CHRONIC INTERSTITIAL (RESTRICTIVE, INFILTRATIVE) LUNG DISEASES, PART 3

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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 pneumoconioses

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 (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

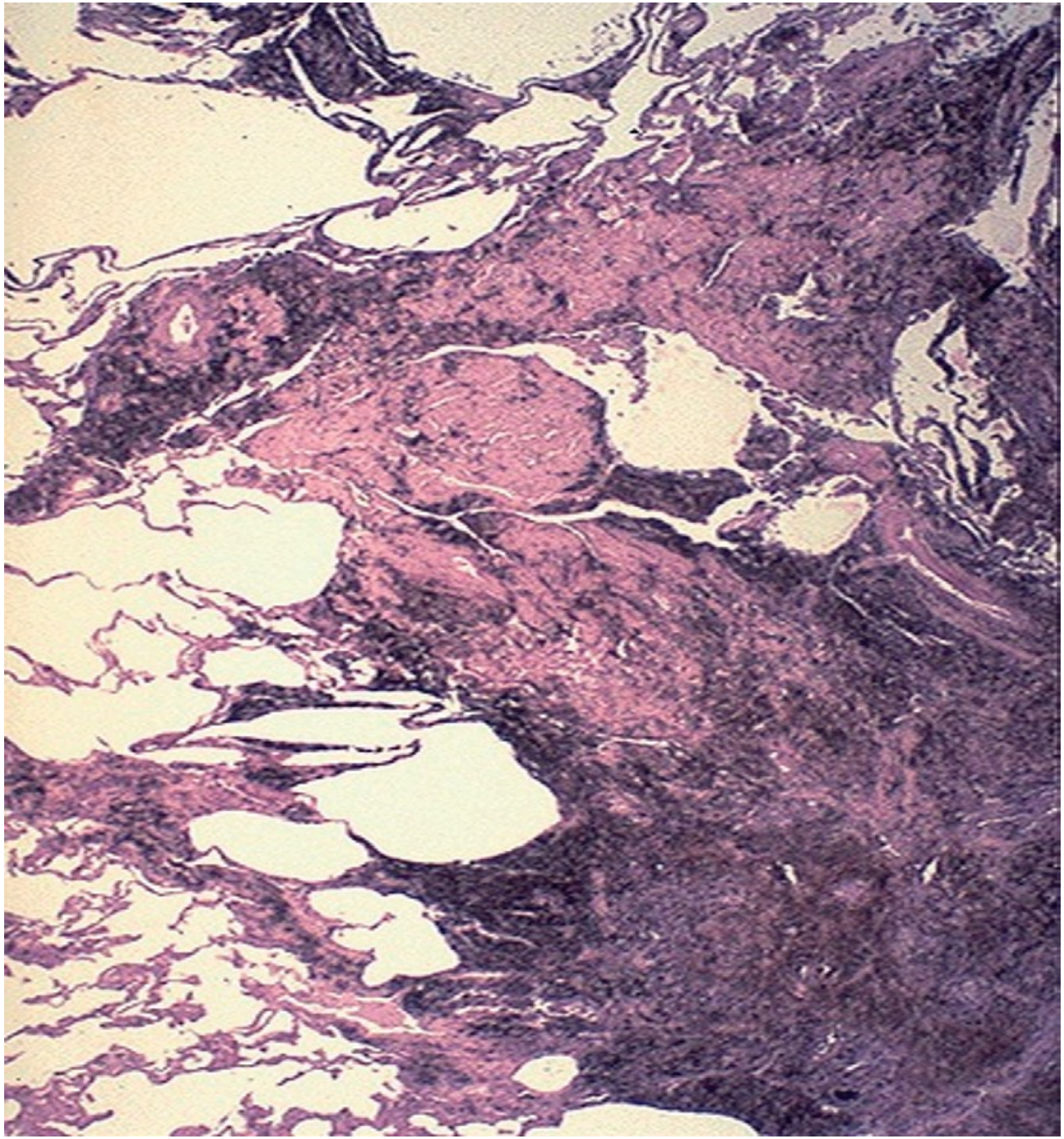
- **centrilobular emphysema** can occur.

- **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 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.**

PNEUMOCONIOSES

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- **Silicosis**
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SLICA:

- naturally occurring mineral.
- accounts for 59% of the earth's crust.
- two types : crystalline silica (toxic) and amorphous.
- Several processes release silica into the air such as:

  crushing ,grinding , and blasting.

SILICOSIS

- **The most prevalent chronic occupational disease in the world**
- Inhalation of crystalline silica mostly in **occupational** settings
- **quartz is most implicated in silicosis**

- Amorphus silica is less pathogenic

- **Workers in sandblasting and hard-rock mining are at high risk.**

PATHOGENESIS

- After **inhalation**, the particles **interact with epithelial cells and macrophages.**

- Activating the **inflammasome** and the release of **inflammatory mediators** by pulmonary macrophages

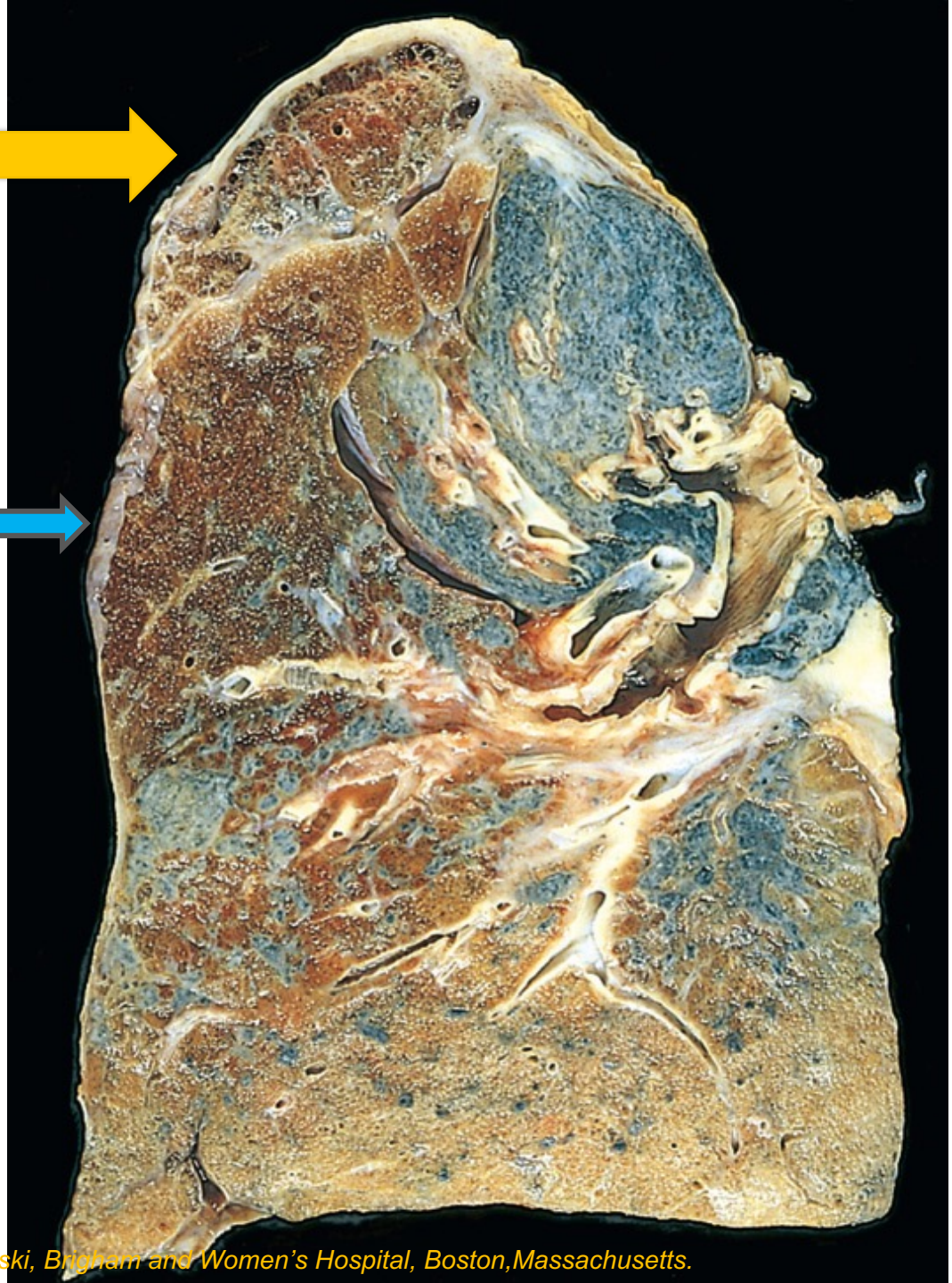
    - IL-1, TNF, fibronectin, lipid mediators, oxygen-derived free radicals, and fibrogenic cytokines.

