General pathology of TUBERCULOSIS

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Tuberculosis

Subject outlines

- Definition
- Epidemiology
- Etiology
- Tissue reaction against TB infection
- Spread of TB infection
- General complications of TB infection
- Primary tuberculosis
- Secondary tuberculosis
- Diagnosis of tuberculosis

Tuberculosis

Definition

Tuberculosis (TB) is a chronic infectious granulomatous disease caused by tubercle bacilli.

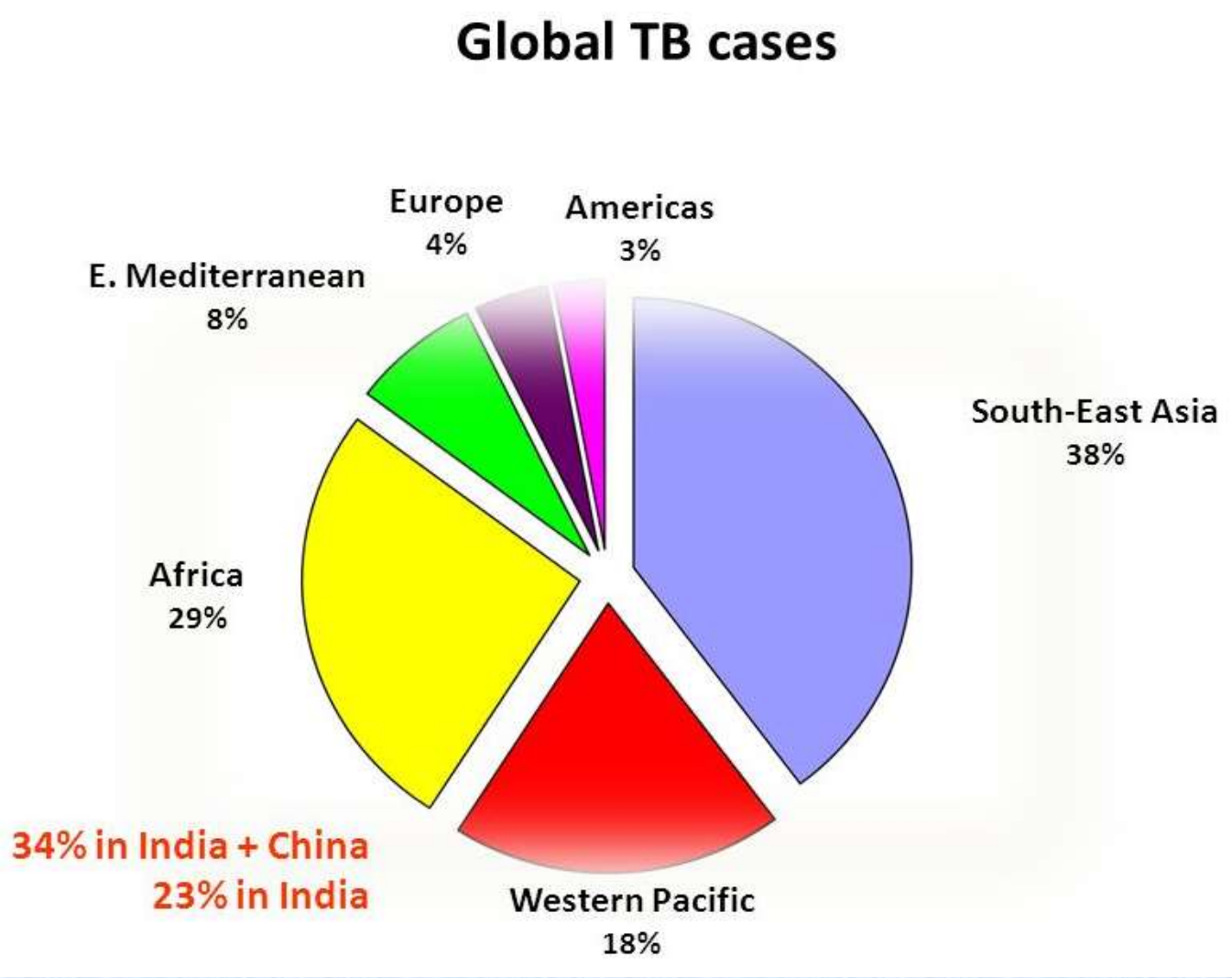
Tuberculosis

❑ Epidemiology:

- It is the most common granulomatous disease worldwide.
- An important cause of death through the world.
- More common in developing countries.
- A common and endemic in Egypt; detected in Egyptian mummies.

Tuberculosis

- **Epidemiology:**



Tuberculosis

- **Etiology:**
  - ***Predisposing factors***
    - Malnutrition
    - Over-crowding
    - Chronic diseases as diabetes millets and renal failure
    - Chronic lung diseases as pneumoconiosis
    - Immunosuppression as AIDS

Tuberculosis

- **Etiology:**
  - ***Causative organism:***

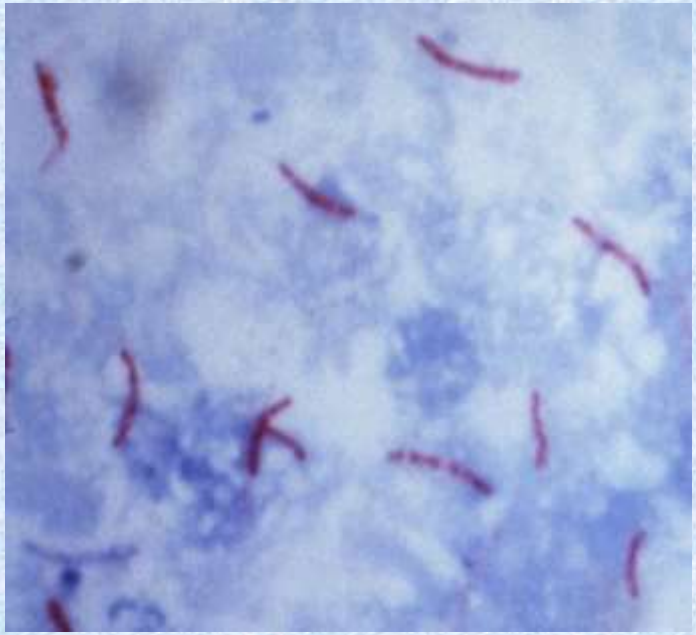
    ***Called* mycobacterium tubercle bacilli**
    - Rod shaped organism
    - Gram-positive bacilli
    - Identified by Ziehl-Nelsen stain
    - Two strains of the bacilli:

      1. Human strain: infection is acquired by inhalation
      2. Bovine strain: infection is acquired by ingestion

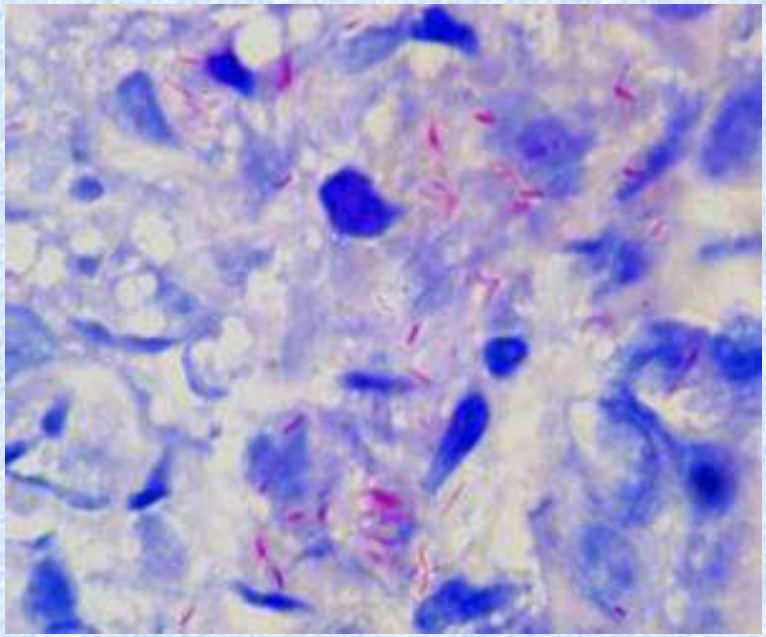
Tuberculosis

- **Etiology:**
  - ***Causative organism:***

    ***Called* mycobacterium tubercle bacilli**



Bacilli in culture



Intracellular bacilli

Tuberculosis

- **Etiology:**
  - ***Pathogenicity of mycobacterium bacilli*.**
    - TB bacilli are non motile
    - TB bacilli are obligatory intracellular organism.
    - TB bacilli don`t liberate exotoxin or endotoxin.

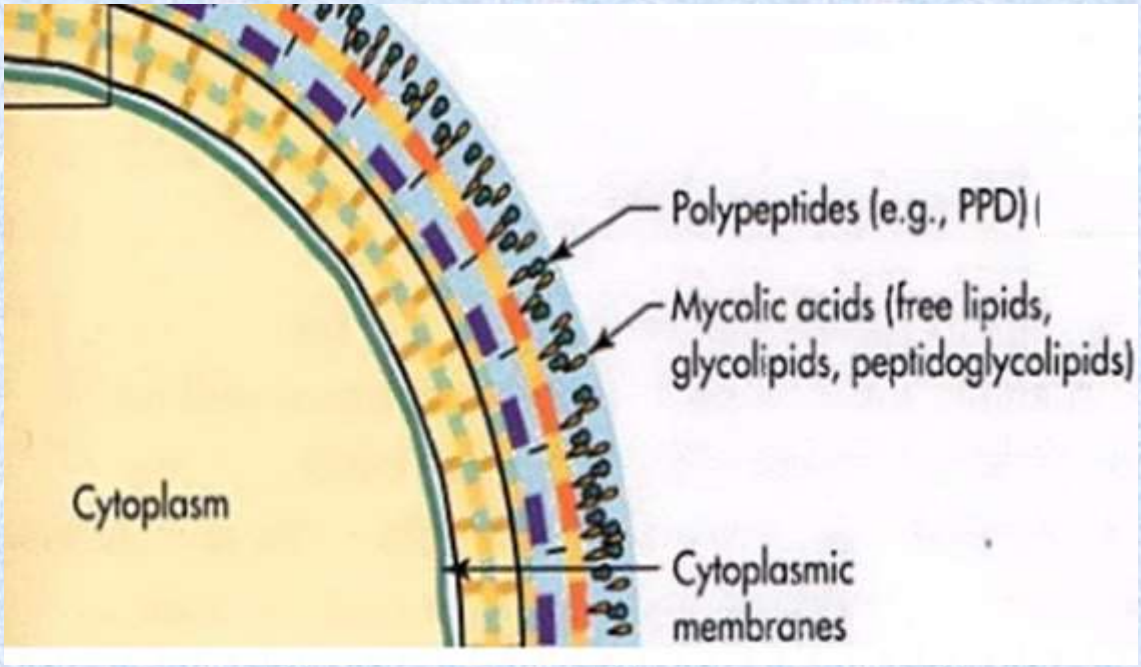
Tuberculosis

- **Etiology:**
  - ***Pathogenicity of mycobacterium bacilli*.**
    - TB bacilli are non motile
    - TB bacilli are obligatory intracellular organism.
    - TB bacilli don`t liberate exotoxin or endotoxin.
    - Pathological effects of TB bacilli **depend on bacterial wall structure that induce immunological tissue reaction.**

