Chronic inflammation - 2
Granulomatous inflammation

Objectives

- List different causes of granuloma
- Describe the formation of a granuloma
- Define a granuloma
- Describe microscopy of a granuloma
- Briefly describe tuberculosis the prototype of granuloma

Types of chronic inflammation

Nonspecific chronic inflammation

- Active inflammation
  Mononuclear cells
- Tissue destruction
- Granulation tissue
- Collagen deposition and fibrosis

Granuloma formation

- Cellular attempt to localize injurious agents which are difficult to eradicate
- Seen in a limited number of conditions
  (infectious/ non infectious)

Granulomatous inflammation

Specific infections	Tuberculosis, Leprosy, Syphilis, Cat-scratch disease, Fungi, Parasites- larvae, eggs and worms
Foreign bodies	Endogenous - keratin, hair shafts, necrotic tissue, cholesterol crystals sodium urate crystals
	Exogenous - Silica, asbestos fibres, suture material, food particles
Chemicals	Beryllium
Drugs	Hepatic granulomas due to Allopurinol, phenylbutazone, sulphonamides
Others	Crohn's disease, sarcoidosis

Granulomatous inflammation

Immune granulomas

- Persistent T-cell response against certain microbes

-Type IV hypersensitivity reaction

(Cell mediated immunity- CMI)

Prototype - TB

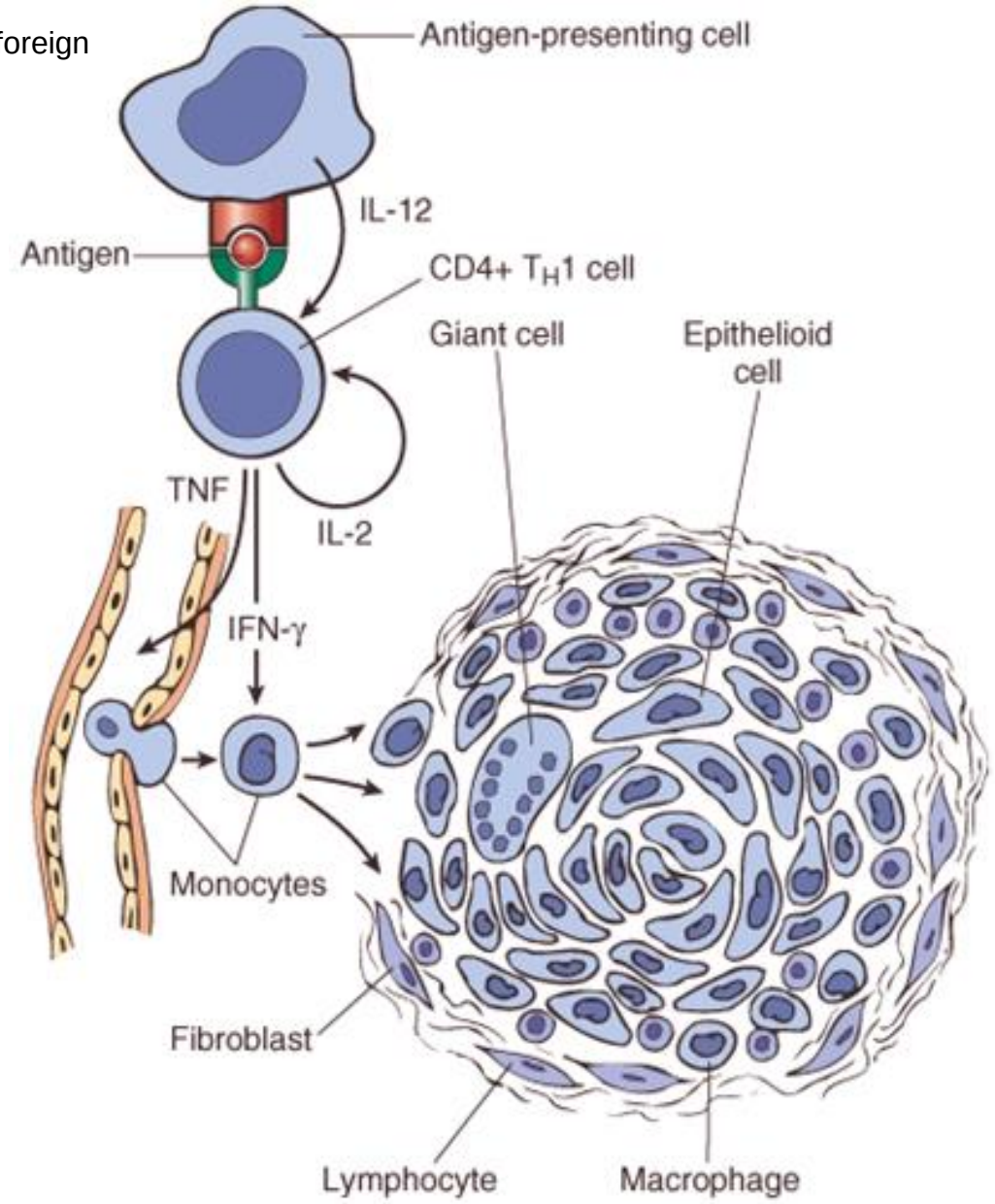
- A protective immune reaction

Foreign body granulomas

- Do not elicit any specific immune response (non-immune)

CMI / type IV hypersensitivity reactions

Macrophage engulf foreign protein antigens



Granuloma formation

Granuloma - Definition

- Consists of microscopic aggregates of "epithelioid cells"
- Surrounded by lymphocytes and occasionally plasma cells
- May contain multinucleated giant cells

- Older lesions develop a peripheral rim of fibroblasts

- With time, the focus of granuloma may get calcified

Epithelioid cells

- These are transformed macrophages
- In Haematoxyllin and eosin (H & E) stained sections, epithelioid cells show

