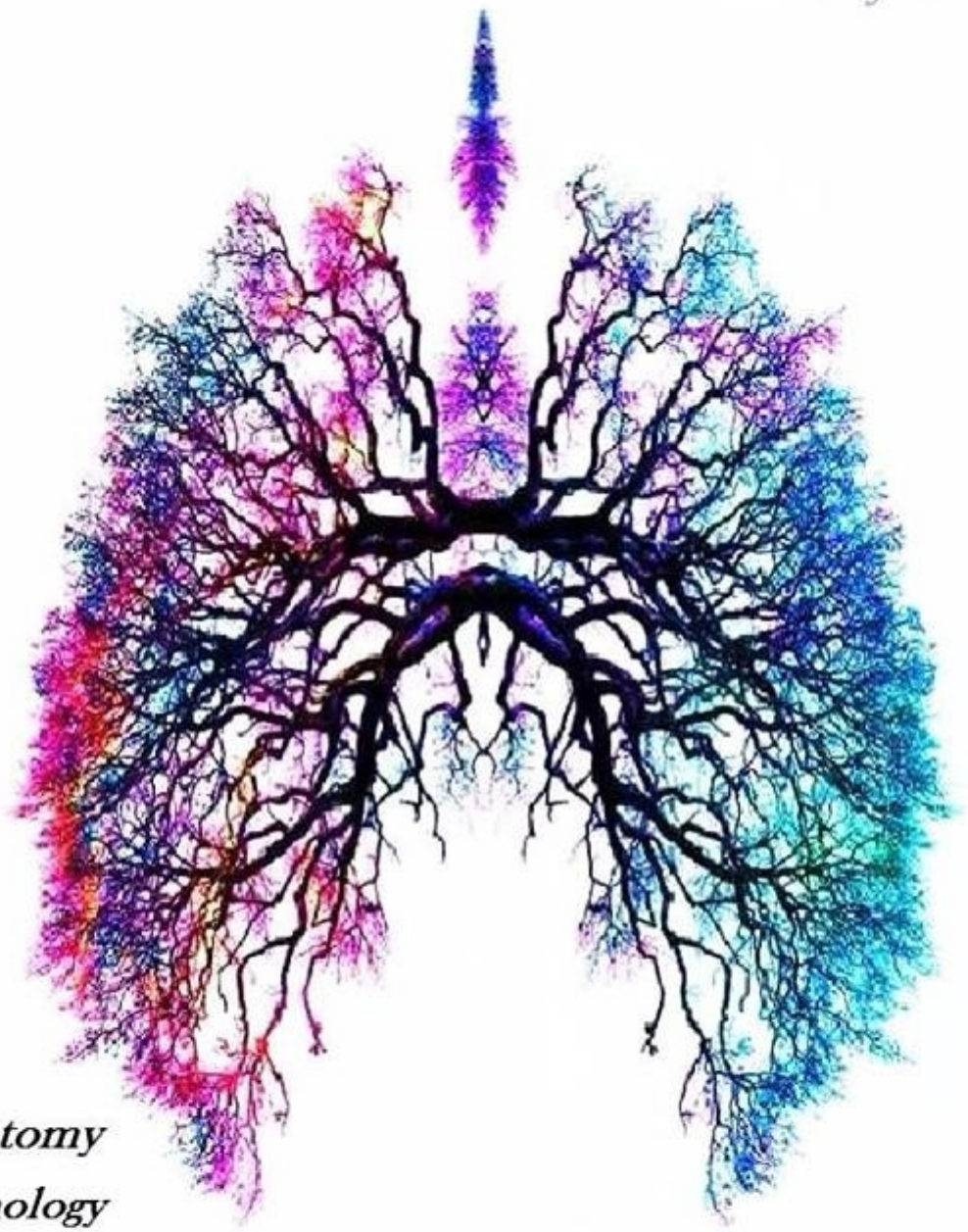
RESPIRATORY SYSTEM

Cover by: Aseil Khatib



- ○ Anatomy
- ● Pathology
- ○ Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL

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Lecture # 5

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IV.CHRONIC INTERSTITIAL (RESTRICTIVE, INFILTRATIVE) LUNG DISEASES

- Are a group of disorders characterized by bilateral, patchy, chronic involvement of the lung connective tissue, mainly the interstitium in the alveolar walls.
- The interstitium is composed of basement membrane of the endothelial and epithelial cells , collagen and fibers and, fibroblasts,

- Many of the entities are of unknown cause , some have an intra-alveolar as well as an interstitial component.
- The similarity in clinical signs, symptoms, radiographic alterations, and pathophysiologic changes justifies their consideration as a group.

