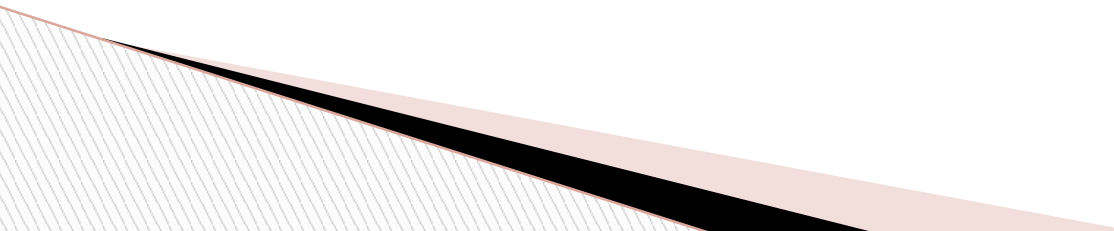


GRANULOMAS

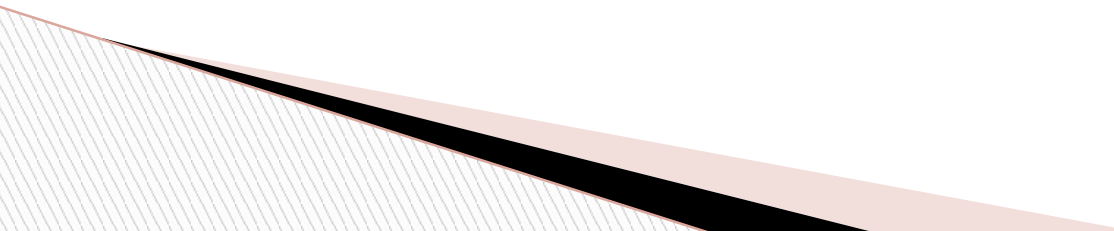
Dr. Dina Saleh

Granuloma

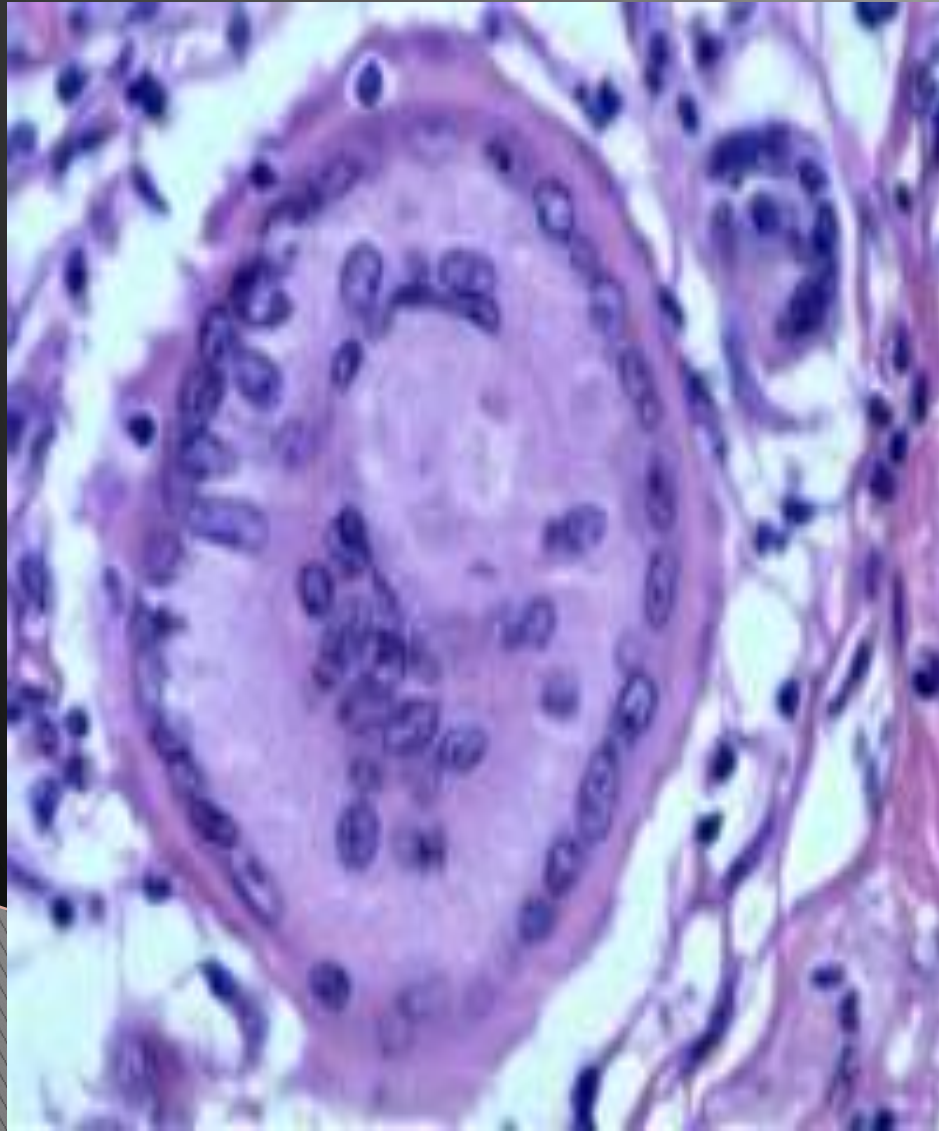
Specialized form of chronic inflammation characterized by small aggregates of modified macrophages (epithelioid cells) that are rimmed at the periphery by lymphocytes.



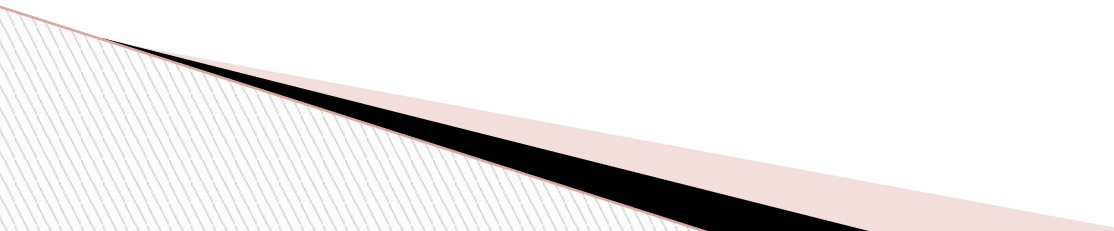
Composition of a Granuloma

- i. Epithelioid cells.
 - ii. Multinucleated giant cells, located centrally, are formed by the fusion of epithelioid cells. Types include *Langhans-type* giant cell (peripheral horseshoe arrangement of nuclei) and *Foreign body type* giant cell (haphazard arrangement of nuclei).
 - iii. Lymphocytes and plasma cells at the periphery
 - iv. Central necrosis occurs in granulomata due to excessive enzymatic breakdown
- 