Tuberculosis

❑ Etiology:

➢ ***Pathogenicity of mycobacterium bacilli.***



- A **lipid capsule** protect organism from digestion
- A **protein layer** (tuberculo-protein): highly antigenic (induces type IV hypersensitivity reaction that result in tissue damage)

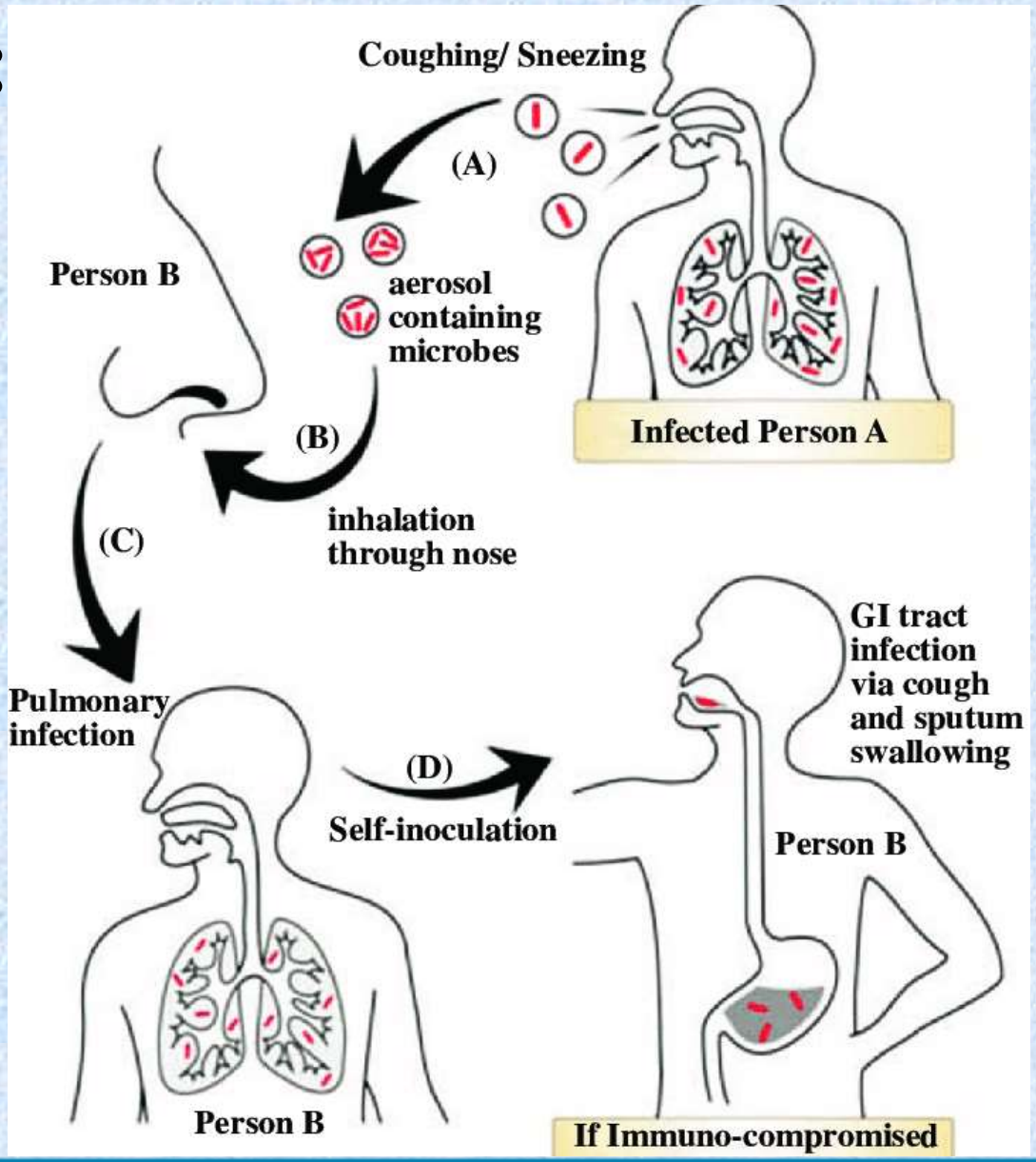
Tuberculosis

❑ Mode of infection:

- Inhalation of infected droplets  Pulmonary or tonsillar TB (commonly by human strain).
- Ingestion of infected milk or swallowing of infected sputum  Intestinal or tonsillar TB (common by bovine strain).
- Inoculation in a skin wound  TB of skin

Tuberculosis

- **Mode of infection:**



Tuberculosis

- **Tissue reaction against TB infection:**

Proliferative reaction

- Mainly cellular reaction
- Occurs mainly in solid organs

Granuloma formation

Exudative reaction

- Mainly fluid excaudate
- Occurs mainly in serous sacs

Tuberculosis

- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**

➢ **Mode of formation:**

- Mycobacteria attract neutrophils that fail to kill the organism.
- Macrophages engulf and destroy organism with liberation of tuberculoproteins
- Tuberculoproteins attract more macrophages that attract and activate T lymphocytes.

Tuberculosis

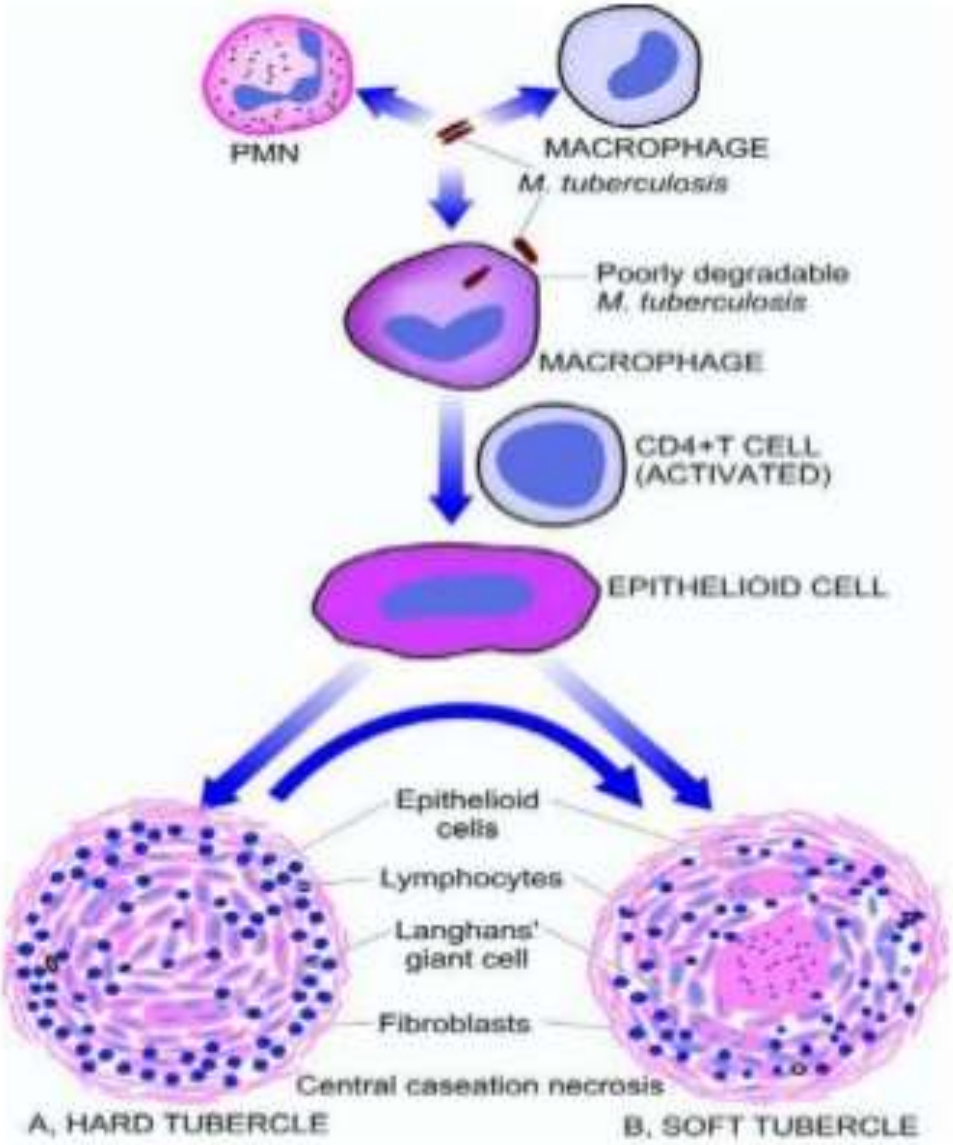
- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**

