Interstitial Lung Diseases and Restrictive Lung Diseases

APPROVED

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Restrictive lung diseases

- An assortment of disparate pulmonary diseases with common feature of reduced VC, small resting lung volumes, but no resistance to expiratory gas flow
- Physiologic consequences of parenchymal pleuropulmonary disease, chest wall abnormalities, neuromuscular disease

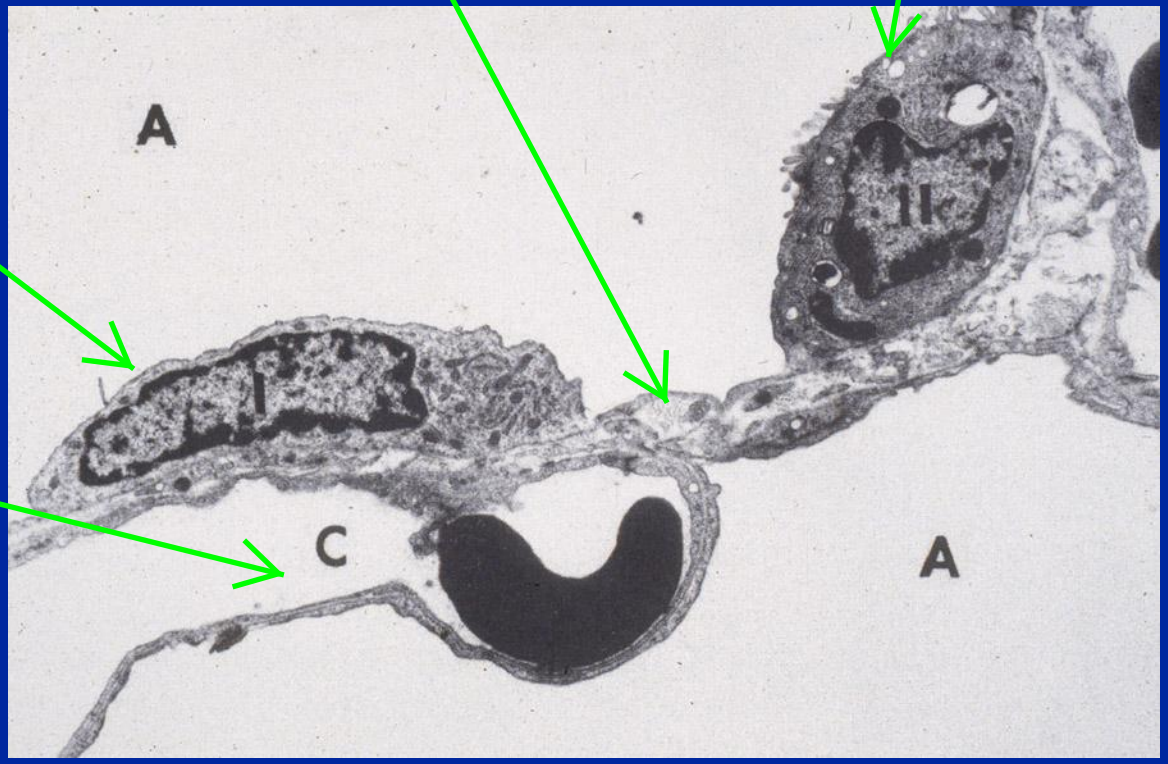
Vital Capacity = maximum amount of air one can expel from fully inhaled lungs

The Intersitium of the lung

- The anatomic space between the basement membrane on which the alveolar pneumocytes reside and the foot processes of the capillary endothelial cells
- May be expanded by edema, inflammation or fibrosis.
- Lymphovasculature may be occluded by metastatic tumor, so-called lymphangitic carcinomatosis

Type II Pneumocyte

Interstitium



Type I Pneumocyte

Capillary

"Interstitium can be expanded by fibrosis, inflammation and so forth"

DISORDERS OF UNKNOWN CAUSE

"This is not a lecture in diagnostic surgical pathology. I don't want you guys to get too caught up in the histology."

- Idiopathic pulmonary fibrosis
- Cryptogenic organizing pneumonia (Bronchiolitis obliterans organizing pneumonia, B.O.O.P.)
- Sarcoidosis
- Idiopathic pulmonary hemosiderosis

Idiopathic pulmoanry fibrosis

Extent to which oxygen passes from lungs into blood. This is determined by the diffusing capacity of the lungs for carbon monoxide

Pulmonary Function Test

Insidious onset of progressive SOB, restrictive physiology on PFT's and reduced DLCO

Buzz word for lung tissue at end stage

Usual interstitial pneumonia

- **"Usual" (UIP) form with diffuse interstitial fibrosis, honeycomb lung and variable chronic inflammation. Poorly responsive to corticosteroids, indication for transplant in younger**

Transplant if patient is young because UIP doesn't respond well to treatment. Provide supportive care if patient is older.

ATS/ERS Classification of Idiopathic Interstitial Pneumonia

American and European Societies that classify these diseases.

We will mostly focus on UIP and NSIP

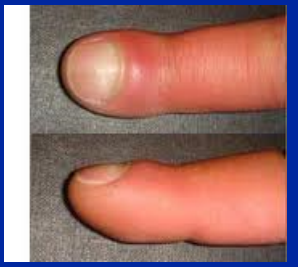
- UIP
- NSIP
- Organizing Pneumonia (COP/BOOP)
- DAD/AIP
- RB-IlD
- DIP
- LIP

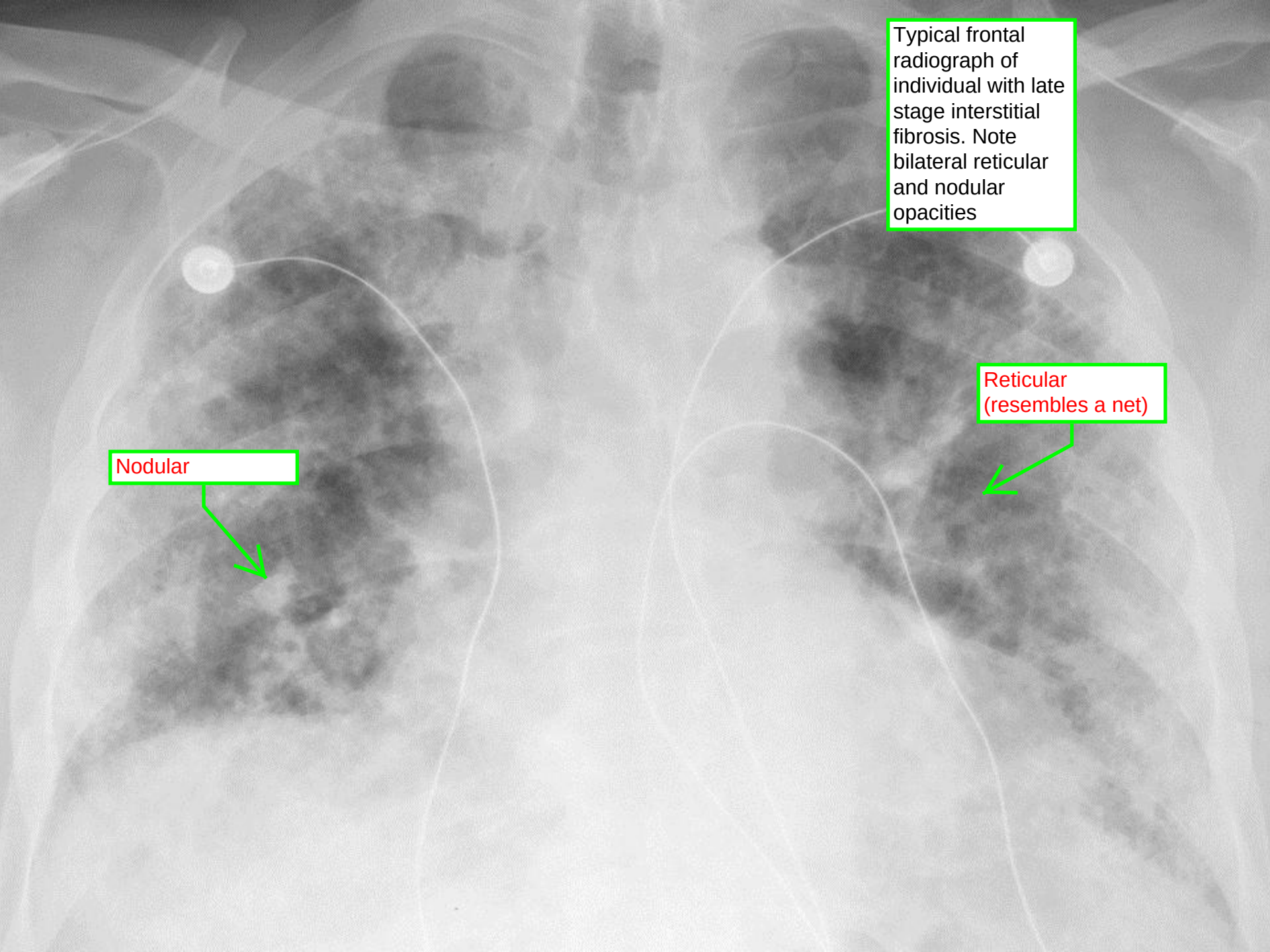
Usual Interstitial Pneumonia (UIP)

Mostly read slide

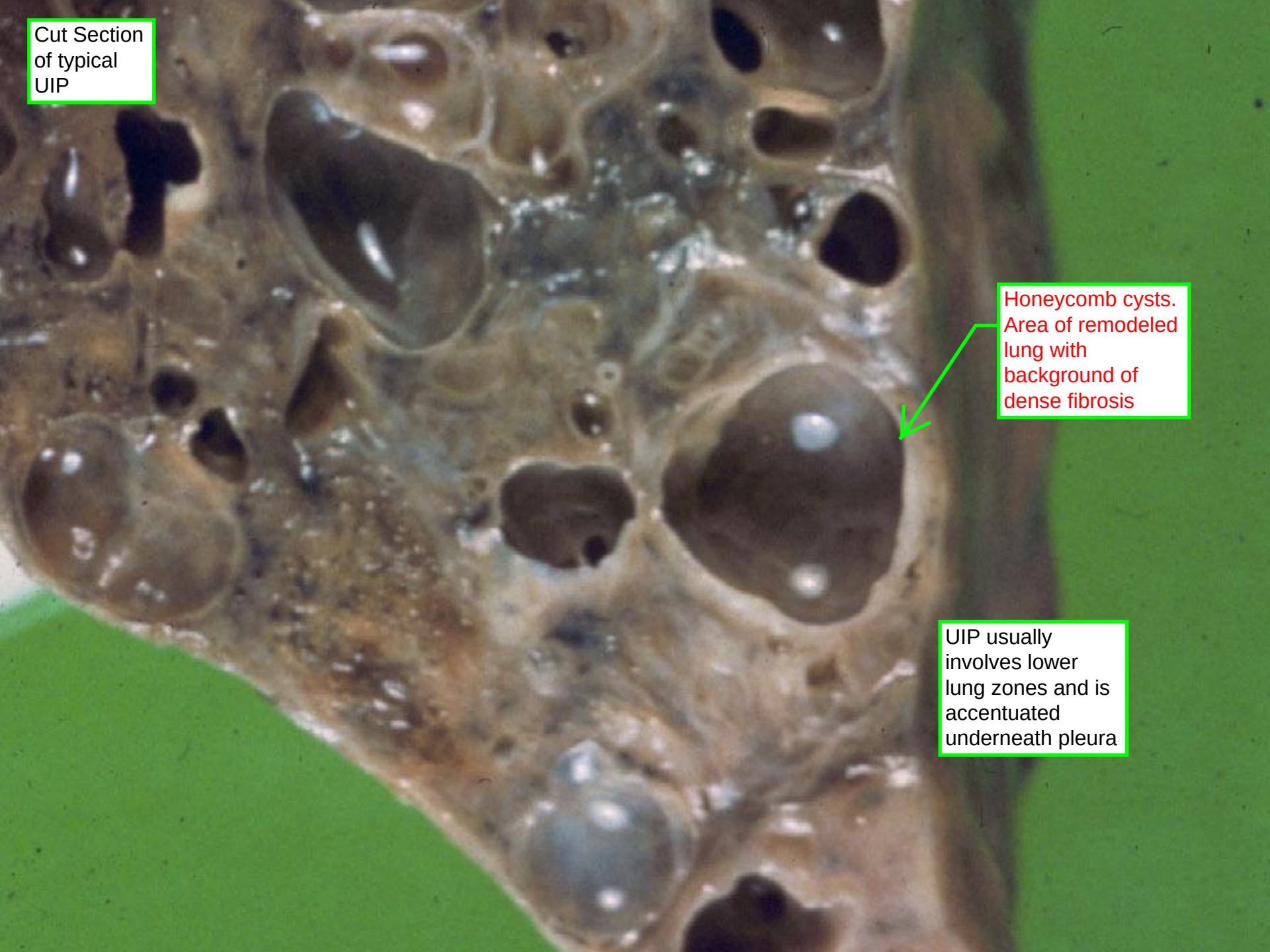
- The *usual* pattern observed by the pathologist histologically at surgical lung biopsy
- When pulmonologists speak of caring for patients with “idiopathic pulmonry fibrosis” they are *usually* referring to the diagnosis of UIP
- Clinical picture of insidious onset of SOB, crackles on lung exam, digital clubbing, and restrictive physiology on PFT’s

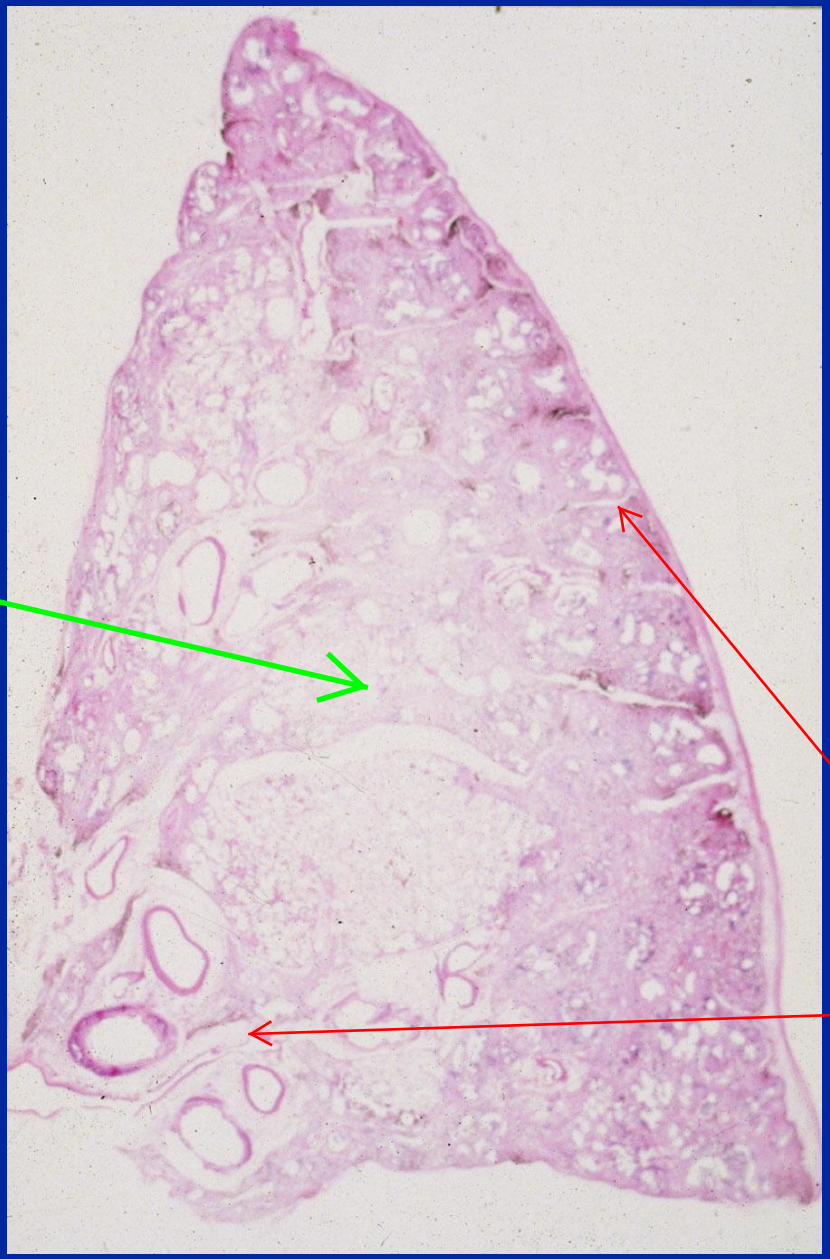
Preserved expiratory flow rates but low lung volumes (opposite of obstructive lung diseases)




Typical frontal radiograph of individual with late stage interstitial fibrosis. Note bilateral reticular and nodular opacities
Reticular (resembles a net)
Nodular

