Chronic interstitial lung diseases-1

Manar Hajeer, MD, FRCpath

School of medicine, university of Jordan

- Synonyms: Restrictive , infiltrative.
- Heterogenous group.
- Pulmonary fibrosis (Bilateral ,Patchy, intra-alveolar and interstitial)
- Many are of unknown cause & pathogenesis.

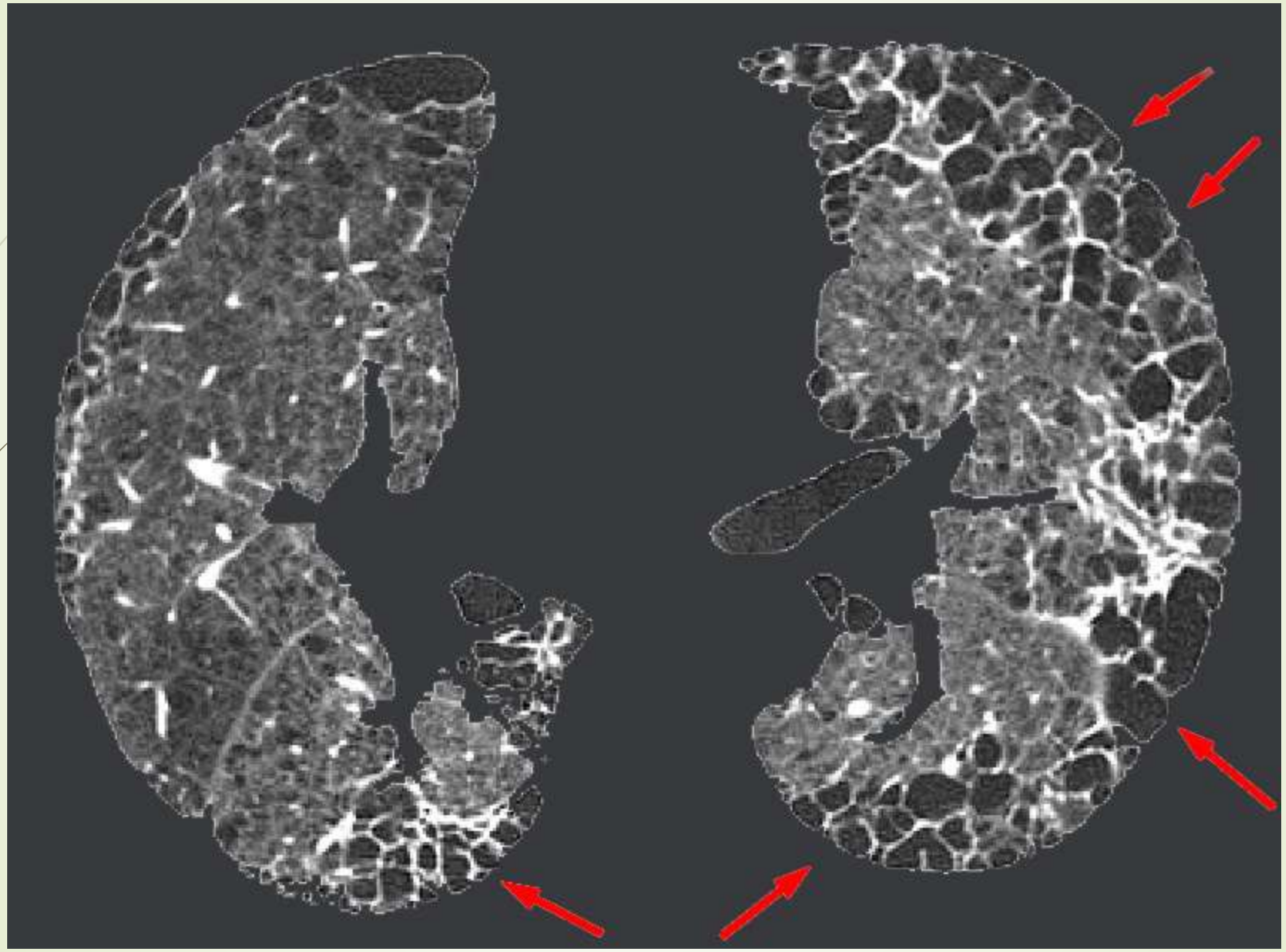
- Categorized according to clinical and histopathologic features.
- **However:**
- Overlap in histology.
- Similar signs and symptoms, radiologic changes & pathophysiology.

Hallmark: Stiff lungs (reduced lung compliance) ++

- Dyspnea (increased efforts to breath)
- Damage of alveolar epithelium and interstitial vessels >> abnormal ventilation-perfusion ratio >>> hypoxia
- Ground-glass shadows on CXR (small nodules & irregular lines)
- With progression >>> respiratory failure >>> pulmonary hypertension >>> Cor pulmonale.

- Lung compliance: measure of lung's ability to stretch or expand

- In advanced cases all show diffuse scarring and gross destruction of lung **(End stage or honeycomb lung)**
- Here, the underlying etiology can not be determined.



Honeycomb lung: dilated irregular air spaces between bands of dense fibrous connective tissue

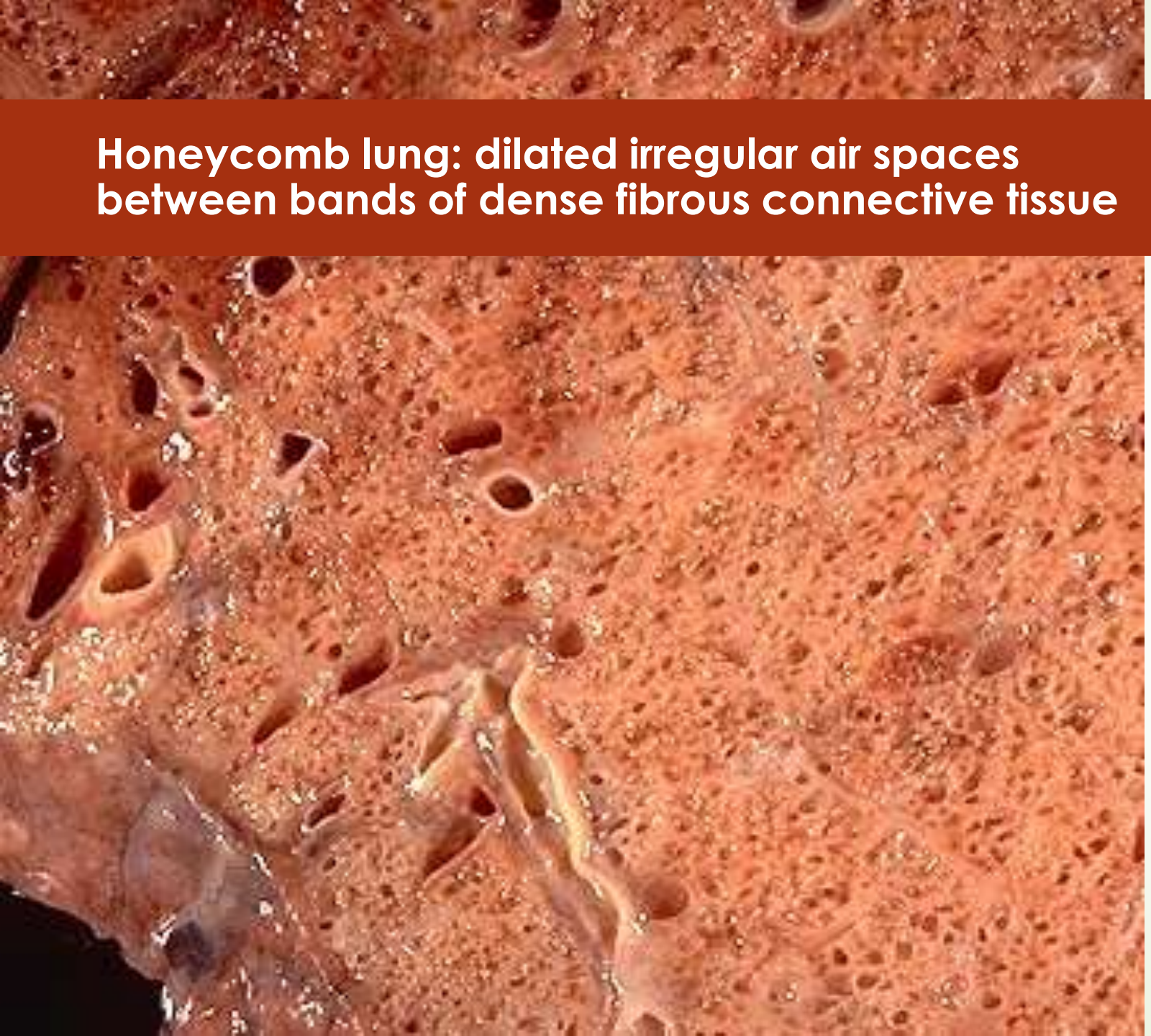


Table 15-5 Major Categories of Chronic Interstitial Lung Disease

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

Granulomatous diseases:

- Sarcoidosis
- Hypersensitivity pneumonitis.

