Respiratory System
RS

Dr. Ola Abu Al Karsaneh

Granulomatous Diseases

1. Sarcoidosis:

- A multisystem disease of unknown etiology.
- The diagnosis of sarcoidosis is always by the exclusion of other causes of granulomas.
- Bilateral hilar lymphadenopathy or lung involvement or both, visible on chest x-ray, is the major presenting feature.

Epidemiology:

- ✓ Affects both genders & all races.
- ✓ Affect adults **younger than 40 years** of age.
- ✓ Higher prevalence among **nonsmokers**.

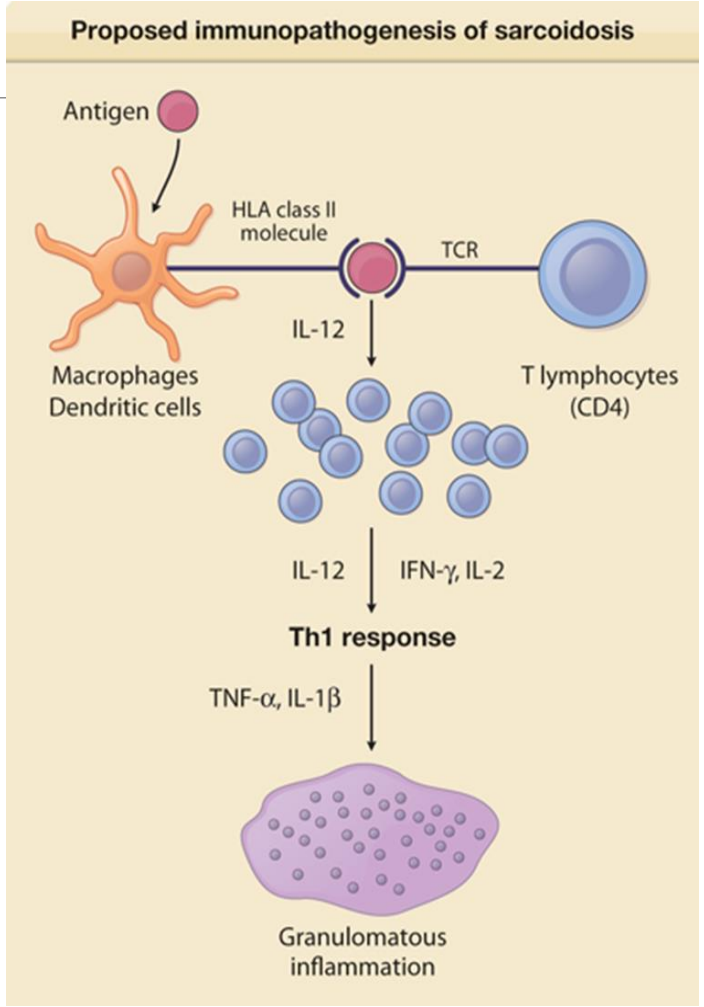
Etiology & pathogenesis:

- It is a disease of disordered **immune regulation** in **genetically** predisposed individuals exposed to certain **environmental agents.**

- Development of a cell-mediated response to an unidentified antigen. The process is driven by **CD4+ helper T cells,** which produce cytokines causing T cell proliferation and macrophage activation

- Polyclonal **hypergammaglobulinemia.**

- After lung transplantation, sarcoidosis **recurs in the new lungs in at least one-third of patients.**



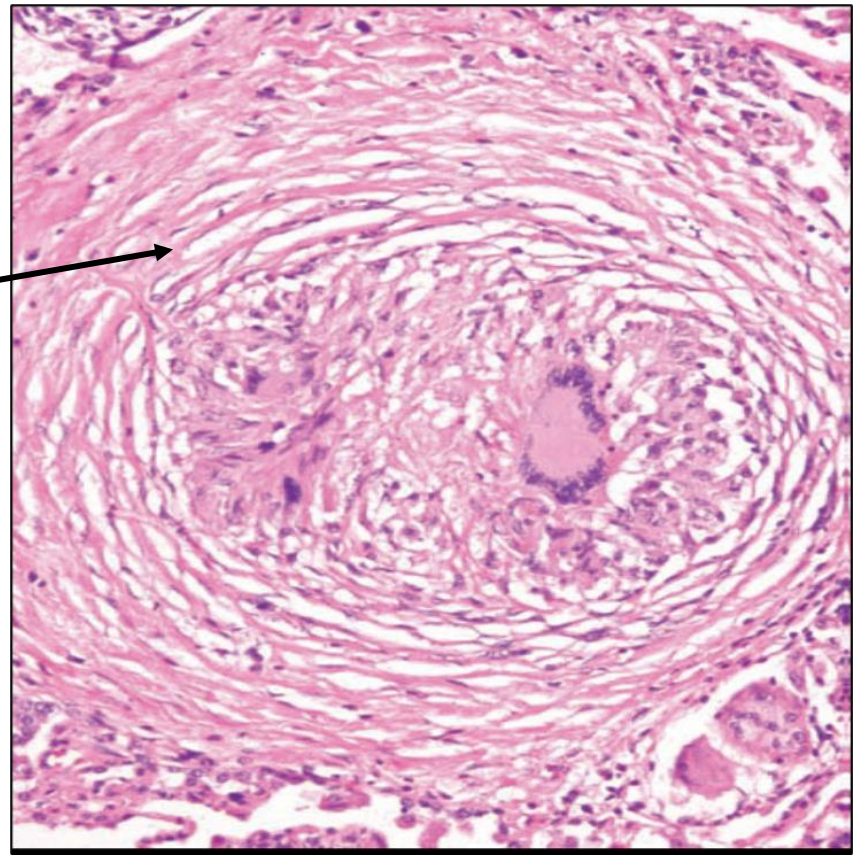
Clinical Features

- Many are asymptomatic, discovered on routine chest film
- Or a gradual appearance of respiratory symptoms (SOB, cough)
- Fever, fatigue, night sweats & anorexia.
- **Cutaneous lesions: Raised, red, tender nodules on the anterior aspects of the legs**
- Spleen, liver, BM: often involved with/without organ enlargement.
- **Hypercalcemia** & hypercalciuria are common.
- **Ocular involvement** + Lacrimal Gland inflammation= SICCA Syndrome