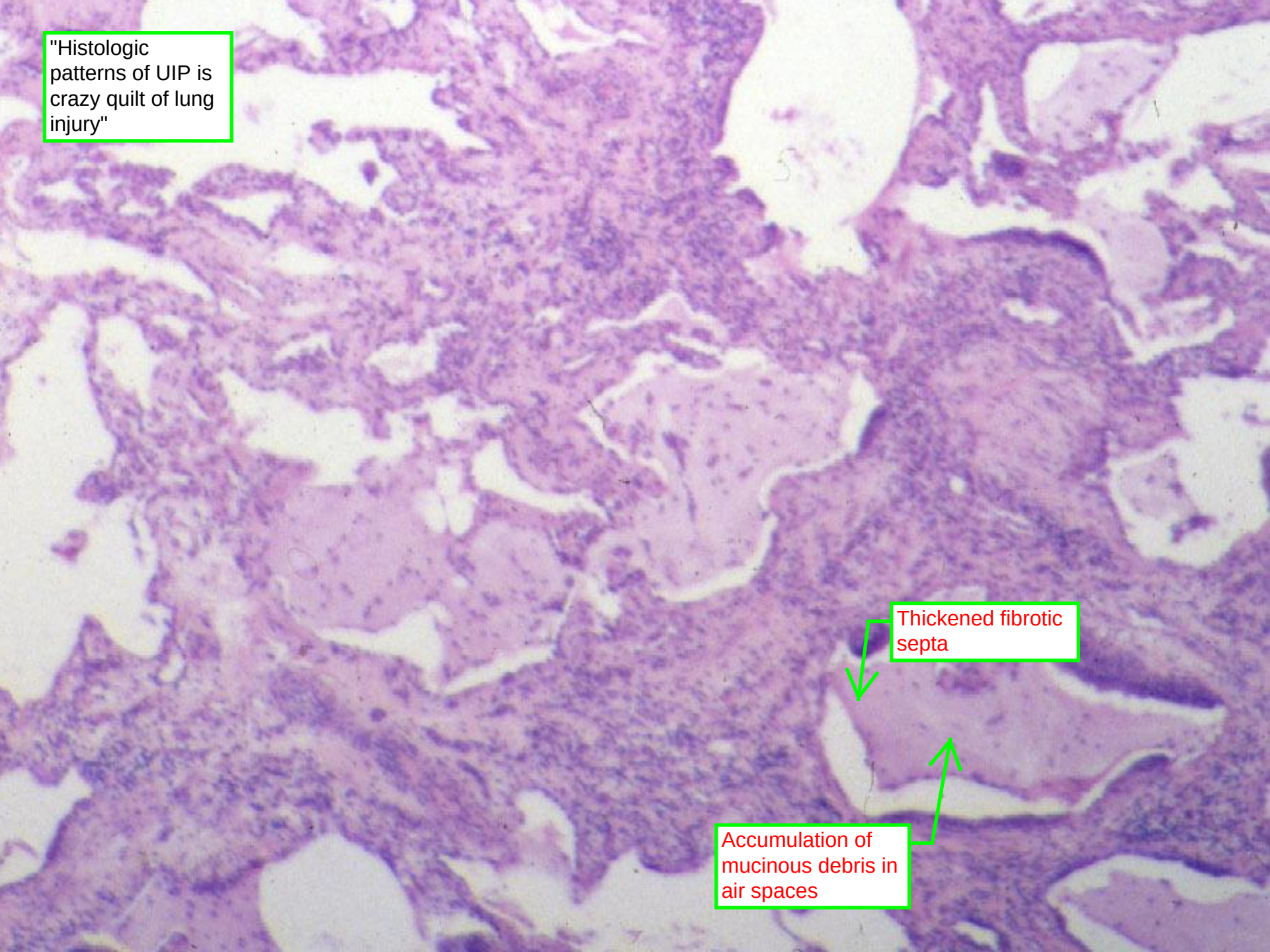

Surface of lung looks pebbled/ cobblestoned
cm

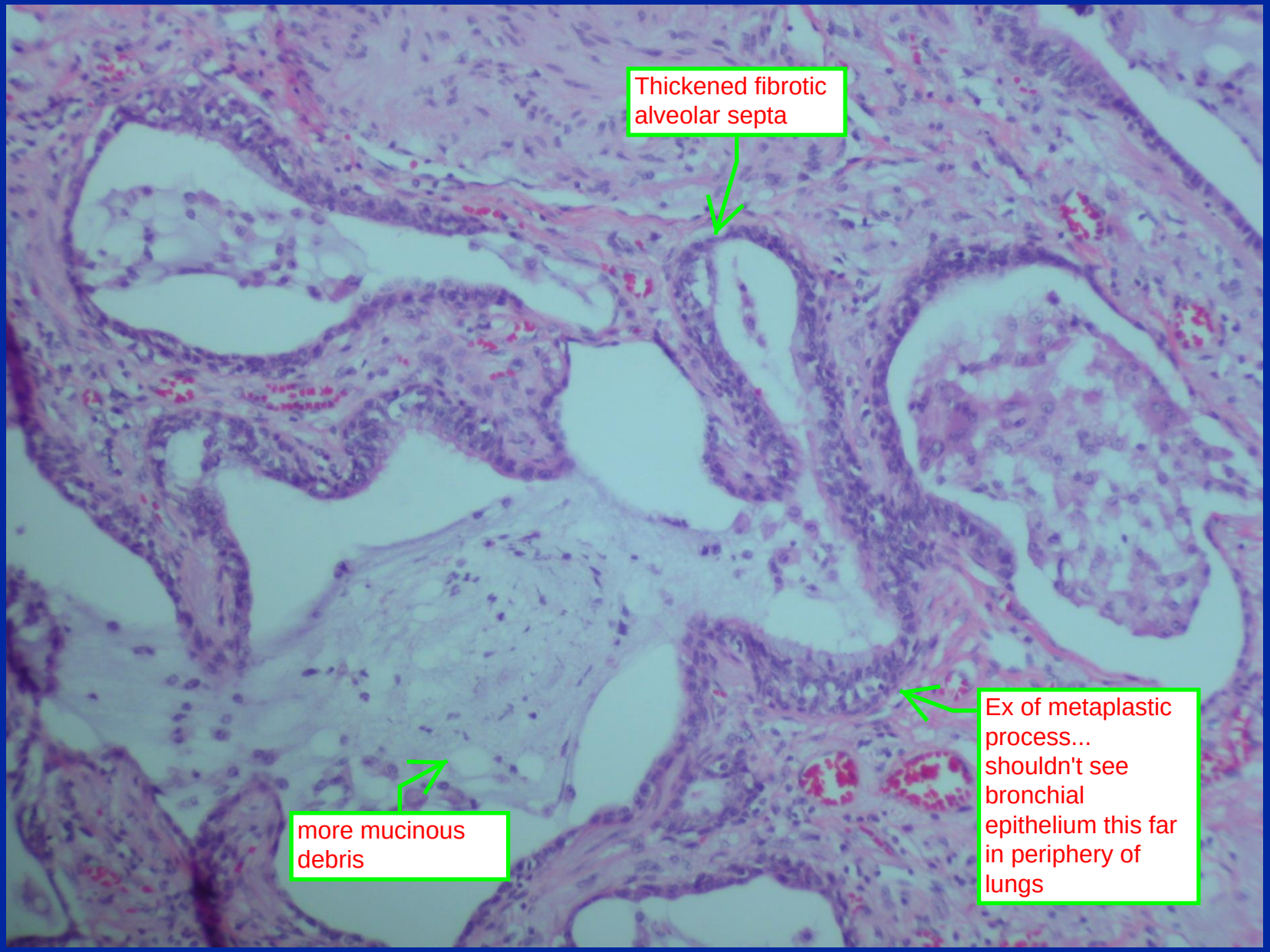

Cut Section of typical UIP
Honeycomb cysts. Area of remodeled lung with background of dense fibrosis
UIP usually involves lower lung zones and is accentuated underneath pleura

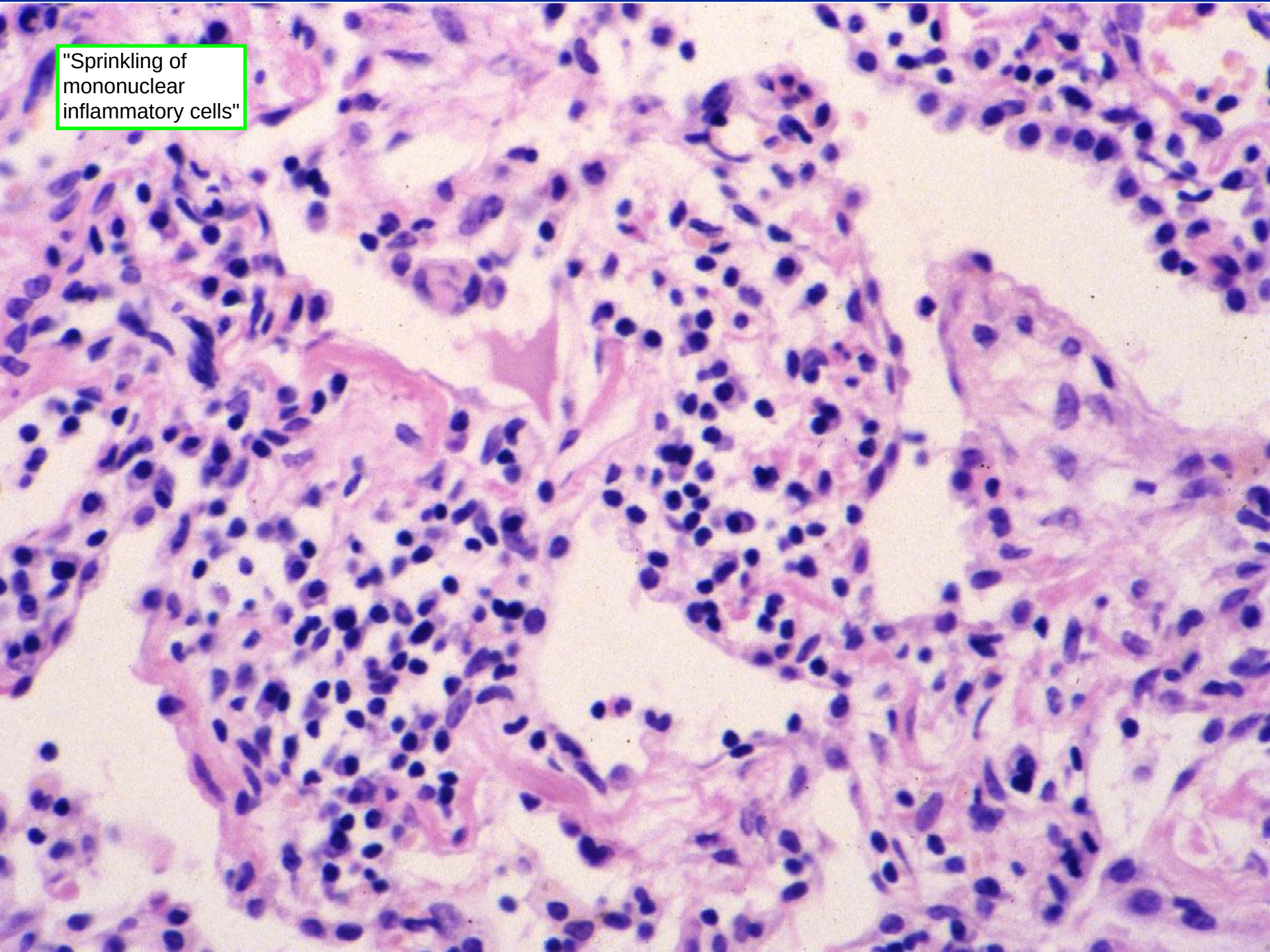


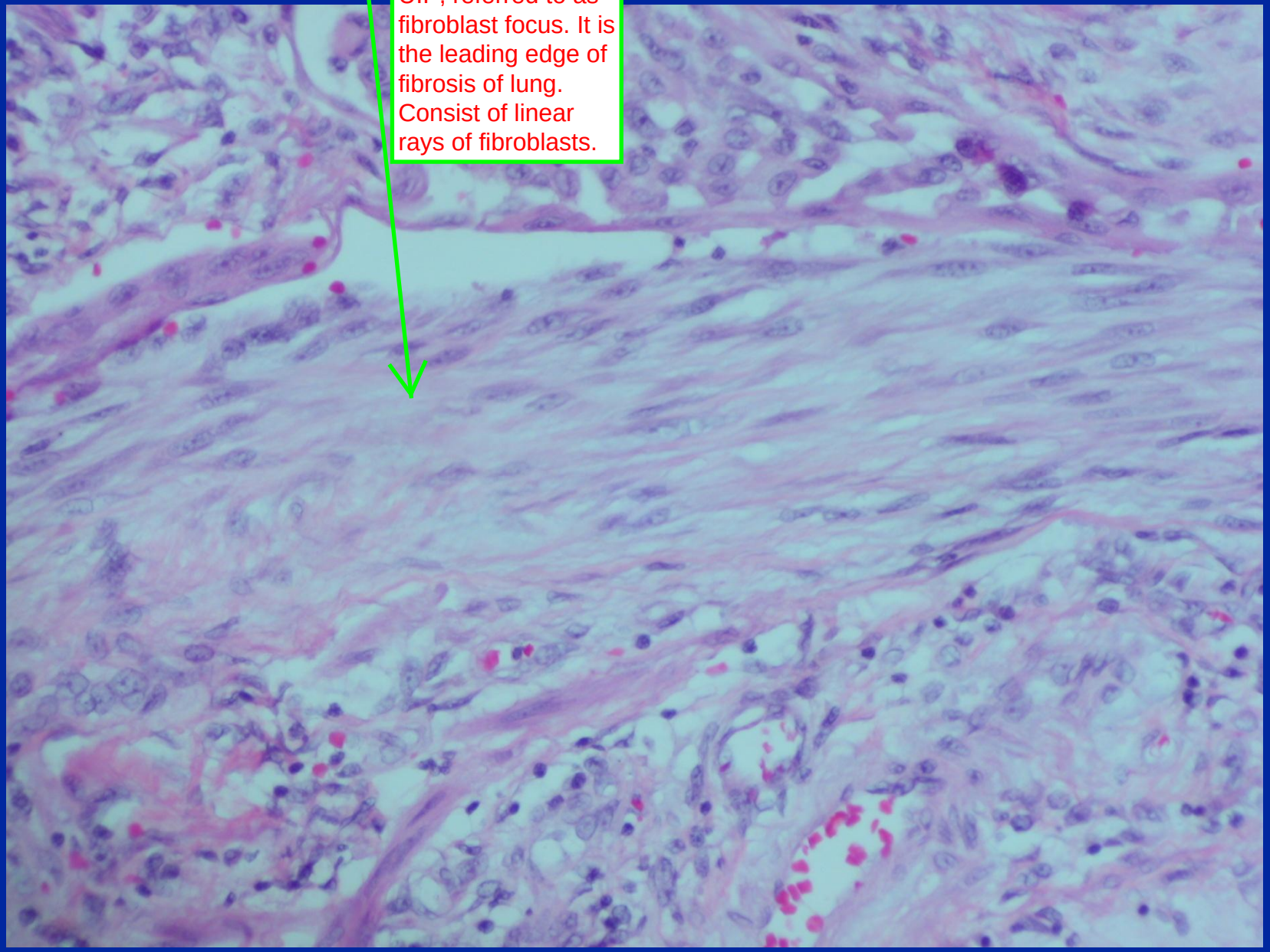
Central part of the lung tends to be spared

Note again with UIP it is accentuated in the lower lung zones and underneath the pleura


"Histologic patterns of UIP is crazy quilt of lung injury"
Thickened fibrotic septa
Accumulation of mucinous debris in air spaces


Thickened fibrotic alveolar septa
Ex of metaplastic process... shouldn't see bronchial epithelium this far in periphery of lungs
more mucinous debris


"Sprinkling of mononuclear inflammatory cells"


Classic lesion with UIP, referred to as fibroblast focus. It is the leading edge of fibrosis of lung. Consist of linear rays of fibroblasts.

Bronchiolitis obliterans organizing pneumonia (BOOP)

- Common response to pulmonary inflammatory injury- seen w/ CVD
- Post-infectious, may be seen adjacent to some other primary process e.g. tumor, may be component of other primary process e.g. HP, or reflect pulmonary toxicity due to drugs
- Idiopathic- cryptogenic organizing pneumonia

