Chronic Inflammation

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Overview of Chronic Inflammation

- Chronic inflammation represents a failure of the initial response (acute inflammation) to deal with the offending agent
- As the offending agent persists, the adaptative immunity system is initiated
- The causes of chronic inflammation are those that are difficult to eradicate
  - Microbes
  - Self-antigens

Acute vs Chronic Inflammation

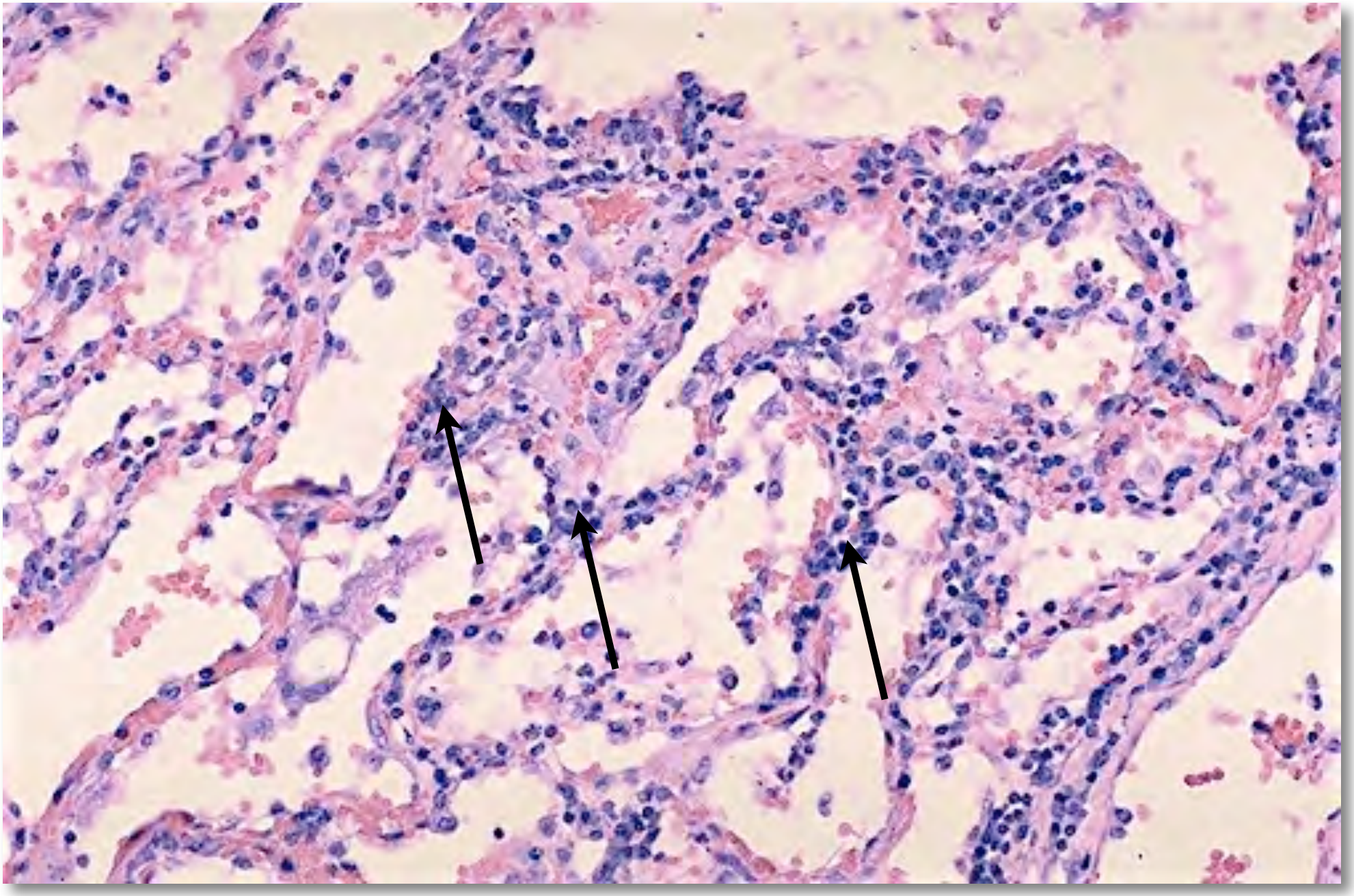
	Onset	Cellular Infiltrate	Cardinal Signs
Acute	Fast (seconds to hours)	Neutrophils	Prominent
Chronic	Slow (days)	Macrophages and Lymphocytes	Less Prominent

