FIBROSING DISEASES

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FIBROSING DISEASES

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

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

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

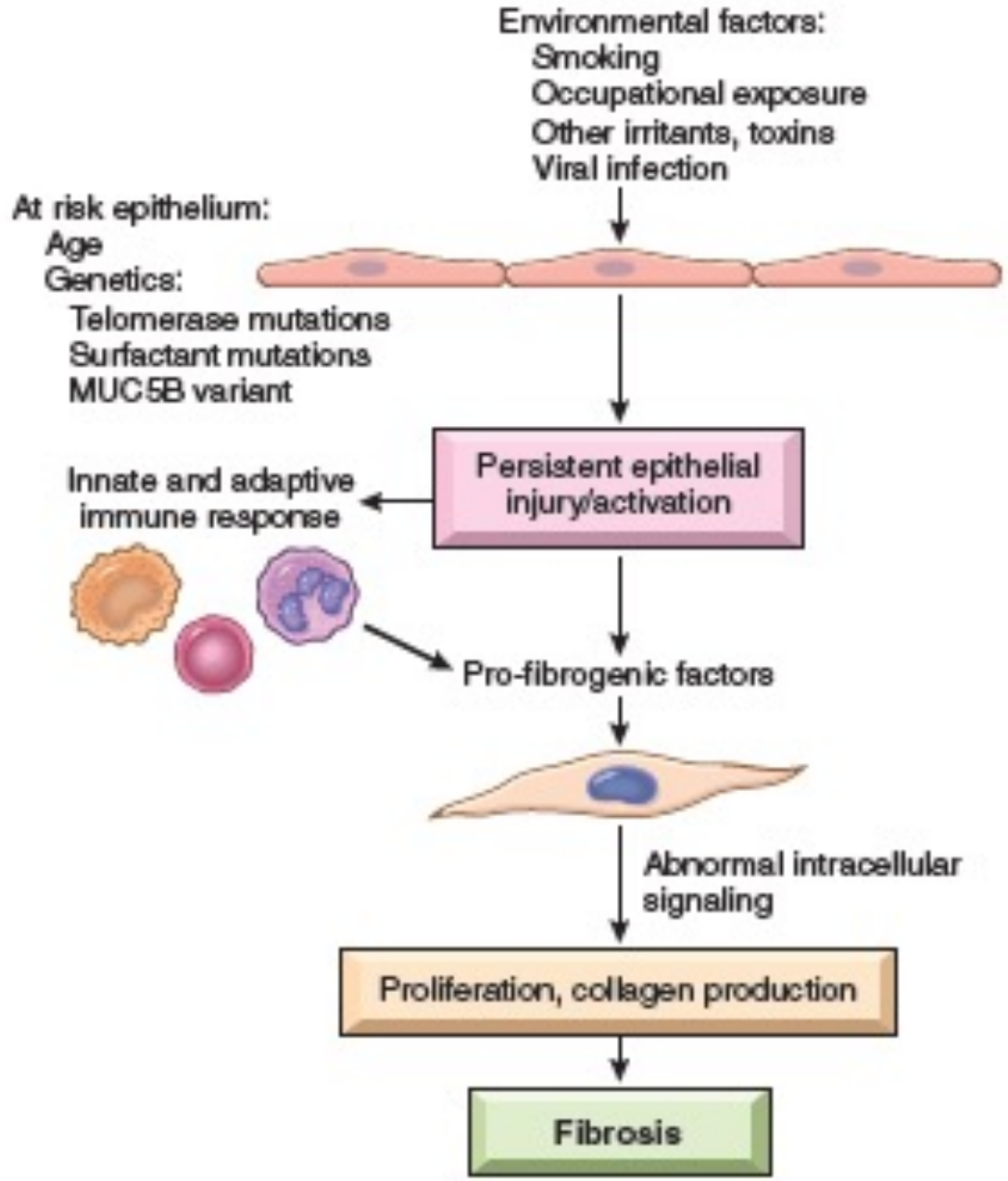

Fig. 13.13 Proposed pathogenic mechanisms in idiopathic pulmonary fibrosis. See text for details.

