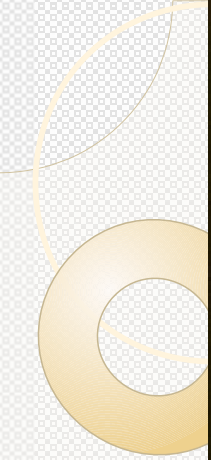




# Granulomatous Inflammation

Dr Sahar Iqbal  
AP pathology





# GRANULOMATOUS INFLAMMATION

- **Definition:** specialized form of chronic inflammation characterized by formation of **granulomas**.
- **Granulomas:** are characterized by collections of activated macrophages, often with T lymphocytes, and sometimes associated with central necrosis.
- **Two types:**
  1. Caseating granulomas and
  2. Non-caseating granulomas

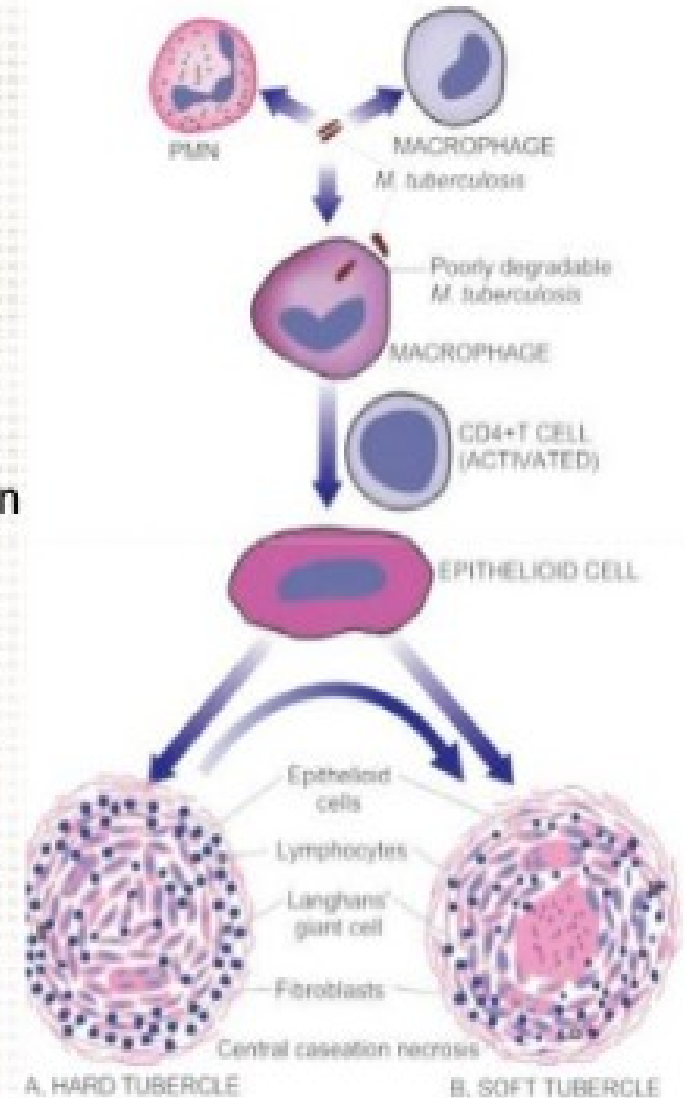
# Mycobacterium tuberculosis

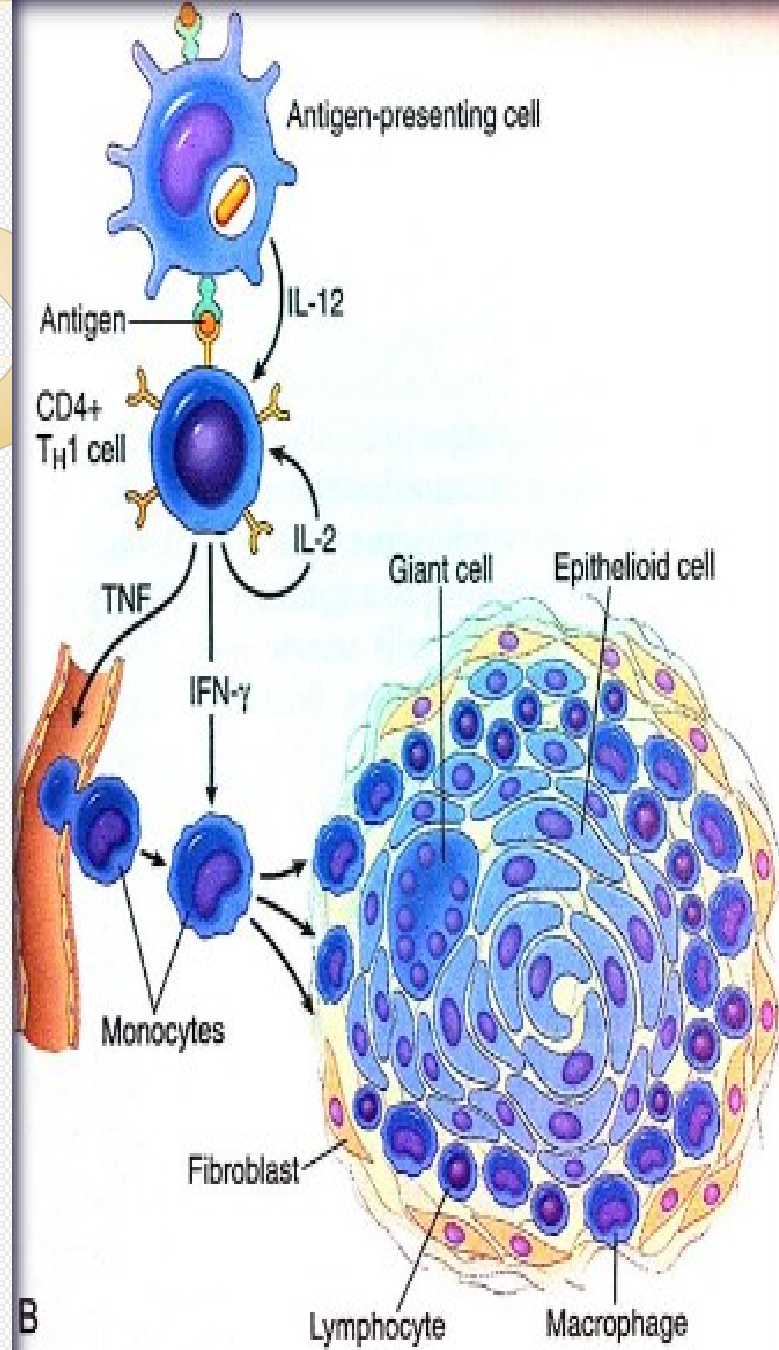
**Acid-fast bacilli**



# Pathogenesis

- No demonstrable toxins
- Virulence mycobacteria reach the alveoli
- Macrophage – initiates phagocytosis, but unable to do so
  - bacterial sulfolipids inhibit the fusion of phagocytic vesicles with lysosomes
- multiply in the pulmonary epithelium or macrophages
- 2 to 4 weeks - destroyed by the immune system, but some survive and are spread by the blood to extrapulmonary sites
- Ability to survive and grow within host cells





