وَقُل رَّبِّ زِدْنِي عِلْمًا

النادي الطبي

RESPIRATORY SYSTEM

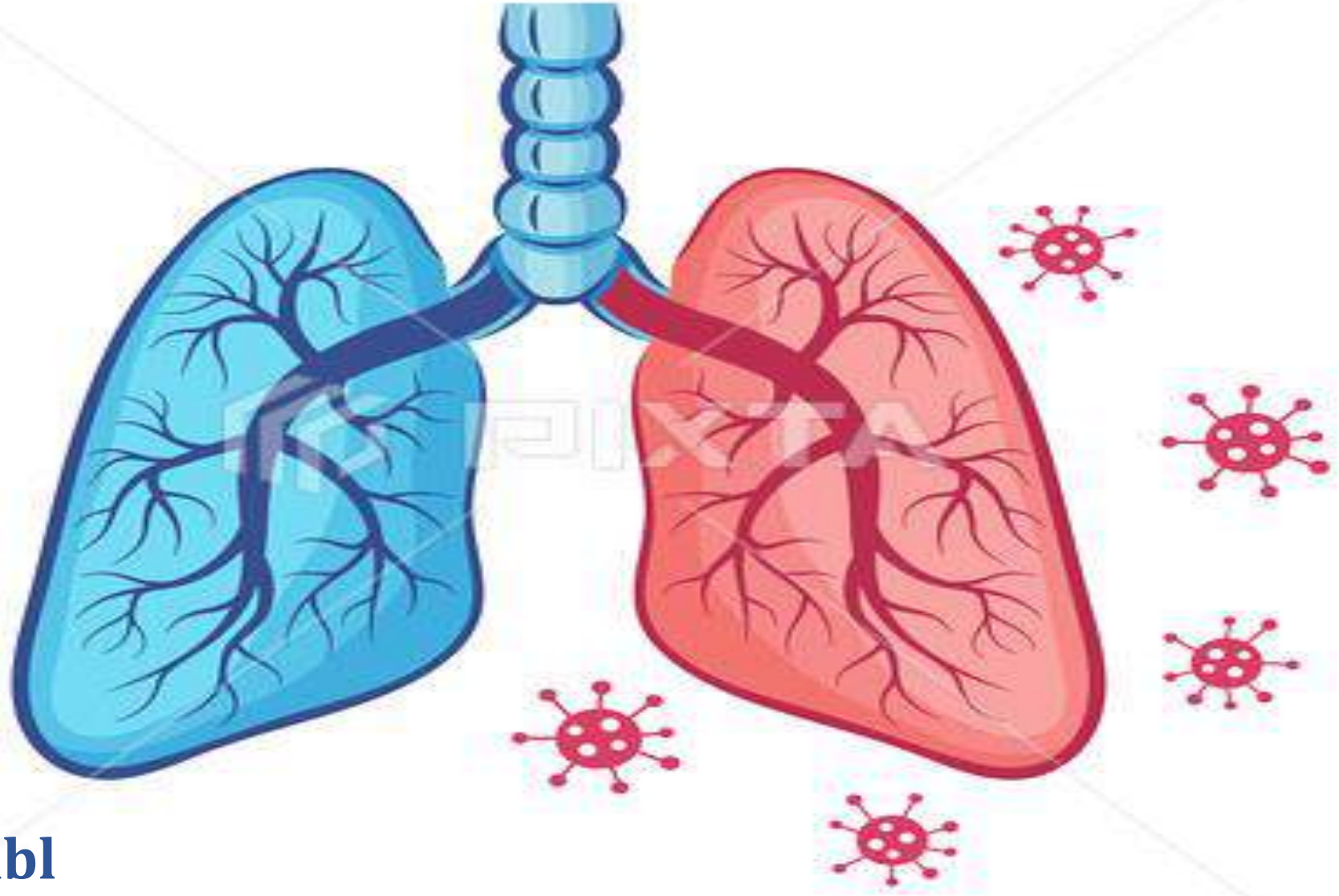
HAYAT BATCH

SUBJECT : _____

LEC NO. : 4

DONE BY : Hala albeshtawe

RESPIRATORY TRACT INFECTIONS - IV



By
Prof. Hala Tabl

Mycobacteria

Medically important Mycobacteria

*M. tuberculosis
*M. bovis
} Causative agents of tuberculosis in man

