

# TUBERCULOSIS

Drug therapy





**BY**

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# 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



# OBJECTIVES ( continue)

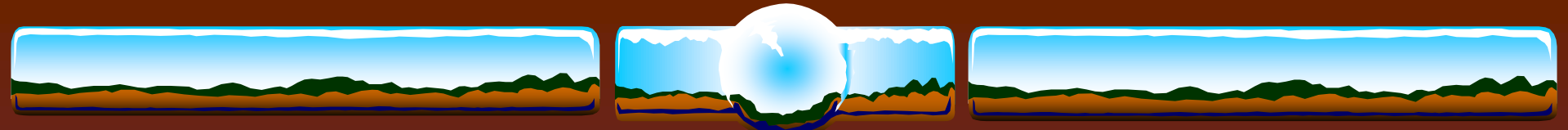
Regarding :

- ❖ The mechanism of action
- ❖ Adverse effects
- ❖ Drug interactions
- ❖ Contraindication
- ❖ Discuss tuberculosis & pregnancy
- ❖ Discuss tuberculosis & breast feeding



# Etiology

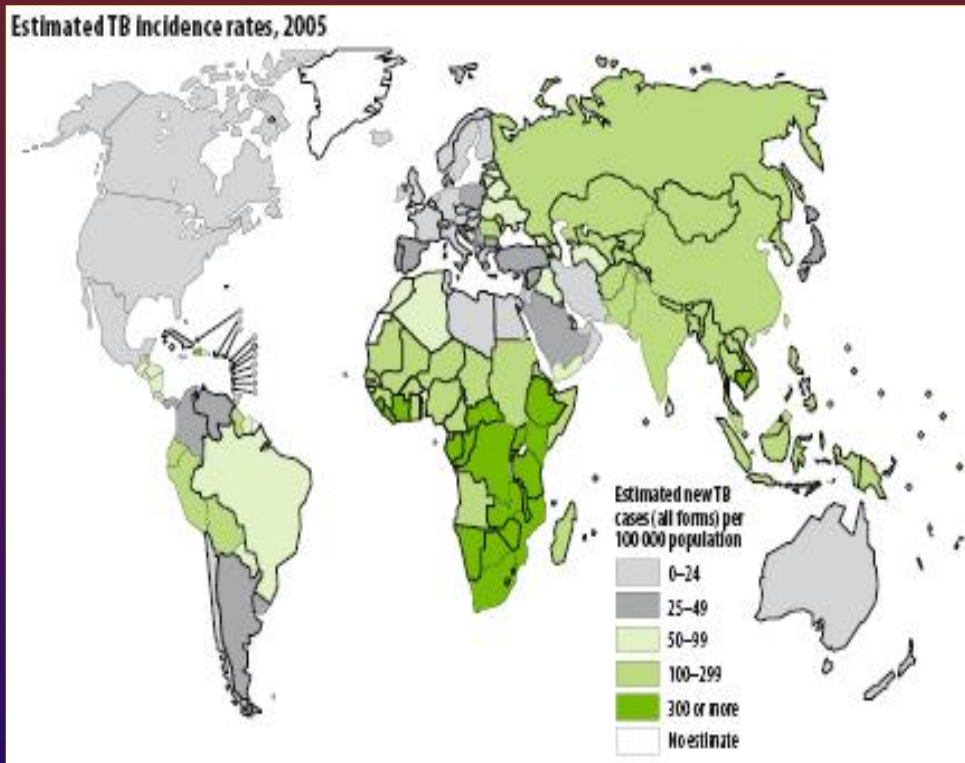
**Mycobacterium tuberculosis**, slow growing, an acid fast bacillus

- 
- ❖ Robert Koch was the first to see *Mycobacterium tuberculosis* with his staining technique in 1882.





# *Disease information:*



• Each year, 1% of the global population is infected.

More than one third of the world's population has tuberculosis.