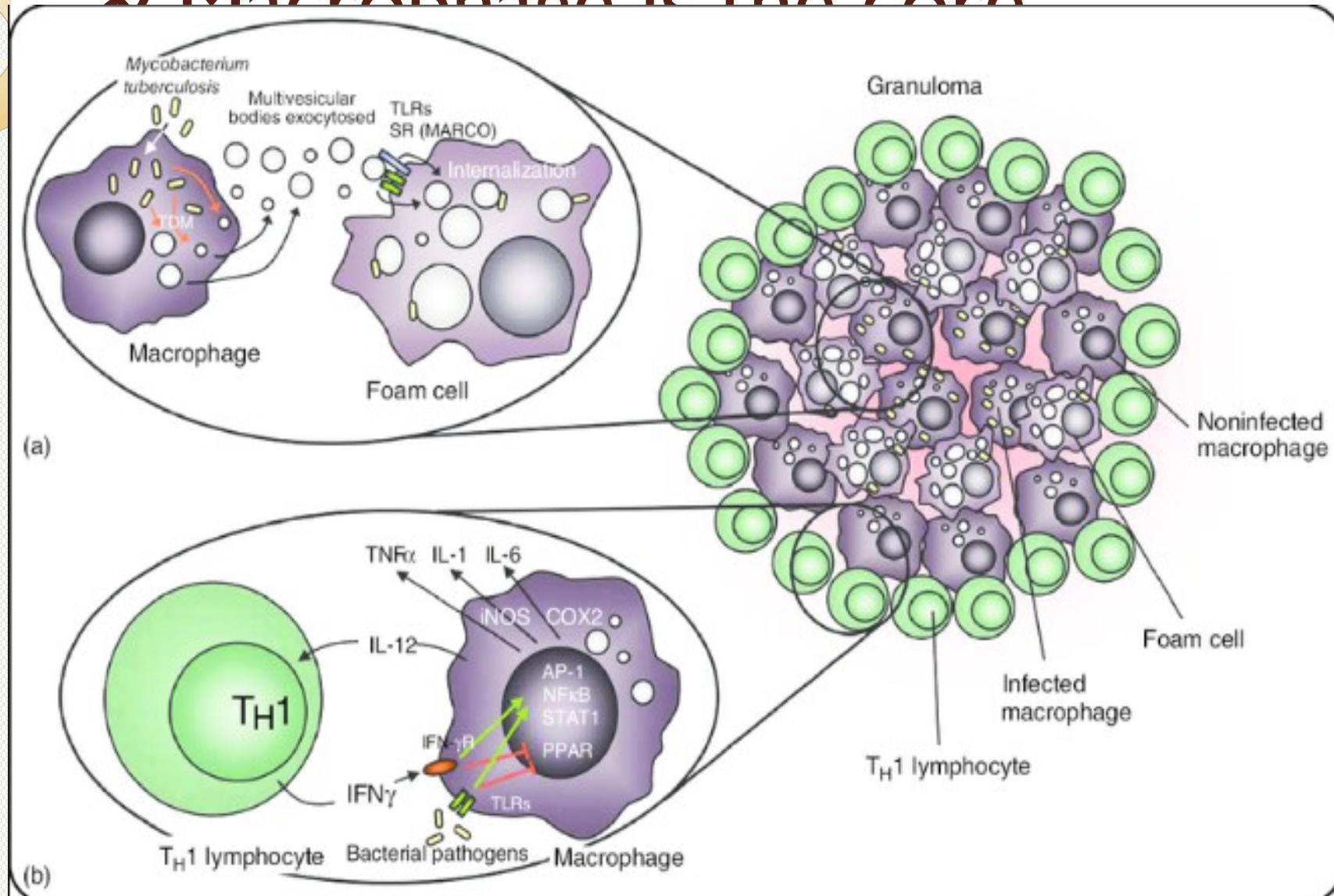
B

Figure 5-15

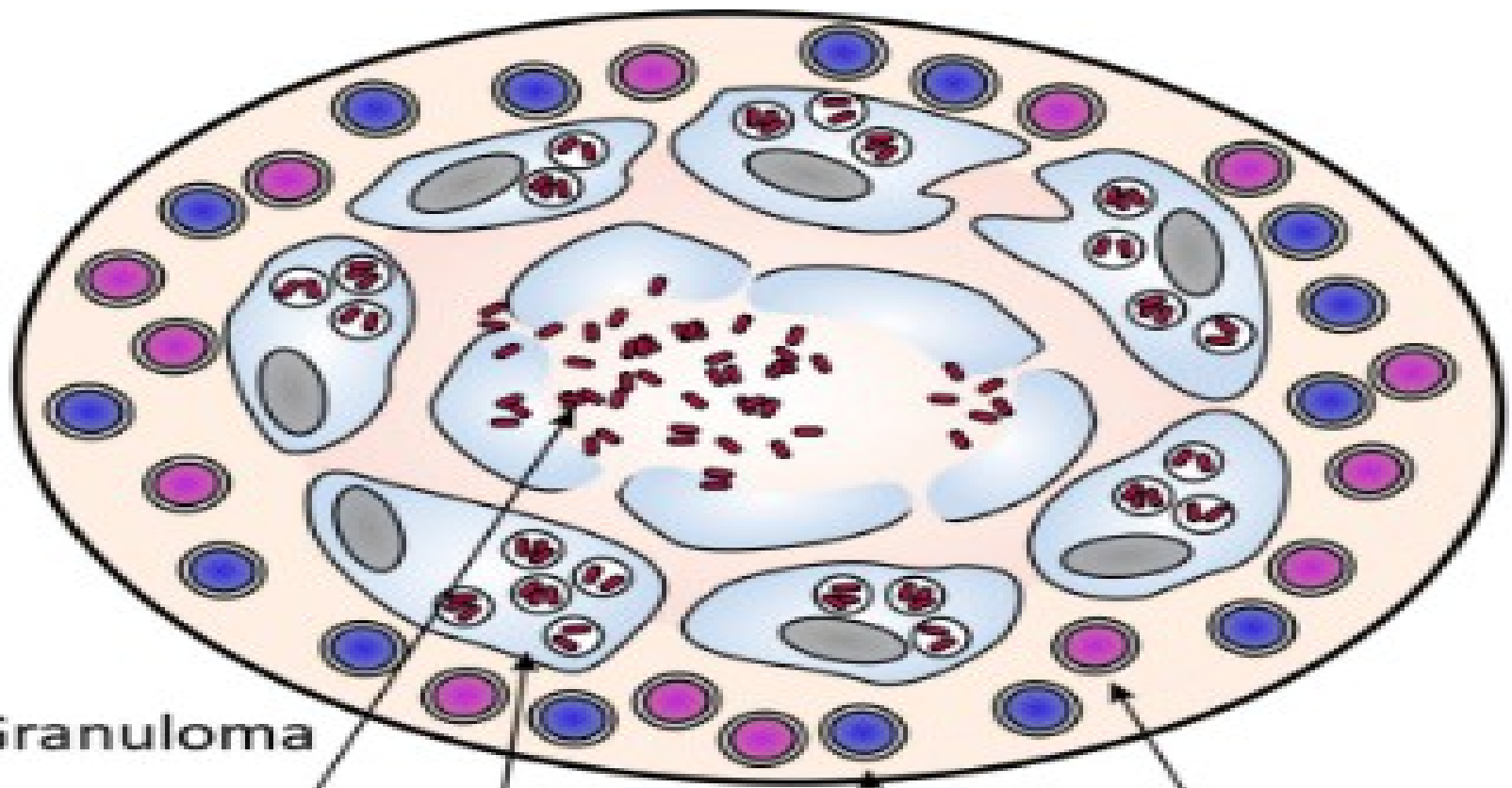
## PATHOGENESIS OF GRANULOMA FORMATION

Events that give rise to the formation of granuloma and role of cytokines in the pathogenesis of granuloma (courtesy Robins Pathologic Basis of Disease, Chapter 5- Diseases of the immune system)

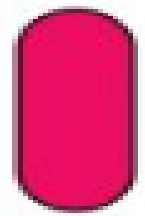
# Cross talk between Lymphocyte & Macrophage is the core