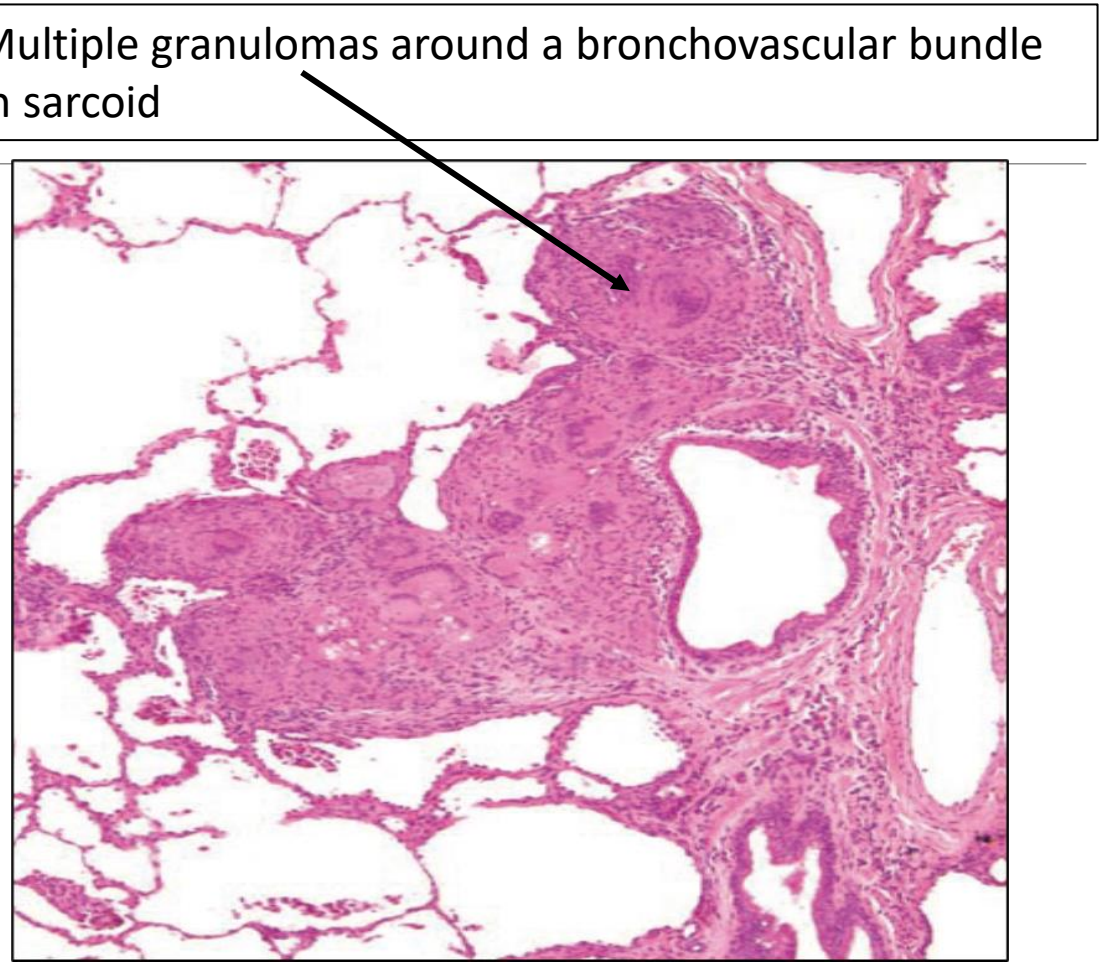
+ Parotid involvement = MIKULICZ Syndrome

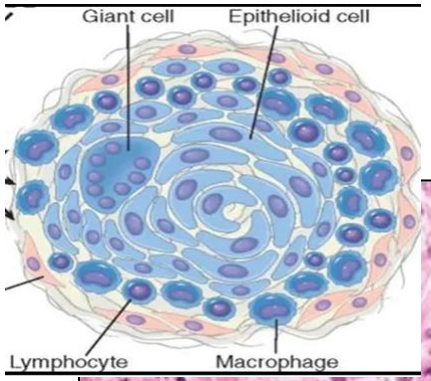
Morphology:

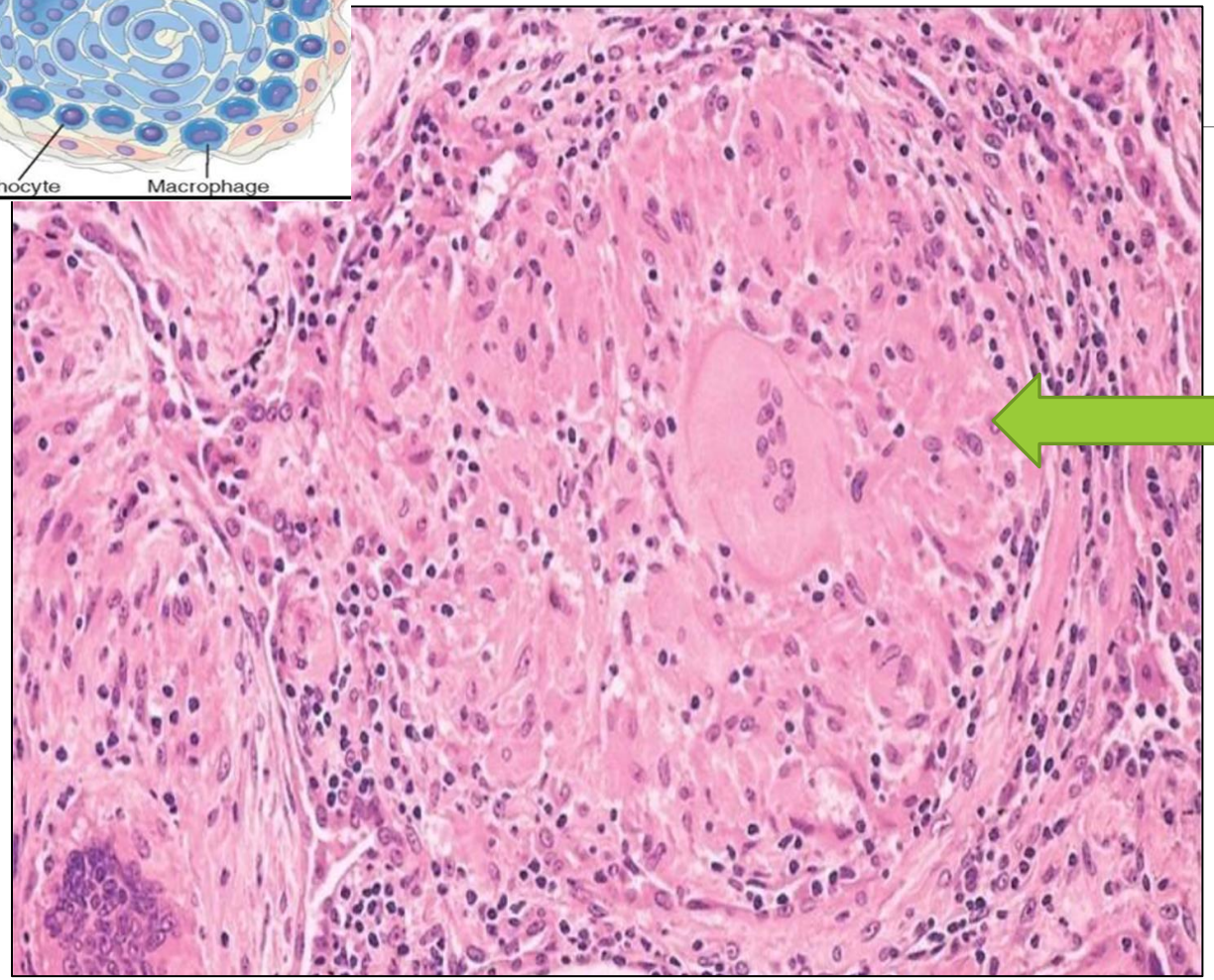
- **Non-caseating granulomas** ➡ **c**ompact collection of epithelioid cells rimmed by an outer zone of T cells and multinucleated giant cells.
- **Fine concentric layers of hyaline collagen** present peripheral to granuloma
- Interstitial **inflammation is UNcommon**
- Two other features seen in granuloma (not specific):
  - Schaumann bodies are laminated concretions composed of calcium & protein.
  - Asteroid bodies: stellate inclusions.

