RSM-
chronic interstitial (restrictive, infiltrative) lung diseases

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21-10-2024

Chronic interstitial diseases

- **Chronic interstitial diseases are a heterogeneous group of disorders characterized by bilateral, often patchy, pulmonary fibrosis mainly affecting the walls of the alveoli.**

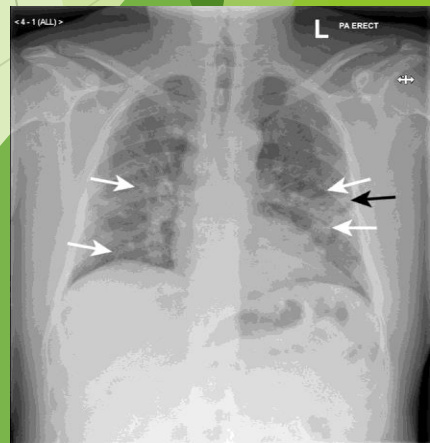
- **Chronic interstitial lung diseases are categorized based on clinicopathologic features and characteristic histology**

Table 13.2 Major Categories of Chronic Interstitial Lung Disease

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

The hallmark of these disorders is

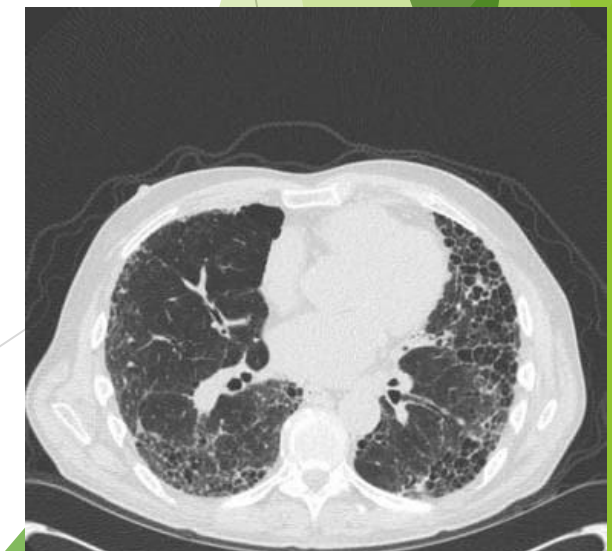
- Reduced compliance (stiff lungs), which in turn necessitates increased effort to breathe (dyspnea).
- Damage to the alveolar epithelium and interstitial vasculature produces abnormalities in the ventilation-perfusion ratio, leading to hypoxia.
- Chest radiographs show small nodules, irregular lines, or “ground-glass shadows.”
- With progression, patients may develop respiratory failure, pulmonary hypertension, and cor pulmonale



I. Fibrosing Diseases:
1. Idiopathic Pulmonary Fibrosis

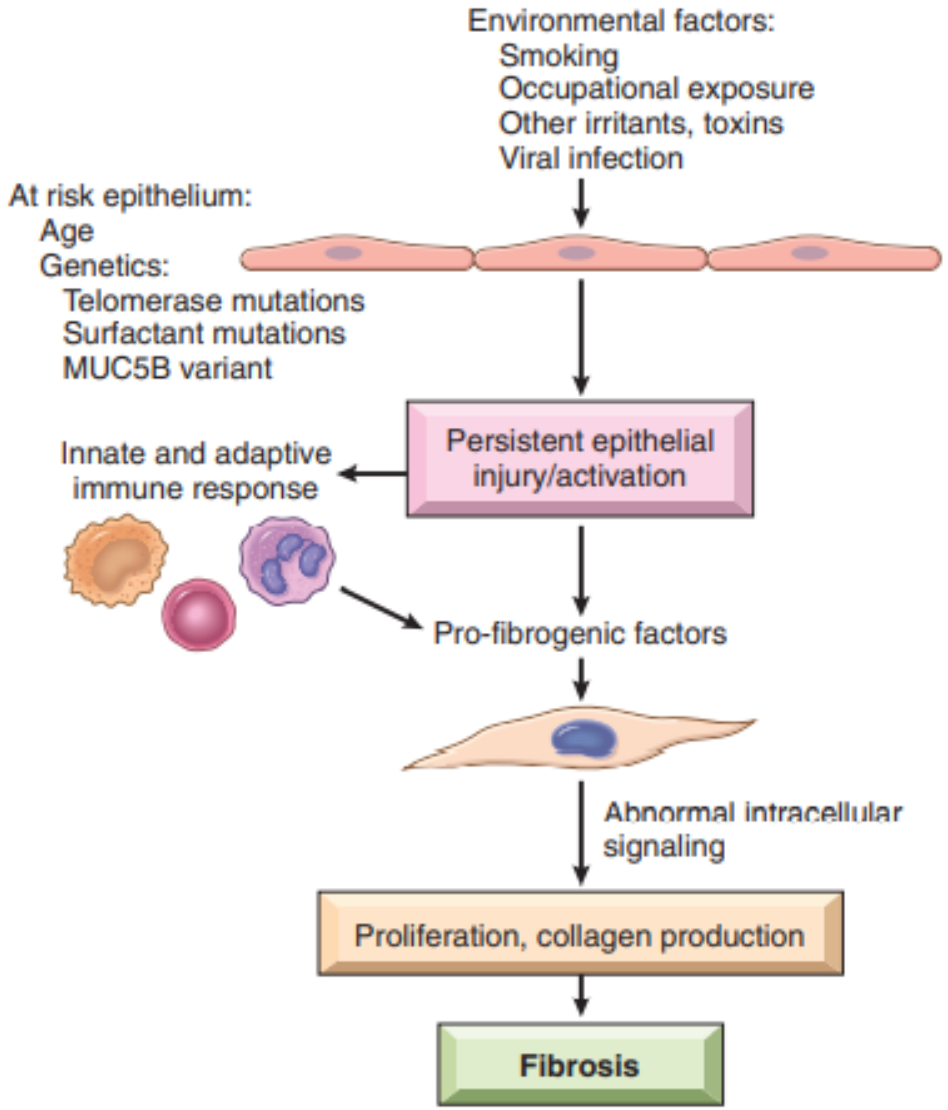
- **Idiopathic pulmonary fibrosis (IPF) refers to a pulmonary disorder of unknown etiology that is characterized by patchy, progressive bilateral interstitial fibrosis.**