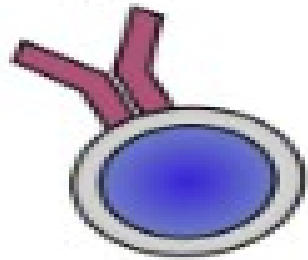


Granuloma



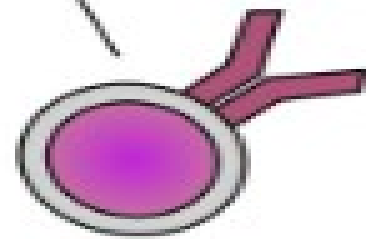
**Macrophage**

IFN- $\gamma$   
TNF- $\alpha$   
iNOS



**CD4+**

IL2  
IFN- $\gamma$



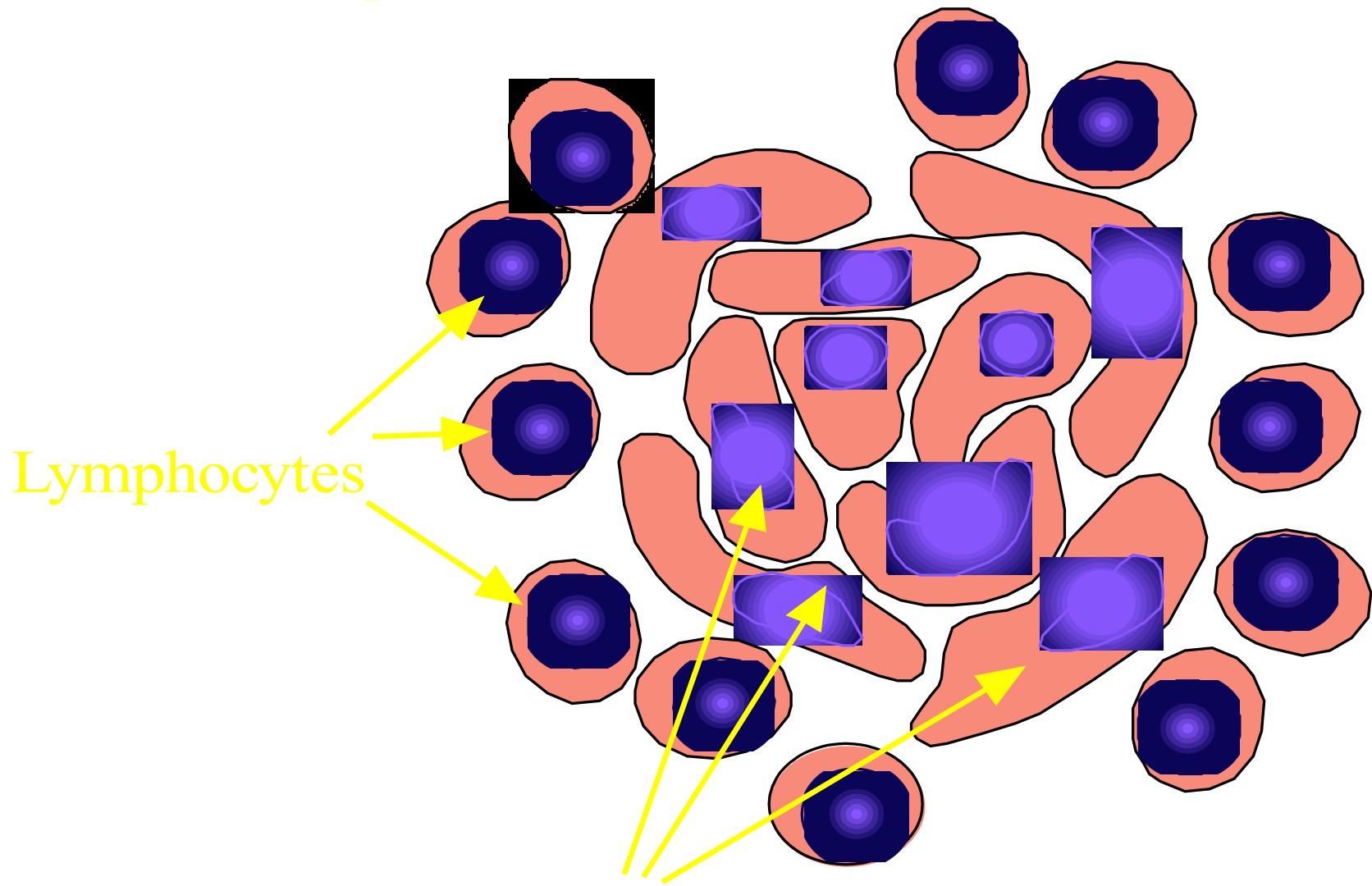
**CD8+**

IFN- $\gamma$   
Perforin  
Granulolysin



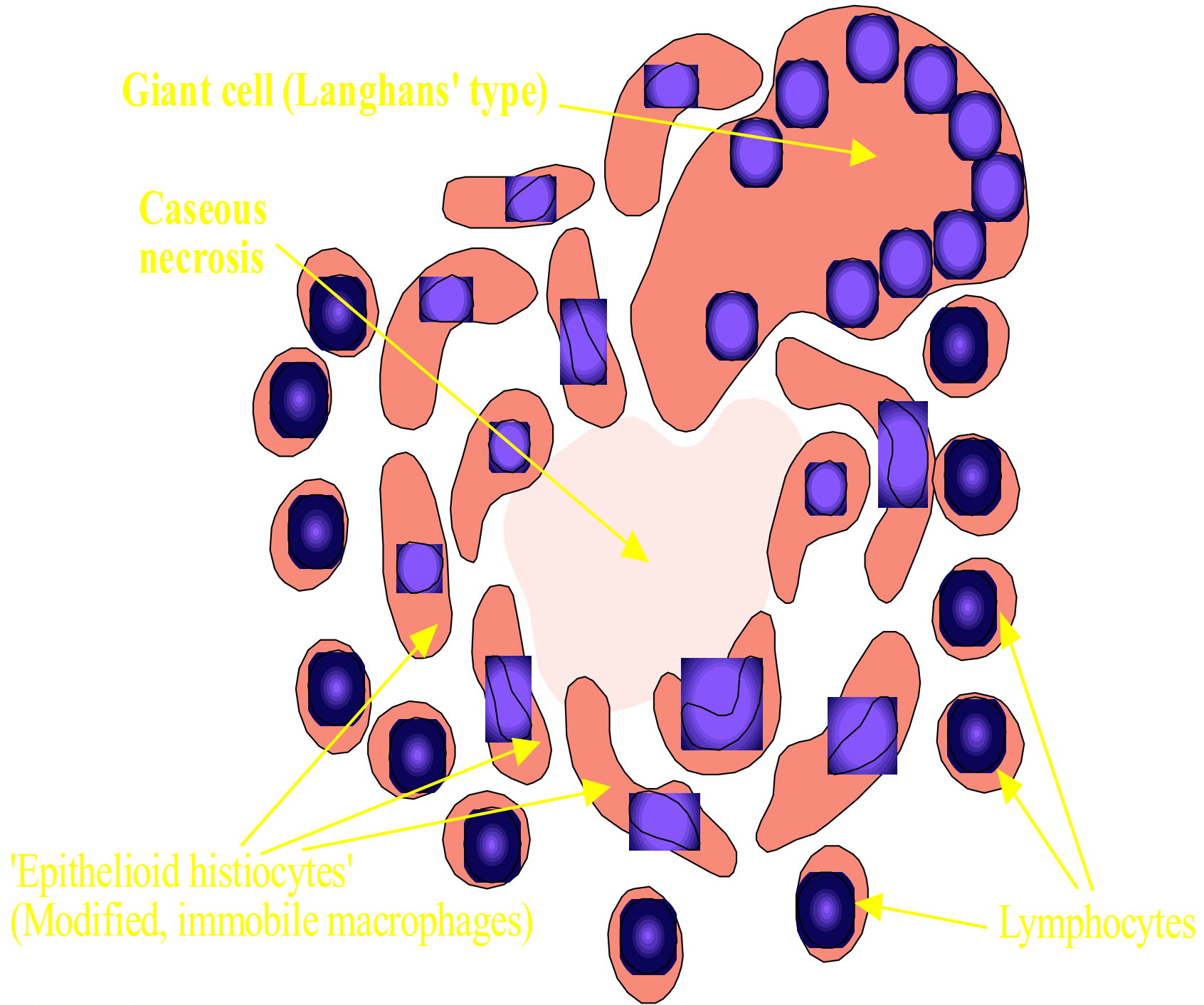
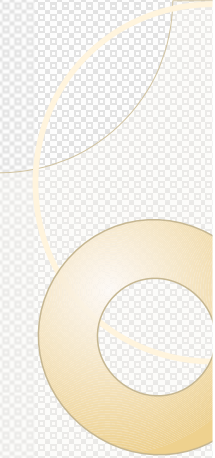


**A small granuloma.**



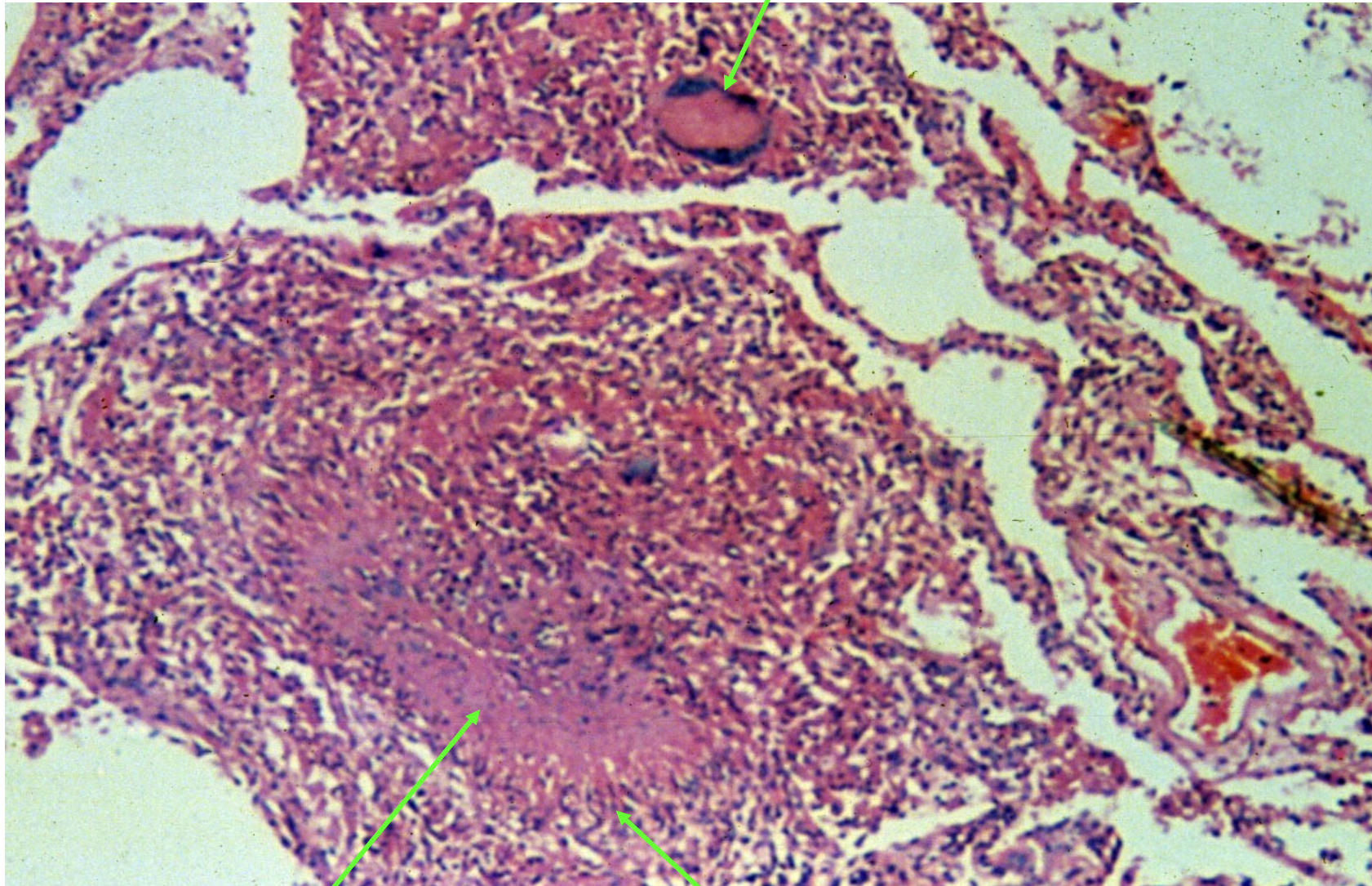
Lymphocytes

'Epithelioid histiocytes'  
(Modified, immobile macrophages)