Chronic Inflammation

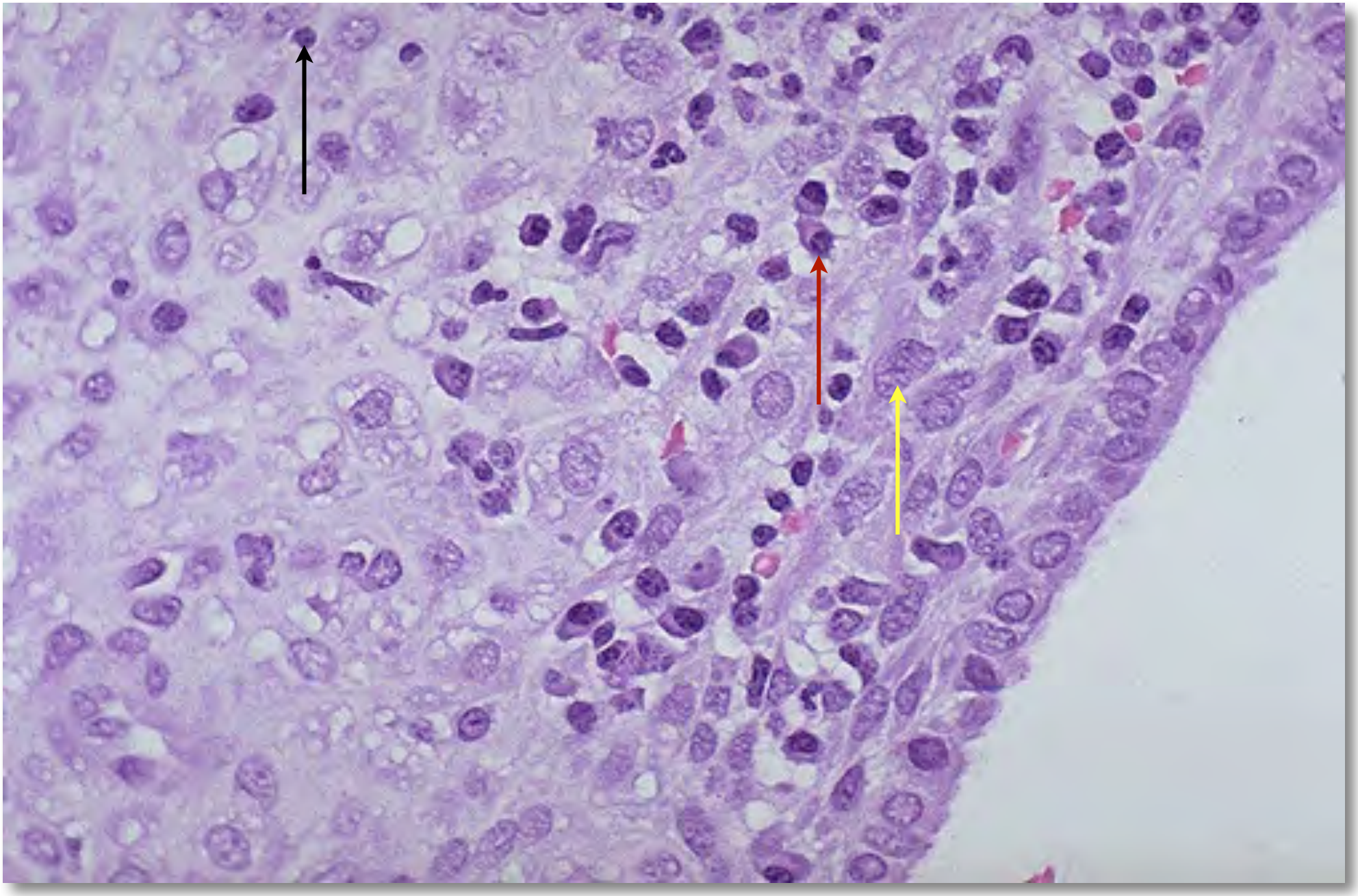
Important cells of chronic inflammation

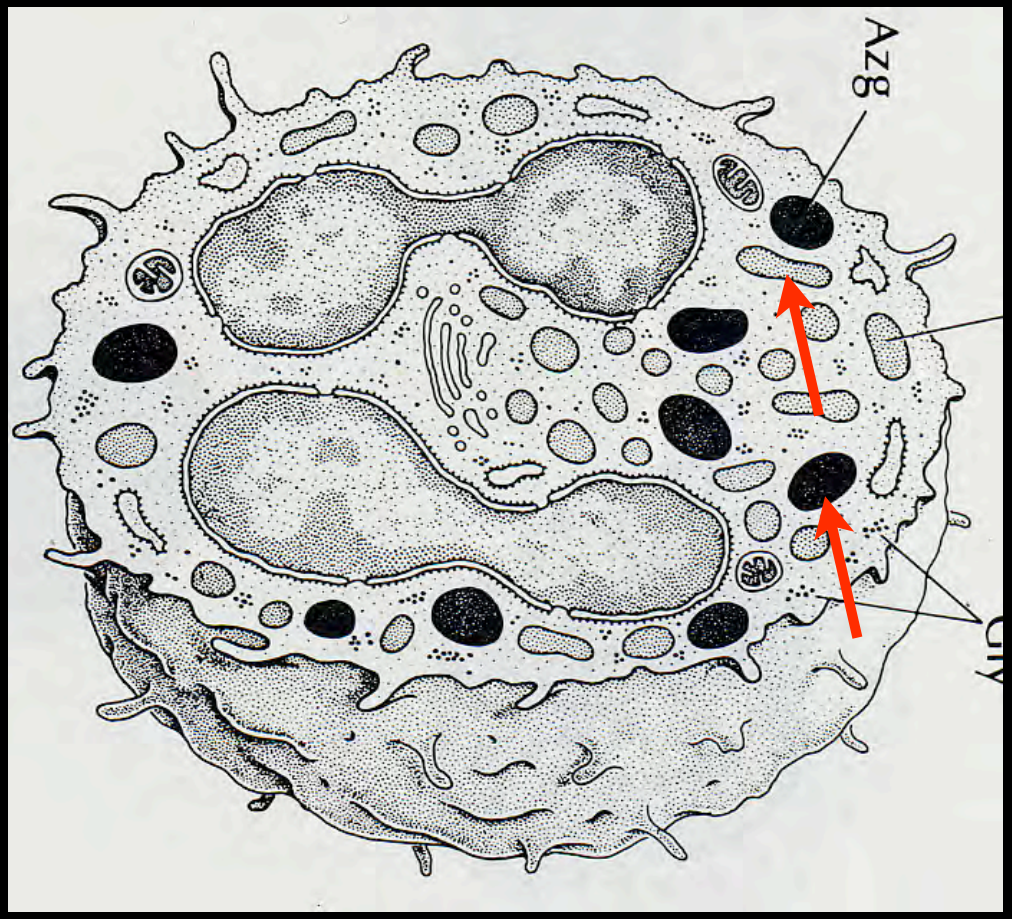
- Monocytes and macrophages
- Lymphocytes
- Plasma cells and T cells
- Eosinophils
- Fibroblasts
- Mast cells
- Endothelial cells

