Respiratory system – Pathology (Fibrosing diseases)

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FIBROSING DISEASES

- **Idiopathic Pulmonary Fibrosis**
- **Nonspecific Interstitial Pneumonia**
- **Cryptogenic Organizing Pneumonia**
- **Pneumoconioses**

IDIOPATHIC PULMONARY FIBROSIS

- Pulmonary disorder of unknown etiology that is characterized by patchy, progressive bilateral interstitial fibrosis.
- cryptogenic Fibrosing alveolitis.
- The radiologic and histologic pattern of fibrosis is referred to as Usual interstitial pneumonia (UIP) pattern.
- Males , Never before 50s

IDIOPATHIC PULMONARY FIBROSIS

- Diagnosis:
  - radiologic and histologic pattern are needed
  - Diagnosis of exclusion

PATHOGENESIS

- This interstitial fibrosis is believed to result from:
- Repeated cycles of epithelial activation/injury by some
- unidentified agent
- Defective repair of alveolar epithelium
- Genetic predisposition

GENETIC FACTORS:

- Germ line mutations leading to loss of telomerase associated with increased risk.
- cellular aging since IPF is a disorder of older adults.
- 35% have a genetic variant in the MUC5B gene that alter the production of mucin
- Smaller number have germ line mutations in surfactant genes.

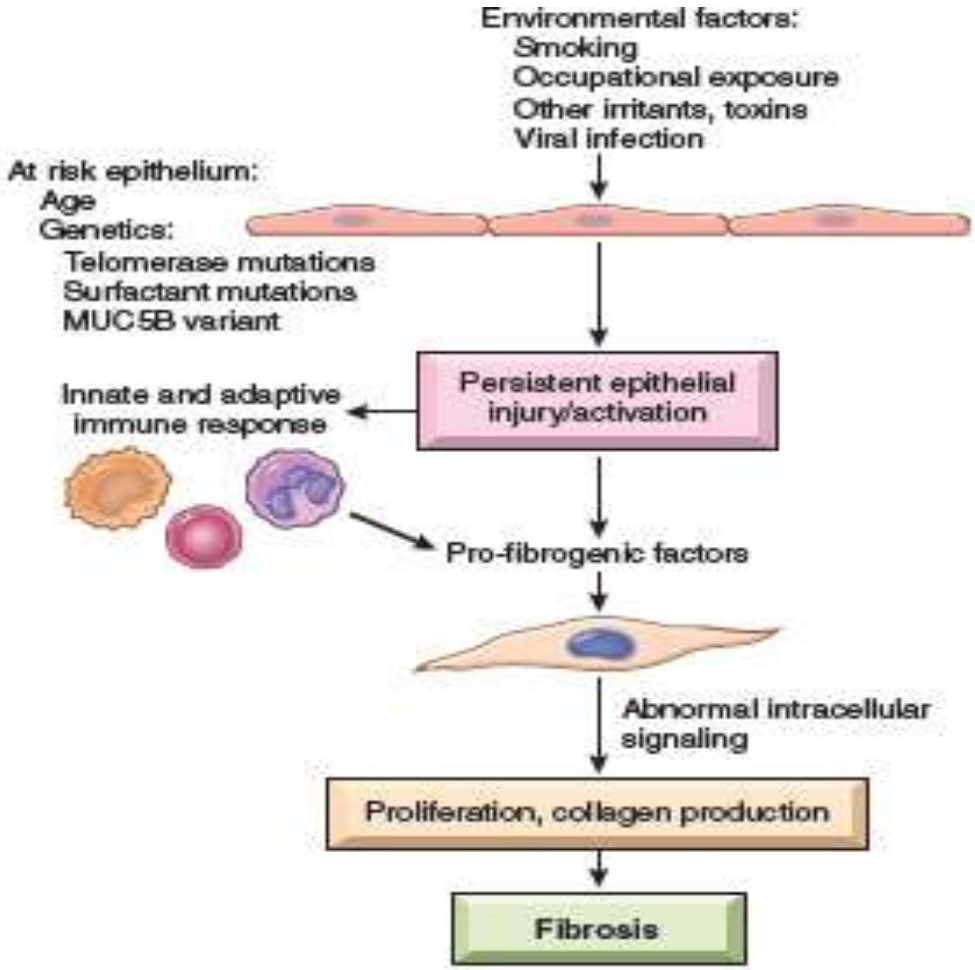


Fig. 13.13 Proposed pathogenic mechanisms in idiopathic pulmonary fibrosis. See text for details.

