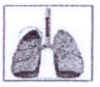
Treatment of Tuberculosis

What is Tuberculosis ?

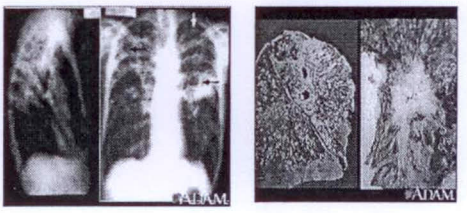


- Tuberculosis is a common , chronic infectious disease caused by *Mycobacterium tuberculosis* (*MTB*) complex.
- 1/3 of human race infected.
- 8 million infected per year.
- About 2 million death per year.

Tuberculosis-continue

- MTB usually attack the lungs, but other organs also affected such as, meninges , kidneys and lymph nodes.
- It spreads through air.
- Most infections are asymptomatic
- 1/3 progress to active disease.

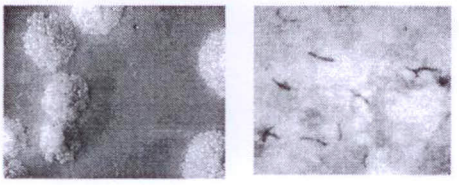
Pulmonary TB



M.tuberculosis

- A small , aerobic , non-motile AFB (acid fast bacilli) .
- ***M. tuberculosis* complex includes** :
  M. tuberculosis (human type),
  M.bovis ,
  M.africanum
  M.microti
  BCG (BCGosis) .

AFB (smear and culture)



Principles of Treatment of TB

The main goal of treatment is to kill tubercle bacilli rapidly.

To prevent emergence of drug resistance.

To control the spread from case to another.

To eliminate the *persistent* bacilli from the host's tissues to prevent *relapse*.

Continue-

- To achieve these effects requires a combination of 2-4 agents with specific activities be given for a sufficient period of time (**6-12 months**) so to prevent drug resistance & relapse.

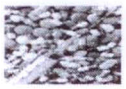
Antituberculosis Drugs

First- Line Drugs
Oral drugs

- Isoniazid
- Rifampin
- Ethambutol
- Pyrazinamide

Second-Line Drugs
Injectable drugs

- Cycloserine
- Ethionamide
- *P*-aminosalicylic acid
- Streptomycin
- Caproeomycin



First-line drugs isoniazid (INH)

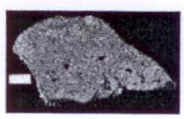
- First line agent for **all forms of TB** caused by a susceptible organism.
- Bactericidal against rapidly dividing cells.
- Used for adults, children and pregnant women.
- *Adverse effects:*
  - Liver toxicity
  - Clinical hepatitis (in patient's with previous liver disease).
  - Peripheral neurotoxicity

Rifampin (RIF)

- First –line agent and **sterilizing** for all forms of TB caused by a susceptible organisms.
- bactericidal against organisms that are dividing rapidly and semidormant bacterial populations.
- Essential component of all short-course regimens (should not be used alone).
- Safe to be used in children and pregnancy.

Adverse effects of RIF

- **Hepatotoxicity**: hepatitis, hyperbilirubinemia
- Orange discoloration of bodily fluids ,eg. Urine.
- Can be used to prove compliance with the treatment.



Pyrazinamide (PZA)

- First line agent for **all forms of TB** caused by a susceptible organisms.
- Has a great activity against dormant or semidormant populations within macrophages or the acidic environment of caseous foci.

PZA- Adverse effects

- **Hepatotoxicity**
- Gastrointestinal symptoms (nausea ,vomiting)
- Dermatitis, transient rash.
- Polyarthralgia
- Acute gouty arthritis

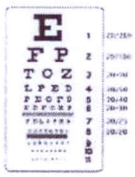
Can be used during pregnancy.

Ethambutol

- A first-line drug for treatment of **all forms of TB .**
- **Included in the first initial regimen to prevent emergence of RIF resistance when INH is resistant.**
- Proven for organisms resistant to either INH or RIF.
- Safe to be used during pregnancy.

Adverse effects of Ethambutol

- Decreased **visual acuity** or decreased red-green color discrimination.
- Not recommended for children whom visual acuity cannot be monitored.
- Cutaneous reaction.



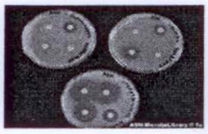
Common Combinations

- **INH+ RIF + Ethambutol or PZN for the first 2 months.**
- Then continue with INH + RIF for the rest 4 months. Duration may increase accordingly.
- Regimen must be taken as prescribed by the doctor, and finish the course.
- Antimicrobial susceptibility testing of the organism is important before the use of these drugs.

Drug susceptibility testing in the lab.

- Using the *comparative principle* i.e. to compare the susceptibility of the pathogenic isolate with that of a known strain.
- Both fluid and solid media can be used for that.
- It takes about **2-4 weeks** to read.

Comparative method


Second-Line Drugs

- Used when the organisms develop resistance to the first line drugs.
- May be used temporarily for patients with acute hepatitis.
- More toxic.

Drug Resistant Tuberculosis

- The bacteria can become resistant to the anti-TB drugs. That is the drugs can no longer kill the bacteria.
- **Resistance develops when these drugs are misused or mismanaged,** *examples:*

When the patients do not complete their full course of treatment.

Wrong prescriptions by doctors, wrong dose, long time taken of the drug, or poor quality.

Multidrug-Resistant TB (MDR)

- **MDR** TB is the Mycobacteria that is resistant to at least **2** of the best anti-TB drugs, **INH + RIF.**
- Extensively drug-resistant TB (**XDR TB**) is TB that is resistant to almost all drugs used including INH and RIF , plus any fluroquinolone and at least one of the 3 injectable second –line drugs.
- Patients infected with **XDR TB** are left with much less options for treatment, and **risk of death**.

Direct Observed Therapy (DOT)

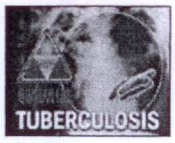
- DOT is the strategy devised to help the patient adhere to treatment.
- A designated person watches TB patient swallow each dose of the prescribed drugs.
- The goal of DOT is to ensure that the patient with active TB receives and adequately complete the treatment to minimize the risk of spreading disease to others and develop resistance.

DOT- continue

- DOT is applied by the WHO in a trial to control and eliminate tuberculosis from the world.

Priority for use of DOT

- Pulmonary TB patients with positive smears.
- Treatment failure
- Drug resistance
- Relapse
- TB + HIV infection
- Psychiatric patients
- Previous non-adherence to therapy
- Children and adolescents



Notes for Consideration

- DOT and monitoring of side effects important.
- Regimen decided according to susceptibility testing.
- Obtain sputum culture at the time of completion of initial course to identify risk of relapse.
- **Extended period of treatment recommended for patients with cavitation on chest-X-ray**.

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- Special consideration in patients with HIV , extra-pulmonary TB **, children** , pregnancy and patients with hepatic diseases.
- Patients with MDR TB.