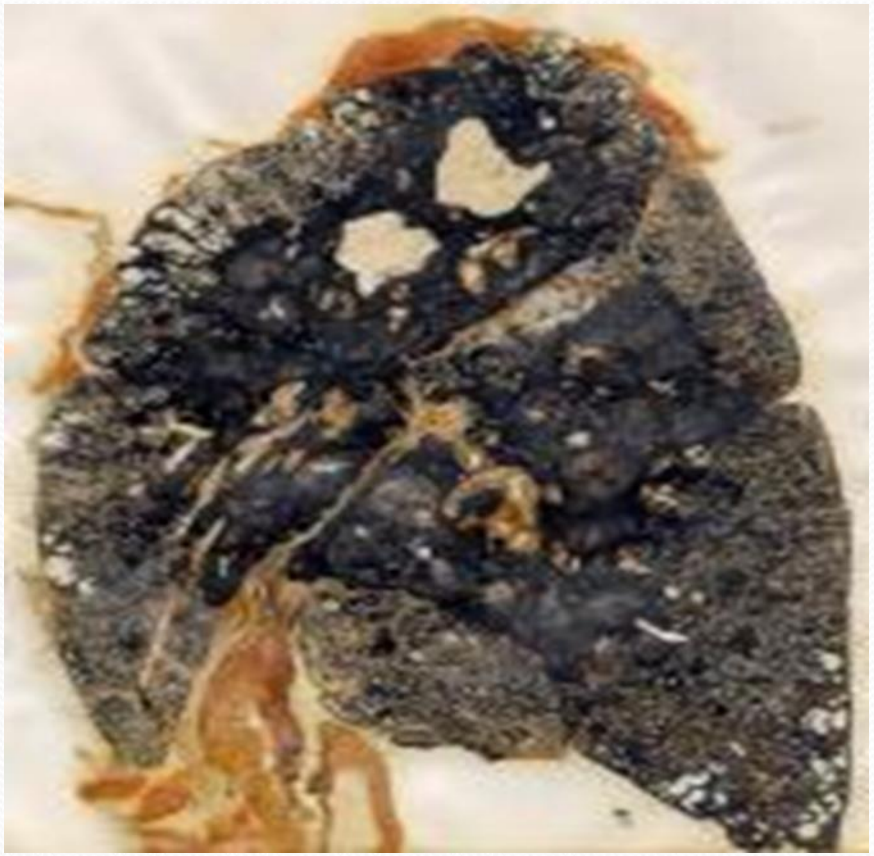




Complicated Coal worker pneumoconiosis

Morphology

- Occurs after many years of underground mine work.
- fibrous scarring appears (complicated CWP) also callled progressive massive fibrosis
- Black scars exceed 2 cm in diameter some times up to 10 cm
- It consists of dense collagen and carbon pigments.
- Miners who have rheumatoid arthritis and PMF are called Caplan's syndrome.
- Complicated coal worker's pneumoconiosis produces cough, dyspnea, and lung function impairment.
- In advanced cases cor pulmonale with right ventricular failure may develop



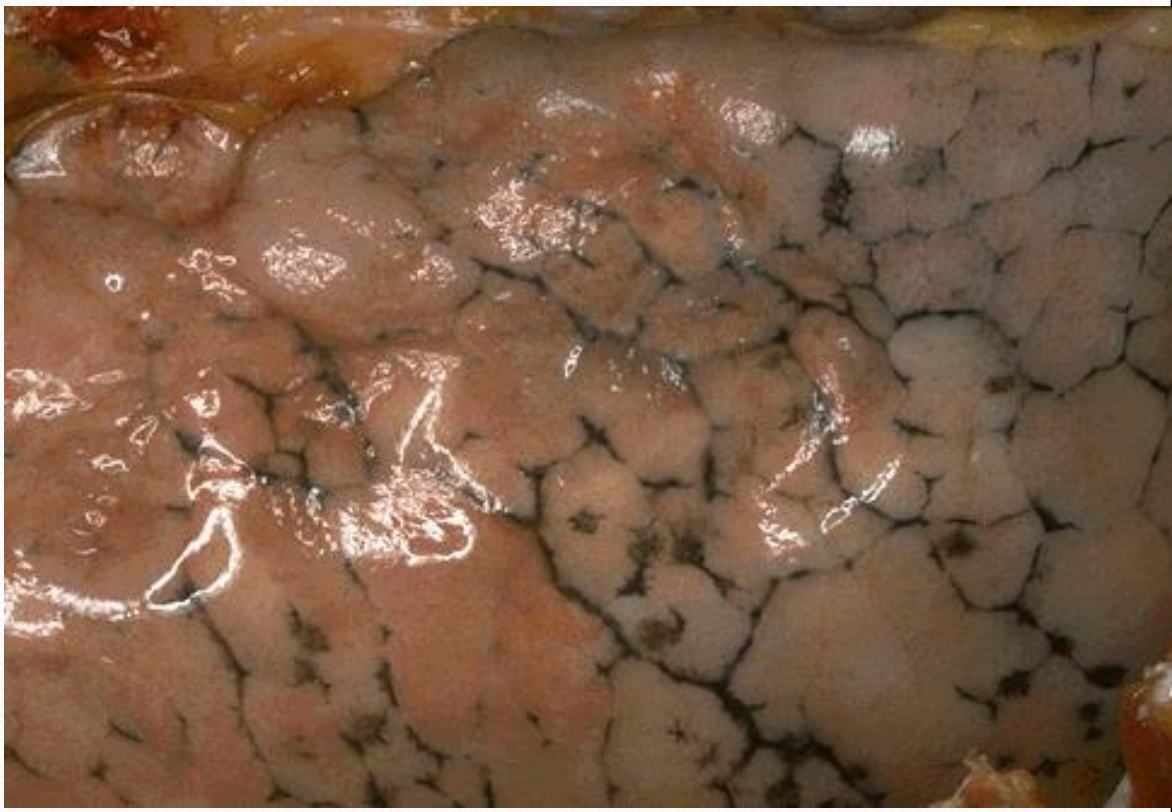
Healthy Tissue

Healthy Tissue
90-year-old
schoolteacher

Progressive
massive fibrosis
40-year-old-miner

Anthracosis

- **Anthracosis** is the asymptomatic accumulation of coal pigment/carbon particles without consequent cellular reaction. Such accumulation can be found in varying degrees among most urban dwellers and in tobacco smokers. Inhaled coal dust enters the terminal bronchioles, and the carbon pigment is engulfed by alveolar and interstitial macrophages.

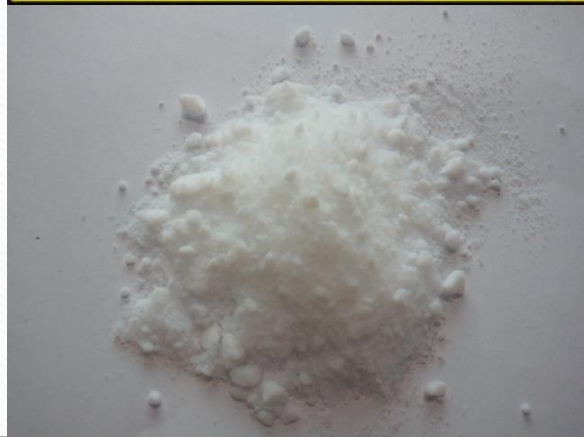


Silicosis

- Silicosis is a fibro-nodular lung disease caused by long term exposure to inhalation of dust containing crystalline silica particles (alpha-quartz or silicon dioxide).
- Encountered in industries: mining of gold, tin, copper and coal, sandblasting, metal grinding, ceramic manufacturing.
- The more common chronic forms manifest after several years of exposure. The symptoms may be indolent or progressive. Chronic silicosis can lead to complicated progressive massive fibrosis. Symptoms often manifest only 1 to 3 decades after initial exposure.
- Silicosis predispose to lung cancer and tuberculosis.