➢ **Mode of formation:**

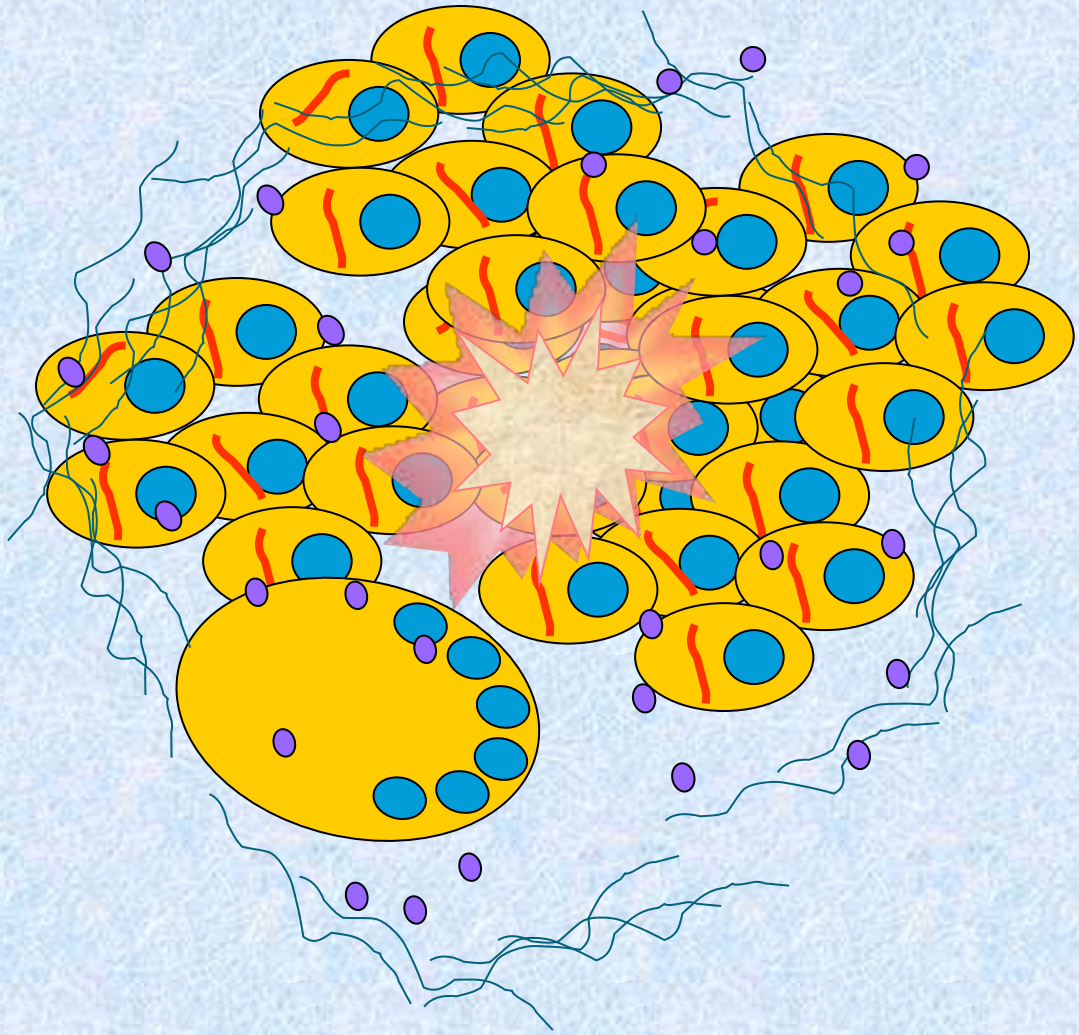
- Macrophages modify to epithelioid cells that are larger in size and have higher phagocytic activity.
- Epithelioid cells fuse to form Langhan`s giant cells.
- Macrophages presents tuberculoprotein to T cells that get sensitized and accumulate around epithelioid cells (Type IV hypersensitivity reaction).
- Type IV reaction induce central necrosis (caseation necrosis)

Tuberculosis

EVOLUTION OF TUBERCLE.



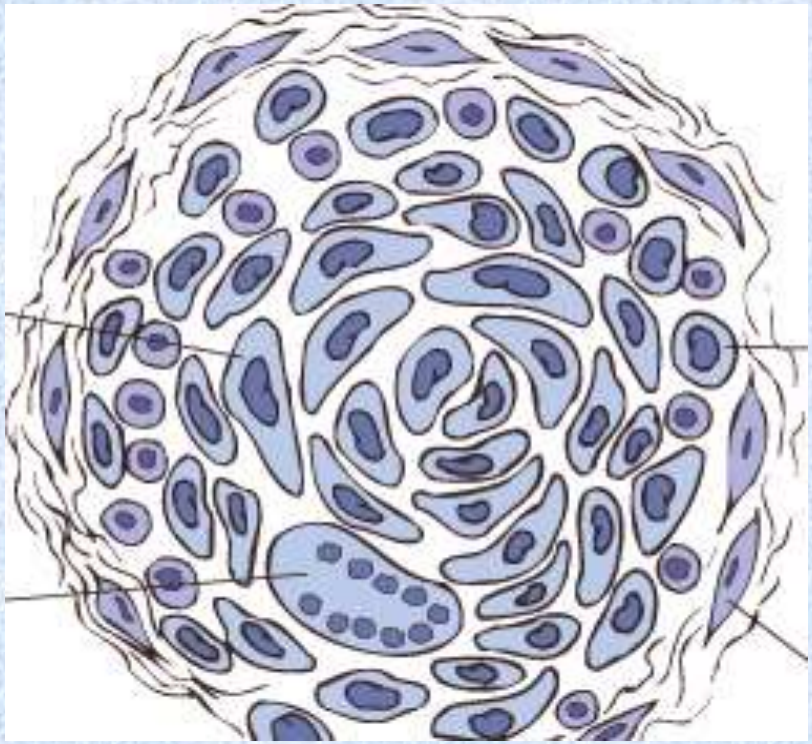
Tuberculosis



Tuberculosis

- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**
    - **Grossly**

- Small microscopic size (1-2mm).
- If caseation occurred → large pale yellow nodule

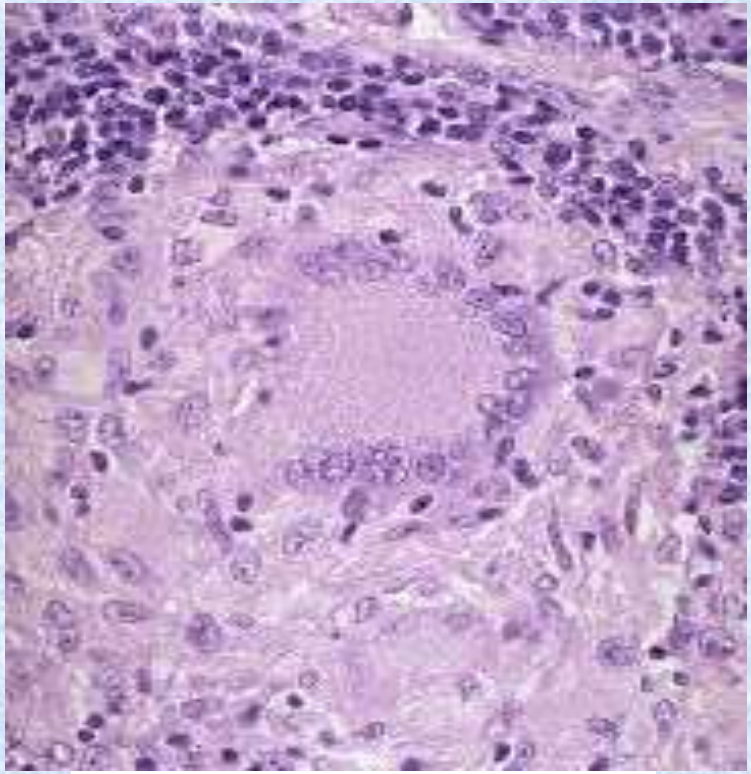


- **Microscopic**

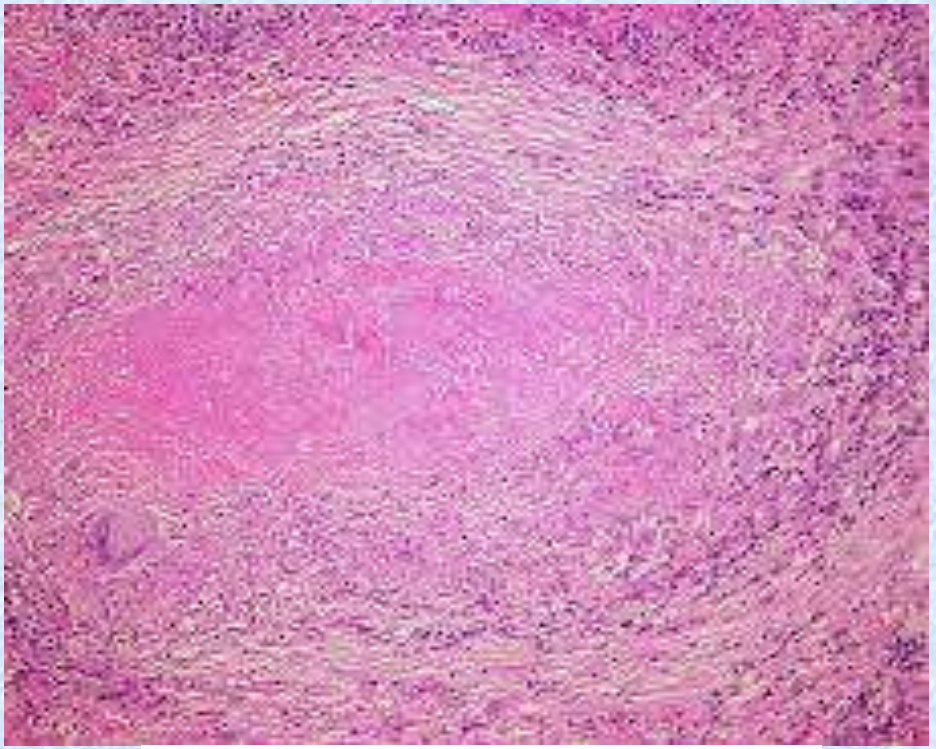
1. **Epithelioid cells**
2. **Langhan`s giant cells**
3. **Lymphocytes**

Tuberculosis

- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**
    - **Microscopic:**



Early granuloma



Caseating granuloma

Tuberculosis

- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**
    - **Microscopic:**

Early granuloma

Caseating granuloma

Where is the organism??

Tuberculosis

- **Tissue reaction against TB infection:**
  - **Proliferative tissue reaction (Tubercle):**
    - **Fate of the tubercle:**

1. Good host immunity:
   - Small tubercles: heals by fibrosis ± calcification
   - Large caseous lesions: surrounded by fibrous capsule with risk of future reactivation with lowered immunity

2. Low host immunity:
   - Direct spread to adjacent tissue.
   - Distant spread to other organs.

Tuberculosis

- **Tissue reaction against TB infection:**
  - **Excudative tissue reaction:**
    - Occurs in serous sacs
    - More common in secondary TB in sensitized patients (have sensitized T cells).
    - Usually due to exposure to a large number of TB bacilli
    - Characterized by more fluid excaudate rich in fibrinogen

Tuberculosis

❑ Spread of TB infection:

1. **Local spread to adjacent tissue:** TB bacilli are none motile but carried by macrophages to surrounding tissues
2. **Spread through natural passages:**
   - Trans-bronchial: from one lung to the other
   - Sputum of pulmonary TB leads to intestinal TB
3. **Lymphatic spread:** TB bacilli are carried to regional LNs by lymphatics
4. **Blood spread:**
   - Occurs if immunity is low and leads to isolated organ TB or miliary TB

