Respiratory System
RS

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Chronic Restrictive Interstitial Lung Diseases

- Heterogeneous group of disorders characterized by bilateral, often patchy, pulmonary fibrosis mainly affecting the walls of the alveoli.

Table 12–3 Major Categories of Chronic Interstitial Lung Disease

Fibrosing
Usual interstitial pneumonia (idiopathic pulmonary fibrosis)
Nonspecific interstitial pneumonia
Cryptogenic organizing pneumonia
Associated with collagen vascular disease
Pneumoconiosis
Associated with therapies (drugs, radiation)
Granulomatous
Sarcoidosis
Hypersensitivity pneumonia
Eosinophilic
Loeffler syndrome
Drug allergy–related
Idiopathic chronic eosinophilic pneumonia
Smoking-Related
Desquamative interstitial pneumonia
Respiratory bronchiolitis

Fibrosing Diseases

1- Idiopathic Pulmonary Fibrosis (IPF):

- Unknown etiology, characterized by patchy, progressive bilateral interstitial fibrosis.
- M > F
- Most patients are > 60 years of age at presentation.
- Diagnosed only after exclusion of all other causes.

- The **radiologic and histologic** pattern of fibrosis is referred to as **usual interstitial pneumonia (UIP).**

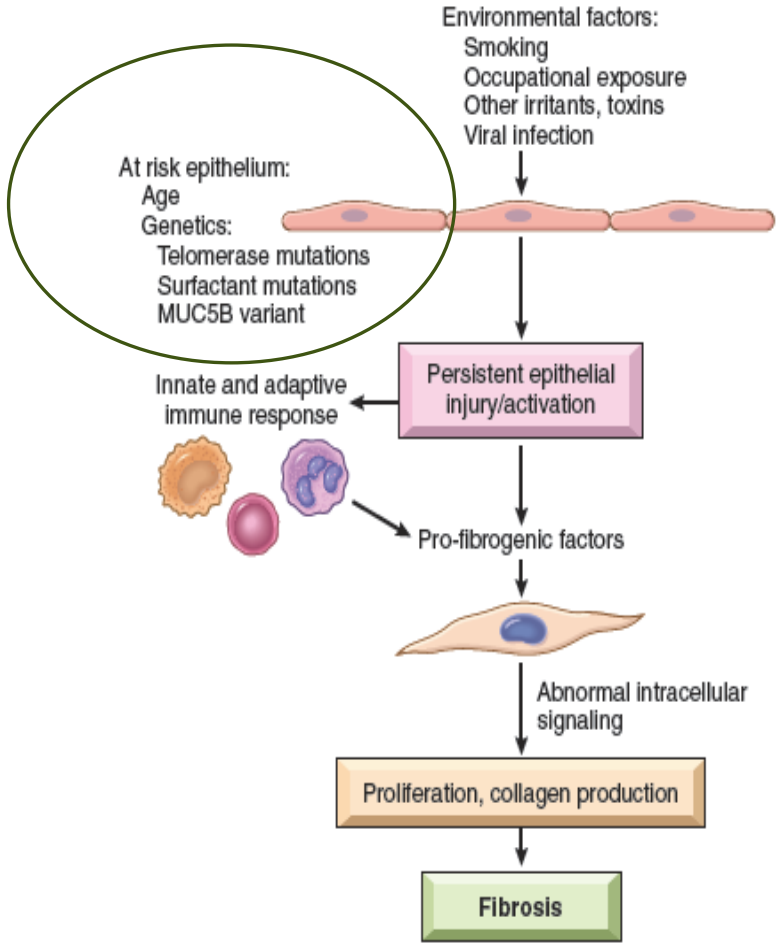
Pathogenesis

-Interstitial fibrosis results from repeated injury and defective repair of the **alveolar epithelium**, often in **a genetically** predisposed individual.

-The cause of the injury is obscure.

-It is hypothesized that abnormal epithelial repair at the sites of chronic injury and inflammation gives rise to exuberant fibroblastic or myofibroblastic proliferation

- Recent data point to excessive activation of profibrotic factors such as TGF-β.



Clinical Features & Examination:

- Insidious presentation
- Nonproductive cough & progressive dyspnea
- Hx of smoking in most.

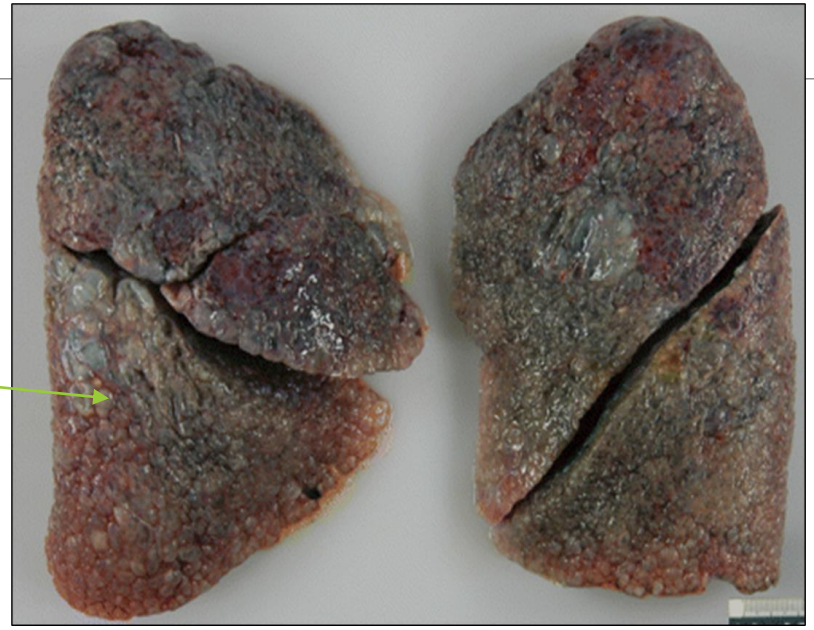
- **PFT**: restrictive results

- **Radiography**: subpleural and lower lobe fibrosis and “honeycombing”.
- **Prognosis**: **Poor**; survival is only 3 to 5 years; lung transplantation is the only definitive treatment

Morphology:

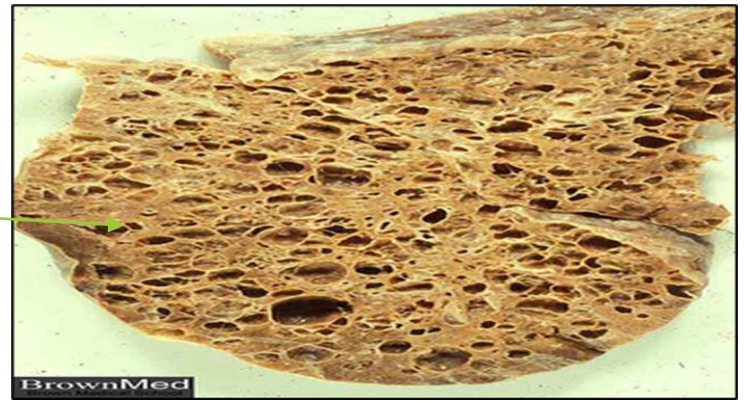
Grossly:

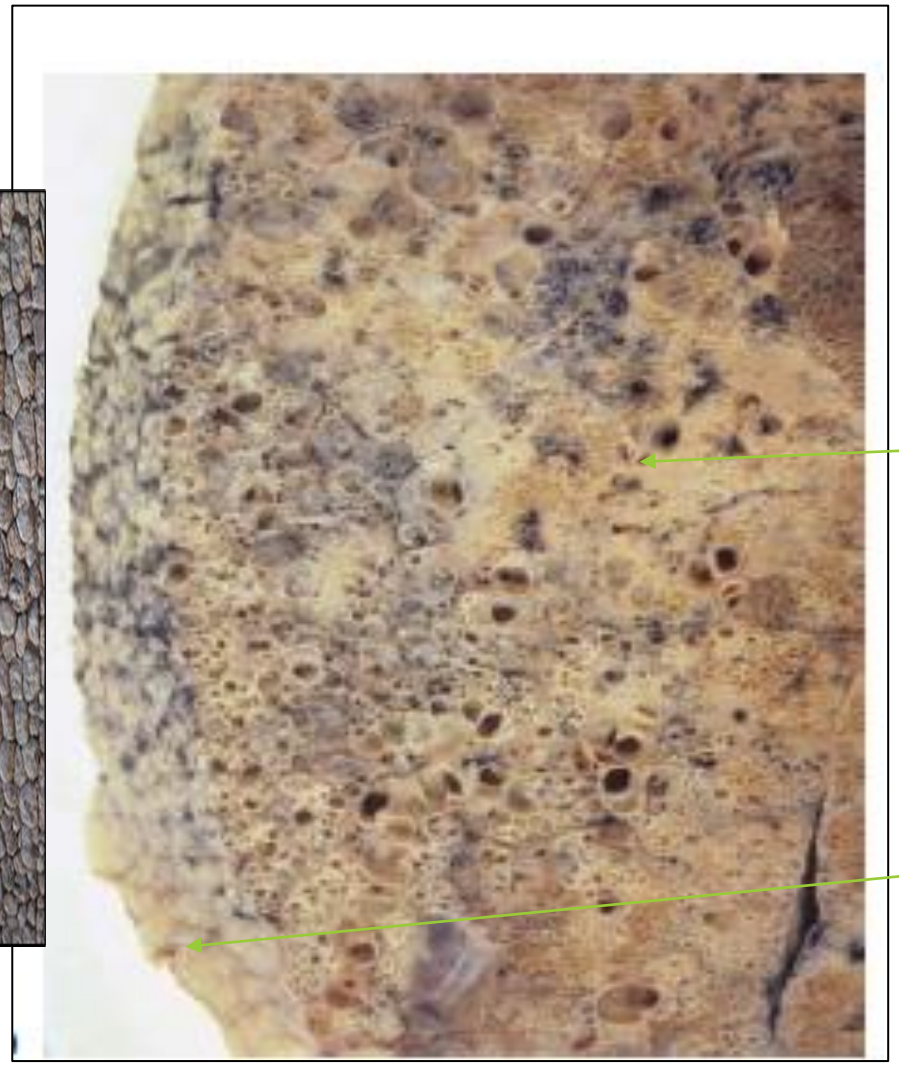
- The pleural surfaces of the lung are cobblestoned due to the retraction of scars along the interlobular septa.

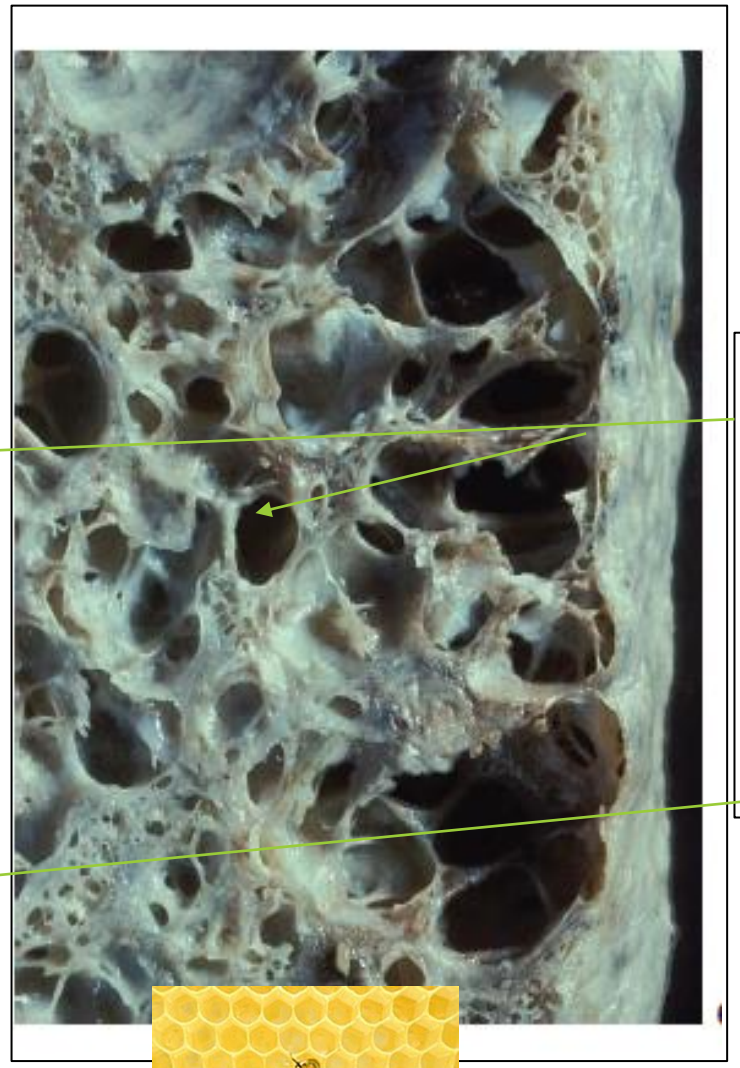


- The cut surface shows firm, rubbery white areas of fibrosis, which occurs preferentially **within the lower lobe, the subpleural regions, and along the interlobular septa**

- Macroscopic Honeycomb.







There are both honeycombing and extensive sheets of fibrous tissue; the pleura is also cobblestoned.

Histologically

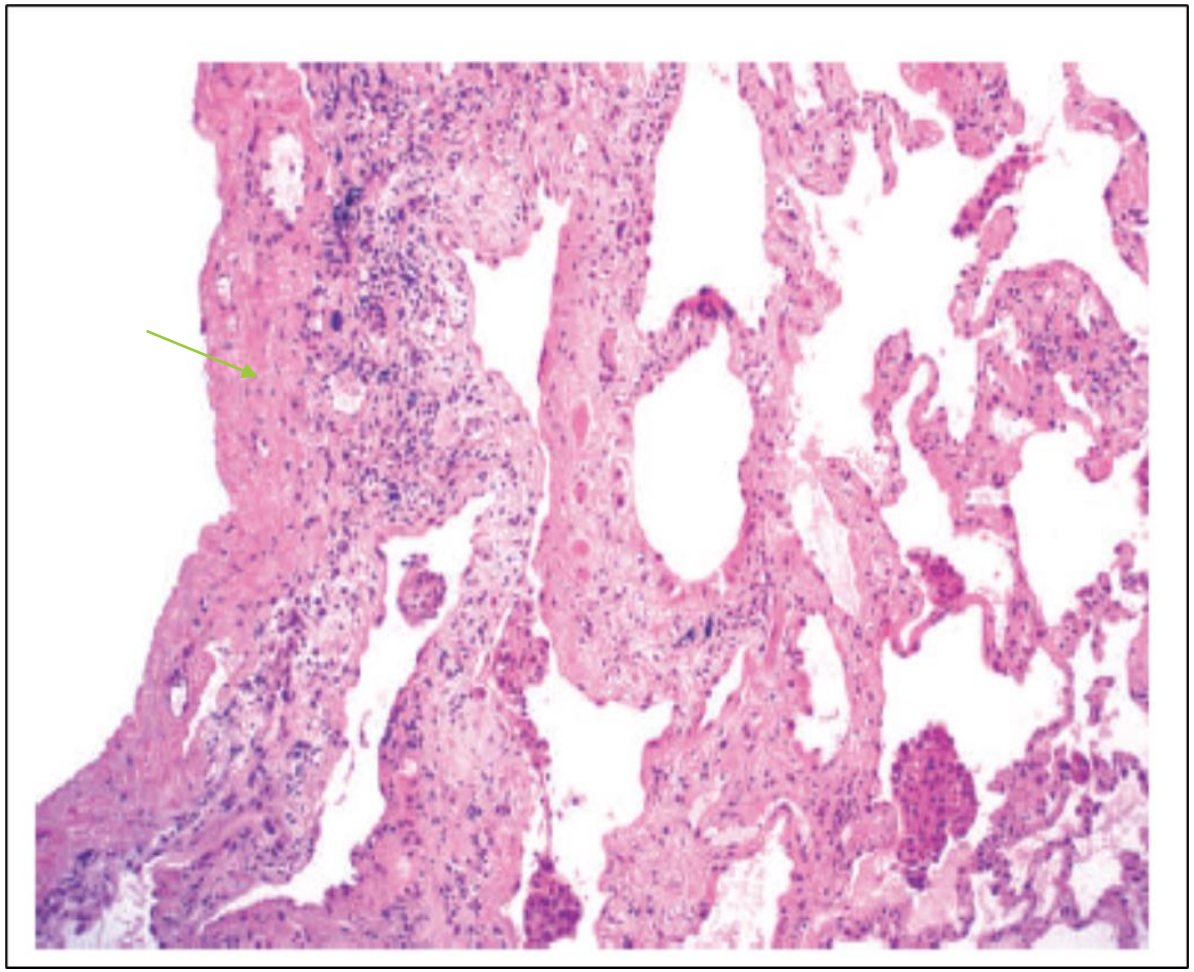
- Patchy interstitial fibrosis, which worsens with time **(Temporal and spatial heterogeneity).**
- Fibrosis with alternating normal lung parenchyma.
- Fibrosis is accentuated subpleural and along the interlobular septae.

