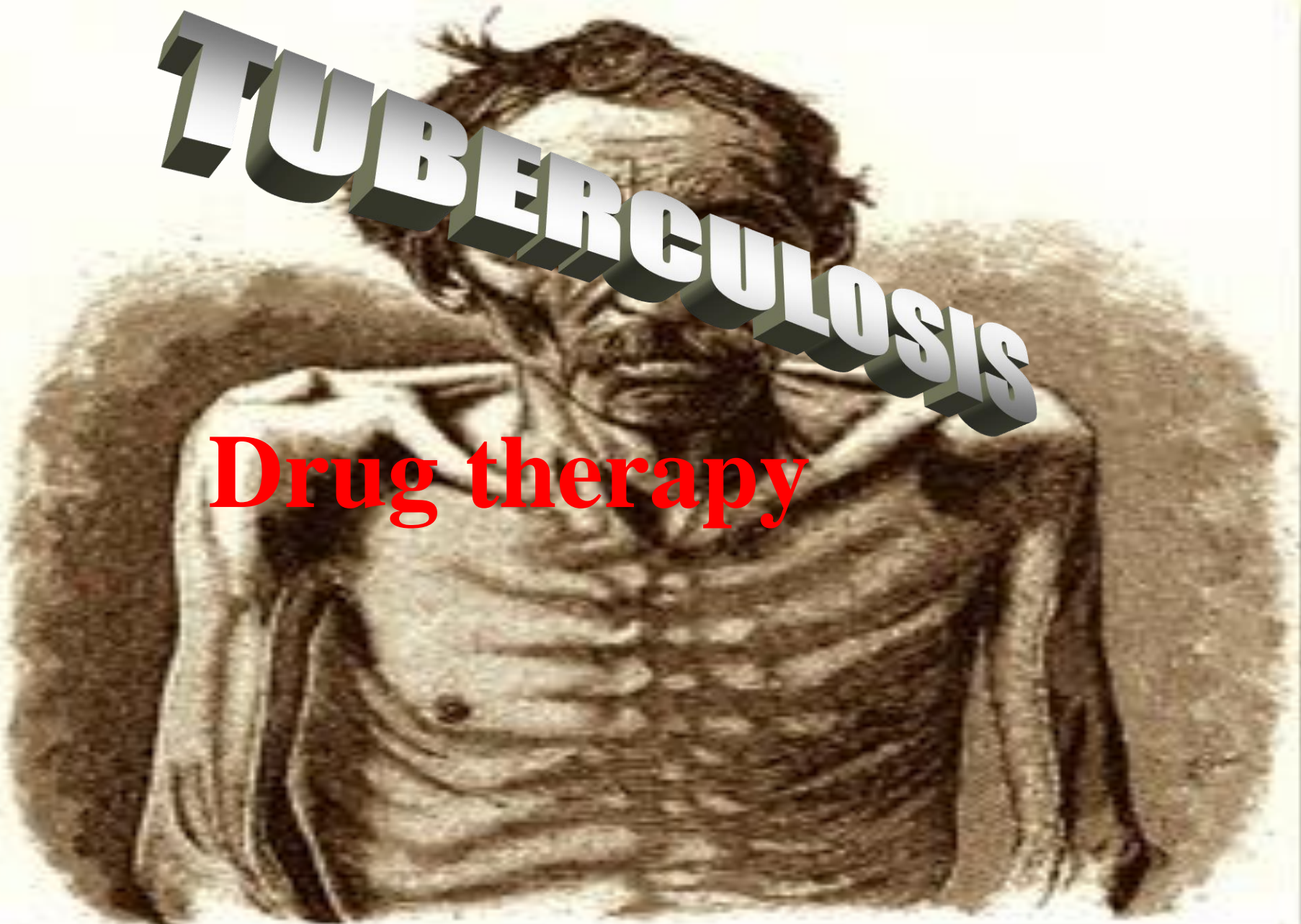


TUBERCULOSIS

Drug therapy





BY

Dr. Ishfaq Bukhari

Associate Professor of Pharmacology

College of Medicine, KSU



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)

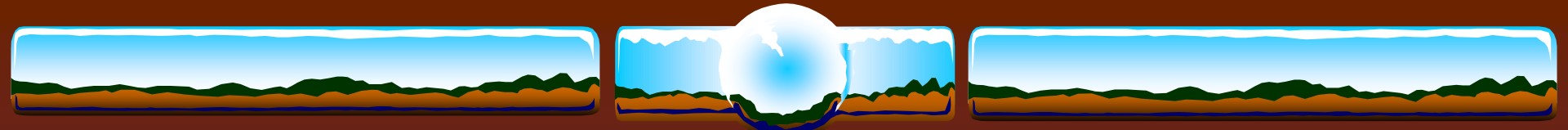
Regarding :

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



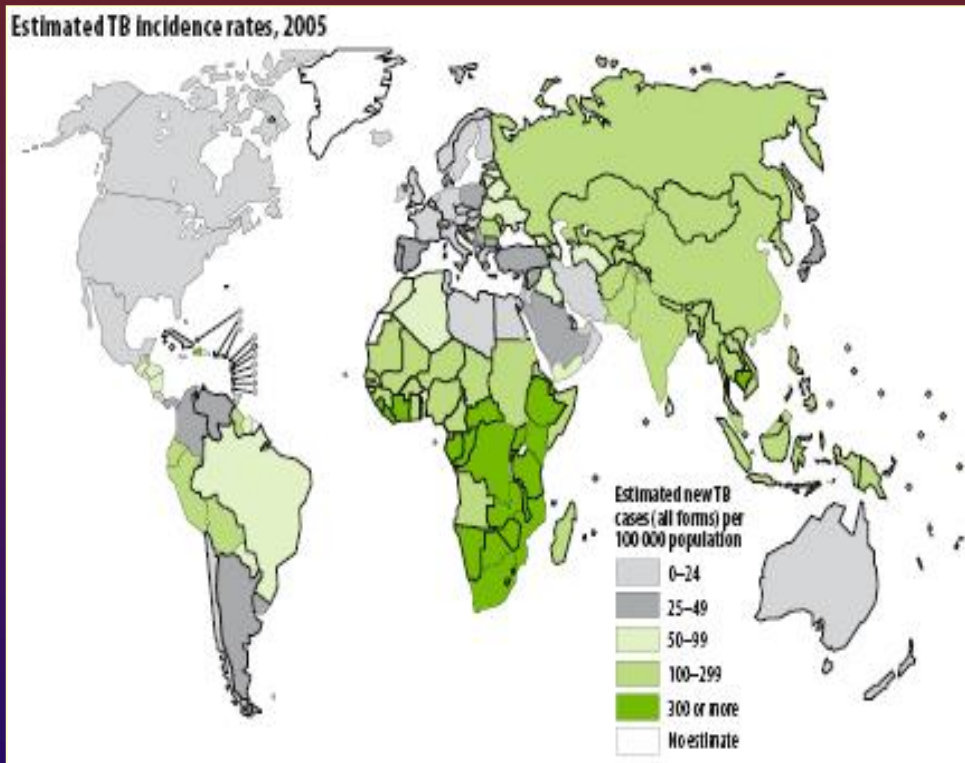
Etiology

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
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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 preferred)



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 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



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



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OBEDY

THE RULES OF HEALTH



WPA FEDERAL ART PROJECT

DIV. 54

BE CLEAN
IN EVERYTHING THAT
CONCERNS YOUR BABY