السل / الدرن

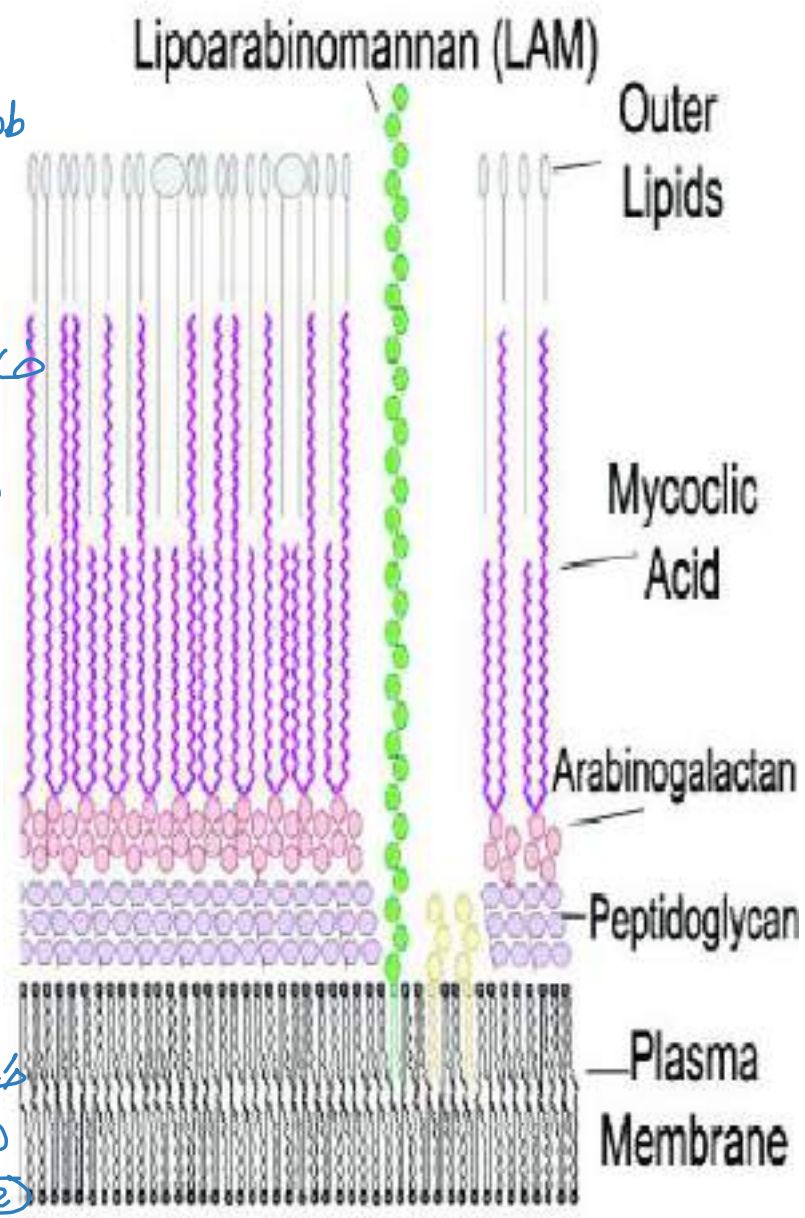
*M. Leprae → Causative agent of leprosy

الجذام

*Atypical mycobacteria

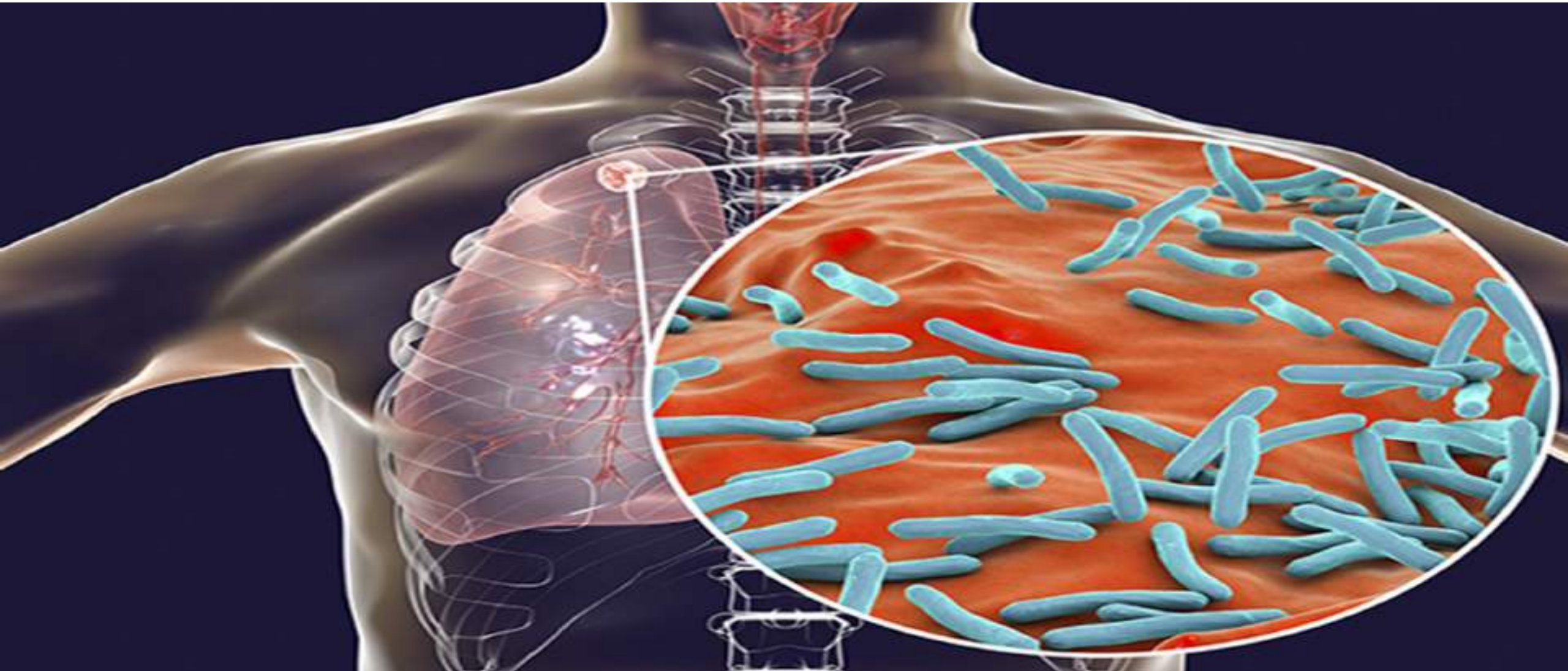
General characters of Mycobacteria:

- Slender rods, non-spore forming, strictly aerobic.
- Difficult to stain with ordinary stains (e.g. Gram stain) because of a **high lipid** content (**mycolic acid**) (40-60%) in the cell wall.
- Stained with special stain **Ziehl-Neelsen (Z.N)** that depend on application of heat and concentrated dye.
- Once stained , they retain the stain and resist decolorization with acids, that is why described as "**acid fast bacilli**" **(AFB).**