  - round, ovoid or elongated vesicular nuclei

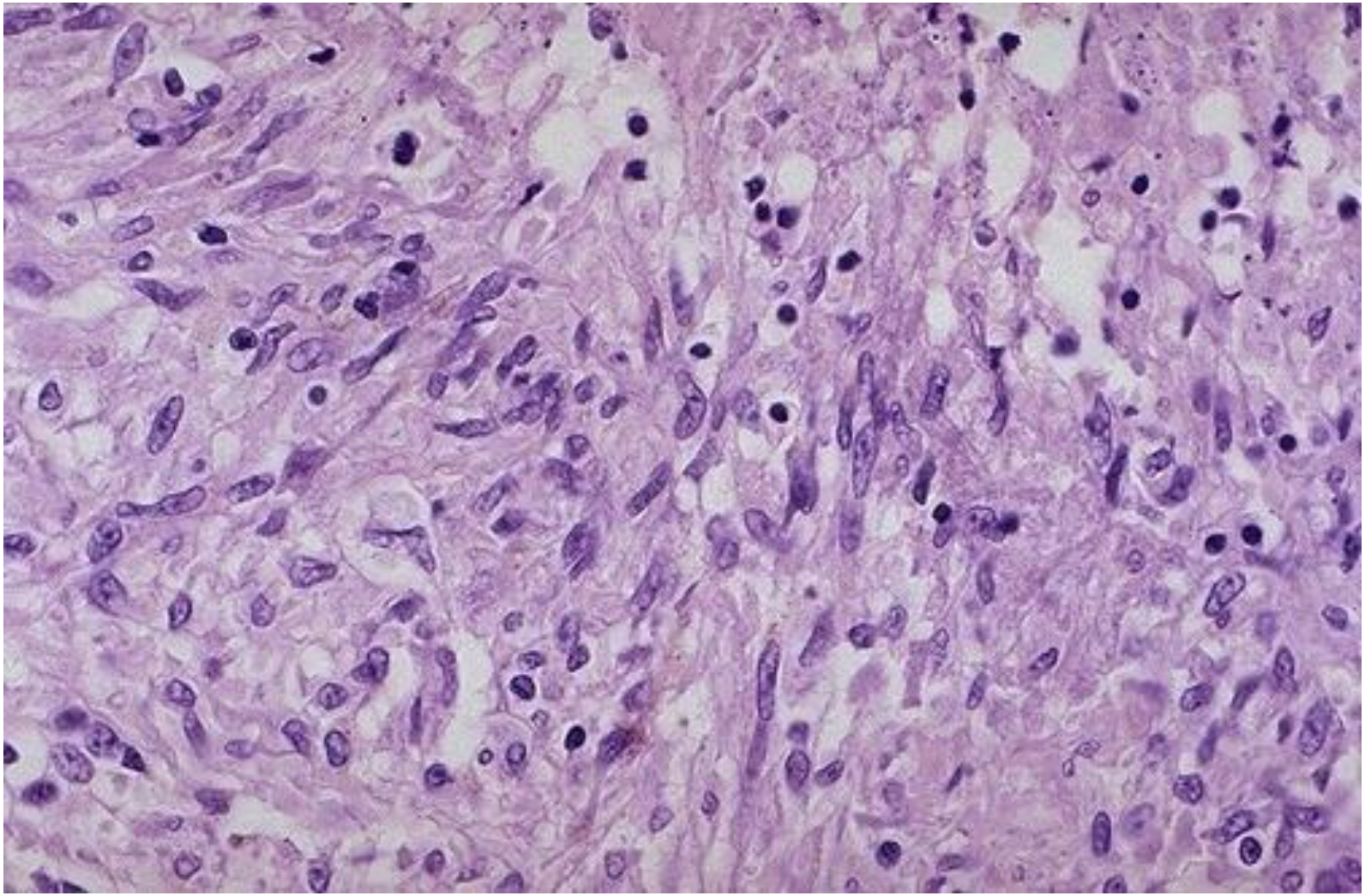
  - pale pink, granular, abundant cytoplasm

  - cytoplasmic borders are not distinct

  - Some nuclei fused and form

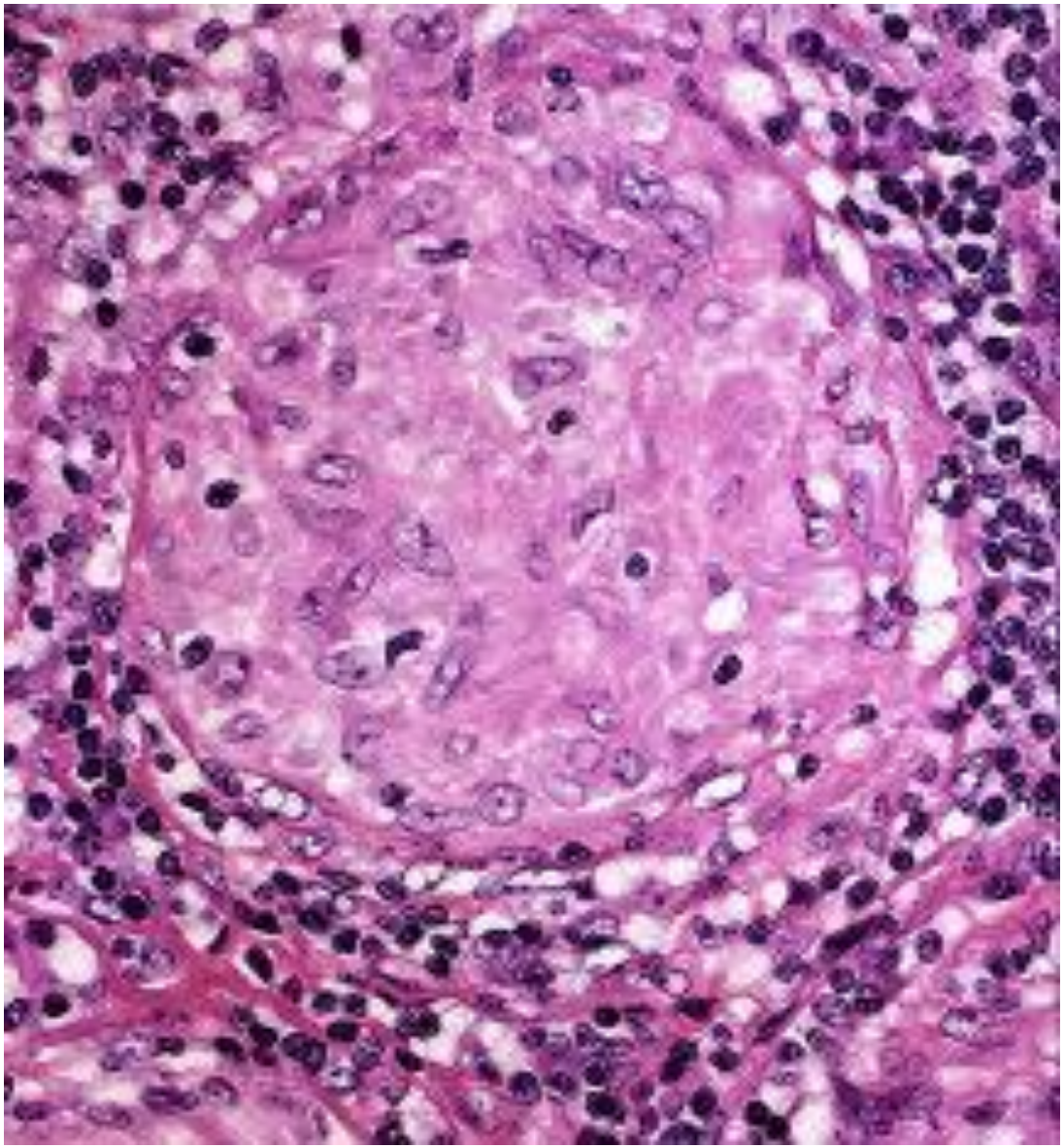
    "multinucleated giant cells"

