Mycobacteria

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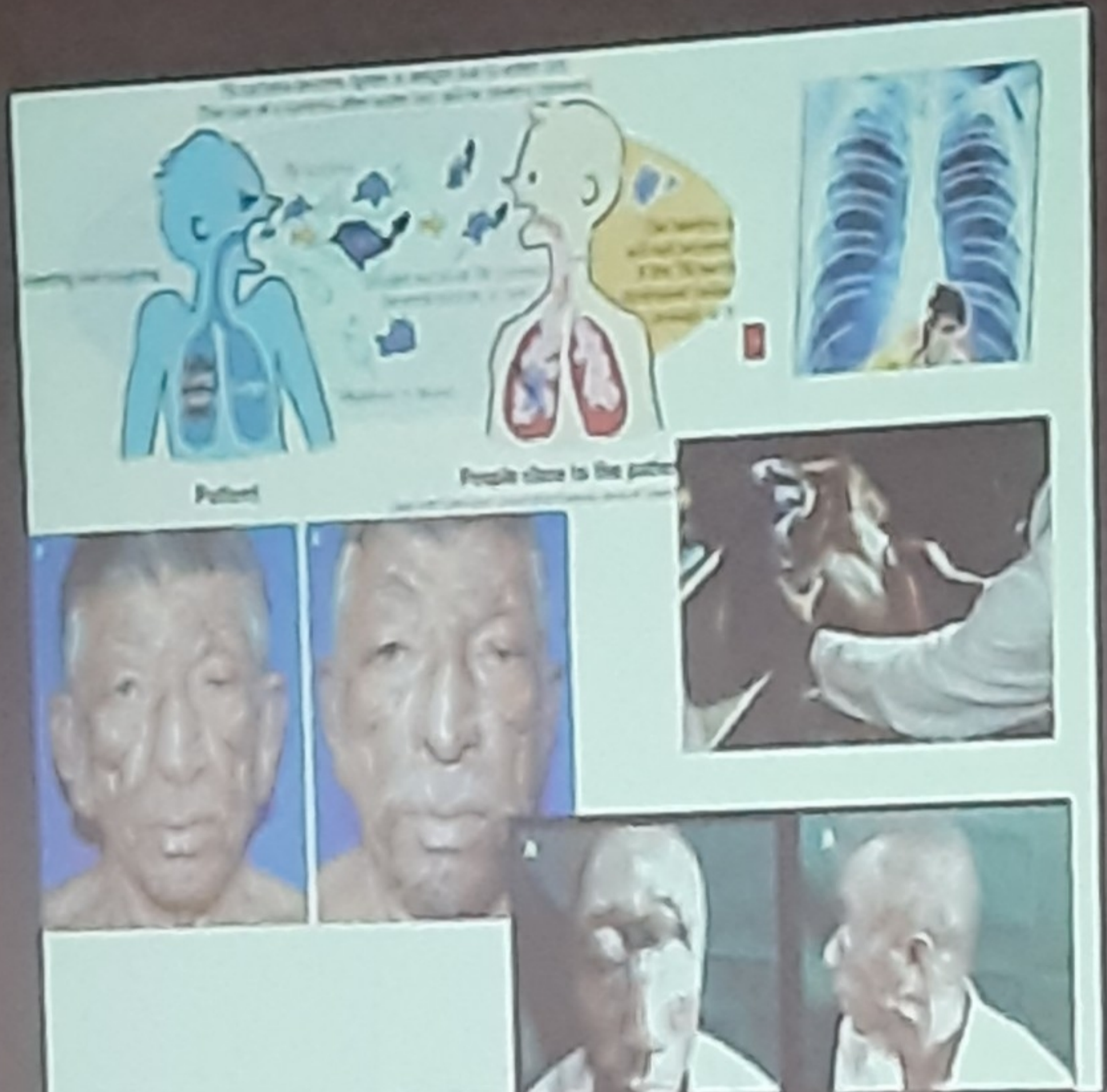


Learning Objectives

- ✓ Describe the structure, epidemiology and main pathogenic features & symptoms of Mycobacteria
- ✓ Discuss Laboratory Diagnosis of MTB symptoms, dormant infections, treatment
- ✓ MDR and XDR TB: what are they, how have they come about, and how
- ✓ Prevention and treatment
- ✓ Leprosy
- ✓ Non-Tubercular Mycobacterium infections

Introduction

- >100 species of mycobacteria

- Major pathogens:
  - *Mycobacterium tuberculosis* (Koch, 1882) - Koch bacillus
  - *Mycobacterium leprae* (Hansen, 1874) - Hansen's bacillus
  - Rest are environmental organisms-collectively known as MOTTs (Mycobacteria Other Than Tuberculosis) or NTM (non-tuberculous mycobacteria) -cause opportunistic infections

Classification of Mycobacterial Species

Mycobacteria

M. TB Complex

- M. tuberculosis
- M. africanum
- M. bovis
- M. microti

M. leprae

Nontuberculous mycobacteria (NTM)
= atypical mycobacteria
= mycobacteria other than TB (MOTT)

- M. avium complex (MAC)
  - M. avium
  - M. intracellulare
- M. kansasii, M. abscessus
- M. fortuitum, M. malmoense, M. xenopi
- M. szulgai, M. chelonae .....