- The hallmark feature of these disorders is reduced compliance (i.e., more pressure is required to expand the lungs because they are stiff), which in turn necessitates increased effort of breathing (dyspnea).
- Chest radiographs show diffuse infiltration by small nodules, irregular lines, or "ground-glass shadows

- With progression, patients can develop respiratory failure, and pulmonary hypertension and cor pulmonale
- Advanced forms of these diseases may be difficult to differentiate because they result in scarring and gross destruction of the lung, referred to as "honeycomb" lung.

- Are divided into two groups

I. Granulomatous diseases

2. Fibrosing diseases

I. Granulomatous diseases

A. Sarcoidosis

- Although sarcoidosis is an example of a restrictive lung disease, **it is important to note that sarcoidosis is a multisystem disease of unknown etiology characterized by noncaseating granulomas in many tissues and organs**.
- Other diseases, including mycobacterial or fungal infections may also produce noncaseating granulomas; so the histologic ***diagnosis of sarcoidosis is one of exclusion***.

Epidemiology

- It occurs throughout the world, affecting both genders and all races and age groups.
- There is a consistent predilection for adults younger than 40 years of age
- A high incidence has been noted among African Americans
- Sarcoidosis is one of the few pulmonary diseases with a higher prevalence among nonsmokers.

ETIOLOGY AND PATHOGENESIS

- Although the etiology of sarcoidosis remains unknown, several lines of evidence suggest that it is a disease of disordered immune regulation in genetically predisposed persons exposed to certain environmental agents

- Immunologic abnormalities in sarcoidosis suggest the development of a cell-mediated response to an unidentified antigen and the process is driven by CD4+ helper T cells. These abnormalities include:

1. Intra-alveolar and interstitial accumulation of CD4+ T_H1 cells
2. Increases in T cell-derived T_H1 cytokines such as IL-2 and IFN-γ, resulting in T cell expansion and macrophage activation, respectively

3. Anergy to common skin test antigens such as purified protein derivative (PPD), that may result from pulmonary recruitment of CD4+ T cells and consequent peripheral depletion

- The role of genetic factors is suggested by

a. Familial clustering of cases and

b. Association with certain human leukocyte antigens (HLA) (class I HLA-A1 and HLA-B8)

- After lung transplantation, sarcoidosis recurs in the new lungs in 75% of patients.

