

# GRANULOMATOUS INFLAMMATION

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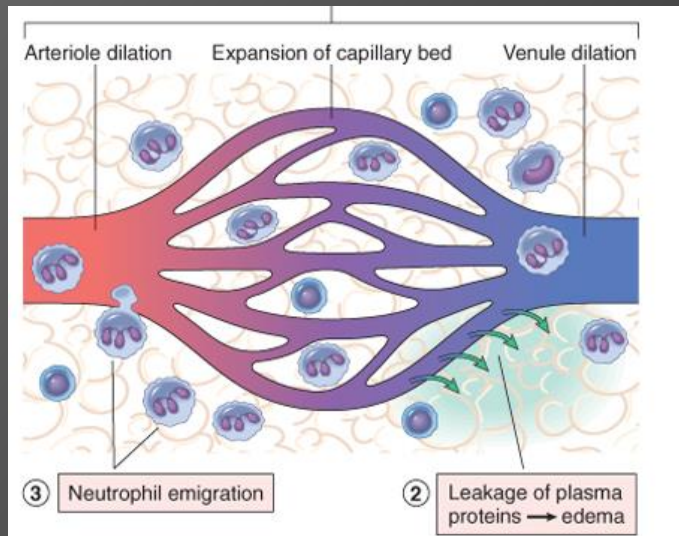
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# Inflammation

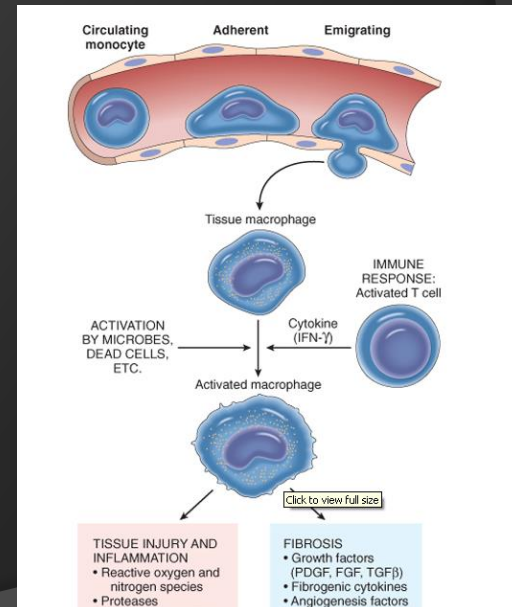
## Acute inflammation

Neutrophils



## Chronic inflammation

Macrophage  
Lymphocytes  
Plasma cells



# OBJECTIVES AND KEY PRINCIPLES TO BE TAUGHT:

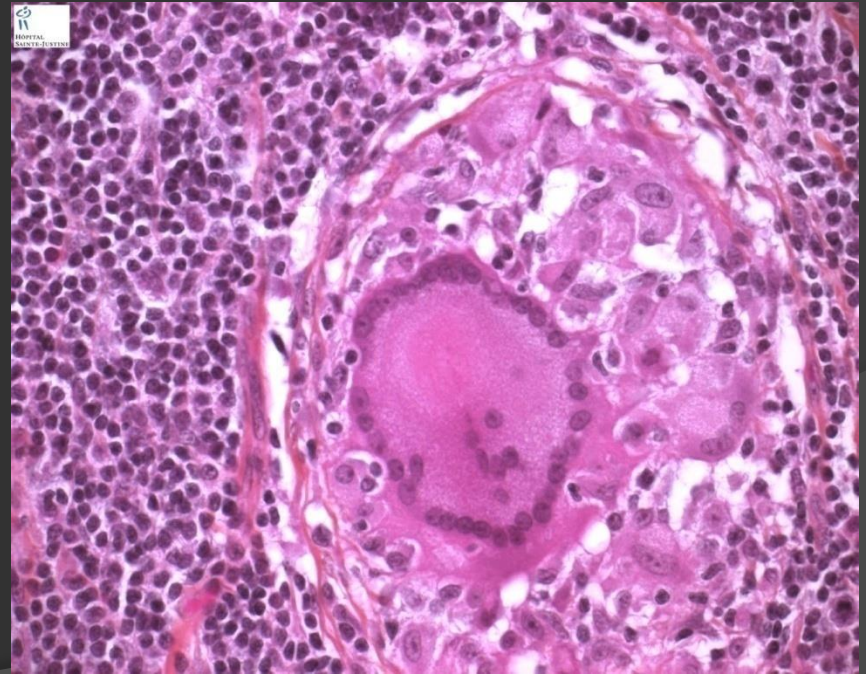
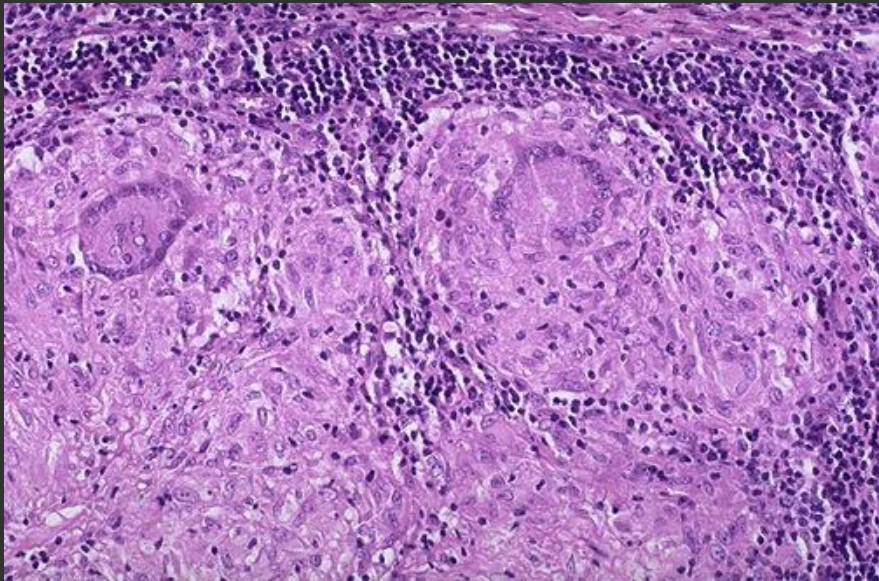
Upon completion of this lecture, the student should:

- Define Granulomatous inflammation.
- Recognize the morphology of granulomas (tubercles) and list the cells found in granuloma along with their appearance.
- Identify the two types of granulomas, which differ in their pathogenesis.
  - Foreign body granulomas
  - Immune granulomas
- List the common causes of Granulomatous Inflammation.
- Understands the pathogenesis of granuloma formation.