- **When mixed with other minerals**, **the fibrogenic effect of quartz is reduced**.

- This fortuitous situation is commonplace, as **quartz** in the workplace is **rarely pure**.

MORPHOLOGY, SILICOTIC NODULES:

- **Macroscopically**:
  - early stages are tiny, barely palpable, discrete, pale-to-black (if coal dust is present) nodules
  - **Upper zones** of the lungs



Courtesy of Dr. John Godleski, Brigham and Women's Hospital, Boston,Massachusetts.

- **Microscopically:**
- **Silicotic nodules:**
    - **Concentrically arranged hyalinized collagen fibers surrounding amorphous center.**
    - With **“whorled”** collagen fibers

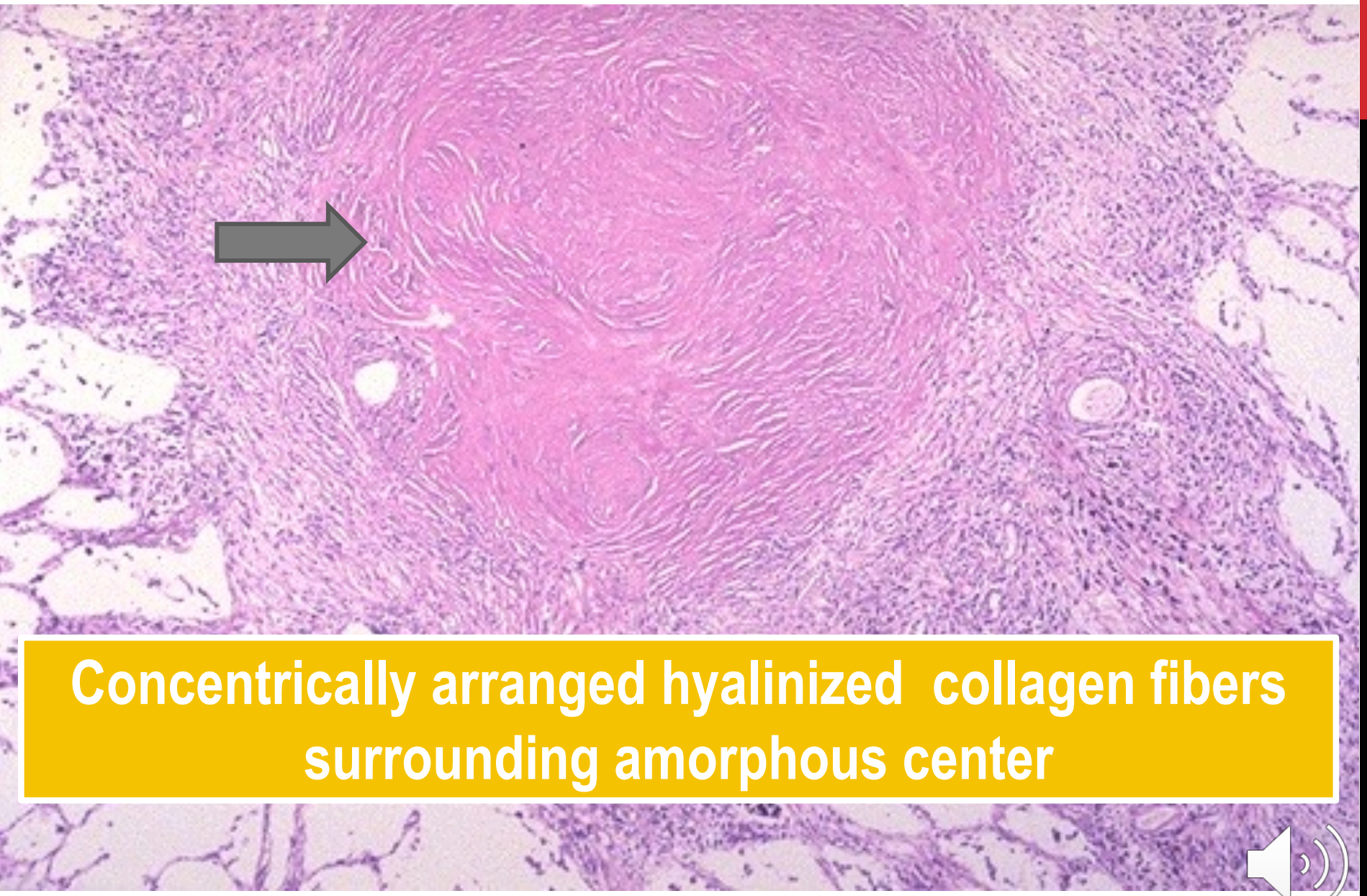
- **Polarized** microscopy reveals weakly birefringent silica

- Nodules may coalesce into **hard, collagenous scars**, with eventual **progression to PMF**

- **Fibrotic lesions** also may occur in **hilar lymph nodes and pleura.**

- The greater degree of exposure to silica and an increasing length of exposure → amount of silicotic nodule formation and the degree of restrictive lung disease.

