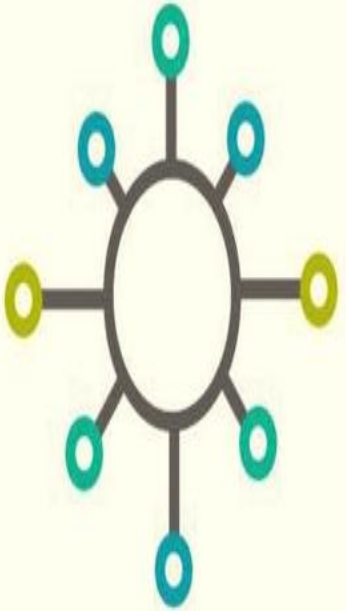


PATHOLOGY
TEAM 436

MEDICINE

KING SAUD UNIVERSITY

GRANULATION TISSUE

What is granulation tissue:

- It is a non specific part of repair response which contains: new blood vessels, fibroblasts, mononuclear cells in an edematous extracellular matrix.
- Granulation tissue is usually associated with chronic inflammation.
- It is a healing phase that follows the acute inflammation.

How is it formed:

- First, we find **acute and chronic inflammatory cells** in the edematous interstitial tissue.
- After the end of acute inflammation period the acute inflammatory cells leave and the inflamed interstitial tissue is dominated by chronic inflammatory cells.
- At the end the fibroblasts dominate the interstitial tissue.

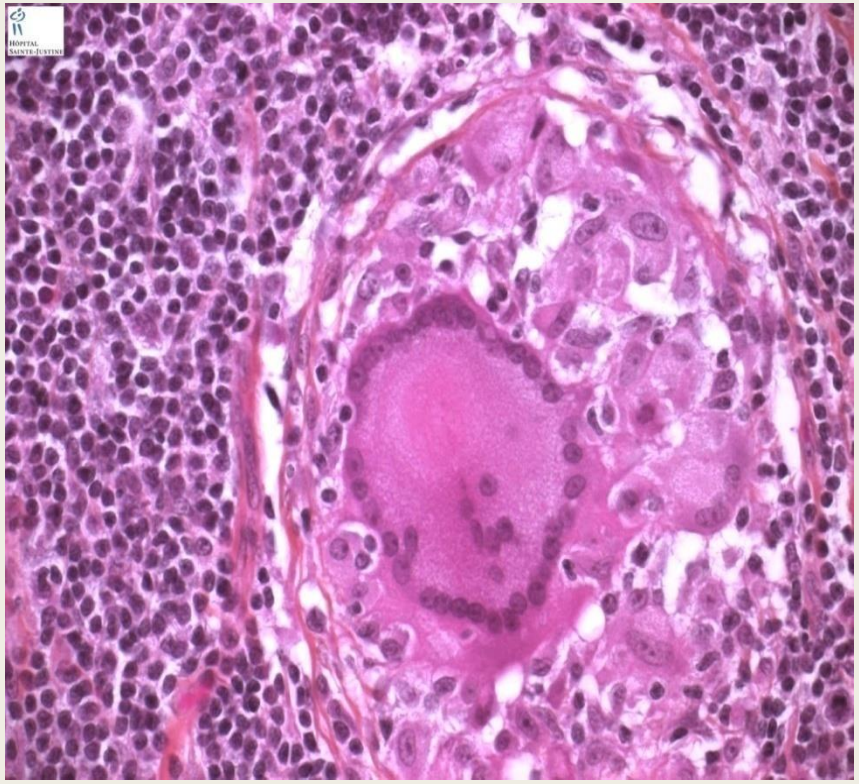
GRANULOMATOUS INFLAMMATION

What is granulomatous inflammation:

- It is a form of chronic inflammation which is characterized by aggregation of **activated macrophages** with **lymphocytes.**
- When we say granuloma we mean granulomatous inflammation.
- Granuloma: is a nodular collection of **epithelioid macrophages** **which are** **surrounded by a rim of lymphocytes**. The reason behind calling them epithelioid macrophages is because the have squamous cell-like appearance.
- There are limited diseases that can cause granulomas thus we need to recognize granuloma very well.

