# Tuberculosis

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# Global Emergency

- **Tuberculosis kills 5,000 people a day**
- **2.3 million die each year**

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- Tuberculosis is infectious disease caused by *Mycobacterium tuberculosis*.

## Types

- Pulmonary TB
  - Primary TB
  - Secondary TB
- Milliary TB
- Extra-pulmonary TB

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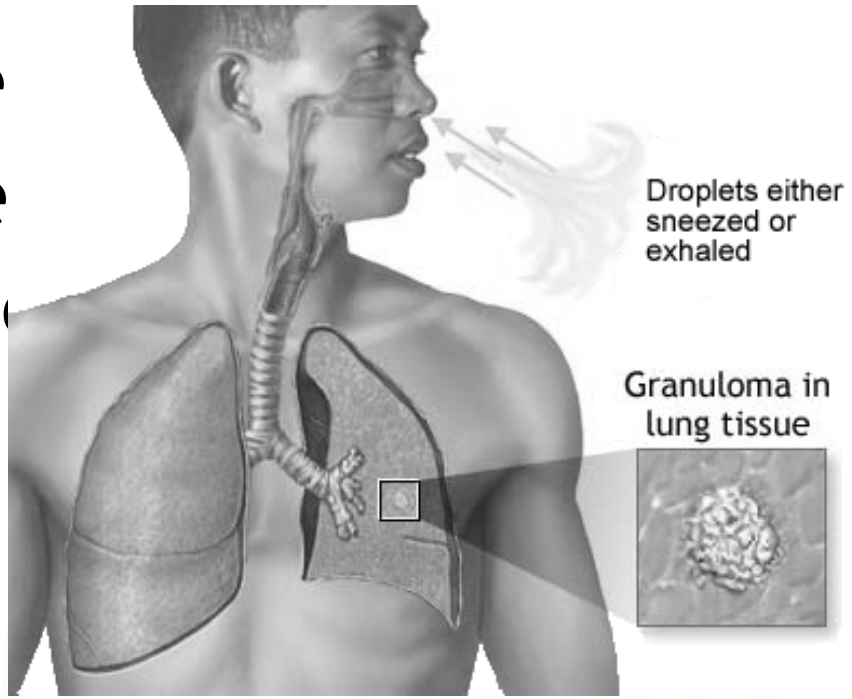
# TRANSMISSION

Respiratory transmission.

- Conditions for transmission:
  - overcrowding
  - poor personal hygie
  - poor public hygiene
  - Immuno compromis

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# Transmission

- Respiratory transmission
- Patients with the active disease expel bacilli into air by:
  - coughing
  - sneezing
  - Shouting
- Bacilli multiply in 4 -6 weeks
- May spreads throughout the body.
- The bacilli implant in areas of high partial pressure of oxygen:
  - lung
  - renal cortex
  - reticuloendothelial system

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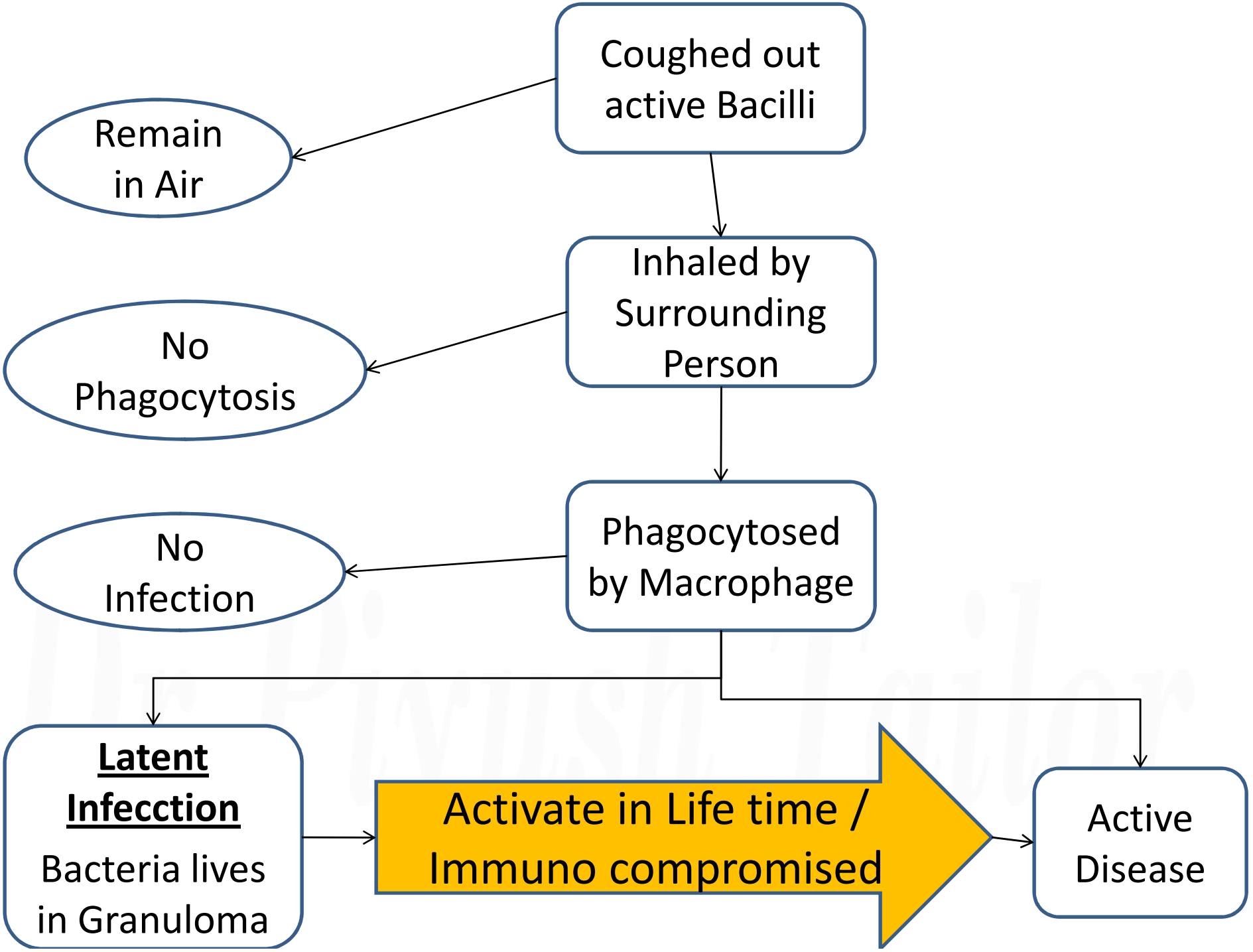
Coughed out active Bacilli
Remain in Air
Inhaled by Surrounding Person
No Phagocytosis
Phagocytosed by Macrophage
No Infection
Latent Infecction
Bacteria lives in Granuloma
Activate in Life time / Immuno compromised
Active Disease

# Risk of infection

- Exposure to amount TB bacilli
- Frequency of exposure to TB bacilli
- Duration of exposure to a person with Pulmonary TB
- Untreated AFB smear positive Pulmonary TB cases are the most infectious

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# Risk factors for disease

- Development of disease depends on individual susceptibility
- HIV increases the risk of getting TB disease
- 10% Life time risk of TB in HIV negative
- 10% Annual risk of TB in HIV positive

