
TUBERCULOSIS
Drug therapy

BY

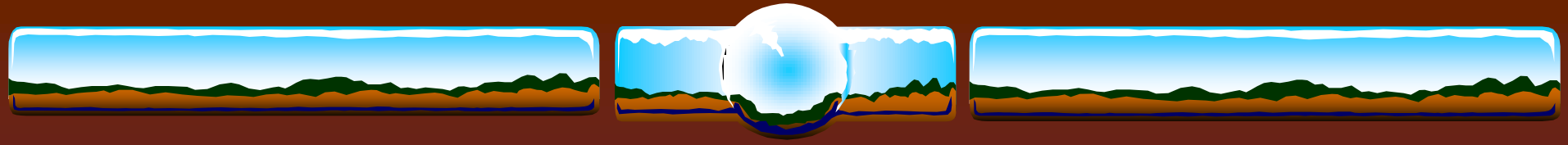
Dr. Ishfaq Bukhari

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

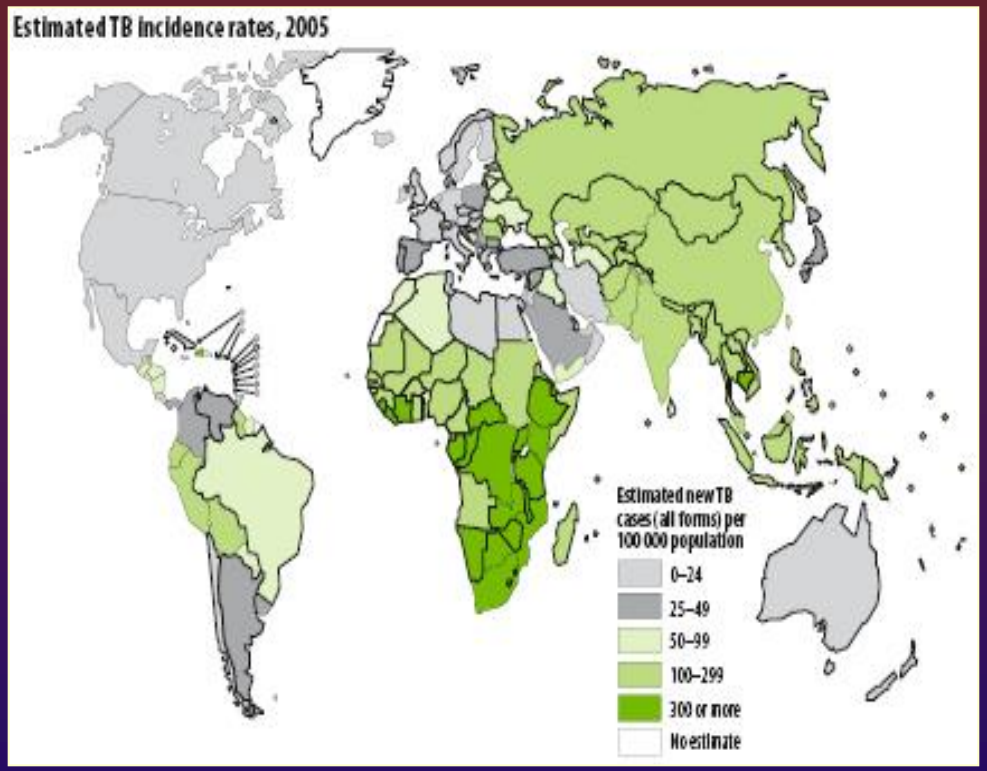
Etiology

Mycobacterium tuberculosis, slow growing, an acid fast bacillus

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

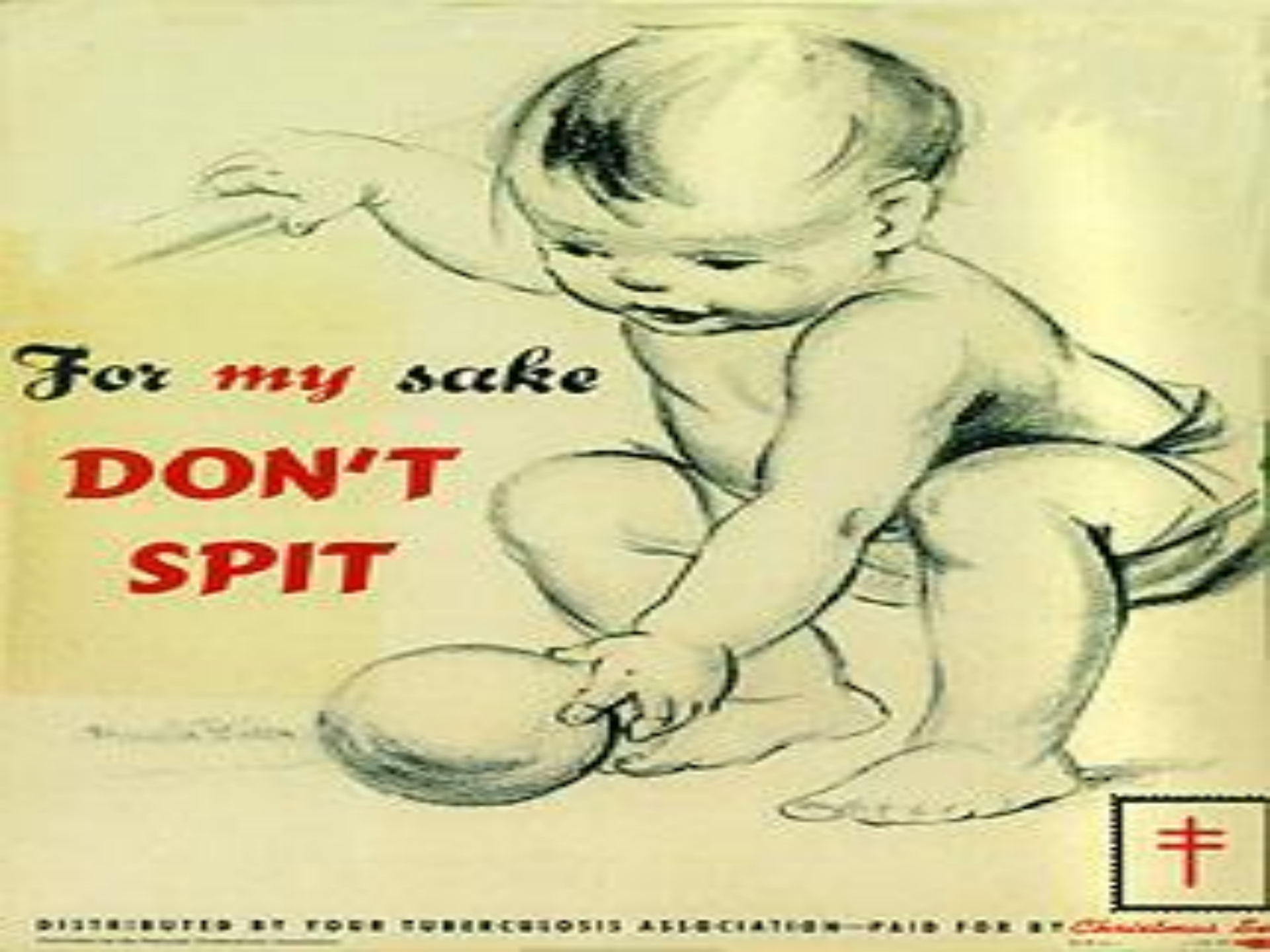

Robert Koch (1843-1910) German physician who was awarded the Nobel Prize in Stockholm 1905

Disease information:



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

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



DISTRIBUTED BY YOUR TUBERCULOSIS ASSOCIATION—PAID FOR BY Christmas Seal

COVER UP!

YOUR COUGHS AND SNEEZES

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

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

- Streptomycin (should not be the first line choice)

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
- Clincally significsnt drug interactios 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-threating 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.

Aminosalicylic Acid (PAS).

- Bacteriostatic
- Inhibits Folic acid synthesis.

Clinical uses

- As a second line agent is used in the treatment of pulmonary & other forms of tuberculosis.

