Mycobacteria

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Background

- The mycobacteria are rod-shaped, aerobic bacteria that do not form spores.
- *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 s 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.

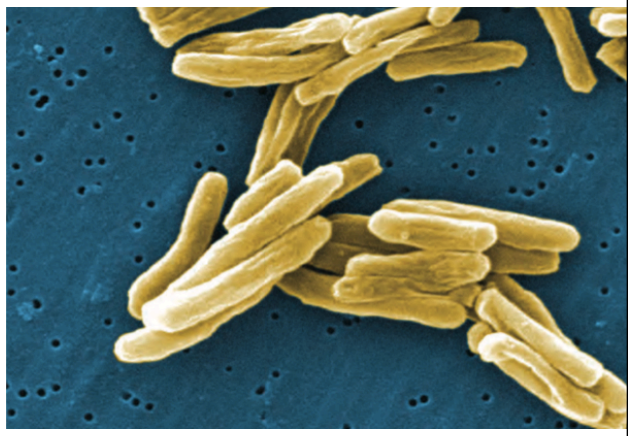
- Tuberculosis , consumption(consume patients ,weight loss), white plaque (extreme pallor seen among patients).

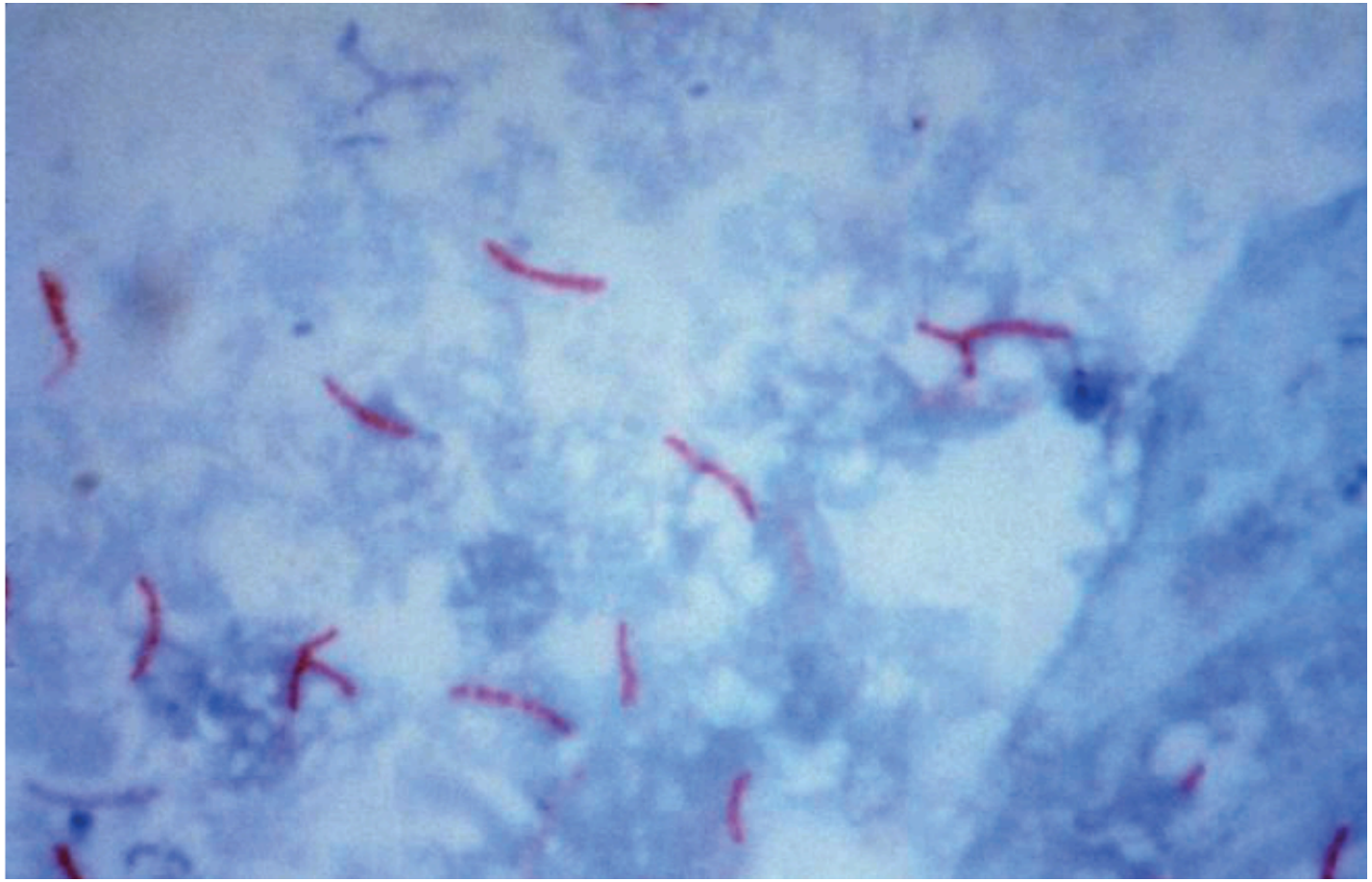
- The family mycobacterium tuberculosis complex(MTC) can cause Tuberculosis (TB) in humans and other livings.