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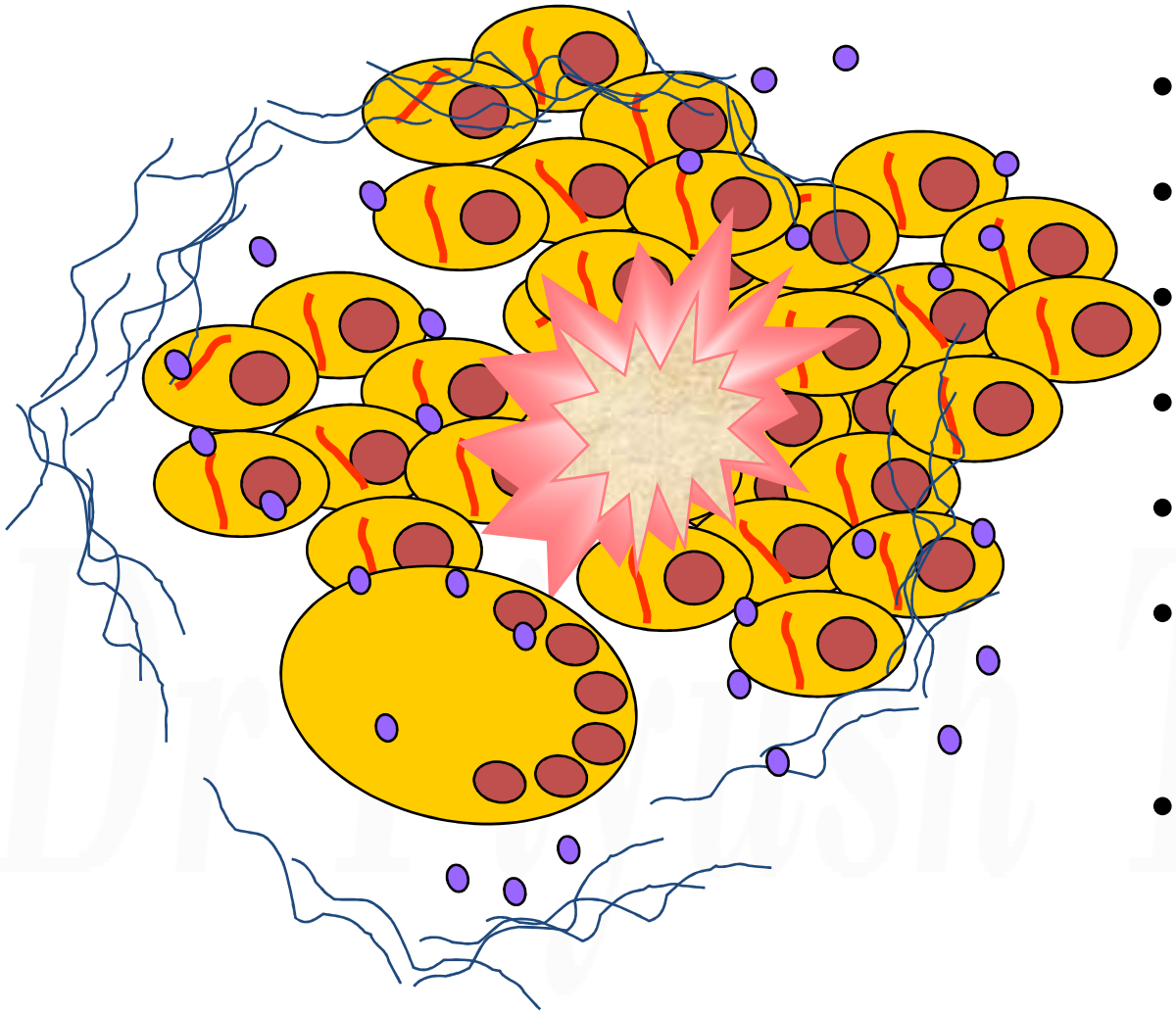
# TB Pathogenesis



- Bacterial entry
- T Lymphocytes.
- Macrophages.
- Epitheloid cells.
- Proliferation.
- Central Necrosis.
- Giant cell formation.
- Fibrosis.

# Morphology of Granuloma

1. Rounded tight collection of chronic inflammatory cells.
2. Central Caseous necrosis.
3. Active macrophages - epithelioid cells.
4. Outer layer of lymphocytes & fibroblasts.
5. Langhans giant cells – joined epithelioid cells.

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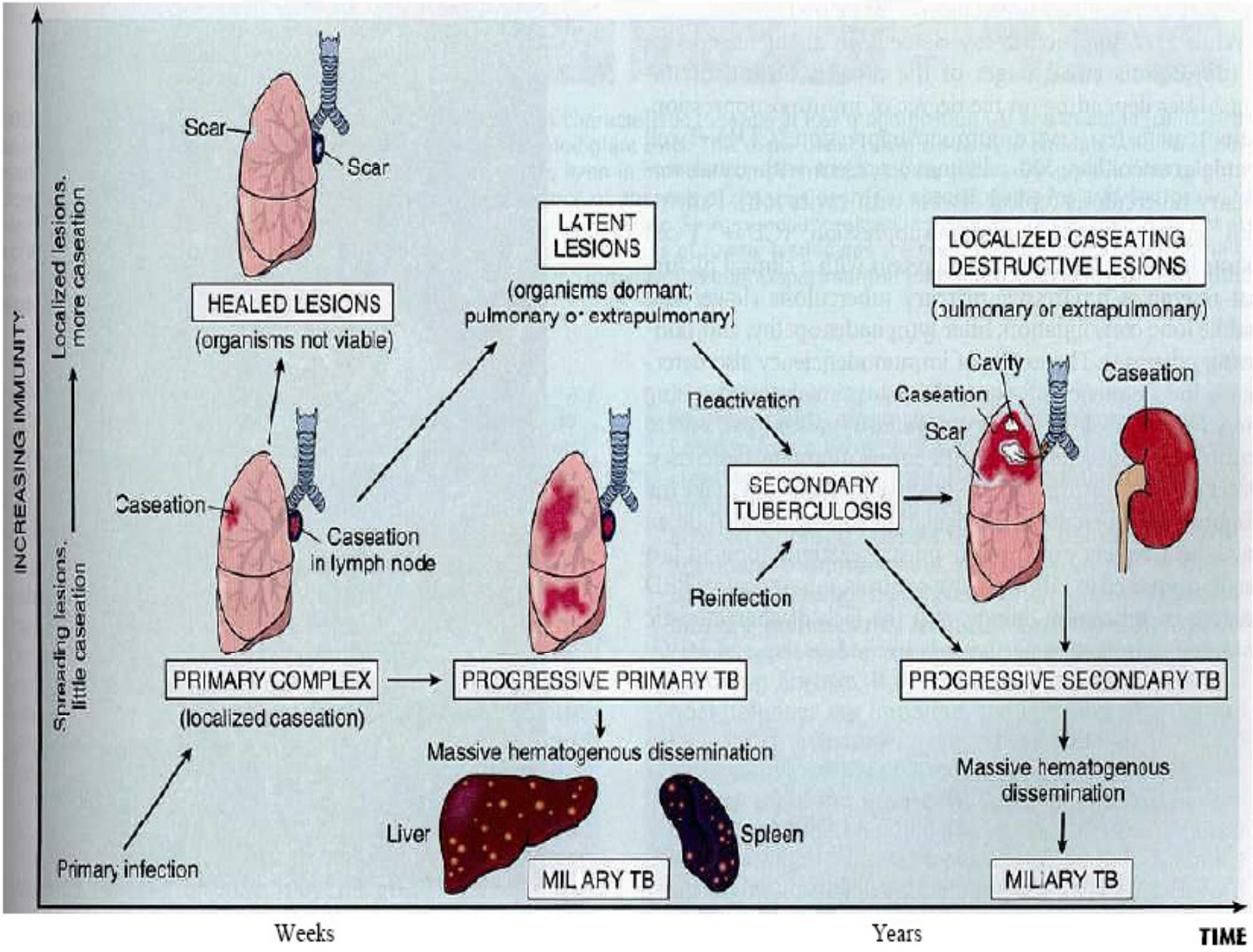
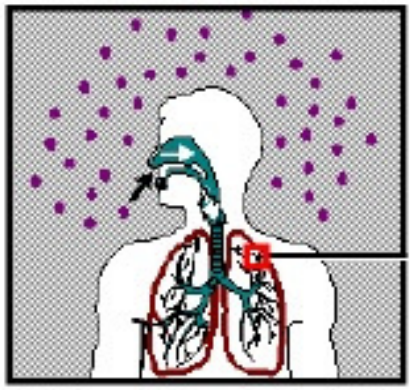