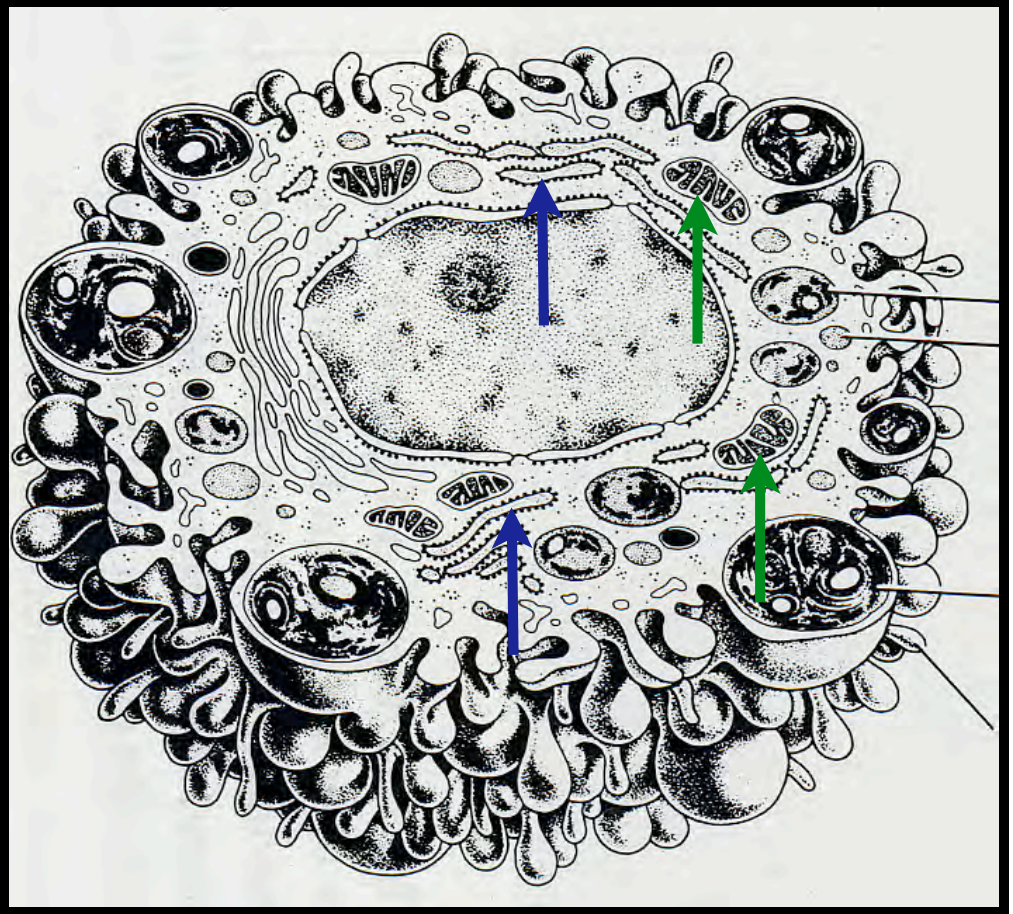
Chronic Interstitial Pneumonia



Chronic Inflammatory Cells



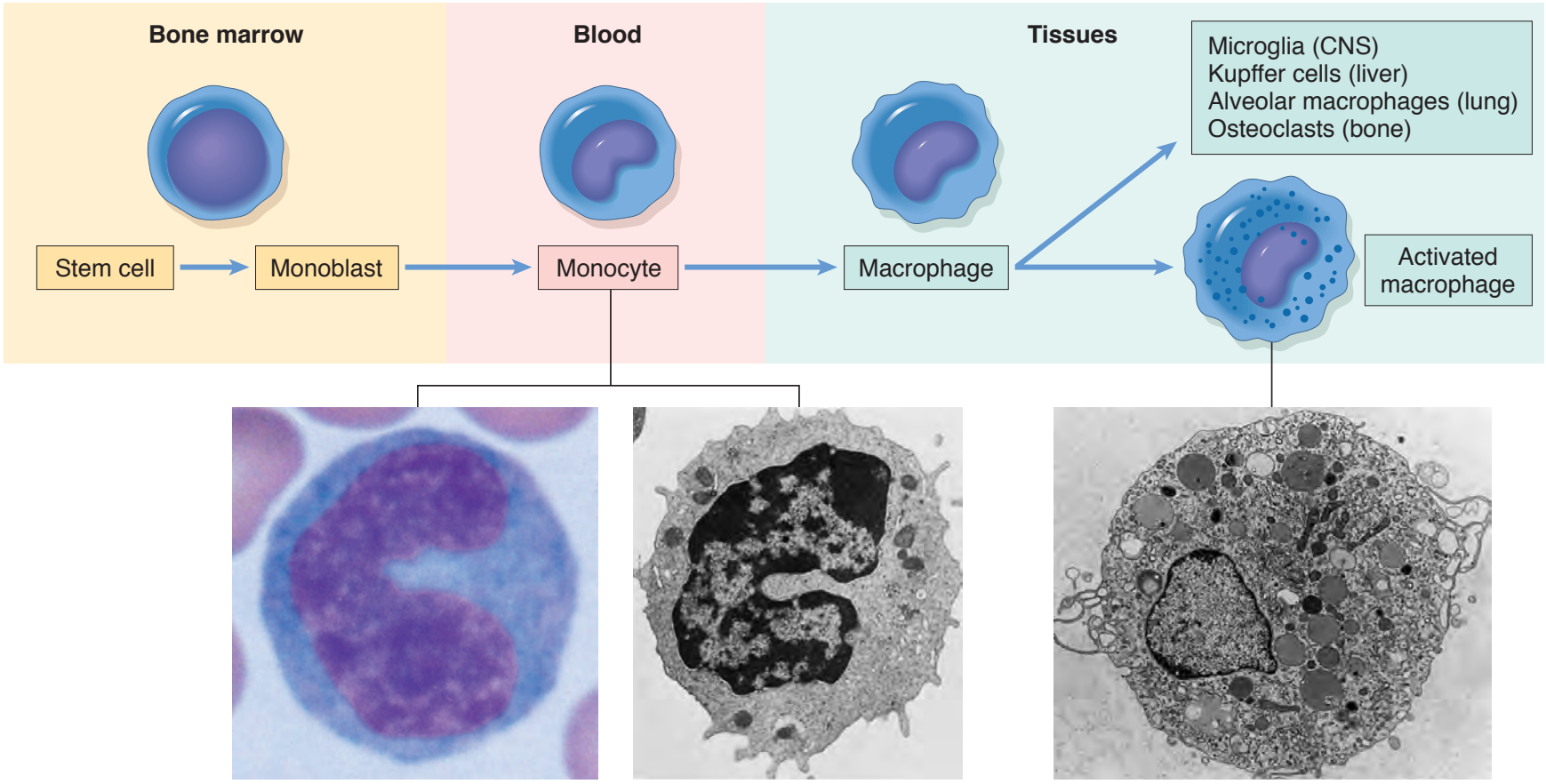




Neutrophil

Macrophage

Maturation of Monocyte to Macrophage



Chronic Inflammation

Macrophages are critical in chronic inflammation

Types of Macrophages

Kupffer cells

Pulmonary alveolar

Histiocytes

Bone marrow

Osteoclasts

Spleen/lymph nodes -APC

Microglia

Langerhans cells

Macrophages of inflammation are mainly derived from circulating monocytes

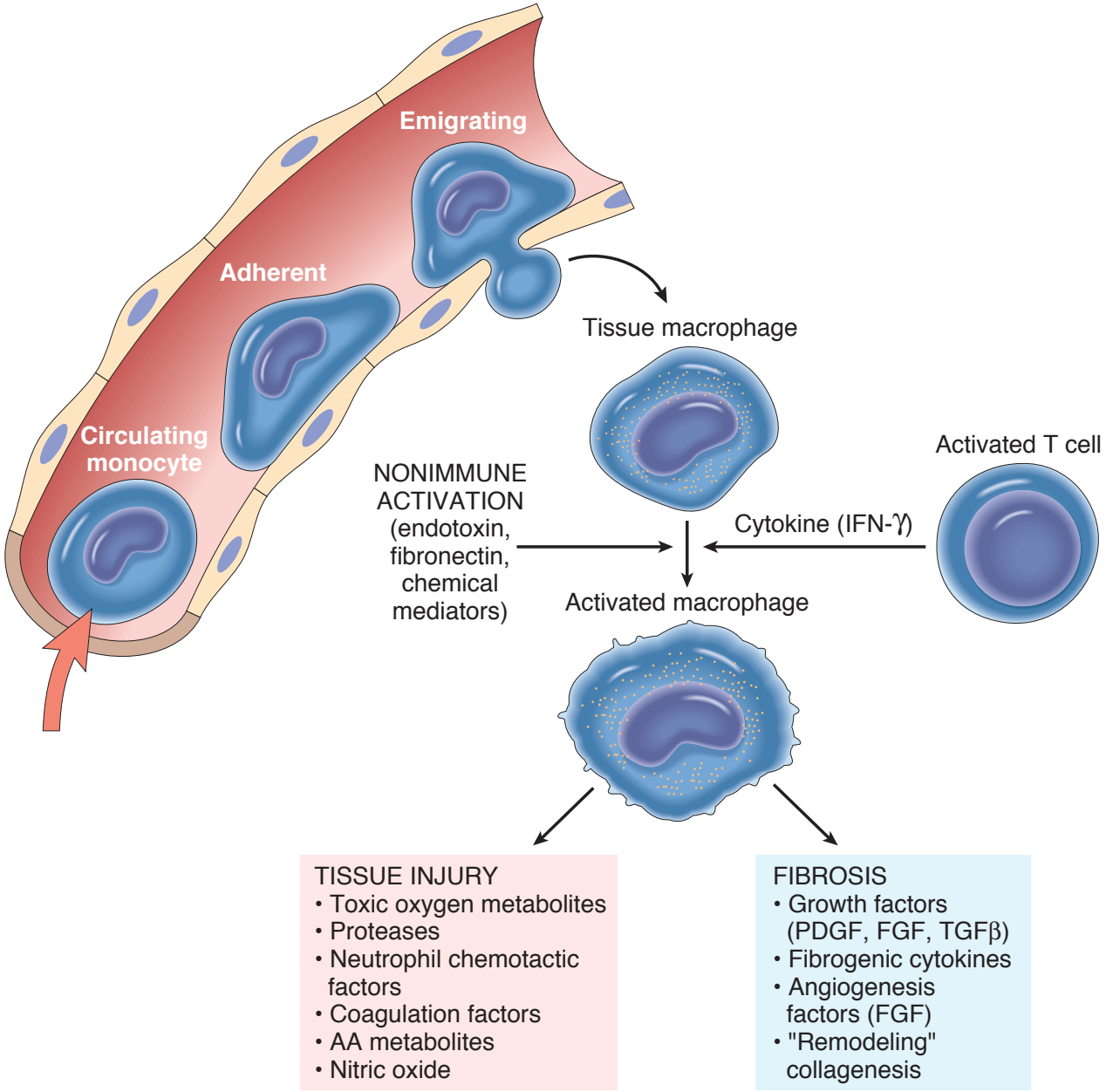
Activated Macrophages

- Size
- Motility
- Metabolic Rate
- Effector Functions:
  - Phagocytosis
  - Secretion
  - Antigen presentation

Signals for Macrophage Activation

- Secreted by injured/distressed cells (e.g. γ-interferon)
- Byproducts of tissue injury, or host response
- Unique microbial molecule(s)

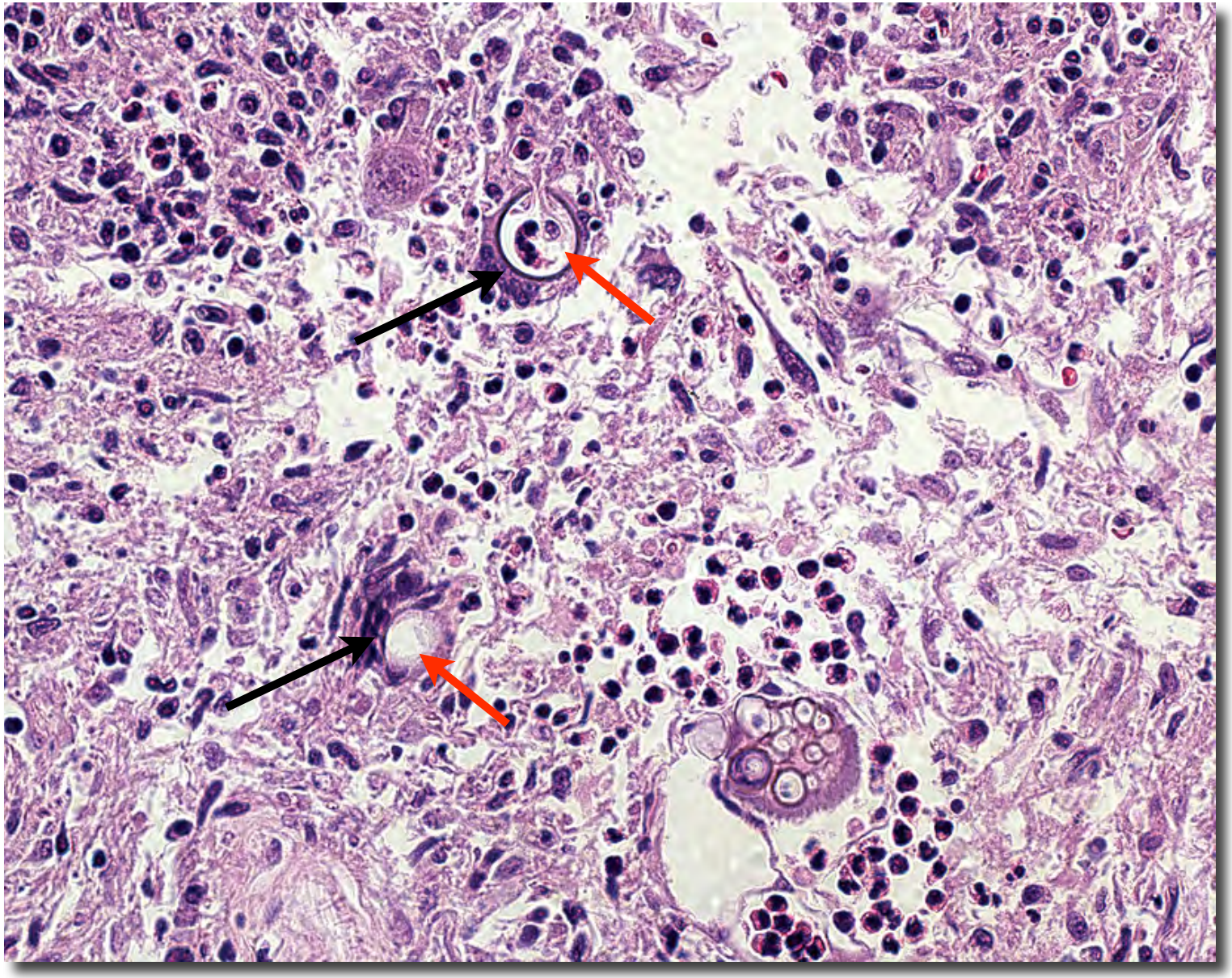
Macrophage Activation



Macrophage Effector Functions:

- Phagocytosis
  - Of pathogens, apoptotic cells, debris, etc.
  - Broad-specificity receptors:
    - Toll-like receptors
    - Scavenger receptors
    - Opsonin receptors!!!!