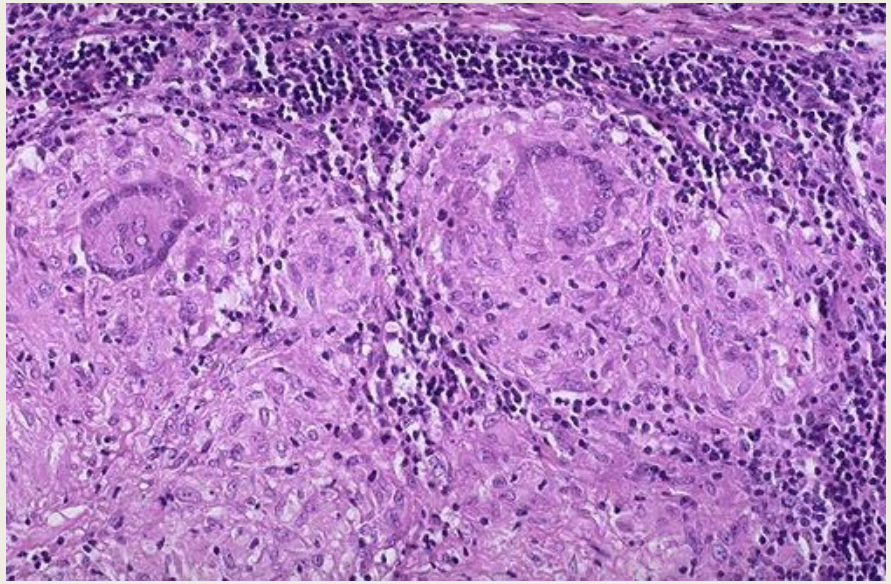
Morphology of granuloma:

- Activated macrophages in granulomas have pink, granular cytoplasm with unclear cell boundaries; these are called **epithelioid cells**.
- The aggregation of these cells are surrounded by a **rim of lymphocytes**.
- Multinucleated giant cells are found in granulomas.
- Older granulomas may have a rim of fibroblasts and connective tissue.
- In granulomas associated with certain infectious organisms (mostly tubercle bacillus), a combination of hypoxia and free radical injury leads to a central zone of **caseous necrosis**.