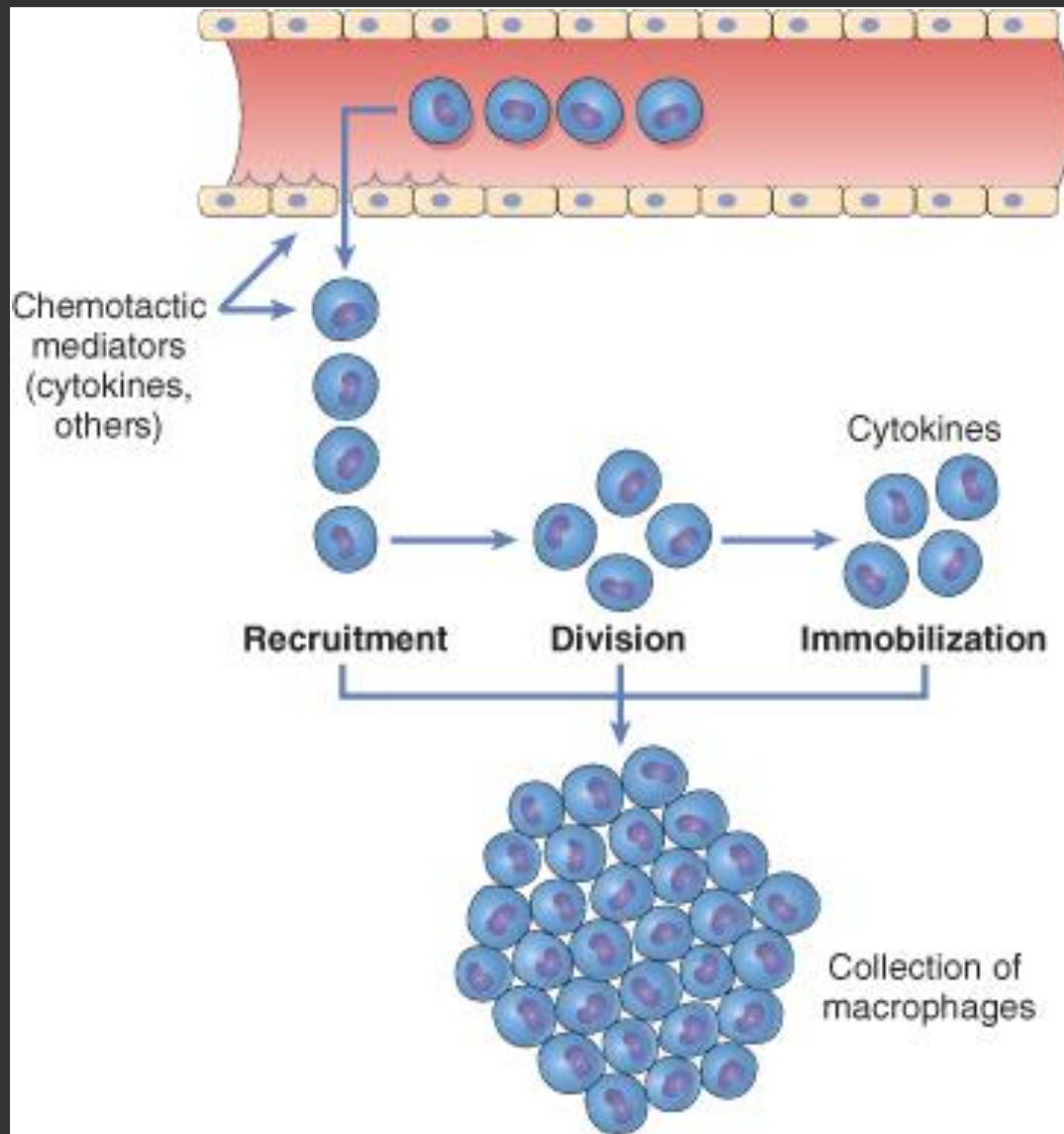
# GRANULOMATOUS INFLAMMATION

A form of chronic inflammation characterized by the formation of granulomas.

- Granuloma = Nodular collection of epithelioid macrophages surrounded by a rim of lymphocytes
- Epithelioid macrophages: squamous cell-like appearance







# Why is it important?

- ⦿ Granulomas are encountered in certain **specific** pathologic states.
- ⦿ Recognition of the granulomatous pattern is important because of the **limited number of conditions** (some life-threatening) that cause it

# Granulomatous Inflammation pathogenesis

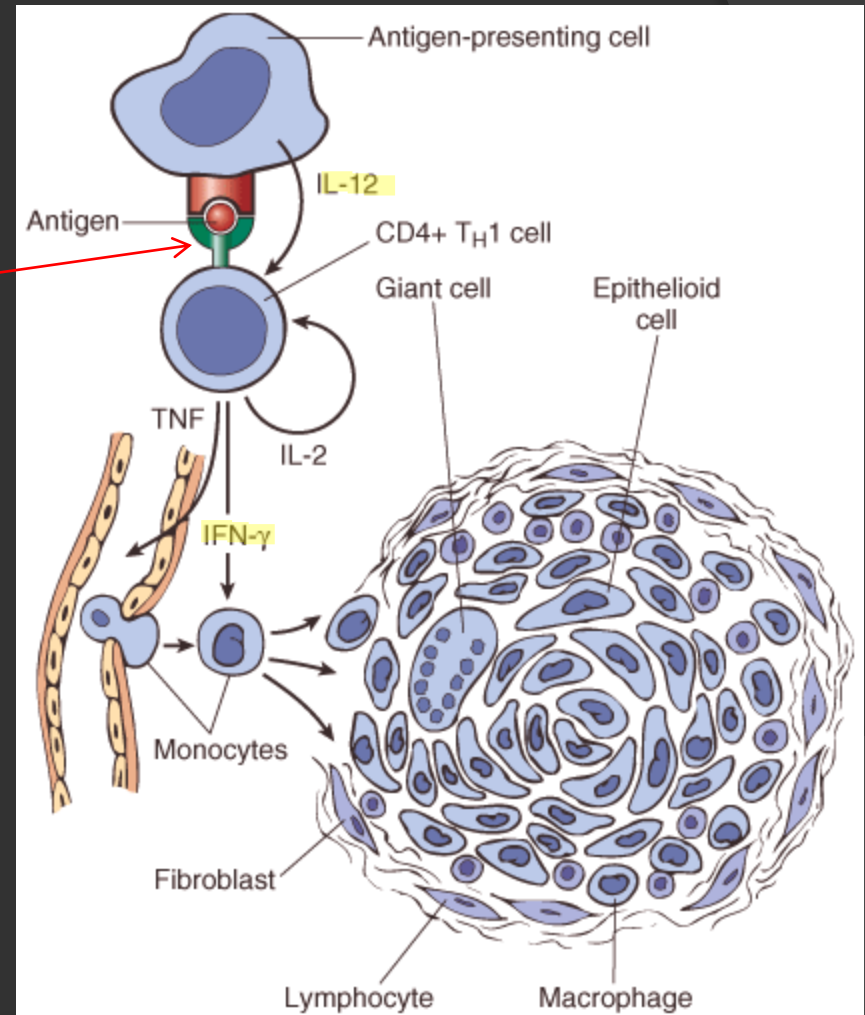
- Neutrophils ordinarily remove agents that incite an acute inflammatory response. However, there are circumstances in which reactive neutrophils **cannot** digest the substances that provoke acute inflammation.



# Granulomatous Inflammation mechanism

- What is the initiating event in granuloma formation?
- deposition of a indigestible antigenic material

*IFN- $\gamma$*  released by the CD4+ T cells of the  $T_H1$  subset is crucial in activating macrophages.



Type IV hypersensitivity

## Epithelioid cell granulomas

1. When macrophages have successfully phagocytosed the injurious agent but it survives inside them.
2. When an active T lymphocyte-mediated cellular immune response occurs. Lymphokines produced by activated T lymphocytes inhibit migration of macrophages and cause them to aggregate in the area of injury and form granulomas.

# Pathogenesis

There are two types of granulomas

## Foreign body granuloma

are incited by relatively inert foreign bodies. Typically, foreign body granulomas form when material such suture are large enough to preclude phagocytosis by a single macrophage

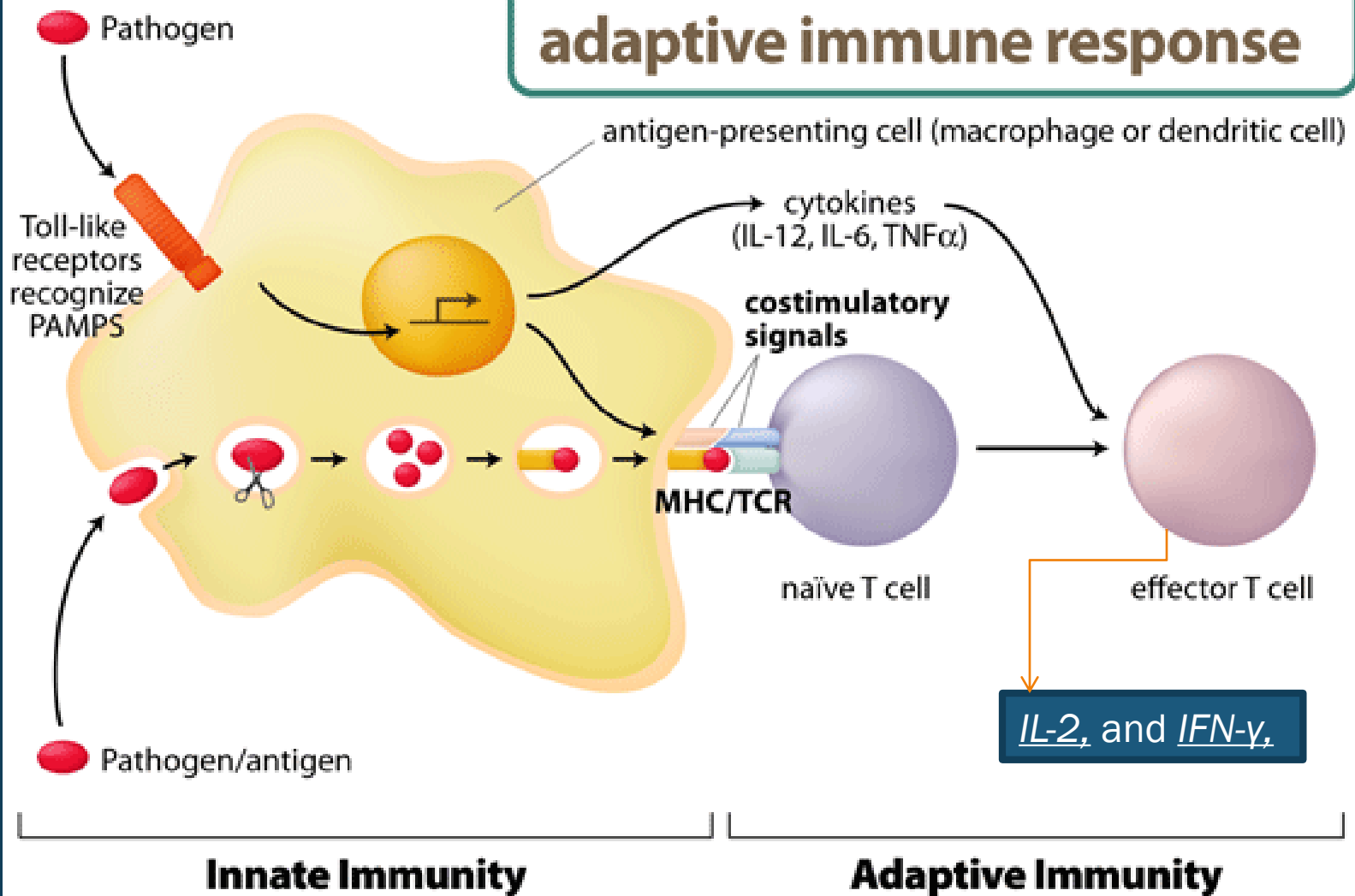
These material **do not incite any specific inflammatory immune response.**

