CHRONIC INTERSTITIAL (RESTRICTIVE, INFILTRATIVE) LUNG DISEASES, PART 1

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It's hard to get the air IN

It's hard to Inhale

lung compliance is Decreased (stiff lungs)

Lung volume and capacity are DEcreased

- **Total lung capacity: (TLC) is the volume of air in the lungs upon the maximum effort of inspiration.**
- **lung compliance: is a measure of the lung's ability to stretch or expand**

CHRONIC INTERSTITIAL LUNG DISEASES

- Called **RESTRICTIVE or INFILTRATIVE**

- are a heterogeneous group of disorders characterized predominantly by inflammation and fibrosis of the lung interstitium (+/- intra-alveolar) associated with pulmonary function studies indicative of restrictive lung disease. (reductions in lung volume, and lung compliance)

- Many entities in this group are of unknown cause and pathogenesis.

- Frequent overlap

- **Clinically:** dyspnea (**increased effort to breathe**), tachypnea, end-inspiratory crackles, and eventual cyanosis.

- **Chest radiographs:** bilateral lesions → small nodules, irregular lines, or ground-glass shadows.

- the damage to the alveolar epithelium and interstitial vasculature results in **abnormal ventilation–perfusion ratio→ hypoxia.**

- With progression→ pulmonary hypertension →respiratory failure and cor pulmonale

- categorized based on **clinical features and histology**

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

- the entities can be distinguished in their early stages, but advanced forms are hard to differentiate

- **When advanced all result in:**
  - diffuse scarring and gross destruction of the lung, referred to as **end-stage or "honeycomb" lung.**
  - hypoxia→ secondary pulmonary hypertension → cor pulmonale.
  - At this stage, the etiology of the underlying diseases may be difficult to determine

HONEYCOMB LUNG

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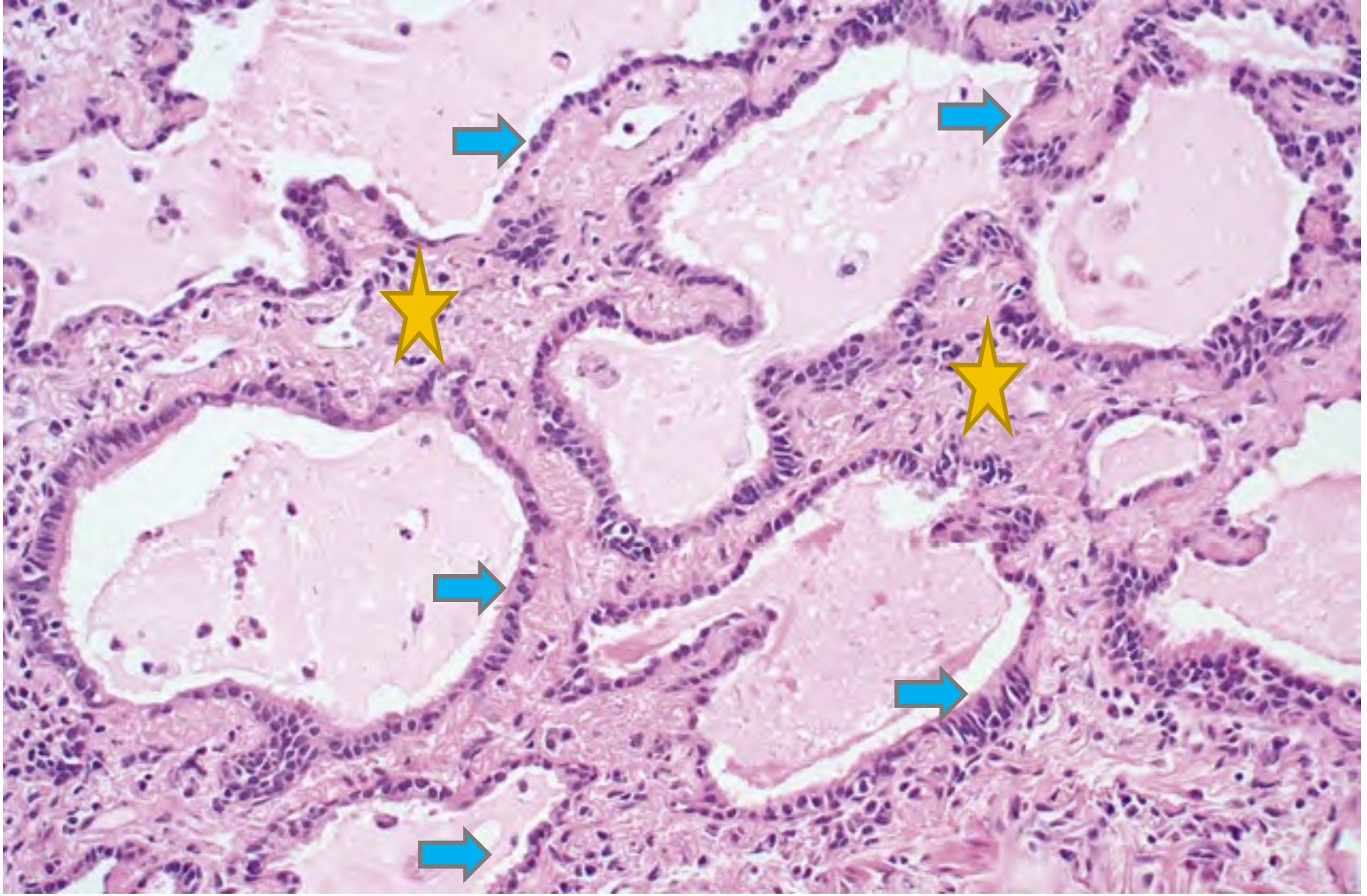

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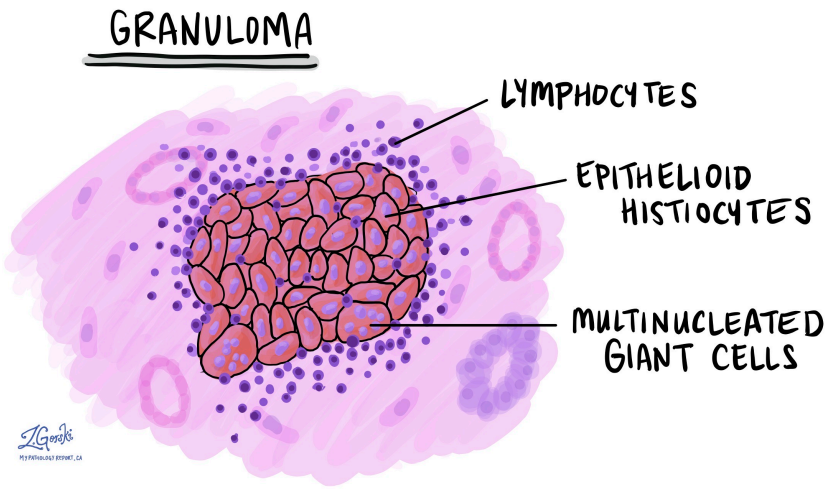
GRANULOMATOUS DISEASES



