GRANULOMA

DR ANJUM

GRANULOMA….. DEFINATION

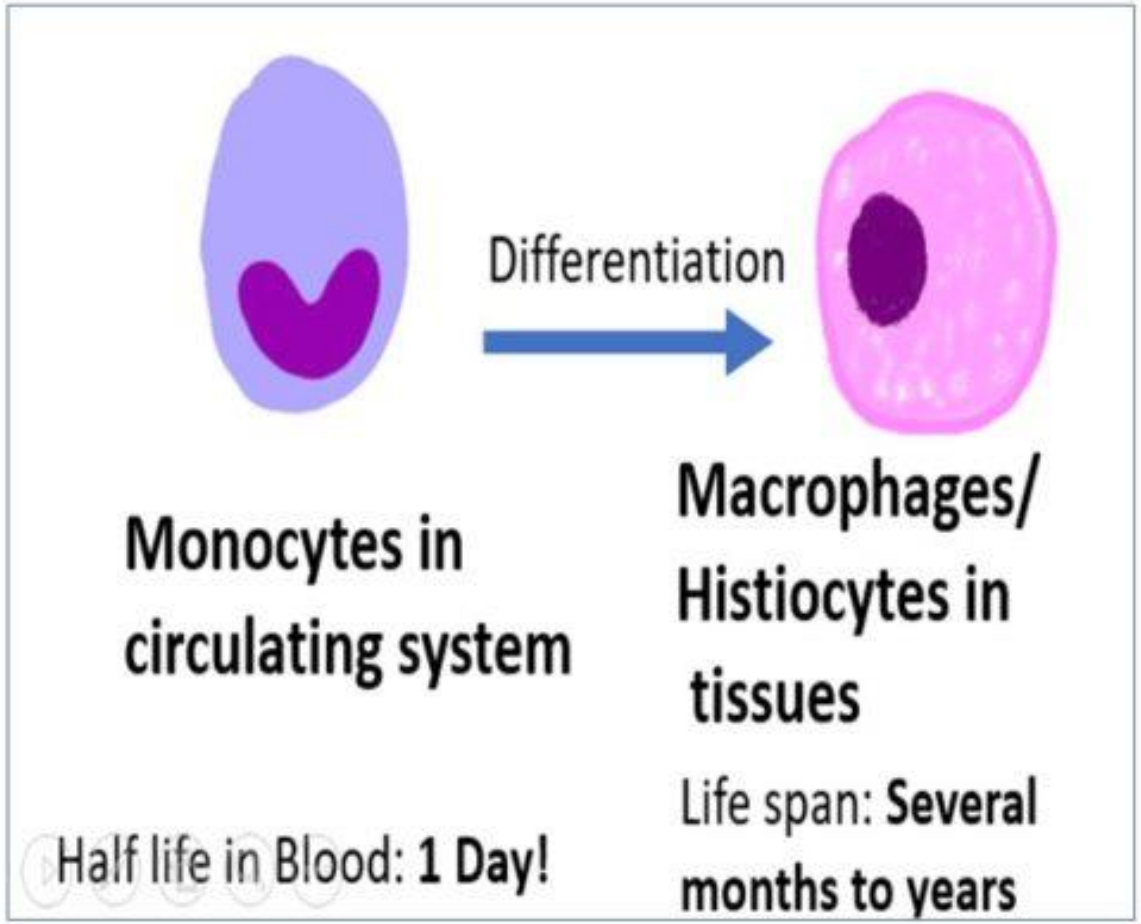
- A **granuloma,** is a focal aggregate of immune cells that forms in response to a **persistent (chronic) inflammatory stimulus**.
- It characteristically shows the compact organization of mature macrophages, which may or may not be associated with other inflammatory cell types.
- In Pathology…….**a granuloma is an organized collection of macrophages**

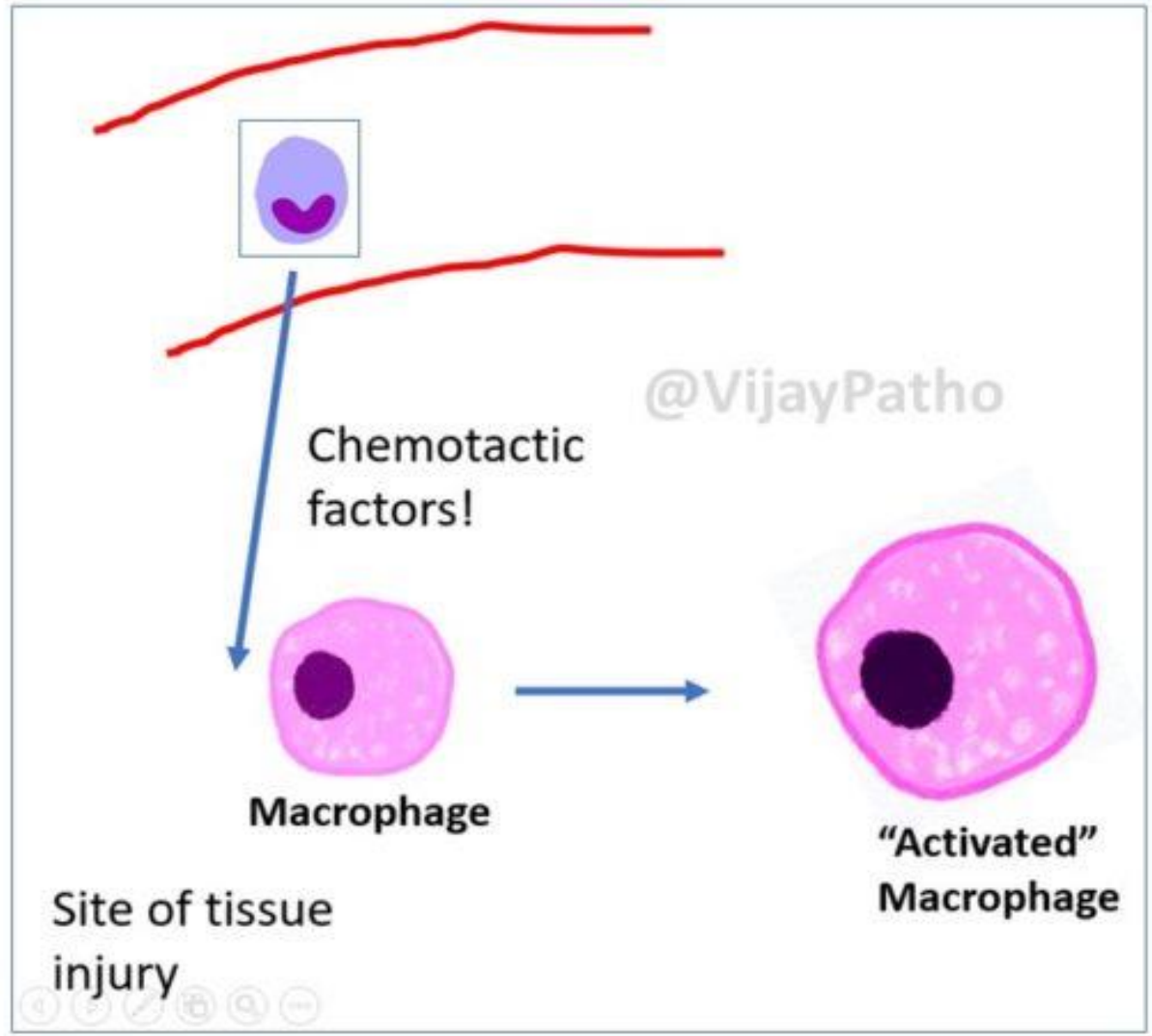
GRANULOMA……INTRODUCTION

- A **granuloma** is an aggregation of **macrophages** that forms in response to chronic **inflammation.**
- This occurs when the **immune system** attempts to isolate foreign substances that it is otherwise unable to eliminate.
- Granulomas are made up of specialized immune cells including **lymphocytes**, **histiocytes**, and **multi-nucleated giant cells**. **Pathologists use the word granulomatous to describe the microscopic look of granulomas inside tissue.**

MACROPHAGES

- The **dominant cells in most chronic inflammatory reactions**.
- These are derived from **hematopoietic stem cells** in the bone marrow in postnatal life.
- They are monocytes in the circulating system. The half life of these monocytes is **one day**.
- These **monocytes differentiates into macrophages/histiocytes** in the tissues.
- The half life of macrophages can vary from **several months to years**. These are diffusely scattered in various connective tissues.


Differentiation
Monocytes in circulating system
Macrophages/ Histiocytes in tissues
Life span: Several months to years
Half life in Blood: 1 Day!


@VijayPatho
Chemotactic factors!
Macrophage
"Activated" Macrophage
Site of tissue injury

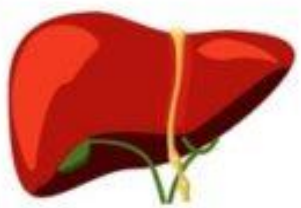
MACROPHAGES

Special names in different locations

Arise from progenitors in the yolk sac or fetal liver very early in embryogenesis

Migrate and persists for life!

