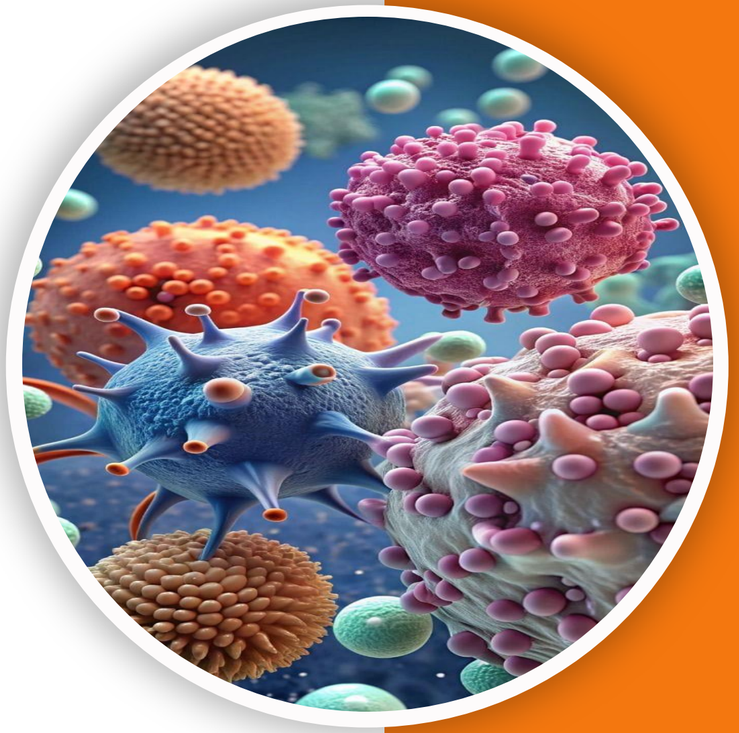
بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Microbiology | Lecture 14

Mycobacterium (Larger Text Size)



Done By : NST Fighter

Mycobacteria

By: Assis. Prof. Nader Alaridah

Mycobacteria

Family of bacteria

- One of the most infectious diseases that has exhausted humanity.
- Three diseases that has exhausted humanity the most :

1) HIV (AIDS).
2) Malaria.
3) **Tuberculosis ;** which is caused by *Mycobacterium.*

Mycobacteria

Mycobacteria is a family of bacteria that i**ncludes 3 sub families** under it (each one cause a different disease) :

1) *Mycobacterium tuberculosis complex* **(MTC) ;** causes **tuberculosis (**السُّل**).**

2) *Mycobacterium leprae* **;** causes **leprosy** (also called Hanson disease),(الجُذام). → can be distinguished by Lion-like faces of infected patients.

3) *Non-tuberculosis mycobacteria* (NMT) ; also called environmental mycobacteria, also other name is *Atypical mycobacteria*, it includes *Mycobacterium avium-intracellulare* (MAI, also called *avium complex,* or MAC).

Background

- The mycobacteria are **rod-shaped** (bacillus), **aerobic** bacteria that do **not form spores**.
- Mycobacteria are **Acid-fast bacilli (AFB) ;** mycobacteria isn't stained by Gram positive nor Gram negative stain; they are identified by acid-fast staining.
- ***Mycobacterium tuberculosis complex*** (MTC) a genetically related group of Mycobacterium species that **can cause tuberculosis in humans.**

- ***Mycobacterium leprae*** causes **leprosy**.

- ***Mycobacterium avium-intracellulare*** (M avium complex, or MAC) and other **nontuberculous (NTM) mycobacteria** frequently infect patients with **AIDS**, are **opportunistic pathogens in other immunocompromised persons**, and occasionally cause disease in patients with normal immune systems.

Mycobacterium Tuberculosis (Mtb)

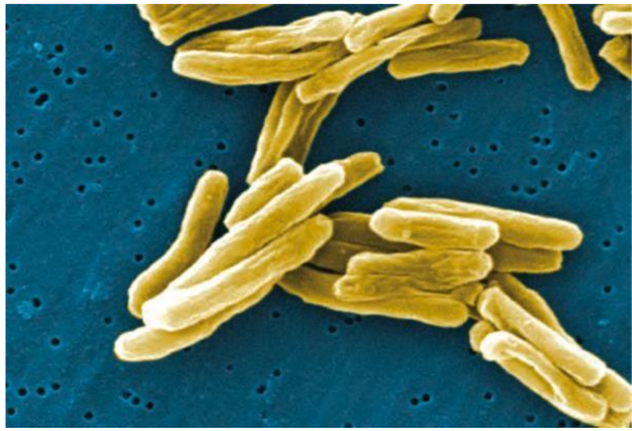
- It was not until the 19th century, when Robert Koch utilized a new staining method (ZN stain) and applied it to sputum from patients discovering the causal agent of the disease Tuberculosis (TB); Mtb or Koch bacillus.

- **It has many Names : Tuberculosis , consumption** (because it **consumes patients,** causing **weight loss**), white plaque (because of extreme pallor (شحوب) seen among patients).

- The family **mycobacterium tuberculosis complex(MTC)** can cause **Tuberculosis (TB) in humans** and other livings (the only thing required from us is in tuberculosis in humans).

- Mycobacterium tuberculosis family includes 11 bacteria : **M. tuberculosis (Mtb)** which is responsible for 70% of tuberculosis cases**,** Mycobacterium **africanum**, Mycobacterium **bovis**, Mycobacterium **microti**, Mycobacterium **caprae**, Mycobacterium **pinnipedii**, Mycobacterium **suricatte**, Mycobacterium **mungi**, Mycobacterium **dassie**, Mycobacterium **oryx** and Mycobacterium **canetti.**

Morphology



- In tissue, **tubercle bacilli** are **thin**, **straight rods** measuring **about 0.3 ~ 3 µ m.**
- Tuberculosis are **intracellular pathogens,** which means that once they are inhaled they get engulfed (phagocytosis) by macrophages inside the cell or circulating monocyte in the circulation and **replicate inside them.**
- True tubercle bacilli are characterized by **"acid fastness"**—that is, **95% ethyl alcohol** containing **3% hydrochloric acid** (acid-alcohol) quickly decolorizes all bacteria except the mycobacteria.
- Mycobacteria are **obligate aerobes** (they need oxygen to produce energy, which explains why 90% tuberculosis cases are pulmonary tuberculosis) and derive energy from the oxidation of many simple carbon compounds.
- The **growth rate** is **much slower** than that of most bacteria. The doubling time of tubercle bacilli is **about 18 hours** (18–24 hours).
- Mycobacteria **tend to be more resistant to chemical agents** (ex. Commonly used disinfectants, we use high concentration of disinfectant to kill them or by sterilisation techniques), **than other bacteria** because of the **hydrophobic nature** (due to **high lipid content**, more than 50% of its dry weight), of the cell surface and **their clumped growth.**

Morphology

Notes :

- Because of tuberculosis slow growth rate (slow doubling time), we need 6-8 weeks to grow them on agar plate.
- Mycobacterium leprea has a slower growth rate than Mycobacterium tuberculosis.
- Mycobacterium leprea **can't** been grown in **VTIRO** (outside a host cell), it only grow in host cell so we use an animal cell model.