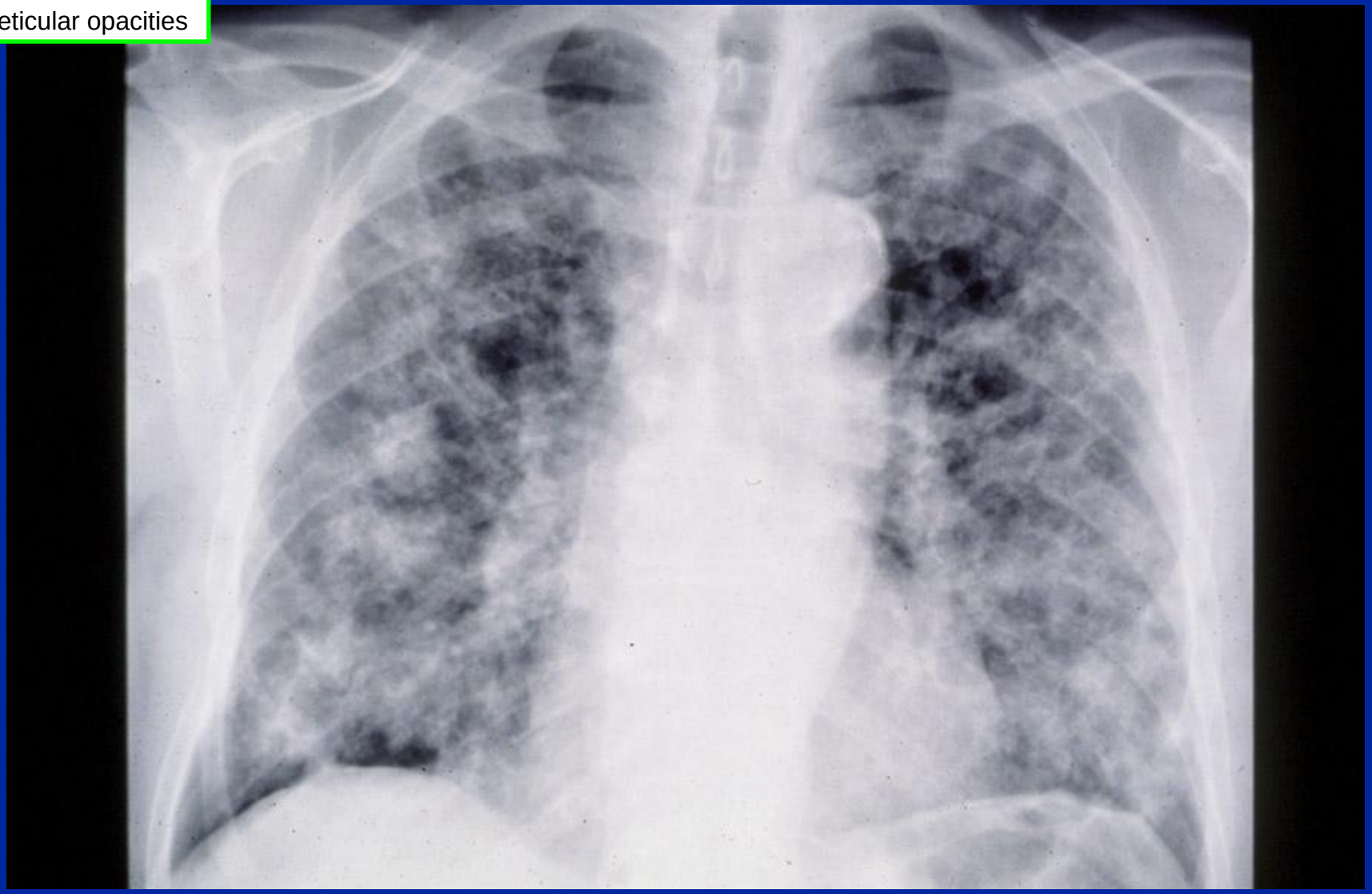
When BOOP occurs without injury

BOOP

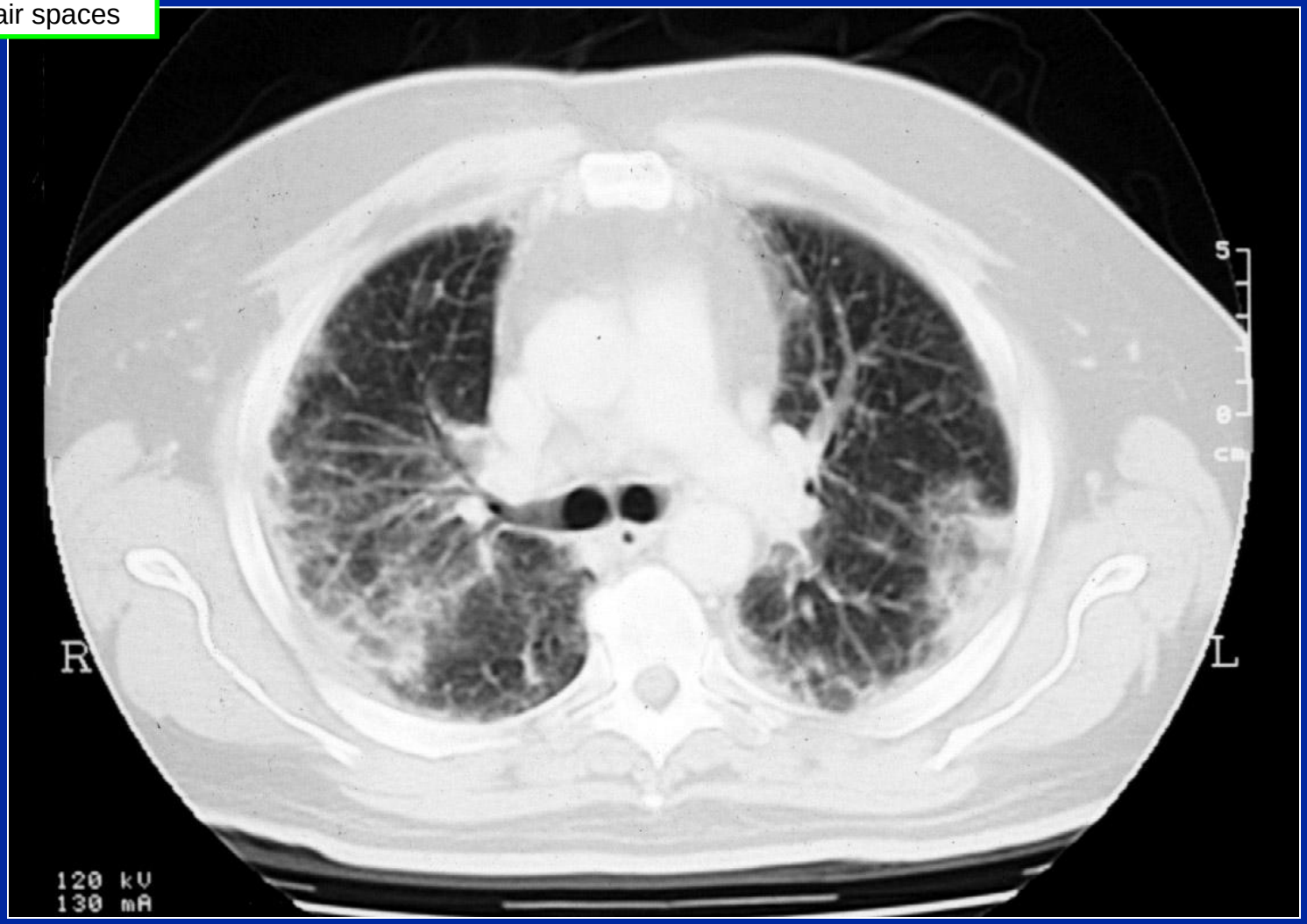
- Clinical features include dyspnea, constitutional symptoms
- good response to steroids, although will relapse if not treated long enough

As long as the lungs are not irreversibly scarred by collagen deposition there is the possibility they will be responsive to therapy.

Appears same as UIP on X-ray with nodular and reticular opacities



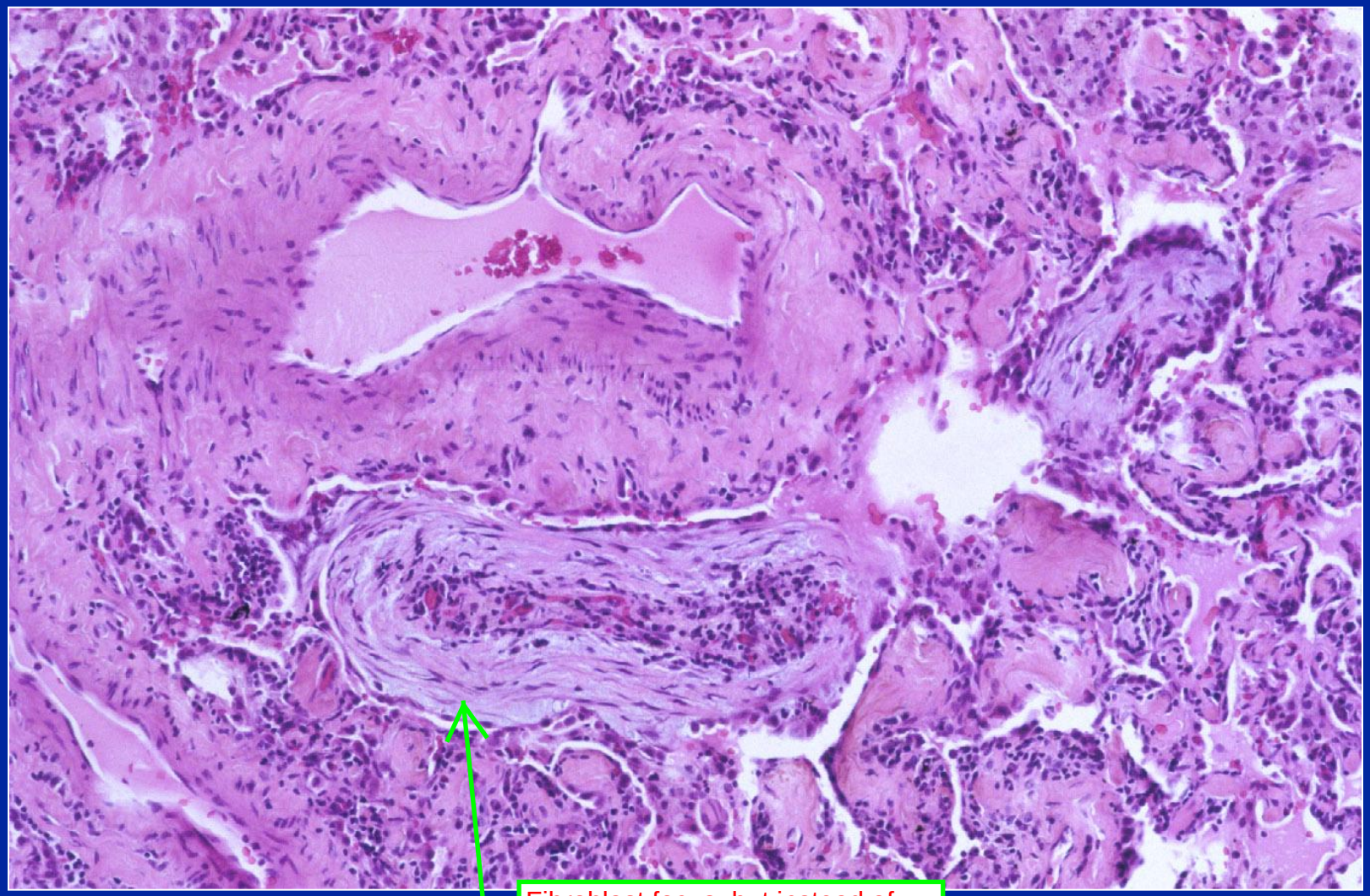
On CT scan still see "fluffy" reticular and nodular infiltrates in the air spaces

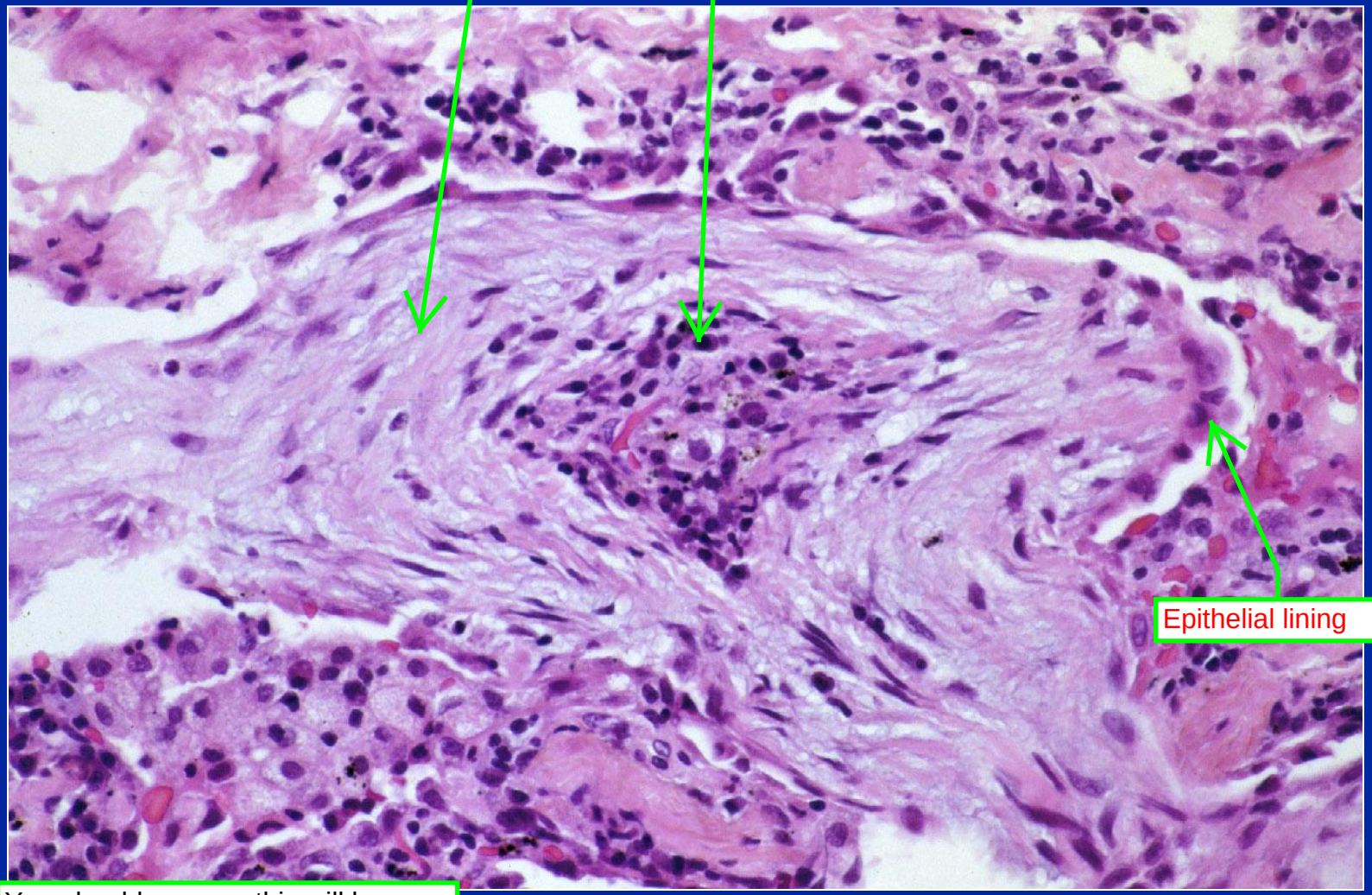


Read slide

Histologic features of BOOP

- Plugs of loose edematous connective tissue in small airways
- Typically have a core of inflammatory cells and epithelialization at periphery


Fibroblast focus, but instead of being in interstitium like in UIP, this is making its way through an alveolar duct



You should assume this will be responsive to therapy because there is no honeycomb pattern indicative of late stage disease

Non-specific Interstitial Pneumonia (NSIP)

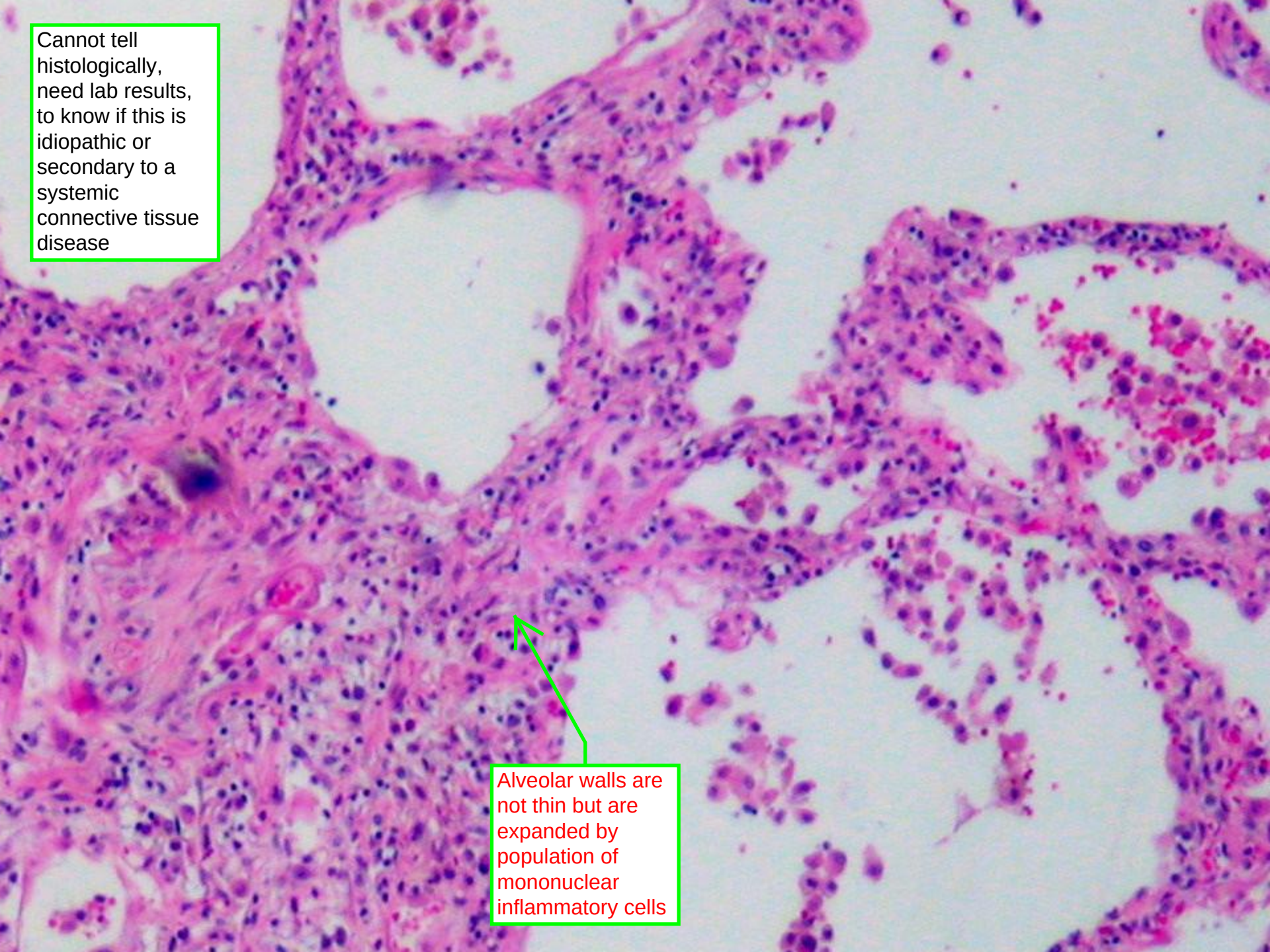
- Cellular Pattern
- Fibrosing Pattern
- Non-idiopathic associations include connective tissue disorders (RA, scleroderma, SLE ,polymyositis and other systemic inflammatory disorders- PBC, Hashimoto's thyroiditis

