Chronic interstitial lung diseases-2

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Table 15-5 Major Categories of Chronic Interstitial Lung Disease

Fibrosing
Usual interstitial pneumonia (idiopathic pulmonary fibrosis)
Nonspecific interstitial pneumonia
Cryptogenic organizing pneumonia
Connective tissue disease-associated
Pneumoconiosis
Drug reactions
Radiation pneumonitis
Granulomatous
Sarcoidosis
Hypersensitivity pneumonitis
Eosinophilic
Smoking Related
Desquamative interstitial pneumonia
Respiratory bronchiolitis-associated interstitial lung disease
Other
Langerhans cell histiocytosis
Pulmonary alveolar proteinosis
Lymphoid interstitial pneumonia

Fibrosing diseases:

- **Usual interstitial pneumonia (idiopathic pulmonary fibrosis)**
- **Nonspecific interstitial pneumonia**
- **Cryptogenic organizing pneumonia**
- **Connective tissue disease-associated**
- **Pneumoconiosis**

- **Drug reactions**
- **Radiation pneumonitis**

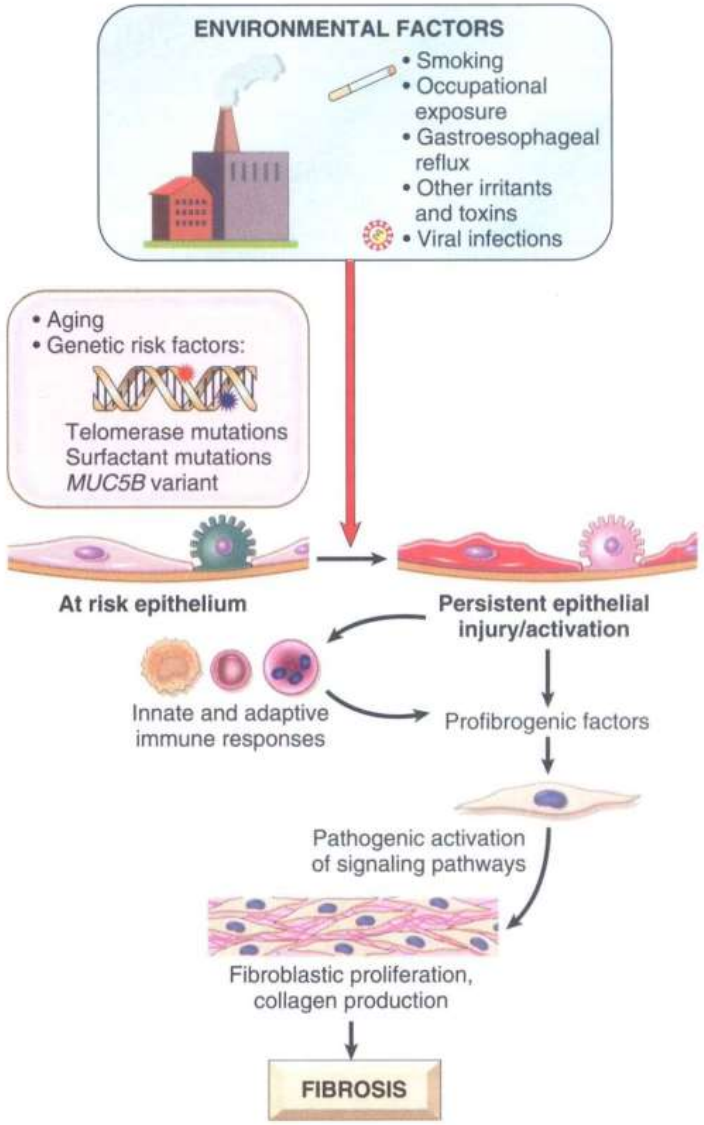
Idiopathic pulmonary fibrosis (Usual interstitial pneumonia)

- Unknown etiology.
- Patchy progressive bilateral interstitial fibrosis.
- “cryptogenic Fibrosing alveolitis”

- Radiologic and histologic pattern of fibrosis (UIP pattern).
- Diagnosis of exclusion.
- Males predominant.
- Never occur before 50.