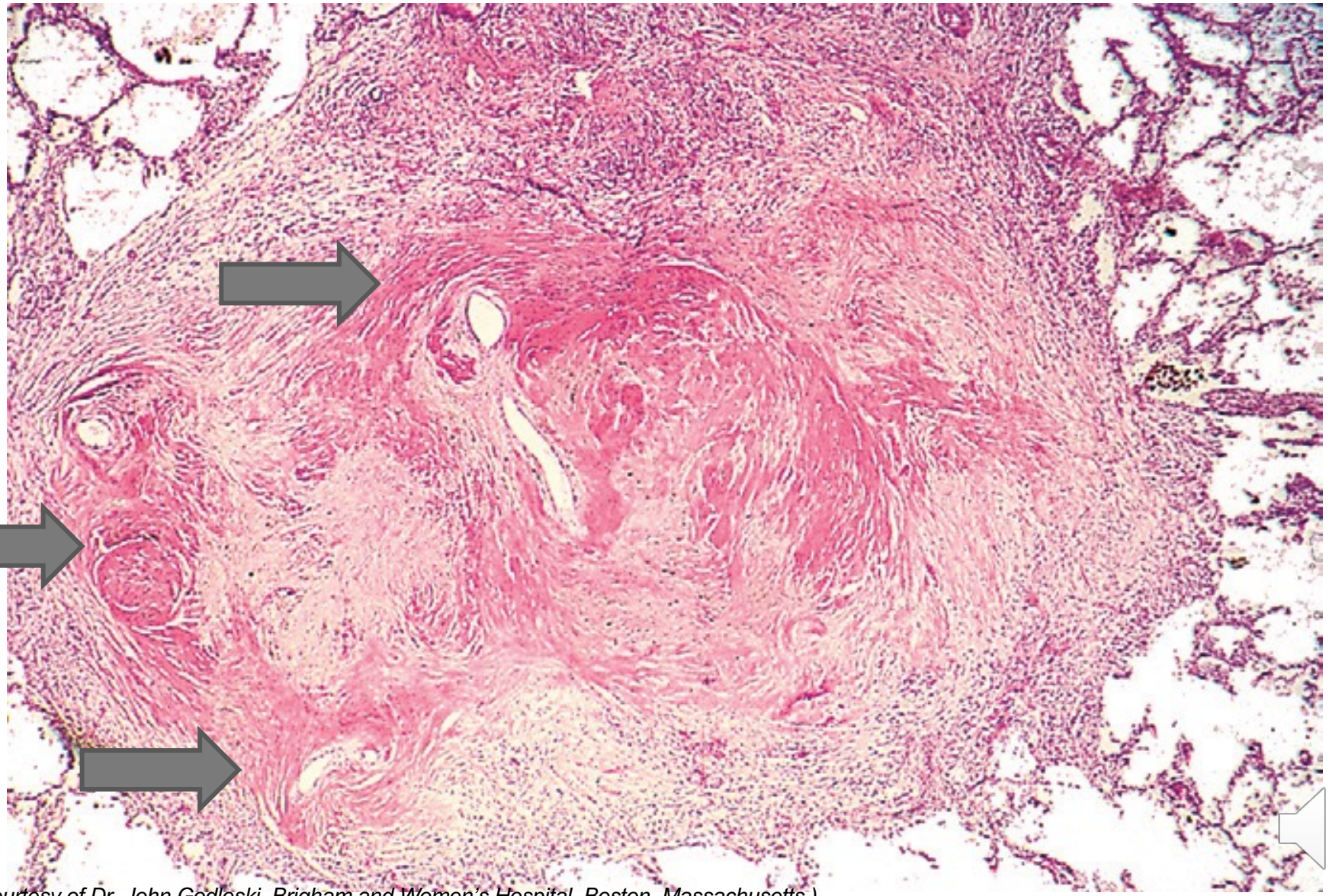
SILICOTIC NODULE



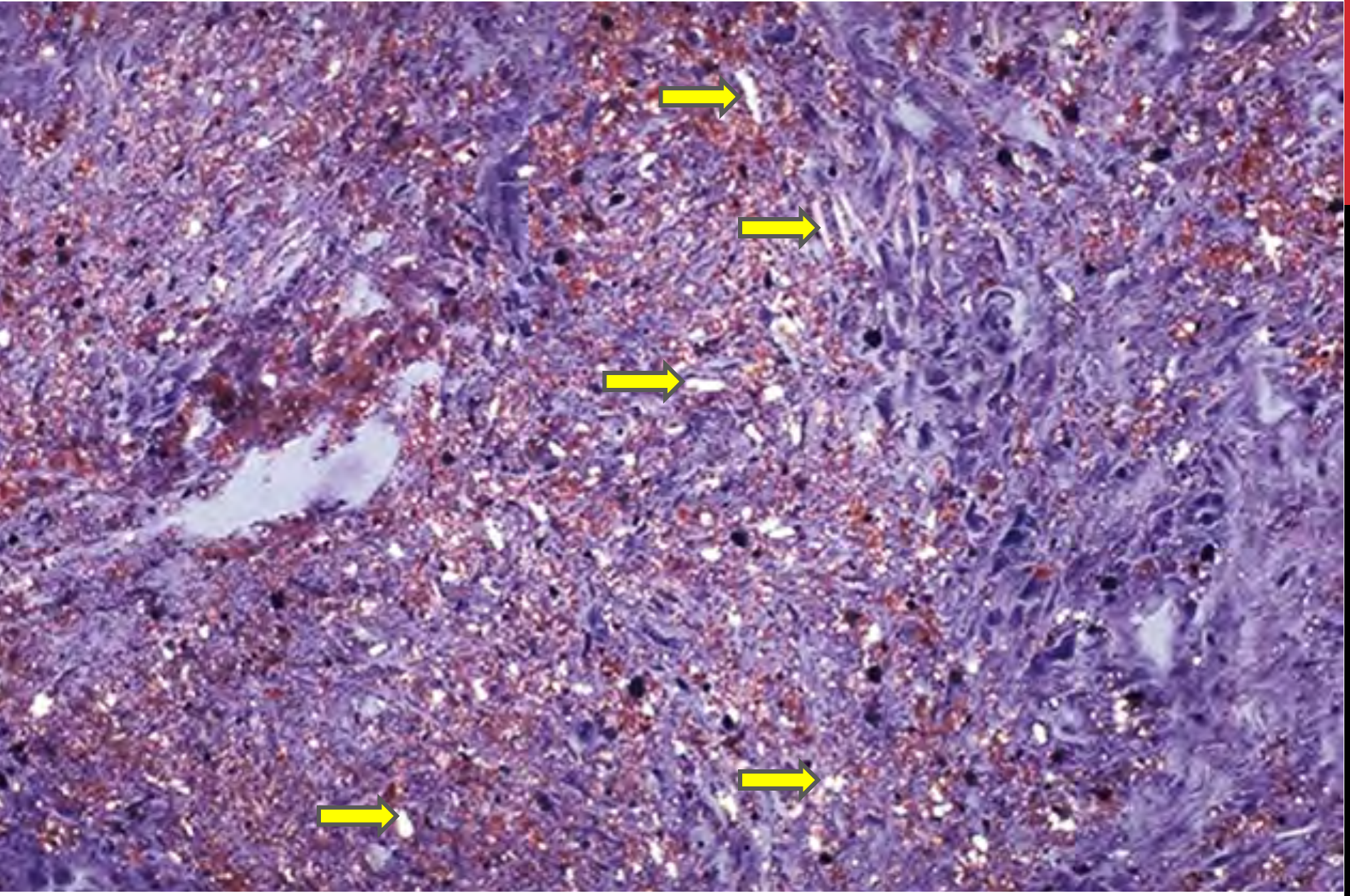
Concentrically arranged hyalinized collagen fibers surrounding amorphous center

Webpath.med.utah.edu

SEVERAL COALESCENT COLLAGENOUS SILICOTIC NODULES



Courtesy of Dr. John Godleski, Brigham and Women's Hospital, Boston, Massachusetts.)