- **it is a disease of aging, virtually never occurring before 50 years of age, mainly in males.**
- **The radiologic and histologic pattern of fibrosis is referred to as usual interstitial pneumonia (UIP).**



Pathogenesis

- **The interstitial fibrosis that characterizes IPF is believed to result from repeated injury and defective repair of alveolar epithelium, often in a genetically predisposed individual.**



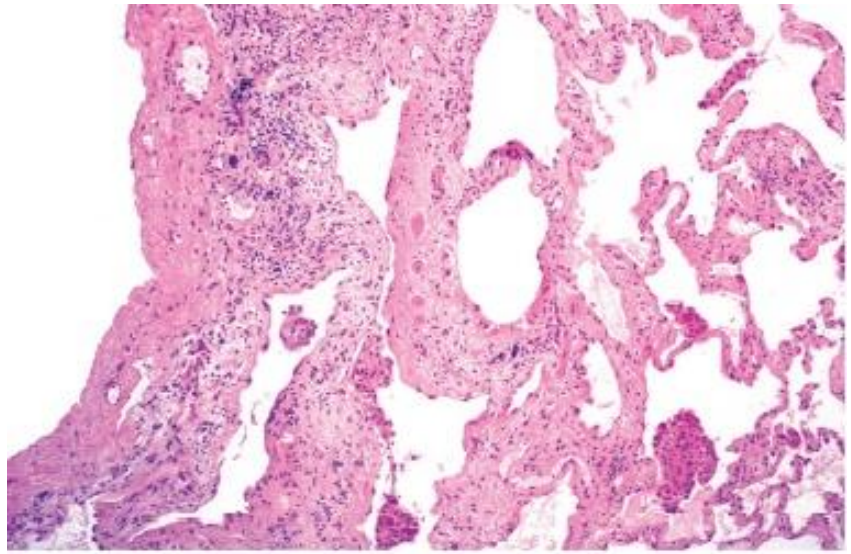
Morphology

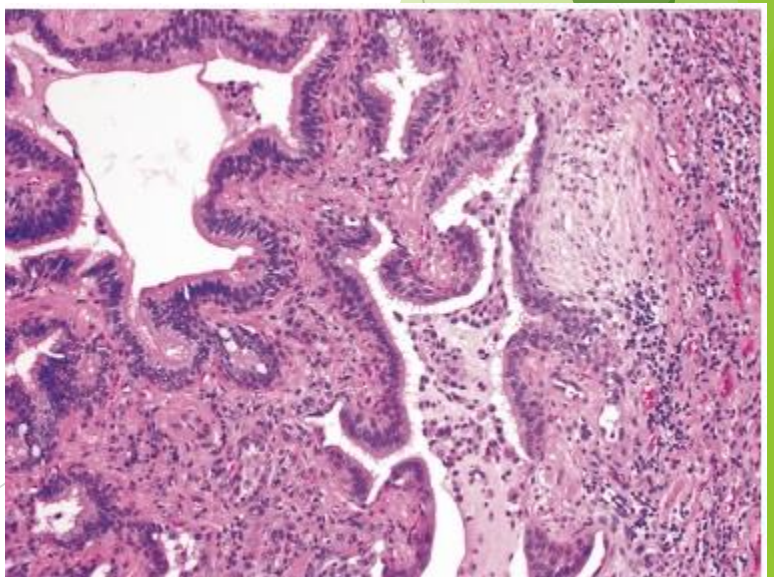
- **Grossly, the pleural surfaces of the lung are cobblestoned due to retraction of scars along the interlobular septa.**

- **The cut surface shows firm, rubbery white areas of fibrosis.**

Histologically, the hallmark is patchy interstitial fibrosis.

- **The earliest lesions demonstrate exuberant fibroblastic proliferation (fibroblastic foci) ,Over time these areas become more collagenous and less cellular.**
- **The dense fibrosis causes collapse of alveolar walls and formation of cystic spaces lined by hyperplastic type II pneumocytes or bronchiolar epithelium (honeycomb fibrosis).**
- **The interstitial inflammation usually is patchy and consists of an alveolar septal infiltrate of mostly lymphocytes and occasional plasma cells**





Clinical Features

- Gradual onset of a nonproductive cough and progressive dyspnea.
- Cyanosis, cor pulmonale, and peripheral edema may develop in later stages of the disease.

- Radiology: (subpleural and basilar fibrosis, reticular abnormalities, and “honeycombing”) often are diagnostic.