lycobacterium: Physiology & Structure

Name from *Myces* and *Bakterion*, Fungus-like Rod

Bacillus

Aerobic

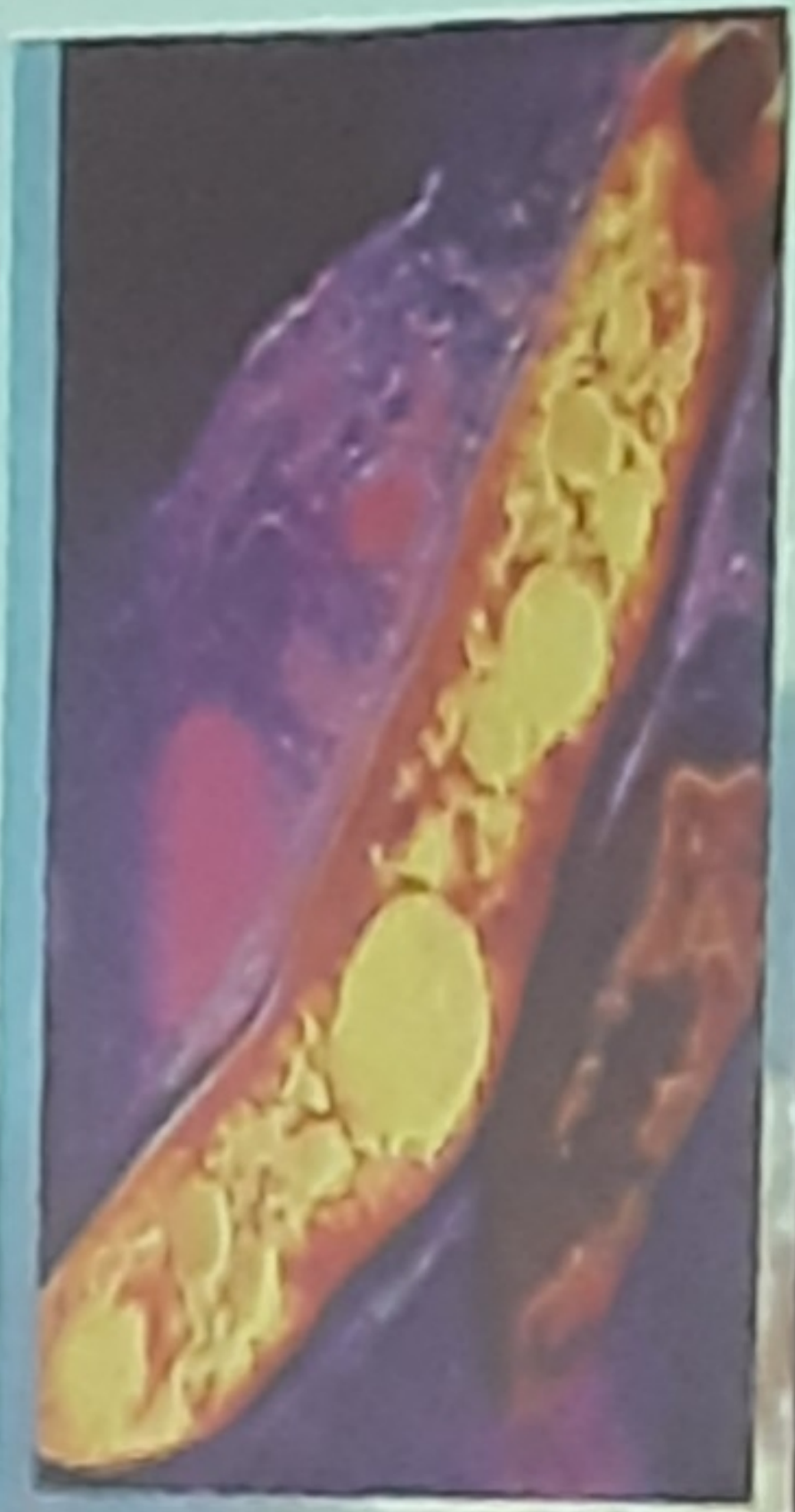
Nonmotile

Acid-Fast Staining

Complex Cell Wall

Intracellular Parasite

Diseases From Immune Response



Virulence factors

No spore, no flagellum, no exotoxin,no endotoxin, no invasive enzyme

- Capsule:polysaccharide;CR3;enzyme; protect
- Lipid/Lipo arabinomannan
- Heat-shock protein/Tuberculin protein: antigenicity.