Silica cystals

CLINICAL FEATURES:

- **Asymptomatic**: detected as fine nodularity in the upper zones of the lung on routine chest radiographs

- **Most patients do not develop shortness of breath until late in the course.**
- after **PMF**: Shortness of breath, pulmonary hypertension and cor pulmonale

- The disease may continue to worsen even if the patient is no longer exposed.

- Silicosis is slow to kill, but impaired pulmonary function may severely limit activity
- **The onset of silicosis can be:**
  - slow and insidious (10 to 30 years after exposure; most common),
  - accelerated (within 10 years of exposure)
  - rapid (in weeks or months after intense exposure to fine dust high in silica; rare).

- **Silicosis → increased susceptibility to tuberculosis.**
  - crystalline silica inhibits the ability of pulmonary macrophages to kill phagocytosed mycobacteria.

- **silica and lung cancer:**
  - Patients with silicosis have **double the risk** for developing lung cancer.

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- **Asbestosis and Asbestos-Related Diseases**

ASBESTOSIS AND ASBESTOS-RELATED DISEASES

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

ASBESTOS

- **Family of crystalline hydrated silicates with a fibrous geometry.**

ASSOCIATED WITH:

(1) parenchymal interstitial fibrosis (asbestosis);

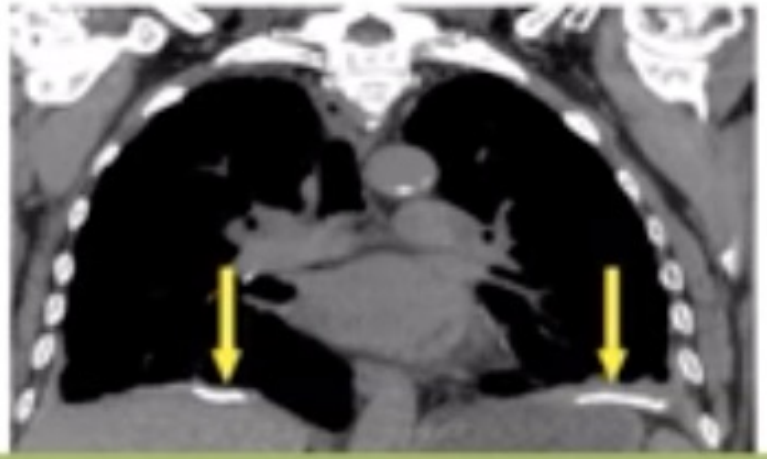
(2) localized fibrous plaques or, rarely, diffuse pleural fibrosis.

(3) pleural effusions

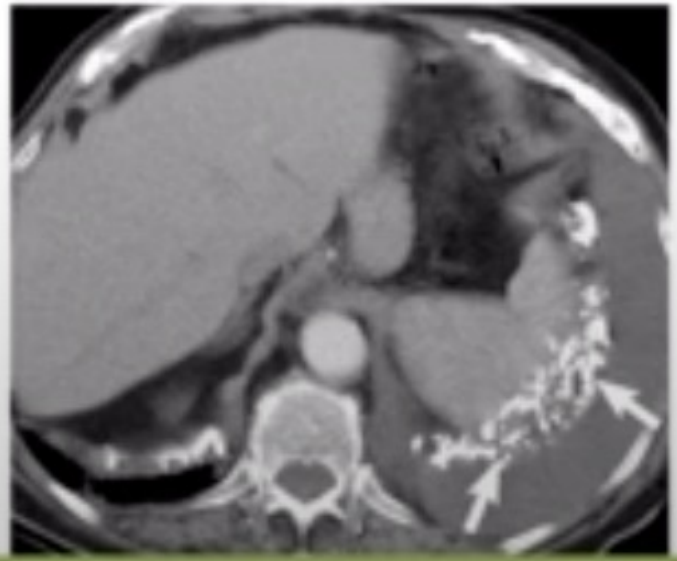
(4) Lung carcinomas

(5) malignant pleural and peritoneal mesotheliomas

(6) laryngeal carcinoma



Pleural Plaques suggest asbestos exposure and do not cause symptoms



Malignant Pleural Mesothelioma: Rare cancer of the lung lining

ASBESTOSIS:
IS SCARRING OF THE LUNG CAUSED BY ASBESTOS EXPOSURE

PATHOGENESIS:

- once phagocytosed by macrophages→ asbestos fibers activate the inflammasome and damage phagolysosomal membranes → release of proinflammatory factors and fibrogenic mediators→

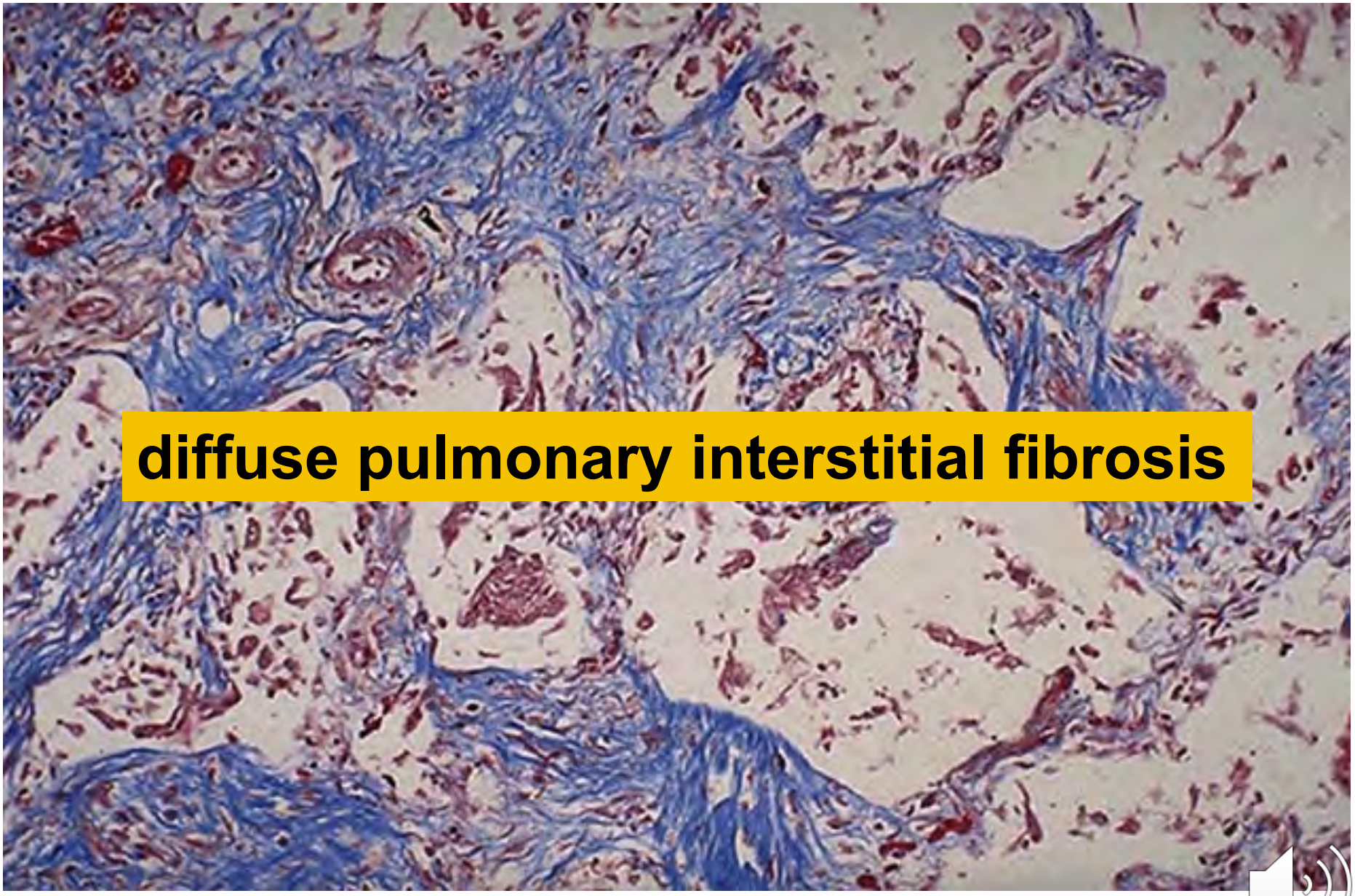
1. cellular and fibrotic lung reactions
2. tumor initiator and a promoter
    - mediated by the oncogenic effects of reactive free radicals generated by asbestos fibers in the distal lung near the mesothelial lining