Epithelioid histiocytes



Abundant eosinophilic cytoplasm , elongated vesicular nuclei and indistinct cell borders

Epithelioid histiocytes



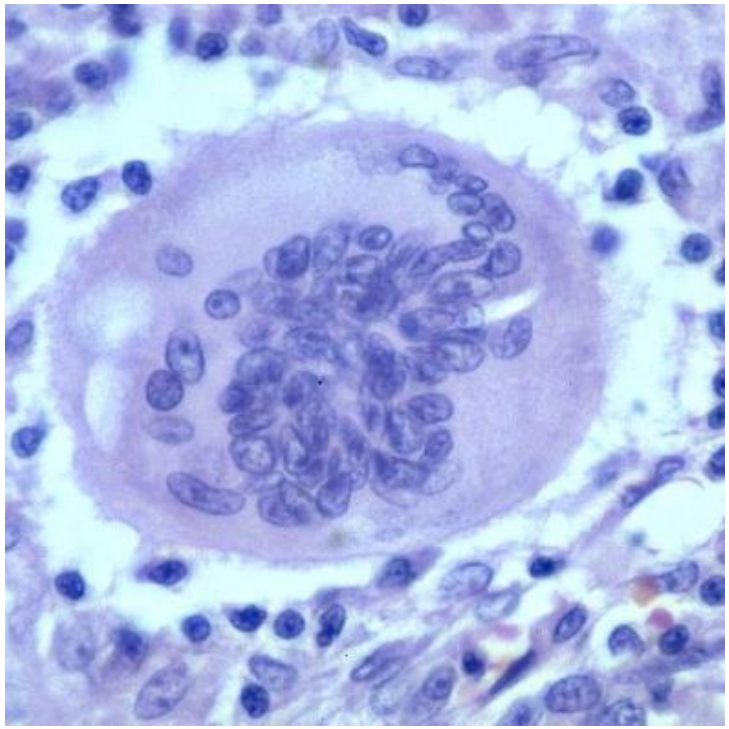
Multinucleated giant cells

- Frequently epithelioid histiocytes fuse to form giant cells
  - Abundant pale cytoplasm
  - contains 20 or more small nuclei

- When nuclei are arranged
  - at the cell periphery - Langhans-type giant cells
  - haphazardly - Foreign body-type giant cells