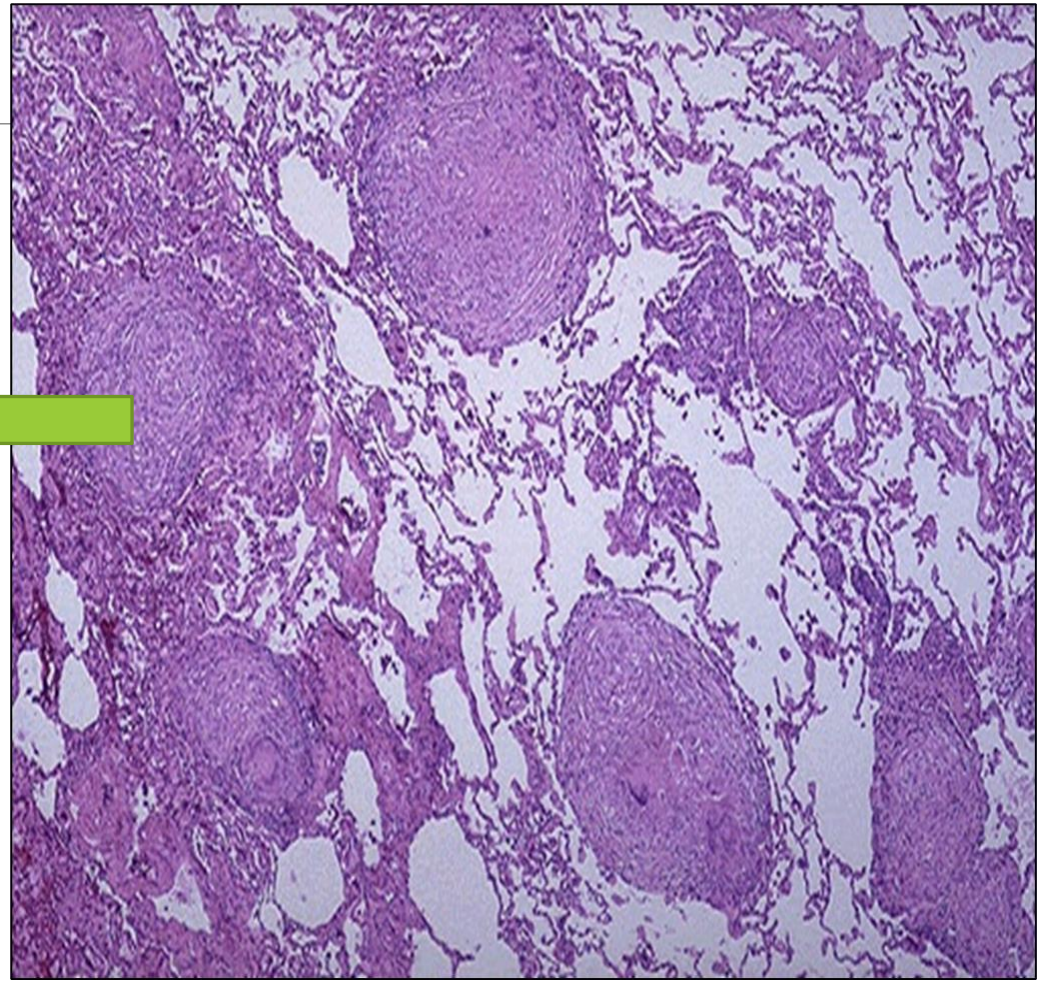


- The lungs are involved in 90% of patients. The granulomas frequently involve the interstitium in the connective tissue around **bronchioles** & **pulmonary venules & in the pleura** i.e. **lymphangitic distribution.**
- Intra thoracic & paratracheal lymph nodes are enlarged