- The earliest lesions demonstrate fibroblastic proliferation **(fibroblastic foci)**

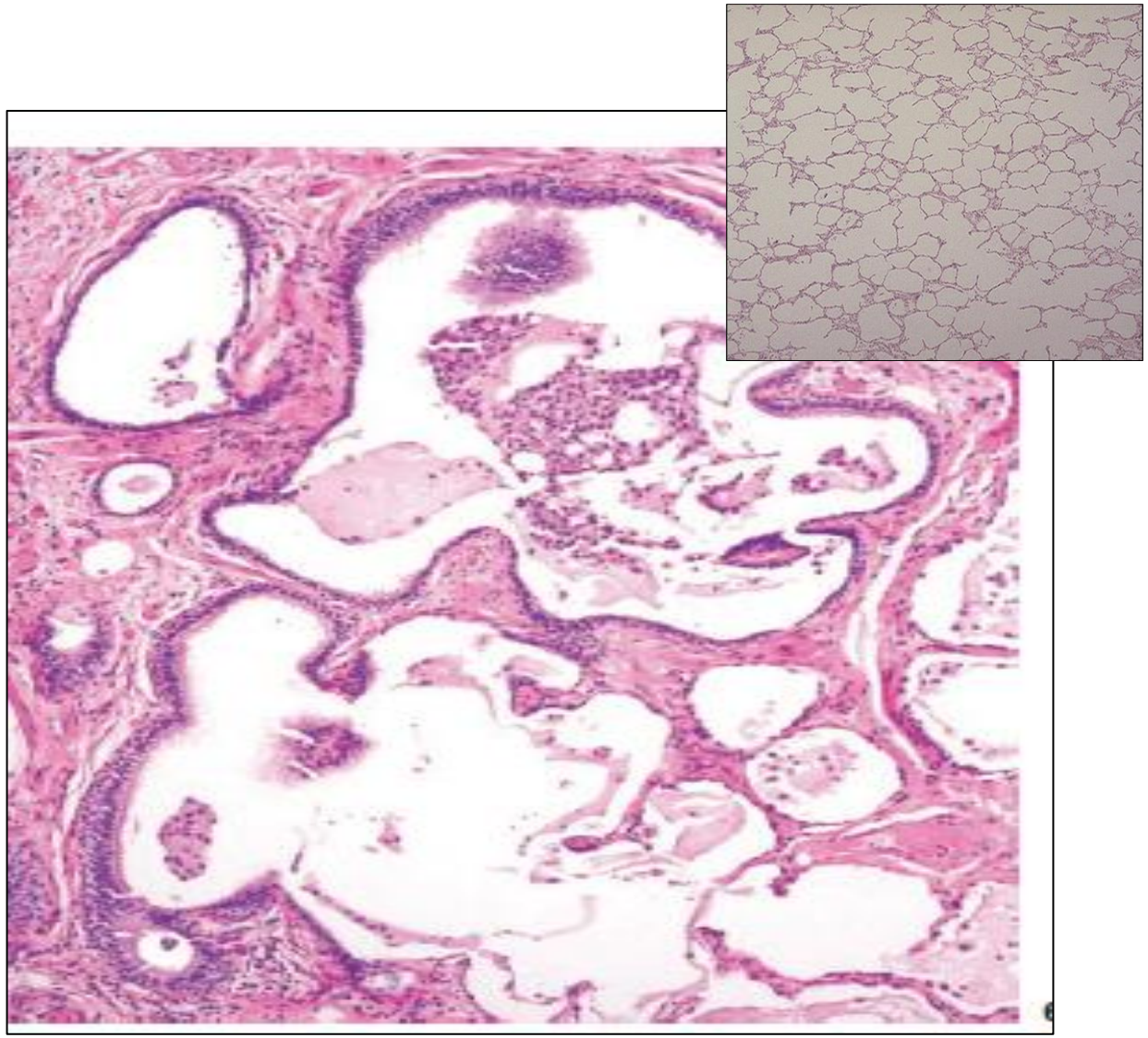
- Over time, these areas become more collagenous and less cellular.

- Dense fibrosis causes the collapse of alveolar walls and the formation of cystic spaces lined by hyperplastic type II pneumocytes or bronchiolar epithelium **(honeycomb fibrosis).**

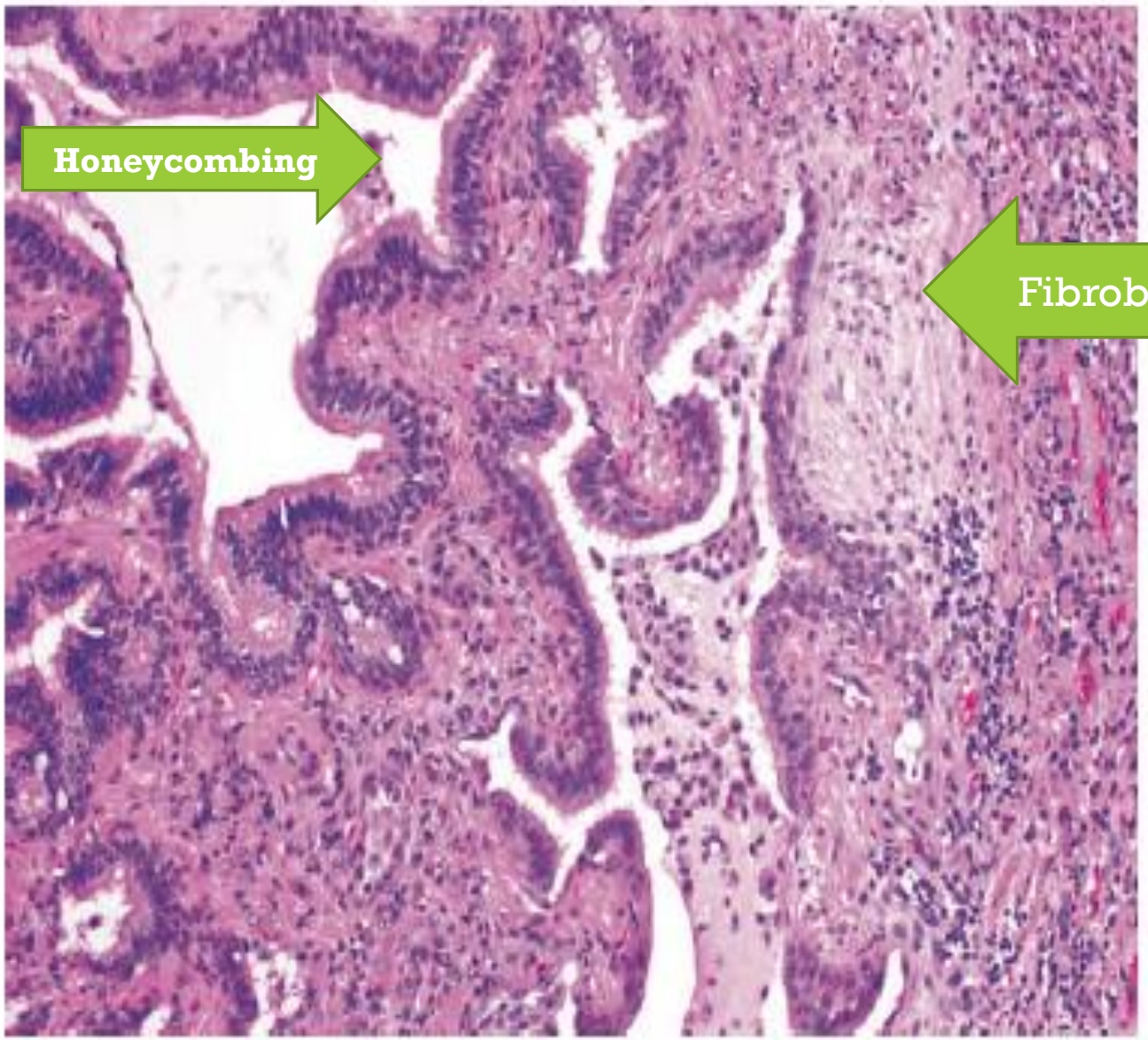
- The interstitial inflammation usually consists of patchy lymphocytes.



