ANTIMYCOBACTERIAL DRUGS

OBJECTIVES

- At the end of lecture , the students should:

- Discuss the etiology of tuberculosis
- Discuss the common route for transmission of the disease
- Discusses the out line for treatment of tuberculosis
- Discuss the drugs used in the first & second line Regarding :
    - The mechanism of action
    - Adverse effects
    - Drug interactions
    - Contraindication
    - Discuss tuberculosis & pregnancy
    - Discuss tuberculosis & breast feeding

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

Tuberculosis

Tuberculosis is caused by the infectious agent known as **Mycobacterium tuberculosis**. This rod-shaped bacterium, also called Koch's bacillus, it is a slow growing , an acid fast bacillus and it was discovered by Dr. Robert Koch in 1882.

Common sites of infections:

- Apical areas of lung.
- Renal parenchyma.
- Growing ends of bones.

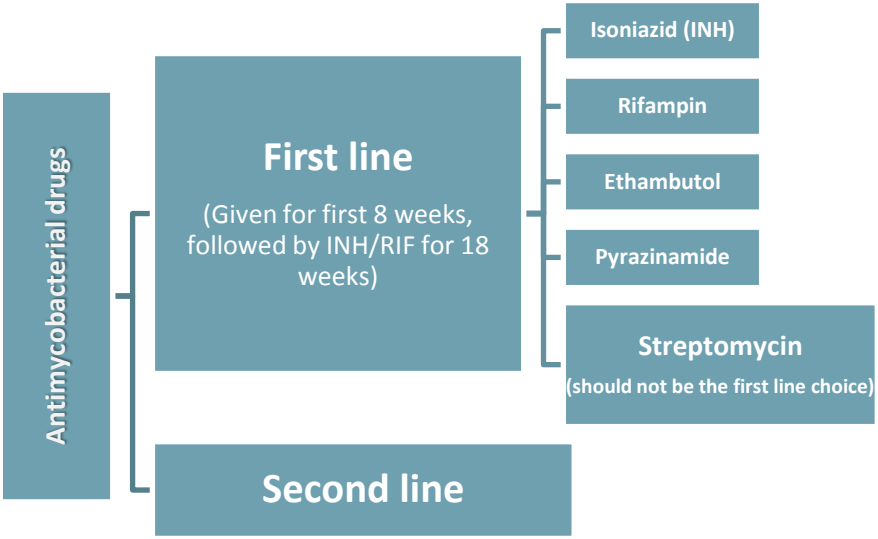
Treatment:

- Preventing development of drug resistance is the most important reason to use drug combination.
- Periods of treatment (minimum 6 months).
- TB can be treated effectively by using **first line** drugs (FLD) **isoniazid** (INH), **rifampin** (RIF), **pyrazinamide** (PZA), **ethambutol** (EMB) and **streptomycin** (SM). However, this first line therapy often fails to cure TB for several reasons. Relapse and the spread of the disease contribute to the emergence of drug resistant bacteria. The emergence of multidrug resistant TB (MDR-TB), i.e. which is resistant to at least isoniazid (INH) and rifampicin (RIF), is of great concern, because it requires the use of **second-line** drugs that are difficult to procure and are much more toxic and expensive than FLDs. source

Robert Koch (1843-1910) German physician who was awarded the Nobel Prize in Stockholm 1905

Some facts about TB:

- Each year, 1% of the global population is infected.
- More than one third of the world's population has tuberculosis.
- A major cause of death worldwide.



- Never use a single drug therapy
- Isoniazid –rifampin combination administered for 9 months will cure 95-98% of cases .
- Addition of pyrazinamide/ethambutol for this combination for the first 2 months allows total duration to be reduced to 6 months.