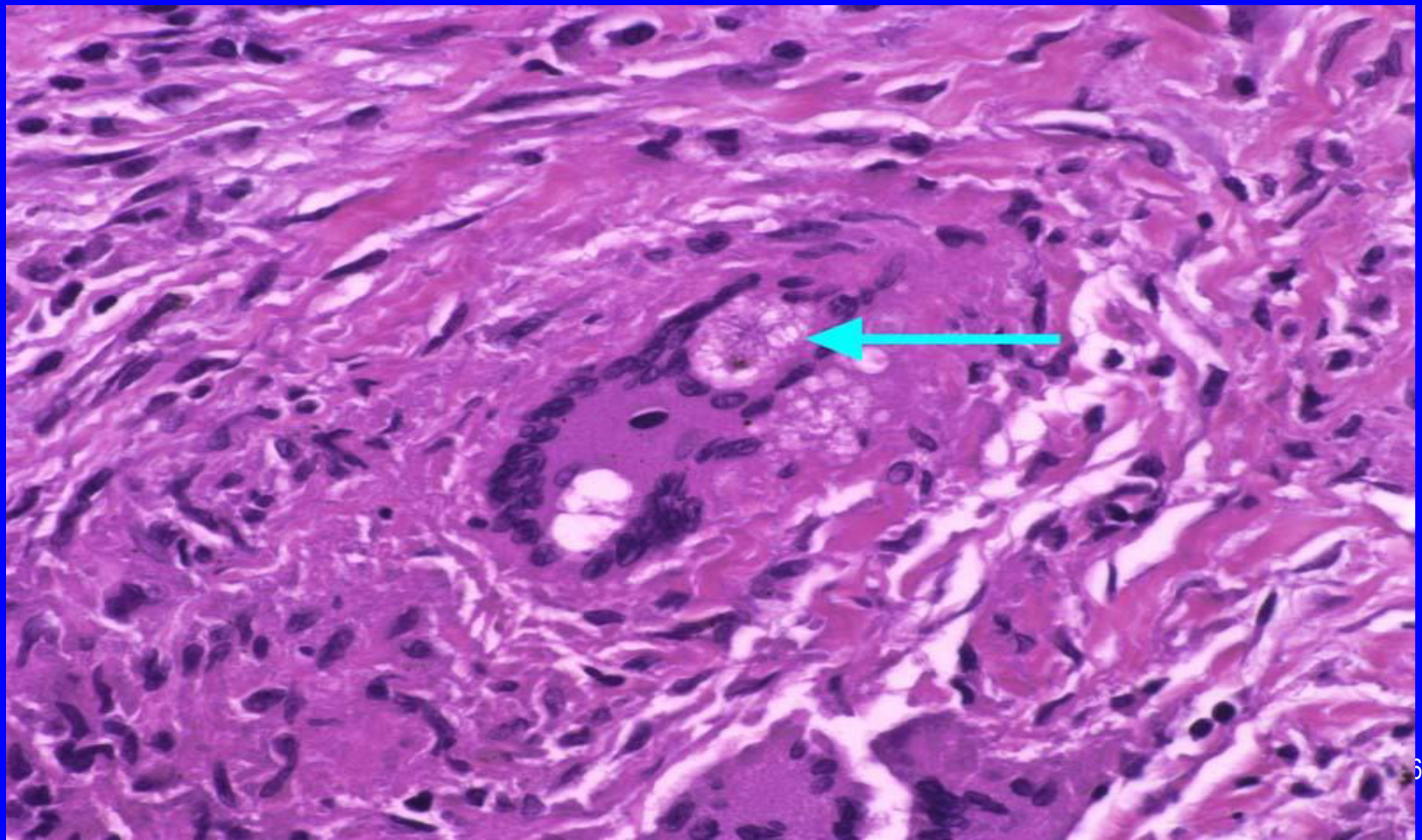
- **MORPHOLOGY**

- The diagnostic histopathologic feature of sarcoidosis is the noncaseating epithelioid granuloma, irrespective of the organ involved