Notes :

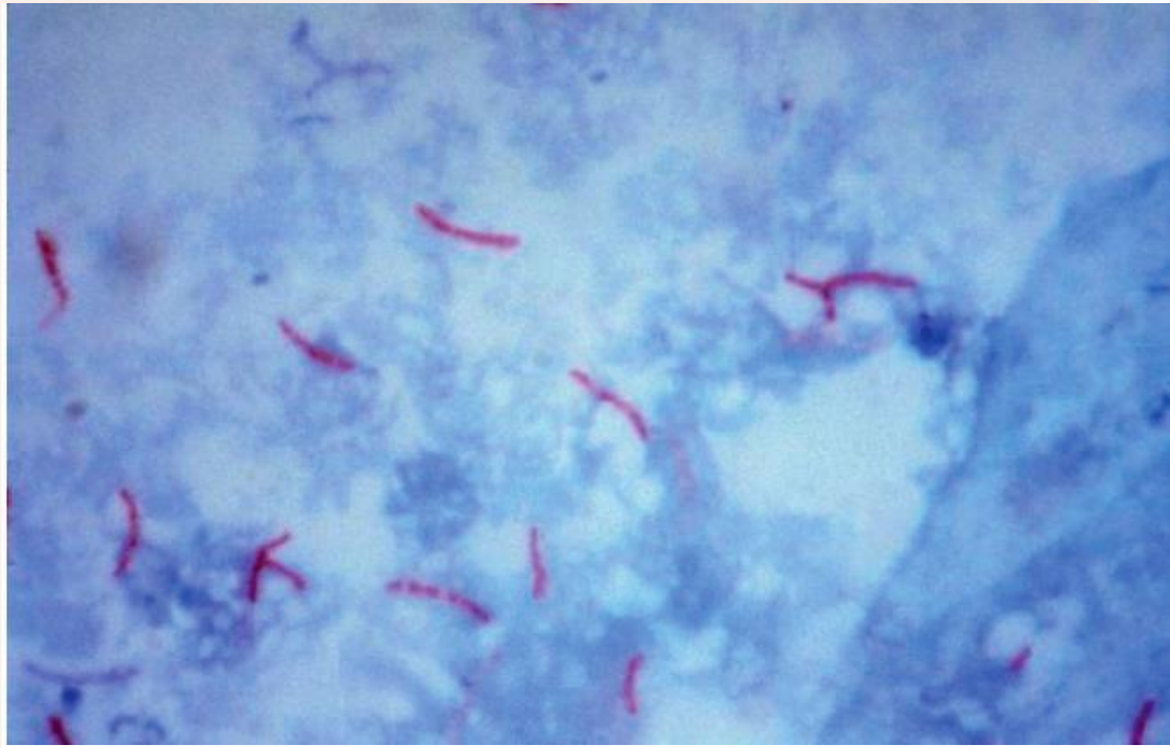
This is a **sputum** sample from a patient infected with tuberculosis.
The sample contains **Mycobacterium tuberculosis (red color)**, which indicates that this patient can infect others (Smer Positive).
If it is **absent**, that **does not** mean the disease is absent – only that the patient is **not** infectious (Smer Negative).

Morphology

Bacilli (slightly curved)

Stain Used

ZN (Ziehl–Neelsen) stain



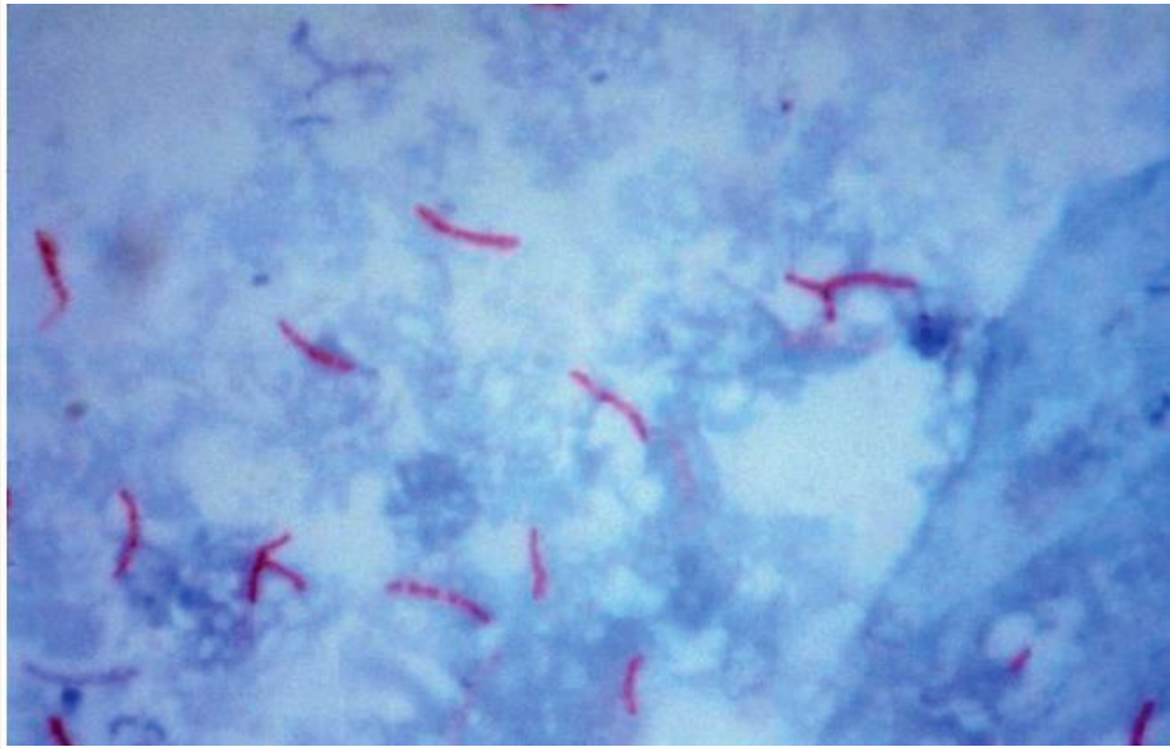
Notes :

Staining Principle

Carbol fuchsin is used to stain the bacteria.
Then, a strong decolorizer (95% ethyl alcohol containing 3% hydrochloric acid – acid-alcohol) is applied to wash out the stain.

However, in Mycobacterium, the stain **is not washed out due to the bacterium's thick lipid layer.**
Therefore, these bacteria are called **acid-fast (because they fast from the acid |** لإنهم يصوموا من الحمض**).**

If we apply a counterstain, Mycobacterium **will not** take up this new stain and will retain its already stained red colour.



Mtb Culture : the gold standard for tuberculosis diagnosis.

- The media for primary culture of mycobacteria should include a **nonselective medium and a selective medium.**

➢ There are **3 systems** for tuberculosis culture :

1) Inspissated egg media (egg based media)— These media (eg, Löwenstein- Jensen) contain defined

salts, glycerol, and complex organic substances (eg, fresh eggs or egg yolks, potato flour, and other

ingredients in various combinations.

- **The inspissated egg** media has developed to **Semisynthetic agar media.**

2) Semisynthetic agar media— These media (eg, **Middlebrook 7H10 and 7H11**) contain defined salts, vitamins, cofactors, oleic acid, albumin, catalase, and glycerol.

Mtb Culture : the gold standard for tuberculosis diagnosis.

- The problem with the **inspissated egg** media and the **semisynthetic media** problem is that they **take long time (about 1 month) for forming colonies of Mycobacteria,** which make diagnoses of the disease or infection take long time.

Mtb Culture : the gold standard for tuberculosis diagnosis.

- There are **3 systems** for tuberculosis culture :

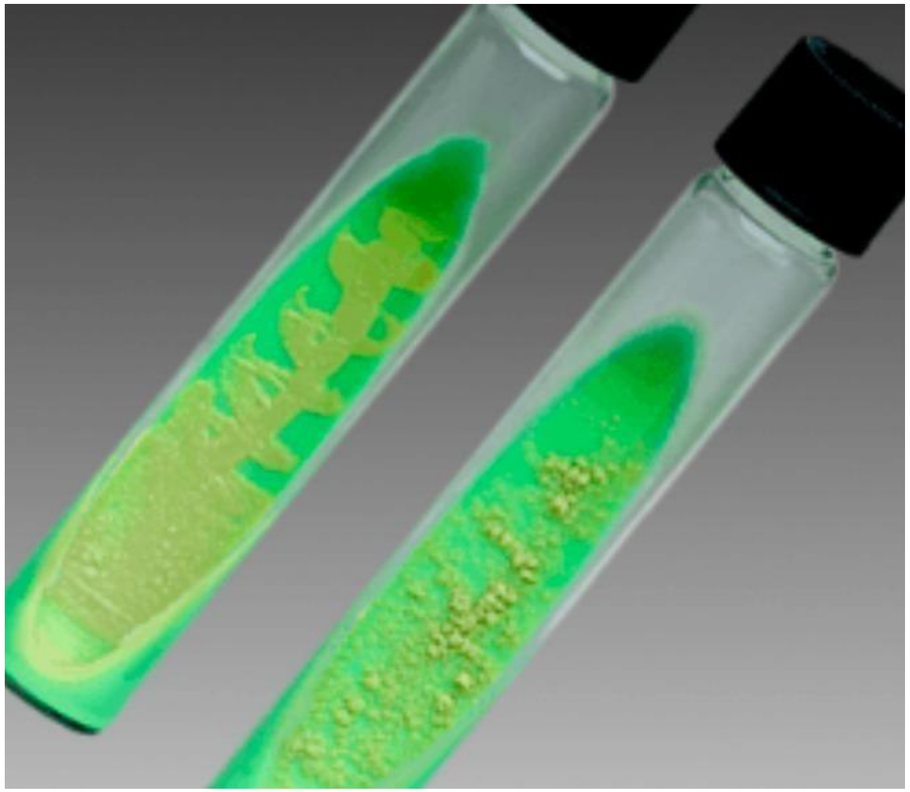
3) **Broth media**— A fluid based system (eg, Middlebrook 7H9 and 7H12) support the proliferation of small inoculate.