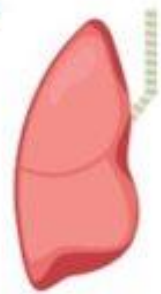
Karl Wilhelm Ritter von Kupffer



Kupffer cells

Sinus histiocytes

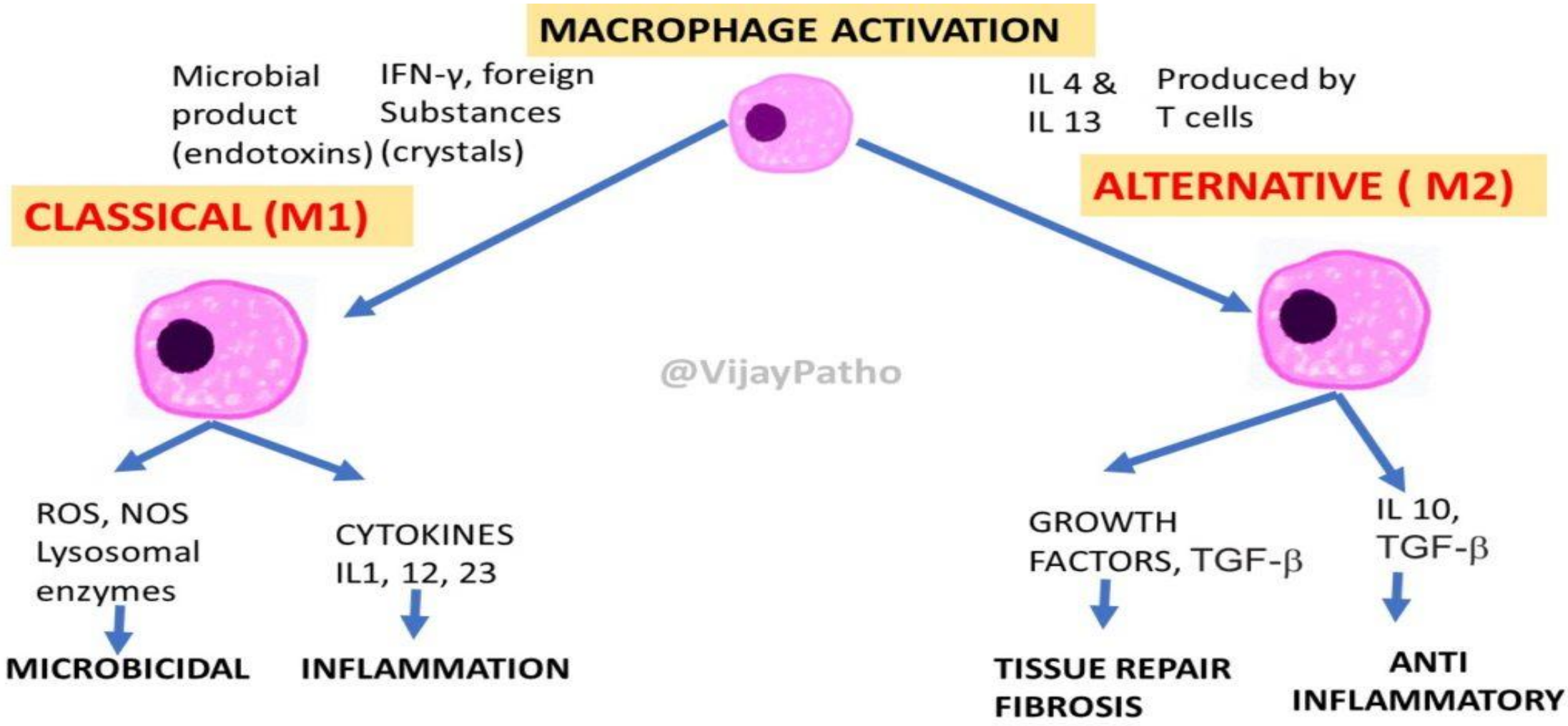
Microglial cells



Alveolar macrophages

- **The monocytes in circulation reach the site of injury due to the presence of various chemotactic factors and differentiate into macrophages.**

  These macrophages have to be "activated" for them to be fully functional.



Inflammatory cells

Infective agent

Elimination /eradication of the infective/offending agent

Infective agent

Unable to eradicate/ eliminate

CONTAIN!

GRANULOMA!

GRANULOMATOUS INFLAMMATION

Form of chronic inflammation

characterized by collections of

"Activated" **M**acrophages | T lymphocytes | sometimes with necrosis

INTRODUCTION

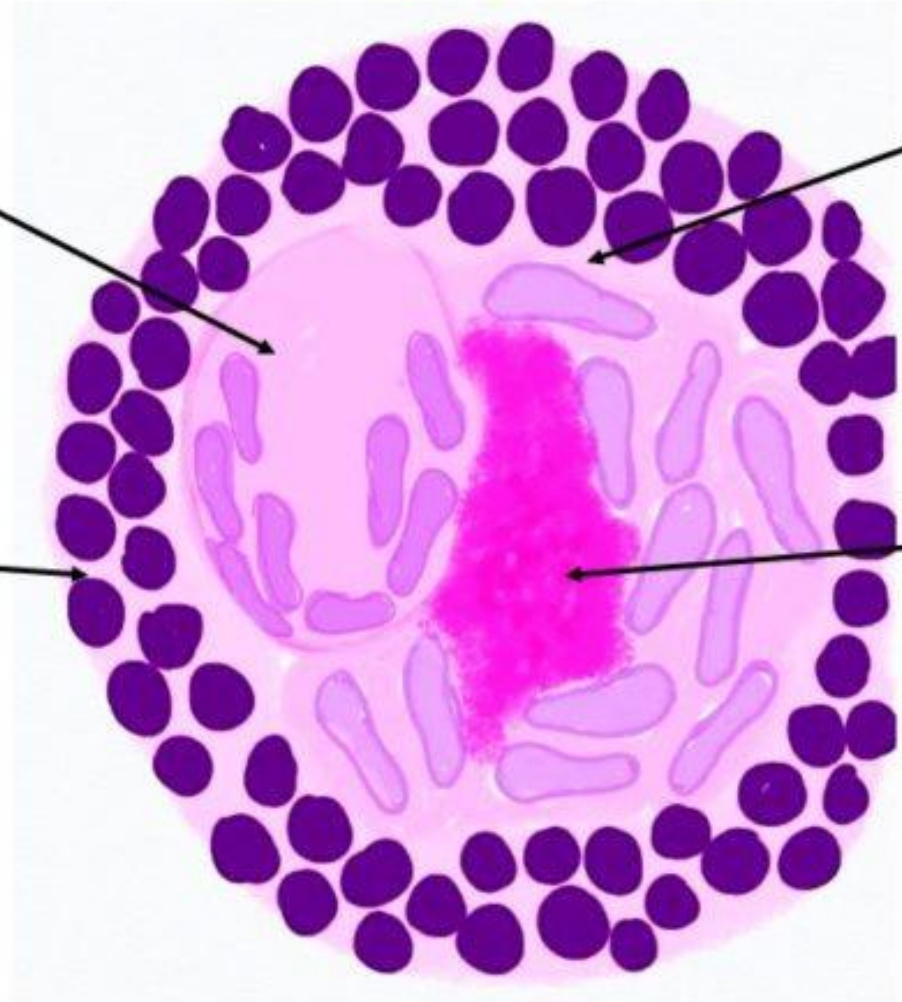
GRANULOMA…..circumscribed lesion of 1 mm in diameter composed predominantly of :

- Modified Macrophages……. **“Epithelioid cells”…..** Are large, polygonal and have **an oval/ elongated pale staining nuclei** and they look like epithelial cells. Ultra structurally, Epitheloid cells also found to have **“tight junctions”(like epithelial cells)** and hence they can aggregate to form granulomas. The nucleus of these cells can be elongated and resemble the shape of sole/slipper and hence it is also referred to as “**Slipper shaped**” nuclei
- Rimmed at the periphery by Lymphoid cells.
- With a collar of Fibroblast proliferation

GRANULOMA

Langhans Giant cell

Epithelioid cells with pale elongated nuclei

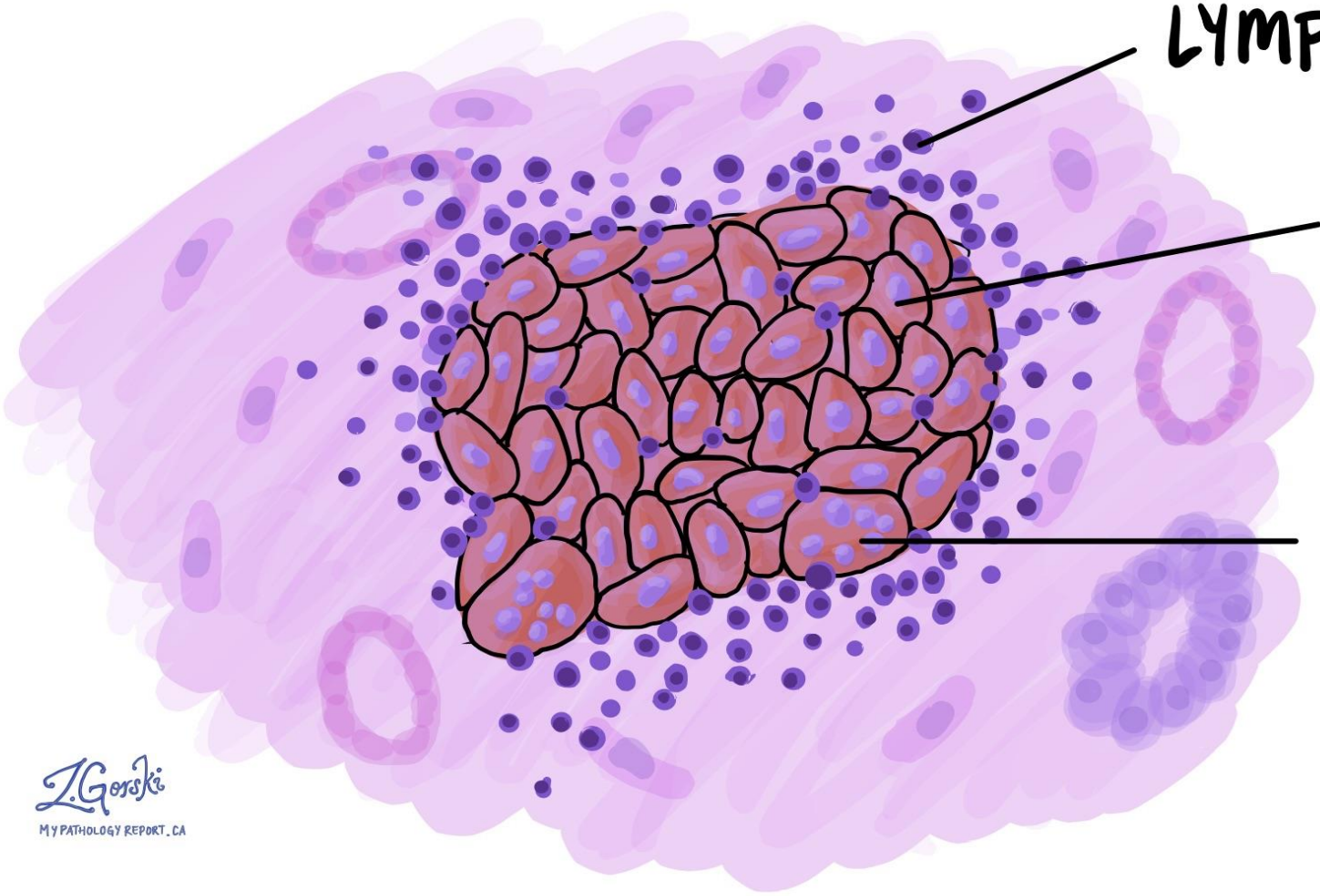


Clusters of epithelioid cells surrounded by lymphocytes

Amorphous, eosinophilic granular debritic material with complete loss of cellular details

