Diseases of the Respiratory System

Chronic Interstitial Lung Diseases (Restrictive, Infiltrative)

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Respiratory block
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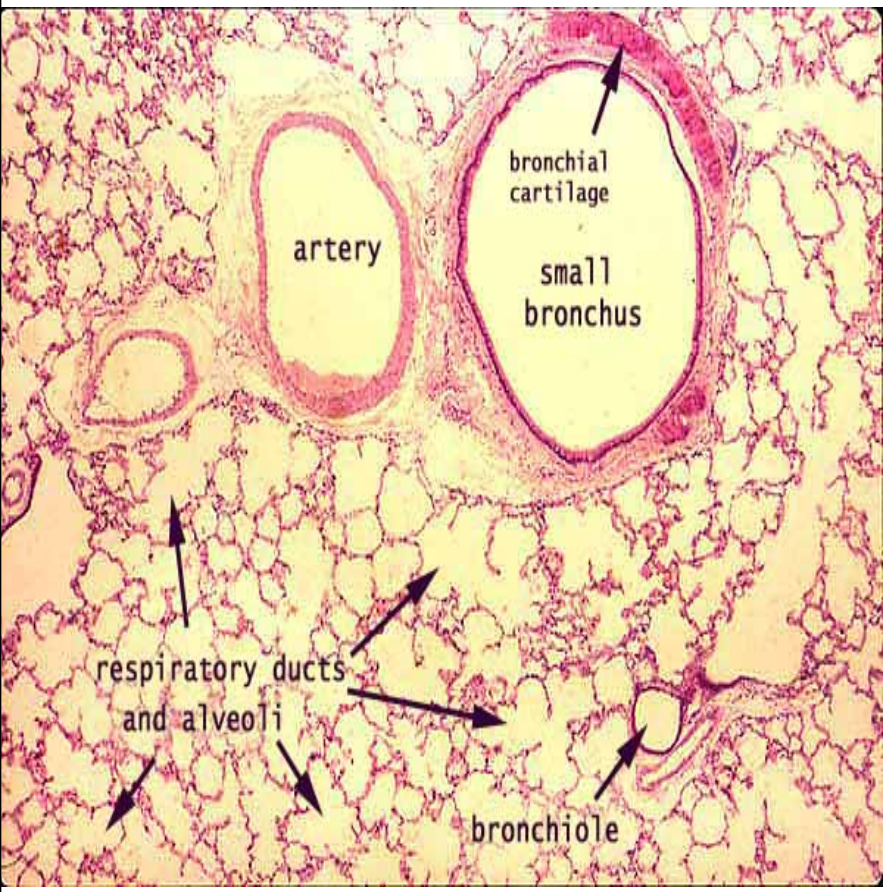
Pathology
Lecture 3

Objectives

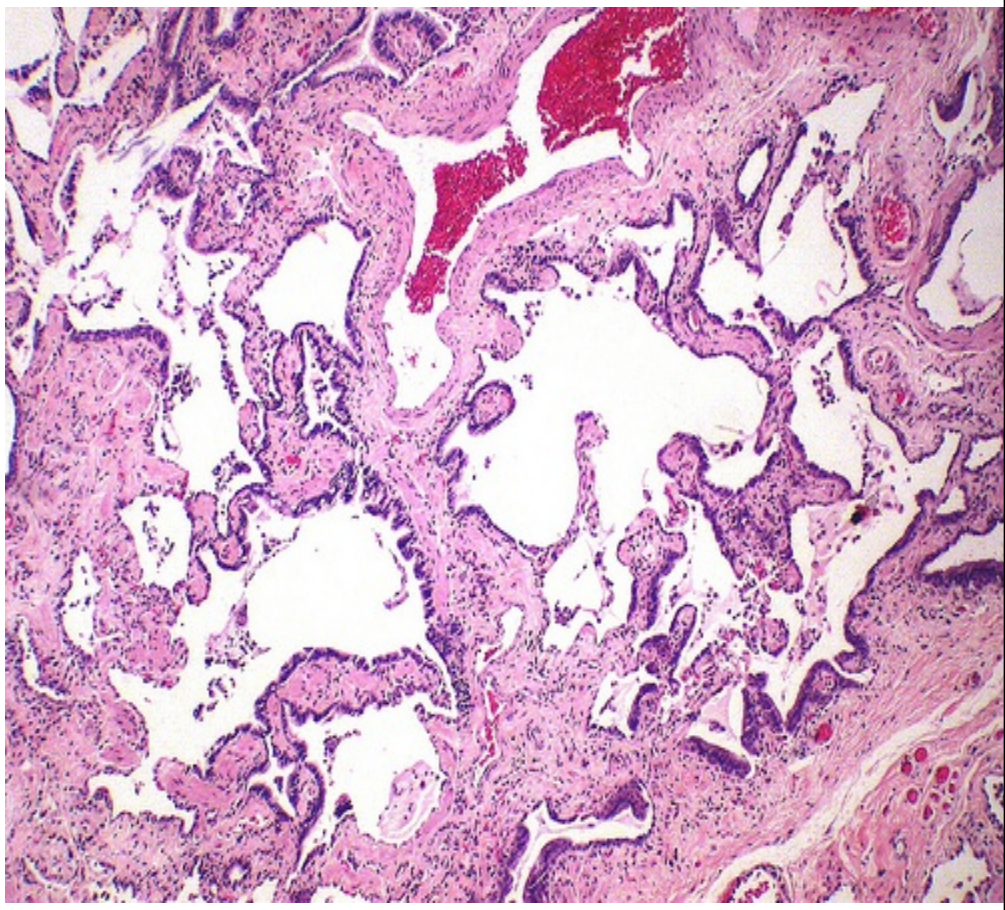
- Understand the structure and constituents of the lung interstitium as well as the restrictive changes which occur in diseases of the interstituim (ILD)
- Know the symptoms of ILD: progressive breathlessness and cough
- Know subtypes of ILD: acute and chronic
- Discuss the causes, morphology and outcome of acute ILD
- Appreciate the pathogenesis of chronic ILD regardless of their type.
- Become aware of the classification of interstitial lung diseases.
- Discuss examples of interstitial lung diseases including:
  - **idiopathic pulmonary fibrosis**
  - **Pneumoconiosis**
  - **Hypersensitivity pneumonitis**
  - **Sarcoidosis**

Interstitial lung diseases

Normal



Honeycomb lung



Restrictive Lung Disease

The restrictive lung diseases are divided into:

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

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

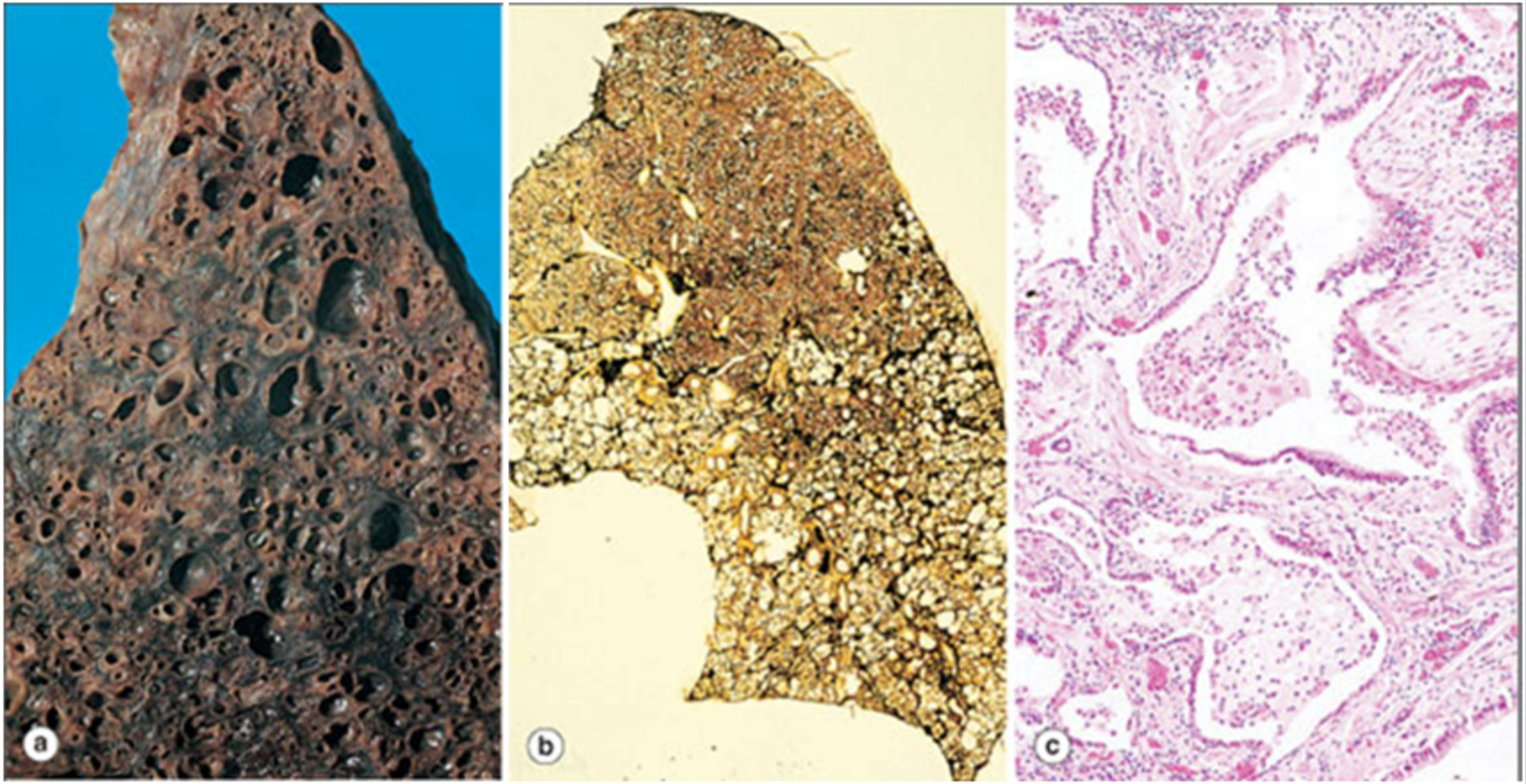
2. **Extrinsic disorders or extraparenchymal diseases:**

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**

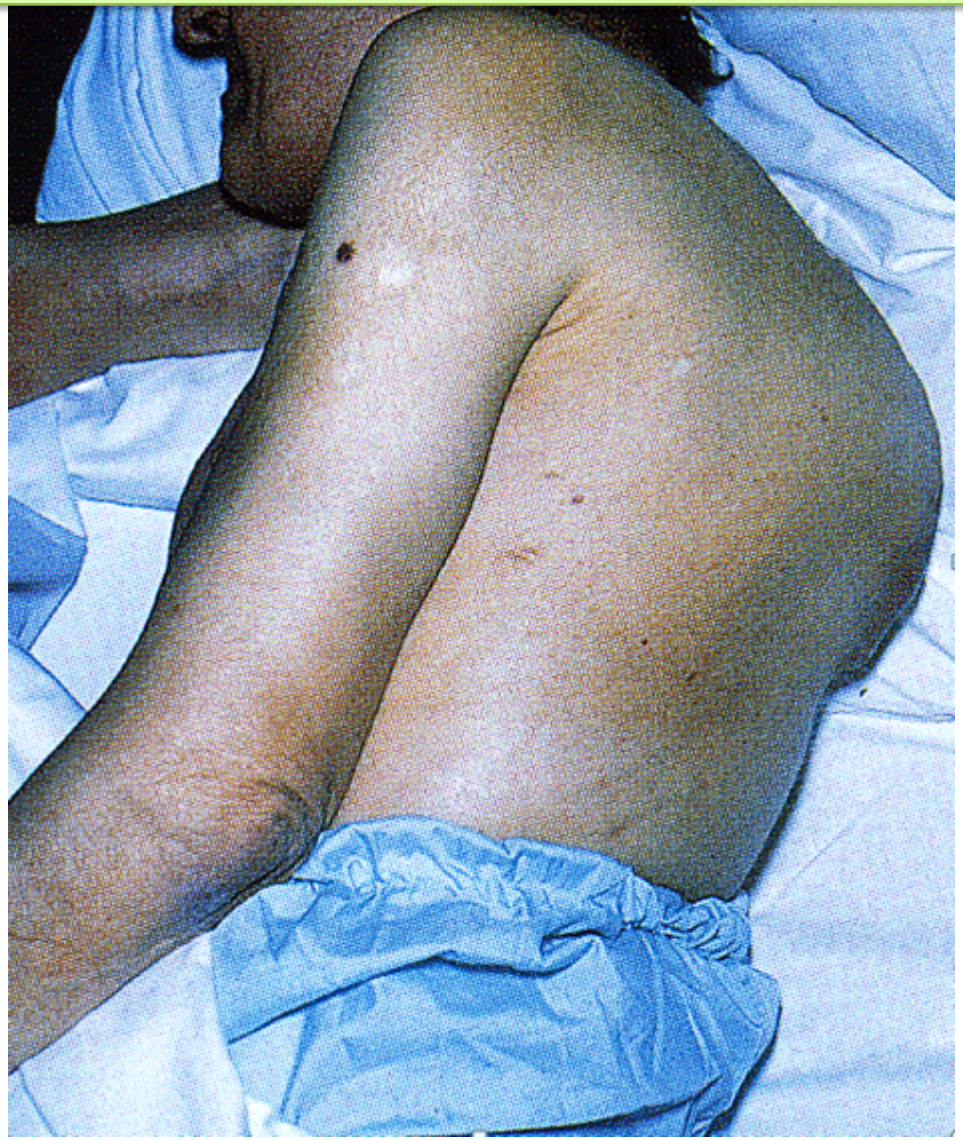
Diseases of Lung

Intrinsic lung diseases



Honeycomb lung. Macroscopically (a) honeycomb lung appears as large (b) the extent of abnormality and interstitial fibrosis can be better appreciated. (c) shows coalescence of air spaces, both alveoli and bronchioles, to form cysts lined with cuboidal epithelium.

Extrinsic disorders or extraparenchymal diseases



Severe kyphoscoliosis of unknown etiology. Flexion (kyphosis) and lateral deviation (scoliosis) of the spine have the combined effect of reducing chest volume. This compromises respiratory function and may cause restrictive lung disease.