PATHOGENESIS

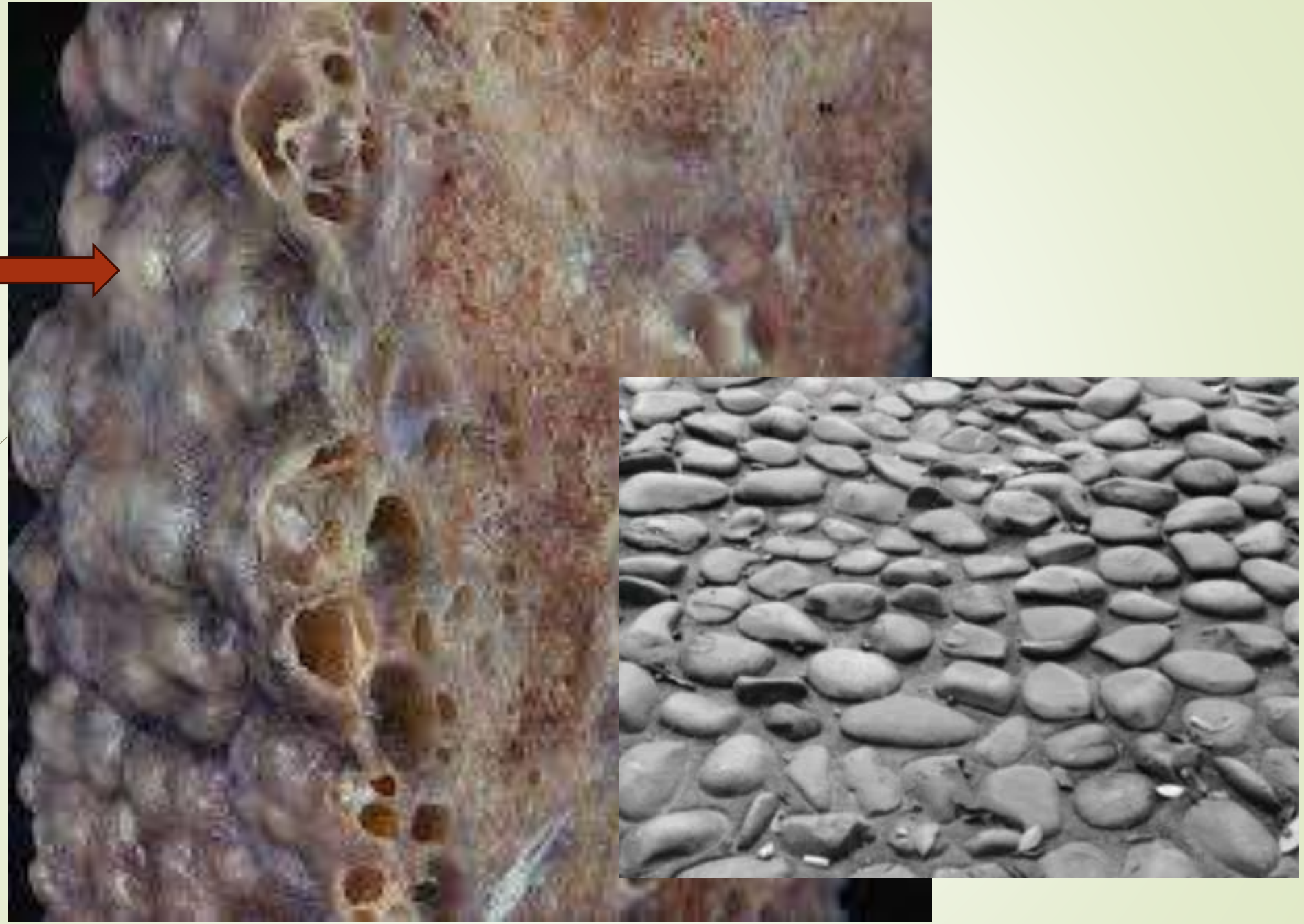
- Repeated injury to alveolar epithelium.
- Defected repair leading to fibroblastic proliferation.
- In genetically predisposed individuals.
- The cause is obscure.


ENVIRONMENTAL FACTORS
• Smoking
• Occupational exposure
• Gastroesophageal reflux
• Other irritants and toxins
• Viral infections
• Aging
• Genetic risk factors:
Telomerase mutations
Surfactant mutations
MUC5B variant
At risk epithelium
Persistent epithelial injury/activation
Innate and adaptive immune responses
Profibrogenic factors
Pathogenic activation of signaling pathways
Fibroblastic proliferation, collagen production
FIBROSIS

MORPHOLOGY

- **MACROSCOPIC:**

- **Cobblestone appearance of pleural surface (retraction of scars along the interlobular septa)**
- **Cut surface shows fibrotic firm, rubbery white areas.**
- **Lower lobe, subpleural regions and along the interlobular septa are mostly affected.**



MICROSCOPIC:

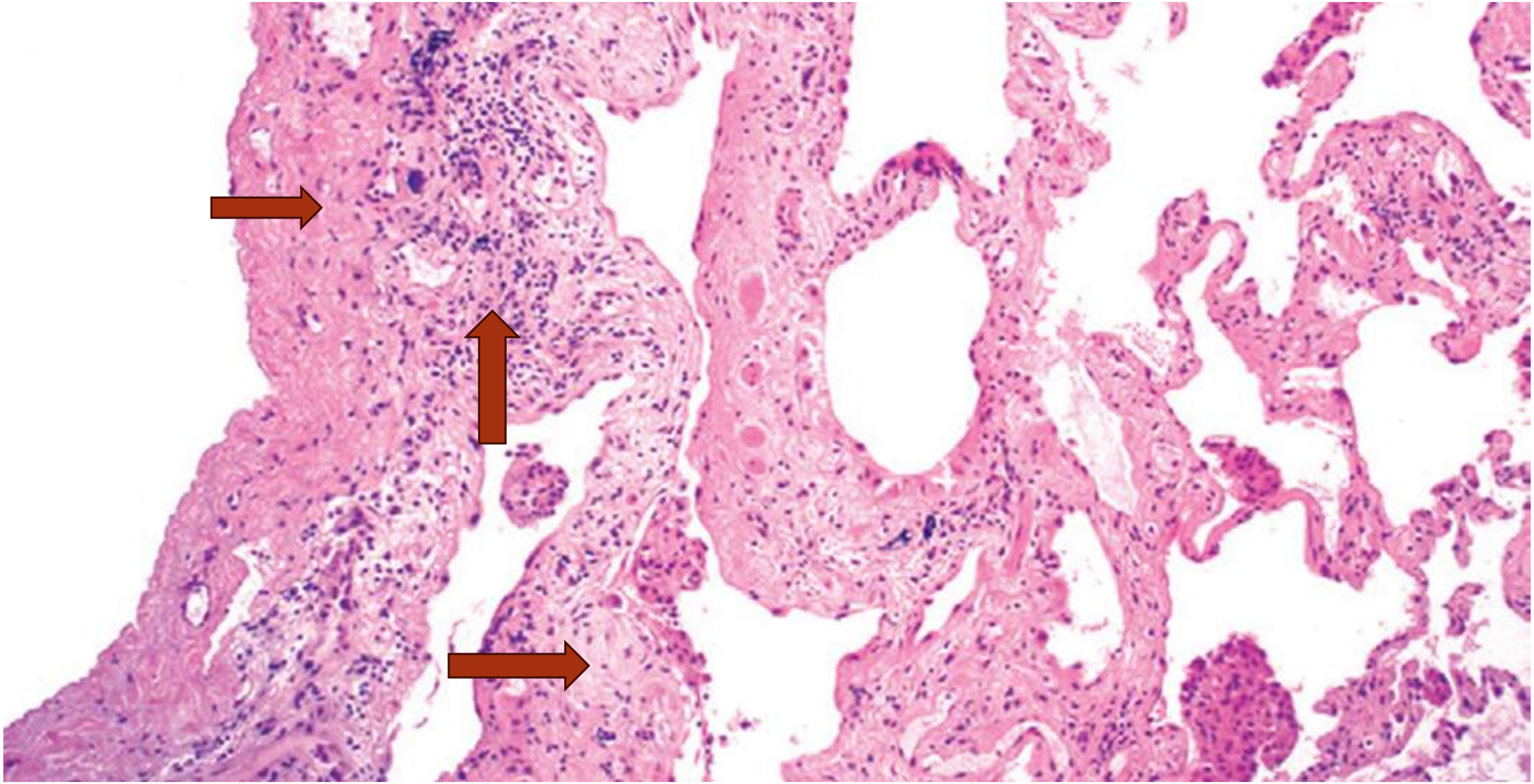
- Usual interstitial pneumonia (UIP) pattern of fibrosis.
- **Hallmark** is patchy interstitial fibrosis (varies in intensity & worsens with time).

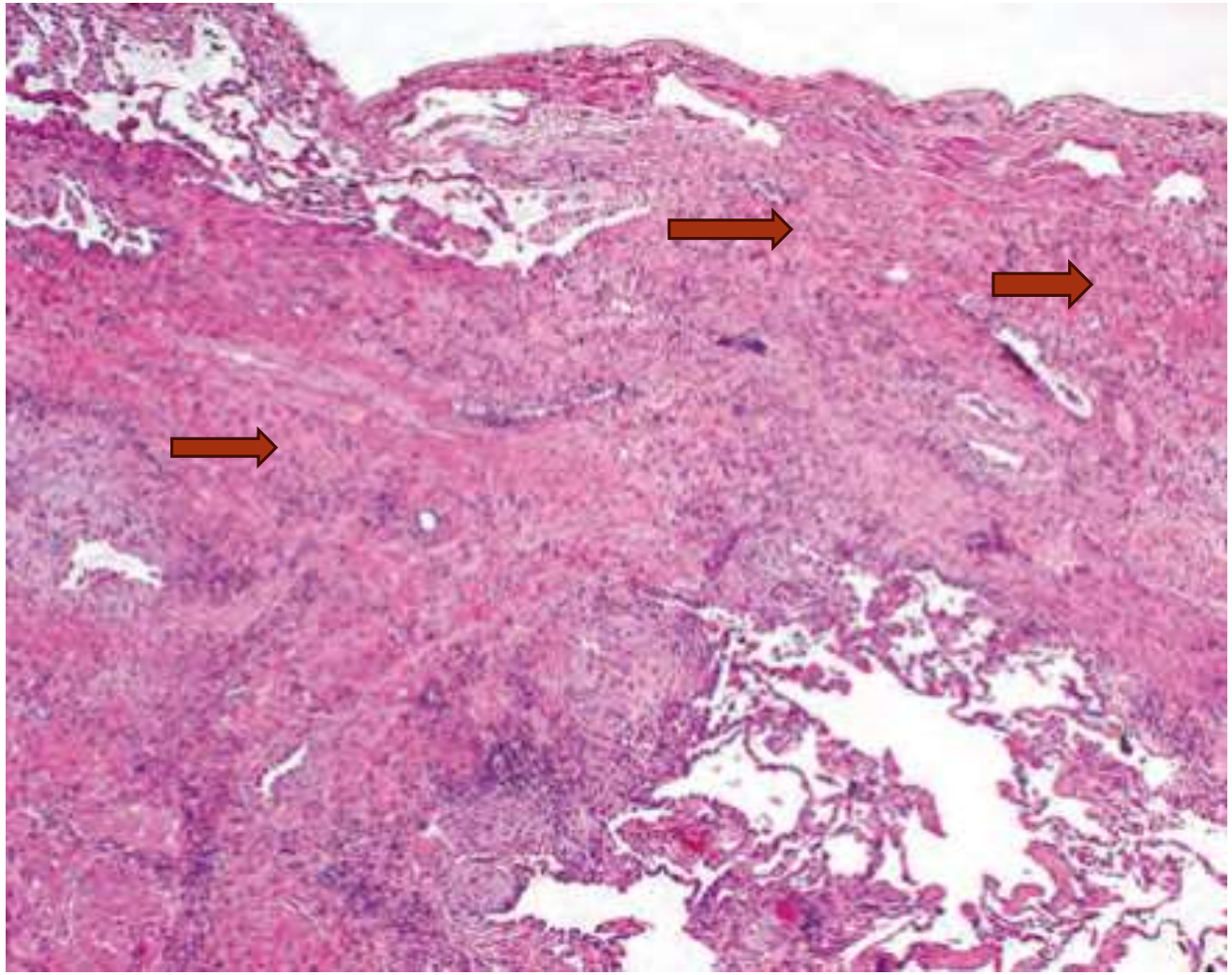
- **The earliest lesions**: Fibroblastic foci.
- **Later**: collagenous and less cellular foci.
- **Advanced**: Honeycomb fibrosis.