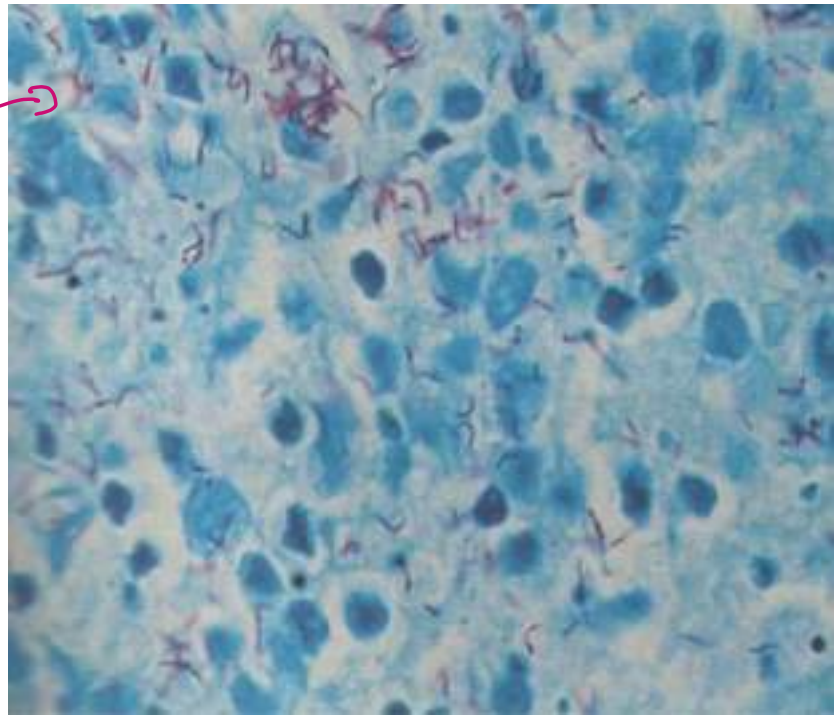
MYCOBACTERIUM TUBERCULOSIS

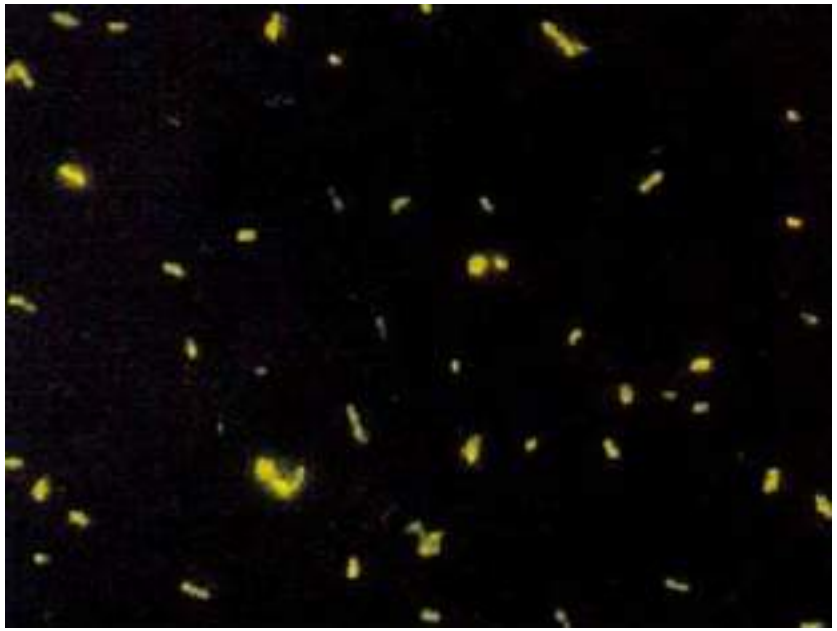
“Tubercle bacillus” “Koch bacillus”



Morphology:

- Thin straight or slightly curved rods.
- Non motile, non-sporing and non-capsulated.
- They stained by **Z.N (Hot)** or **Kinyoun (Cold)** stain and appear as thin **pink rods** arranged singly or in small groups **in a contrasting blue background.**
- They can be stained by **fluorochrome** (fluorescent) stains (e.g. auramine, rodamine).





Cultural characters:

affect the more oxygenated area in the body

- They are **obligate aerobe** (upper lobe of the lung).

- They are **slow growers**, growth appears after 4-6 weeks (doubling time 18 hs in contrast to <1 hour in most bacteria).

- Types of media:

enriched media يحتاج

1) Egg based media such as **Lowenstein-Jensen (L-J)** medium & Dorset's egg medium.

اسرع للخروج من ال media التي قبلها

2) Agar based media e.g. Middlebrook's 7H10,7H11 agar.

3) Fluid media e.g., Middlebrook's 7H9.

L-J medium

Resistance & Sensitivity:

***They are highly resistant to :**

- Dryness (survives in dried sputum for long periods).
- Chemicals, many acids and alkalis.
- Antibiotics.

***They are killed by:**

- Sunlight
- U.V. rays
- 5%phenol
- Heat (60°C for 20 min.) (**Pasteurization can kill them in milk**).

Virulence Factors:

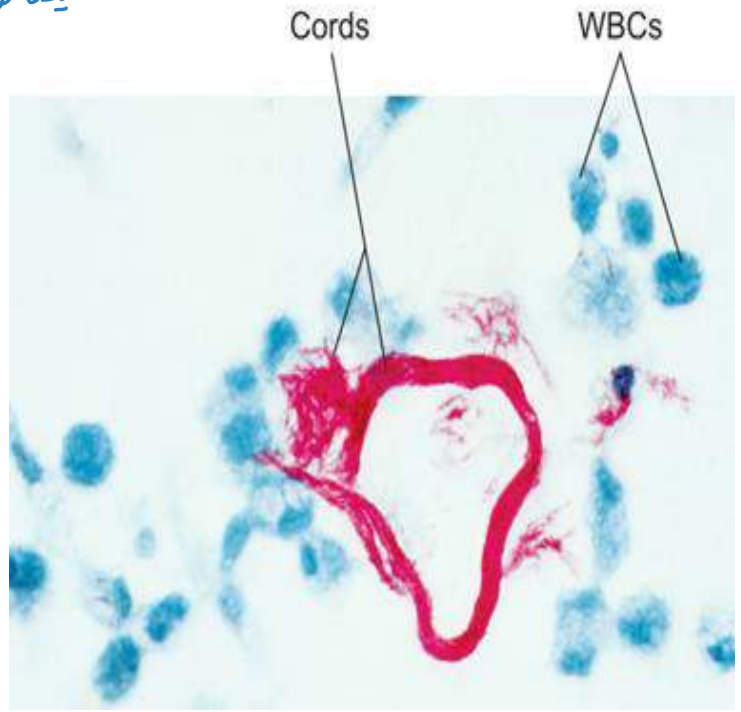
1. **High lipid of cell wall (Mycolic acids),** responsible for:

   Resistance to: Antibiotics, acidic and alkaline compounds, Osmotic lysis via complement.

virulent strain secrete virulent factor

يتكاثر الـ organism ويرتبط ببعضه الهدف إصنع الحواجز من الـ diffusion إلى خلايا

2. **Cord factor:** Virulent strains grow in a characteristic "Serpentine" cordlike pattern.



يحتوي بعض البروتينات على protein kinases يمزع عنع phago lysosomal fusion

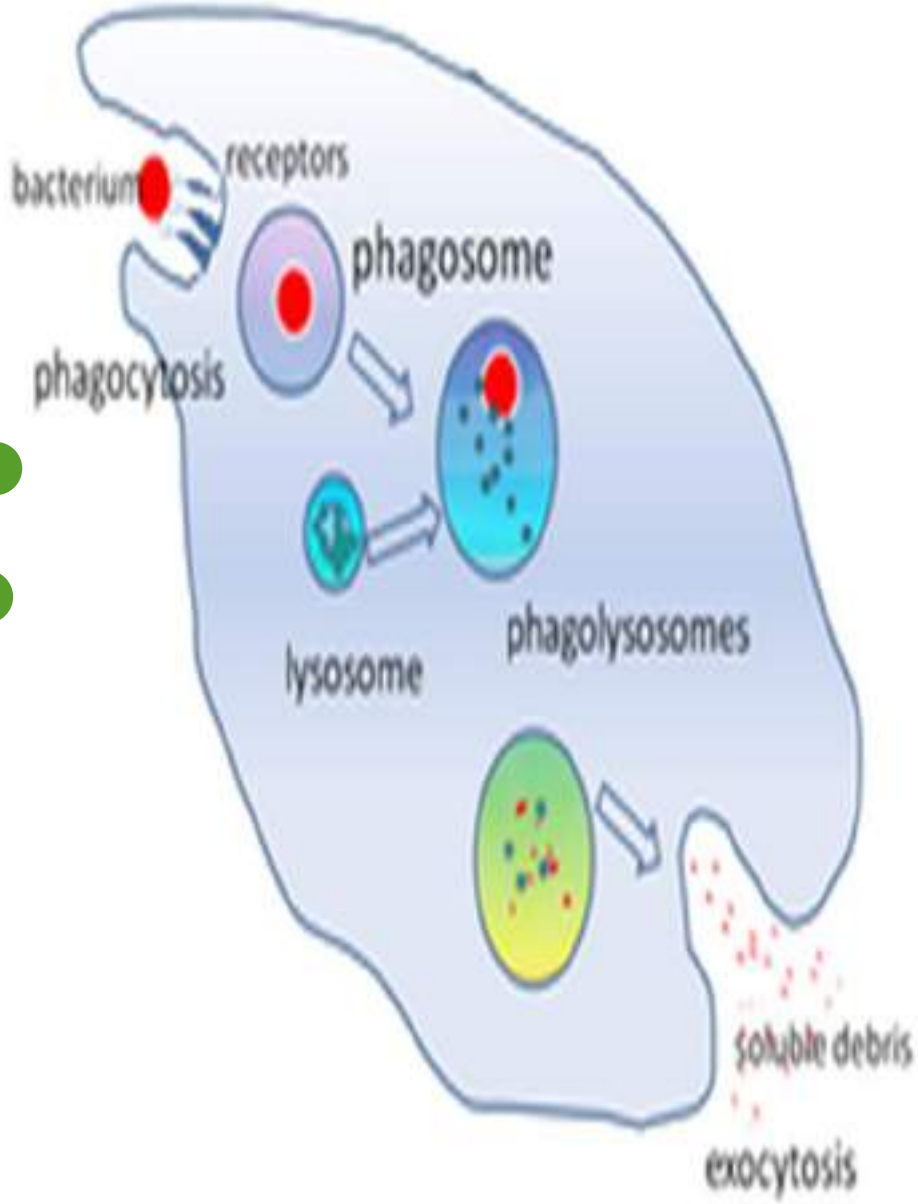
3. **Exported repetitive protein Erp & PKnG:**