Indication of 2nd line treatment

- Resistance to the drugs of 1st line.
- Failure of clinical response
- There is contraindication for first line drugs.
- Used in typical & atypical tuberculosis
- 2nd line drugs are more toxic than 1st line drugs

First Line Drugs

DRUG	Mechanism Of Action	Site of Action	Clinical uses	Adverse effects	Drug Interactions
Isoniazid	**Bactericidal** for **resting** bacilli. **Bactericidal** for **rapidly growing** bacilli ; Inhibits the synthesis of mycobacterial cell wall (inhibit the synthesis of **mycolic acid**)	**intracellular** & **extracellular** bacilli	Treatment of **TB** Treatment of **Latent TB** in patients with positive tuberculin skin test **Prophylaxis** against active TB in individuals who are in great risk.	Peripheral neuritis (pin & needle sensation in the feet) Optic neuritis &atrophy (Pyridoxine (Vit B6) should be given in both cases) Hepatitis (toxic metabolites)	Enzyme **inhibitor** Slow and fast acetylators.
Rifampin	**Bactericidal ;** Inhibits RNA synthesis by binding to DNA dependent RNA polymerase enzyme.		Treatment of **TB** **Prophylaxis**.	Harmless **red-orange discoloration of body secretions** (saliva, sweat .....) **Tell the patient about this effect**. Hepatitis Flu-like syndrome Hemolytic anemia	Enzyme **inducer**
Ethambutol	**Bacteriostatic ;** Inhibitor of mycobacterial arabinosyl transferase (alters the cell barrier) disrupts the assembly of mycobacterial cell wall.		Treatment of **TB** in combination with other drugs.	Impaired visual acuity red-green color blindness. Ethambutol is contraindicated in children **under 5 years**.	-
Pyrazinamide	**Bacteriostatic** ; Mechanism of action is unknown	**Intracellular** Bacilli	**Mycobacterial infections** mainly in multidrug resistance cases. It is important in **short – course** (6 months) regimen. **Prophylaxis** of TB.	Hepatotoxicity (common) Hyperuricemia (gouty arthritis) Drug fever & skin rash	-
Streptomycin	**Bactericidal ;** Inhibitors of protein synthesis by binding to 30 S ribosomal subunits.	**Extracellular** bacilli	**Severe** , life-threating form of **TB** as meningitis, disseminated disease.	Ototoxicity Nephrotoxicity Neuromuscular block	-

Second Line Drugs

Drugs	Mechanism	Clinical uses	Adverse Effects
Ethionamide	Inhibits the synthesis of mycolic acid.	As s secondary line agent, treatment of **TB**.	**Terratogenic** Poorly tolerated because of: **Severe** gastric irritation& neurological manifstaion
Rifabutin	RNA inhibitor. Cross-resistance with rifampin is complete. Enzyme **inducer**	Effective in prevention & treatment of **TB**. In prevention & treatment of **atypical TB**.	GIT intolerance. Orange-red discoloration of body secretions.
Aminosalicylic Acid (PAS)	Bacteriostatic ; Inhibits Folic acid synthesis.	As a second line agent is used in the treatment of **pulmonary** & **other forms of TB**.	GIT upset. Crystalluria.
Fluoroquinolones (ciprofloxacin)		Effective against multidrug- resistant tuberculosis.	

TB & Pregnancy:

- Untreated TB represents **a great** risk to the pregnant women & her fetus than the treatment itself.
- First line (INH, ethmabutol, and rifampicin) drugs are given for 9 months in normal doses.
- **Streptomycin NOT used.**

TB & Breast feeding:

- It is not a contraindication to receive drugs, but **caution** is recommended.

1-What is the minimum period of time the T.B patient should
take drugs ?

A- 2 weeks
B- 2 months
C- Till the patient feels better
D- 6 months

2- A 3-years-old child came to hospital with his parents, after examination, the doctor diagnosed him with T.B, which one of the following drugs the doctor shouldn't give hem ?

A- Rifampin
B- Streptomycin
C- Ethambutol
D- Isoniazid

3- A pregnant woman came to KKUH with T.B complaining , which one of the following drugs the doctor shouldn't give her?

A- Rifampin
B- Streptomycin
C- Isoniazid
D- Ethambutol

4- A Patient with a history of gouty arthritis, which one of the following drugs we should not be given to him ?

A- Rifampin
B- Ethambutol
C- Pyrazinamide
D- Streptomycin

5- Someone who has TB, had a car driving test but he did not pass it because he ran a red light and he said he saw it green. What's the most likely drug he's taking ?

A- Ethambutol
B- Rifampin
C- Isoniazid
D- Pyrazinamide

Done By:
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5- A
4- C
3- B
2- C
1- D