

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 interstitium (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**

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:

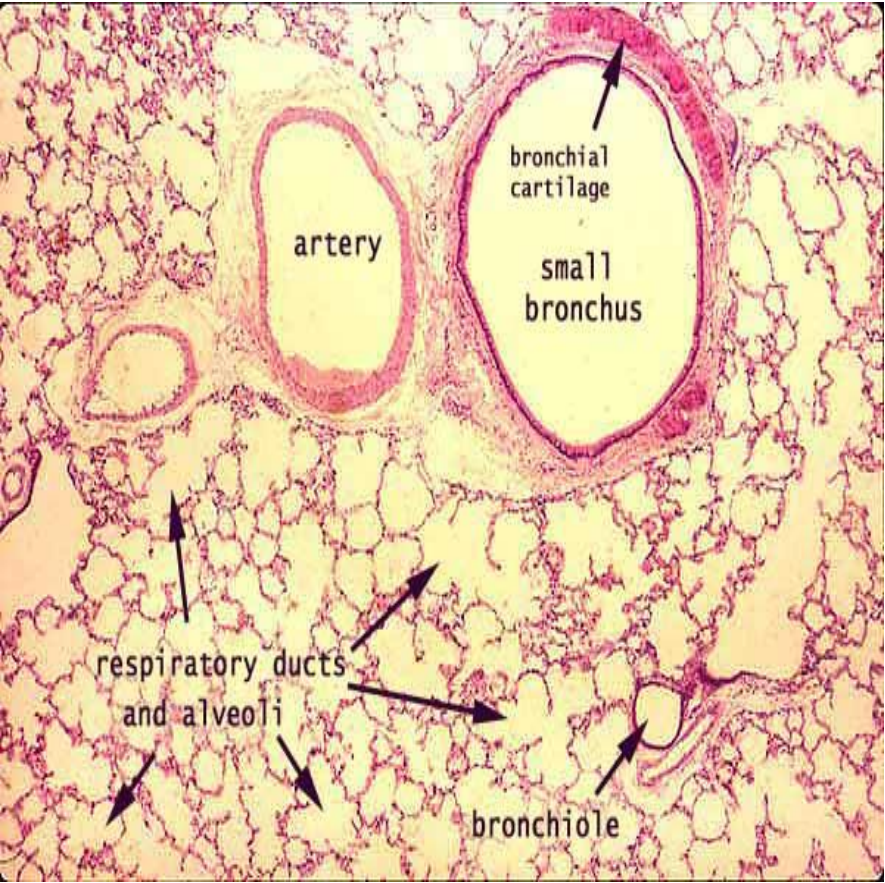
The chest wall, pleura, and respiratory muscles are the components of the respiratory pump, and they need to function normally for effective ventilation.

Abnormalities of the chest wall include:

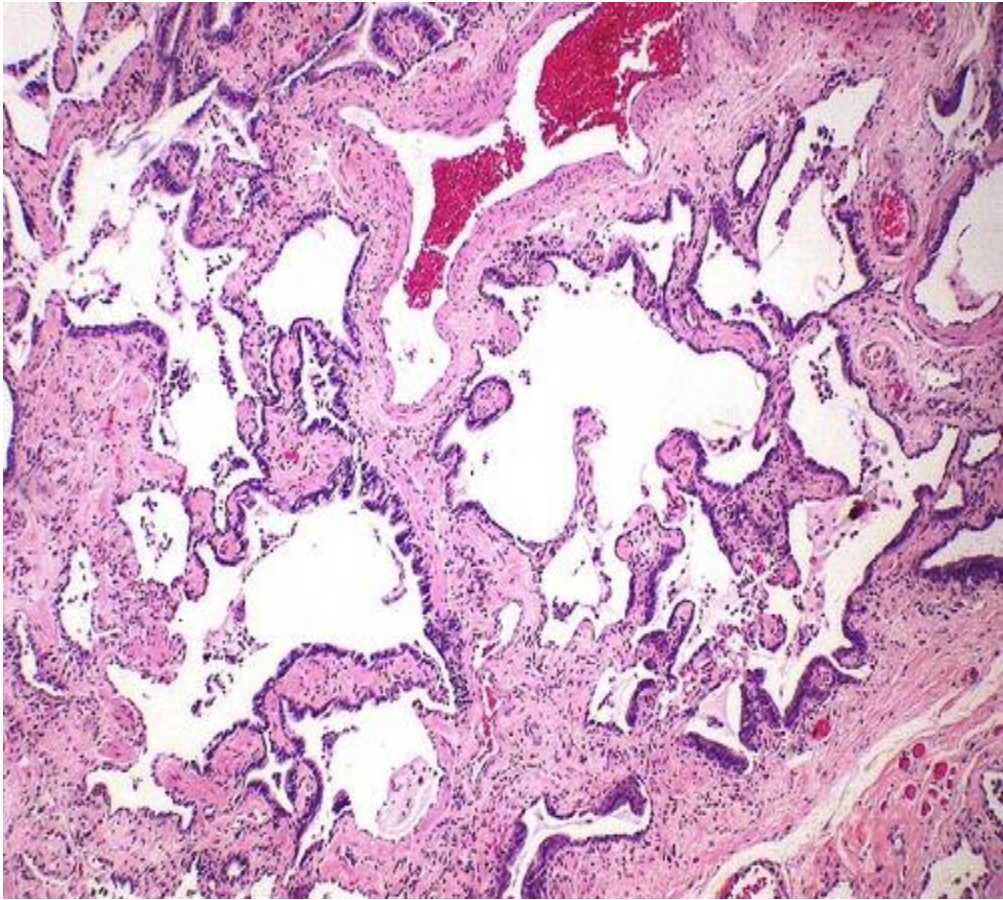
- bony abnormalities (kyphosis or kypho-scoliosis)
- massive pleural effusion
- morbid obesity
- neuromuscular disease of respiratory muscles

Interstitial lung diseases

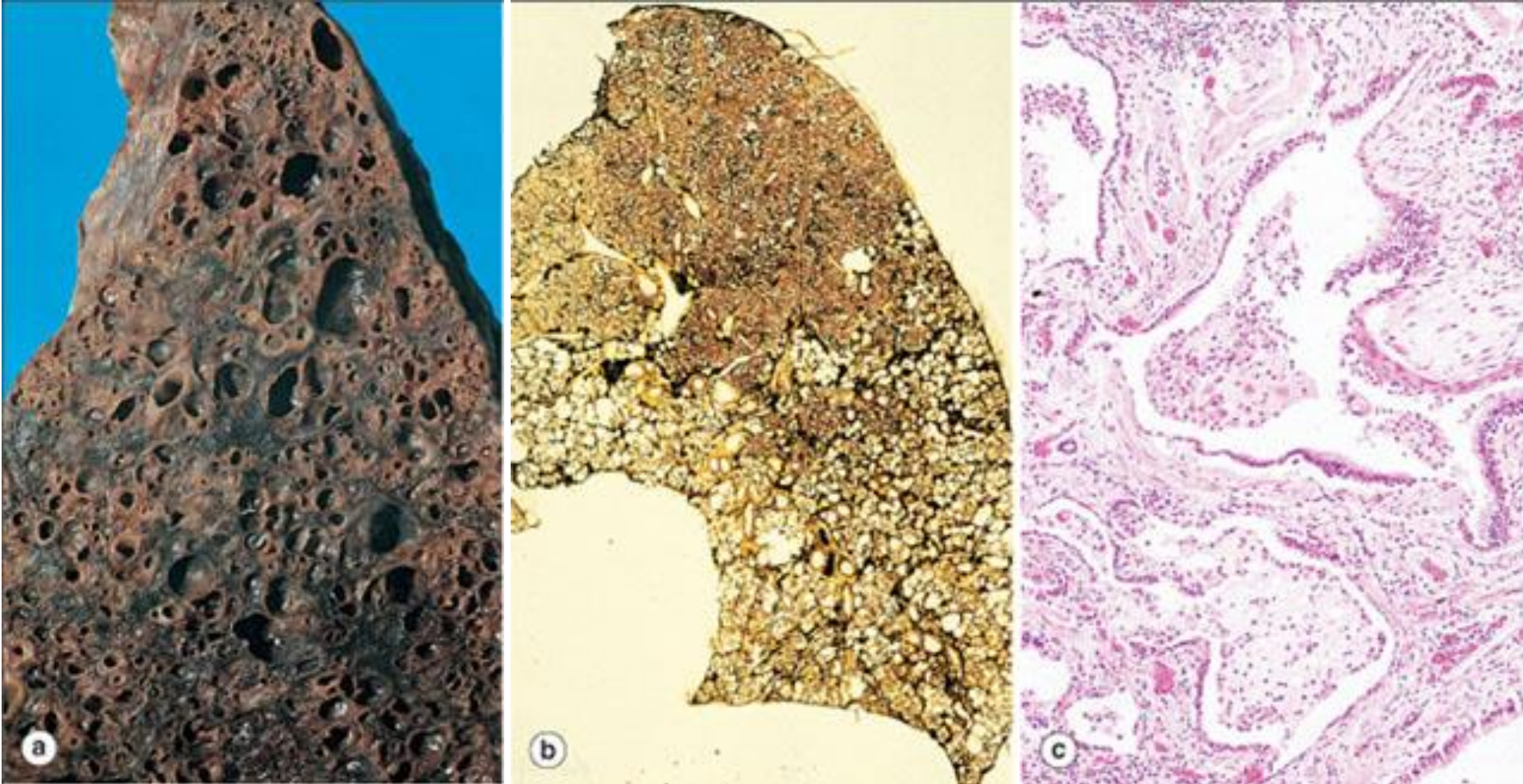
Normal



Honeycomb lung



Diseases of Lung



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.



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.

Acute restrictive lung diseases (INTRINSIC TYPE)

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

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 fractures, head injury, burns, radiation)