Sarcoidosis

- Multisystem disease
- Unknown etiology
- Noncaseating granulomas in many tissues and organs
- Diagnosis of sarcoidosis is one of exclusion

Clinical presentation:

- Major presentation: bilateral hilar lymphadenopathy or lung involvement (or both) on CXR.
- Occasionally: Eye and skin involvement

Epidemiologic trends:

- Adults younger than 40 years.
- African Americans (2-3 times greater than in Europeans).
- Higher prevalence among nonsmokers
- Recur in transplanted lungs.

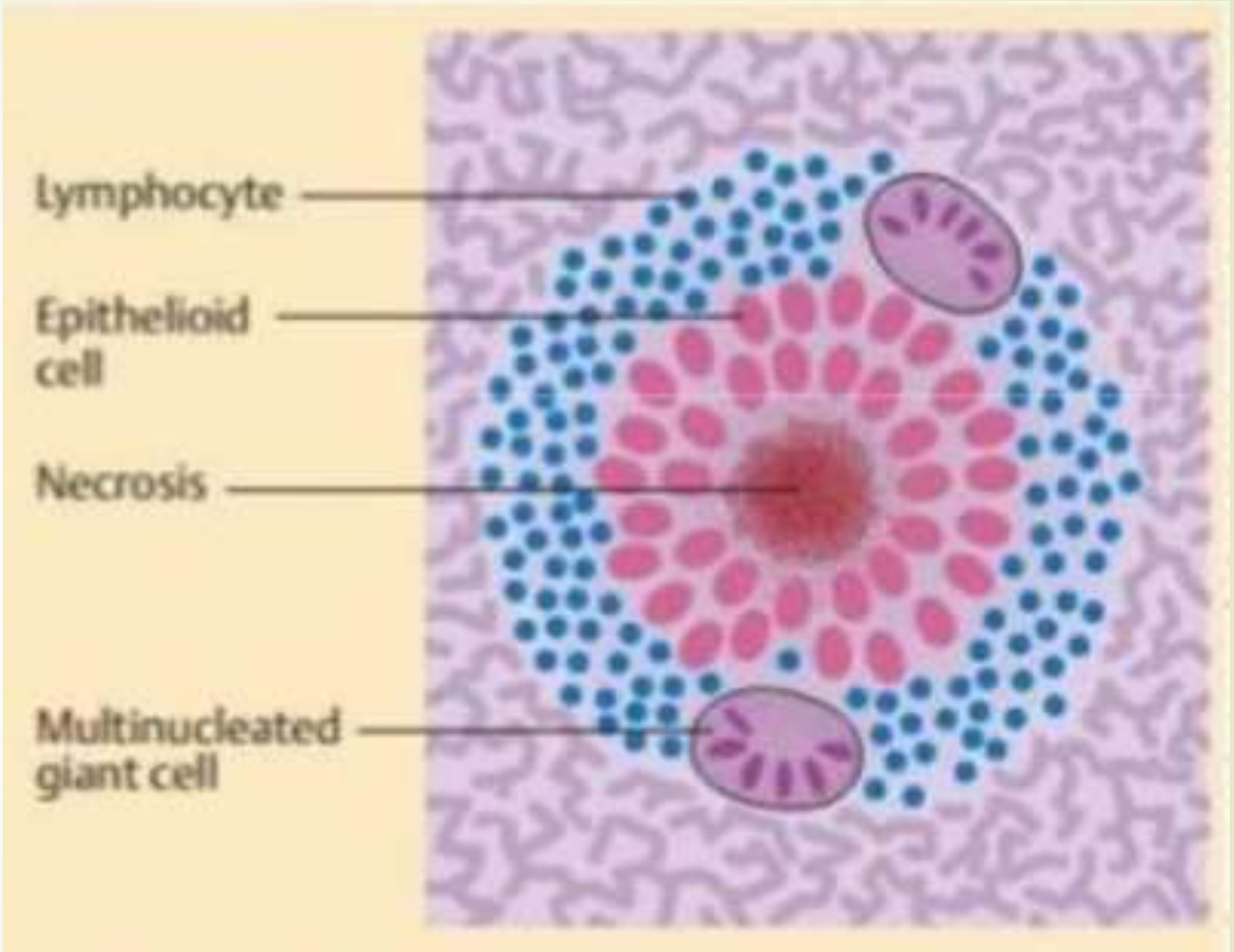
ETIOLOGY AND PATHOGENESIS:

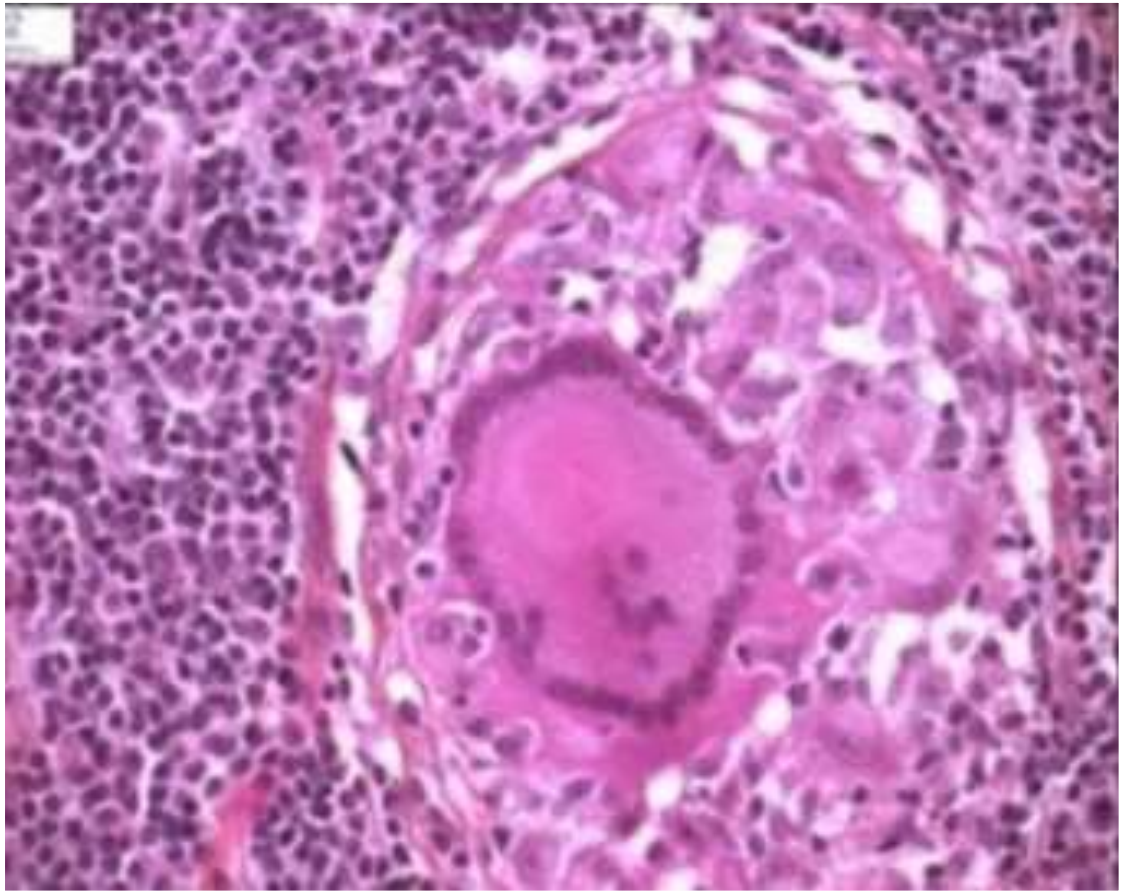
- Disordered immune regulation in genetically predisposed persons exposed to certain undefined environmental agents.
- Cell-mediated response to an unidentified antigen, driven by CD4+ helper T cells
- Increases in TH1 cytokines such as IL-2 and IFN-γ >>> T cell expansion and macrophage activation.