- It includes M. tuberculosis (Mtb), 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.
- 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 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.
- Mycobacteria tend to be more resistant to chemical agents than other bacteria because of the hydrophobic nature of the cell surface and their clumped growth,





Mtb Culture

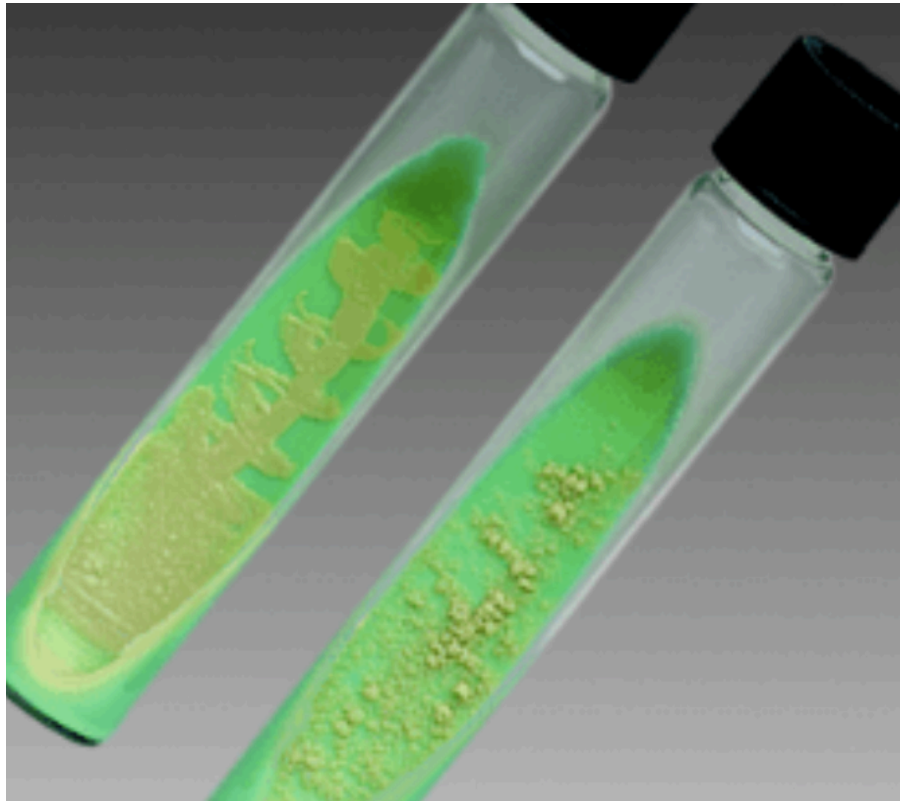
- The media for primary culture of mycobacteria should include a nonselective medium and a selective medium.

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

- Inspissated egg 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.

- Broth media— (eg, Middlebrook 7H9 and 7H12) support the proliferation of small inoculate.