   Inhibit phago-lysosomal fusion.

The main pathogenesis in TB

Pathogenesis:

- Tubercle bacilli do not contain or produce toxins.
- Their pathogenicity depends upon the fact that the organism **survives and multiplies in macrophage** within a vacuole called a phagosome as it produces a specific protein that prevents phago-lysosomal fusion and so, escape the degradation by lysosomal enzymes.
- It is an intracellular organism.



Immunity Against Tuberculosis:

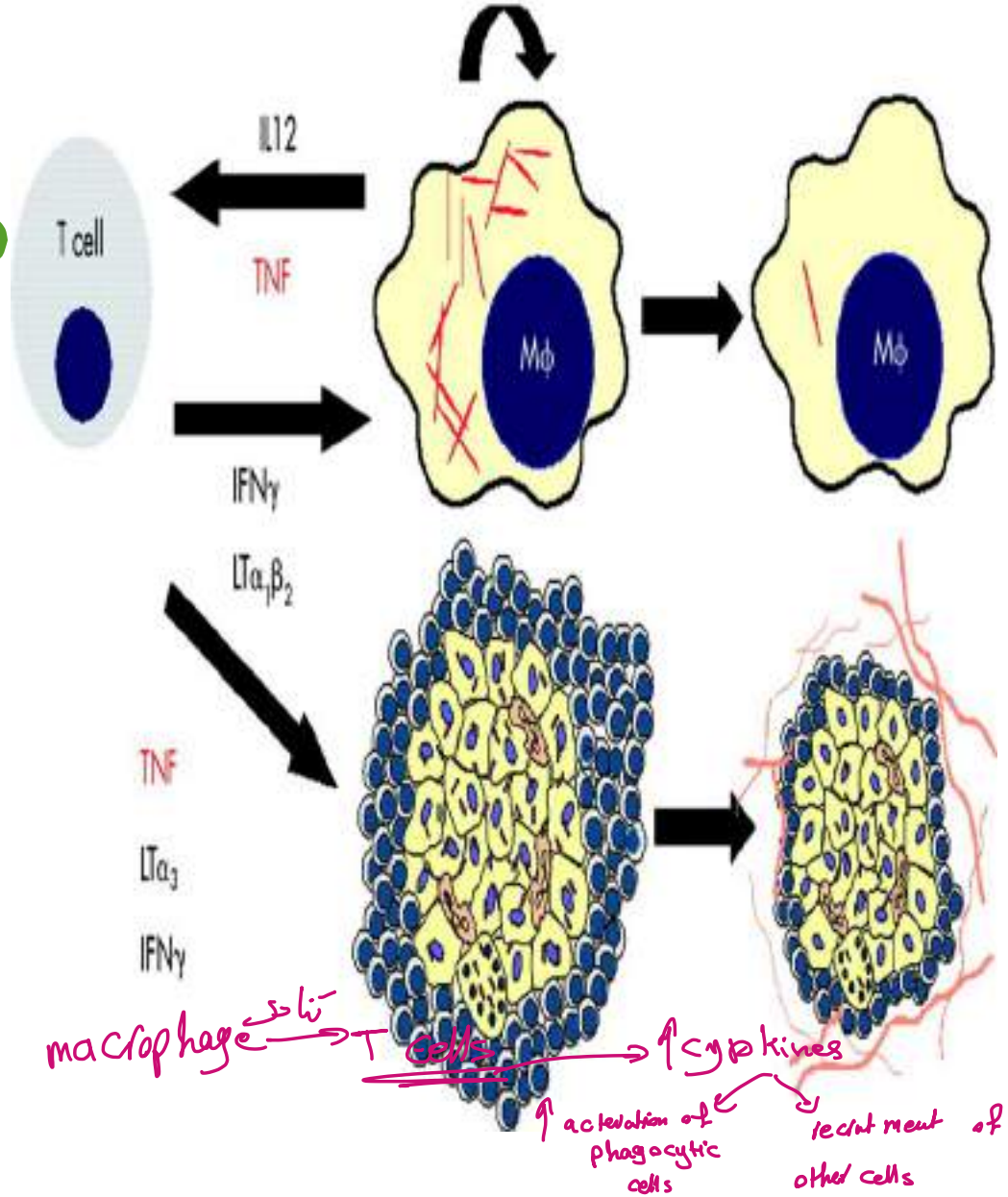
The immunity against TB is about cell mediated immunity

