Chronic inflammation 1

What is inflammation?

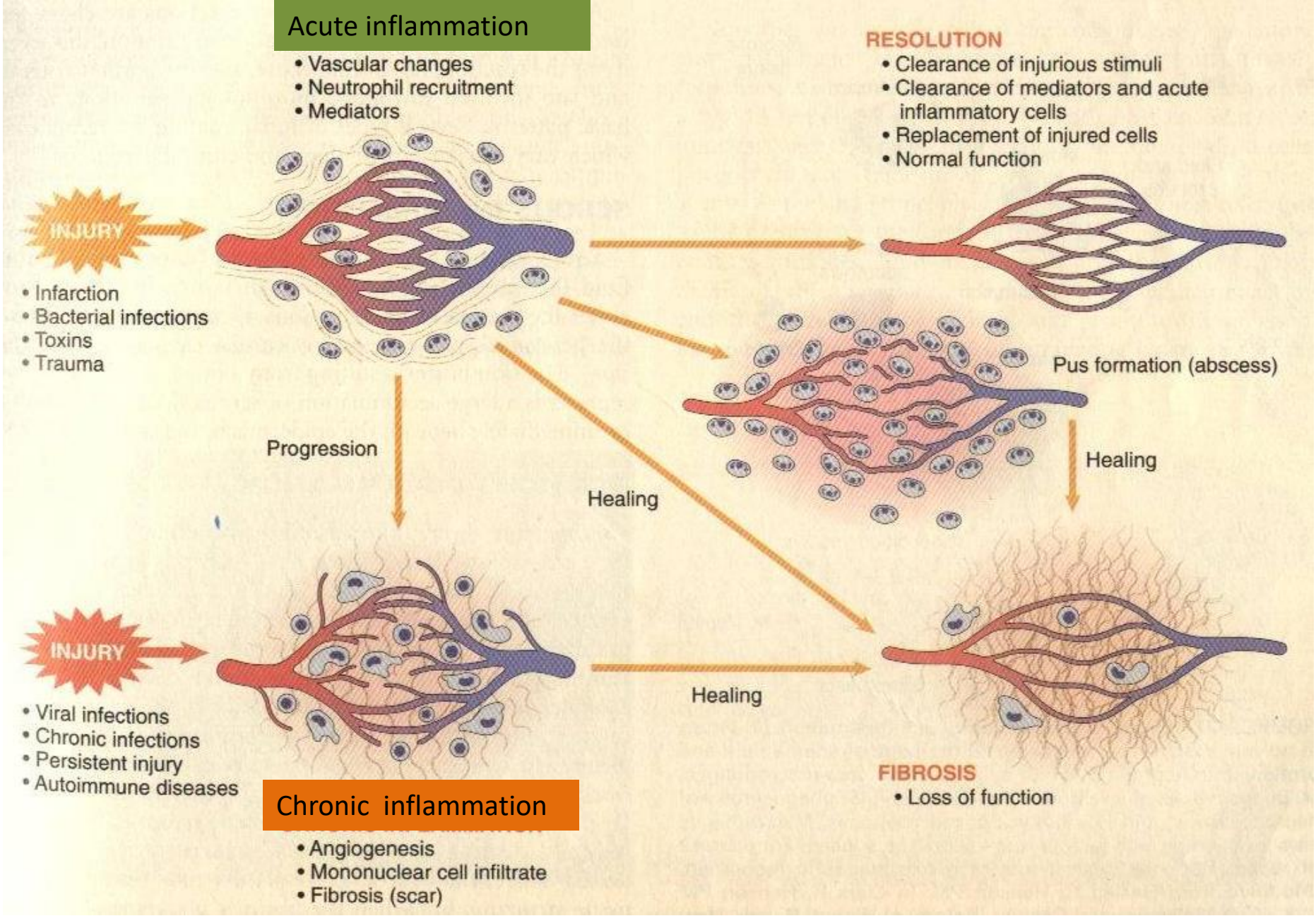
- A protective **host response**
- Destroys and eliminates causative agents and damaged/necrotic host tissue
- Initiates healing and repair

A process essential for survival

What are the types of inflammation ?

Acute inflammation

Chronic inflammation


Acute inflammation
• Vascular changes
• Neutrophil recruitment
• Mediators
RESOLUTION
• Clearance of injurious stimuli
• Clearance of mediators and acute inflammatory cells
• Replacement of injured cells
• Normal function
INJURY
• Infarction
• Bacterial infections
• Toxins
• Trauma
Pus formation (abscess)
Progression
Healing
Healing
INJURY
• Viral infections
• Chronic infections
• Persistent injury
• Autoimmune diseases
Healing
FIBROSIS
• Loss of function
Chronic inflammation
• Angiogenesis
• Mononuclear cell infiltrate
• Fibrosis (scar)

Objectives

- Define chronic inflammation (CI)
- Describe the cellular interactions in chronic inflammation
- Describe the macroscopic and microscopic features of chronic inflammation
- List systemic manifestations of chronic inflammation

Chronic inflammation

Inflammation of **prolong duration** (weeks/months/years)

characterized by

- ongoing inflammation

    macrophages, lymphocytes and plasma cells

- tissue destruction/ necrosis and

- tissue repair with new vessel formation and fibrosis

    occurring at the same time

Chronic inflammation (CI)

- Usually **begins as a chronic process**
  (Starts *denovo / "*Chronic inflammation *abinitio"*)
  - No recognizable initial phase of acute inflammation

- May progress from acute inflammation

Causes of *De Novo* Chronic inflammation

- Persistent infection by microorganisms
- Prolonged exposure to potentially toxic agents
- Immune-mediated inflammatory diseases

Persistent infection by microorganisms that are resistant to phagocytosis and intracellular killing

eg.

Tuberculosis infection

- Evokes a delayed type hypersensitivity reaction

- May result in granuloma formation

Immune mediated inflammatory diseases

Due to inappropriate activation of immune system

- Autoimmune diseases

  Rheumatoid arthritis

  Hashimoto thyroiditis

- Unregulated immune responses against common environmental substances

  Allergic diseases

Prolonged exposure to potentially toxic agents

- Endogenous material

  eg. keratin - ruptured epidermoid cyst

  uric acid crystals - gout

  hair - pilonidal sinus

- Exogenous material

  eg. Silica - Silicosis

  asbestos fibers, suture material,

  bone particles,implanted prosthesis

CI - Progress from acute inflammation

- Usually due to persistent suppurative inflammation

  Chronic abscess - eg. lung,

  osteomyelitis

- Poorly drained abscess may result in

  sinus formation

- Repeated attacks of inflammation with healing

  eg. - Chronic cholecystitis

  - Chronic pyelonephritis

Usually shows a mixture of acute and chronic inflammatory cells

Cells in chronic inflammation

- **Macrophages** ("Macro"- big; "Phage"- eat)
- **Lymphocytes**
- Plasma cells
- Eosinophils
- Mast cells

Depending on the type of the cellular infiltrate sometimes it would be possible to suggest the possible aetiological agent