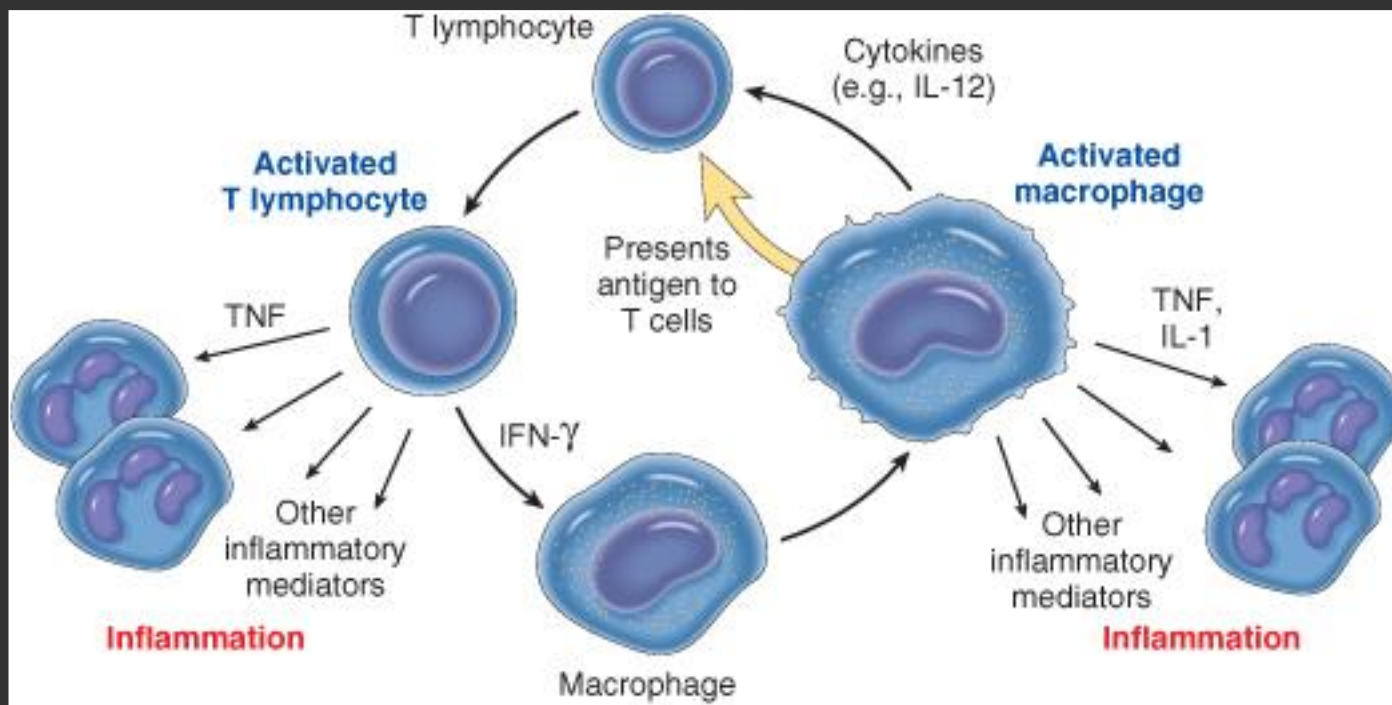
The foreign material can usually be identified in the center of the granuloma, by polarized light (appears refractile).

## Immune granuloma

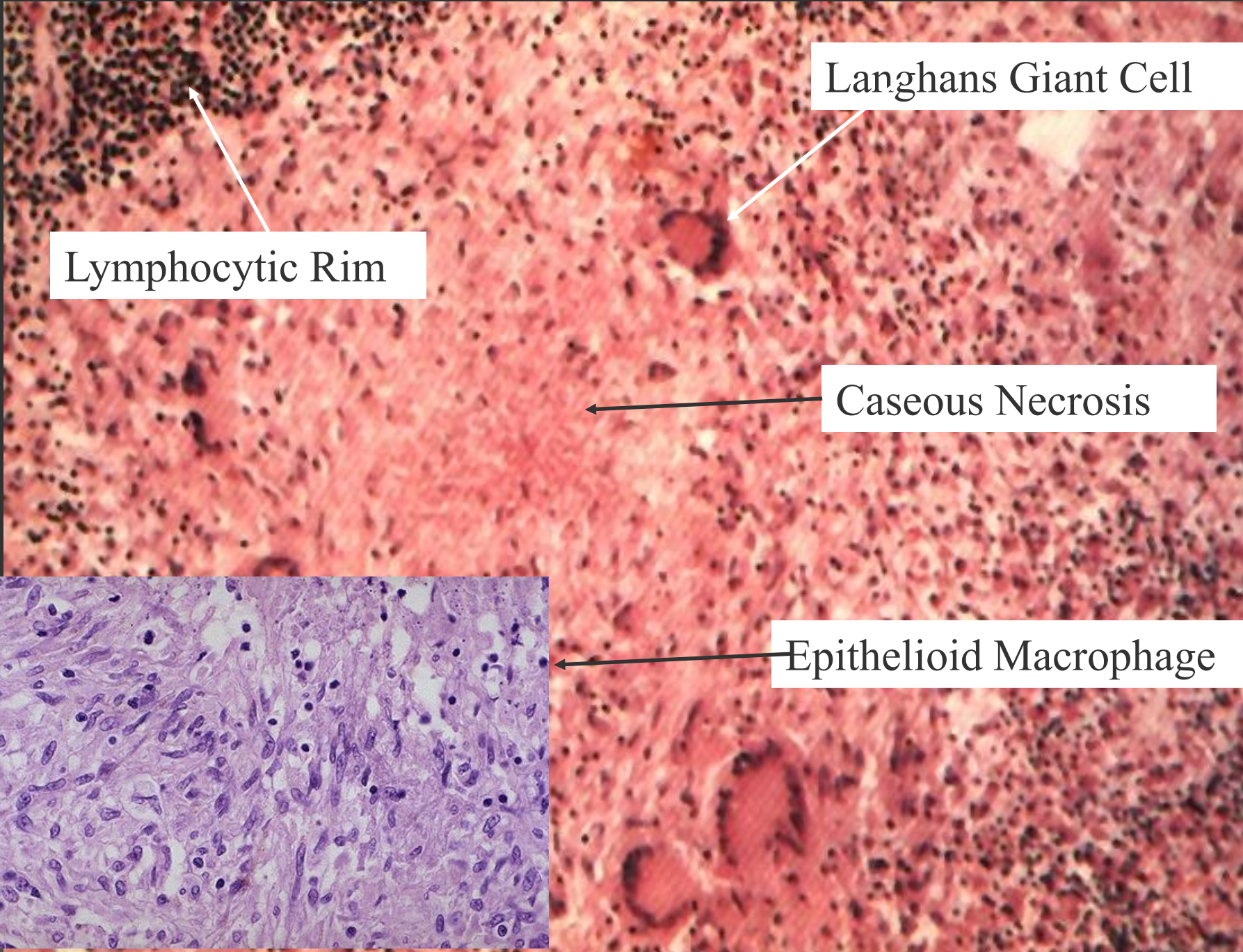
are caused by insoluble particles, typically microbes, that are capable of inducing a **cell-mediated immune response.**