Know subtypes of ILD: acute and chronic

Acute restrictive lung disease

(INTRINSIC TYPE)

Acute restrictive lung diseases (INTRINSIC TYPE)

1. **Adult respiratory distress syndromes (ARDS)**
2. **Neonatal respiratory distress syndromes (NRDS)**

ARDS

Can be caused by many conditions:

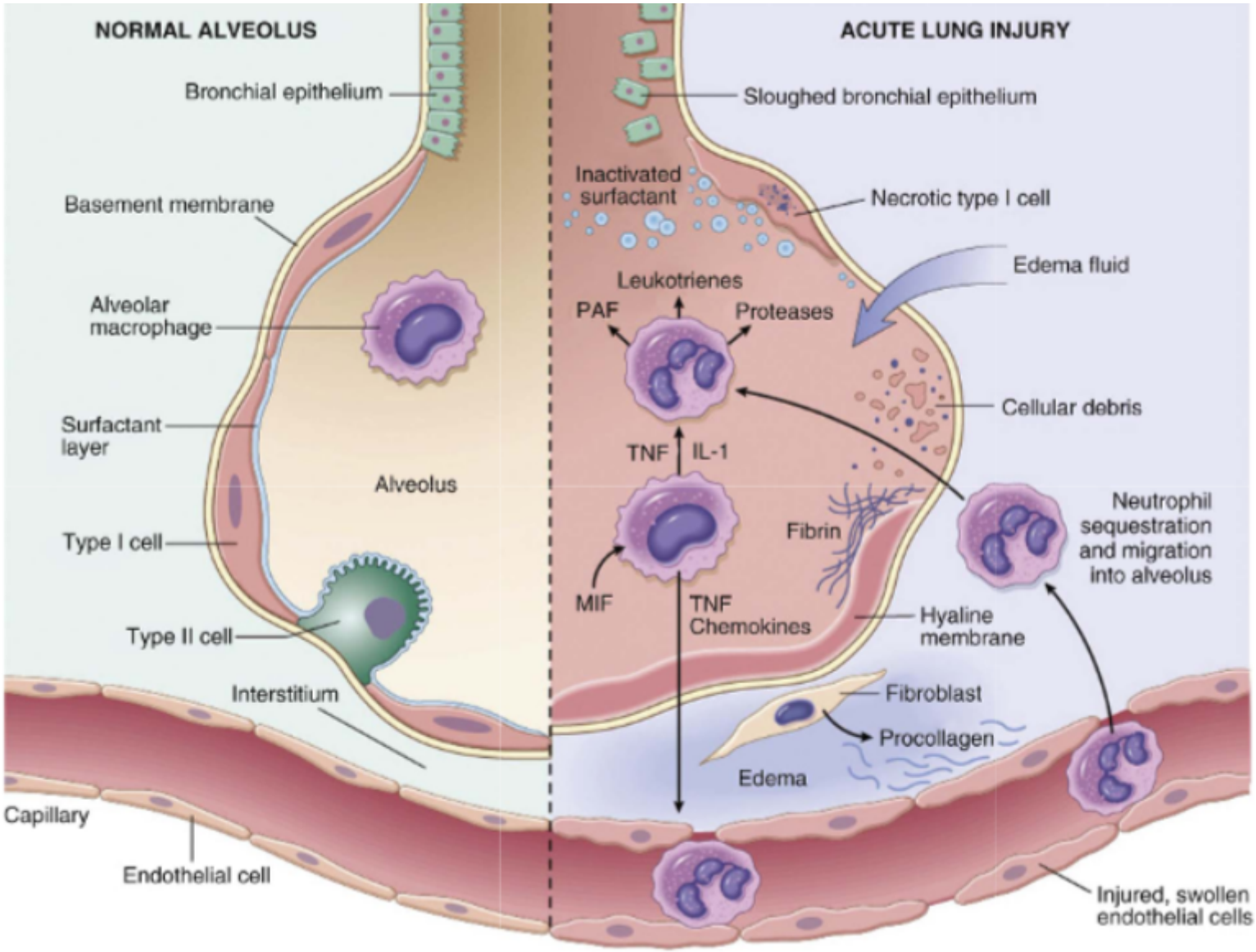
Pneumonia and sepsis are the most common causes

Direct injury to lung

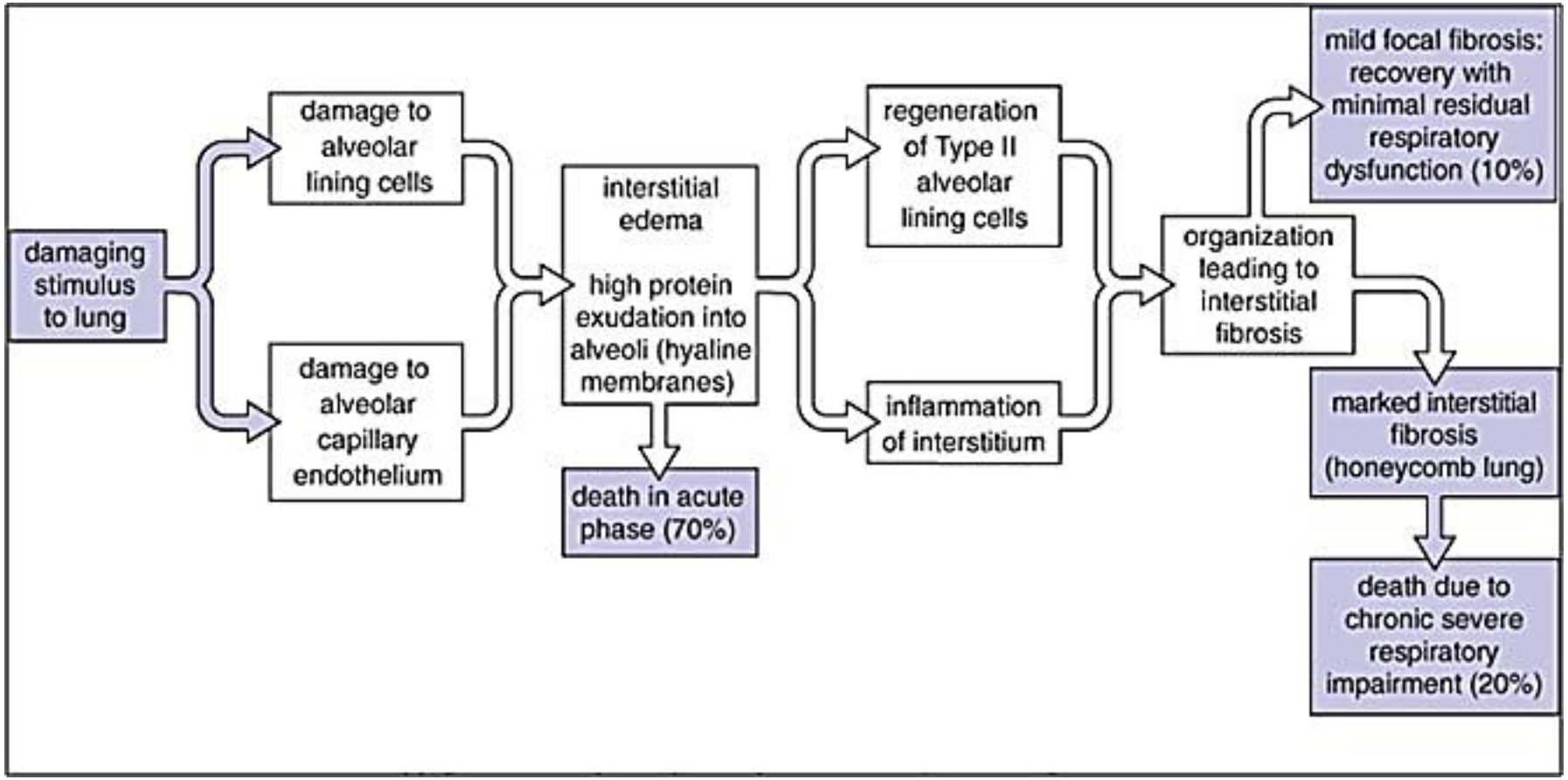
- **Pneumonia**
- **Aspiration of gastric contents**
- **Pulmonary trauma**
- **Fat embolism**
- **Near drowning**
- **Toxic inhalation injury (irritants such as chlorine, O2 toxicity)**
- **Post lung transplant**
- **Severe acute respiratory syndrome (SARS): The virus is a coronavirus that destroys the type II pneumocytes and causes diffuse alveolar damage**

Indirect injury to lung:

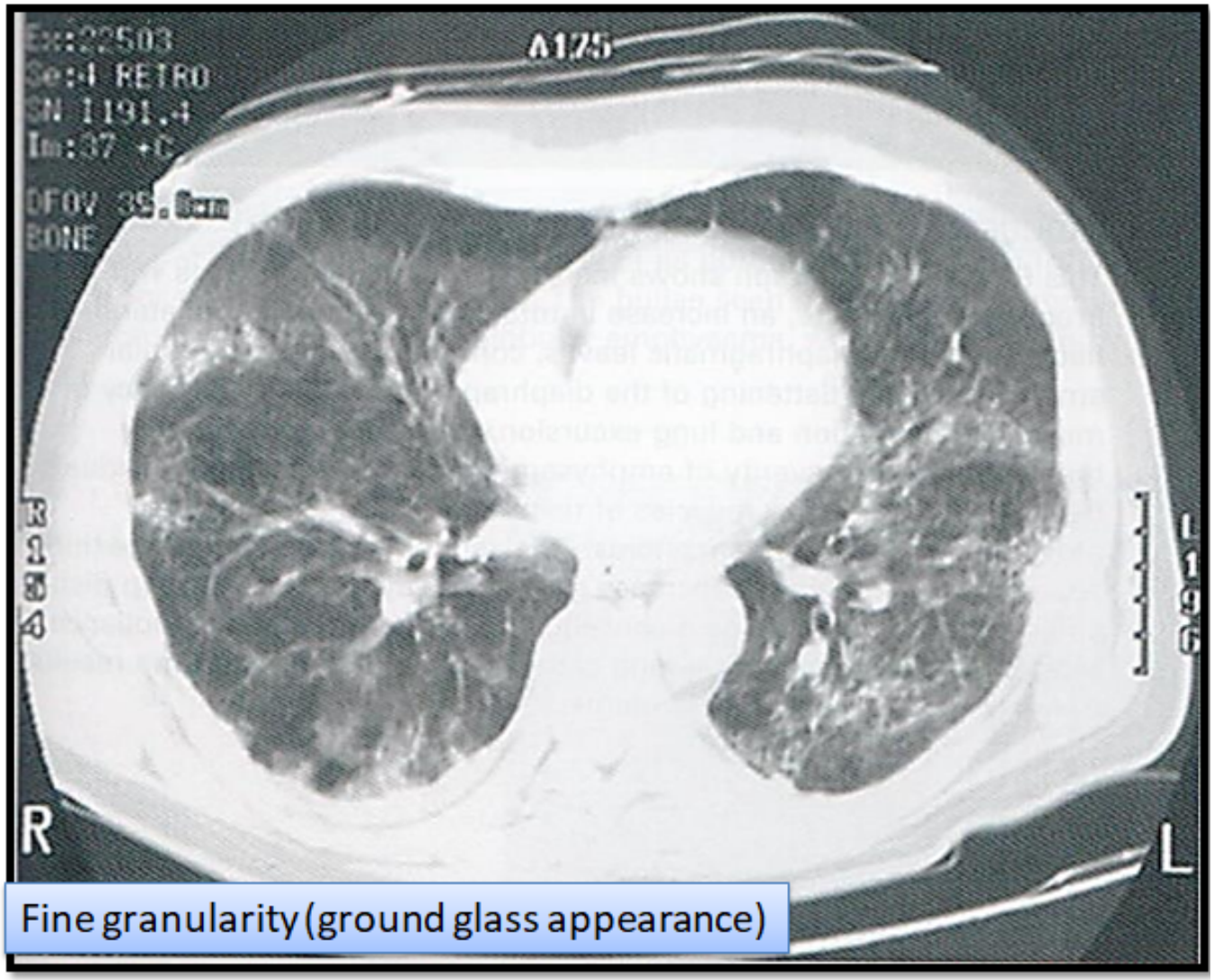
- **Sepsis**
- **Severe trauma** (e.g. bone fracture, head injury, burns, radiation)
- **Shock**
- **Cardiopulmonary bypass**
- **Acute pancreatitis**
- **Transfusion**
- **Uremia**
- **Overdose with street drugs such as heroin**
- **Therapeutic drugs such as bleomycin**
- **Hematologic conditions e.g multiple transfusion, coagulation disorders**


NORMAL ALVEOLUS
ACUTE LUNG INJURY
Bronchial epithelium
Sloughed bronchial epithelium
Inactivated surfactant
Necrotic type I cell
Basement membrane
Edema fluid
Leukotrienes
PAF
Proteases
Alveolar macrophage
Cellular debris
Surfactant layer
TNF
IL-1
Alveolus
Type I cell
Fibrin
Neutrophil sequestration and migration into alveolus
MIF
TNF Chemokines
Hyaline membrane
Type II cell
Fibroblast
Interstitium
Procollagen
Edema
Capillary
Endothelial cell
Injured, swollen endothelial cells