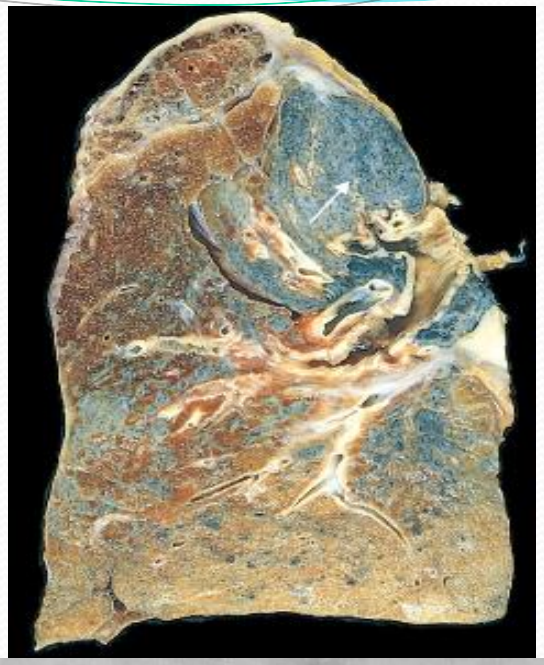
Pathogenesis:

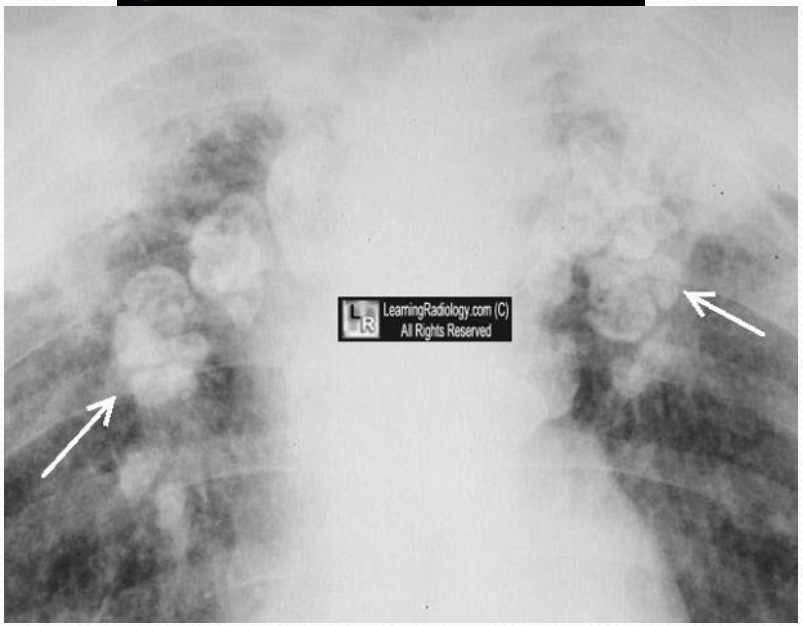
- Crystalline silica is highly fibrogenic.
- Scattered lymphocytes and macrophages are drawn rapidly with fibrosis.
- Some particles are transported to lymph nodes.



Morphology of Silicosis

- Tiny collagenous nodules that enlarge forming stony-hard large fibrous scars usually in the upper lobes.
- The lung parenchyma between the scars may be compressed or emphysematous.
- Calcifications may appear (eggshell calcification) .
- Similar collagenous nodules within the lymph nodes.
- Fibrous pleural plaques may develop.





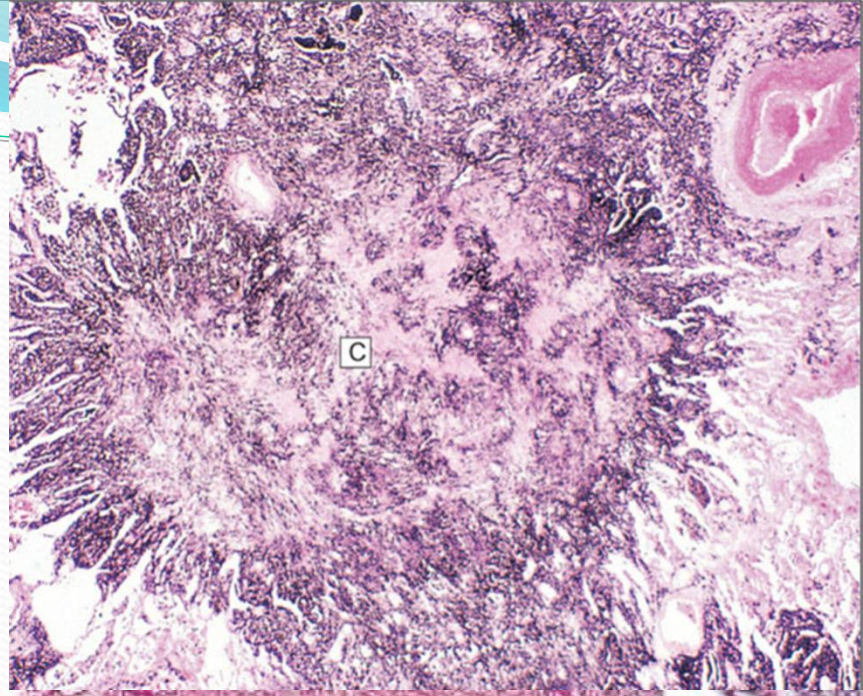
Morphology of Silicosis

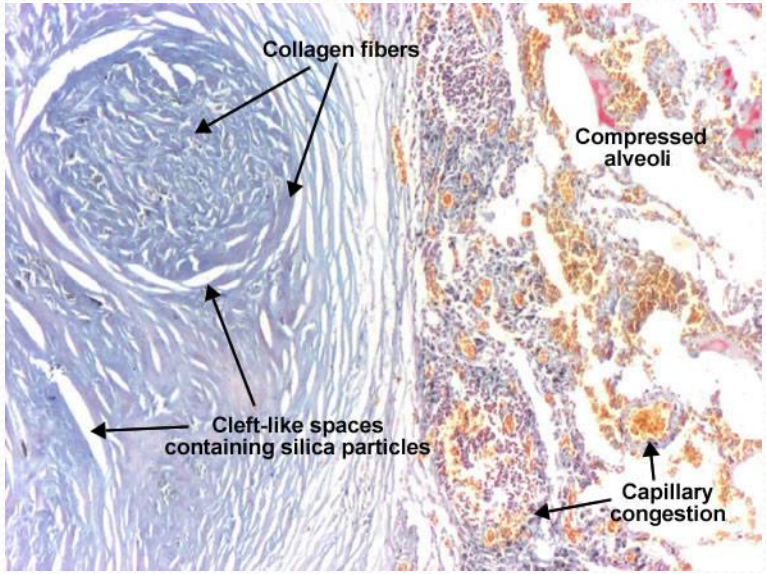
-Hyalinized collagen fiber surround an amorphous center (fibrous nodules).

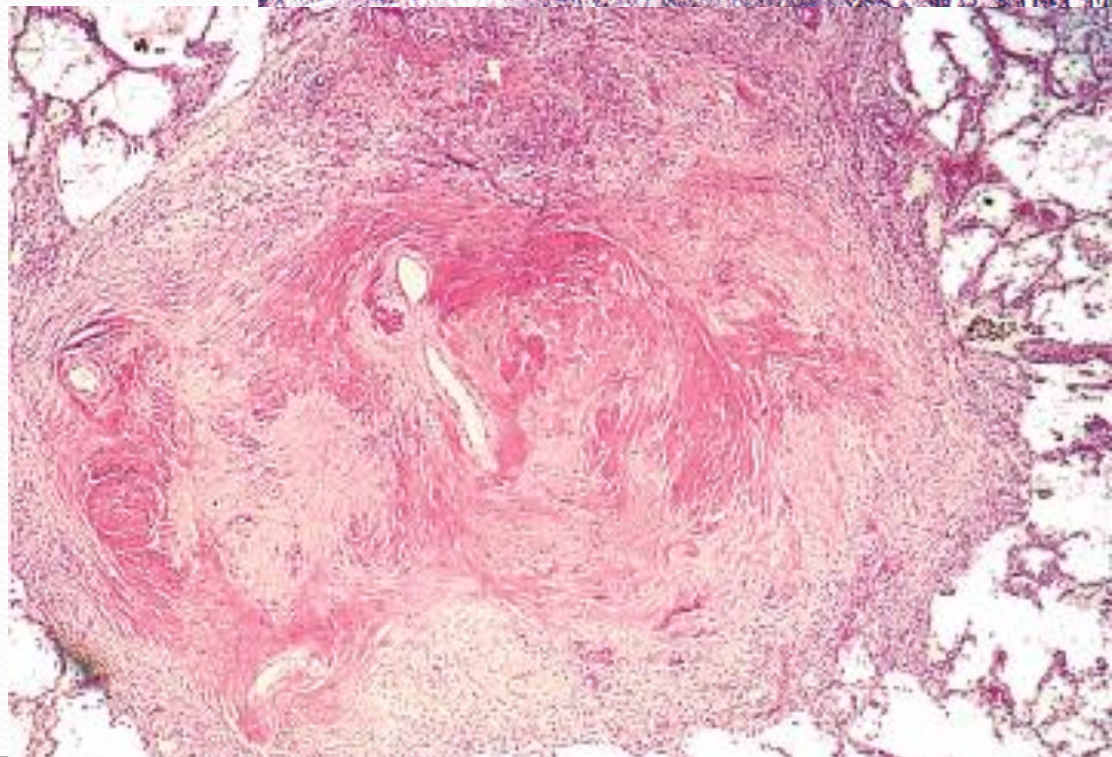
- Scarring progress to PMF.

-Scarring extending and encroching the pulmonary arteries.

-Cor pulmonale.