eg. **Predominance of eosinophils in parasitic infections**

Macrophage

- Normally diffusely scattered in most tissue

CNS- Microglia
Lung- Alveolar macrophages
Bone- Osteoclasts

Liver-Kupffer cells
Spleen and lymph nodes - Sinus histiocytes

Bone marrow →  → 

- Larger
- Greater phagocytic capacity

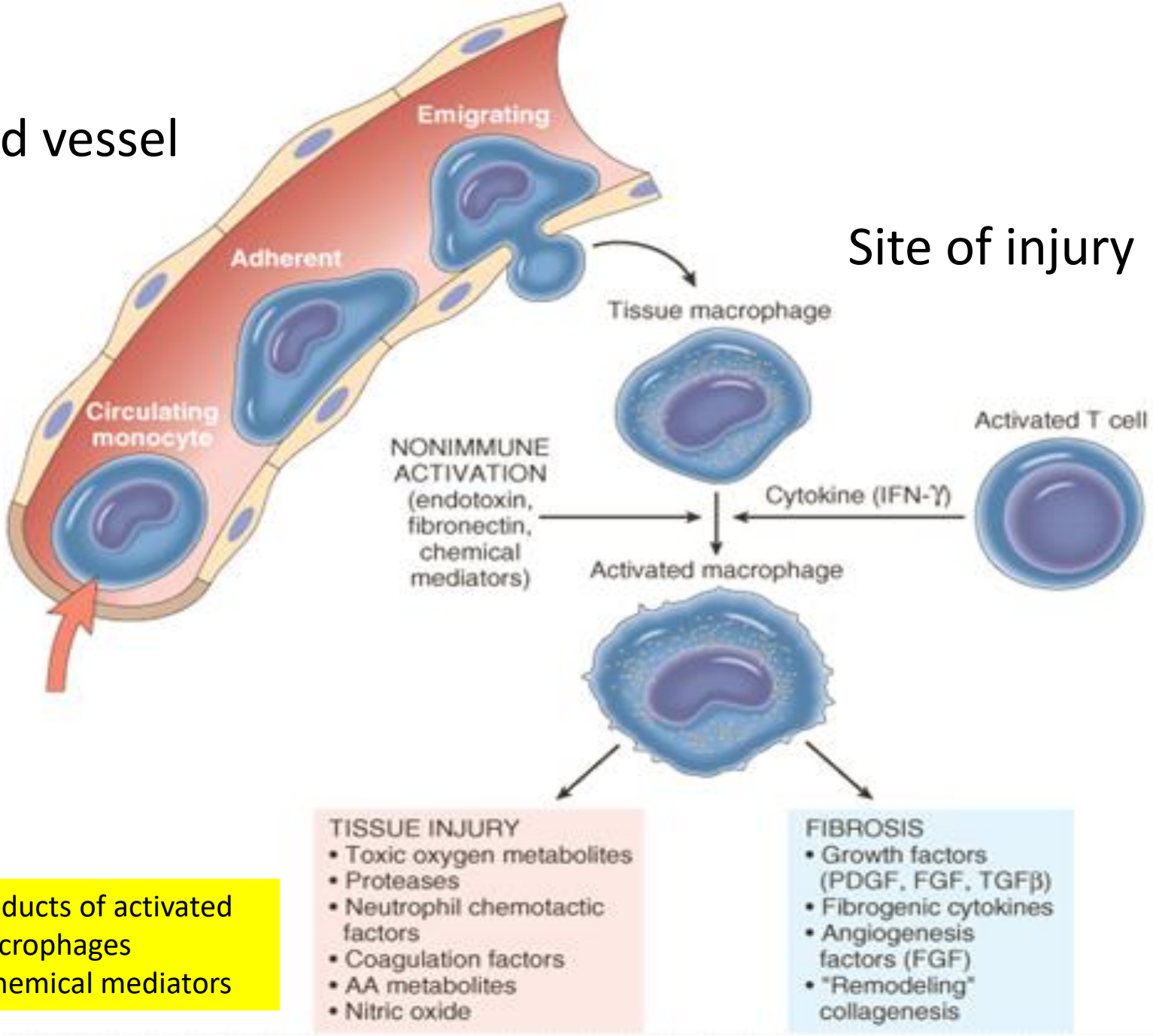
Half life – about 1 day

Longer half life

Blood

Tissue

Blood vessel



Products of activated macrophages
- Chemical mediators

Macrophages

- If the stimulus is eliminated, macrophages eventually disappear

  - die/enter into the lymphatics and lymph nodes

- In chronic inflammation, accumulation persists, and this is mediated by different mechanisms
  - **Recruitment of monocytes from the circulation**
  - Local proliferation of macrophages
  - Immobilization of macrophages within the site of inflammation

Lymphocytes

- Both T and B lymphocytes migrate to a site of injury following

  - an immune stimulus (infections) or

  - a non immune stimulus (infarction/tissue trauma)

- Use the similar adhesion molecules and chemokines that recruit other leukocytes

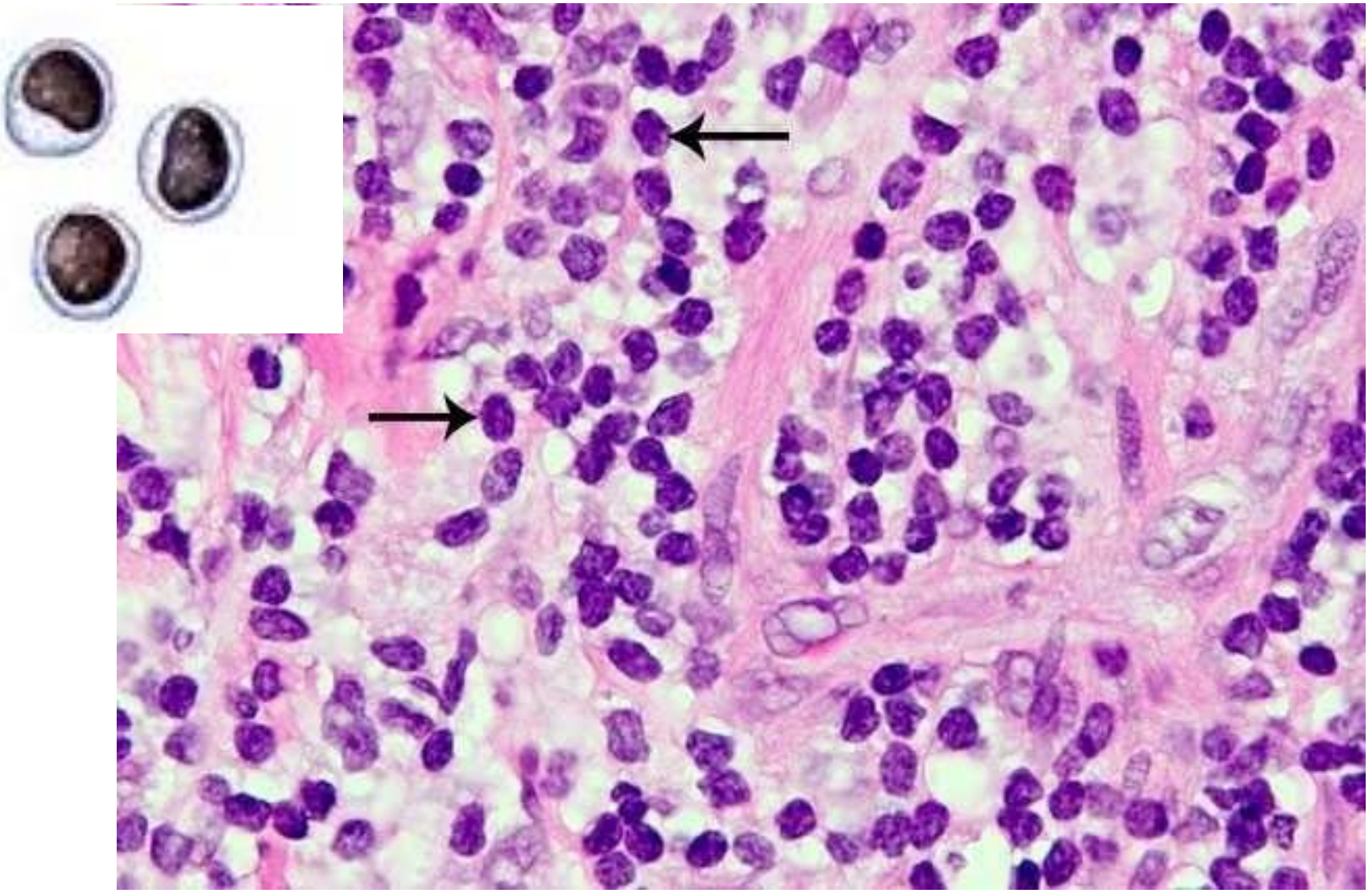
Lymphocytes

- T- lymphocytes
  - Recruit and activate macrophages

  - Recruit other lymphocytes

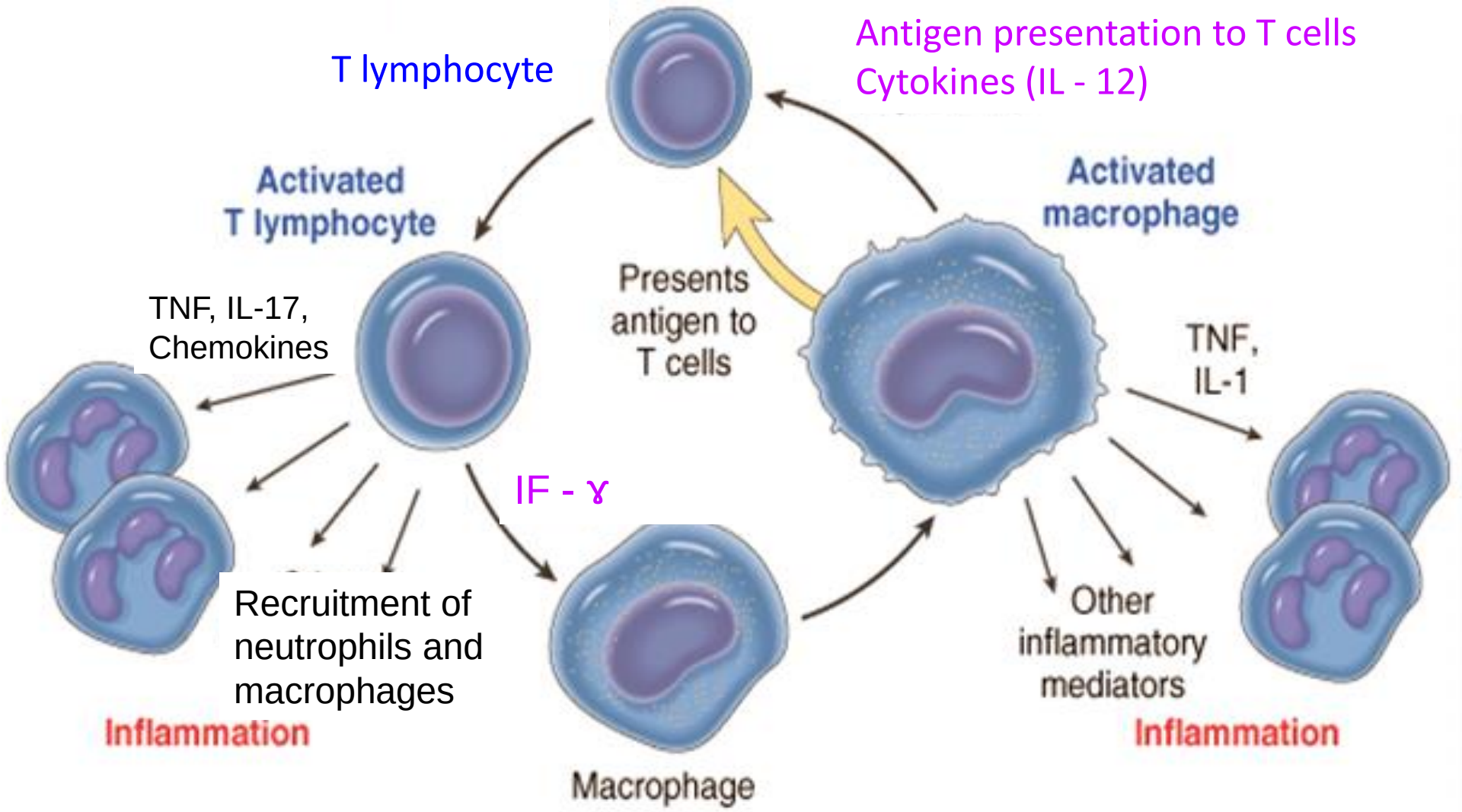
  - Produce inflammatory mediators

  - Destroy target cells by producing perforin, a cytolytic protein stored in and released by cytoplasmic granules