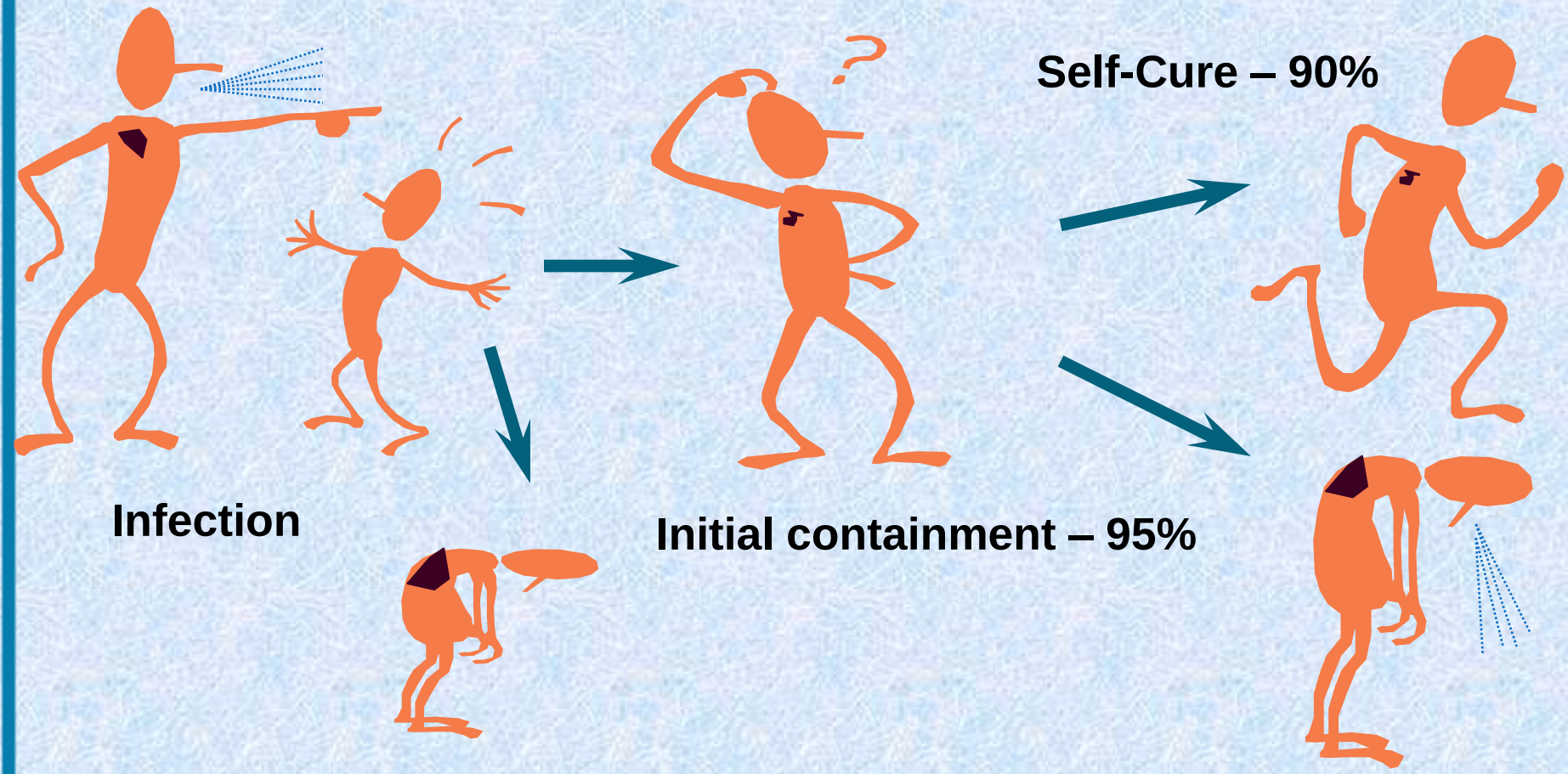
Tuberculosis

❑ Factors affecting course of TB infection:

1. **Age**: children and elderly people are susceptible to infection
2. **Dose of infection**: large dose of TB bacilli → disease.
3. **Previous exposure to TB bacilli**:
   - Usually induces immunity against TB bacilli (protective)
   - Previous exposure to T.B. bacilli may comes from:
     - BCG vaccination
     - Previous infection
4. **Immune status of the patient:** Patients with immuno-deficiency (AIDS patients) are more liable to suffer T.B.
5. **Presence of other diseases:** as DM, chronic lung diseases, renal failure) ↑ risk of TB infection.

Tuberculosis

- **Factors affecting course of TB infection:**



Tuberculosis

- **General complications of TB infection:**

1. **Haemorrhage**
2. **Reactivation**
3. **Spread**
4. **Organ destruction and extensive fibrosis.**
5. **Secondary amyloidosis**

Tuberculosis

- **Types of TB:**

Primary TB

Secondary TB

Tuberculosis

❑ Types of TB:

Primary TB	Secondary TB
• TB infection for first time	• Re-infection
• Exogenous infection	• Exogenous or endogenous
• More common in young age (childhood type)	• More common in adult life (adult type)
• Tissue reaction is slow	• Tissue reaction is rapid
• Tissue damage is minimal	• Tissue damage is prominent
• Lymph nodal reaction: prominent	• Lymph nodal reaction: mild
• Primary sites: lung, intestine, skin and tonsils	• Affect any organ
• Tissue reaction depends on innate immunity	• Tissue reaction depends on hypersensitivity reaction

Primary TB

Tuberculosis

❑ Primary TB:

❖ General features:

- Infection by TB bacilli for the first time.
- Common in young age
- Exogenous source of infection
- Most cases are asymptomatic (flu-like illness) and ± 5% develop a significant disease

❖ Primary sites of TB

1. Lung **3. Tonsils**

2. Intestine **4. Skin**

Primary Tuberculosis

❖ **Main pathological features (the primary complex):**

1. TB lesion at the primary site of infection: epithelioid cell granuloma with or without caseation (**Describe !**)
2. TB lymphangitis
3. TB lymphadenitis (**usually the prominent lesion**)

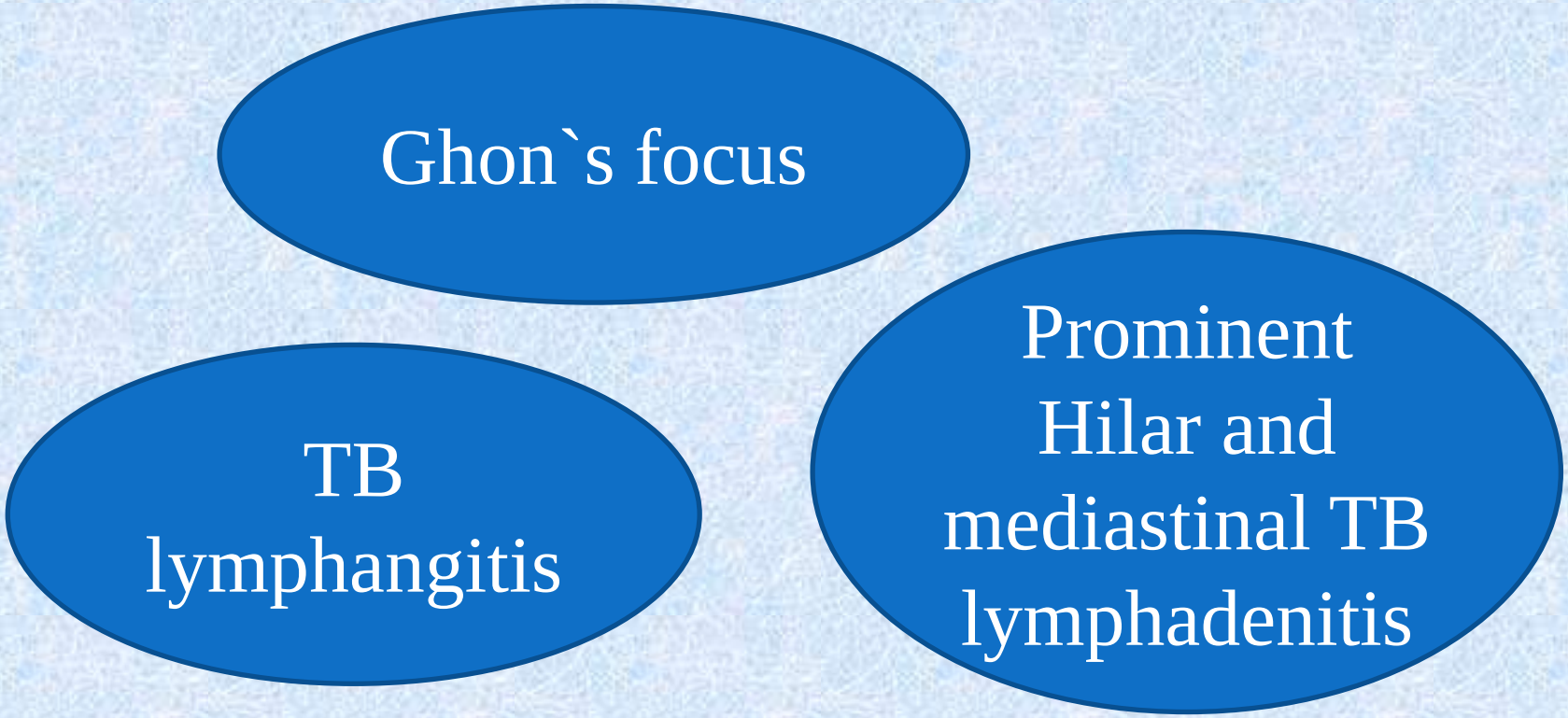
❖ **According to primary sites of TB; the known primary complexes are:**

- Primary pulmonary complex → for pulmonary TB
- Primary intestinal complex → for intestinal TB
- Primary cervical complex → for tonsillar TB
- Primary cutaneous complex (rare) → for skin TB

Primary Tuberculosis

A. Primary pulmonary TB:

- **Etiology:**
  - Inhalation of TB bacilli; usually human strain
- **Pathology (primary pulmonary complex):**



Primary Tuberculosis

A. Primary pulmonary TB:

- **Etiology:**
  - Inhalation of TB bacilli; us
- **Pathology (primary pulmo**

Gross: small (few mm), sub-pleural; upper zone of lower lobes of lower zones of upper lobe
MP: Epithelioid cell granuloma