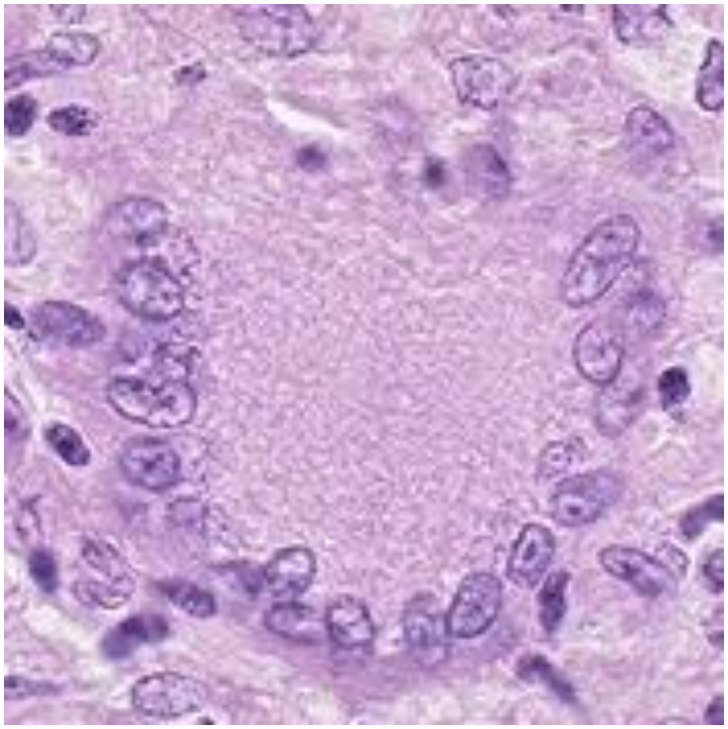
Multinucleated giant cells

Foreign body-type



Haphazardly arranged nuclei

Langhans-type



Nuclei at the periphery
“Horse shoe” shaped

No functional difference

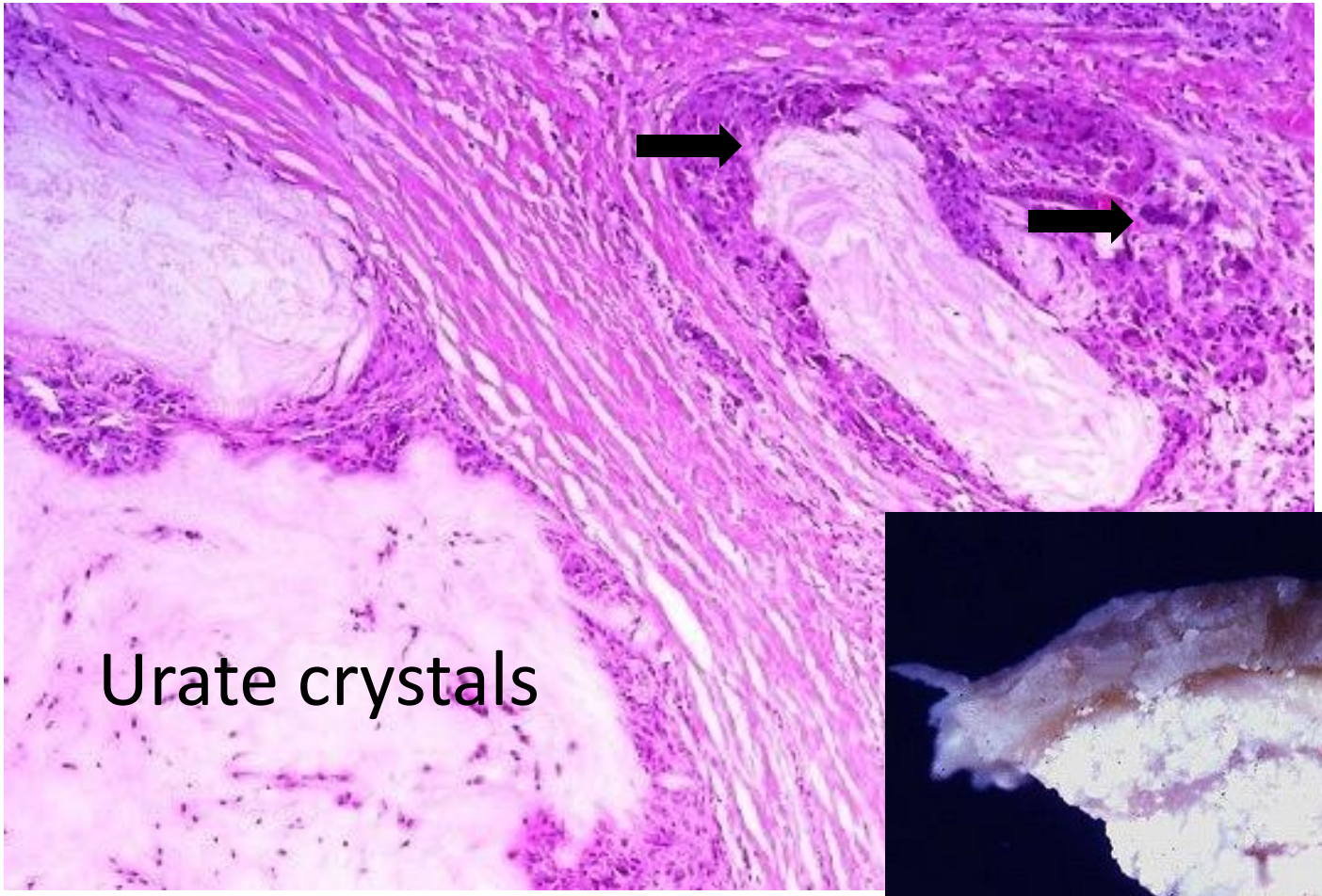
Foreign body type giant cells

