CHRONIC INTERSTITIAL (RESTRICTIVE, INFILTRATIVE) LUNG DISEASES, PART 2

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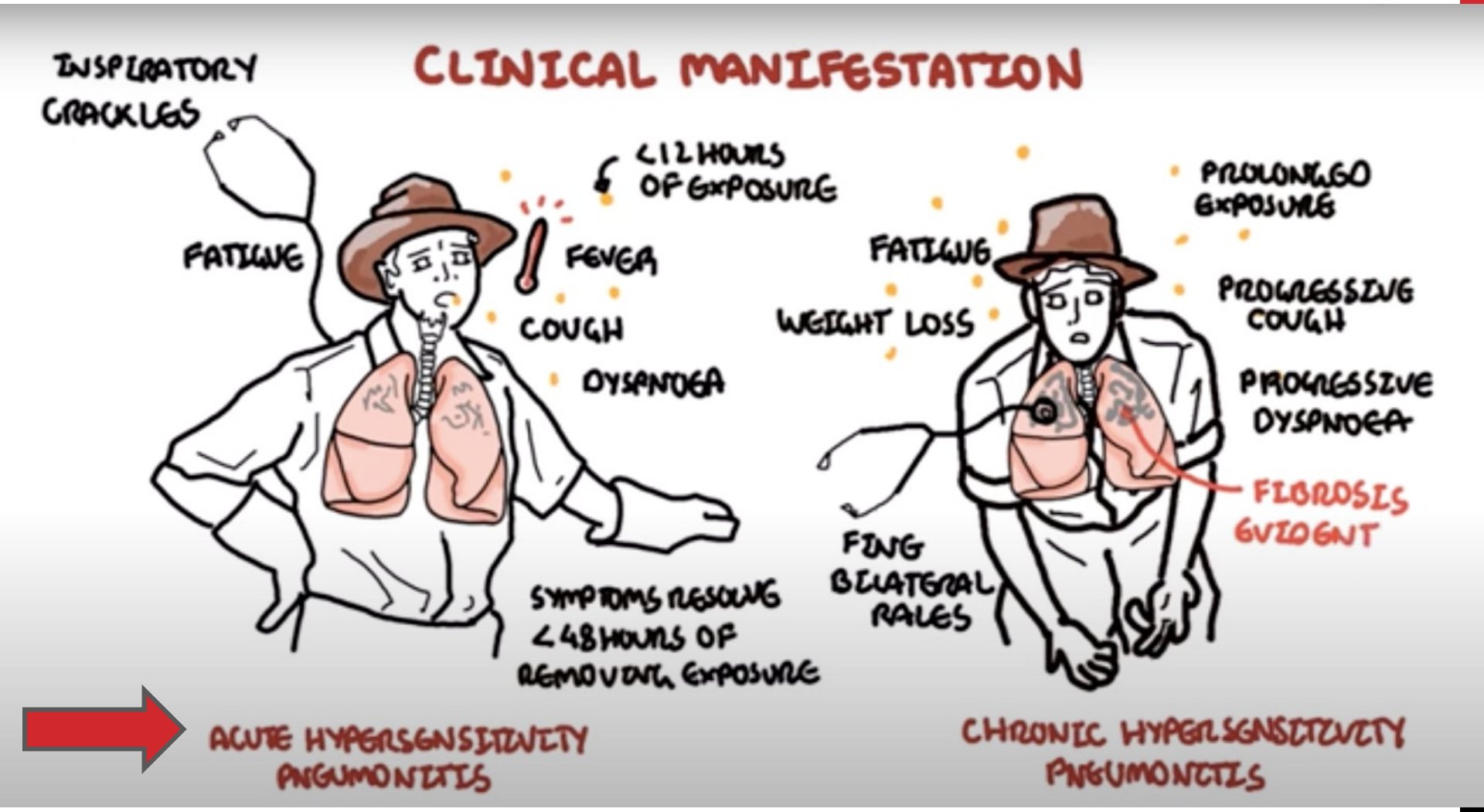
CLINICAL FEATURES

- **Acute reaction**: fever, cough, dyspnea, and constitutional signs and symptoms arising **4 to 8** hrs after exposure (influenza like)

- If antigenic exposure is terminated after acute attacks of the disease, **complete resolution** of pulmonary symptoms occurs within days.