# Innate immunity is critical to adaptive immune response









Langhans Giant Cell

Lymphocytic Rim

Caseous Necrosis

Epithelioid Macrophage





Lymphocytes

Epithelioid histiocytes

Necrosis

Multinucleated cell



# Granulomatous Inflammation

## Causes

### Non-immune granuloma

- **Foreign body**
  - Suture
  - Graft material
  - talc (associated with intravenous drug abuse)

### Immune granuloma:

- **Bacteria**
  - Tuberculosis
  - Leprosy
  - Actinomycosis
  - Cat-scratch disease
- **Parasites**
  - Schistosomiasis
  - Leishmaniasis
- **Fungi**
  - Histoplasmosis
  - Blastomycosis
- **Metal/Dust**
  - Berylliosis

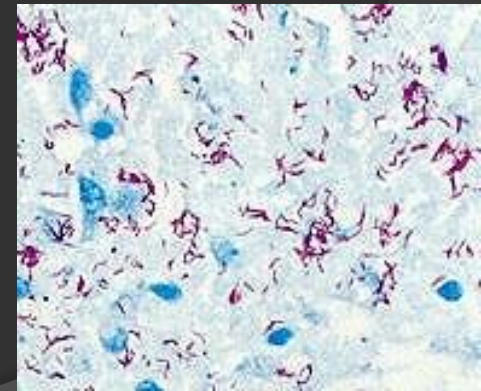
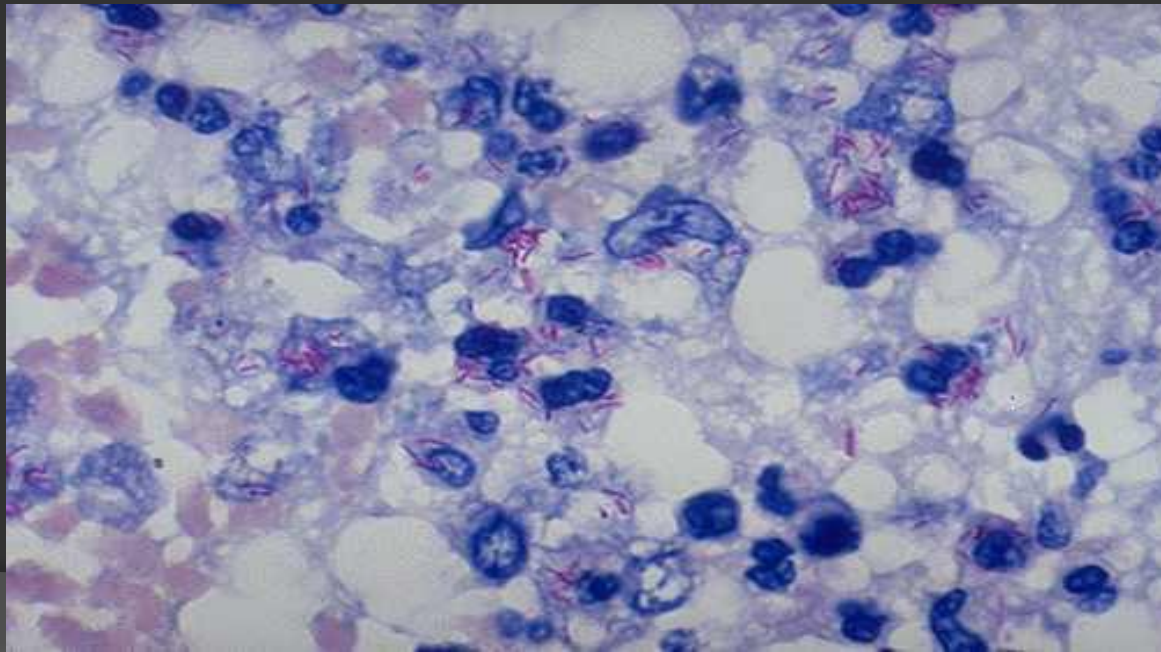
**unknown**

Sarcoidosis  
Crohn's disease

# Tuberculosis

## *Mycobacterium tuberculosis*

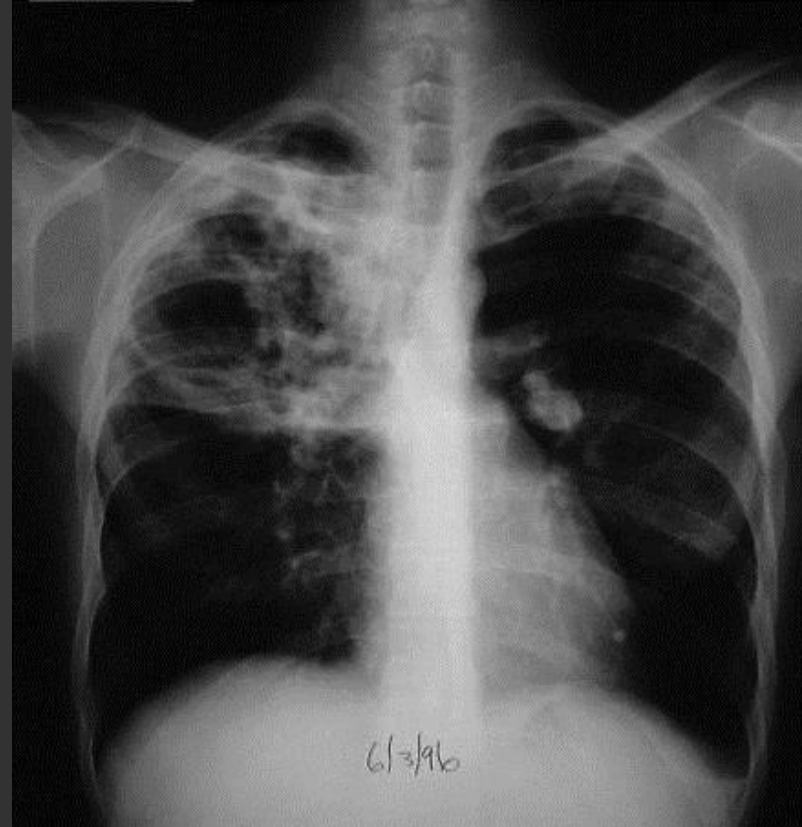
- Mycobacteria – ‘fungus like..
- slender rods
- acid fast bacilli [AFB] (i.e., they have a high content of complex lipids that readily bind the Ziehl-Neelsen [carbol fuchsin] stain and subsequently resist decolorization).



# Pathogenesis of TB

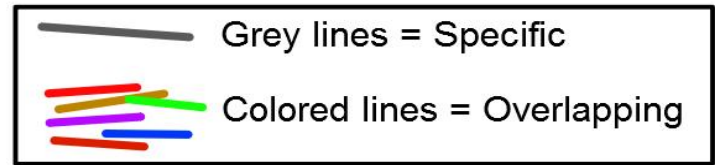
- Cord factor is a glycolipid molecule found in the cell wall of *Mycobacterium tuberculosis* and similar species.
- It protects *M. tuberculosis* from the defenses of the host
- Cord factor presence increases the production of the cytokines interleukin-12 (IL-12), IL-1 $\beta$ , IL-6 and TNF which are all pro-inflammatory cytokines important for granuloma formation