Ghon`s focus

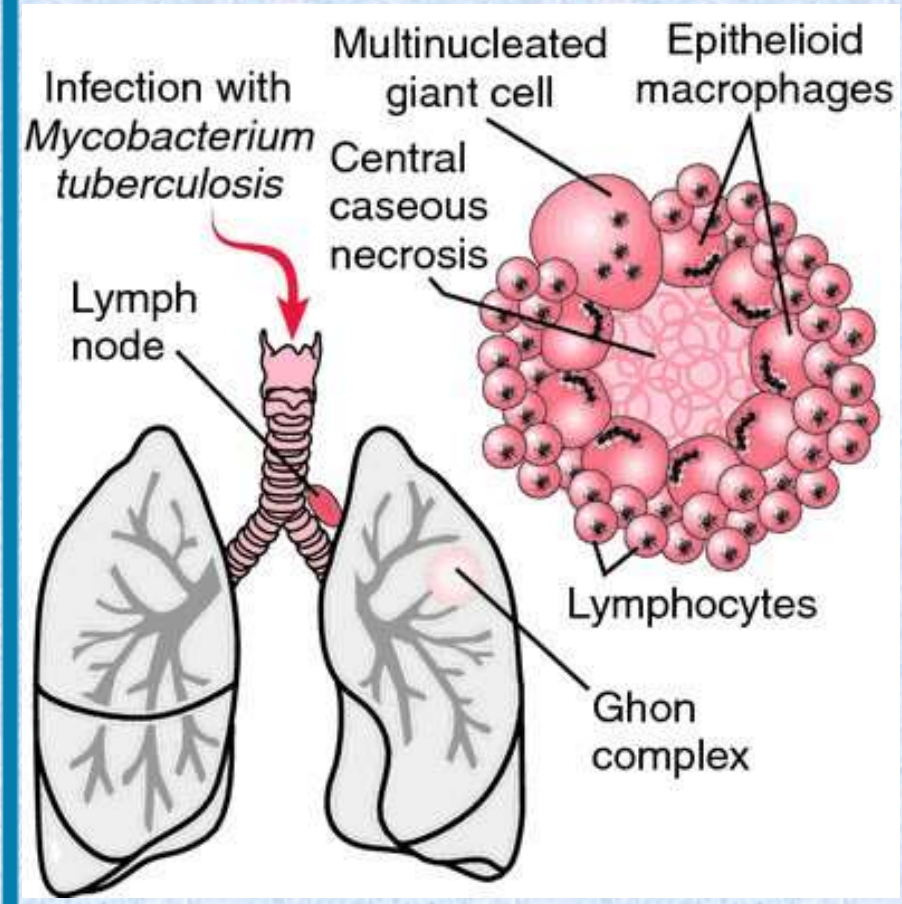
TB lymphangitis

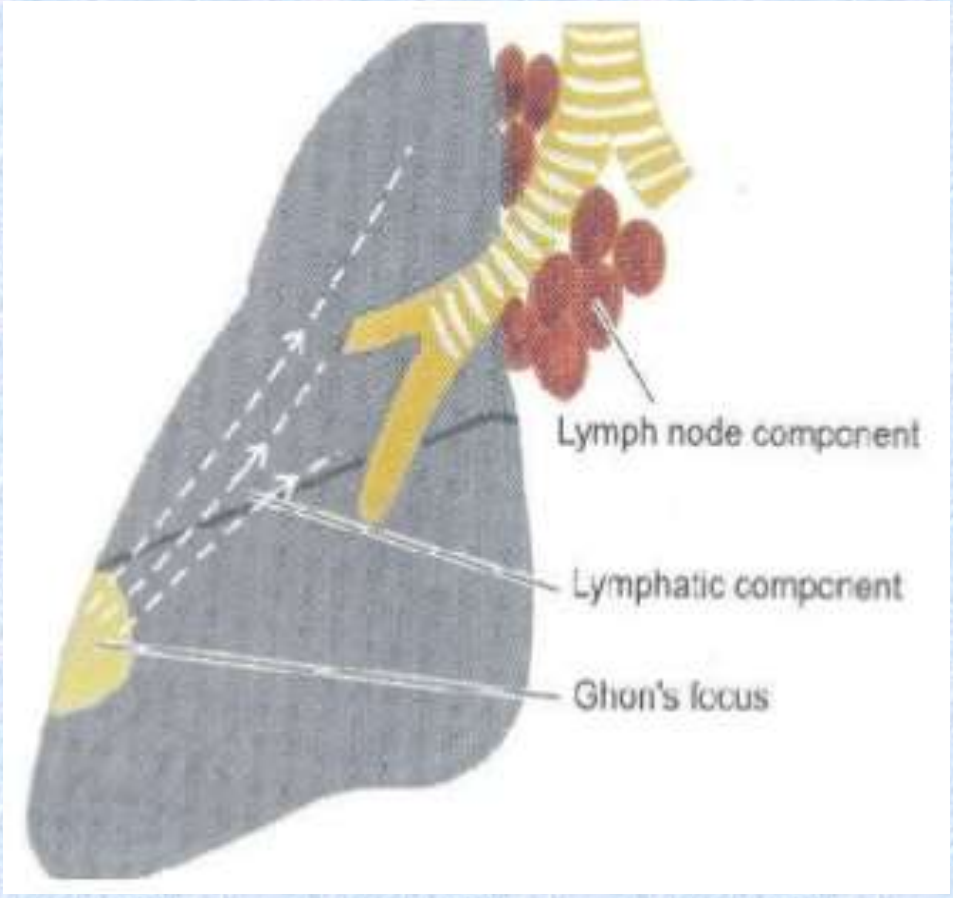
Prominent Hilar and mediastinal TB lymphadenitis

Primary Tuberculosis

A. Primary pulmonary TB:

❖ Pathology (primary pulmonary complex):

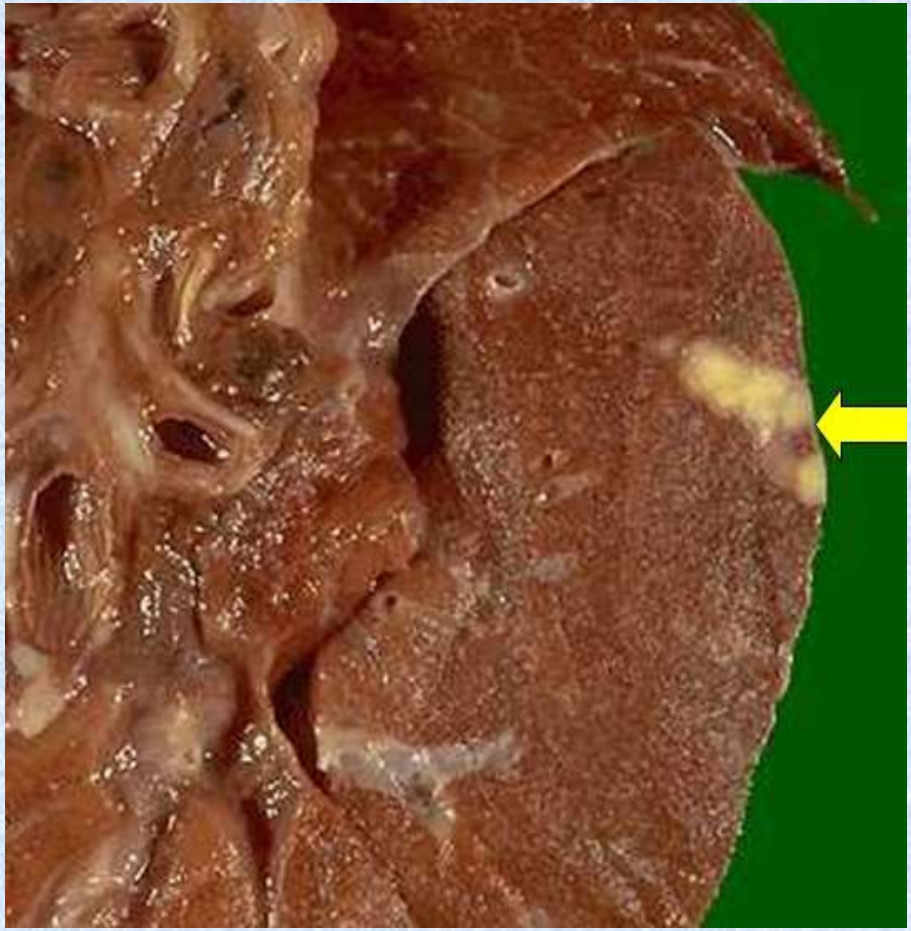


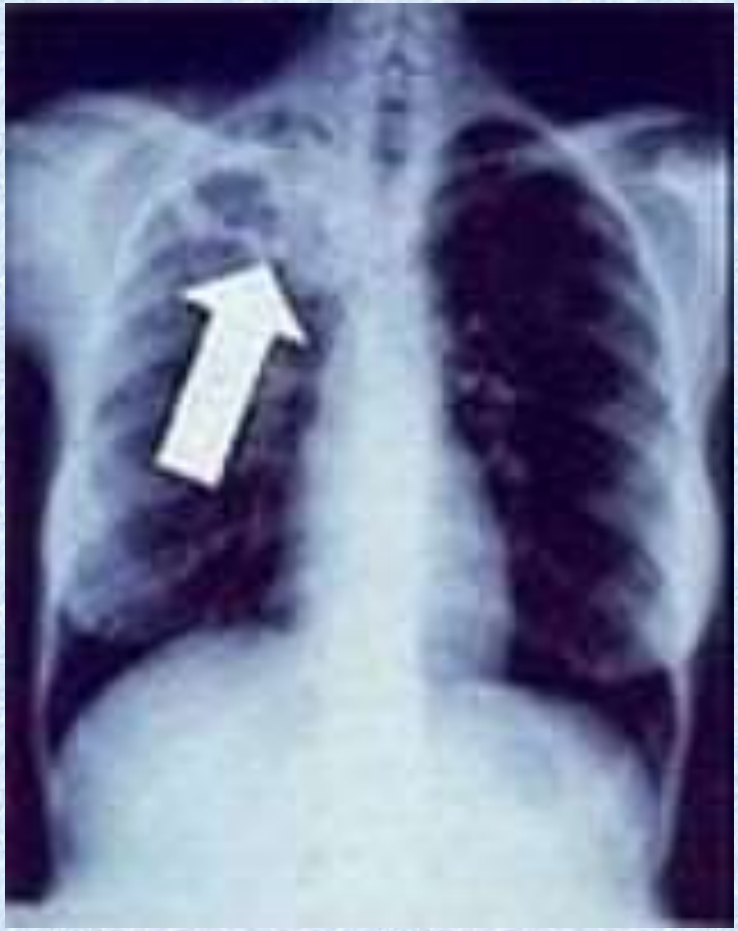


Primary Tuberculosis

A. Primary pulmonary TB:

- **Pathology (primary pulmonary complex):**





Primary Tuberculosis

A. Primary pulmonary TB:

❖ **Clinically:**

- The patients presents with enlarged hilar/mediastinal LN

❖ **Fate:**

1. Localization and healing by fibrosis: occurs in 95% of cases
2. Spread:
   a. Direct: to pleura or pericardium
   b. Trans-bronchial to lower lung lobes, to other lung, to tonsils or intestine by sputum
   c. Lymphatic
   d. Blood spread:
      - Goode immunity: no effect
      - Low immunity: isolated organ TB or miliary TB
3. Encapsulation and reactivation leading to secondary TB

Primary Tuberculosis

B. Primary intestinal TB:

- **Etiology:**
  - Ingestion of TB bacilli; usually bovine strain
- **Pathology (primary intestinal complex):**

Small intestinal ulcer

TB lymphangitis

Prominent mesenteric lymphadenitis (Tabes mesenterica)

Primary Tuberculosis

B. Primary intestinal TB:

- **Etiology:**
  - Ingestion of TB bacil
- **Pathology (primary in**

Gross: small girdle ulcers at terminal ileum (payers patch).
MP: Epithelioid cell granuloma