Diseases of Lung

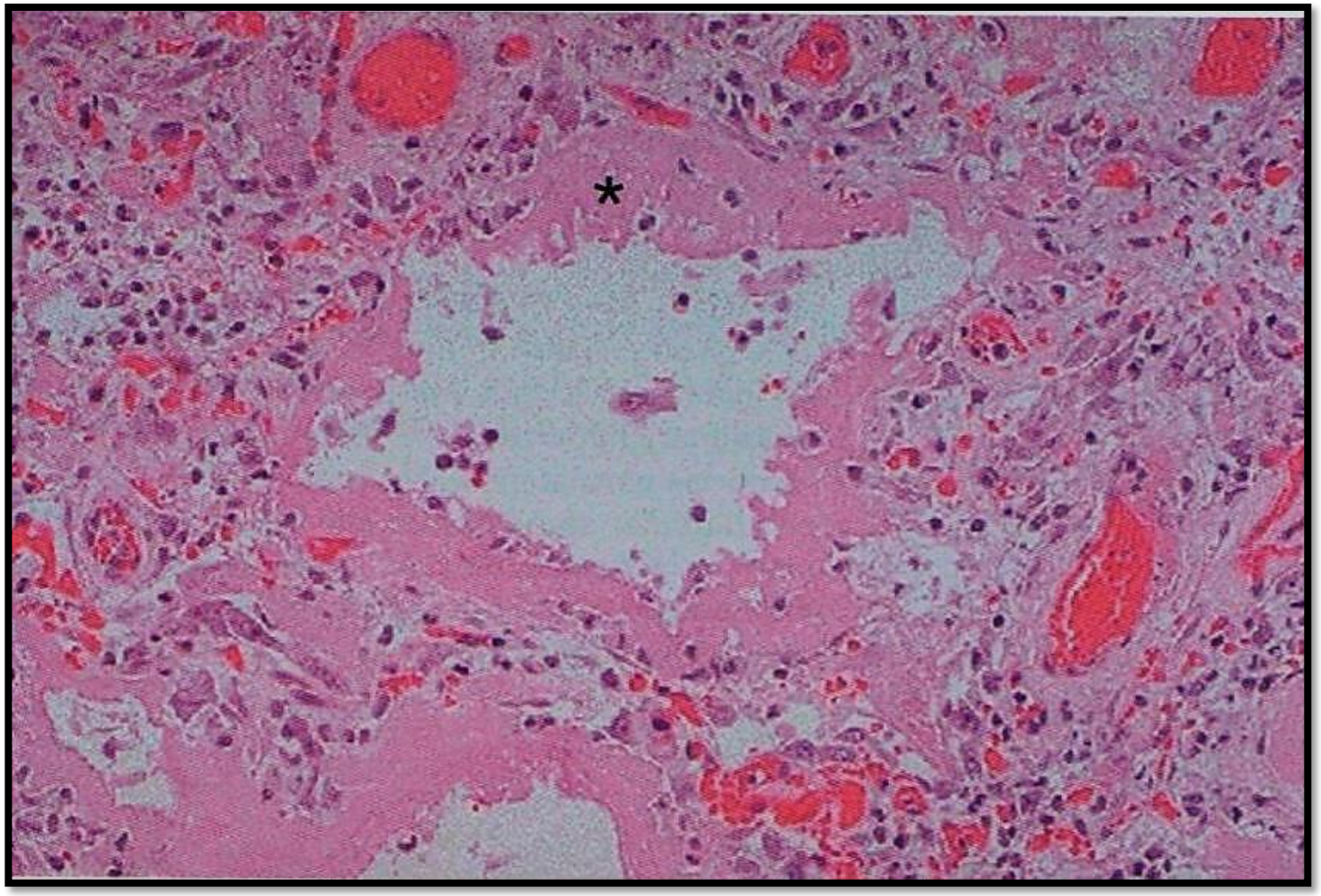


The main events and outcomes of ARDS

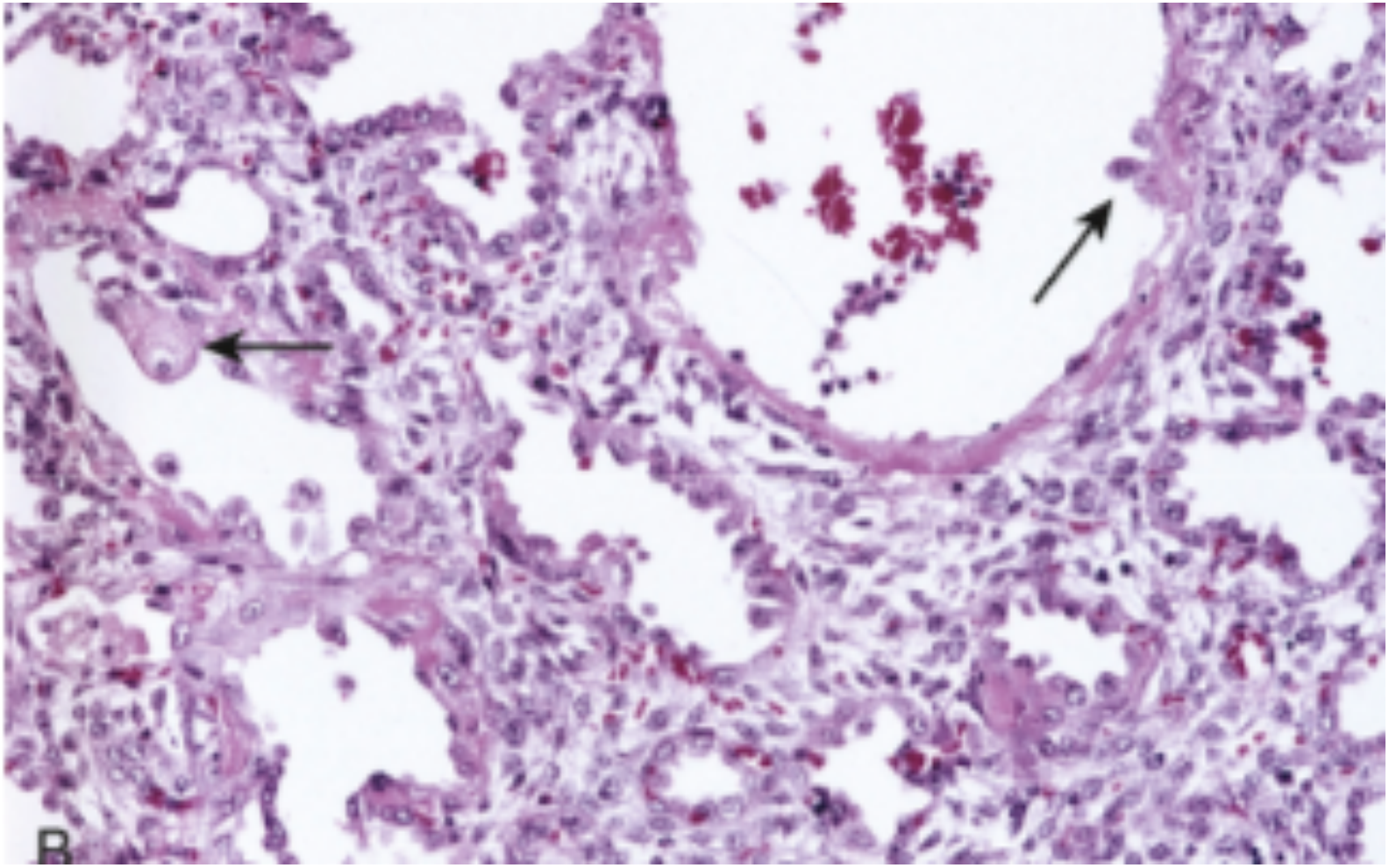


Diffuse alveolar damage, CT image

Diffuse alveolar damage, gross: lung edema



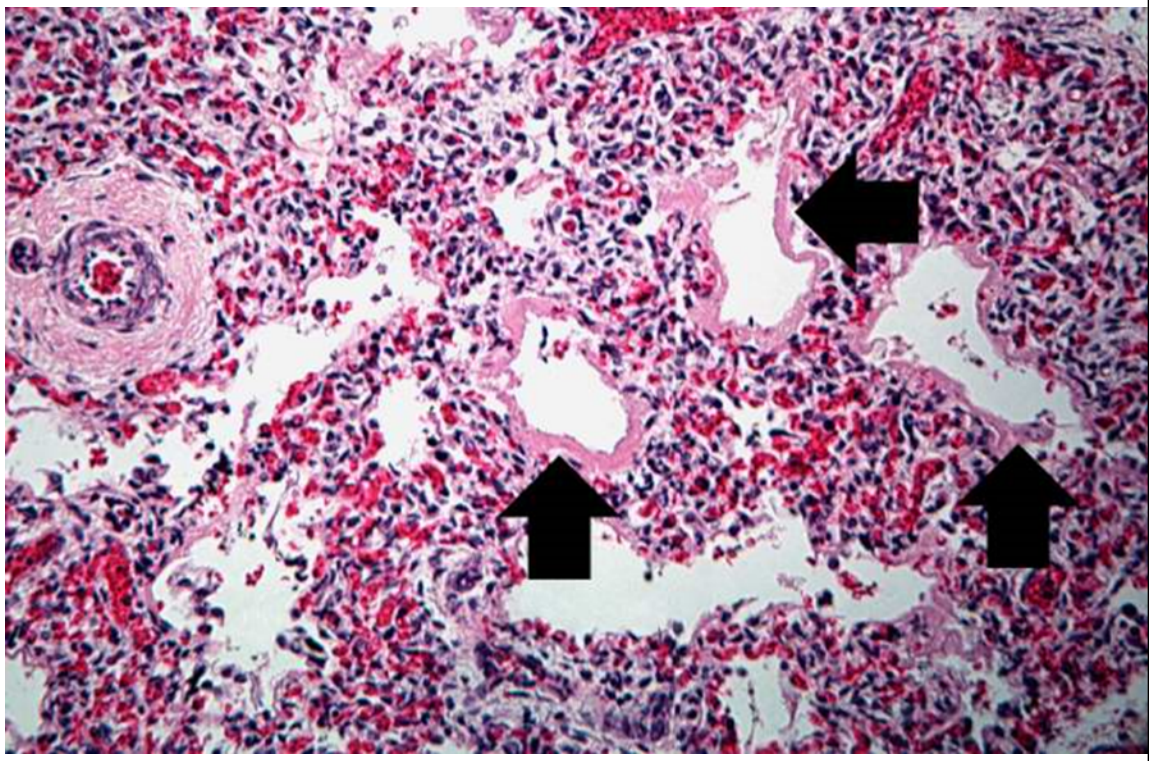
Diffuse alveolar damage, microscopic



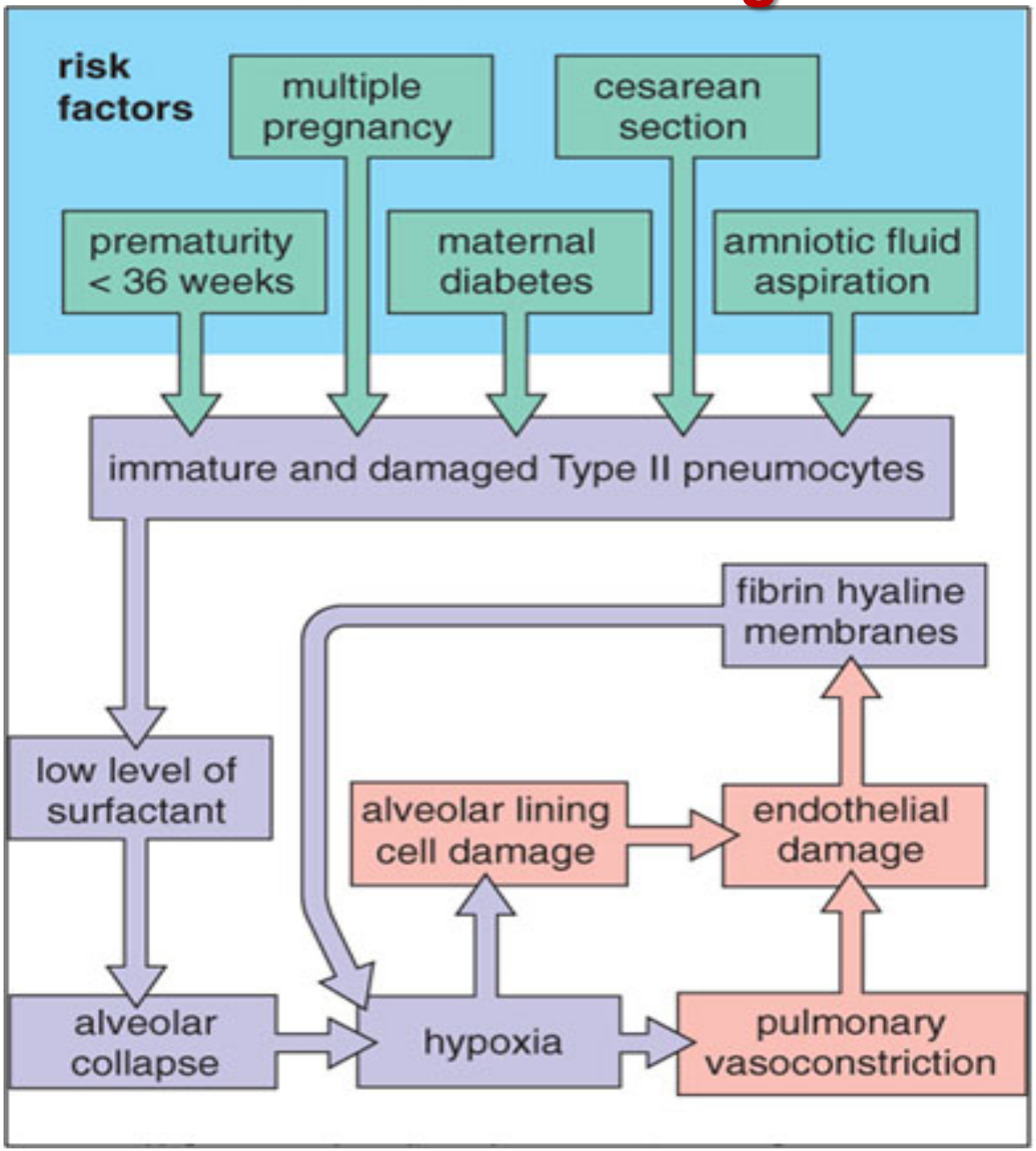
The healing stage is marked by resorption of hyaline membranes and thickening of alveolar septa by inflammatory cells, fibroblasts, and collagen. Numerous reactive type II pneumocytes also are seen at this stage (arrows), associated with regeneration and repair.

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 newborns, most often as a result of immaturity.



Diseases of Lung



Pathogenesis of NRDS.

Chronic restrictive lung disease

(INTRINSIC TYPE)

Major Categories of Chronic Interstitial Lung Disease

Idiopathic fibrosing:

Usual interstitial pneumonia (idiopathic pulmonary fibrosis)

Occupational: Pneumoconiosis

Anthracosis and coal worker's pneumoconiosis,
Silicosis
Berylliosis
Asbestosis

Immune diseases:

Sarcoidosis
Goodpasture syndrome
Hypersensitibity pneumonitis (extrinsic allergic alveolitis)
Systemic lupus erythematosus
Systemic sclerosis (scleroderma)
Wegener granulomatosis

Drug:

Chemotherapy, methotrexate, bleomyxin toxicity
Amiodarone: antiarrythemic drug (cause pulmonary fibrosis and pneumonitis)

Smoking related:

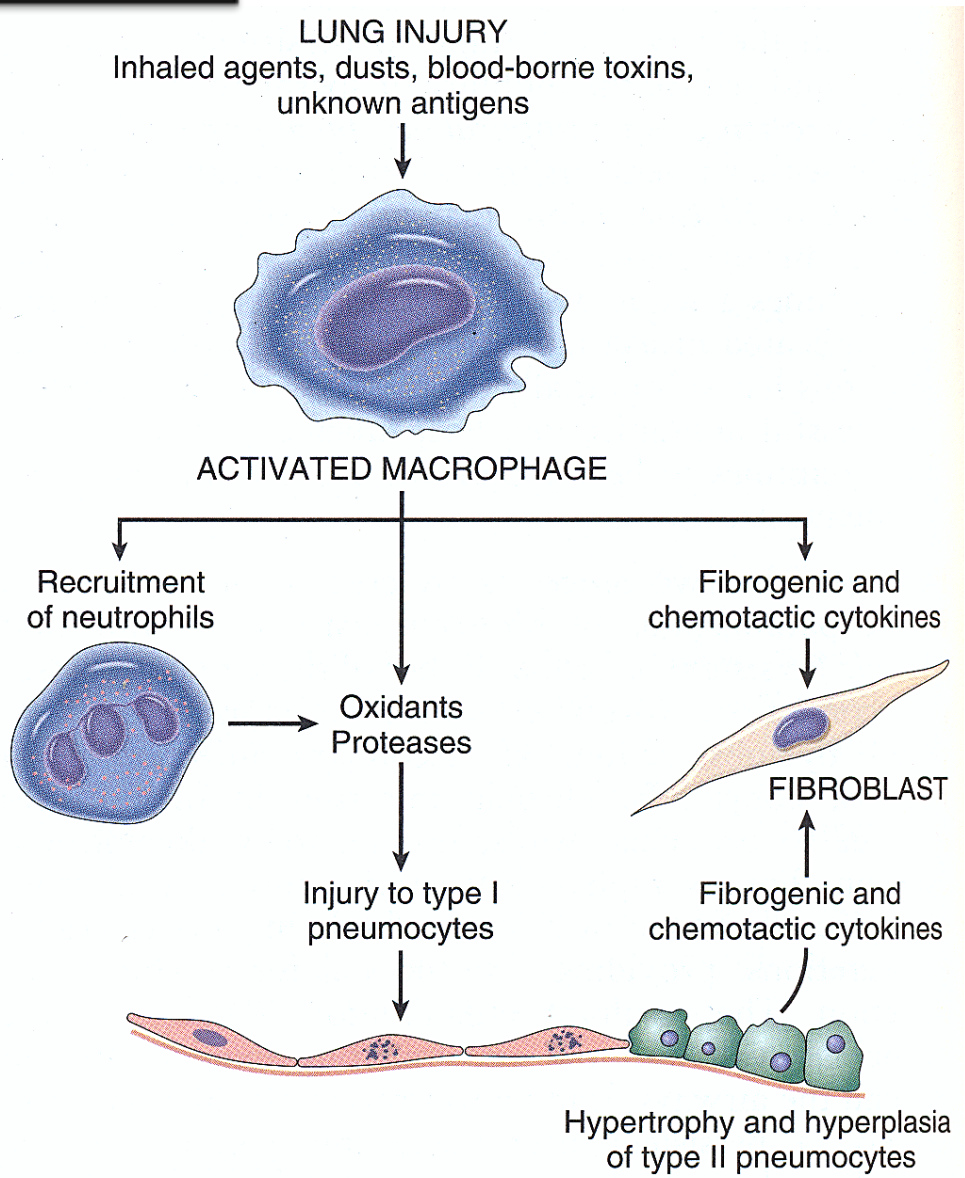
Eosinophilic granuloma
Desquamative interstitial pneumonia
Respiratory bronchiolitis-associated interstitial lung disease