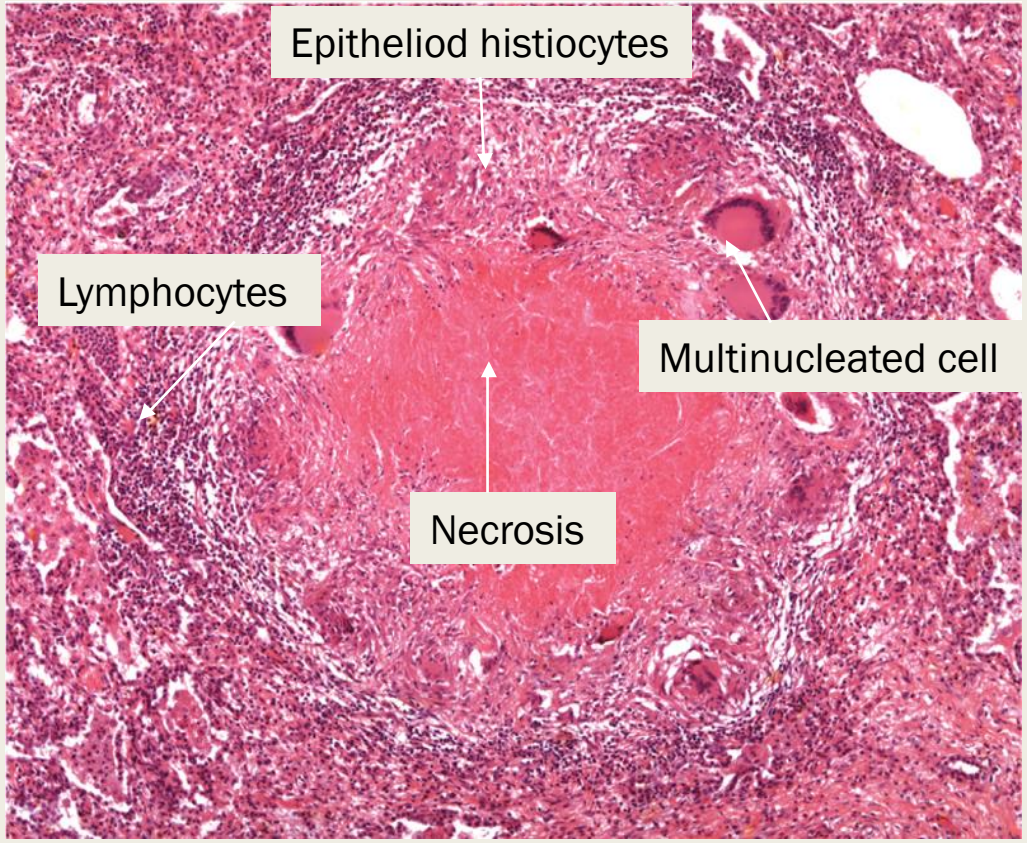


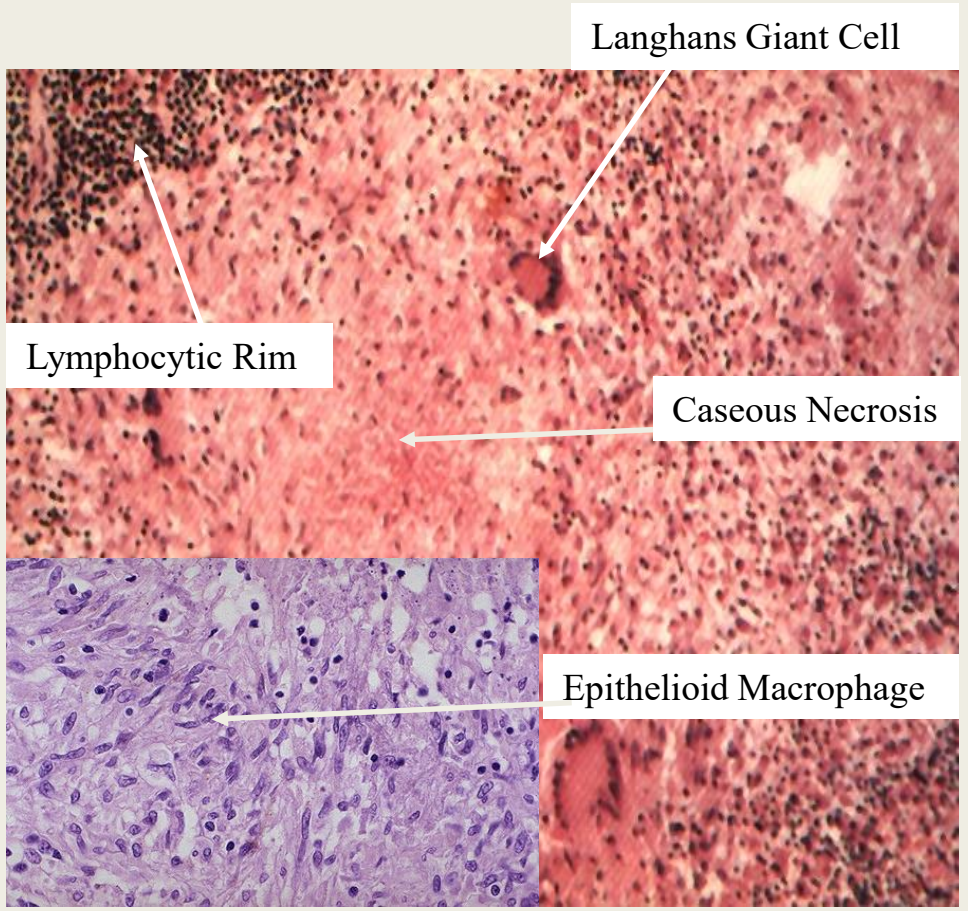
Morphology of granuloma:

- It appears as eosinophilic amorphous, structure less, granular debris, with complete loss of cellular details.
- The granulomas associated with Crohn disease, sarcoidosis, and foreign body reactions tend to not have a caseous necrotic centers.



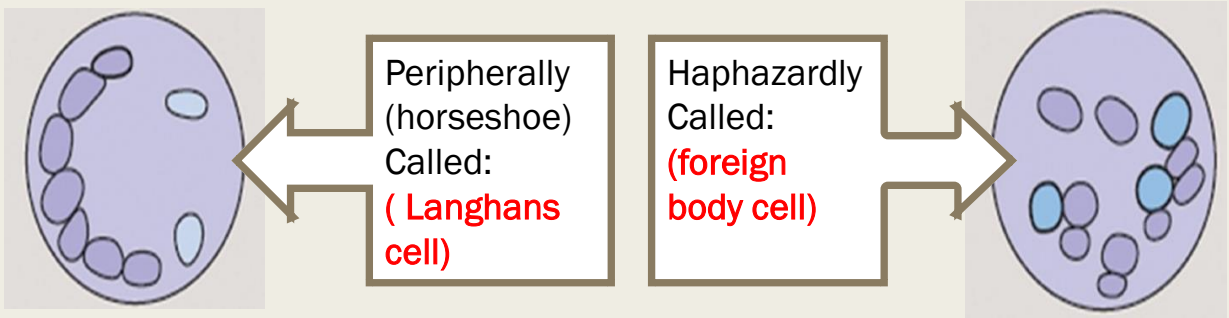
Morphology of granuloma:





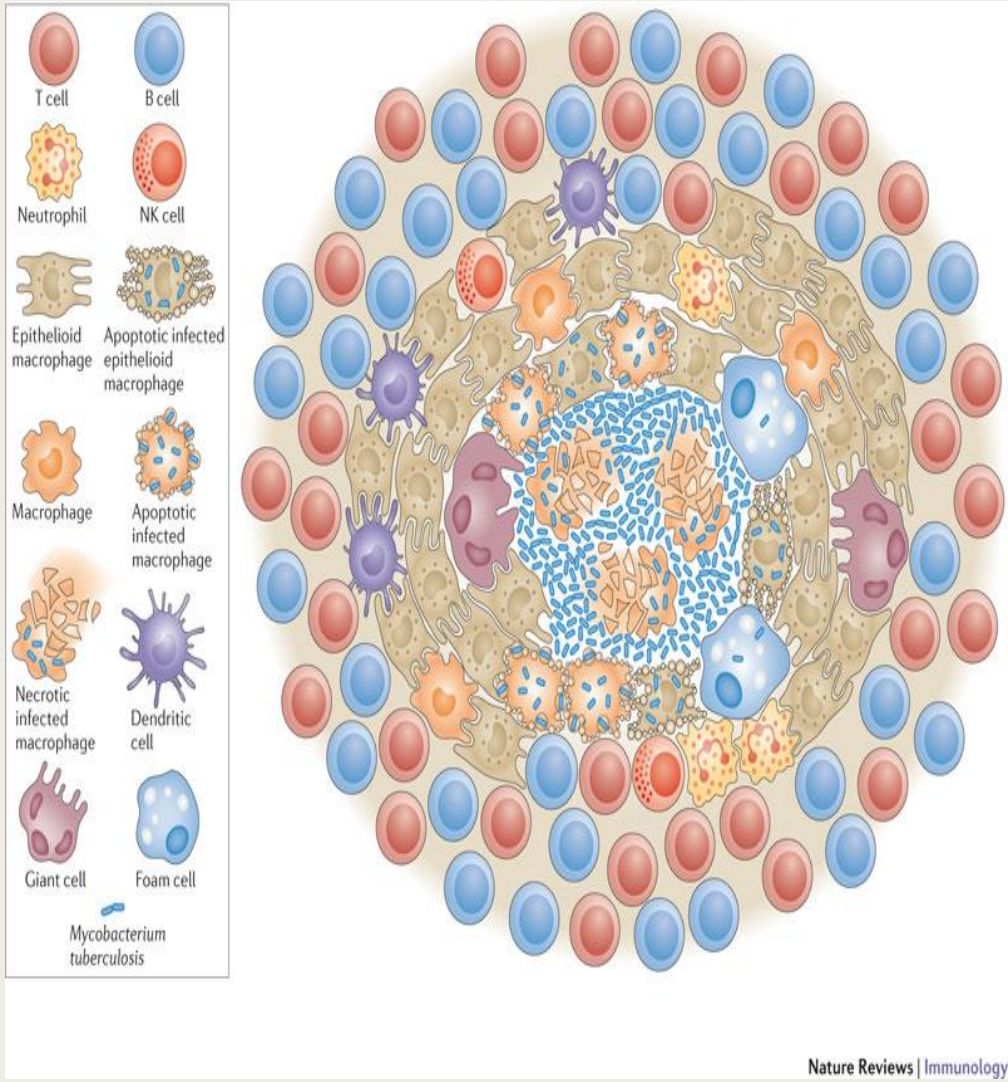
Distinctive cells found in granuloma:

- Epithelioid cells: are activated macrophages that resemble an essential characteristic of granuloma and are surrounded by a rim of lymphocyte.
- Giant cells (Langhans cells): multinucleated cells form from the cytoplasmic fusion of the cytoplasm of macrophages.
- Giant cells nuclei are arranged in two ways:



- Don't mix up langhans cells with langerhan's cells which are antigen presenting cells.
- Note that histiocytes and macrophages are the same.
- Fibroblasts: older granuloma may have a rim of fibroblasts and connective tissue.
- Lymphocytes: mediate cellular immune response.
- Macrophages: phagocytose the injurious agent
- Monocytes.

Granuloma of TB



Pathogenesis of granulomatous inflammation:

- 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.
- When neutrophils fail to digest the antigen, the CD4+ T cells release INF-γ to activate the macrophages which is going to:
- 1- phagocytize the antigen which is in this case survive the digestion thus they become infected, danger resembling macrophages.
- 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 of immune type granulomatous inflammation is known as type IV hypersensitivity reaction

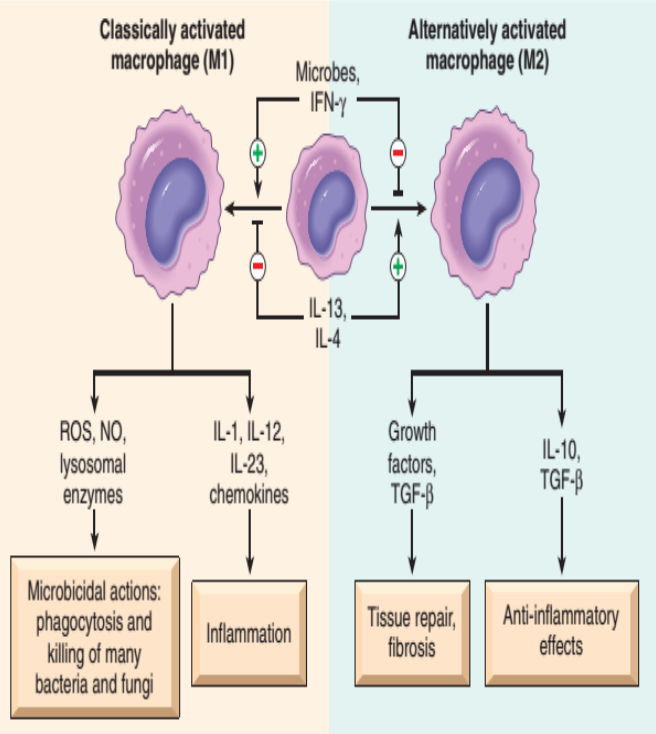


Figure 2–21 Pathways of macrophage activation. Different stimuli activate monocytes/macrophages to develop into functionally distinct populations. Classically activated macrophages are induced by microbial products and cytokines, particularly IFN-γ, and are microbicidal and involved in potentially harmful inflammation. Alternatively activated macrophages are induced by IL-4 and IL-13, produced by T_H2 cells (a helper T cell subset) and other leukocytes, and are important in tissue repair and fibrosis. IFN-γ, interferon-γ; IL-4, IL-13, interkeukin-4, -13.