- Caused by foreign bodies that cannot be phagocytosed by a single macrophage
- May form granulomas
- Foreign material may be present within the granuloma

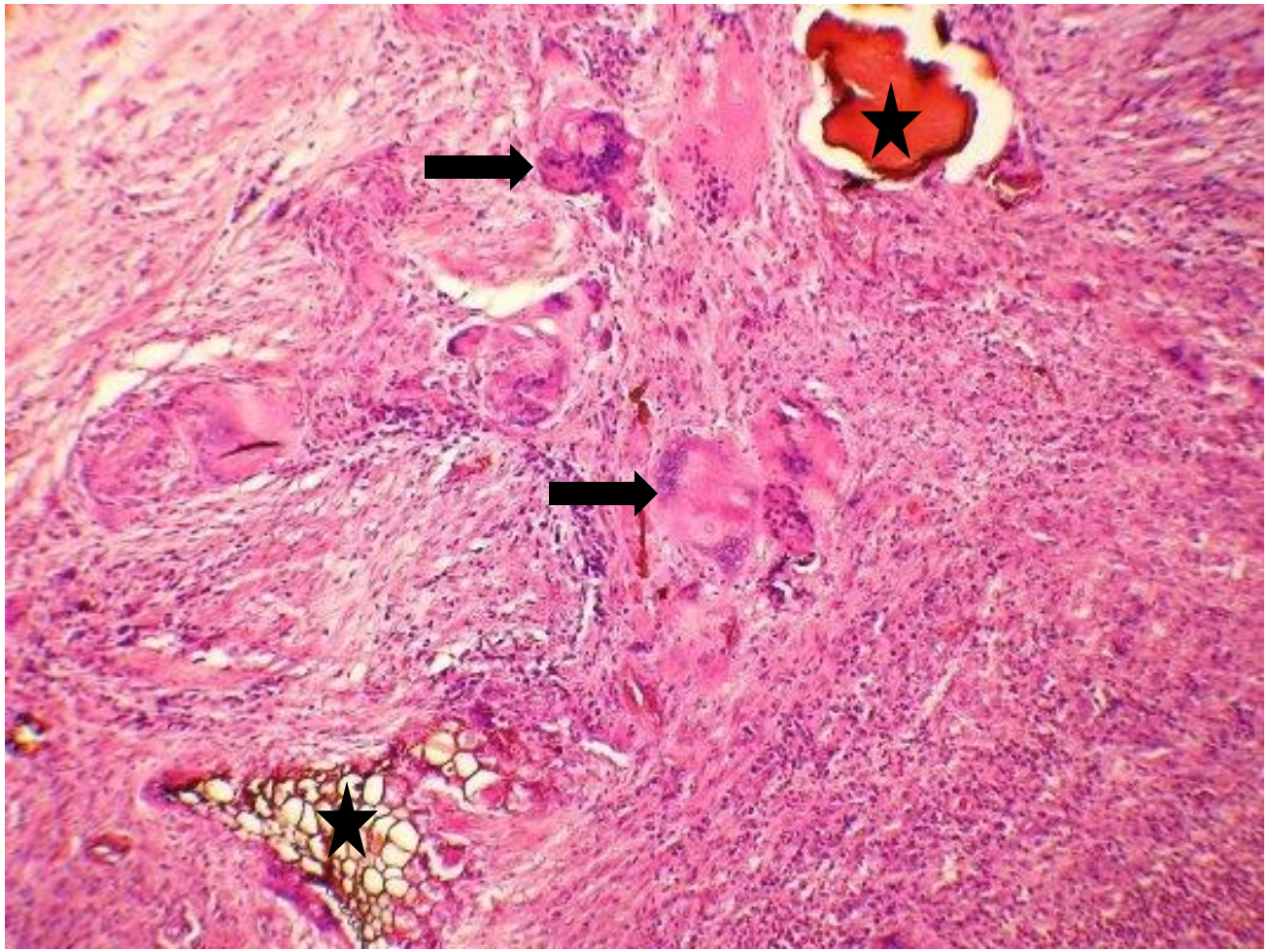
Skin

Note: Foreign-body type giant cells (arrows)