Lipid

a. Phospholipid

monocytes proliferate, cause tubercles

b. Wax D

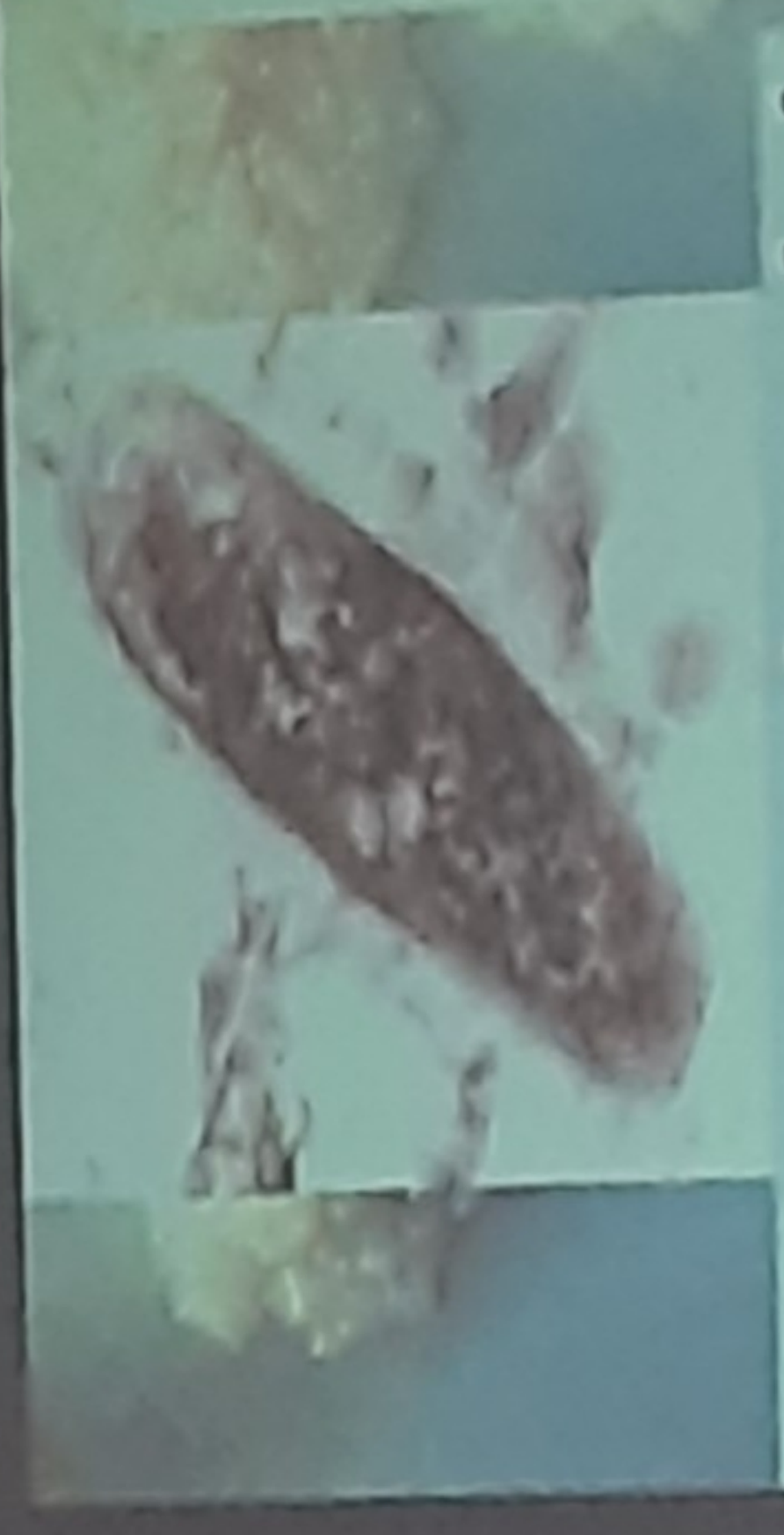
c. Sulfatide

suppress phagosome

d. Cord factor (trehalose-6,6-dimycolate)

destroy mitochondria, cause chronic granulomatosis, suppress WBC

Cell Wall



- Complex
- Contains Mycolic Acid
  - Lipids account for 60% of Cell Wall Weight
- Responsible for Many Characteristics
  - Acid Fastness
  - Slow Growth
  - Antibiotic Resistance
  - Antigenicity
  - Clumping

Mycobacterium tuberculosis

Pathogenesis

- Modes of transmission
  - Droplet infection
    - Person to person by inhalation aerosols
    - *M.tuberculosis* (Pulmonary tuberculosis)
  - Ingestion of milk
    - Infected cattle
    - *M.bovis* (Intestinal tuberculosis)
  - Contamination of abrasion
    - Laboratory workers (Skin infection)

Epidemiology

- 2 Billion People Infected World Wide
  - ✓ONE-THIRD of the human population
- 8.8 Million New Cases / Year
- 2 Million Deaths / Year
- Kenya is one of the 22 countries most affected by TB in the world

Primary infection

Latent TB infection
(immunocompetent)

Progressive primary TB
(immunocompromised, children)

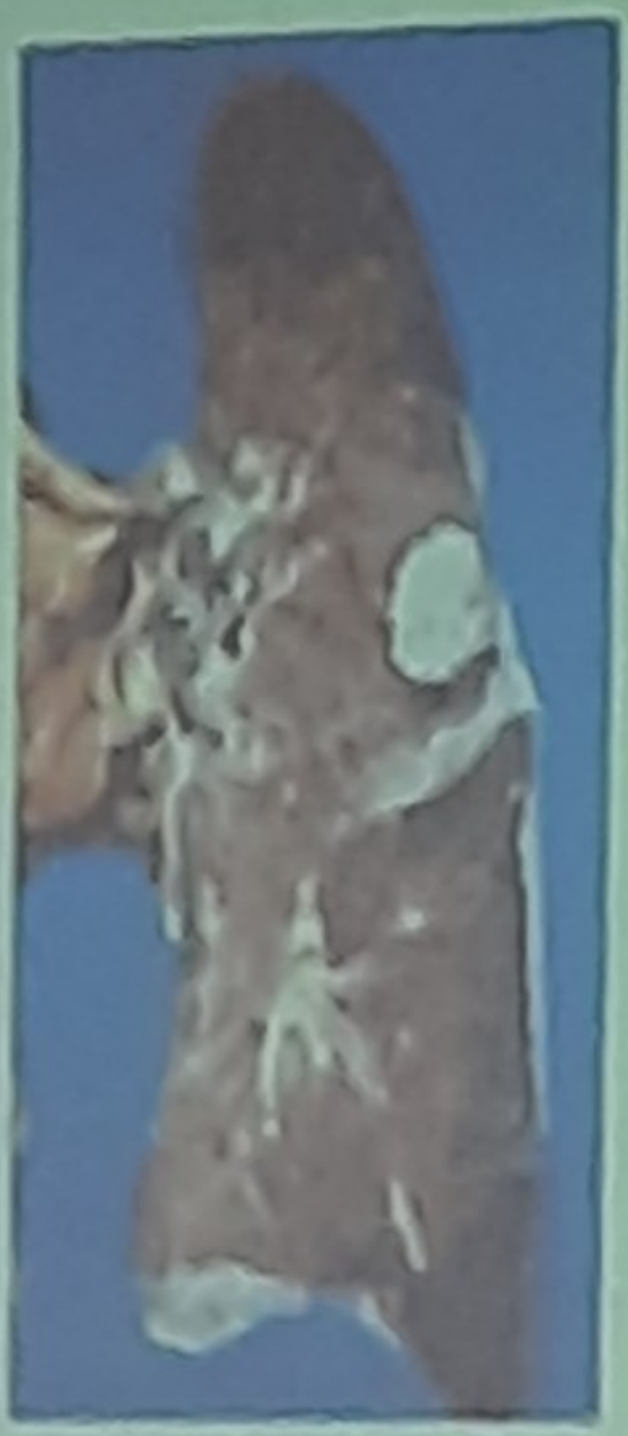
Post-primary TB/ Secondary TB/Adult-type TB
Reactivation disease
(develops when immunity is suppressed)