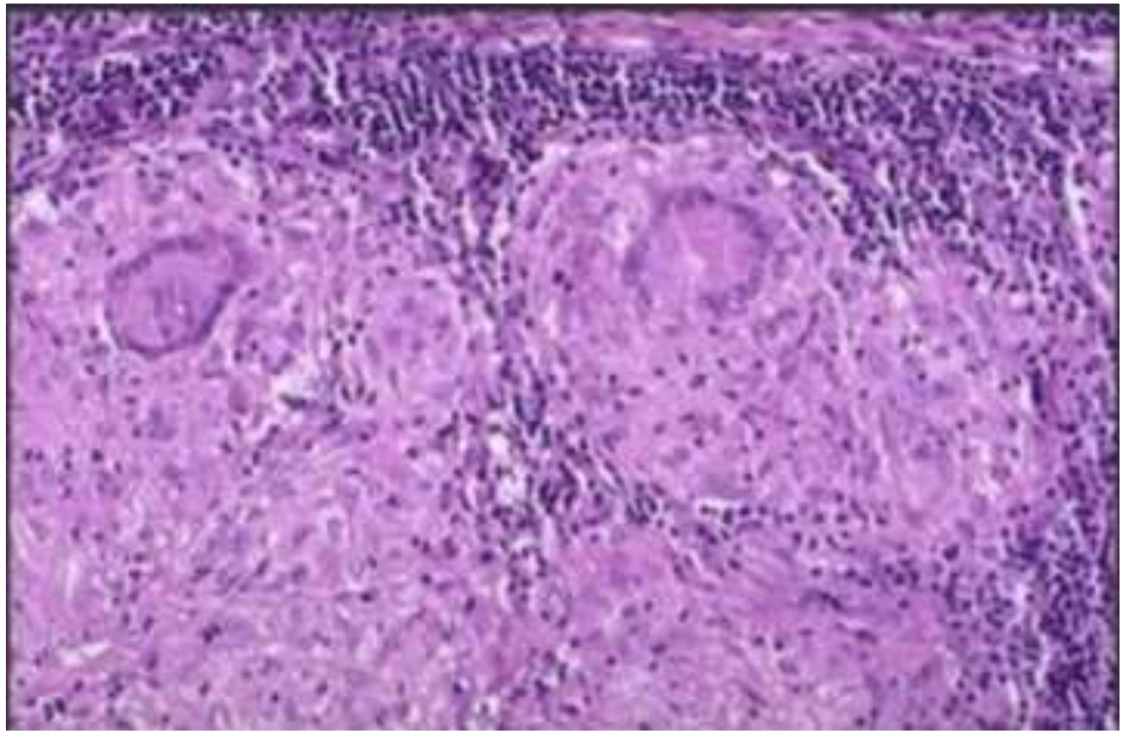
Morphology:

- **Cardinal feature: noncaseating epithelioid granulomas** (Epithelioid macrophages, multinucleated giant cells, rim of CD4+ T cells)
- Caseation necrosis typical of tuberculosis is absent.
- Overtime, granulomas replaced by hyalinized scars.

Composition of granuloma:

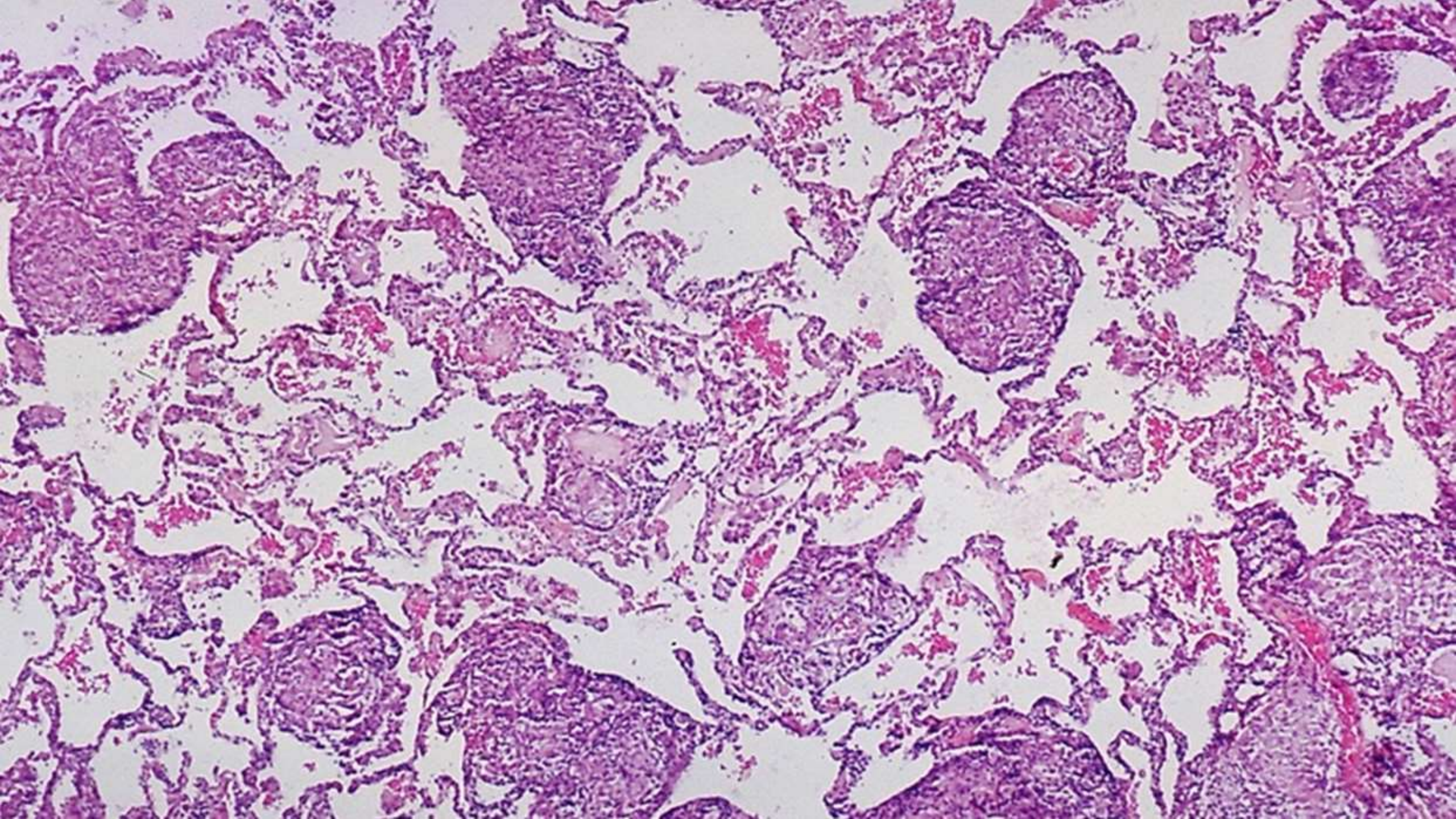


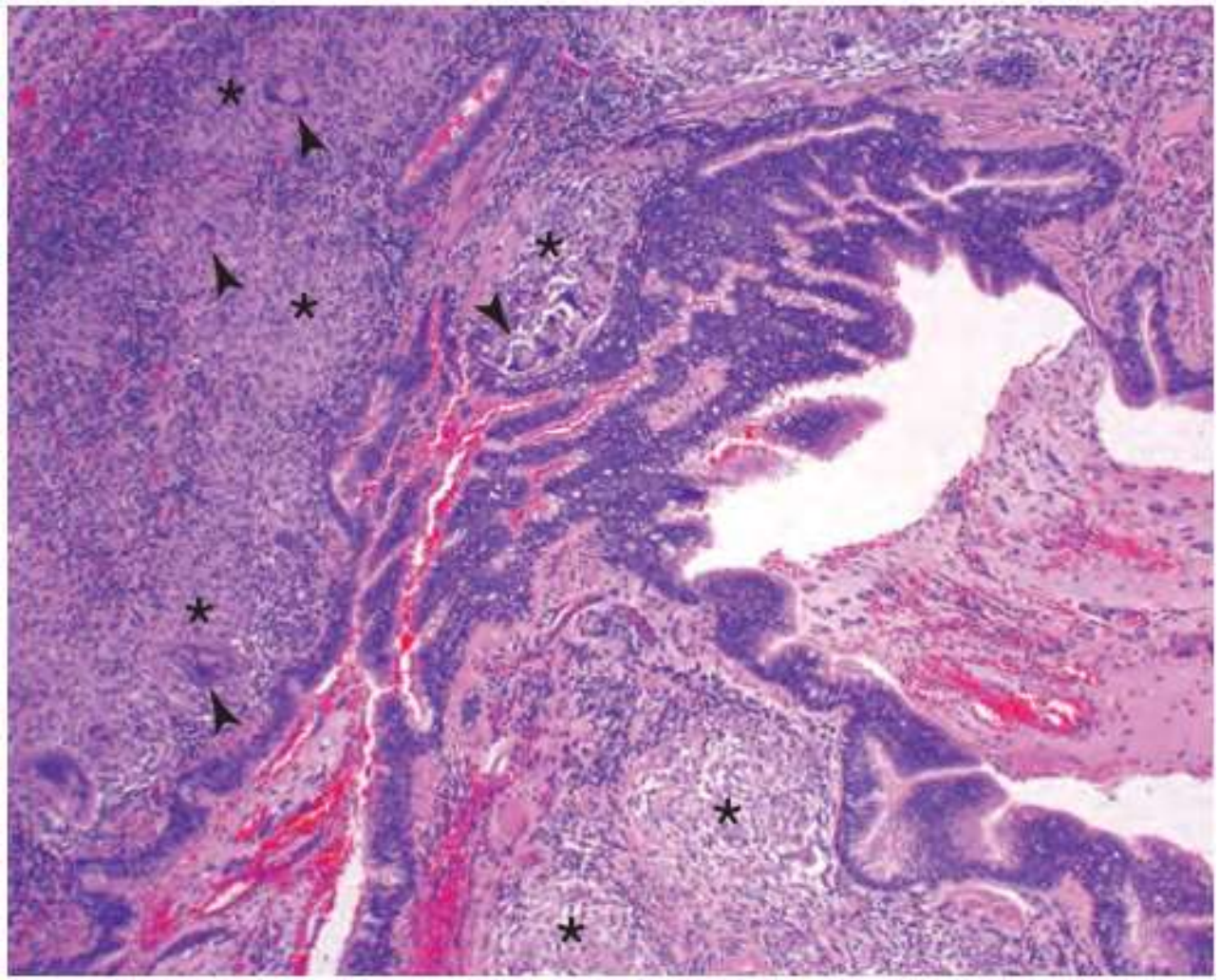


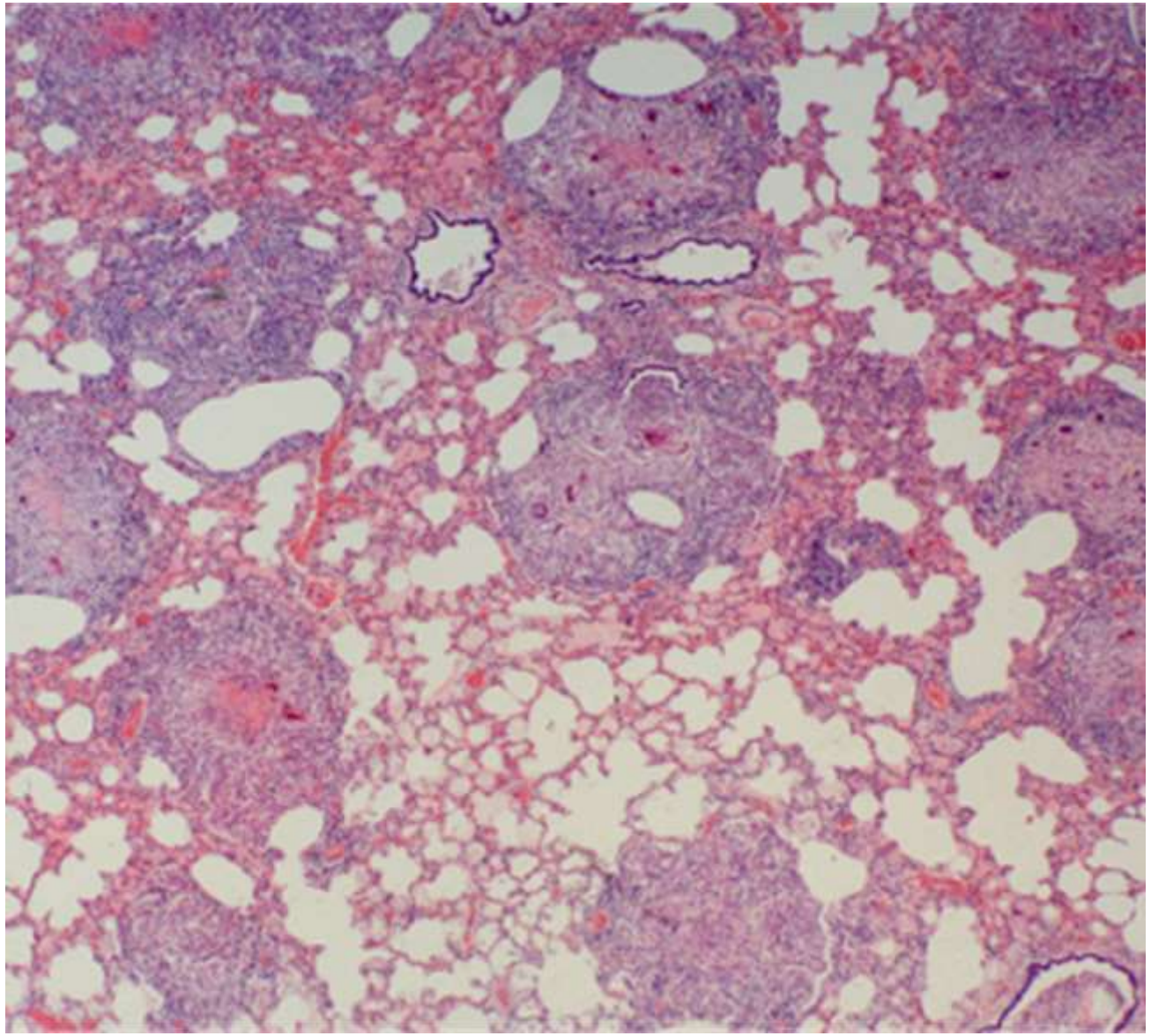


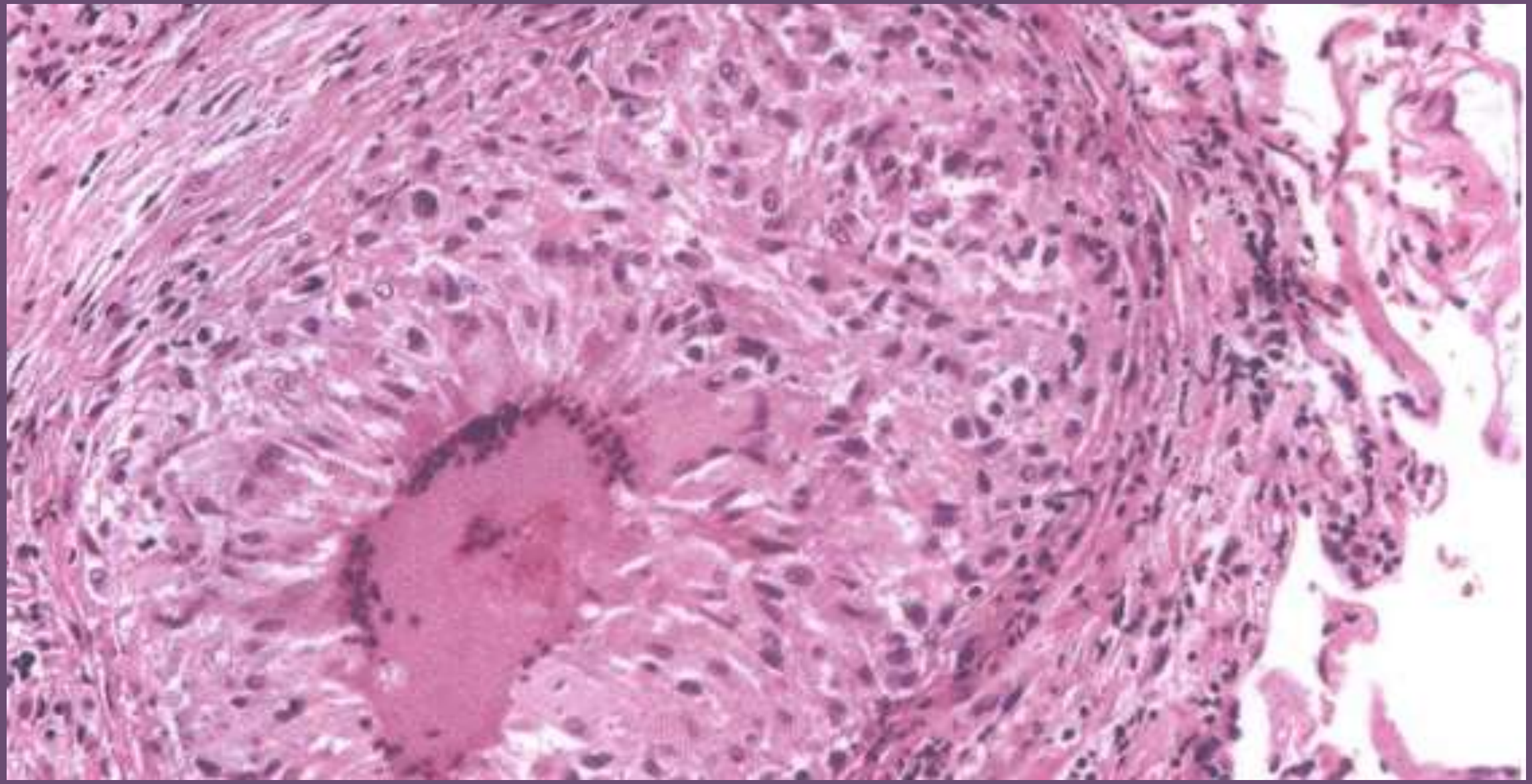
- **In the granulomas:**