Lymphocytes - scant cytoplasm and round nuclei without prominent nucleoli

Macrophage - Lymphocyte interactions in Chronic inflammation

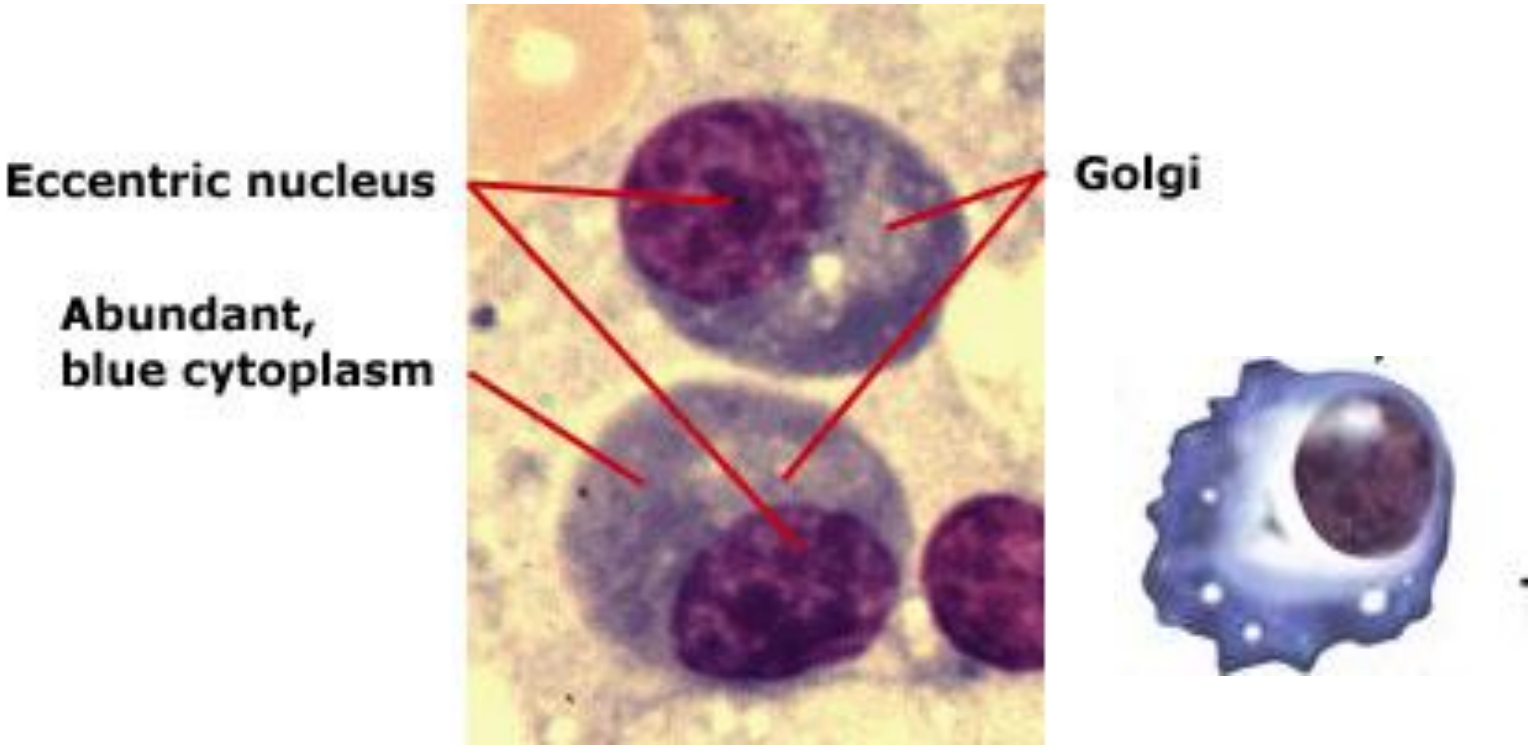


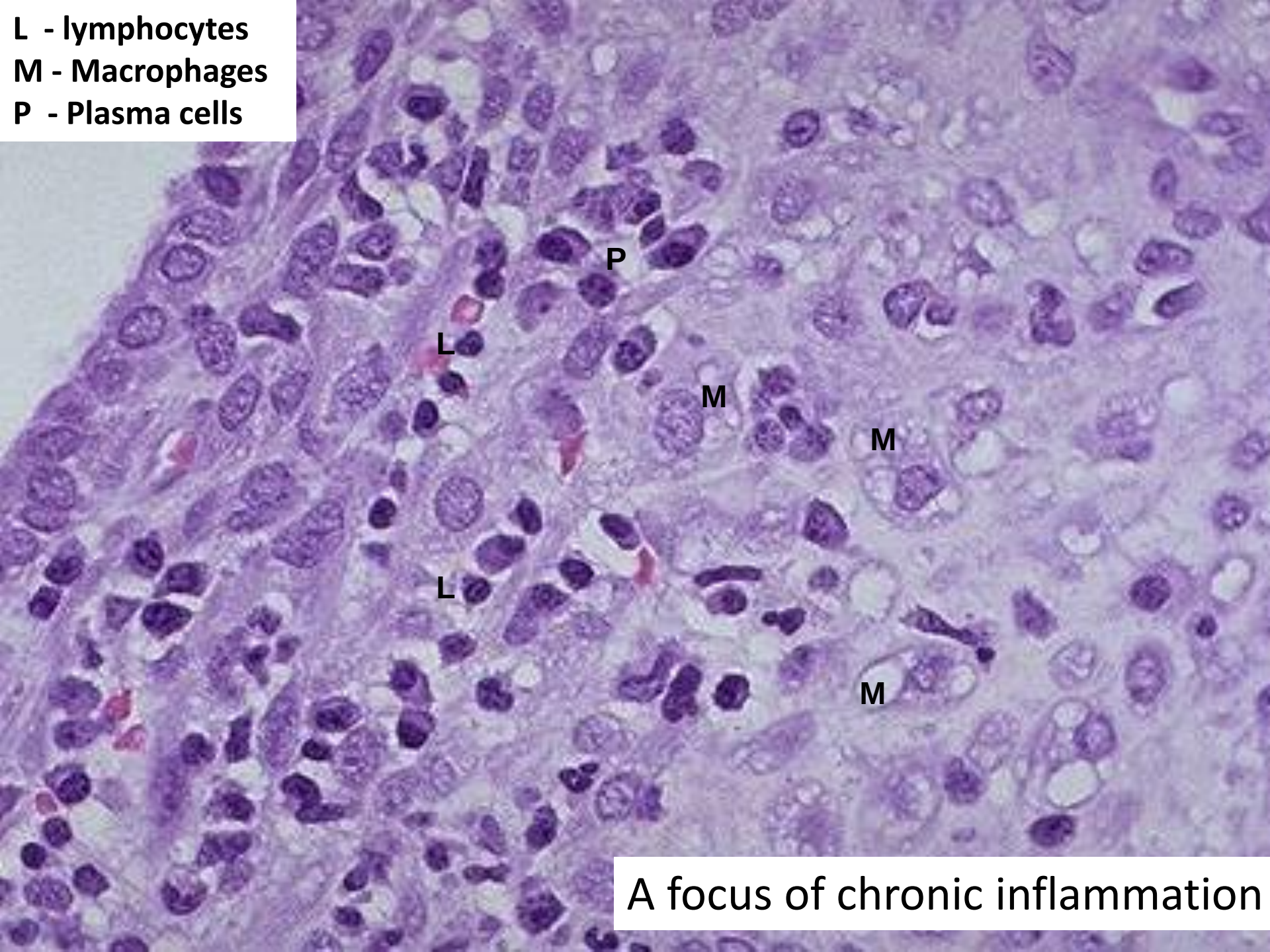
Macrophage - lymphocyte interactions in chronic inflammation

Other cells involved in chronic inflammation

Plasma cells

- Develop from activated B lymphocytes after exposed to antigens
  - Produce antibodies