Mtb Colonies



Mtb Cell wall

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

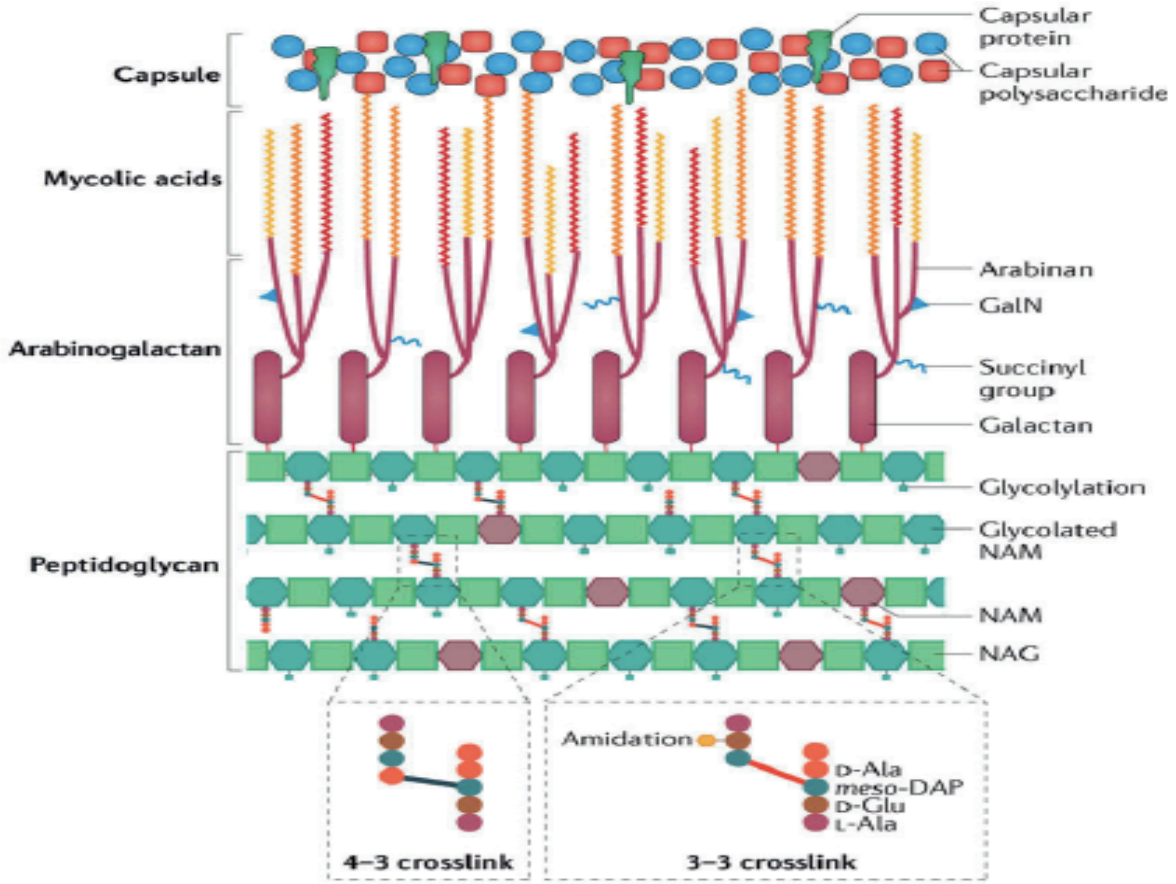
- It consists of an inner layer and an outer layer that surrounds the plasma membrane. The inner compartment is composed of three distinct macromolecules — peptidoglycans (PG), arabinogalactans (AG) and mycolic acids (MA) — covalently linked together to form a complex known as the MA-AG-PG complex.

- 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.

- 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.