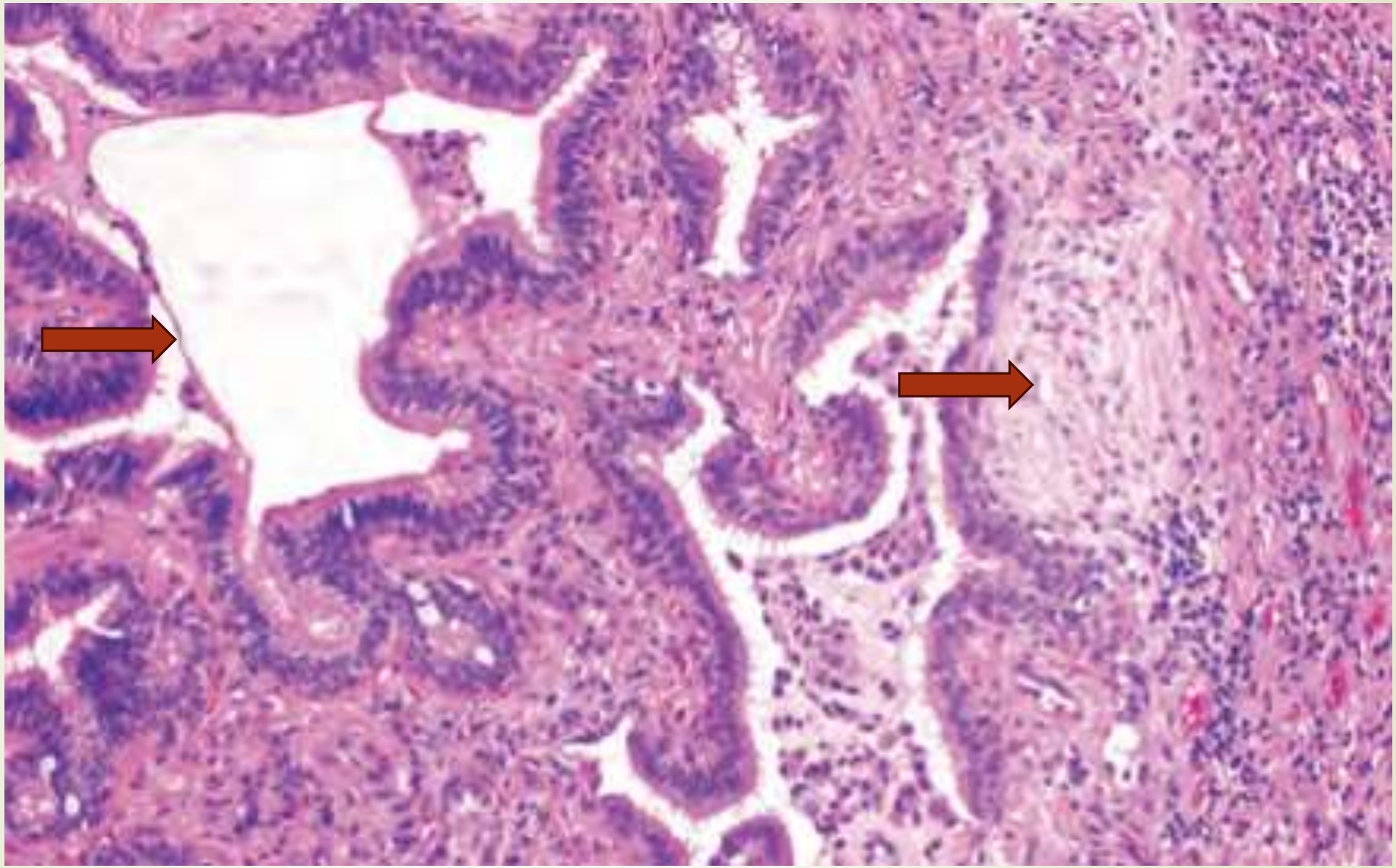
- **Typical finding: Coexistence of early and late lesions (temporal heterogeneity).**

Microscopic:

- Mild-moderate inflammation in fibrotic areas (lymphocytes, few plasma cells, neutrophils, eosinophils, and mast cells)
- Secondary pulmonary arterial hypertensive changes (intimal fibrosis and medial thickening)