Shock

Cardiopulmonary bypass

Acute pancreatitis

Transfusion

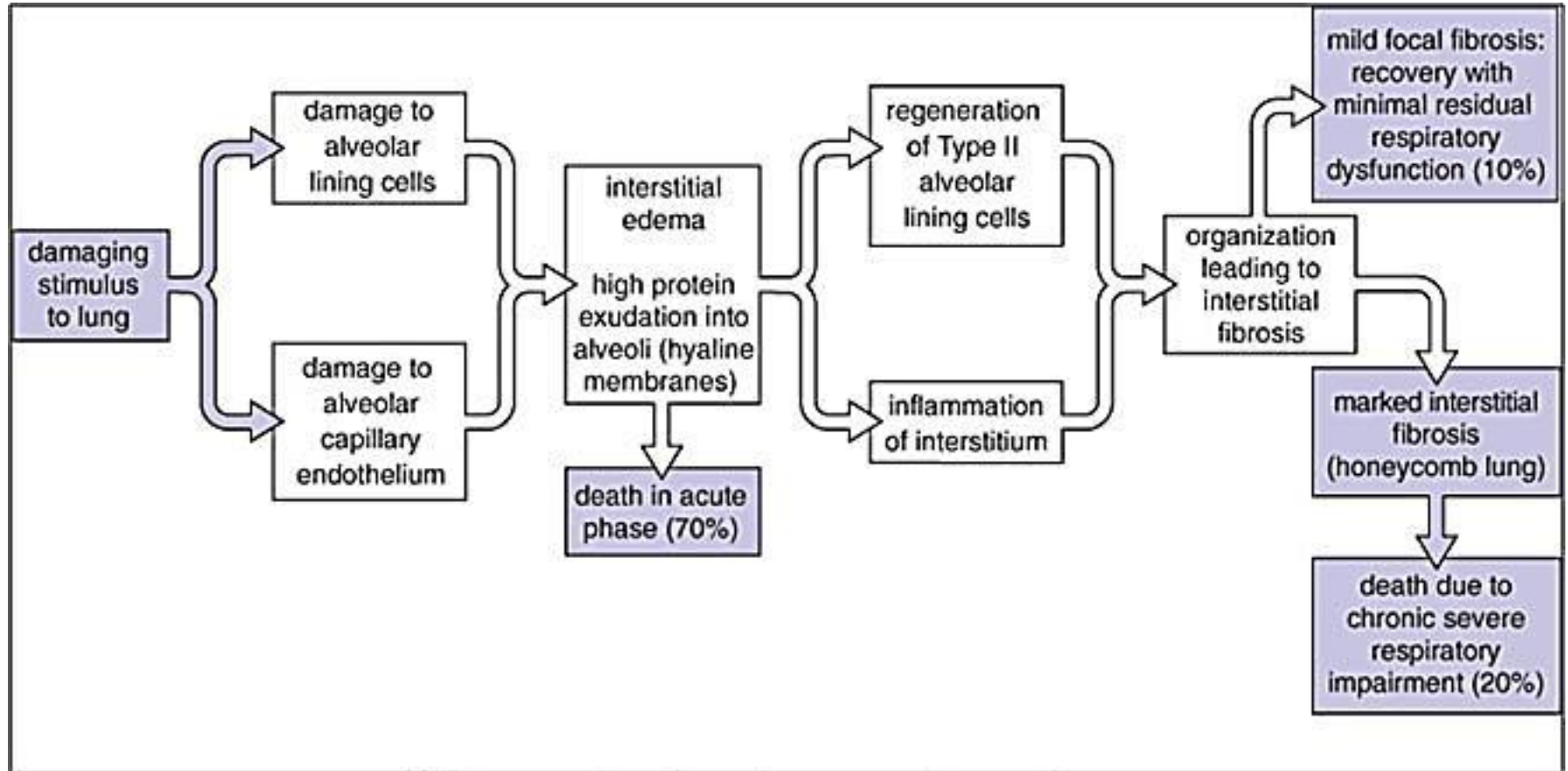
Uremia

Overdose with street drugs such as heroin

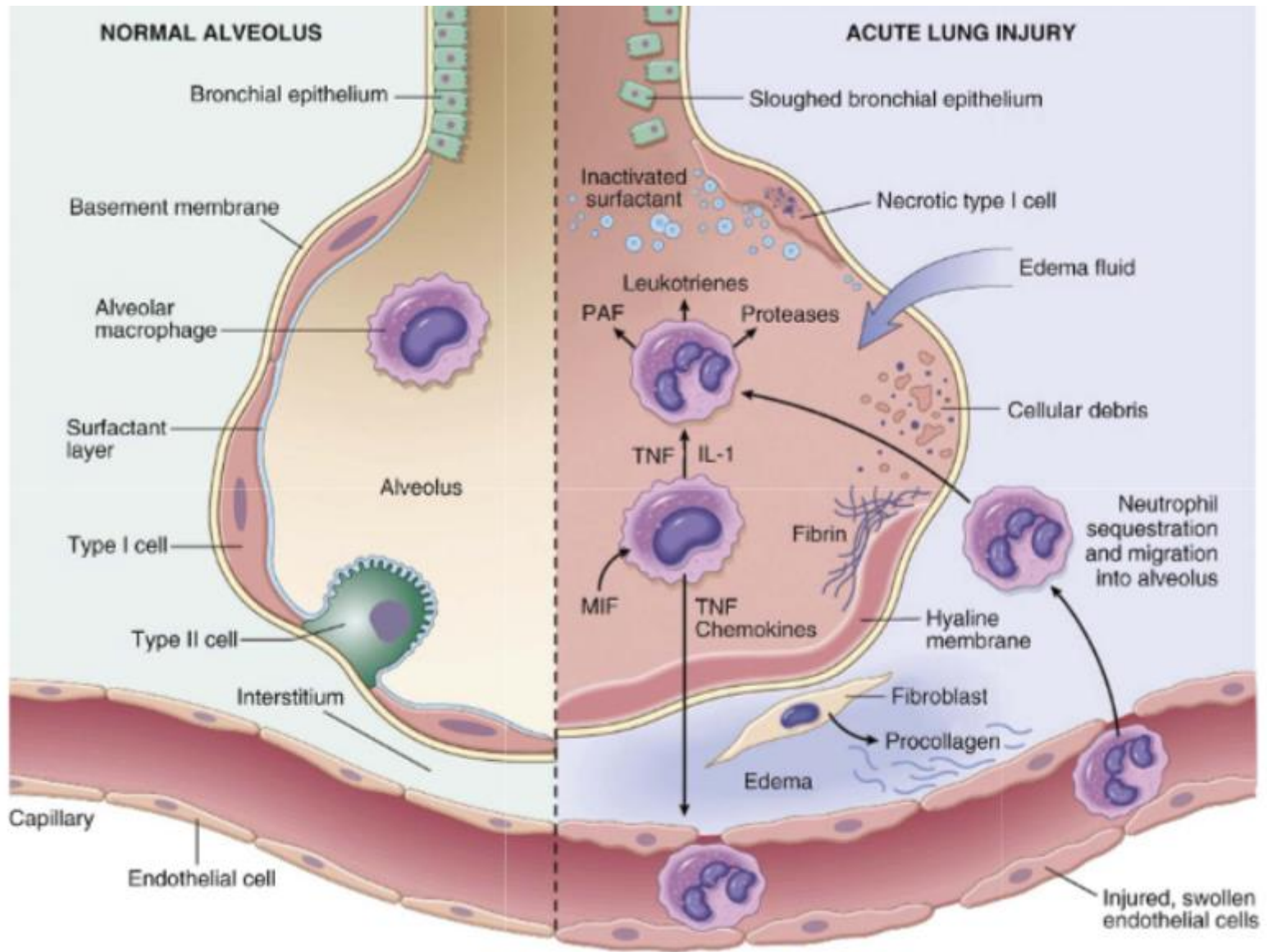
Therapeutic drugs such as bleomycin

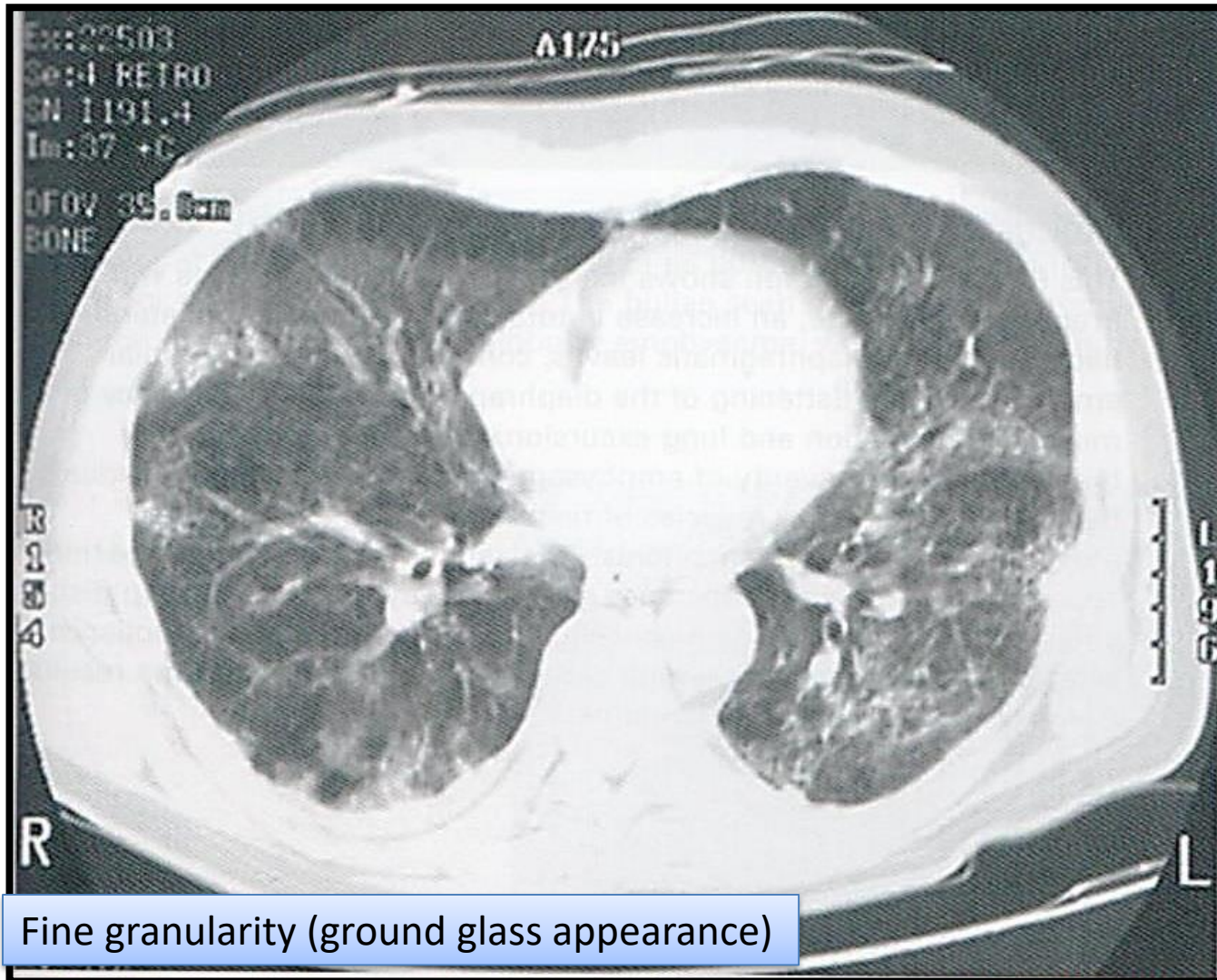
Hematologic conditions e.g multiple transfusion, coagulation disorders

Diseases of Lung



The main events and outcomes of ARDS.