- Broth media allows us to diagnose tuberculosis in almost 10 days which fasten the diagnosis process.

Even if Mycobacteria colonies are not found, it does not mean the absence of the disease, but rather the absence of Mycobacteria in the sample taken.

Mtb Colonies

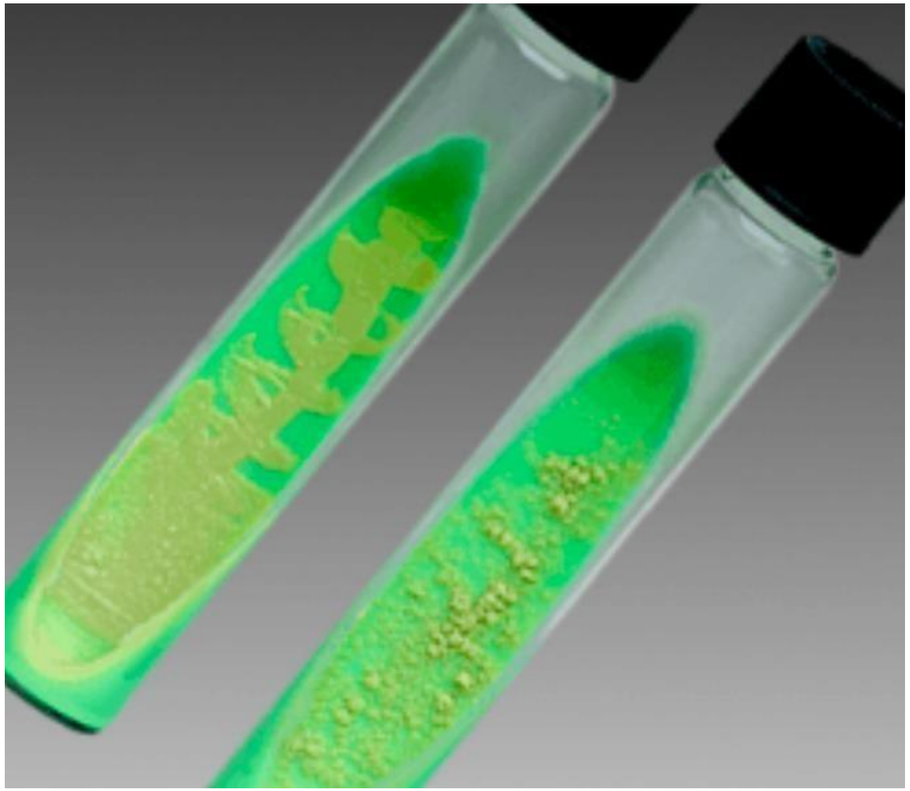
Löwenstein-Jensen (LJ) Medium



- It is an **egg-based (inspissated egg) medium** used for the **culturing** of ***Mycobacterium* species.**
- It can be recognized by its distinct **green color**, which comes from **malachite green.**
- **Malachite green** serves as a **selective agent** that:
  - **Inhibits** the growth of the bacteria **normal flora.**
  - **Allows** the growth of **pathogenic mycobacteria**, such as ***Mycobacterium tuberculosis.***

Mtb Colonies

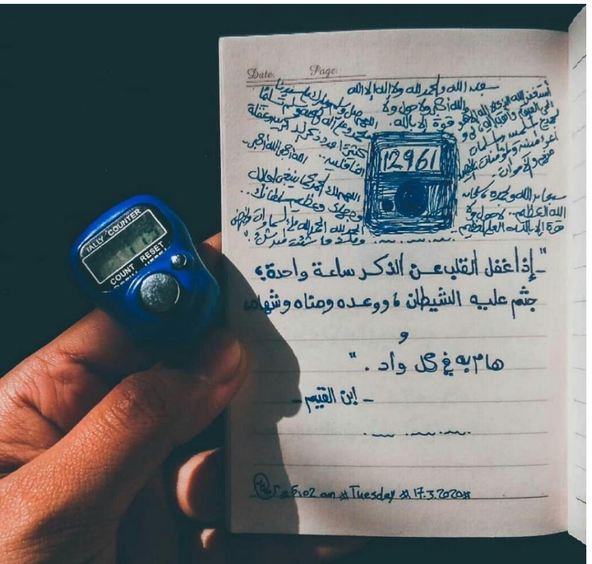
- This selective property is particularly useful because most tuberculosis cases (about 90%) are pulmonary, and **sputum samples from the lungs often contain abundant normal flora.**



Mtb Colonies

Middlebrook 7H10 and 7H11

- It is a **semisynthetic medium**
- Colonies have a distinct shape which is **rough, dry, and crimped.**



الزمه فإنه لك منجاة

Mtb Cell wall

High lipid content and waxes.

- The mycobacterial cell wall is a complex structure that is required for cell growth, resistance to antibiotics and virulence.

- It consists of an **inner layer** and an **outer layer** that surrounds **the plasma membrane** (Two layers rather than plasma membranes).

- The inner compartment is composed of **three distinct macromolecules** — **peptidoglycans (PG), arabinogalactans (AG) and mycolic acids (MA)** (MA are long chain fatty acids (78–90 carbon)— covalently linked (Heavily cross linked) together to form a complex known as the MA-AG-PG complex.

- The peptidoglycan layer surrounds the plasma membrane and comprises long polymers of the repeating disaccharide **N-acetyl glucosamine–N-acetyl muramic acid (NAG–NAM)** that are **linked via peptide bridges.**

Mtb Cell wall

- Most of the arabinan is ligated with long-carbon-chain mycolic acids, which form the characteristic thick waxy lipid coat of mycobacteria and are major contributors to the impermeability of the cell wall and to virulence.

- **Mycolic acids (long-chain fatty acids C78–C90)**, waxes, and phosphatides , can be found in Mtb cell wall and **make up 50%** of the dry weight of the mycobacterial cell envelope.

- These mycolic acids are esterified to glycerol and trehalose where trehalose can contain one or two molecules of mycolic acids forming **trehalose dimycolates (TDM) (Cord Factor)** **responsible of cirbintine growth** (When Mycobacteria are grown in broth media, they form rope-like structures known as cord. Mycobacteria clump to the cord forming clusters all along the cord) and **trehalose monomycolates (TMM).**