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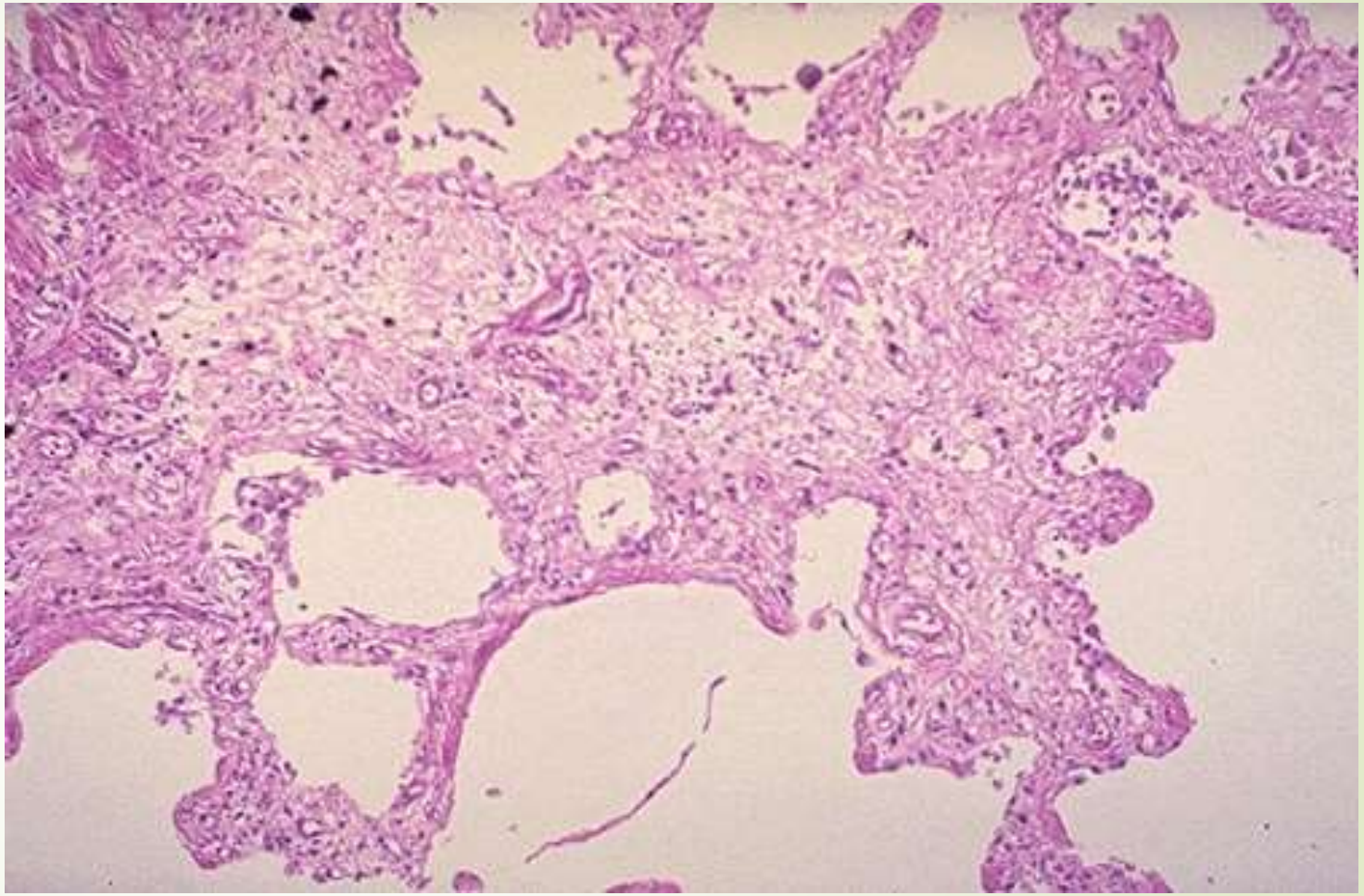

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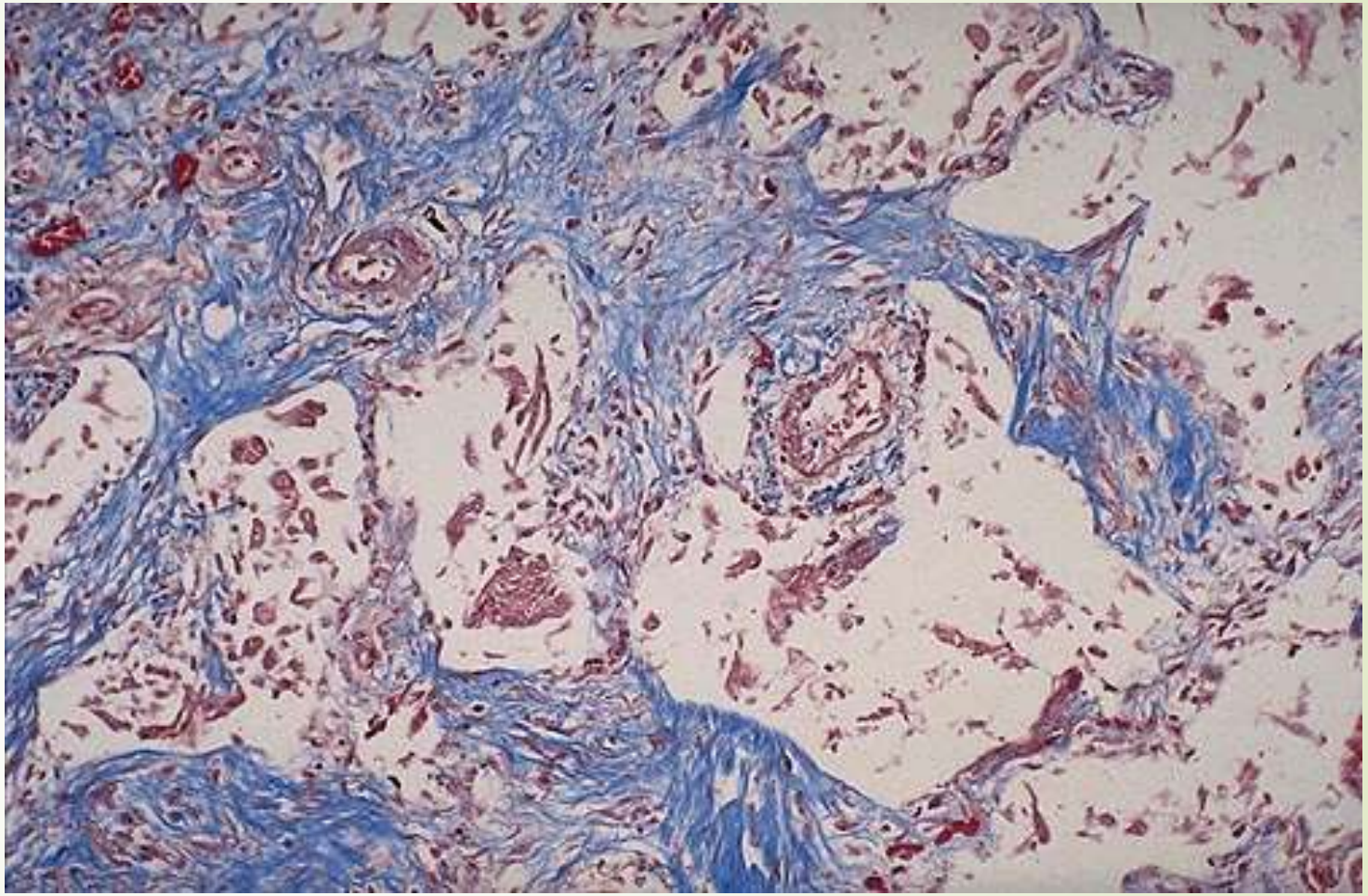
- **Masson trichrome special stain for fibrosis.**