GRANULOMATOUS DISEASES

- **Sarcoidosis**
- **Hypersensitivity pneumonitis**

SARCOIDOSIS

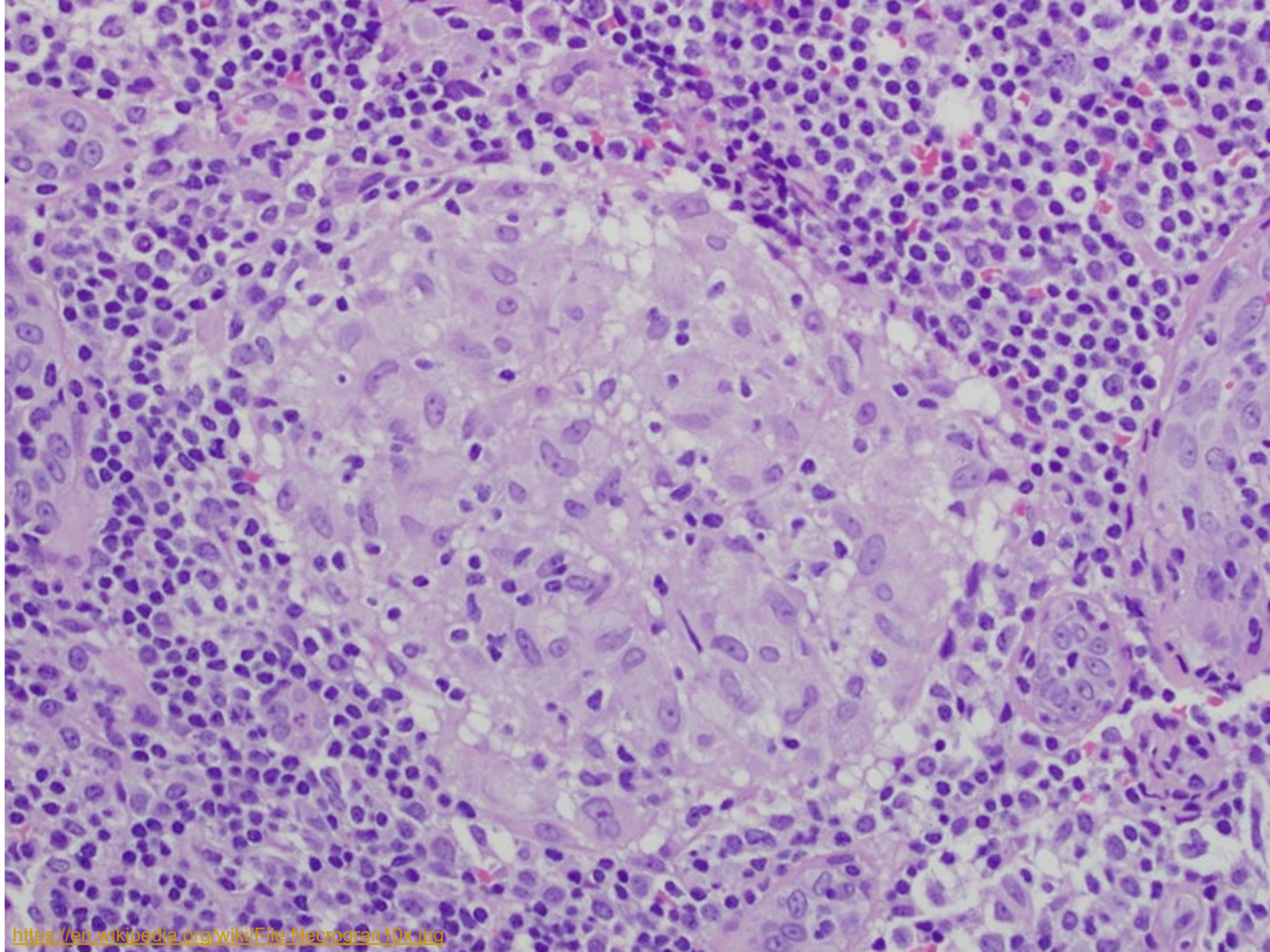
- **Systemic granulomatous disease of unknown etiology**
- characterized by **noncaseating granulomas** in many tissues and organs.
- Diagnosis **of exclusion**.
- Clinically
- can present as an acute or chronic illness or restrictive lung disease

ETIOLOGY AND PATHOGENESIS

- the etiology is **unknown**

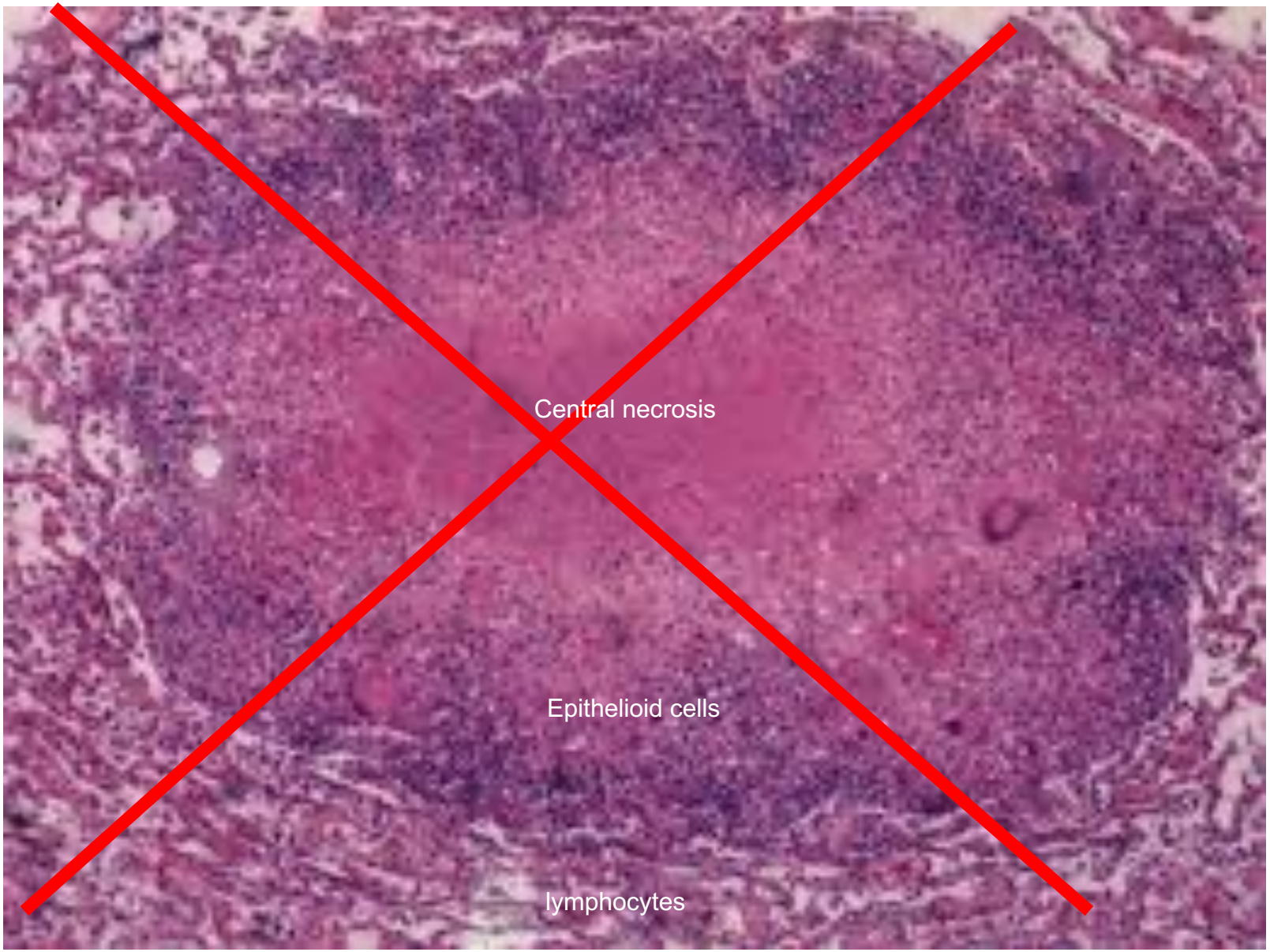
- research evidences suggest that it's a **Disordered immune** regulation in **genetically predisposed persons exposed to certain environmental agents**.