Typical Progression of Pulmonary Tuberculosis

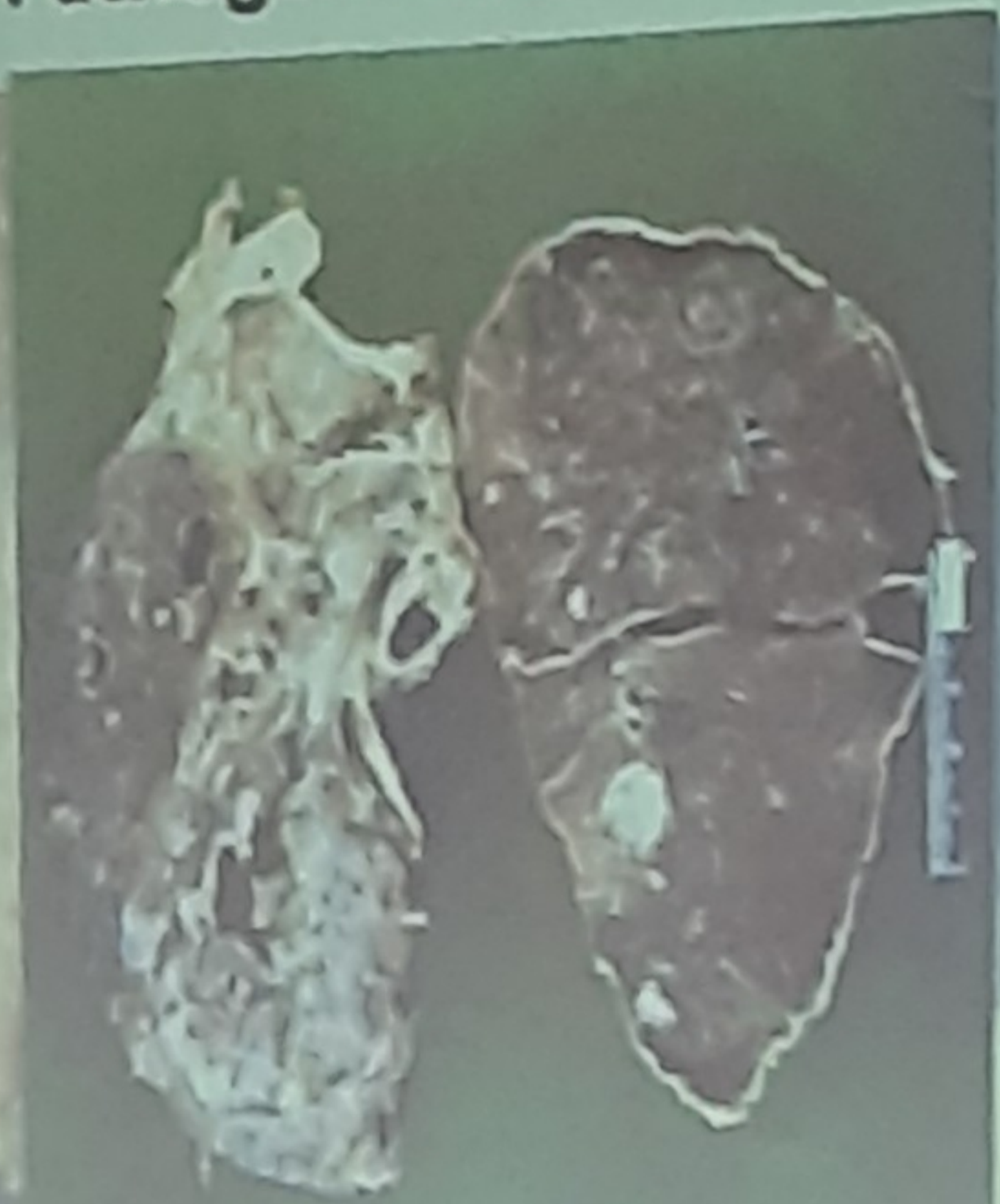
- Pneumonia
- Granuloma formation with fibrosis
- Caseous necrosis
  - Tissue becomes dry & amorphous (resembling cheese)
  - Mixture of protein & fat (assimilated very slowly)
- Calcification
  - Ca^{++} salts deposited
- Cavity formation
  - Center liquefies & empties into bronchi