Skin - Gouty tophus

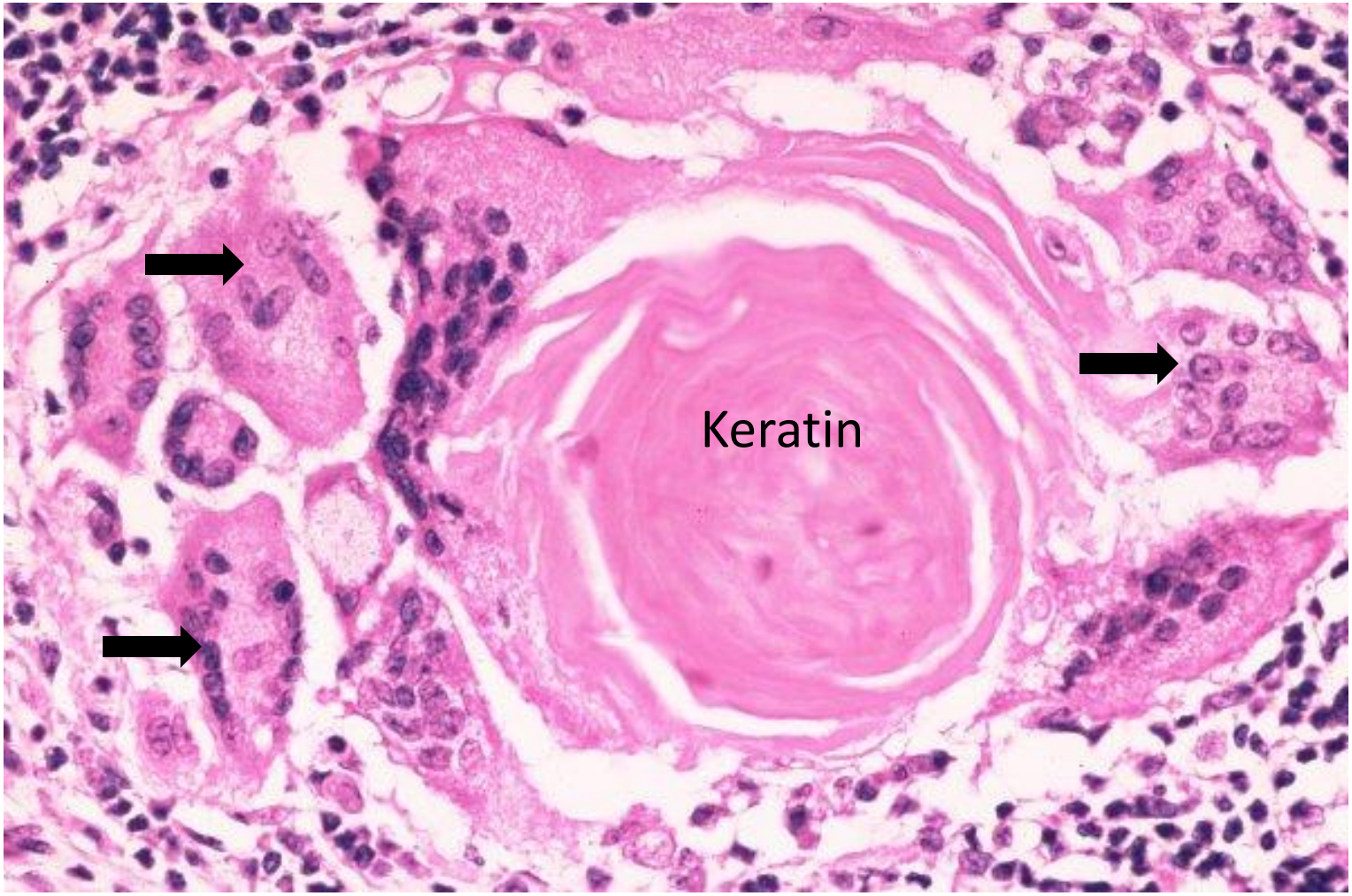


Bowell wall - perforated diverticulitis



Note : Multiple foreign body type giant cells
Foreign bodies (food particles and fecal material)

Keratin



Macroscopy

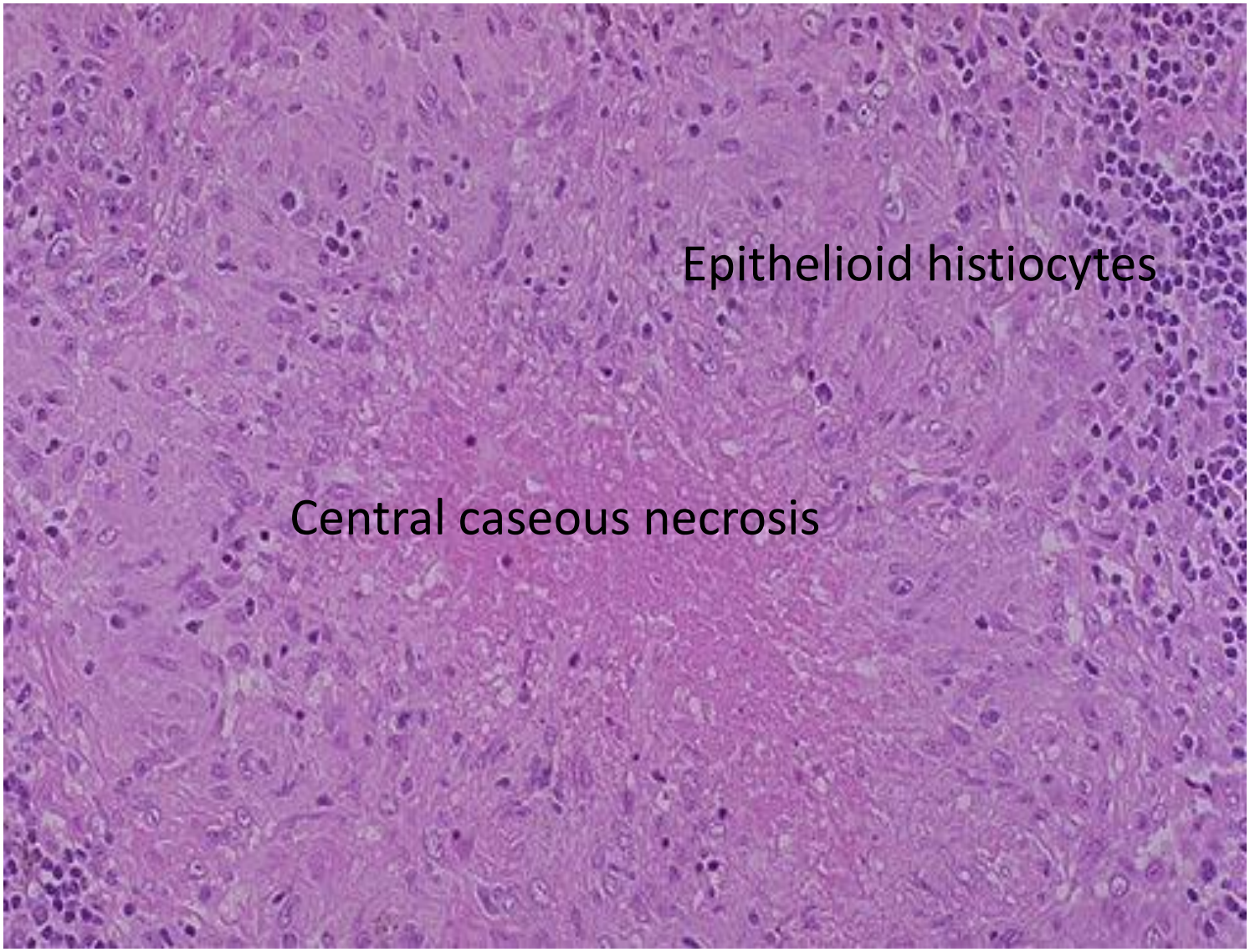
- Areas of caseous necrosis
- Macroscopy