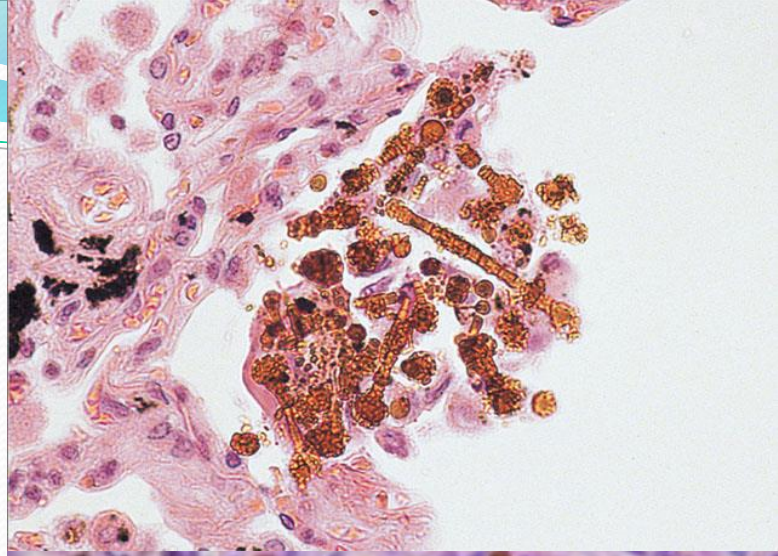


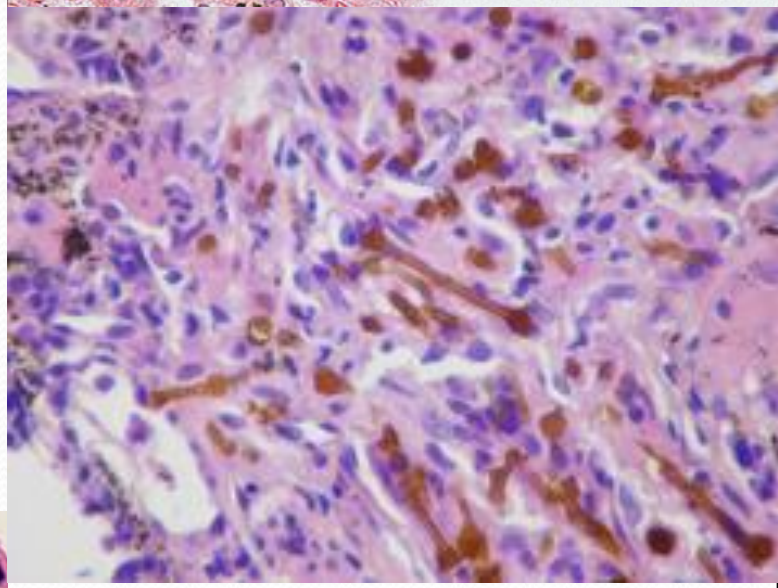


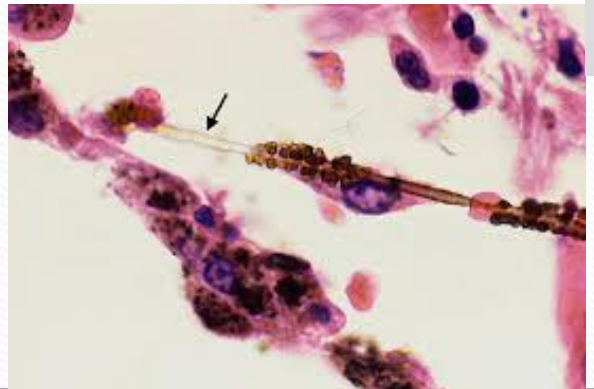


Asbestosis

- Pneumoconiosis caused by asbestos inhalation is called asbestosis.
- Asbestos is a group of naturally occurring, heat-resistant fibrous silicates. Asbestos fibers are long and thin. They can curved or straight.
- All types of asbestos (crocidolite and amosite) are fibrogenic to lungs.
- **Asbestosis** occurs decades after exposure has ended.
- Characterized by scars containing asbestos bodies.
- They can cause
  - pleural effusion.
  - pleural adhesions.
  - parietal pleural fibrocalcific plaques
  - Some types of asbestos are carcinogenic (especially crocidolite) and prolong asbestos exposure can predisposes to bronchogenic carcinoma and malignant mesothelioma.

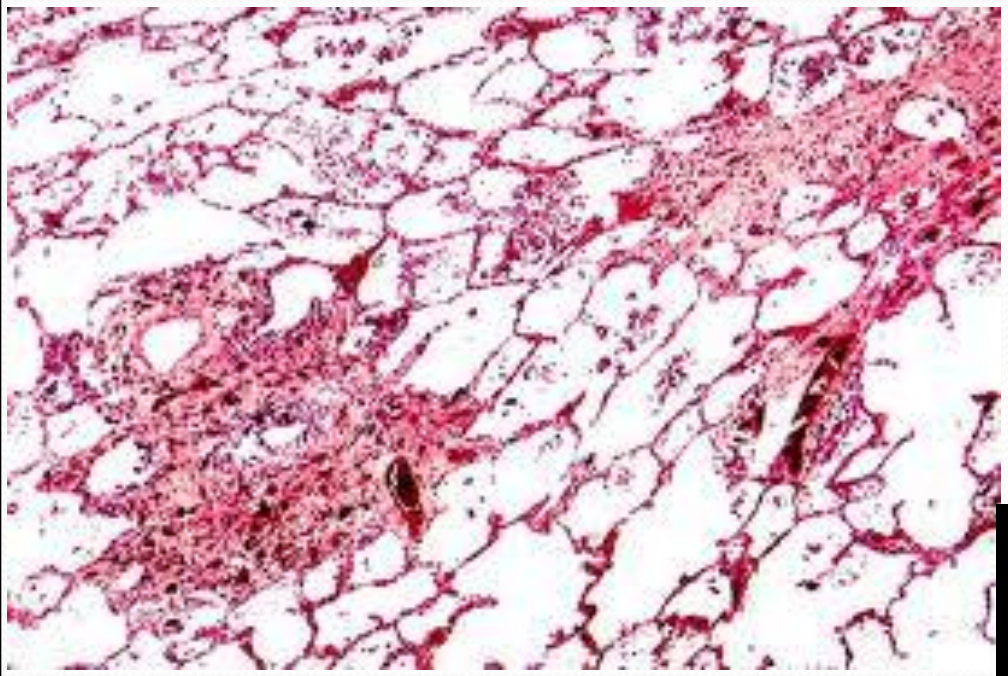




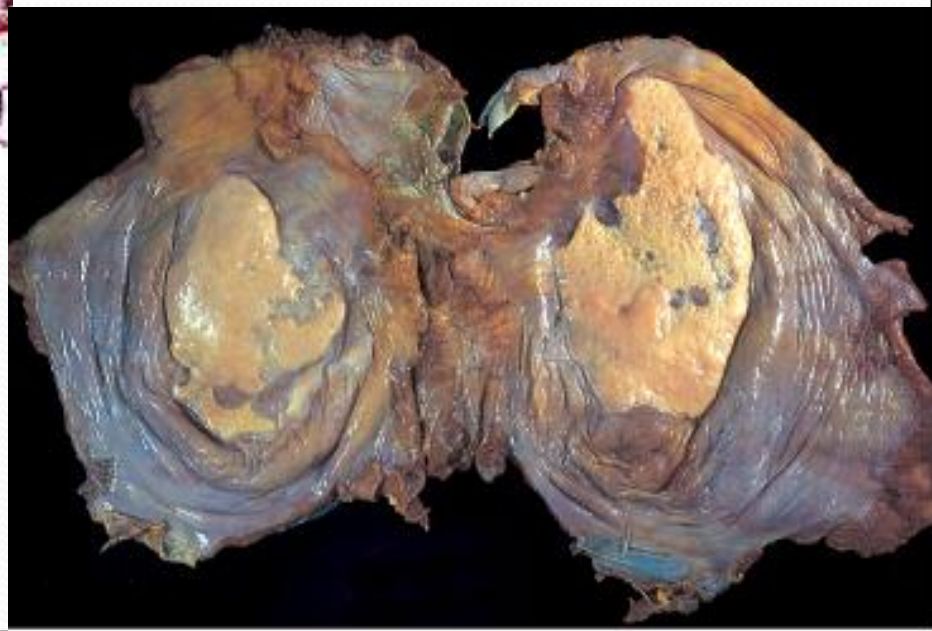


Asbestos bodies are long, thin asbestos fibers coated with hemosiderin and protein to form brown filaments with a beaded or drumstick pattern.

- scarring containing asbestos bodies.