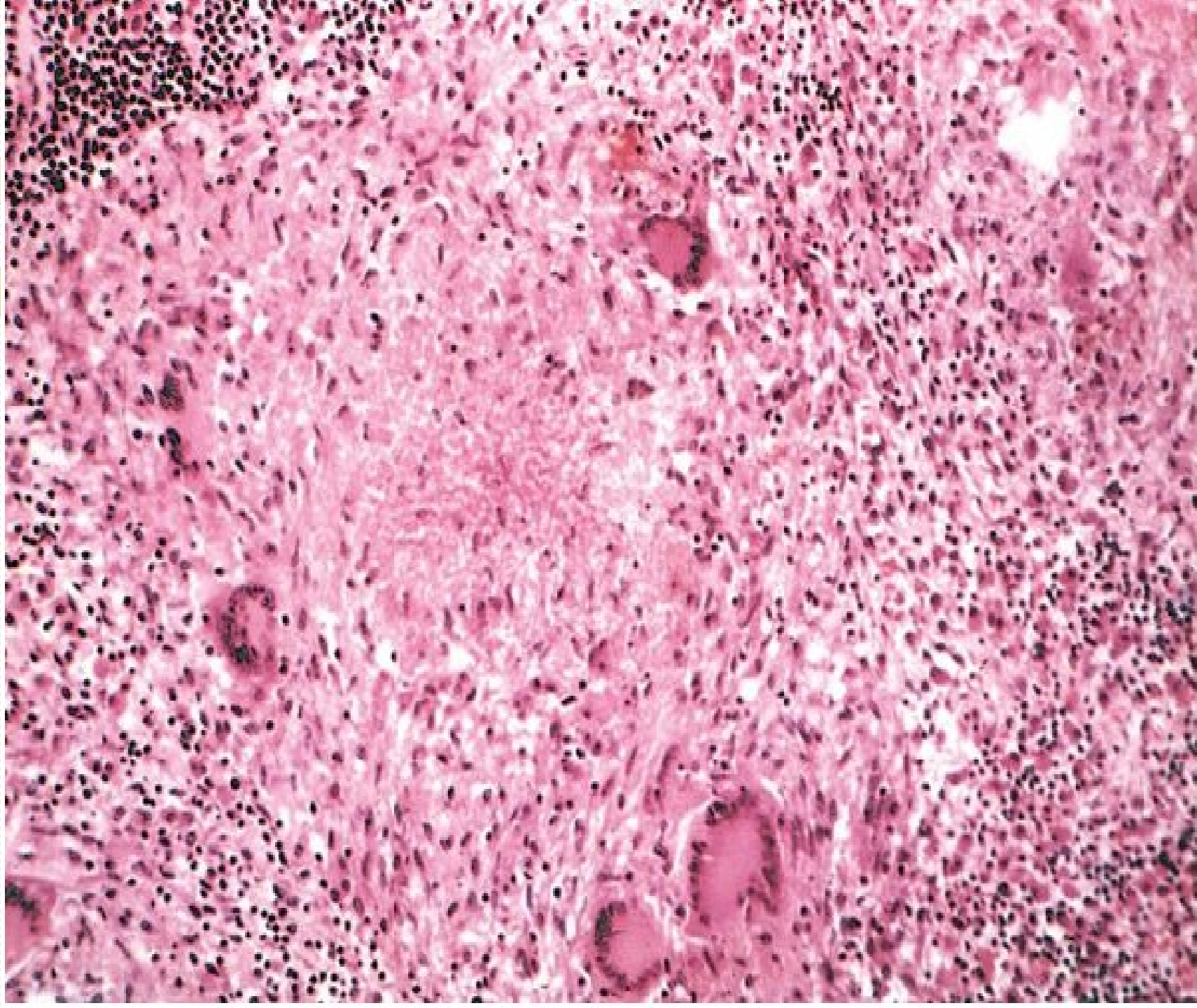
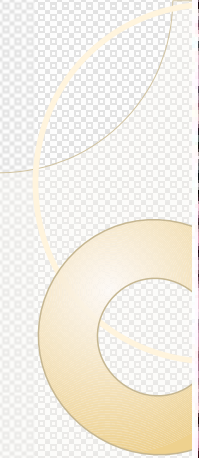


Langhans' type giant cell



Caseous necrosis

'Epithelioid' macrophages





# Two main types of Granulomas

## Foreign body granuloma

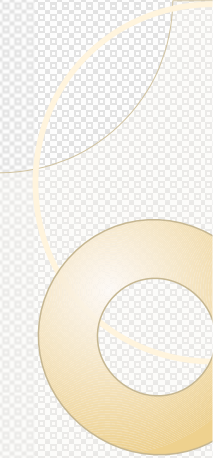
are incited by relatively inert foreign bodies. Typically, foreign body granulomas form when material such as suture are large enough to preclude phagocytosis by a single macrophage

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

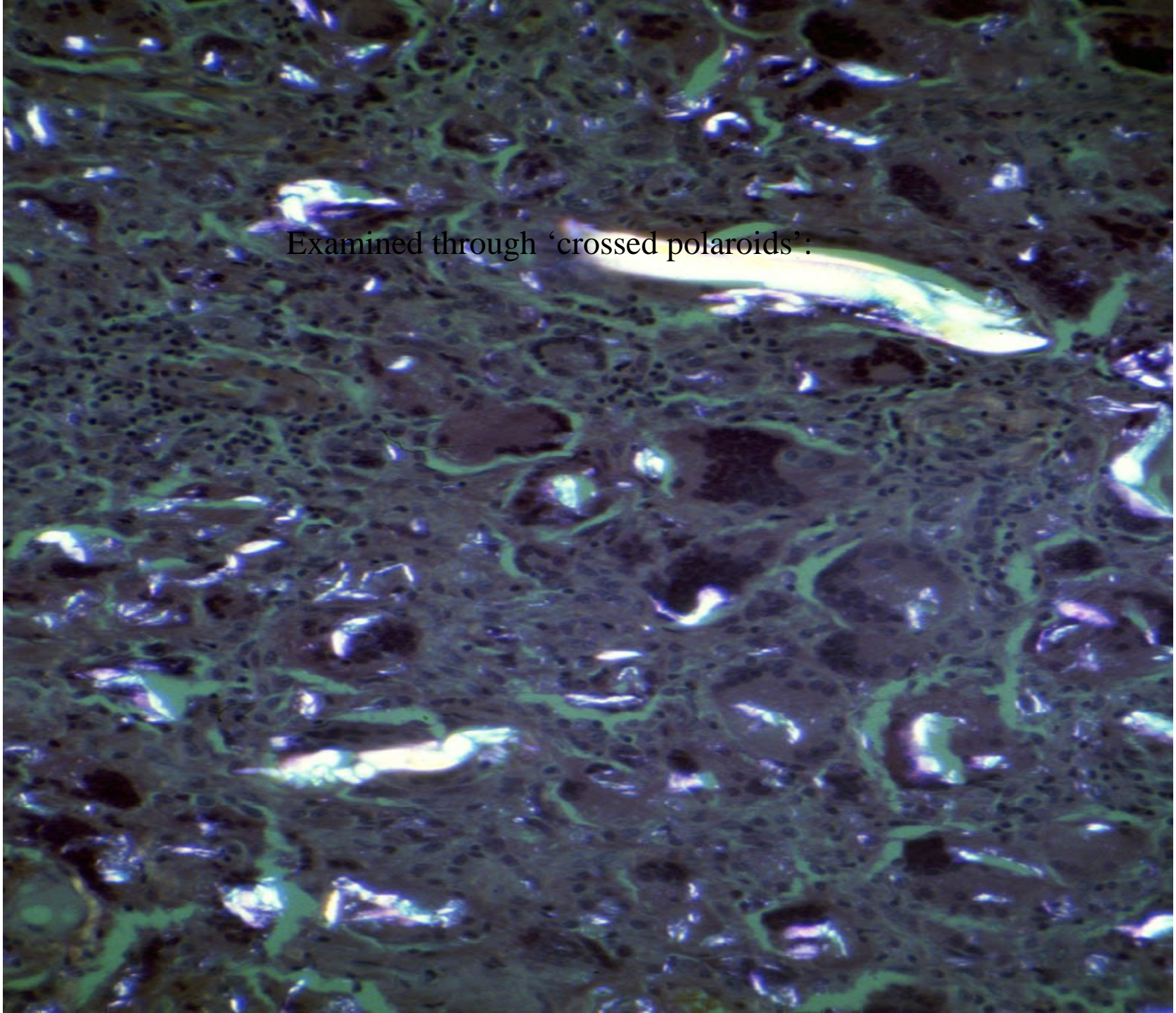
The foreign material can usually be identified in the center of the granuloma, by polarized light (appears refractile).

## Immune granuloma

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

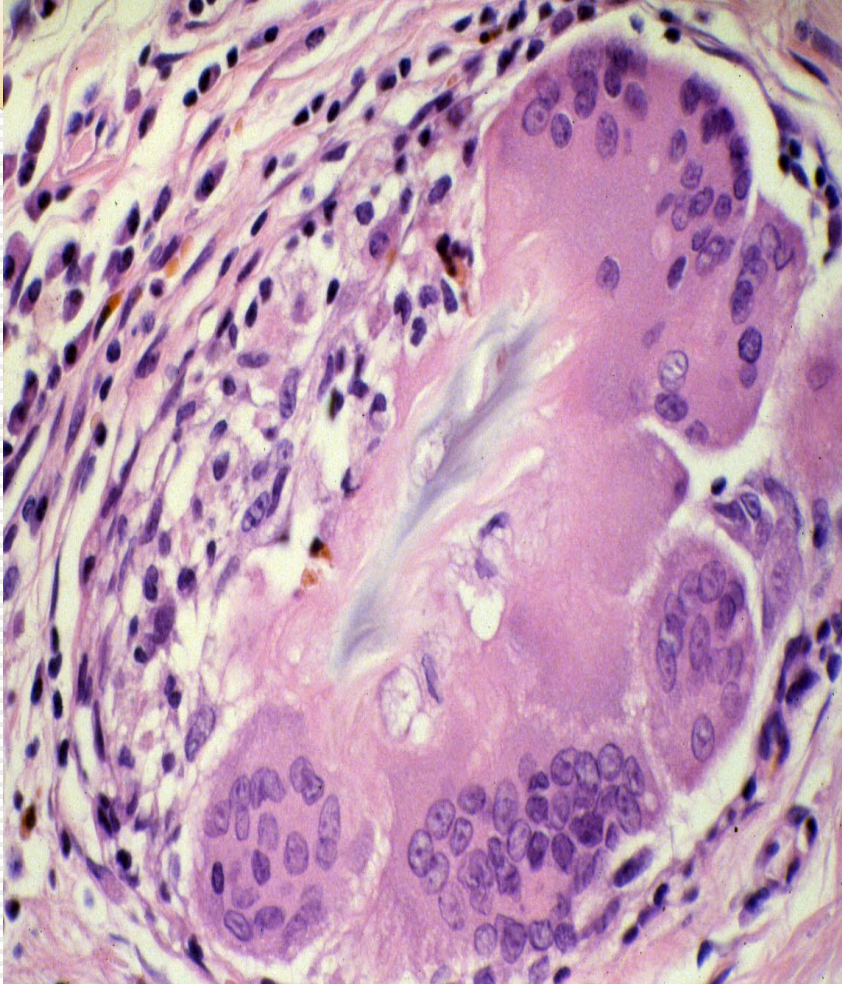


Examined through 'crossed polaroids':