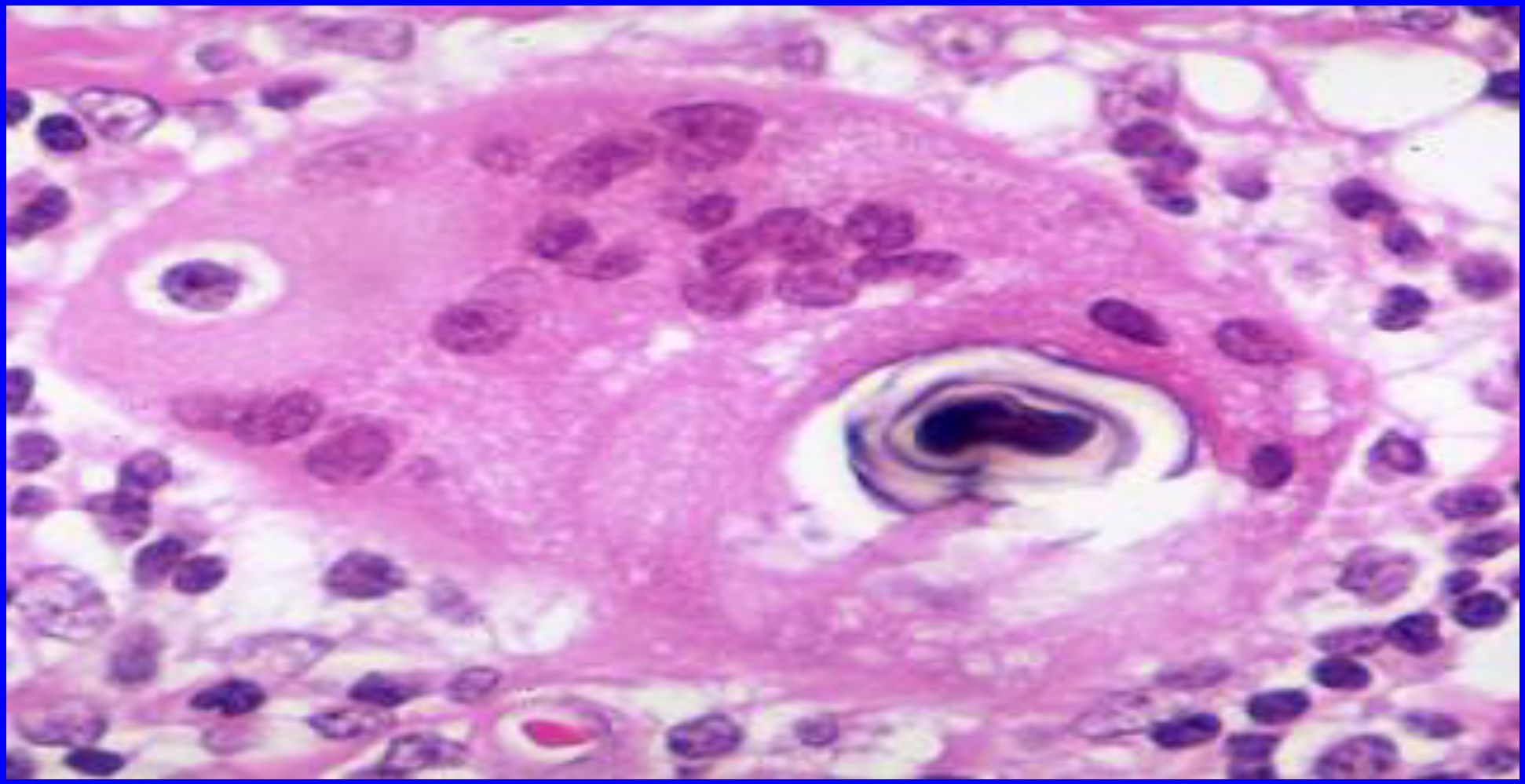
Two other microscopic features are sometimes seen:

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

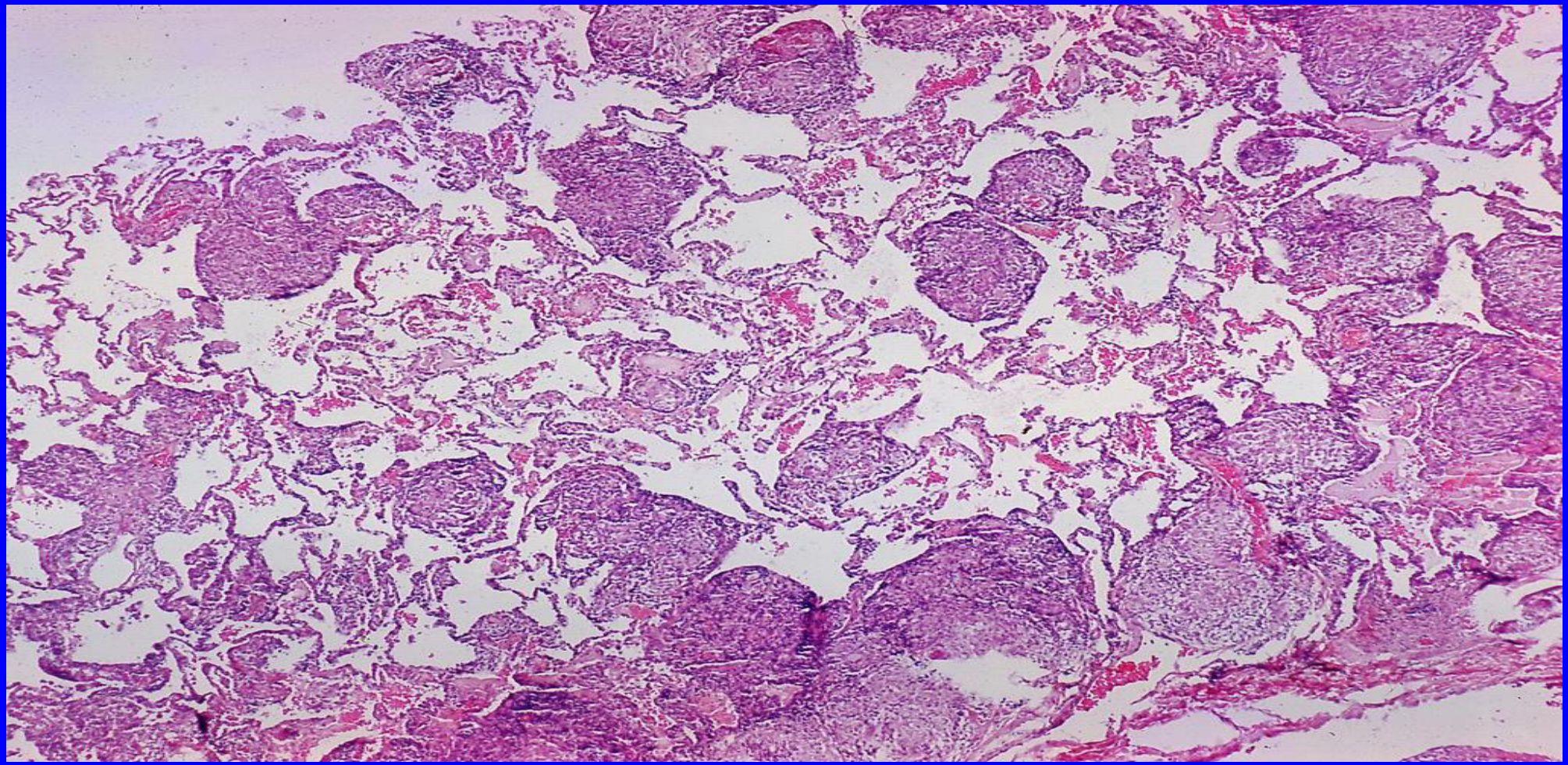
Asteroid bodies



Shaumann bodies



sarcoidosis



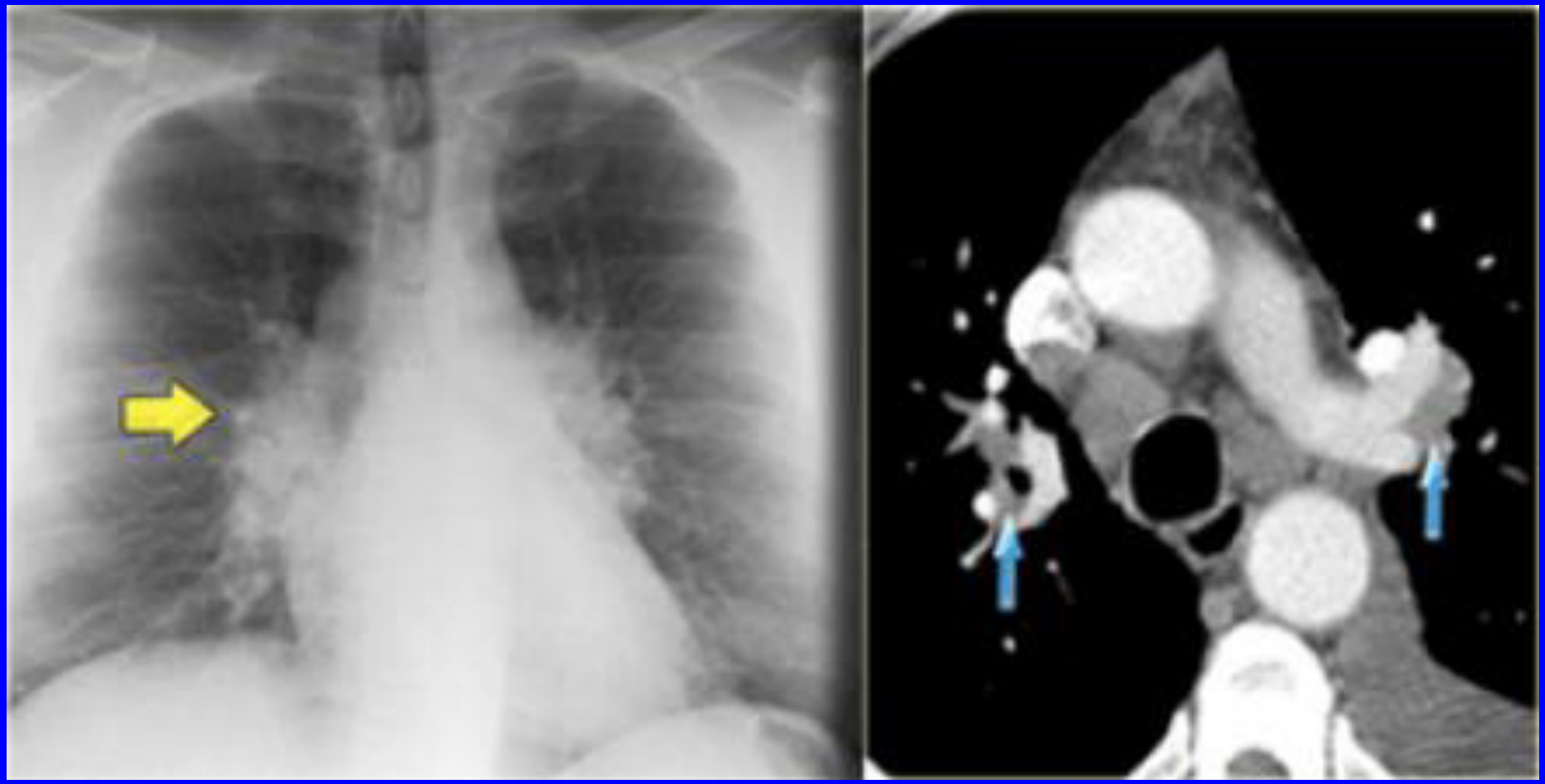
- Their presence (1&2)is not required for diagnosis of sarcoidosis-they also may occur in granulomas of other origins.
- Caseation necrosis typical of tuberculosis is absent.