INCREASING IMMUNITY
Localized lesions, more caseation
Spreading lesions, little caseation
Scar
Scar
HEALED LESIONS
(organisms not viable)
LATENT LESIONS
(organisms dormant; pulmonary or extrapulmonary)
LOCALIZED CASEATING DESTRUCTIVE LESIONS
(pulmonary or extrapulmonary)
Reactivation
Cavity
Caseation
Scar
Caseation
Caseation
Caseation in lymph node
SECONDARY TUBERCULOSIS
Reinfection
PRIMARY COMPLEX
(localized caseation)
PROGRESSIVE PRIMARY TB
PROGRESSIVE SECONDARY TB
Massive hematogenous dissemination
Massive hematogenous dissemination
Liver
Spleen
MILIARY TB
MILIARY TB
Primary infection
Weeks
Years
TIME

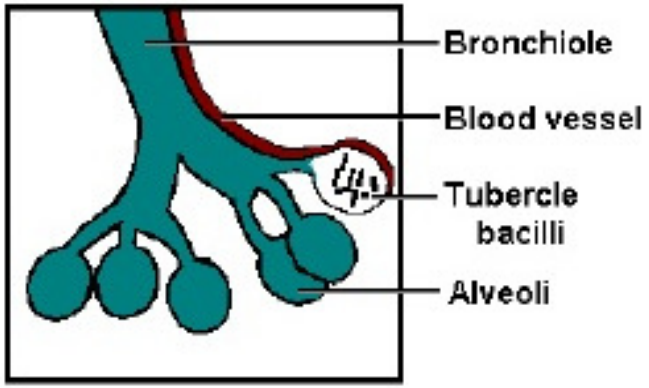
# PATHOGENESIS

1



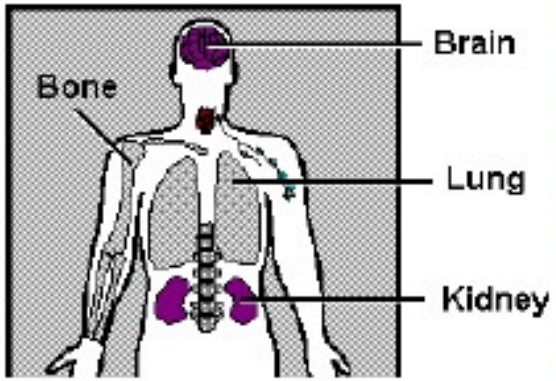
Droplet nuclei containing tubercle bacilli are inhaled, ente the lungs, and travel to the alveoli

2



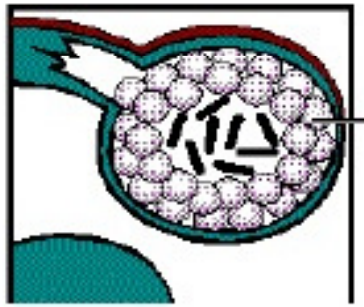

Tubercle bacilli multiply in the alveoli

3



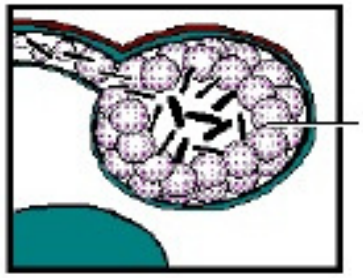

A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the lungs, kidneys, brain, or bone

4



Macrophages form a hard shell & keeps bacilli under control

5



Hard shell breaks down and tubercle bacilli escape and multiply (in this example, TB disease develops in the lungs)

# Types of tuberculosis

- Primary tuberculosis:
  - develops in a previously unexposed person
  - And therefore person is not sensitized .
- Secondary tuberculosis:
  - develop in previously infected person.
  - And therefore person is previously sensitized.
- Miliary Tuberculosis :
  - Consolidation scattered through the lung parenchyma .

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# Primary tuberculosis

- Infection of an individual who has not been previously infected or immunized.

- Pathogenesis:
  - Inhalation of bacilli
  - Implant in the distal airspaces
  - Development of Sensitization
  - Gray-white inflammatory consolidation
  - “Ghon focus”

# Primary tuberculosis - Ghon's Complex

- Pulmonary component (Ghon's Focus)
- Lymph node component
  - Hilar & Tracheo-bronchial
- Lymphatic component