- Cell-mediated response to an unidentified antigen, driven by **CD4+ helper T cells**



https://en.wikipedia.org/wiki/File:Necrogran10x.jpg

- Caseation necrosis typical of tuberculosis is **ABSENT.**



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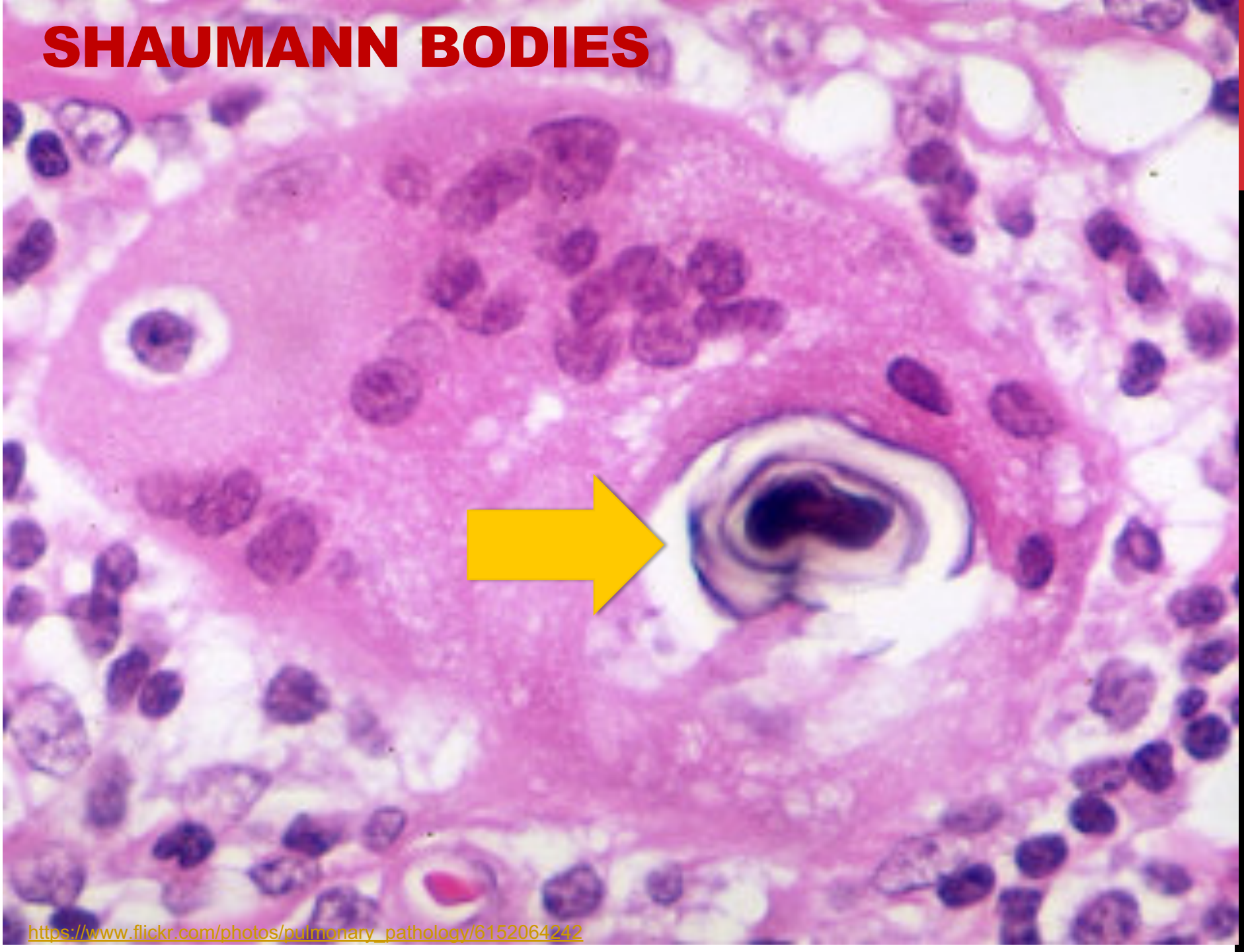
SHAUMANN BODIES



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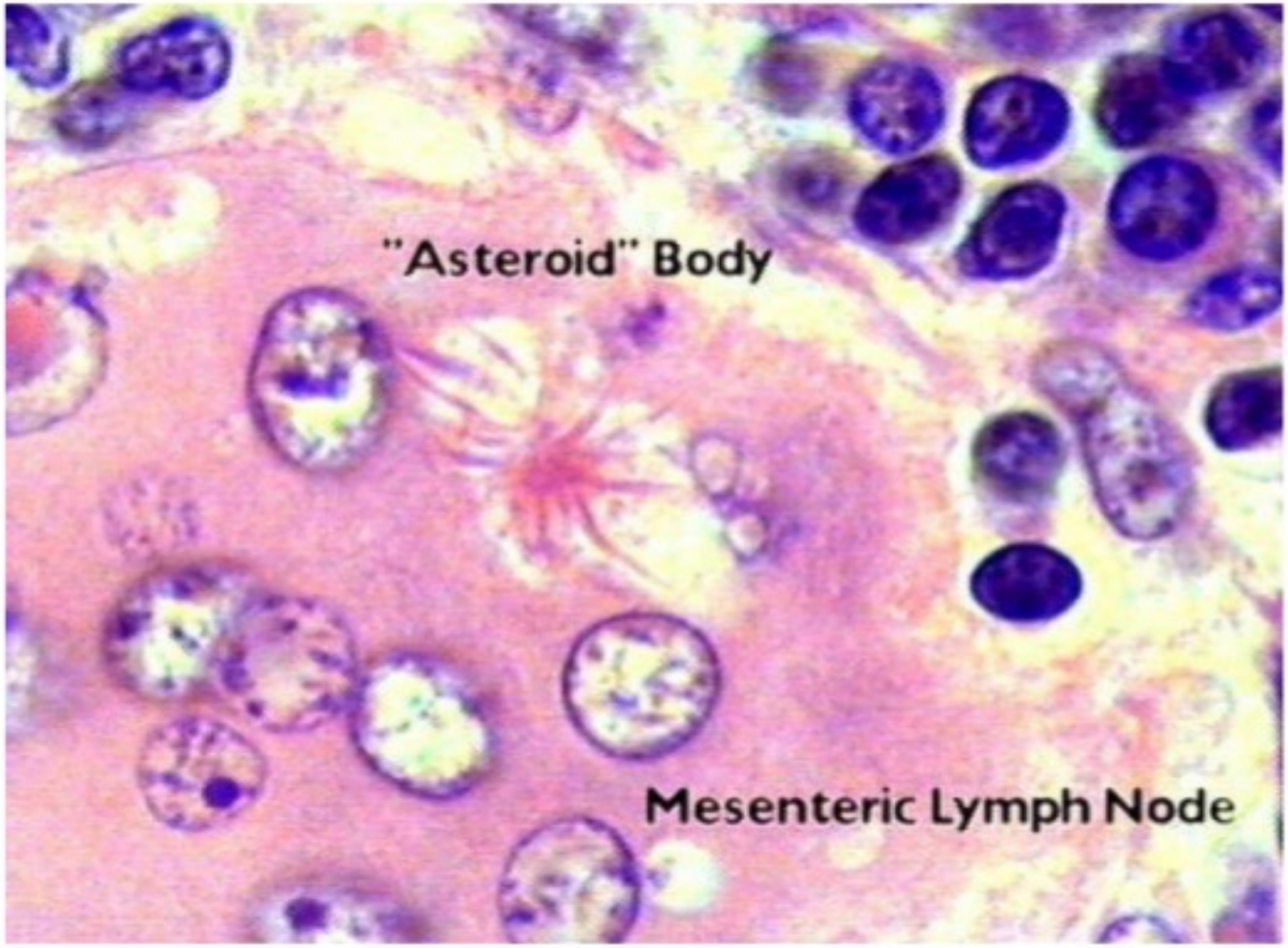
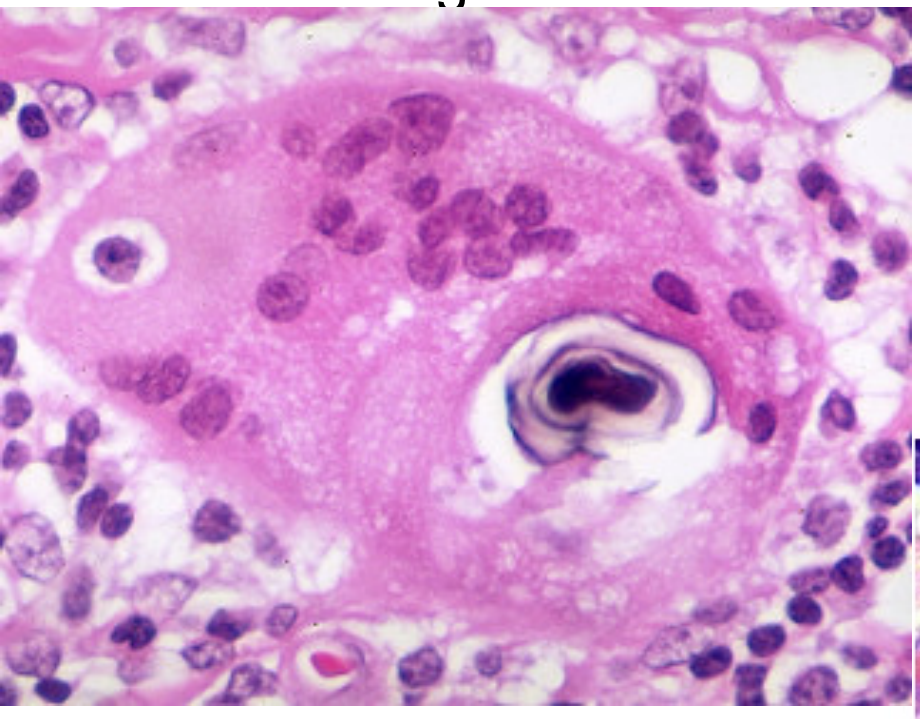
Asteroid body