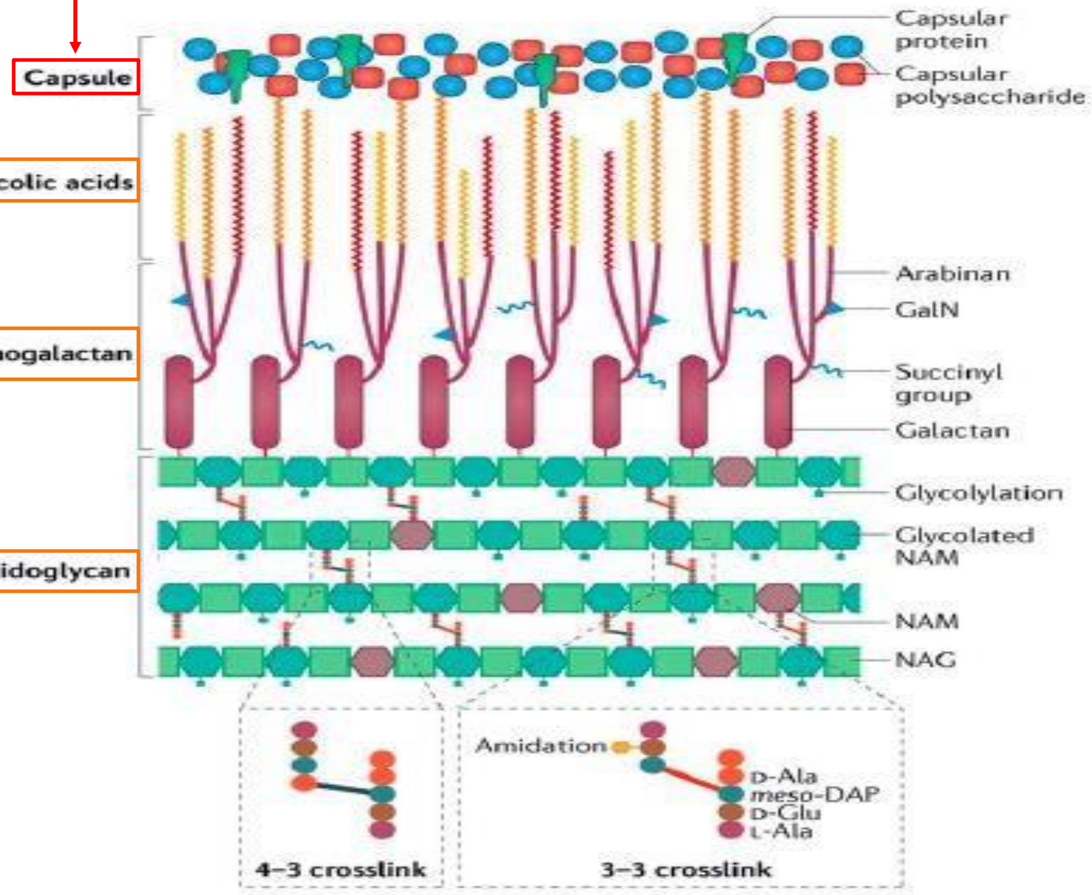
Misnomer ; mycobacteria is not capsulated, this is a capsule like layer composed of proteins, lipids, and polysaccharides.

Mycobacterium are named like this due to their unique cell wall component **Mycolic acid.**

They have many of the mycobacterium **virulence factors.**

Peptide chains heavily **cross linked** by **NAG & NAM.** Like peptidoglycan of Gram positive bacteria .

Mtb Cell wall

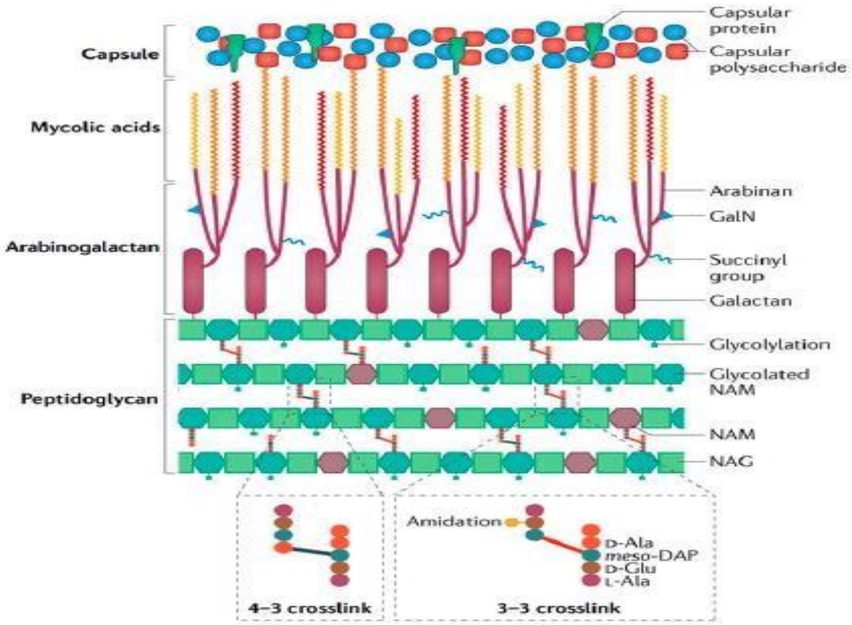


Mycobacterium are non-toxin activity bacteria, they don't contain any toxin (like gram negative) and they don't produce any toxin material.

contain major phosphatidylinositol mannosides (PIMs), which play roles in immune modulation and virulen

Mtb Cell wall

The Mycobacterium species have two well-known **virulence factors** present in their cell wall:



1) LAM (Lipoarabinomannan).

2) LM (Lipomannan).

These molecules **prevent phagolysosomal fusion,** which is the fusion between the **phagosome (containing the Mycobacterium)** and the **lysosome inside the phagocytic cell.**

They are complex glycolipids composed of arabinogalactan **derived carbohydrates** linked with **lipids from the capsule like** layer of the cell wall.

3) Trehalose dimycolates (TDM) (Cord Factor). (Already explained).

4) Capsule-structure contains many **phosphatidylinositol mannosides (PIMs),** which play roles in virulence.

Epidemiology

- Two TB-related conditions exist; **latent TB infection (LTBI) and TB disease**. If not treated properly, **TB disease can be fatal**. People who have **latent** TB infection **do not feel sick, do not have any symptoms, and cannot spread TB to others, but!** once it gets immunocompromised, they develop active tuberculosis (tuberculosis disease).

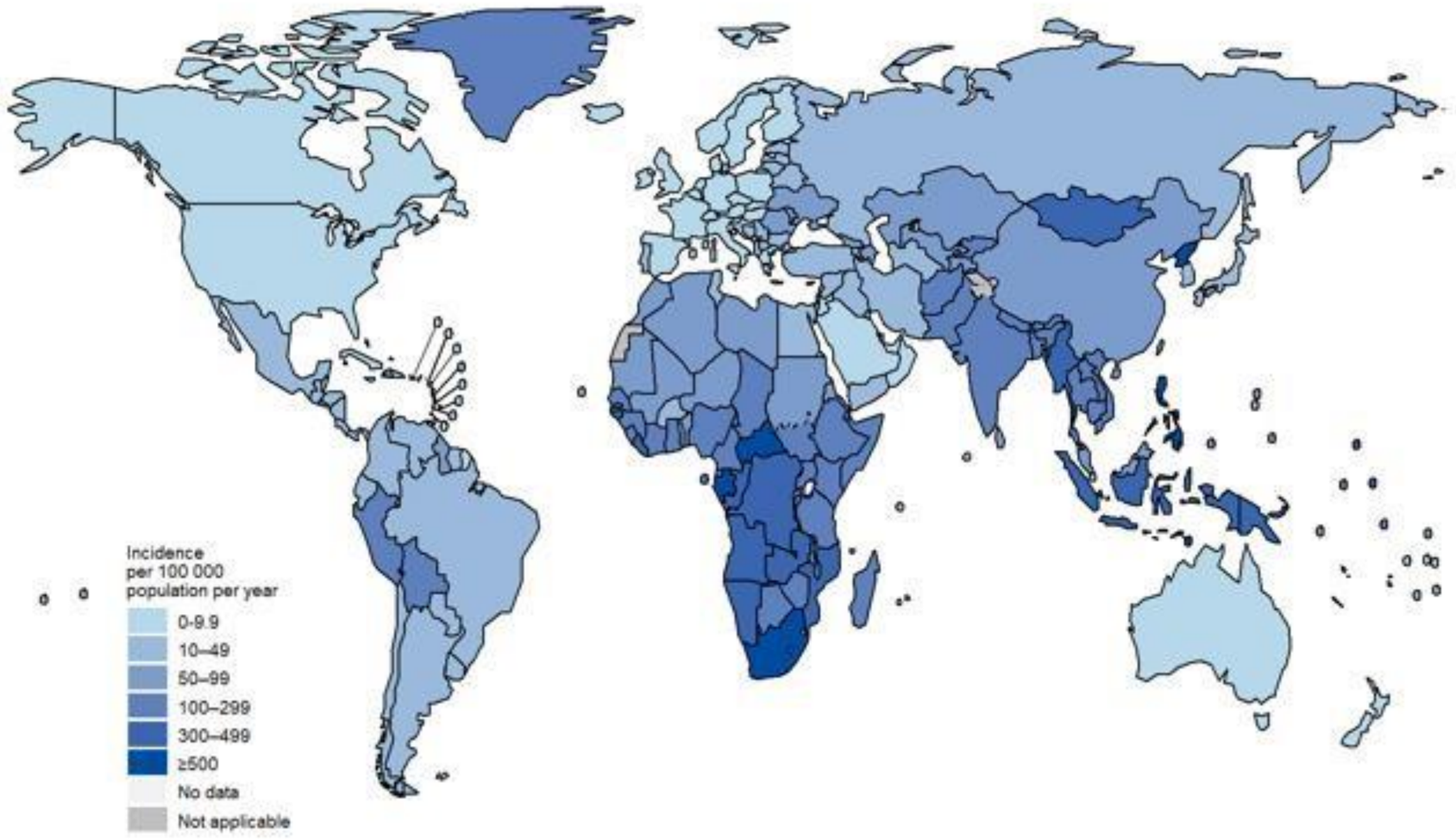
- About **one third** of the worlds population **is infected with TB bacteria (TB latency).**

- However, only **small proportion** of those infected **will become sick with TB.**

- TB remains a leading cause of infectious diseases morbidity and mortality. In 2015, an estimated 10.4 million new TB cases were seen world wide.