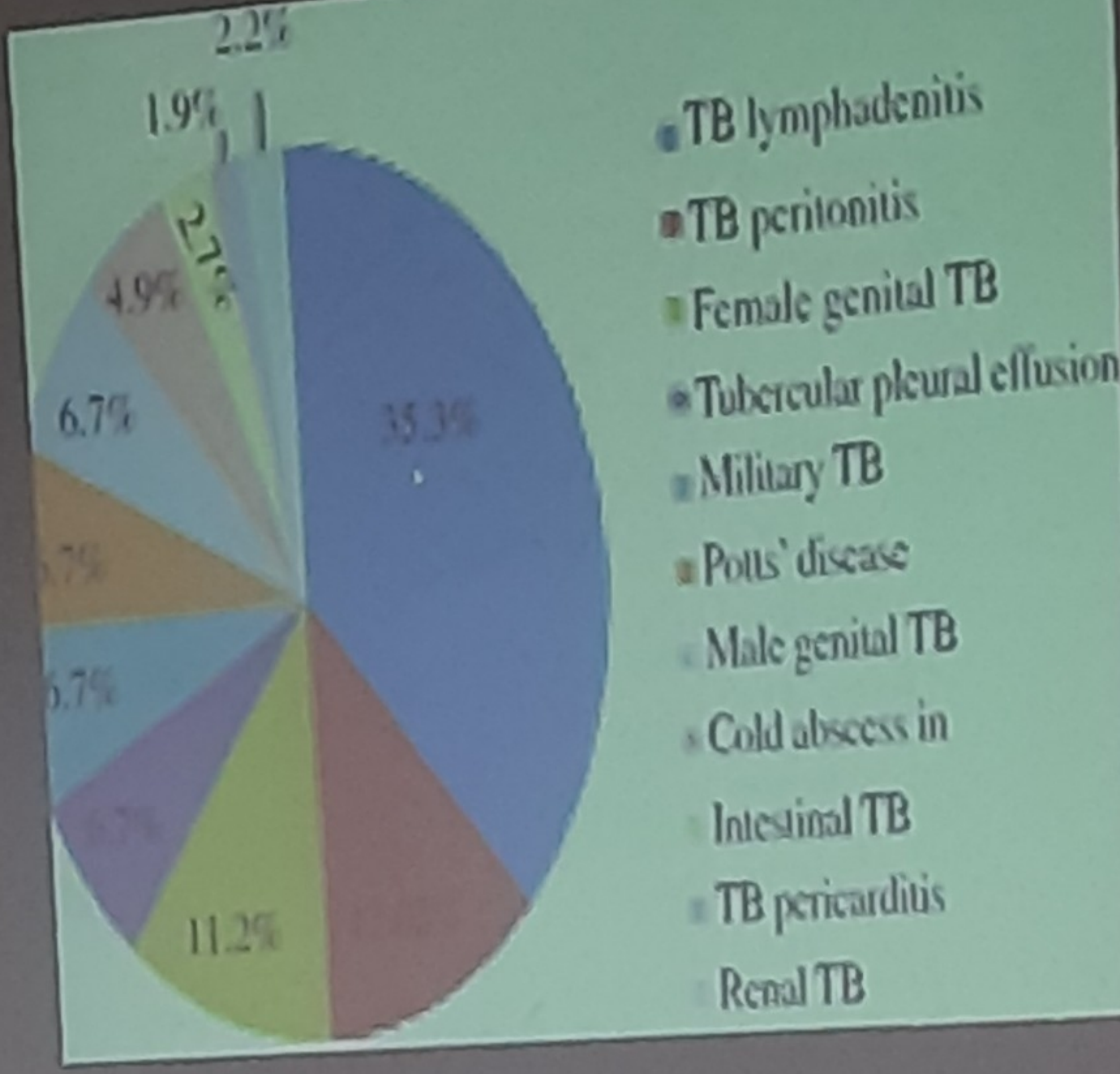
Ghon complex

- Nodules in lung tissue and lymph nodes
- Caseous necrosis inside nodules
- Calcium may deposit in the fatty area of necrosis
- Visible on x-rays