- With the acute form, the **diagnosis** is obvious because of the **temporal relationship** of symptom onset and exposure to the antigen.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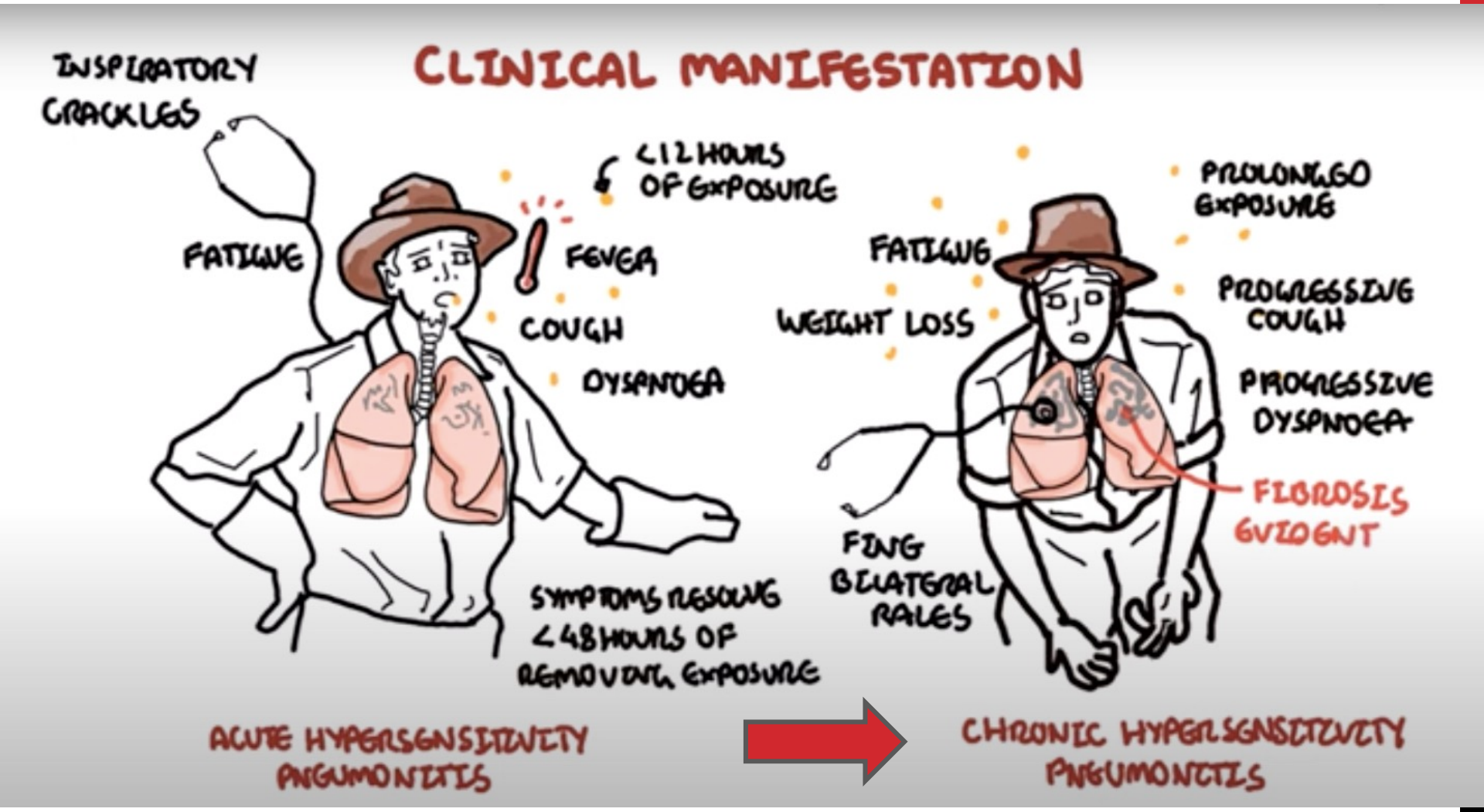
INSPIRATORY CRACKLES
FATIGUE
<12 HOURS OF EXPOSURE
FEVER
COUGH
DYSPNOEA
SYMPTOMS RESOLVE <48 HOURS OF REMOVAL EXPOSURE
ACUTE HYPERSENSITIVITY PNEUMONITIS
FATIGUE
WEIGHT LOSS
PROLONGED EXPOSURE
PROGRESSIVE COUGH
PROGRESSIVE DYSPNOEA
FIBROSIS EVIDENT
FINE BILATERAL RALES
CHRONIC HYPERSENSITIVITY PNEUMONITIS

- Failure to remove the agent from the environment results in **Irreversible chronic interstitial pulmonary disease**.