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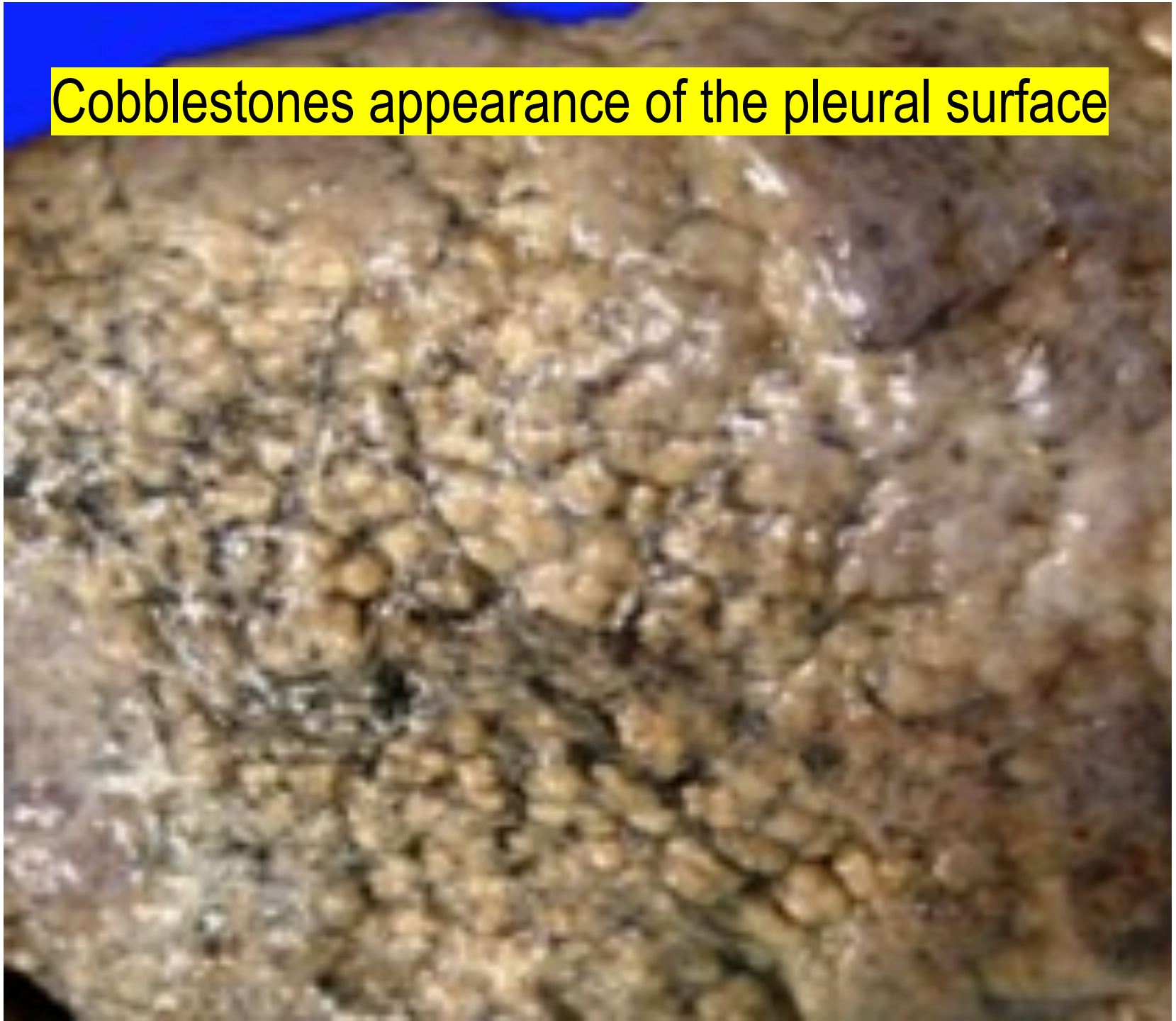
MORPHOLOGY, MACROSCOPIC:

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

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


Cobblestones appearance of the pleural surface

- 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:

Fibrosis:

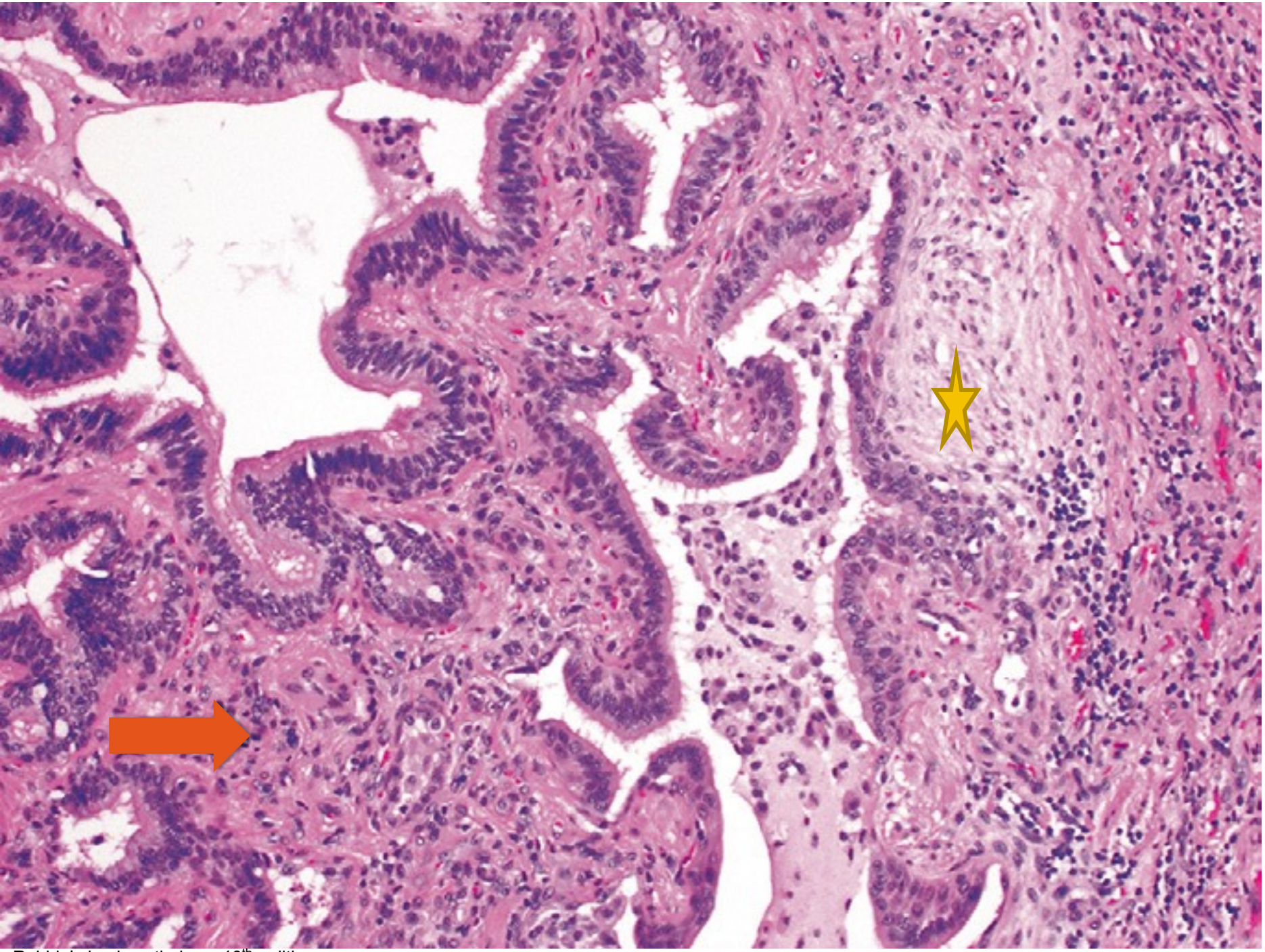
- Hallmark is **patchy** interstitial fibrosis, **which varies in intensity and worsens with time**.