- Treatment:
- Anti-inflammatory therapies .
- anti-fibrotic therapies

2. Pneumoconioses

- lung disorders caused by inhalation of mineral dusts.
- The mineral dust pneumoconioses—the three most common of which are caused by inhalation of :

- coal dust.
- Silica.
- asbestos.

} stem from exposure in the workplace

Table 13.3 Mineral Dust–Induced Lung Disease

Agent	Disease	Exposure
Coal dust	Simple coal worker's pneumoconiosis: macules and nodules Complicated coal worker's pneumoconiosis: PMF	Coal mining
Silica	Silicosis	Sandblasting, quarrying, mining, stone cutting, foundry work, ceramics
Asbestos	Asbestosis, pleural effusions, pleural plaques, or diffuse fibrosis; mesothelioma; carcinoma of the lung and larynx	Mining, milling, and fabrication of ores and materials; installation and removal of insulation

Pathogenesis

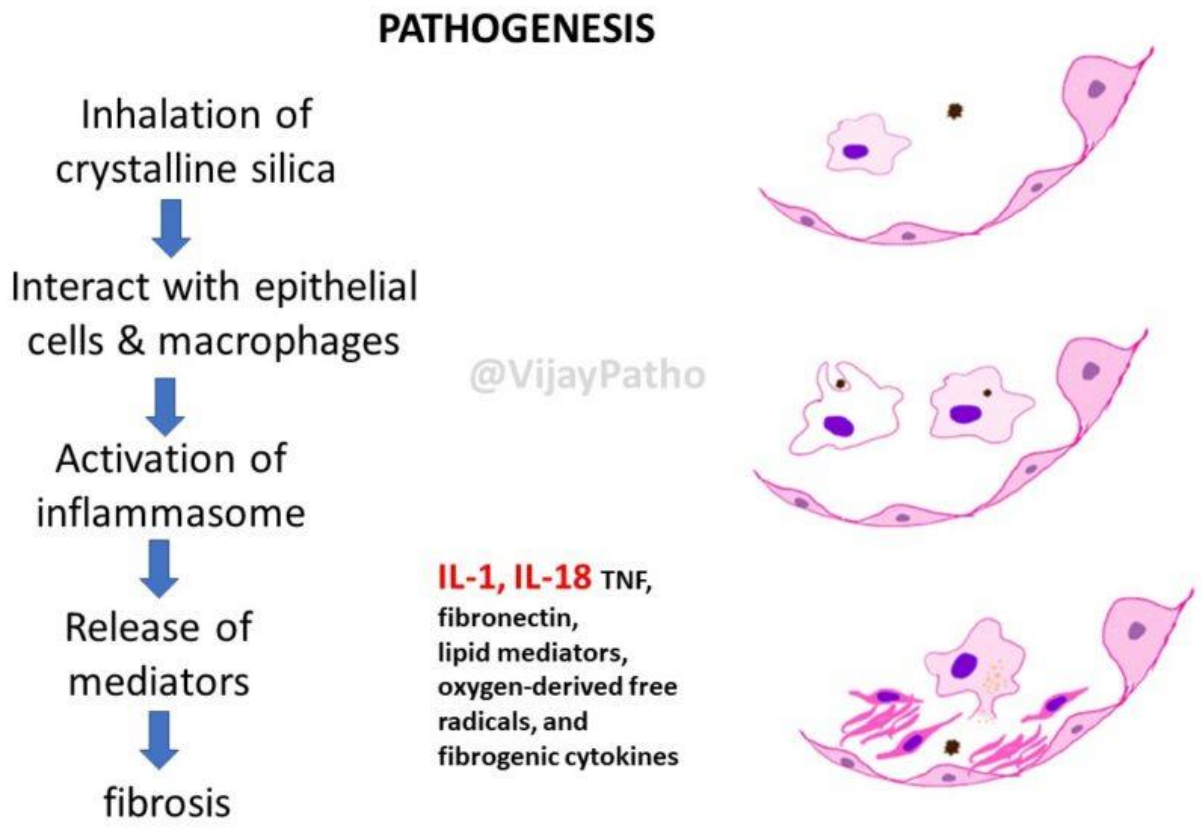
- **The reaction of the lung to mineral dusts depends on many variables, including:**
- ✓ **size.**
- ✓ **Shape.**
- ✓ **solubility.**
- ✓ **reactivity of the particles.**

- ✓ **Tobacco smoking worsens the effects of all inhaled mineral dusts, more so with asbestos than other particles.**

- For example, particles greater than 5 to 10 µm are unlikely to reach distal airways, whereas particles smaller than 0.5 µm move into and out of alveoli, often without substantial deposition and injury