# Tuberculosis





# Symptoms of Tuberculosis



**(Established)  
pulmonary tuberculosis**

Poor appetite

**Miliary tuberculosis**

Productive cough

**Return of  
dormant  
tuberculosis**

Night sweats

Cough with  
increasing mucus  
Coughing  
up blood

**Primary  
pulmonary  
tuberculosis**

Weakness

Fever

Structural  
abnormalities

Dry cough

Weight loss

**Extrapulmonary  
tuberculosis**

*Common sites:*

**Tuberculous  
pleuritis**

Meninges

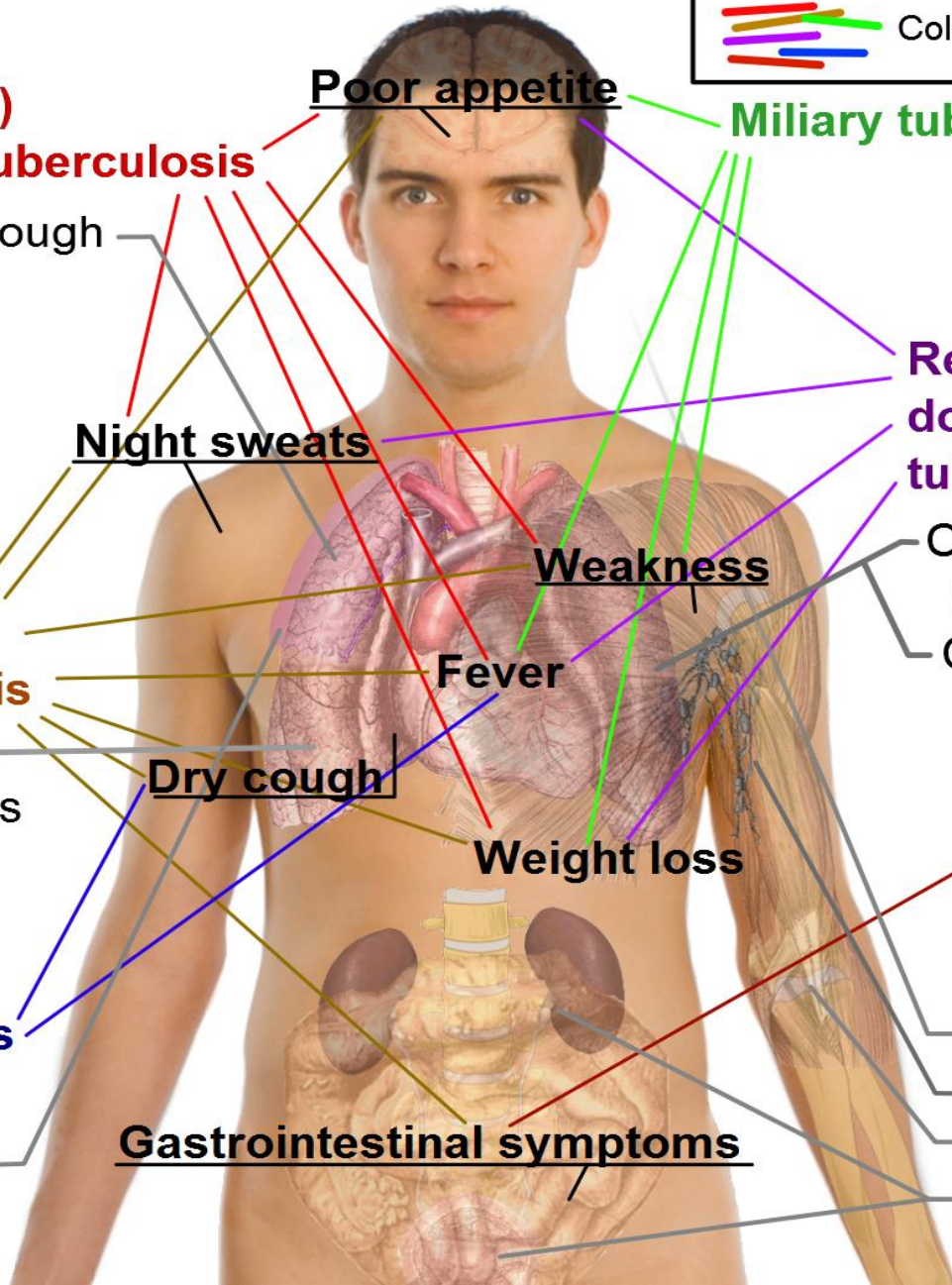