- On primary infection, the patient develops:

1- **Cell mediated immunity (CMI) (Delayed-type = type IV hypersensitivity)** (Granuloma formation) that leads to localization of tubercle bacilli, retards their multiplication, limits their spread.

Patients deficient in cellular immunity, such as AIDS patients, are more susceptible to disseminated (miliary) tuberculosis.

2- Circulating antibodies forms but has little role.



Human Tuberculosis (TB)

- Caused mainly by the **human** and **bovine** types.
- **Human** type is transmitted airborne by **inhalation** of respiratory aerosol (droplet nuclei <5μm) which expelled from active TB patient when cough, speak, sneeze,.. These nuclei remain suspended in air for several hours. Its initial site of infection is the **lung**.
- **Bovine** type is transmitted mainly by **ingestion** of unpasteurized milk of infected cattle **(zoonosis)** and its initial site of infection is the **intestine**.

نوع يأتي من الحيوانات

Primary site of infection

Primary pulmonary tuberculosis:

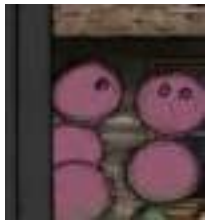
- Characterized by a small lesion called "**Primary complex**" which consists of:
  1. * Ghon focus (T.B. granuloma) in the lung (mid-zone).
  2. * Lymphangitis and lymphadenitis of the draining lymph nodes.

- The T.B granuloma become surrounded by fibrous tissue (Tubercle), undergone central caseation necrosis (cheese like).

- **Fate of primary lesion:**
  - In most cases, it is asymptomatic and tubercles heal by fibrosis and calcification leaving the person immune and hypersensitive **(tuberculin positive)**.
  - Small foci containing **dormant viable** organisms **(Simon foci)** may be formed and often become sites of reactivation **(Latent TB)**
  - Only small % (immunocompromised) progress into active or disseminated T.B.

Secondary pulmonary tuberculosis:

- Is the most common form of **clinical** tuberculosis.
- It may be: **reactivation** of old primary lesion or **reinfection.**
- Occurs mainly in **immunocompromised,** debilitated or diabetic patients.
- **Spread of the organism occurs by two mechanisms:**



1) Local spread: -To other parts of the lungs (upper lobe), OR

-A tubercle **cavitate,** erode a bronchus, empty its contents, and spread the organism to other persons if expectorated **(Open TB).**

2) Hematogenous spread: which result in **miliary T.B.**

Symptoms of active TB disease:

Cough lasting 3+ weeks

Coughing up blood or sputum *(phlegm from deep inside the lungs)*

Chest pain

Weakness or fatigue

No appetite

Weight loss

Fever and/or chills

Night sweats

Note that the sputum is yellowish green or may be coughing blood (hemoptysis).

Laboratory Diagnosis

Specimens: Sputum (3 consecutive days) or broncho-alveolar lavage.

1- Direct microscopic examination:

***Z.N stain & Kinyoun:** low sensitivity (Require large number of bacilli).

-Positive film is highly suggestive, **negative film does not exclude T.B**.

***Flourochrome stain:** More sensitive and allow more rapid screening than Z.N.

2- Culture:

-Culture is the **gold standard and the most conclusive** method.

-L.J medium **(up to 8 weeks)** or more rapid Middlebrook 7H9 **(~3 weeks)**.

3- Polymerase Chain Reaction (PCR): Rapid & sensitive.

Tuberculin Test "Mantoux test"

Principle: It is skin allergic test used to detect **cell mediated immunity** to tubercle bacilli which become detectable **few weeks** after natural infection or BCG vaccine.