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

mild to moderate **inflammation** within the fibrotic areas (lymphocytes, few plasma cells, neutrophils, eosinophils, and mast cells).

+/- Foci of squamous metaplasia and smooth muscle hyperplasia

pulmonary arterial hypertensive changes (intimal fibrosis and medial thickening).



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CLINICAL FEATURES

- **55 to 75 years old at presentation**

- **Gradual onset of Nonproductive cough** and **progressive dyspnea on exertion.**

- **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**
- Median survival after diagnosis **3 years**
- **lung transplantation is the only definitive treatment**.

MANAGEMENT:

- Anti-inflammatory therapies
- Anti-fibrotic therapies

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NONSPECIFIC INTERSTITIAL PNEUMONIA (NSIP)

- despite its name it has **Distinct clinical, radiologic, and histologic features.**

- **Chronic bilateral interstitial lung disease of Unknown etiology**

- **Better prognosis** than IPF**.**

- Clinically: female nonsmokers in their 6th decade of life with Dyspnea and cough of several months

NONSPECIFIC INTERSTITIAL PNEUMONIA

- **Idiopathic or associated** with collagen vascular disorders such as rheumatoid arthritis.

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

- Key features on radiology: bilateral, symmetric, predominantly lower lobe reticular opacities.

Histology:

NSIP is divided into cellular and fibrosing patterns.

- **The cellular pattern**: mild to moderate **chronic** interstitial **inflammation** (lymphocytes and a few plasma cells), in a uniform or patchy distribution.
- **The fibrosing pattern**: diffuse or patchy interstitial **fibrotic lesions of the same stage of development** (an important distinction from UIP).

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CRYPTOGENIC ORGANIZING PNEUMONIA

- Uncommon
- Unknown etiology (BUT seen as a response to infections or inflammatory injury of the lungs (viral and bacterial pneumonia, inhaled toxins, drugs, connective tissue disease, and graft-versus-host disease in BM transplant recipients).
- Cough and dyspnea
- CXR: subpleural or peribronchial patchy airspace consolidation (radiopaque or white areas).

- Microscopically:
  - **Masson bodies:** Intraalveolar plugs of loose organizing connective tissue (of the same age) within alveolar ducts, alveoli, and often bronchioles
  - the underlying lung architecture is normal.
  - no interstitial fibrosis or honeycomb lung.

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

- The prognosis for these patients is dependent on the underlying disorder.

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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**

- However, 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.

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PATHOGENESIS:

- **The development of a pneumoconiosis depends on:**

  (1) the **amount** of dust retained in the lung and airways (concentration in air, duration and the effectiveness of clearance mechanisms)

  (2) the **size and shape** of the particles:

  Particles that are 1 to 5 μm in diameter are the most dangerous

  (3) particle **solubility and reactivity**.

  (4) other irritants: **concomitant tobacco smoking** worsens the effects of all inhaled mineral dusts, more so with asbestos.

- **The pulmonary alveolar macrophage is a key cellular element** of lung injury and fibrosis.

PNEUMOCONIOSES

- **Coal Worker's Pneumoconiosis (CWP)**
- **Silicosis**
- **Asbestosis and Asbestos-Related Diseases**

COAL WORKER'S PNEUMOCONIOSIS (CWP)

- lung disease caused by inhalation of coal particles and other admixed forms of dust.
  - Coal is mainly carbon+/- trace metals, inorganic minerals, and crystalline silica.
    - Contaminating silica in the coal dust can favor progressive disease.
- Coal workers may also develop **emphysema and chronic bronchitis** independent of smoking.

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 pneumoconiosis

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, in draining lymph nodes or in organized lymphoid tissue along the bronchi or in the lung hilus.