Lymph nodes

Bone and joint sites

Genitourinary tract

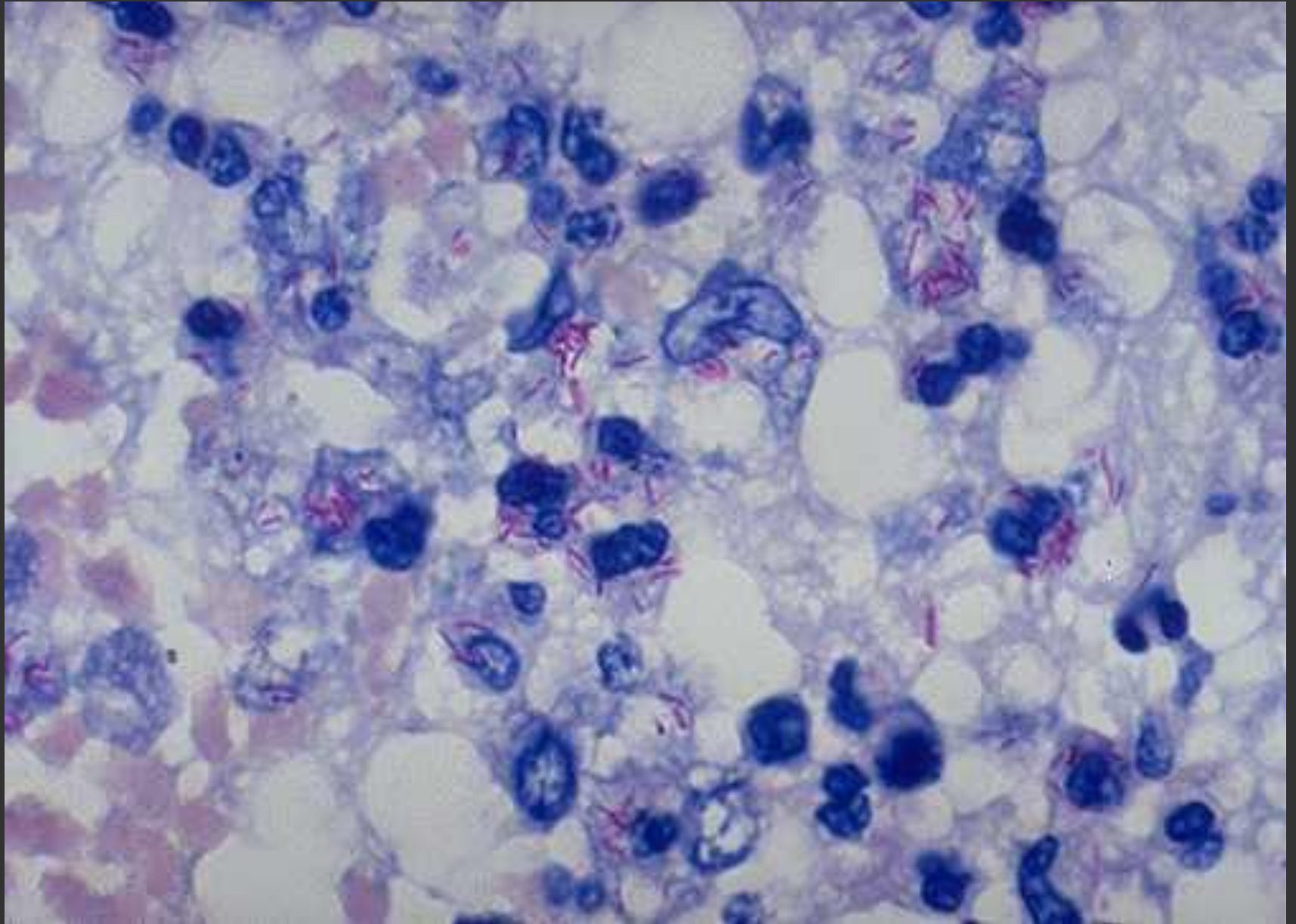
Chest pain

Gastrointestinal symptoms

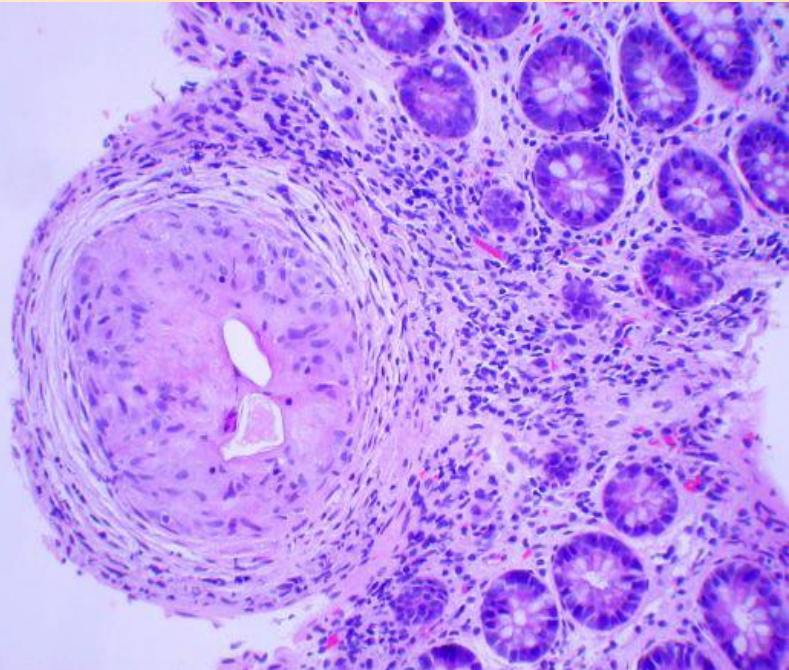
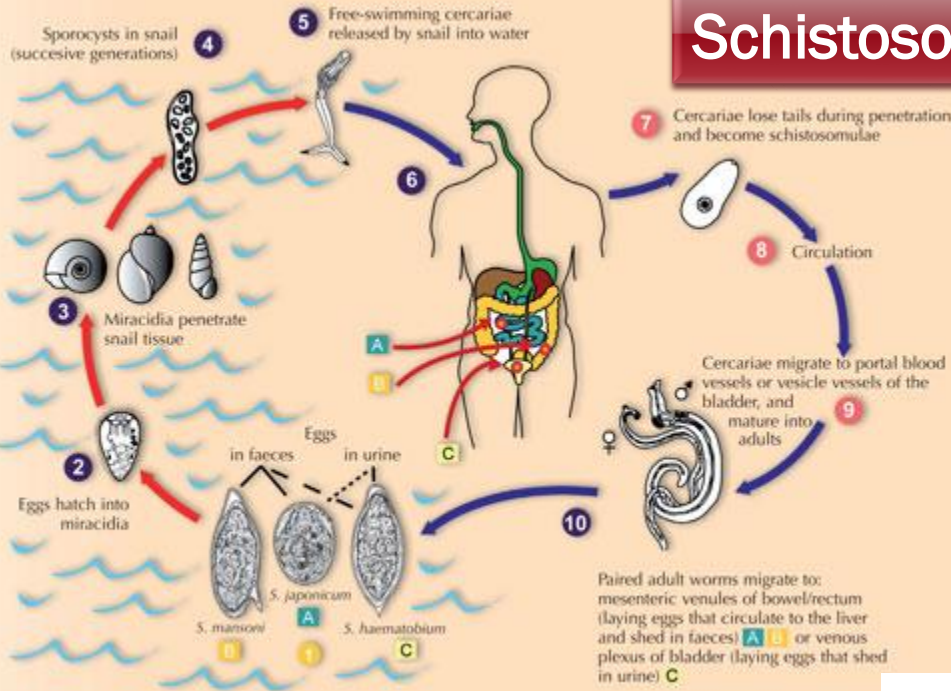




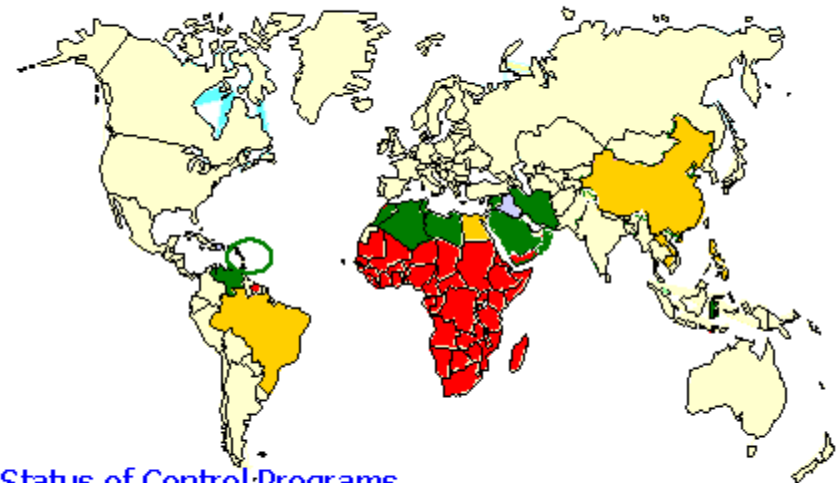
# Sputum , TB bacilli



# Schistosomiasis



## Global Distribution of Schistosomiasis

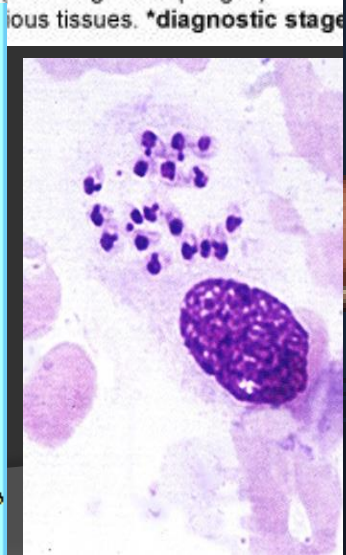
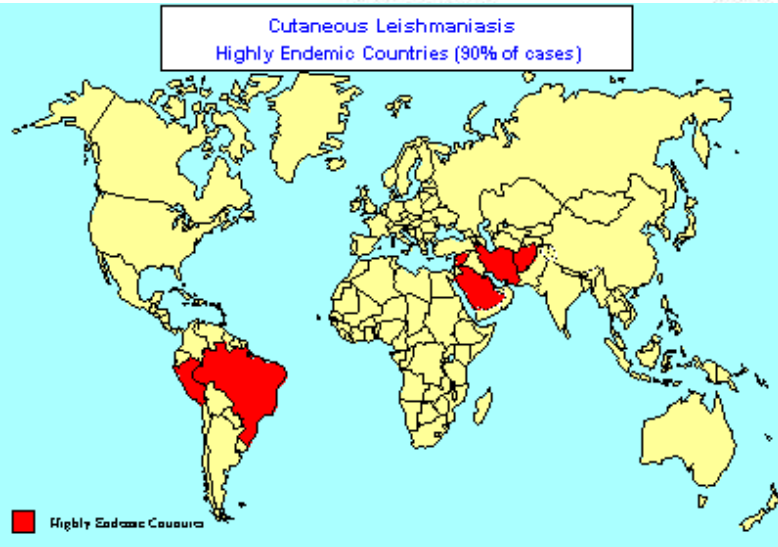
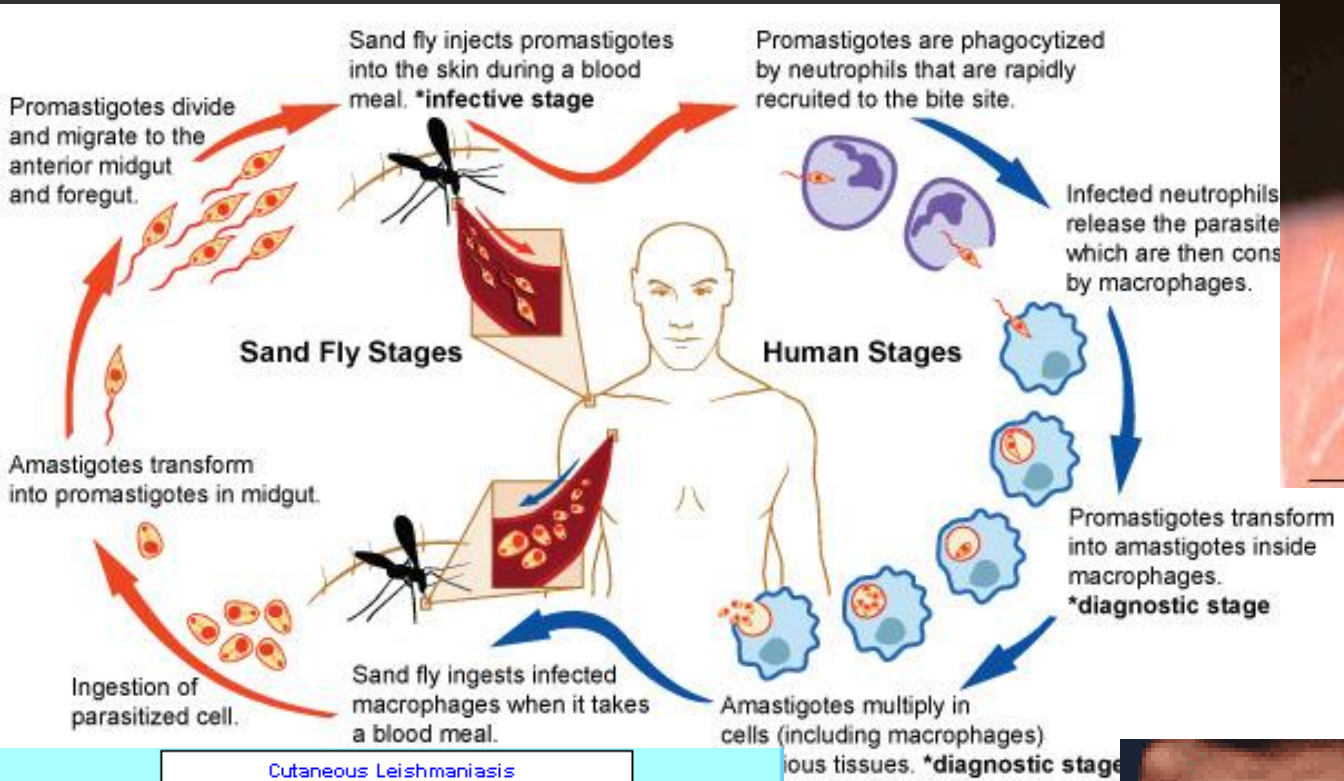


