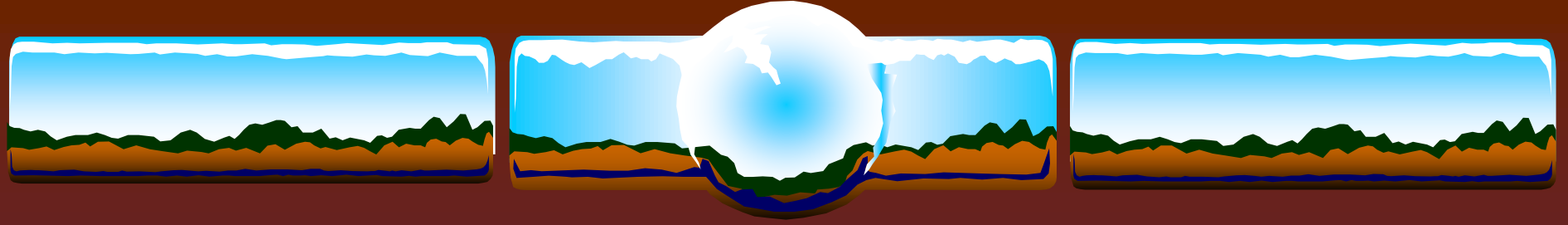


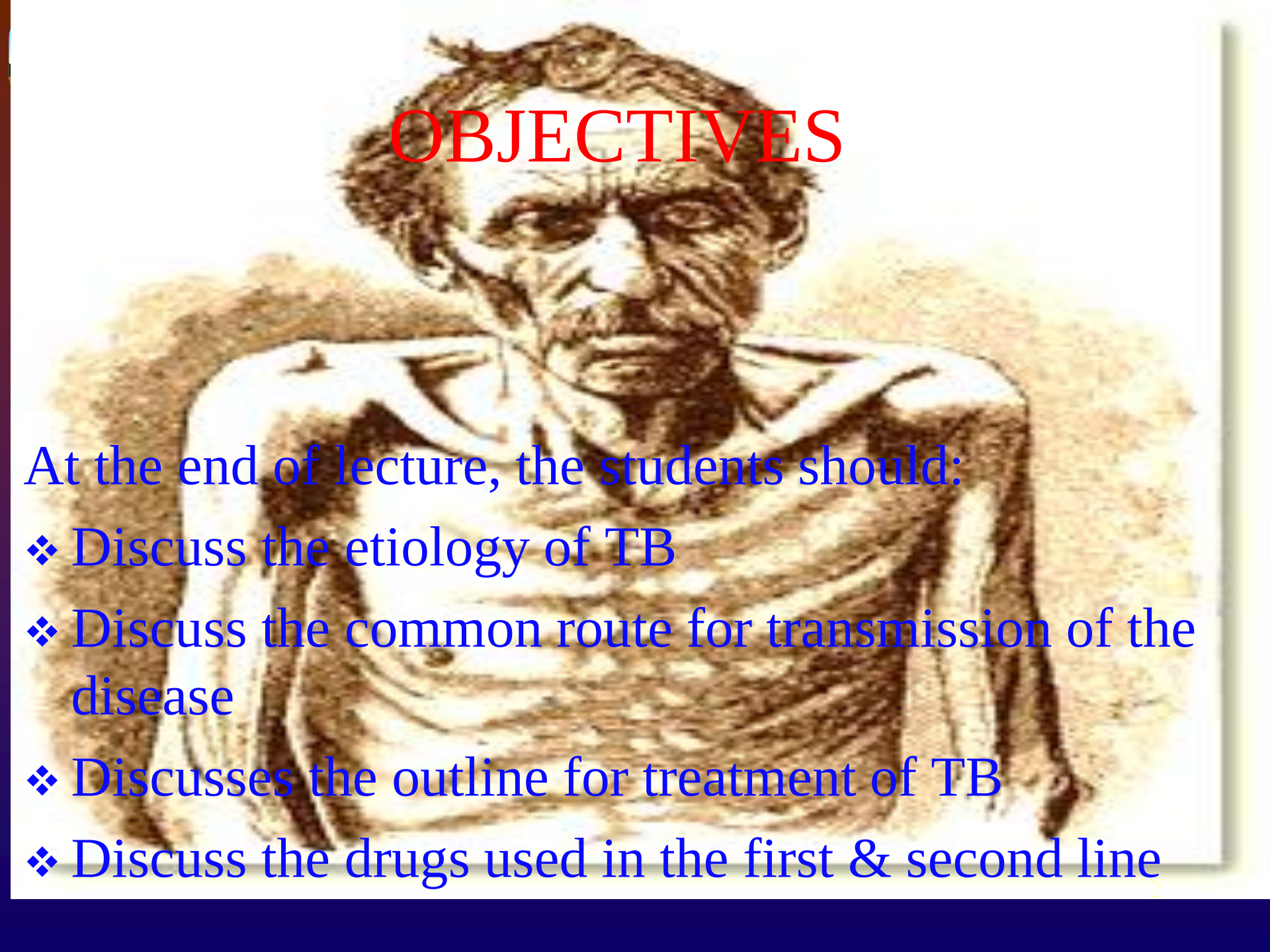
TUBERCULOSIS

Pulmonary TB

Drug therapy

Dr. Ishfaq

Dr. Aliah



OBJECTIVES

At the end of lecture, the students should:

- Discuss the etiology of TB
- Discuss the common route for transmission of the disease
- Discusses the outline for treatment of TB
- Discuss the drugs used in the first & second line

OBJECTIVES (Cont’)

Drugs

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

Robert Koch was the first

to isolate mammalian *Mycobacterium tuberculosis* with his staining technique in 1882.

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. The mycobacteria survive & multiply within macrophages**
- **Renal parenchyma**
- **Growing ends of bones.**

Treatment of Tuberculosis

- Drugs combination is important to prevent development of drug resistance.
- Periods of treatment (minimum 6 months)

- Drugs are divided into 2 groups:

1. First line
2. Second line.

Antimycobacterial drugs

First line

1- Isoniazid (INH)

2- Rifampin

3- Ethambutol

4- Pyrazinamide

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

5- Streptomycin (should not be the 1st line choice).

Never use a single drug therapy

- INH –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.

INH

- Bacteriostatic for resting bacilli
- Bactericidal for rapidly growing bacilli
- Effective against intracellular & extracellular bacilli.

Mechanism of Action

- Inhibits the synthesis of mycolic acid, an important component of mycobacterial cell wall
- Penetrates into macrophages & is active against both intracellular & extracellular organisms.

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.

ADRs

- **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 & alcohol use.

Drug Interactions

- INH inhibits cytochrome P450 2C19 isoform (enzyme inhibitor)
- Slow & fast acetylators.

Rifampin

- **Bactericidal**
- **Mechanism of action:**

Binds to bacterial DNA- dependent RNA polymerase enzyme & thus inhibits RNA synthesis.

Site of Action (similar to INH)

- Intracellular bacilli
- Extracellular bacilli

Clinical uses