- Foreign body type giant cells

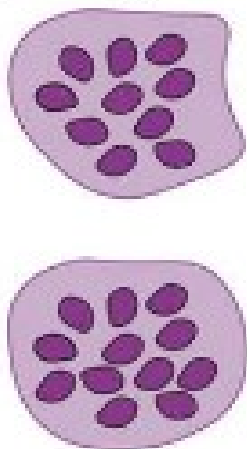


- Langhans type giant cells

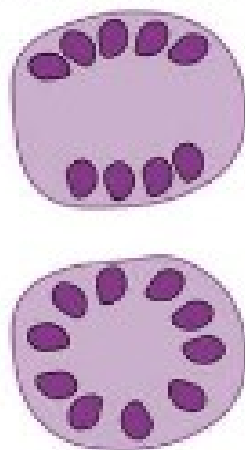


## Inflammatory multinucleated giant cells

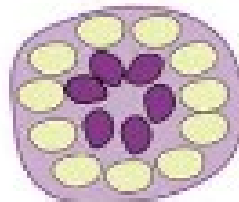
### Foreign body giant cells



### Langerhans' giant cells

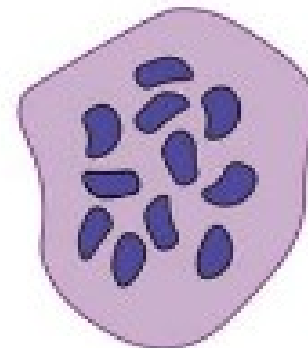


### Tuonon giant cells

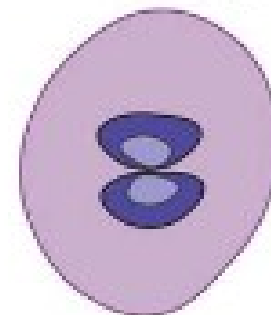


## Tumor giant cells

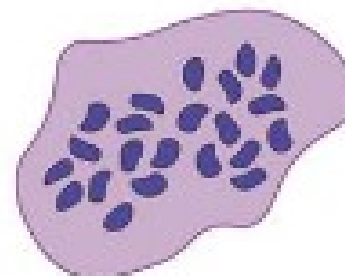
### Anaplastic cancer giant cells



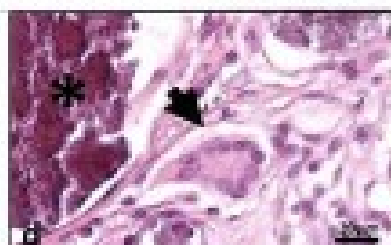
### Reed-Sternberg cells



### Osteoclastic tumor giant cell



## Multinucleated giant cells within biomaterial implantation beds

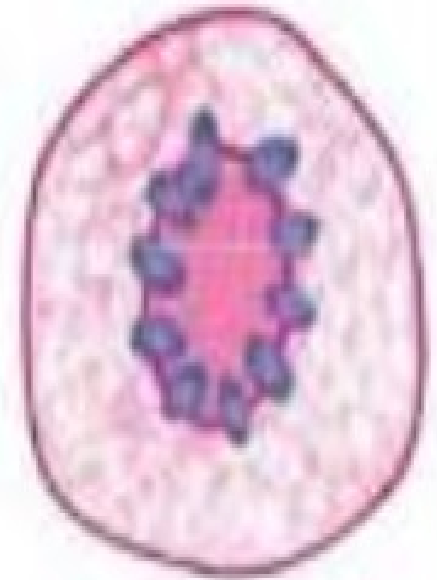




**A, Foreign body type**



**B, Langhans' type**



**C, Touton type**

TB may be  
pulmonary or  
extra-  
pulmonary



**Pulmonary TB**  
is most  
common form

# SYMPTOMS

Main symptoms of  
**Pulmonary tuberculosis**

## Central

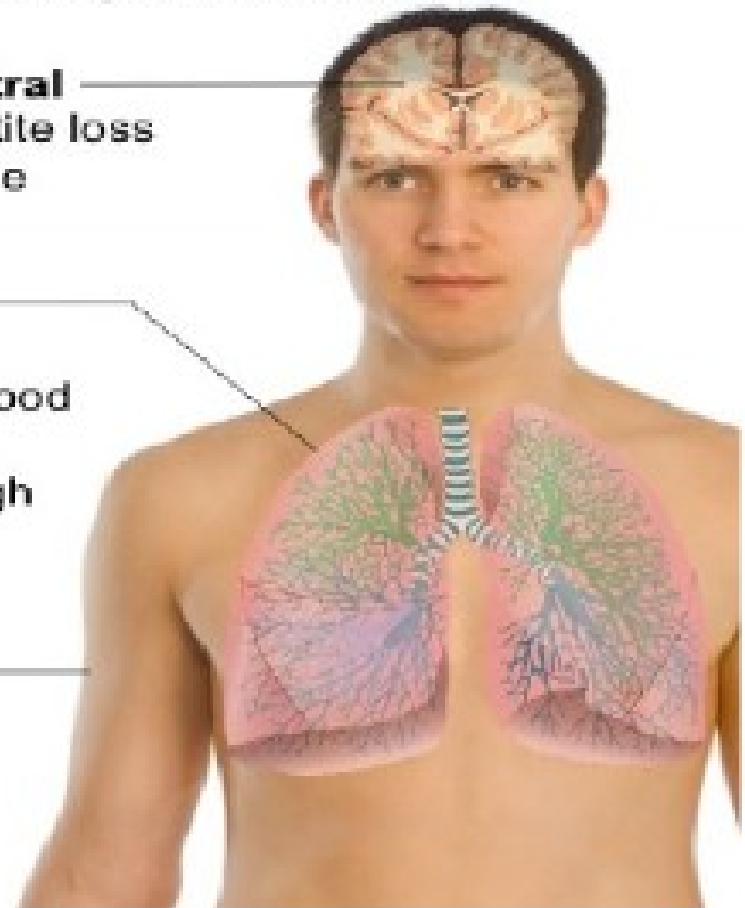
- appetite loss
- fatigue

## Lungs

- chest pain
- coughing up blood
- productive,  
prolonged cough

## Skin

- night sweats,
- pallor





The diagram illustrates the human respiratory system, including the trachea and bronchi. It compares two states of Tuberculosis (TB) infection. On the left, the lungs are labeled 'Latent TB' and show a small, isolated cluster of blue rod-shaped bacteria within a yellow circular capsule. On the right, the lungs are labeled 'TB Disease' and show a larger, more active cluster of blue rod-shaped bacteria, with some bacteria appearing to be spreading or multiplying. The background of the lungs is a light pink color, and the trachea and bronchi are shown in white and grey.