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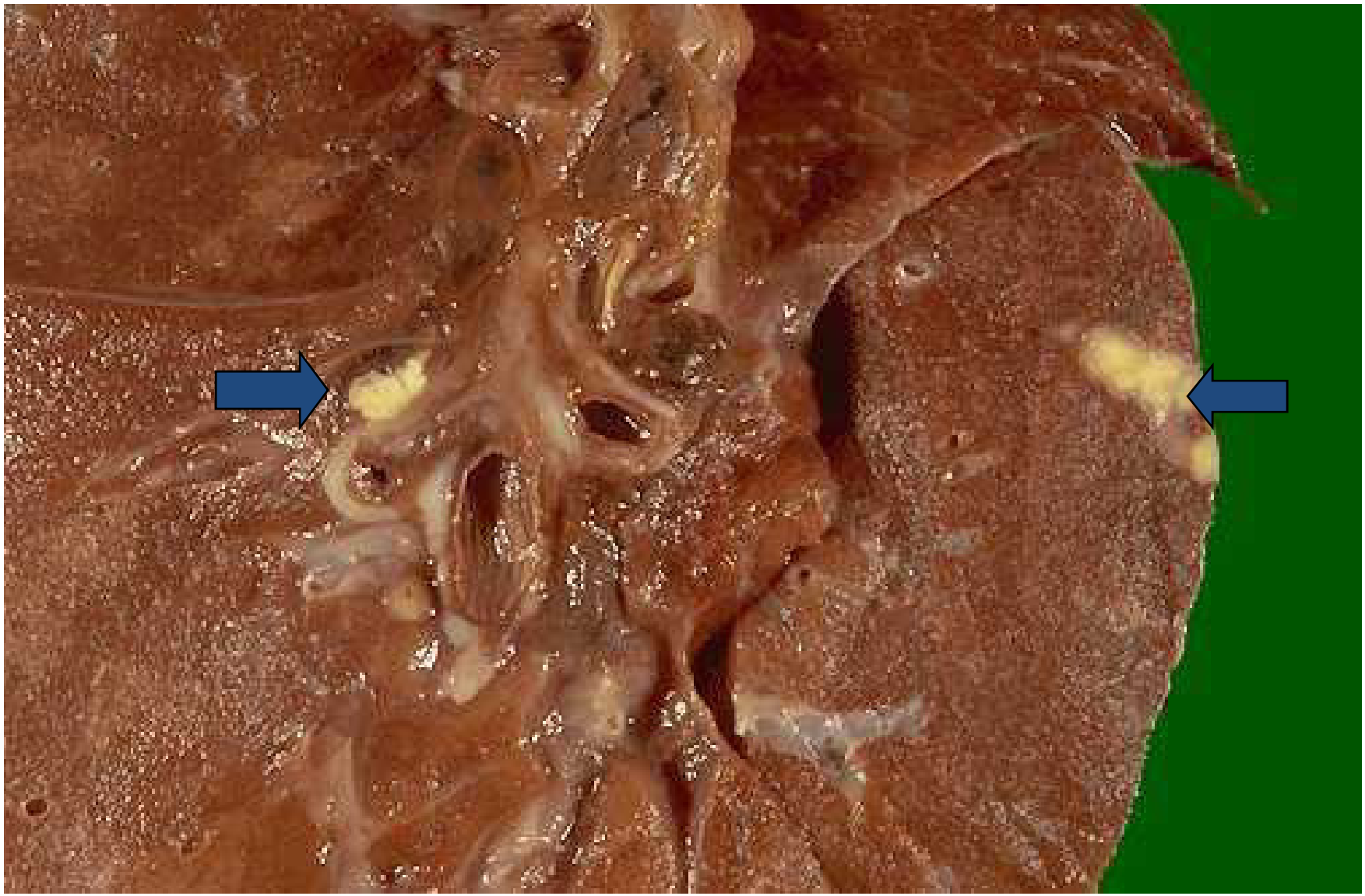
# Ghon Complex



# Fate of primary tuberculosis

- Heal by fibrosis→ calcification
- Progressive primary tuberculosis
- Primary miliary tuberculosis

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# Secondary tuberculosis

- Infection of an individual who has been previously infected or sensitized

- The infection may be acquired from
  - Endogenous source:
    - Reactivation of dormant primary complex
  - Exogenous source

Dr. Rajesh Kalor

# Fate of secondary tuberculosis

- Heal with fibrous scarring and calcification
- Progressive pulmonary TB
- Tuberculous caseous pneumonia
- Miliary tuberculosis

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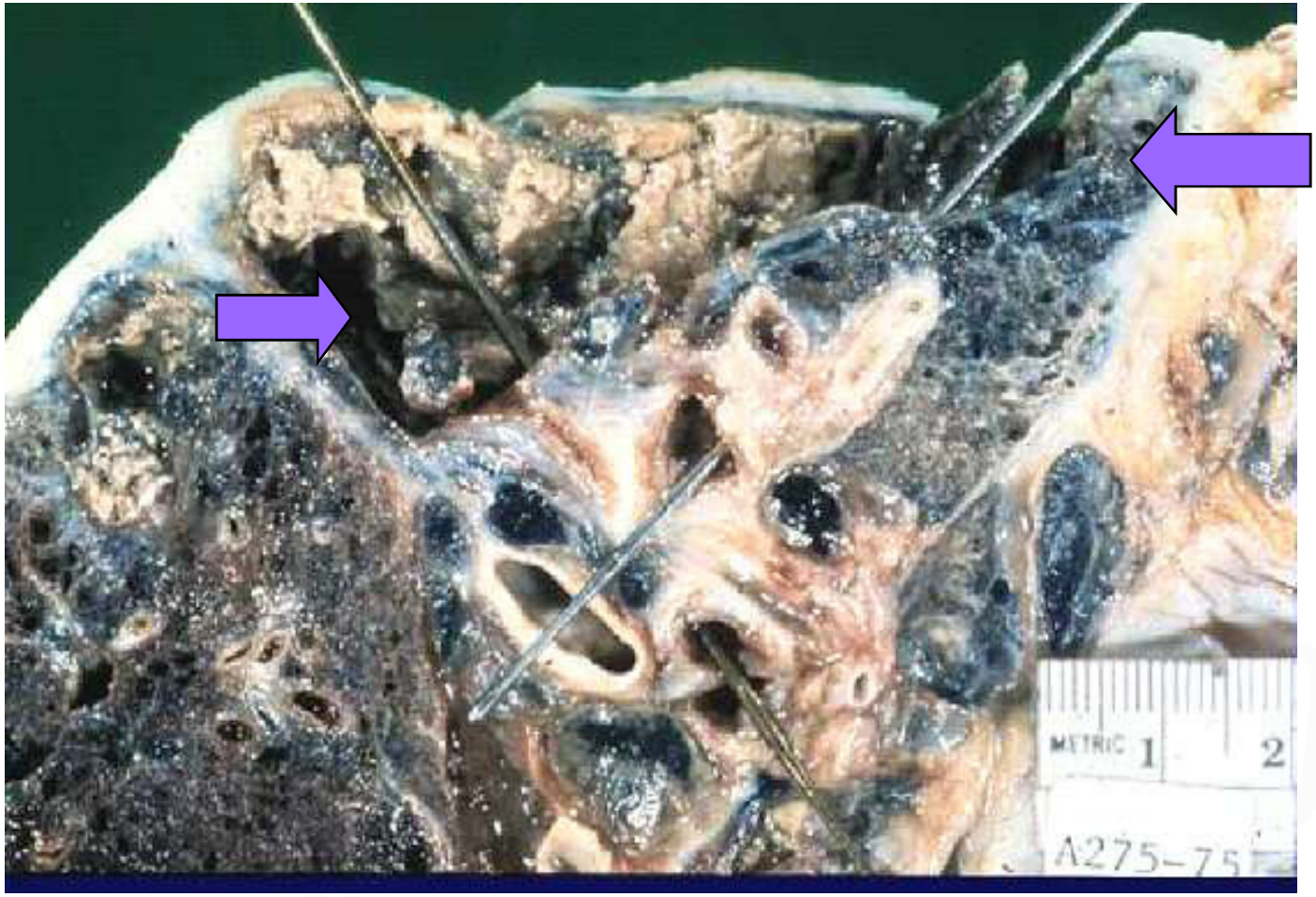
# Cavitary Secondary TB



# Cavitary Secondary TB

- **Due to high oxygen tension**
- **Favourable environment for bacilli**
- In Open Tuberculosis
  - Bacilli implant on the mucosal lining of air passages
  - Producing endobronchial / endotracheal TB