- TB is considered an airborne infectious disease although M. tuberculosis complex organisms can be spread **through un-pasteurised milk**, **direct inoculation** and other means.

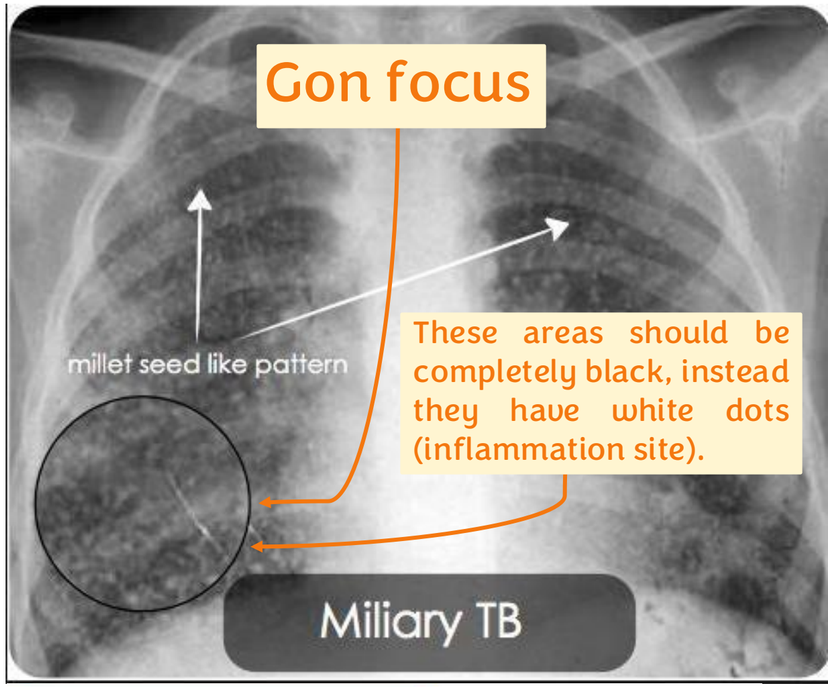
Estimated TB incidence rates, 2020

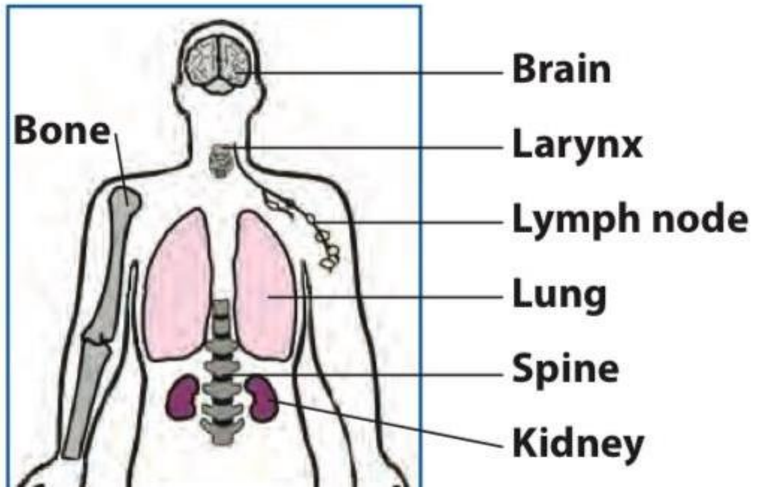


Tuberculosis TB

the mark for tuberculosis is the granuloma formation

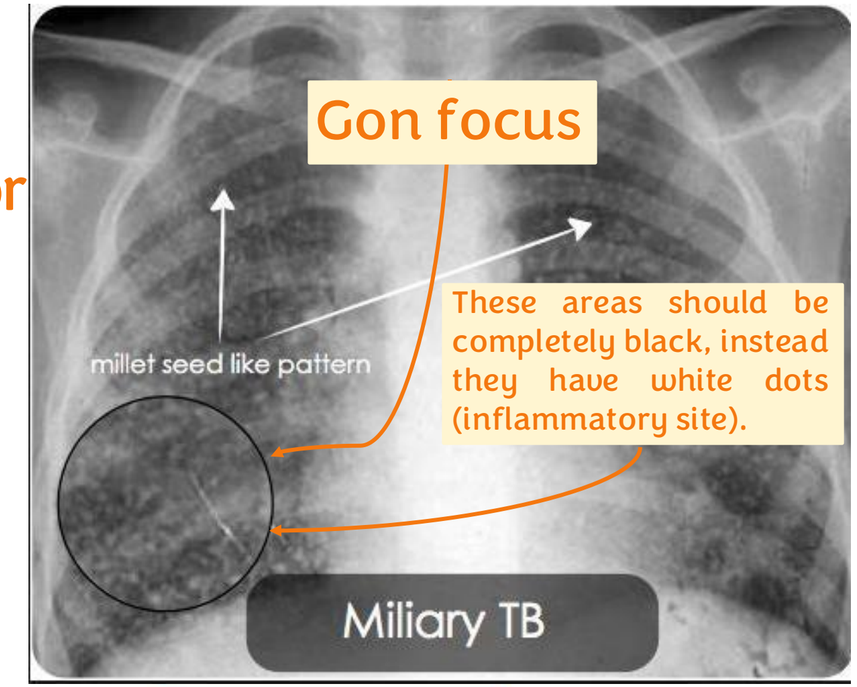
- The **primary site** of TB is usually **lung** (pulmonary, 90% of tuberculosis cases), from which it **can get disseminated into other parts of the body**. The other routes of spread can be contiguous involvement from adjacent tuberculous lymphadenopathy or primary involvement of extrapulmonary organ.
- Spread – Lymphatic vs hematogenous (Miliary).
- **TB bacteria can attack any part of the body** (they prefer well oxygenated organs) such as the pleura ,L.N. ,pericardium, **kidney**, **spine**, **brain** and abdomen (abdominal Tuberculosis) also some of them infect lymphnodes in children causing lymphadenitis collectively known as **extrapulmonary TB** (10% of tuberculosis cases)
- Primary Infection(Active) and Reactivation Types of Tuberculosis.





Tuberculosis TB

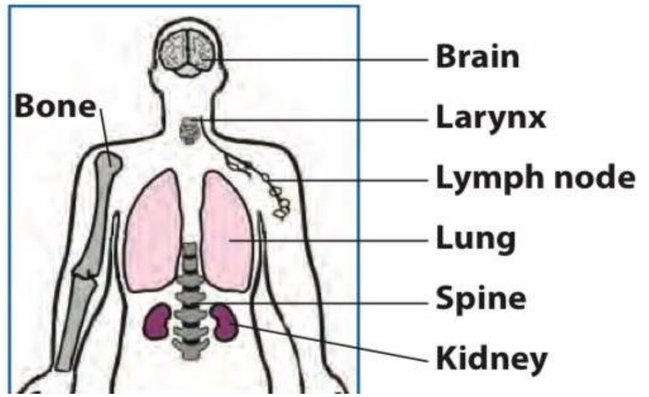
- Spread – Lymphatic vs hematogenous (Miliary).