## Latent TB

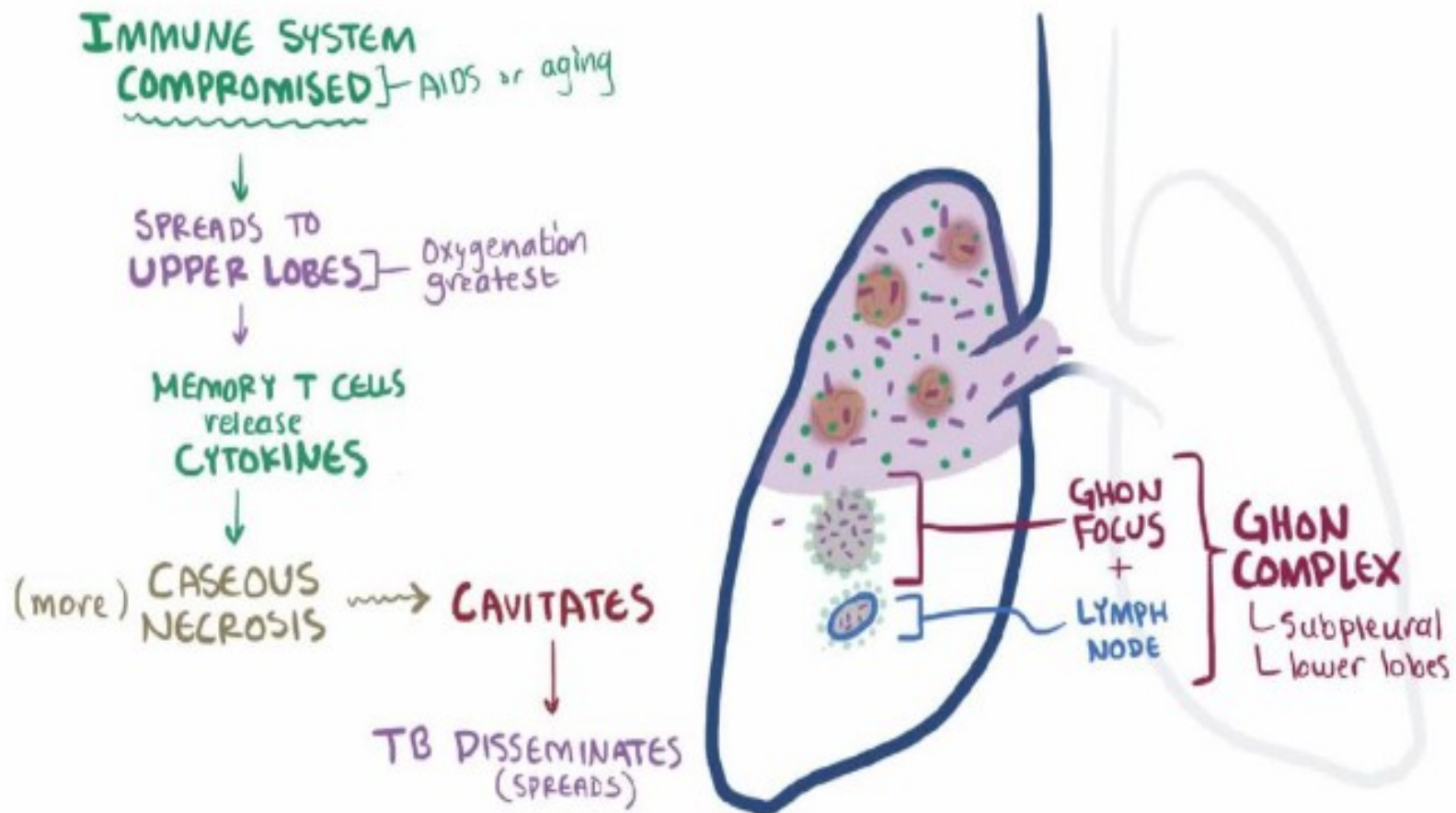
- TB lives but doesn't grow in the body
- Doesn't make a person feel sick or have symptoms
- **Can't** spread from person to person
- Can advance to TB disease

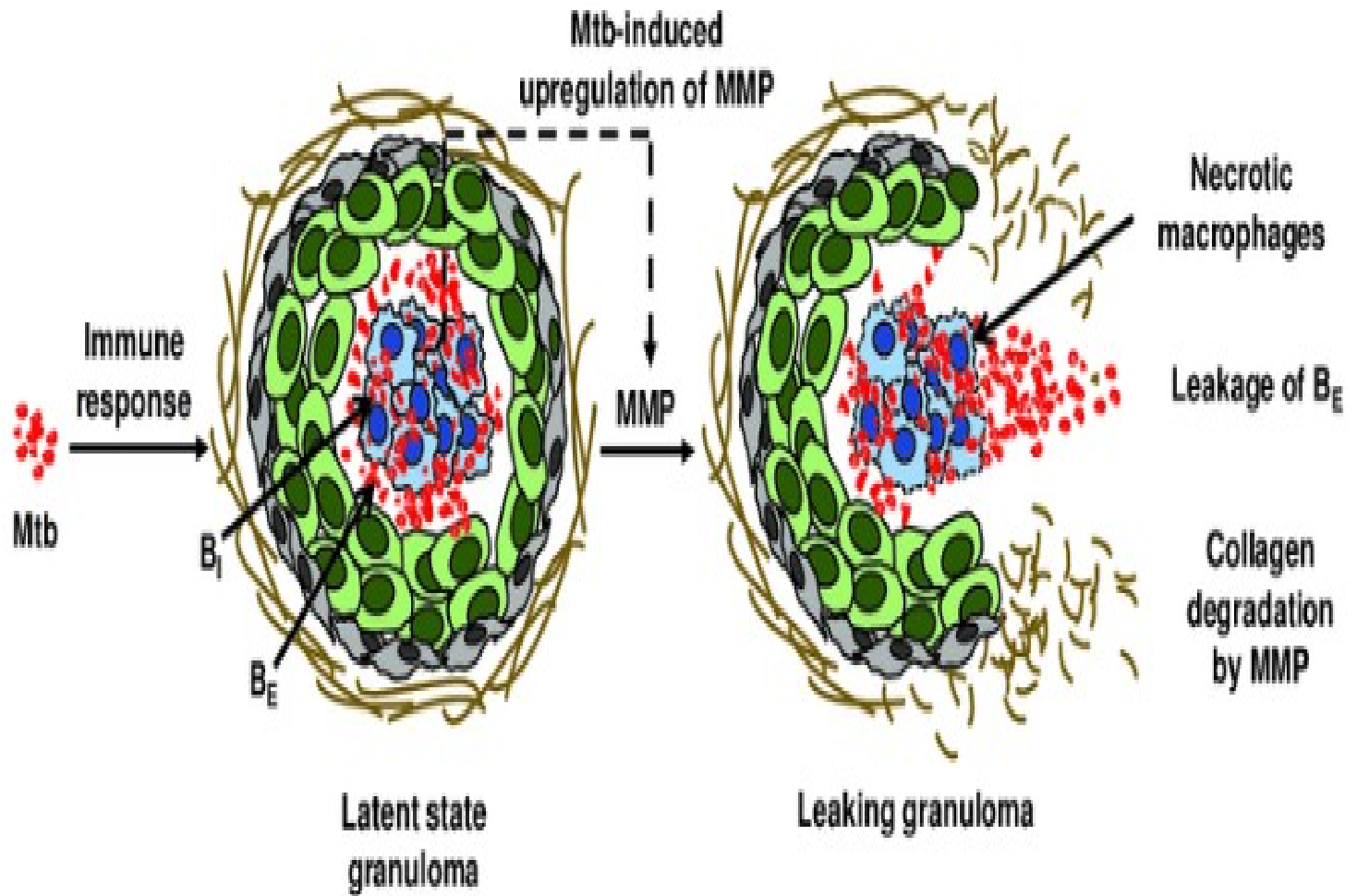
## TB Disease

- TB is active and grows in the body
- Makes a person feel sick and have symptoms
- **Can** spread from person to person
- Can cause death if not treated

