



King Saud University
College of Medicine
1st Year, 3rd Block

Drugs Used in Tuberculosis

9



RESPIRATORY BLOCK

Tuberculosis

**Mycobacterium tuberculosis*, slow growing, an acid fast bacillus.

*Common sites of infections :

→Apical areas of lung

→Renal parenchyma

→Growing ends of bones

Treatment Of Tuberculosis

*Preventing development of drug resistance is the most important reason to use **drug combination**.

*Periods of treatment (**minimum 6 months**)

*Drugs are divided into two groups:

1- First line

2- Second line

Antimycobacterial drugs (First line)

1- Isoniazid (INH)

2- Rifampin*

3- Ethambutol

4- Pyrazinamide*

5- Streptomycin (should not be the first choice)

*Given for first 8 weeks, followed by INH/RIF for 18 weeks

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

1 st line	Isoniazid (INH)	Rifampin	Ethambutol	Pyrazinamide	Streptomycin
F E A T U R E S	<ul style="list-style-type: none"> -Bactericidal for rapidly growing bacilli and bacteriostatic for resting bacilli. - Inhibits the synthesis of mycobacterial cell wall (inhibit the synthesis of mycolic acid). 	<ul style="list-style-type: none"> -Bactericidal. - Inhibits RNA synthesis by binding to DNA dependent RNA polymerase enzyme. 	<ul style="list-style-type: none"> - Bacteriostatic. - Inhibitor of mycobacterial arabinosyl transferase (alters the cell barrier) disrupts the assembly of mycobacterial cell wall. 	<ul style="list-style-type: none"> - Bactericidal. - Mechanism of action is Unknown. 	<ul style="list-style-type: none"> - Bactericidal. - Inhibitors protein synthesis by binding to 30 S ribosomal subunits.
Site of Action	<ul style="list-style-type: none"> - Active against intracellular & extracellular bacilli. 	<ul style="list-style-type: none"> - Similar to INH 	<ul style="list-style-type: none"> - Similar to INH 	<ul style="list-style-type: none"> - Active against Intracellular Bacilli 	<ul style="list-style-type: none"> - Active mainly on extracellular bacilli
Clinical uses	<ul style="list-style-type: none"> - TB. - Latent TB. - Prophylaxis against TB. 	<ul style="list-style-type: none"> - TB. - Prophylaxis against TB. 	<ul style="list-style-type: none"> -TB in combination with other drugs 	<ul style="list-style-type: none"> -Multidrug resistance of TB. -Prophylaxis against TB -important in Short course. 	<ul style="list-style-type: none"> - Severe cases of TB, as meningitis
Adverse effects	<ul style="list-style-type: none"> - Peripheral neuritis (pin & needles sensation in the feet). - Optic neuritis atrophy. (Pyridoxine -vitamin B₆- should be given in both cases). - Hepatitis. 	<ul style="list-style-type: none"> - Harmless red-orange discoloration of body secretions (saliva, sweat,...). - Hepatitis. - Flu-like syndrome. - Hemolytic anemia. 	<ul style="list-style-type: none"> - Impaired visual acuity. - Red-green color blindness. - contraindicated in children under 5 years. 	<ul style="list-style-type: none"> - Hepatotoxicity. - Hyperuricemia. - Fever. - Skin rash. 	<ul style="list-style-type: none"> - Ototoxicity. - Nephrotoxicity - Neuromuscular block.
Drug Interactions	<ul style="list-style-type: none"> - Slow and fast acetylators individuals. - Fast acetylator may need high dosage. 	<ul style="list-style-type: none"> - Enzyme inducer 			

2nd line Drugs

Indication of 2nd line treatment: 1- Resistance to the drugs of 1st line. 2- Failure of clinical response. 3- There is contraindication for first line drugs. 4- Used in typical & atypical tuberculosis. 5- **2nd line drugs are more toxic than 1st line drugs.**

	Ethionamide	Fluoroquinolones (Ciprofloxacin)	Rifabutin
Mechanism Of Action	Inhibits the synthesis of mycolic acid.	-	-RNA inhibitor. -Cross-resistance with Rifampin. -Enzyme inducer.
Clinical Uses	As a secondary line agent ,treatment of TB.	Effective against multidrug- resistant tuberculosis.	-Effective in prevention &treatment of T.B. -In prevention & treatment of atypical TB.
Adverse Effects	-Poorly tolerated Because of : Severe gastric irritation & Neurological manifestations.	-	1-GIT intolerance. 2-Orange-red discoloration of body secretions.

Aminosalicylic Acid (PAS)

act as:

- 1- bacteriostatic.
- 2- Inhibits Folic acid synthesis.

Clinical uses:

As a second line agent in the treatment of pulmonary & other forms of TB.

Adverse effects:

- 1-GIT upset.
- 2-Crystalluria. (excretion of crystals in the urine, causing renal irritation)

TB with

1-pregnancy:

-Untreated TB represents a great risk to the pregnant & her fetus than the treatment itself.

-First line (INH, Ethambutol and rifampicin) drugs are given for 9 months in normal doses

Pyrazinamide & Streptomycin not used

2- Breast Feeding:

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

SUMMARY

Drug	Mech. Action	Clinical uses	Adverse effect
Isoniazid ^{1,2,*,**}	Inhibit synthesis of mycolic acid.	TB, Latent TB and prophylaxis	Peripheral neuritis Hepatitis
Rifampin ^{*,1,2}	Inhibit RNA synthesis	TB, prophylaxis	Red-orange discoloration of body secretions, Hepatitis
Ethambutol ^{**1,2}	disrupts the assembly of mycobacterial cell wall.	TB in combination with other drugs	Impaired visual acuity red-green color blindness
Pyrazinamide ^{*,1}	Unknown	Mycobacterial infections Important in(6months) course Prophylaxis	Hepatotoxicity Hyperuricemia (CI in gout)
Streptomycin ^{*,2}	Inhibit protein synthesis	Severe , life-threatening form of T.B. as meningitis	Ototoxicity Nephrotoxicity
Ethionamide	Inhibit synthesis of mycolic acid.	TB	Terratogenic, Severe gastric irritation
Fluoroquinolones	Effective against multidrug- resistant tuberculosis.		
Rifabutin	RNA inhibitor	Prevention and treatment of (TB, atypical TB)	GIT intolerance Orange-red discoloration of body secretions.
Aminosalicylic Acid ^{**}	Inhibits Folic acid synthesis.	TB	GIT upset, crystallurea

Red:1st line drugs. Green:2nd line. **:Bacteriostatic. *:Bactericidal. 1:Intracellular effect. 2:Extracellular effect.

MCQs

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-Which one of the following inhibit RNA syntheses (by binding to DNA dependent RNA polymerase enzyme) ?

- A- Rifampin
- B- Pyrazinamide
- C- Rifabutin
- D- A and C

3-Which one of the following inhibit protein syntheses ?

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

4-Which one of the following inhibit cell wall (mycolic acid) syntheses ?

- A- Ethionamide
- B- Isoniazid
- C- Streptomycin
- D- A and B

5- 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

6- 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

7- 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

8- All of the following drugs act on (intracellular and extracellular) except ?

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

9- 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

10- A TB patient taking Isoniazid, but the doctor warned him about the sever side effects of it and prescribed a drug that would minimize the side effects. What's that drug ?

- A- Paracetamol
- B- Pyridoxine
- C- Colchicine
- D- Salbutamol

1-D 2-D 3-A 4-D 5-C 6-B 7-C 8-C 9-A 10-B



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**We hope that we made this lecture easier for you
Good Luck !**