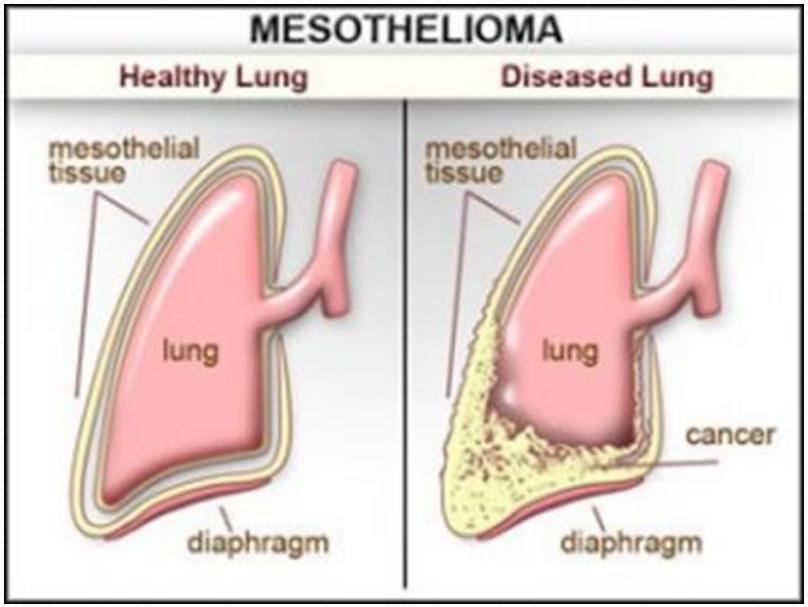
- parietal pleural fibrocalcific plaques

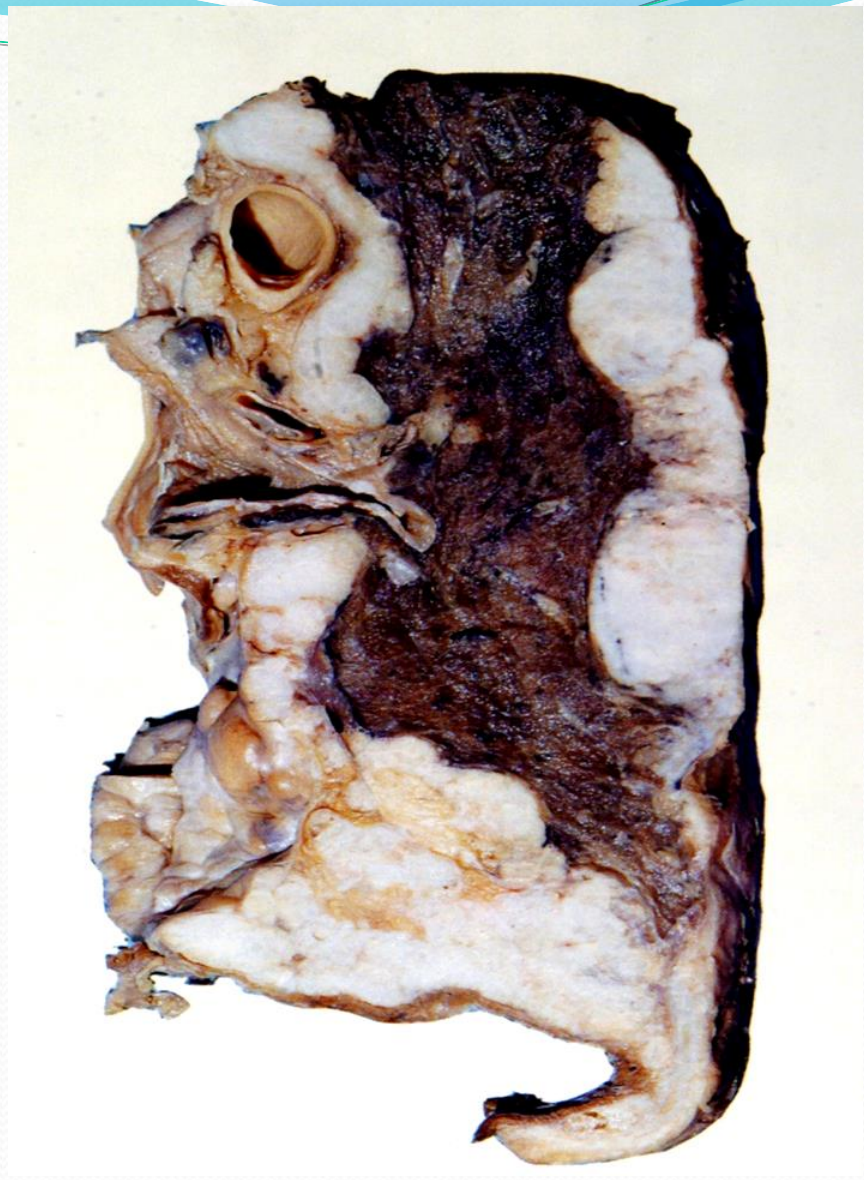


Asbestosis

- Both bronchogenic carcinoma and mesothelioma develop in workers exposed to asbestos.

The risk of bronchogenic carcinoma is fivefold and for mesothelioma is 1000 fold greater





Pleural mesothelioma

Asbestosis

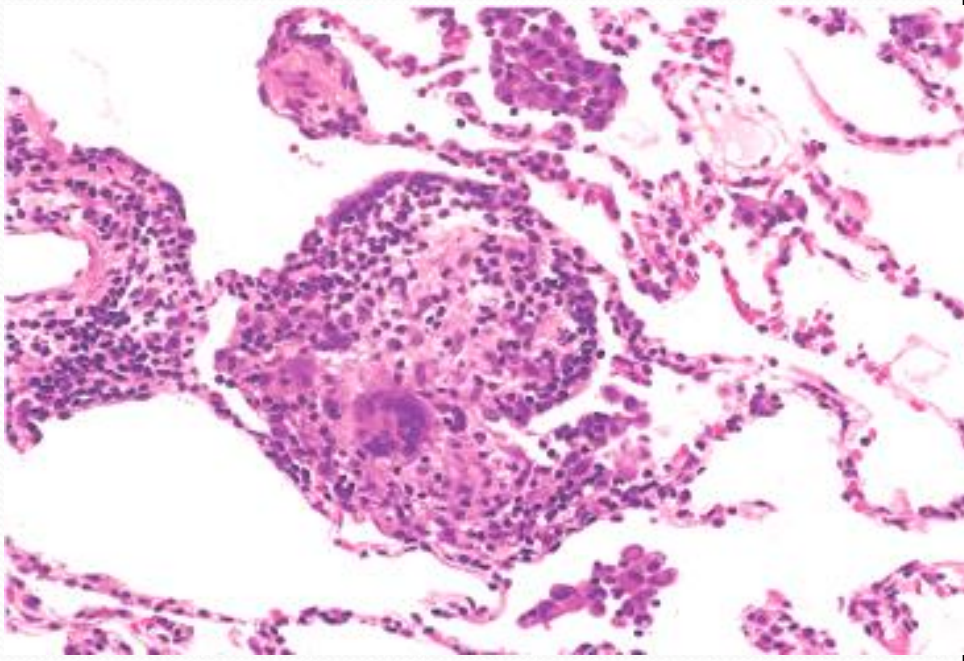
- Products containing asbestos are - Pipes, sheets, vinyl-asbestos floor tiles, asbestos paper in filtering and insulating products, textile products etc.
- Therefore the people in the following occupations are at risk: Insulation workers, boilermakers, pipefitters, plumbers etc.
- Symptoms usually appear after a latent period of 20 years or longer. This latent period may be shorter after intense exposure.
- Dyspnea upon exertion is the most common symptom and worsens as the disease progresses. Patients may have a dry cough and chest discomfort.

Hypersensitivity pneumonitis

- Hypersensitivity pneumonitis an immunologically mediated (type III and IV)interstitial lung disease caused by intense and often prolonged exposure to inhaled organic dust(i.e. dusts containing organic antigens).
- An immunologically mediated inflammatory lung disease primarily affects the alveoli and is therefore often called allergic alveolitis.
- These dusts come from sources such as dairy and grain products, animal droppings and animal proteins etc. Poultry and other bird handlers are commonly exposed to droppings, feathers, and serum proteins of pigeons etc.
- The most common antigens are thermophilic *Actinomycetes* species and avian proteins and the most common diseases are farmer's lung and bird fancier's/handler's lung.
- It is an occupational restrictive disease

Hypersensitivity Pneumonitis

- It is characterized by diffuse inflammation of lung parenchyma and airways in previously sensitized persons.
- Hypersensitivity pneumonitis can present as acute, subacute (intermittent) or chronic progressive.
- Morphology: is characterized by noncaseating interstitial granulomas (IV hypersensitivity reaction), bronchiolitis, interstitial pneumonitis, and diffuse interstitial fibrosis.
- Clinical course is variable