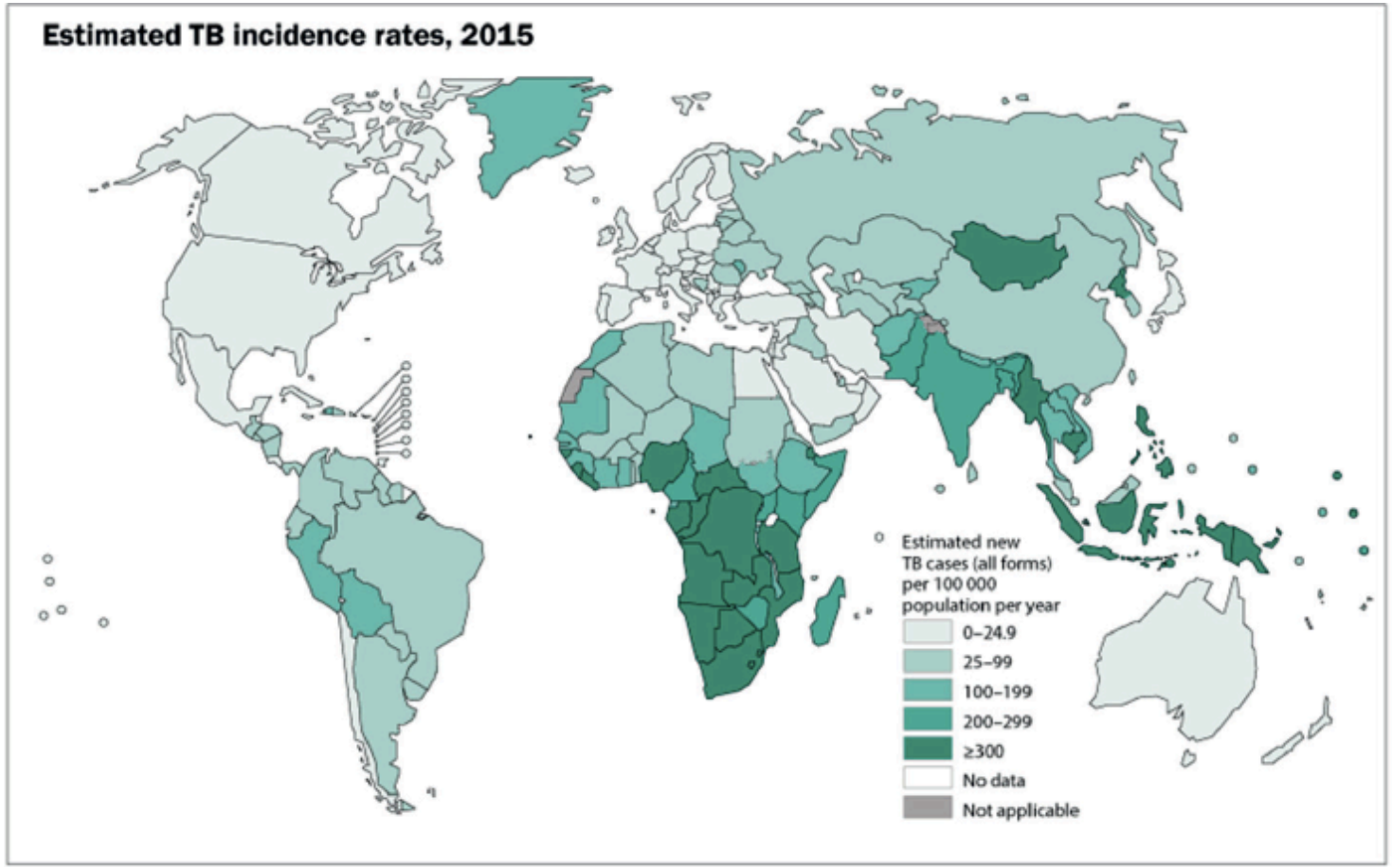
- Mycolic acids (long-chain fatty acids C78–C90), waxes, and phosphatides , can be found in Mtb cell wall and make up 50% of the dry weight of the mycobacterial cell envelope.

- 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) and trehalose monomycolates (TMM).