Types of granuloma:

Non-immune granuloma

- Aroused by relatively immobile foreign bodies.
- Foreign body granuloma forms when material such as, suture , are large enough to block phagocytosis.
- These materials don't provoke any specific inflammatory immune response.
- Can be identified in the center of the granuloma, by polarized light (appears refractile).

Foreign body

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

Immune granuloma:

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

Bacteria

- ***Tuberculosis***
- ***Leprosy***
- ***Actinomycosis***
- ***Cat-scratch disease***

Parasites

- ***Schistosomiasis***
- ***Leishmaniasis***

Fungi

- ***Histoplasmosis***
- ***Blastomycosis***

Metal/Dust

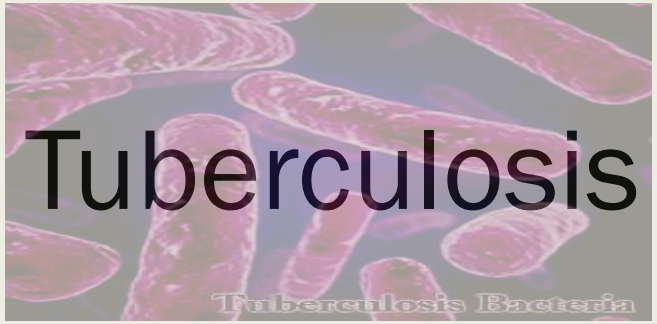
- ***Berylliosis***

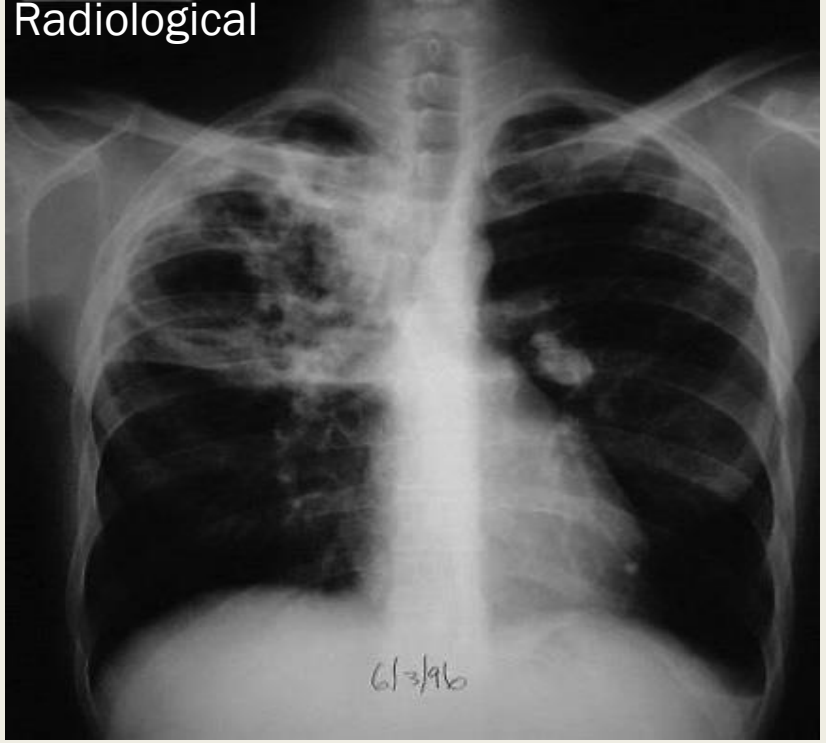
Diseases with granulomatous inflammation:

Table 2–8 Examples of Diseases with Granulomatous Inflammation

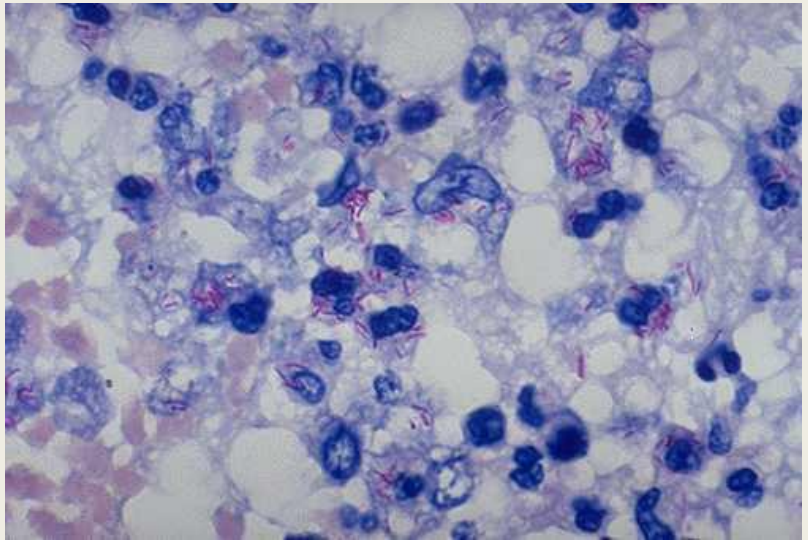
Disease	Cause	Tissue Reaction
Tuberculosis	*Mycobacterium tuberculosis*	Caseating granuloma (tubercle): focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells; central necrosis with amorphous granular debris; acid-fast bacilli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

Tuberculosis

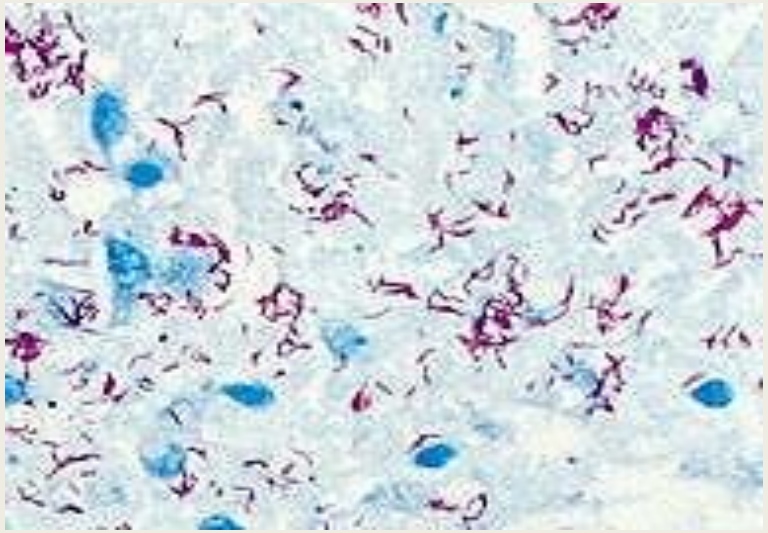




- *Mycobacterium tuberculosis*
- Mycobacteria means (fungus like).
- slender rods shaped.
- acid fast bacilli [AFB] (i.e. they have a high content of complex lipids that readily bind the Ziehl-Neelsen [carbol fuchsin] stain and subsequently resist decolorization).