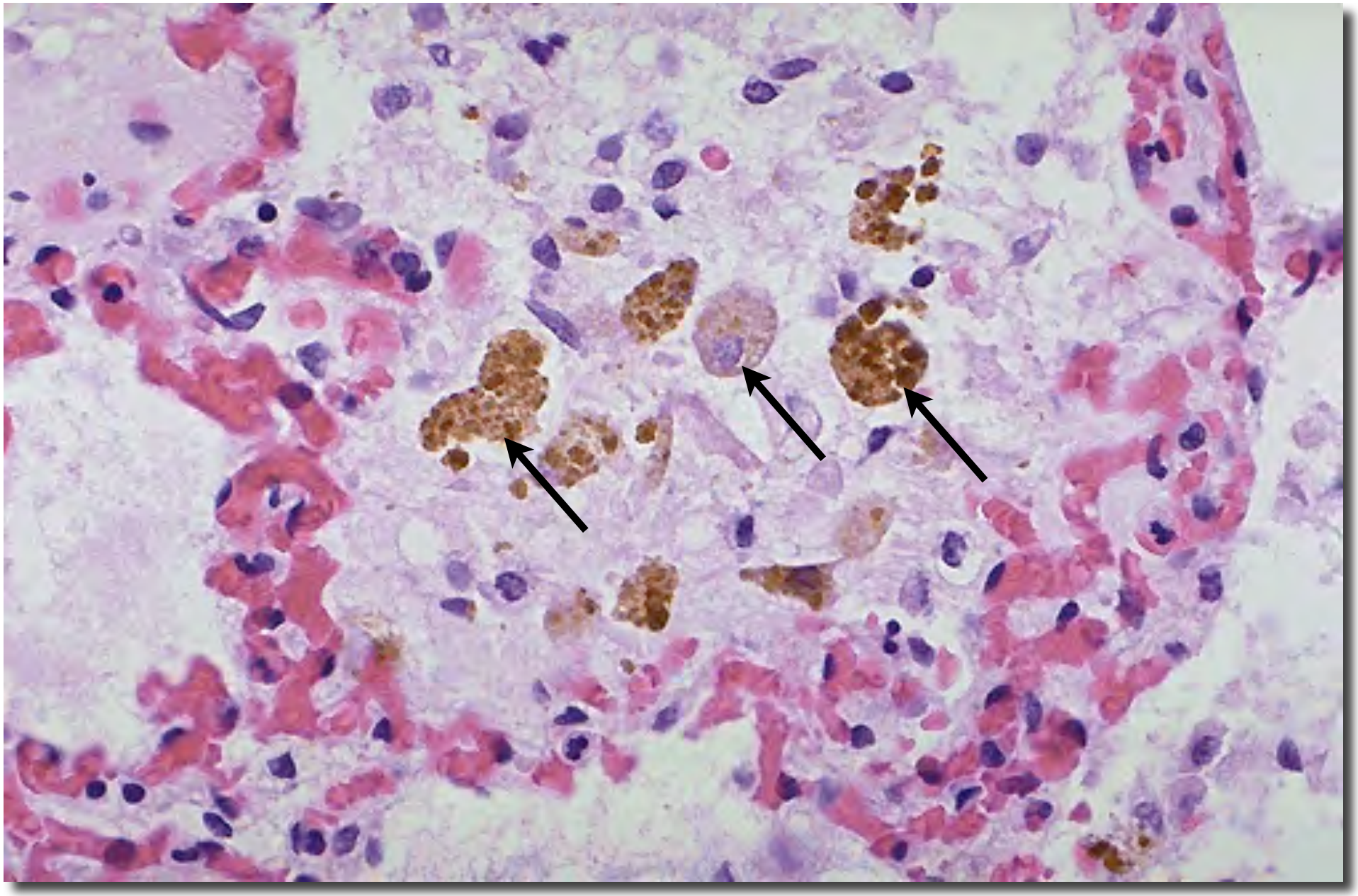
Coccidiodomyocosis Meningitis



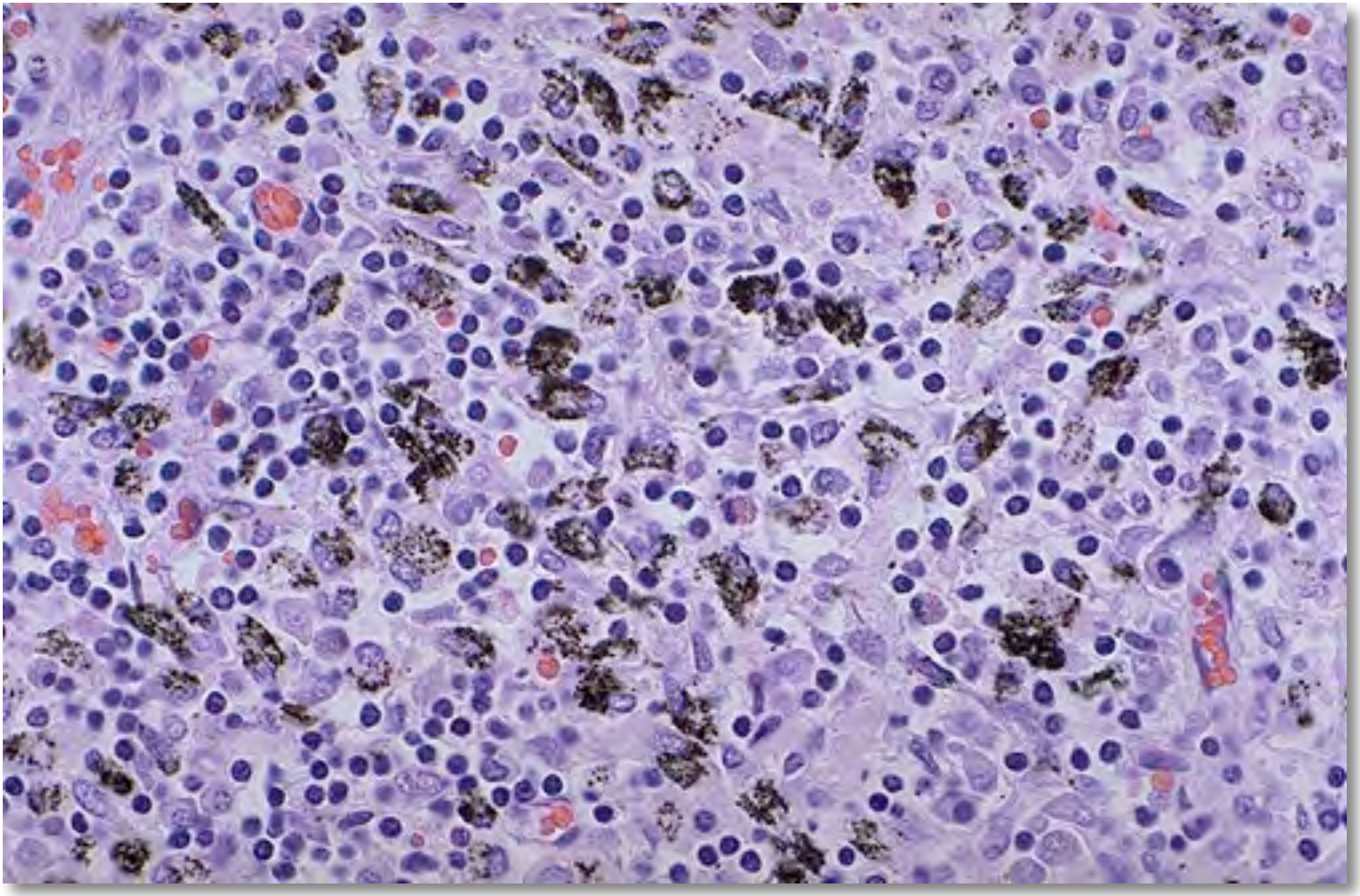
Macrophage Effector Functions:

- Phagocytosis
  - Same as for neutrophils except:
    - Digestion is slower, but can continue longer
    - Indigestible material can be sequestered