- Once Mycobacteria are inhaled, they are engulfed (phagocytosed) by macrophages within the lung tissue or by circulating monocytes in the bloodstream. The bacteria are capable of replicating inside these cells.

- The infected macrophages then migrate to the alveoli of the lungs. In response, the immune system attempts to contain the infection by forming a granuloma, which is the hallmark of tuberculosis (TB).

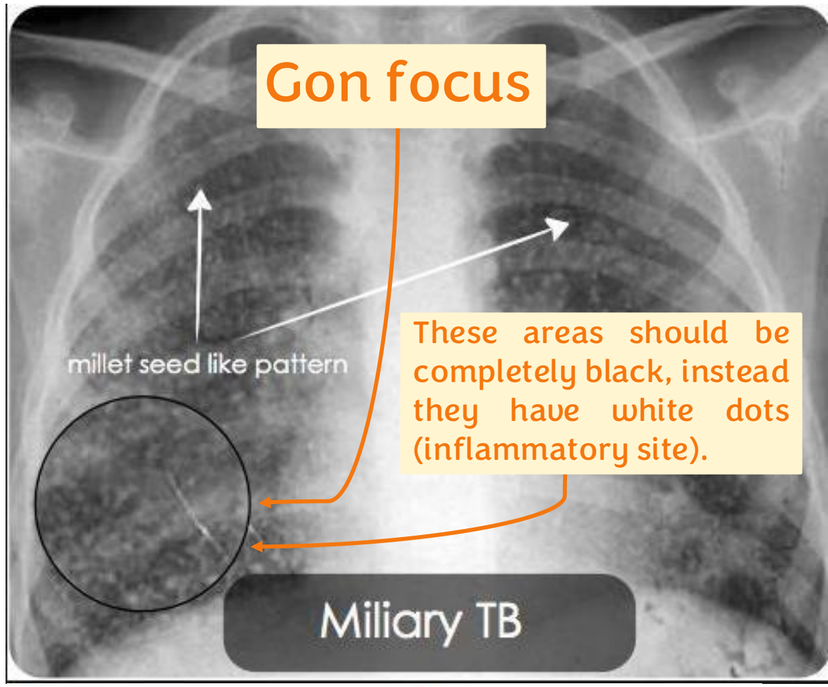
- On chest X-ray, this granuloma appears as a Ghon focus.



- In children, due to their immature immune system, the granulomas (Ghon focus) may erode into nearby structures and lymph nodes. The infection can then spread (disseminate) to other parts of the body – most notably to the brain, where it may cause meningitis, as the blood-brain barrier (BBB) is also still immature in children.

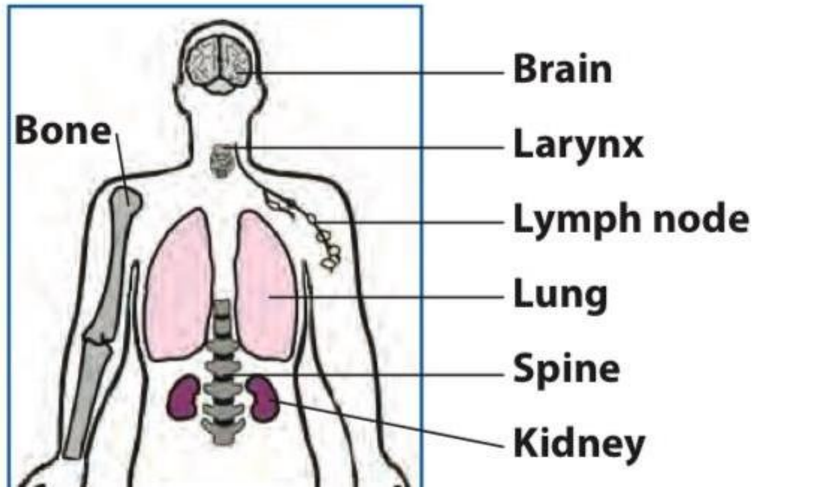
Tuberculosis TB

- Spread – Lymphatic vs hematogenous (Miliary, since they appear at the chest. X-ray as a milt seeds like pattern).



When the infection involves both the primary lung lesion and the regional lymph nodes, the lesion is referred to as a Ghon complex.

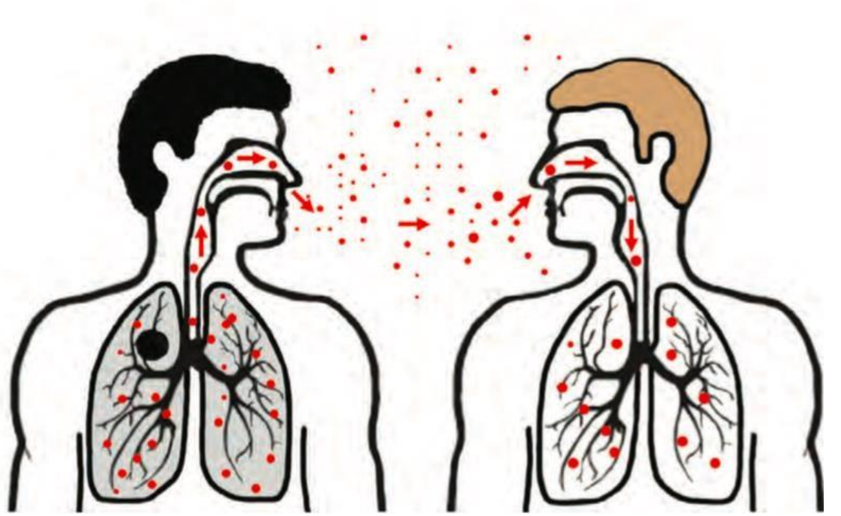
Mycobacterium tuberculosis infection can either:
Begin in the lungs and later spread to other organs (secondary infection), or
Directly involve extrapulmonary sites without showing any pulmonary symptoms.



In contrast, Mycobacterium bovis mainly causes extrapulmonary tuberculosis, often affecting the abdomen, since it is usually transmitted through ingestion of contaminated milk.

Transmission

Polmunary tuberculosis mainly transmitted through Generated irozoles, Droplet nuclei, coughs, and sneezes.



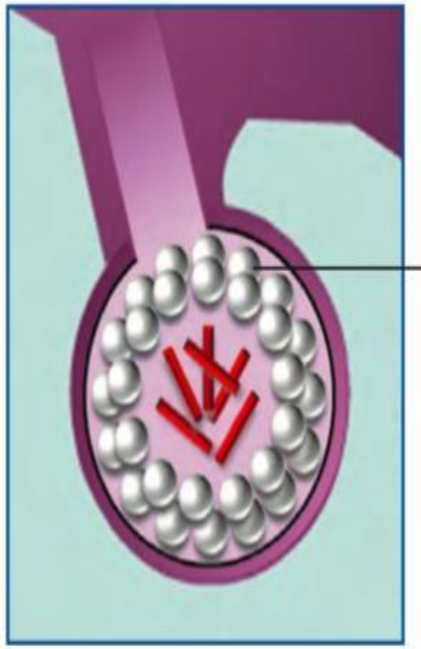
- TB is considered an airborne infectious disease although M. tuberculosis complex organisms **can be spread through unpasteurised milk, direct inoculation and other means.**

- The underlying pathophysiology of TB is the "**10/3/1 formula.**

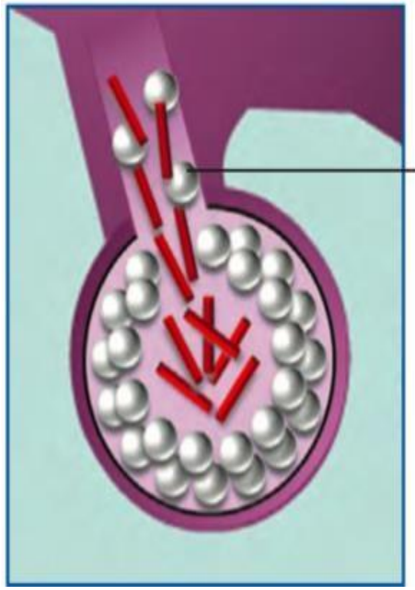
For every 10 people, 3 have latent tuberculosis, one have tuberculosis disease, and 6 of them don't have any form of tuberculosis (their immune system get rid of them somehow ☺).