- Treatment of TB
- Prophylaxis
- Against other bacterial infection such as meningococcal & staphylococcal infections.

ADRs

- **Harmless red-orange discoloration of body secretions (saliva, sweat, urine, 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

- **Rifampicin** strongly induces most cytochrome P450 isoforms

Clinically significant drug interactions: warfarin, methadone will be metabolized faster.

Ethambutol

- Bacteriostatic

- Inhibits mycobacterial arabinosyl transferase; essential enzyme for mycobacterial cell wall synthesis

Thus disrupts the assembly of mycobacterial cell wall.

Site of Action (similar to INH)

Intracellular & extracellular bacilli

Clinical uses

Treatment of TB in combination with other drugs.

ADRs

- Impaired visual acuity

Red-green color blindness

- Ethambutol is contraindicated in children under 5 years.

Pyrazinamide (PZA)

- **Bacteriostatic**

- **Mechanism of action: Pyrazinamide is converted to pyrazinoic acid—the active form which disrupts mycobacterial cell membrane metabolism & transport functions**
- **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.

PZA

ADRs

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

Streptomycin

- Bactericidal
- Inhibits of protein synthesis by binding to bacterial 30S ribosomal subunits
- Active mainly against extracellular bacilli.

Clinical uses

- **Injectable drug used in severe, life-threating form of T.B. as meningitis, disseminated disease.**

ADRs

- **Ototoxicity (Vertigo & hearing loss) may be permanent**
- **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

Mechanism of action: Inhibits the synthesis of mycolic acid.

Clinical uses:

As a secondary line agent for treatment of TB (po).

ADRs of Ethionamide

Teratogenic

Poorly tolerated

Because of :

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

Fluoroquinolones (Ciprofloxacin)

Effective against multidrug- resistant TB.

Rifabutin

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

Clinical uses of Rifabutin

- Effective in prevention & treatment of TB
- In prevention & treatment of atypical TB.