Radiation Reactions

Occur after radiation with diffuse alveolar damage, severe atypia of hyperplastic type II cells and fibroblasts

Pathogenesis of Chronic Interstitial Lung Disease

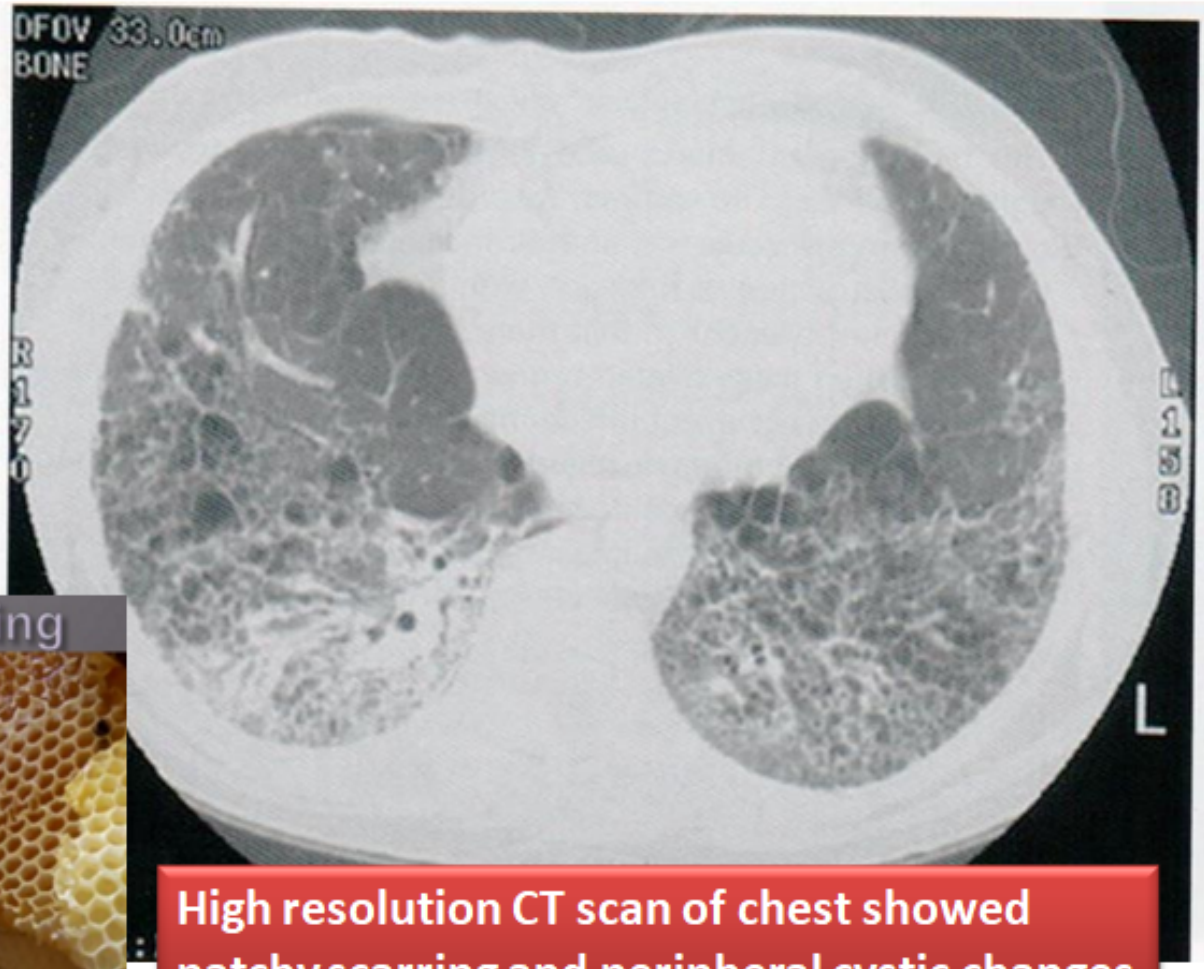
- **Lung injury**
- **Influx of inflammatory cells into the alveoli and alveolar walls**
- **Release of chemical mediators and promotion of fibrosis**
- **Distortion of the normal structure of alveoli**



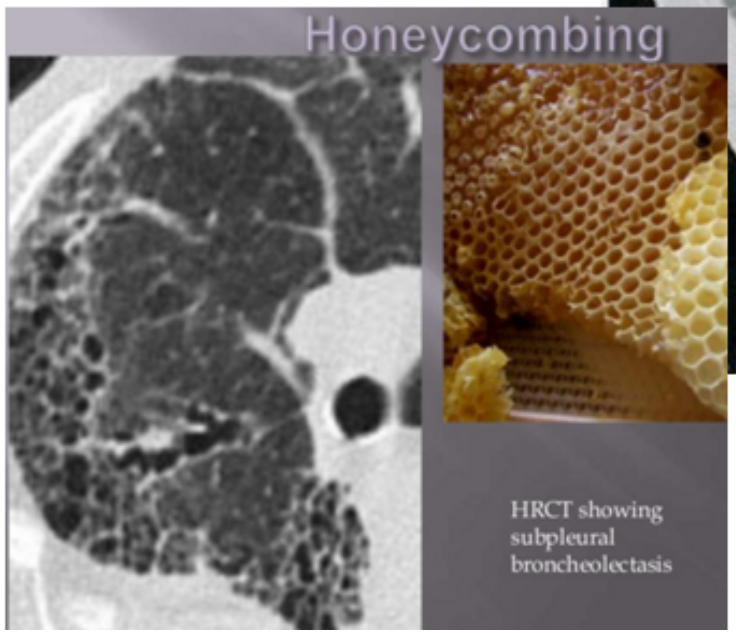
Idiopathic pulmonary fibrosis (**Usual interstitial pneumonia**)

Usual interstitial pneumonia

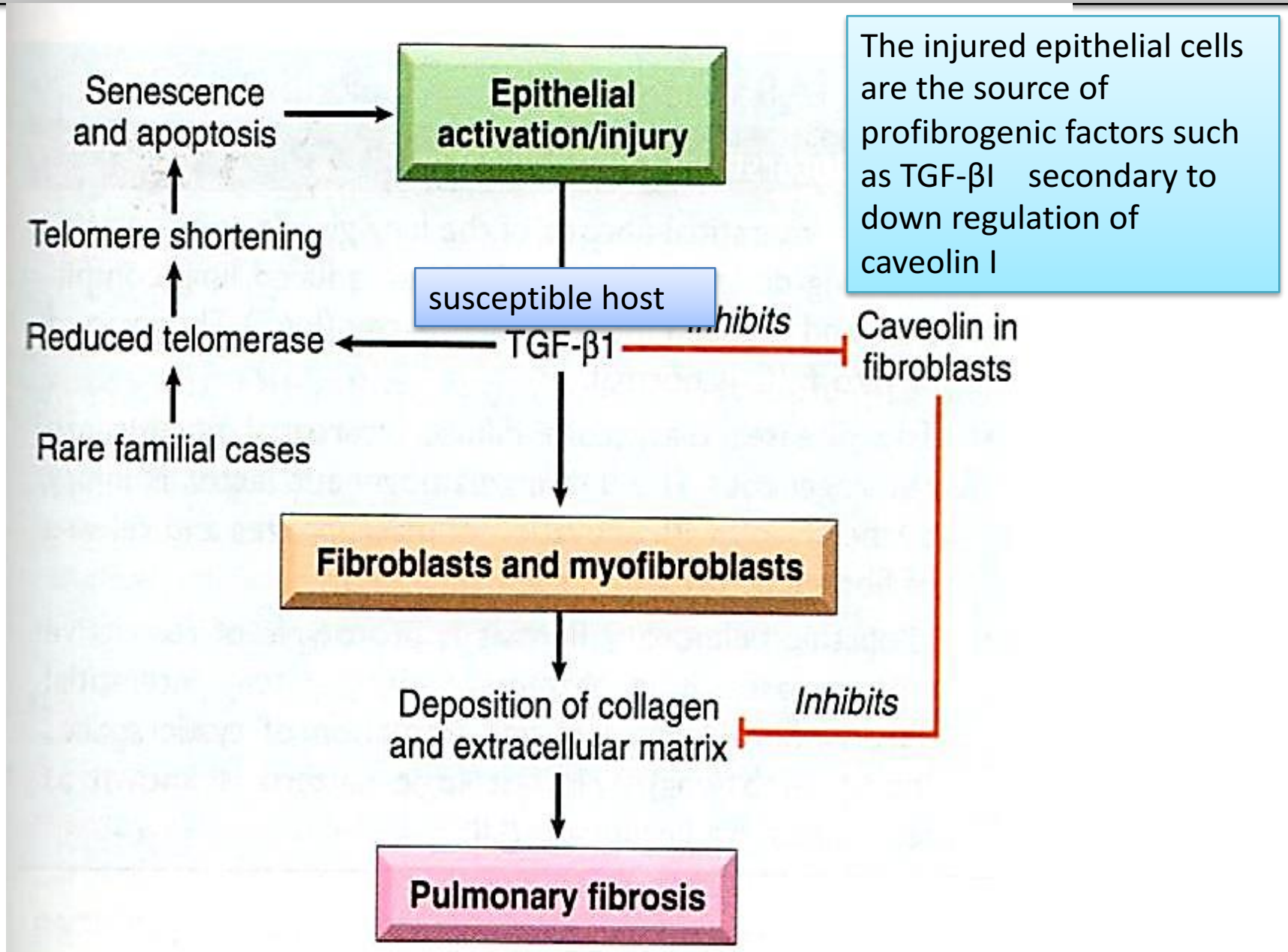
- **Progressive dyspnea and dry cough**
- **Age: Adults 30 to 50 years**
- **Progressive subpleural fibrosing disorder**
- **Honeycomb lung**
- **Prognosis: poor**



High resolution CT scan of chest showed patchy scarring and peripheral cystic changes