- The presence of both bodies is not required for diagnosis of sarcoidosis, and they may also occur in granulomas of other origins.



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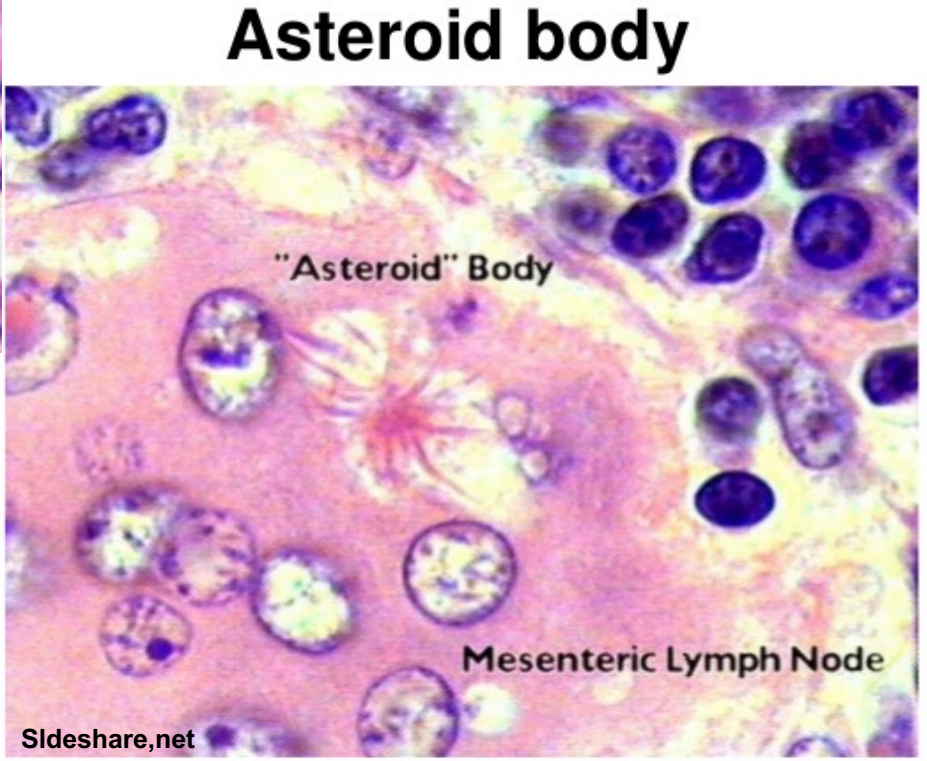

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MOST COMMONLY INVOLVES:

- Lungs
- lymph nodes
- Skin
- eye and lacrimal glands
- Spleen, Liver, BM

MORPHOLOGY, LUNGS:

- **90%** of patients.

- Granulomas involve the **interstitium**

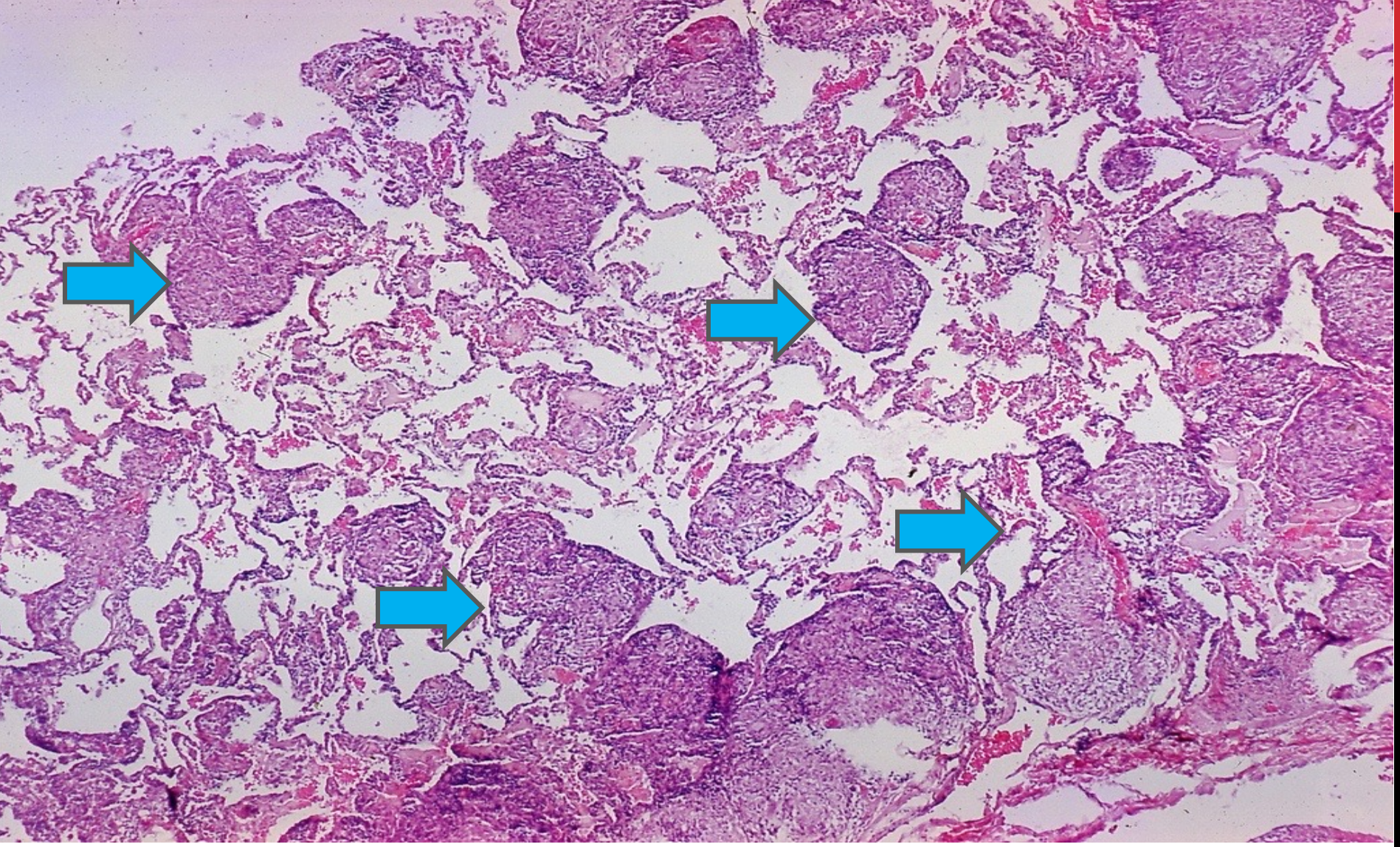
+/- alveolar lesions and pleural involvement