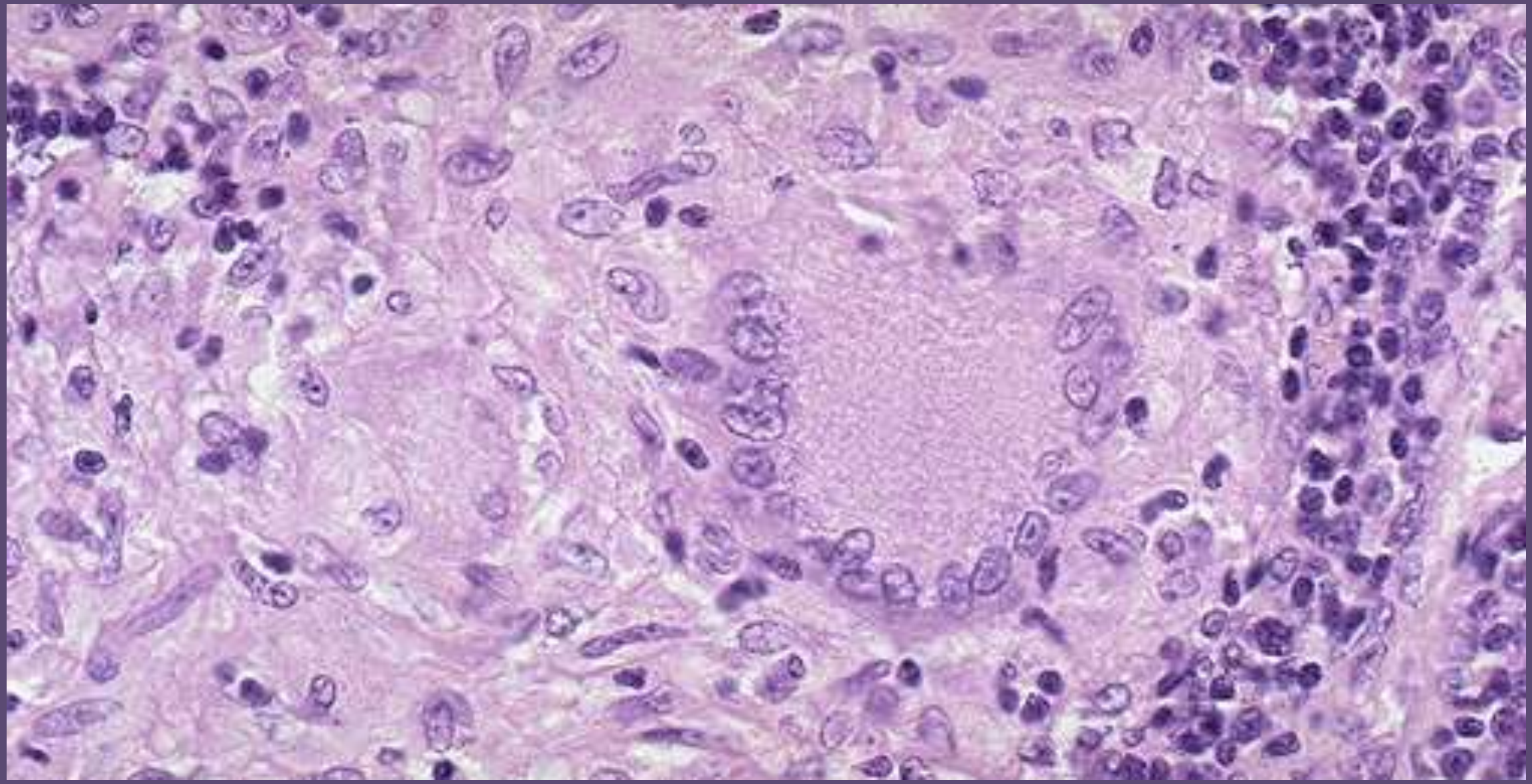
- **1- Schaumann bodies,** laminated concretions composed of calcium and proteins
- 2- **Asteroid bodies** stellate inclusions enclosed within giant cells.