Hypersensitivity pneumonitis

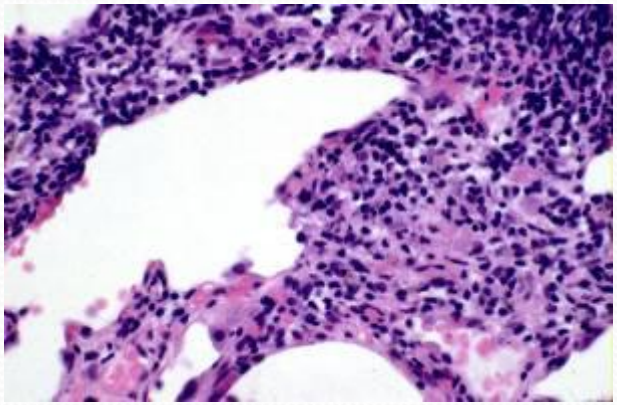
- **Immunologically mediated disorder affecting airways and interstitium.**

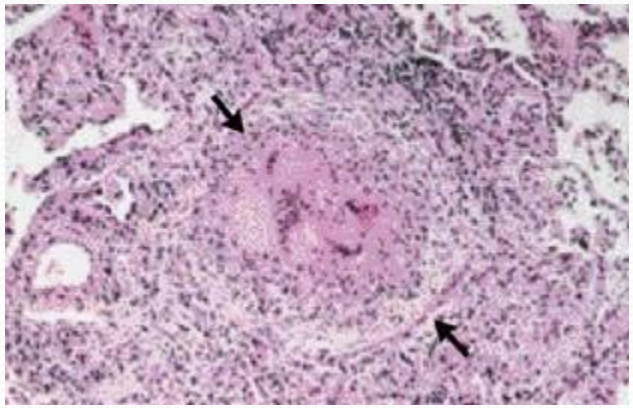
Farmer's lung
Thermophilic actinomycetes in hay

Pigeon breeder's

Air-condition lung
Thermophilic bacteria

Sugarcane bagasse
(Bagassosis)



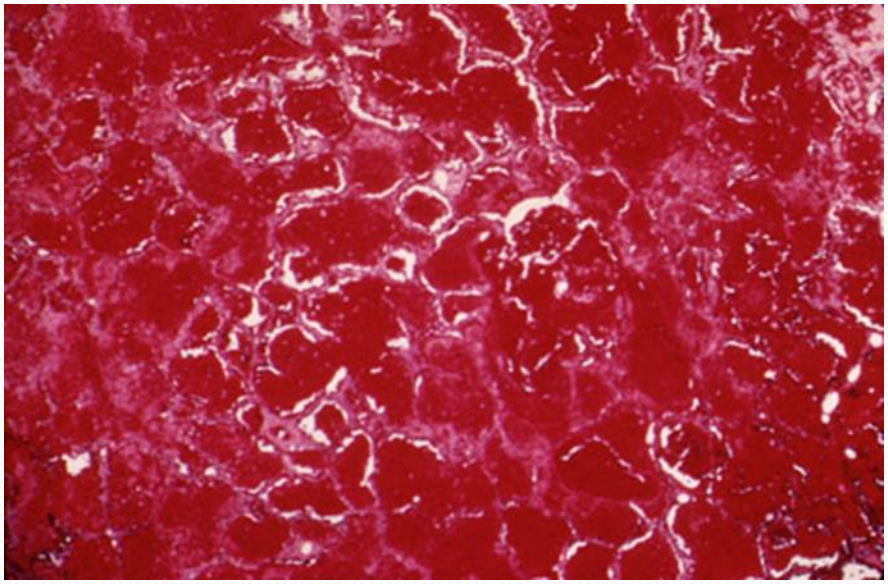


Goodpasture Syndrome/ Anti-GBM disease

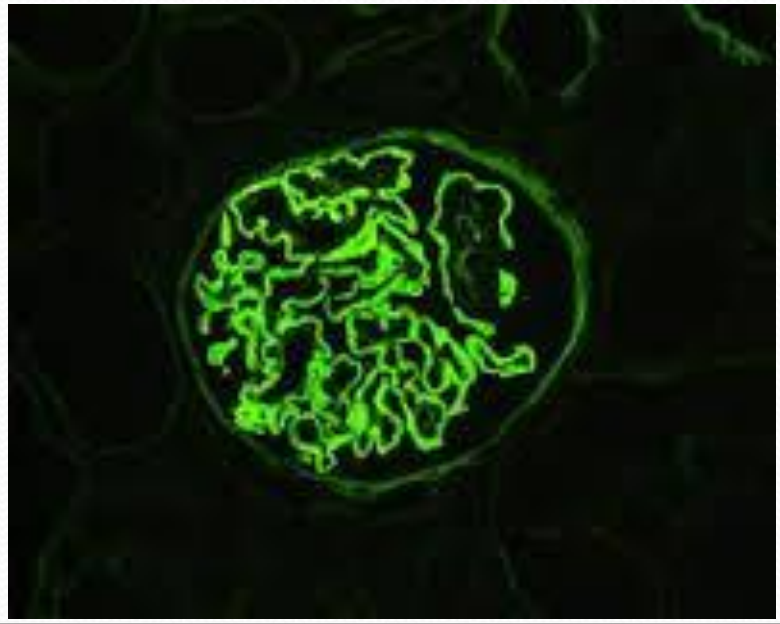
- Rare disease
- Is a triad of
  - diffuse pulmonary hemorrhage,
  - glomerulonephritis,
  - circulating anti-alveolar and anti-glomerular basement membrane (anti-GBM) antibodies
- Anti-GBM disease is an autoimmune disorder.
- The anti-GBM antibody can usually be found in serum.
- Most of the patients have pulmonary symptoms (hemoptysis and dyspnea) and renal symptoms (hematuria, proteinuria, red cell casts and renal failure) and arthralgias.
- The lung will show features of acute necrotizing alveolitis with marked hemorrhage.
- Kidney may show rapidly progressive glomerulonephritis that may lead to renal failure.

Goodpasture syndrome

Iron stain in sputum



Immunofluorescence of renal biopsy staining for IgG in a linear pattern in patient with anti-glomerular basement membrane (anti-GBM) disease

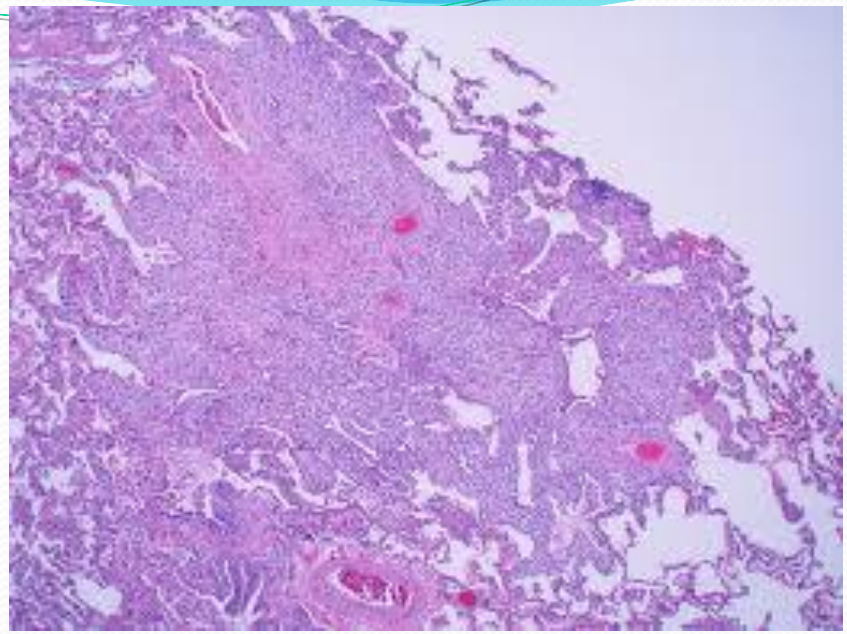


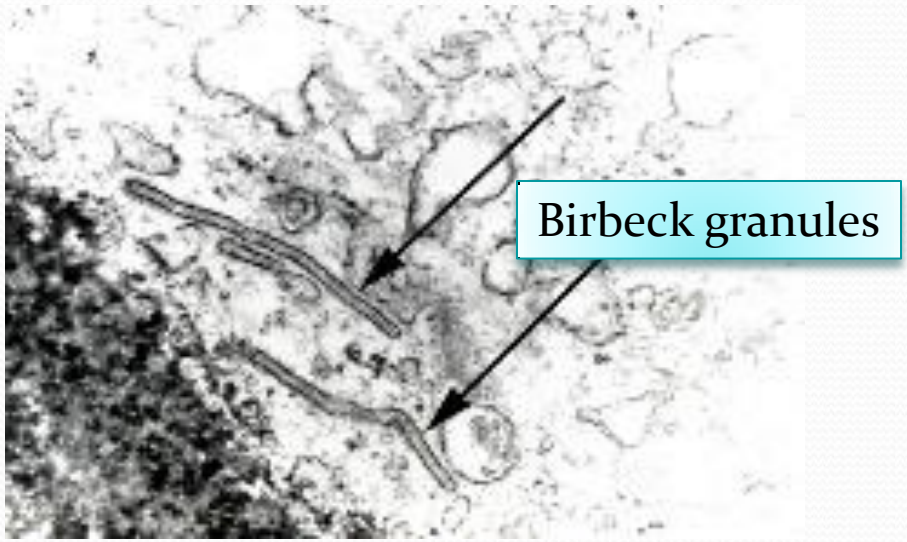
Eosinophilic Granuloma/pulmonary histiocytosis X/pulmonary Langerhan cell histiocytosis X