- Lesions are common along the lymphatics, around bronchi and blood vessels,
- high frequency of granulomas in the bronchial submucosa

- The **BAL** fluid contains abundant CD4+ T cells.

- strong tendency for lesions to heal in the lungs→ varying stages of fibrosis and hyalinization are often found.

- **In 5-15% of cases → honeycomb lung**



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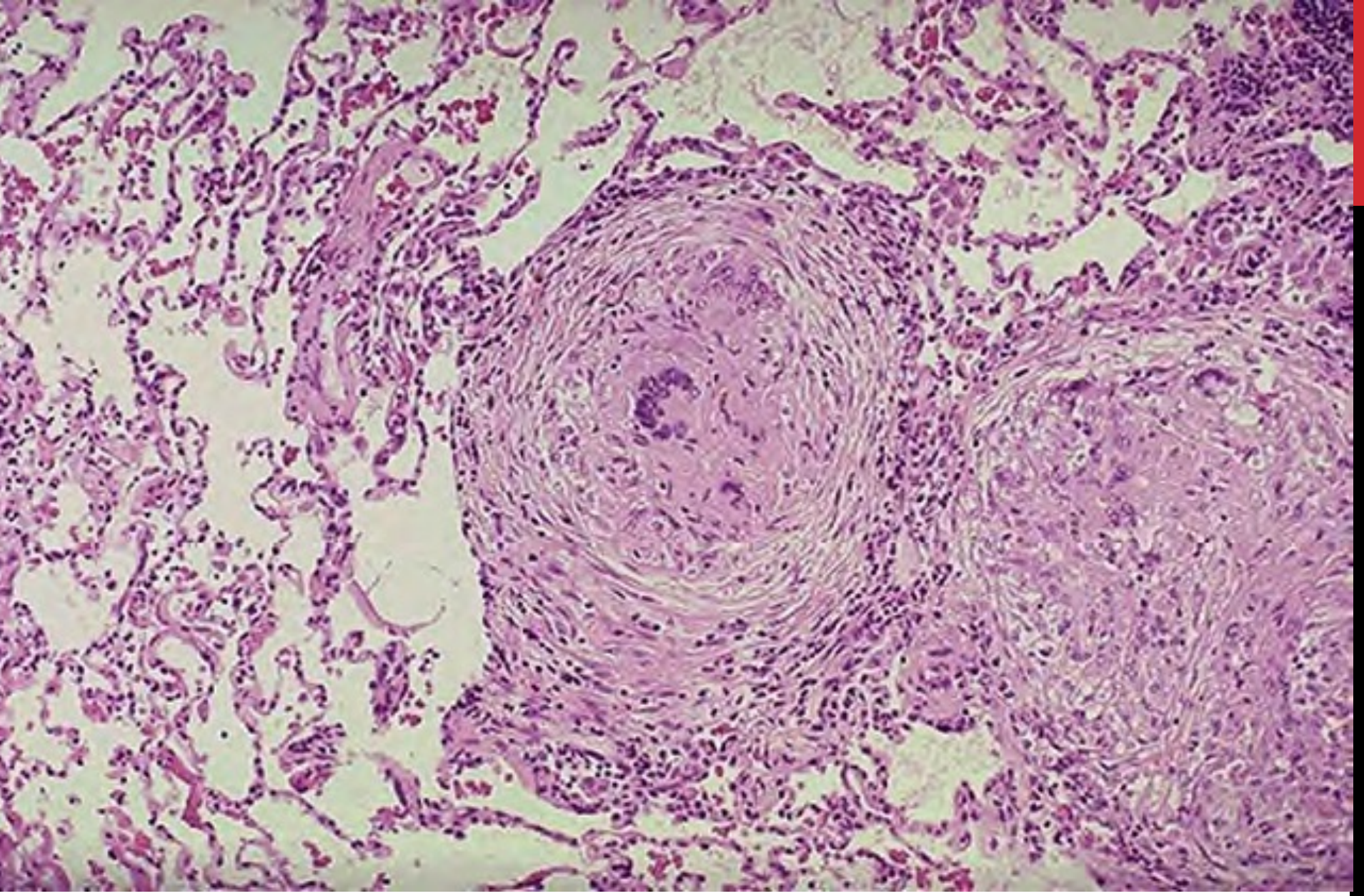