Types of giant cells



Examples of granulomatous inflammation

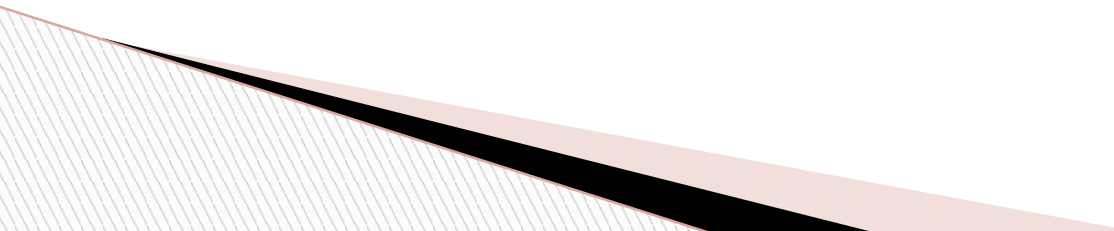
1. Bacterial : Tuberculosis, leprosy, syphilitic gumma, cat scratch disease.
 2. Parasitic : Schistosomiasis, toxoplasmosis.
 3. Fungal : cryptococcosis.
 4. Inorganic dusts : Silicosis.
 5. Foreign body : suture, breast prosthesis.
 6. Unknown etiology : Sarcoidosis, crohn's disease.
- 

Tuberculosis

- It is a chronic infectious granulomatous inflammation.
- It is caused by the bacillus *Mycobacterium tuberculosis*.
- It typically affects the lungs (**pulmonary TB**) but can also affect other sites (**extrapulmonary TB**).
- *M. tuberculosis* is carried in **airborne particles**, called droplet nuclei, of 1– 5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing.

Pathogenesis of tuberculosis:

TB bacillus does not produce exotoxins or endotoxins, so its pathogenicity is related to escape killing by MQs and inducing immune response:

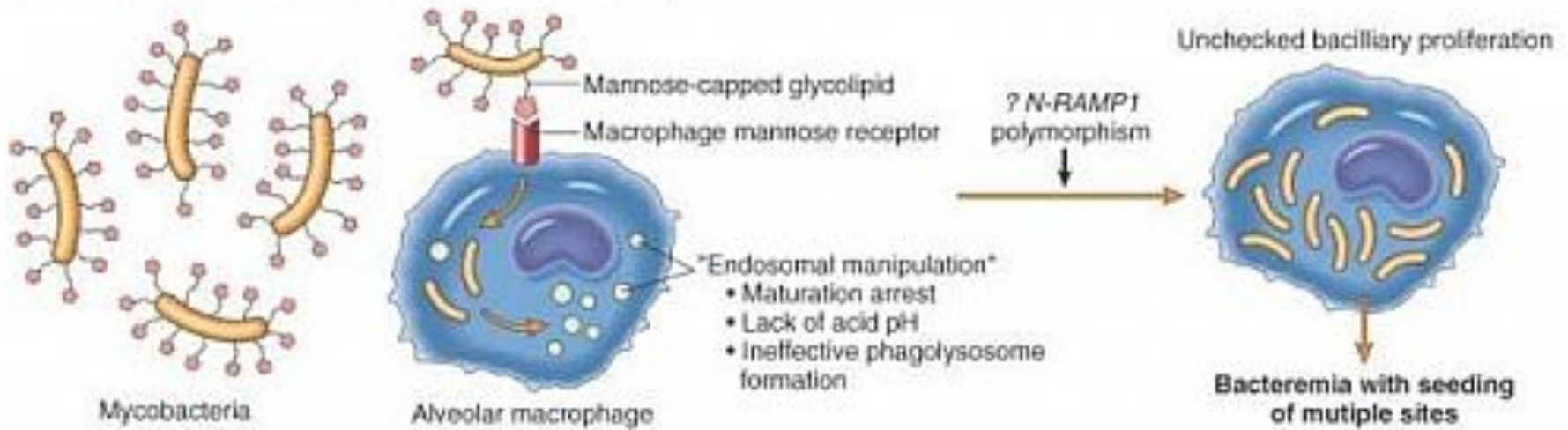


Steps in the pathogenesis of TB

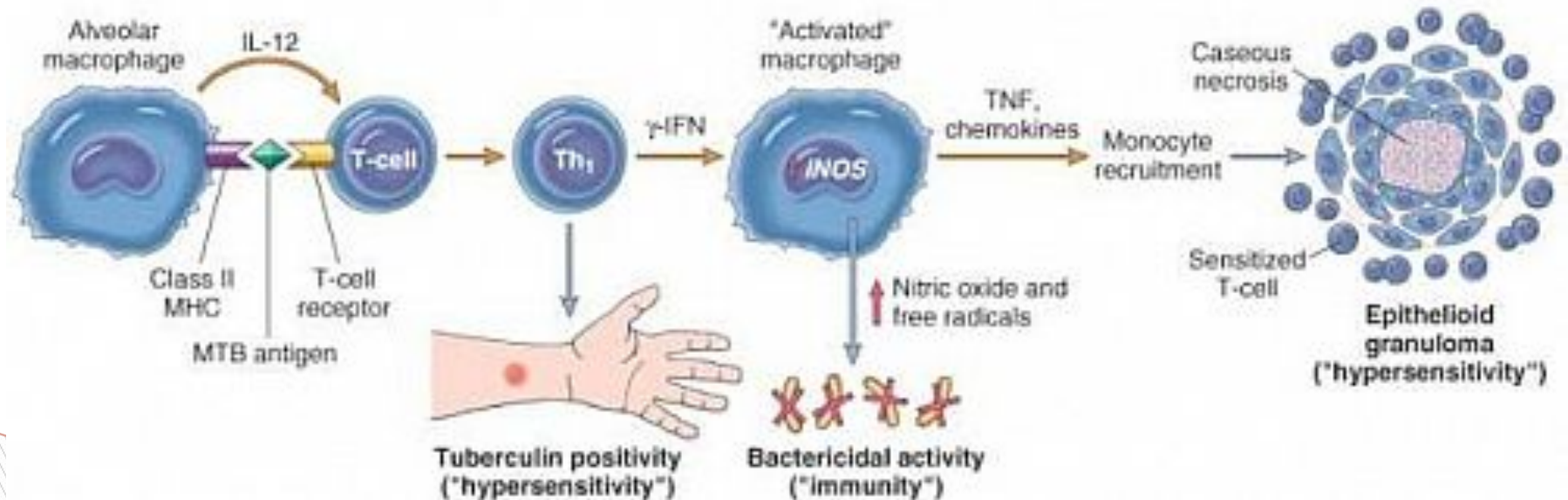
Primary TB infection

- a. The bacteria are **phagocytosed by alveolar macrophages**, but the macrophages **cannot** digest them. This leads to unchecked bacillary **replication**.
- b. **T-cell sensitization**.
- c. **T- cell activation** which cause:
 - Release of **IFN- γ** leading to macrophage activation
 - Positive skin test
- d. **Granuloma formation** (activated macrophage mediated):
 - Mononuclear cells recruitment
 - Release of growth factors (e.g. **TGF-B**) which stimulate fibroblast proliferation and collagen synthesis.