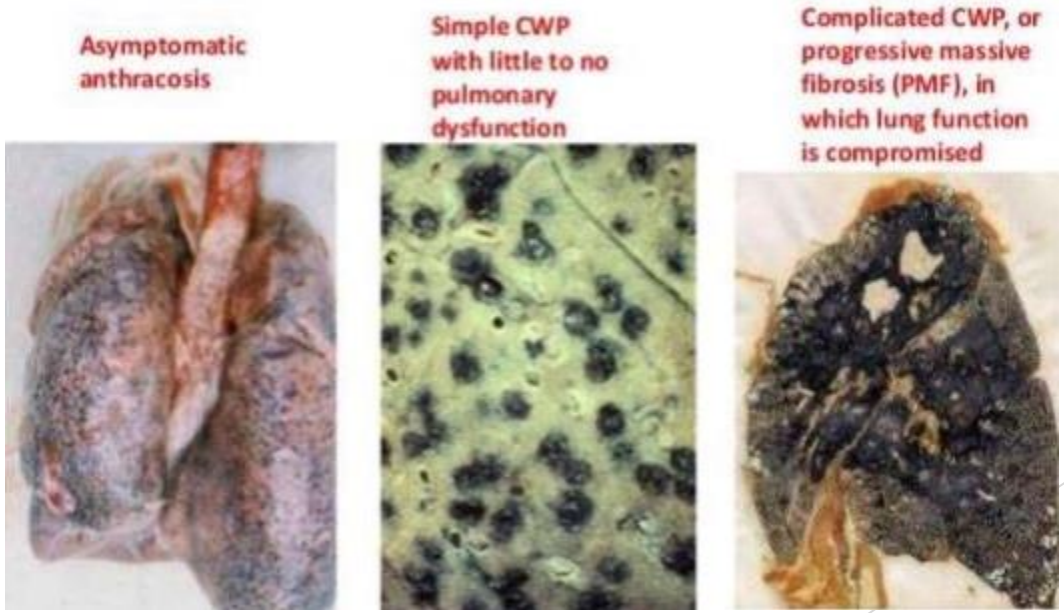
- Particles that are 1 to 5 µm in diameter are the most dangerous, because they get lodged at the bifurcation of the distal airways

✓The pulmonary alveolar macrophage is a key cellular element in the initiation and perpetuation of inflammation, lung injury and fibrosis.

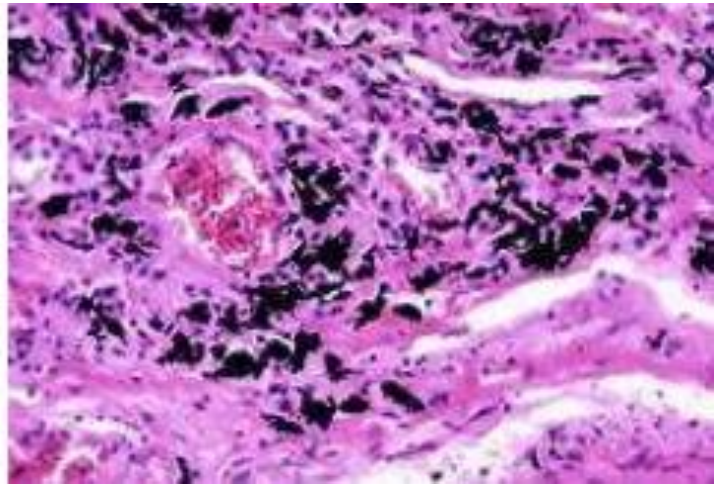


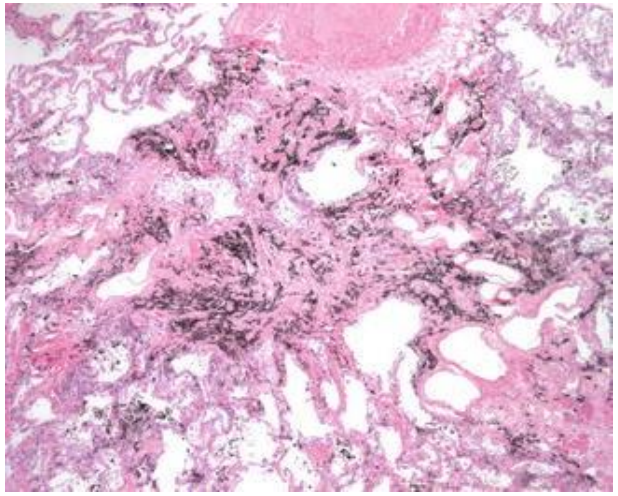
A. Coal Worker's Pneumoconiosis

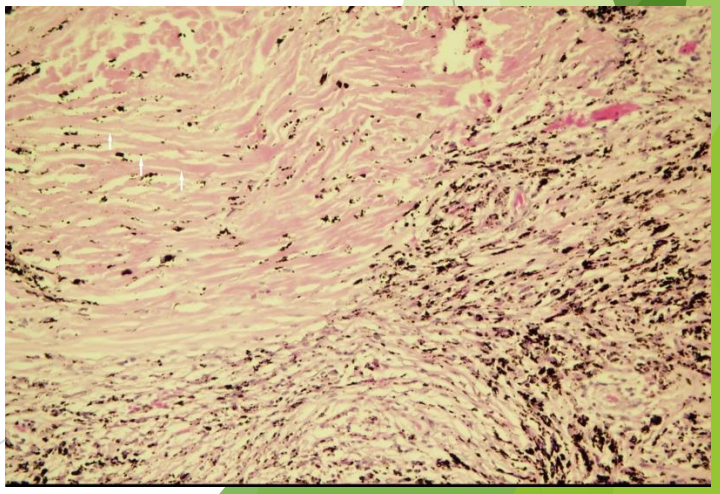
- The spectrum of lung findings in coal workers is wide, ranging from :
- Asymptomatic anthracosis, in which pigment deposits without a perceptible cellular reaction.
- Simple coal worker's pneumoconiosis (CWP), in which macrophages accumulate with little to no pulmonary dysfunction.
- Complicated CWP or progressive massive fibrosis (PMF), in which fibrosis is extensive and lung function is compromised