  Soft, yellow-white, granular cheesy material

- Microscopy

  Amorphous, structurless, granular debris with complete loss of cellular details

TB granuloma



Tuberculin skin test

- What is the rationale behind performing this test?

Tuberculin skin test

- Detect the delayed hypersensitivity/ CMI to *M. tuberculosis* antigen

- Does not differentiate between infection and disease

- False positive and false negative reactions may occur

  - find the causes

Tuberculin skin test

- Following intracutaneous injection of tuberculin in previously sensitized individual (2- 4 weeks later) ,

- reddening and induration of the site

appear in 8 to 12 hours

- reach a peak in 24 to 72 hours

- slowly subsides thereafter

Tuberculin skin test

- Accumulation of mononuclear cells around small veins and venules at the site if injection (perivascular cuffing)

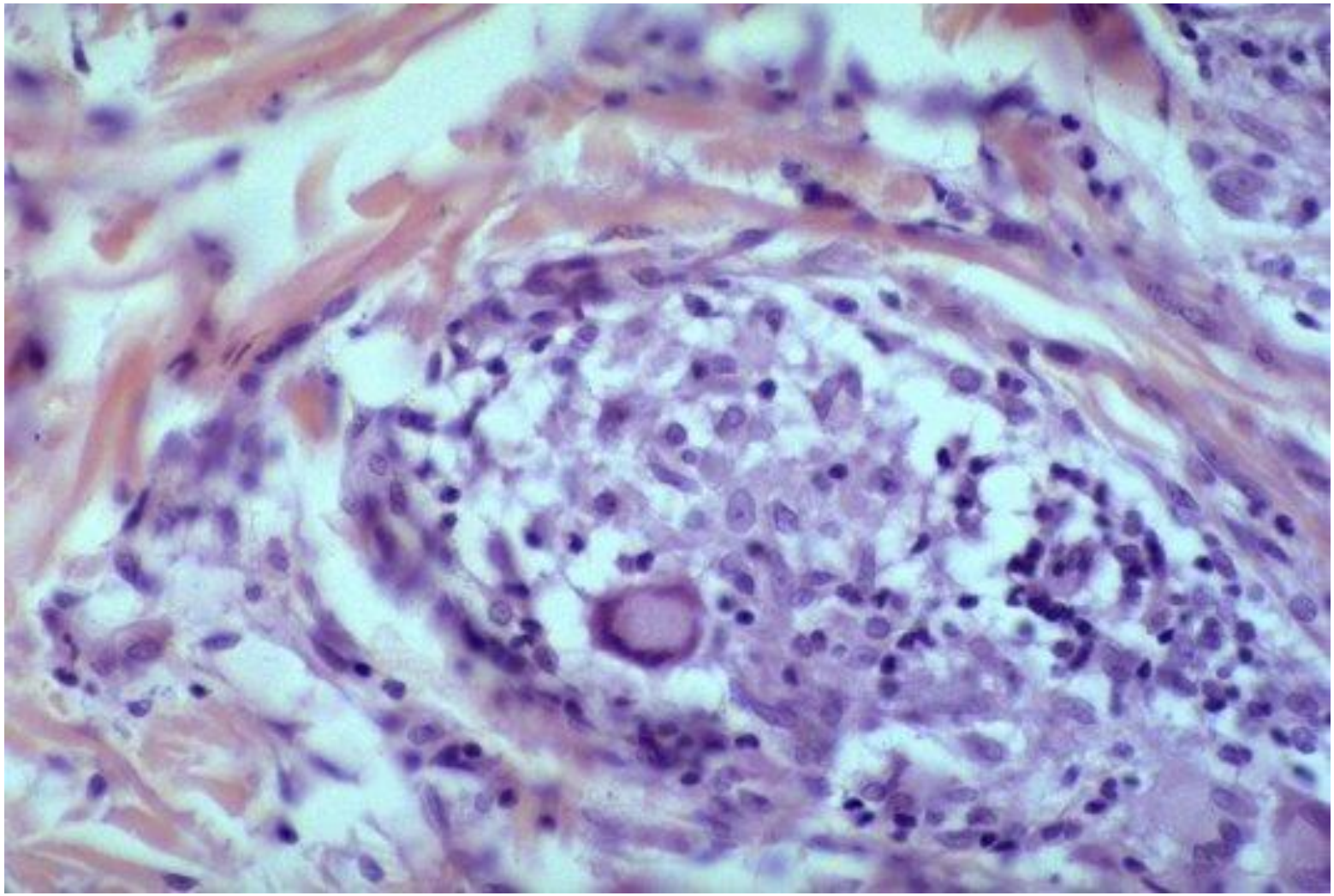
- Increased micro-vascular permeability

  - plasma proteins escape - dermal edema

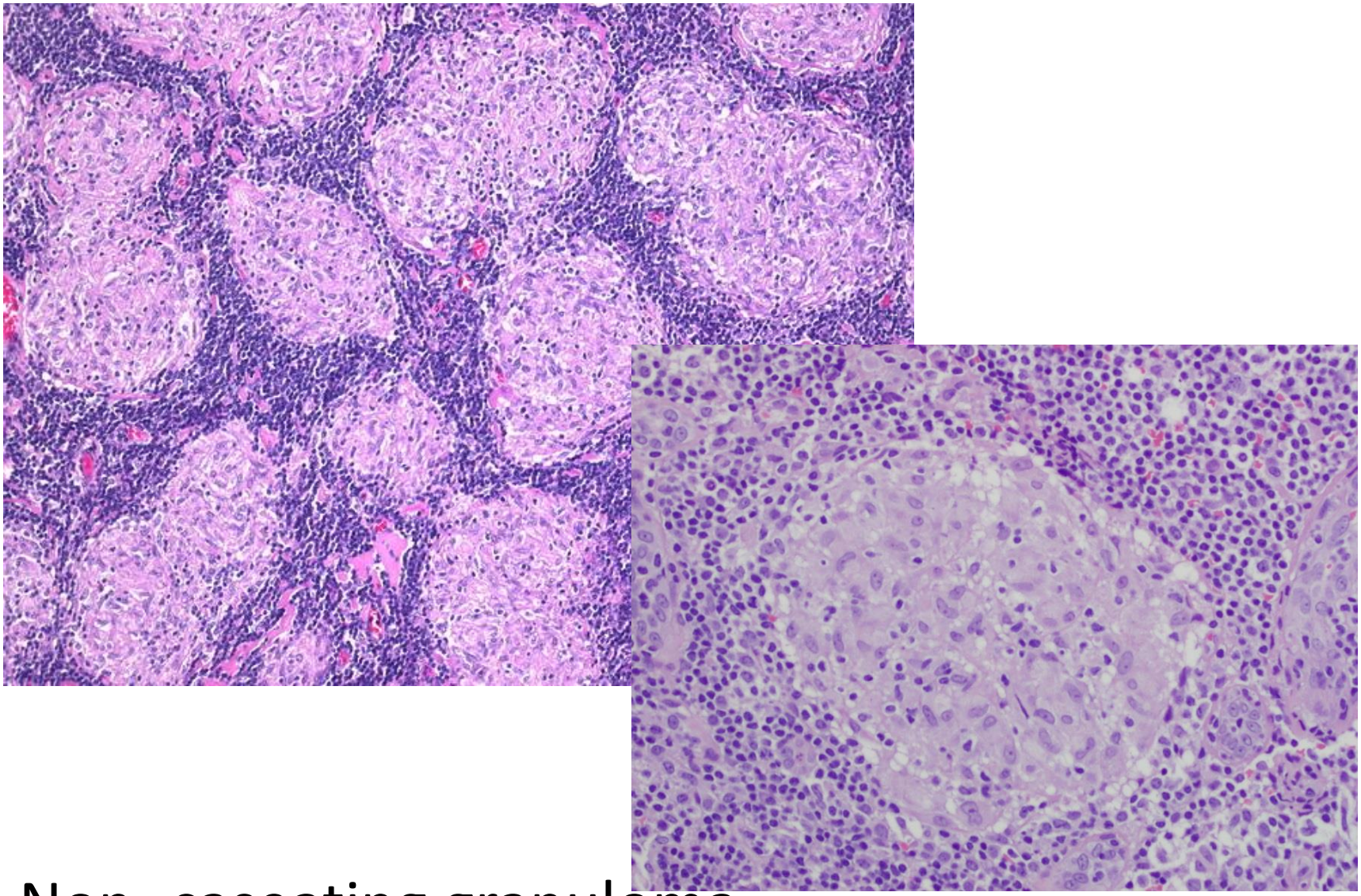
  - fibrin deposits in the interstitium - induration