CASEOUS NECROSIS on gross examination

GRANULOMA

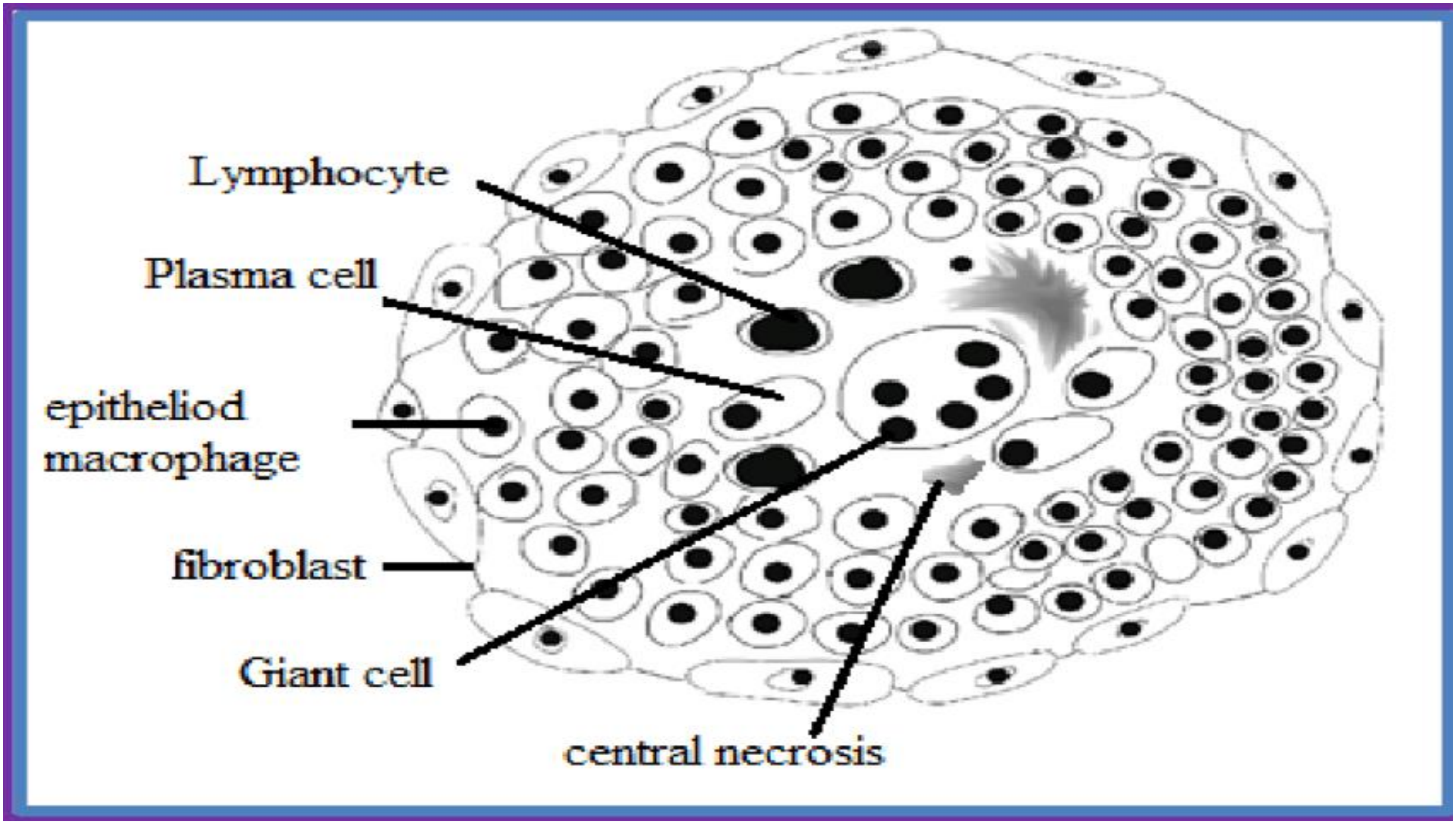


LYMPHOCYTES

EPITHELIOID HISTIOCYTES

MULTINUCLEATED GIANT CELLS

L.Gorski
MYPATHOLOGYREPORT.CA


Lymphocyte
Plasma cell
epitheliod
macrophage
fibroblast
Giant cell
central necrosis

Granuloma

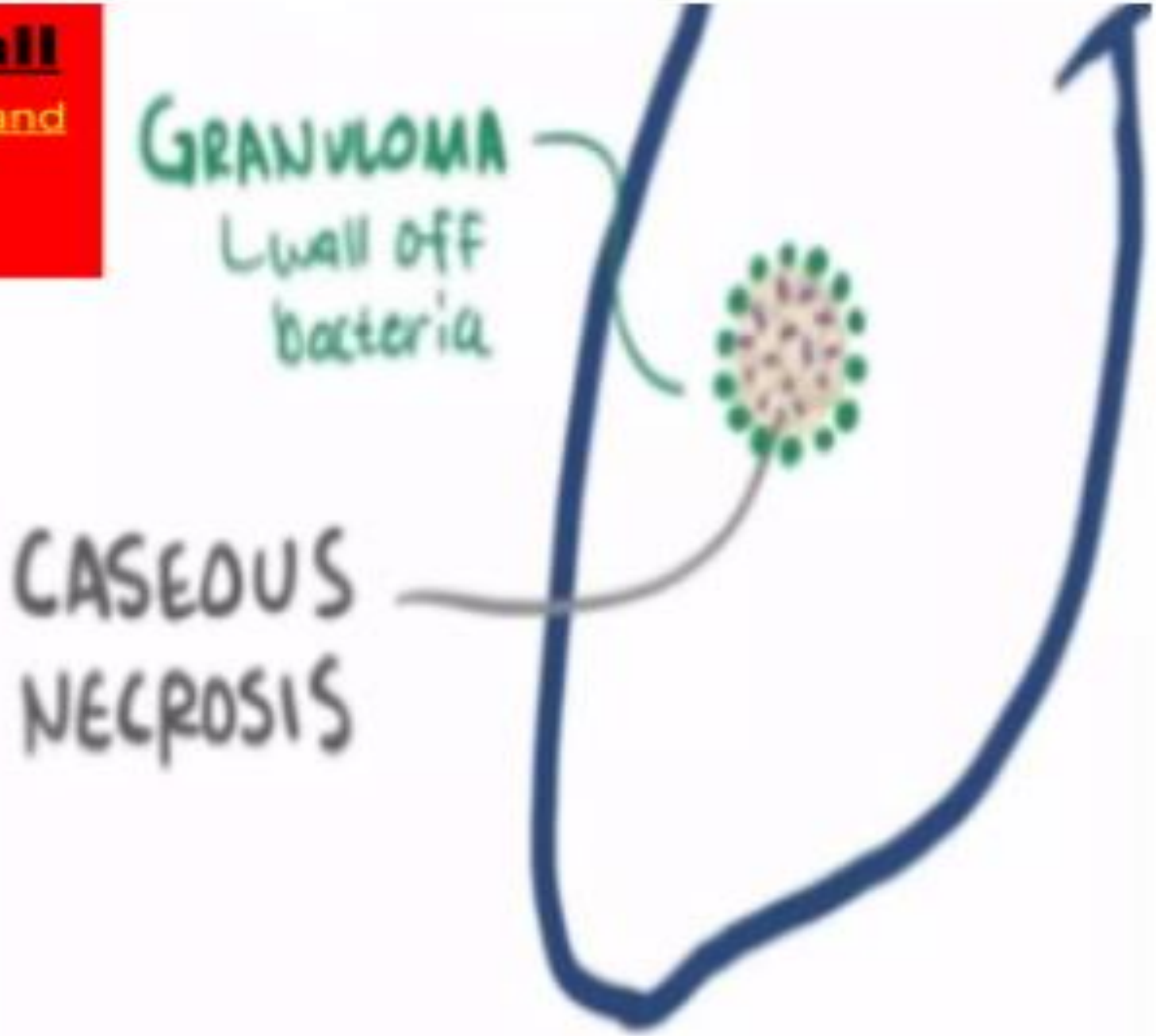
is NOT

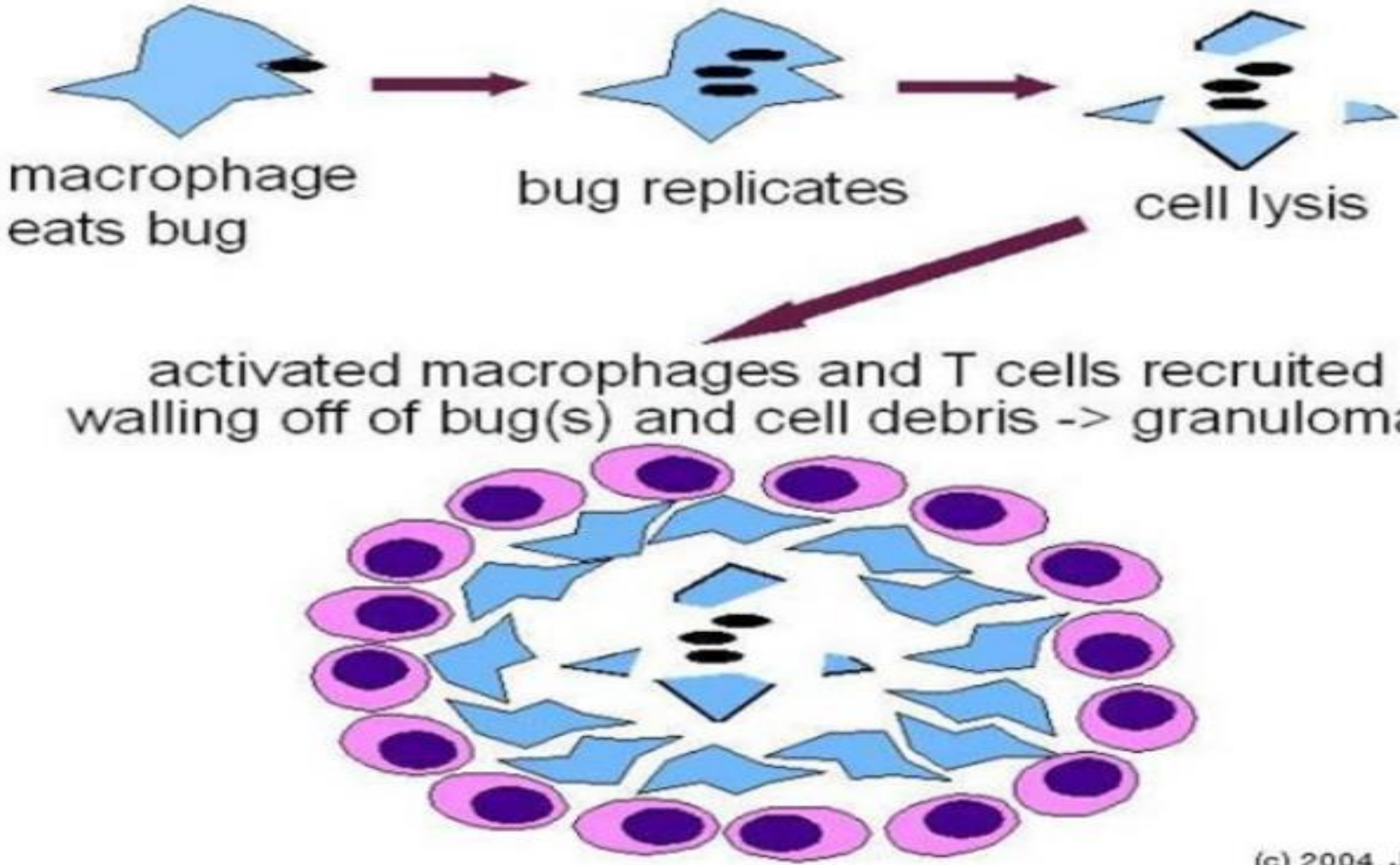
a Granulation Tissue

MECHANISM OF GRANULOMA FORMATION

- **GRANULOMA FORMATION**…..to deal with those pathogens that have escape the **HOST IMMUNE SYSTEM** by various means…..**like resisting phagocytosis and killing within the macrophages.**
- Granuloma try to **wall off…** these organisms and prevent their further growth and spread.

Granulomas try to **wall off** these organisms and prevent their further growth and spread.




macrophage
eats bug
bug replicates
cell lysis
activated macrophages and T cells recruited
walling off of bug(s) and cell debris -> granuloma
(c) 2004, Jenifer Cobur

MAIN CAUSES OF GRANULOMATOUS INFLAMMATION

- Mildly irritant 'foreign' material

- Mycobacteria: Tuberculosis, leprosy
- Syphilis
- Other rare infections e.g. some fungi
- Unknown causes: Sarcoid
  Wegener's granulomatosis
  Crohn's disease

DIFFERENCE BETWEEN A NECROTIZING AND A NON-NECROTIZING GRANULOMA?