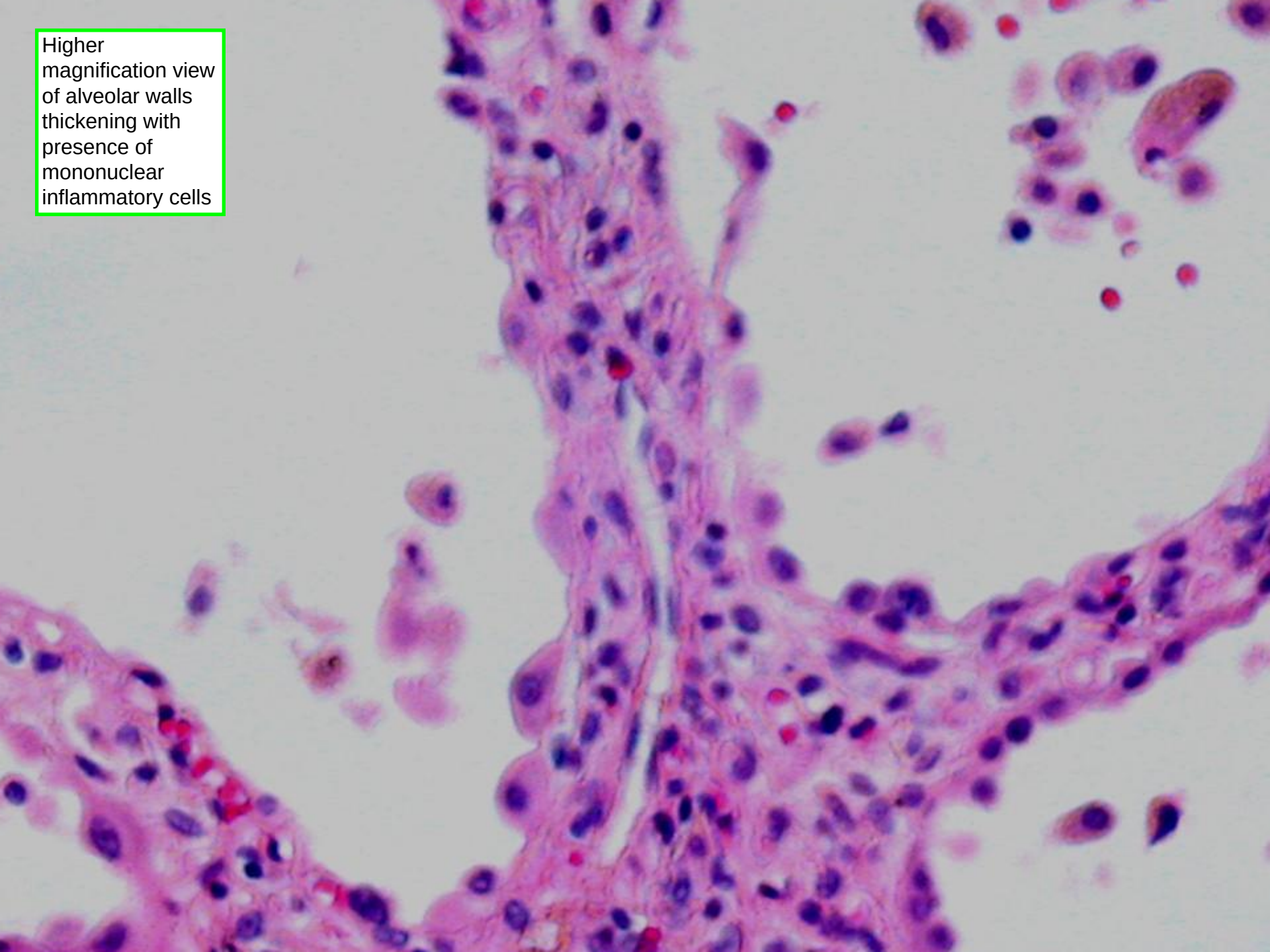
Rheumatoid arthritis

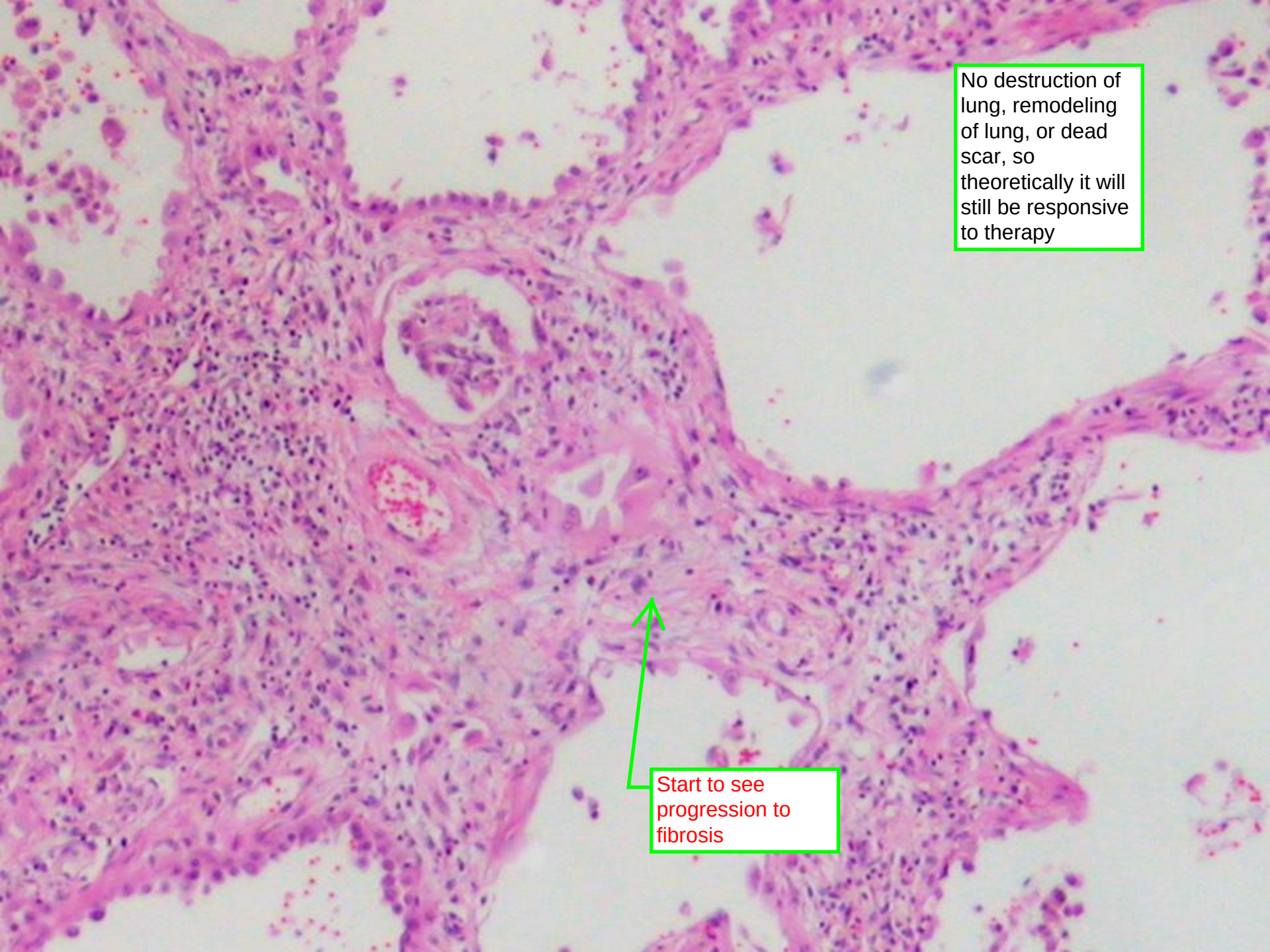
Lupus

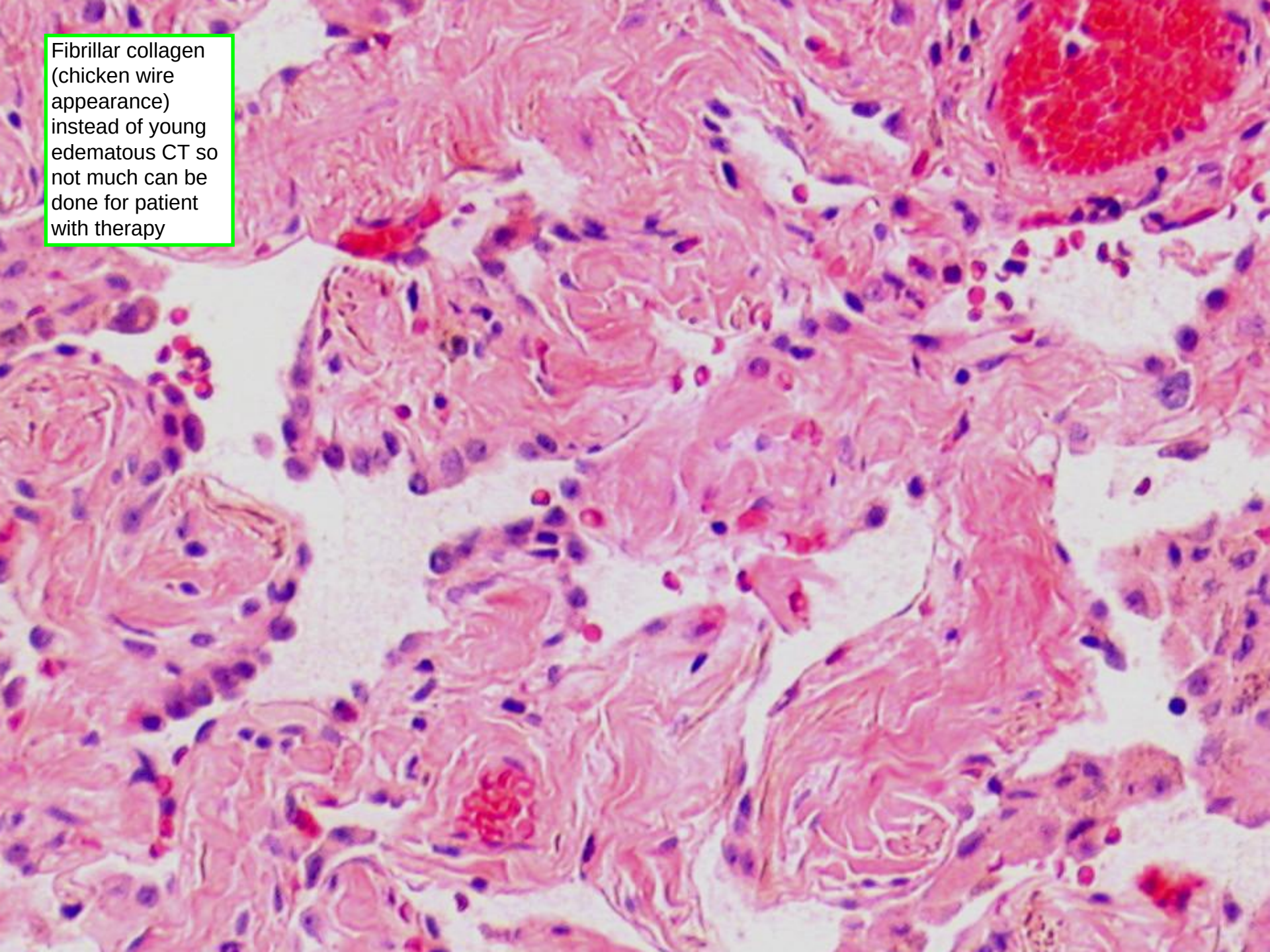
Primary biliary cirrhosis

Patient often presents with systemic inflammatory process as well


Cannot tell histologically, need lab results, to know if this is idiopathic or secondary to a systemic connective tissue disease
Alveolar walls are not thin but are expanded by population of mononuclear inflammatory cells


Higher magnification view of alveolar walls thickening with presence of mononuclear inflammatory cells


No destruction of lung, remodeling of lung, or dead scar, so theoretically it will still be responsive to therapy
Start to see progression to fibrosis


Fibrillar collagen (chicken wire appearance) instead of young edematous CT so not much can be done for patient with therapy

Sarcoidosis

Can involve many different organ systems (CNS, skin, etc.)

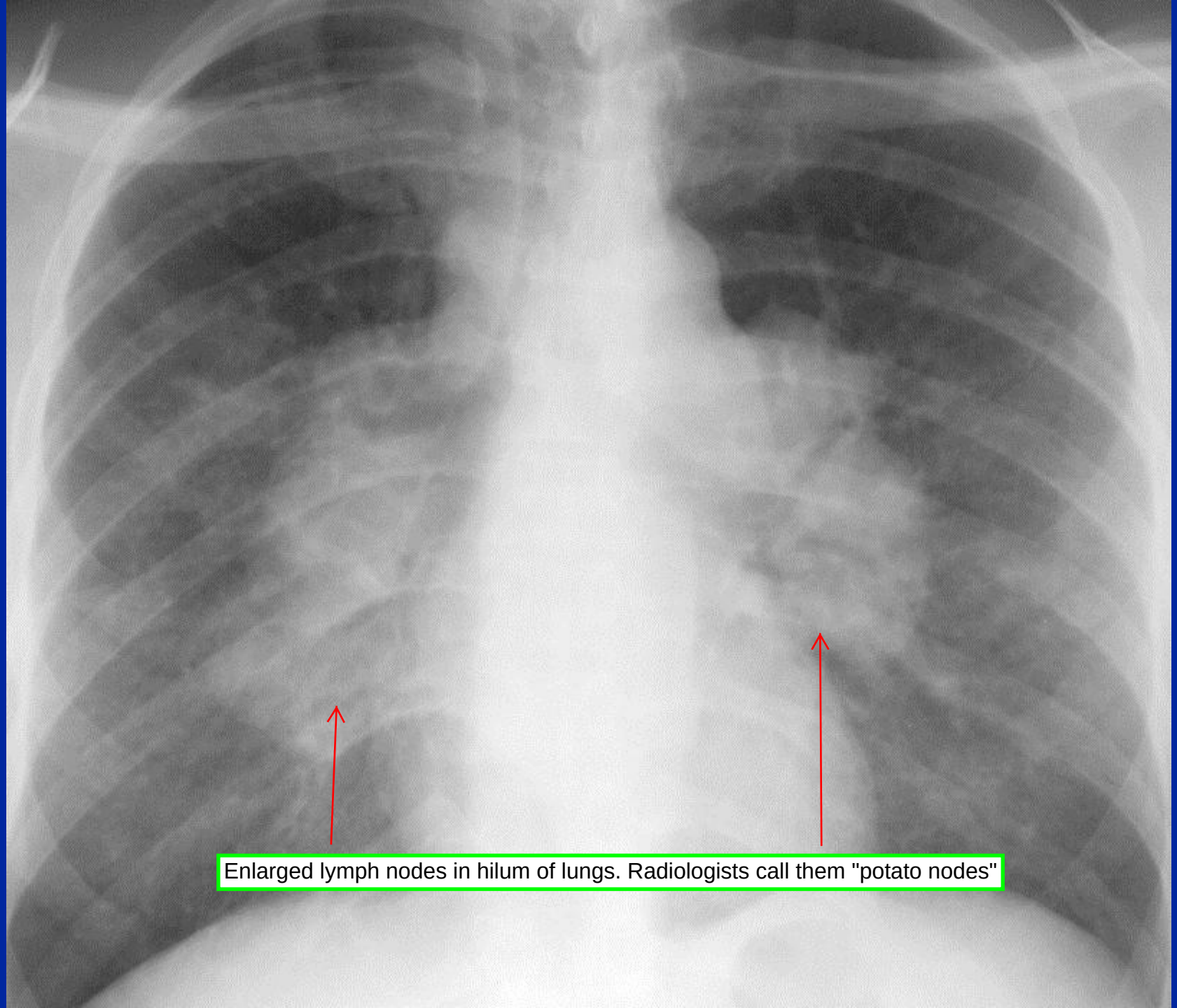
- Idiopathic systemic disease characterized by the presence of non-necrotizing epithelioid granulomata in many tissues and organs
- Epidemiology- highest rates in USA in southeast among AA, disease originally described in northern European women, rare in China and SE Asia

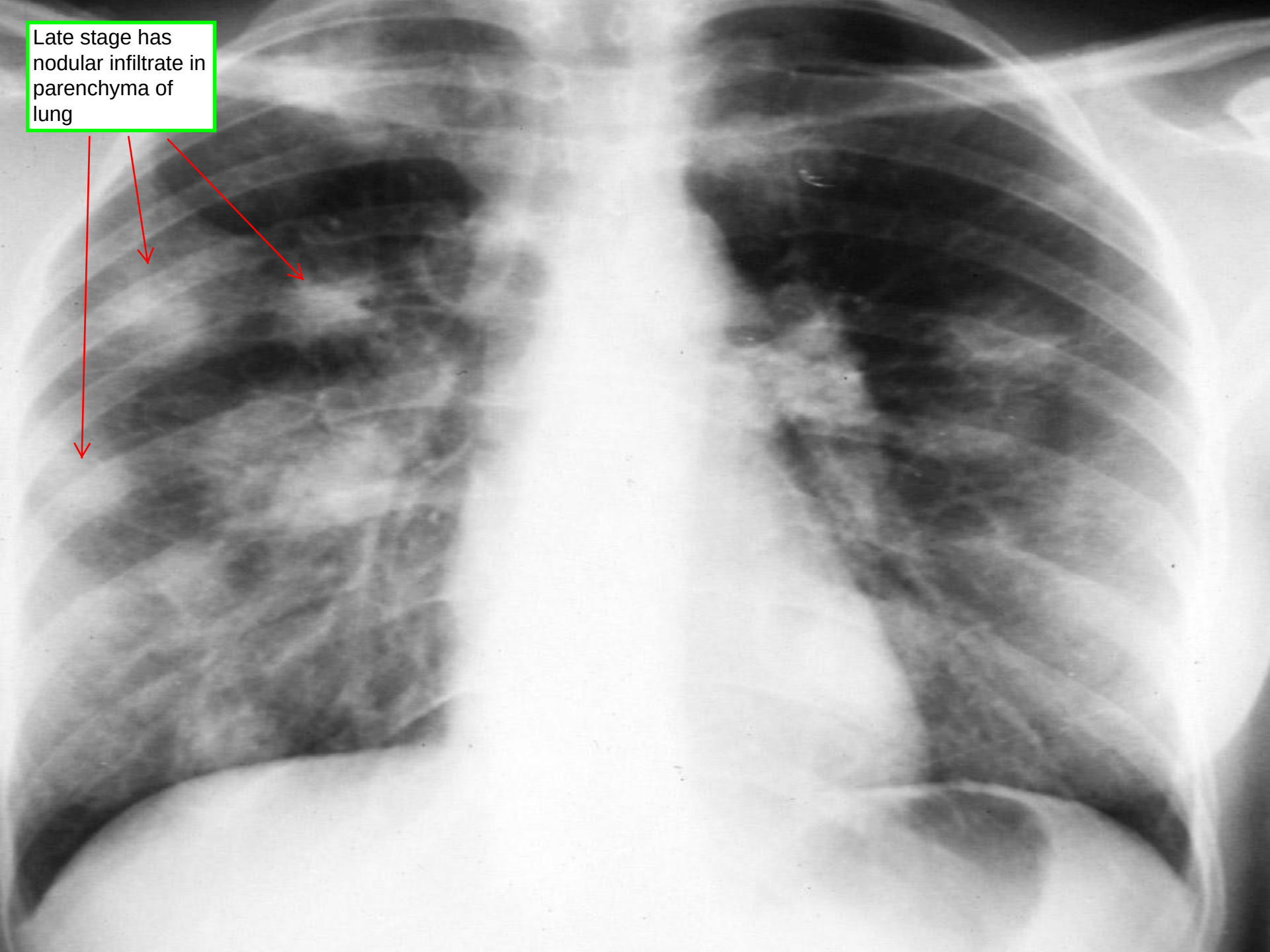
No one knows what exactly causes sarcoidosis