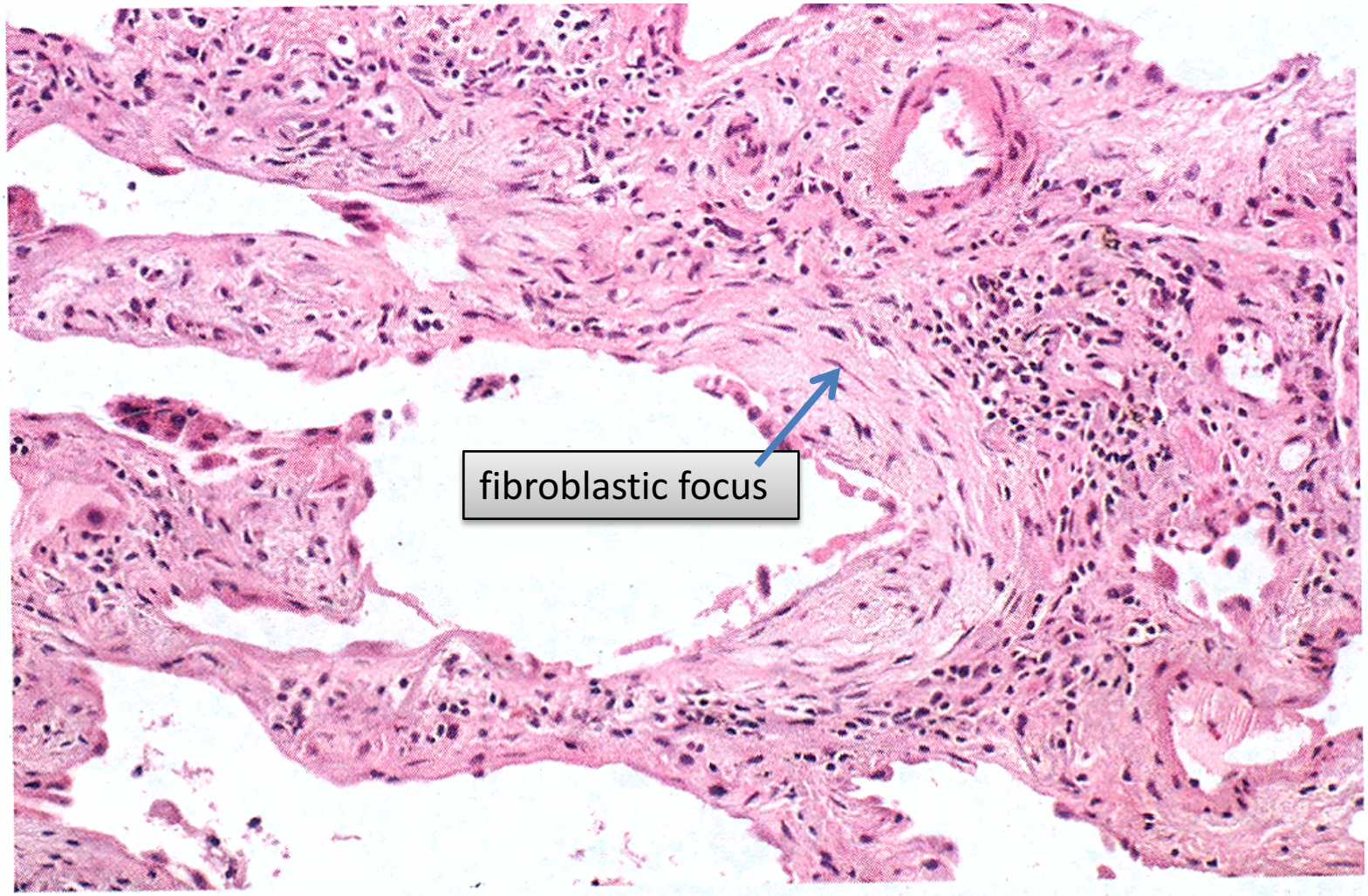


Pathogenesis of idiopathic pulmonary fibrosis

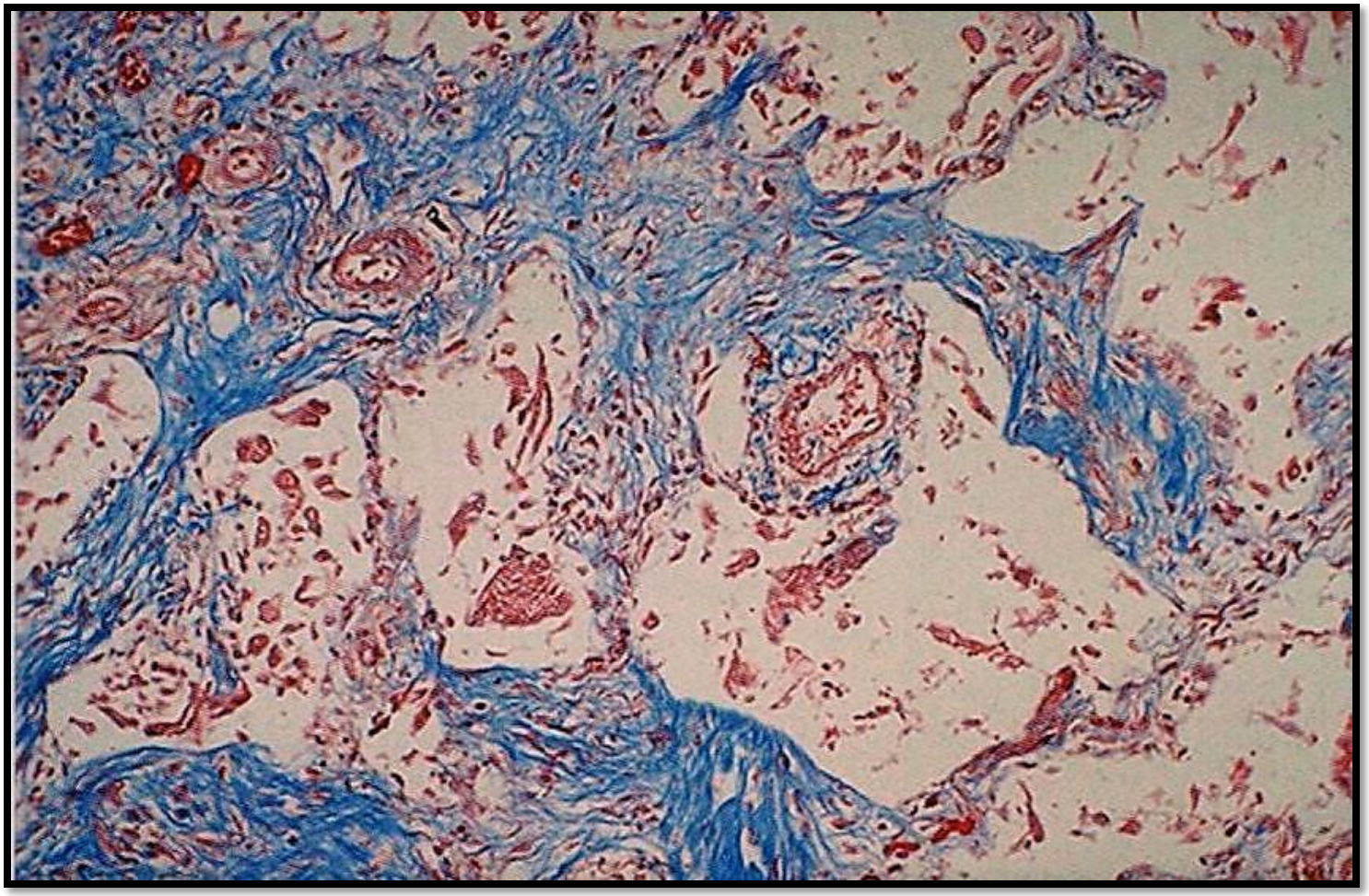


The injured epithelial cells are the source of profibrogenic factors such as TGF-βI secondary to down regulation of caveolin I

Honeycomb change, gross
Fibrosis in the subpleural region



Usual interstitial pneumonia. Fibroblastic focus with fibers running parallel to surface and bluish myxoid extracellular matrix.



Interstitial fibrosis, microscopic

Idiopathic pulmonary fibrosis
(**Usual interstitial pneumonia**)

A restrictive lung diseases characterized by reduced lung compliance. It is characterized by subpleural patchy interstitial fibrosis, fibroblastic foci and formation of cystic spaces (honeycomb lung).

Causes

- Unknown? Genetic
- The resulting injury to alveolar epithelial cells set in motion event that lead to increase local production of fibrogenic cytokines such as TGF-β

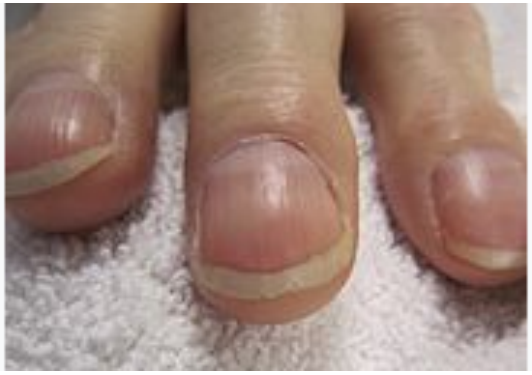
Clinical features

- Gradually increasing *dyspnea on exertion* and dry cough
- Most patients are 55 to 75 years
- X ray: early: ground glass fine granularity, advanced: honeycomb lung

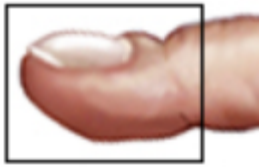
Complications

- Hypoxemia, *cyanosis* and clubbing
- gradual deterioration in pulmonary status despite medical treatment
- The median survival is about 3 years

Clubbing of nail



- Periosteal reaction of distal phalanx with bulbous swelling of the connective tissue in the terminal phalanxes.
- a symptom of diseases of the heart or lungs which cause chronically low blood levels of oxygen.



Pathogenesis:
The megakaryocytes bypass the breakdown within the pulmonary circulation and enter the systemic circulation. They are then trapped within the capillary beds within the extremities, such as the digits, and release platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) leading to hypertrophy of connective tissua.

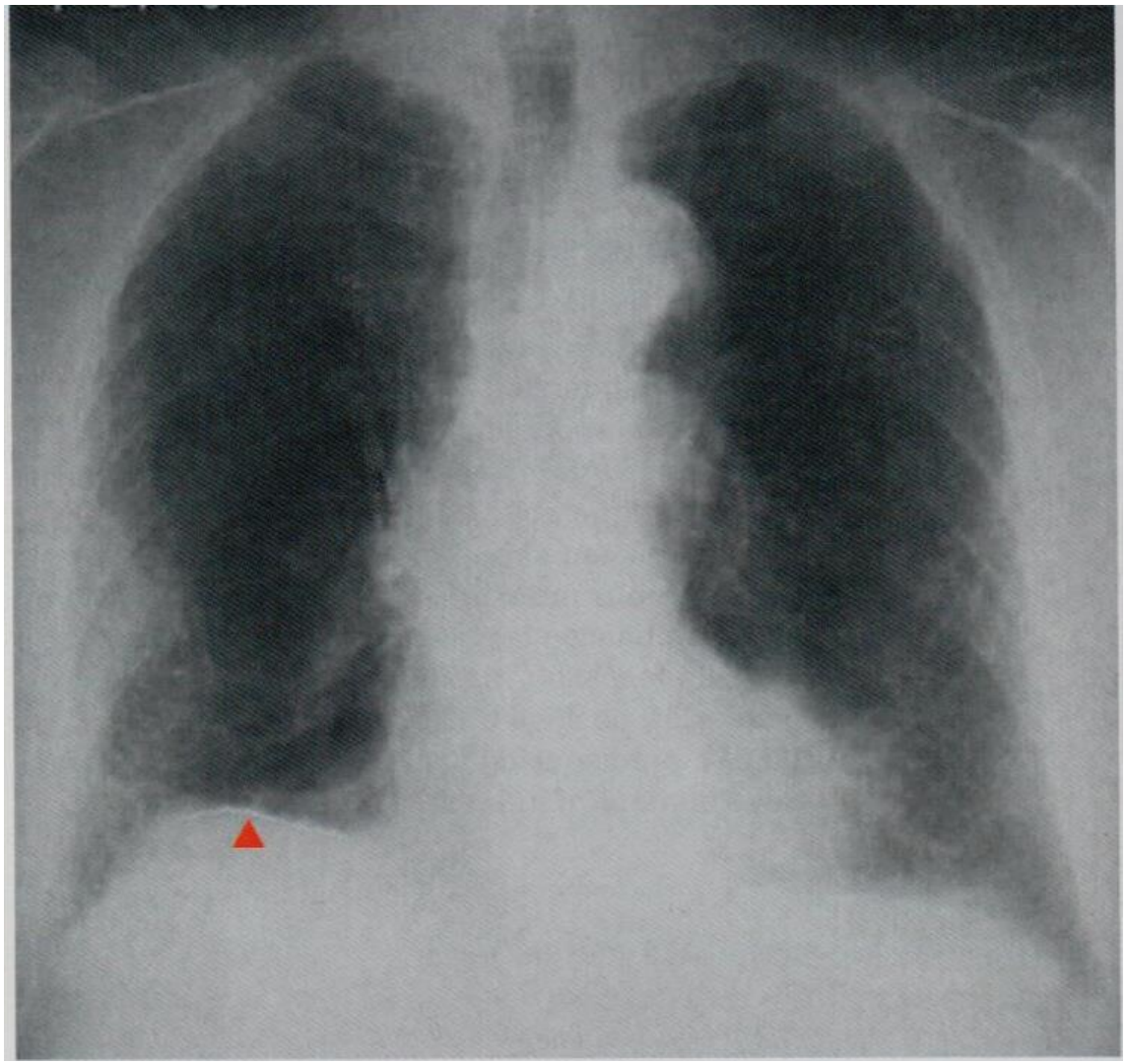
Occupational: Pneumoconiosis

Anthracosis and coal worker's pneumoconiosis,
Silicosis
Berylliosis
Asbestosis

The development of pneumoconiosis depends 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.**

Robbins Basic Pathology Table: 13.3 page 508

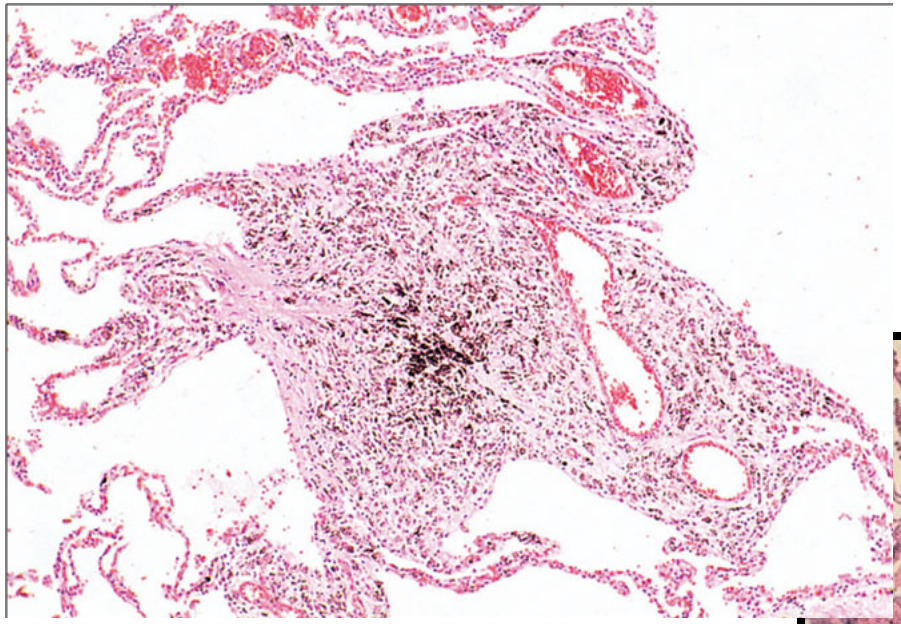


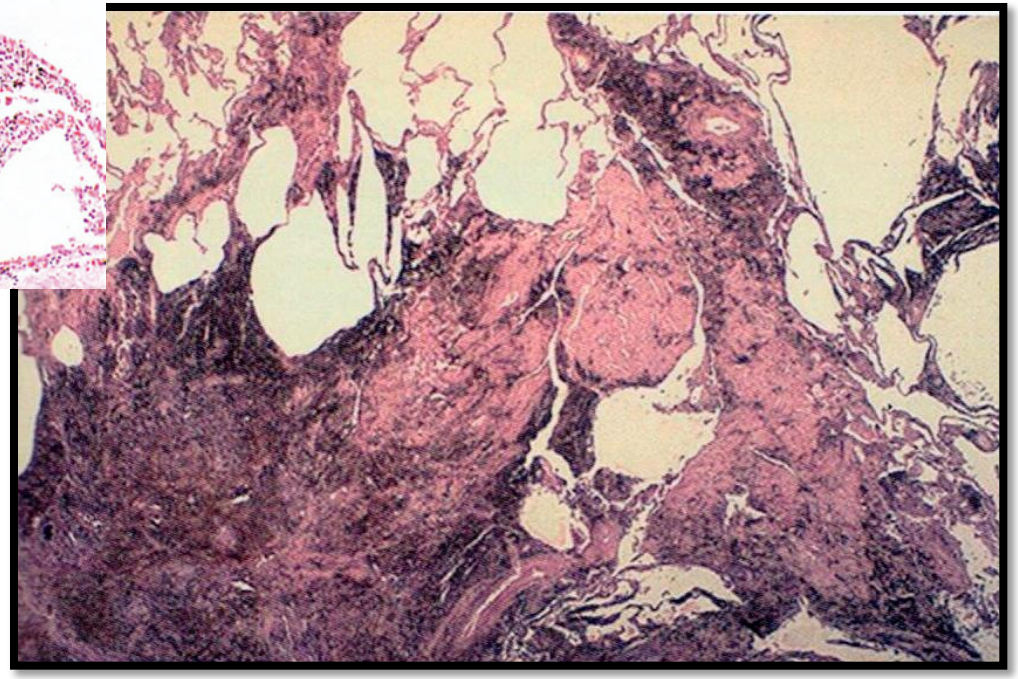
Pneumoconiosis, radiograph

Coal worker's pneumoconiosis

to progressive massive fibrosis (complicated coal worker's pneumoconiosis).
(a) Cut surface (b) thin section of whole lung.