- Pulmonary anthracosis:
- Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages, which then accumulate in the connective tissue along the pulmonary and pleural lymphatics and in draining lymph nodes.
- Simple CWP is characterized by the presence of :
- Coal macules: consists of dust-laden macrophages and small amounts of collagen fibers .
- Larger coal nodules:
- Complicated CWP (PMF) :
- Caused by coalescence of coal nodules. consist of dense collagen and pigment







Clinical Features

- **CWP usually is a benign disease that produces little defect in lung function.**
- **If PMF develops, there is increasing pulmonary dysfunction, pulmonary hypertension, and cor pulmonale.**

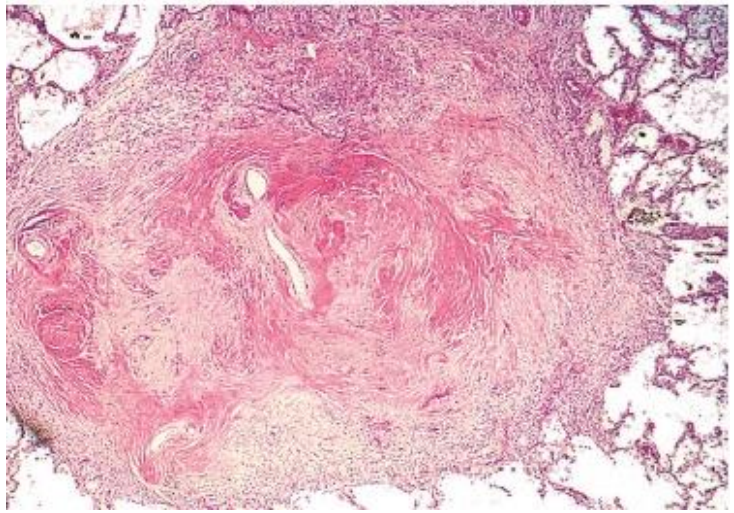
- **There is no increased frequency of lung carcinoma in coal miners, a feature that distinguishes CWP from both silica and asbestos exposures**

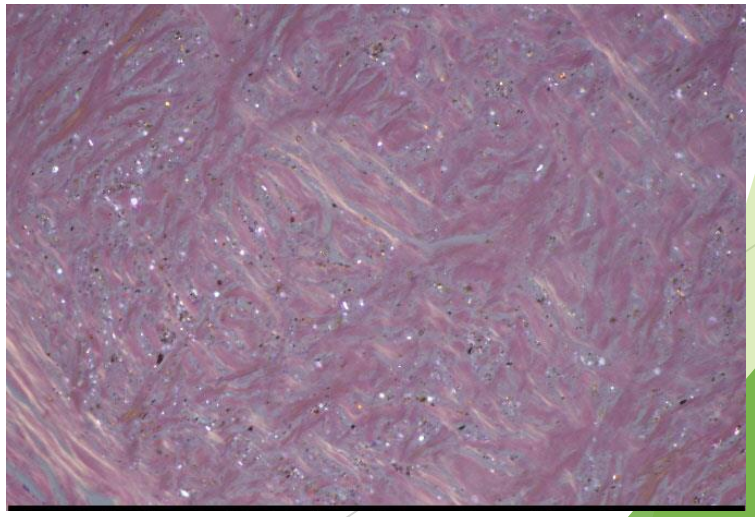
B. Silicosis

- **Silicosis is currently the most prevalent chronic occupational disease in the world.**
- **It is caused by inhalation of crystalline silica, mostly in occupational settings.**
- **Silica occurs in both crystalline and amorphous forms, but crystalline forms (including quartz) are by far the most toxic and fibrogenic**

MORPHOLOGY

- Silicotic nodules in their early stages are tiny, barely palpable, discrete, pale-to-black (if coal dust is present) nodules in the upper zones of the lungs.
- Microscopically:
- the silicotic nodule demonstrates concentrically arranged hyalinized collagen fibers surrounding an amorphous center.
- The “whorled” appearance of the collagen fibers is quite distinctive for silicosis.
- Examination of the nodules by polarized microscopy reveals weakly birefringent silica particles.





Clinical Features

- Silicosis usually is detected in asymptomatic workers on routine chest radiographs, which typically show a fine nodularity in the upper zones of the lung.
- Most patients do not develop shortness of breath until late in the course.
- patients with PMF develop pulmonary hypertension and cor pulmonale as a result of chronic hypoxia–induced vasoconstriction and parenchymal destruction.
- Silicosis is associated with an increased susceptibility to tuberculosis

c. Asbestosis and Asbestos-Related Diseases

- Asbestos is a family of crystalline hydrated silicates with a fibrous geometry. On the basis of epidemiologic studies.
- Asbestos acts as a tumour initiator and promoter
- occupational exposure to asbestos is linked to:
- parenchymal interstitial fibrosis (asbestosis).
- localized fibrous plaques.
- pleural effusions.
- lung carcinoma.
- malignant pleural and peritoneal mesothelioma.
- laryngeal carcinoma.
-

Pathogenesis

- As with silica crystals, once phagocytosed by macrophages.
- Asbestos fibers activate the inflammasome.
- Damage phagolysosomal membranes.
- Stimulating the release of proinflammatory factors and fibrogenic mediators.