Two groups: based on how the granulomas look when viewed under the microscope

1. **Necrotizing and**
2. **Non-necrotizing**

- **Necrosis** is a type of **cell death** and **necrotizing granulomas** contain dead cells at their center.
- **Necrotizing granulomas** are important because they are more likely to be related to infections such as tuberculosis. As a result, your pathologist may order additional special stains such as a **silver stain or acid-fast stain** to look for infectious organisms
- In contrast, **non-necrotizing granulomas** are made up entirely of immune cells.

MORPHOLOGY

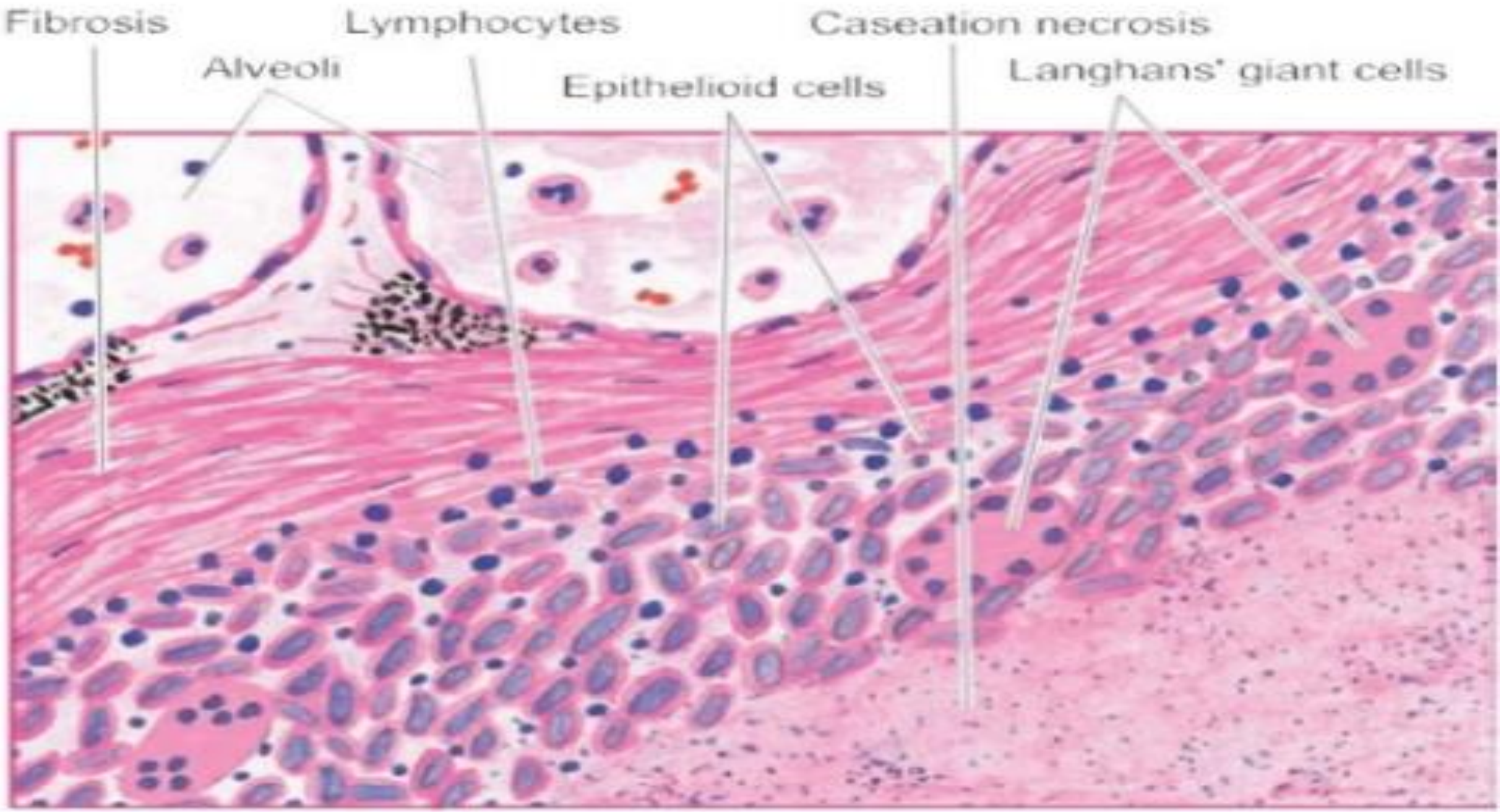
CONCENTRIC LAYERS OF GRANULOMA :

4 concentric layers in a granuloma, from inside to out:

1. **Necrosis +/-**
2. **Foamy bubbly cytoplasm , abundant.**
3. **Giant cells, Epitheloid cells and Macrophages….** Especially prominent in immune granulomas. Lymphocytes secrete mediators that activate and alter macrophages and macrophage-derived cells located centrally.
4. **Lymphocytes**
5. **Fibroblasts…….Walls off the lesion.**

EPITHELOID CELLS

- Epithelioid **histiocytes** (**Epithelioid cells**) are activated **macrophages** resembling **epithelial cells**:
- **elongated,** with **finely granular, pale eosinophilic (pink) cytoplasm** and
- **central, ovoid nucleus (oval or elongate), which is less dense than that of a lymphocyte.**
- They have **indistinct shape contour**, often appear to merge into one another and can form **aggregates** known as **giant cells**.


Fibrosis
Lymphocytes
Caseation necrosis
Alveoli
Epithelioid cells
Langhans' giant cells

GIANT CELLS

- A **giant cell** is a mass formed by the union of several distinct cells (usually macrophages), often forming a granuloma.
- It can arise in response to an infection, such as from tuberculosis, herpes, or HIV, or foreign body.

TYPES OF GIANT CELLS

1. Langhans giant cell
2. Foreign-body giant cell
3. Touton giant cells
4. Giant-cell arteritis
5. Reed–sternberg cell

Also as in subependymal giant cell astrocytoma

GIANT CELLS

Cells with nuclei are arranged in 'HORSESHOE' shaped pattern. Can be seen in one or both the poles

Langhans

NOT Langerhans!

Contain regular nuclei scattered throughout cytoplasm

Foreign body

Ring of nuclei surrounding central cytoplasm. peripheral cytoplasm is vacuolated

Touton

Contain hyperchromatic pleomorphic nuclei scattered throughout cytoplasm

Tumor

CASEOUS NECROSIS

- Combination of **coagulative and liquefactive necrosis**.
- Encounter principally in the **center of tuberculous necrosis**.
- **Appear as soft , friable, whitish gray debris resembling cheesy material**.