Clinical Features:

- Gradual onset of nonproductive cough and progressive dyspnea.
- Cyanosis, Cor pulmonale, and peripheral edema may develop later.

- P/E: “dry” or “Velcro”-like crackles during inspiration.
- CXR: subpleural and basilar fibrosis and “honeycombing”.

- Clinical and radiologic findings often are diagnostic.

Prognosis:

- Progression despite medical therapy.
- Mean survival is 3 years or less.
- Lung transplantation only definitive therapy

- Anti-inflammatory & immunosuppressive therapy (little benefit)
- Antifibrotic therapy (main Tx)

Fibrosing diseases:

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- Nonspecific interstitial pneumonia
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- Drug reactions
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Nonspecific Interstitial Pneumonia (NSIP)

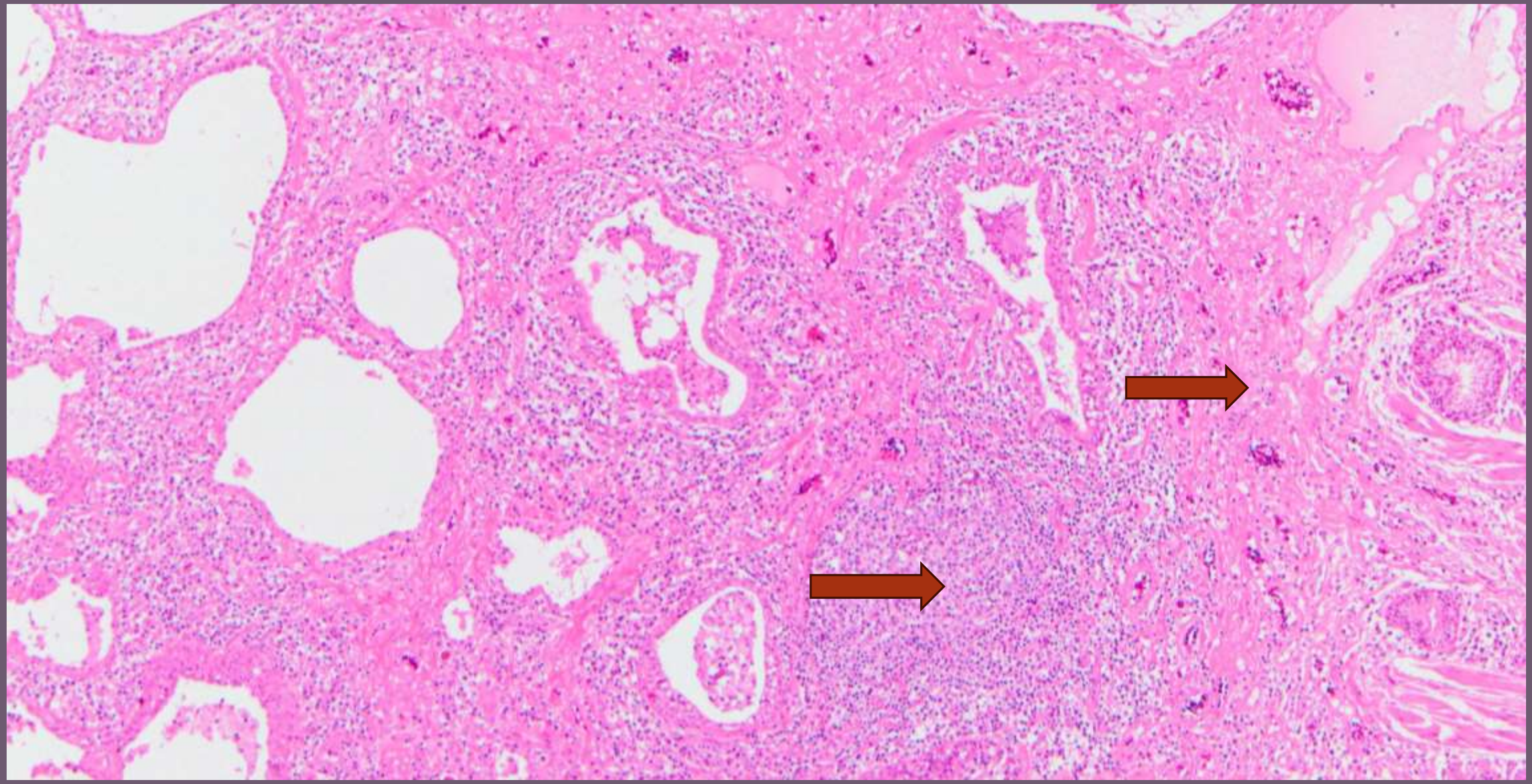
- Chronic bilateral interstitial lung disease
- **Distinct clinical, radiologic, and histologic features.**