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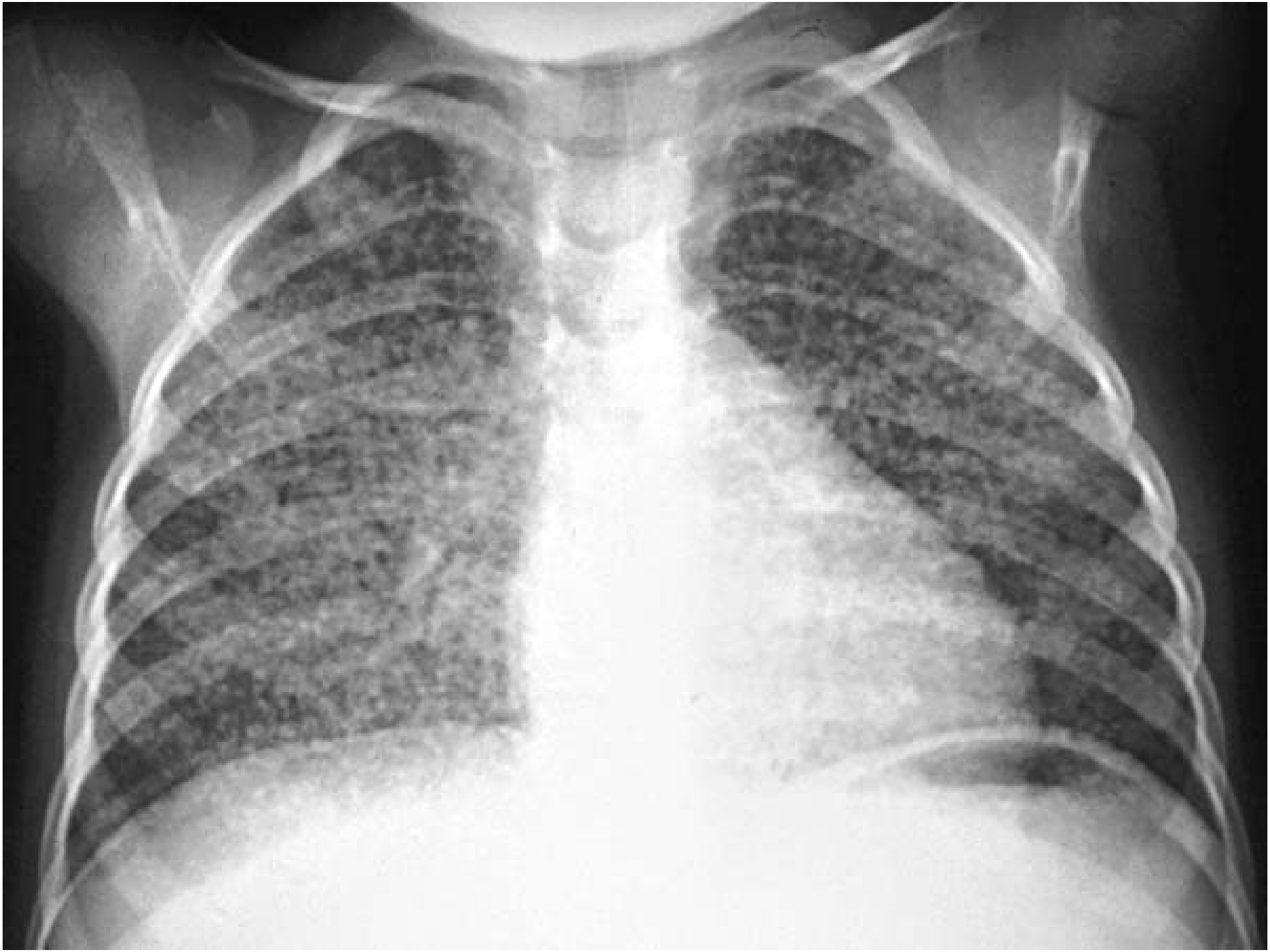
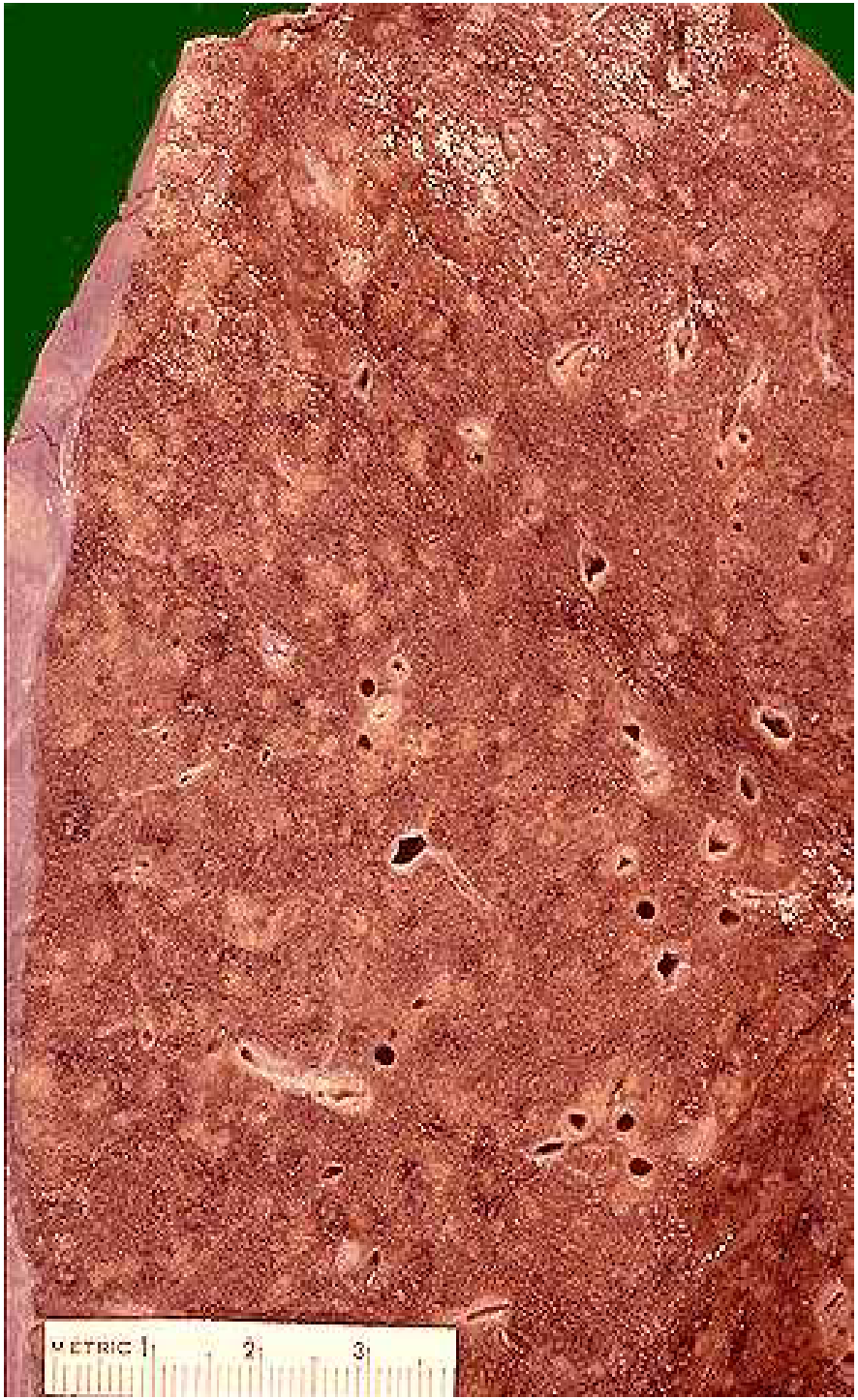
# Miliary pulmonary tuberculosis

- **Pathogenesis :**
- Organisms drain in lymphatic
- Spread in lymphatic ducts
- Organism enter into right side of heart through venous return
- Enter in Pulmonary arteries
- Make microscopic scattered lesion in lung parenchyma
- Granuloma & Caseous necrosis formation.