Pathogenesis & Immunity



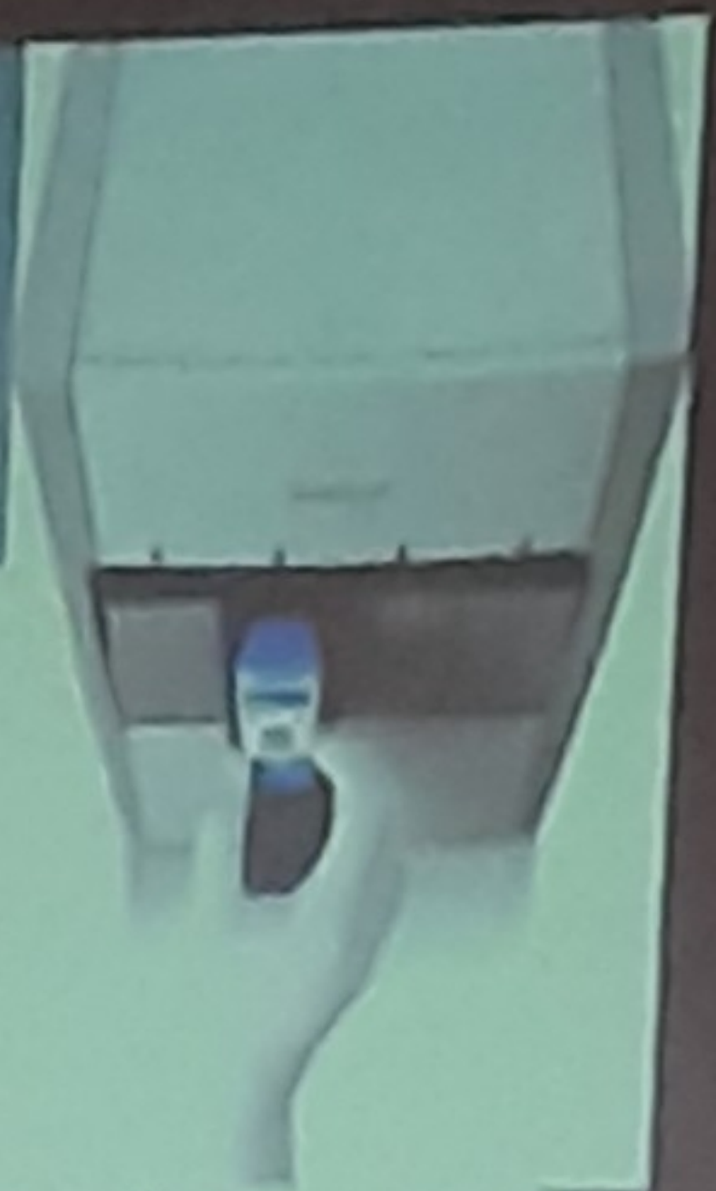

2.2%
1.9%
2.7%
4.9%
6.7%
35.3%
11.2%
TB lymphadenitis
TB peritonitis
Female genital TB
Tubercular pleural effusion
Military TB
Pott's disease
Male genital TB
Cold abscess in
Intestinal TB
TB pericarditis
Renal TB

Laboratory diagnosis

- Specimen
  - Sputum (expectorated or induced)
  - Pleural fluid
  - Gastric washings
  - Urine
  - Aspirates
  - CSF
  - Fine needle aspirates
  - Tissue biopsies

- Staining of specimen using
  - Ziehl Neelsen (ZN) stain –acid-fast bacilli (AFBs)
  - Kinyoun staining
  - Fluorescence microscopy using auramine O or rhodamine stain

- Culture – Gold standard in TB diagnosis - require incubation for 6 – 8 weeks before declaring negative
  - Solid culture (Lowenstein Jensen, Middlebrook)
  - Semi automated Liquid culture Bactec 460
  - Automated Liquid culture system (MGIT – mycobacterial growth indicator tube)
- <u>No gold standard for diagnosis of LTBI</u>