Small intestinal ulcer

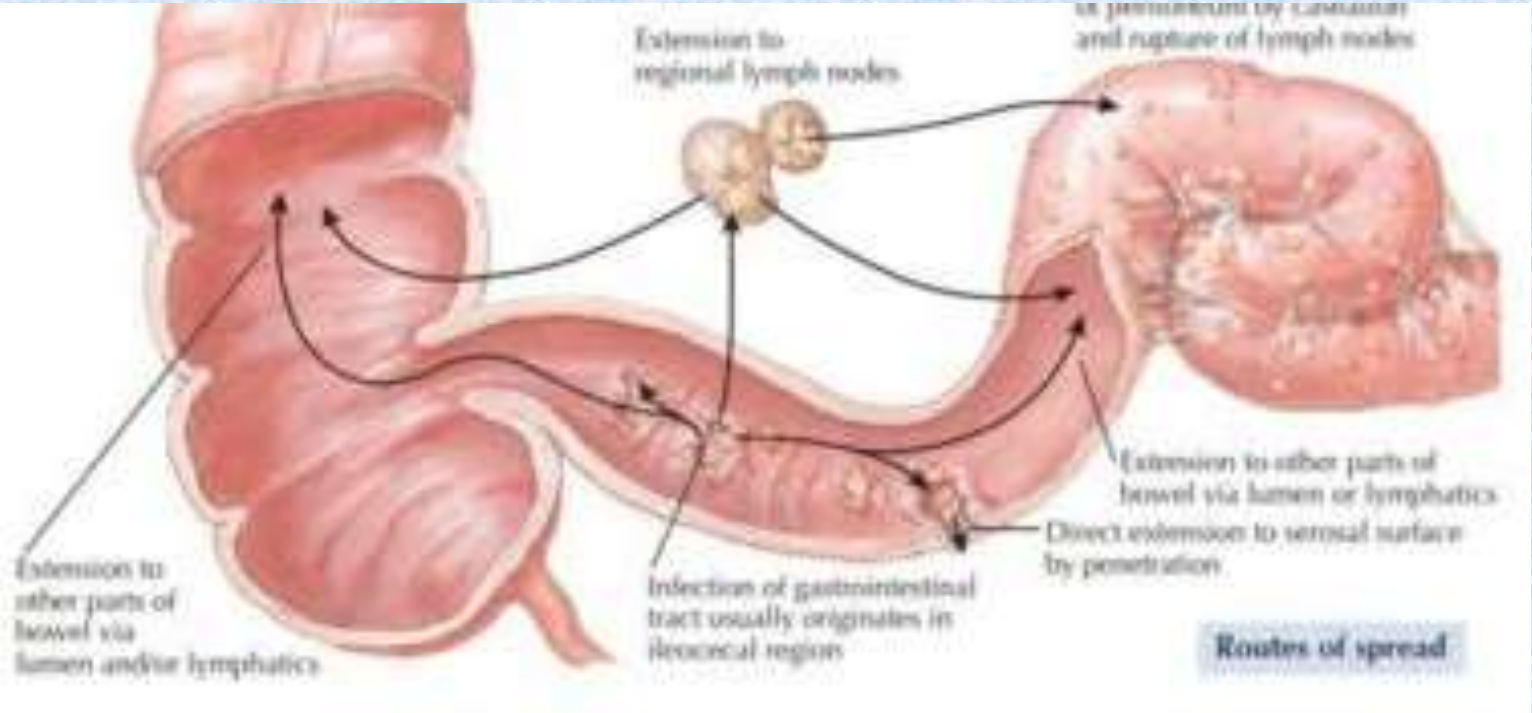
Prominent mesenteric lymphadenitis (Tabes mesenterica)

TB lymphangitis

Primary Tuberculosis

B. Primary intestinal TB:

- **Pathology (primary intestinal complex):**



Primary Tuberculosis

B. Primary intestinal TB:

❖ **Clinically:**

- The patients presents with ***enlarged mesenteric LN*** (***Tabes mesentrica***)

❖ **Fate:**

1. Localization and healing by fibrosis: occurs in most cases
2. Spread:
   a. Direct: to peritoneum
   b. Lymphatic
   c. Blood:
      - Good immunity: no effect
      - Low immunity: isolated organ TB or miliary TB

Primary Tuberculosis

C. Primary tonsillar TB:

- **Etiology:**
  - Ingestion or inhalation of TB bacilli.
- **Clinically:**
  - The patients presents with enlarged cervical LN
- **Pathology (primary cervical complex):**

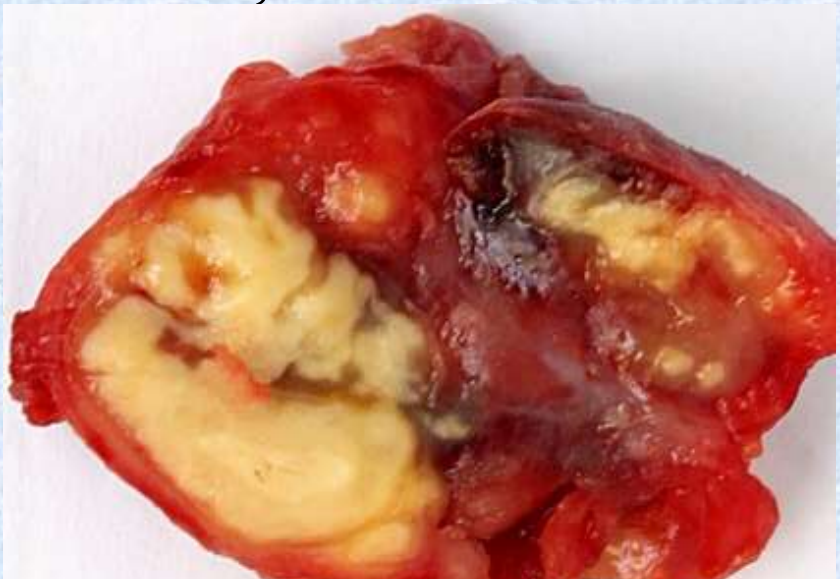
Small tonsillar ulcer or nodule

Prominent cervical lymphadenitis

TB lymphangitis

Primary Tuberculosis

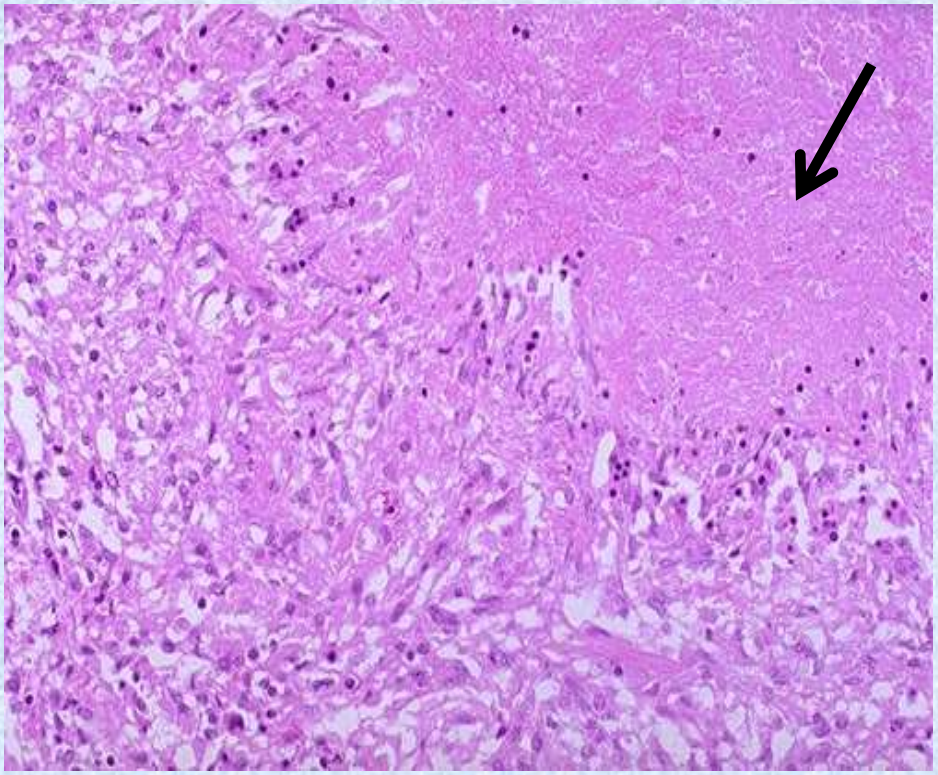
- **TB lymphadenitis:**
  - **Etiology:**
    - A component of primary complex in cases of primary TB.
    - Also can be involved in secondary TB
  - **Sites**
    - Pulmonary hilar, mediastinal, mesenteric and cervical LNs
  - **Pathology:**



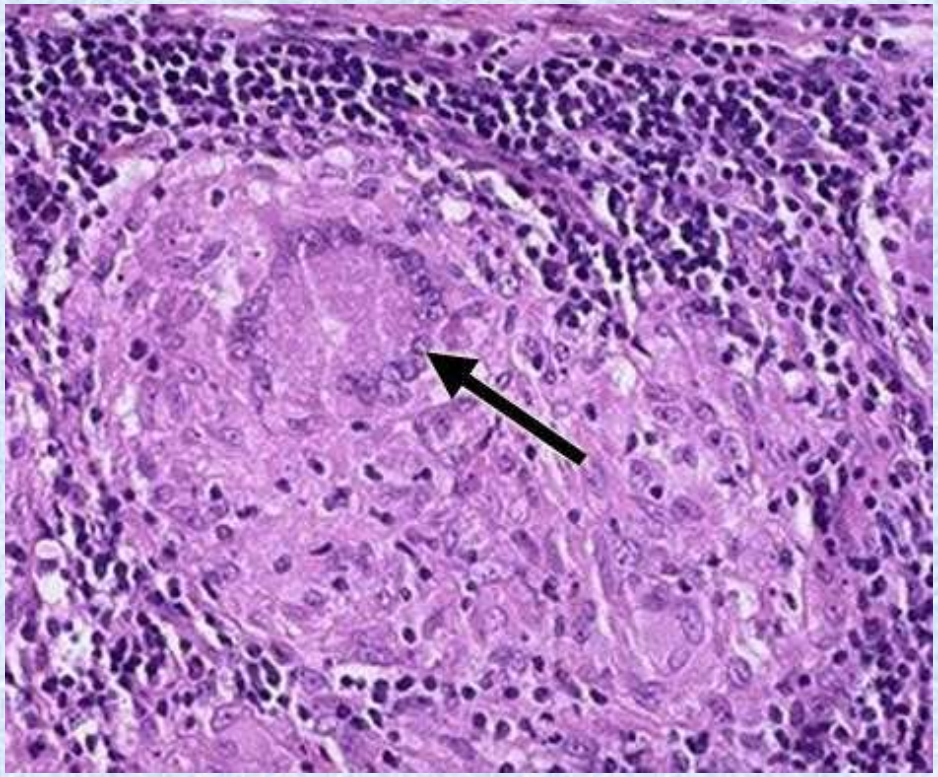
Caseating TB of LN, yellow caseating material