Simple CWP:

- **Presence of coal macules and nodules**
  - **Coal macules (1 to 2 mm in dm):** dust-laden macrophages & small amounts of collagen fibers arrayed in a delicate network

- located primarily adjacent to respiratory bronchioles

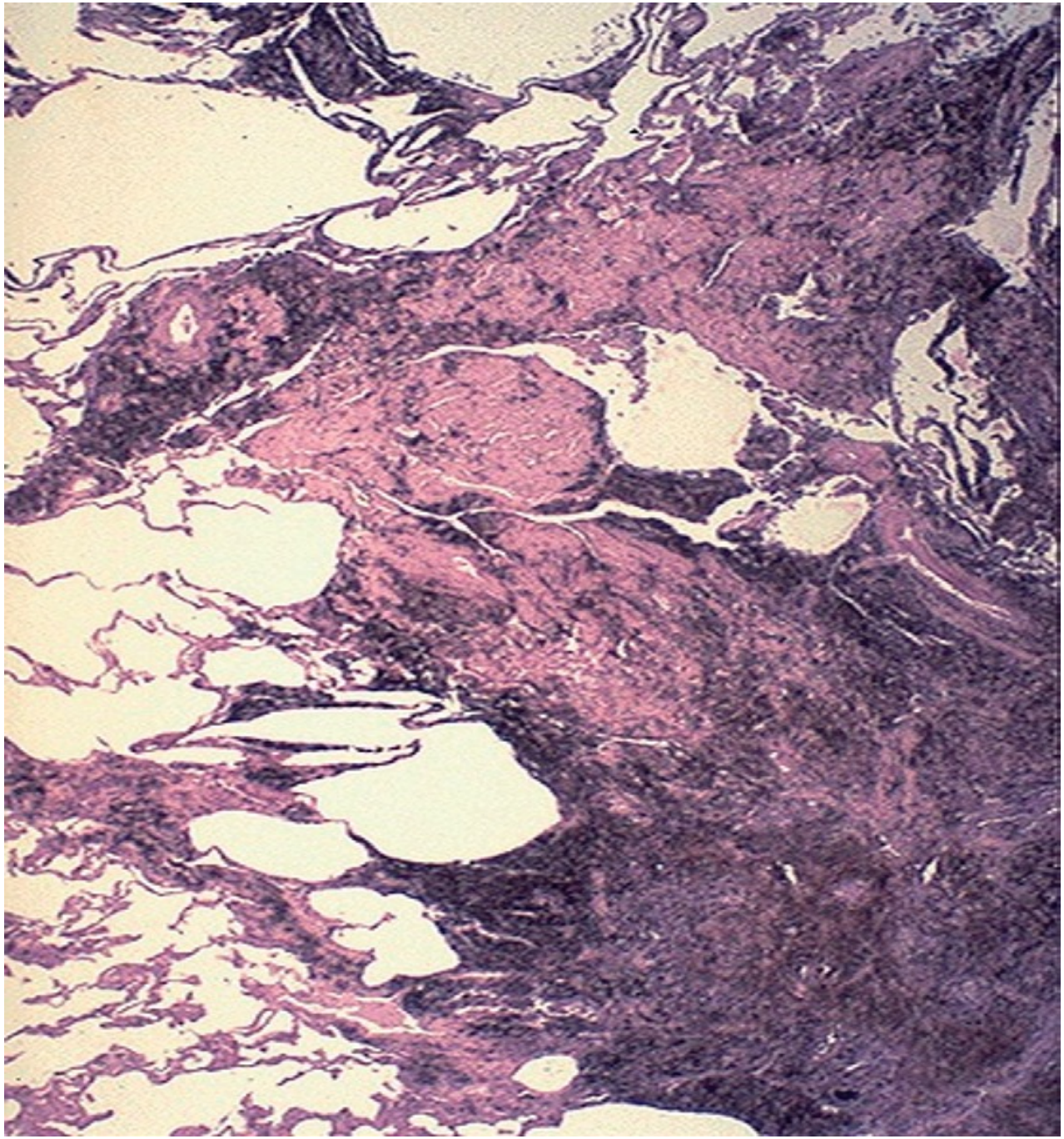
- **centrilobular emphysema** can occur.

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

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.

- **complicated CWP**:
  - The mild forms do not to affect lung function significantly.
  - 10% of complicated CWP progress to PMF: increasing pulmonary dysfunction, pulmonary hypertension, and cor pulmonale.
  - The Progression from CWP to PMF is linked to higher coal dust exposure levels and total dust burden.

- once established PMF tends 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!