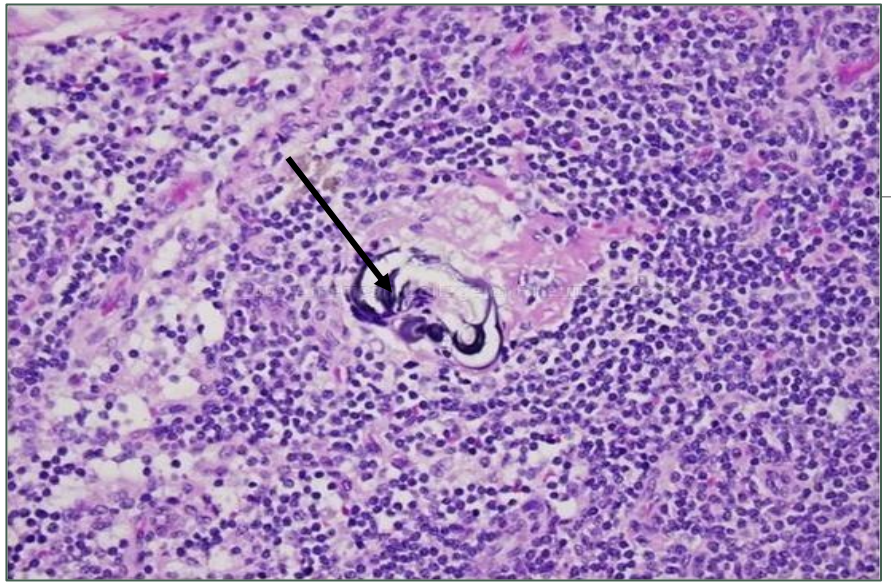


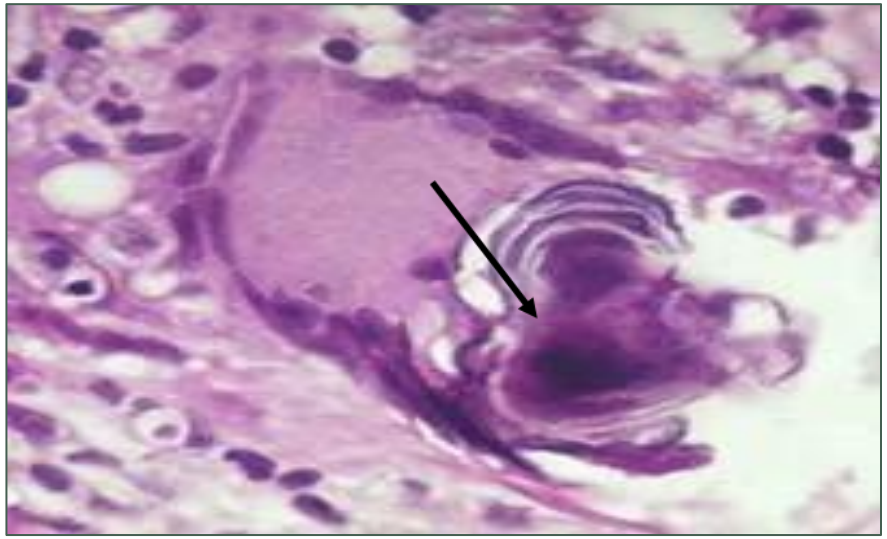

Giant cell
Epithelioid cell
Lymphocyte
Macrophage



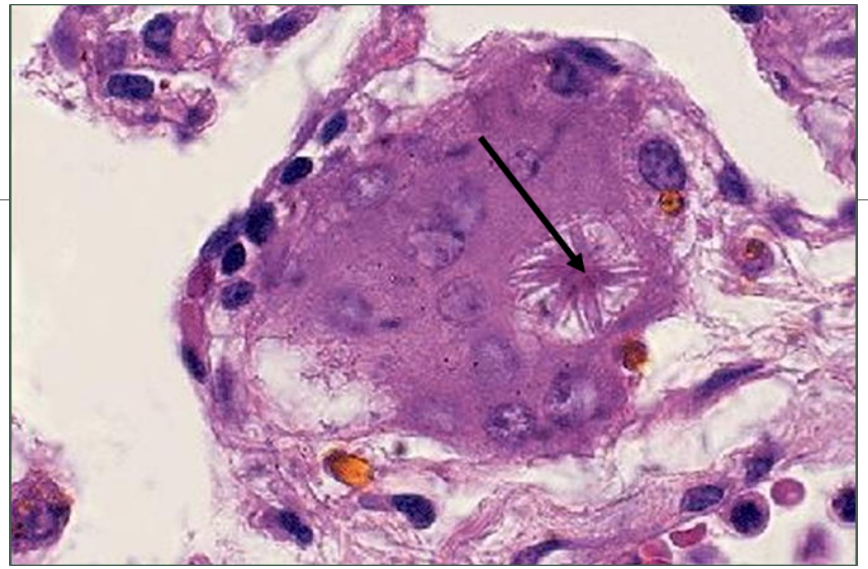


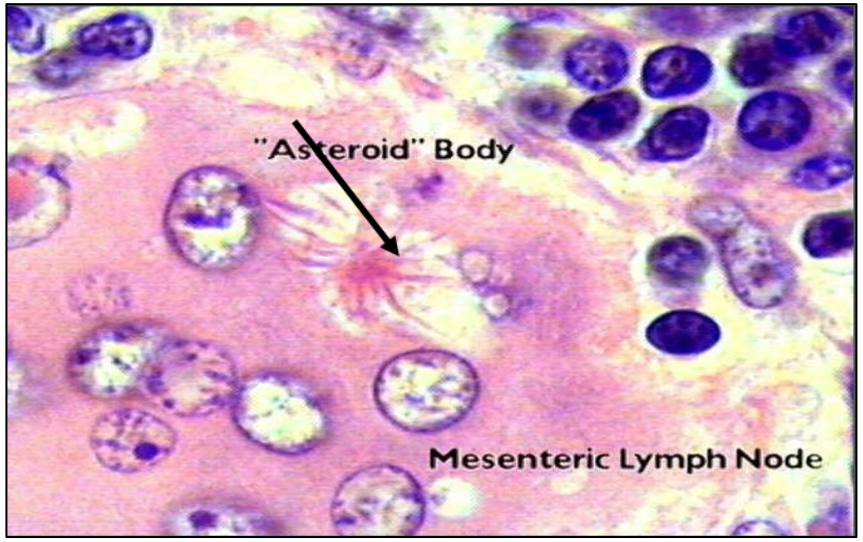
Schaumann Bodies





Asteroid Bodies





2- Hypersensitivity Pneumonitis :

- Is an immunologically mediated inflammatory lung disease that primarily affects the **alveoli** and **interstitium** and is often called ***allergic alveolitis***.

- Results from sensitivity to inhaled organic and sometimes inorganic antigens

- Manifests predominantly as a **restrictive l**ung disease.

- The responsible occupational and household exposures are diverse, but the syndromes share common clinical and pathologic findings.

An immunologically mediated disease, evidence:

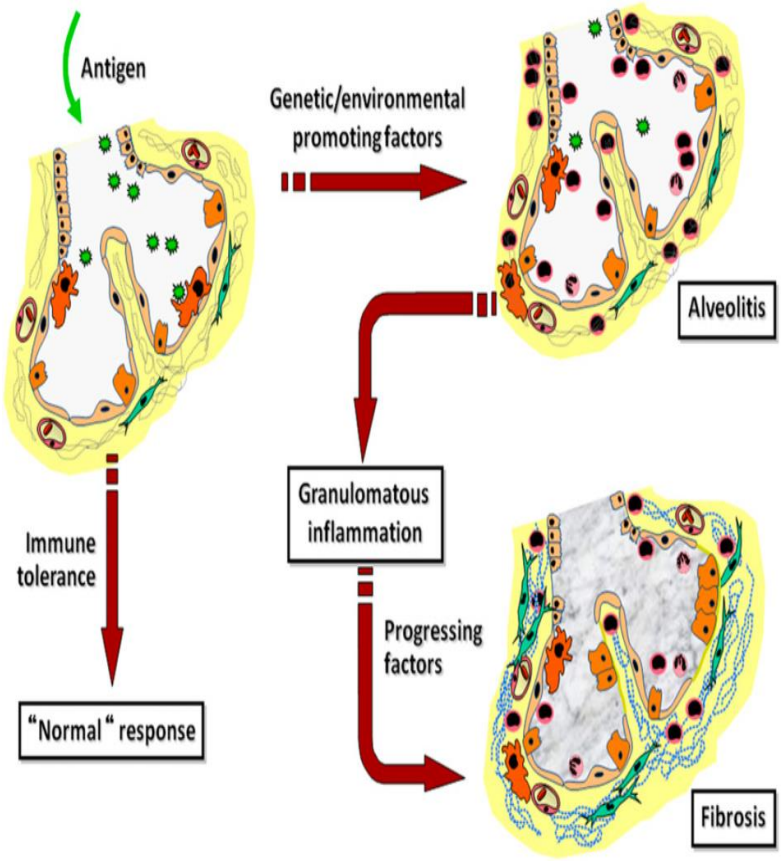
- Bronchoalveolar lavage shows increased numbers of T lymphocytes.
- Most affected patients have specific antibodies against the offending antigen in their serum (type **III reaction**).
- Complement and immunoglobulins have been demonstrated within vessel walls by immunofluorescence (**type III reaction**).
- Noncaseating granulomas are found in the lungs of two-thirds of affected patients (**type IV reaction**).

Clinical Features

- Presentation depends on the duration & intensity of exposure to the antigen :
  - Acute
  - Subacute
  - Chronic

Acute: direct irritant effect: fever, cough, dyspnea, and constitutional Sx and symptoms arising 4 to 8 hours after exposure.

Chronic: insidious onset of cough, dyspnea, malaise, and weight loss.



Morphology:

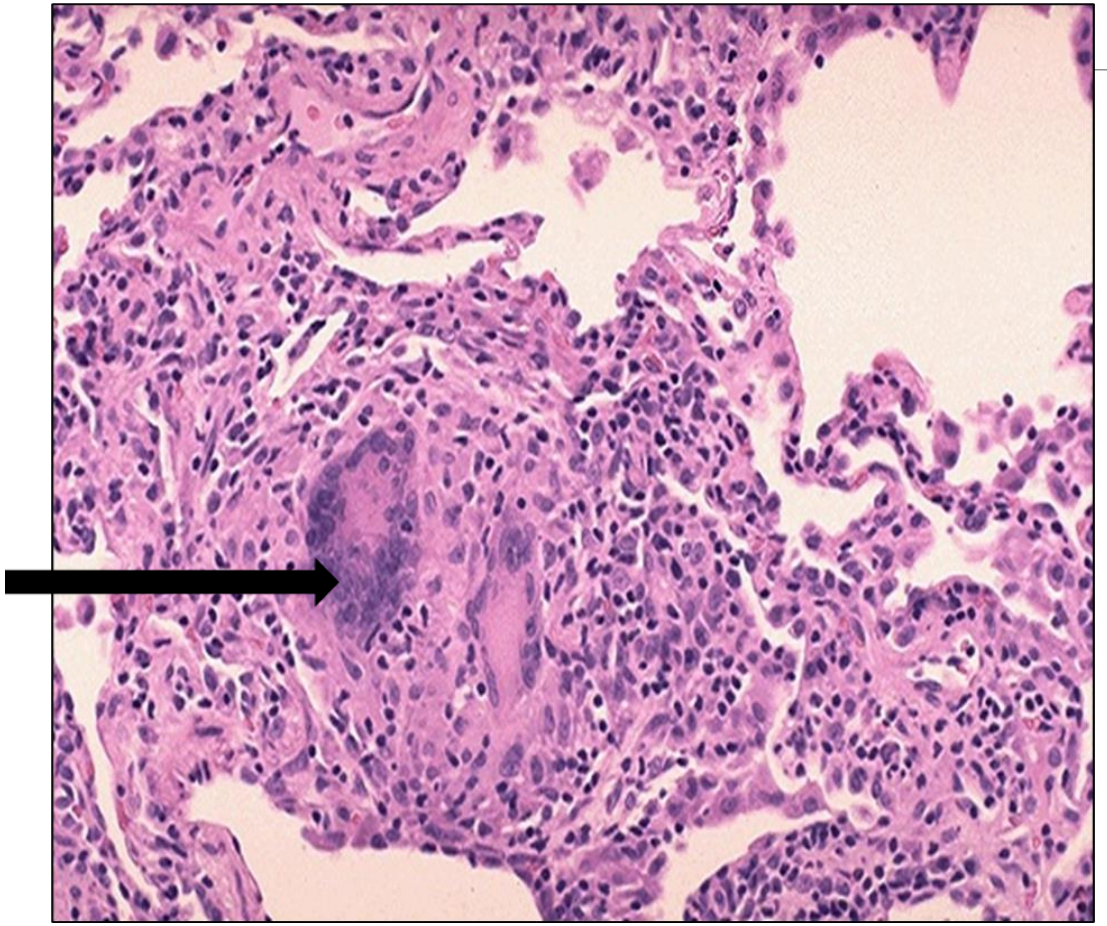
Histologic changes are characteristically centered on bronchioles **(Bronchiolocentric)**:

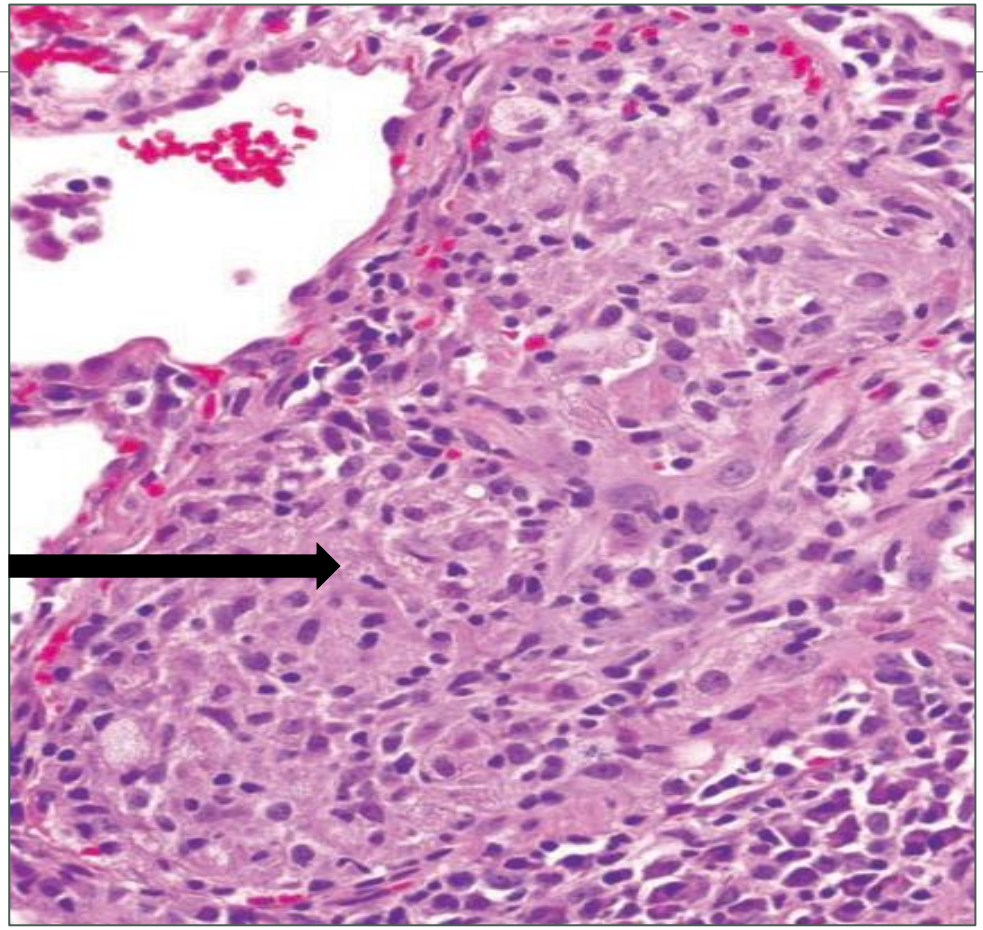
(1) Interstitial **pneumonitis**, consisting primarily of lymphocytes, plasma cells, and macrophages (eosinophils are rare)

(2) "Loose," poorly formed interstitial **noncaseating granulomas** in two-thirds of patients.

(3) Chronic inflammation may involve walls of bronchioles (**bronchiolitis**)

- Interstitial fibrosis (in chronic cases).





Smoking –Related Interstitial Diseases

1. Desquamative Interstitial Pneumonia(DIP)

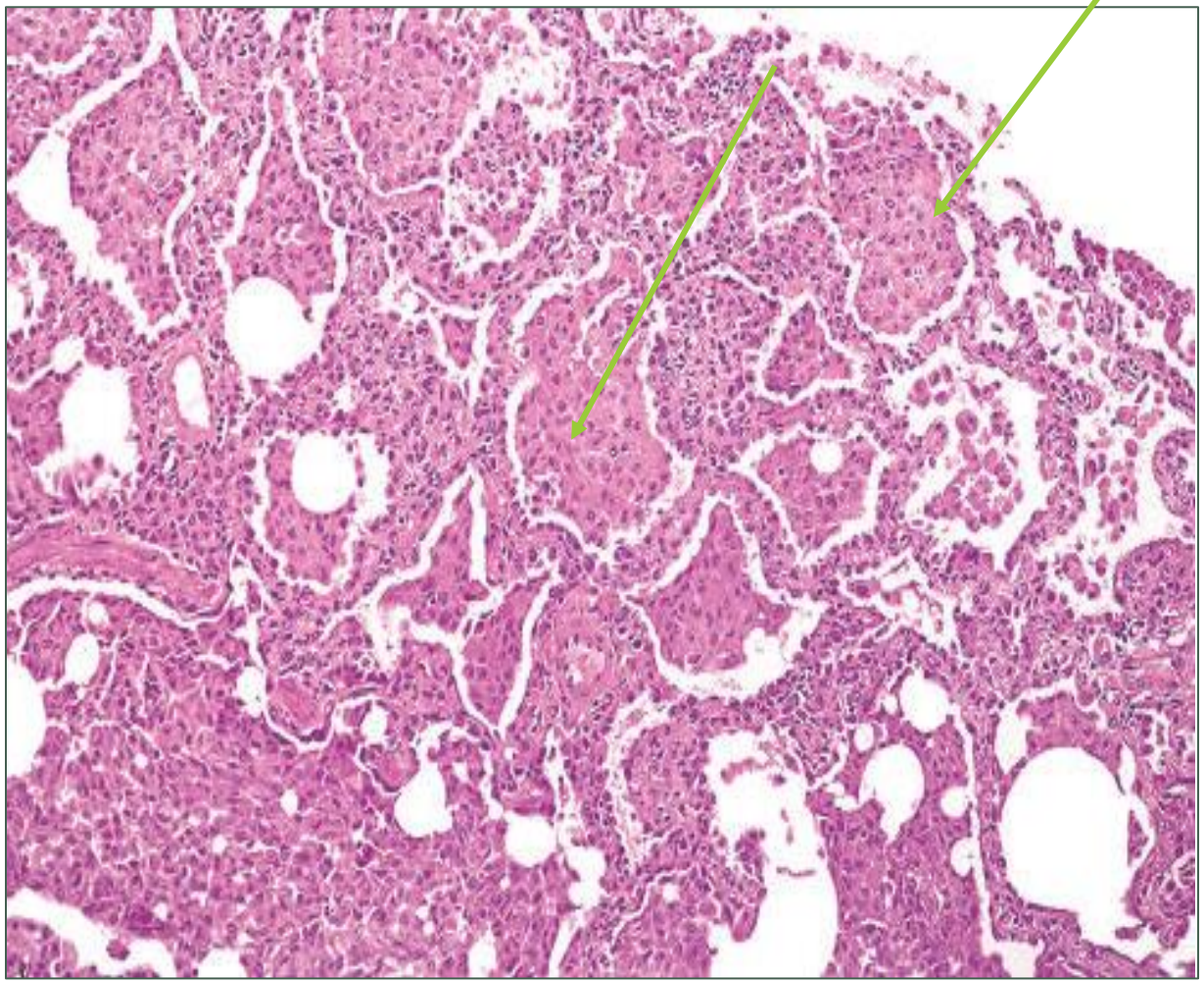
- In 4^{th} to 5^{th} decades, M>F.
- Dyspnea and dry cough.
- PFT: shows a **mild restrictive** abnormality.