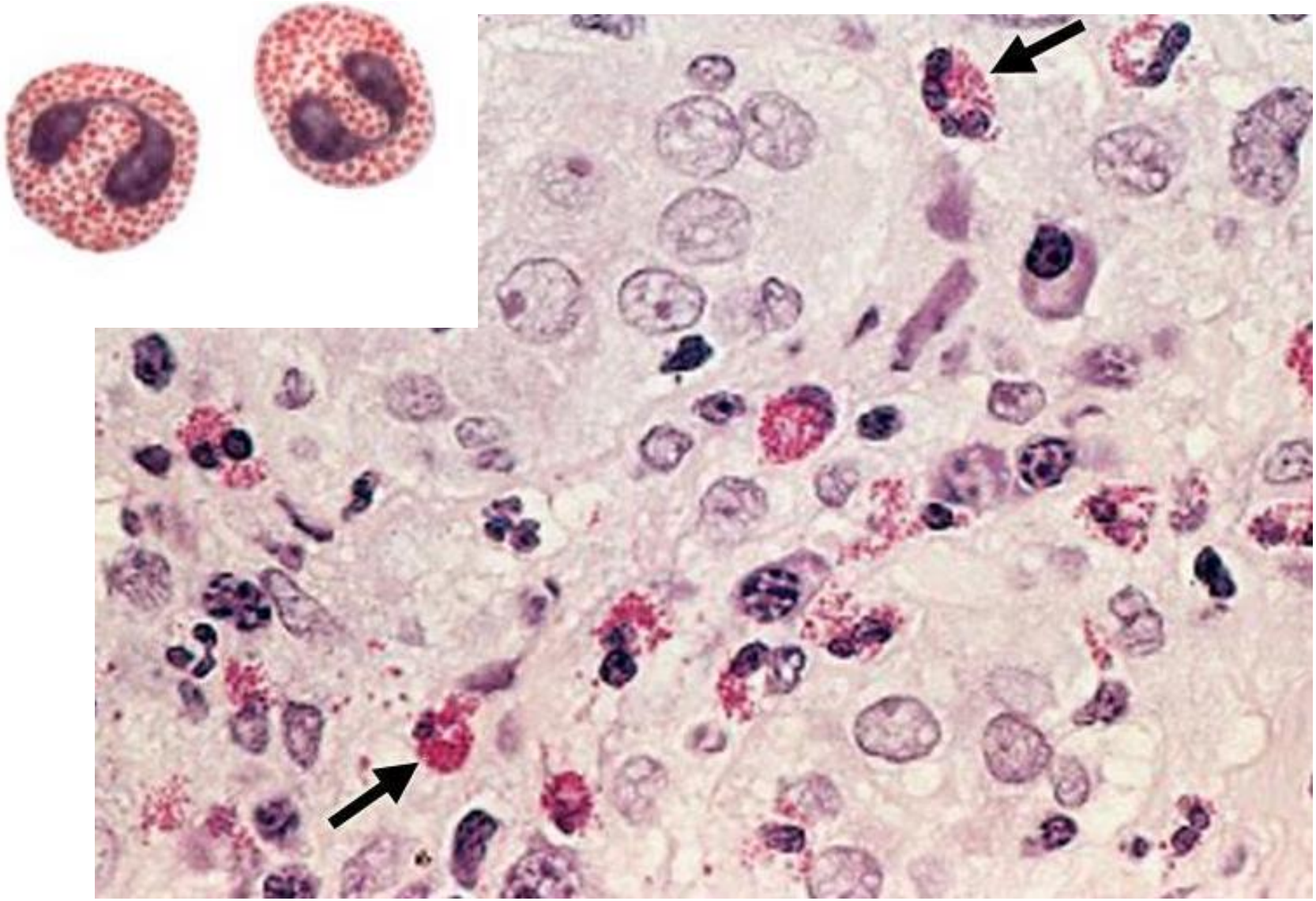
A focus of chronic inflammation

Eosinophils

- Abundant in
- Immune reactions mediated by immunoglobulin E (IgE)
- Parasitic infections

- Migrate from the peripheral blood into tissue

- Eosinophil granules contain major basic protein
  - Toxic to parasites, also lyses mammalian epithelial cells

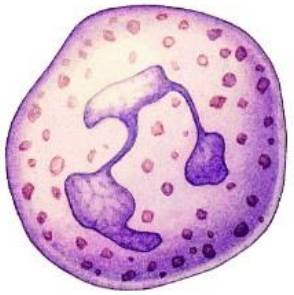


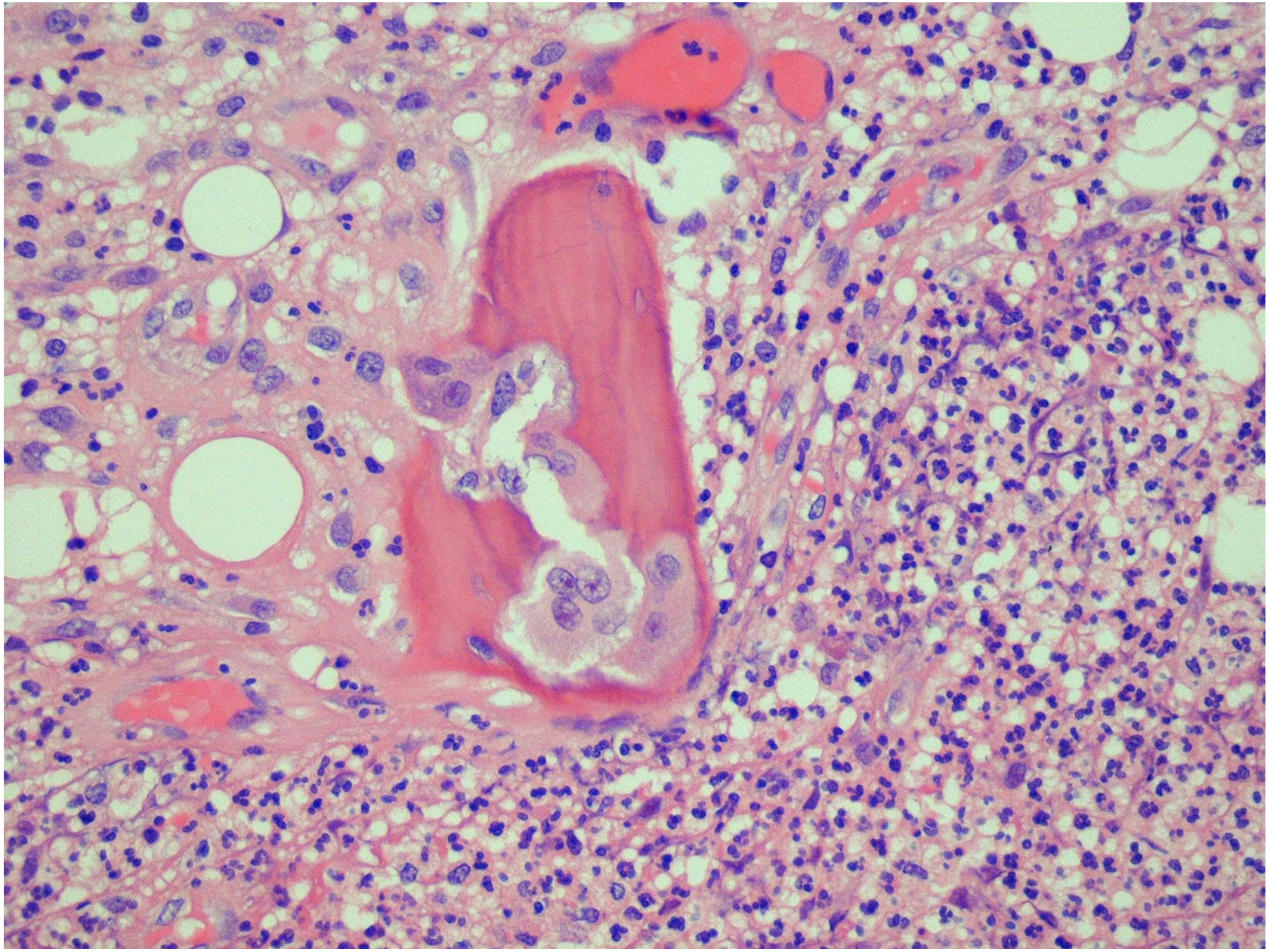
Eosinophils - Brightly eosinophilic coarse cytoplasmic ganules and (arrow) bi-lobed nuclei (arrow)
- Some show degranulation

Neutrophils in chronic inflammation

- Presence of neutrophils is characteristic of acute inflammation

- Some chronic inflammation continue to show neutrophils and usually form chronic abscesses
  - inflammation caused by foreign material
  - actinomyces infection
  - chronic osteomyelitis
  - smoking related chronic lung damage





Chronic osteomyelitis

Macroscopic features of Chronic inflammation

CI - Macroscopic appearance

Extremely variable

eg.

- Chronic ulcer - Chronic peptic ulcer of the stomach
- Chronic abscess - may lead to cavitation (eg. lung)
- Fistulae, sinuses
- Due to fibrosis