- Chronic disease characterized by insidious onset of **progressive cough, dyspnea, malaise, fatigue and weight loss.**

- **Restrictive pattern on PFT**

- **Dx:**
  - **clinical, radiological** (high resolution CT: ground glass opacity) and **pathological examination**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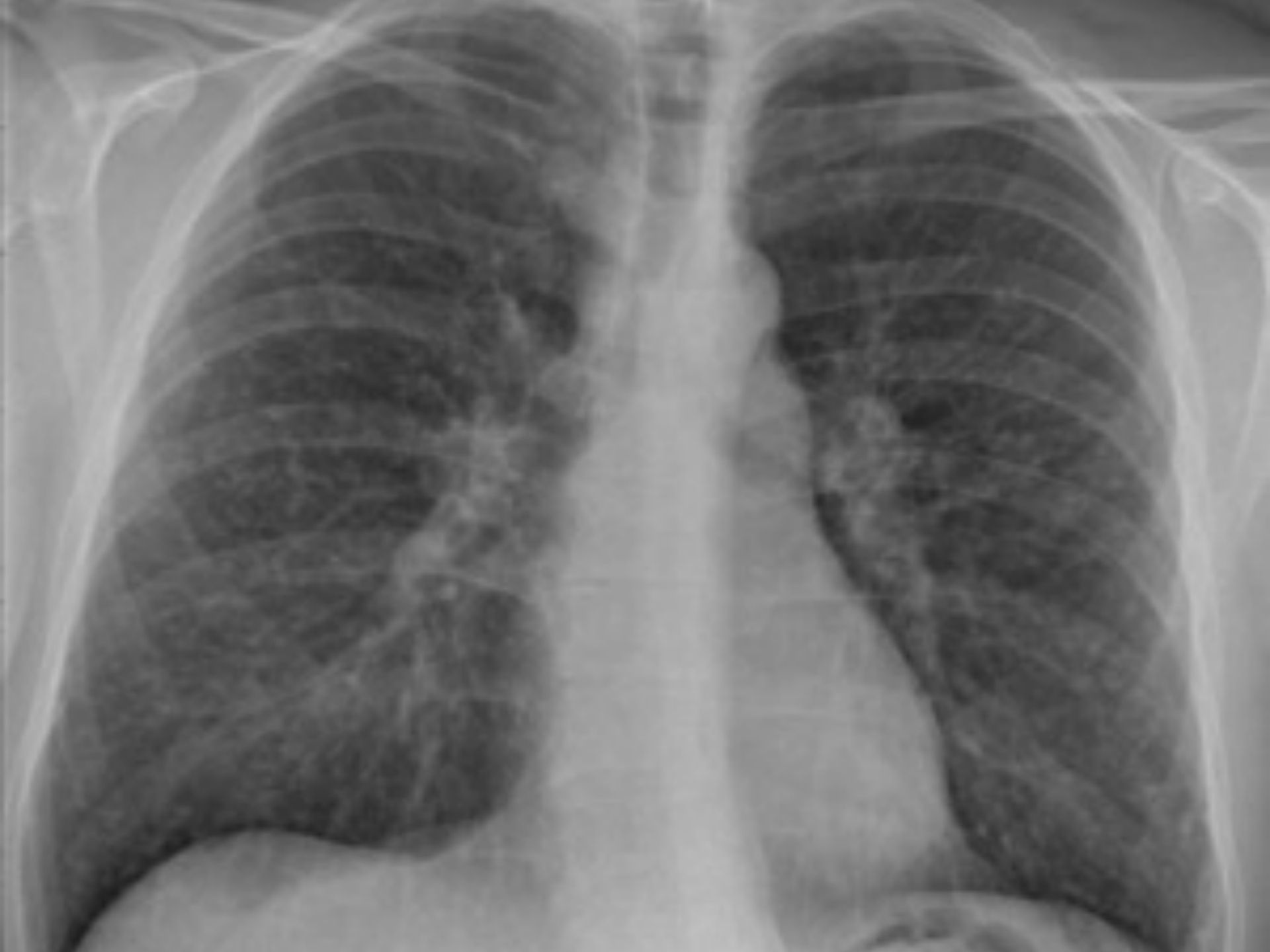
A 61-year-old lady noted increasing dyspnea and a nonproductive cough for 5 months. On examination, her temperature is 37.7° C. A CXR shows prominent hilar lymphadenopathy with reticulonodular infiltrates bilaterally. A transbronchial biopsy showed interstitial fibrosis and small, discrete noncaseating granulomas. One granuloma contains an asteroid body in a giant cell. The medical history indicates that she smoked cigarettes for 10 years, but stopped 5 years ago. Which of the following is the most likely cause of her illness?