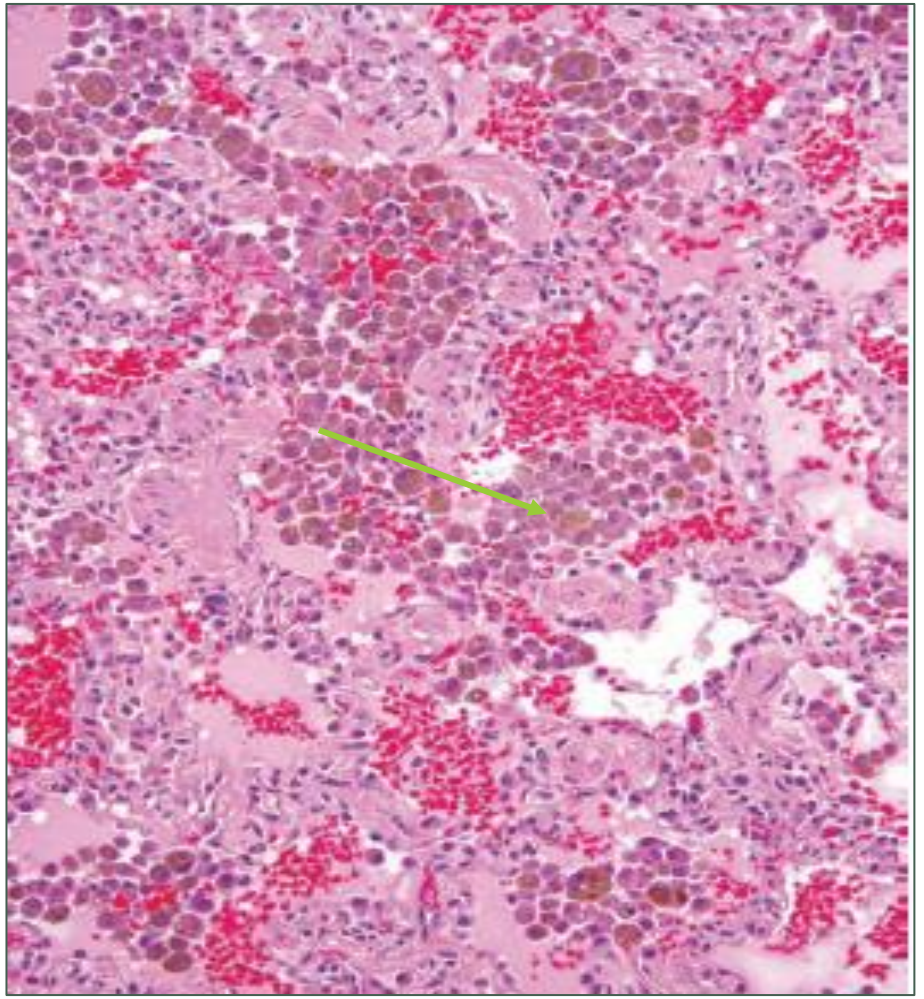
Morphology:

- **Widespread** process
- Accumulation of large numbers of **macrophages** containing dusty-brown pigment ***(smoker's macrophages)*** in the air spaces.
- The alveolar septa are thickened by a sparse inflammatory infiltrate.
-Interstitial fibrosis, when present, is mild.

❖ Overall

Good prognosis and an excellent response to steroids and smoking cessation,





2. Respiratory Bronchiolitis Associated Interstitial Lung Disease (RB-ILD)

- Clinically similar to DIP.

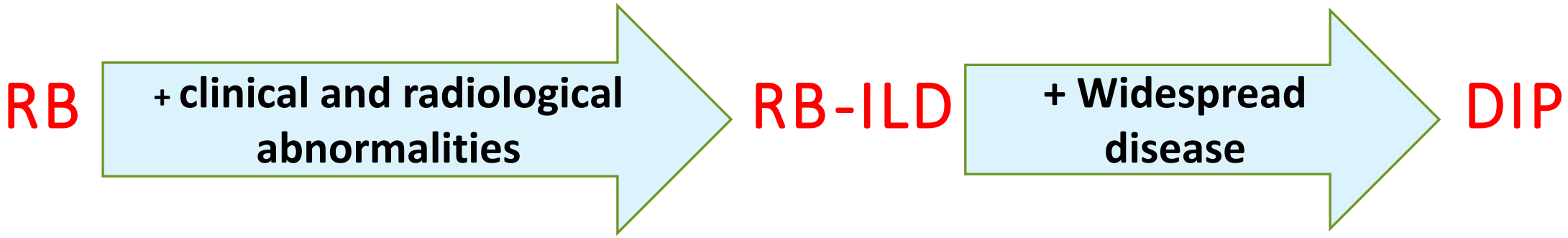
Morphology:

Respiratory bronchiolitis (RB) is a common lesion found in smokers characterized by the presence of pigmented intraluminal macrophages in a “bronchiolocentric” distribution.

- Mild peribronchiolar fibrosis is also seen.

- The changes are **patchy.**

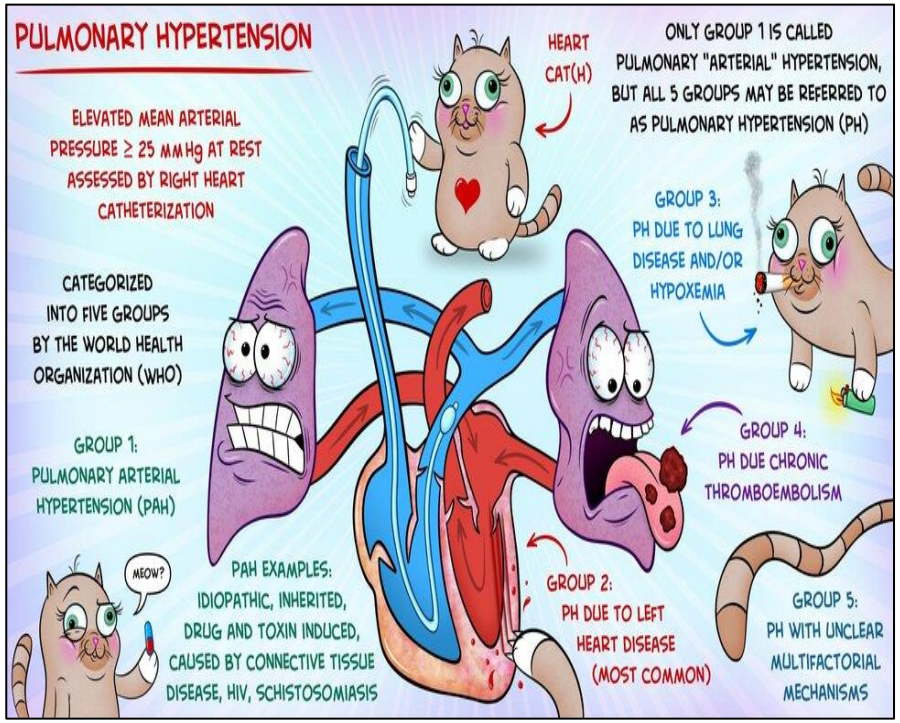
The term RB-ILD is used for patients who develop significant pulmonary symptoms, abnormal pulmonary function, and imaging abnormalities.


RB
+ clinical and radiological abnormalities
RB-ILD
+ Widespread disease
DIP

PULMONARY DISEASES OF VASCULAR ORIGIN

1. Pulmonary Hypertension:

- Normal pulmonary blood pressure is 1/8 of systemic blood pressure.
- Pulmonary hypertension is considered when the mean pulmonary pressure exceeds 1/4 the systemic blood pressure.