Alveolar Sac: Hemosiderin-laden Macrophages

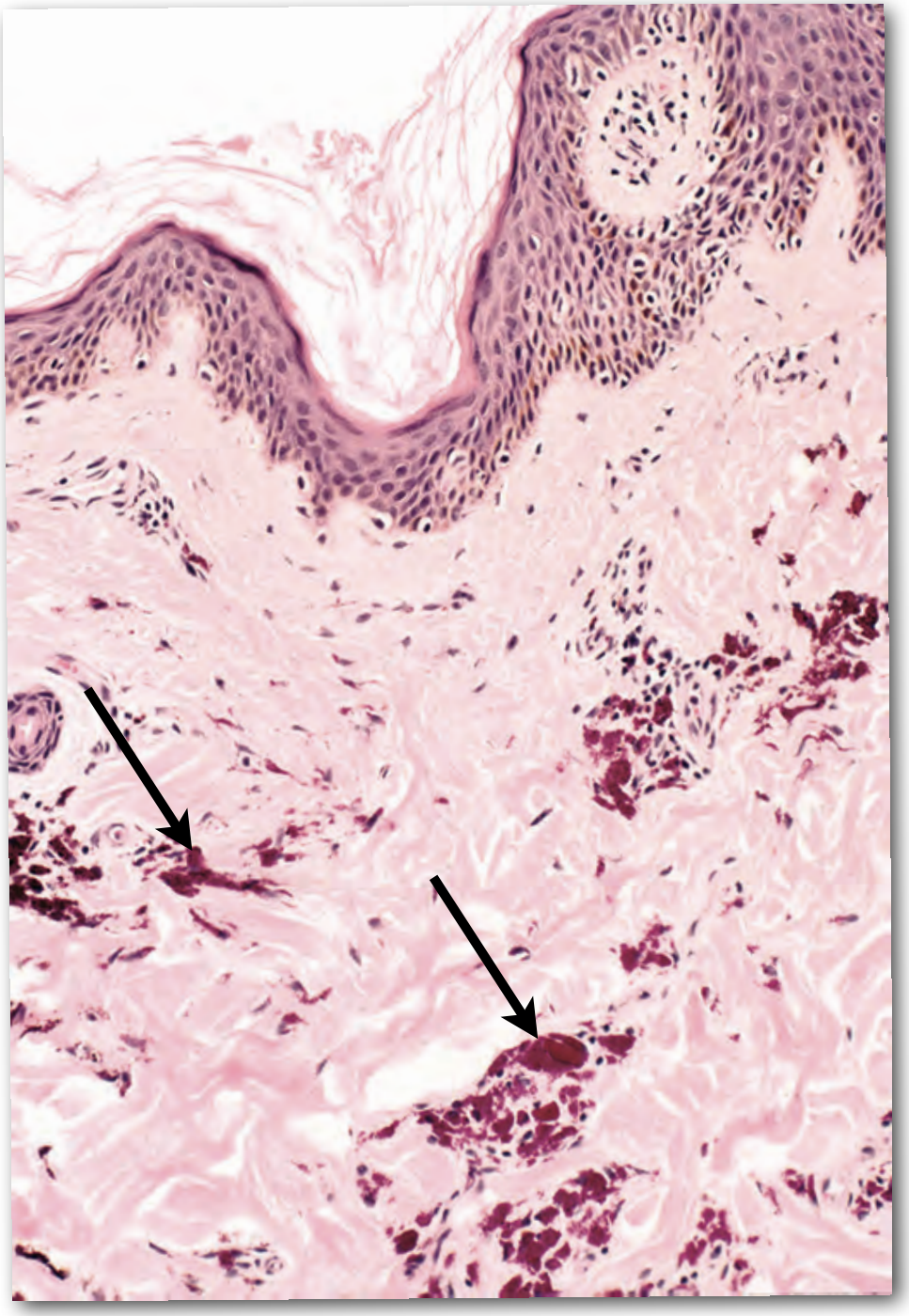


Lymph Node: Anthracosis




GRATEFUL DEAD

Tattoo Pigment

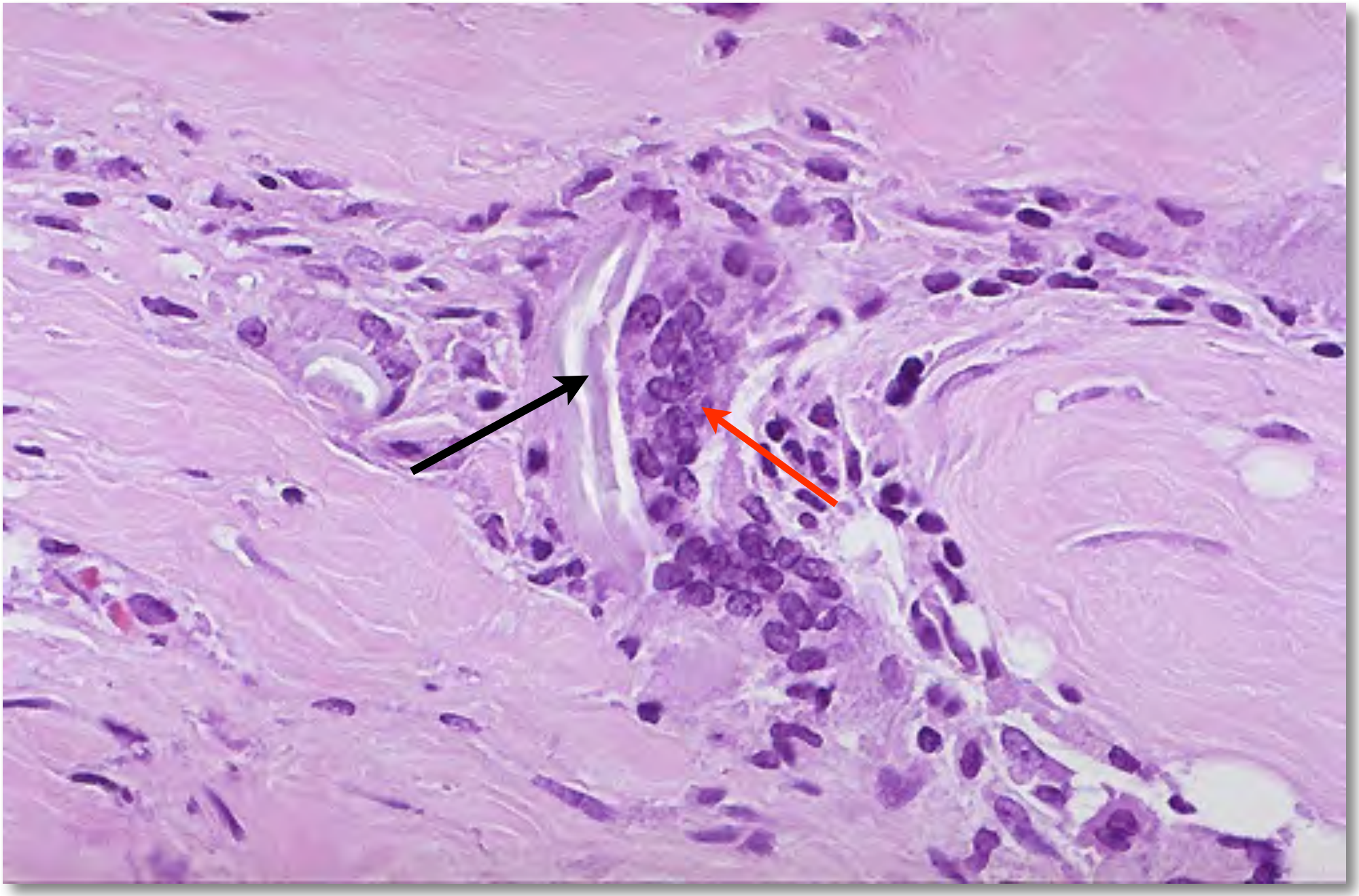



PINK FLOYD

Macrophage Effector Functions:

- Phagocytosis
  - Same as for neutrophils except:
    - Digestion is slower, but can continue longer
    - Indigestible material can be sequestered
    - Formation of multinucleated-giant cells and and epithelioid cells

Foreign-Body Giant Cell Reaction: Suture



Foreign-Body Giant Cell Reaction: Vegetable Material

Macrophage Effector Functions:

- Phagocytosis
- Secretion
  - Antimicrobial enzymes
  - Proteases, other enzymes
  - Reactive oxygen species, nitric oxide, hydrogen peroxide
  - Complement & coagulation proteins

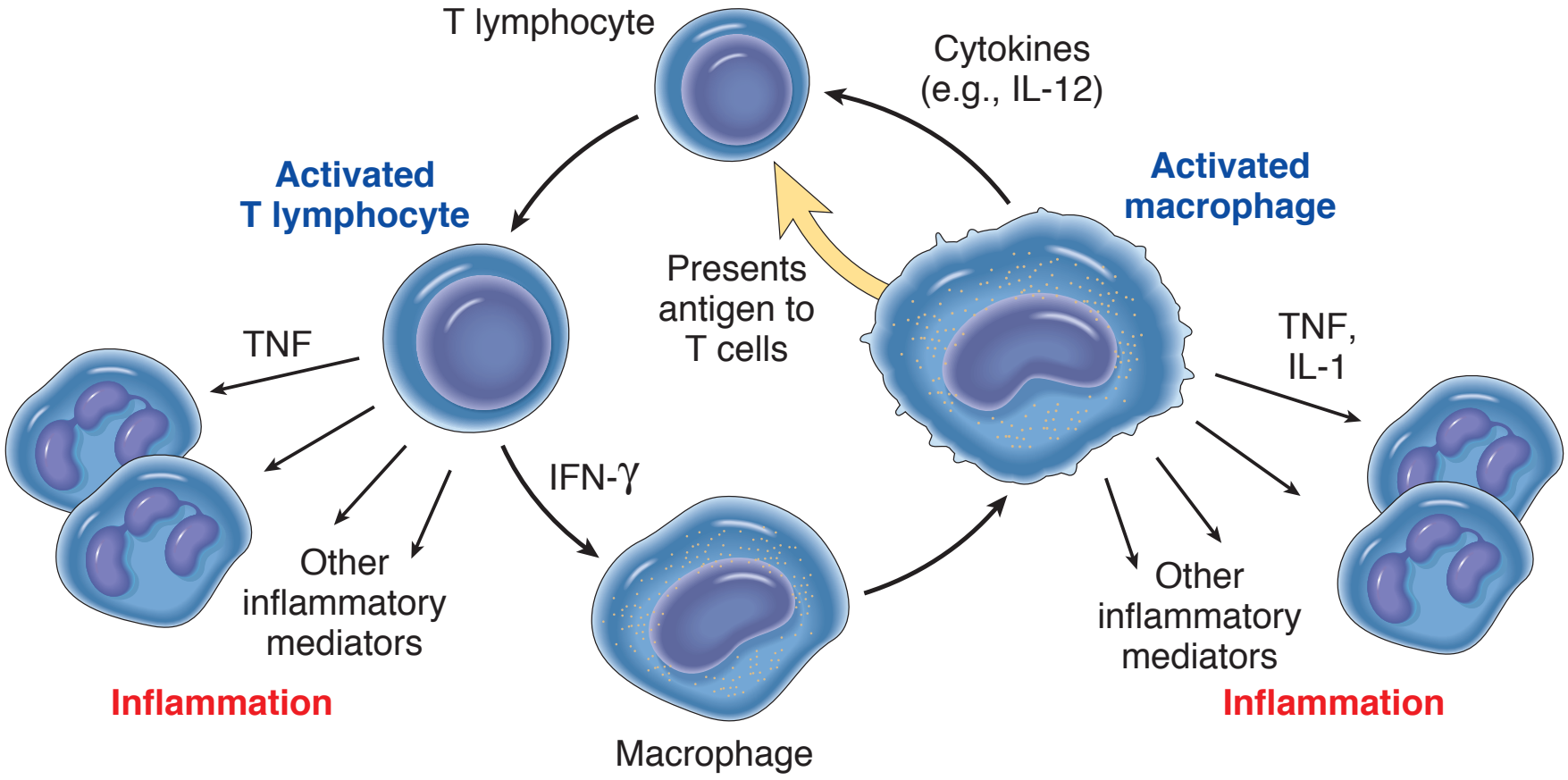
Macrophage Effector Functions:

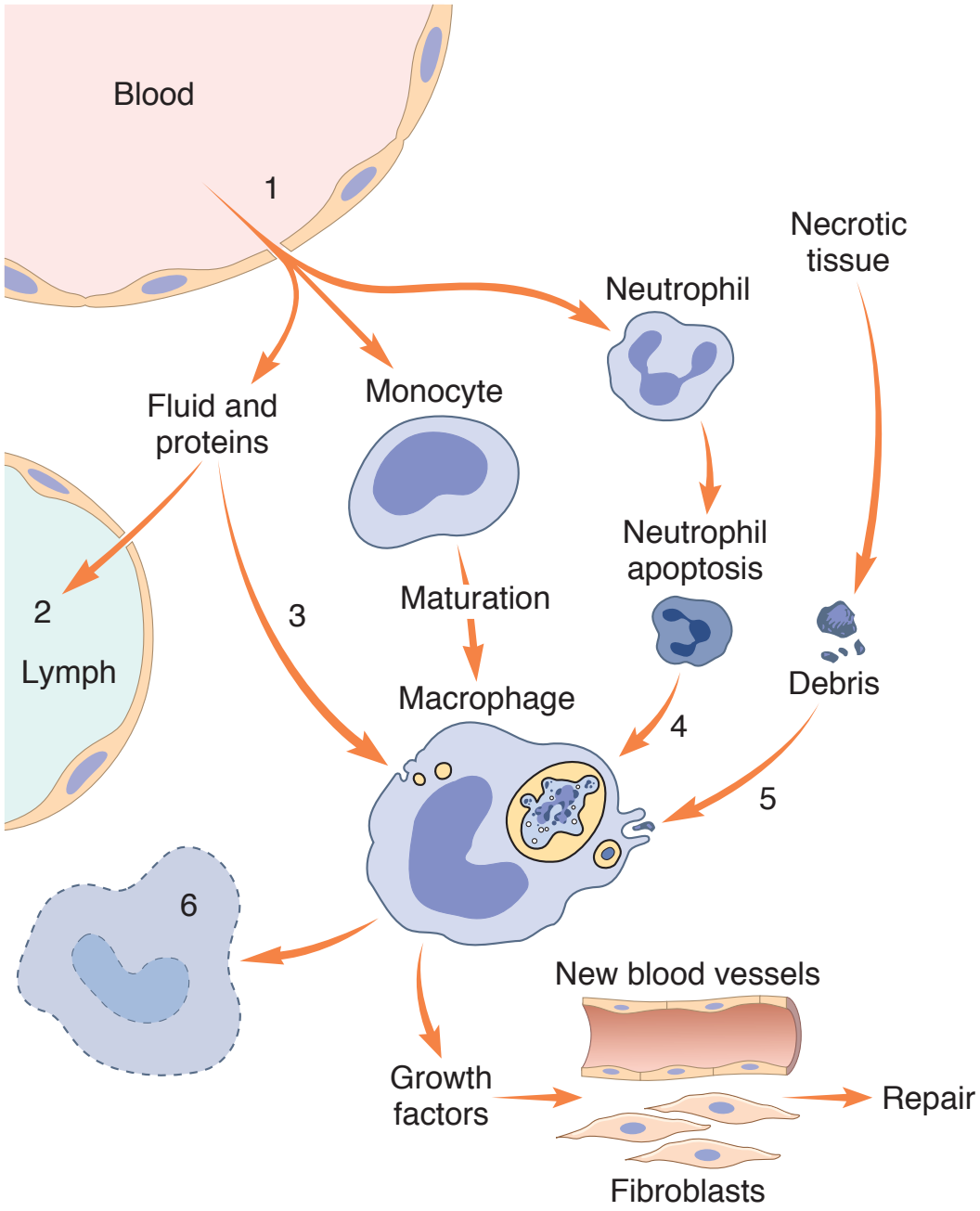
- Secretion
  - Chemokines (e.g. lymphocyte attractants)
  - Cytokines
    - Interleukin-1 & -6 resulting in fever
    - Release GM-CSF leads to increased BM neutrophil production and release and prevents apoptosis of neutrophils
    - Interleukin-12 attracts lymphocytes and controls lymphocyte differentiation
  - Other inflammatory mediators (e.g. prostaglandins)

Macrophage Effector Functions:

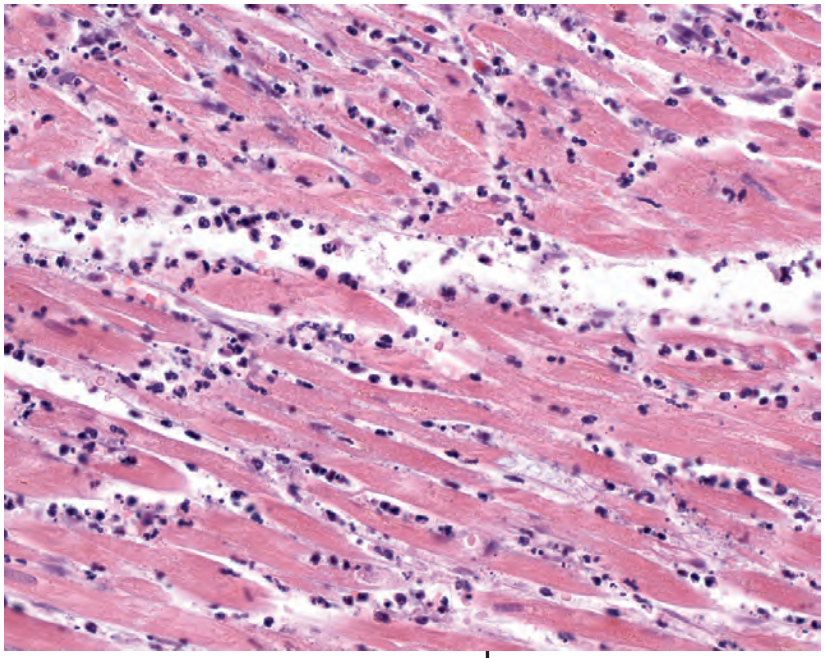
- Phagocytosis
- Secretion
- Antigen presentation!!!
  - Macrophage-lymphcyte collaboration

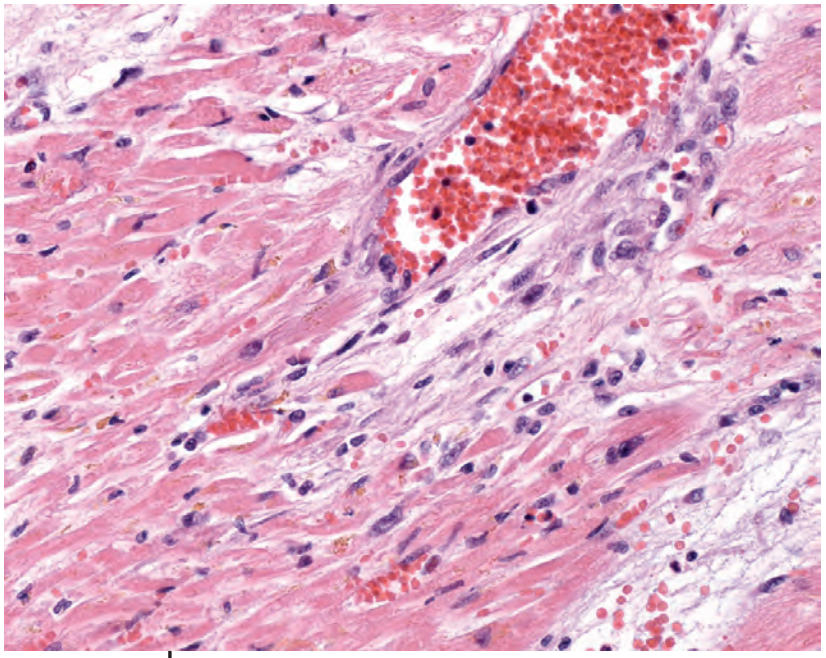
Macrophage-Lymphocyte Interactions in Chronic Inflammation

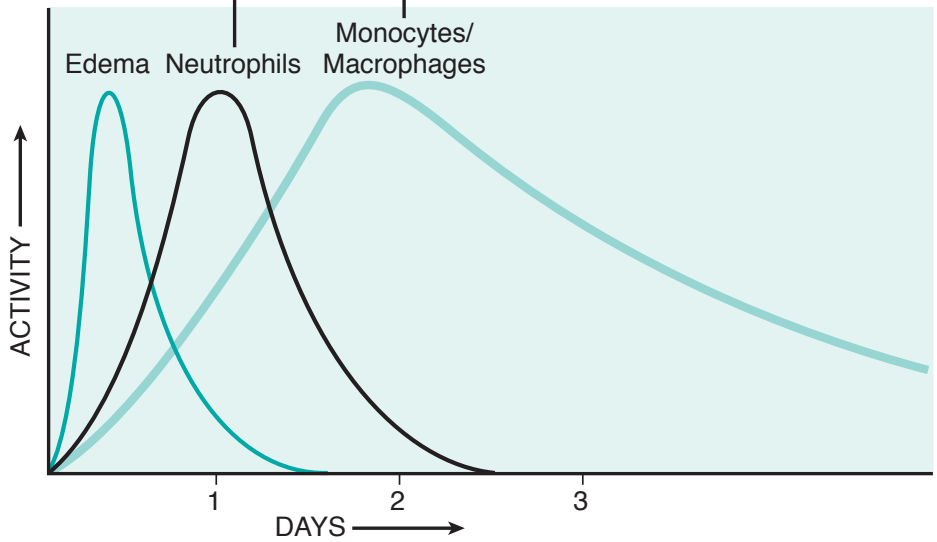



Blood
1
Necrotic tissue
Neutrophil
Fluid and proteins
Monocyte
Neutrophil apoptosis
2
Lymph
3
Maturation
Debris
Macrophage
4
5
6
New blood vessels
Growth factors
Repair
Fibroblasts