Adverse effects

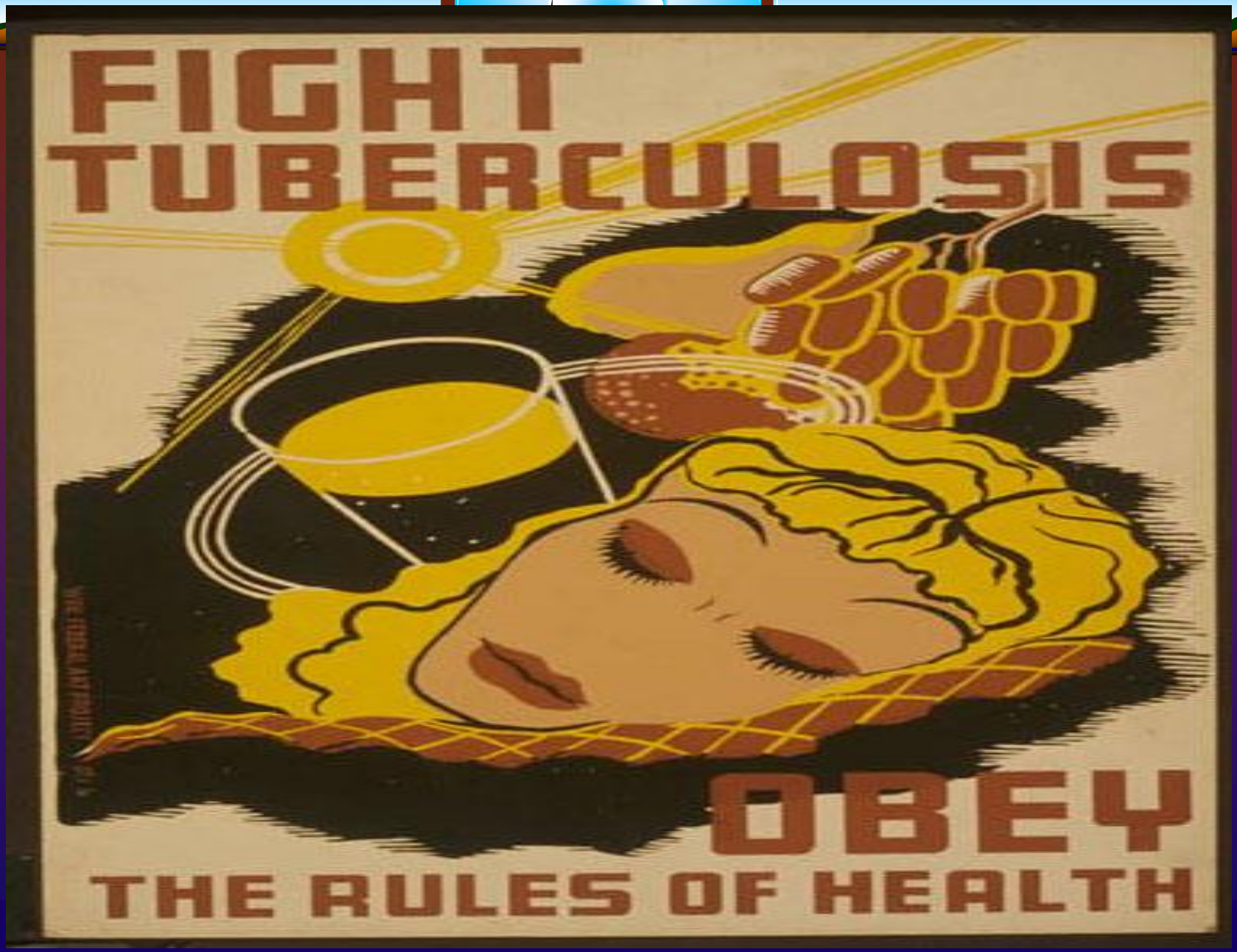
- GIT upset
- Crystalluria

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
OBEY
THE RULES OF HEALTH


WPA FEDERAL ART PROJECT
BE CLEAN
IN EVERYTHING THAT
CONCERNS YOUR BABY