A. PRIMARY PULMONARY TUBERCULOSIS (0-3 weeks)



B. PRIMARY PULMONARY TUBERCULOSIS (>3 weeks)



Mantoux (tuberculin) skin test

Intradermal injection of 0.1 ml of purified protein derivative (PPD) . Delayed hypersensitivity develops in infected or previously infected individual with tubercle bacilli. Positive test is identified as an indurated area of at least 5mm in diameter that peaks in 48-72 hours .



GROSS

Primary pulmonary TB

– Ghon foci:

- **Shape:** gray-white, caseous nodule
- **Size:** small (1 – 1.5 cm in diameter)
- **Location:** subpleural

– Typically seen at **lower part of the upper lobe** or the **upper part of the lower lobe**

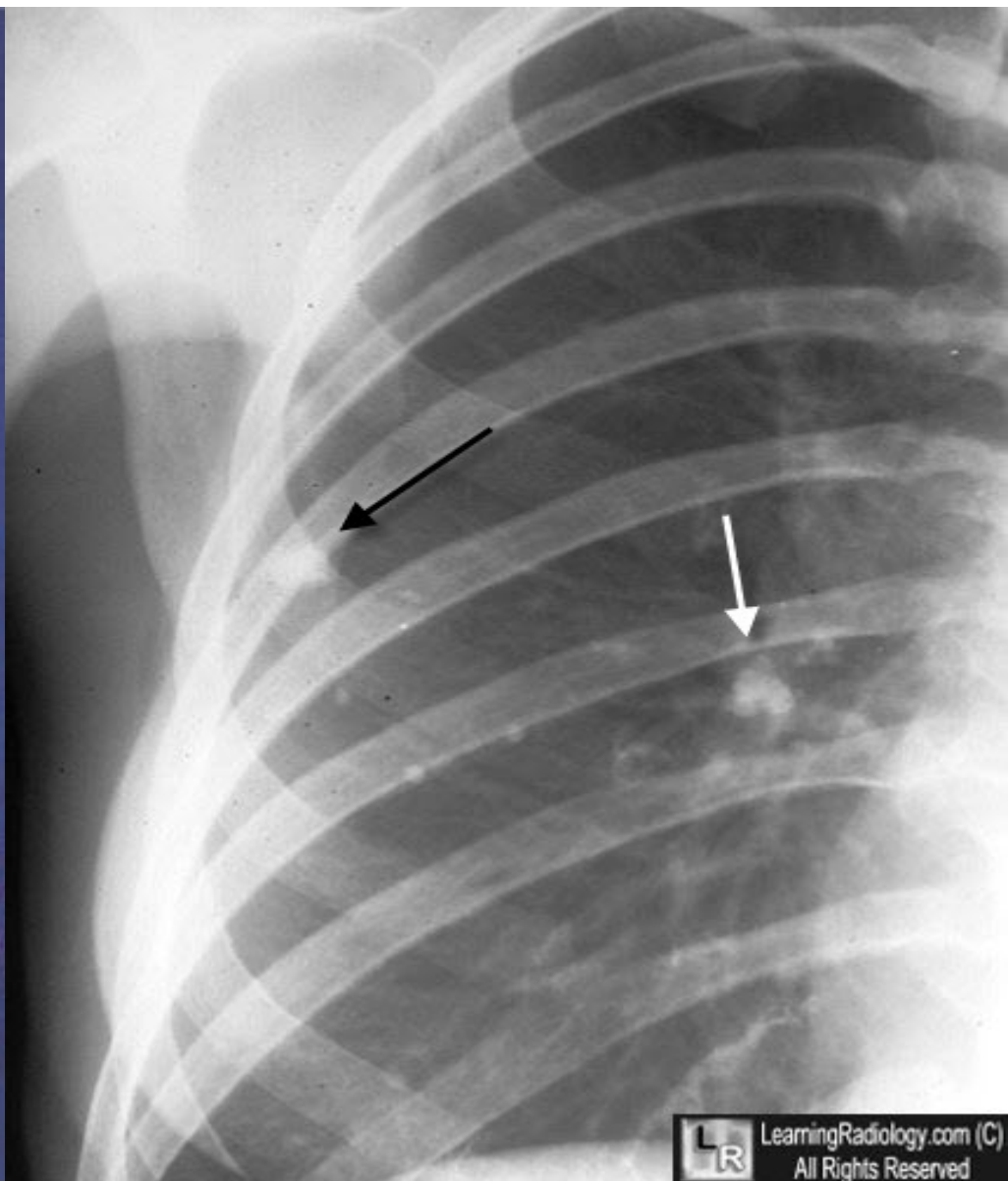
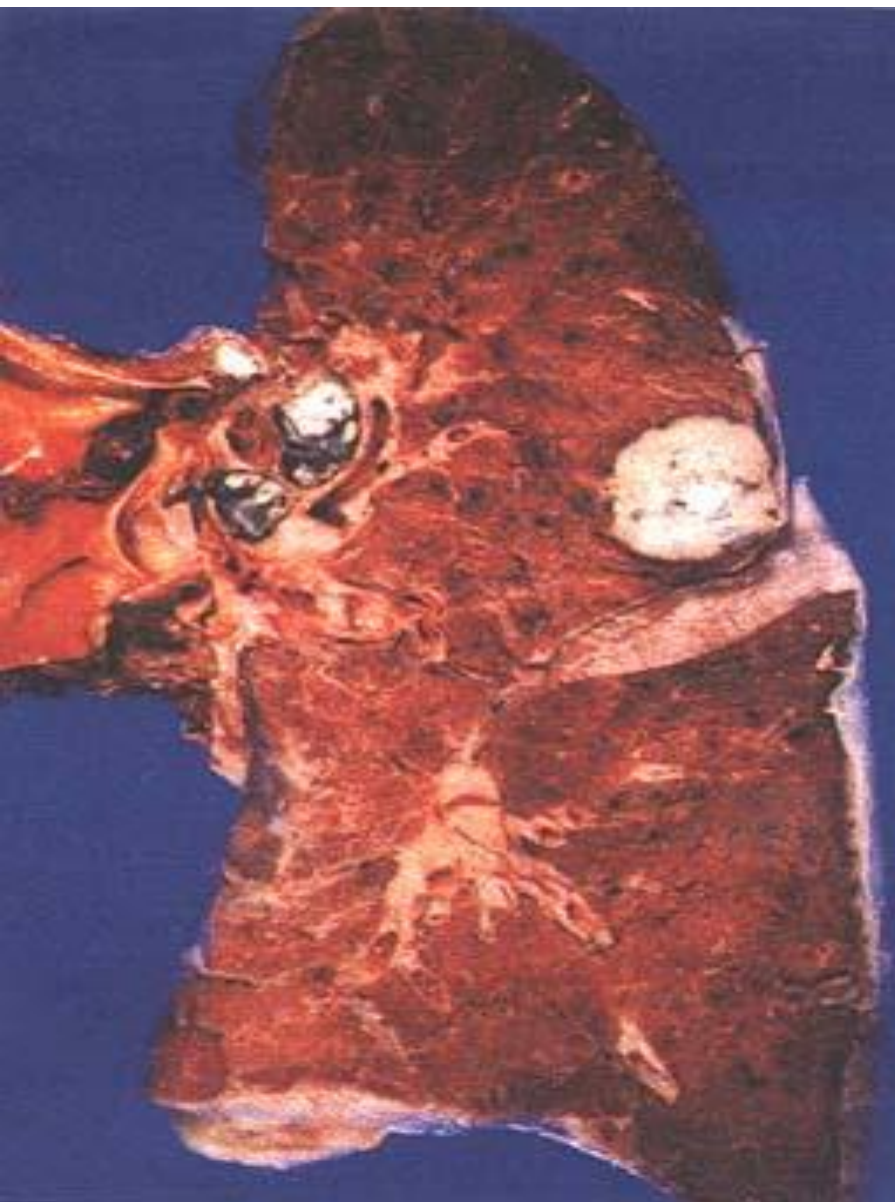
• **Outcome:**