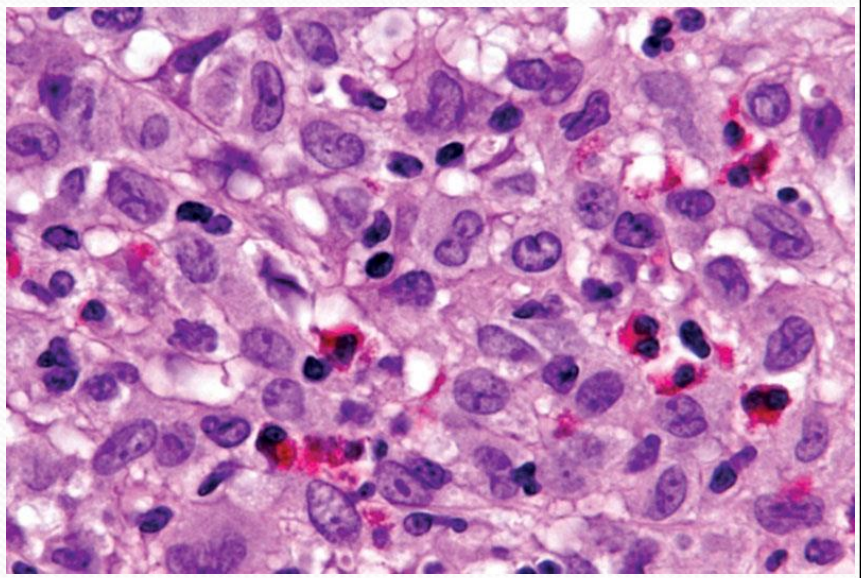
- is an uncommon interstitial lung disease in which there is accumulation of Langerhans cells in the lungs.
- It is considered as a form of smoking-related interstitial lung disease.
- Some patients recover completely after they stop smoking, but others develop long-term complications such as pulmonary fibrosis and pulmonary hypertension.
- It chiefly affects young adults in the third or fourth decades of life.
- It is a localized form of Langerhan cell histiocytosis.
- It commonly involves the lungs. Other organ systems like bone, skin and lymph nodes may also be affected.

Eosinophilic Granuloma

- In pulmonary Langerhans cell histiocytosis X there is infiltration of the lungs by activated Langerhans cells and eosinophils. They form nodules around the bronchioles, causing destruction of the airway walls. In late stages of the disease, fibrotic stellate scarring.
- They may be identified by immunohistochemical staining with CD1a or by the presence of rod like Birbeck granules via electron microscopy.







Idiopathic Pulmonary Fibrosis/ usual interstitial pneumonia/ fibrosing alveolitis/ Hamman-Rich syndrome

UIP

Idiopathic Pulmonary Fibrosis/ usual interstitial pneumonia/ fibrosing alveolitis/ Hamman-Rich syndrome (UIP)

- UIP is progressive fibrosing disorder of unknown cause. It is an idiopathic interstitial pneumonia with diffuse interstitial fibrosis and inflammation.
- Adults 30 to 50 years

- It has a poor prognosis. Respiratory and heart failure may develop within few years. No effective therapy is available for the treatment of idiopathic pulmonary fibrosis. Lung transplant is the only solution.

Etiology

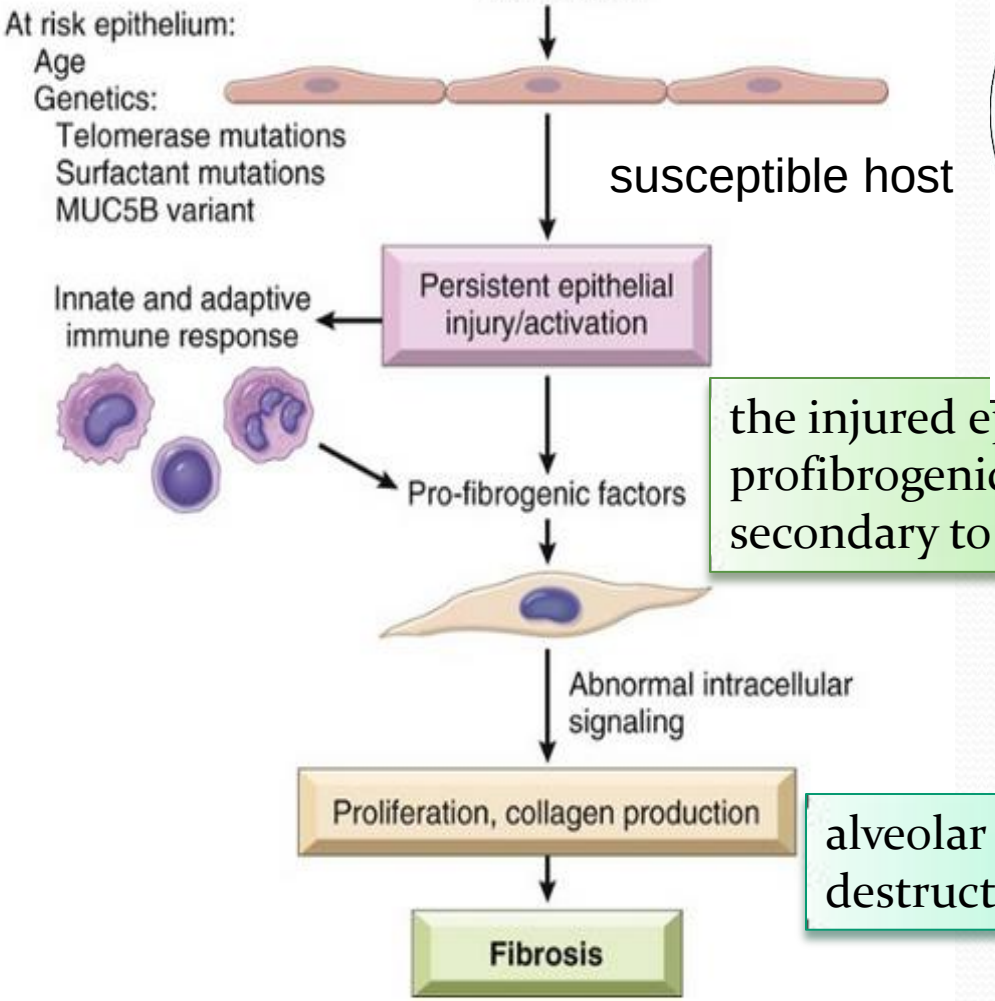
Idiopathic Pulmonary Fibrosis/ usual interstitial pneumonia/ fibrosing alveolitis/ Hamman-Rich syndrome (UIP)

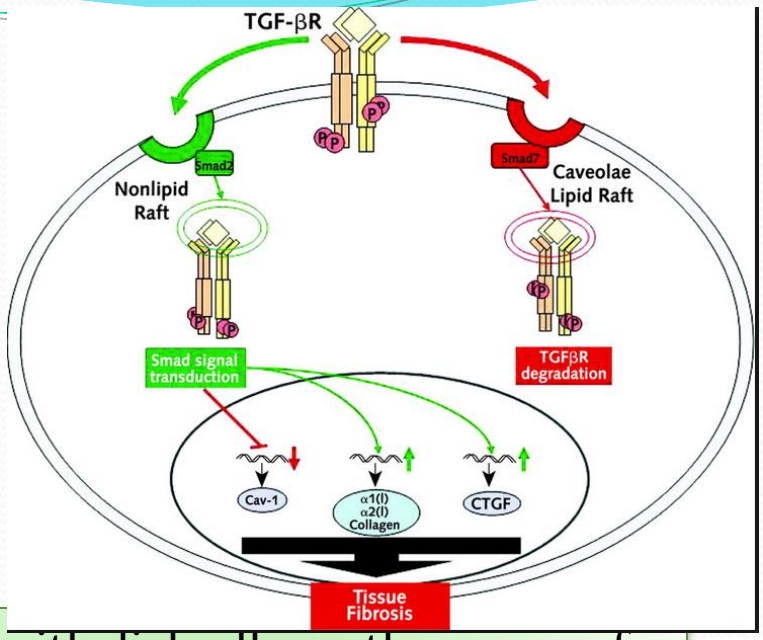
The etiology of UIP remains undefined. The current hypothesis is that:

1. Exposure to an inciting agent (eg. smoke, environmental pollutants, dust, viral infections, gastroesophageal reflux disease etc) in a susceptible host leads to alveolar damage, fibrosis and irreversible destruction of the lung parenchyma.
2. Some idiopathic pulmonary fibrosis are familial.
3. Certain medication drugs (bleomycin, and nitrofurantoin) are associated with development of pulmonary fibrosis.