Primary Tuberculosis

- **TB lymphadenitis:**



Caseating TB of LN, yellow caseating necrosis, arrow



Early TB of LN, NO caseation, Langhan`s giant cell, arrow

Primary Tuberculosis

- **TB lymphadenitis:**
  - **Fate:**

1. Localization and healing by fibrosis: the common course
2. Spread:
   a. Direct spread: To
      - Skin (in cases of cervical LN): form a sinus.
      - Mediastinum or pericardium (cases of pulmonary hilar or mediastinal LNs
      - To peritoneum (in cases of intestinal TB): TB peritonitis

   b. Lymphatic: to other lymph node groups
   c. Haematogenous:
      - Good immunity: no effect
      - Low immunity: isolated organ TB or miliary TB

Secondary TB

Secondary Tuberculosis

- **Means**: re-exposure to TB infection in a previously sensitized patient
- **More of infection**:
  a. Endogenous: reactivation of an old TB lesion
  b. Exogenous: re-infection in a previously infected or previously immunized patient
- **Pathologically**:
  - **Can involve any organ**
  - The site of TB infection show the main pathological lesions
  - Lymph node involvement is usually mild and insignificant

Secondary Tuberculosis

A. Secondary pulmonary TB:

❖ **Mode of infection**

- Re-infection by repeated inhalation of TB bacilli
- Reactivation of old encapsulated Ghon`s focus

❖ **Pathological forms**

1. Chronic fibro-caseous pulmonary TB (more common):
   - Chronic prolonged course

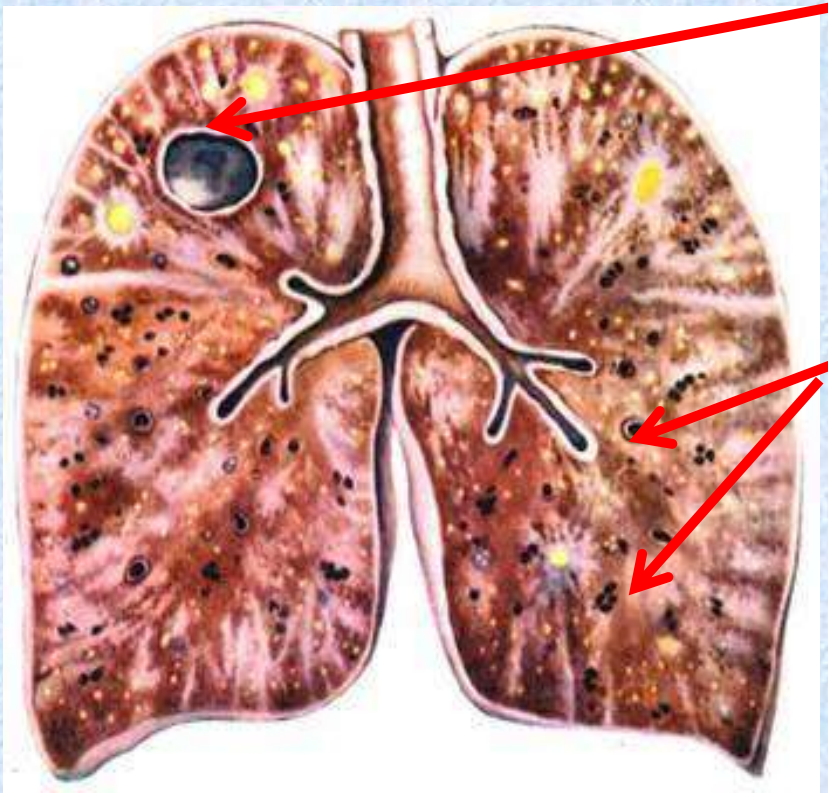
2. TB bronchopneumonia:
   - Acute fatal course

Secondary Tuberculosis

A. Secondary pulmonary TB:

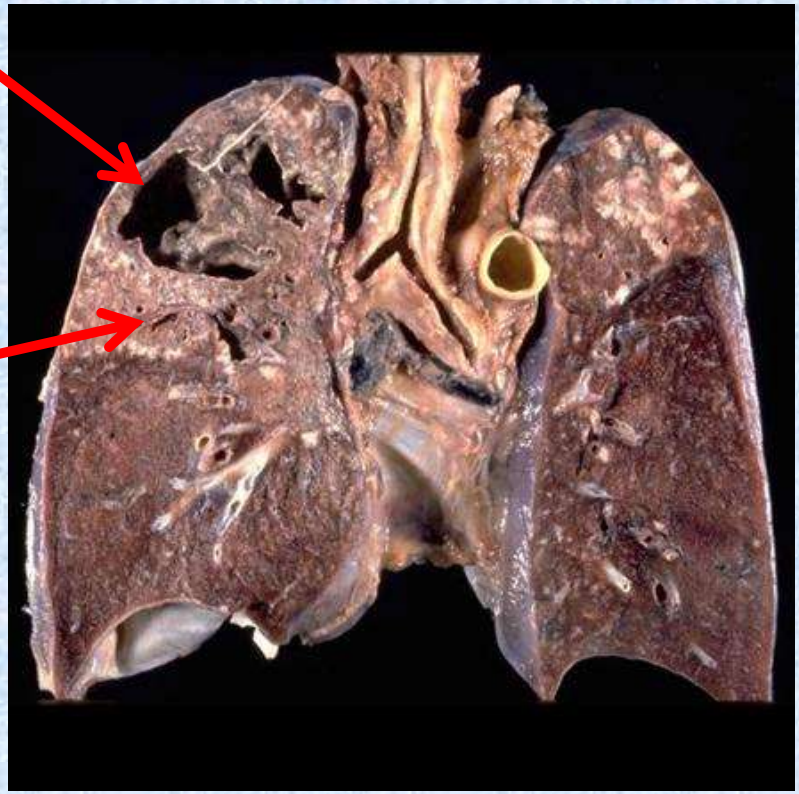
1. Chronic fibro-caseous pulmonary TB

- ***Grossly***



Apical cavity

Acinar lesions



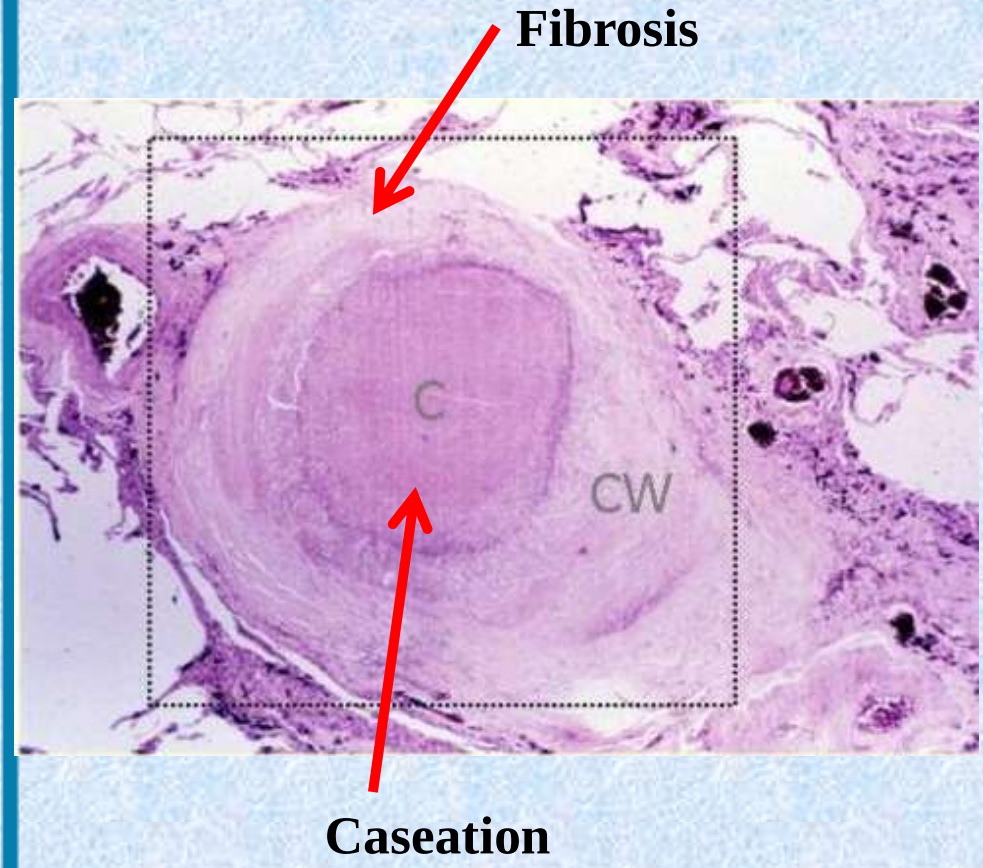
Insignificant mild enlarged hilar LN

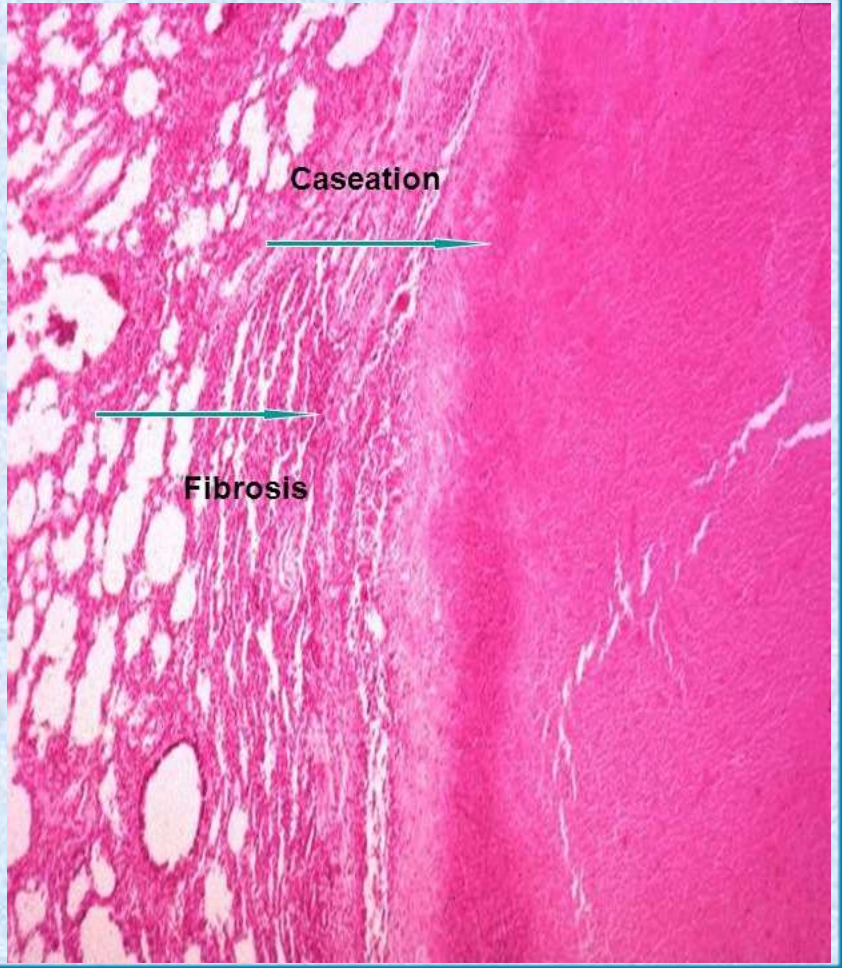
Secondary Tuberculosis

A. Secondary pulmonary TB:

1. Chronic fibro-caseous pulmonary TB

- ***MP***





Secondary Tuberculosis

A. Secondary pulmonary TB:

1. Chronic fibro-caseous pulmonary TB

- ***Clinically***

1. Weakness & weight loss
2. Night sweats
3. Low grade fever
4. Chest pain and Dyspnea
5. Haemoptysis
6. Pleural effusion