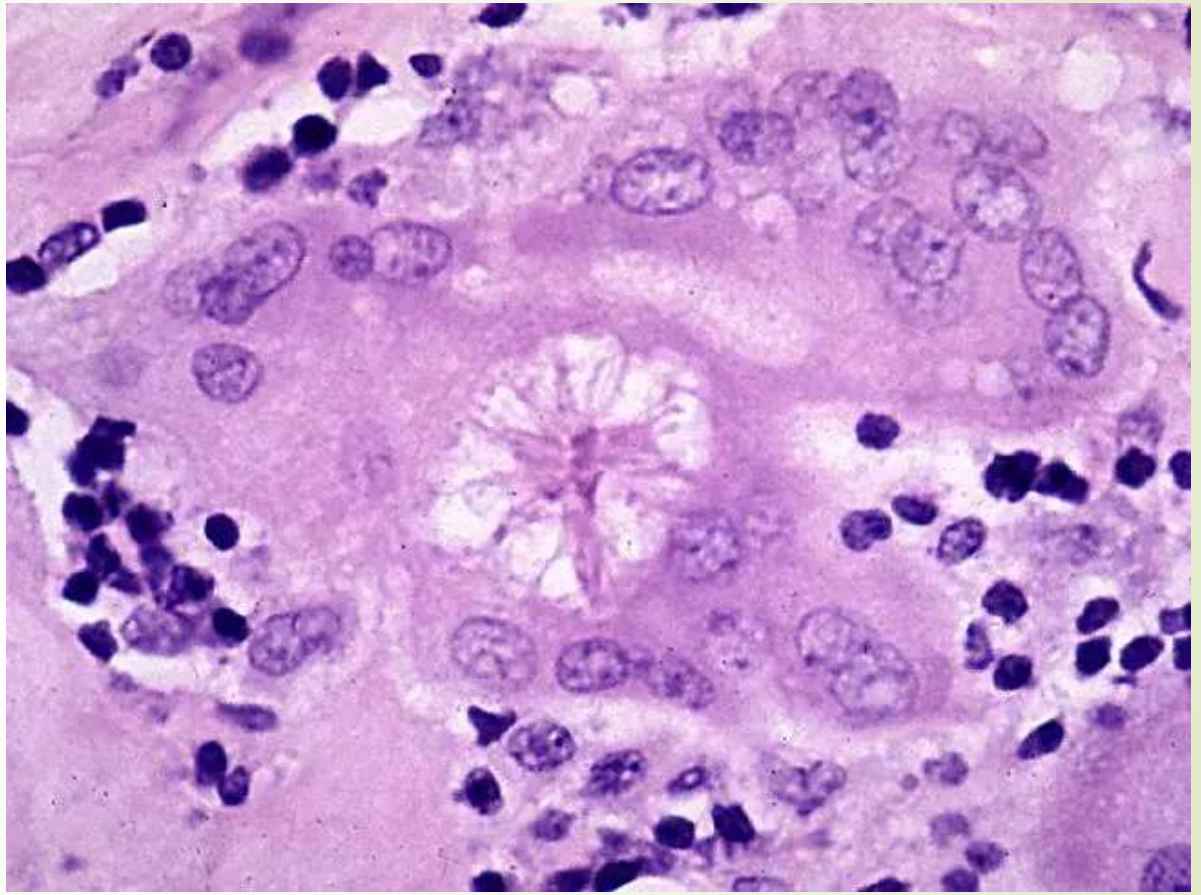


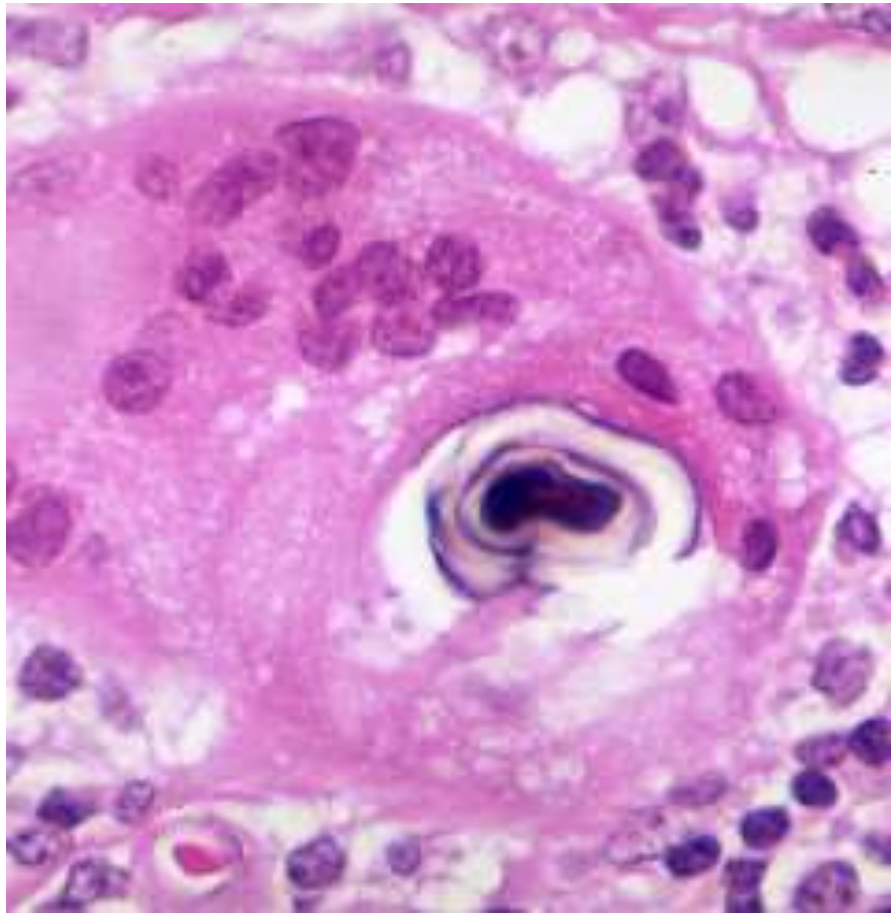






Asteroid bodies





Schaumann bodies

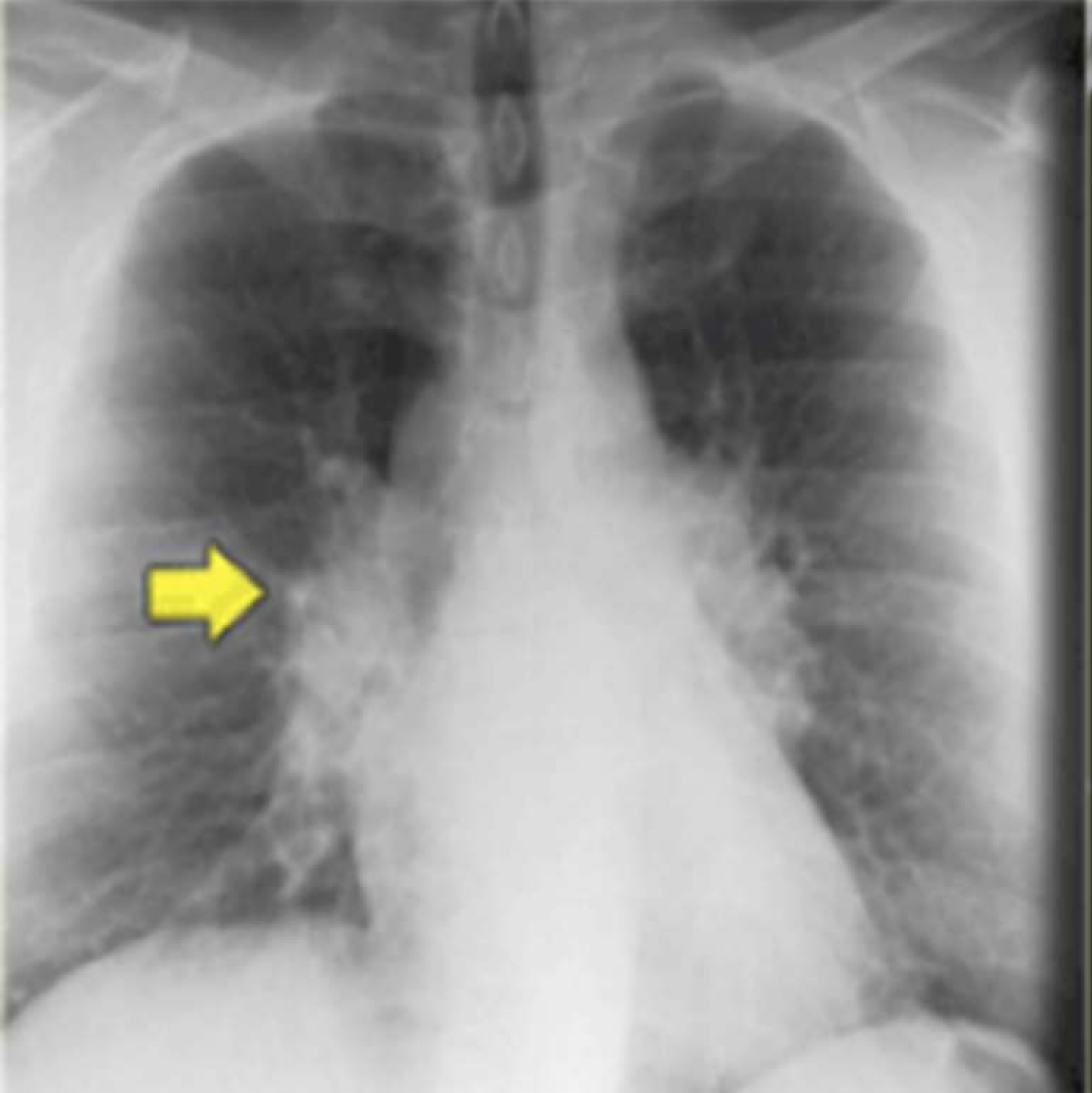
Lung involvement:

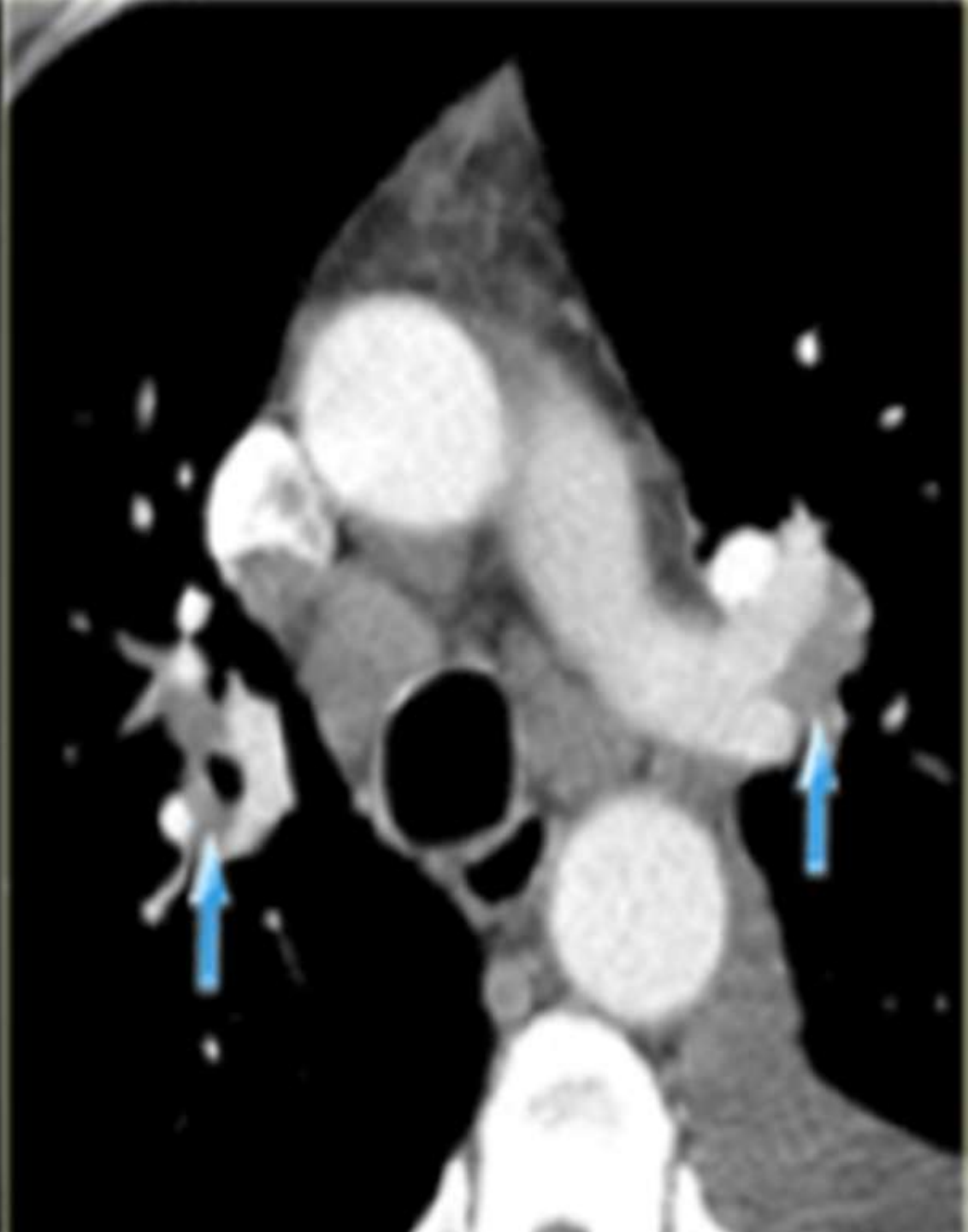
- **Involved in 90% of patients.**
- **Granulomas predominantly involve the interstitium NOT air spaces. (Peribronchial, periveunular and pleural distribution)**
- **BAL fluid contains abundant CD4+ T cells.**
- **Eventually replaced by diffuse interstitial fibrosis (honeycomb lung) in 5-15% of cases.**

Lymph nodes involvement:

- Enlarged Hilar and paratracheal lymph nodes (75% to 90%)
- Peripheral lymphadenopathy in 1/3.

- The nodes “unlike TB” are:
- Non-matted
- Nonadherent
- Do not ulcerate
- Noncaseating.



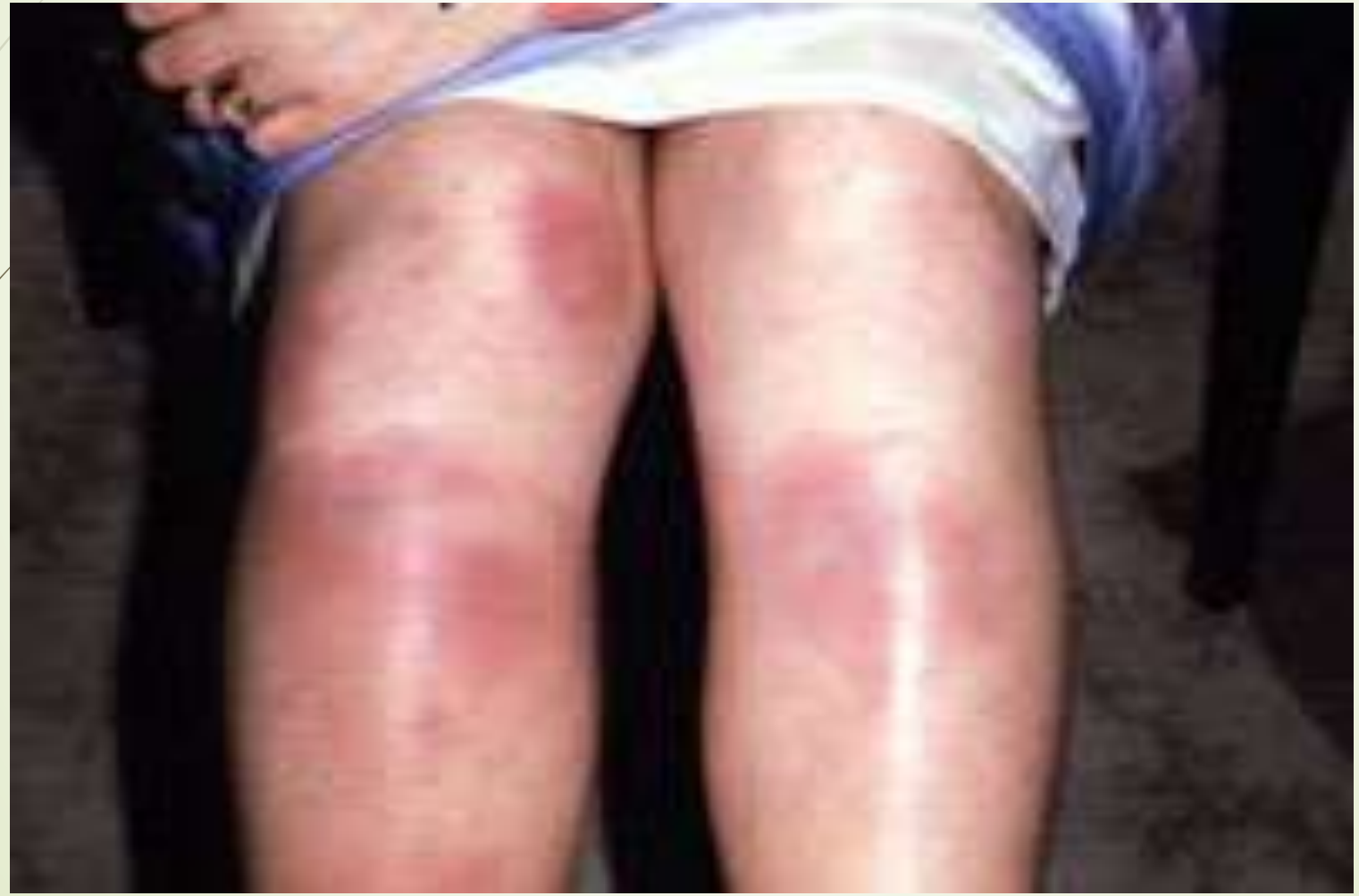


Skin lesions:

- In 25% of patients.
- **1- Erythema nodosum:**
- Hallmark of acute sarcoidosis
- Panniculitis
- Raised, red, tender bilateral nodules (anterior aspects of the legs).
- Granulomas are uncommon in these lesions.