Pathogenesis of Idiopathic Pulmonary Fibrosis/ usual interstitial pneumonia/ fibrosing alveolitis/ Hamman-Rich syndrome (UIP)

smoke, environmental pollutants, dust, viral infections, gastroesophageal reflux disease

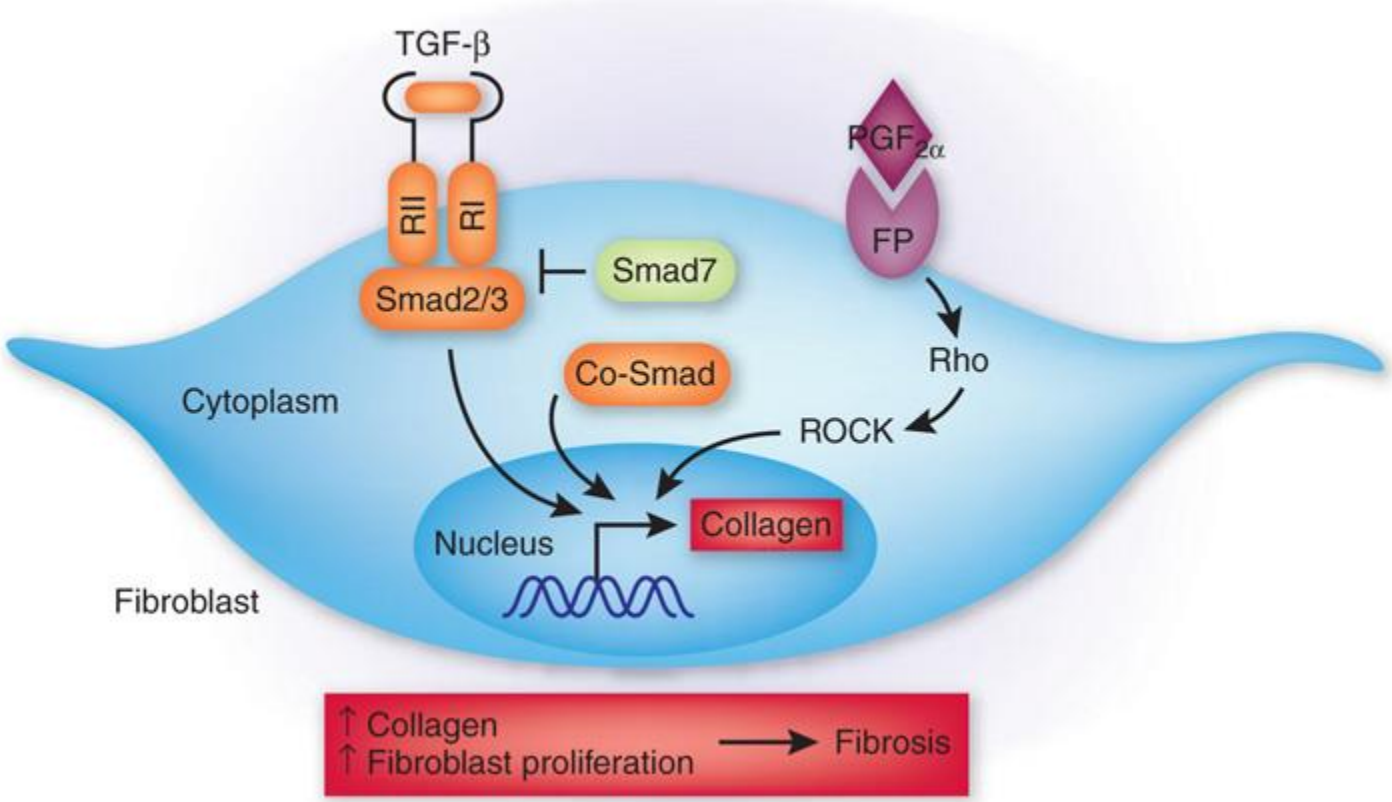




the injured epithelial cells are the source of profibrogenic factors such as TGF-β secondary to downregulation of caveolin I

alveolar damage, fibrosis and irreversible destruction of the lung parenchyma.

Profibrogenic factors: TGF-β



$PGF_{2\alpha}$, produced locally during lung injury or fibrosis binds to its cognate G protein–coupled receptor FP. This binding activates the small GTPase Rho signaling pathway, leading to collagen synthesis through mechanisms yet to be delineated. The potent profibrotic factor TGF-β acts independently through Smads to further enhance collagen production by fibroblasts. The increase in collagen, together with $PGF_{2\alpha}$-FP–induced fibroblast proliferation, contribute to the pathogenesis of *in vivo* pulmonary fibrosis.

Clinical features
Idiopathic Pulmonary Fibrosis/ usual interstitial pneumonia/ fibrosing alveolitis/ Hamman-Rich syndrome (UIP)

- Most patients present with exertional dyspnea and a nonproductive cough.
- A chest radiograph and high-resolution computed tomography typically reveals diffuse reticular opacities.
- Histology of IPF shows features of usual interstitial pneumonia with a heterogeneous, patchy appearance. There are alternating areas of healthy lung and abnormal lung with interstitial inflammation, fibrosis, and honeycomb change.
- The diagnosis of idiopathic pulmonary fibrosis relies on a combination of clinical, laboratory, radiologic, and/or pathologic data.

Morphology of UIP

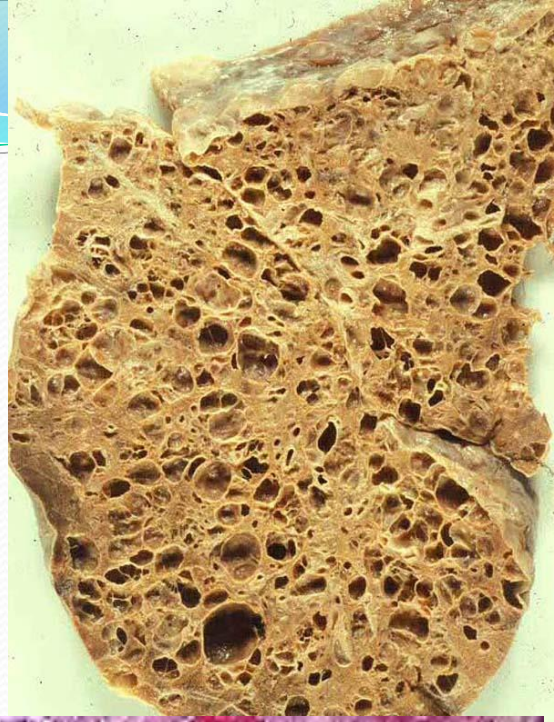
- The morphologic changes vary according to the stage of the disease.
- Early cases:

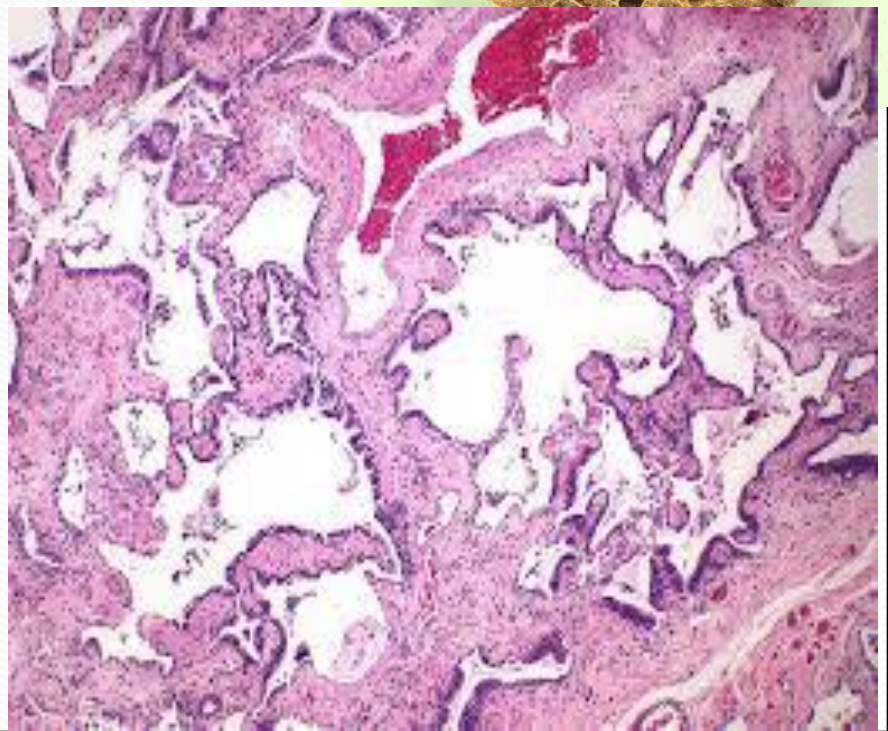
  -Intra-alveolar and interstial inflammation.