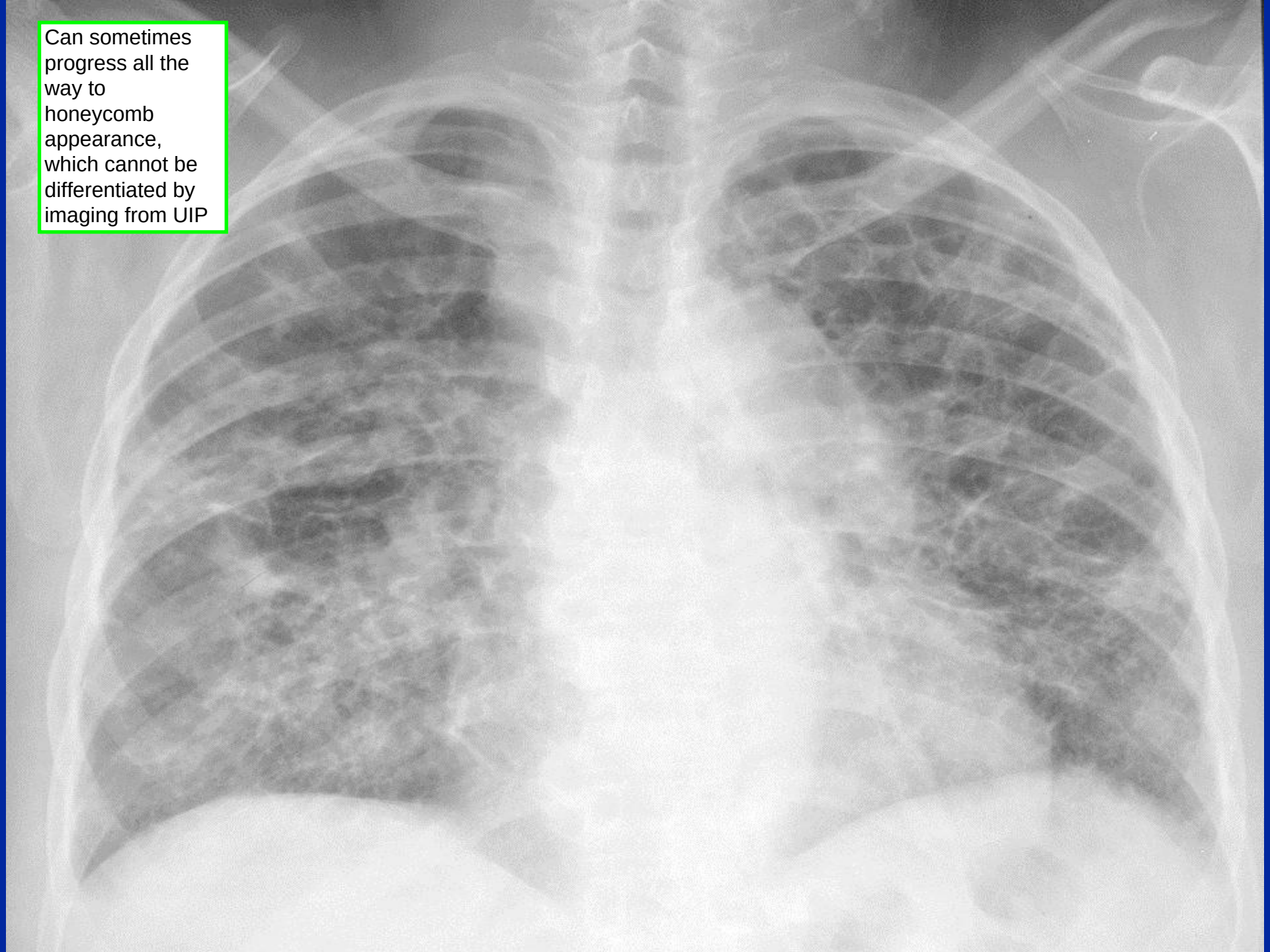
Pulmonary sarcoidosis

- Variable clinical presentation- from the asymptomatic to severe impairment with CNS/cardiac ocular/cutaneous involvement, constitutional symptoms
- Typical bilateral hilar lymphadenopathy +/- parenchymal infiltrates on CXR

Usually malignant processes present unilaterally so when it is bilateral in a young individual think sarcoidosis


Enlarged lymph nodes in hilum of lungs. Radiologists call them "potato nodes"


Late stage has nodular infiltrate in parenchyma of lung


Can sometimes progress all the way to honeycomb appearance, which cannot be differentiated by imaging from UIP

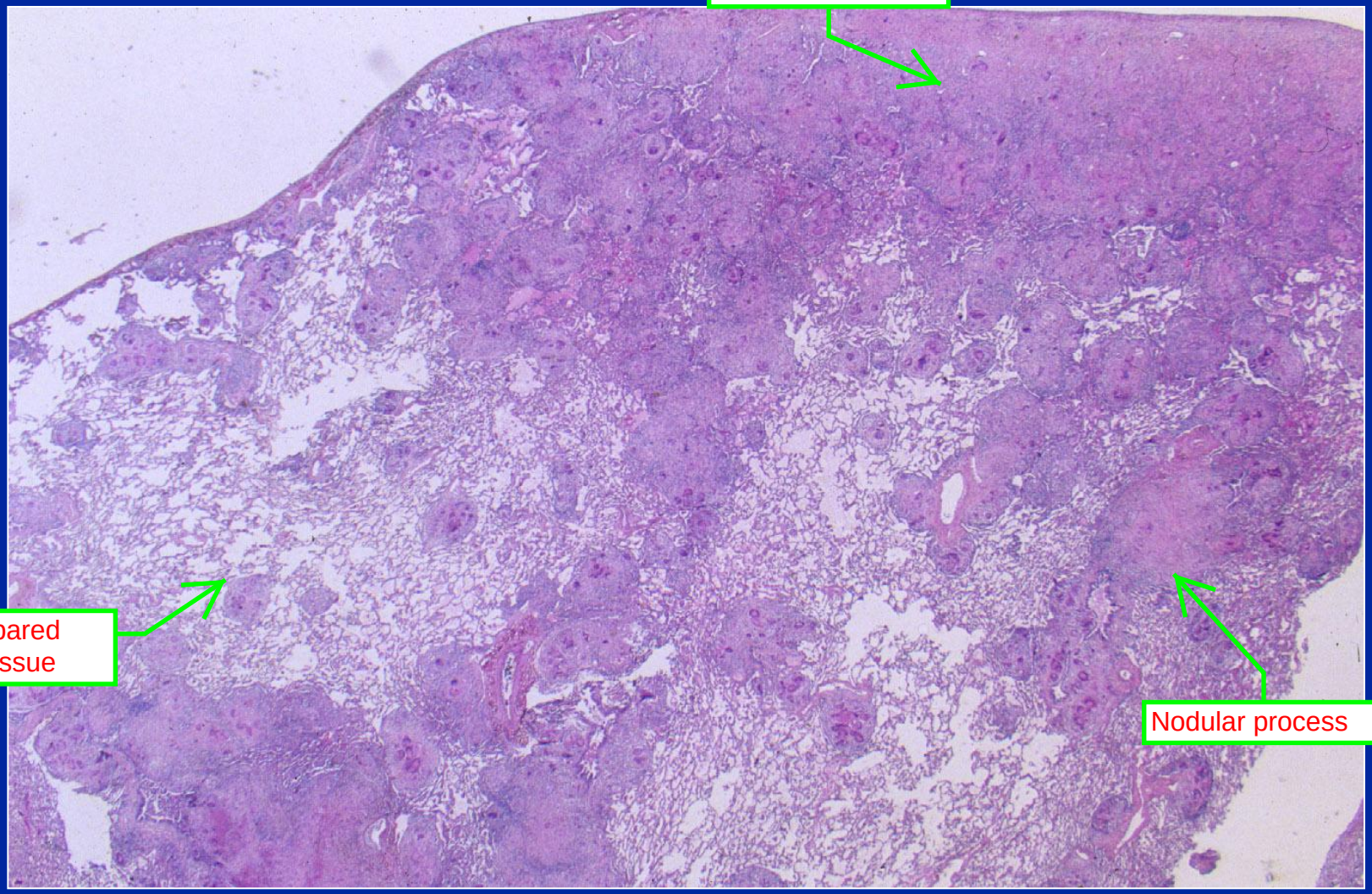
Pathology of sarcoidosis

- Compact, non-necrotizing granulomata comprised of epithelioid histiocytes, giant cells with inclusions in lymph nodes or in lymphovascular distribution, notably in the walls of airways
- Diagnose by excluding its mimics: mycobacteria, fungi, Be

Sarcoidosis- clinical course

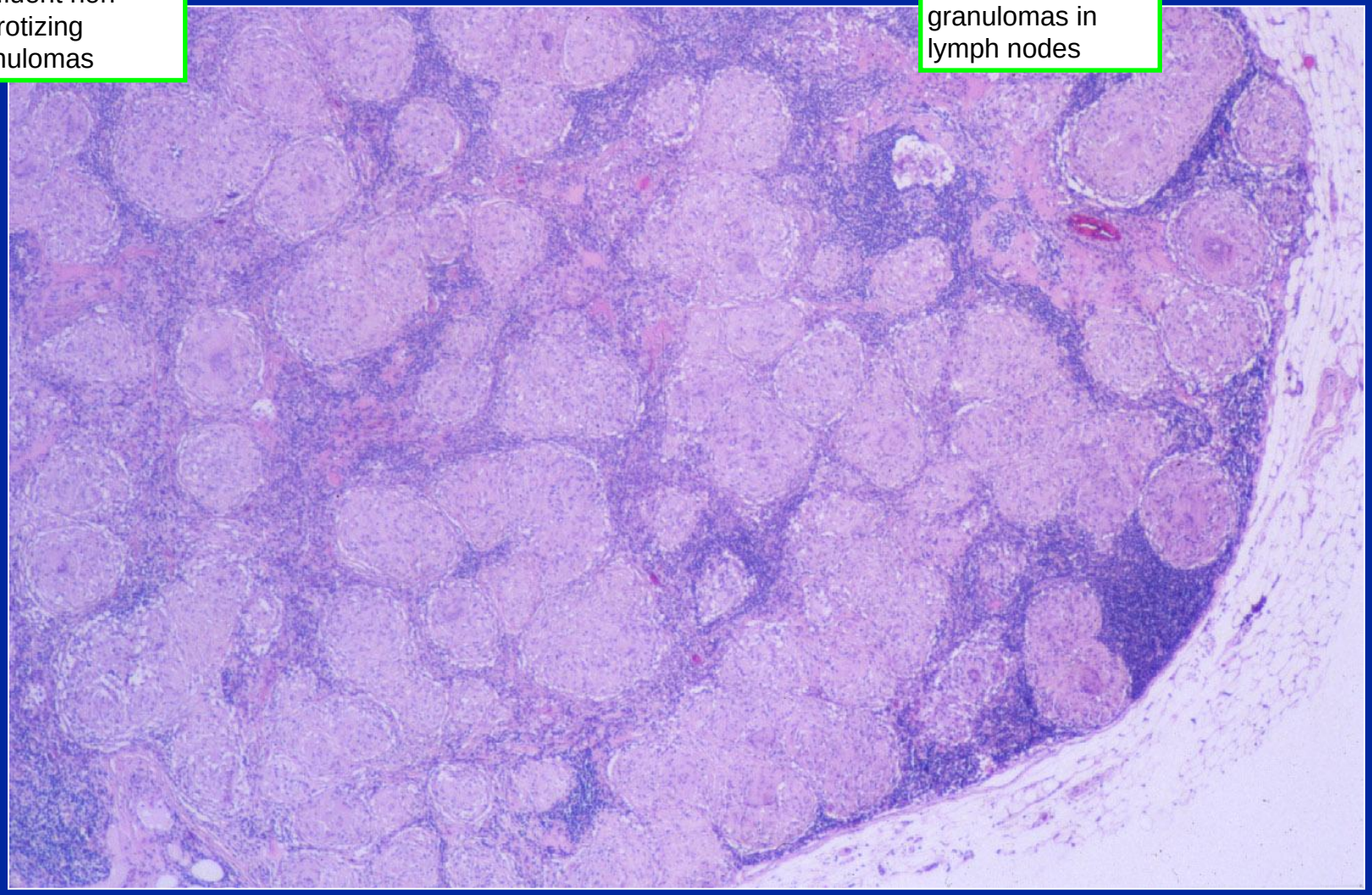
- Highly variable, may be present as an asymptomatic radiographic abnormality, most have respiratory or constitutional complaints
- Corticosteroids are the mainstay of therapy, 60-80% will recover, 10% die from CNS or cardiac involvemnt pulmonary fibrosis. Poor transplant candidates

Because this is a systemic disease a lung transplant may not be enough

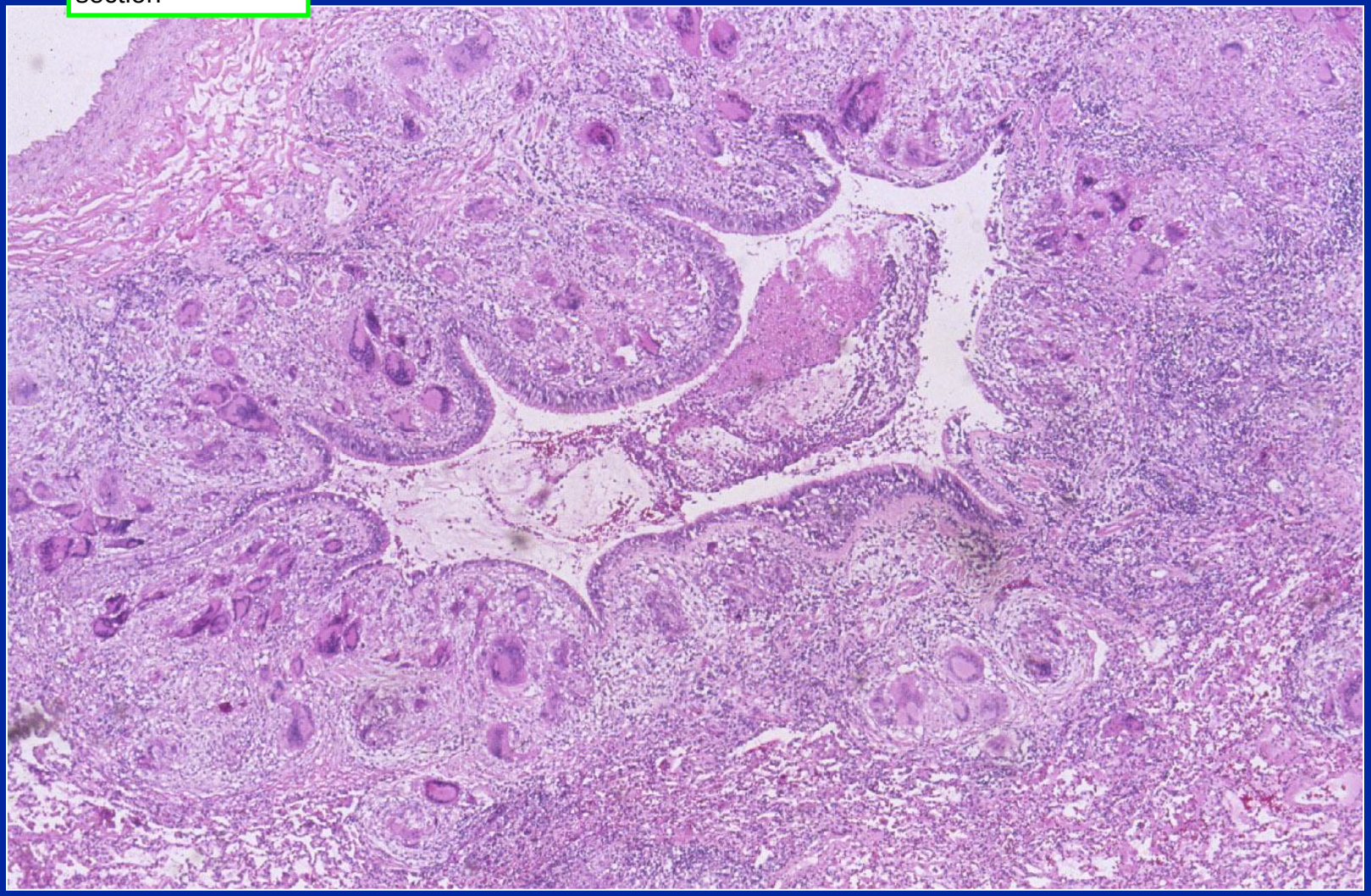

Sheet of granulomas near pleura that have grown together
Area of spared alveolar tissue
Nodular process

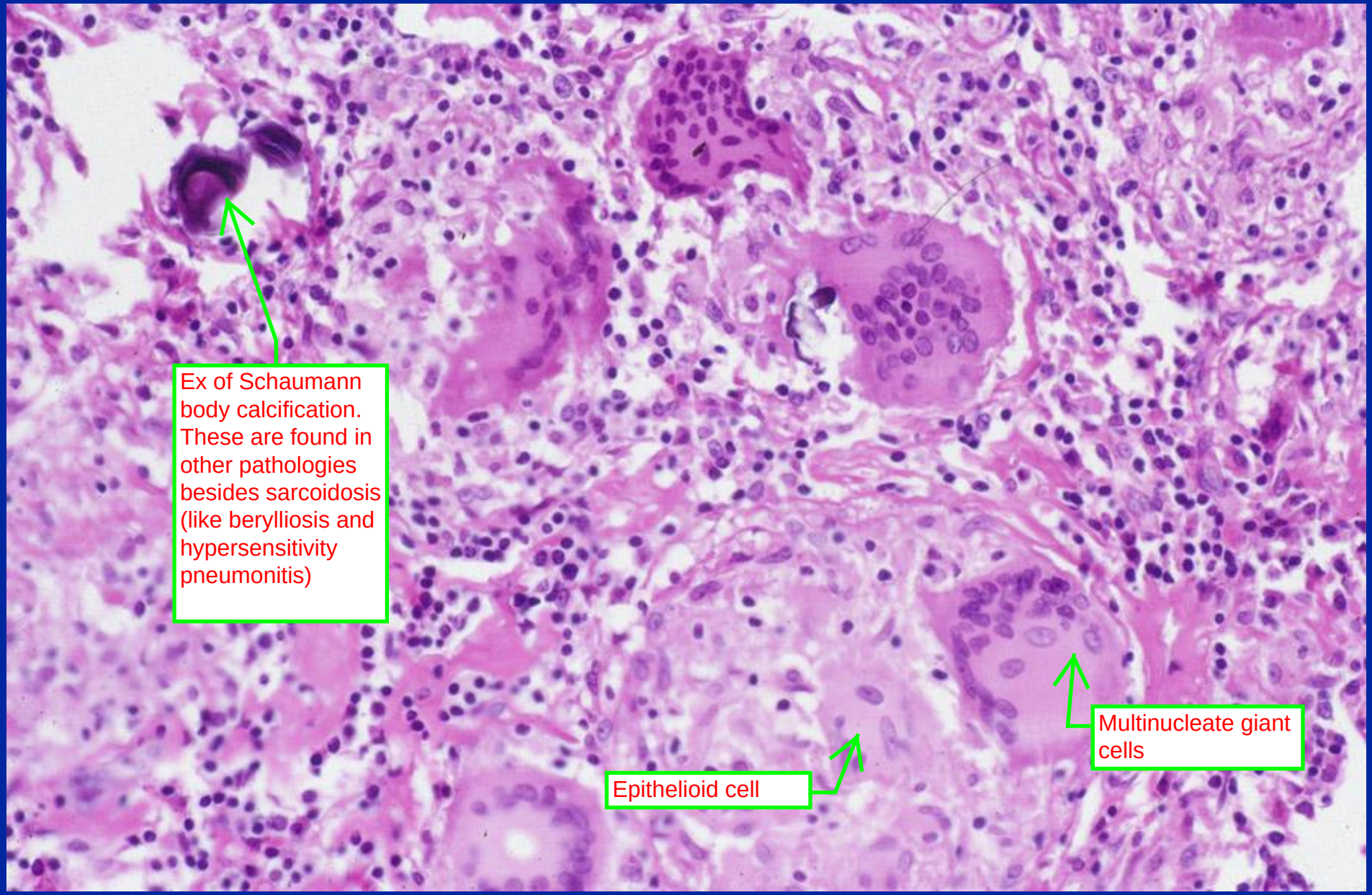
Lymph nodes also have pattern of diffuse and confluent non-necrotizing granulomas