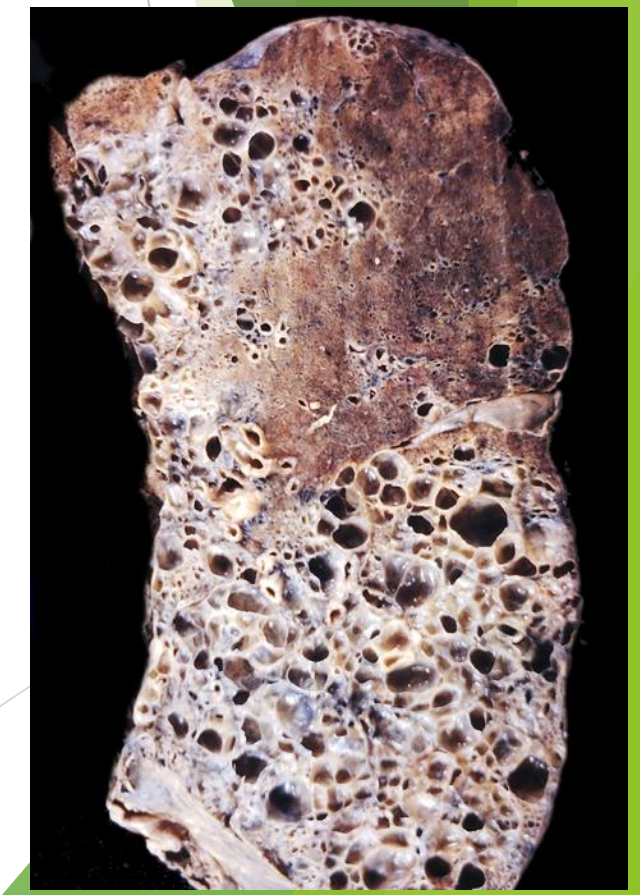
MORPHOLOGY

- Asbestosis is marked by diffuse pulmonary interstitial fibrosis, characterized by the presence of asbestos bodies, which are seen as golden brown, fusiform or beaded rods with a translucent center.

- Asbestos bodies apparently are formed when macrophages attempt to phagocytose asbestos fibers; the iron “crust” is derived from phagocyte ferritin.

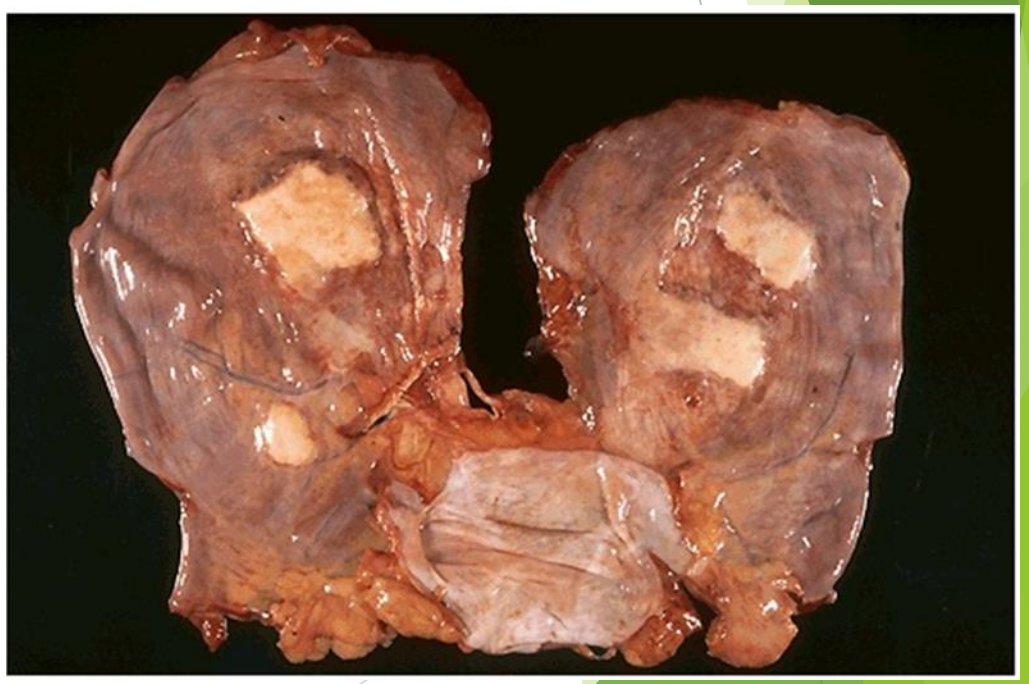
- asbestosis begins in the lower lobes and subpleurally, spreading to the middle and upper lobes of the lungs as the fibrosis progresses.

- Contraction of the fibrous tissue distorts the normal architecture, creating enlarged air spaces enclosed within thick fibrous walls; eventually, the affected regions become honeycombed



MORPHOLOGY

- Pleural plaques are the most common manifestation of asbestos exposure and are well-circumscribed plaques of dense collagen often containing calcium.



Clinical Features

- Progressively worsening dyspnea appears 10 to 20 years after exposure.
- cough and production of sputum.
- The disease may remain static or progress to congestive heart failure, cor pulmonale, and death.
- Both lung carcinoma and malignant mesothelioma develop in workers exposed to asbestos

II. Granulomatous Diseases
Sarcoidosis

- Sarcoidosis is a multisystem disease of unknown etiology characterized by noncaseating granulomatous inflammation in many tissues and organs.