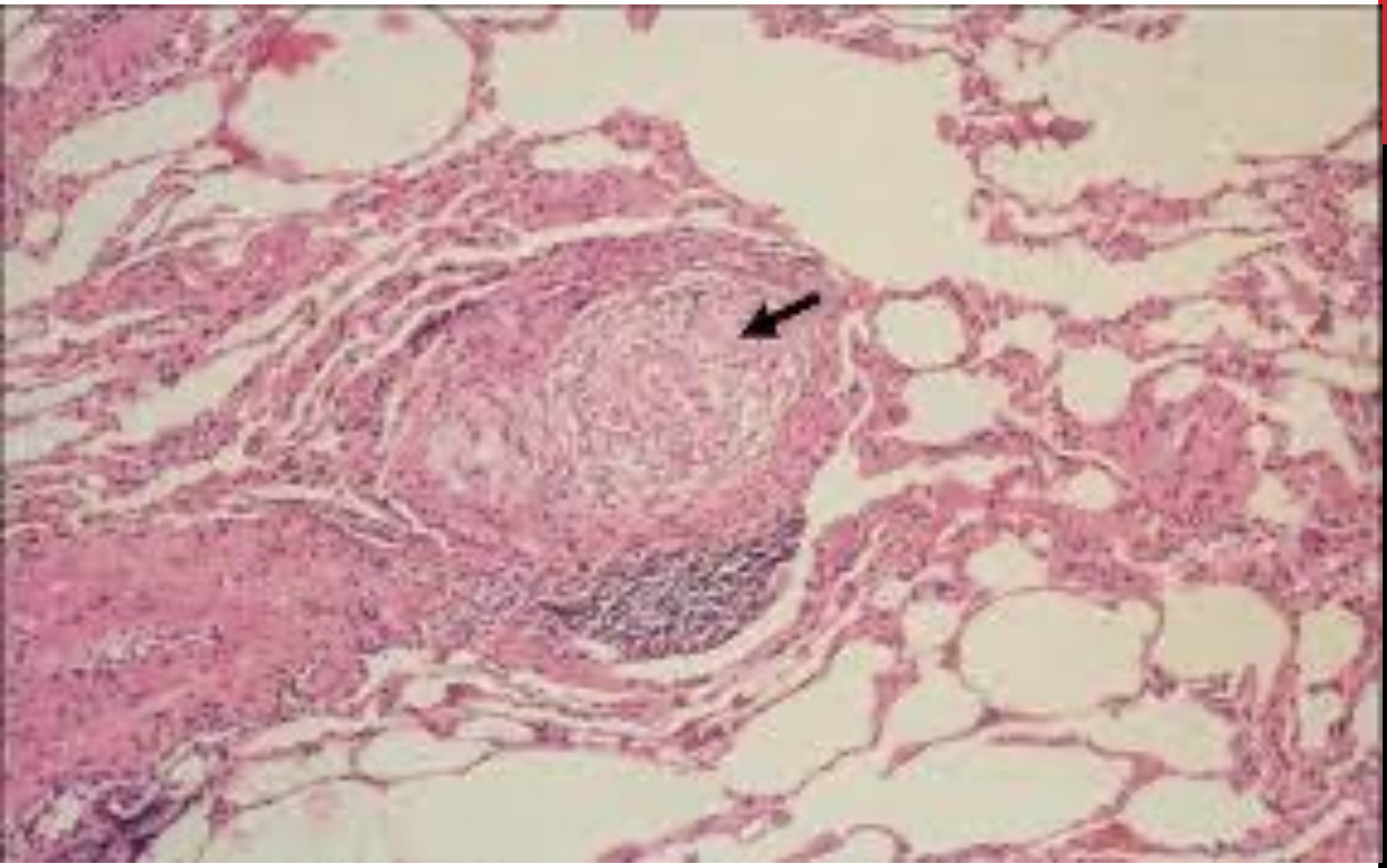
A T cell-mediated response to unknown antigen