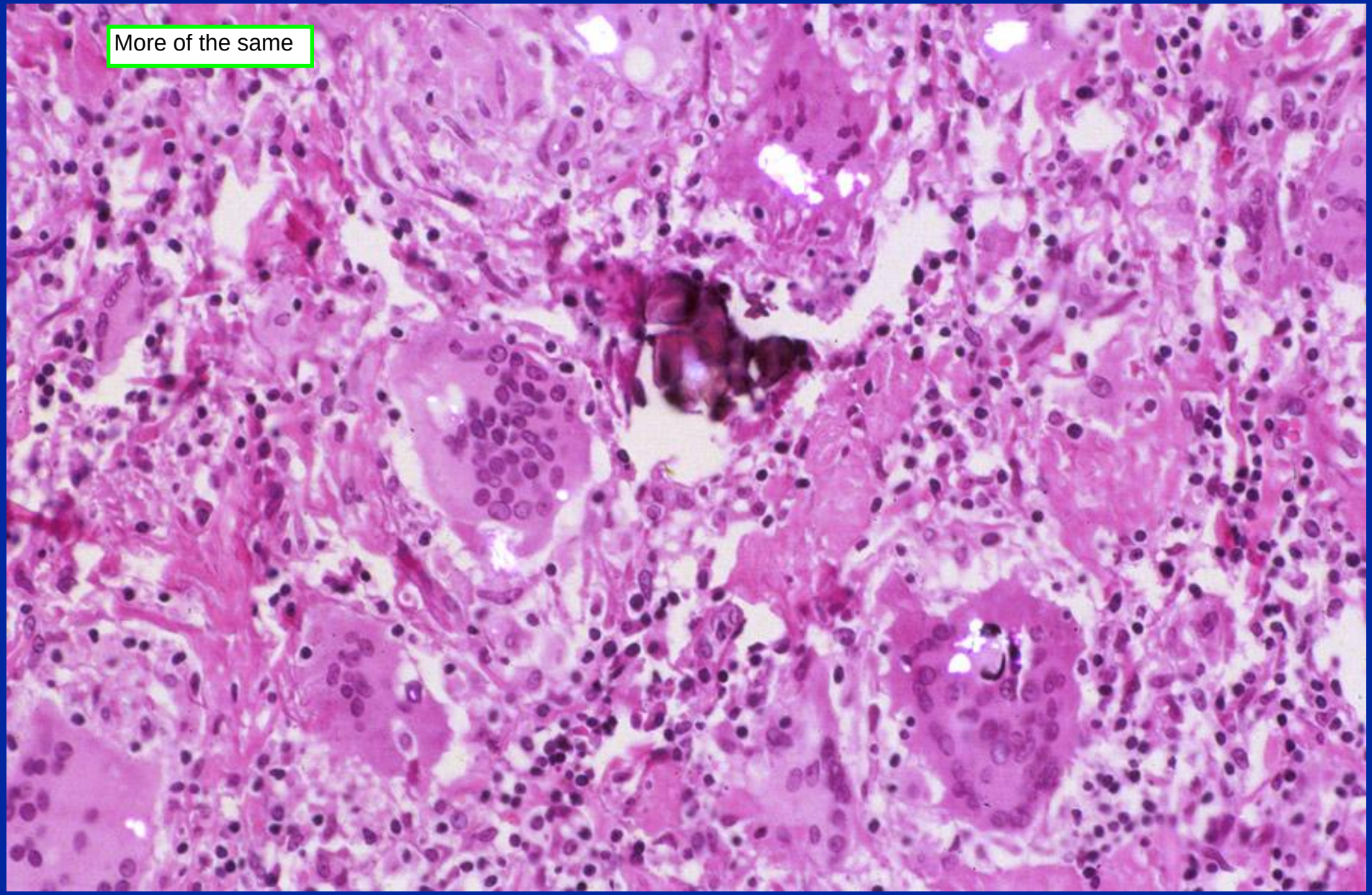
Few things besides sarcoidosis can cause wall-to-wall granulomas in lymph nodes



Appreciate granulomas in wall of airway cross-section




Ex of Schaumann body calcification. These are found in other pathologies besides sarcoidosis (like berylliosis and hypersensitivity pneumonitis)
Epithelioid cell
Multinucleate giant cells

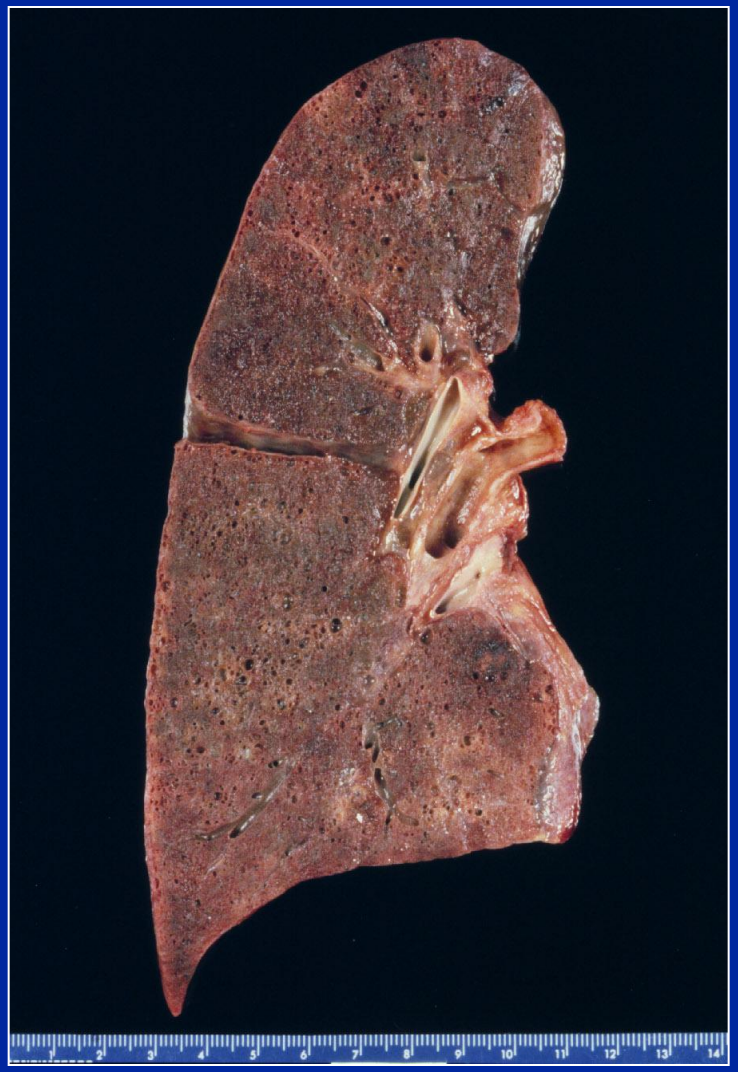

More of the same

Idiopathic pulmonary hemosiderosis

- **Disease of children and young adults characterized by anemia, hemoptysis and pulmonary infiltrates**
- **Pathology features injury to alveolar epithelium and interstitial fibrosis in addition to varying degrees and ages of intraalveolar hemorrhage**
- **Not associated with anti-BM AB's**

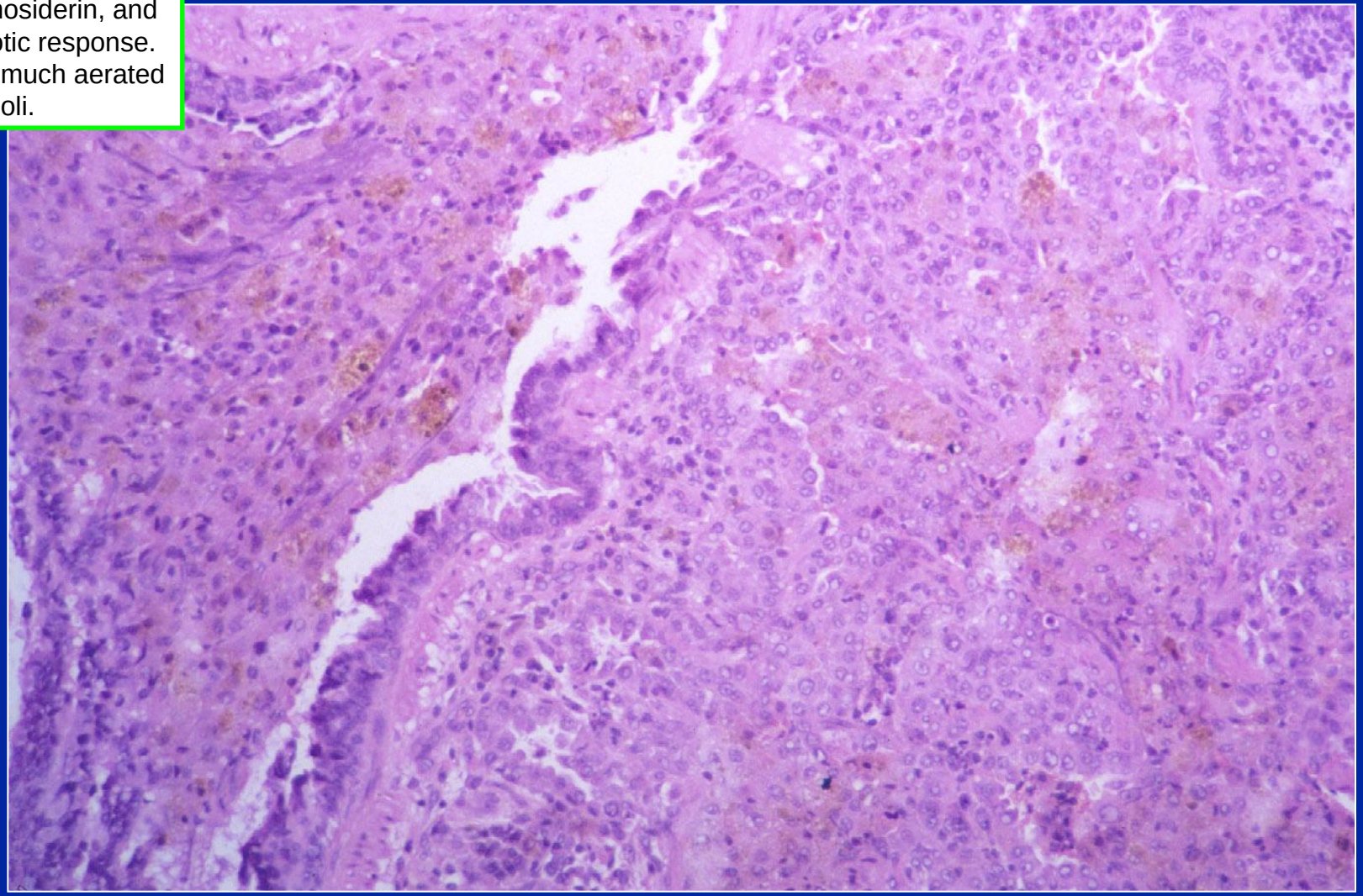
Extravasated blood is good at causing fibrosis, such as during hemothorax due to trauma

Anti-basement membrane antibodies, such as Goodpastures

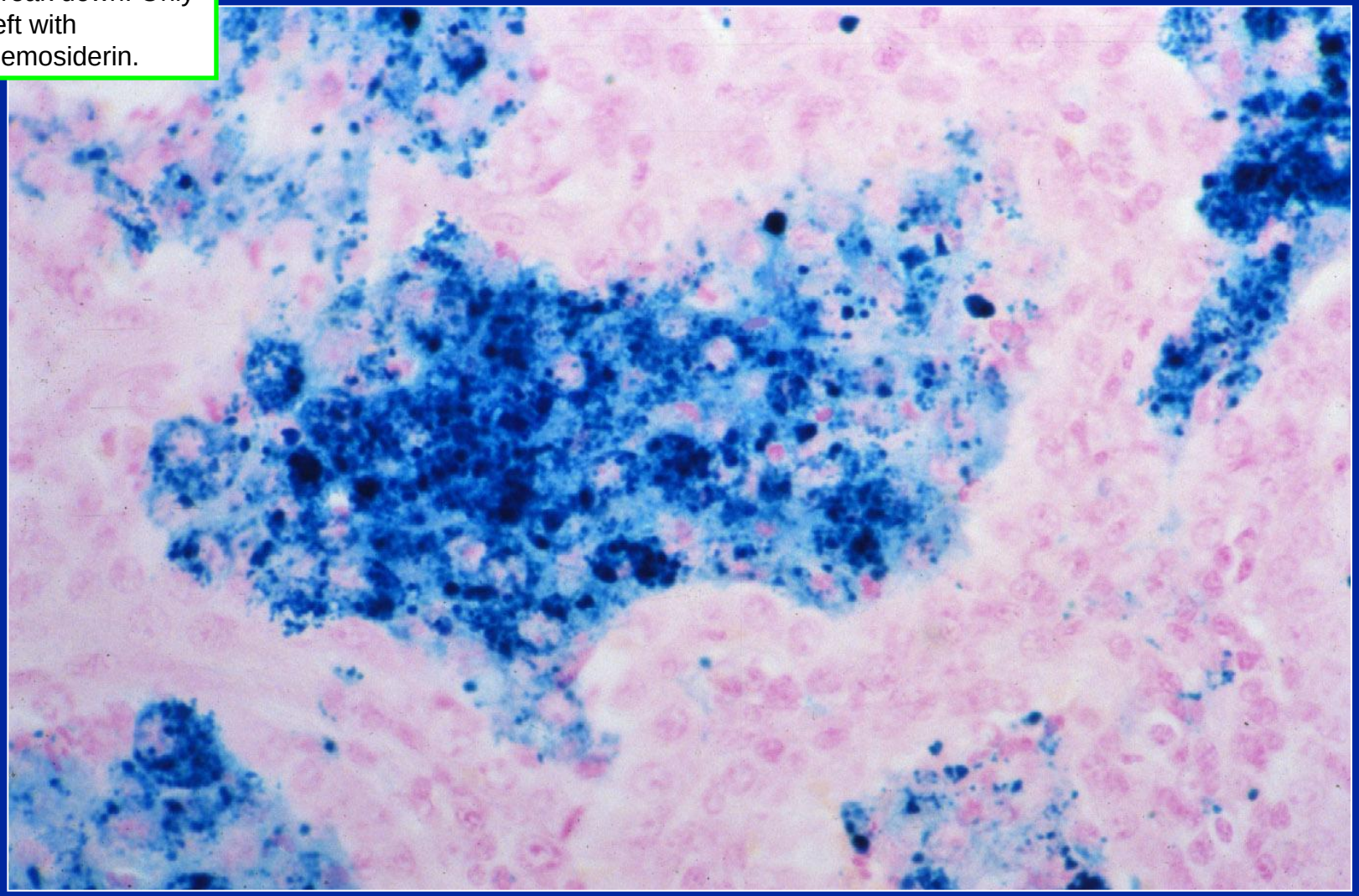


Brick red discoloration due to extravasated blood ending up in alveolar spaces

Not a lot of aerated lung tissue... mostly old blood, hemosiderin, and fibrotic response. Not much aerated alveoli.



Pearls Iron stain. Erythrocytes (source of iron) break down. Only left with hemosiderin.



Read slide

ILD RELATED TO CIGARETTE SMOKING

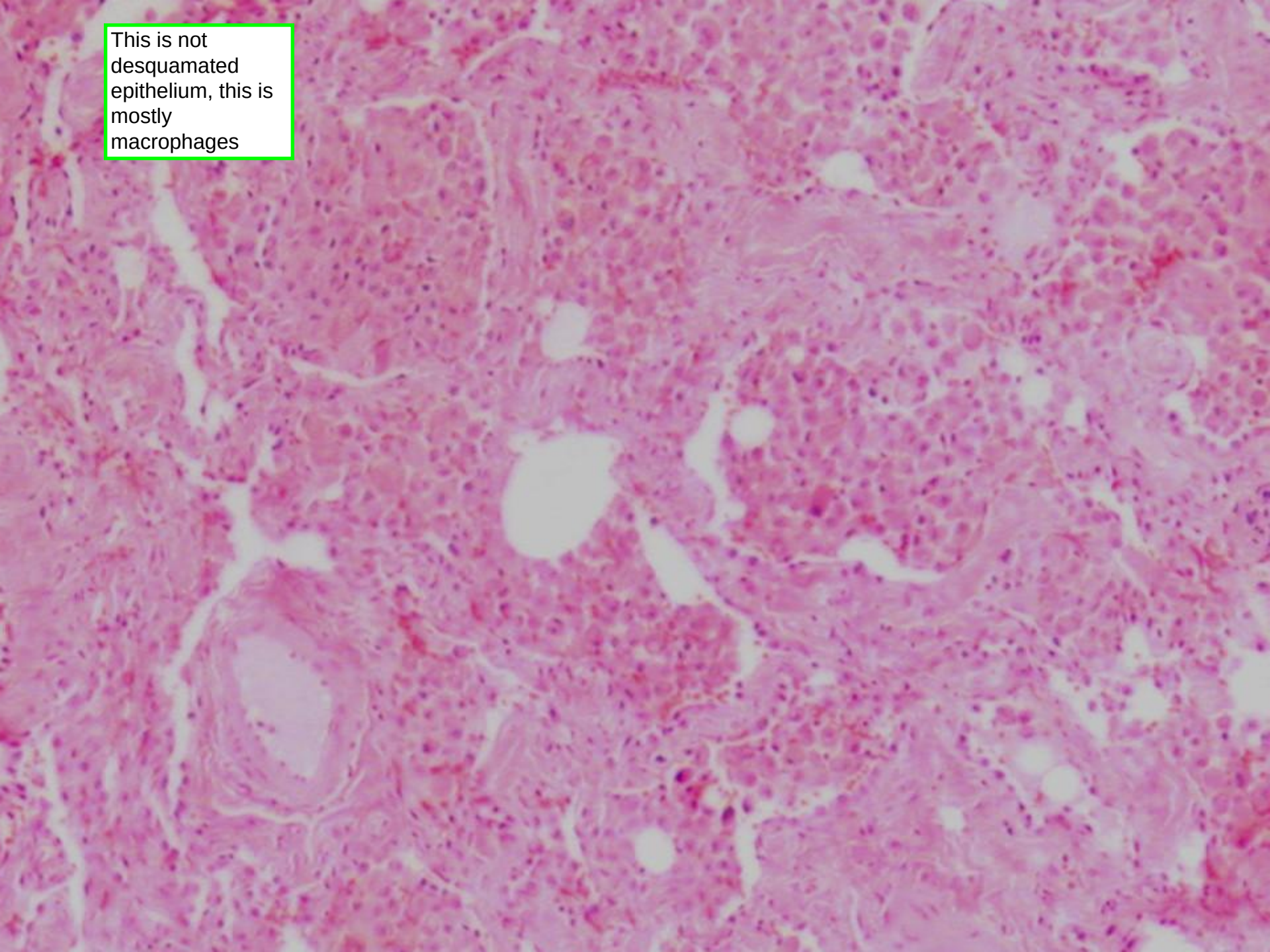
- Desquamative interstitial pneumonia (D.I.P.)
- Pulmonary Langerhans cell histiocytosis (Eosinophilic granuloma)
- Respiratory bronchiolitis associated interstitial lung disease (R.B.I.L.D.)