Causes of pulmonary hypertension:

1- Chronic obstructive or interstitial lung disease

2- Congenital or acquired heart diseases

3- Recurrent thrombo-emboli

4- Connective tissue disorders (as systemic sclerosis)

5- Primary or idiopathic pulmonary hypertension: when all the above causes are absent.

- **Rare cases are familial form due to autosomal dominant mode of inheritance.**

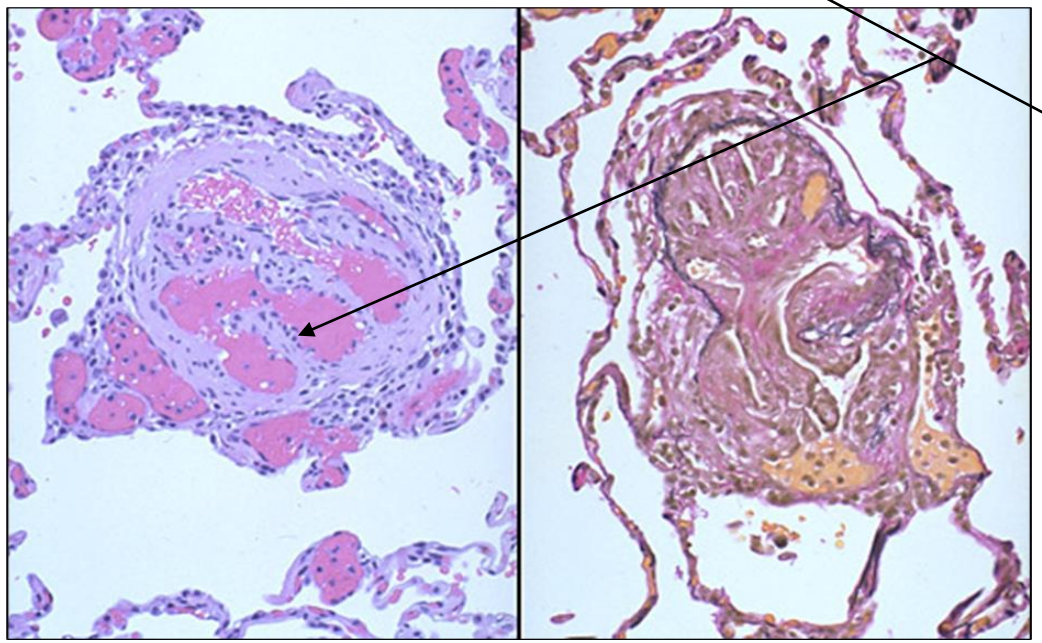
Morphology :

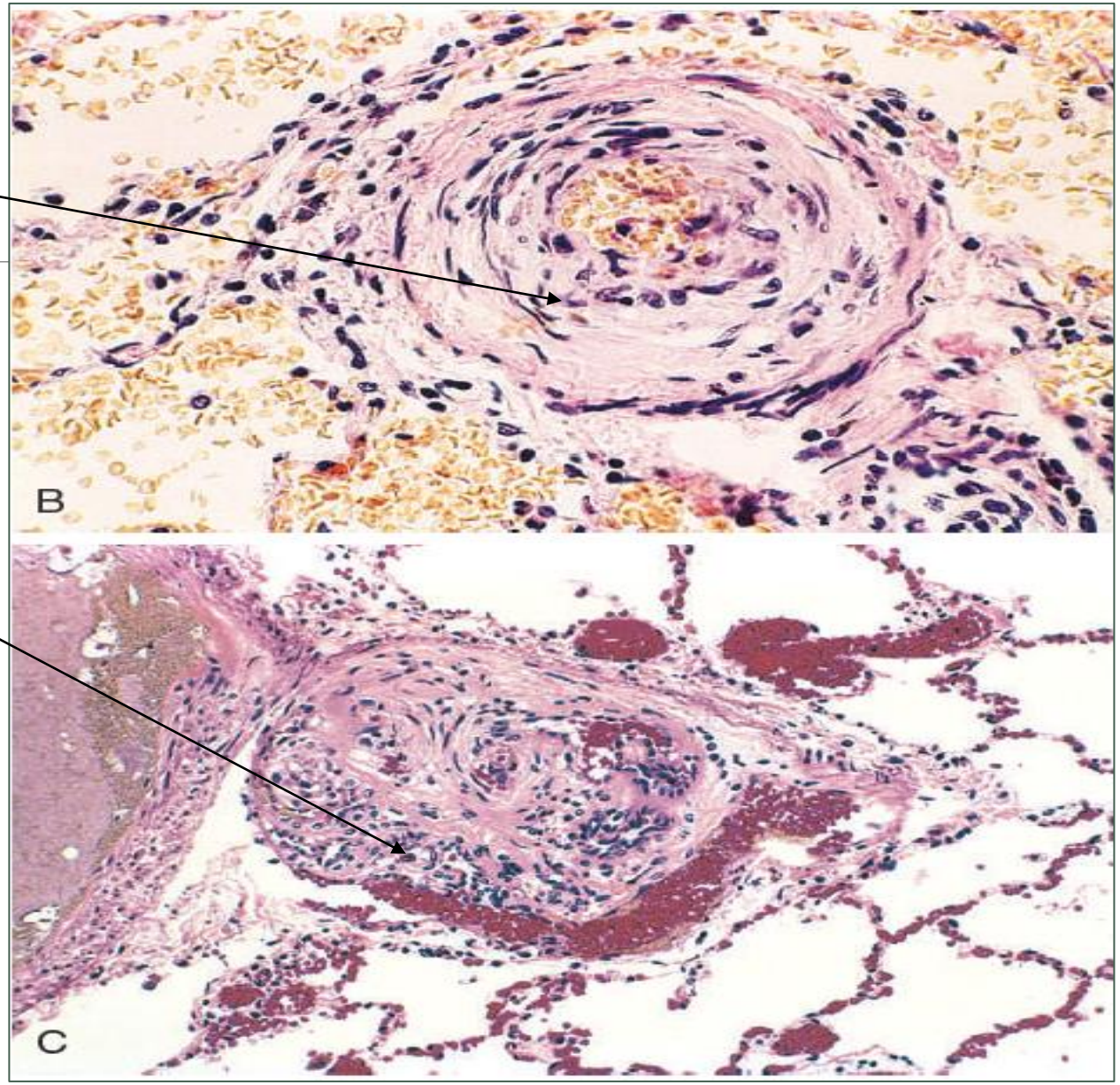
- All forms of pulmonary hypertension are associated with **medial hypertrophy of the pulmonary muscular and elastic arteries, pulmonary arterial atherosclerosis, and right ventricular hypertrophy**.

- The arterioles and small arteries are most prominently affected by **medial hypertrophy and intimal fibrosis**

- **An uncommon but characteristic pathologic change is the plexiform lesion (**a tuft of capillary formations producing a network, or web, that spans the lumen of a dilated, thin-walled, small artery).

(B)Marked medial hypertrophy.
(C) Plexiform lesion characteristic of advanced pulmonary hypertension was seen in small arteries.





2. Diffuse Alveolar Hemorrhage Syndromes

1. Good pasture syndrome:

- An **autoimmune** disease in which **lung and kidney** injury are caused by circulating autoantibodies against certain domains of **type IV collagen** in the basement membranes of renal glomeruli and pulmonary alveoli.