Capsule
Mycolic acids
Arabinogalactan
Peptidoglycan
Capsular protein
Capsular polysaccharide
Arabinan
GalN
Succinyl group
Galactan
Glycolylation
Glycolated NAM
NAM
NAG
Amidation
D-Ala
meso-DAP
D-Glu
L-Ala
4–3 crosslink
3–3 crosslink

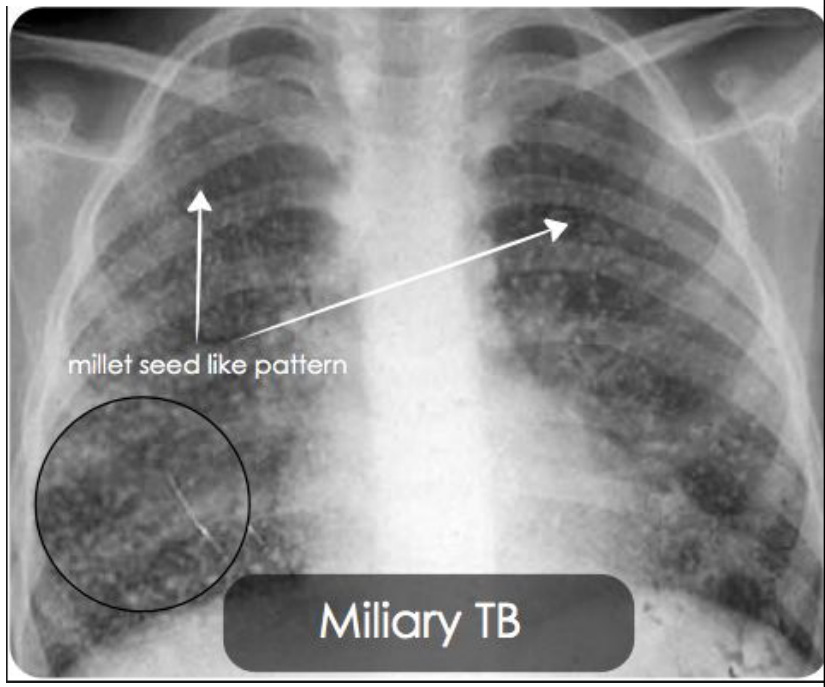
Epidemiology

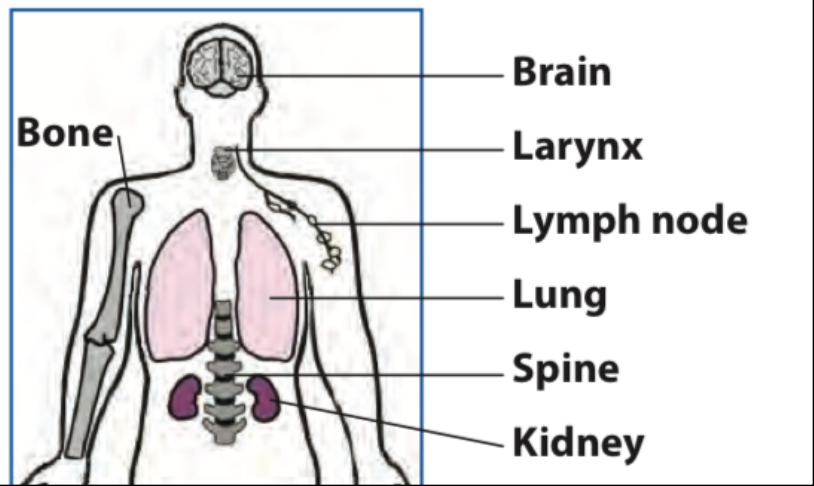
- Two TB-related conditions exist; latent TB infection (LTBI) and TB disease. If not treated properly, TB disease can be fatal. People who have latent TB infection do not feel sick, do not have any symptoms, and cannot spread TB to others
- About one third of the worlds population is infected with TB 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, and direct inoculation.


Estimated TB incidence rates, 2015
Estimated new TB cases (all forms) per 100 000 population per year
0–24.9
25–99
100–199
200–299
≥300
No data
Not applicable