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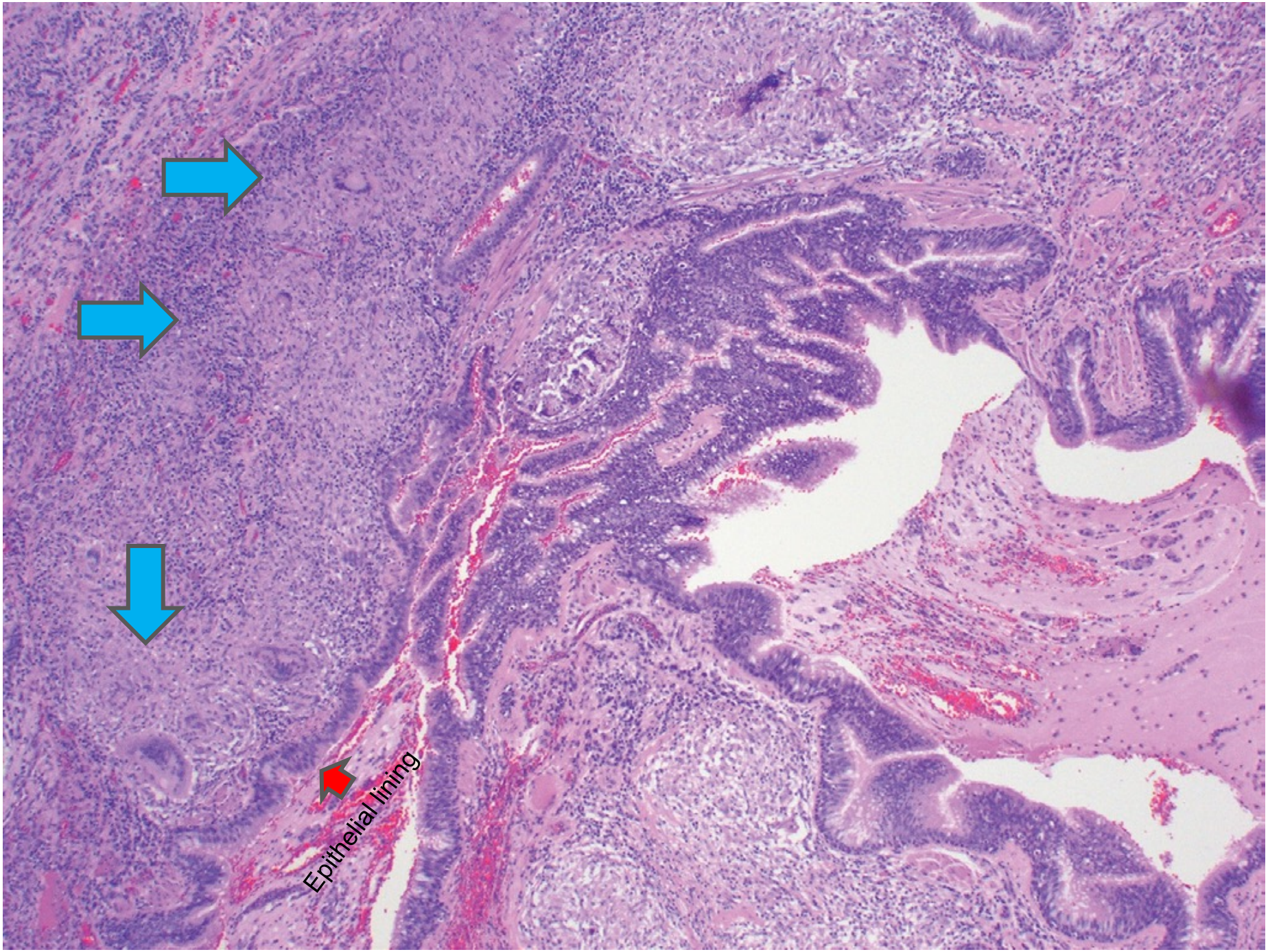

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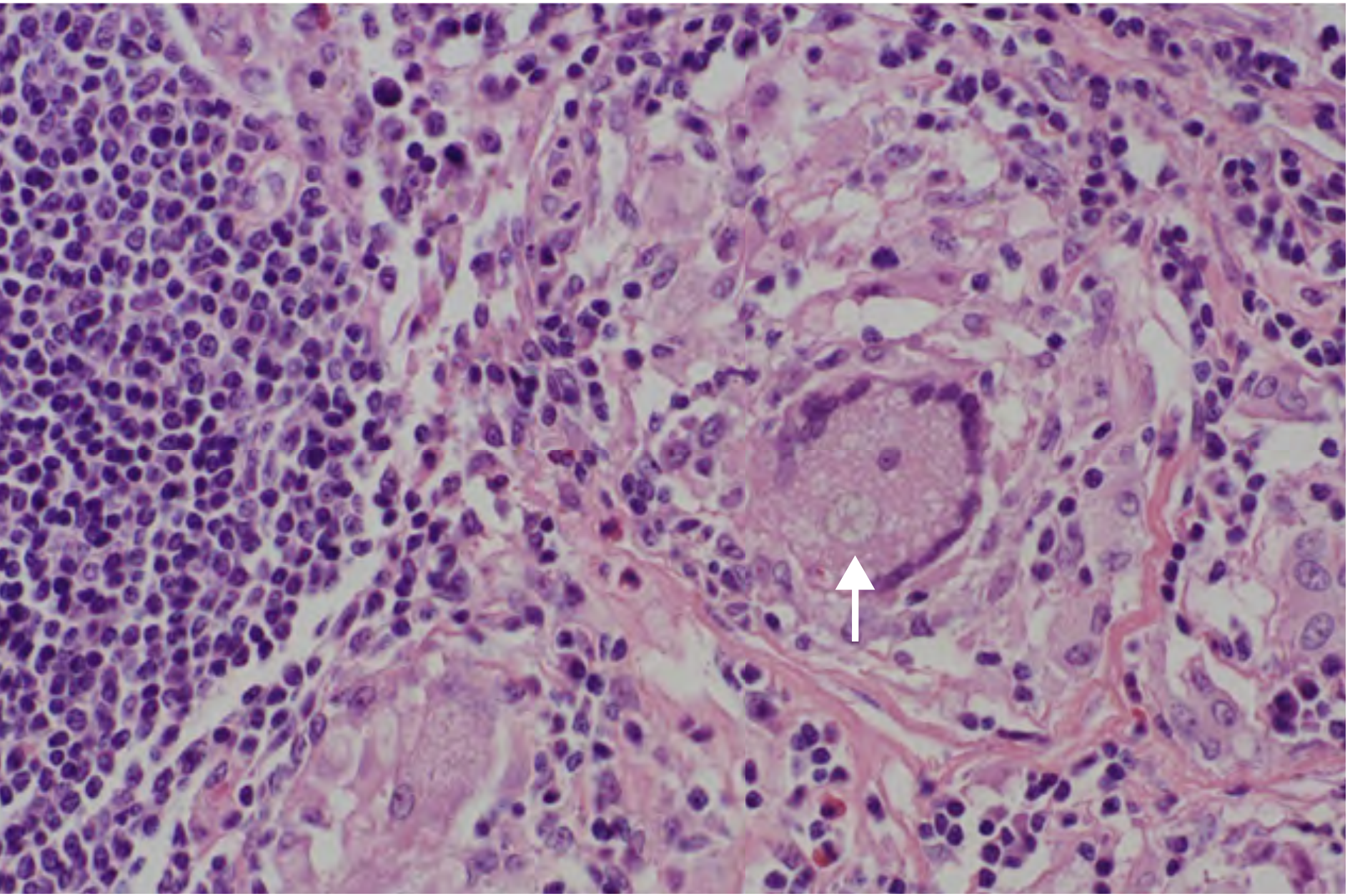
MORPHOLOGY, LYMPH NODES:

- **in almost all cases, any node can be affected.**
- **Particularly the hilar and mediastinal nodes**
- The nodes:
  - Enlarged painless
  - firm, rubbery texture
  - Discrete “nonmatted” , nonadherent and do not ulcerate “ unlike TB”