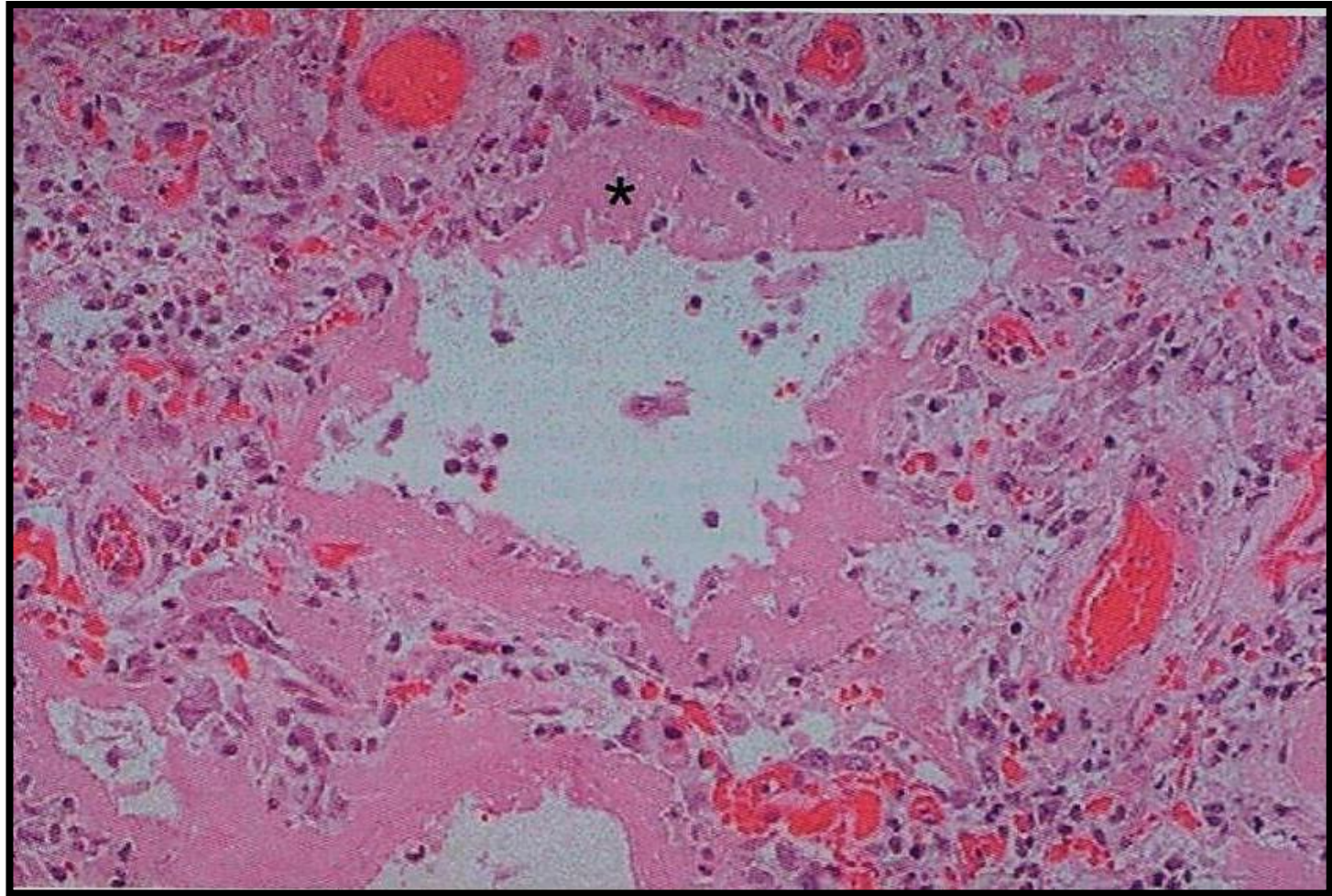




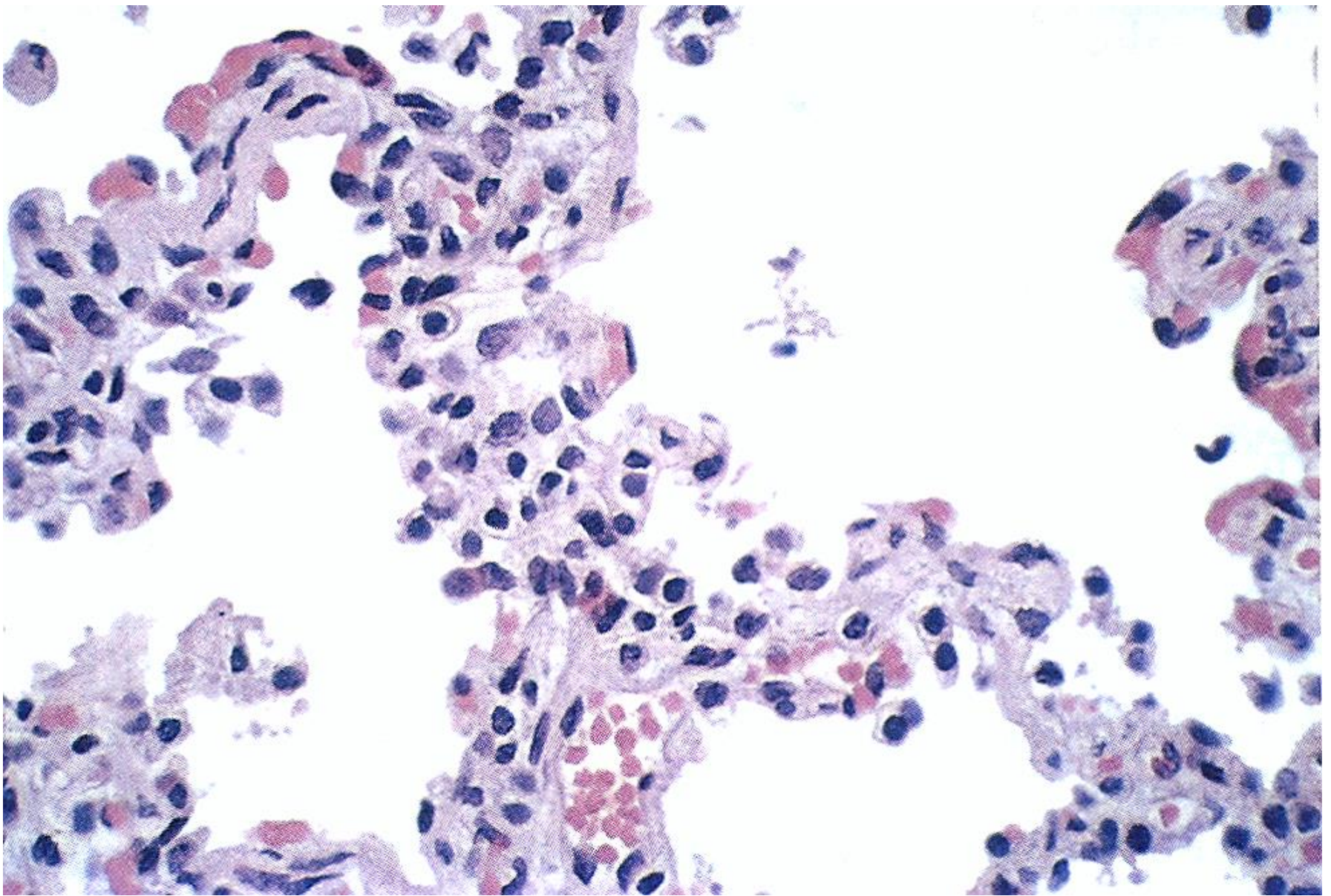
Diffuse alveolar damage, CT image



Diffuse alveolar damage, gross: lung edema



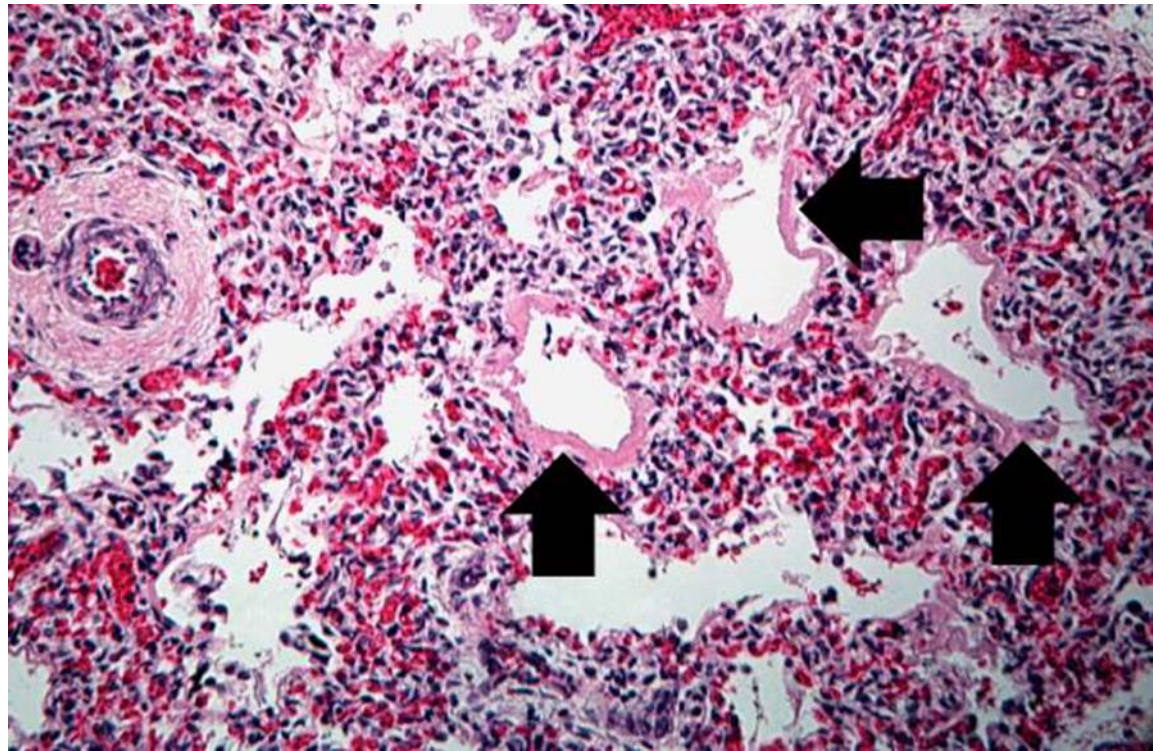
Diffuse alveolar damage, microscopic



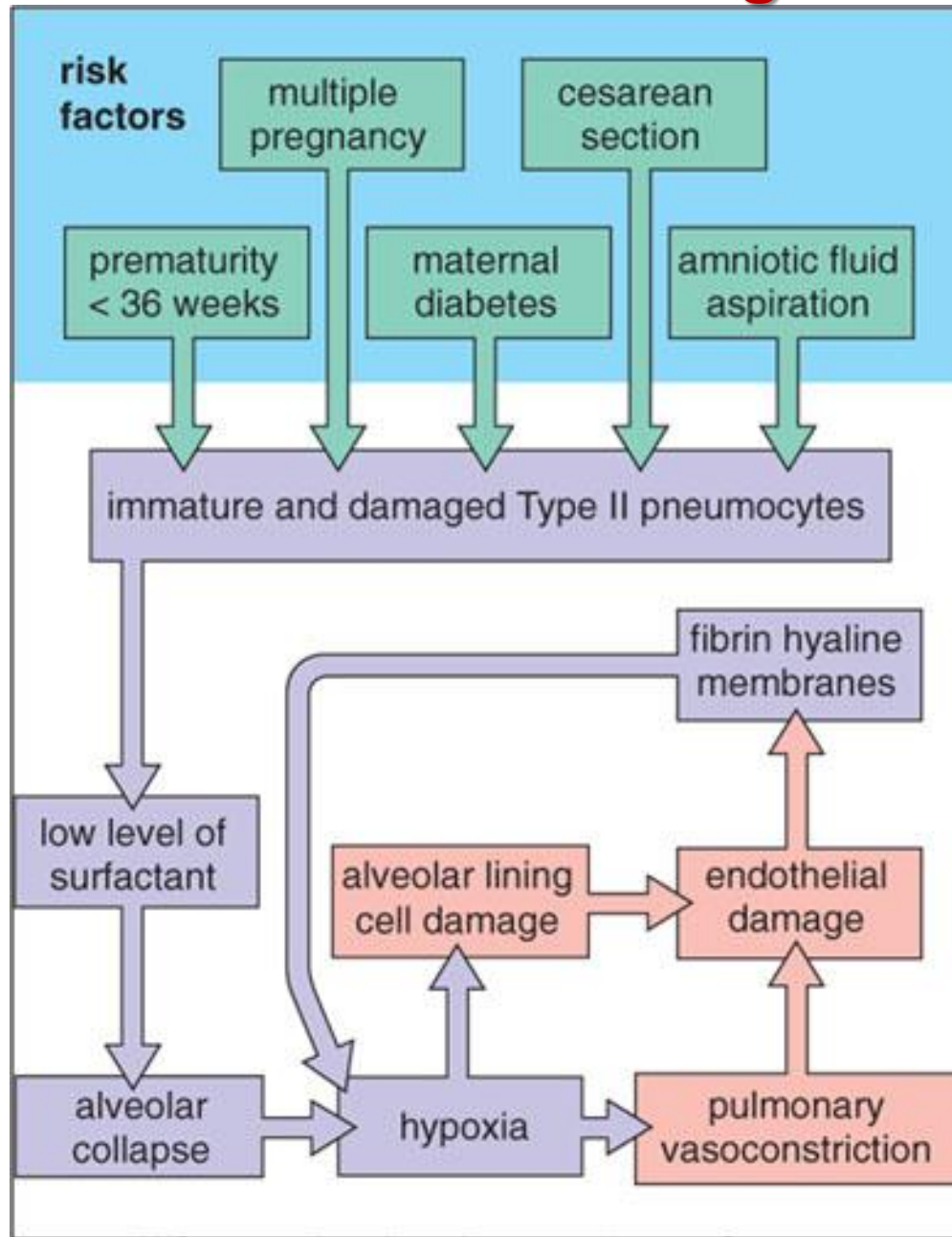
Atypical pneumonia

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

Hypersensitivity pneumonitis
(extrinsic allergic alveolitis)

Systemic lupus erythematosus

Systemic sclerosis (scleroderma)

Wegener granulomatosis

Drug:

Chemotherapy, methotrexate, bleomycin toxicity

Smoking related:

Eosinophilic granuloma

Desquamative interstitial pneumonia

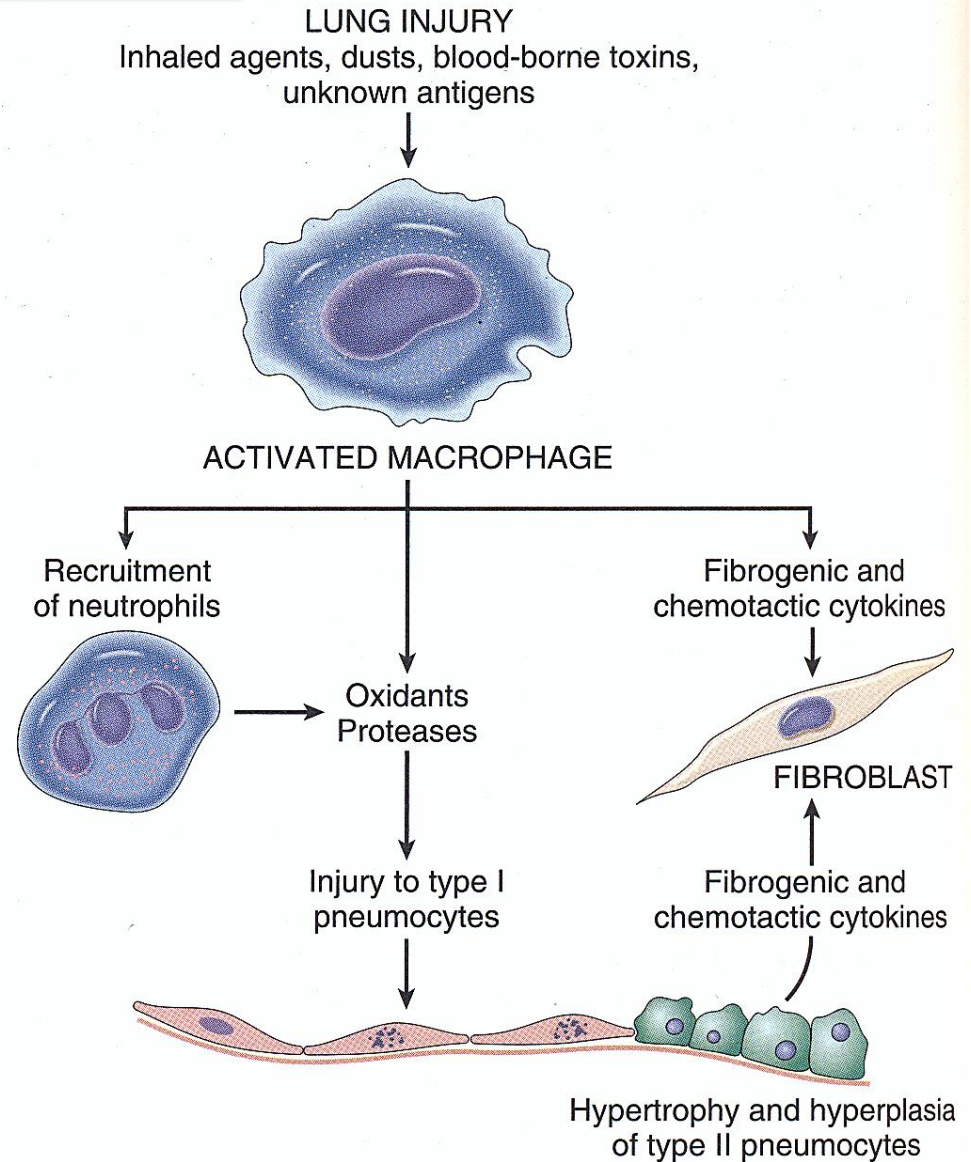
Respiratory bronchiolitis-associated interstitial lung disease

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**



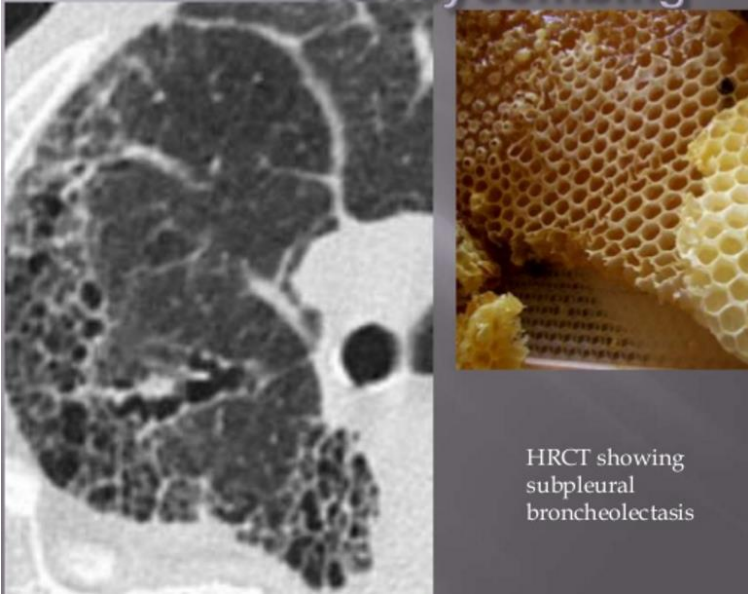
Idiopathic pulmonary fibrosis (Usual interstitial pneumonia)