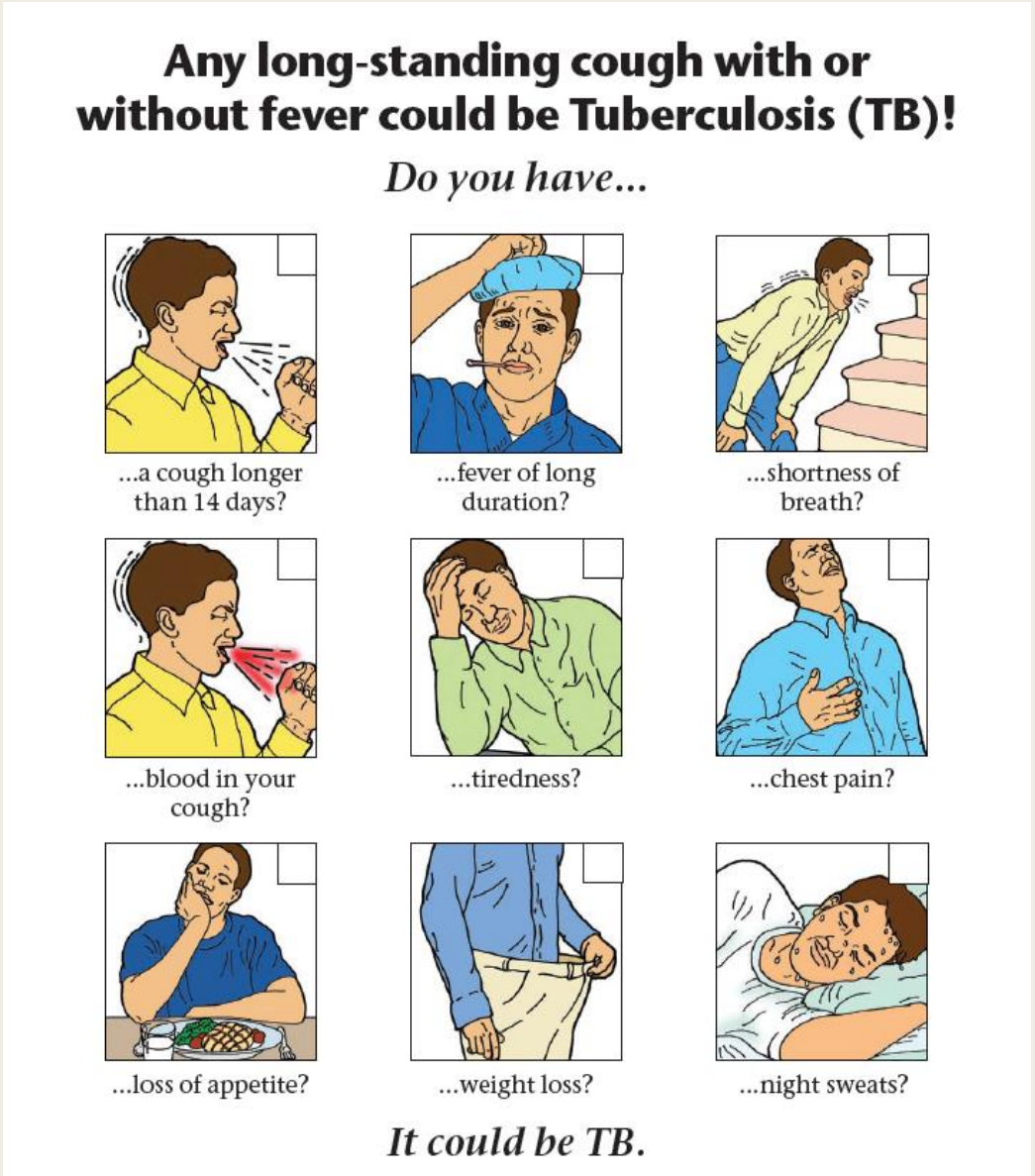
Under Microscope



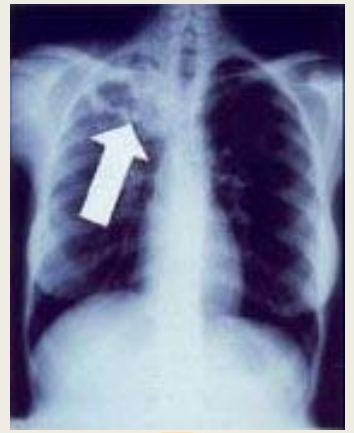
Pathogenesis of TB:

- Cord factor: it is a glycolipid molecule found in the cell wall of **Mycobacterium tuberculosis** and similar species.
- It protects mycobacterium tuberculosis from the defenses of the host.
- Cord factor presence increases the production of:
- 1. cytokines Interleukin-12 (IL-12)
- 2. IL-1β
- 3. IL-6
- 4. Tumor necrosis factor (TNF).