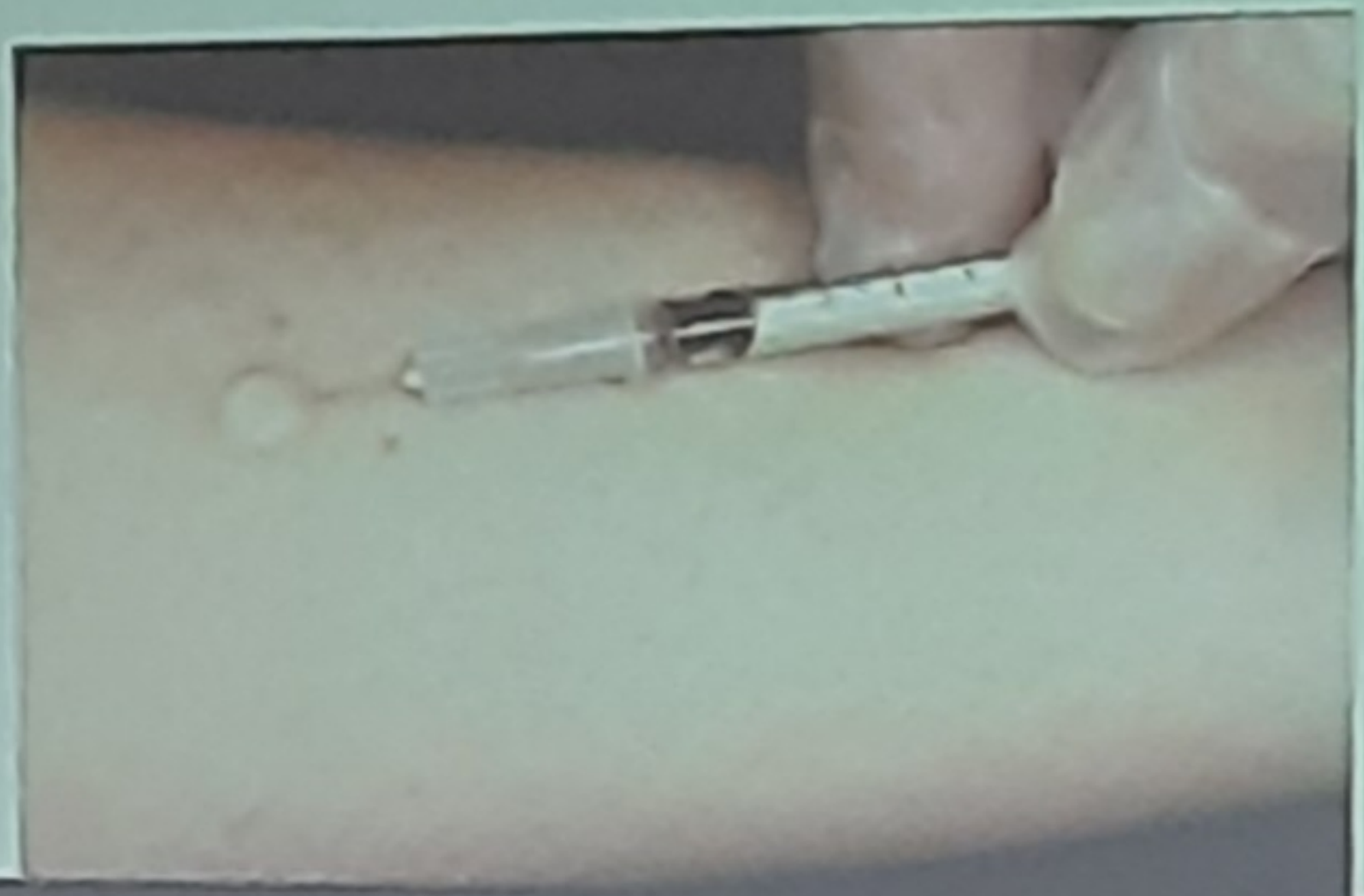


To confirm *M.tuberculosis* from culture:

- Growth rate
- Colonial morphology
- Ziehl Neelsen staining results
- Molecular – PCR – from culture; some direct from sputum
- Gene/Xpert - is a nucleic acid amplification test, that can identify (MTB) DNA and resistance to rifampicin (RIF)

- Immunological diagnostic tests
  - Tuberculin skin test – does not distinguish between vaccination and disease. Usually negative in patients with advanced AIDS

  - QuantiFERON , T-SPOT TB – Detect interferon γ. For active & latent TB



Treatment

- 1st line: isoniazid, rifampicin/ rifabutin, ethambutol, pyrazinamide, streptomycin

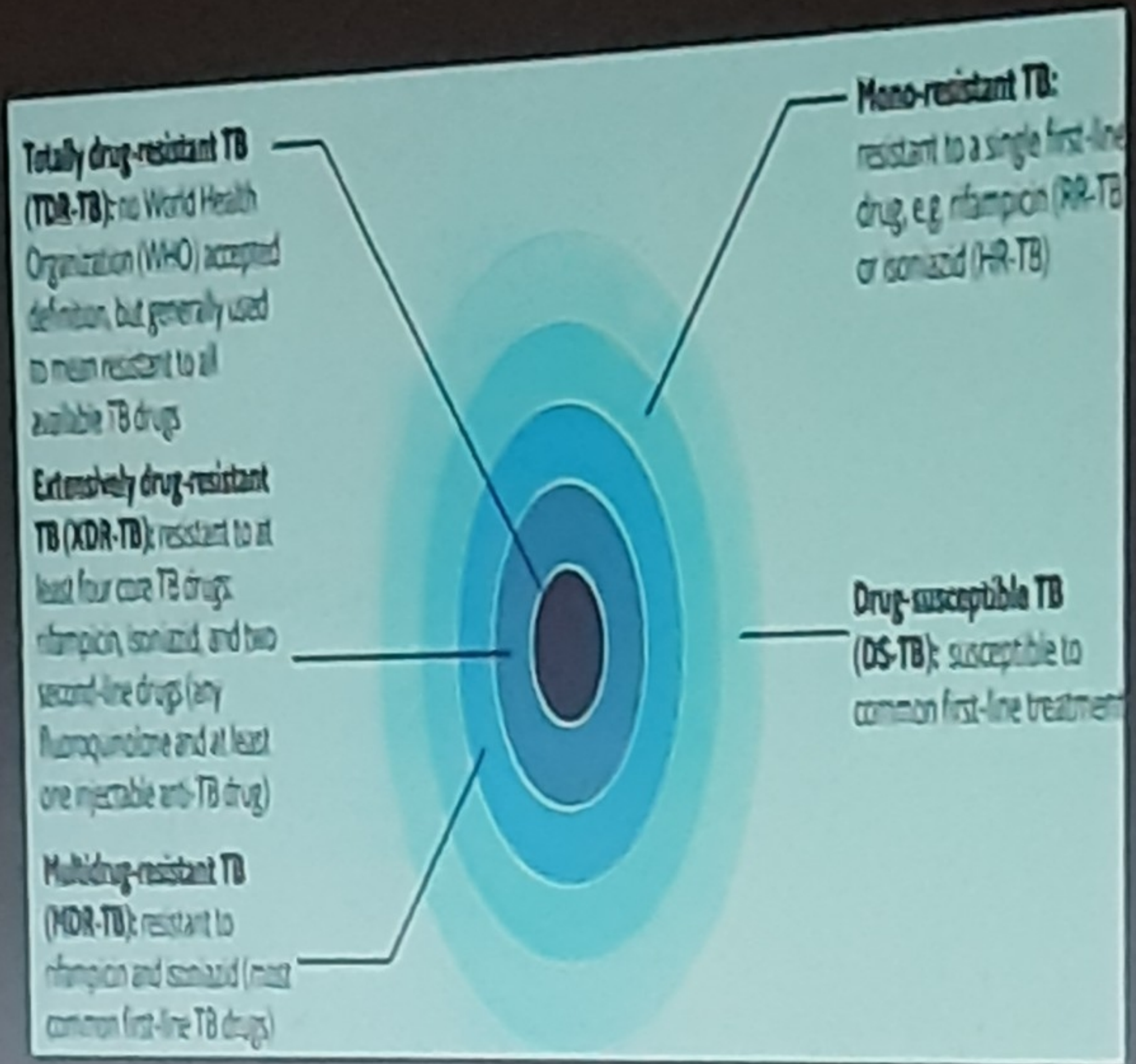
- 2nd line: para-amino salicylic acid, cycloserine, quinolones (ofloxacin/ ciprofloxacin/ levofloxacin/ etc), amikacin, kanamycin, capreomycin, ethionamide