Usual interstitial pneumonia

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

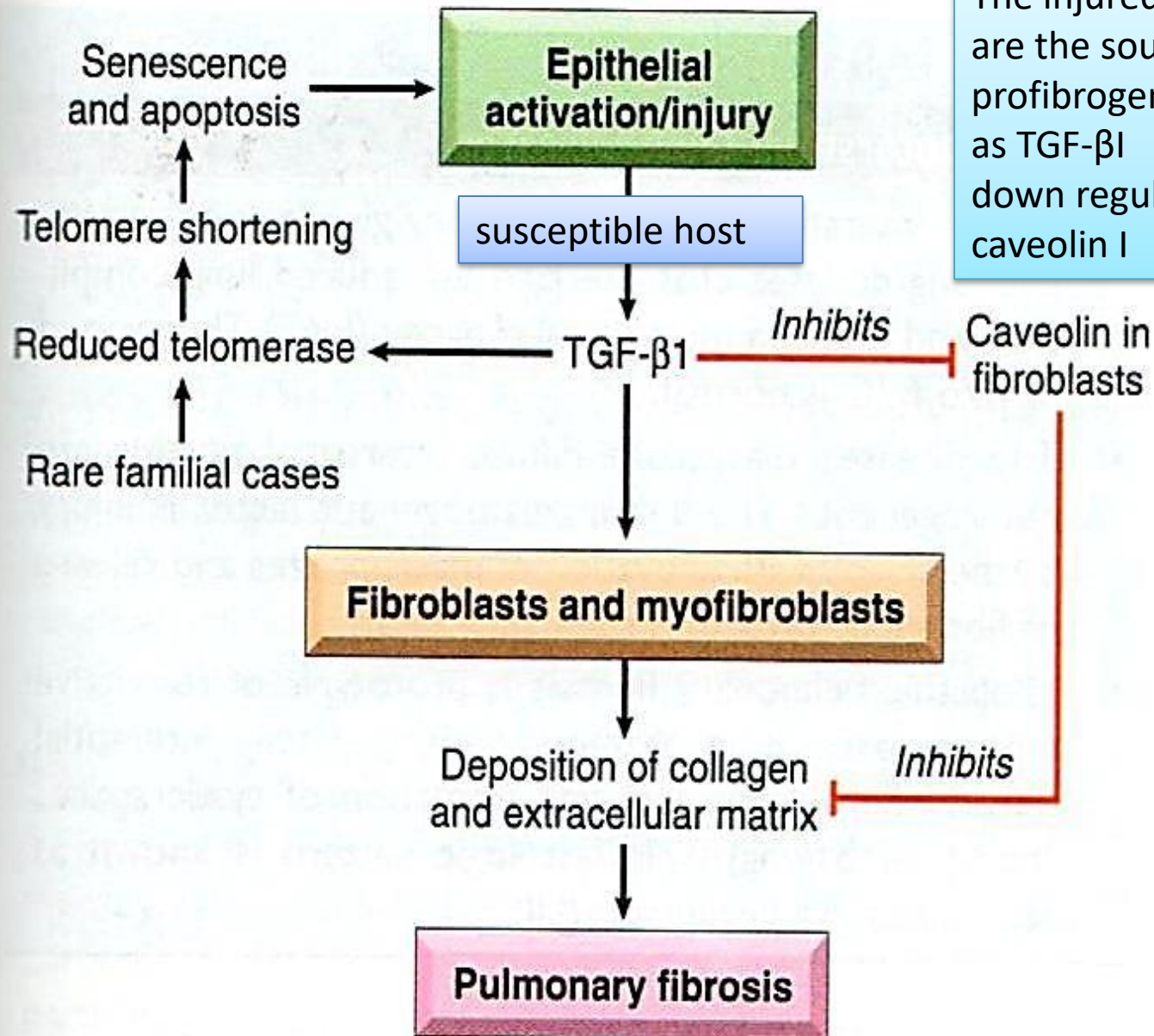


Honeycombing



HRCT showing
subpleural
bronchoectasis

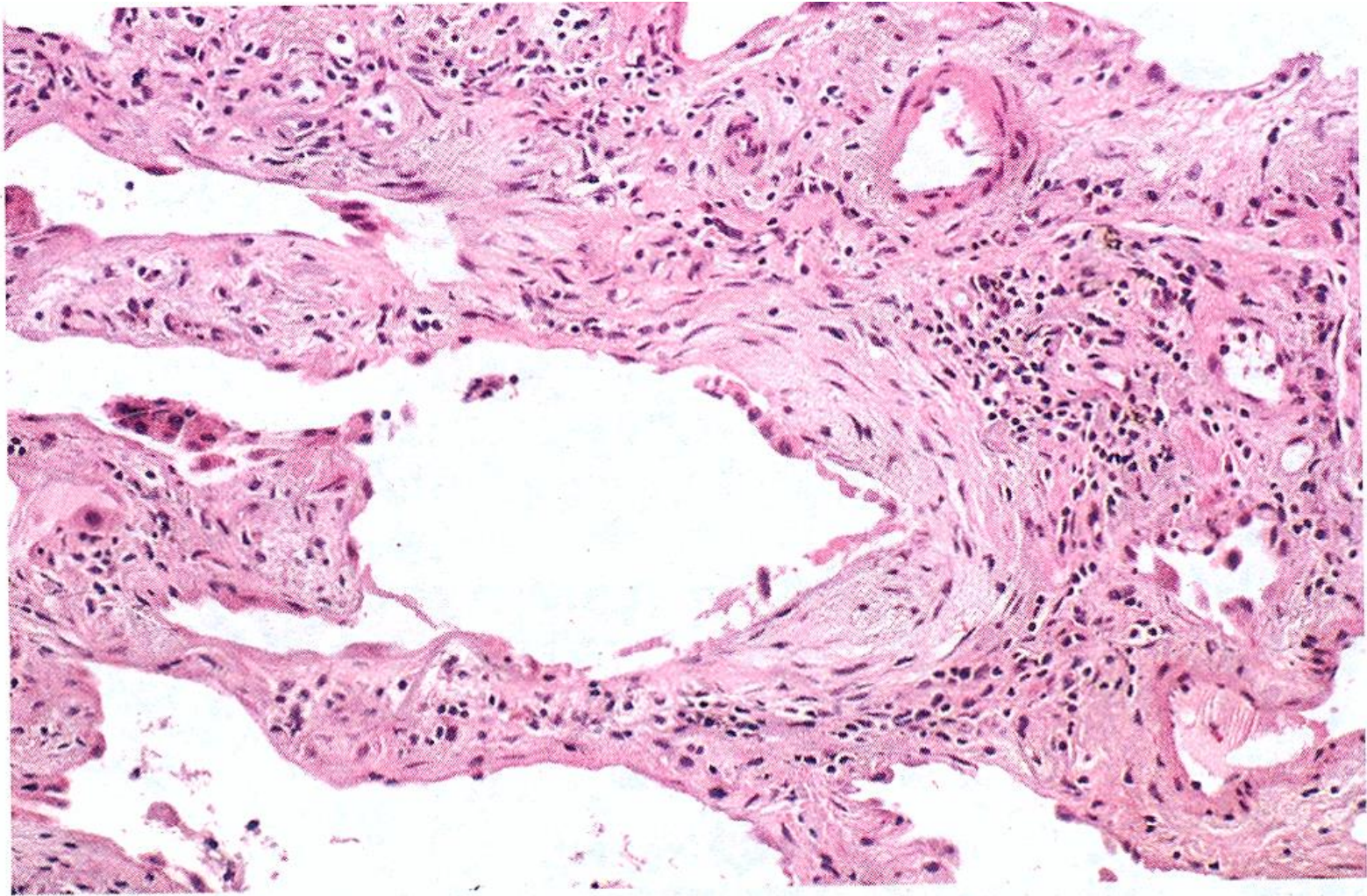
Pathogenesis of idiopathic pulmonary fibrosis



The injured epithelial cells are the source of profibrogenic factors such as TGF-β1 secondary to down regulation of caveolin I