B Deposition of immune complexes

C Infection with atypical mycobacteria

D Smoke inhalation with loss of bronchioles





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	sarcoidosis	Hypersensitivity pneumonitis
Workplace related	no	yes
Noncaseating granuloma	Well defined	Poorly defined
Bilateral hilar lymphadenopathy	yes	no
Hypercalcimia and hypercalciuria	yes	no
BAL:	T helper are dominant	Both increased but T cytotoxic are more
Other organs involvement: eye, skin, bone..etc	yes	no

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

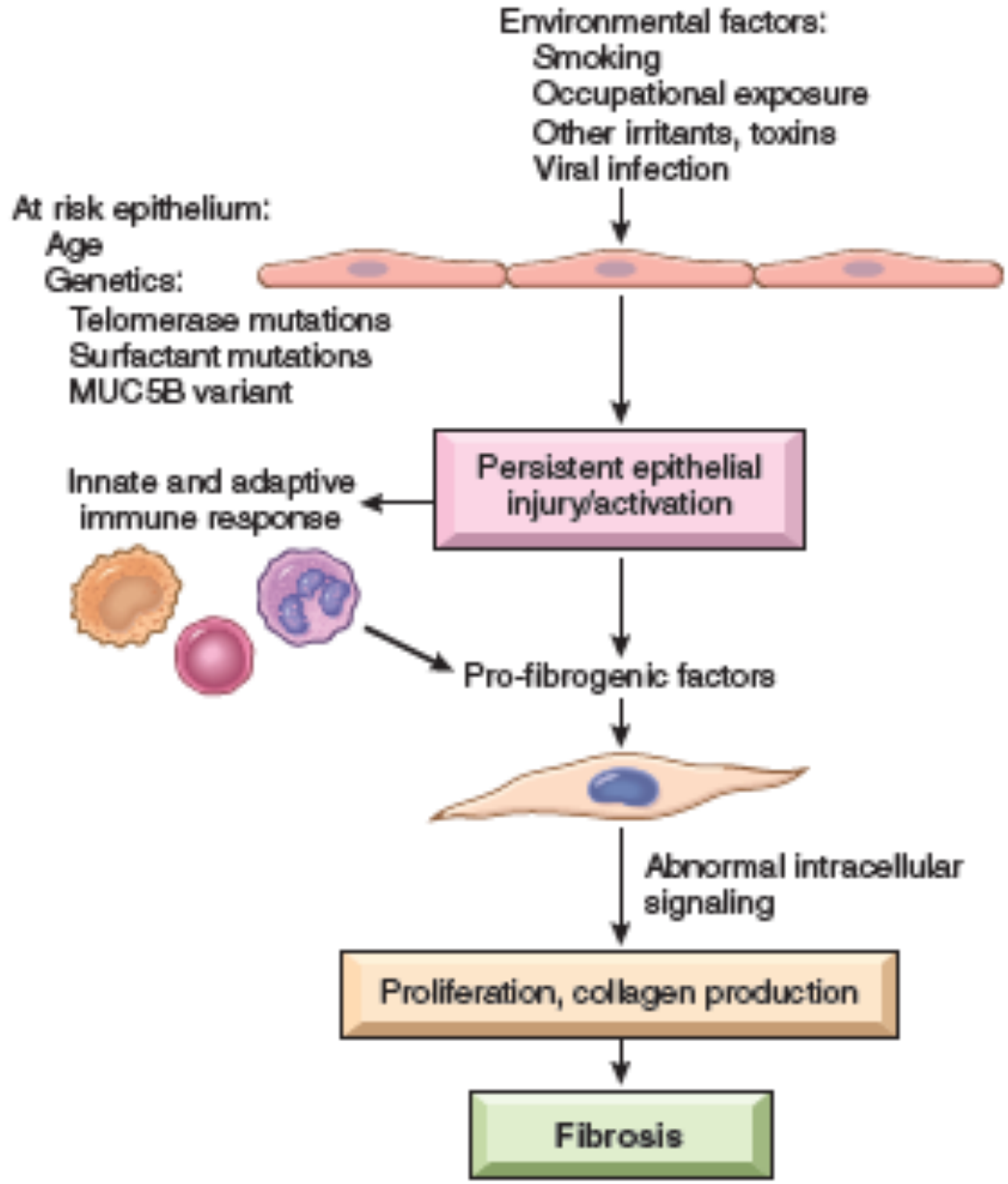

Fig. 13.13 Proposed pathogenic mechanisms in idiopathic pulmonary fibrosis. See text for details.