Pathogenesis

- Mycobacteria are in droplets when infected persons cough, sneeze, or speak. The droplets evaporate, leaving organisms that are small enough, when inhaled, **to be deposited in alveoli**
- Inside the alveoli, the host's immune system responds by **release of cytokines and lymphokines that stimulate monocytes and macrophages.**
- Mycobacteria **begin to multiply within macrophages.** Some of the macrophages develop an enhanced ability **to kill the organism**, but others **may be killed by the bacilli.**
- The cells form a barrier shell, called a **granuloma**, that keeps the bacilli contained and under control **(LTBI**).
- If the immune system **cannot** keep the tubercle bacilli under control, the bacilli **begin to multiply rapidly** (**TB disease).**



Special immune cells form a barrier shell (in this example, bacilli are in the lungs)

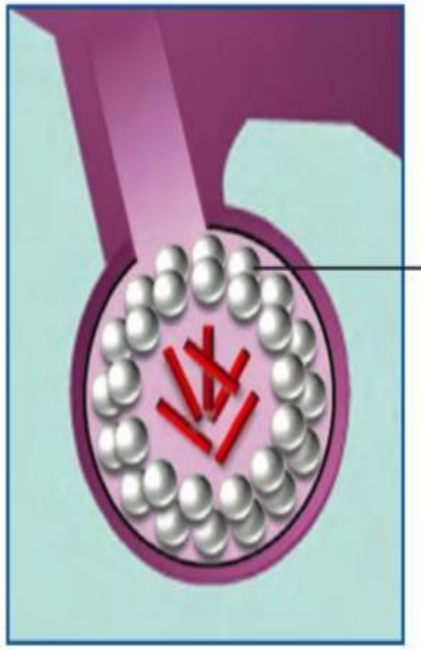


Shell breaks down and tubercle bacilli escape and multiply

Pathogenesis

- If the macrophages **succeed in killing Mycobacterium tuberculosis**, this will be followed by **healing of the granuloma (previously seen on the X-ray image).**

- The healing can occur either by **absorption or calcification,** which may result in **caseous necrosis**, which result in **alveoli opening,** leading to **spread of the bacteria to nearby tissues, lymph nodes, and then disseminate to other organs of the body** if the infection is not fully controlled.



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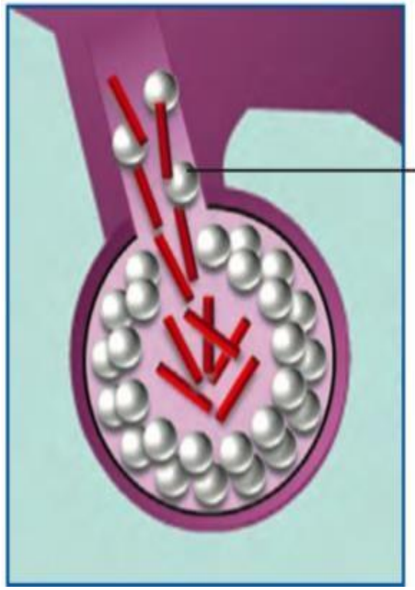


Shell breaks down and tubercle bacilli escape and multiply

Pathology

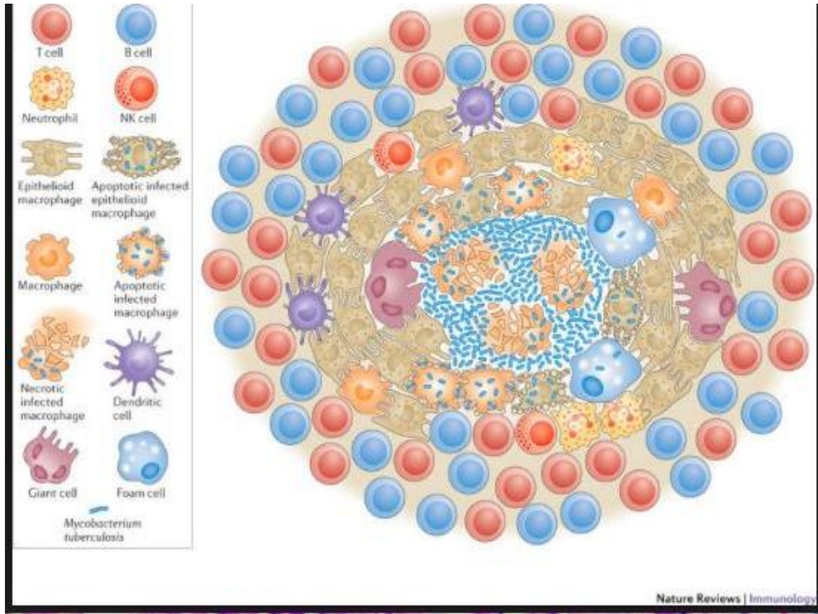
- **Exudative type**—This consists of an **acute inflammatory reaction** with **edema fluid**; polymorphonuclear leukocytes (neutrophils) ; and, later, monocytes around the tubercle bacilli, trying to contain the mycobacteria. This type is seen particularly in lung tissue, where it resembles bacteria pneumonia.

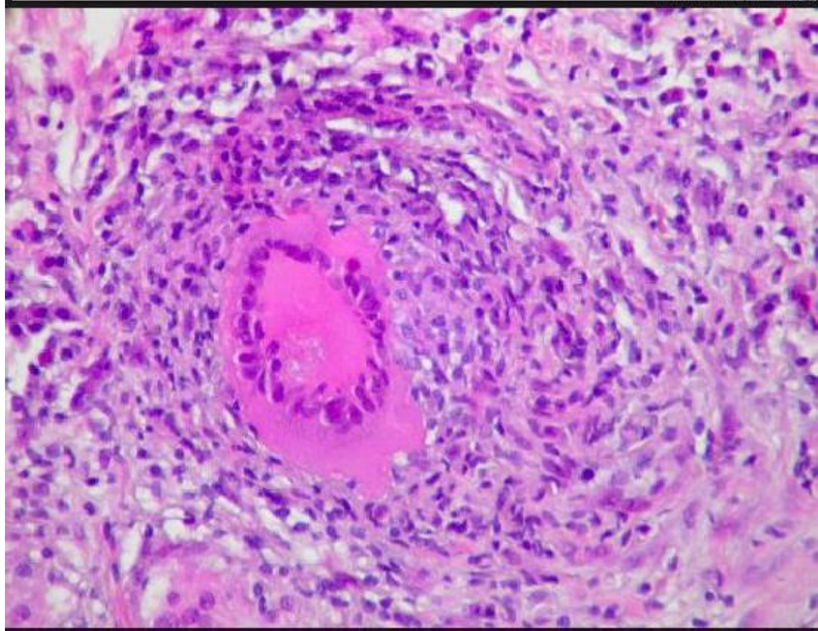
- **Productive type**—When fully developed, this lesion, a chronic granuloma, consists of three zones:

1) a central area of large, multinucleated giant cells containing tubercle bacilli.

2) a mid zone of pale epithelioid cells, often arranged radially.

3) a peripheral zone of fibroblasts, lymphocytes, and monocytes (B Cells & T cells).





Primary Infection and Reactivation
Types of Tuberculosis

- An acute exudative lesion develops and rapidly spreads to the lymphatics and regional lymph nodes. The exudative lesion in tissue often heals rapidly.
- In primary infections, the involvement may be **in any part of the lung but is most often at the base.**
- The reactivation (someone has latent tuberculosis, and then develop tuberculosis disease), type is usually caused by **tubercle bacilli that have survived in the primary lesion.**
- The reactivation type almost always begins **at the apex of the lung, where the oxygen tension (PO2) is highest.**

Clinical manifestation

- Classic clinical features associated with active pulmonary TB are **coughing, weight loss/anorexia, fever, night sweats, haemoptysis (coughing blood)** **not hematemesis (vomiting blood)**, **dyspnea (chest pain) and malaise/fatigue**, **short of breath (Disnea).**

- Tuberculosis is usually a chronic disease; it presents slowly with weight loss, low-grade fever, and symptoms related to the organ system infected. Because of its slow course, it may be confused with cancer. Whenever you have an infection of any organ system, tuberculosis will be somewhere on your differential diagnosis list.