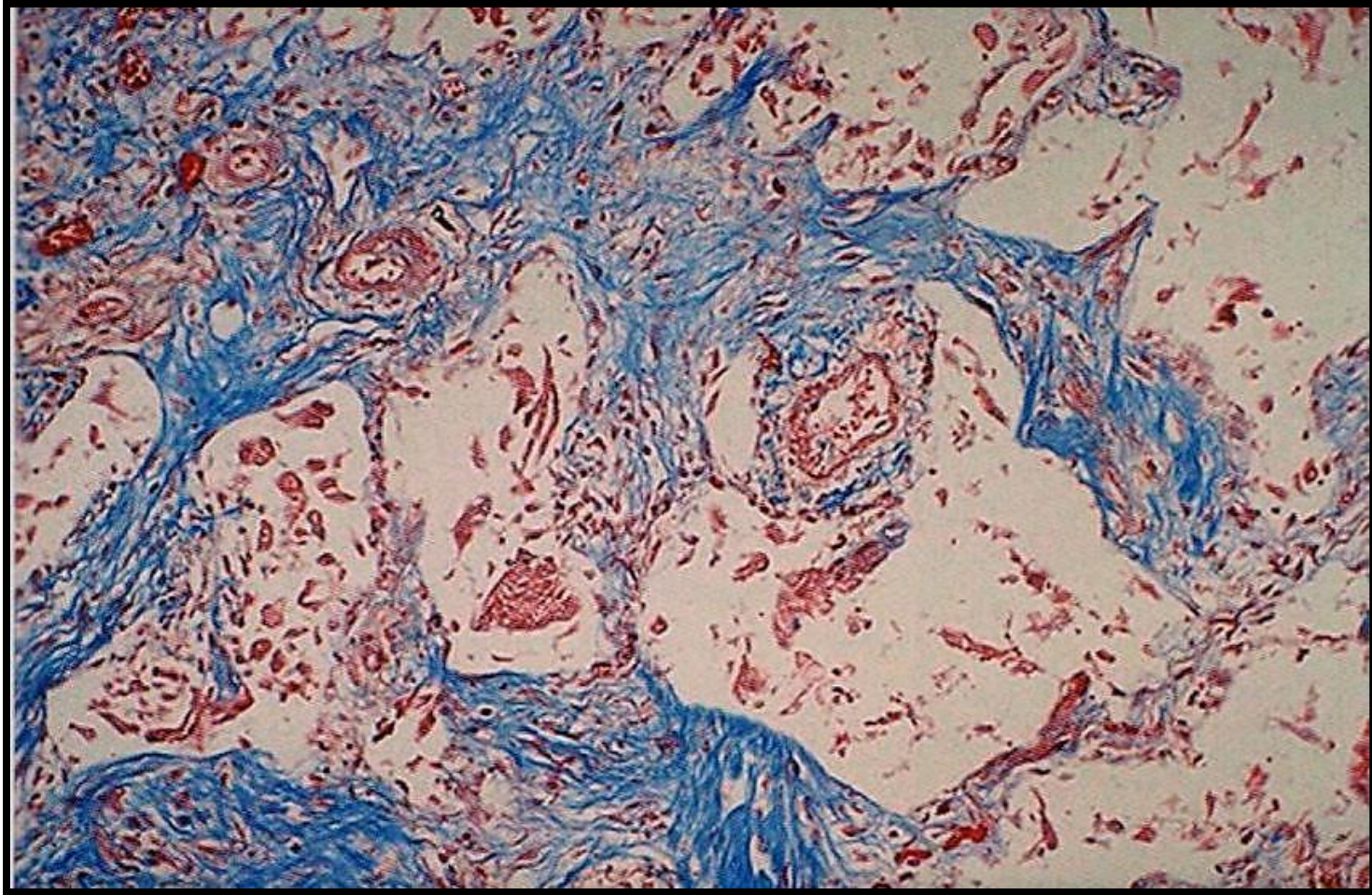


Honeycomb change, gross
Fibrosis in the subpleural region



F

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

Occupational: Pneumoconiosis

Anthracosis and coal worker's pneumoconiosis,

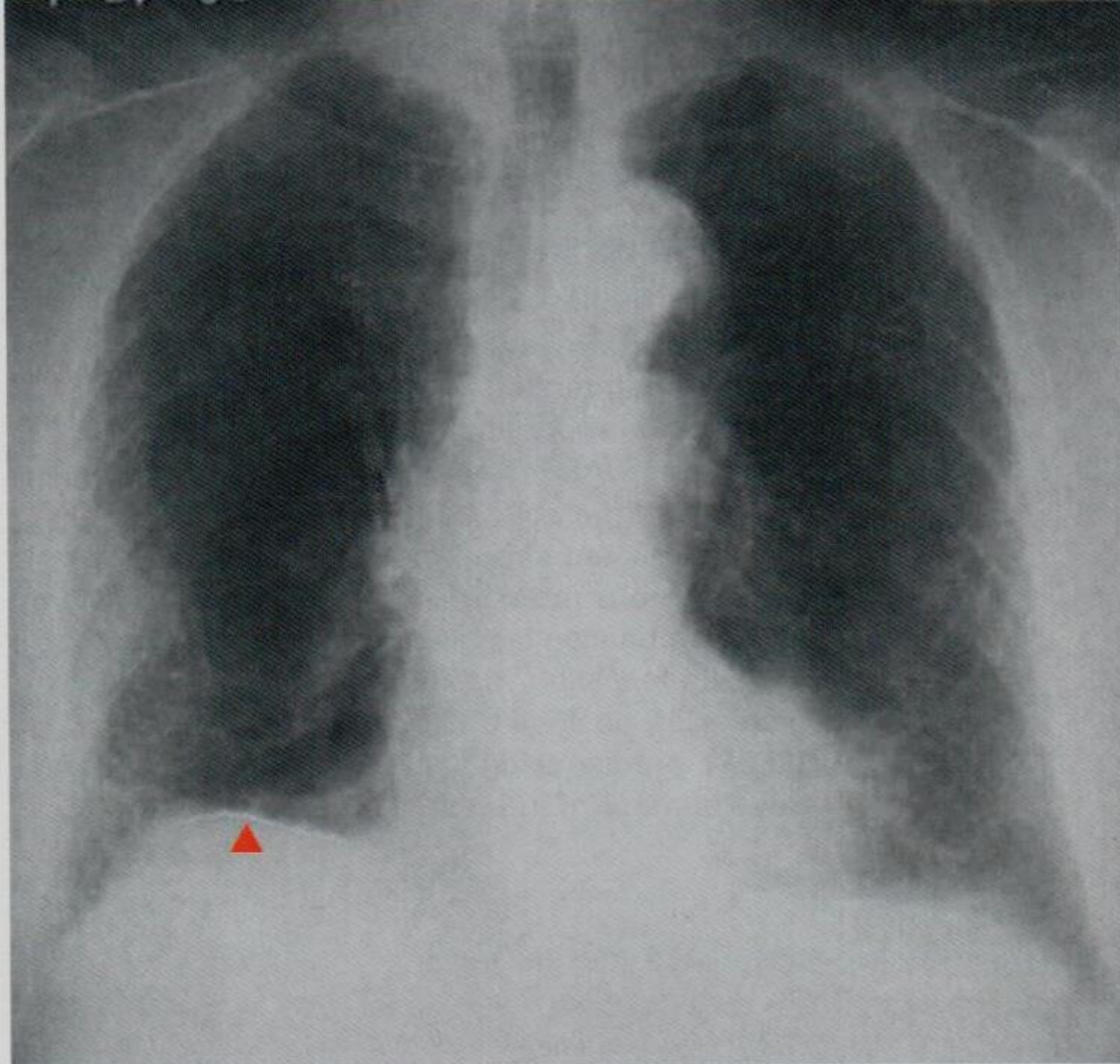
Silicosis

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 (1-5 μ) shape.**
- **Their solubility and physiochemical activity.**
- **The possible additional effects of other irritants, tobacco smoking.**

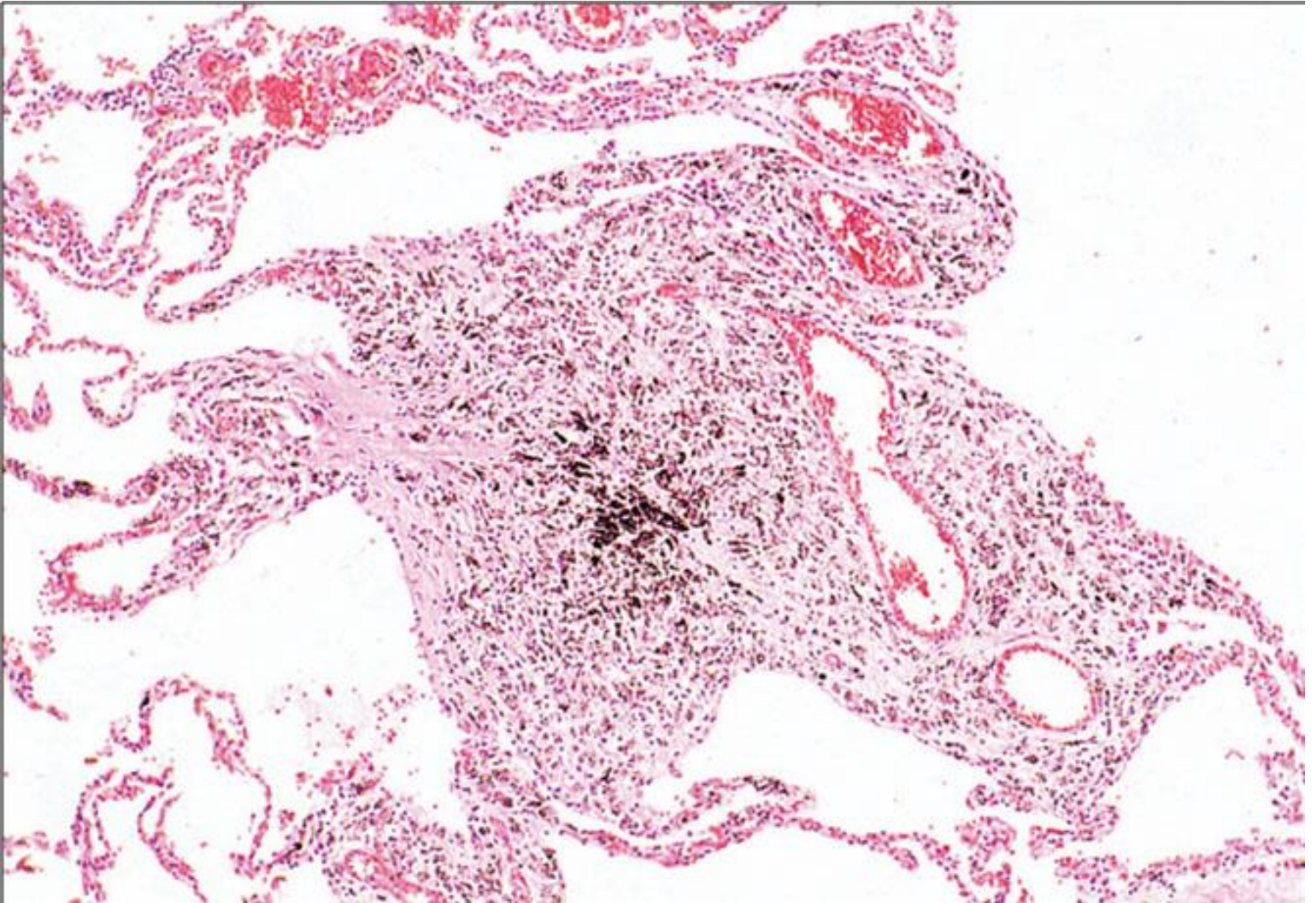


Pneumoconiosis, radiograph



Coal worker's pneumoconiosis, microscopic

Diseases of Lung



Varies from anthracosis to Simple coal worker's pneumoconiosis to.....

Diseases of Lung

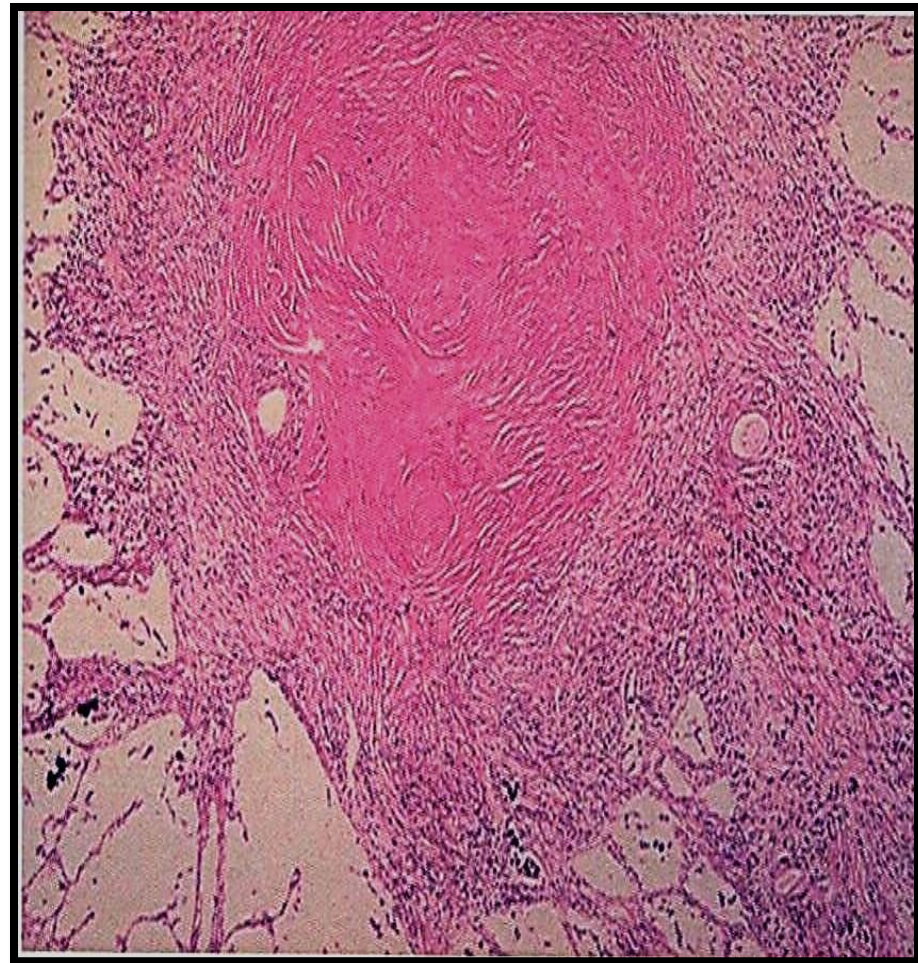
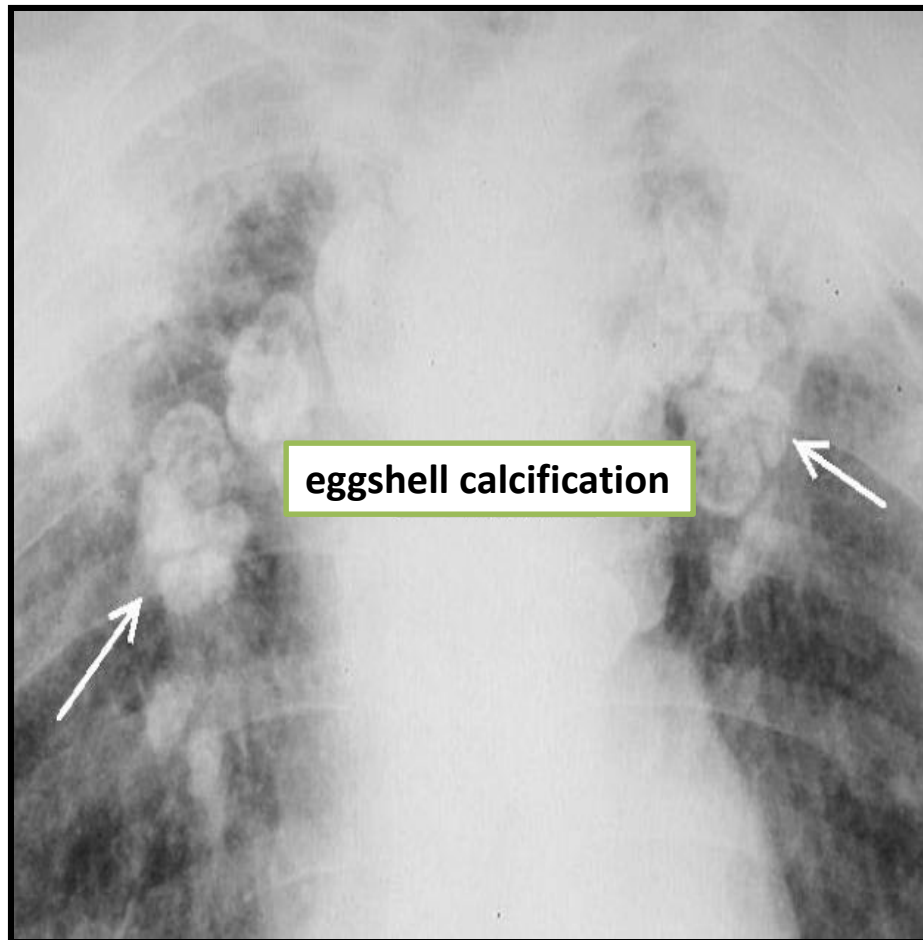
Coal worker's pneumoconiosis