For *my* sake  
**DON'T  
SPIT**





# COVER UP! YOUR COUGHS AND SNEEZES

Actual photograph of a sneeze



**SPRAY SPREADS**  
**COLDS • FLU • TUBERCULOSIS**



THE ANNUAL SALE OF *Christmas Seals* MADE THIS POSTER POSSIBLE



# Tuberculosis

## 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

- ❖ Isoniazid (INH)
- ❖ Rifampin
- ❖ Ethambutol
- ❖ Pyrazinamide
- ❖ Streptomycin (should not be the first line 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.**





# Isoniazid

- ❖ **Bacteriostatic for resting bacilli.**
- ❖ **Bactericidal for rapidly growing bacilli.**
- ❖ **Is effective against intracellular & extracellular bacilli**



# Mechanism Of Action

- ❖ Inhibits the synthesis of mycobacterial cell wall ( inhibit the synthesis of mycolic acid )



# Clinical uses

- ❖ **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 .**



# Adverse effects

## ❖ Peripheral neuritis

(pin & needles sensation in the feet )

## ❖ Optic neuritis & atrophy.

(Pyridoxine should be given in both cases )

## ❖ Hepatitis (toxic metabolites)

❖ Hepatitis with INH, is age dependent; it is rare in persons younger than 20 years , risk increases with age and alcohol use



# Drug Interactions of INH

- ❖ **Enzyme inhibitor**
- ❖ **Slow and fast acetylators.**





# Rifampin

- ❖ **Bactericidal**

- ❖ **Inhibits RNA synthesis**

**by binding to DNA dependent RNA  
polymerase enzyme.**



# Site of Action (similar to INH)

- ❖ Intracellular bacilli
- ❖ Extracellular bacilli



# Clinical uses

❖ Treatment of TB

❖ Prophylaxis.



## Adverse effects

- ❖ **Harmless red-orange discoloration of body secretions ( saliva, sweat, tears .....). Tell the patient about this effect. Can permanently stain contact lenses.**
- ❖ **Hepatitis less common compared to INH**
- ❖ **Flu-like syndrome**
- ❖ **Hemolytic anemia**



# Drug Interactions

- ❖ **Enzyme inducer**
- ❖ **Clinically significant drug interactions such as warfarin, methadone will be metabolized faster**





# Ethambutol

❖ **Bacteriostatic**

❖ **Inhibitor of mycobacterial arabinosyl transferase ( alters the cell barrier )**  
disrupts the assembly of mycobacterial cell wall.



# Site Of Action (similar to INH)

❖ Intracellular & Extracellular bacilli



# Clinical uses

- ❖ **Treatment of tuberculosis in combination with other drugs.**



# Adverse effects

- ❖ Impaired visual acuity
- ❖ red-green color blindness.
- ❖ Ethambutol is contraindicated in children under 5 years.



# Pyrazinamide

- ❖ **Bacteriostatic**
- ❖ **Mechanism of action is unknown .**



# Site Of Action

- ❖ Active against **Intracellular Bacilli**



## Clinical uses

- ❖ **Mycobacterial infections mainly in multidrug resistance cases.**
- ❖ **It is important in short –course (6 months) regimen.**
- ❖ **Prophylaxis of TB .**



# Adverse effects

- ❖ **Hepatotoxicity (common)**
- ❖ **Hyperuricemia (gouty arthritis)**
- ❖ **Drug fever & skin rash**





# Streptomycin

- ❖ Bactericidal
- ❖ Inhibitors of protein synthesis by binding to 30 S ribosomal subunits.
- ❖ Active mainly on **extracellular bacilli**



# Clinical uses

- ❖ Severe , life-threatening form of T.B. as meningitis, disseminated disease.



# Adverse Effects

- ❖ **Ototoxicity**
- ❖ **Nephrotoxicity**
- ❖ **Neuromuscular block**



# Indication of 2<sup>nd</sup> line treatment

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



# Ethionamide

❖ Inhibits the synthesis of mycolic acid



# Clinical uses

- ❖ As a secondary line agent ,treatment of TB.



# Adverse Effects

**Terratogenic**

**Poorly tolerated**

**Because of :**

- ❖ **Severe gastric irritation &**
- ❖ **Neurological manifestations**



# Fluoroquinolones (Ciprofloxacin )

- ❖ Effective against multidrug-resistant tuberculosis.





# Rifabutin

- ❖ RNA inhibitor
- ❖ Cross –resistance with rifampin is complete.
- ❖ Enzyme inducer



# Clinical uses

- ❖ **Effective in prevention & treatment of T.B.**
- ❖ **In prevention & treatment of atypical TB.**



# Adverse Effects

❖ **GIT intolerance**

❖ **Orange-red discoloration of body secretions.**



# TB & Pregnancy

- ❖ **Untreated TB represents a great risk to the pregnant woman & 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

# FIGHT TUBERCULOSIS



WPA FEDERAL ART PROJECTS

# OBEDY

THE RULES OF HEALTH





WPA FEDERAL ART PROJECT

DIV. 54

**BE CLEAN**  
IN EVERYTHING THAT  
CONCERNS YOUR BABY