Different types of granulomas

Leprosy - Tuberculoid leprosy

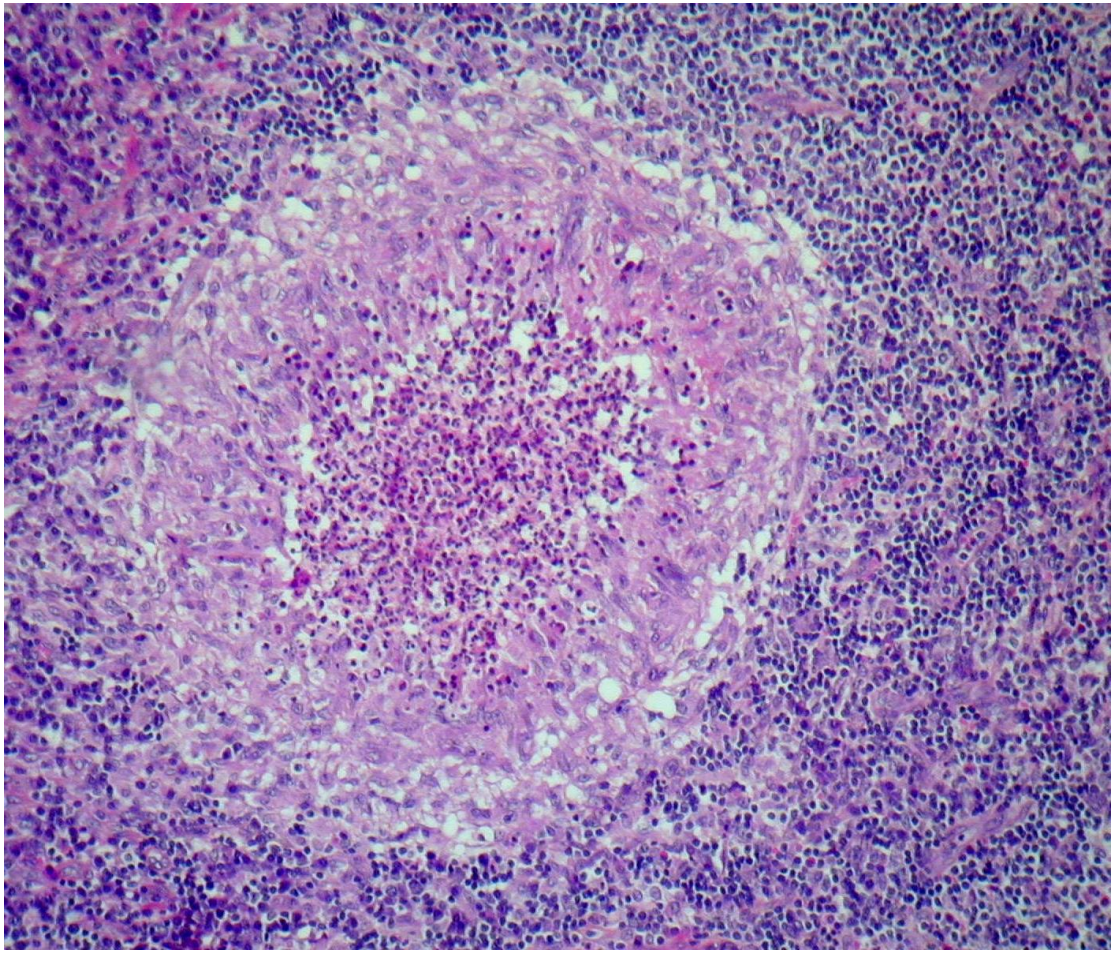


Sarcoidosis - Granuloma



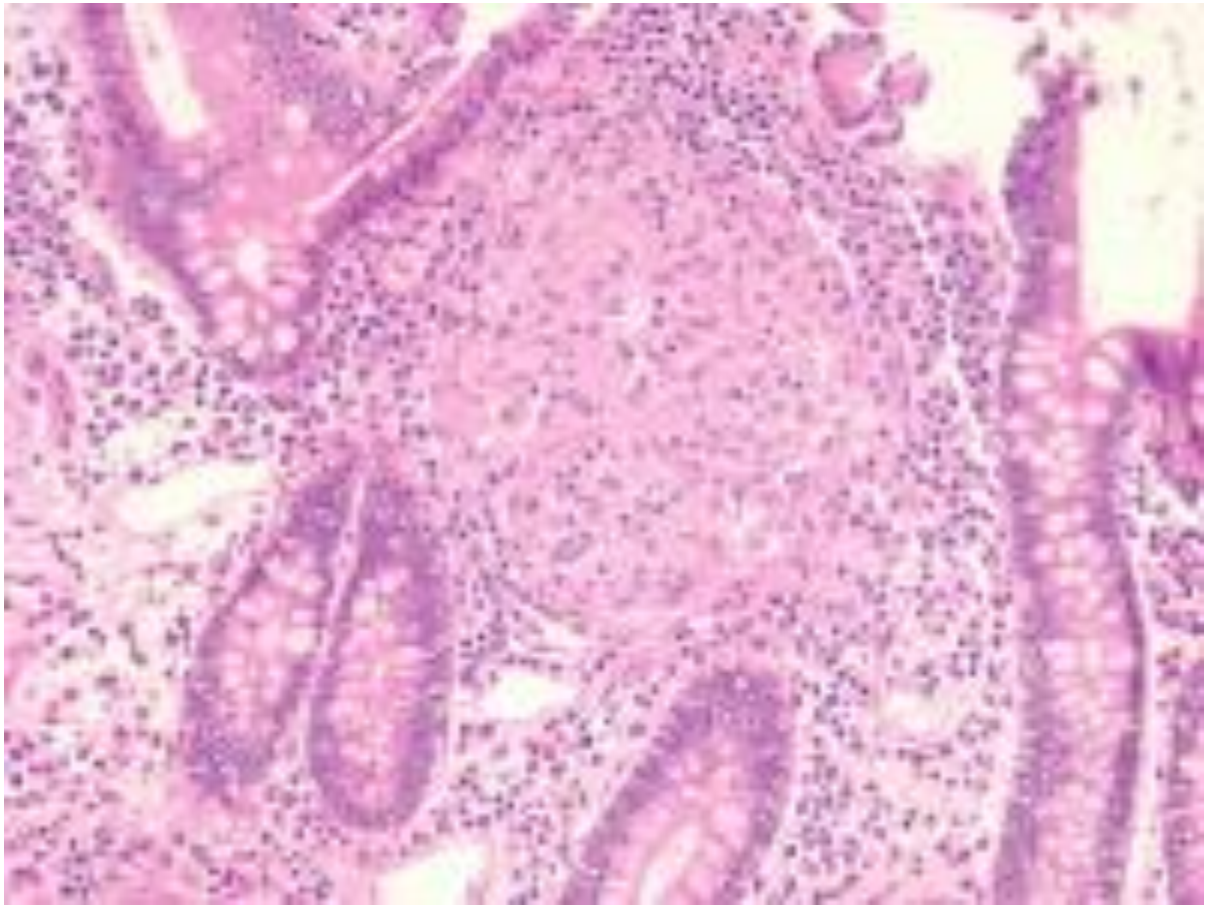
Non- caseating granuloma

Cat-scratch disease



Central granular debris and neutrophils
Giant cells - Uncommon
Aetiology - Gram - negative bacillus

Crohn's disease



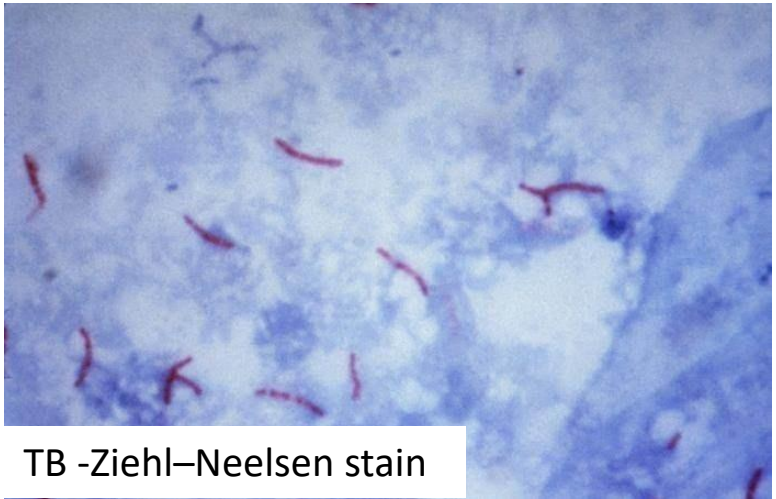
Non - caseating granuloma

Aetiology – Immune reaction against intestinal bacteria, self antigens

Granulomatous inflammation
- Diagnosis -

- Morphological patterns of granulomatous inflammation is sufficient for a reasonably accurate diagnosis

- However special stains and other ancillary tests are useful for confirmation



TB -Ziehl–Neelsen stain

Granulomatous inflammation - Summary

- A specific type of chronic inflammation
- Seen only in limited number of conditions
- There are immune and non-immune granulomas
- Microscopic appearance of granulomas vary in different disease processes