  - Thickening of the walls of hollow viscera

    eg. gall bladder in chronic cholecystitis

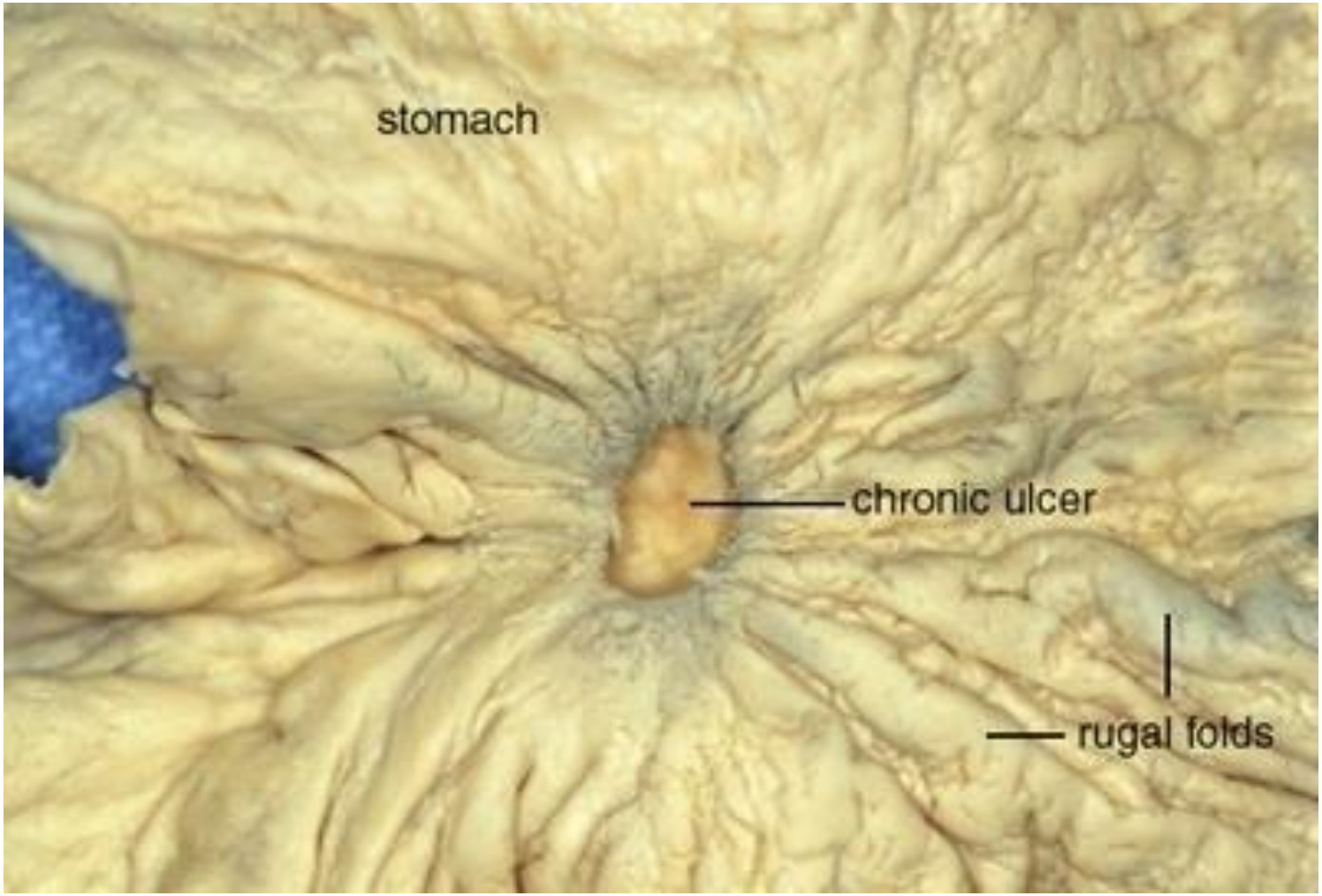
  - Adhesions

  - Stenosis / strictures

- Mass formation - Differential diagnosis - tumour

Skin - chronic ulcer - Macroscopy

Chronic peptic **ulcer** - Macroscopy



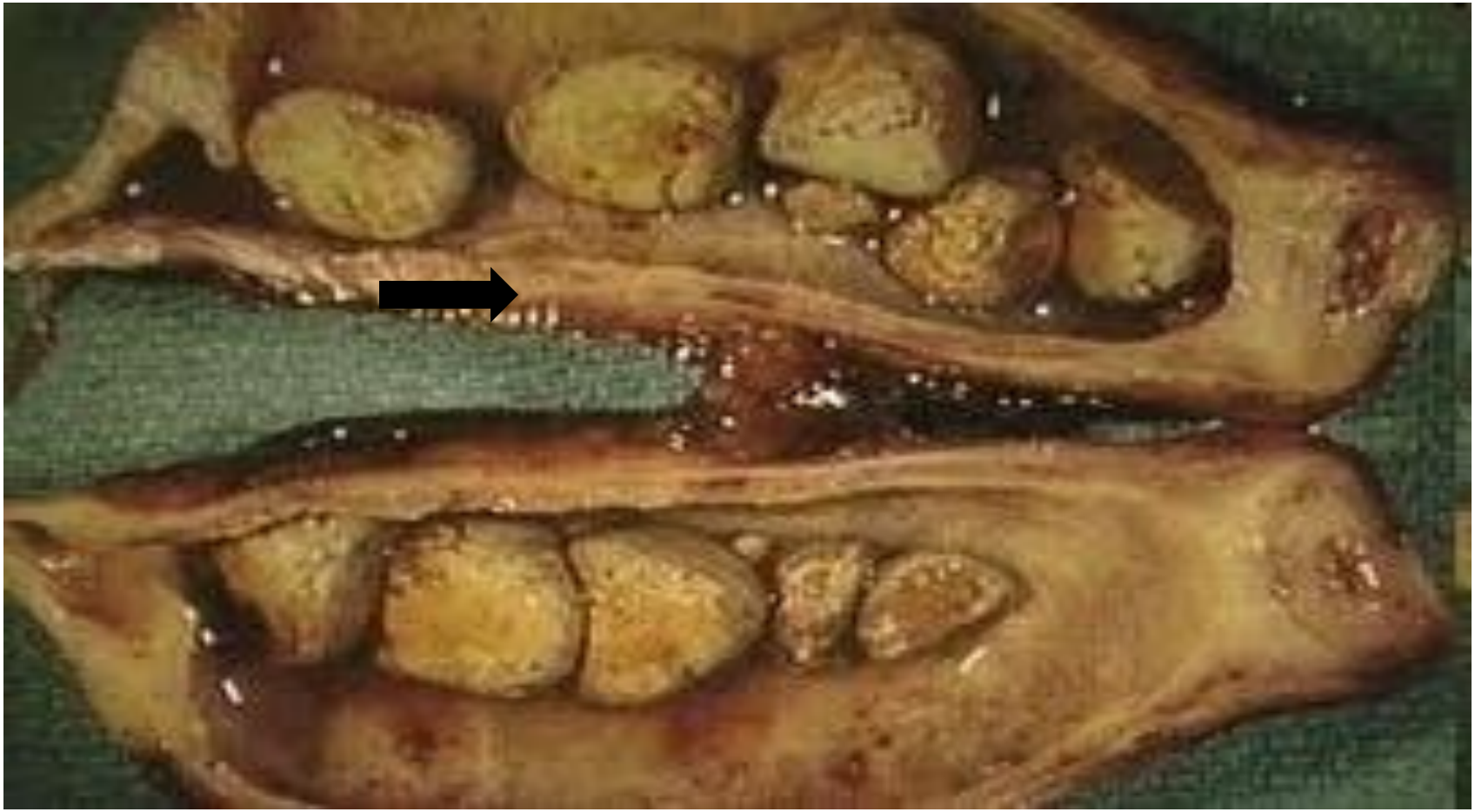
Lung

Abscess

Cavitation

thickened walls due to fibrosis

Gall bladder - Chronic cholecystitis



Macroscopy - **Thickened wall**

- Gall stones

Kidney - Chronic pyelonephritis

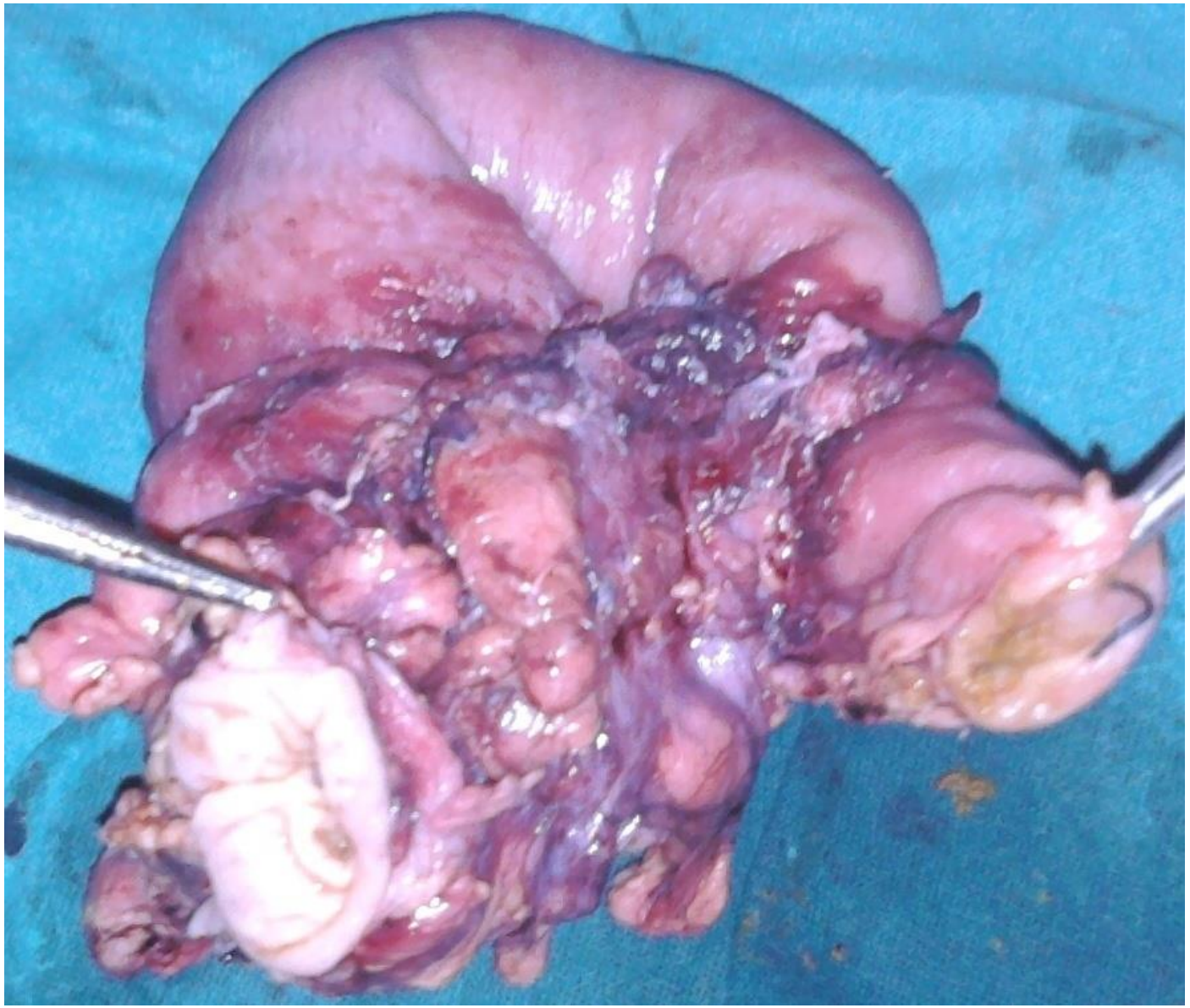
Surface **scarring**

Normal kidney

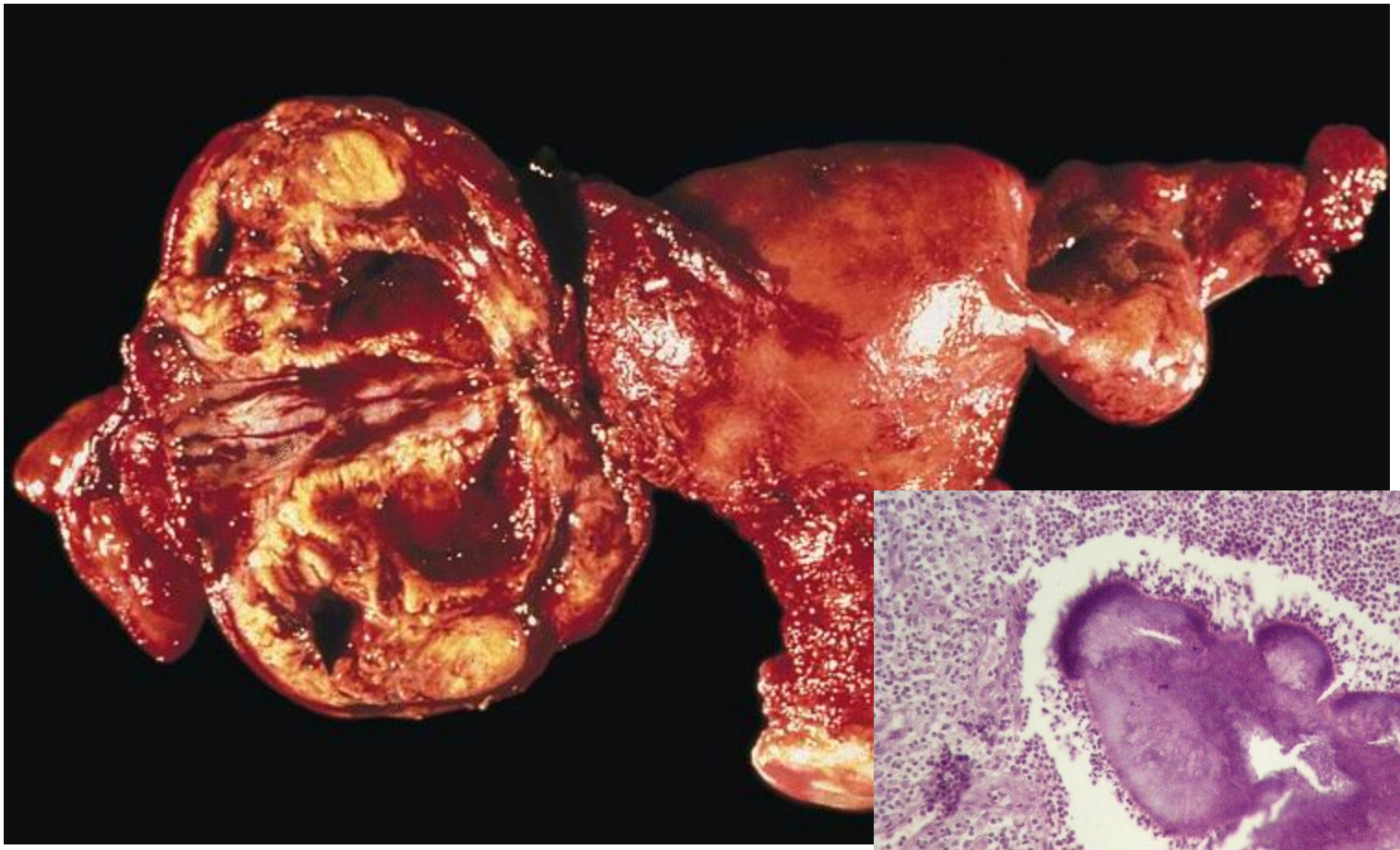
Lung

Scarring - Chronic inflammation of the bronchi dilation and scarring

Ileocaecal mass in tuberculosis



Female genital organs