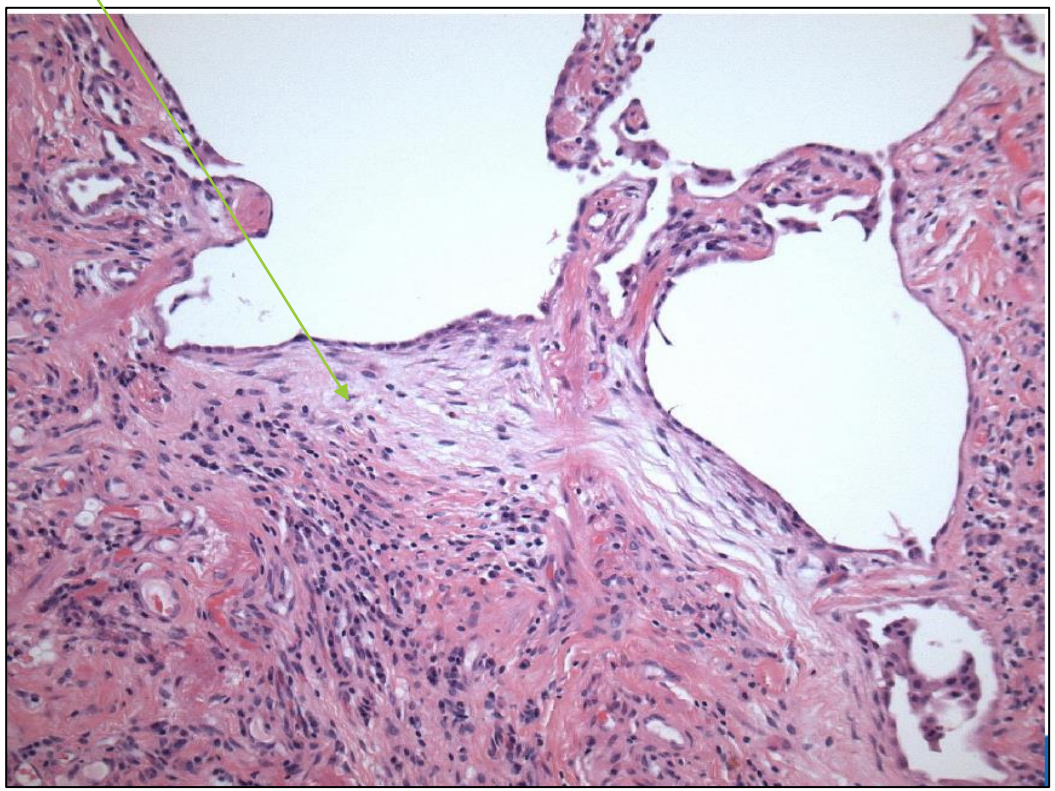
More pronounced fibrosis in the subpleural region