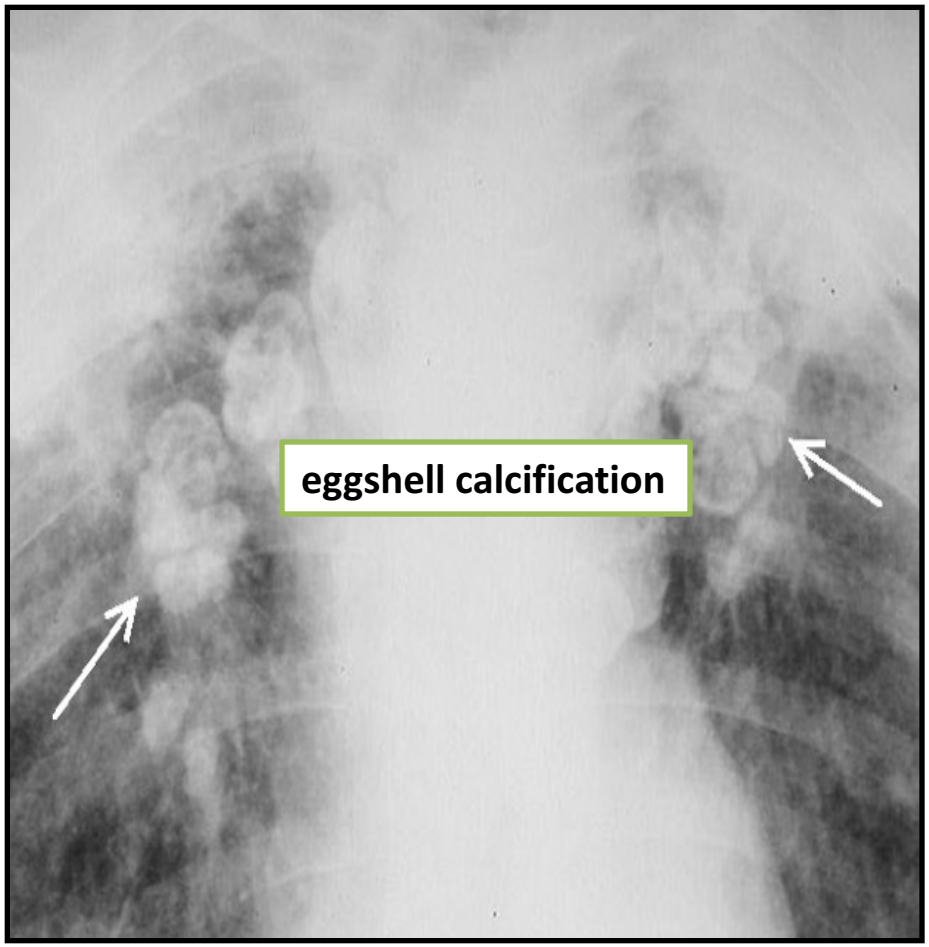
Coal worker's pneumoconiosis

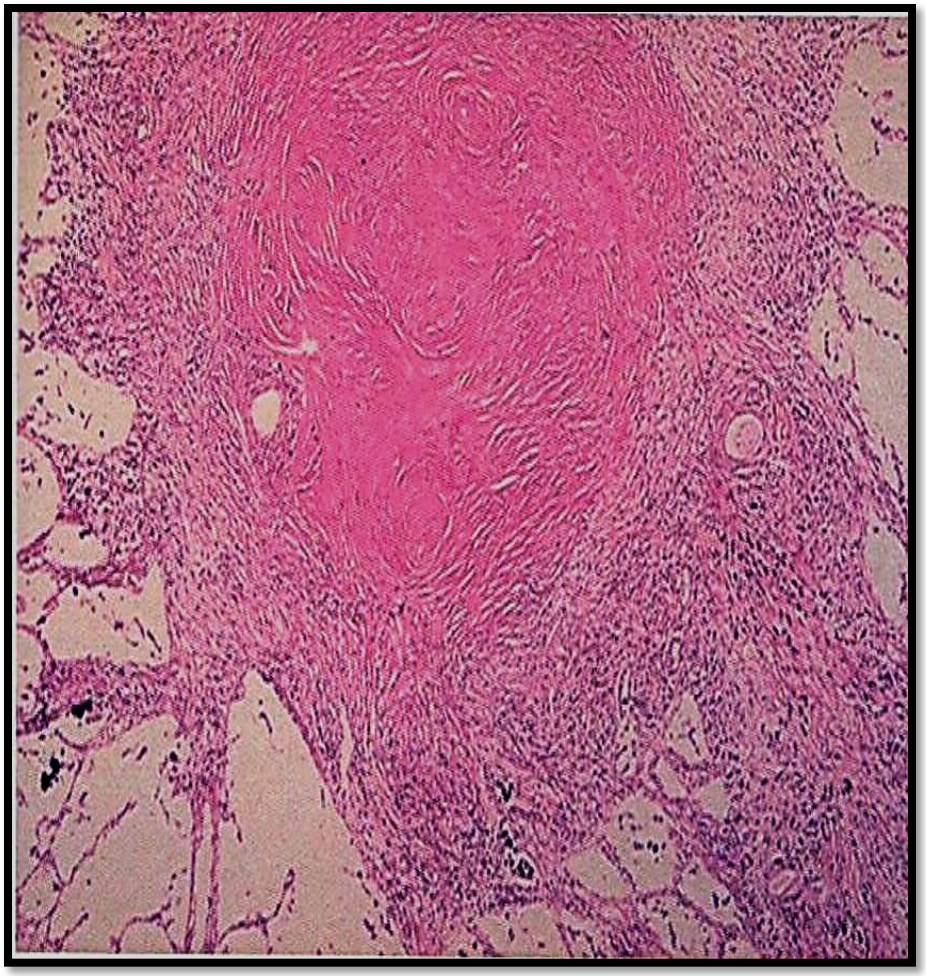




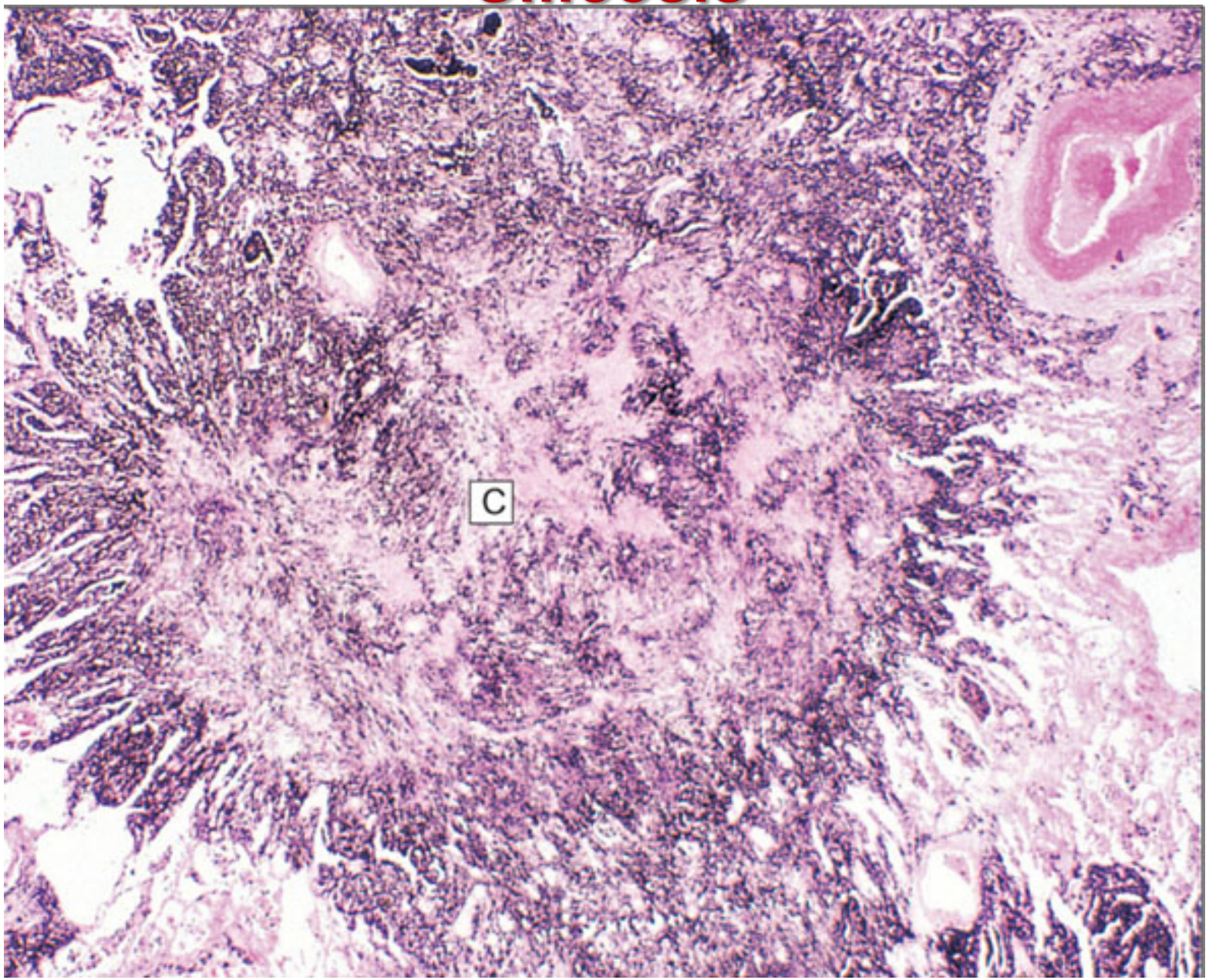
microscopic

Silicosis



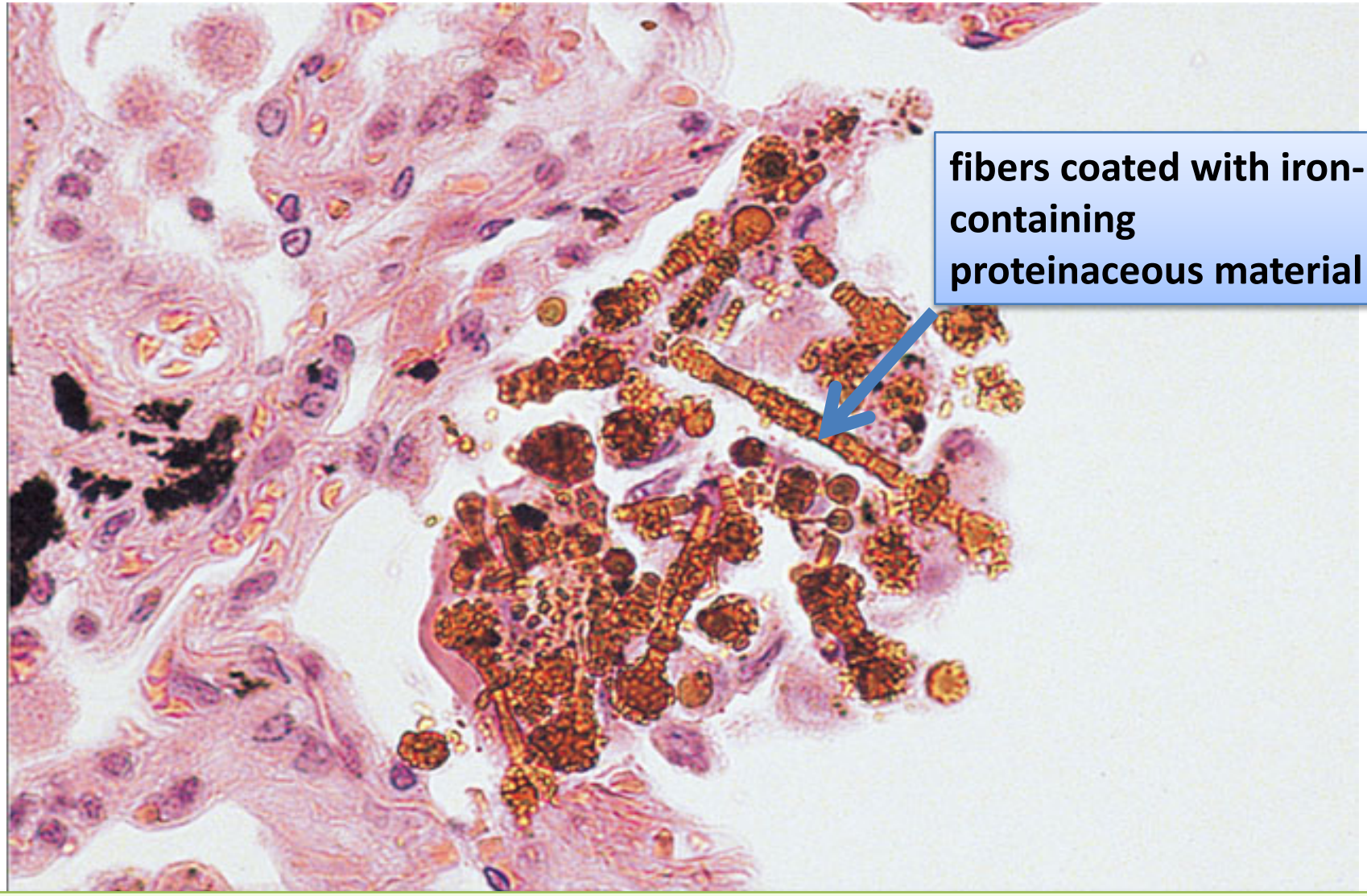


Silicosis



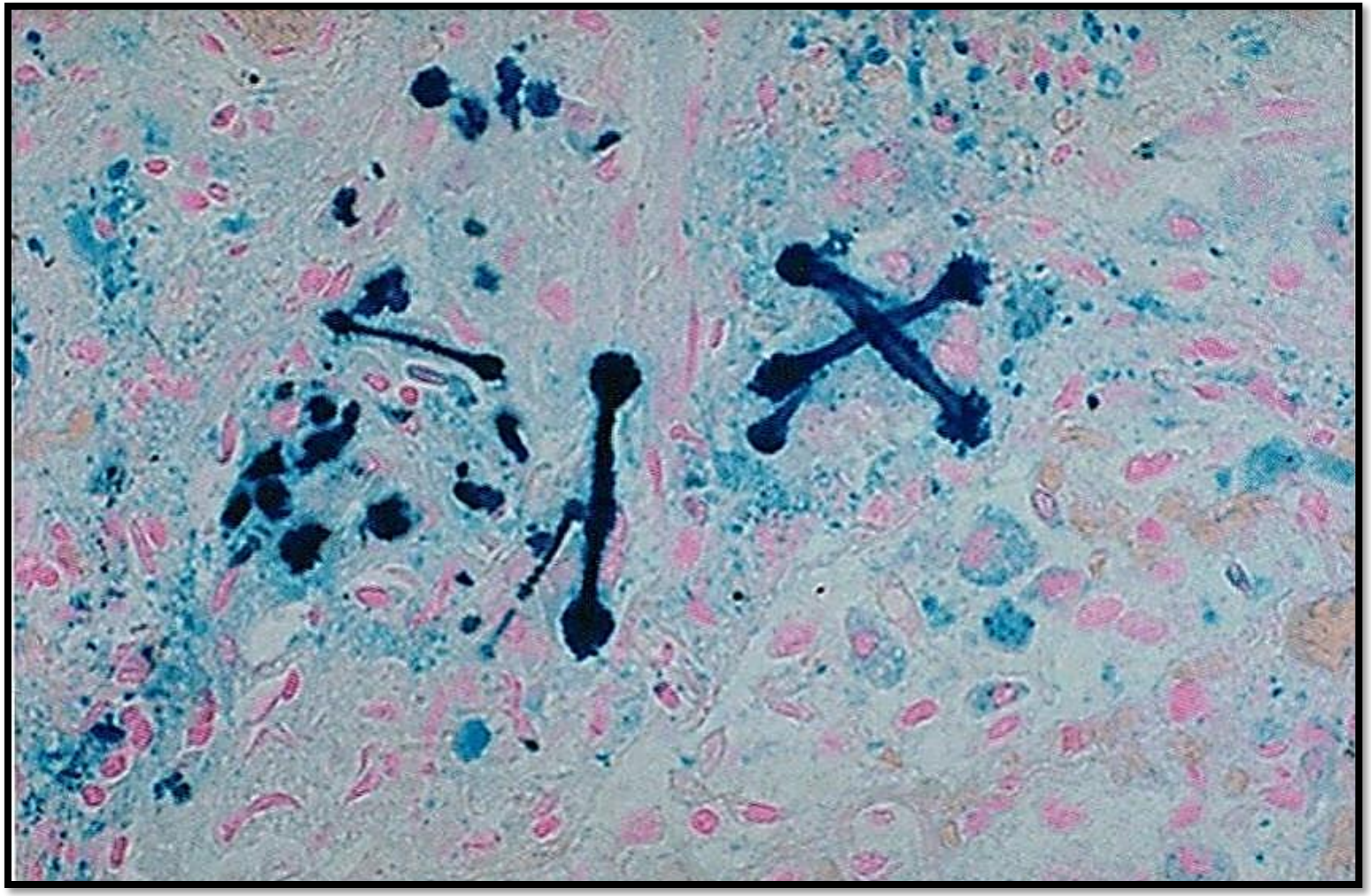
Silicosis of lung. In silicosis, nodules of collagen (C) contain silica particles.