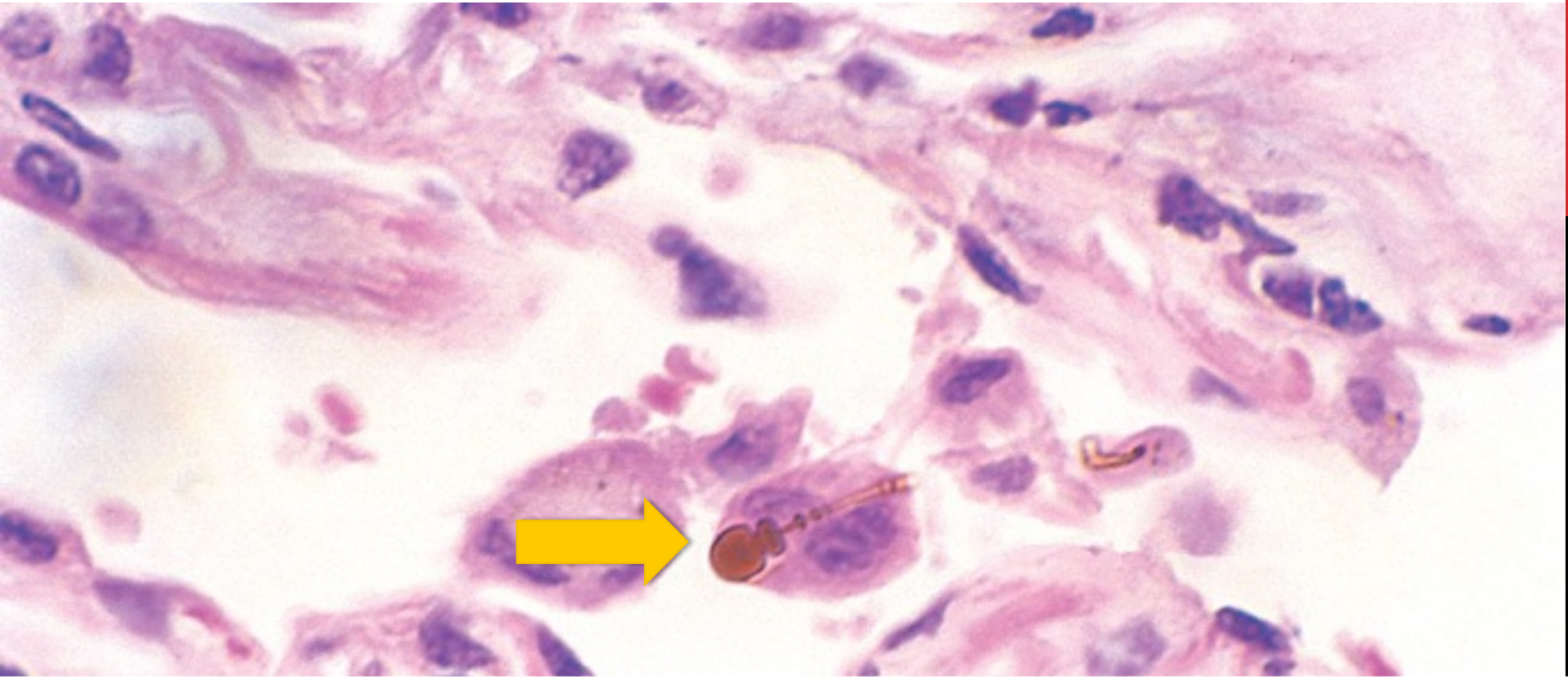
- **Asbestos and tobacco:**
  - The adsorption of carcinogens in tobacco smoke onto asbestos fibers results in remarkable **synergy** between tobacco smoking and the development of lung carcinoma in asbestos workers→ Smoking enhances the effect of asbestos by interfering with the mucociliary clearance of fibers.
- asbestos workers →**fivefold increase** of lung carcinoma with asbestos exposure alone
- Asbestos exposure and smoking toge

→a **55-fold increase** in the risk.