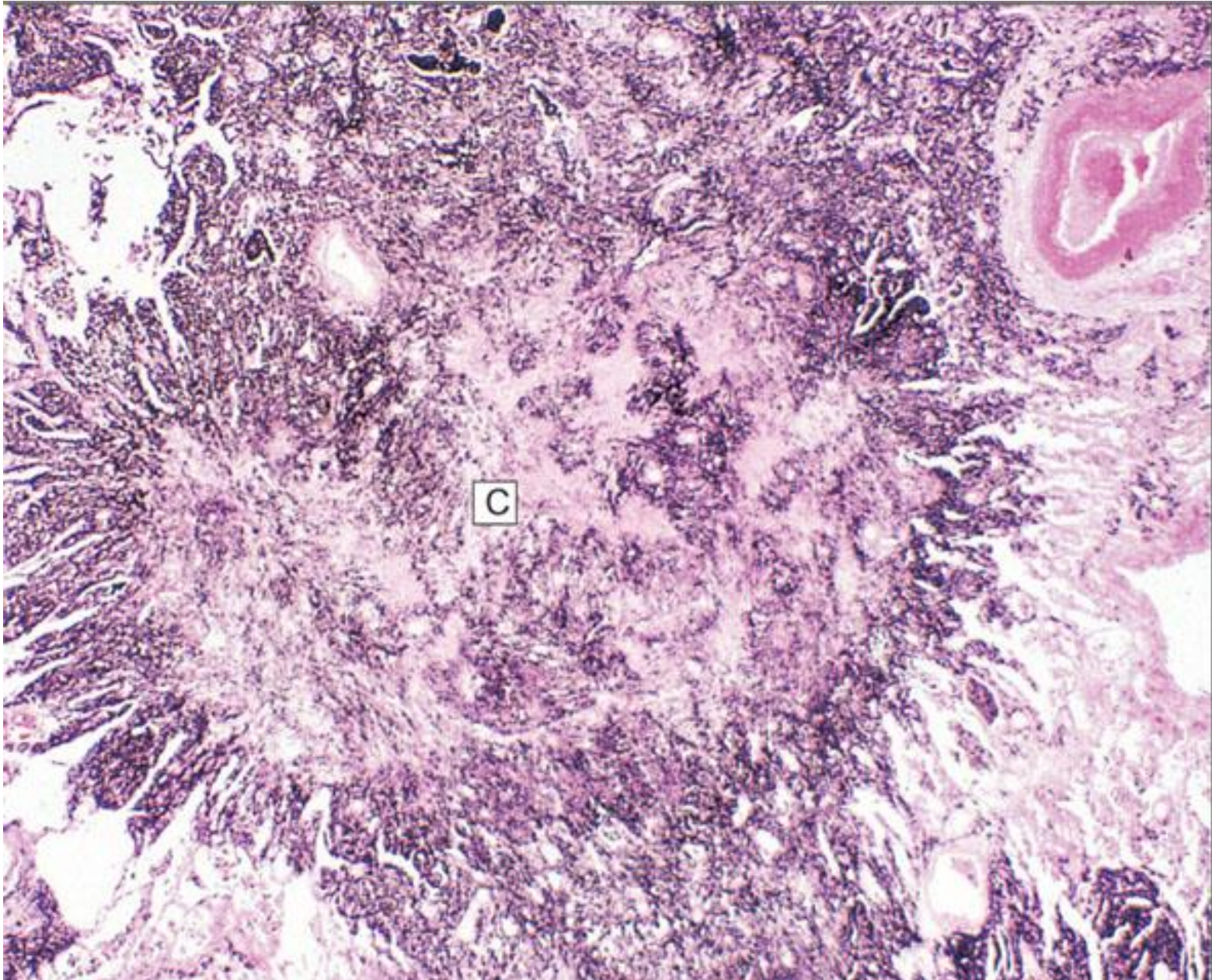
to progressive massive fibrosis (complicated coal worker's pneumoconiosis).

(a) Cut surface (b) thin section of whole lung.

Silicosis

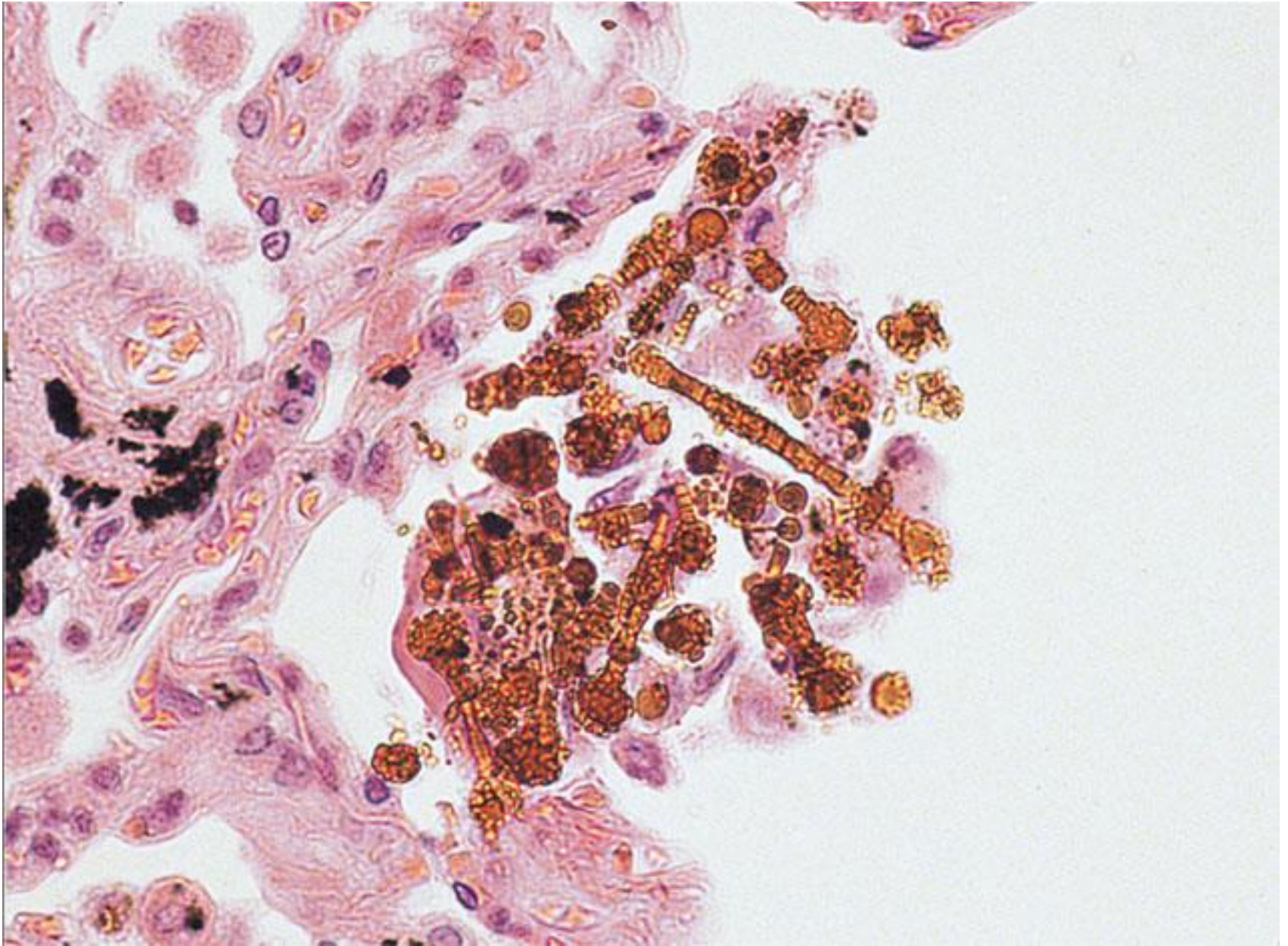


Silicosis



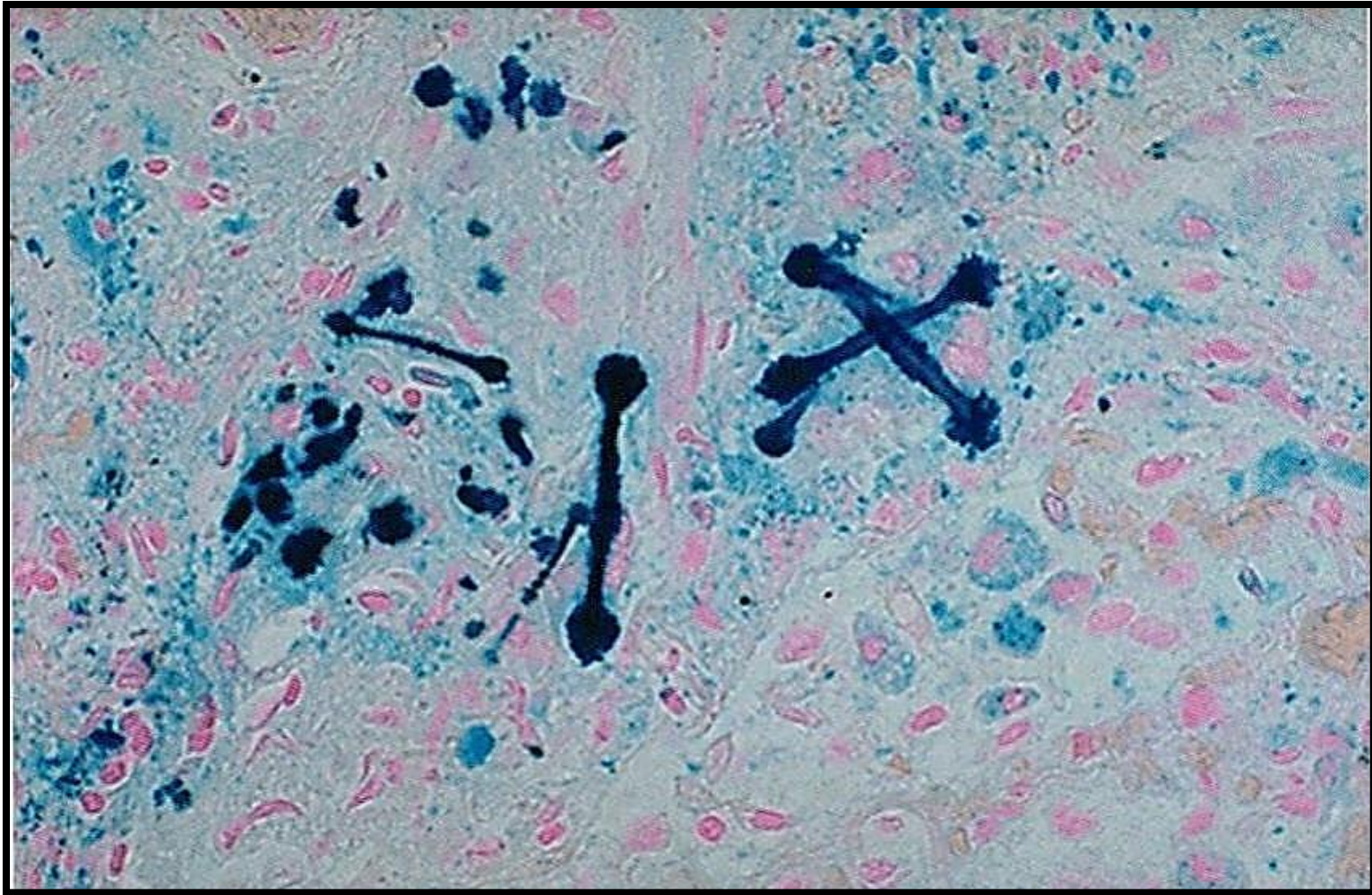
Silicosis of lung. In silicosis, nodules of collagen (C) contain silica particles.

Asbestosis



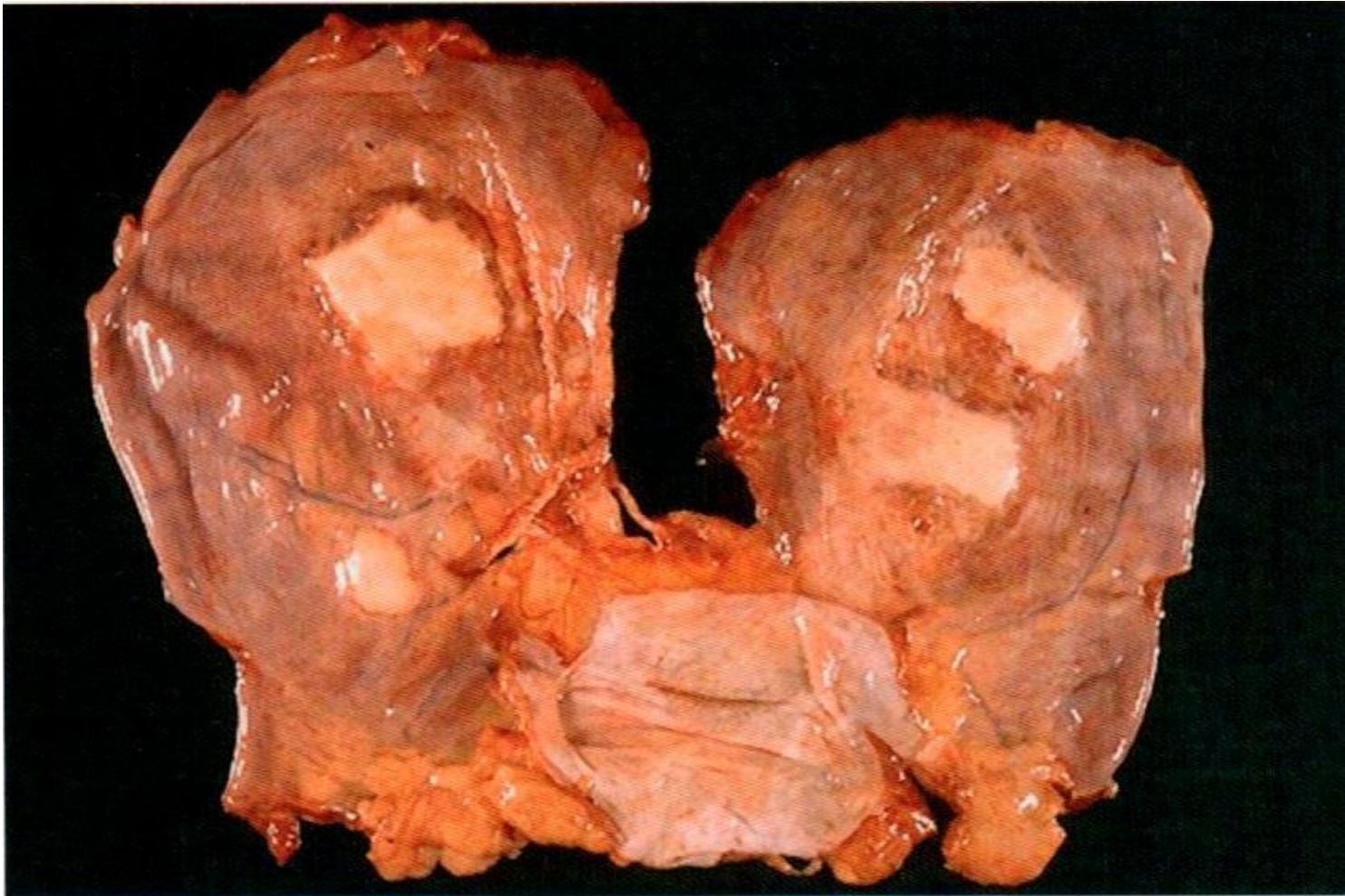
Asbestos bodies. Asbestos bodies are long, thin asbestos fibers coated with hemosiderin and protein to form brown filaments with a beaded or drumstick pattern.