- It is one of the great imitators

Laboratory diagnostic methods

the gold standard (definitive diagnosis) for tuberculosis diagnosis is Microbiology (culture).

We usually take **phlegm** as a sample from the patient, in **children** we can't take phlegm we take **bronchoalviolar lavage (BAL).**

❖ Smear microscopy

- Three specimens from each patient with suspected TB should be examined microscopically for **Acid Fast Bacilli AFB (classically Ziehl-Neelsen)** or mycobacteria can be **demonstrated by yellow fluorescence after staining with auramin.** (If we don't find tuberculosis, this means that the sample don't contain it not the absent of the disease).

❖ Culture

- Both liquid and solid mycobacterial cultures should be performed for every specimen, and recovered isolates should be according to standard criteria (Lowenstein-Jensen or Middlebrook 7H10), **Radiometric broth culture (BACTEC radiometric system)** and **mycobacterial growth indicator tube (MGIT).** (Takes 2 weeks for mycobacteria growth if present).
- Culture for **acid fast bacilli** is the **most specific test** for TB and **allows direct identification and determination of susceptibility of the causative organism.**

Laboratory diagnostic methods

❖ A **nucleic acid amplification test (NAAT)**, **Tuberculin skin tests (TSTs)**, **Interferon-gamma release assays (IGRAs)** **are commonly used as well.**

➢ The **Tuberculin Skin Test (TST)** is performed by injecting **purified protein derivative (PPD)**, which is extracted from **Mycobacterium tuberculosis**, intradermally into the **patient's forearm**.

➢ **After 48 hours**, the induration – Edema – **(hard, raised swelling)** at the injection site is measured and **the size of the induration** helps determine whether the test is positive or negative for tuberculosis infection.

➢ **Interpretation of Results:**

- **Normal individuals** (general population): Induration **> 15 mm** → **Positive**.
- **Intermediate-risk groups** (e.g., homeless individuals, IV drug users, healthcare workers due to close contact with patients): Induration **> 10 mm** → **Positive**.

Laboratory diagnostic methods

❖ Tuberculin skin tests (TSTs)

- **High-risk individuals** (HIV/AIDS patients): Induration **> 5 mm** → **Positive.**

➢ **The hard thing is to interpret this positive result (Next slide).**

Laboratory diagnostic methods

❖ Tuberculin skin tests (TSTs)

- **Interpreting a positive TST** result can be **difficult.**

- A significant portion of patients who test positive **may not actually have active tuberculosis** – this is referred to as a **false positive result.**

- The **two** main **confounding factors** that can **cause a false positive TST** are:

1) **BCG vaccination:**

Common in Jordan and many other countries, as most individuals receive the BCG vaccine within the first month
after birth.

The vaccine can cause the immune system to react to the test, even without actual infection.

Laboratory diagnostic methods

❖ **Tuberculin skin tests (TSTs)**

2) **Environmental (non-tuberculous) mycobacteria:**
Exposure to environmental mycobacteria can also stimulate a cross-reactive immune response, leading to a positive test result.

- It's also important to note that a positive TST only indicates that the **immune system recognizes Mycobacterium antigens**, meaning the person has been exposed at some point.

- **However, it does not provide information about when the infection occurred, nor can it distinguish between active and latent tuberculosis.**

Laboratory diagnostic methods

❖ **Interferon-gamma release assays (IGRAs)**

- Contains antigens that are present at **Mycobacteria tuberculosis** but **not** present at **mycobacteria bovis** (the one that we are vaccinated against).
- As a result **it doesn't give a false positive** because of **vaccine** or **environmental mycobacteria.**
- The test provides a **positive** or **negative** result, indicating whether the patient's immune system **recognizes M. tuberculosis antigens.**
- However, **similar to the Tuberculin Skin Test (TST)**, the **IGRA cannot determine when the infection occurred, nor can it distinquish between active and latent**

keep going.

Treatment

- The course of TB treatment **depends** on whether the individual is in the **latent or active stage, and on his or her probability of risk.**

- Treatment of TB usually involves a **drug cocktail, or a mixture of multiple drug**s, with an **intensive initial 2-month phase** followed by a **slower 4- to 6-month continuation phase** the main anti-tuberculosis drugs used in the chemotherapy of TB are:

1) **isoniazid (INH)**, cases **hallucination.**
2) **rifampin (RIF)** cases **red body fluid** (urine and droplets become orange colour).
3) **pyrazinamide (PZA)** cases **optic neuritis.**
4) **Either ethambutol (EMB)** cases **hyperuricemia** **or streptomycin (SM).**

- Isoniazid preventive therapy IPT is the recommended treatment for LTBI but the
- regimen's main drawback is the duration of therapy

Prevention

- The best way to prevent TB is to diagnose and **isolate infectious cases rapidly** and to administer appropriate treatment until **patients are rendered noninfectious (usually 2–4 weeks after the start of proper treatment)** and the disease is **cured**.

- Additional strategies include **BCG vaccination and treatment of persons with LTBI who are at high risk of developing active disease.**

- Mycobacterium bovis **Bacillus Calmette–Guérin (BCG)**, an attenuated vaccine derived from M. bovis, is the **only licensed vaccine against tuberculosis (TB).**

OTHER MYCOBACTERIA

- The nontuberculous mycobacteria (NTM) is a **diverse group of organisms commonly found in the environment** (water, soil, and in birds, M.avium found in birds), and the group includes both saprophytes and human pathogens.

- The NTM can be further classified into the **rapid growers (grow in <7 days)** and **slow growers** (most of them). Each group can be subdivided on the **basis of pigment production.**

- Mycobacterium avium Complex (MAC or MAI).

- MAC organisms infrequently **cause disease in immunocompetent humans.**
- MAC infection is one of the most common **opportunistic infections of bacterial origin in patients with AIDS.**

The nontuberculous mycobacteria (NTM) Classification:

- Slowly growers (more than 7 days to grow):

- Mycobacterium kansasii (causes a pulmonary disease, but not tuberculosis, remember these are non tuberculosis mycobacteria), Mycobacterium marinum (causes aquarium granuloma, especially in people who have fishes), and Mycobacterium ulcerans soft tissue infection. (**Photochromogene** They produce a pigment in the presence of light).

- Mycobacterium scrofulaceum (**scotochromogens**: they produce a pigment in the absence of light).

- Mycobacterium avium complex, or (MAI). (**Nonchromogenes** : they don't produce pigments whether in the presence or absence of light).

The nontuberculous mycobacteria (NTM) Classification:

- Fast growers (less than 7 days to grow) :

- Mycobacterium fortuitum Complex ,Mycobacterium chelonae-abscessus, M. smegmatis.

The nontuberculous mycobacteria (NTM)

- In order to **distinguish** between Mycobacteria **tuberculosis** from **non-tuberculosis** mycobacteria, we use **nisine test :**

- **Tuberculosis** Mycobacteria are **Nisine Positive.**

- **Non-Tuberculosis** Mycobacteria are **Nisine Negative .**

Mycobacterium leprae

- Mycobacterium **leprae** is an acid-fast rod.
- It is impossible to grow this bacterium In **vitro**, **it needs an animal model.**
- It causes the famous disease **leprosy**.
- The bacteria appear to grow better in **cooler body temperatures closer to the skin surface, and Shawn cells of the nerves.**
- Skin lesion consistent with leprosy and with definite sensory loss.
- The severity of the disease is dependent on the host's cell-mediated immune response to the bacilli (which live intracellular, like Mtb).

Pathogenesis

- Lepromatous leprosy (LL), infectious one.
- borderline lepromatous (BL)
- Tuberculoid leprosy (TL), control the mycobacterium leprosy.

Clinical manifestation

- The onset of leprosy is insidious.

- The lesions involve the **cooler tissue of the body**, including the **skin, superficial nerves, nose, pharynx, larynx, eyes, and testicles.**

Diagnosis

- skin or nasal mucosa or a biopsy of earlobe skin are smeared on a slide.

- Smears are stained by the Ziehl-Neelsen technique. Biopsy of skin or of a thickened nerve gives a typical histologic picture.

- No serologic tests are of value.

Treatment

- Sulfones such as dapsone are first-line therapy for both tuberculoid and lepromatous leprosy.

- RMP or clofazimine generally is included in the initial treatment Regimens.

THE END

رسالة من الفريق العلمي:

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			