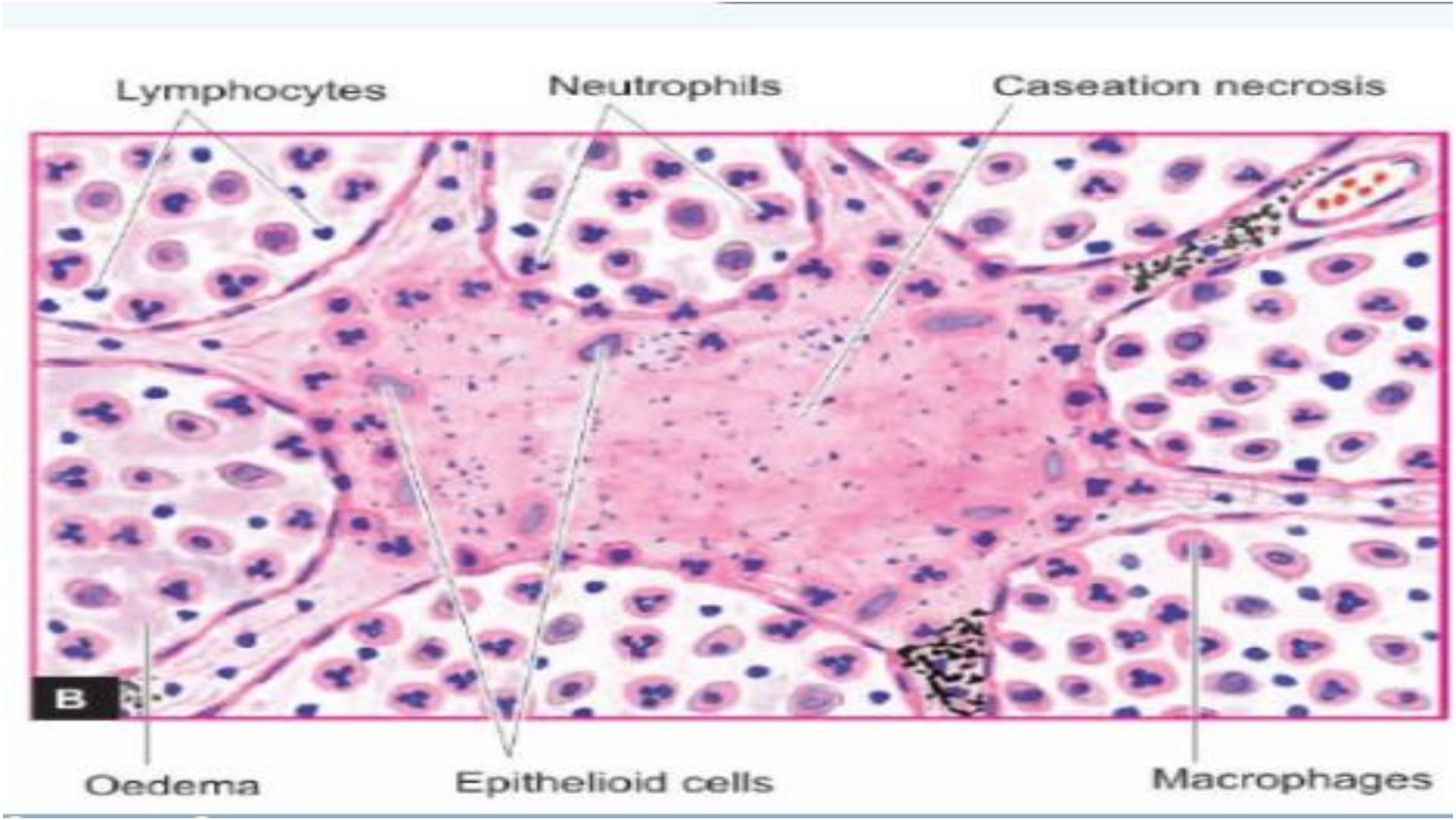
MORPHOLOGY

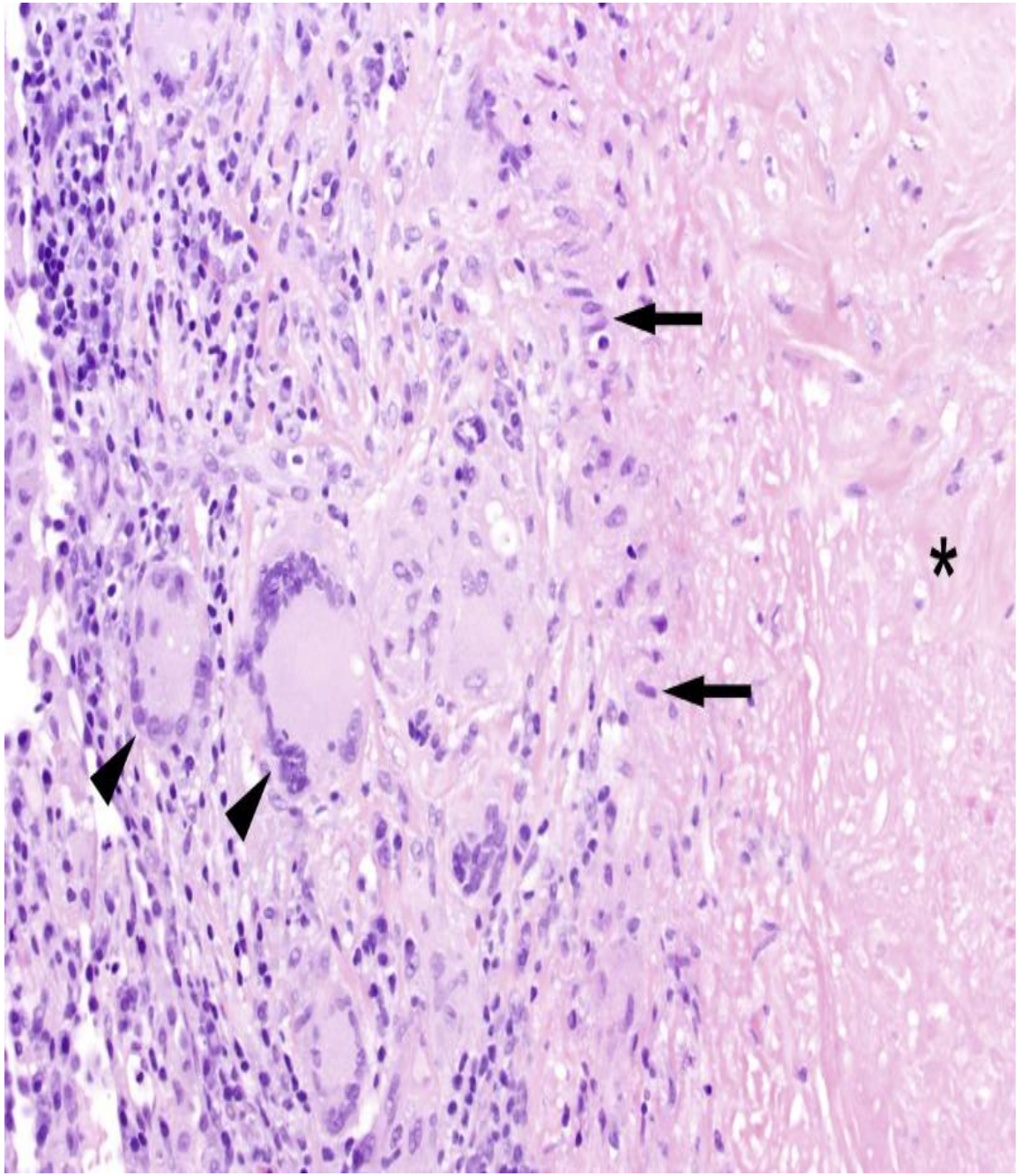
GROSSLY :

- **Foci of Caseous necrosis**.....due to effects of lipopolysaccharides present in the capsule of the **tubercle bacilli , Mycobacterium tuberculosis.**

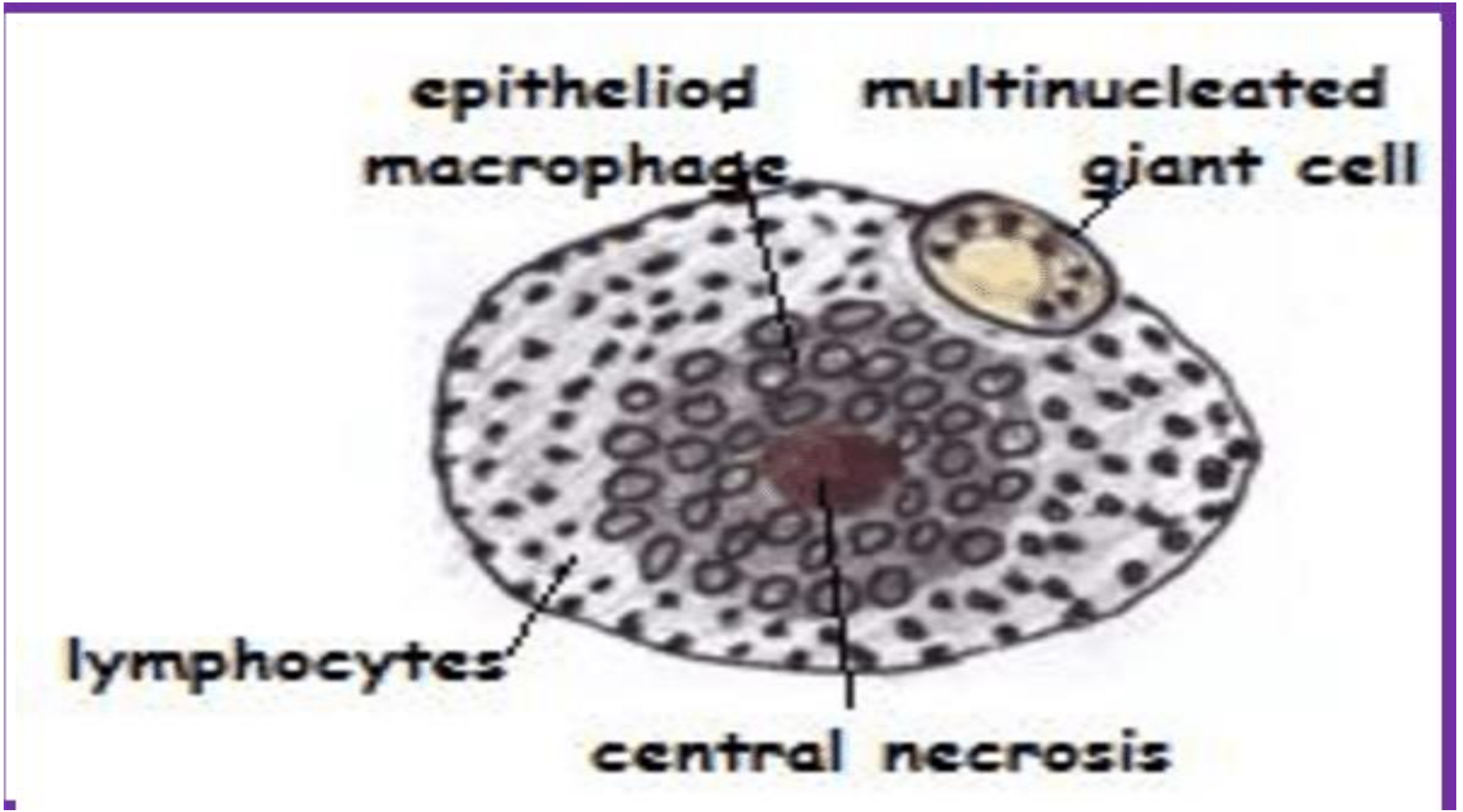
MICROSCOPICALLY

1. *the* ***necrosed foci*** *are* *structureless*, eosinophilic, and contain granular debris.
2. The surrounding tissue shows **characteristic granulomatous inflammatory reaction** consisting of **epithelioid cells** with
3. interspersed giant cells of **Langhans' or foreign body** type and
4. **peripheral mantle** **(layer, covering, Ring, collar)** **of** lymphocytes.
5. **Fibrous cup**.


Lymphocytes
Neutrophils
Caseation necrosis
B
Oedema
Epithelioid cells
Macrophages



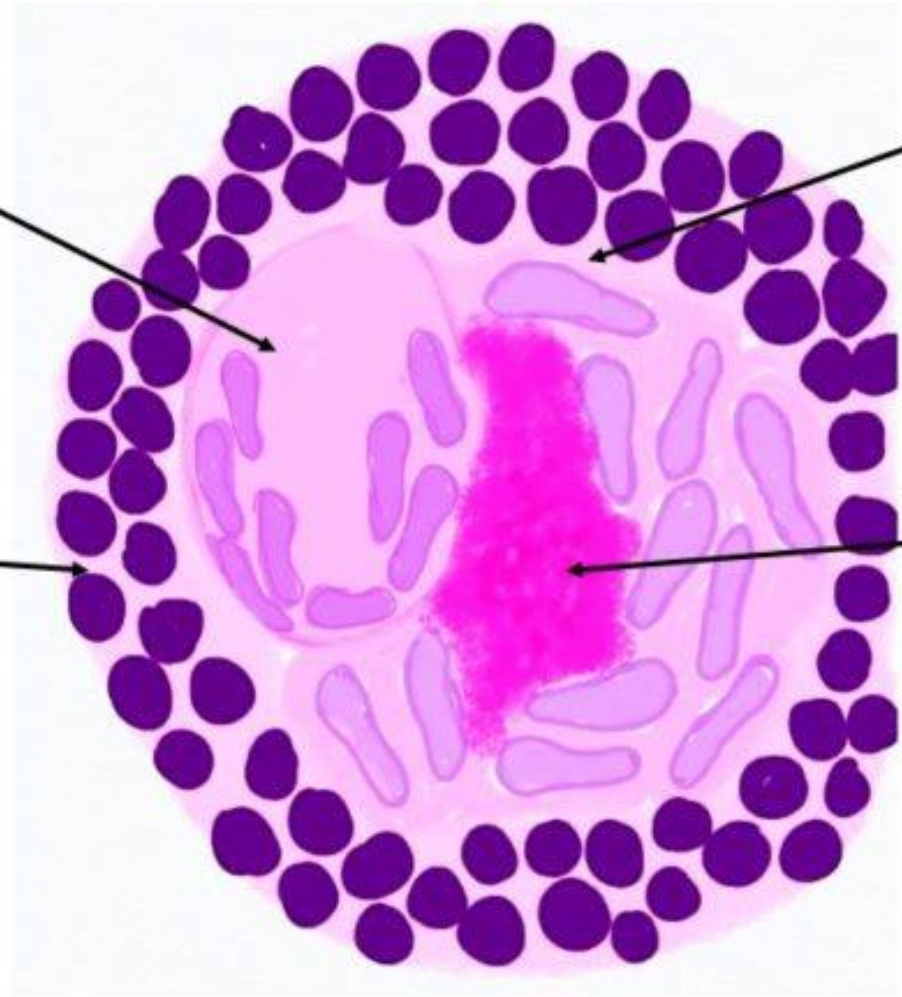
- **Necrotizing granuloma** seen in mycobacterial tuberculosis showing ……
- A peripheral rim of **Epithelioid histiocytes (arrows)** surrounding the **central necrotic region** (asterisk)
-)Some **Histiocytes** are also forming **multinucleated giant cells (arrow heads**).
- External to the rim of histiocytes is an **outer rim of lymphocytes and plasma cells**.