Involved organs:

1. The **lungs** are involved at some stage of the disease in 90% of patients:

- The granulomas predominantly involve the interstitium rather than air spaces, with some tendency to localize in the connective tissue around bronchioles and venules and in the pleura

sarcoidosis



- The bronchoalveolar lavage contains abundant CD4+ T cells.
- In 5% to 15% of patients, the granulomas eventually are replaced by diffuse interstitial fibrosis, resulting in a so-called honeycomb lung.

2. Intrathoracic hilar and paratracheal lymph nodes are enlarged in 75% to 90% of patients, while a third present with peripheral lymphadenopathy.
3. Skin lesions are encountered in approximately 25% of patients

a.Erythema nodosum,

- The hallmark of acute sarcoidosis, consists of raised, red, tender nodules on the anterior aspects of the legs.
- Sarcoidal granulomas are uncommon in these lesions.

b. Subcutaneous nodules

- Are discrete and painless
- These usually reveal abundant noncaseating granulomas.

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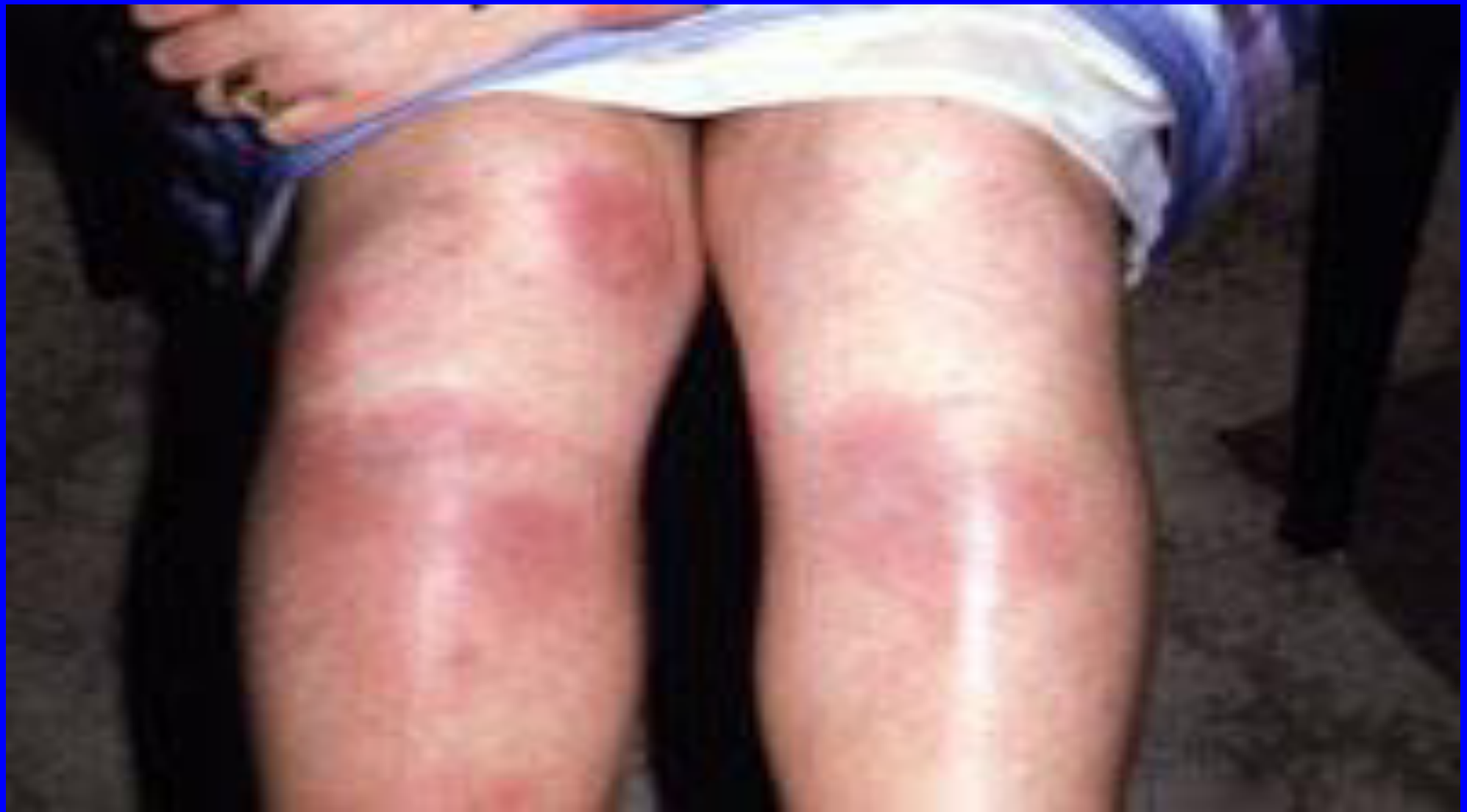
Erythema Nodosum



4. Involvement of the eye and lacrimal glands occurs in about one fifth to one half of patients and the ocular involvement takes the form of iritis or iridocyclitis and may be unilateral or bilateral

- As a consequence, corneal opacities, (less commonly) total loss of vision may develop.
- These ocular lesions are frequently accompanied by inflammation in the lacrimal glands, with suppression of lacrimation (sicca syndrome).

5. Unilateral or bilateral parotitis with painful enlargement of the parotid glands

- Some patients develop xerostomia (dry mouth).

Note:

- Combined uveoparotid involvement is designated **Mikulicz syndrome**.

6. It affects spleen, liver and Bone marrow.

***Note*:**

- Other findings include hypercalcemia and is not related to bone destruction but rather are caused by increased calcium absorption secondary to production of active vitamin D by the mononuclear phagocytes in the granulomas.

Clinical Features

1.In many affected persons the disease is

a. Entirely asymptomatic,

b. Discovered on routine chest films as bilateral hilar adenopathy or

c. As an incidental finding at autopsy.

2. In others, peripheral lymphadenopathy, cutaneous lesions, eye involvement, splenomegaly, or hepatomegaly may be presenting manifestations.
3. In about two thirds of symptomatic cases, there is gradual appearance of respiratory symptoms (shortness of breath, dry cough, or vague substernal discomfort) or constitutional signs and symptoms (fever, fatigue, weight loss, anorexia, night sweats

- Because of the variable and nondiagnostic clinical features, resort is frequently made to lung or lymph node biopsies.
- ***The presence of noncaseating granulomas is suggestive of sarcoidosis, but other identifiable causes of granulomatous inflammation must be excluded***

Clinical course:

- Sarcoidosis follows an unpredictable course characterized by either progressive chronicity or periods of activity interspersed with remissions.

- The remissions may be spontaneous or initiated by steroid therapy and often are permanent.
- Overall, 65% to 70% of affected persons recover with minimal or no residual manifestations.
- Another 20% develop permanent lung dysfunction or visual impairment.
- 10% to 15%, succumb to progressive pulmonary fibrosis and cor pulmonale.