Acute Myocardial Infarct







Chronic Granulomatous Inflammation

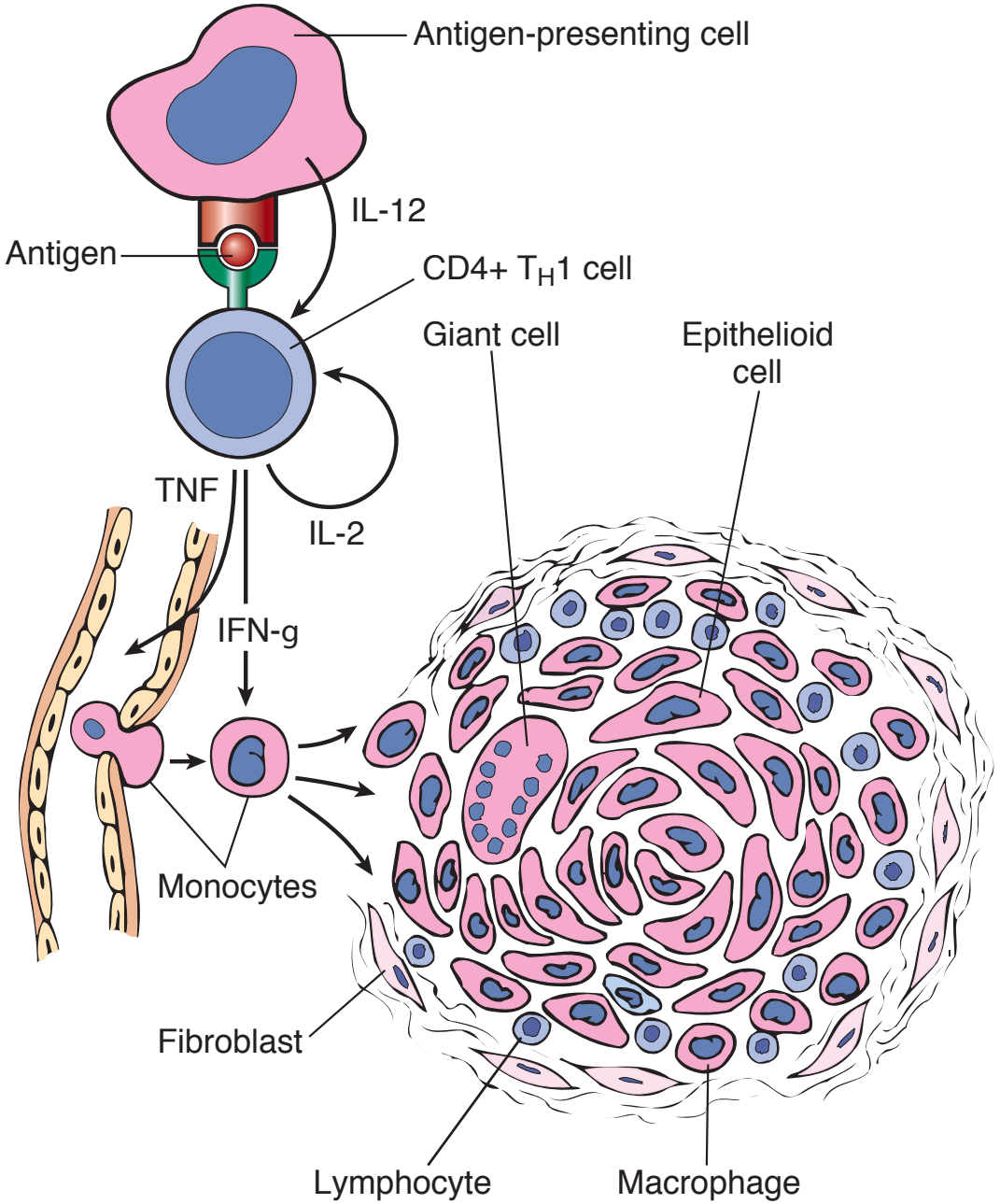
Definition

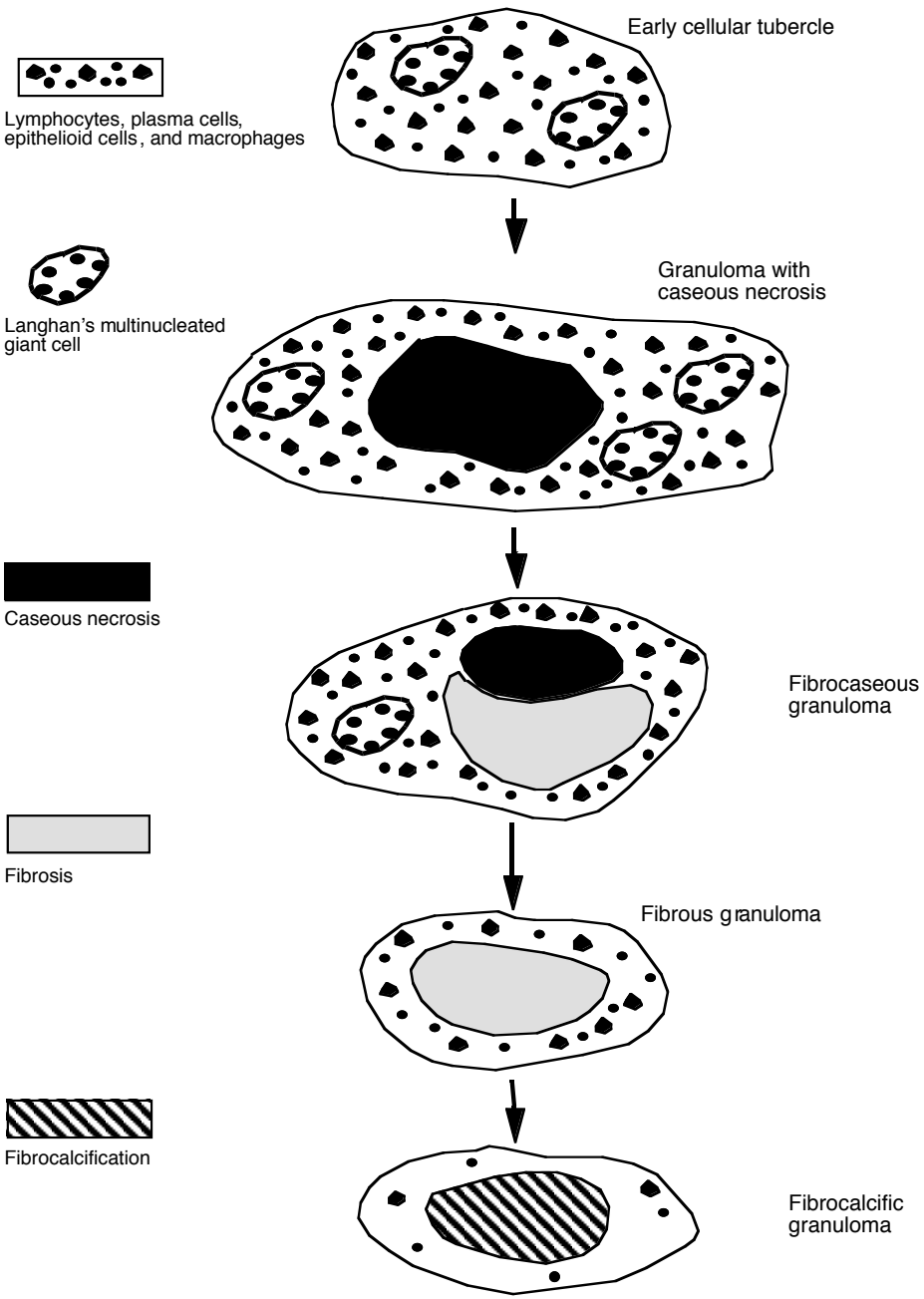
- Granulomas - collections of modified macrophages (epithelioid cells), usually surrounded by a rim of lymphocytes with scattered fibroblasts

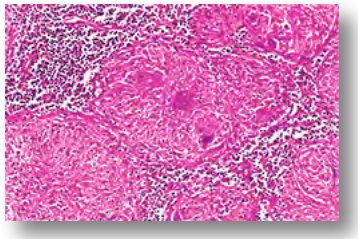
Granulomatous Diseases

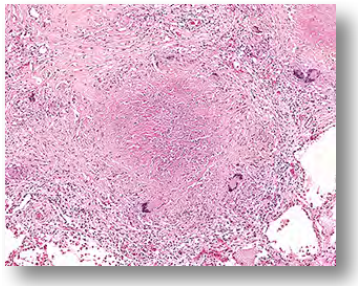
Tuberculosis	Silicosis
Leprosy	Beryllium disease
Syphilis	Sarcoidosis
Parasitic and fungal infections	Foreign body

Granuloma Formation

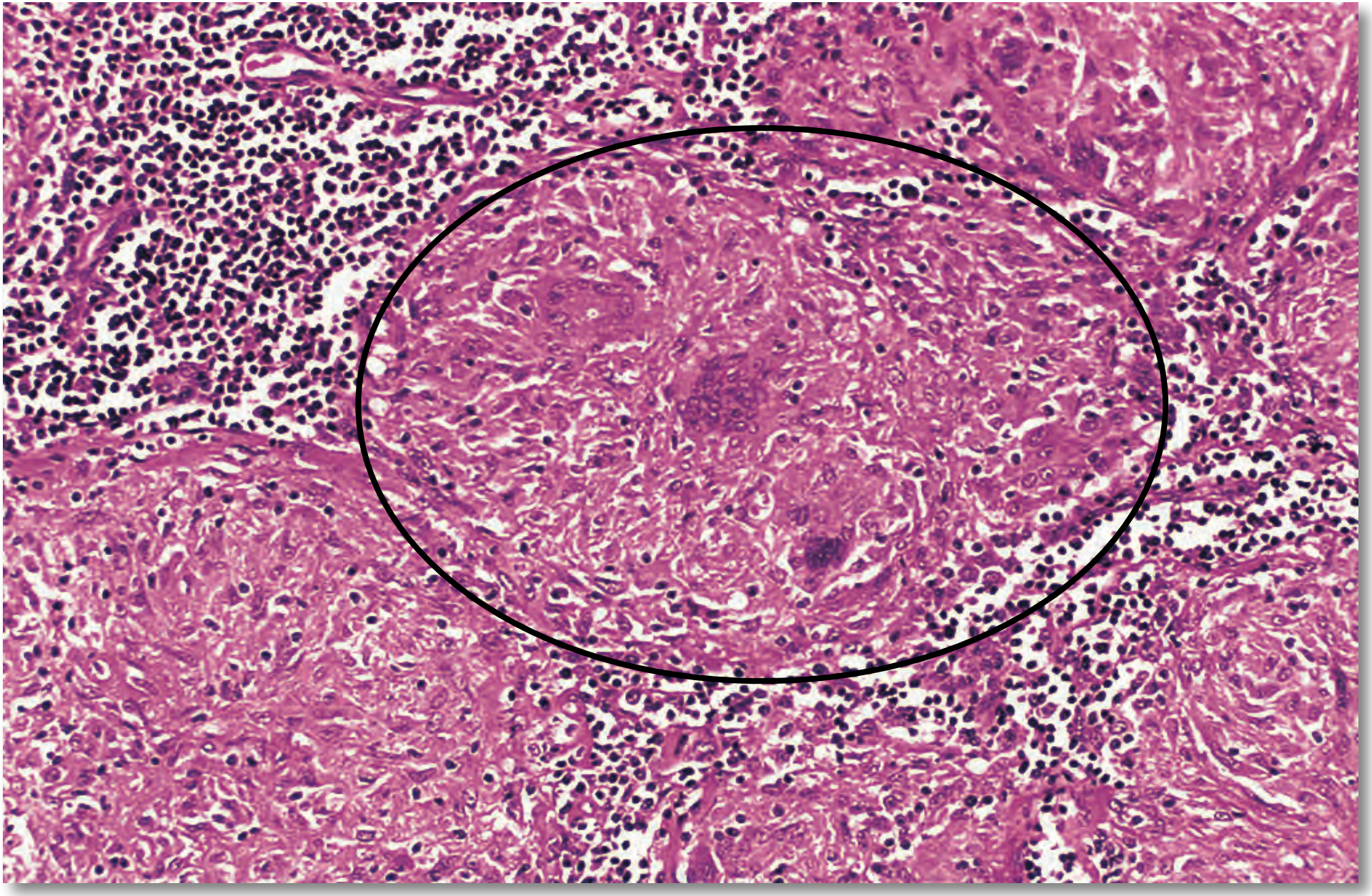



Early cellular tubercle
Lymphocytes, plasma cells, epithelioid cells, and macrophages
Granuloma with caseous necrosis
Langhan's multinucleated giant cell
Caseous necrosis
Fibrocaseous granuloma
Fibrosis
Fibrous granuloma
Fibrocalcification
Fibrocalcific granuloma