Microscopic Honeycombing



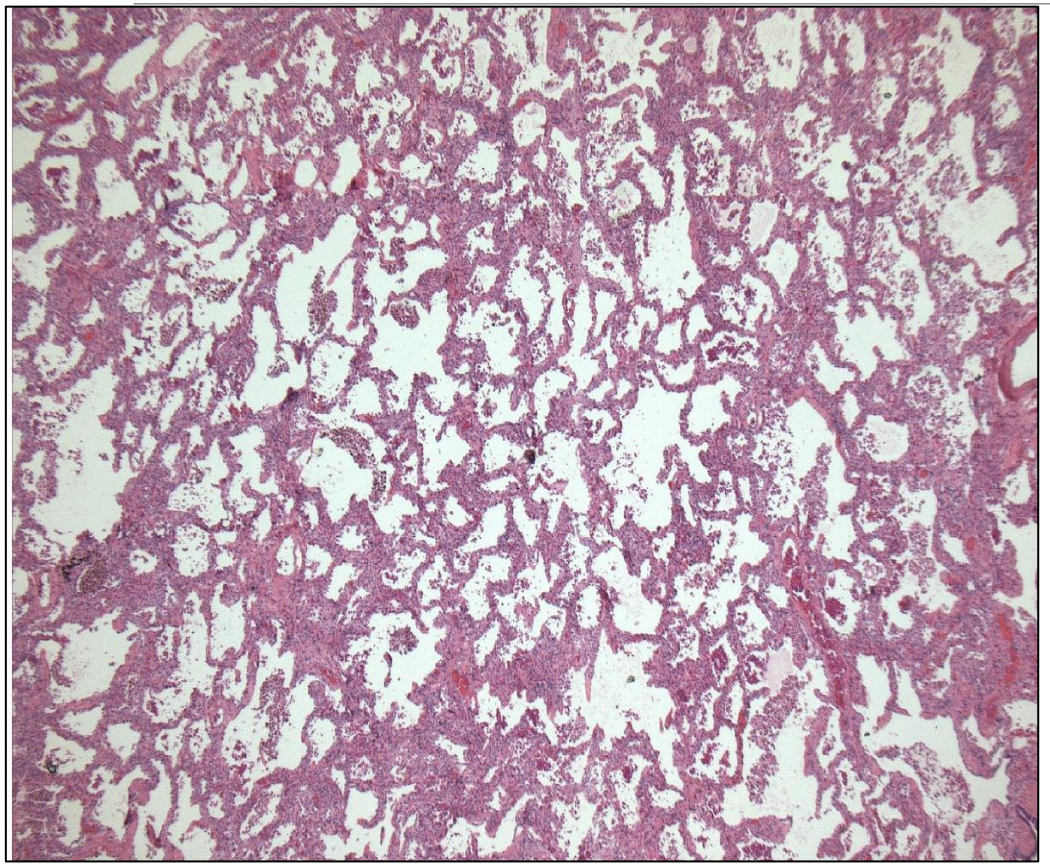
Fibroblastic focus

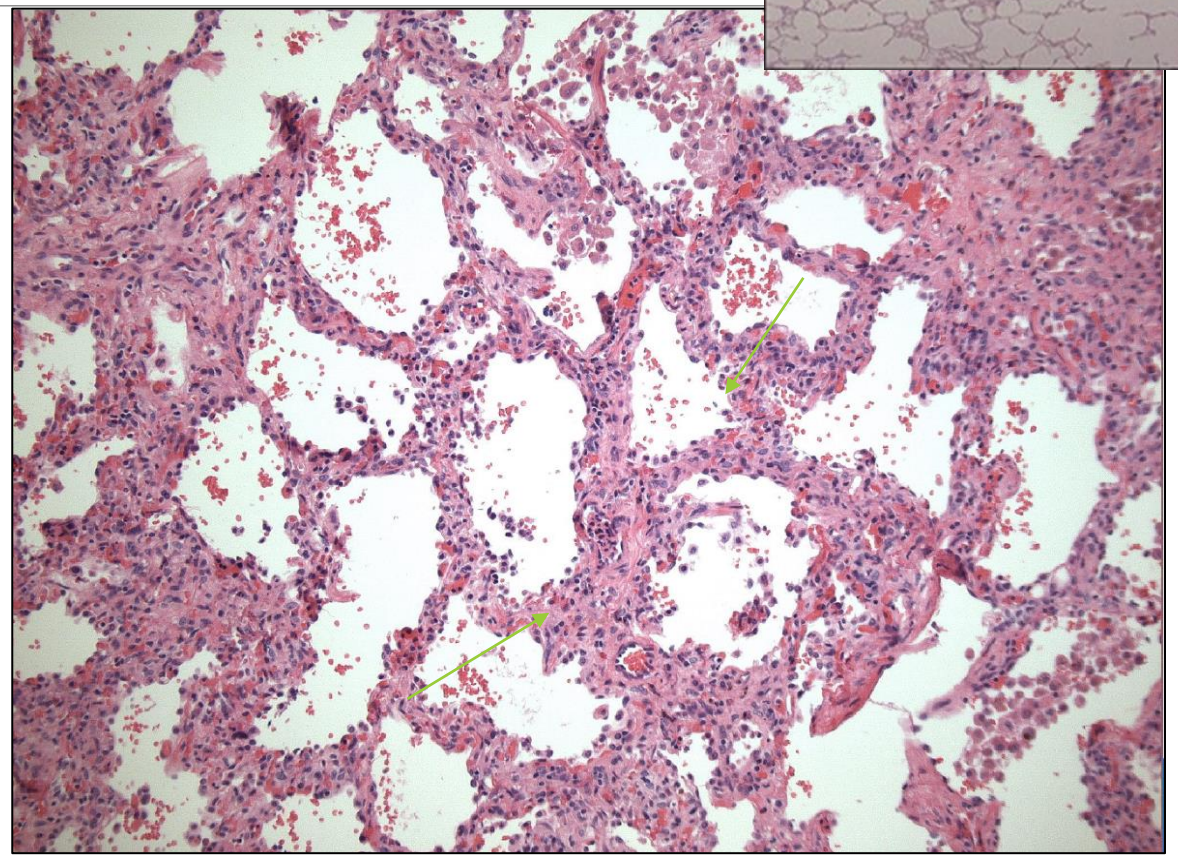


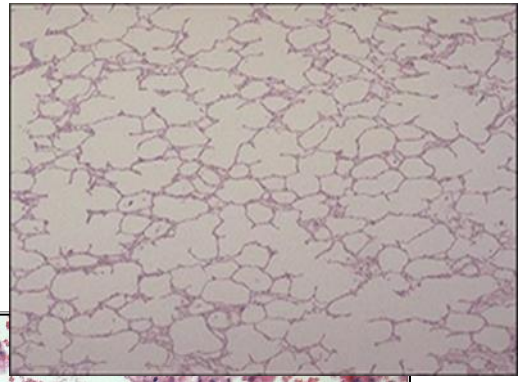
2- Nonspecific Interstitial Pneumonia (NSIP)

- A chronic bilateral interstitial lung disease of unknown etiology.
- It has a **more diffuse pattern (homogenous)** & **without heterogeneity**
- Better prognosis than UIP.
- Radiography: bilateral ground-glass opacities **(GGOs)**
- **Histologically:**
  - ✓ Mature fibrosing pattern: Alveolar septal fibrosis.
  - ✓ Cellular pattern: interstitial inflammation (lymphocytes & plasma cells)
  - ✓ Mixed pattern
  - **- The fibrotic and inflammatory process follows the original alveolar walls.**

NSIP





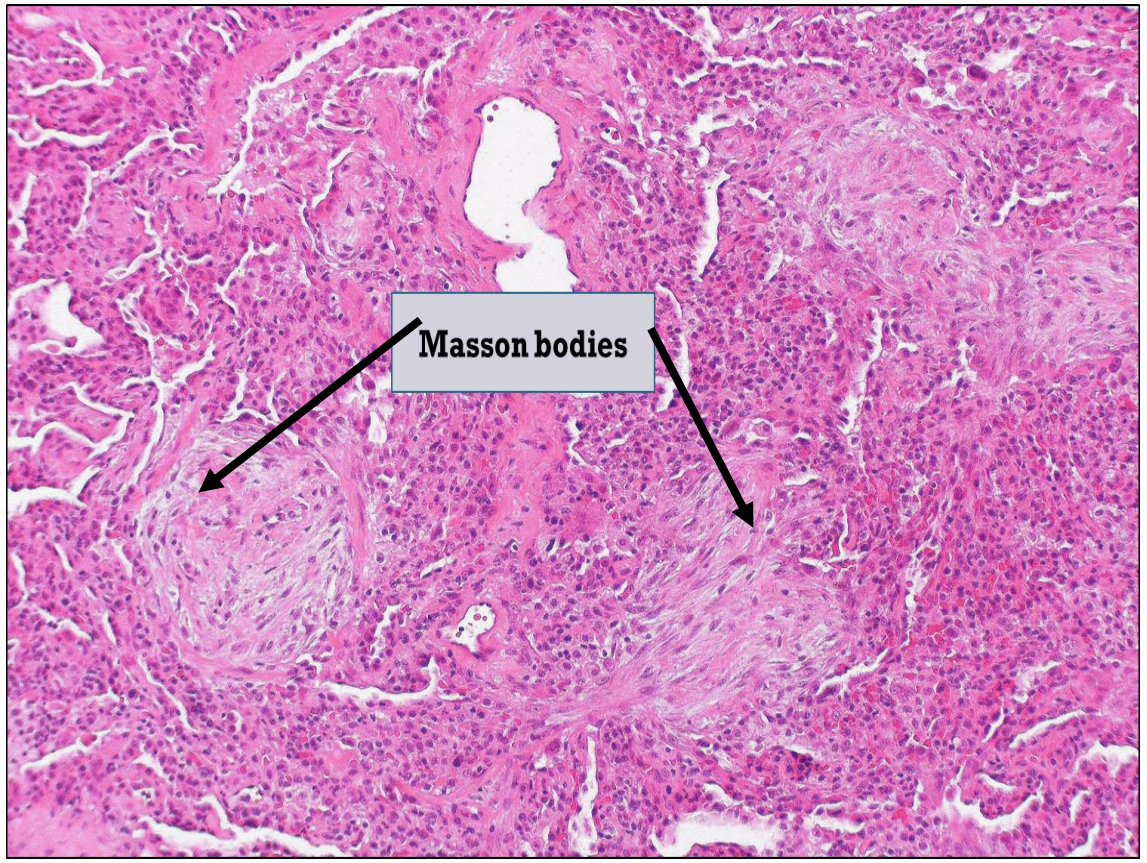


3 -Cryptogenic Organizing Pneumonia (COP) :

- ✓ Many causes (inflammatory, drug reaction …) but mainly cryptogenic.
- ✓ Cough and dyspnea.
- ✓ Chest radiographs: airspace **consolidation.**

Histologically

- ✓ Polypoid plugs of fibrosis in bronchioles & alveolar ducts & alveoli **(Masson bodies).**
- ✓ Interstitial inflammation, no temporal heterogeneity.
- ✓ No destruction of lung architecture.



4- “Collagen” Vascular Diseases:

- Many connective tissue diseases can involve the lung at some point in their course.
- Pulmonary involvement can take different histologic patterns:

⟹ NSIP, UIP, vascular sclerosis and organizing pneumonia

- ✓ Rheumatoid Arthritis
- ✓ SLE (“Lupus”)
- ✓ Progressive Systemic Sclerosis (Scleroderma)

5. Pneumoconiosis:

- A lung reaction to inhalation of mineral dust.

The term includes diseases caused by organic and inorganic particulates, and some also include chemical fumes and vapor-induced lung diseases.

- The most common & clinically significant lung diseases are those caused by :

- Coal dust
- Silica
- Asbestos

Pathogenesis:

The reaction of lung tissue to mineral dust depends on many variables:

1. The amount of the particles.
2. The size, shape & concentration of the particles.
3. Solubility & cytotoxicity of particles.

- Most inhaled dust is entrapped in mucus & rapidly removed from the lung by ciliary movement.

- Some dust particles become impacted at alveolar ducts where macrophages phagocytose the trapped particles.

- The more reactive particles activate the inflammasome and induce the production of several products that mediate an inflammatory response & initiate fibroblastic proliferation & collagen deposition

1. Coal- workers pneumoconiosis :

A condition affecting the **coal- mine workers** characterized by **black** lung.

The spectrum of lung findings includes:

1- **Asymptomatic anthracosis:** pigment deposits without a cellular reaction.