Signs, symptoms and diagnosis of TB



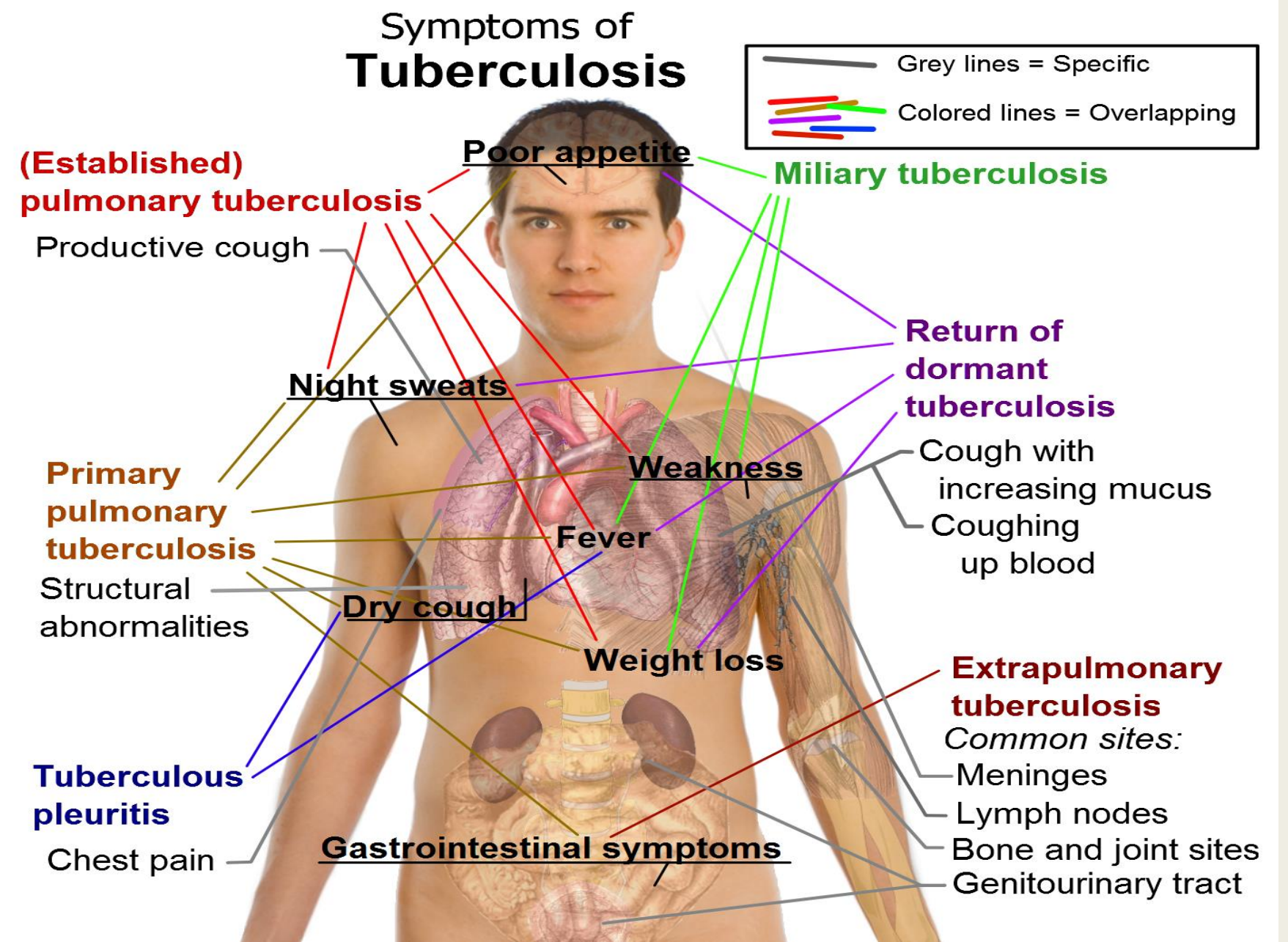
- X-ray



- Sputum smear microscopy

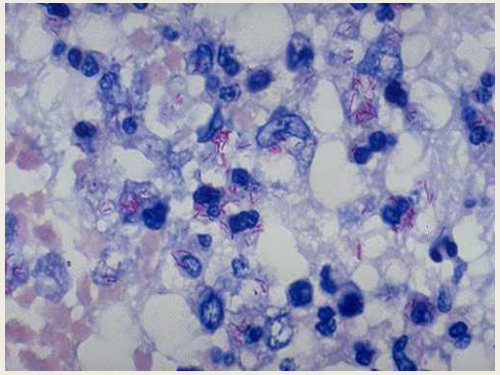
- Culture

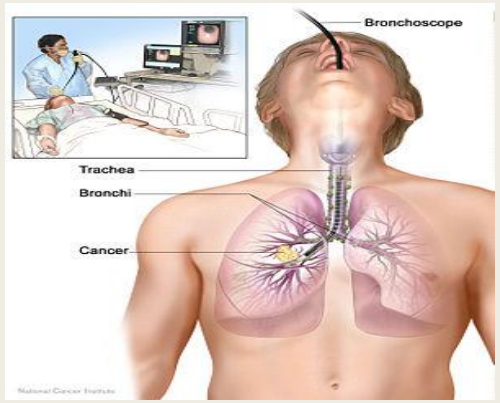
Symptoms of TB:

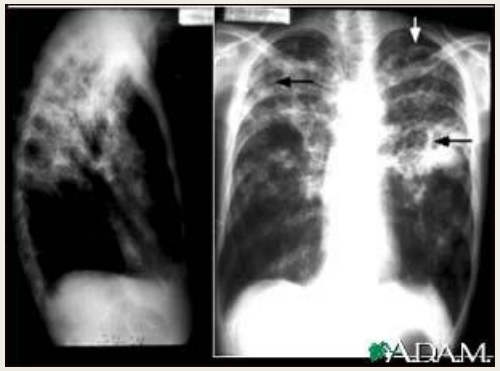


Diagnosis of pulmonary TB:

- *Sputum smear Acid fast stain (>10,000 CFU/ml)*
- *Bronchoscopy*
- *Chest X-Ray*
- *Tuberculin skin testing (TST)*







Team Leaders:
Fahad Alzahrani – Ashwaq Almajed

Boys:

+Abdulaziz Al-Hussainy

+Faisal Algharbi

+Abdulaziz AlMohammed

+Abdullah Altwiraqi

+Abdullah Al-Aseri

+Abdullah Bassam

+Essam Alshahrani

+Fahad Alaskar

+Faris Aljaafar

+Mohammed Hakami

+Mohammed Almania

+Moayed Ahmed

+Moataz Altokhais

+Waleed Almajlad

+Waleed Al-askah

Girls:

+Nehal Beyari

+Najd AlTheeb

+Muneerah Alzayed

+Atikah Kadi

+Ghada AlHadlaq

+Atheer AlRsheed

+Amal AlShaibi

+Haneen Alsubki

+Doaa Walid

+Rania Alessa

+Raneem Alghamdi

+Reema Alshayie

+Ghadah Almazrou

+Fatimah AlTassan

+Lama AlTamimi

+Njoud Alenezy

+Aldanah Almutib

+Ghadah AlMuhana

+Deena AlNowiser