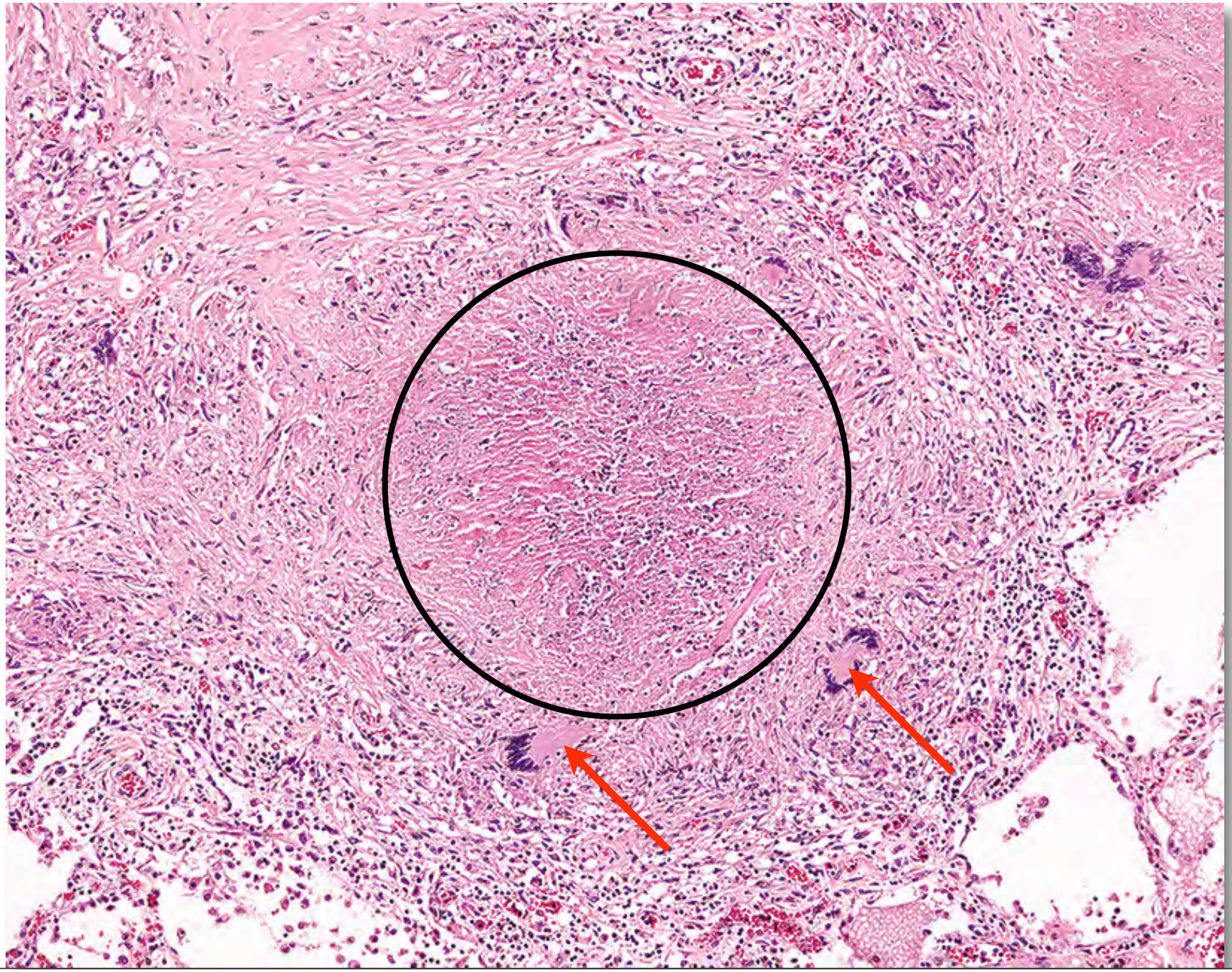


Non-Caseating Granuloma



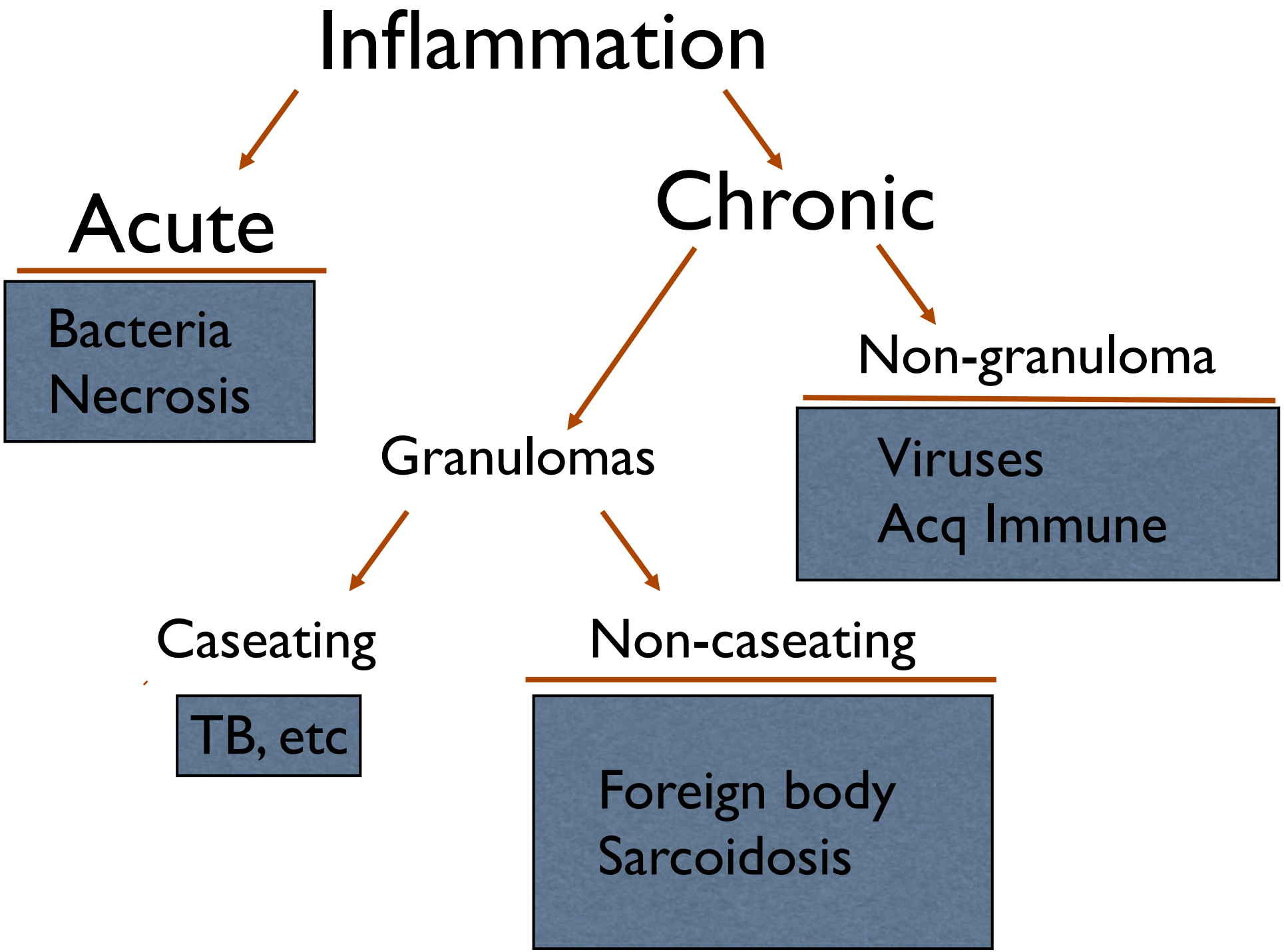
Caseating Granulomatous Inflammation

Caseating Granuloma



Clinical Correlates

- Macrophages and lymphocytes collaborate
- Macrophages accumulate slowly in inflamed tissues
- Inflammatory infiltrate composed mainly of macrophages and lymphocytes = chronic inflammation
- Cardinal signs and associated clinical features of chronic inflammation - “fever and night sweats” due TNF and IL-1
- Number of monocytes circulating in peripheral blood rarely increases significantly


Inflammation
Acute
Bacteria
Necrosis
Chronic
Granulomas
Caseating
TB, etc
Non-caseating
Foreign body
Sarcoidosis
Non-granuloma
Viruses
Acq Immune