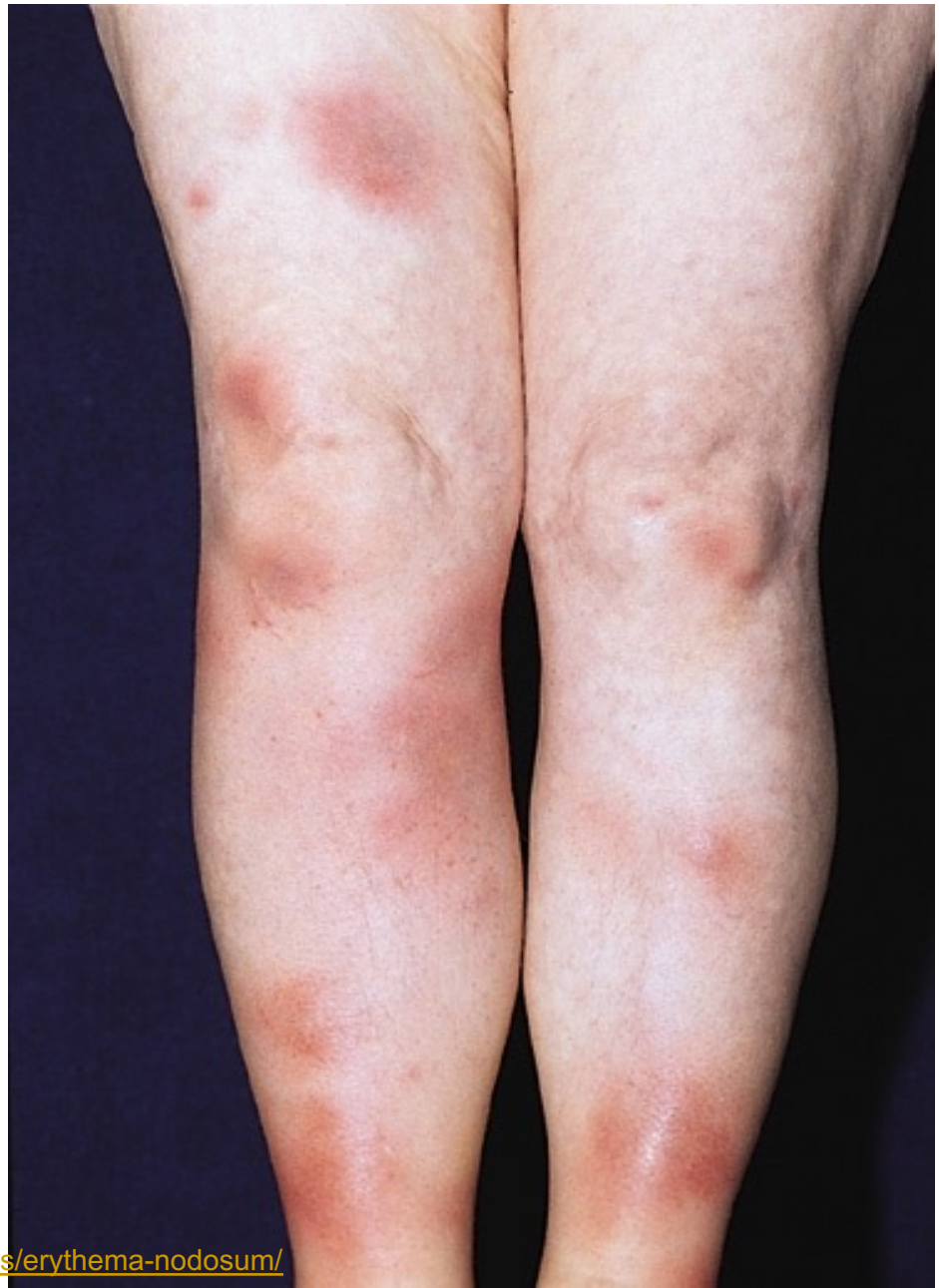
+/- sometimes calcified



MORPHOLOGY, SKIN:

- 25% of patients.
- **Erythema nodosum:**
  - **Hallmark of acute sarcoidosis**
  - Raised, red, tender nodules on the anterior aspects of legs.
  - Sarcoidal granulomas are uncommon in EN.
- **Subcutaneous nodules:**
  - discrete painless
  - abundant noncaseating granulomas
- Others: erythematous plaques; or flat lesions

ERYTHEMA NODOSUM



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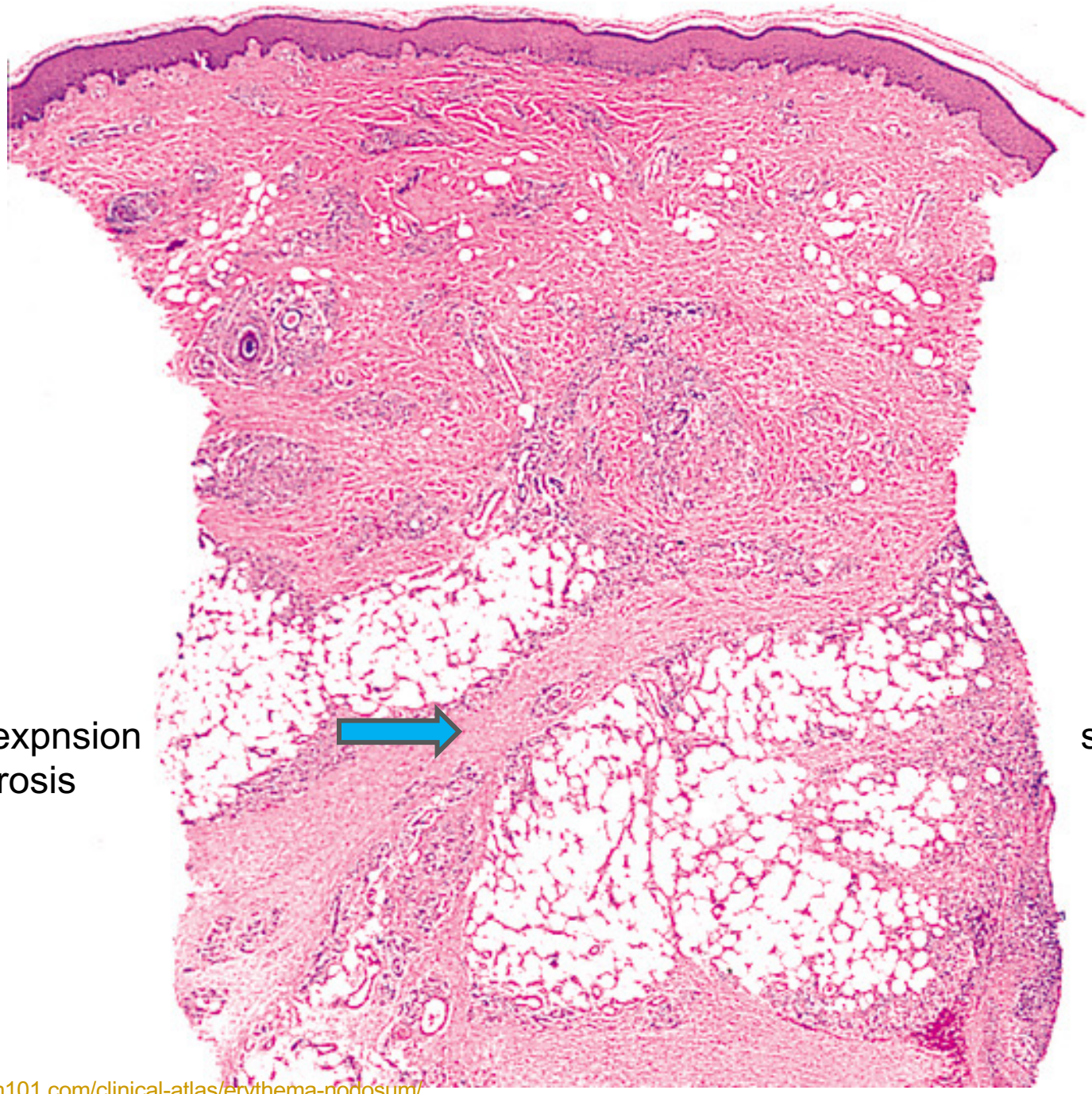

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MORPHOLOGY, EYE AND LACRIMAL GLANDS :

- 20-50% of cases.

- UVEITITS (MOST COMMON):
  - iritis or iridocyclitis, unilateral or bilateral.
  - posterior uveal tract disease (choroiditis)

- Corneal opacities, glaucoma, and even total loss of vision

- **SICCA SYNDROME**: Inflammation in the lacrimal glands, with suppression of lacrimation.

- < 10% of patients; Unilateral or bilateral parotitis with painful enlargement of the parotid glands .