2- **Simple coal worker pneumoconiosis (CWP) :** with little to no pulmonary dysfunction

3- **Complicated CWP** or **progressive massive fibrosis (PMF):** lung function is compromised

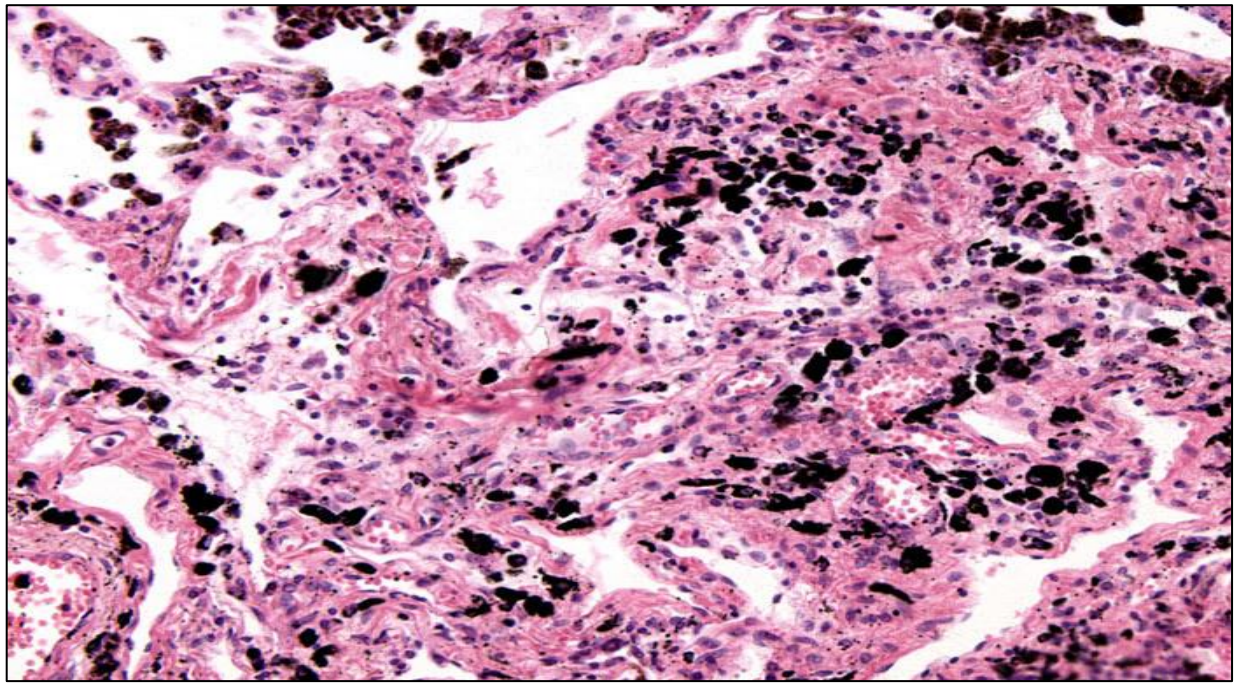
Clinically:

- Benign disease that produces little decrement in lung function.
- In PMF, there is increasing pulmonary dysfunction, pulmonary hypertension, and cor pulmonale.
  - Less than 10% of cases of simple CWP progress to PMF.
- **No increased frequency of lung carcinoma** in coal miners.

Morphology :

Pulmonary anthracosis:

- Inhaled carbon particles are engulfed by alveolar & interstitial macrophages & then accumulate in the connective tissue and in lymph nodes.

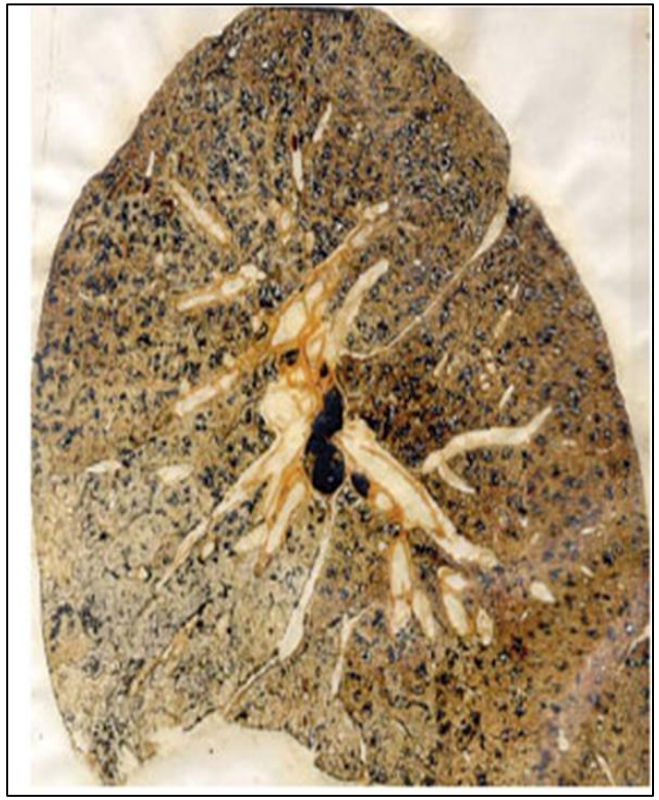


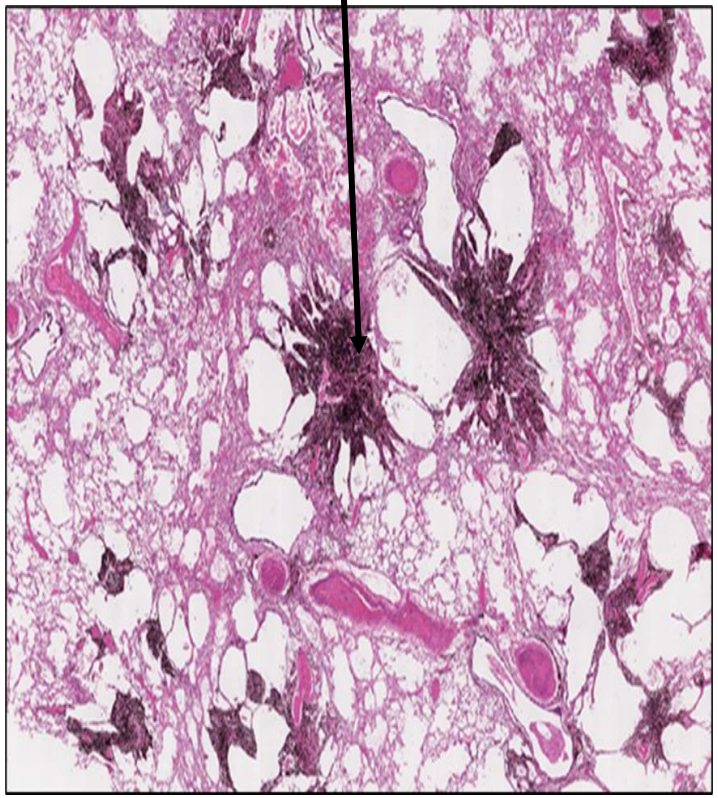
❑ Simple coal-worker pneumoconiosis :

- Coal macules & larger coal nodules around the bronchovascular bundles.

- Consist of carbon-laden macrophages, in addition to a small amount of collagen fibers.

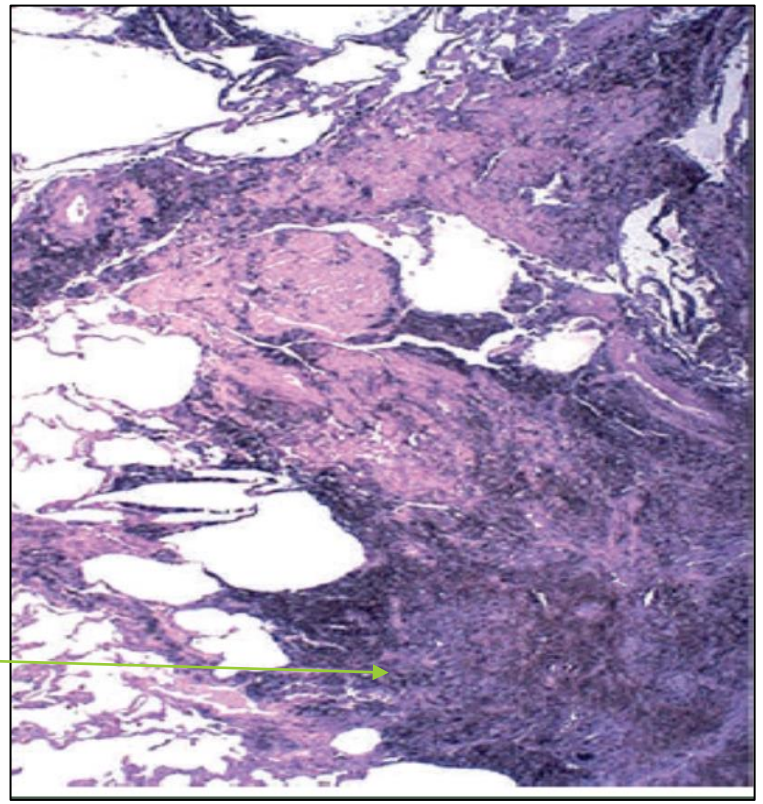
- Although these lesions are scattered throughout the lung, **the upper lobes** are more heavily involved.