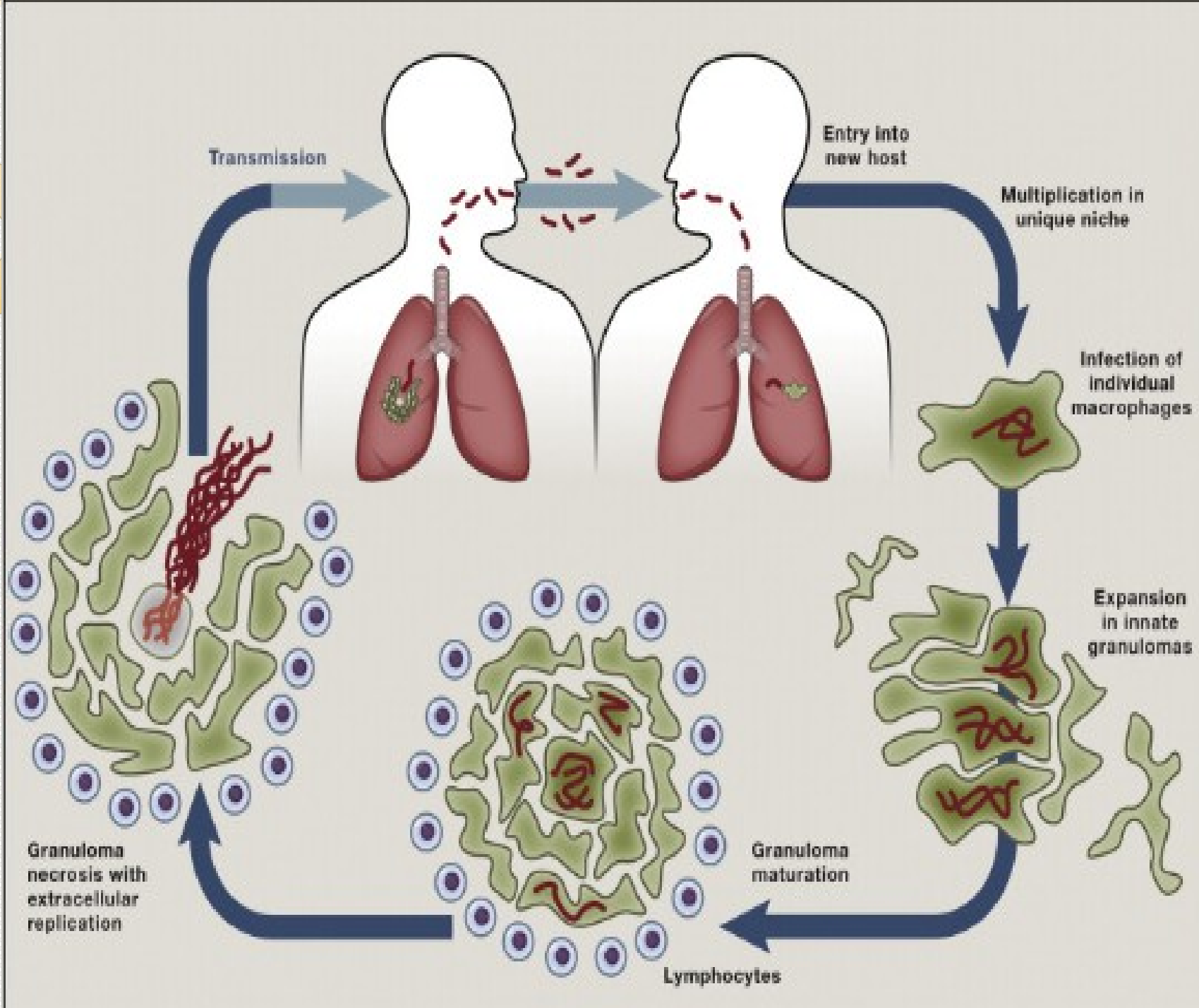
# Ghon focus & Ghon complex

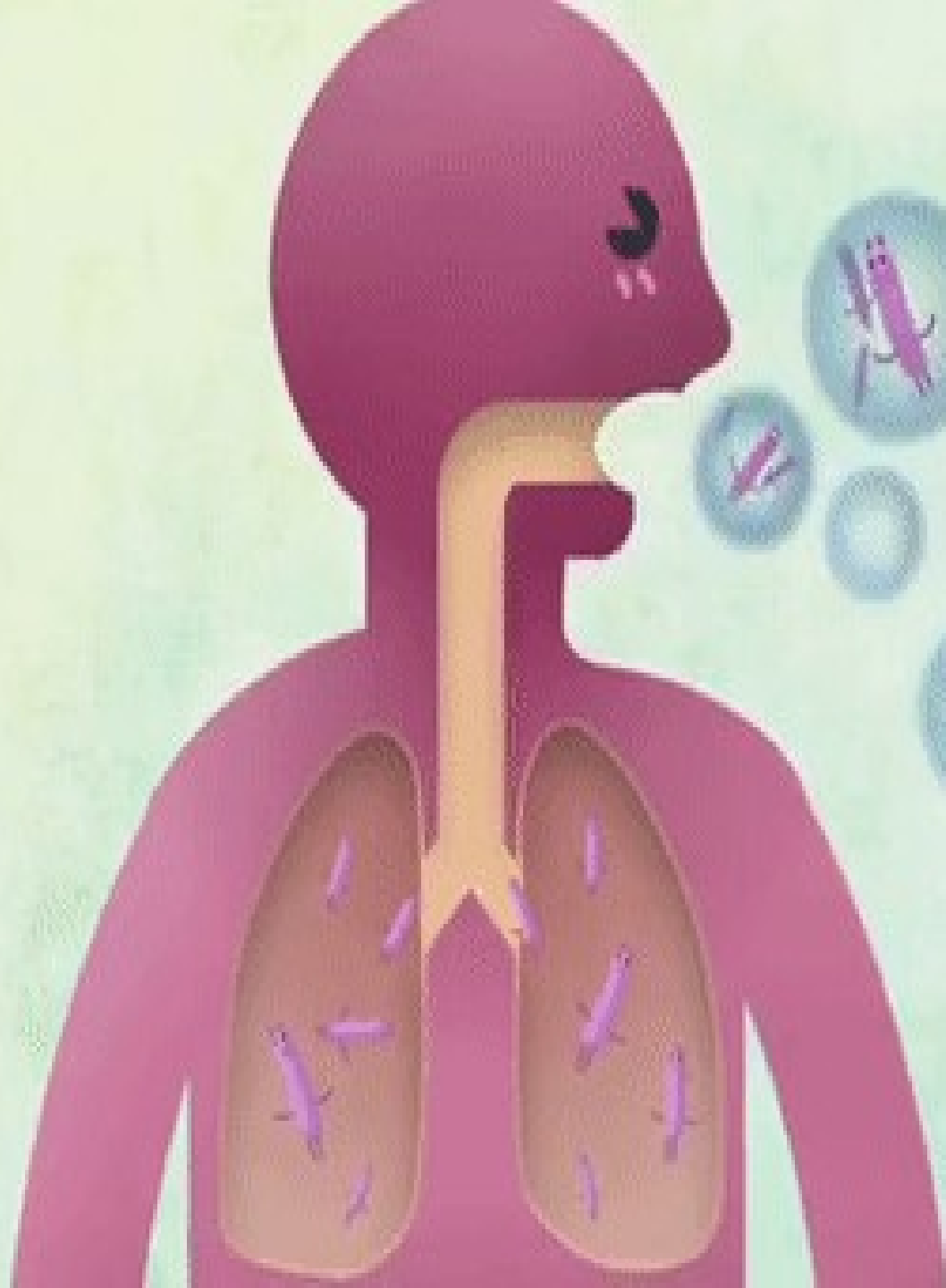
## MYCOBACTERIUM TUBERCULOSIS (TB)



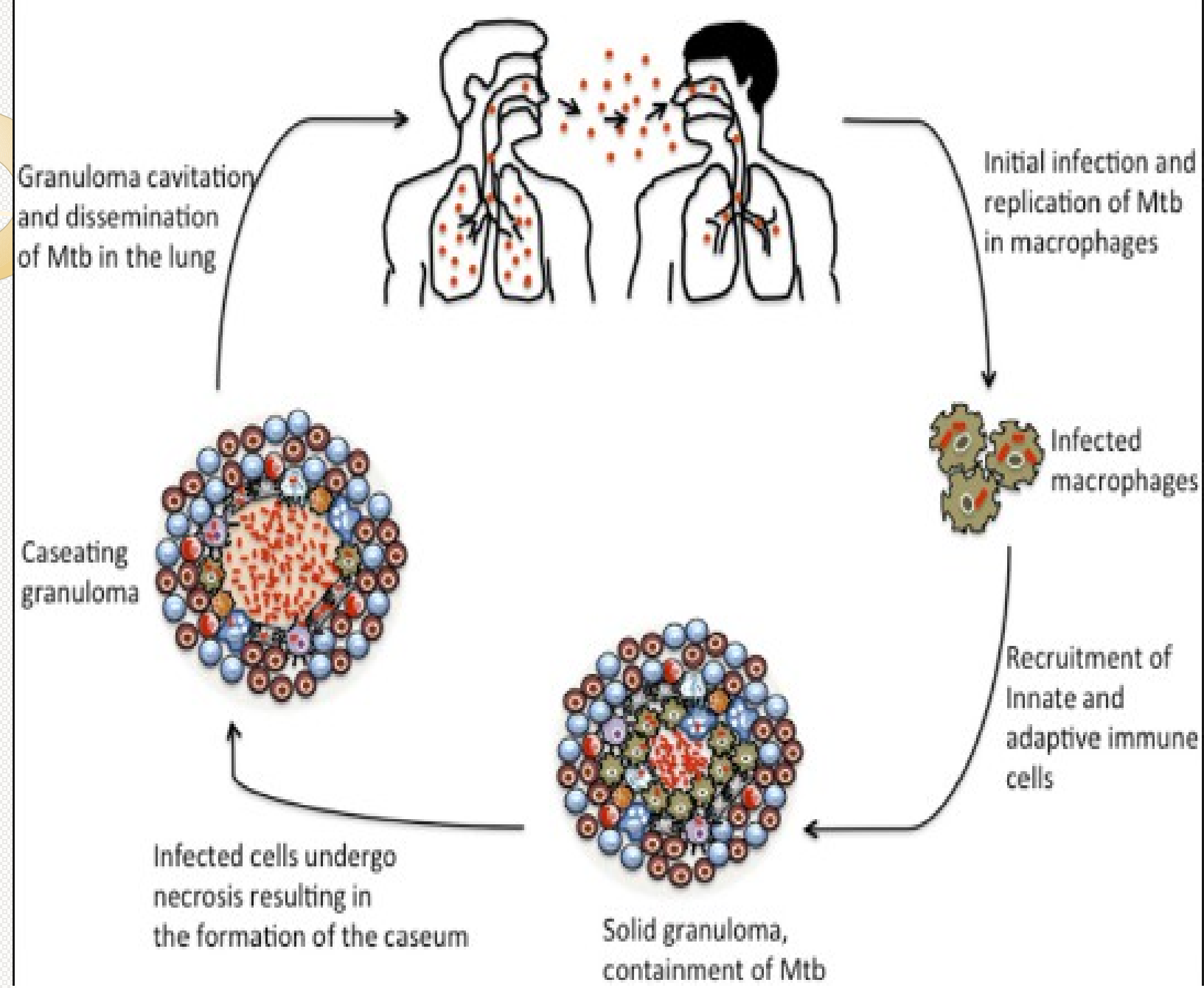








# Transmission of Mtb



# Ways to better recovery in Tuberculosis

Compliance and regular treatment and medication



Compliance and regular treatment and medication



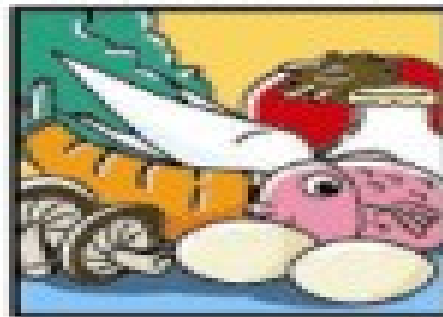
Compliance and regular treatment and medication



Lead a happy life



Balanced diet



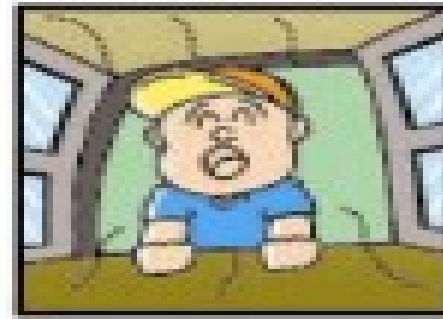
Adequate rest



Adequate exercise



Fresh air





# Lab diagnosis

- CBC & ESR
- Special stains-ZN stain highlights acid fast bacilli in sputum samples
- Microscopic examination-revealed caseating granulomas
- PCR (Molecular nucleic acid techniques)