epithelioid macrophage
multinucleated giant cell
lymphocytes
central necrosis

GRANULOMA

Langhans Giant cell

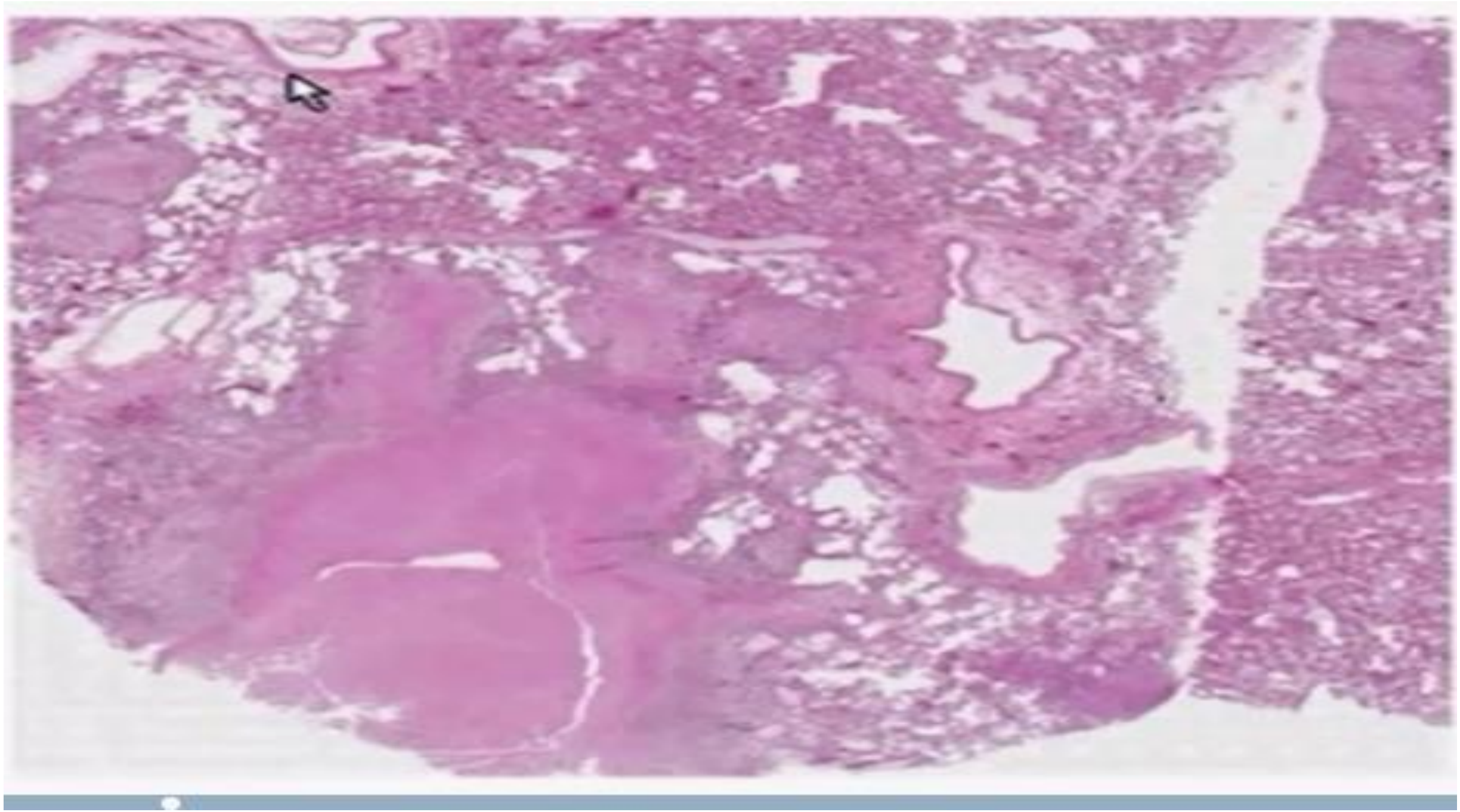
Epithelioid cells with pale elongated nuclei

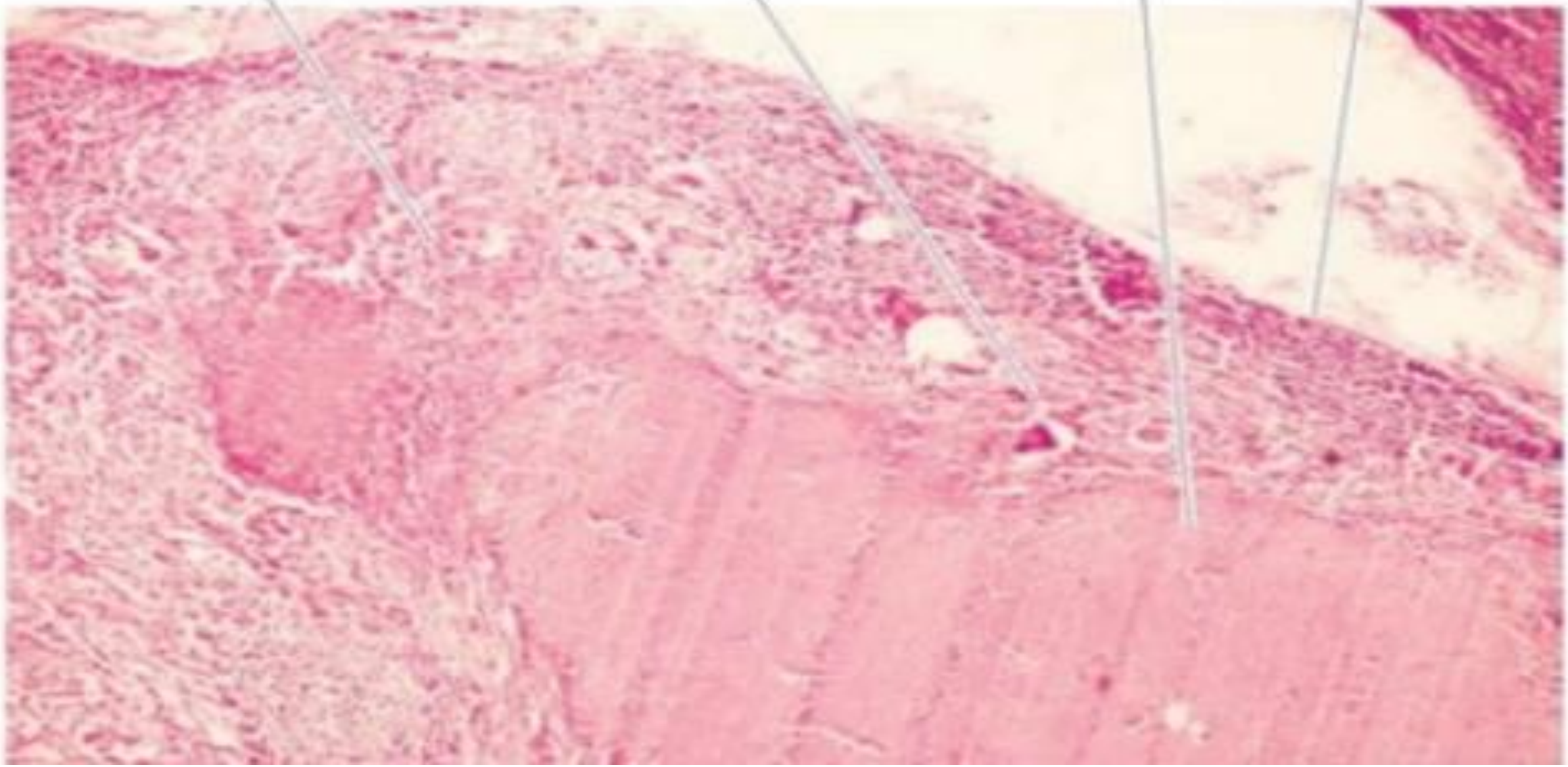


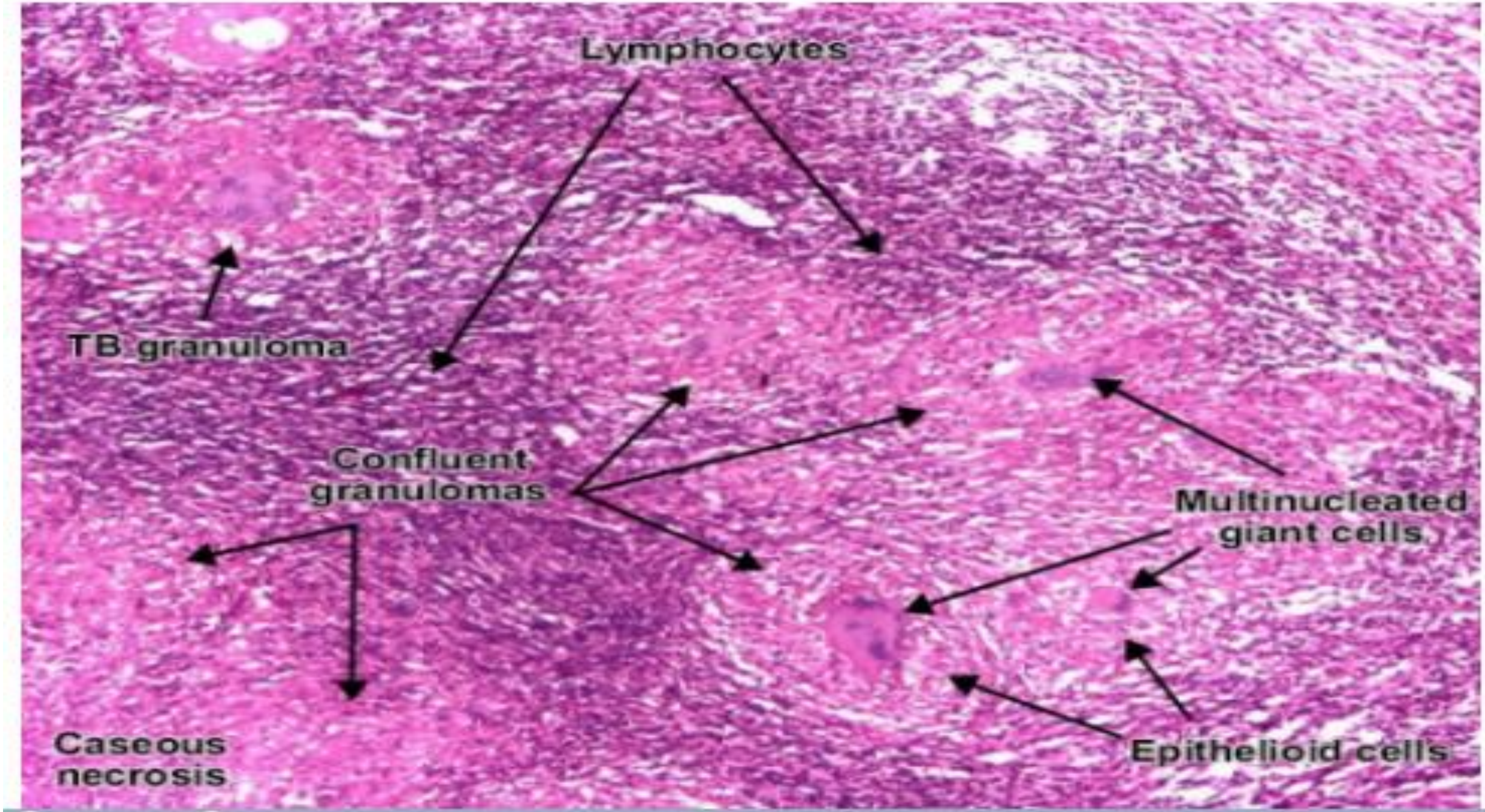
Clusters of epithelioid cells surrounded by lymphocytes