- **2- Subcutaneous nodules**
- Discrete painless
- Abundant noncaseating granulomas.

Erythema Nodosum



Eye & lacrimal glands

- 20% - 50% of cases.
- Iritis or iridocyclitis, unilateral or bilateral.
- Corneal opacities, glaucoma, and even total loss of vision
- The posterior uveal tract disease (choroiditis, retinitis, and optic nerve involvement).
- Sicca syndrome: inflammation of lacrimal glands >>> suppression of lacrimation >> dry eyes.

Salivary glands:

- **Parotid glands: unilateral or bilateral parotitis + painful enlargement <10% >>>> Xerostomia: dry mouth.**
- **Mikulicz syndrome: Combined uveo-parotid involvement.**

Spleen, liver and bone marrow:

- **The spleen:**
- **Granulomas three fourths of cases.**
- **Enlarged in 10%.**

- **The liver:**
- **Granulomas in the portal triads**
- **Hepatomegaly or abnormal LFT in one third.**

- **Bone marrow involvement in 40% of patients.**

Hypercalcemia and hypercalciuria:

- **Not related to bone destruction.**
- **Production of active vitamin D by the mononuclear phagocytes in the granulomas.**

Clinical Features:

- **Many cases are asymptomatic**
- Incidental on routine CXR (bilateral hilar adenopathy) or at autopsy.

- **Symptomatic**
- **Two thirds** gradual respiratory symptoms (shortness of breath, dry cough, substernal discomfort OR constitutional symptoms (fever, fatigue, weight loss, anorexia, night sweats).
- Peripheral lymphadenopathy, cutaneous lesions, eye involvement, splenomegaly, or hepatomegaly.

Diagnosis:

- **Noncaseating granulomas is suggestive of sarcoidosis, but exclusion of other causes is a must (TB)**

- **Diagnosis requires:**
- **1-Clinical findings**
- **2-Radiologic findings**
- **3-Histologic findings of granulomas in involved sites**
- **4-Exclusion of other causes**

Outcome:

- **Unpredictable course**
- **Progressive chronicity OR**
- **Periods of activity interspersed with remissions**
- **Remissions may be spontaneous or by steroid therapy (often permanent).**

- 65% to 70% recover with minimal or no residual manifestations.
- 20% develop permanent lung dysfunction or visual impairment.
- 10% to 15% progressive pulmonary fibrosis and Cor pulmonale.

Granulomatous diseases:

- Sarcoidosis
- Hypersensitivity pneumonitis.

Hypersensitivity pneumonitis.

- Immunologically mediated: Most patients have antibodies against offending antigens
- Primarily affects the alveoli (allergic alveolitis).
- Occupational exposure (sensitivity to inhaled antigens such as in moldy hay)
- Restrictive lung disease with decreased diffusion capacity, lung compliance, and total lung volume.

Many syndromes:

- **Inhalation of organic dust containing antigens (spores of thermophilic bacteria, fungi, animal proteins, or bacterial products)**

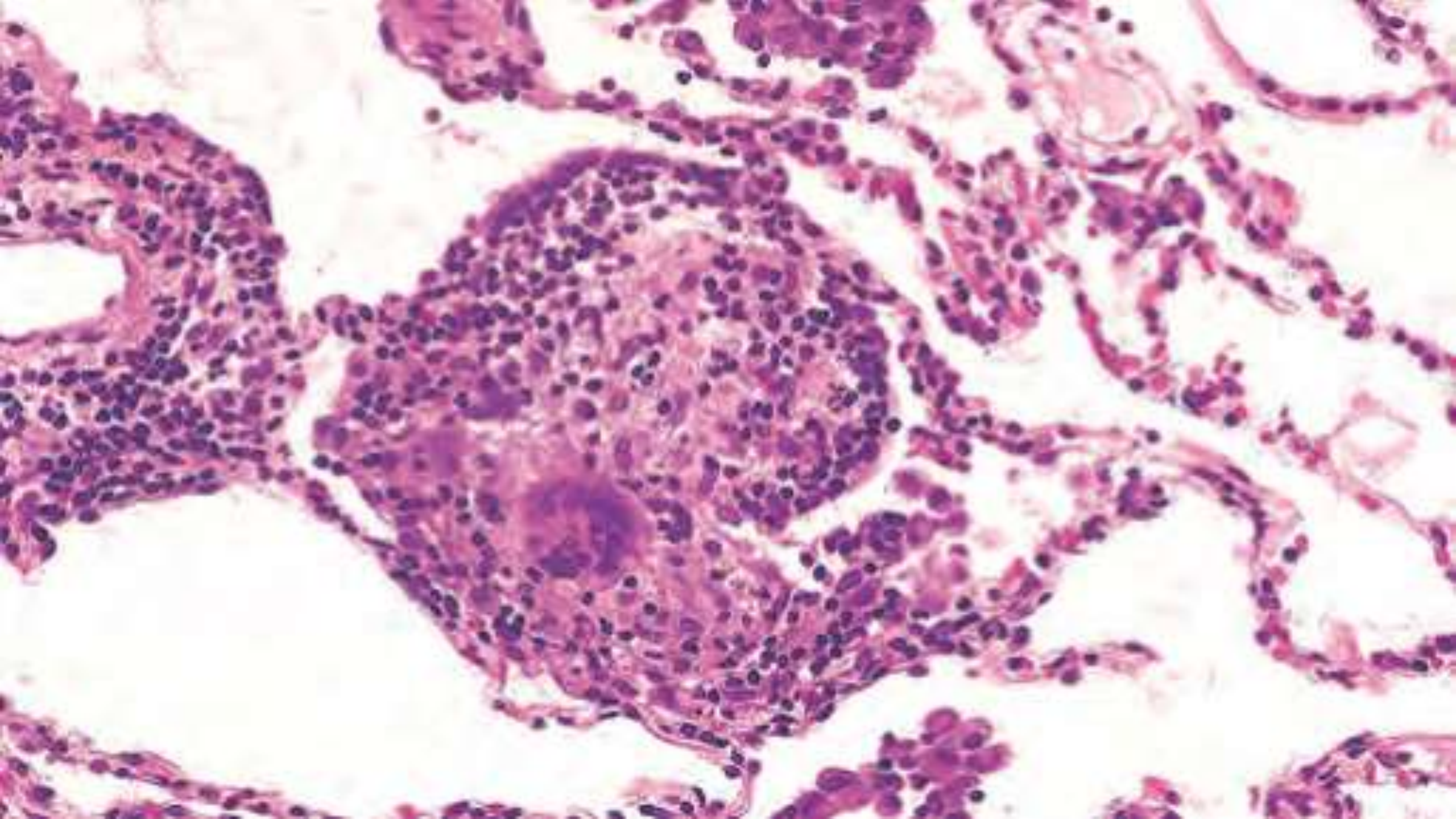
- **Farmer's lung:** dusts generated from humid, warm, newly harvested hay that permits the rapid proliferation of the spores of thermophilic actinomycetes.
- **Pigeon breeder's lung:** proteins from serum, excreta, or feathers of birds.
- **Humidifier or air-conditioner lung**: thermophilic bacteria in heated water reservoirs

Morphology:

- **Acute**: neutrophils may be seen.

- **Chronic (Interstitial pneumonitis):**
- Patchy mononuclear infiltrates (peribronchiolar accentuation).
- Lymphocytes predominate + plasma cells & epithelioid cells.
- Interstitial (peribronchiolar) noncaseating loose granulomas (two thirds of cases)

- **Advanced chronic**: diffuse interstitial fibrosis



Clinical Features

- **Acute reaction**: fever, cough, dyspnea, and constitutional signs and symptoms (4 to 8 hours after exposure)
- **Chronic disease:** insidious onset of cough, dyspnea, malaise, and weight loss.
- **If antigenic exposure is terminated: Complete resolution of symptoms within days.**
- **Continuous exposure: Irreversible chronic disease.**