Poor term. It is not desquamative or interstitial.

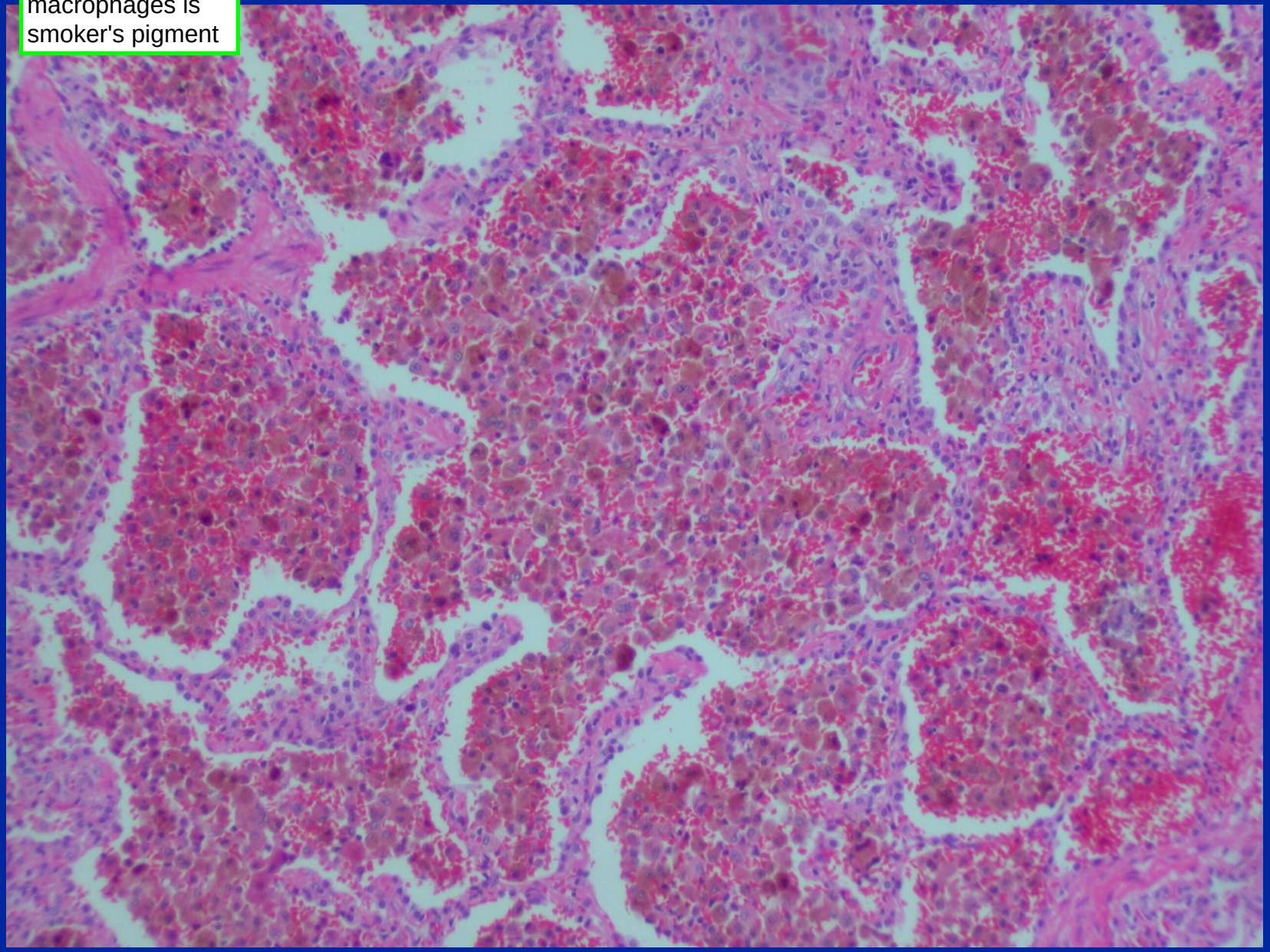
DESQUAMATIVE INTERSTITIAL PNEUMONIA

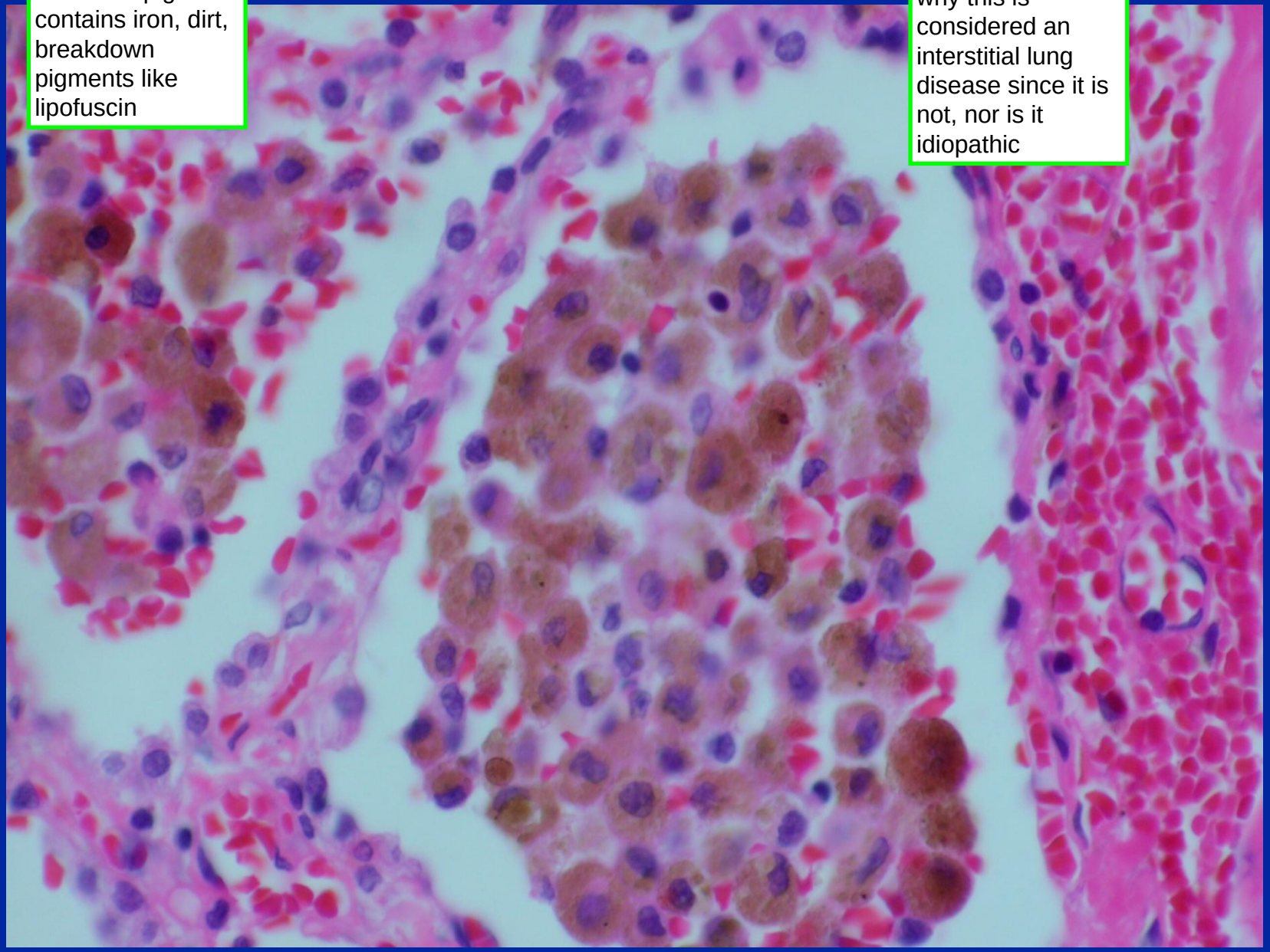
(D.I.P.)

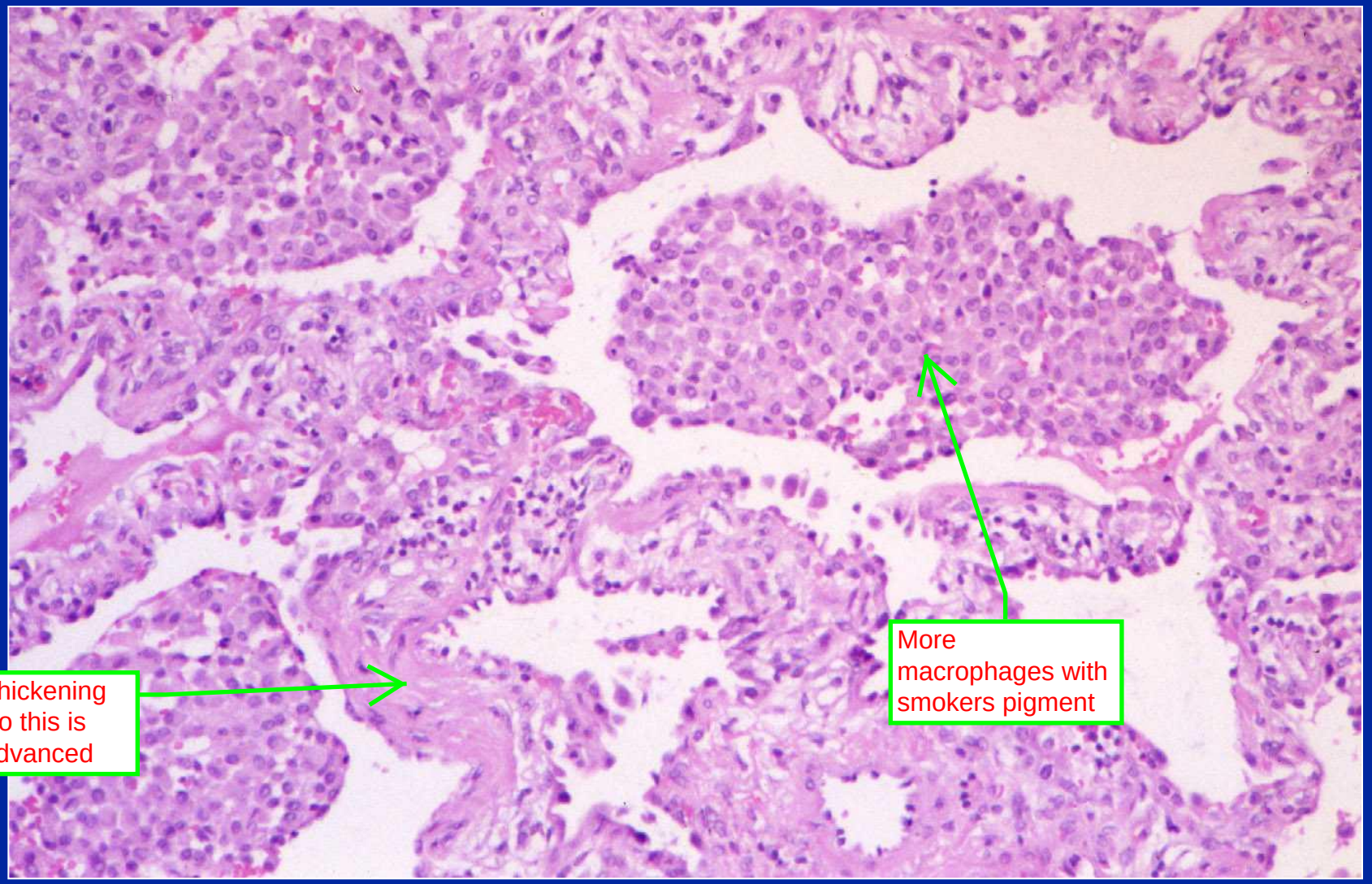
Desquamative means when epithelium sloughs


This is not desquamated epithelium, this is mostly macrophages

Brown tinge to macrophages is smoker's pigment



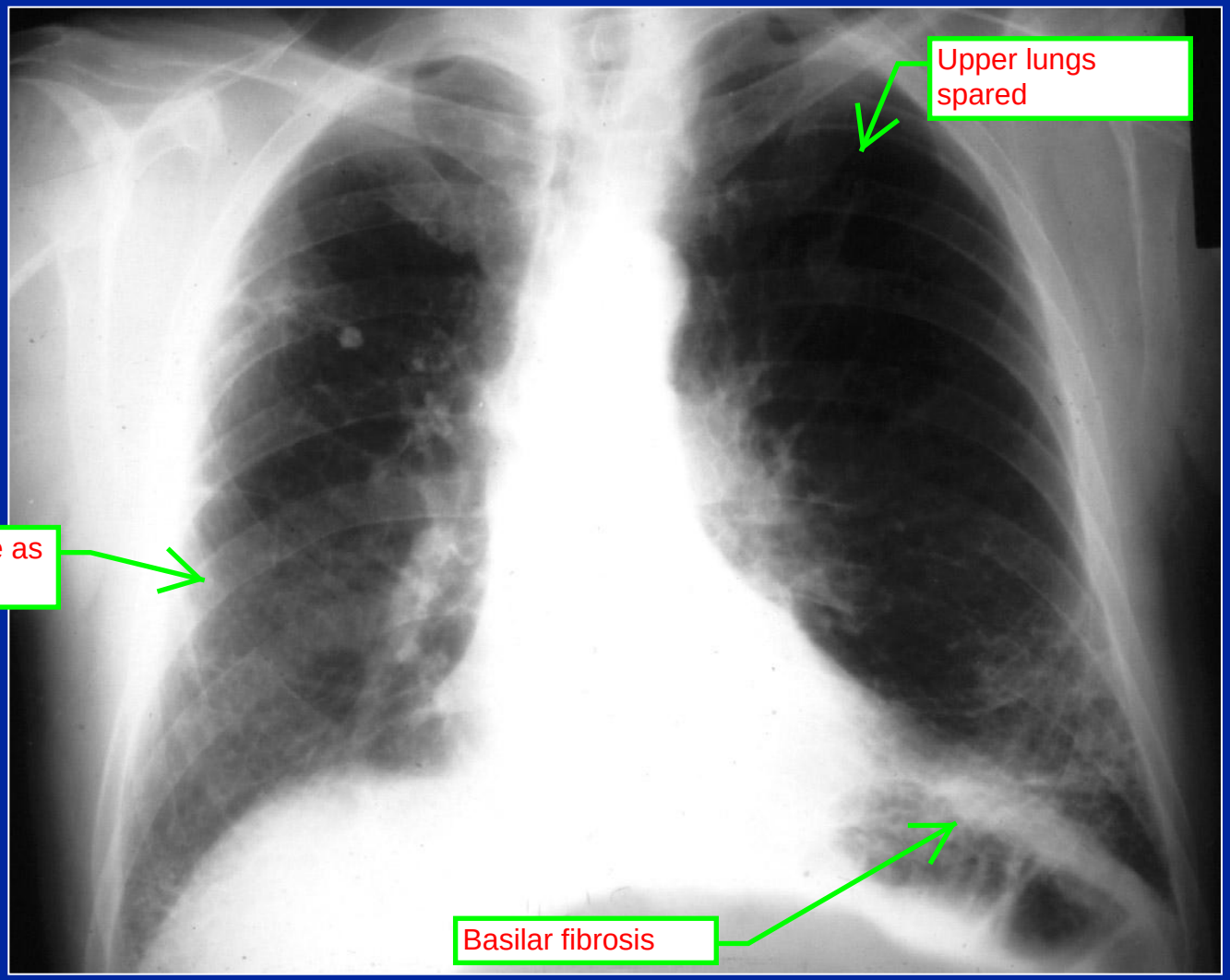

Smoker's pigment contains iron, dirt, breakdown pigments like lipofuscin
He has no idea why this is considered an interstitial lung disease since it is not, nor is it idiopathic


Some thickening of CT so this is more advanced
More macrophages with smokers pigment