MORPHOLOGY, MACROSCOPIC:

- Cobblestones appearance of the pleural surface, due to retraction of scars along the interlobular septa.

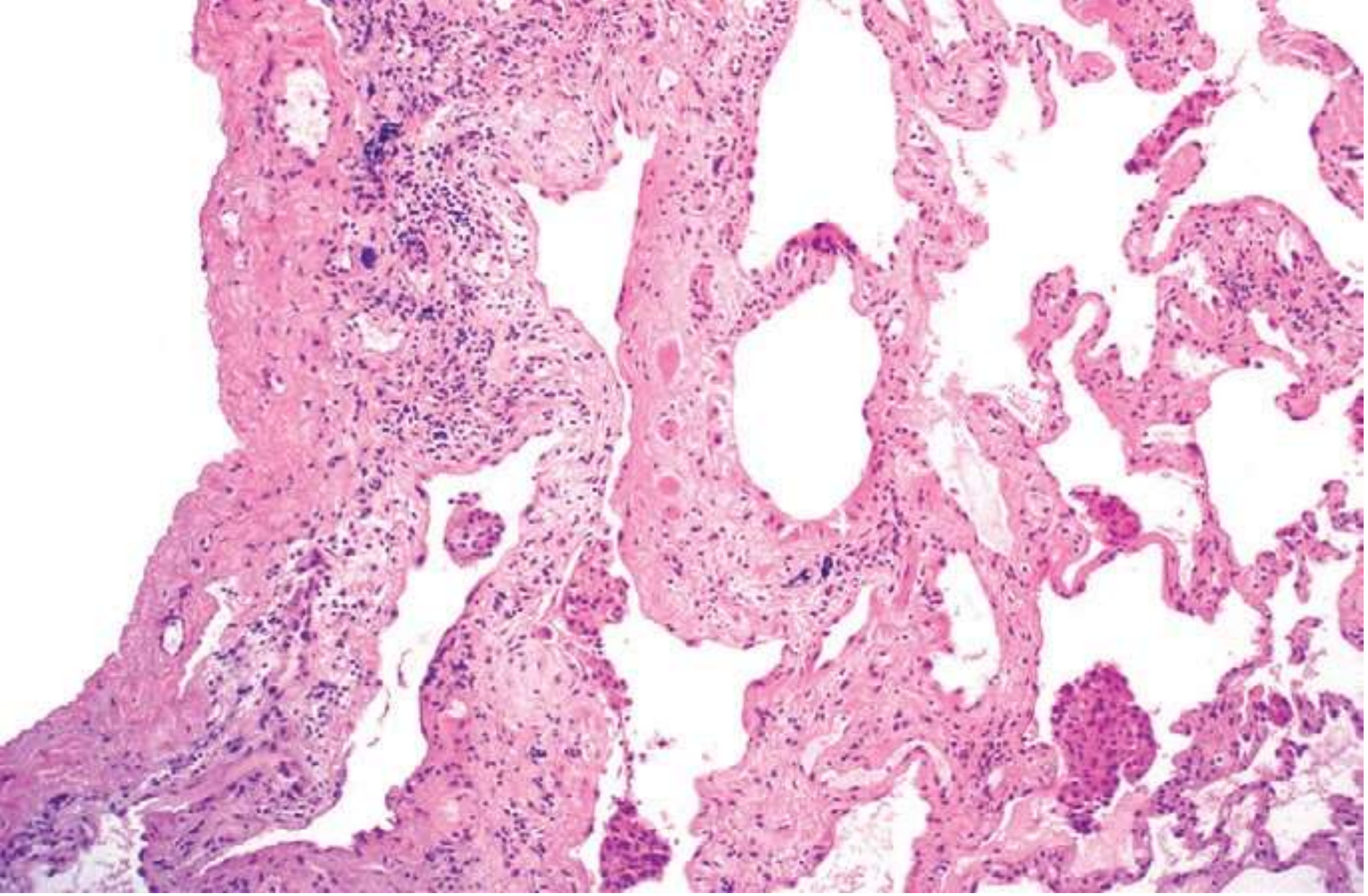
https://en.wikipedia.org/wiki/Cobblestone