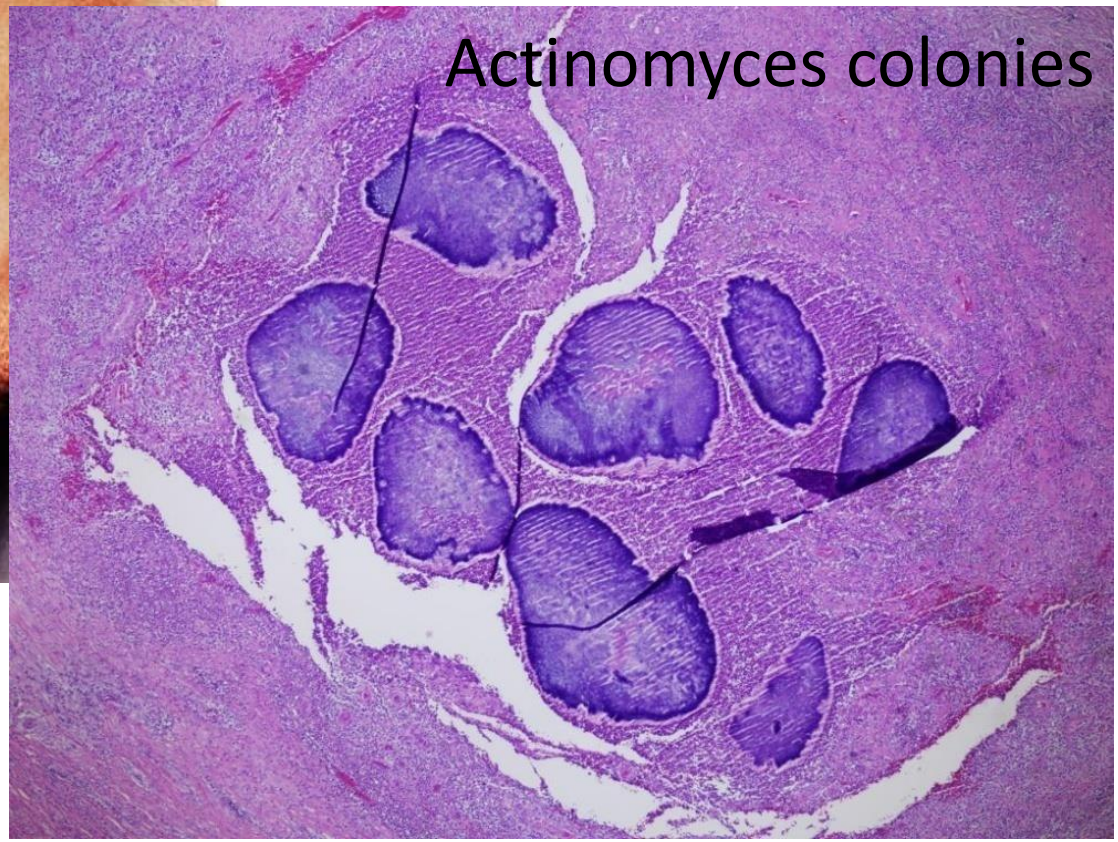


Tubo-ovarian **mass formation**

Actinomyces colonies

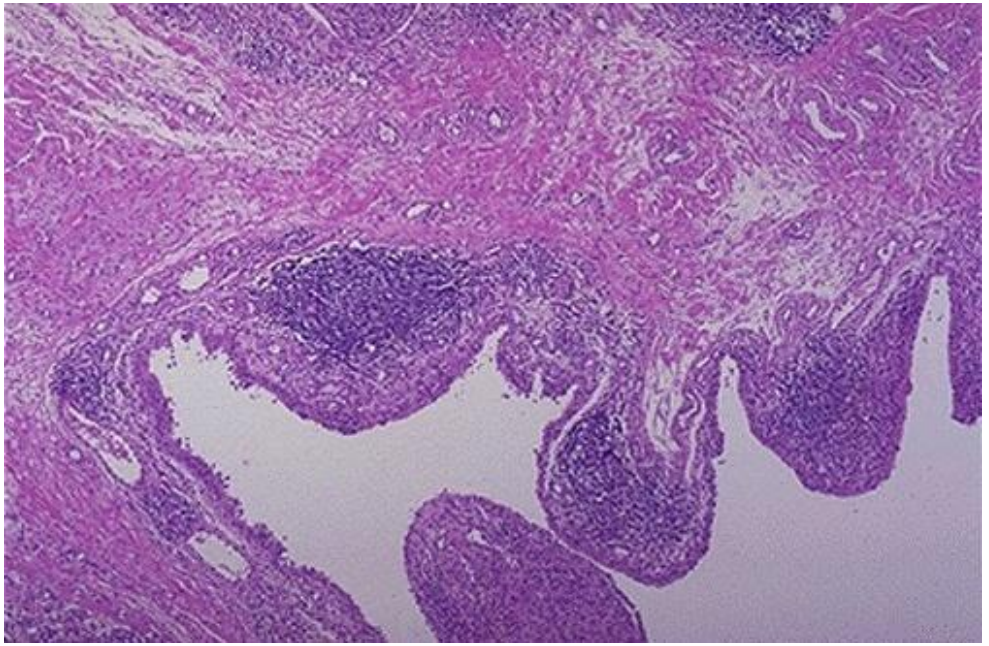
Sinus formation

Sinus formation



Rheumatoid arthritis

Macroscopy
Joint **deformities**



Microscopy
Aggregates of lymphocytes

Microscopic features of chronic inflammation

CI - Microscopy

- Inflammatory cells , mainly consists of
  - lymphocytes , macrophages and plasma cells (mononuclear cell infiltrate)
  - Some macrophages form multinucleated giant cells
- Destruction of normal tissue

  may show necrotic areas

  eg. Caseous necrosis in TB granulomas

- “Granulation tissue”

  Inflammatory cells , proliferating vessels,

  fibroblasts, collagen deposition and later fibrosis

  (Granulomatous inflammation - “granuloma”)