- Most cases → Good health / receiving therapy: heals with **fibrosis/calcification**
- Some cases → Bad health conditions: **progressive pulmonary TB – miliary TB**

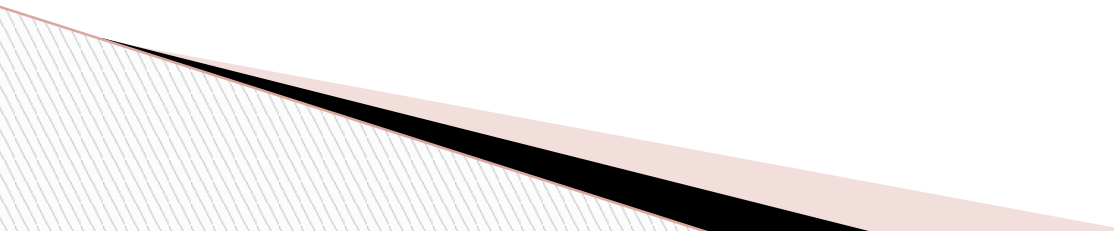
– **Ghon complex:**

- Ghon foci (red arrow) + **enlarged, caseous hilar lymph nodes** (blue arrow)





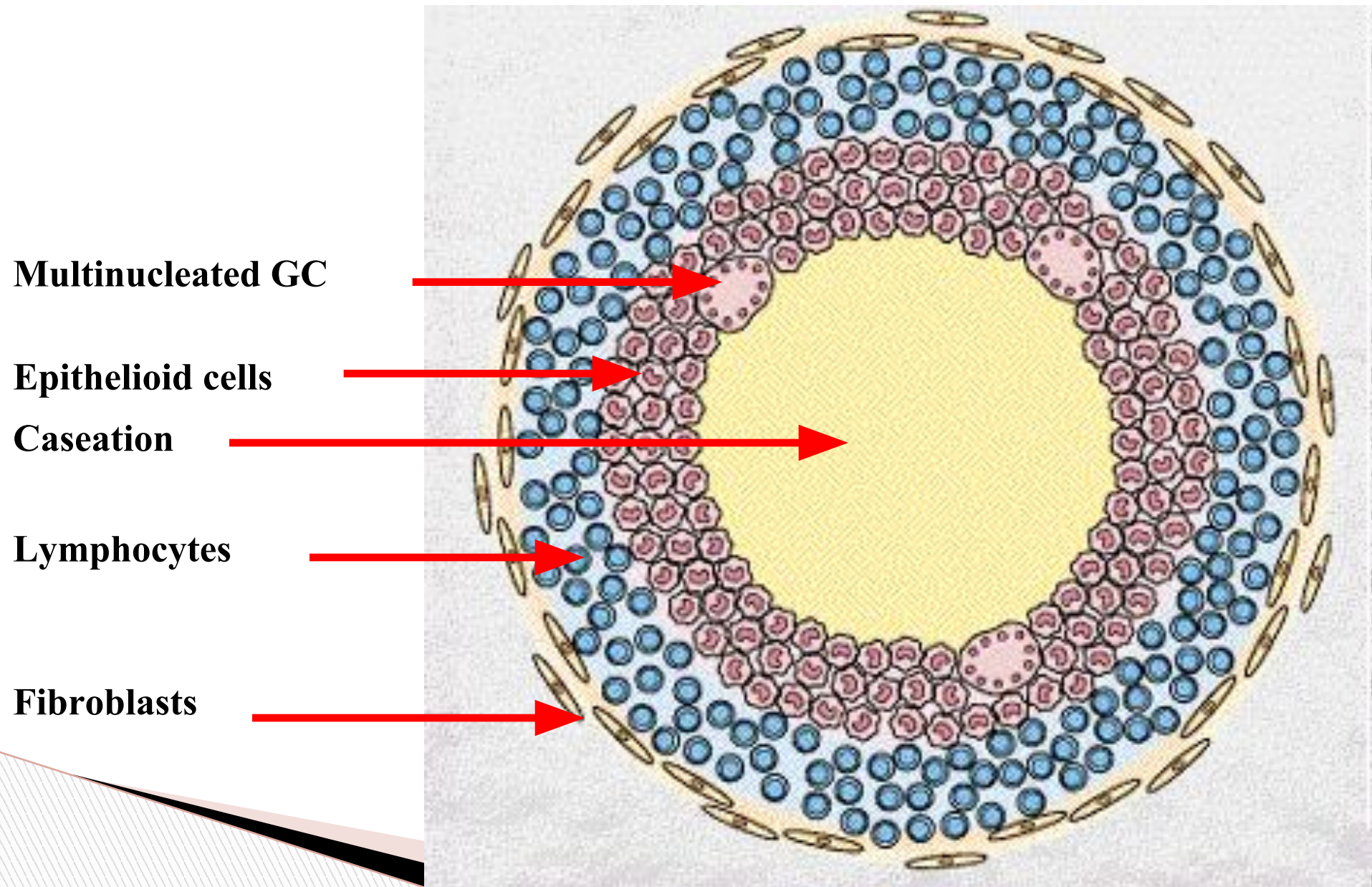
Secondary TB infection

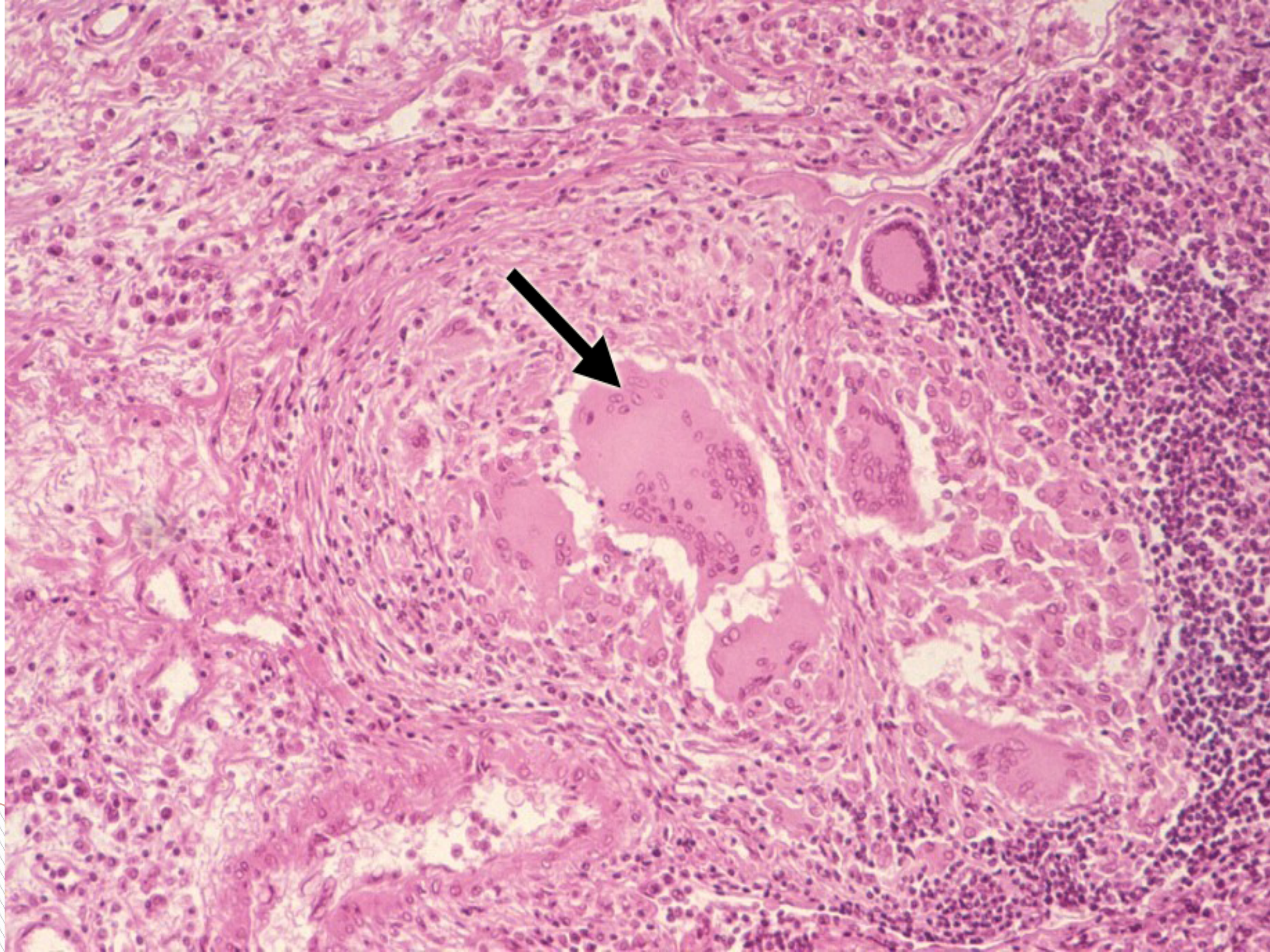
- Occurs in **previously sensitized** host.
 - **Re-activation** of latent infection/ **Re-exposure** to the bacilli.
 - **Rapid** immune response (TH1 cells are already present) rapid macrophage activation & bacilli destruction.
 - Cause **more tissue necrosis** than primary TB.
- 