- Idiopathic.
- Frequent association with connective tissue diseases (RA)

- Better prognosis than IPF.
- Dyspnea and cough of several months

- **Cellular and fibrosing patterns:**
- **Cellular pattern:** mild-to-moderate chronic interstitial inflammation (lymphocytes and a few plasma cells) in a uniform or patchy distribution.
- **Fibrosing pattern:** diffuse or patchy interstitial fibrosis but uniform in the areas involved

- **Temporal heterogeneity characteristic of UIP is ABSENT**
- **Fibroblastic foci typically ABSENT**



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Cryptogenic Organizing Pneumonia

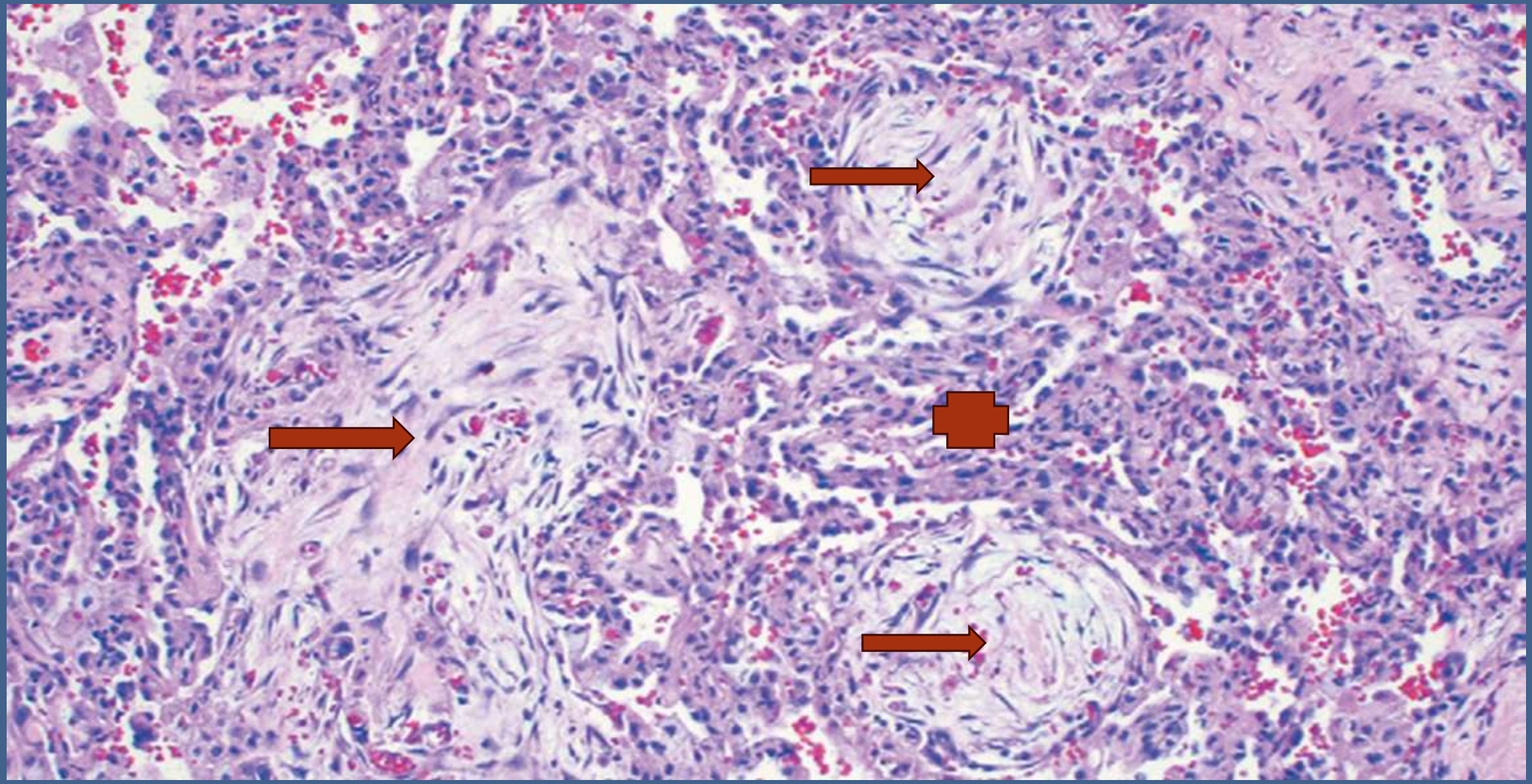
- Uncommon.
- Unknown etiology.
- Cough and dyspnea.
- CXR: subpleural or peri bronchial patchy air space consolidation.