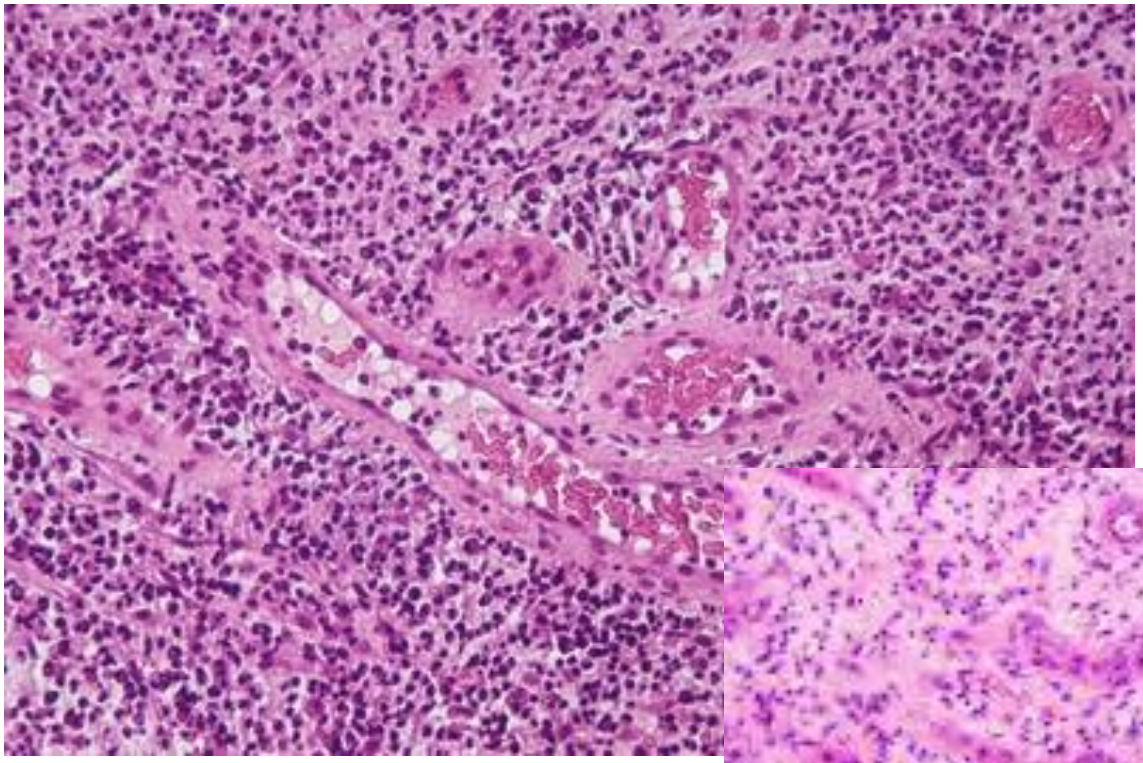
- Regeneration of specialized cells

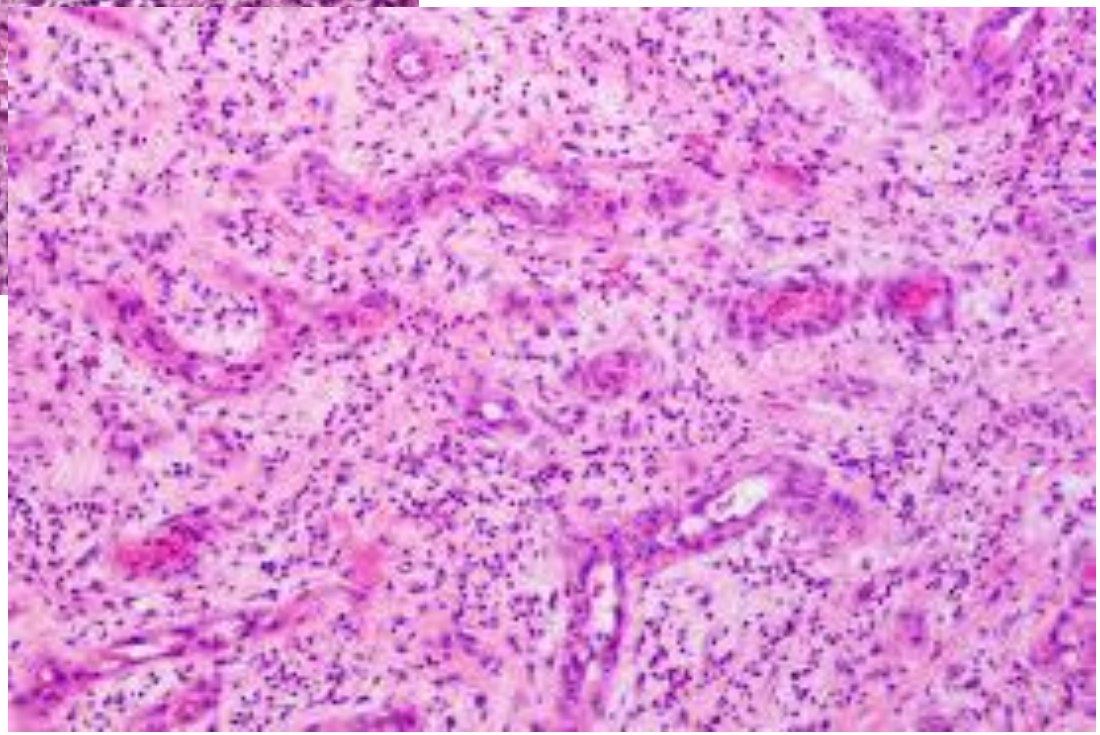
  eg . Epithelial regeneration in an ulcer edge

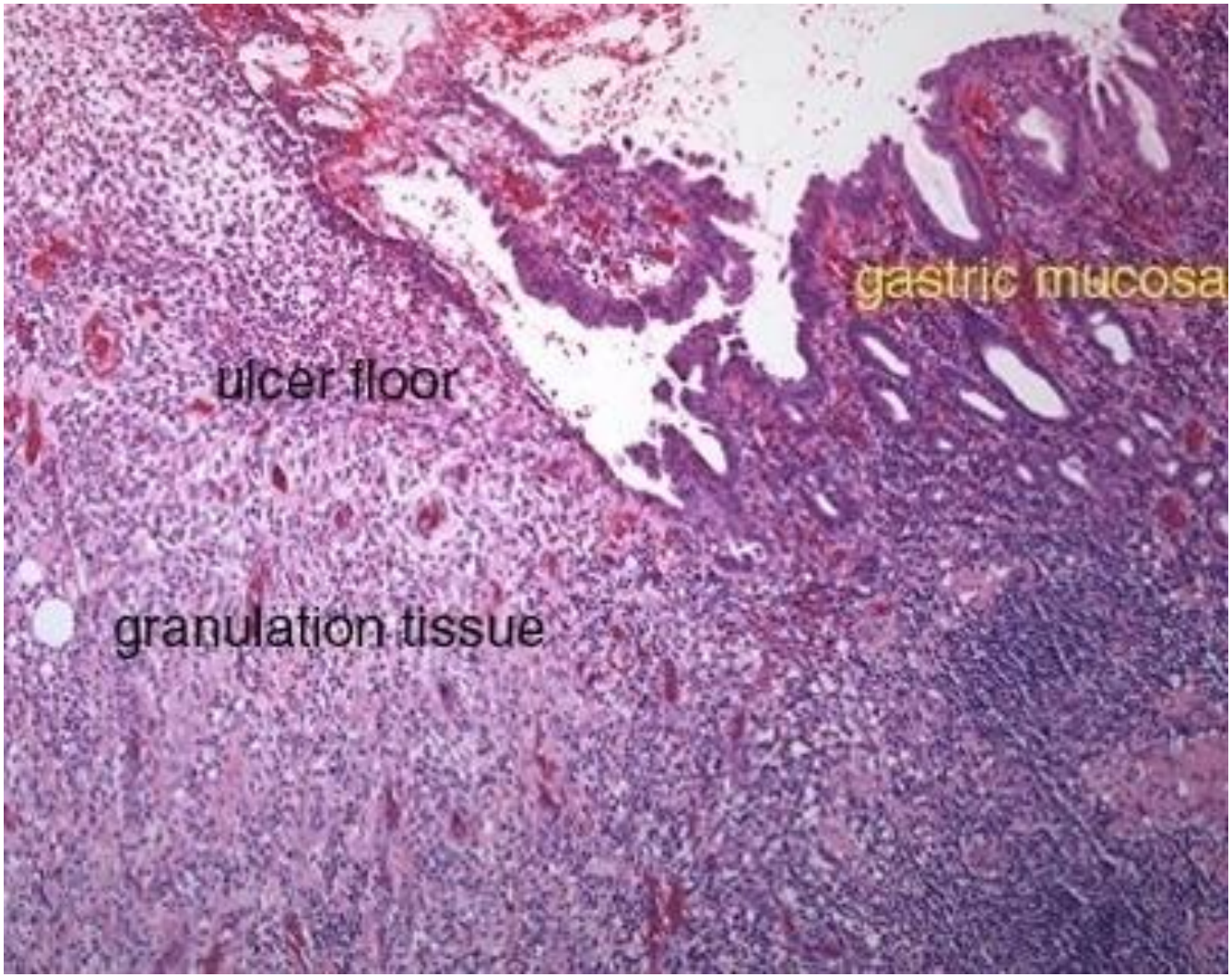
  - may show reactive changes

  (may mimic dysplasia in epithelia)