Asbestosis



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

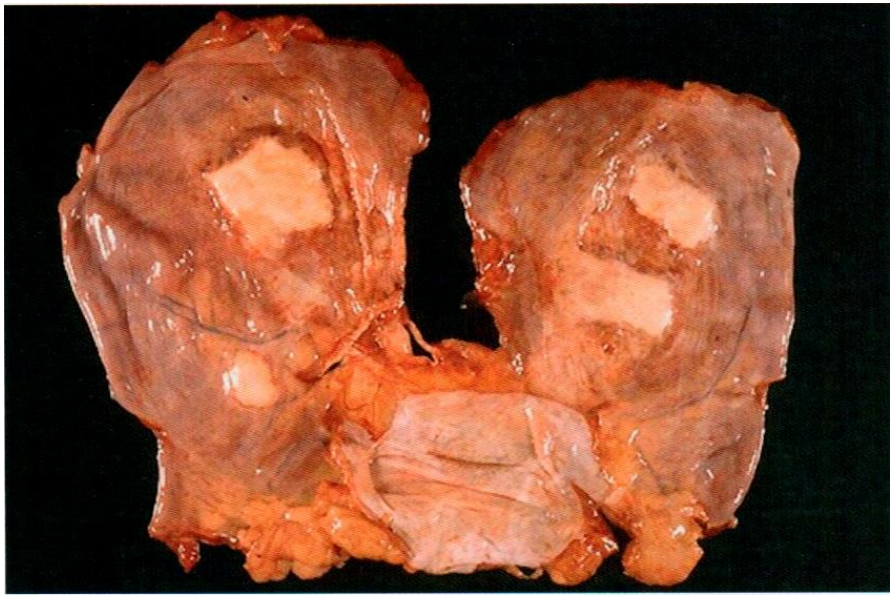
Asbestosis



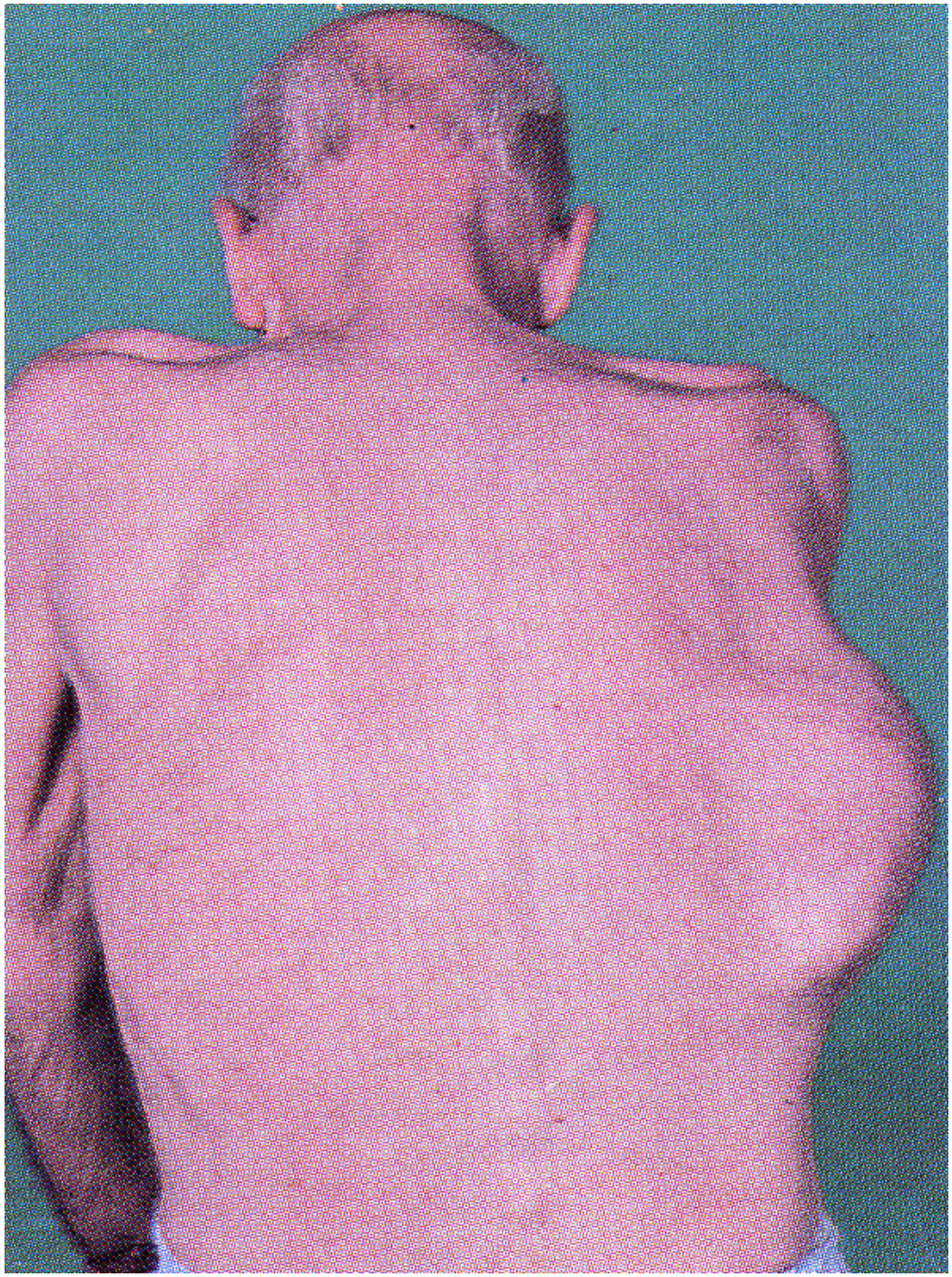
Ferruginous bodies, microscopic

Asbestosis

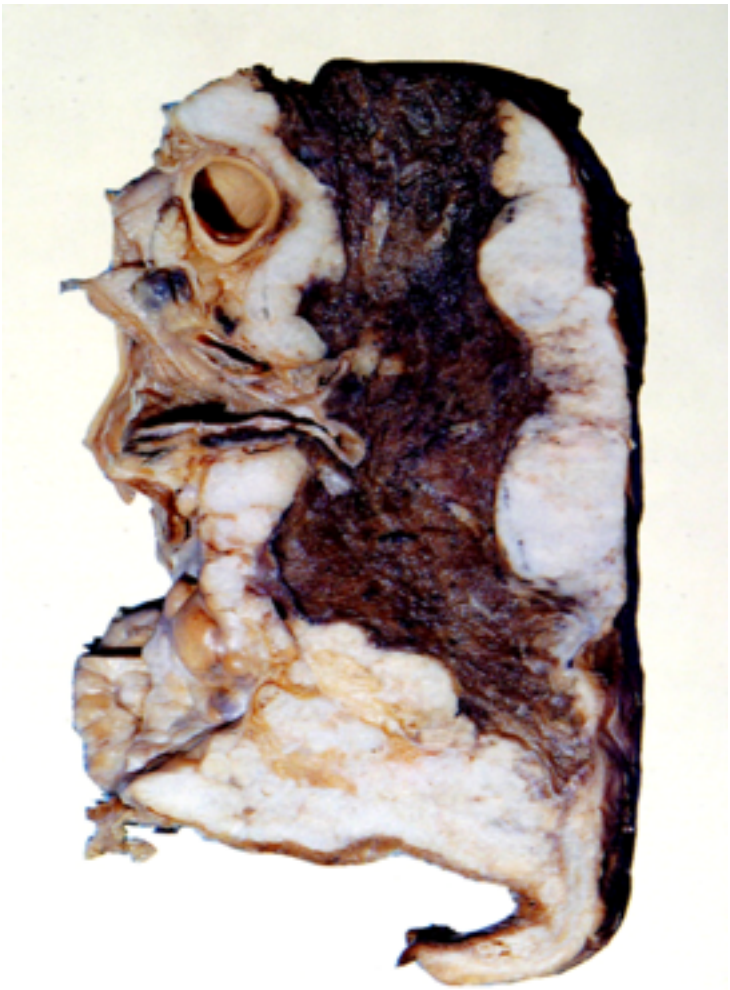
- Parenchymal interstitial fibrosis (asbestosis)
- Pleural effusion.
- Pleural adhesions.
- Parietal pleural fibrocalcific plaques
- Some types of asbestos are carcinogenic (especially crocidolite) and prolong asbestos exposure can predisposes to bronchogenic carcinoma, malignant mesothelioma and laryngeal carcinoma.



Pleural fibrous plaques



Mesothelioma. This patient presented with an asbestos link pleural plaque.



Pneumoconiosis

A nonneoplastic lung reaction to inhalation of mineral dusts (size: 1-5 μm) and fumes encountered in the workplace

Coal related pneumoconiosis

- **Simple Coal worker pneumoconiosis:** Black macules 1 to 5 mm are scattered through the lung
- **Complicated coal worker's:** produces cough, dyspnea, and lung function impairment. Complication: cor pulmonale

Silicosis

- Industrial exposure: mining of gold, tin, copper and coal, sandblasting, metal grinding, ceramic manufacturing
- stony-hard large fibrous scars
- eggshell calcification
- Fibrous pleural plaques may develop
- predispose to lung cancer and tuberculosis

Asbestosis

- Asbestos bodies are long, thin asbestos fibers coated with hemosiderin and protein (ferrogenous bodies)
- lead to lung scars containing asbestos bodies.
- They can cause pleural effusion, pleural adhesions, parietal pleural fibrocalcific plaques' and mesothelioma.
- Some types are carcinogenic and the risk of bronchogenic carcinoma is fivefold and for mesothelioma is 1000 fold and laryngeal carcinoma

Immune Granulomatous Diseases

Sarcoidosis

- A multisystem disease of unknown etiology, > female
- noncaseating granulomas in various tissues:-
- lymph node enlargement (almost all cases), eye involvement [dry eyes], iritis, skin lesions (erythema nodosum, painless subcutaneous nodules), and viscera (liver, skin, marrow). Lung involvement occurs in 90% of cases, with formation of granulomas and interstitial fibrosis

Hypersensitibity pneumonitis (extrinsic allergic alveolitis)

- inhalation of organic dust containing antigens:-
  - *Farmer's lung:* thermophilic actinomycetes or Micropolyspora faeni (spores in mouldy hay).
  - *Pigeon breeder's lung:* excreta, or feathers of birds
  - *Air-conditioner lung:* thermophilic bacteria
- Interstitial pneumonitis, with lymphocytes, plasma cells, macrophages and noncaseating granulomas peribronchiolar
- If exposure is continuous, lead to progressive respiratory failure, dyspnea, and cyanosis and a decrease in compliance

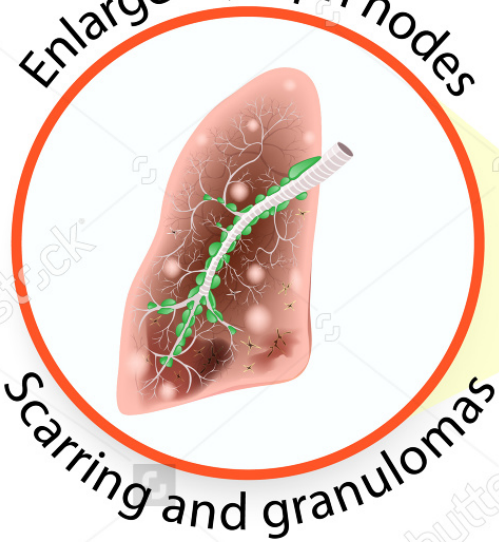
Sarcoidosis

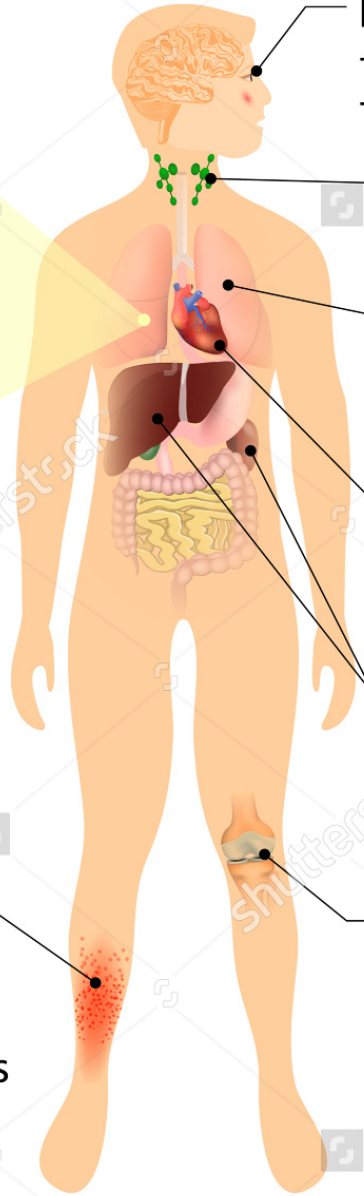
The prognosis of sarcoidosis is unpredictable.

It can progressive and chronic. It may present as episodes of activity.

Granuloma: small, non caseating

Majority of the patients respond well to treatment.





