Microbiology lecture 1

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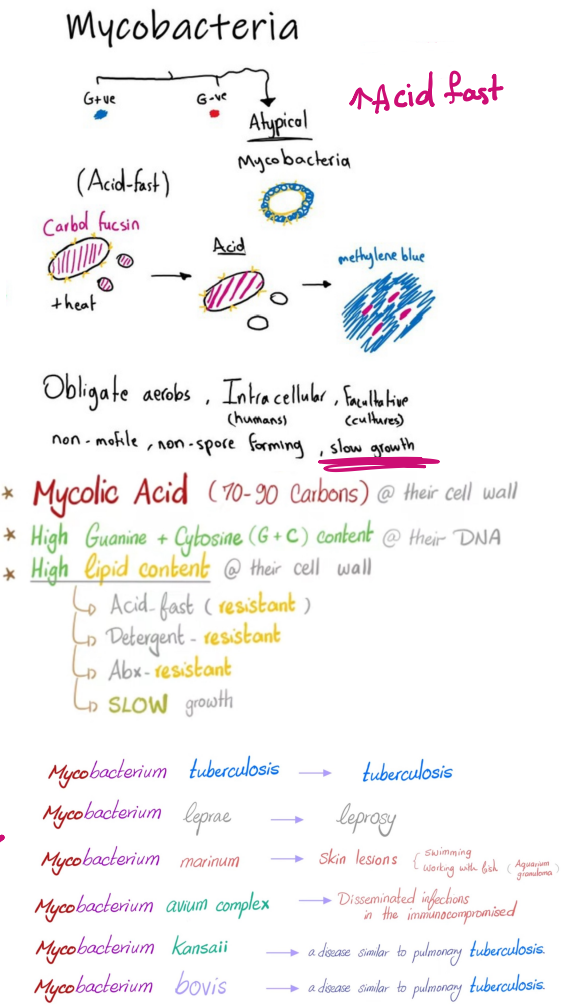
Tuberculosis (TB)

1. Biology and the Mycobacterium tuberculosis Complex (MTBC):

• Fundamental Biology: Mycobacteria are acid-fast bacilli (AFB) and obligate aerobes. They are characterized by extremely slow growth, with replication taking 15 to 20 hours. While they do not form spores, they are highly resistant to drying and disinfectants due to their unique cell wall.

• The Cell Wall: This is the most defining feature of the genus, containing a peptidoglycan core linked to an arabinogalactan layer and thick mycolic acids (long-chain fatty acids). Surface glycolipids, such as 1 cord factor, are toxic to macrophages and drive the formation of granulomas. A capsule also helps mediate interactions with phagocytes to favor bacterial survival.

• The MTBC Family: The M. tuberculosis complex includes several species that cause TB, though M. tuberculosis is the main human pathogen. Other members include:
M. bovis: Causes zoonotic TB via unpasteurized milk or animal contact.
M. africanum: Endemic to West Africa.
M. microti, M. caprae, and M. canettii: Infect rodents, goats/ cattle, or are geographically restricted, respectively.



2. Immunopathogenesis and Clinical Outcomes:

• Early Infection: TB is transmitted through the inhalation of aerosolized droplet nuclei. Once in the alveoli, the bacilli interact with host innate immune cells via Pattern Recognition Receptors (PRRs) like Toll-like receptors (TLRs) and C-type lectin receptors.

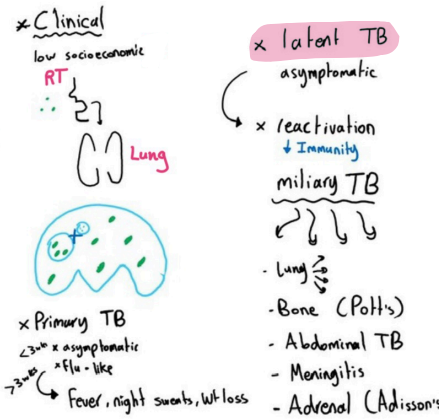
• Intracellular Survival: As a facultative intracellular pathogen, MTB has evolved mechanisms to survive within macrophages, including inhibiting phagosome-lysosome fusion, resisting oxidative stress, and preventing the acidification of the phagosome. The component lipoarabinomannan (LAM) further suppresses the immune response, delaying adaptive immunity for 2 to 4 weeks.

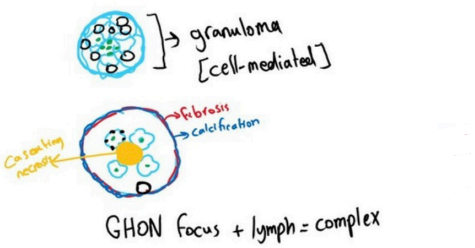
• Lesion Formation: Initial replication leads to a primary pulmonary lesion called a Ghon focus. When combined with involvement of the draining regional lymph nodes, it is termed a Ghon complex.