Asbestosis



Ferruginous bodies, microscopic

Asbestosis



Pleural fibrous plaques, gross

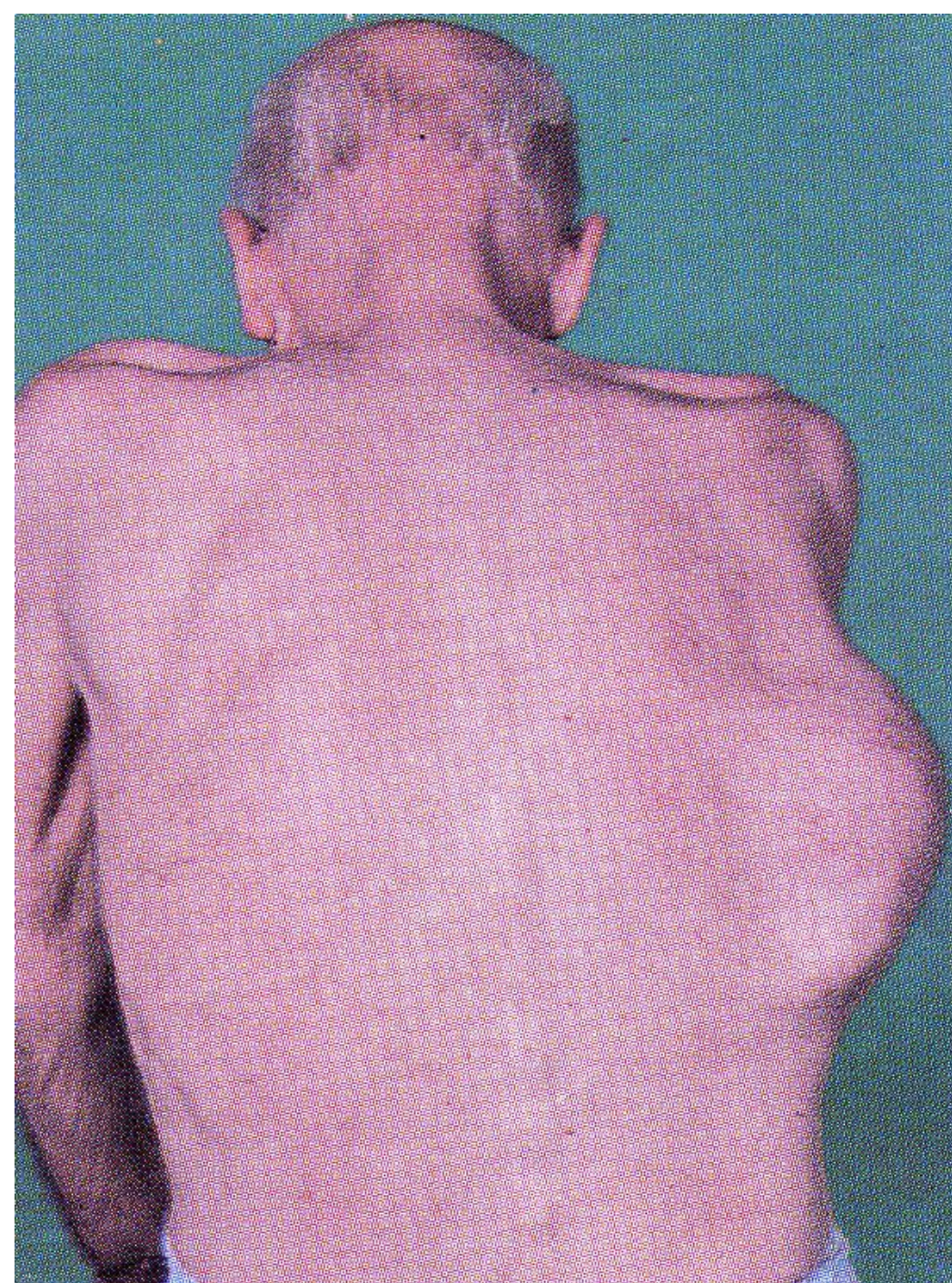
Asbestosis

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



Pleural fibrous plaques, microscopic

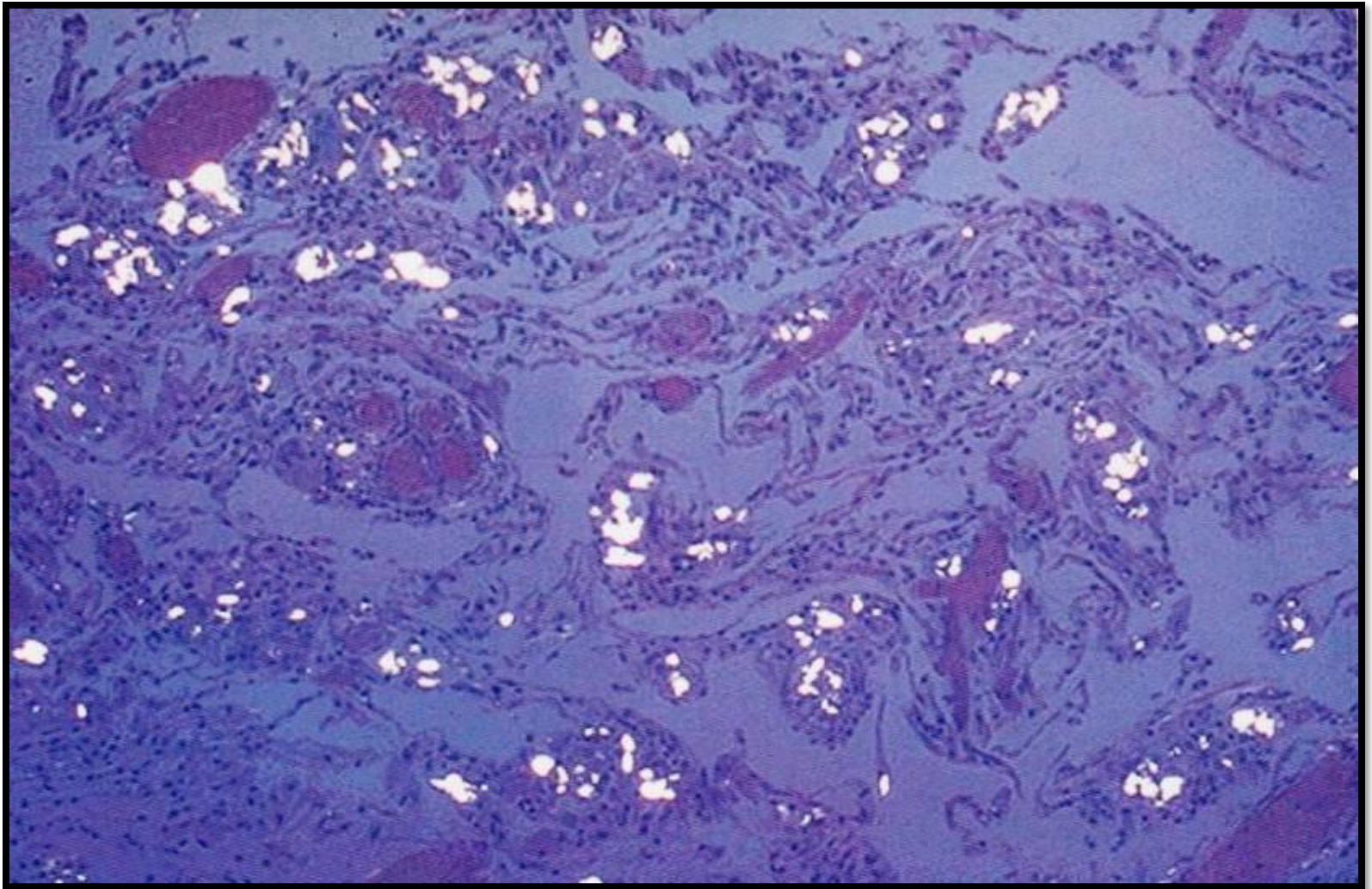
Mesothelioma. This patient presented with an asbestos link pleural plaque.



Diseases of Lung



Pleural mesothelioma



Injection drug use, microscopic

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

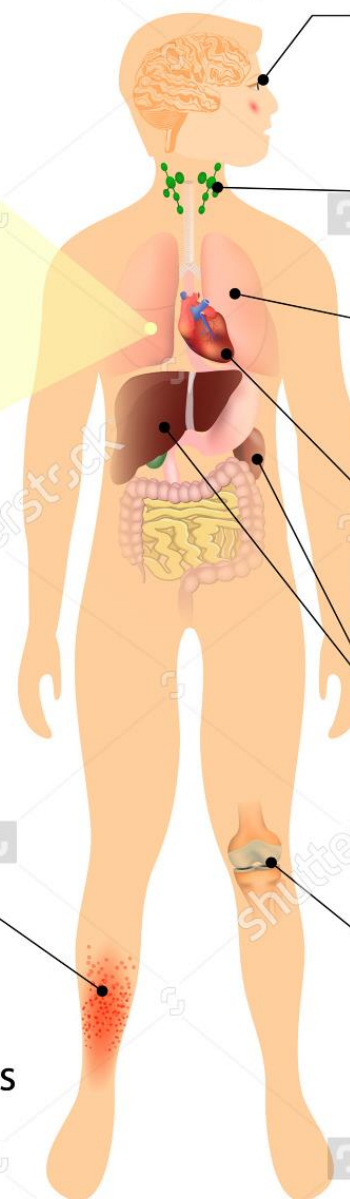
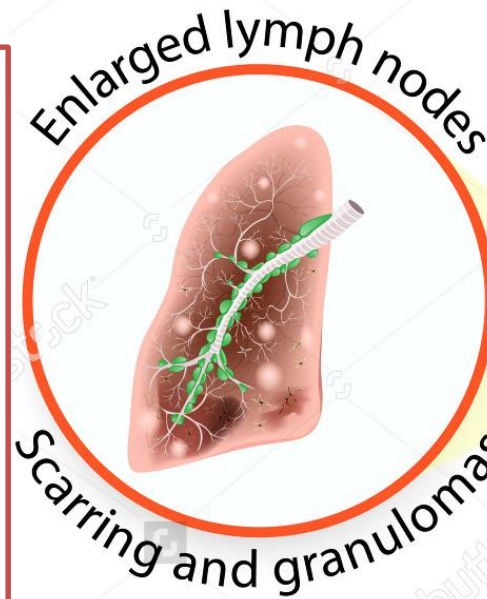
Sarcoidosis

The prognosis of sarcoidosis is unpredictable.