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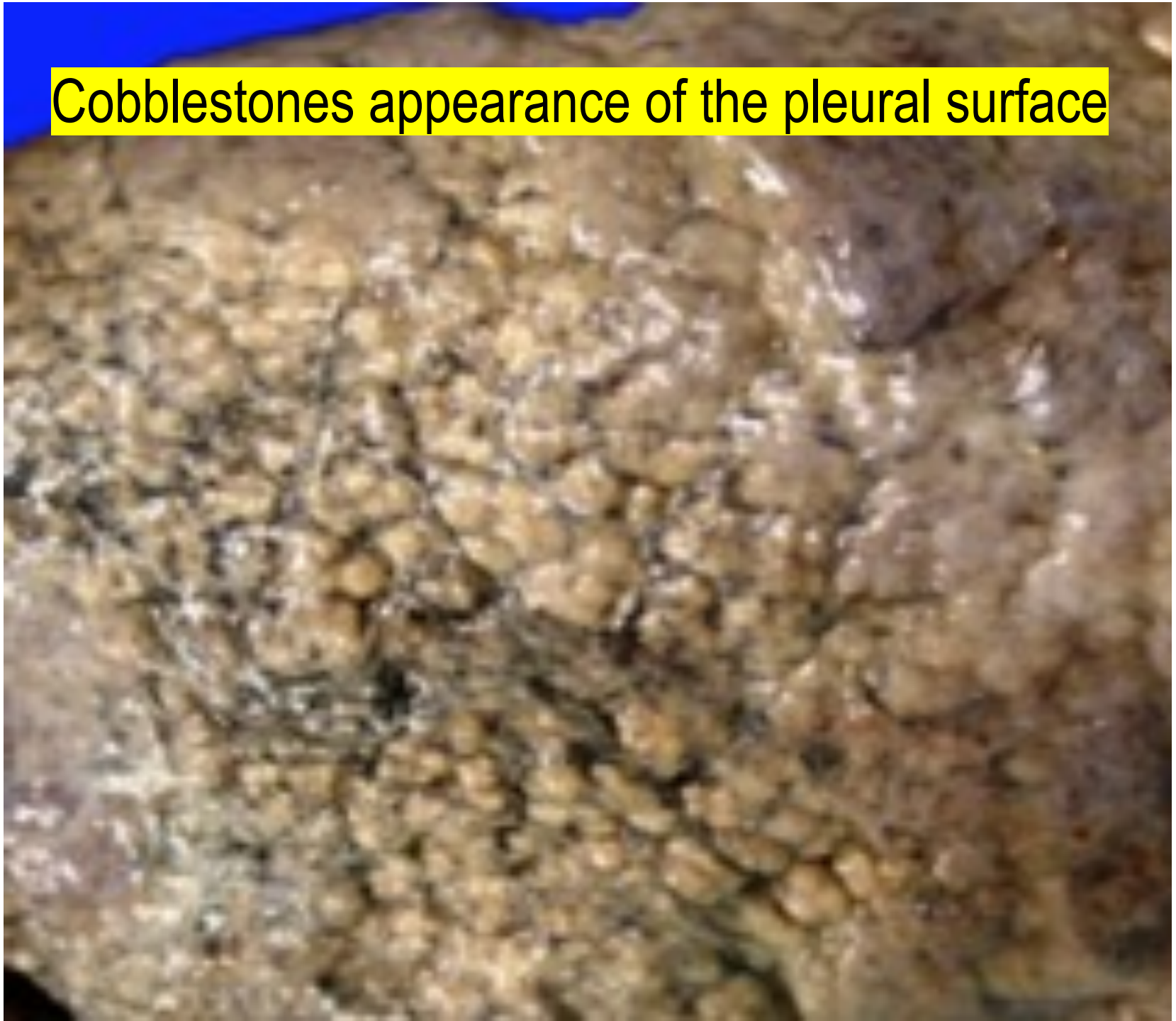
MORPHOLOGY, MACROSCOPIC:

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


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:

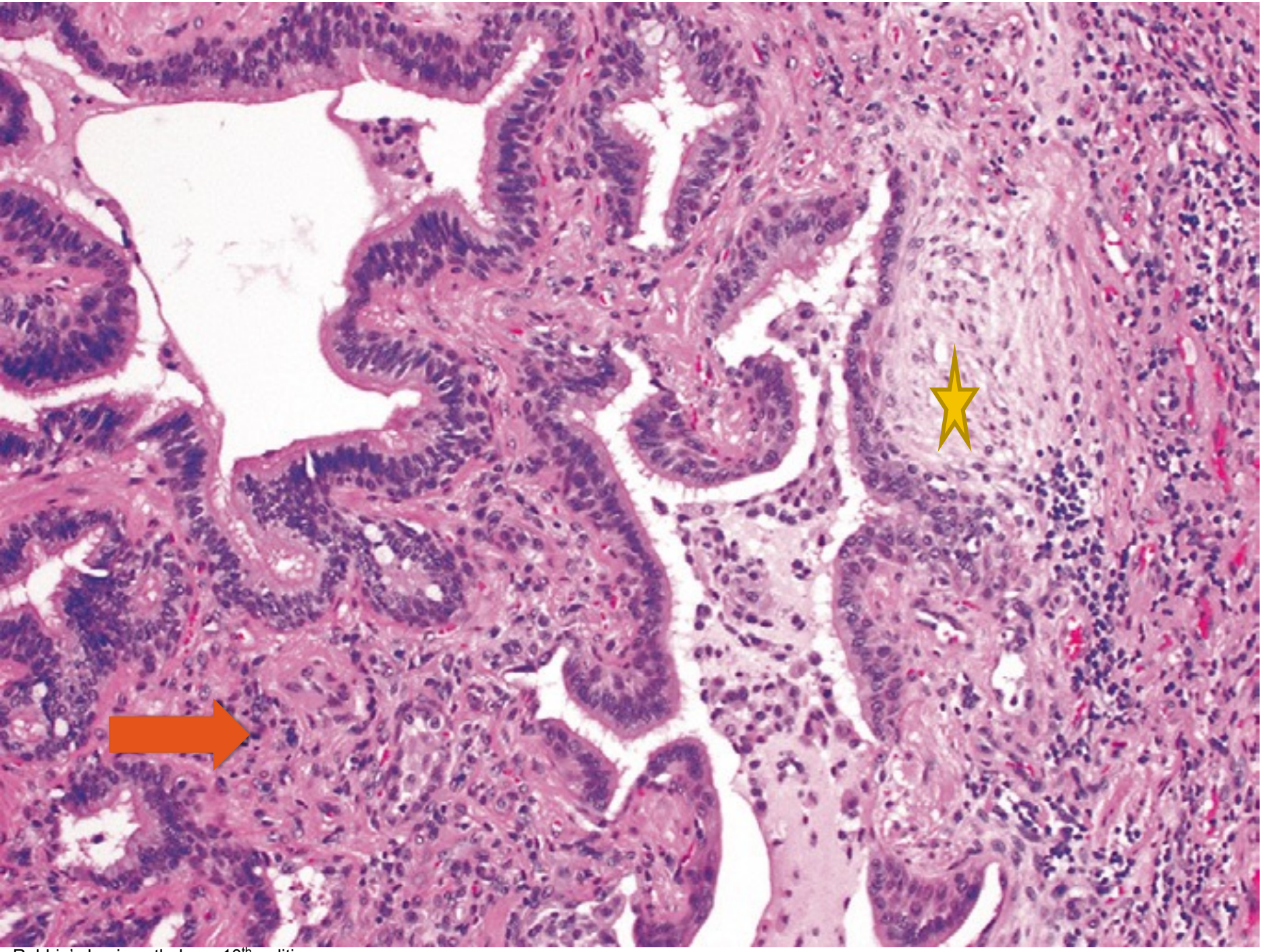
- Hallmark is **patchy** interstitial fibrosis, **which varies in intensity and worsens with time**.

- **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

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).

CRYPTOGENIC ORGANIZING PNEUMONIA

- Uncommon
- Unknown etiology (BUT seen as a response 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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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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https://www.pennlive.com/news/2019/03/cold-case-findings-generating-news-throughout-pa.html

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.

THANK YOU!