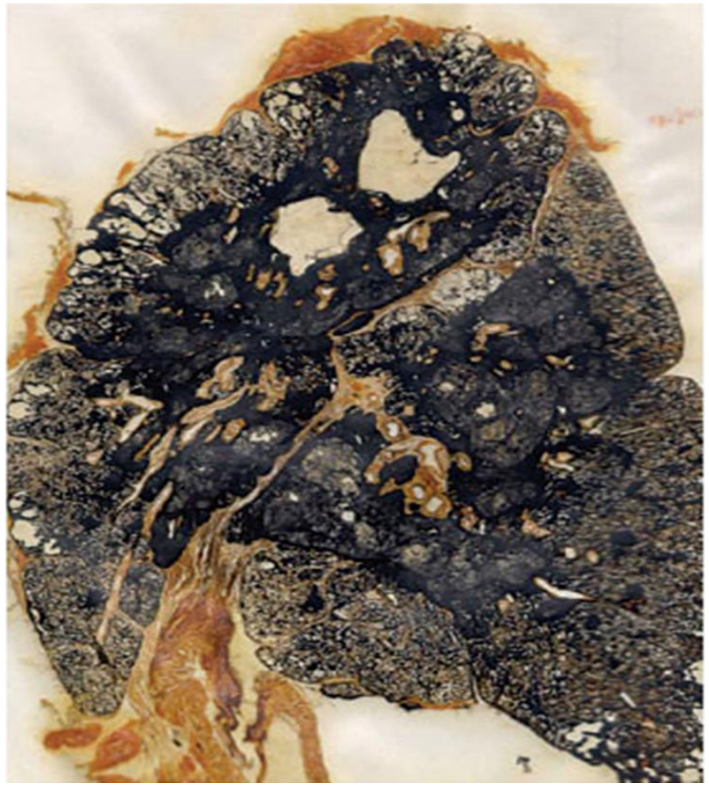




❑ Complicated CWP ,also called progressive massive fibrosis (PMF):

- Occurs on a background of simple CWP by coalescence of coal nodules and generally requires many years to develop.
- It is characterized by intensely blackened scars larger than 2 cm in diameter.
- They are usually multiple.
- Microscopically: the lesion consists of dense collagen and pigment.





2. Silicosis :

- Is the **most prevalent** chronic occupational disease.
- It is caused by the inhalation of crystalline silica.
- Silica occurs in both crystalline (quartz the most common) and amorphous forms.
- Workers in sandblasting, ceramics, glass, and stone cutting.

- Slowly progressive, often impairing pulmonary function.

- Silicosis is associated with an increased susceptibility to tuberculosis.

- The relationship between silica and lung cancer is unsettled, but most studies suggest that silica exposure is associated with some increase in risk.

Morphology

- Tiny palpable nodules in the **upper zones** of the lungs.

Microscopically:

- **Concentrically (whorled) arranged hyalinized collagen** fibers surrounding an amorphous center.
- Fibrotic lesions also may occur in **hilar lymph nodes** and the pleura.
- **Fibrotic calcified nodules in hilar lymph nodes → X-ray: Eggshell calcification.**

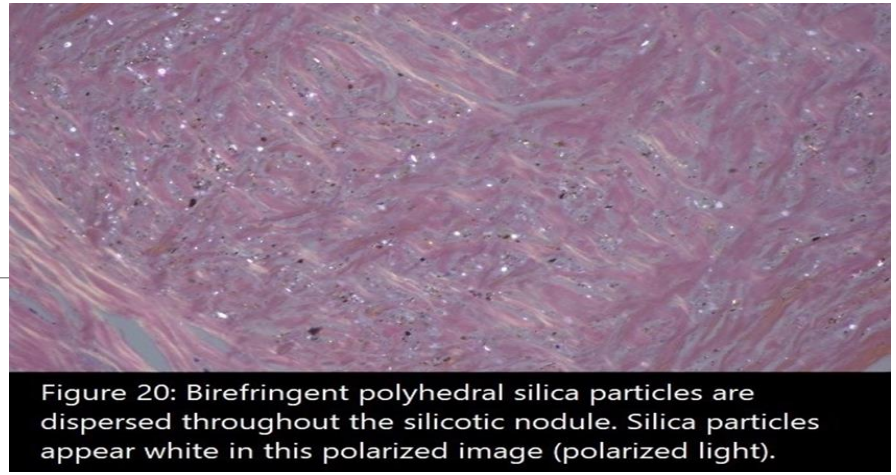
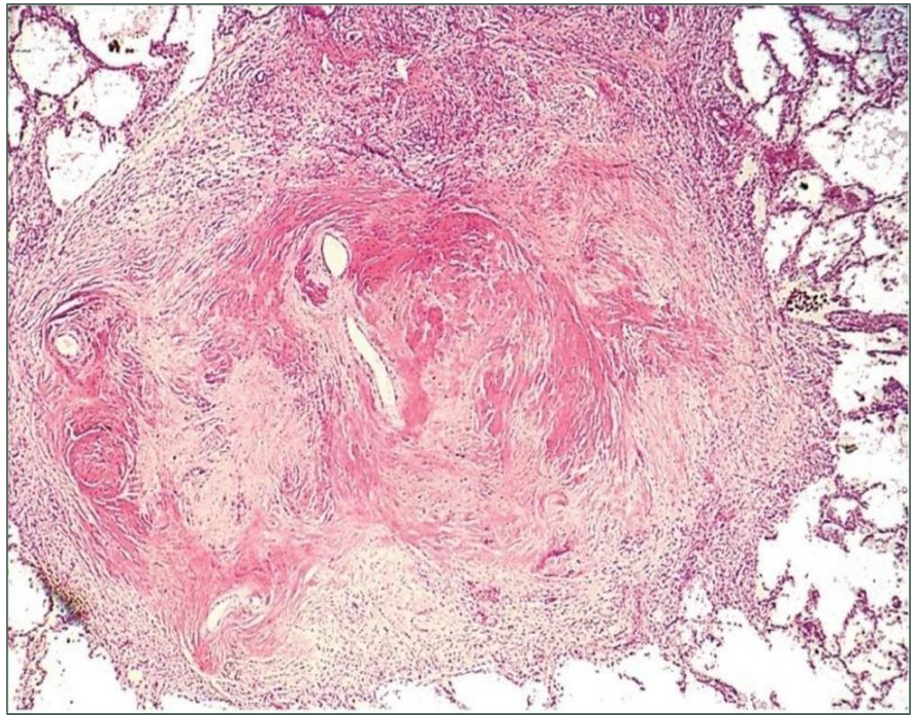


Figure 20: Birefringent polyhedral silica particles are dispersed throughout the silicotic nodule. Silica particles appear white in this polarized image (polarized light).



3. Asbestosis and asbestos-related diseases:

-Asbestos is a family of crystalline hydrated silicates with a fibrous geometry.

- Workers in installation & insulation materials, shipbuilders…

Occupational exposure to asbestos is linked to:

1- Parenchymal interstitial fibrosis (asbestosis).

2- Localized fibrous plaques (**most common**).

3- Pleural effusions

4- Lung carcinoma.

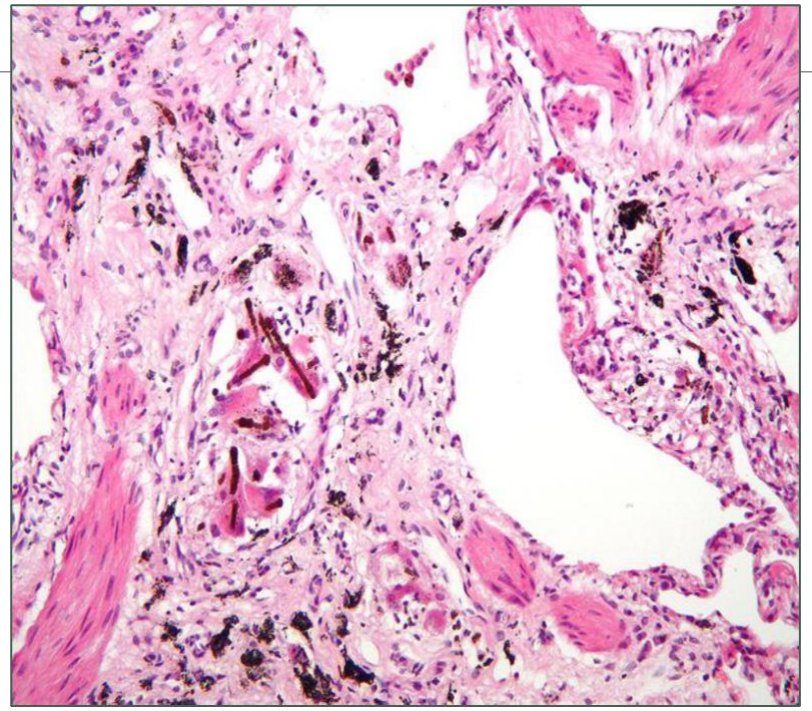
5- Malignant pleural & peritoneal mesothelioma .