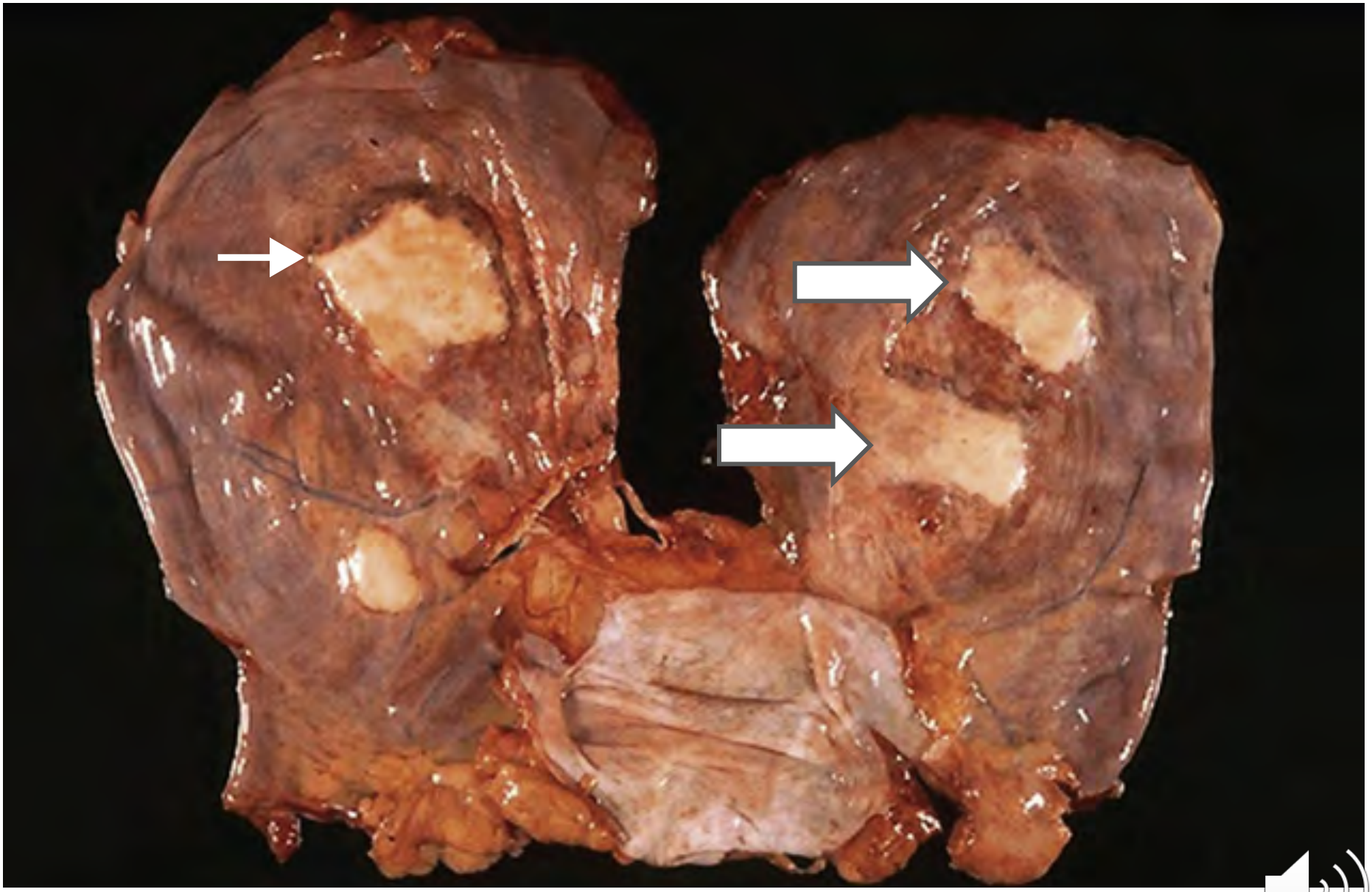
https://health.clevelandclinic.org/even-smoking-just-one-or-two-cigarettes-a-day-increases-your-risk-of-lung-disease/