### Status of Control Programs

- almost eradicated
- ongoing large-scale control programmes
- limited or no control



# Leishmaniasis



# Leprosy



LEPROSY: NEW CASE DETECTION RATES 2005



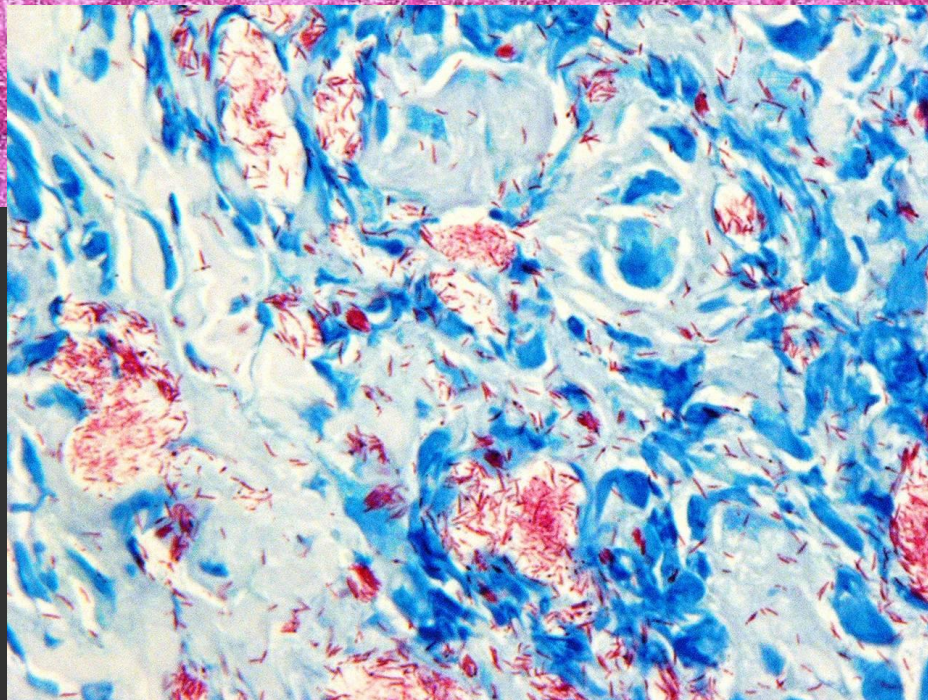
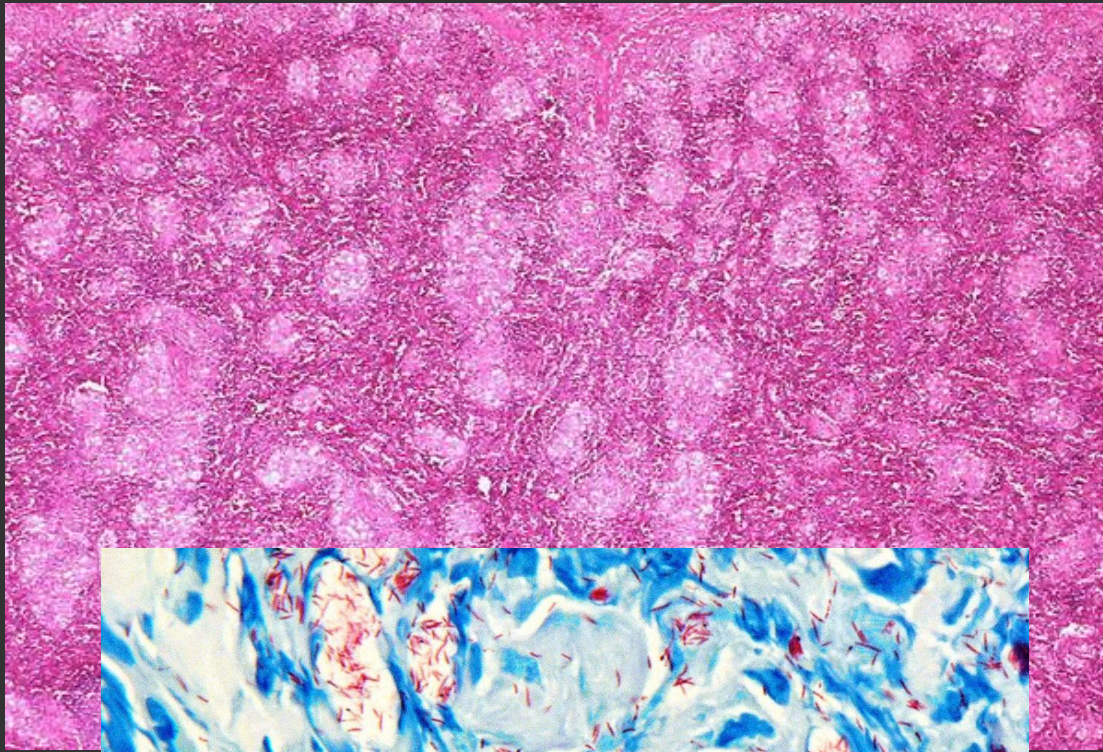
SOURCE: WHO

New case detection rates 2005 (per 100,000 population)