- can manifest in many different ways:
  - Bilateral hilar lymphadenopathy or lung involvement (or both), visible on chest radiographs, is the major finding at presentation in most cases.

  - Eye and skin involvement each occurs in about 25%

Etiology and Pathogenesis

- it is a disease of disordered immune regulation in genetically predisposed individuals exposed to certain environmental agents.

- Several immunologic abnormalities in sarcoidosis suggest the development of a cell-mediated response to an unidentified antigen. The process is driven by CD4+ helper T cells:….clues:

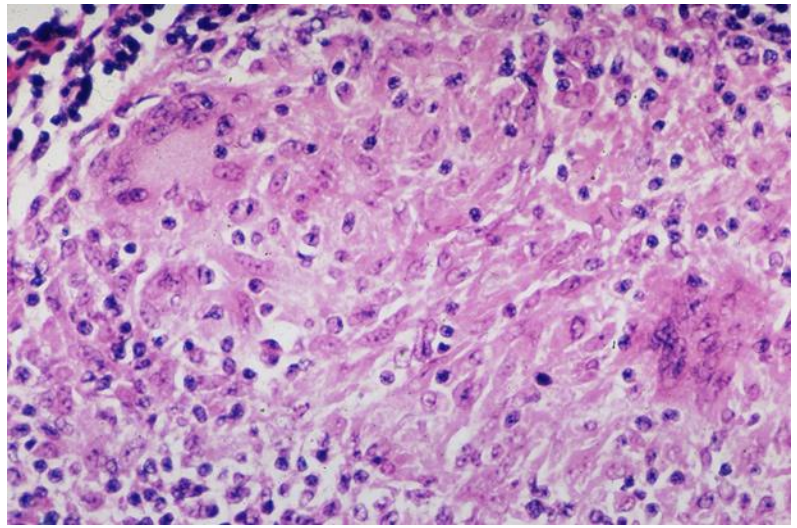
- Intraalveolar and interstitial accumulation of CD4+ TH1 cells, with peripheral T cell cytopenia.

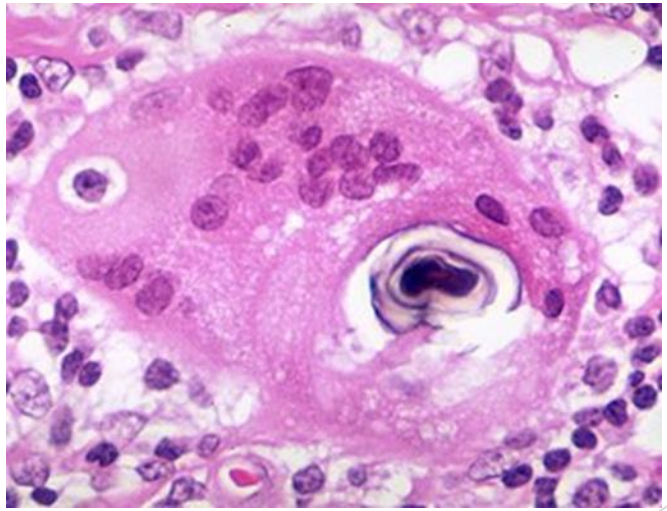
- Increases in TH1 cytokines such as IL-2 and IFN-γ, resulting in T cell proliferation and macrophage activation, respectively.

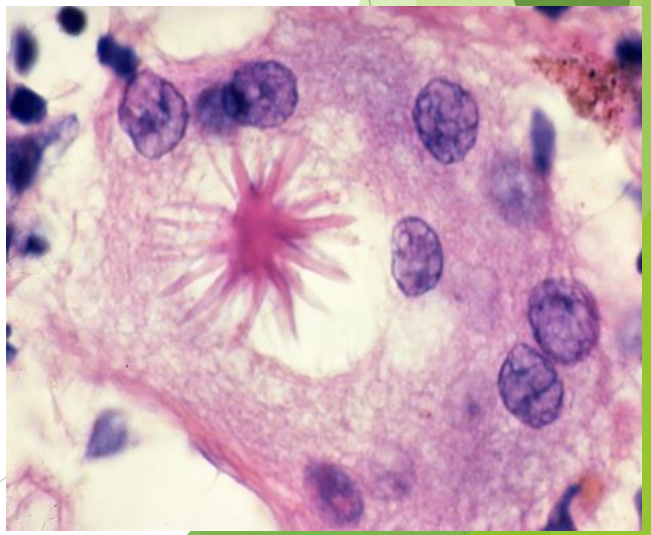
- Increases in several cytokines in the local environment (IL-8, TNF, macrophage inflammatory protein-1α) that favor recruitment of additional T cells and monocytes and contribute to the formation of granulomas.
- Anergy to common skin test antigens such as Candida or purified protein derivative (PPD).
- Polyclonal hypergammaglobulinemia.
- Familial and racial clustering of cases, suggesting the involvement of genetic factors

Morphology

- The cardinal histopathologic feature of sarcoidosis, irrespective of the organ involved, is the **nonnecrotizing epithelioid granuloma.**
- Schaumann bodies: laminated concretions composed of calcium and proteins.
- asteroid bodies: stellate inclusions enclosed within giant cells