Tuberculosis TB

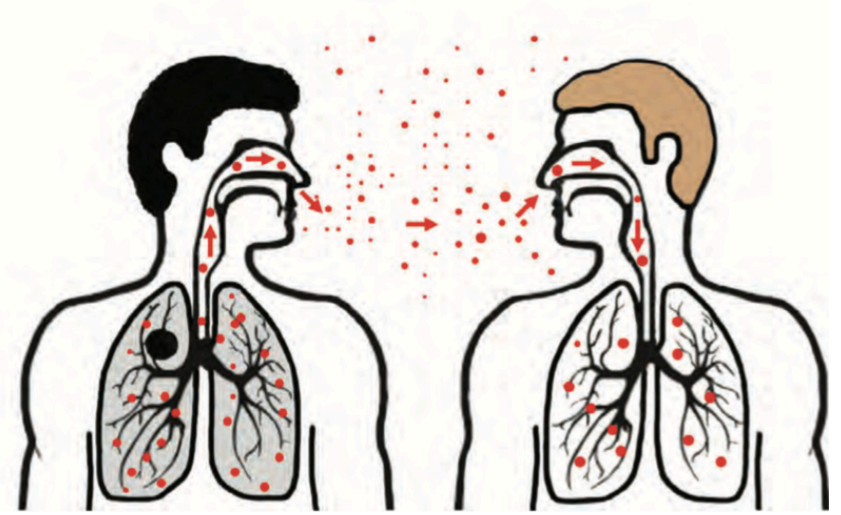
- The primary site of TB is usually lung, from which it can get disseminated into other parts of the body. The other routes of spread can be contiguous involvement from adjacent tuberculous lymphadenopathy or primary involvement of extrapulmonary organ.
- Spread – Lymphatic vs hematogenous (Miliary).
- TB bacteria can attack any part of the body such as the pleura ,L.N. ,pericardium, kidney, spine, brain and abdomen (abdominal Tuberculosis) collectively known as extrapulmonary TB.
- Primary Infection(Active) and Reactivation Types of Tuberculosis.





Transmission

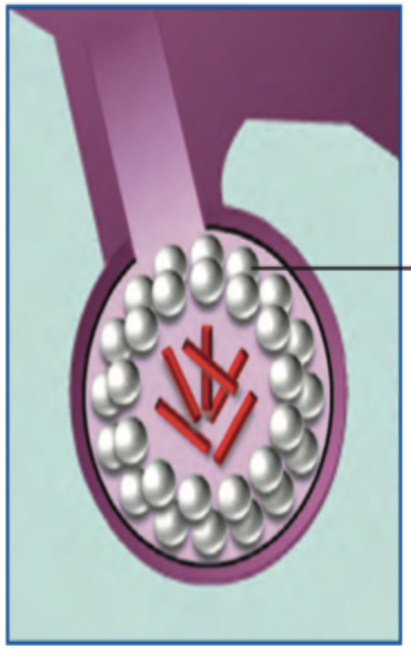
- TB is considered an airborne infectious disease although M. tuberculosis complex organisms can be spread through unpasteurised milk, direct inoculation and other means.



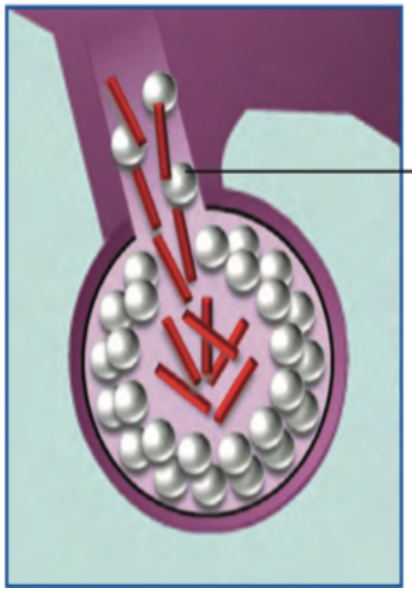
- The underlying pathophysiology of TB is the “10/3/1 formula.

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

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 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 (PO_2) is highest.

Clinical manifestation

- Classic clinical features associated with active pulmonary TB are coughing, weight loss/anorexia, fever, night sweats, haemoptysis (coughing blood), dyspnea (chest pain) and malaise/fatigue.

- 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

❖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.

❖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).
- Culture for acid fast bacilli is the most specific test for TB and allows direct identification and determination of susceptibility of the causative organism

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

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 drugs, 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: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) 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, 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. 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)

- Mycobacterium kansasii ,Mycobacterium marinum and Mycobacterium ulcerans.
- Mycobacterium scrofulaceum.
- Mycobacterium avium complex, or (MAI).
- Mycobacterium fortuitum Complex ,Mycobacterium chelonae-abscessus.

THE END