MORPHOLOGY

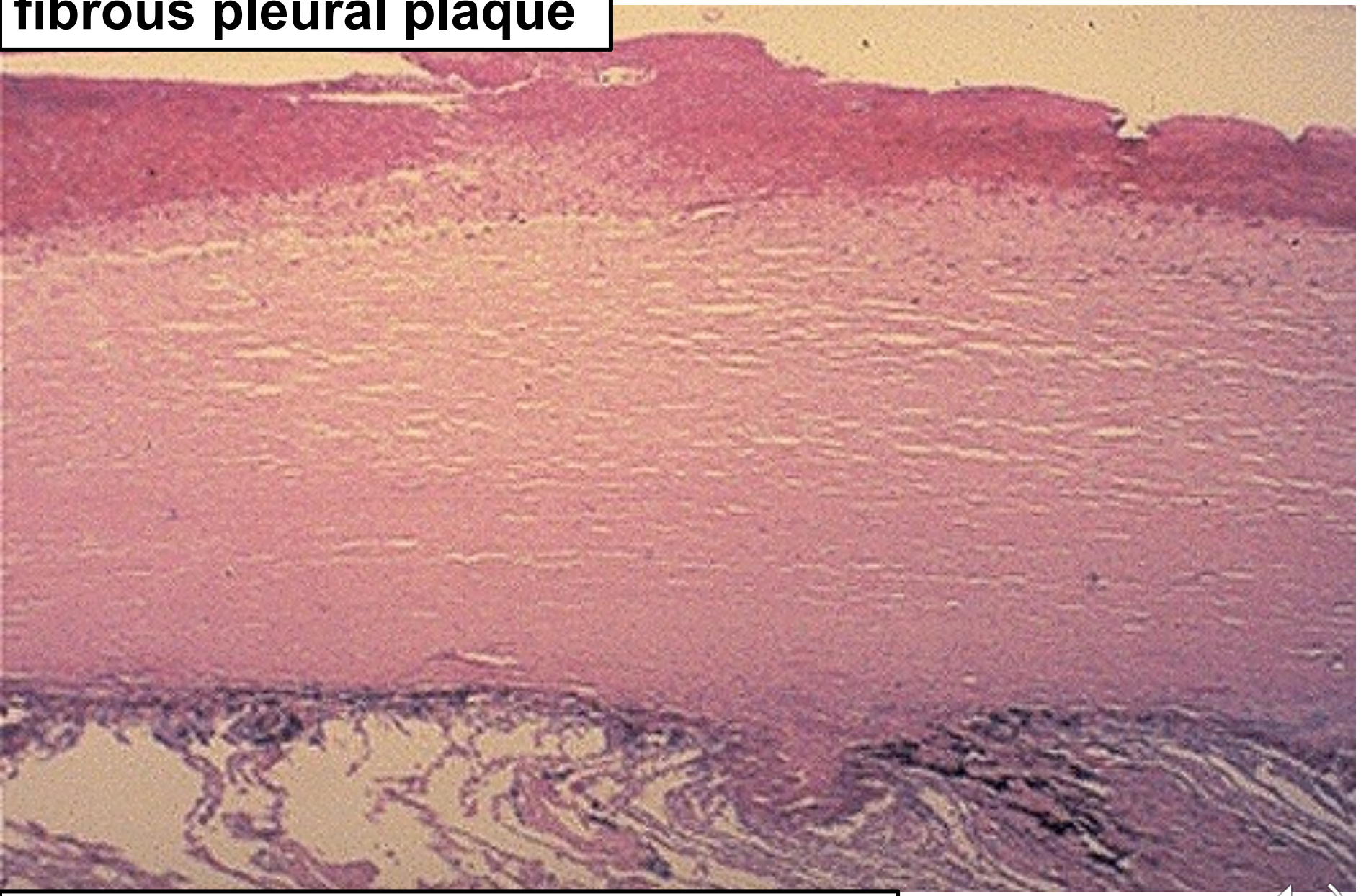

diffuse pulmonary interstitial fibrosis



Asbestos body with beading and knobbed ends

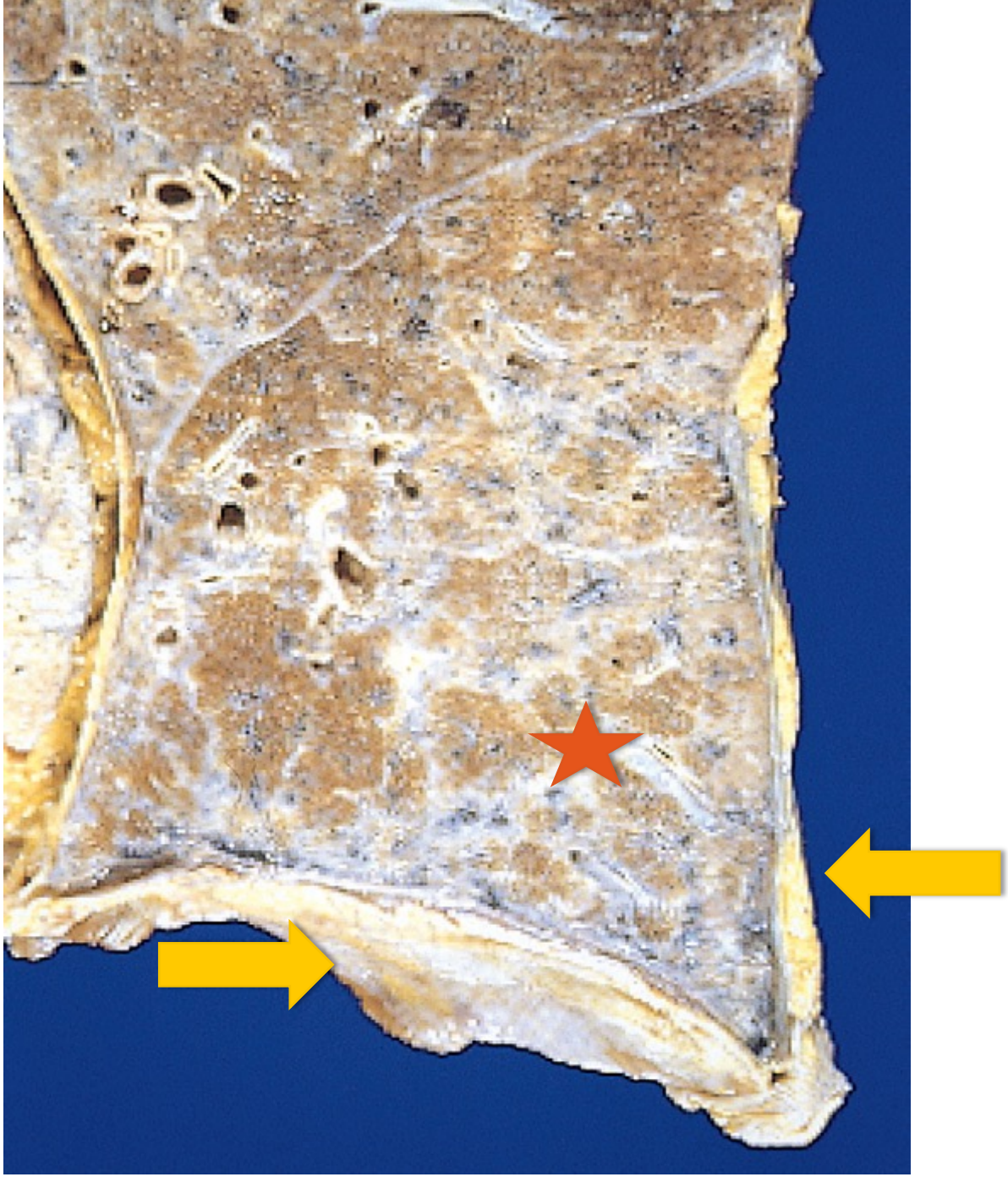


fibrous pleural plaque



dense laminated layers of collagen (pink)

Robbin's and Cotran Atlas of pathology, 3rd edition



Robbin’s Basic pathology, 10 th edition

MORPHOLOGY

- **Diffuse pulmonary interstitial fibrosis** indistinguishable from UIP.
- **Asbestos bodies:**
  - golden brown, fusiform or beaded rods with a translucent center.
  - Formed of asbestos fibers coated with an iron-containing proteinaceous material
- Begins in the **lower lobes and subpleurally**

Robbin's Basic pathology, 10 th edition

- **Pleural plaques:**
  - the most common manifestation of asbestos exposure
  - well-circumscribed plaques of dense collagen containing calcium
  - anterior and posterolateral aspects of the parietal pleura and over the domes of the diaphragm

CLINICAL FEATURES:

- Progressively worsening dyspnea **10 to 20 years after first exposure. (typically, after 20-30 years after exposure)**.
- Dyspnea is the first manifestation (by exertion, but later at rest).
- cough and production of sputum (due to smoking mainly).
- **static or progress** to honeycomb lung, congestive heart failure, cor pulmonale, and death.

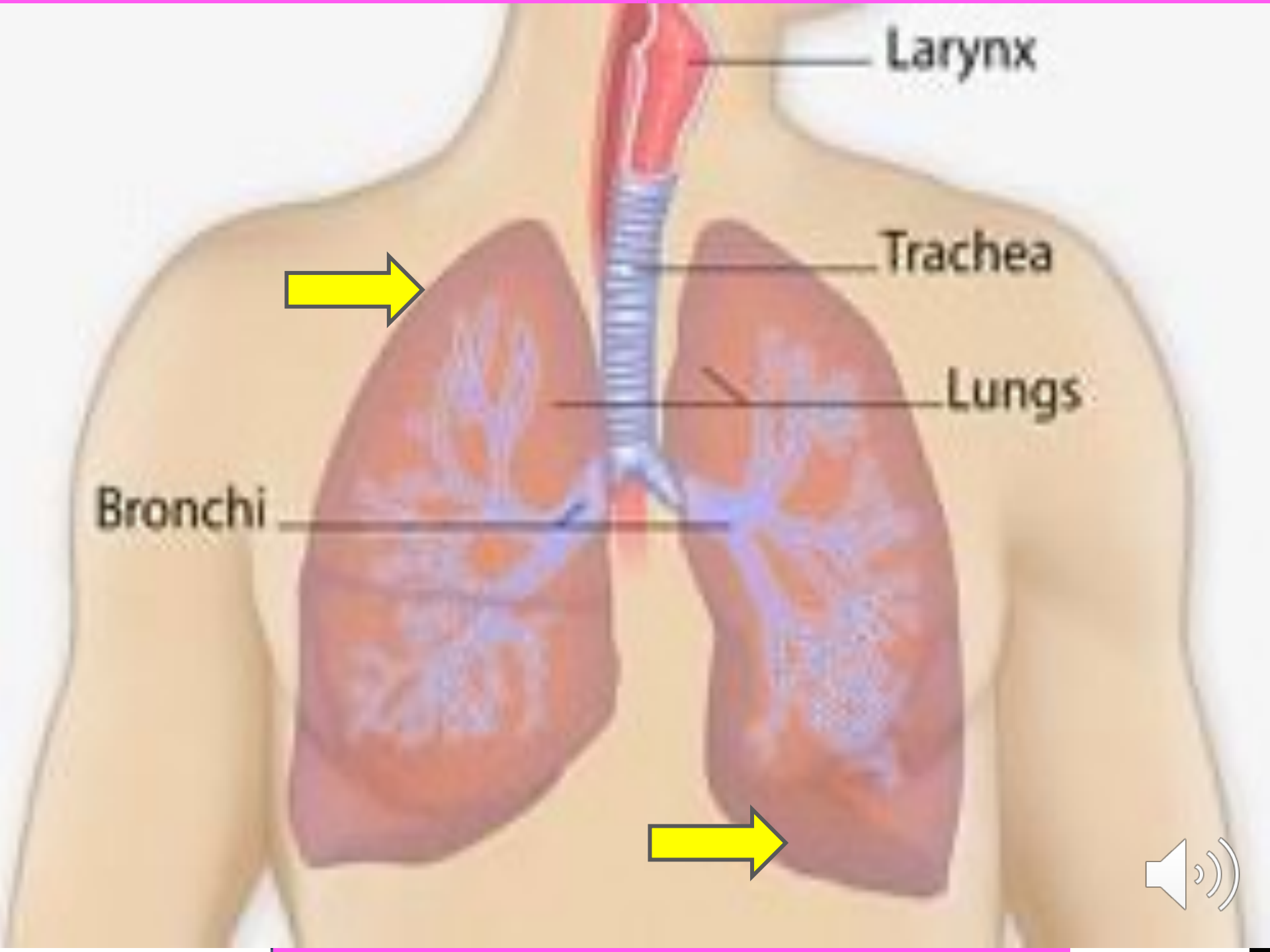
- Pleural plaques are usually asymptomatic