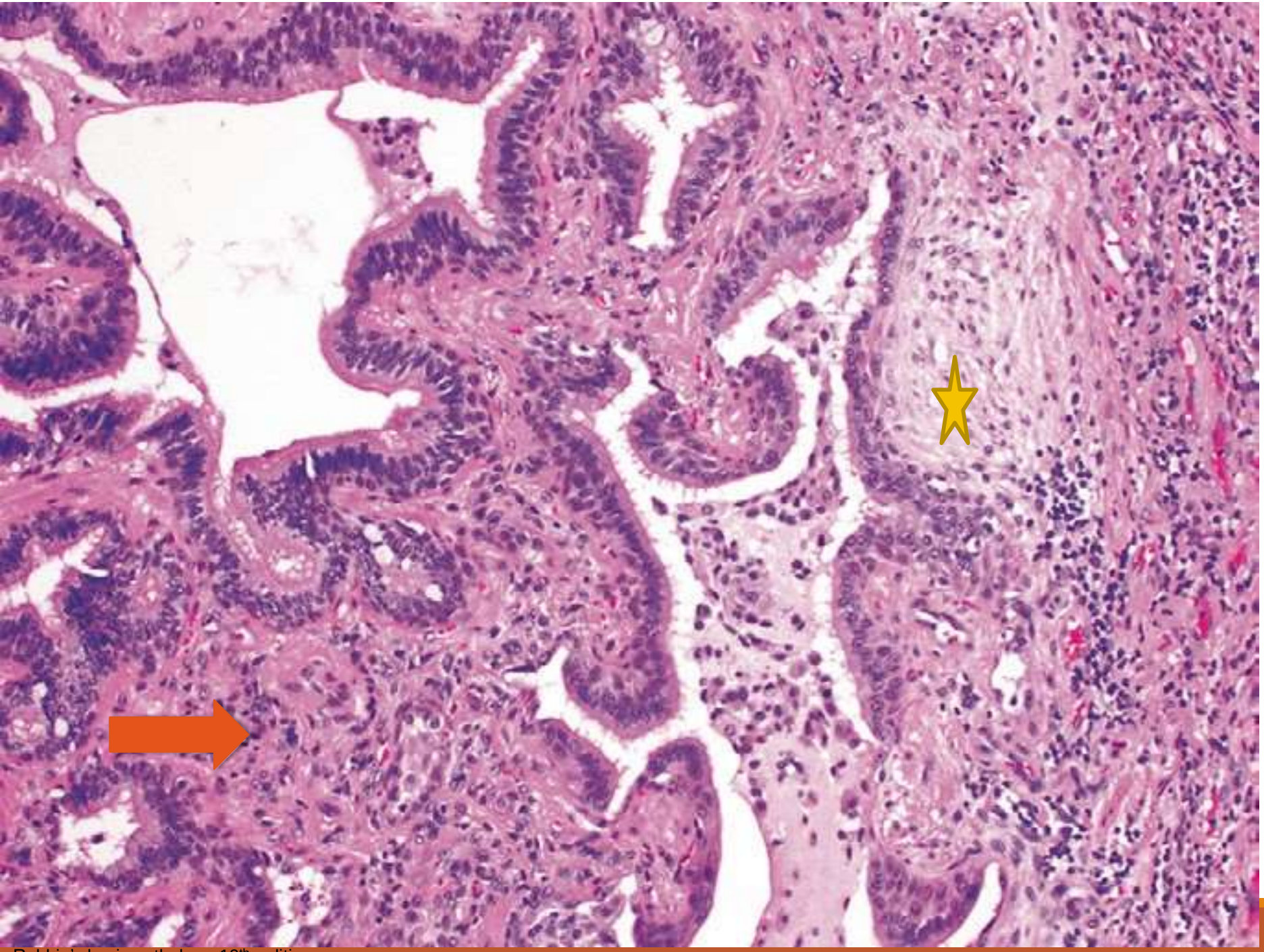
- The cut surface shows fibrosis (firm, rubbery white areas)
- Lower lobe and subpleural regions and along the interlobular septa are mostly affected.
- Usual interstitial pneumonia (UIP) pattern of fibrosis

MORPHOLOGY, MICROSCOPIC:

- Hallmark is patchy interstitial fibrosis, which varies in intensity and worsens with time.