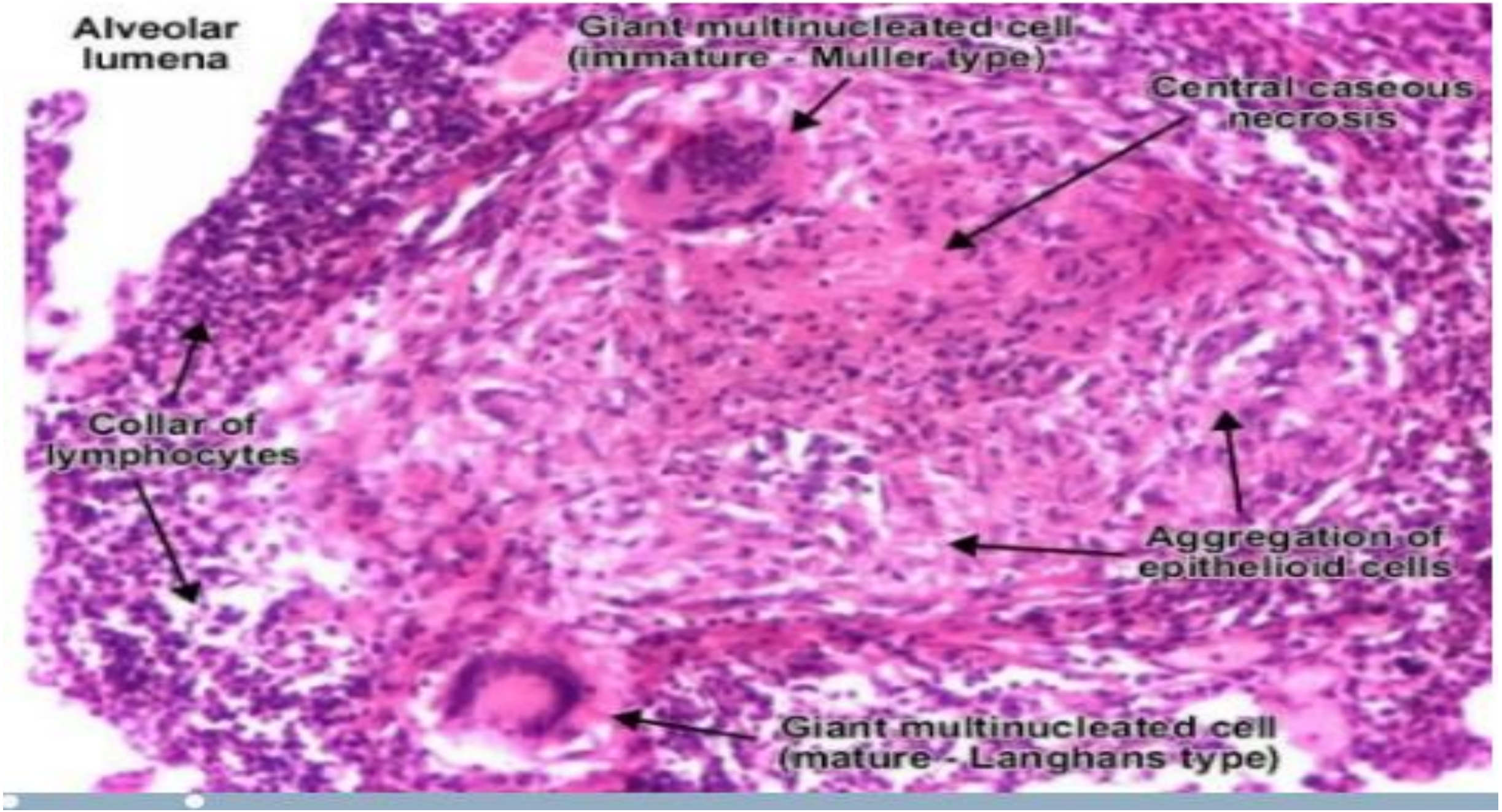
Amorphous, eosinophilic granular debritic material with complete loss of cellular details