  - Hyperplasia of type II pneumocytes
- Advancing disease:

  -prominent interstitial fibrosis.

  -Alternating areas of fibrosis and normal tissue will be seen.
- In the end, the lung consists of spaces lined by cuboidal or columnar epithelium separated by inflammatory fibrous tissue (honeycomb lung). It is the end stage of lung disease

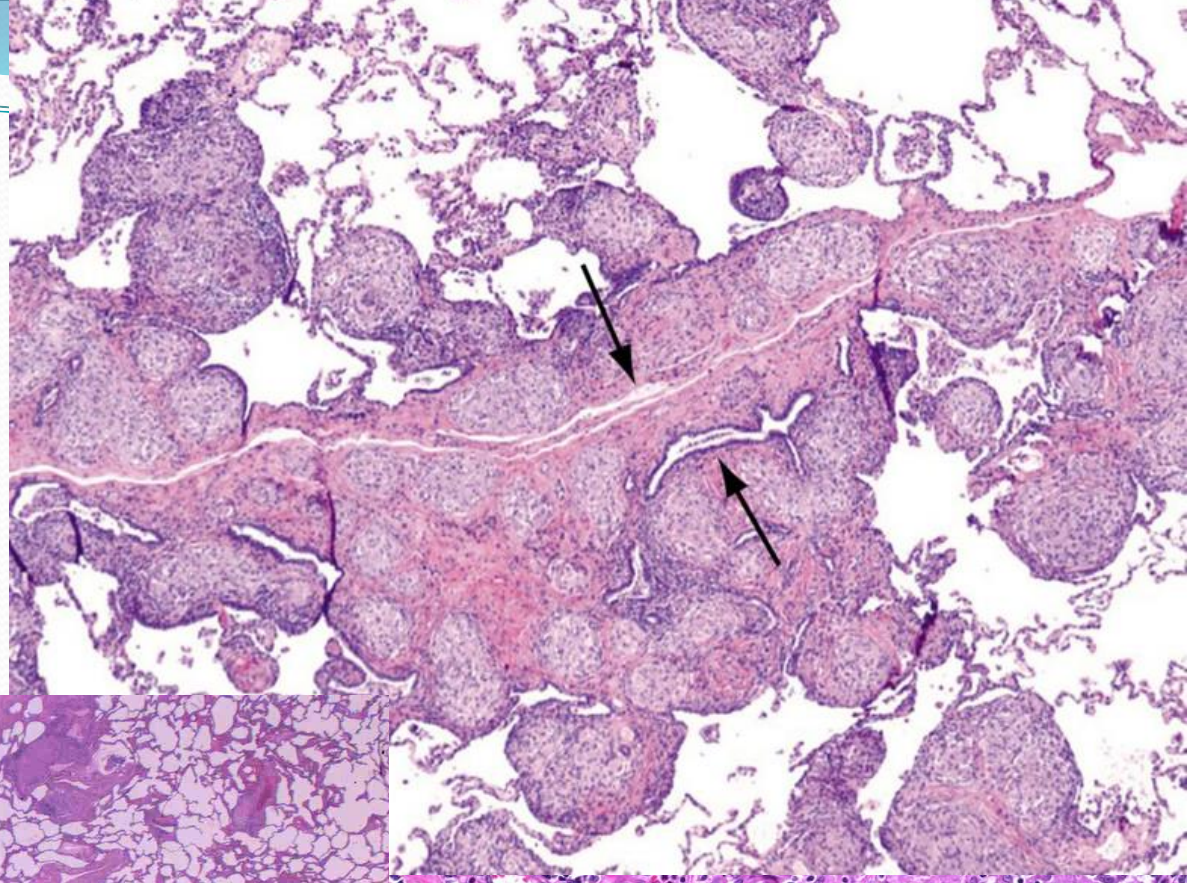


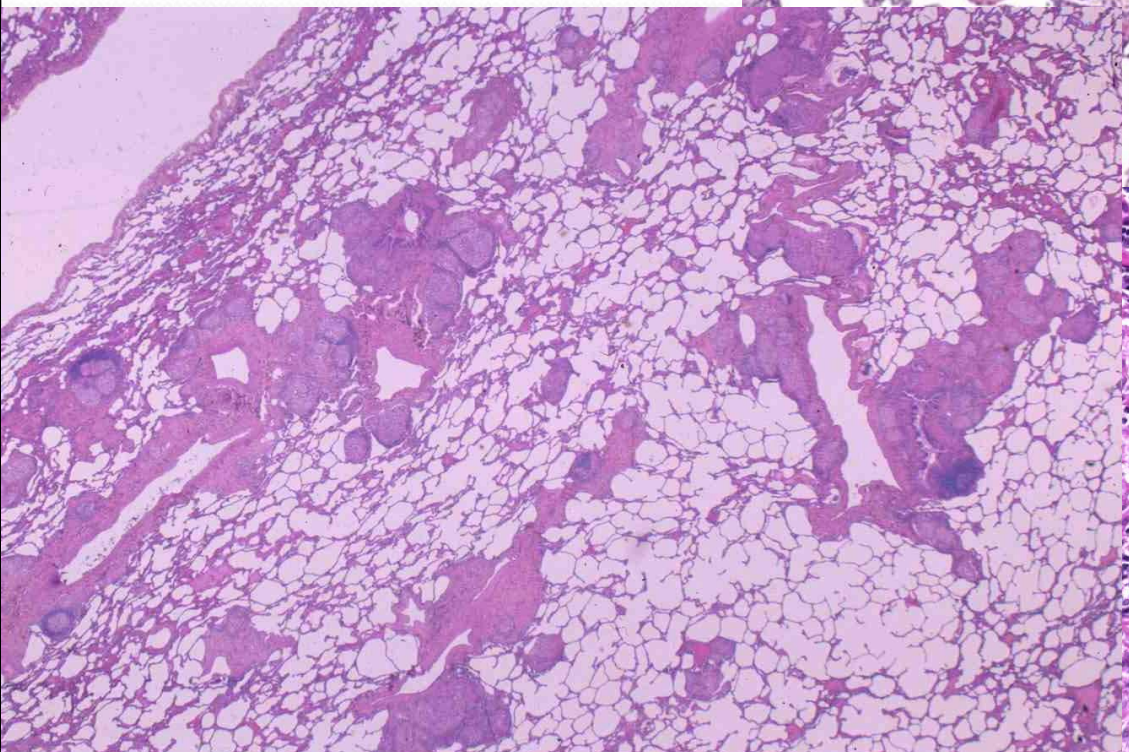


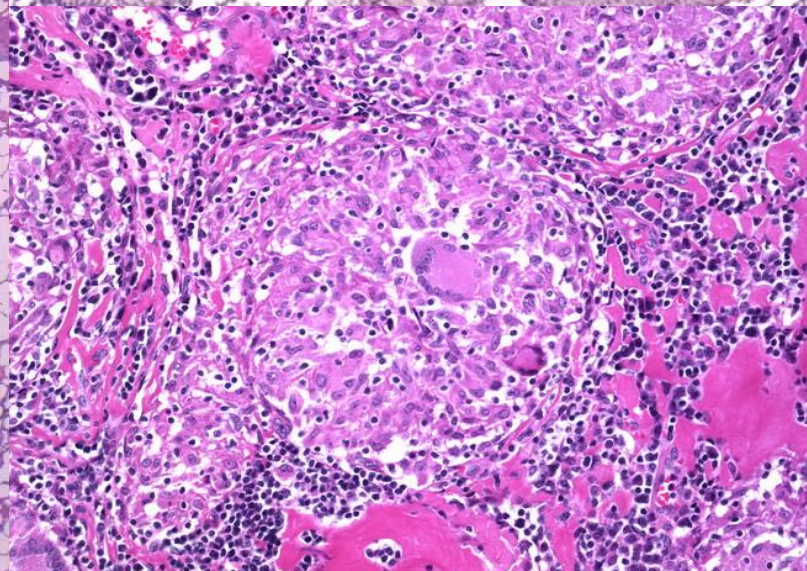
Sarcoidosis

- Sarcoidosis is a multisystem inflammatory disease of
  - unknown cause/etiology
  - that predominantly affects the lungs and intrathoracic lymph nodes.
  - characterized by non-caseating/ non-necrotizing granulomas in affected organ tissues.
  - affecting all races
  - affecting both sexes equally
- Other organs that may be involved include eyes, skin, liver, spleen and bone marrow. Occasionally kidney, heart, CNS and endocrine organs may be involved.

- Sarcoidosis granulomas in the lung







Sarcoidosis

- Clinically the patient may present with fever, anorexia, and arthralgias, dyspnea on exertion, cough and chest pain. Depending on the organs involved the patient can have dermatological, occular, cardiac or neural(rare) manifestations.
- The prognosis of sarcoidosis is unpredictable. It can progressive and chronic. It may present as episodes of activity. Majority of the patients respond well to treatment. A small percentage of patients may die of the complications of sarcoidosis.