METRIC 1 2 3

# Pulmonary TB Clinical features

- Low grade fever ( evening rise )
- Sweating
- Cough (productive)
  - Dry
  - Purulent
  - Haemoptysis
- Weight loss
- Loss of appetite
- Lymphadinopathy

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- Non immunocompromised patients
  - 10% latent infections turns to active TB in life time.
- HIV patients
  - 10% of turns to active TB each year.

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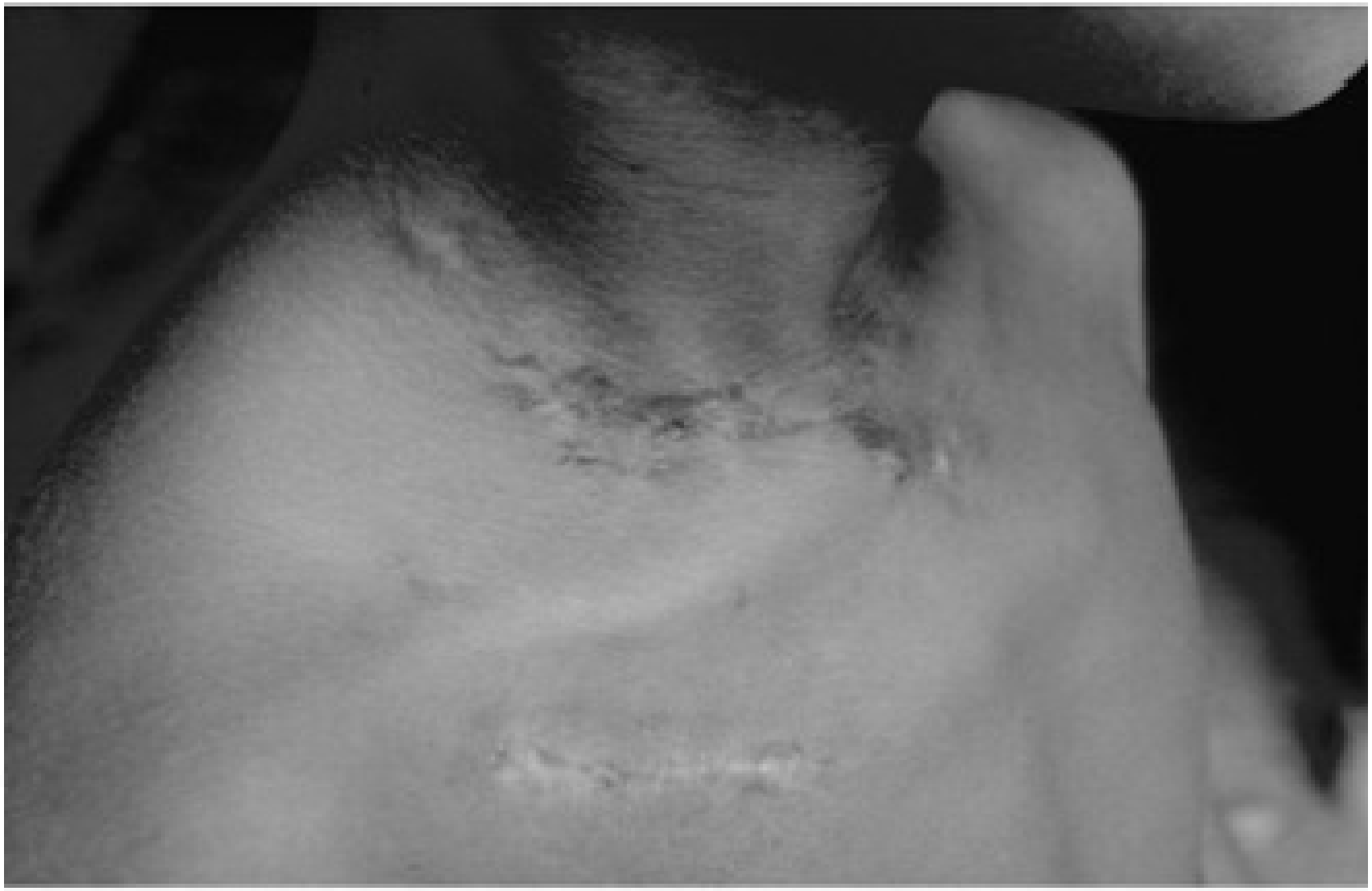
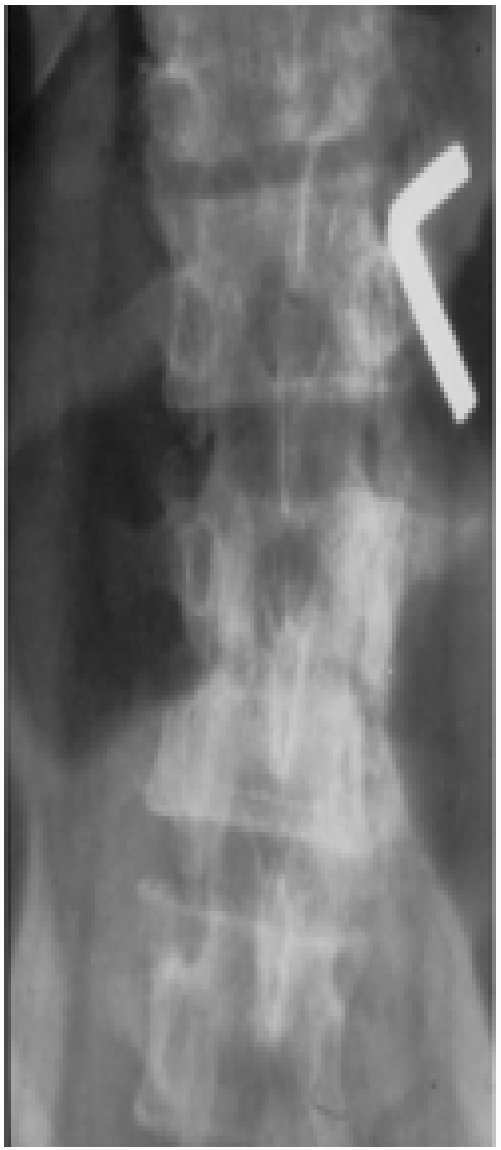
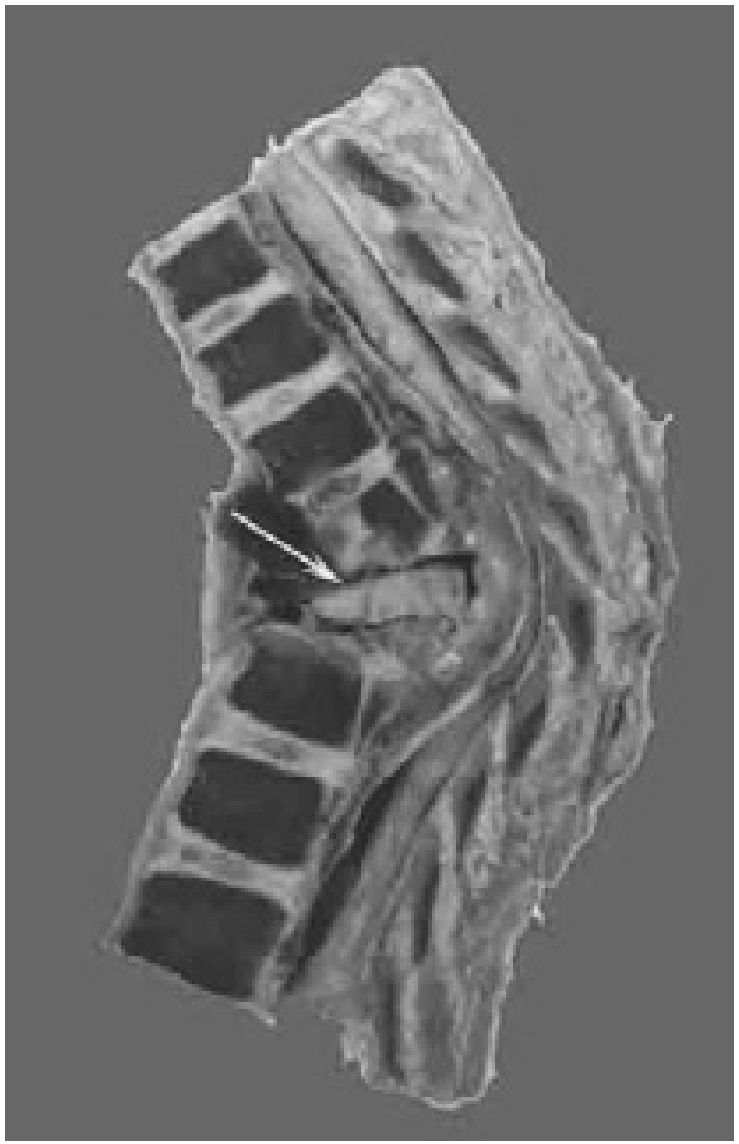
# Cervical