# Diagnostic tests

## Direct

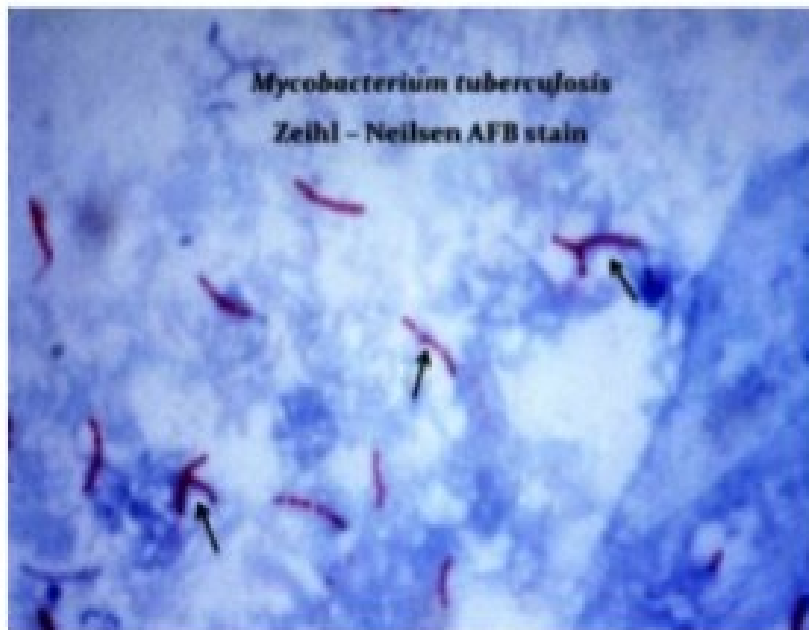
- Microscopy
- Culture
- Molecular nucleic acid techniques
- Antigen detection
- Phage based assays
- Liquid chromatographic tests

## Indirect

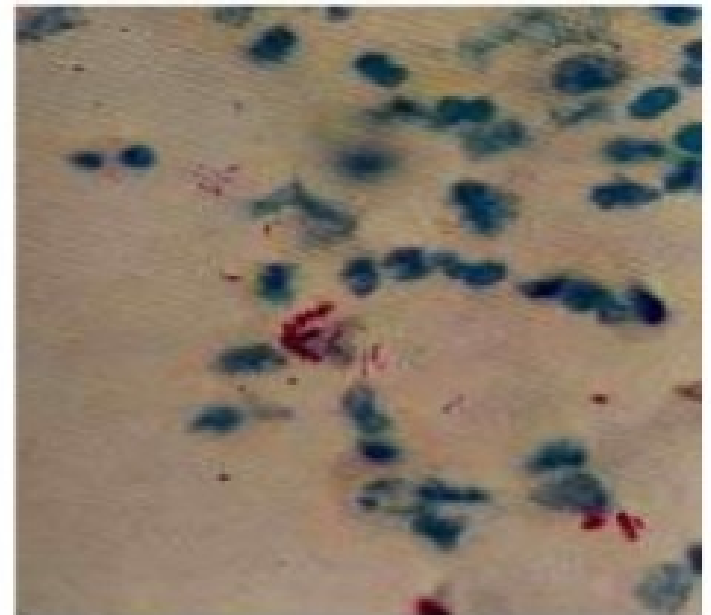
- Tuberculin skin testing (TST)
- Interferon  $\gamma$  assays
- Serological tests

# Microscopy

smears stained by the Ziehl-Neelsen method.



*M. tuberculosis* in sputum



*M. tuberculosis* in urine



Colonies of *Mycobacterium tuberculosis* on Lowenstein-Jensen (LJ) Medium



# Tuberculosis



Vaccination

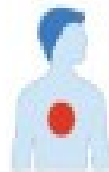
Medication



X-RAY



*Mycobacterium tuberculosis*



Chest pain

## Signs and symptoms



Fever



Nights sweats



Cough



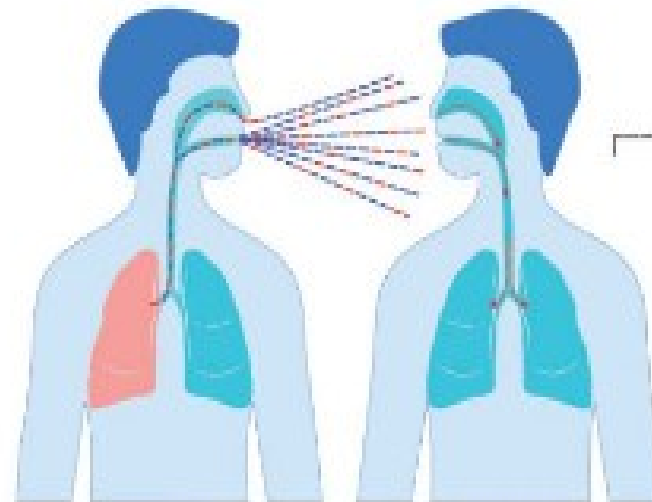
Weight loss



Loss of appetite



Fatigue



Tuberculosis transmitted from person via droplets from the lungs of people with active TB

## Risk



HIV



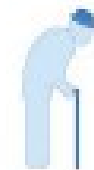
Genetics



Smokers



Children



Elderly



Diabetes



Alcoholism



Inject illicit drugs

# GRANULOMATOUS INFLAMMATION

## Infective causes:

- Tuberculosis
- Leprosy
- Cat-scratch disease
- LGV
- Brucellosis
- Syphilis
- Mycotic infections

## Non-Infective causes:

- Sarcoidosis
- Berylliosis
- Reactions to irritant lipids
- Autoimmune diseases
- Crohn's disease

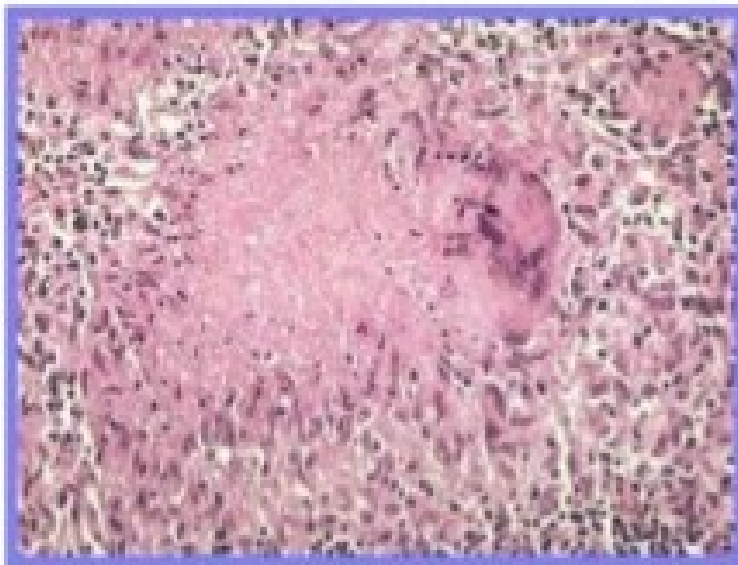
**TABLE 2-8 -- Examples of Diseases with Granulomatous Inflammation**

<b>Disease</b>	<b>Cause</b>	<b>Tissue Reaction</b>
Tuberculosis	<i>Mycobacterium tuberculosis</i>	Caseating granuloma (tubercle): focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells; central necrosis with amorphous granular debris; acid-fast bacilli
Leprosy	<i>Mycobacterium leprae</i>	Acid-fast bacilli in macrophages; noncaseating granulomas
Syphilis	<i>Treponema pallidum</i>	Gumma: microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells necrotic without loss of cellular outline
Cat-scratch disease	Gram-negative bacillus	Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon
Sarcoidosis	Unknown etiology	Noncaseating granulomas with abundant activated macrophages
Crohn disease (inflammatory bowel disease)	Immune reaction against intestinal bacteria, self-antigens	Occasional noncaseating granulomas in the wall of the intestine, with dense chronic inflammatory infiltrate

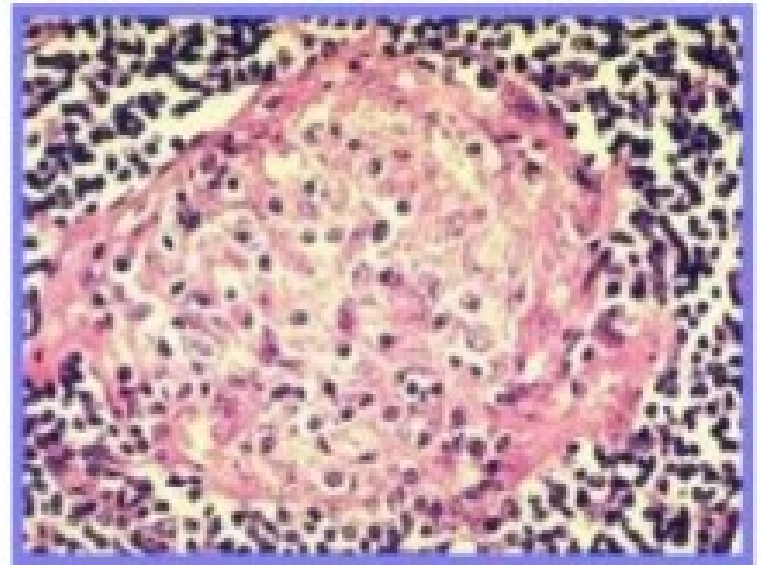
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Sarcoidosis is a multisystem disorder of unknown etiology characterized by non caseating granuloma which affects mainly lungs but can also occur in other organs .



**Caseating granulomas**  
**TB**



**Non caseating granulomas**  
**Sarcoidosis**



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**THANK YOU FOR YOUR  
ATTENTION**



**YESSSS. FINALLY OVER!**