OUTCOMES:

- The risk for developing **lung carcinoma** is increased **5-fold** for asbestos workers

- Concomitant **cigarette smoking** increases the risk for lung carcinoma **but not for mesothelioma**.

- **Lung or pleural cancer** associated with asbestos exposure carries a **poor prognosis**.

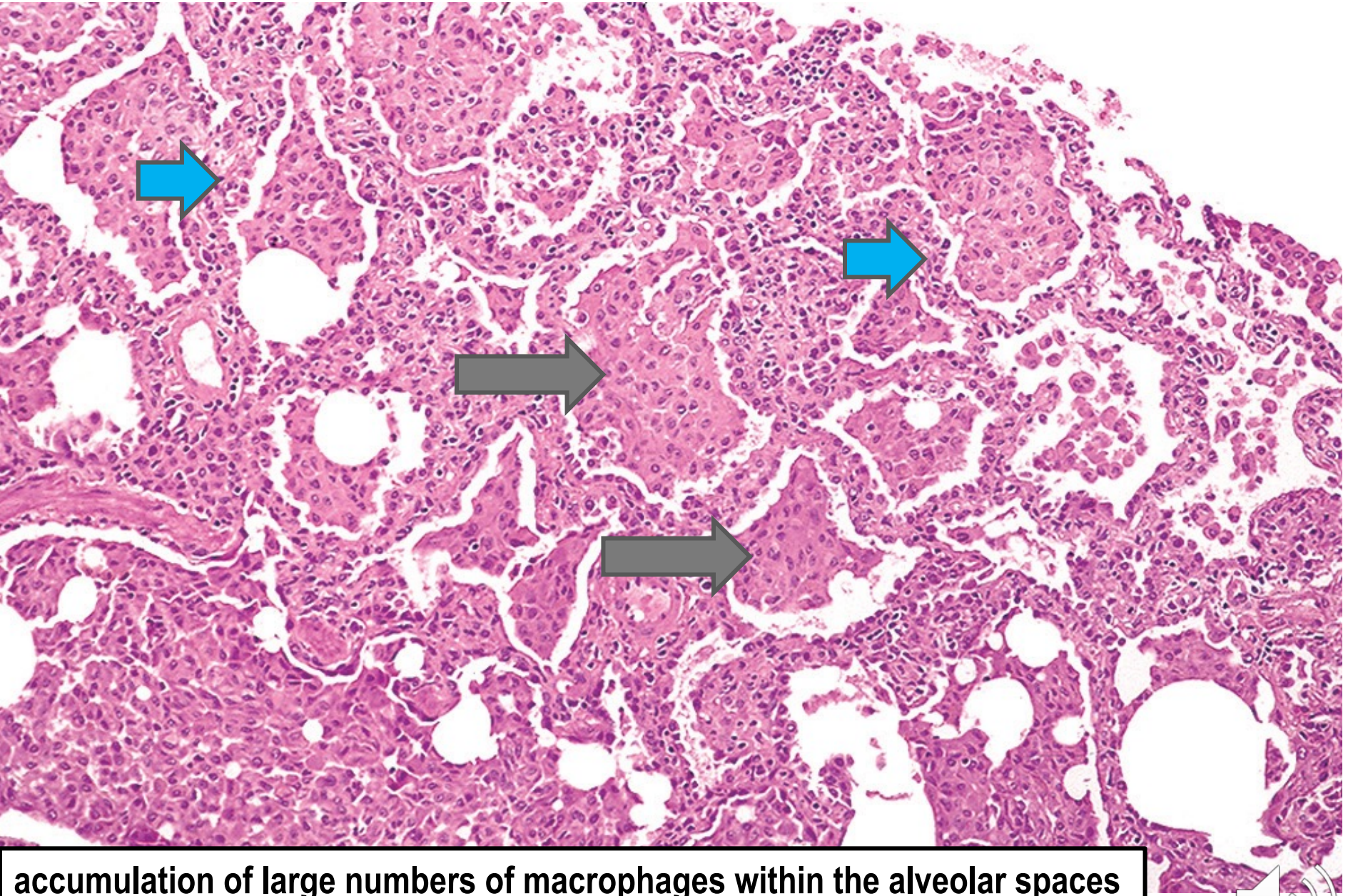

Larynx
Trachea
Lungs
Bronchi

SMOKING-RELATED INTERSTITIAL DISEASES

https://health.clevelandclinic.org/even-smoking-just-one-or-two-cigarettes-a-day-increases-your-risk-of-lung-disease/

SMOKING-RELATED INTERSTITIAL DISEASES

- Desquamative interstitial pneumonia (DIP)
- respiratory bronchiolitis



accumulation of large numbers of macrophages within the alveolar spaces

only slight fibrous thickening of the alveolar walls.

Outcome:

- Male= females, 4th-5th decade, all are smokers
- Insidious onset of dyspnea and dry cough over weeks or months
- PFT→ mild restrictive abnormality
- good prognosis
- excellent response to steroids and smoking cessation, however,

some patients progress despite therapy.

RESPIRATORY BRONCHIOLITIS – ASSOCIATED INTERSTITIAL LUNG DISEASE

- common lesion in smokers
- Histology:
  - presence of pigmented intraluminal macrophages akin to those in DIP, but in a "bronchiolocentric" distribution (first- and second-order respiratory bronchioles).
  - Aggregates of smokers' macrophages: Respiratory bronchioles, alveolar ducts, and peribronchiolar spaces
  - Mild peribronchiolar fibrosis.
  - Centrilobular emphysema is common but not severe
  - Desquamative interstitial pneumonia is often found in different parts of the same lung.

RESPIRATORY BRONCHIOLITIS – ASSOCIATED INTERSTITIAL LUNG DISEASE

- Symptoms are usually mild→ gradual onset of dyspnea and cough in 4th to 5th decade smokers with average exposures of over 30 pack-years of cigarette smoking.
- Cessation of smoking usually results in improvement.

- The term respiratory bronchiolitis-associated interstitial lung disease is used for patients who develop significant pulmonary symptoms, abnormal pulmonary function, and imaging abnormalities.

THANK YOU!