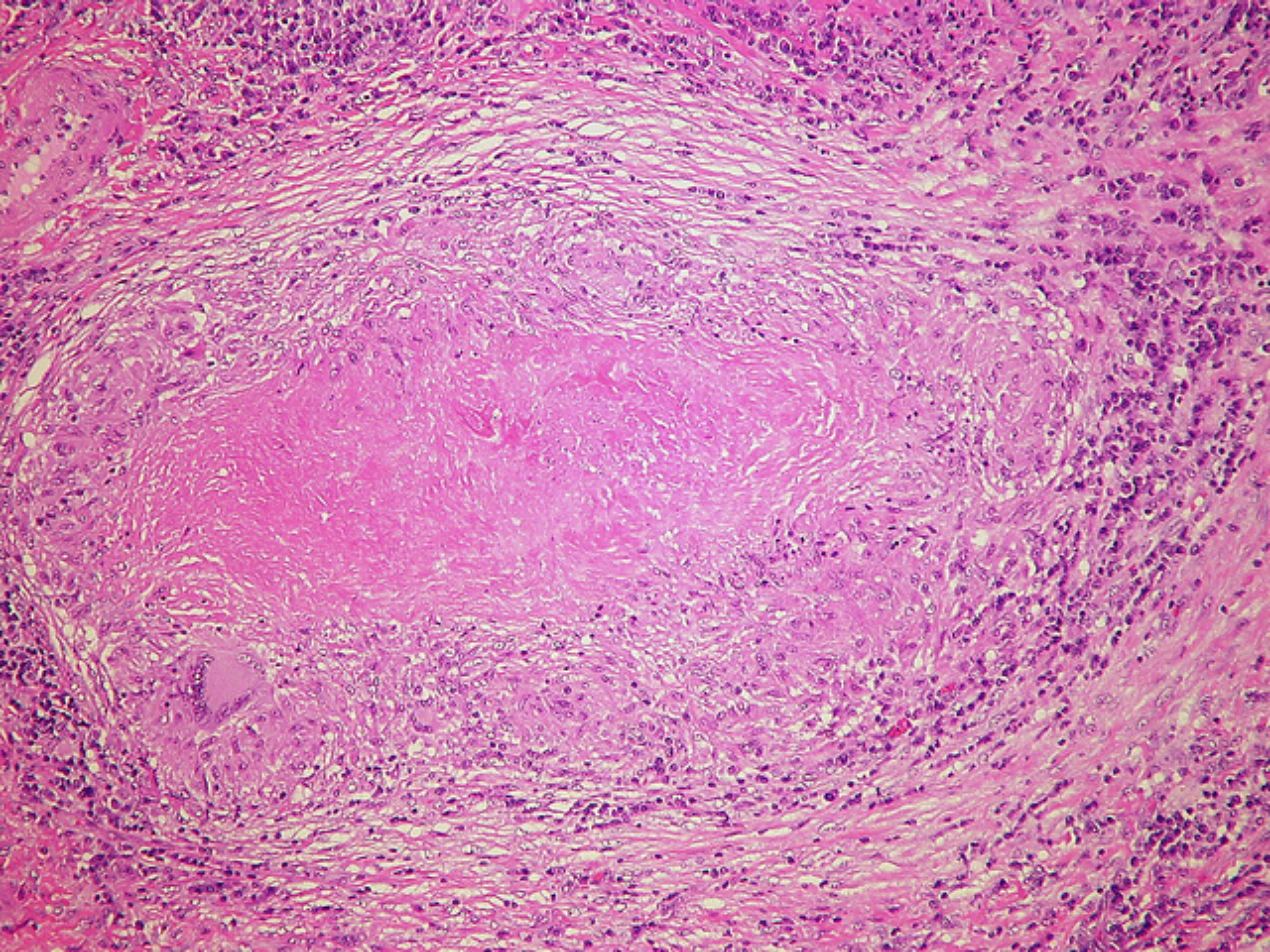
CLINICAL

	Primary TB	Secondary TB
Patient	Non-sensitized Usually children	Previously sensitized Usually adults
Source of infection	Exogenous (initial infection)	Exogenous (re-infection) Endogenous (re-activation)
Pulmonary lesion	Ghon foci (subpleural granuloma) NO cavitation	Apical cavitation
Hilar lymph nodes	Early involved (part of Ghon complex)	NOT early involved
Clinical presentation	Asymptomatic Flu-like symptoms	General manifestations (malaise, anorexia, weight loss, fever, night sweats) Pulmonary manifestations (productive cough, hemoptysis, chest pain)
Disease course	Most cases: Controlled <ul style="list-style-type: none">• Healed (without viable organisms)• Latent (with dormant organisms)	Most cases: Active <ul style="list-style-type: none">• Localized (pulmonary)• Miliary

Diagram of typical TB granuloma (Tubercle)

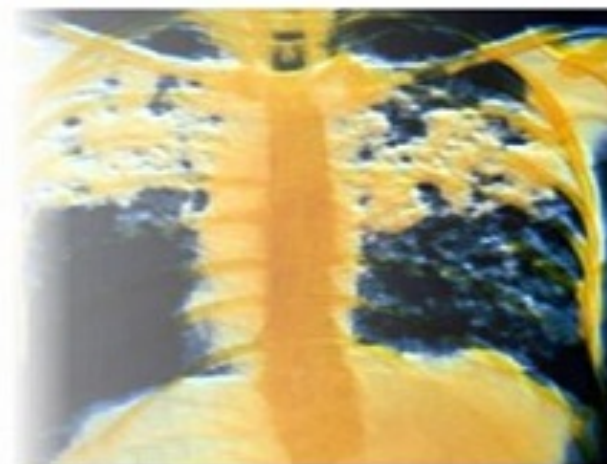
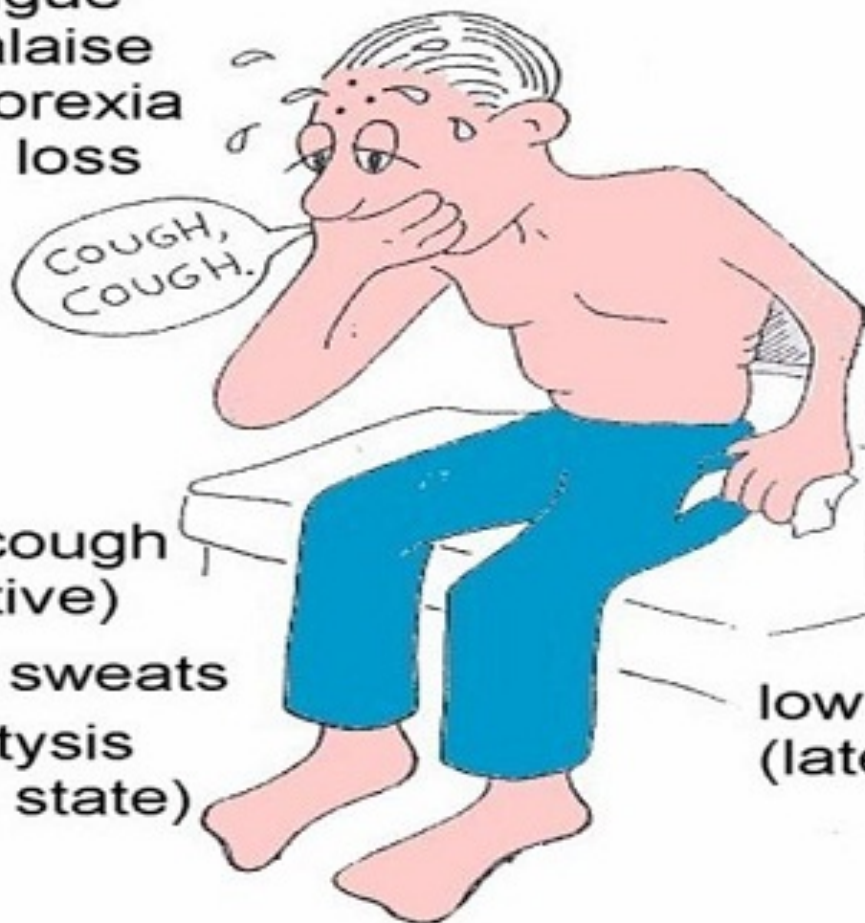






TUBERCULOSIS (TB)

- fatigue
- malaise
- anorexia
- wt. loss



chronic cough
(productive)

night sweats

hemoptysis
(advanced state)

low grade temp.
(late afternoon)

Treatment:

TB medications 6 to 12 months
bedrest until symptoms
resp isolation until
negative sputum
frequently out-pt basis

Diagnostic:

TB skin test
chest x-ray
bacteriologic
sputum studies

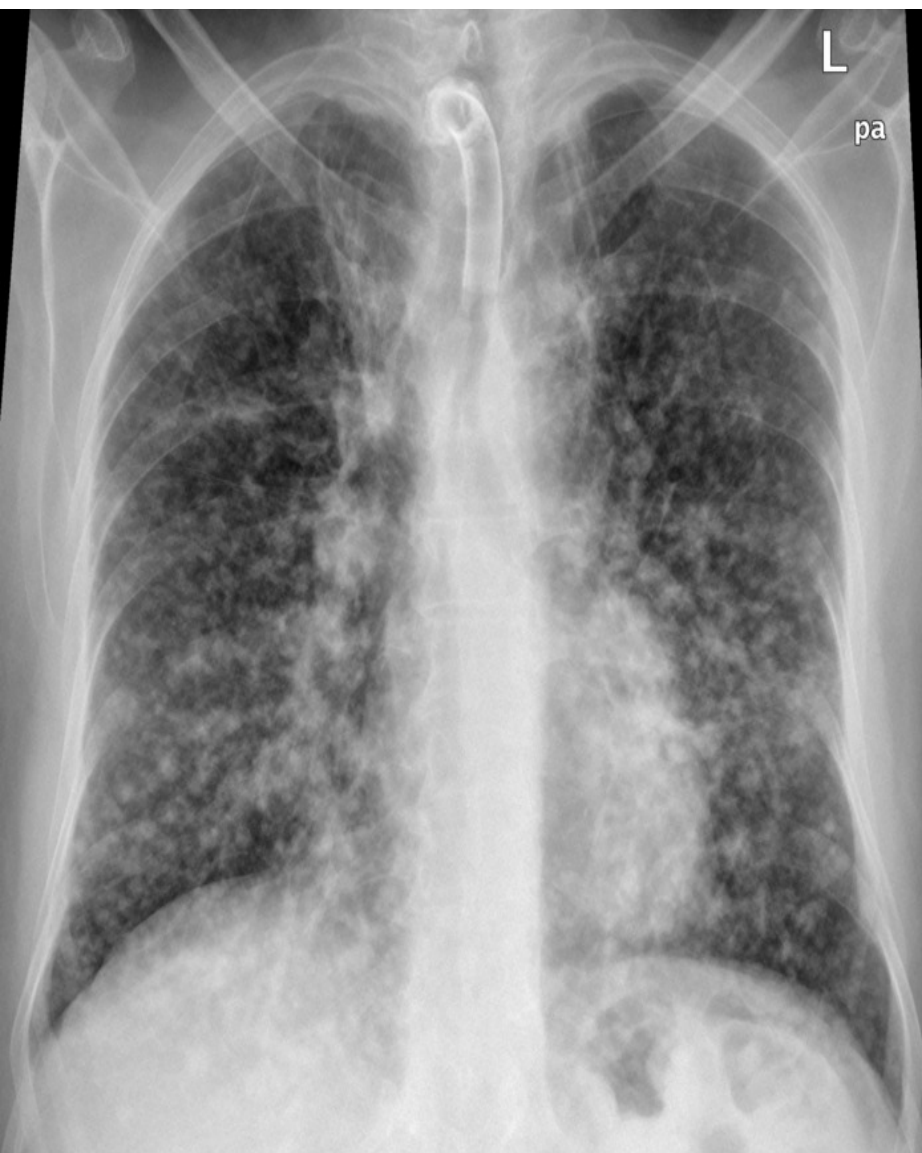
❖ *Miliary tuberculosis*

If large no. of bacilli enter the pulmonary venous circulation and are seeded systemically , then innumerable tubercles appear scattered in many organs all over the body.

Gross : there are innumerable millet seed-sized (1-2mm)

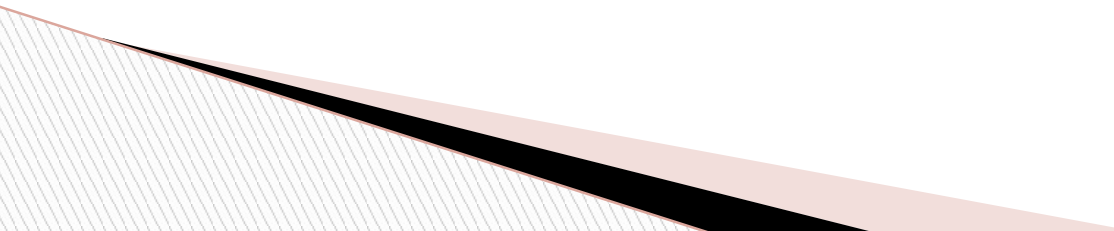
yellowish-white foci of consolidation (tubercle) without grossly visible caseation . They appear in different organs like lungs, liver, spleen, adrenals, etc.

Microscopic: The lesions of miliary TB show multiple tubercles with minute areas of caseation necrosis.