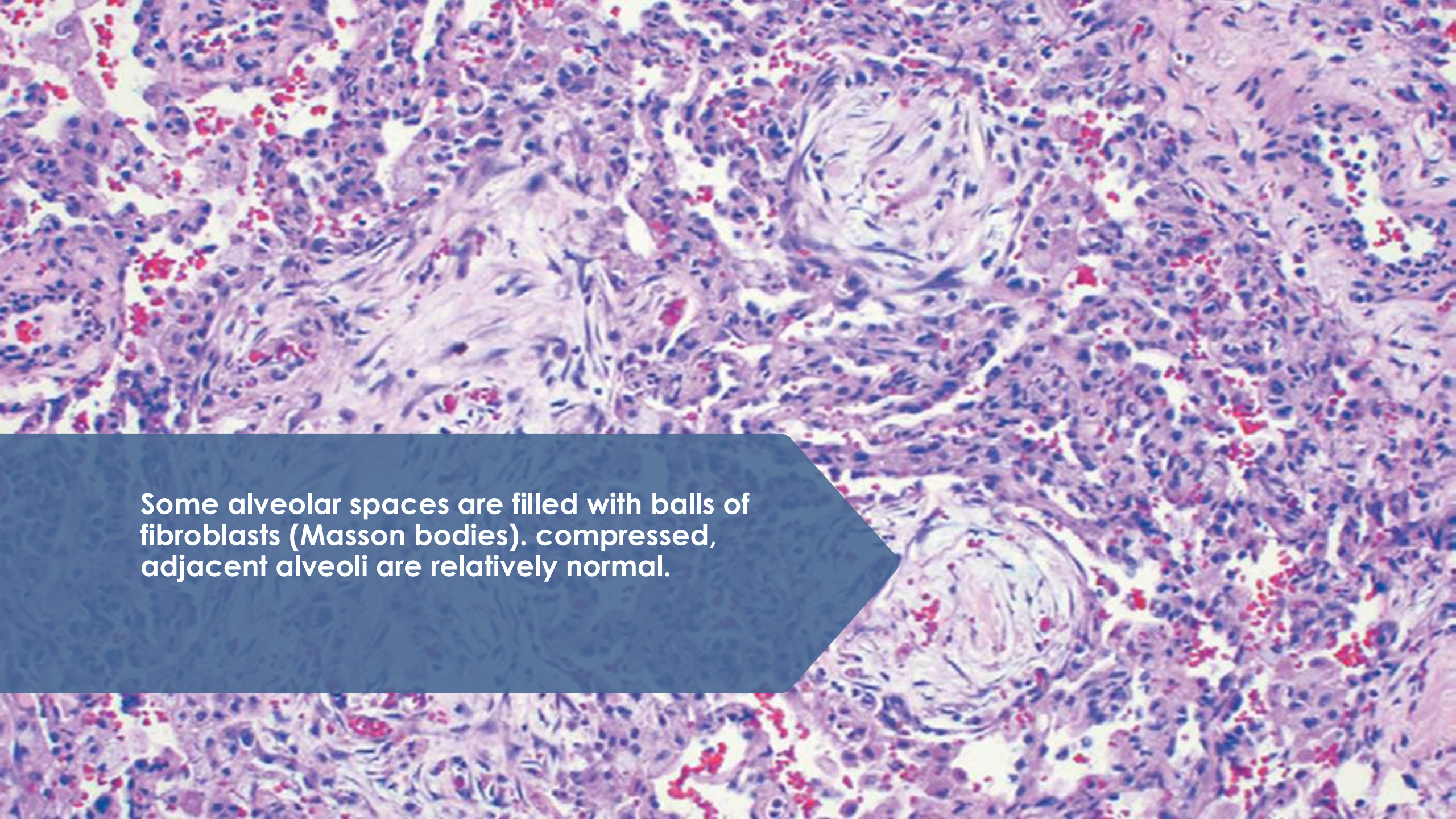
- Some patients recover spontaneously.
- Most patients require Tx with oral steroids.

Morphology: Microscopic

- Polypoid plugs of loose organizing connective tissue within alveolar ducts, alveoli, and bronchioles (Masson bodies).
- Connective tissue is all the same age.

- Underlying lung architecture is normal.
- No interstitial fibrosis or honeycomb lung.




Some alveolar spaces are filled with balls of fibroblasts (Masson bodies). compressed, adjacent alveoli are relatively normal.

- Similar changes are seen in infections (e.g., pneumonia) or inflammatory injury (e.g., collagen vascular disease, transplantation injury) , in this case not “cryptogenic”

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Pneumoconiosis

- Lung reaction to inhalation of mineral dusts, organic and inorganic particulates, chemical fume and vapor.
- Coal dust, silica, and asbestos are most common mineral dust.
- Nearly always result from occupational exposure.
- However, in asbestos the increased risk of cancer extends to family members of asbestos workers.

Table 12–4 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:
Reaction of lung to mineral dust depends on:

- **Amount** of dust retained in the airways & lung.

- **Size and Shape**
- Particles that are 1 to 5 μm in diameter are the most dangerous

- **Solubility of particles**
- Soluble particles produce acute lung injury

- **Proinflammatory properties**
- Coal dust is inert, silica and asbestos provoke greater immune response

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

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