# Supra clavicular

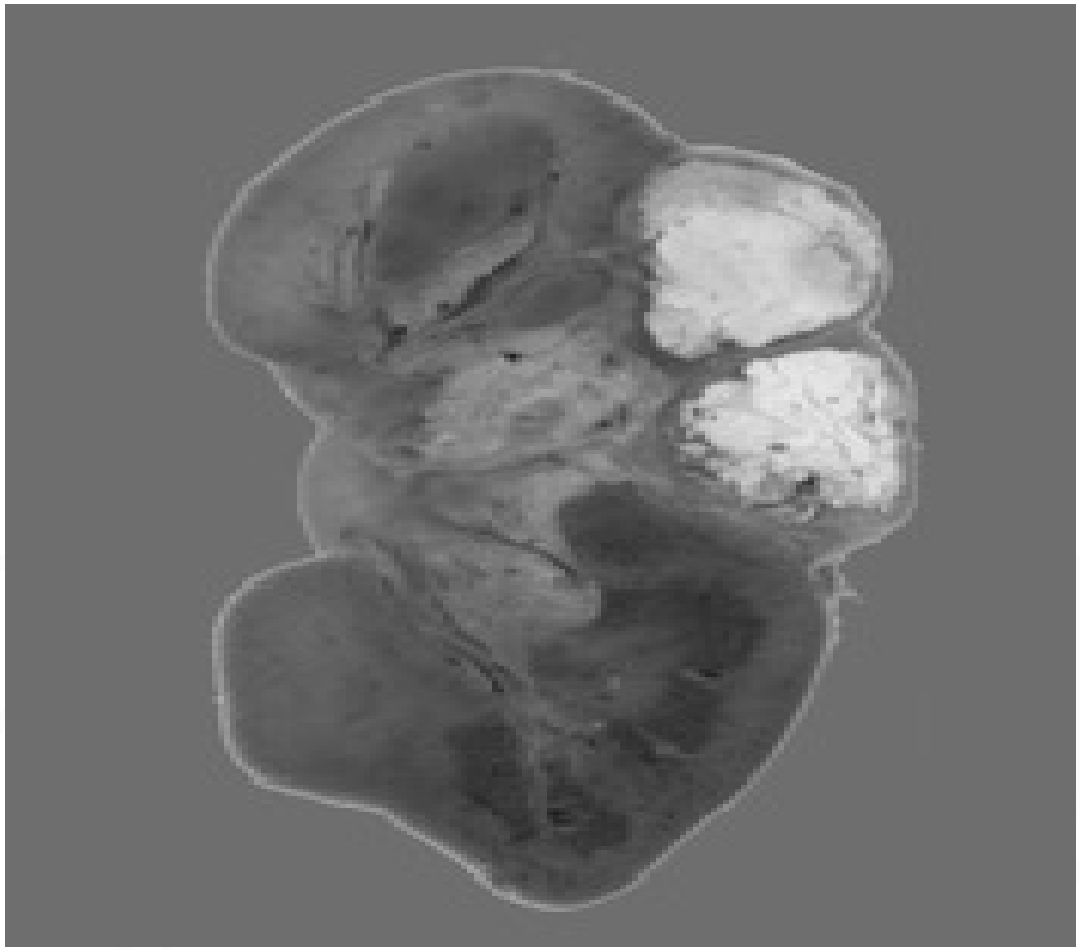


# Potts spine

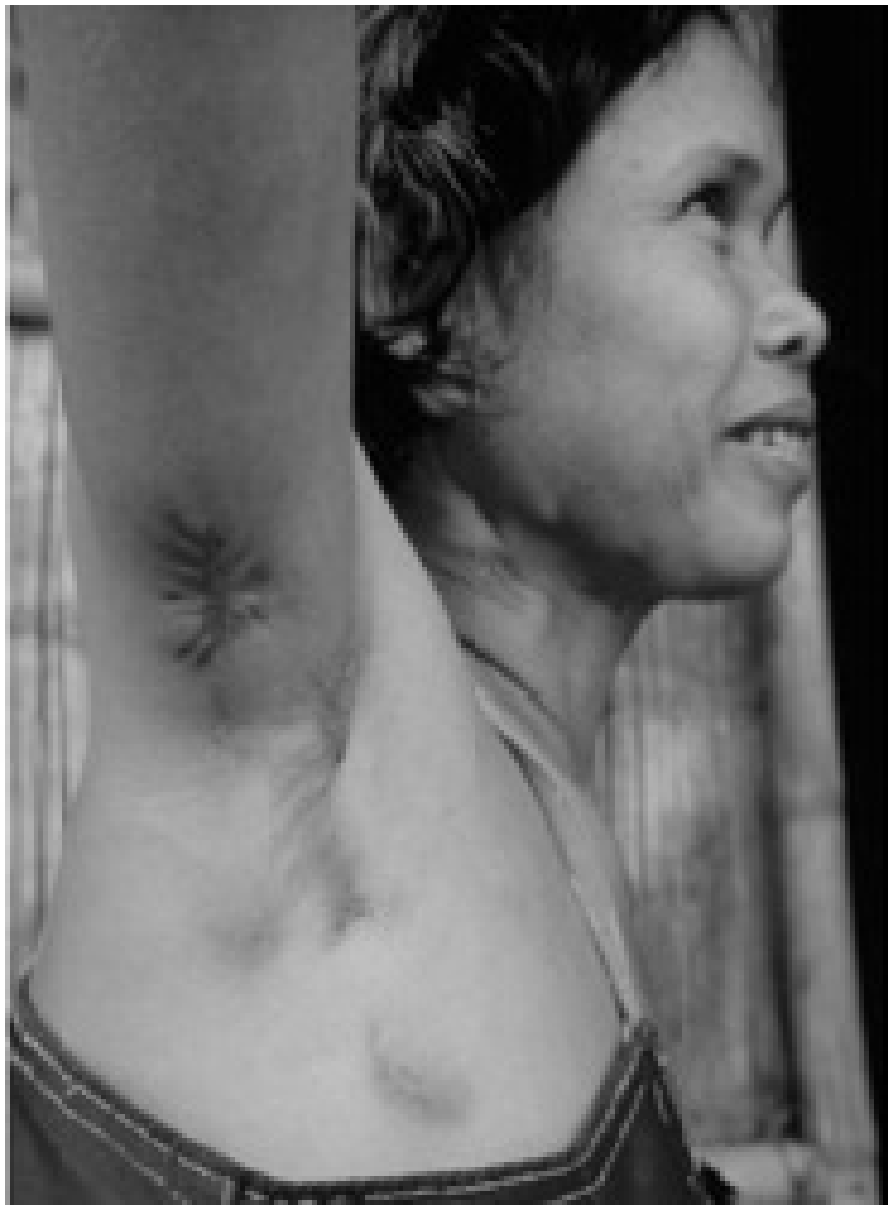




# Supra renal tuberculosis



# Axillary tuberculosis



# Diagnosis of TB

- Zeil Nielson Stain
  - For Acid Fast Bacilli
- Adenosine deaminase test
- Culture most sensitive and specific test.
  - Conventional media = 3-6 weeks.
  - Automated techniques within = 9-16 days
- PCR
- Mantoux test

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# Diagnosis

- Clinical history
- Signs of fever, pleural rub,crackles
- Investigations:
- X ray chest
- Intradermal PPD
- Mantoux
- ZN staning
- PCR
- DNA probing

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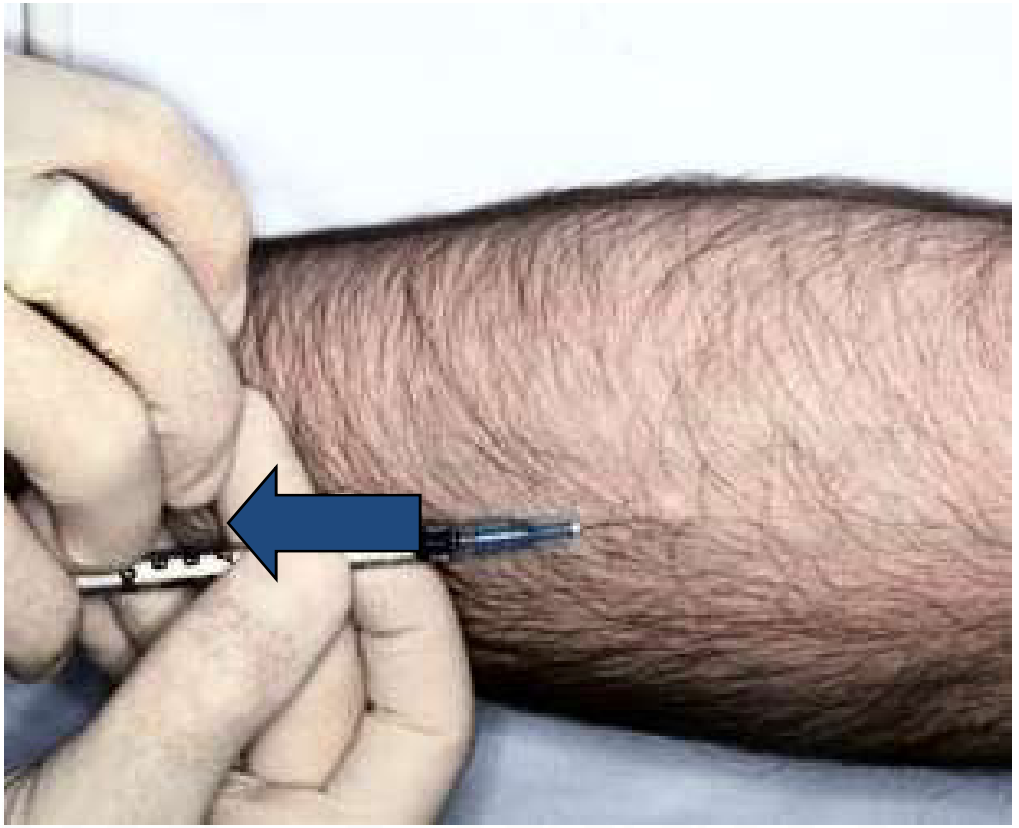
# Mantoux test

- Infection with mycobacterium tuberculosis leads delayed hypersensitivity reaction which can be detected by Mantoux test
- About 2 to 4 weeks after infection, intracutaneous injection of purified protein derivative (PPD) of M.tuberculosis induces a visible and palpable induration that peaks in 48 to 72 hours

# PPD Tuberculin Testing

- Sub cutaneous
- Weal formation
- Itching – no scratch.
- Read after 72 hours.
- Induration size.
- 5-10-15mm



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# Induration Size & Interpretation

- Less than 5 mm
  - No exposure to tubercular bacilli.
- Between 5-9 mm
  - Due to Atypical mycobacteria
  - BCG vaccination.
  - May in HIV or Immunosupression patient
- 10 mm or more
  - Tubercular disease

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# Classification of Drugs

- 3 Groups of Drugs
  - First Line:
    - *Most effective and have lowest toxicity.*
    - **Isoniazid Rifampin**
  - Second Line:
    - *Less effective and more toxic effects*
    - **p-amino salicylic acid, Streptomycin, Ethambutol**