• Determinants of Outcome:

o Latent TB (LTBI): A robust Th1-mediated response involving IFN-Y (to activate macrophages) and TNF-a (to maintain granulomas) contains the infection.

o Active TB: If the immune response is weak-due to HIV, malnutrition, or age—the granuloma fails, leading to uncontrolled bacterial replication and disease progression. The sources outline a spectrum of seven clinical states, ranging from innate clearance (State O) to highly infectious cavitary disease (State VI).





3. Clinical Features and Diagnosis

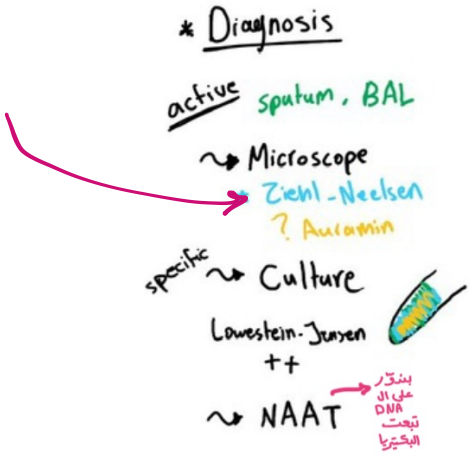
• Symptoms: The onset of respiratory TB is typically gradual and insidious. Dominant symptoms include a persistent cough (90-95% of cases), fever, night sweats, and weight loss. While 70-75% of cases are pulmonary, TB can also be exclusively extrapulmonary or a combination of both.

• Diagnostic Tools:

• AFB Smear Microscopy: Uses Ziehl-Neelsen or Kinyoun stains; it is rapid but cannot distinguish between MTB and NTM.

• GeneXpert MTB/RIF: An automated PCR test that detects MTB DNA and resistance to rifampicin within two hours.

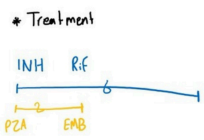
• Culture: The gold standard for diagnosis; liquid culture (MGIT) provides results in 7-14 days, while solid media (Lowenstein-Jensen) takes 3-8 weeks.

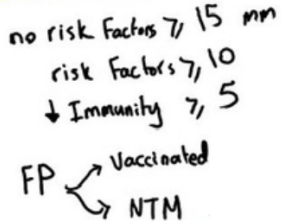


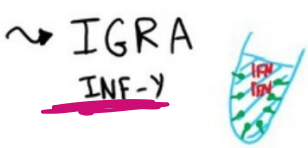
• Immunological Tests: IGRAs (Interferon-y Release Assays) and Tuberculin Skin Tests (TST) detect infection, though TST can produce false positives if the patient has received the BCG vaccine.

4. Treatment, Resistance, and Prevention:

• Standard Therapy: The RIPE regimen consists of an intensive phase (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol) for two months, followed by a four-month continuation phase of Isoniazid and Rifampicin.





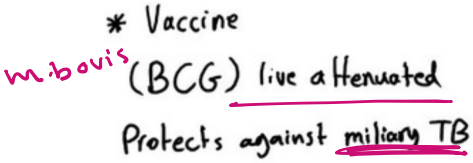


• Drug Resistance: Resistance develops via spontaneous mutations, often worsened by poor treatment adherence.

• MDR-TB: Resistant to both Isoniazid and Rifampicin.

• XDR-TB: MDR-TB plus resistance to at least one fluoroquinolone and one other "Group A" drug (like bedaquiline).

• Prevention: Directly Observed Therapy (DOT) is a core WHO strategy to ensure adherence. The BCG vaccine, a live attenuated strain of M. bovis, is highly effective in children against severe forms like TB meningitis but has variable efficacy in preventing adult pulmonary TB.



Non-Tuberculous Mycobacteria (NTM)

1. Overview and Classification

Unlike the MTBC, NTM are environmental organisms found in soil and water. They are generally not transmitted person-to-person. They are classified into two major groups:
• Slow Growers: Take more than two weeks to grow (e.g., M. avium complex [MAC], M. kansasii, M. xenopi).
• Rapid Growers: Grow within seven days (e.g., M. abscessus, M. fortuitum, M. chelonae).

2. Pathogenesis and Clinical Significance

• Risk Factors: NTM typically cause pulmonary disease in patients with pre-existing conditions like COPD, cystic fibrosis, or bronchiectasis. In severely immunocompromised patients, such as those with advanced AIDS, NTM can cause disseminated disease.
• Immune Control: Similar to TB, control of NTM depends on cell-mediated immunity and the IFN-γ/macrophage activation axis. Defects in this pathway lead to poor intracellular killing.
• Clinical Presentation: NTM infections often present as chronic, indolent respiratory infections with cough, sputum production, fatigue, and weight loss. A major challenge in treating NTM is their high level of intrinsic drug resistance.

3. Key Distinctions from TB

The sources highlight that while MTB is an obligate pathogen requiring a host, NTM live free in the environment. Furthermore, while infection rates for TB are generally decreasing in developed countries, NTM infection rates are increasing.