It can be 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

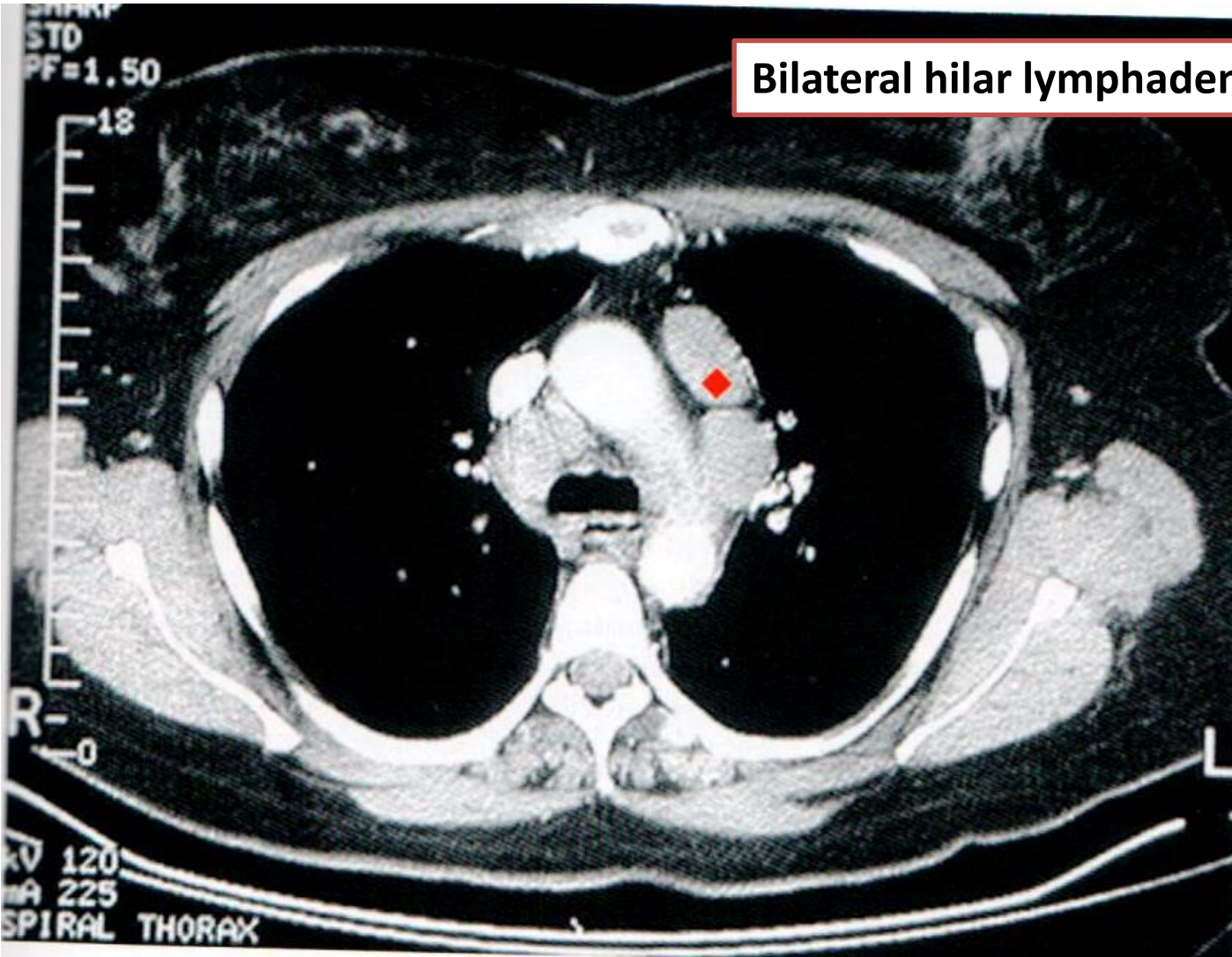
Lungs
- hacking cough
- cough up blood

Heart
- complications

Liver and spleen
- enlargement

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

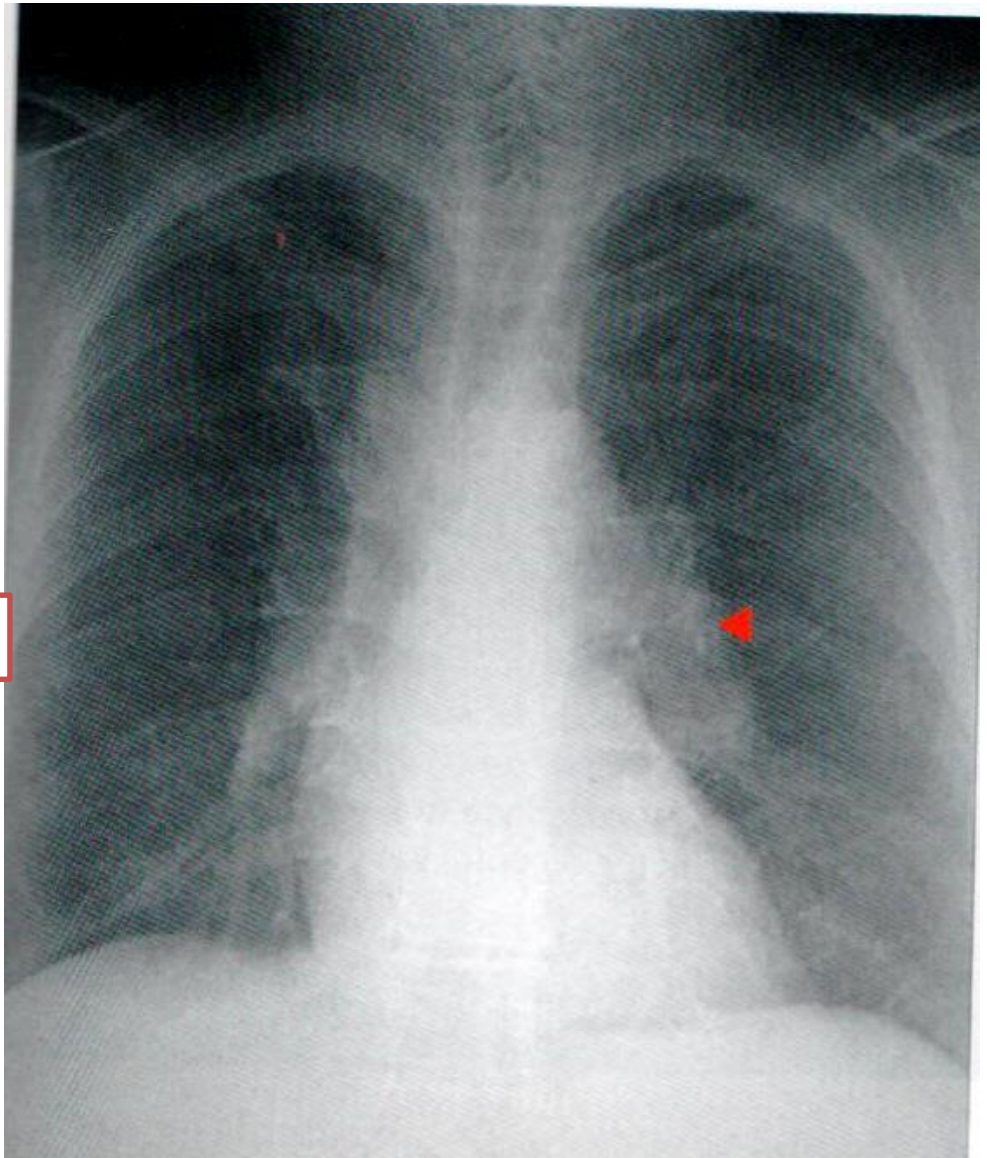
Joints
- pain
- arthritis
- swelling of the knees



Bilateral hilar lymphadenopathy

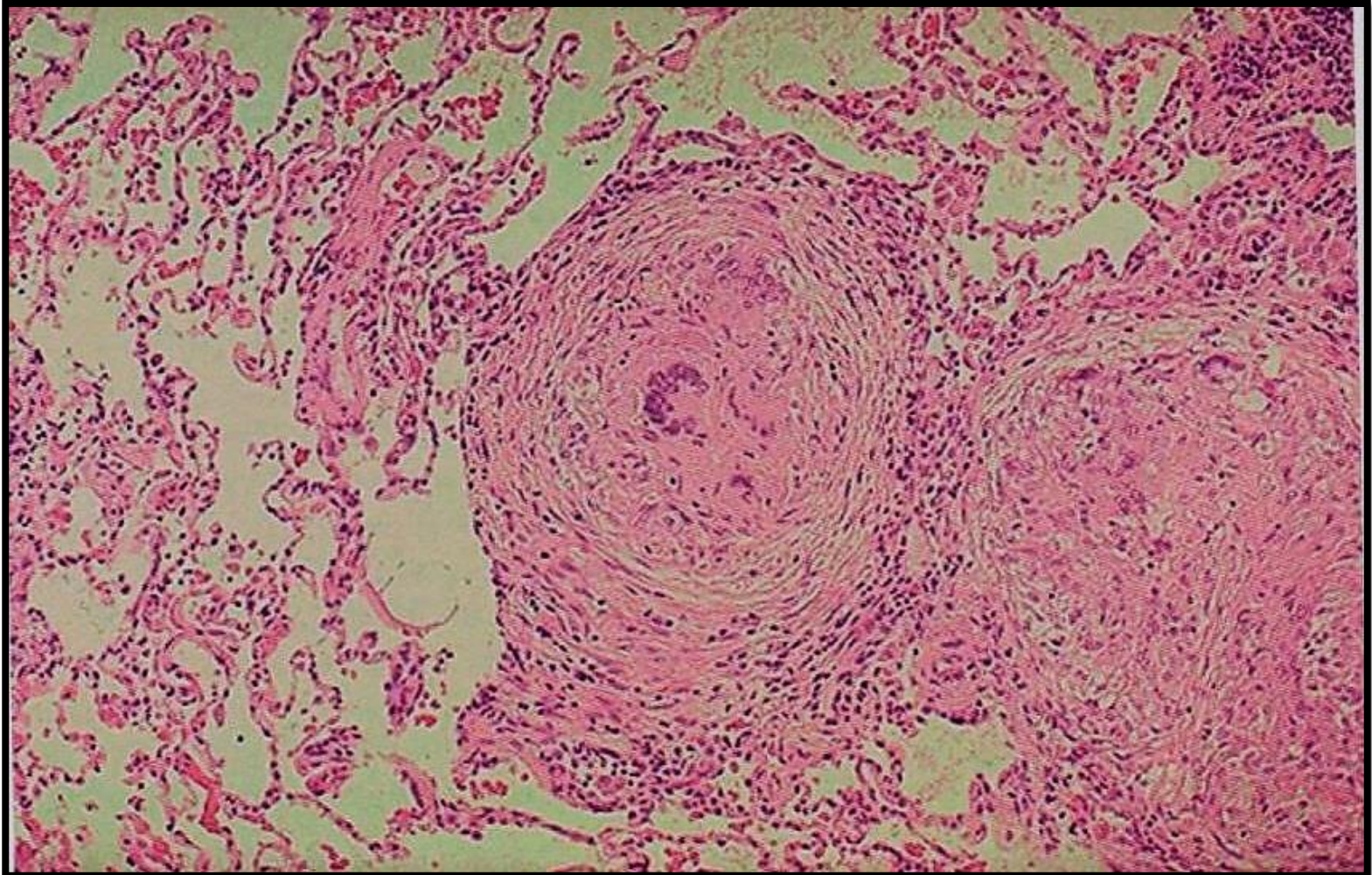
Sarcoidosis, CT image

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



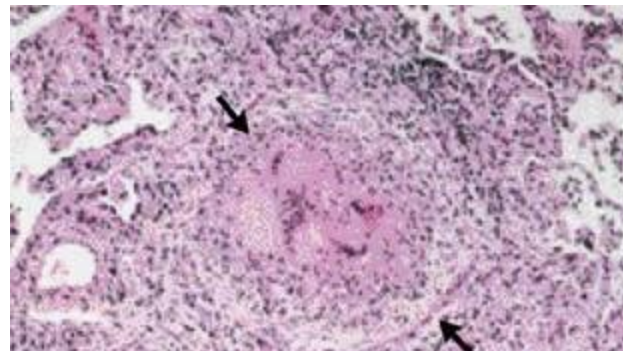
Pigeon breeder's
(*psittacosis*)



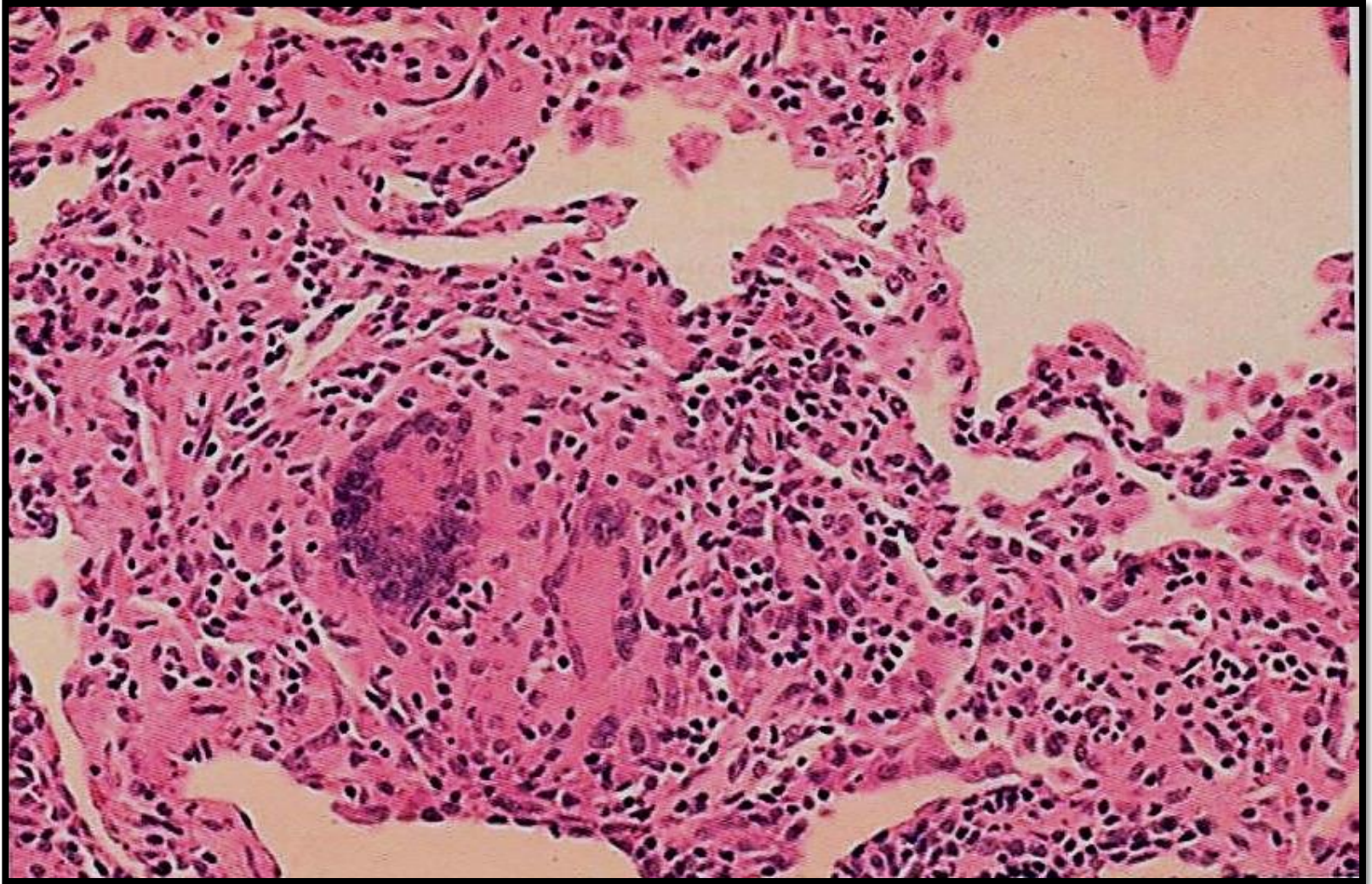
Air-cooler lung
Thermophilic bacteria



Sugarcane bagasse
(Bagassosis)



pneumonitis with non-necrotizing granulomas



Hypersensitivity pneumonitis, microscopic noncaseating interstitial granulomas and chronic inflammation along the bronchiols

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

Hypersensitivity 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