  - Third Line
    - *Least effective and most toxic.*
    - **Amikacin, Kanamycin, Capreomycin, Viomycin, Kanamycin, Cycloserine**

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| Drugs | Short | Dose (mg) | Dose for pediatric (mg/kg) | Commom Side effects |
|---|---|---|---|---|
| Isoniazide | H | 600 | 10-15 | |
| Rifampicin | R | 450 | 10 | Reddish / Orange color urine |
| Pyrazinamide | Z | 1500 | 35 | |
| Ethambutol | E | 750 | 15 | Impaired vision |
| Streptomycin | S | 1200 | 30 | Ototoxicity |

**RNTCP = Revised National Tuberculosis Control Programme**

**DOTs = Direct Observation Therapy**

| Category | Type of Patient | Regimes |
|---|---|---|
| I | ✓New Sputum smear Positive | 2(HRZE)3 |
| | ✓Seriously ill sputum smear-negative | 4(HR)3 |
| | ✓Seriously ill Extra-pulmonary | |
| II | ✓Sputum smear-Positive Relapse | 2(HRZES)3 |
| | ✓Sputum smear-Positive Failure | 1(HRZE)3 |
| | ✓Sputum smear-Positive Treatment After default | 5(HRE)3 |
| III | ✓Sputum smear-Negative Not seriously ill | 2(HRZ)3 |
| | ✓Extra-pulmonary, Not seriously ill | 4(HR)3 |

# Drug Interaction

- Competition between Isoniazid and Phenytoin (anticonvulsant).
- They both compete for drug metabolism enzymes.
- Phenytoin interferes with metabolism of isoniazid by reduction in excretion or enhancement of effect of isoniazid

Dr Eyush Lalor

# WARNING!

Rifampin and Isoniazid are the most effective drugs

These 2 drugs should never be given alone!

They are always used in combination because resistance occurs to one drug alone very rapidly.

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**"Troubles are often the tools by which God fashions us for better things."**

**Exams…!**

- **Henry Ward Beecher**

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# Thank you

Dr Piyush Kolor