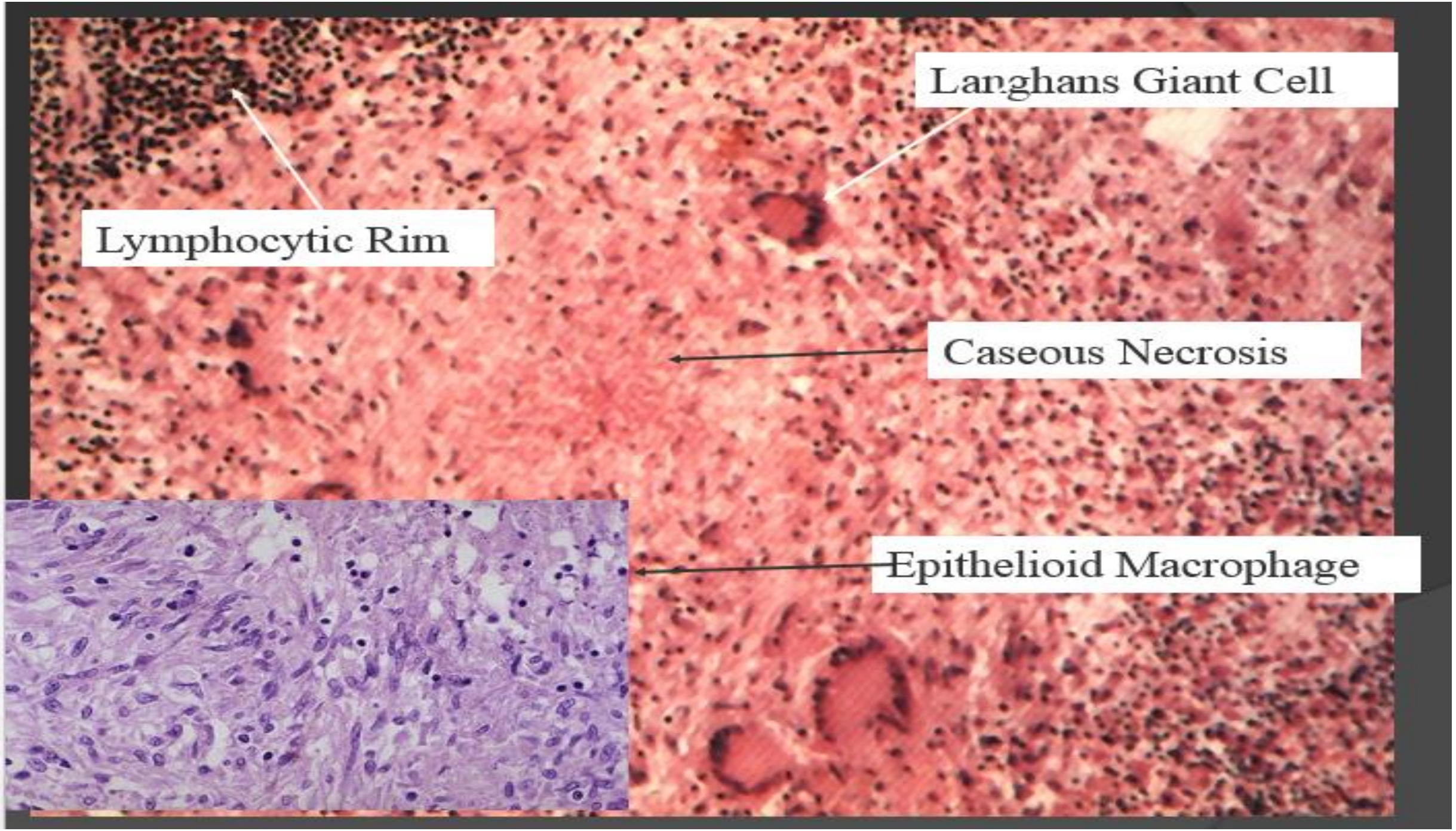
CASEOUS NECROSIS
on gross examination

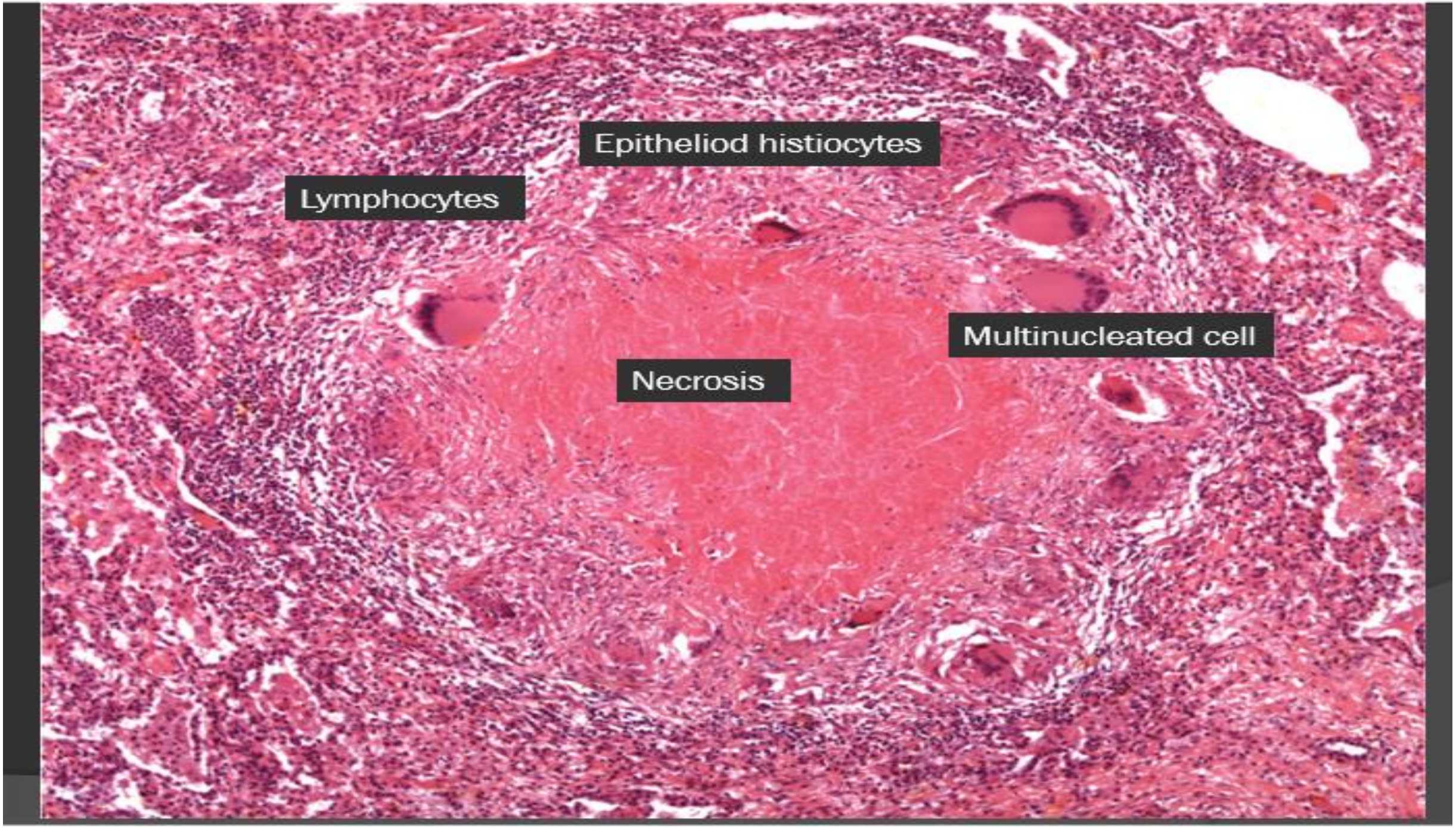



Epithelioid cell granuloma
Lymphoid tissue

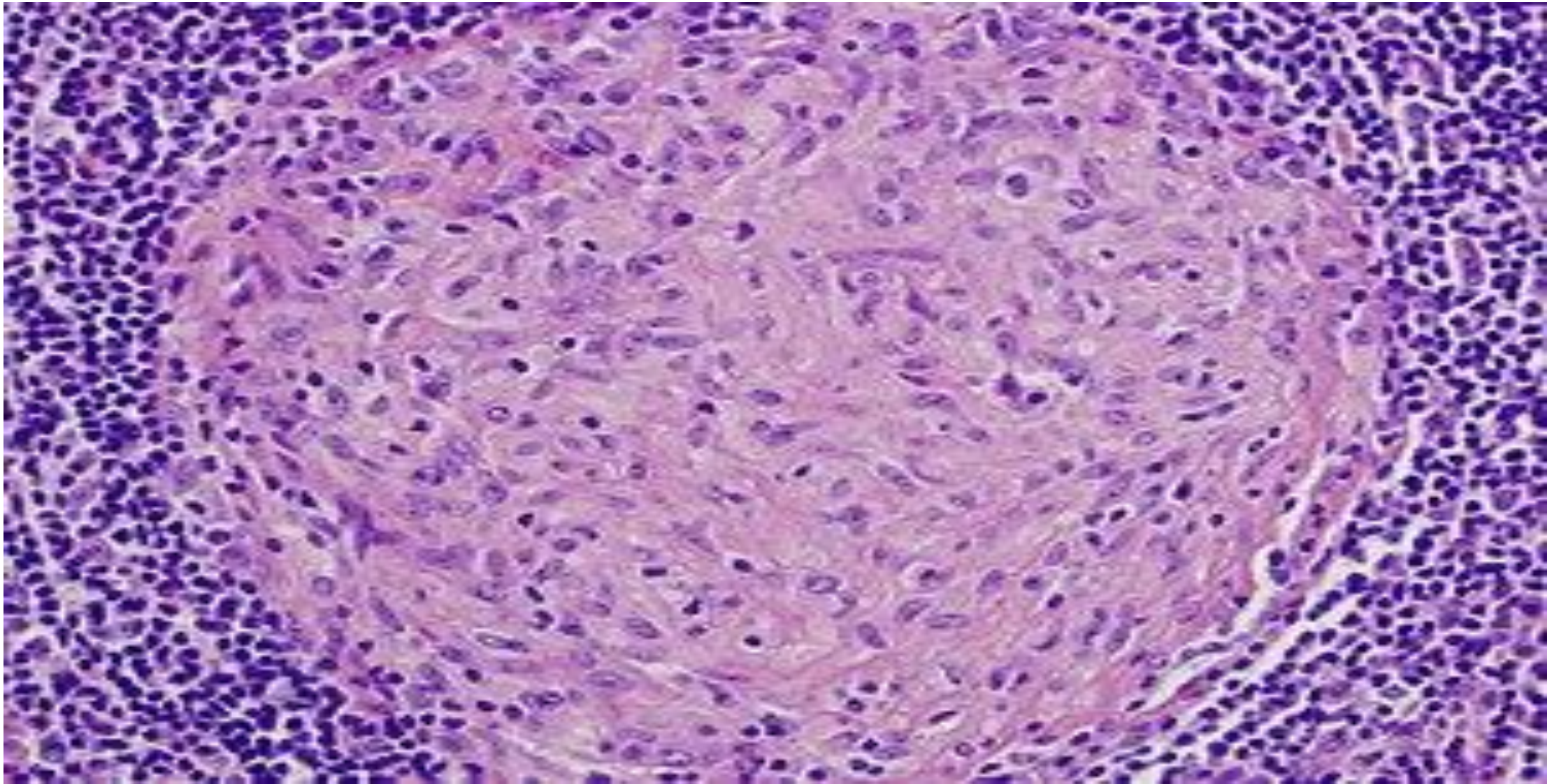

Lymphocytes
TB granuloma
Confluent granulomas
Multinucleated giant cells
Caseous necrosis
Epithelioid cells


Alveolar lumena
Giant multinucleated cell (immature - Muller type)
Central caseous necrosis
Collar of lymphocytes
Aggregation of epithelioid cells
Giant multinucleated cell (mature - Langhans type)

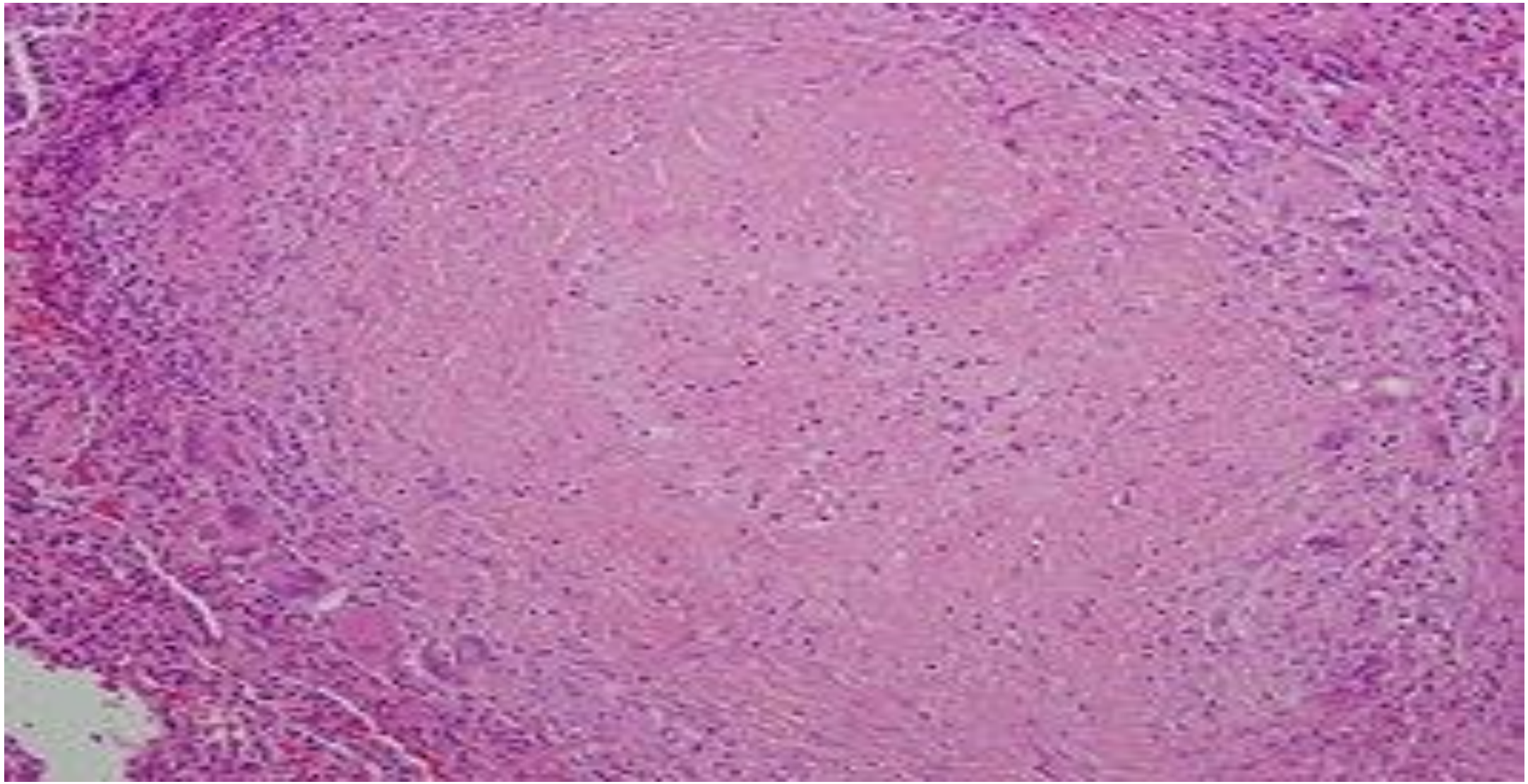

Langhans Giant Cell
Lymphocytic Rim
Caseous Necrosis
Epithelioid Macrophage


Epitheliod histiocytes
Lymphocytes
Multinucleated cell
Necrosis

GRANULOMA ……WITHOUT NECROSIS



GRANULOMA ……WITH CENTRAL NECROSIS



EXAMPLES OF GRANULOMATOUS INFLAMMATION

BACTERIAL

1. Tuberculosis
2. Leprosy
3. Syphilis
4. Brucellosis
5. Listeriosis

EXAMPLES OF GRANULOMATOUS INFLAMMATION

FUNGAL:

1. Histoplasmosis
2. Blastomycosis
3. Hypersensitivity Pneumonitis

HELMINTHIC :

1. Schistosomiosis
2. Trichinosis

EXAMPLES OF GRANULOMATOUS INFLAMMATION

FOREIGN BODY TYPE :

1. Silica granulomatosis
2. Foreign body pneumonitis

VIRAL :

1. Cat-scratch disease
2. Lymphogranuloma venerum

DIFFERENCE BETWEEN GRANULATION TISSUE AND GRANULOMA

- The **key difference** between granulation tissue and granuloma is that…… **granulation tissue refers to new connective tissue and tiny blood vessels that form on the surface of a wound during the healing process while granuloma is an organized collection of macrophages that forms in response to persistent inflammation.**

Granulation Tissue vs Granuloma

More Information Online WWW.DIFFERENCEBETWEEN.COM

	Granulation Tissue	Granuloma
DEFINITION	Granulation tissue is a highly vascularized, newly formed connective tissue on the surface of a wound	Granuloma is an organized collection of macrophages formed in response to chronic inflammation
A RESULT OF	Wound healing process	Inflammation
CONTENT	Connective tissue having fibroblasts, mononuclear cells and numerous tiny blood vessels	Aggregate of macrophages surrounded by lymphocytes
FUNCTION	Replaces dead or necrotic tissue, fills the wound and protects the wound surface from microbes	Surround and destruct antigens
APPEARANCE	Light red or dark pink in color	Cheese-like


THANK YOU
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