→ *Necrotizing hemorrhagic interstitial pneumonitis* and *rapidly progressive glomerulonephritis.*

- **M>F, in teens or twenties, in active smokers.**

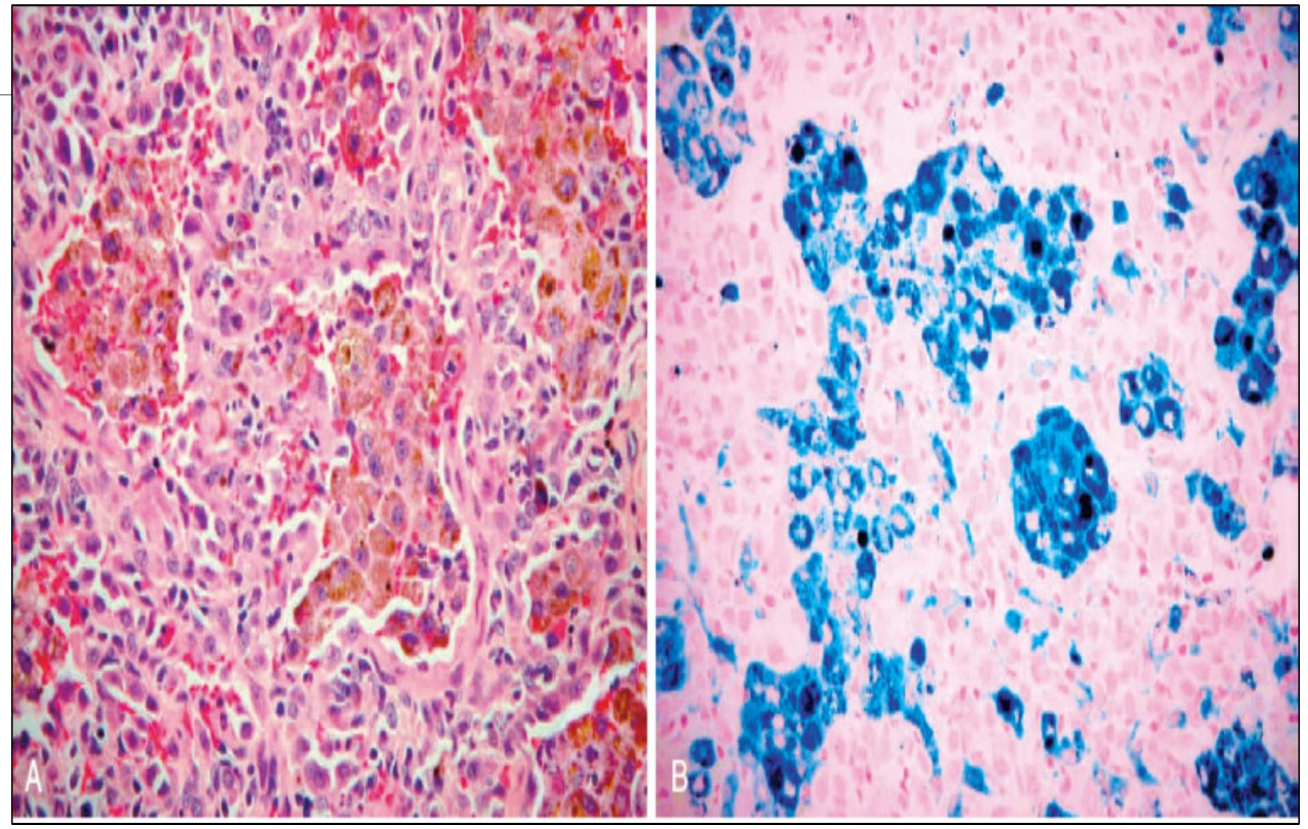
Morphology:

- The lungs are heavy with areas of red-consolidations.

Microscopically: -

1. Focal necrosis of alveolar walls with intraalveolar hemorrhage and hemosiderin.
2. Fibrous thickening of septa, and hypertrophic type II pneumocytes.

- **A linear pattern of immunoglobulin deposition in renal glomeruli.**



(B)Prussian blue stain: an iron stain that highlights the abundant intracellular hemosiderin

2. Granulomatosis and polyangiitis (GPA):

- Formerly called Wegener's granulomatosis, is one of the vasculitis.

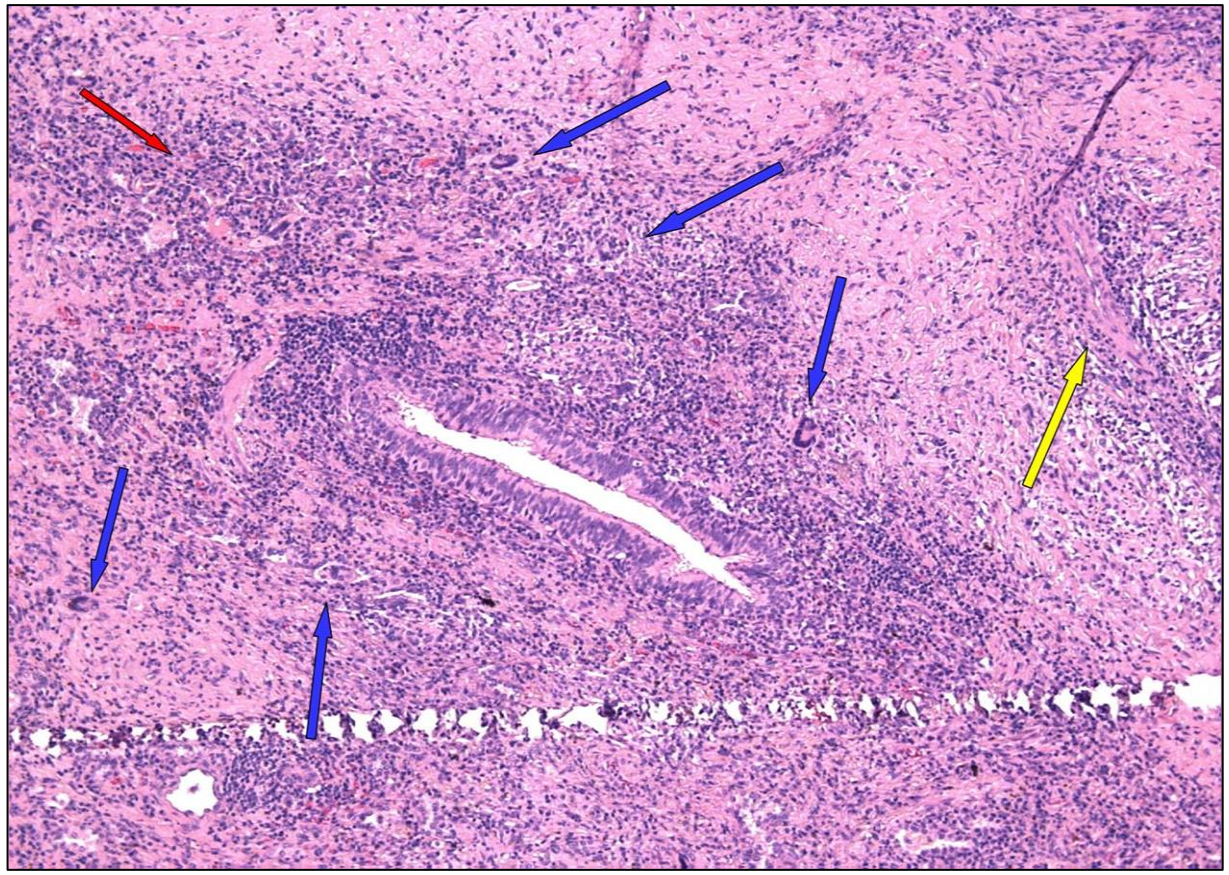
- Causes inflammation of the blood vessels in the nose, sinuses, throat, lungs, and kidneys.

- More than 80% of patients develop upper-respiratory or pulmonary manifestations.

❖ **Anti-neutrophil cytoplasmic antibodies (PR3- ANCAs) are present in close to 95% of cases.**

Morphology:

The lung lesions are characterized by a combination of necrotizing vasculitis (“angiitis”) and parenchymal necrotizing granulomatous inflammation.



Lung biopsy: liquefactive necrosis, lymphocytes, plasma cells (red arrow) and multinucleated giant cells (blue arrow) that generally do not form well-defined granulomas and a destructive, leukocytoclastic angiitis involving arteries and veins (yellow arrow)

Thank you