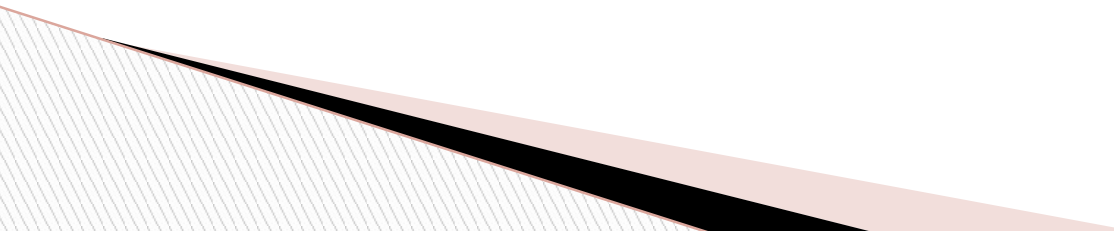


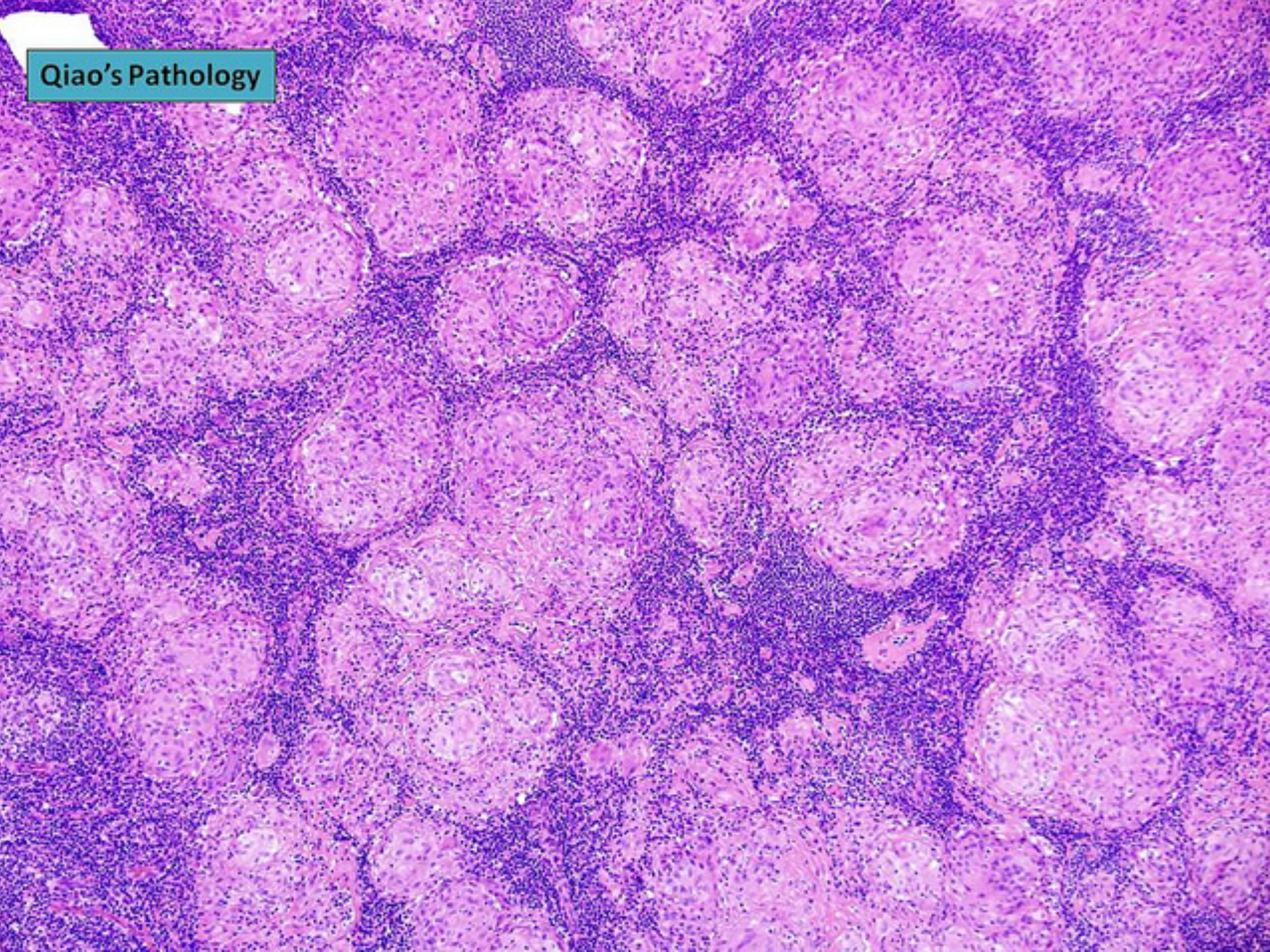
Sarcoidosis

It is a multisystem disease of unknown cause (evidences suggest that it is a disease of disordered immune regulation in genetically predisposed persons exposed to certain environmental agents). It is commonly manifested in the thoracic organs (90% of cases).



Microscopically:

- ❖ Small, non-caseating , well-circumscribed , epithelioid cell granulomas containing giant cells and surrounded peripherally by fibroblasts.