- Xerostomia (dry mouth).

- **Mikulicz syndrome:** Combined uveoparotid involvement.

MORPHOLOGY, SPLEEN, LIVER, BM:

- **Spleen:**
  - In ¾ of cases spleen contains granulomas.
  - In 10% only it becomes enlarged.

- **Liver:**
  - Granulomas in portal triads
  - 1/3 hepatomegaly or abnormal liver function.

- **Bone marrow:**
  - 40% of patients.

- **Hypercalcemia and hypercalciuria.**
  - not related to bone destruction
  - caused by increased calcium absorption secondary to production of active vitamin D by the macrophages that form the granulomas

CLINICAL FEATURES

- **Mostly, Entirely asymptomatic**.

- **Symptomatic in others:**
  - Peripheral lymphadenopathy, cutaneous lesions, eye involvement, splenomegaly, or hepatomegaly.

  - 2/3 → gradual respiratory symptoms (**shortness of breath**, dry cough, or chest discomfort) or Constitutional signs and symptoms (fever, fatigue, weight loss, anorexia, night sweats).

DIAGNOSIS

- A definitive diagnostic test for sarcoidosis **does not exist**

- **Noncaseating granulomas** is suggestive of sarcoidosis, but exclusion of other causes is a must.

- Diagnosis:
  - ✓ **Clinical findings**
  - ✓ **Radiologic findings**
  - ✓ **Histologic findings:** Identification of noncaseating granulomas in involved tissues
  - ✓ Exclusion of other disorders with similar presentations, radiology or histologic findings.
    - In particular, **tuberculosis must be excluded**.

COARSE:

- **Unpredictable course**
- **Progressive chronicity**
- Periods of activity interspersed with remissions
- Remissions may be spontaneous or by steroid therapy

OUTCOME:

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

GRANULOMATOUS DISEASES

- Sarcoidosis
- **Hypersensitivity pneumonitis**

HYPERSENSITIVITY PNEUMONITIS

- a spectrum of immunologically mediated, predominantly interstitial lung disorders caused by intense, prolonged exposure to inhaled organic antigens (Often occupational)

- Called **allergic alveolitis**:
  - Primarily affects the **alveoli**
  - Related to the inhalation of organic dust containing antigens made up of the spores of thermophilic bacteria, fungi, animal proteins, or bacterial products.

- **Numerous syndromes** are described depending on the occupation or exposure of the individual, examples:
  - **Farmer's lung** →exposure to dusts generated from humid, warm, newly harvested hay that permits the rapid proliferation of the spores and mold.
  - **Humidifier or air-conditioner lung:** caused by thermophilic bacteria in heated water reservoirs.
  - **Hot tub lung:** nontuberculous Mycobacterium
  - **Pigeon breeder's lung:** proteins from serum or feathers

- >300 allerogen →development of hypersensitivity pneumonitis most of which are related to occupational exposure.


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IMMUNOLOGIC BASIS

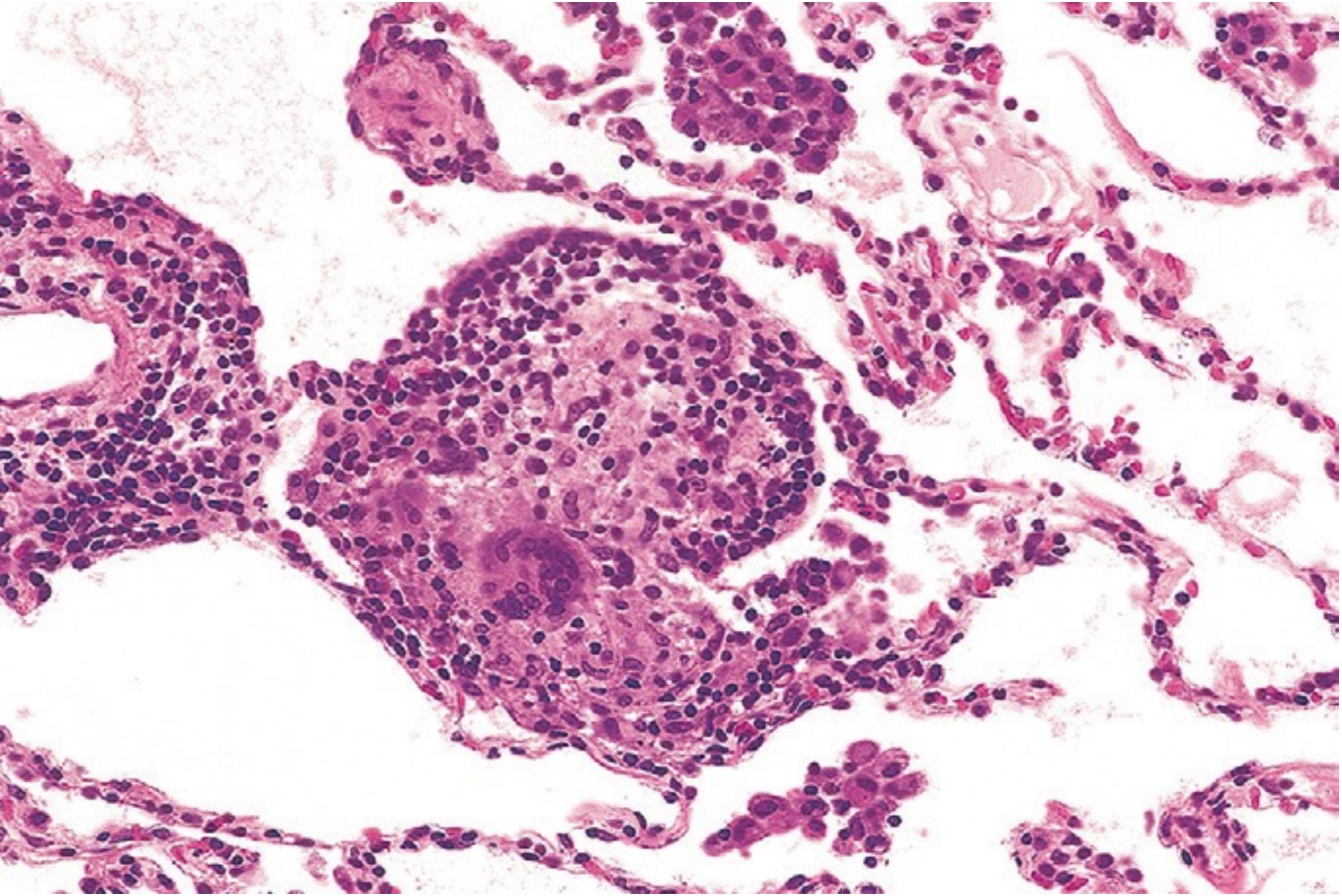
- BAL specimens demonstrate increased numbers of both CD4+ and CD8+ lymphocytes.
- specific antibodies against the offending antigen in serum.
- Complement and immunoglobulins within vessel walls by IF.
- 2/3 of patients, Noncaseating granulomas in the lungs.

MORPHOLOGY

- Histologic changes are centered on **bronchioles,** including:
  - **interstitial pneumonitis:** lymphocytes, plasma cells, and macrophages (eosinophils are rare) in the **pulmonary interstitium**
  - **“Loose,” poorly formed granulomas, without necrosis in > 2/3** of cases, usually in **a peribronchiolar location**
  - **interstitial fibrosis** with fibroblastic foci, honeycombing, and obliterative bronchiolitis (in late stages).

- > 50% intra-alveolar infiltrate is seen

- In advanced chronic cases, **bilateral, upper-lobe–dominant interstitial fibrosis (UIP pattern) occurs**.



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THANK YOU!