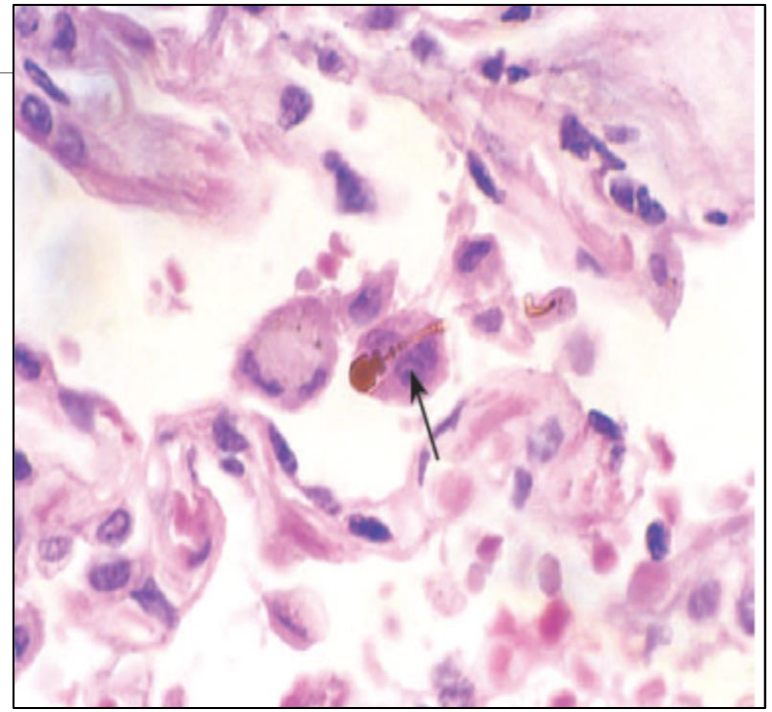
6-Laryngeal carcinoma (extra-pulmonary)

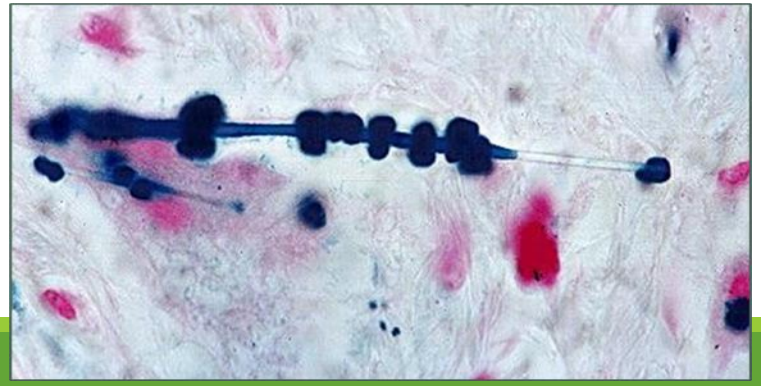
Morphology

- Diffuse interstitial fibrosis, with **asbestos bodies** which are golden brown fusiform or beaded rods with a translucent center, they consist of asbestos fibers coated with an iron-containing proteinaceous material.

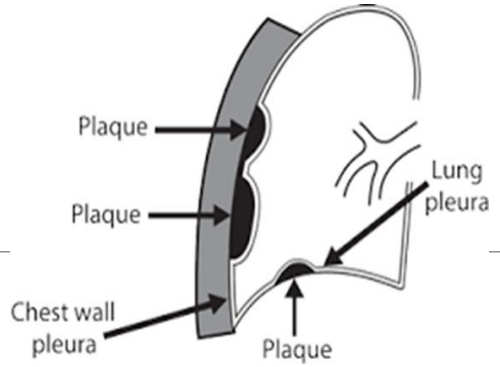
- Asbestosis **begins in the lower lobes.**

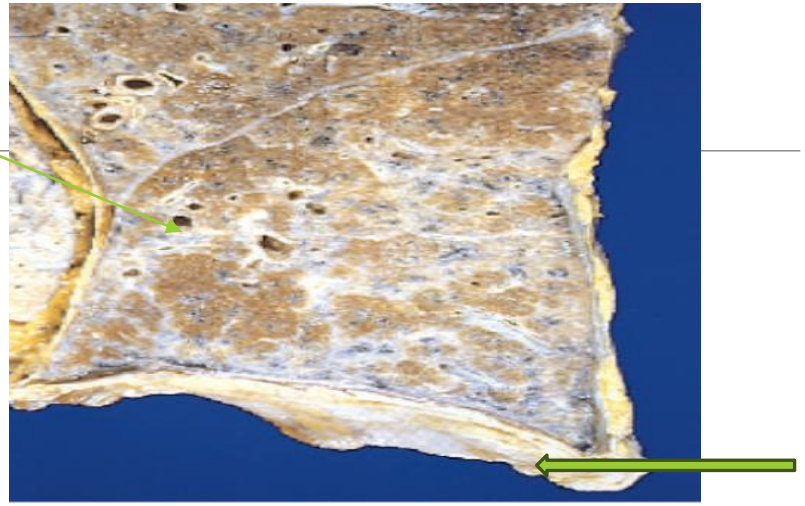




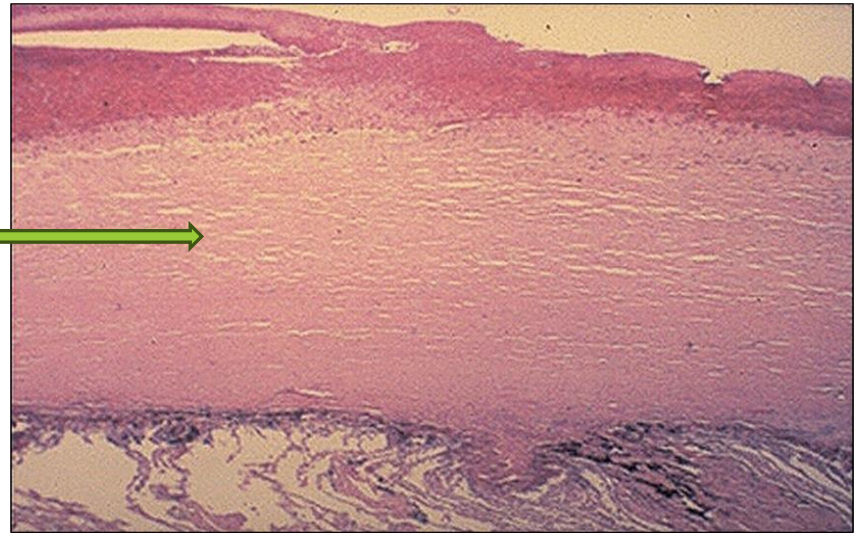


Pleural plaques:





- The most common manifestation of asbestos exposure.
- Well-circumscribed plaques of dense collagen often containing calcium develop on the parietal pleura & over the dome of the diaphragm.
- **They do not contain asbestos bodies** ; they only rarely occur in persons who have no history of asbestos exposure.



6. Drug- and Radiation-Induced Pulmonary Disease

- *Bleomycin* (anti-cancer agent) *and* *Amiodarone*(an anti-arrhythmic agent)

⟹ pneumonitis and interstitial fibrosis.

- *Radiation pneumonitis*

Acute radiation pneumonitis:

- Typically occurs 1 to 6 months after therapy.
- Fever and dyspnea.
- Pleural effusion and pulmonary infiltrates in the irradiated lung bed.
- These signs and symptoms may resolve with corticosteroid therapy

or progress to ***chronic radiation pneumonitis*** associated with pulmonary fibrosis.

Thank You