- Temporal heterogeneity is typical (early and late lesions coexist):
- Fibroblastic foci are fibroblastic proliferations and
- considered the earliest lesions.
- Late lesions are more collagenous and less cellular and may show honeycomb fibrosis





Robbin's basic pathology, 10th edition

CLINICAL FEATURES

- Gradual onset of Nonproductive cough and progressive dyspnea.
- On physical exam, “dry” or “Velcro”-like crackles during inspiration.
- Cyanosis, cor pulmonale, and peripheral edema may develop later.
- Radiologic findings include subpleural and basilar fibrosis, reticular abnormalities, and “honeycombing”

OUTCOME:

- The overall prognosis remains poor
- survival is only 3 to 5 years
- lung transplantation is the only definitive treatment.

MANAGEMENT:

- Anti-inflammatory therapies
- Anti-fibrotic therapies

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NONSPECIFIC INTERSTITIAL PNEUMONIA (NSIP)

- Chronic bilateral interstitial lung disease of Unknown etiology
- despite its name it has Distinct clinical, radiologic, and histologic features.
- Better prognosis than IPF.
- Dyspnea and cough of several months

NONSPECIFIC INTERSTITIAL PNEUMONIA

- frequent association with collagen vascular disorders such as rheumatoid arthritis.

- characterized by patchy but uniform mild to moderate interstitial chronic inflammation and/or fibrosis.

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CRYPTOGENIC ORGANIZING PNEUMONIA

- Uncommon
- Unknown etiology
- Cough and dyspnea
- CXR: subpleural or peribronchial patchy airspace consolidation.

- Microscopically, Intraalveolar plugs of loose organizing connective tissue.

- Some patients recover spontaneously while most require treatment, usually with oral steroids.

A 59 year old lady works as electrical engineer and nonsmoker, has a 4-month history of increasing dyspnea. On examination she is afebrile and normotensive. Chest CT shows lower lobe reticular opacities. A transbronchial biopsy is performed and microscopically shows patchy interstitial inflammation with lymphocytes and plasma cells. No organisms are identified. Her condition slowly worsens over the next 10 years. Which of the following is the most likely diagnosis?

A) Desquamative interstitial pneumonitis

B) Hypersensitivity pneumonitis

C) Idiopathic interstitial fibrosis

D) Nonatopic bronchial asthma

E) Nonspecific interstitial pneumonia

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PNEUMOCONIOSES

- lung reaction to inhalation of mineral dusts, organic and inorganic particulates, chemical fume and vapor.

- The most common mineral dust are induced by inhalation of

  Coal dust, silica, and asbestos.

- usually related to workplace exposure, except for Asbestos

- In Asbestos:
  - The risk of cancer is increased in family members of asbestos workers and to individuals exposed outside of 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

PMF, Progressive massive fibrosis.

PATHOGENESIS:

- The reaction depends on size, shape, solubility, and reactivity of the particles.
- Particles that are 1 to 5 µm in diameter are the most dangerous
- The pulmonary alveolar macrophage is a key cellular element of lung injury and fibrosis.
- Tobacco smoking worsens the effects of all inhaled mineral dusts, more so with asbestos .

PNEUMOCONIOSES

- **Coal Worker's Pneumoconiosis (CWP)**
- **Silicosis**
- **Asbestosis and Asbestos related diseases**

COAL WORKER'S PNEUMOCONIOSIS

- Spectrum of changes:
  - Asymptomatic anthracosis: pigment accumulates without
  - a cellular reaction.

  - Simple coal worker's pneumoconiosis (CWP):
  - accumulations of macrophages with little to no pulmonary
  - dysfunction

  - Complicated CWP or progressive massive fibrosis
  - (PMF) : extensive fibrosis and compromised lung function.
    - less than 10% of cases of simple CWP progress to PMF.

- PMF is generic
  - confluent fibrosing reaction in the lung
  - can be a complication of any one of the pneumoconioses
- Coal is mainly carbon, in addition to other inorganic minerals

MORPHOLOGY:

- Pulmonary Anthracosis:
  - Seen also in urban dwellers and tobacco smokers.
  - Inhaled carbon pigment is engulfed by alveolar or interstitial macrophages
  - accumulate in the connective tissue along the pulmonary and pleural lymphatics and in draining lymph nodes.