Granulation tissue - Microscopy

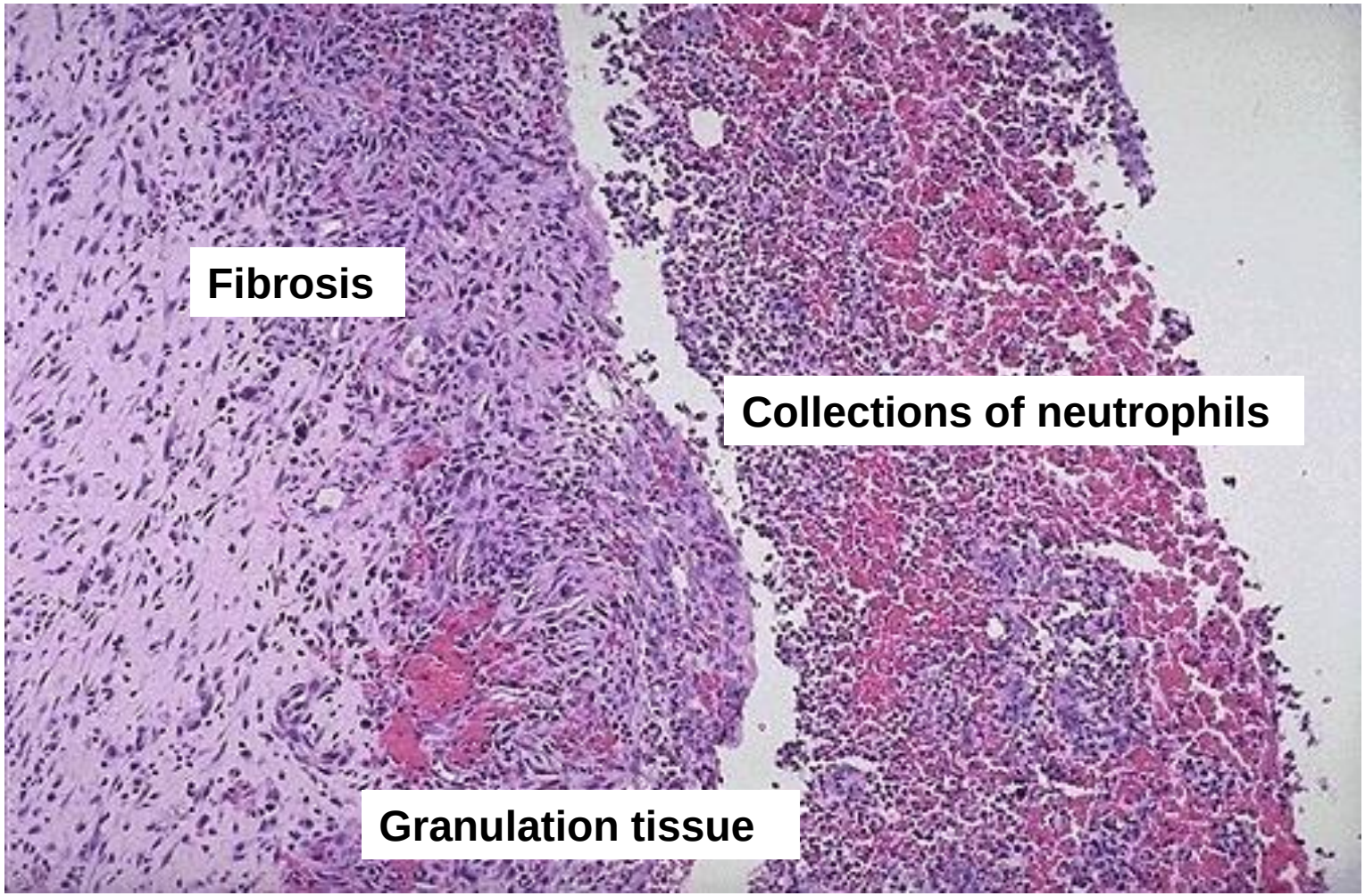






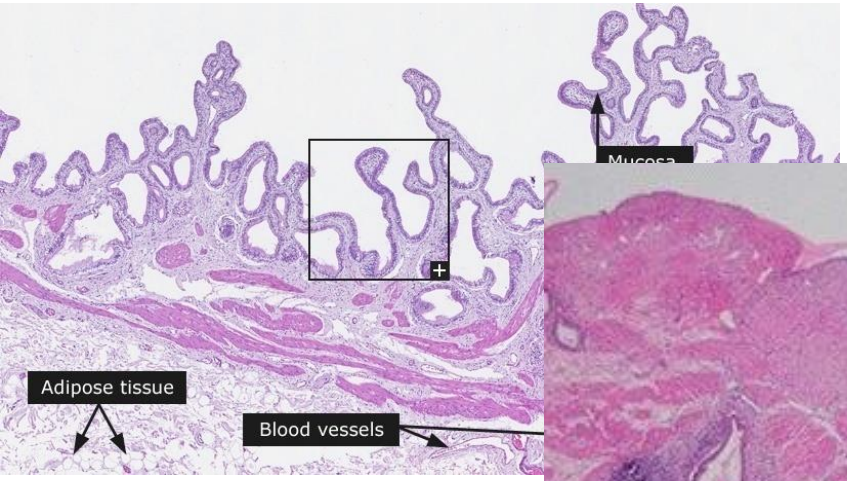
Chronic peptic ulcer - Microscopy

Chronic abscess



Chronic cholecystitis

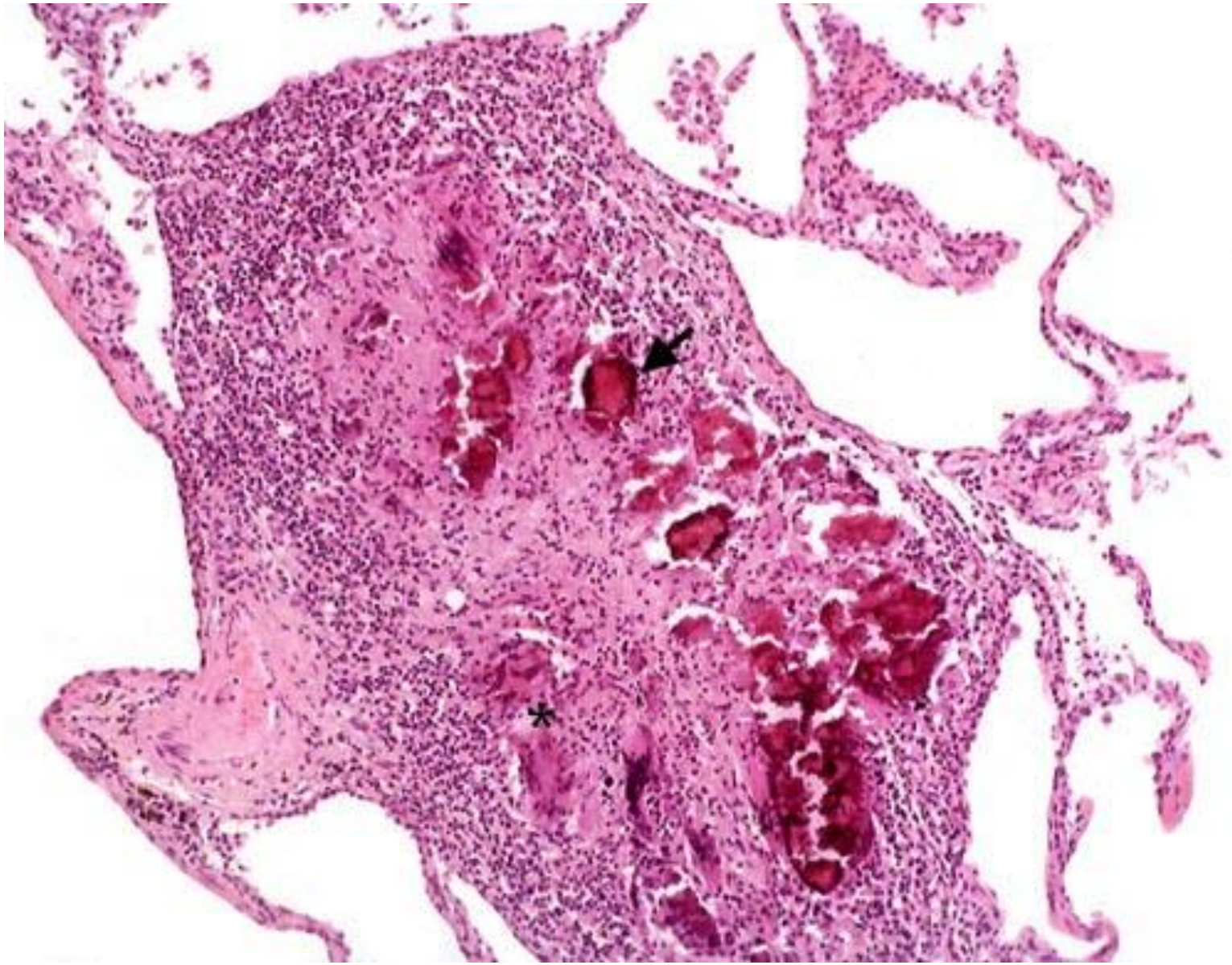
Normal gall bladder



Fibrosis (arrow) and thickening of the wall

Outcomes of chronic inflammation

- Tissue destruction
- Replacement by fibrosis and scar formation
- Amyloidosis
- Calcification



Lung - Granulomatous inflammation with calcification

Systemic effects of chronic inflammation

- Low grade fever
- Loss of weight
- Anaemia - anaemia of chronic disorders
  Usually normocytic normochromic anaemia
- Leucocytosis
  Relative lymphocytosis and monocytosis
- Raised erythrocyte sedimentation rate (ESR)
- Hepatomegaly, splenomegaly and lymphadenopathy
- Amyloidosis
  eg. tuberculosis, bronchiectasis, chronic osteomyelitis, rheumatoid arthritis, IBD

Anaemia in chronic diseases

- Reduced erythroid proliferation in BM
- Low serum iron

  Reduced total iron binding capacity

  Abundant stored iron in the mononuclear phagocytic system
- Inappropriately low renal erythropoietin generation
- This is caused by the action of cytokines , IL-1 , TNF-α and interferon ɣ

CI - Summary

- CI - Inflammation of prolong duration with active inflammation , tissue destruction and repair occurring together
- Main cells - macrophages and T lymphocytes
- Macroscopy - extremely variable
- Microscopy - Inflammation, tissue damage and granulation issue formation and fibrosis
- Outcomes would be tissue destruction , fibrosis , calcification and amyloidosis
- Systemic manifestations

Acute inflammation

- Rapid onset
- Short duration
- Characterised by
  - **Fluid and plasma protein exudate**
  - **Neutrophil predominance**
- Usually resolves but may progress to a chronic stage

Chronic inflammation

- Insidious onset
- Longer duration
- Characterised by
  - **Lymphocytes and macrophages**
  - **Tissue destruction**
  - **Blood vessel proliferation**
  - **Fibrosis**