■ 22 to 26.9 people ■ 14 to 22 ■ 12 to 14 ■ 10 to 12 ■ Less than 10



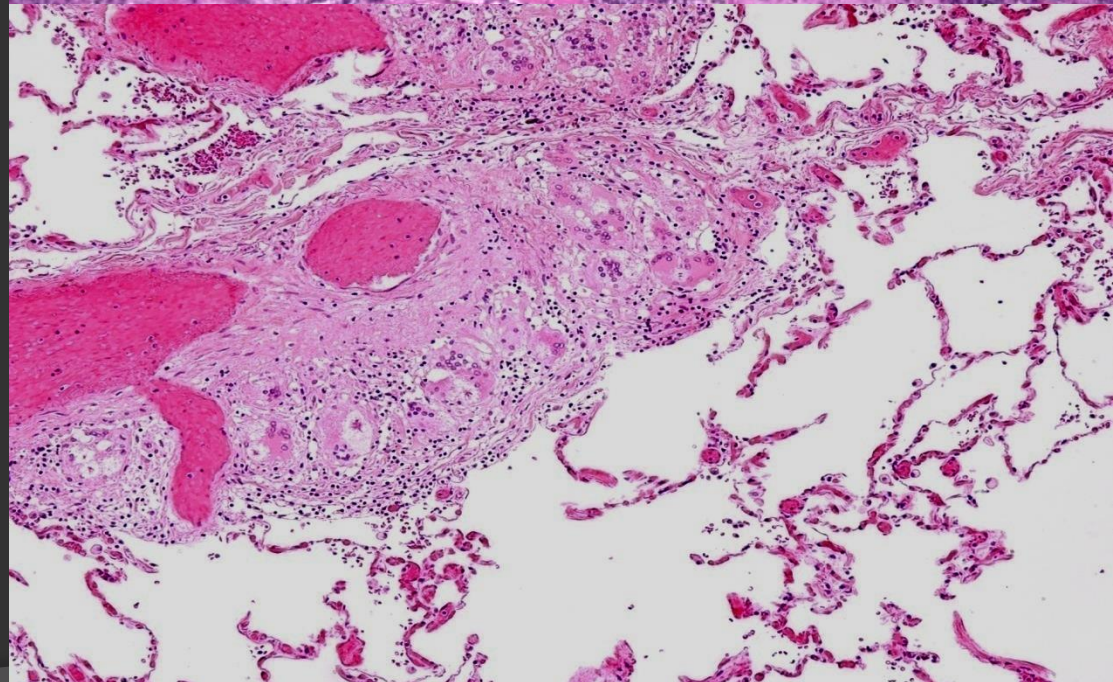
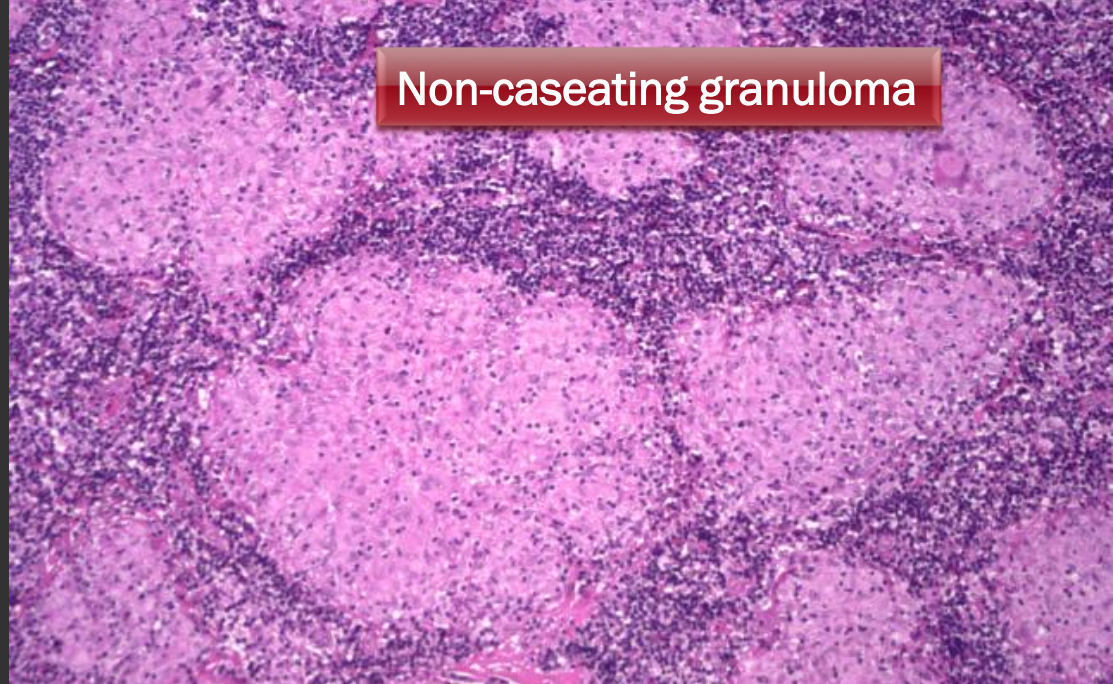
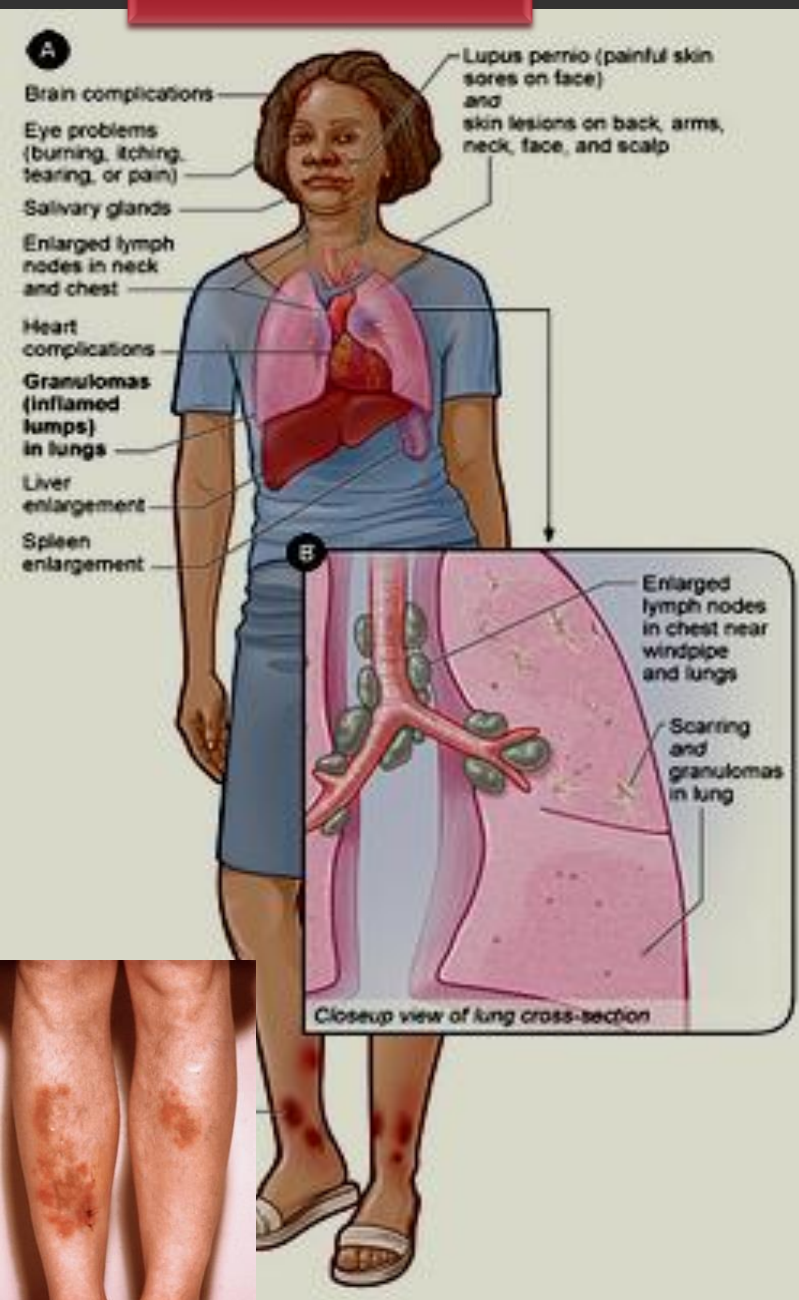
# Leprosy





# Sarcoidosis

## Non-caseating granuloma





# Match A and B

**A**

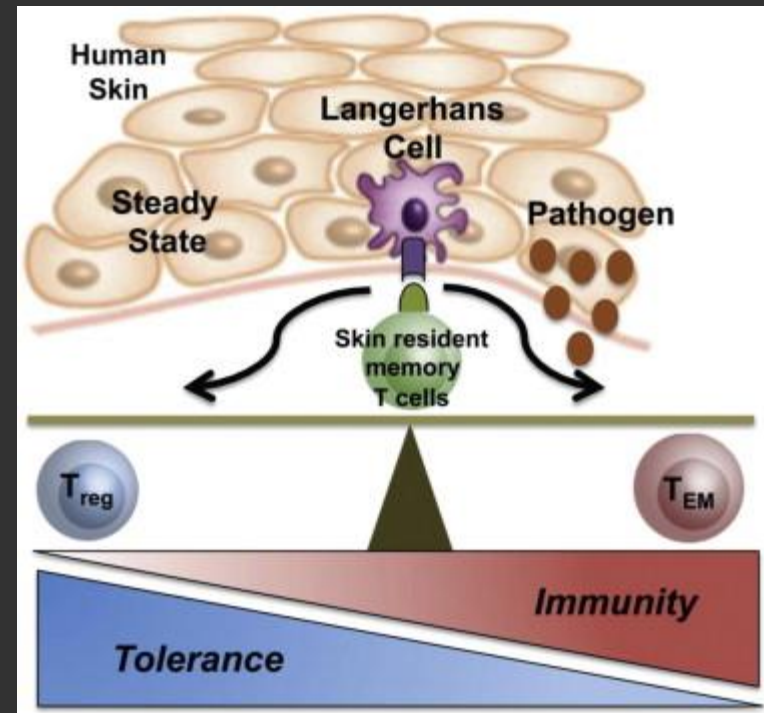
- 1) The most important cell in granulomatous inflammation
- 2) A cytokines that is important in activating macrophages and transforming them into epithelioid cells
- 3) Multinucleated cell in TB
- 4) Antigen presenting cells
- 5) pathogenesis of immune type granulomatous inflammation
- 6) Microscopic finding of TB
- 7) Found in the cell wall of TB

**B**

- a. **IFN- $\gamma$**
- b. **Langhans cells**
- c. **Epithelioid histiocytes**
- d. **Cord factor**
- e. **Langerhan's cells**
- f. **Type IV hypersensitivity reaction**
- g. **Caseating granuloma**

# Langerhan's` cells

- Antigen presenting cells



◎ Which of the following diseases does not cause granulomatous inflammation

- a) Cat-scratch disease
- b) Actinomycosis
- c) **Sarcoidosis**
- d) Leishmaniasis
- e) Staphylococcus infection

# TAKE HOME MESSAGES:

- ⦿ Granulomatous inflammation is a distinctive pattern of chronic inflammation characterized by aggregates epithelioid macrophages
- ⦿ Damaging stimuli which provoke a granulomatous inflammatory response include: Microorganisms which are of low inherent pathogenicity but which excite an immune response.
- ⦿ Granulomata are produced in response to:
  - Bacterial infection
  - parasitic infection: e.g. Schistosoma infection
  - Certain fungi cannot be dealt with adequately by neutrophils, and thus excite granulomatous reactions.
  - Non-living foreign material deposited in tissues, e.g. keratin from ruptured epidermal cyst.
  - Unknown factors, e.g. in the disease 'sarcoidosis' and Crohn's disease