Simple CWP:

Presence of coal macules and nodules
Coal macules : dust-laden macrophages small amounts of collagen fibers arrayed in a delicate network

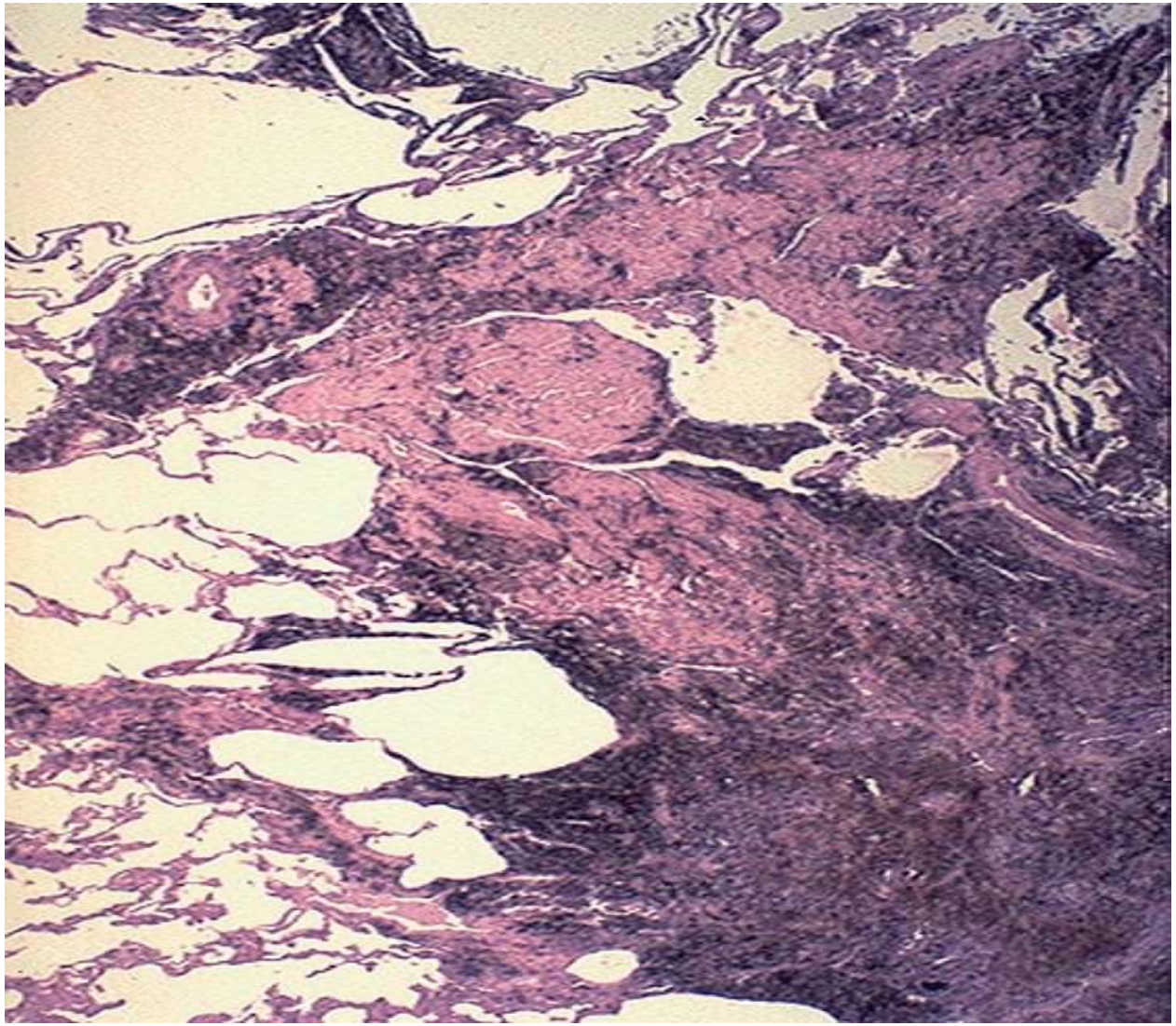
Upper lobes and upper zones of the lower lobes are more heavily involved.

centrilobular emphysema can occur.

MORPHOLOGY:

Complicated CWP (PMF):

- coalescence of coal nodules that develops over many years
- multiple, dark black scars >2 cm & up to 10 cm consist of dense collagen and pigment



Klatt EC: Robbins and Cotran atlas of pathology, *ed 2, Elsevier, Philadelphia, p 121.)*

CLINICAL FEATURES

- CWP: benign disease that produces little effect on lung function
- PMF: increasing pulmonary dysfunction, pulmonary ht, and cor pulmonale.
- The Progression from CWP to PMF is linked to higher coal dust exposure levels and total dust burden.

- once established PMF has a tendency to progress even in the absence of further exposure.

- No increased risk of lung carcinoma in coal miners.

- Distinguishes CWP from silica and asbestos exposures.

THANK YOU!