Tuberculosis Treatment:

If you forget your TB drugs, you'll die and might need a **PRIEST.**

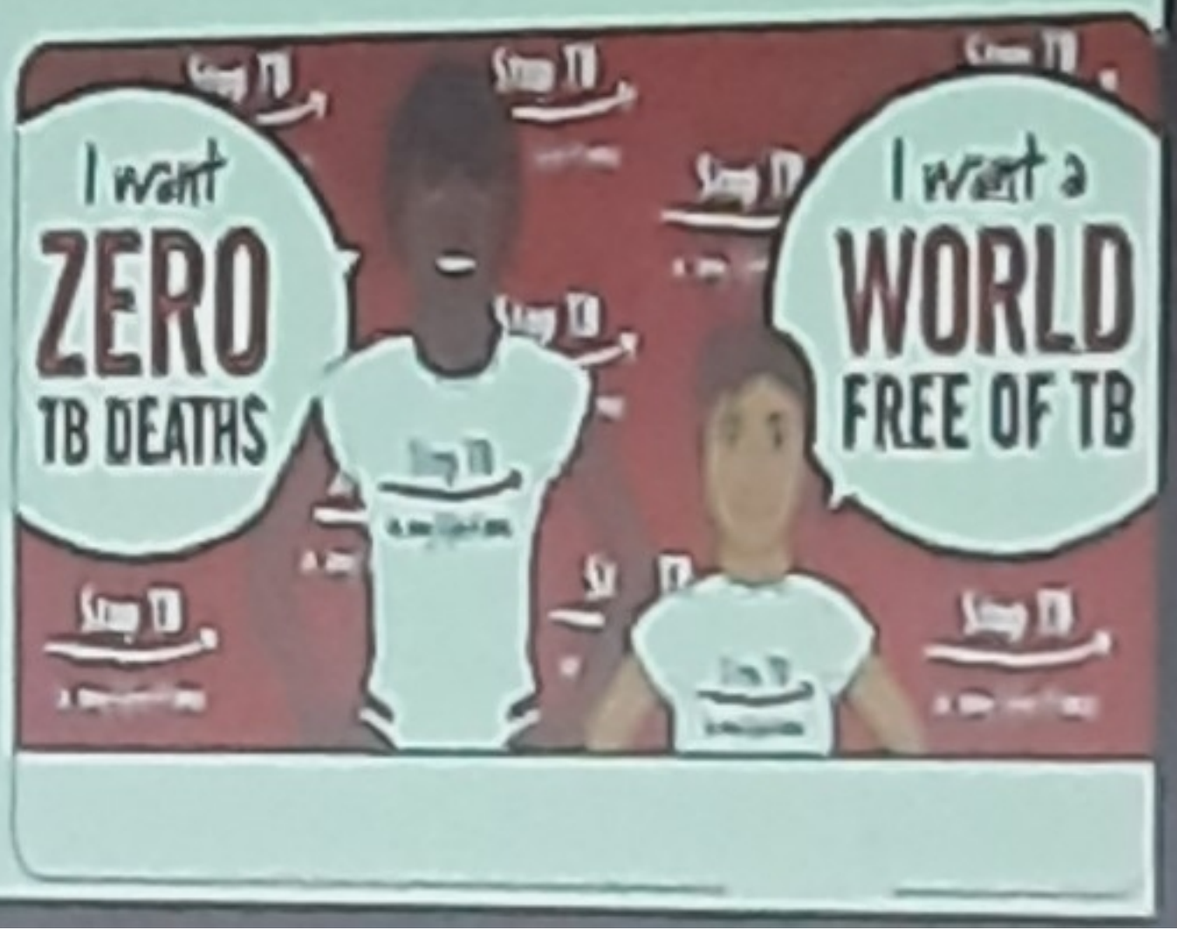
- Pyrazinamide
- Rifampin
- Isoniazid
- Ethambutol
- STreptomycin

- Drug resistance
  - **Multidrug resistant TB (MDR TB):** TB that is resistant to at least rifampicin & isoniazid
  - **Extensively drug resistant TB (XDR TB):** TB which is resistant to isoniazid and rifampin, plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)


Totally drug-resistant TB (TDR-TB): no World Health Organization (WHO) accepted definition, but generally used to mean resistant to all available TB drugs
Extensively drug-resistant TB (XDR-TB): resistant to at least four core TB drugs: rifampicin, isoniazid, and two second-line drugs (any fluoroquinolone and at least one injectable anti-TB drug)
Multi-drug-resistant TB (MDR-TB): resistant to rifampicin and isoniazid (most common first-line TB drugs)
Mono-resistant TB: resistant to a single first-line drug, e.g. rifampicin (RR-TB) or isoniazid (HR-TB)
Drug-susceptible TB (DS-TB): susceptible to common first-line treatment

Prevention and control

- BCG vaccine
- Respiratory isolation of persons with suspected TB till noninfectious
- Ventilation of household
- Contact tracing
- Nutrition
- Chemoprophylaxis
- Vit D??



•"Initiating ART **2 weeks after** the start of tuberculosis treatment significantly **improved survival among HIV-infected adults** with CD4 T-cell counts of 200 [cells/mm^3] or lower," the researchers concluded. CAMELIA study

• "**Deferral of the initiation of ART to the first 4 weeks** of the continuation phase of tuberculosis therapy in those with higher CD4 T-cell counts reduced the risks of IRIS and other adverse events related to ART without increasing the risk of AIDS or death."SAPIT study