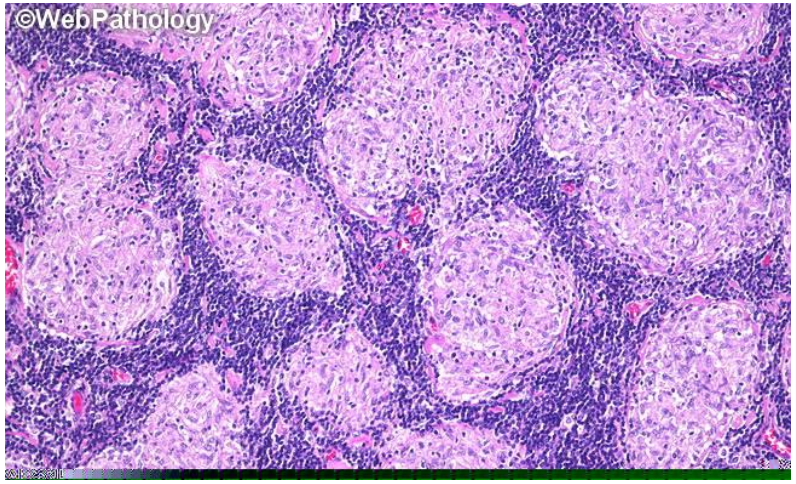


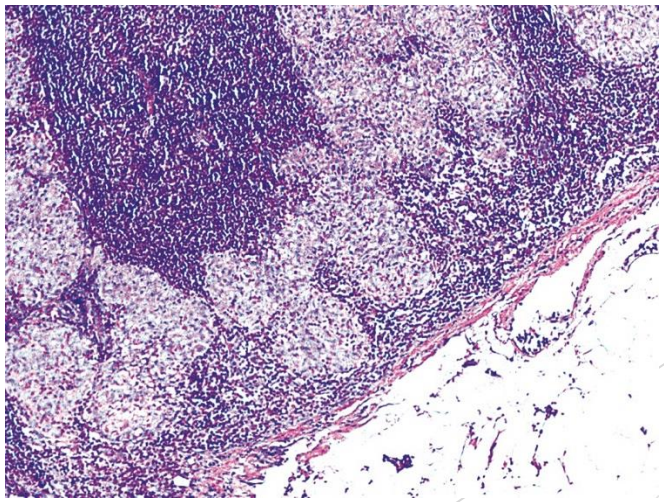


Which organs?????

- 1. lung:
- The granulomas predominantly involve the interstitium rather than air spaces,
- The bronchoalveolar lavage fluid contains abundant CD4+ T cells.
- The granulomas eventually are replaced by diffuse interstitial fibrosis, resulting in a so-called “honeycomb lung”.

- 2. Intrathoracic hilar and paratracheal lymph nodese:
- They are enlarged, painless and have a firm, rubbery texture.

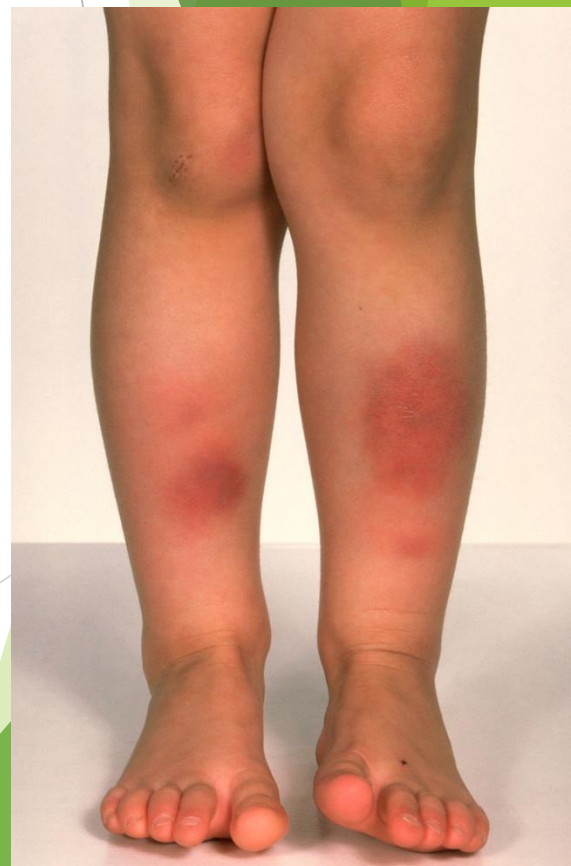




- 3. skin:
  - Erythema nodosum, the hallmark of acute sarcoidosis, consists of raised, red, tender nodules on the anterior aspects of the legs.

- 4. eye and lacrimal glands:
  - optic nerve involvement and total vision loss.
  - Unilateral or bilateral parotitis with painful enlargement of the parotid glands.

  - 5. spleen, liver and bone marrow.



Clinical Features

- Asymptomatic, discovered on routine chest films as bilateral hilar adenopathy or as an incidental finding at autopsy.
- Peripheral lymphadenopathy, cutaneous lesions, eye involvement, splenomegaly, or hepatomegaly.
- Respiratory symptoms (shortness of breath, dry cough, or vague substernal discomfort).

- Definitive diagnostic test for sarcoidosis does not exist, and establishing a diagnosis requires the presence of clinical and radiologic findings.

- Sarcoidosis follows an unpredictable course characterized by either progressive chronicity or periods of activity interspersed with remissions

THANK YOU

GOOD LUCK