Procedure:

Intradermal injection of 0.1ml of **PPD (Purified Protein Derivative).**

Read the test **48-72 hours**.

Measure the diameter of the induration using mm ruler.

"**Only the induration**", which is localized hard papule, is measured, even if there is surrounding erythema).

Interpretation of Tuberculin test

An induration of 5 or more mm	An induration of 10 or more mm	An induration of 15 or more mm
Considered positive for: 1. People with previous history of TB. 2. Close contacts of TB patients. 3. People with HIV infection.	Considered positive for: 1. People in endemic areas where TB is common. 2. Healthcare workers. 3. People with certain medical conditions such as diabetes. 4. Unvaccinated children younger than 4 years old.	considered positive even in absence of any risk factor for TB.

Positive Tuberculin dose not differentiate between active or latent T.B

➢ Negative Test:

A negative test means that there is no infection at all or a very old healed one.

Tuberculin is a good negative test.

➢ False Negative Test:

1. Anergy: is the inability to react because of a weakened immune system, e.g.

Severe T.B, HIV infection, Some viral infections or cancer.

2. Recent T.B: it takes 2-10 weeks for tuberculin test to become positive.

➢ False Positive Test:

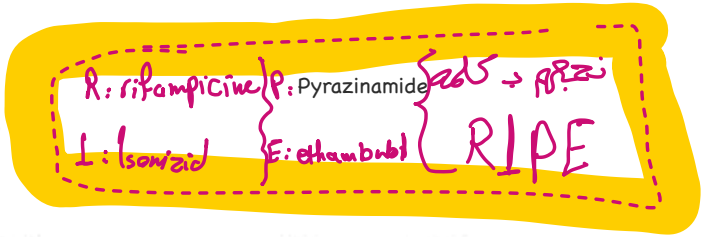
1-Infection with other non-tuberculous mycobacteria.

2- BCG vaccine (The test reactivity induced by vaccine wanes with time).

Treatment:

- **First line anti-tuberculous drugs:** more effective with less side effects.

Isoniazid (INH), Rifampicin, Pyrazinamide, Ethambutol.



- **Second line anti-tuberculous drugs:** less effective with more side effects.

Fluorquinolones, Streptomycin, Amikacin, …

- Second line drugs can be used in patients whose infecting strains are resistant to the first line drugs.

Treatment of TB should be:

1-Long Duration:

Response of tuberculosis to treatment is slow, this is due to the facts that:

- Intracellular location of the organisms.
- Caseous material interferes with penetration of the drugs.
- The slow growth of the organism.
- Metabolically inactive "persisters" within the lesion in chronic cases which may not be eradicated easily by antit-uberculous drugs (source of reactivation in the future).

2- In Combination: 2-4 drugs simultaneously to:

- Reduce development of resistance.
- Reduce toxicity of the drugs.

Resistant mutants Worldwide problem

- **Multidrug resistant TB (MDR-TB):** means tubercle bacilli resistant to both isoniazid (INH) and rifampicin. 1st line
- **Extensively (Extremely) drug resistant TB (XDR-TB):** It is defined as MDR + resistance to fluorquinolones and at least one second-line injectable drugs. Results from inadequate treatment of MDR-TB. 1st + 2nd
- Because drug resistance is a problem, antibiotic sensitivity testing should be performed for all isolated organisms.

Prevention:

Vaccination: BCG “Bacillus of Calmette-Guérin” vaccine:

- This is a **living attenuated** vaccine prepared from a **bovine** strain.
- It is given as a **single dose** of 0.1 ml by intradermal injection in the left deltoid region.
- It is given to all children during the first month of life.
- It is also given to adults exposed to infection e.g. nurses, doctors and contacts of the case.
- It should **NOT** be given to immunocompromised people.
- It loses its effectiveness over time, usually within 5 to 15 years

ATYPICAL MYCOBACTERIA

Non-tuberculous mycobacteria “NTM”
Mycobacteria other than tuberculosis “MOTT”

- They normally found in soil and water.
- Transmission is from the environment. **NO** person to person transmission.
- They are of **low pathogenicity** for man but occasionally they cause **opportunistic** infections especially in **immunocompromised** persons.
- They cause pulmonary diseases which are **indistinguishable** clinically, radiologically and histologically from that caused by the human tubercle bacilli, but tend to be **more chronic and difficult to be eradicated.**
- e.g. **M. Avium Complex (MAC)** (M. avium, M. intracellulare, M. chimera).