 - ❖ Typically , granuloma of sarcoidosis are " naked" i.e. either little or no peripheral rim of lymphocytes.
- 

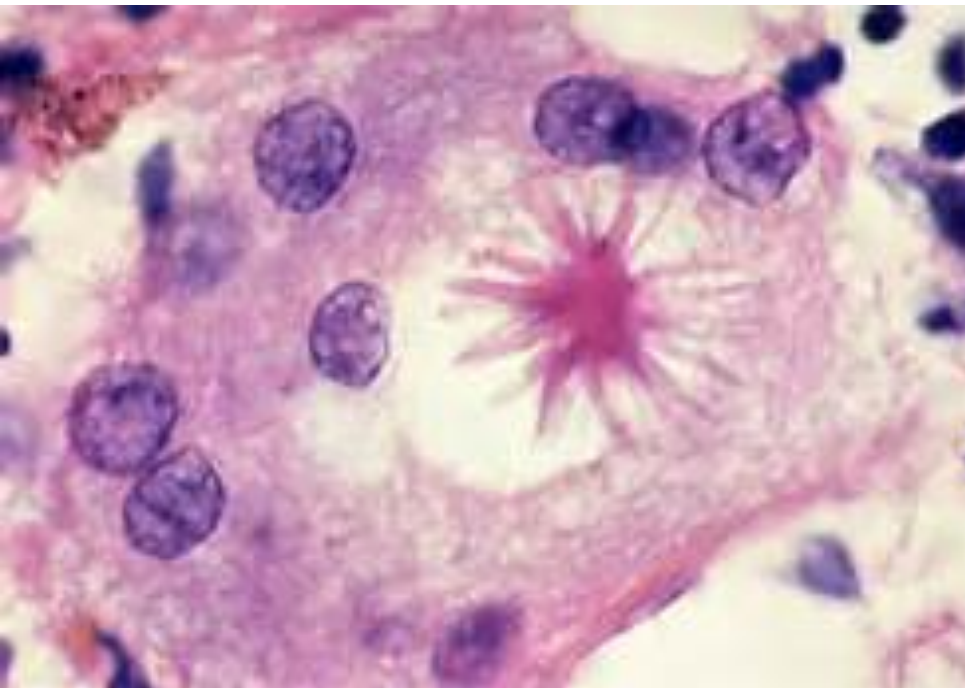


❖ Giant cells in sarcoid granuloma may contain cytoplasmic inclusions:

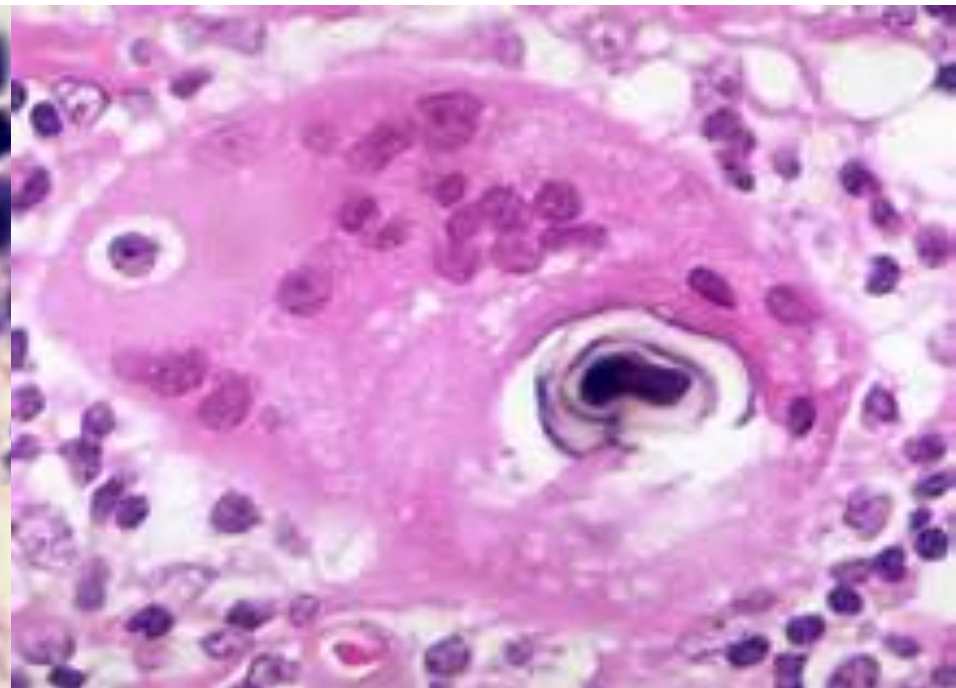
-*Asteroid bodies*: eosinophilic star-shaped inclusions.

-*Schaumann bodies*: concentric laminations of calcium and of iron salts complexed with proteins .

Asteroid body



Schaumann body



**THANK
YOU**

THANK