Eye
- dry eyes
- blurry vision

Lymph nodes
- enlarged

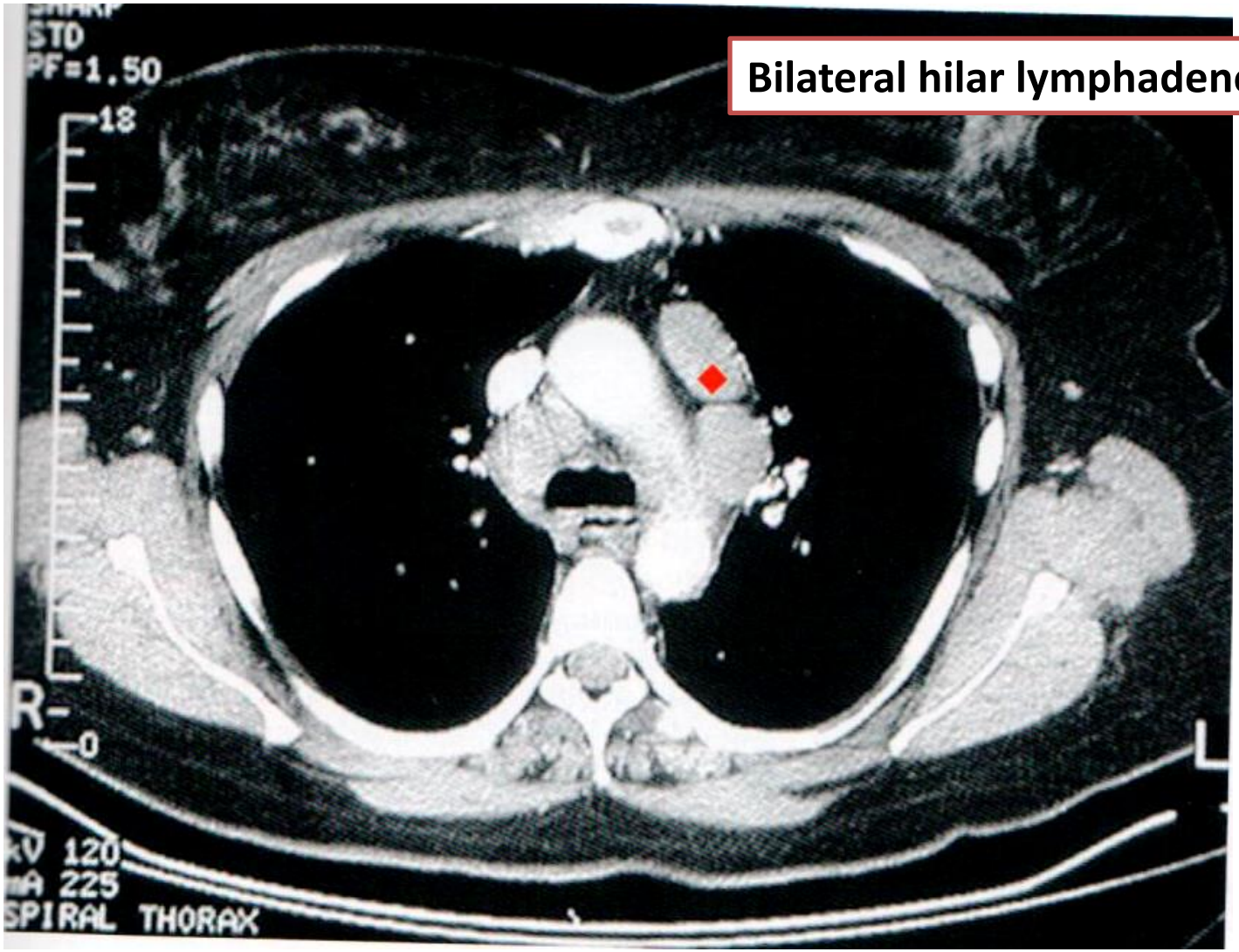
Lungs
- hacking cough
- cough up blood

Heart
- complications

Liver and spleen
- enlargement

Skin
- rashes
- lupus pernio
- erythema nodosum
- skin lesions on back
- subcutaneous nodules

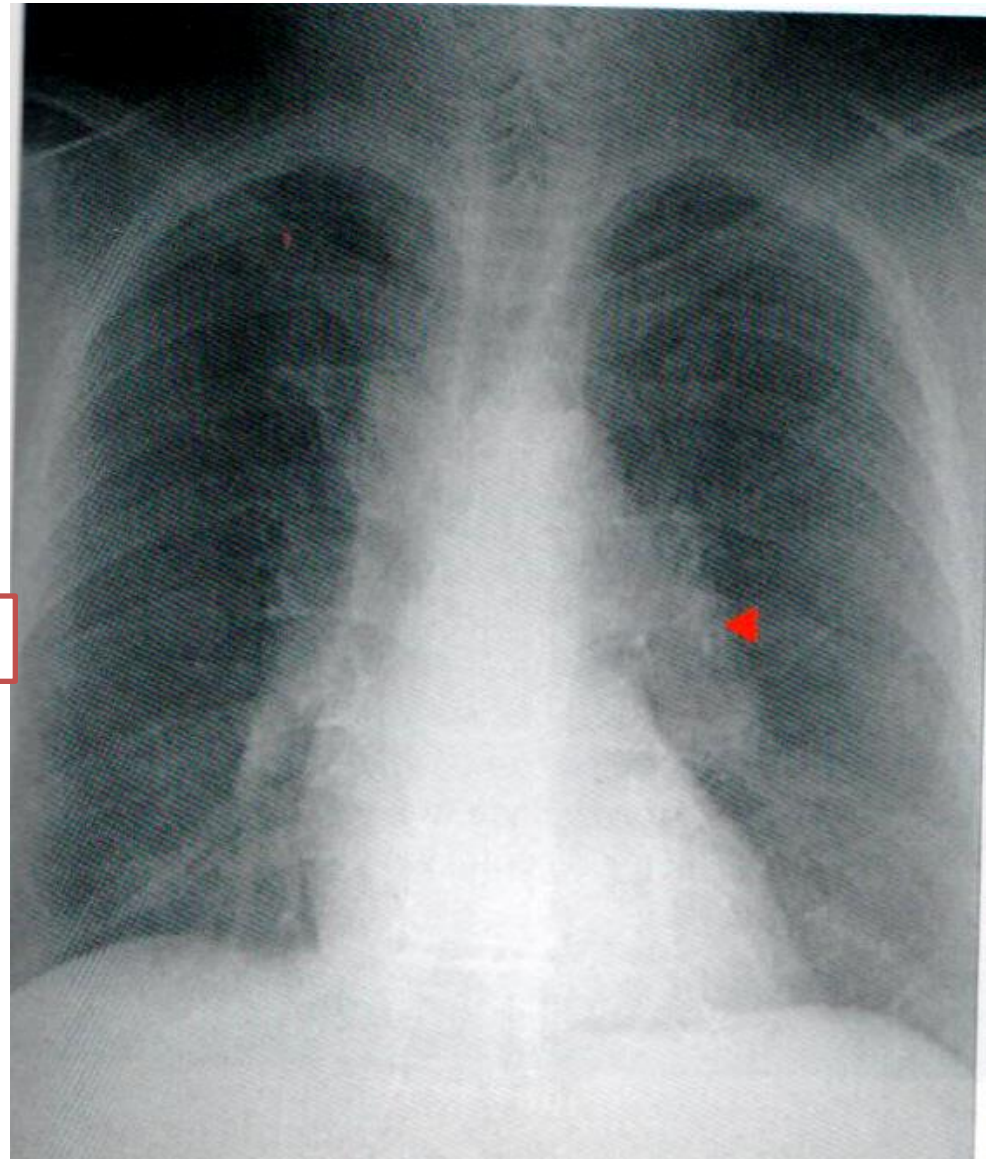
Joints
- pain
- arthritis
- swelling of the knees



Bilateral hilar lymphadenopathy

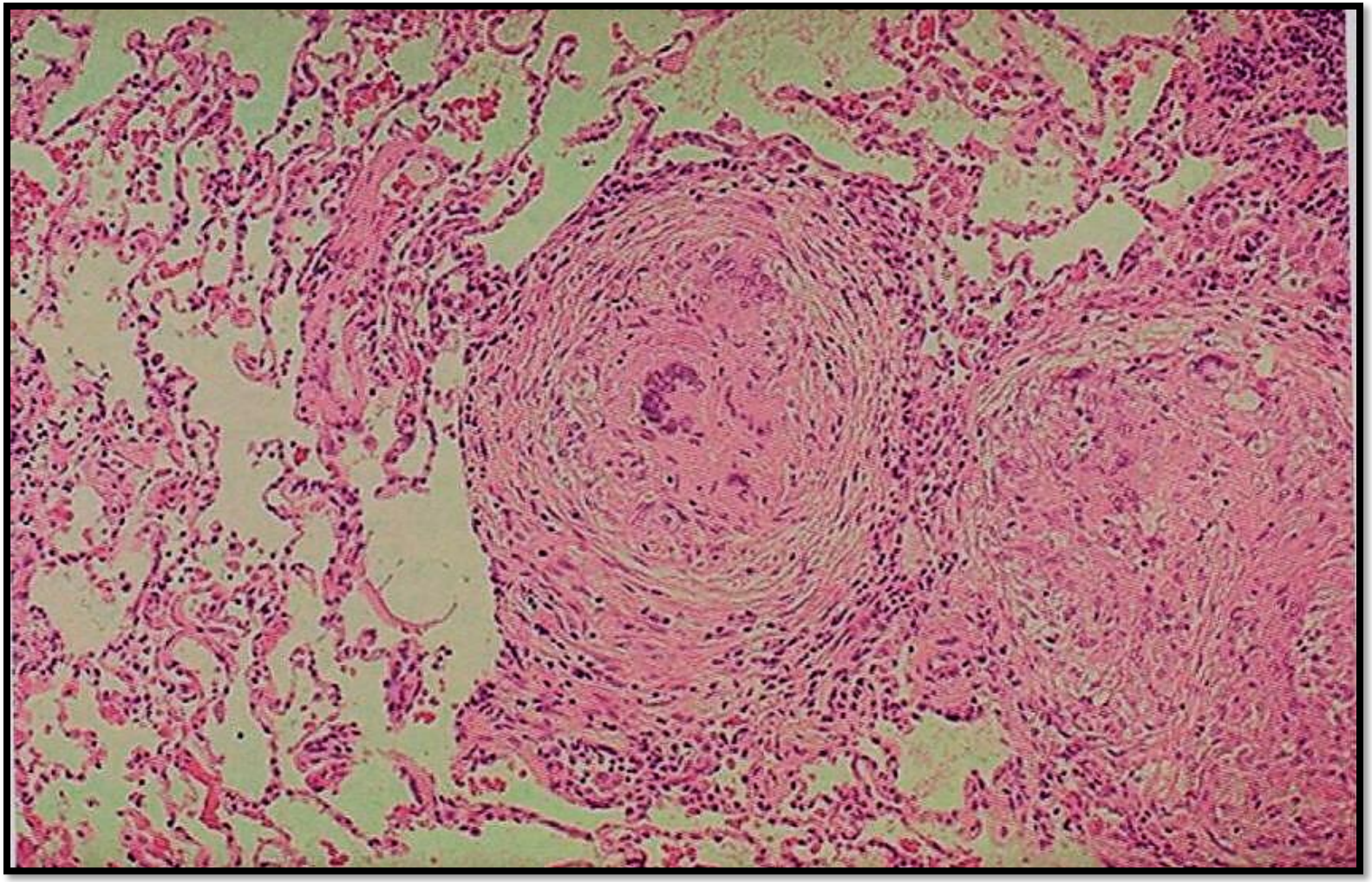
Sarcoidosis, CT image

Bilateral hilar lymphadenopathy



Sarcoidosis, radiograph

Sarcoidosis



Sarcoidosis, microscopic
noncaseating interstitial granulomas

Hypersensitivity pneumonitis

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

Farmer's lung

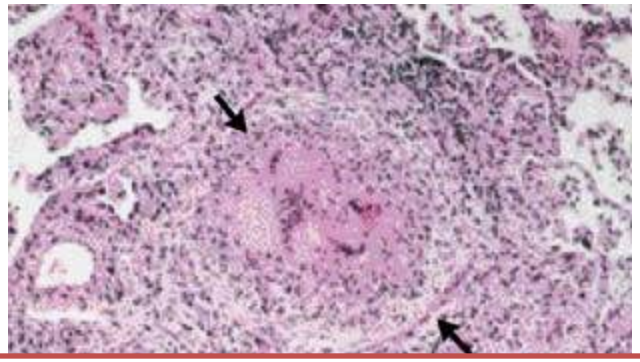
Thermophilic actinomycetes or Micropolyspora faeni in hay

Pigeon breeder's (*psittacosis*)

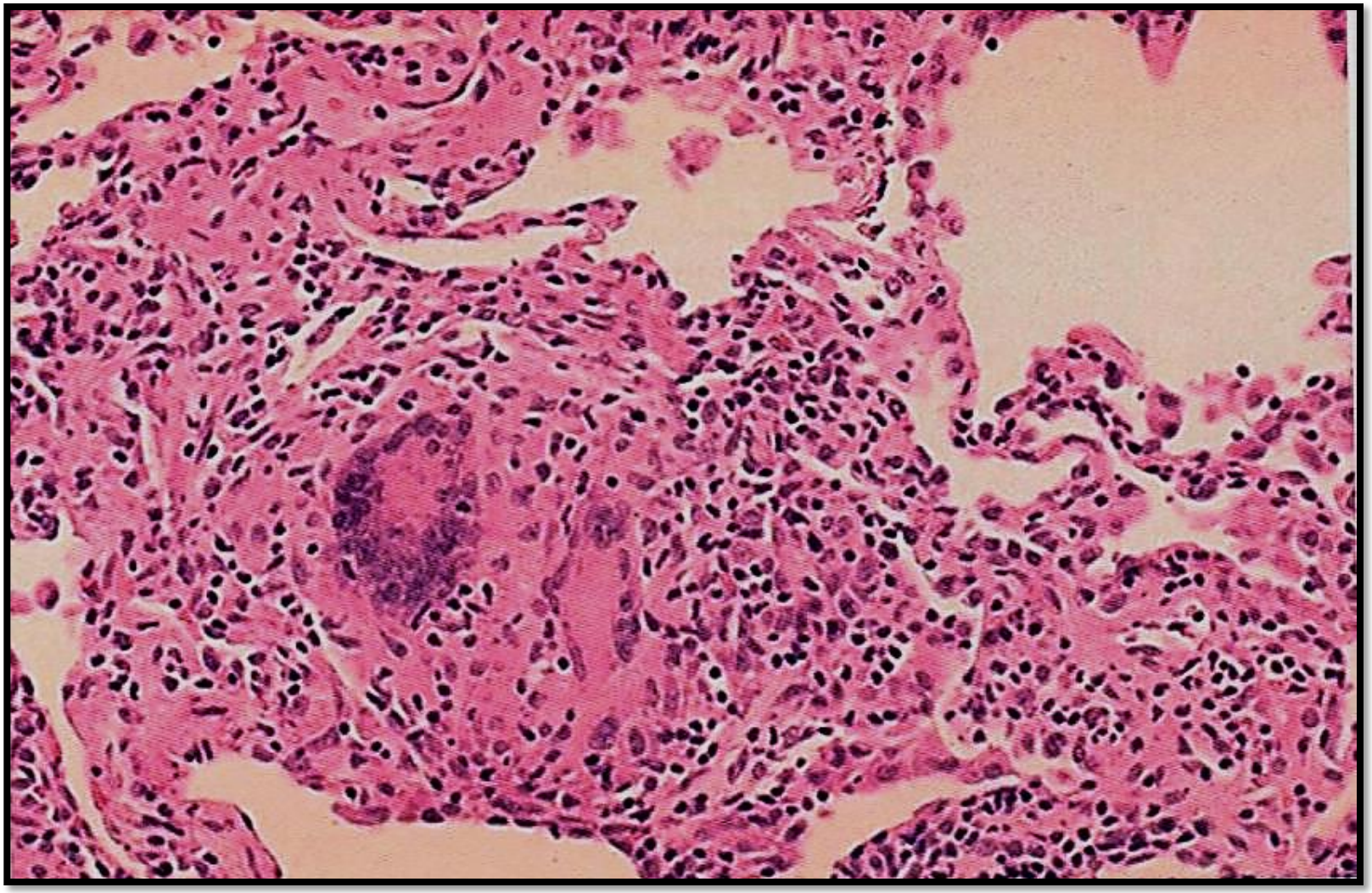
Air-cooler lung

Thermophilic bacteria

Sugarcane bagasse (Bagassosis)



pneumonitis with non-necrotizing granulomas



Hypersensitivity pneumonitis, microscopic

noncaseating interstitial granulomas and chronic inflammation along the bronchiols