COLLAGEN VASCULAR DISORDER RELATED ILD

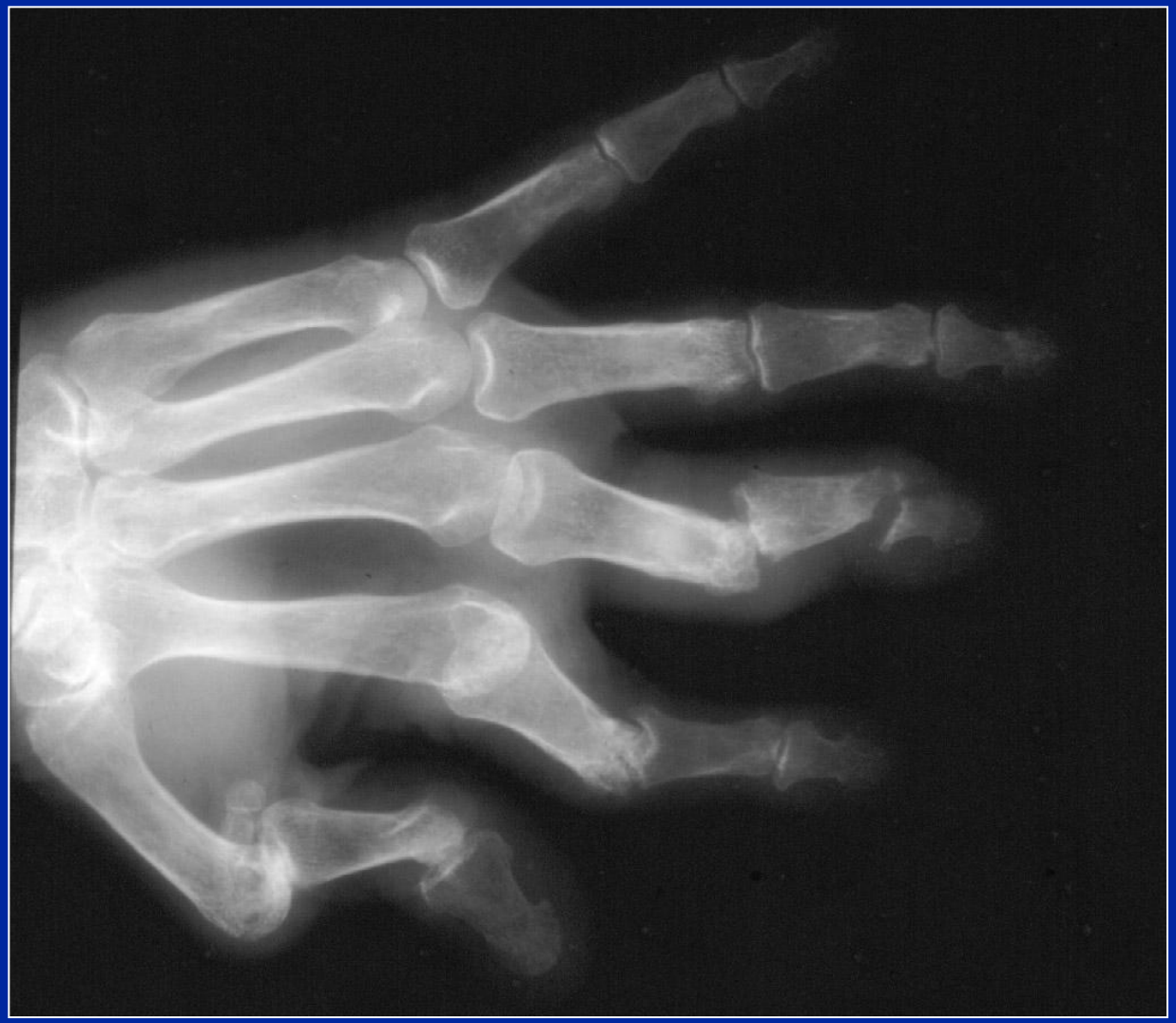
- **Rheumatoid arthritis**
- **Scleroderma**
- **Systemic lupus erythematosus**
- **Sjogren's syndrome**
- **Polymyositis/dermatomyositis**
- **Mixed connective tissue disorder**

All of the previous diseases are seen both idiopathically and with systemic disorders like these. Often SOB that leads them to Dr visit

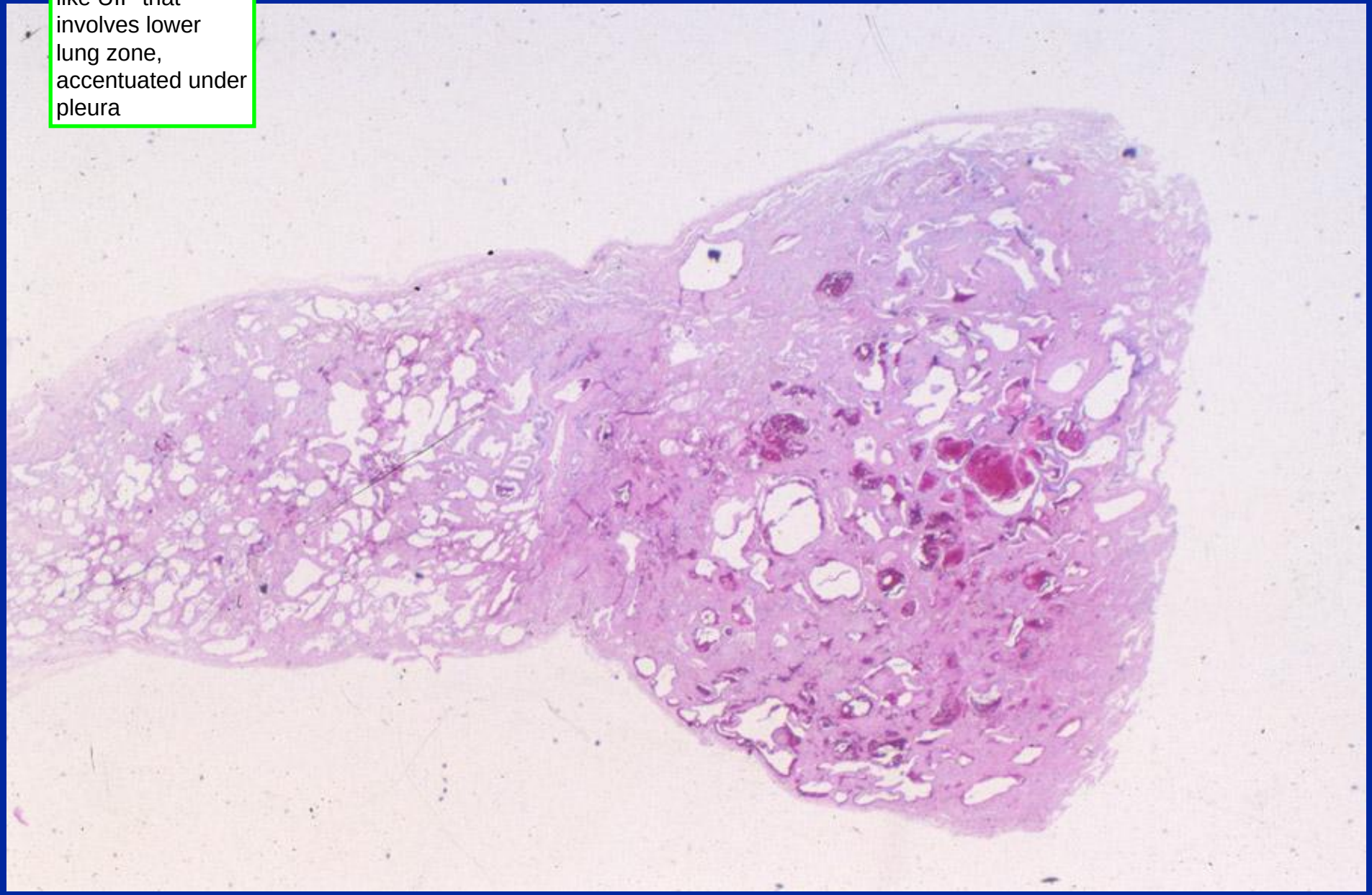


Maybe it's UID...

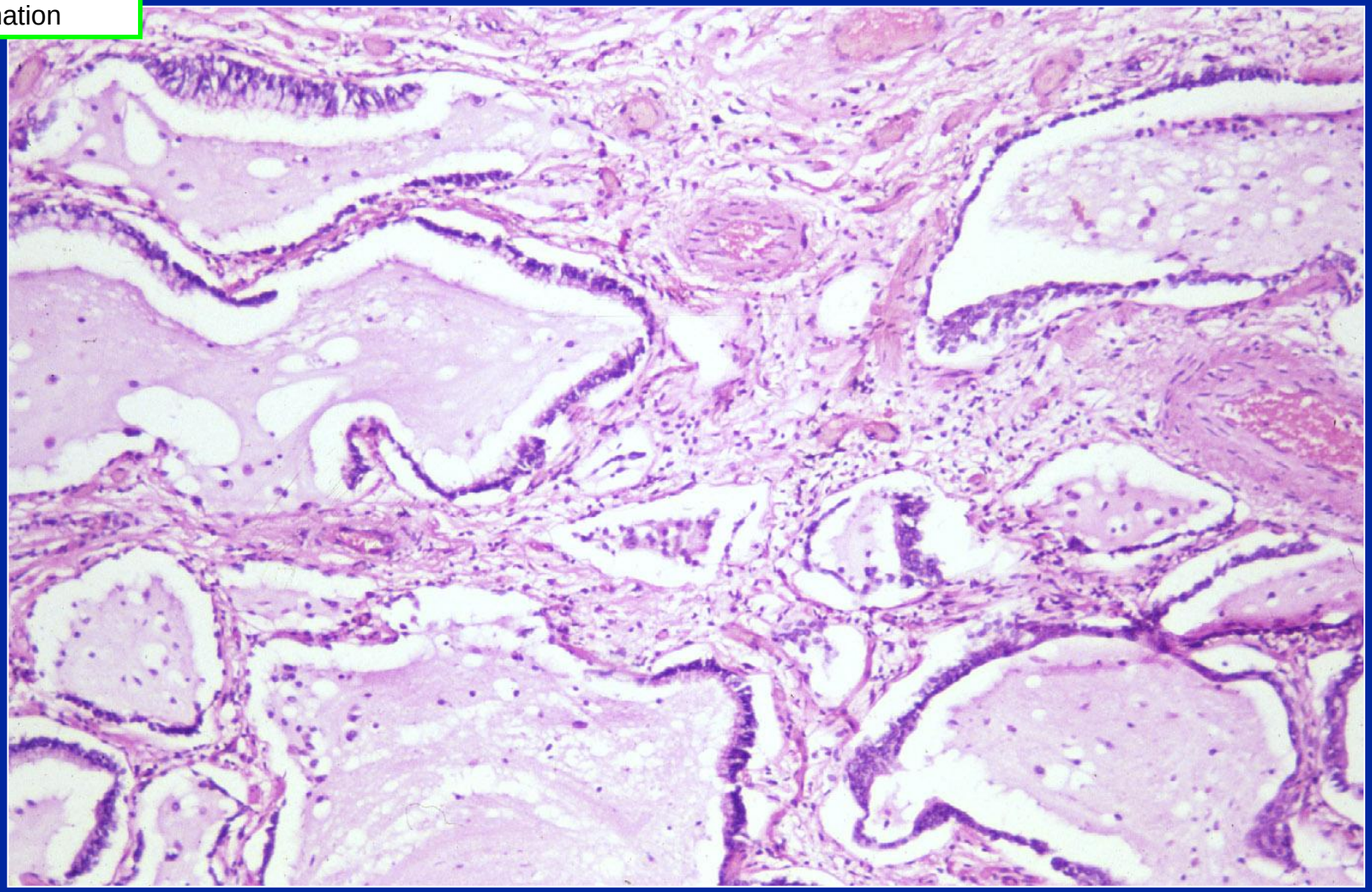
... But there's also swan-neck deformities and ulnar deviation characteristic of rheumatoid arthritis



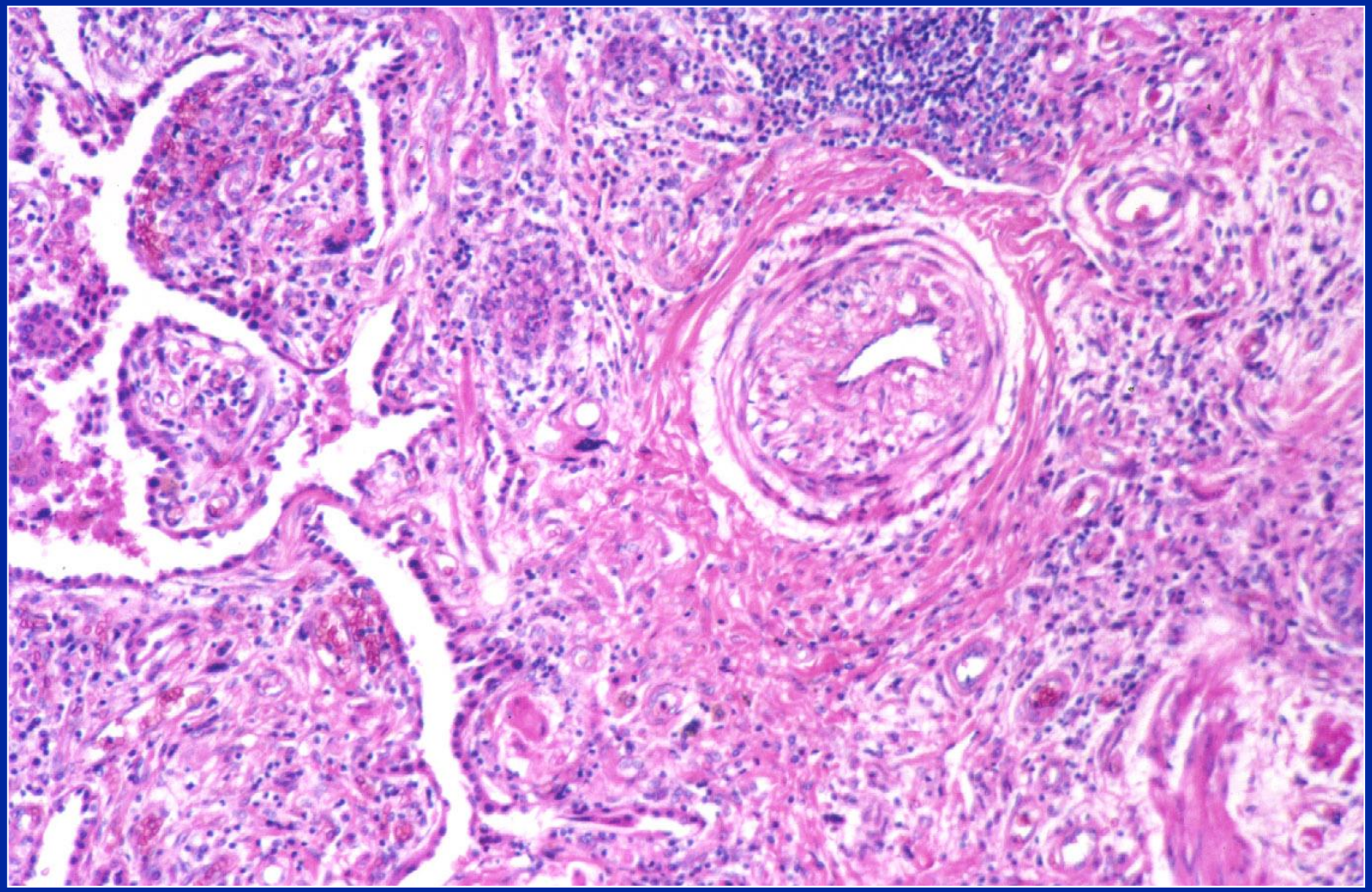
...back to looking like UIP that involves lower lung zone, accentuated under pleura



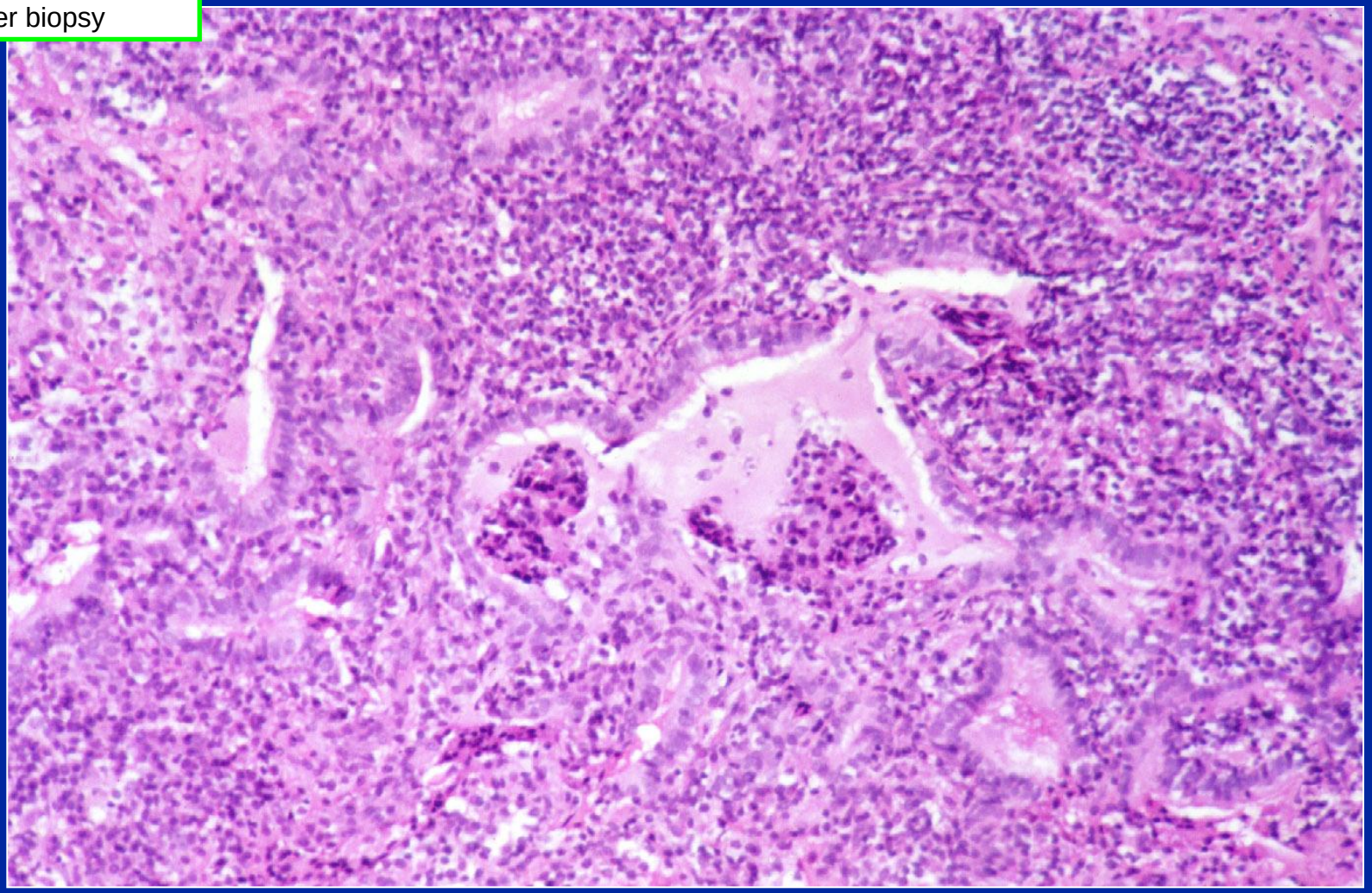
Can see bronchial metaplasia, mucinous debris, interstitial inflammation



More fibrosis and inflammation... very exciting



Often don't know if it is connective tissue disease or idiopathic until after biopsy




We Can Do It!