ADRs

- GIT intolerance
- Orange-red discoloration of body secretions.

Para AminoSalicylic acid (PAS)

- Bacteriostatic
- Inhibits folic acid synthesis thus slows bacterial cell growth & multiplication

Clinical uses

- As a second line agent is used in the treatment of chronic pulmonary & other forms of TB
- Help to slow development of resistance to other drugs, especially INH & streptomycin.

ADRs

- GIT upset, peptic ulceration & hemorrhage
- Crystalluria.

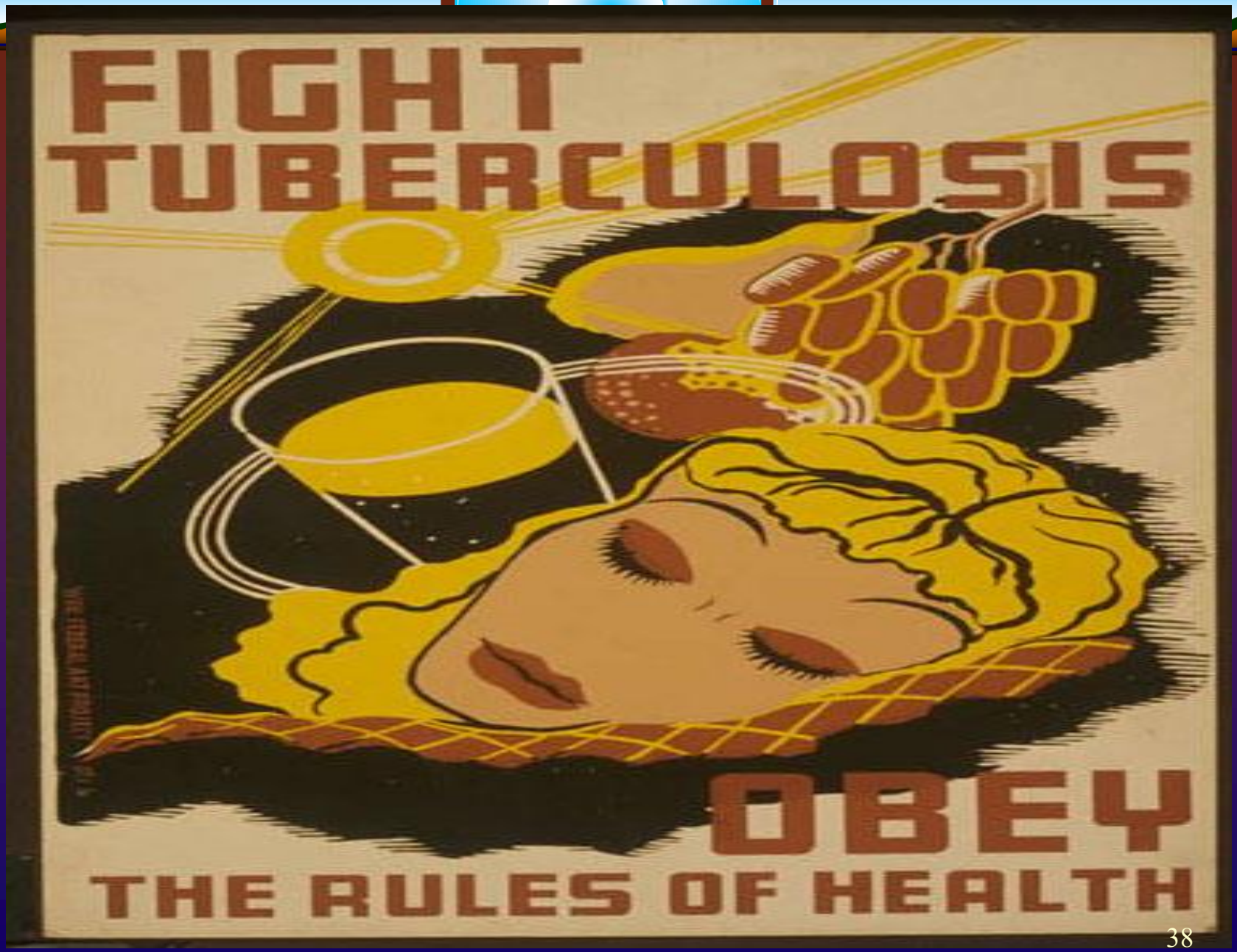
TB & Pregnancy

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

- First line (INH, ethmabutol & 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