- ***Complications***

1. Haemoptysis (coughing of blood)
2. Rupture of the cavity lead to pneumothorax
3. Spread; pleura, other lung or distant spread **to ??**
4. Pulmonary fibrosis with right side heart failure

Secondary Tuberculosis

A. Secondary pulmonary TB:

2. Acute TB bronchopneumonia

- ***Grossly***
  - Both lungs are involves by large number of small caseous TB lesions
  - Pleural is commonly involved (TB pleurisy)

- ***MP:***
  - Numerous caseating TB granulomas (**Describe!**)

- ***Fate/Complications***
  1. A fatal condition
  2. Can lead to miliary systemic TB

Secondary Tuberculosis

B. Secondary intestinal TB:

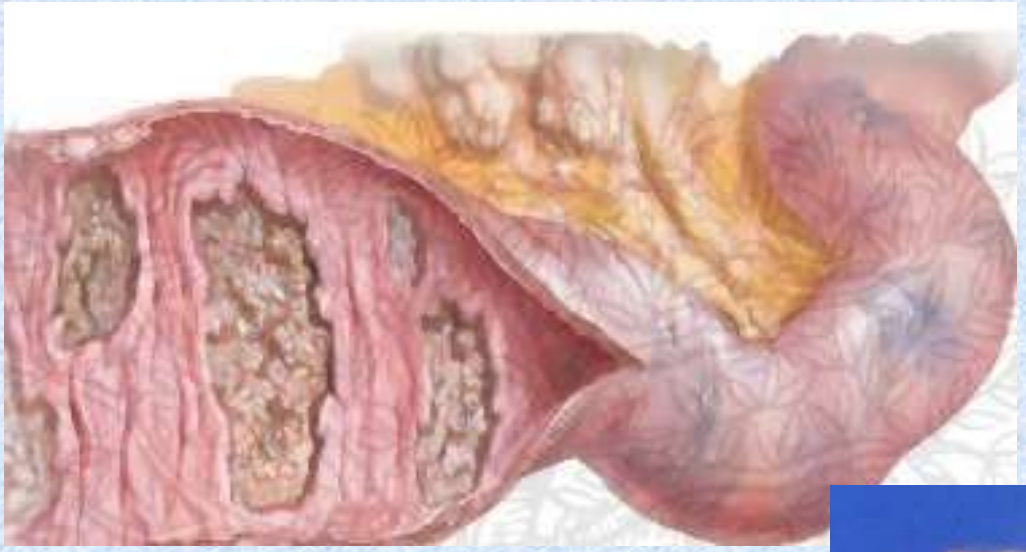
- **Mode of infection**
  - Re-infection by repeated ingestion of TB bacilli
  - More commonly; swallowing of infected sputum in a patient with chronic fibro-caseous pulmonary TB

- **Pathological features**
  - ***Grossly:*** TB ulcers of the intestine
  - ***MP:*** Formation of granulomatous reaction (caseating or non caseating) in intestinal wall

Secondary Tuberculosis

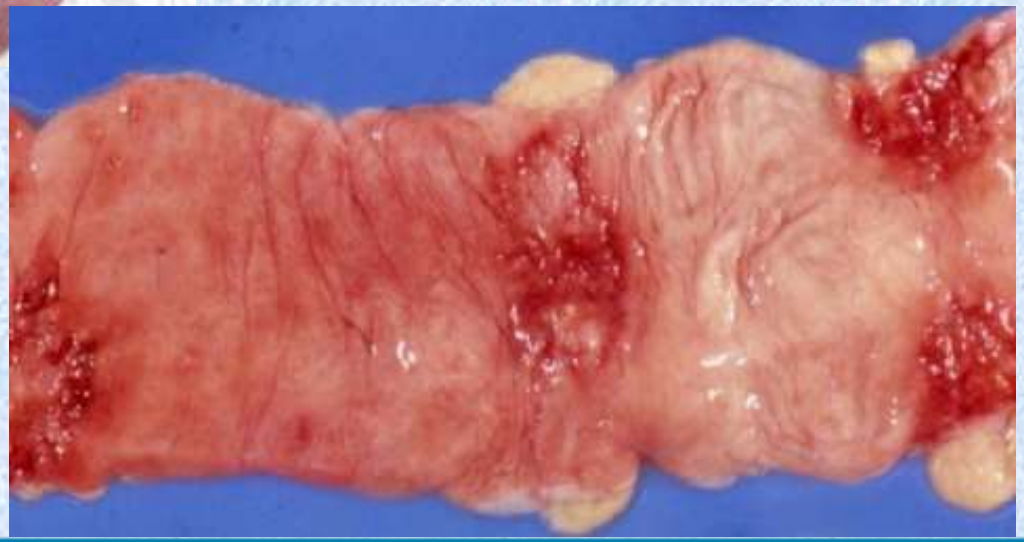
B. Secondary intestinal TB:

❖ **Pathological features**



TB ulcer::

- Multiple, girdle ulcers with undermined edge
- Mild enlarged mesenteric LN



Secondary Tuberculosis

B. Secondary intestinal TB:

❖ **Complications**

1. Intestinal hemorrhage (melena)
2. Intestinal perforation and peritonitis
3. Intestinal fistula
4. Spread to adjacent structures as peritoneum or distant spread …... **Describe!!**
5. Intestinal fibrosis with secondary intestinal obstruction

Secondary Tuberculosis

C. Secondary TB of other organs:

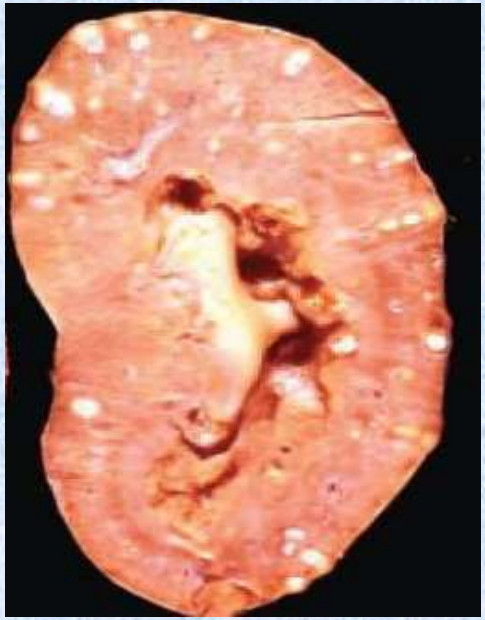
Secondary TB may involve any organ; examples are:

- Skin
- Kidney
- Bone
- Vertebra
- Urinary bladder
- Epididymis
- Peritoneum
- Meningitis

Secondary Tuberculosis

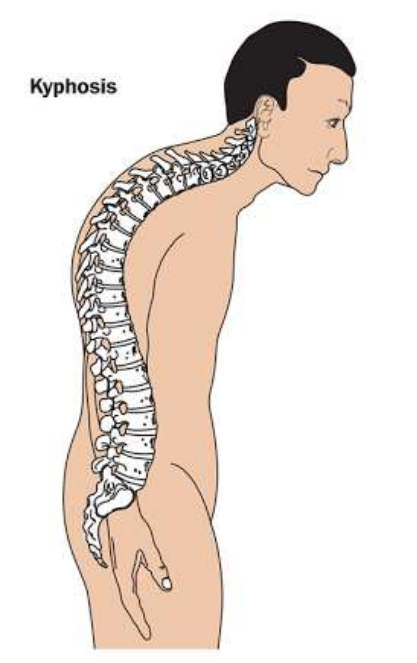
TB of kidney:

- Occurs secondary to pulmonaryTB
- Mostly by haematogenous spread
- Pathological features:
  - Dilated calyces
  - Multiple small granules/nodules at cortico-medullary zone
- Complications:
  1. Haematuria
  2. Spread of infection
  3. Renal failure



Secondary Tuberculosis

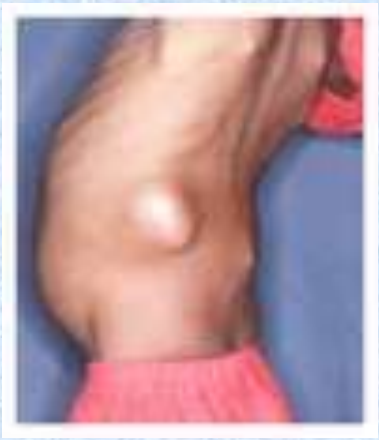
TB of vertebra (Pott`s disease):



- Usually secondary to pulmonary TB.
- By haematogenous spread

- Sites:
  - Involves thoracic, lumber and cervical vertebrae in this order

- Pathological features & complications
  1. Kyphosis
  2. Formation of cold abscess
  3. Paraplegia



Tuberculosis

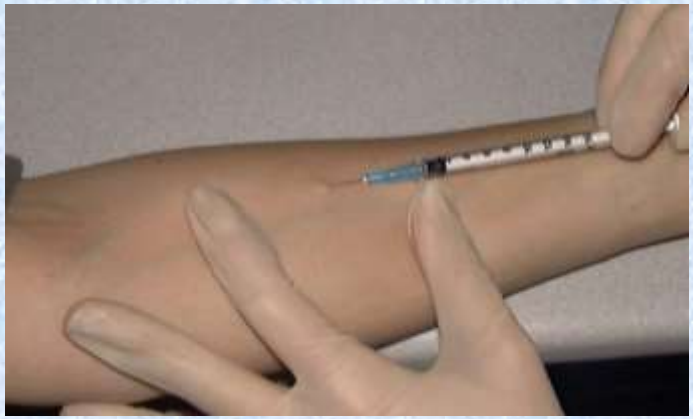
- **Diagnosis of TB infection:**
  - Clinical suspicion
  - Radiological features
  - Bacteriological studies
  - Histopathological findings

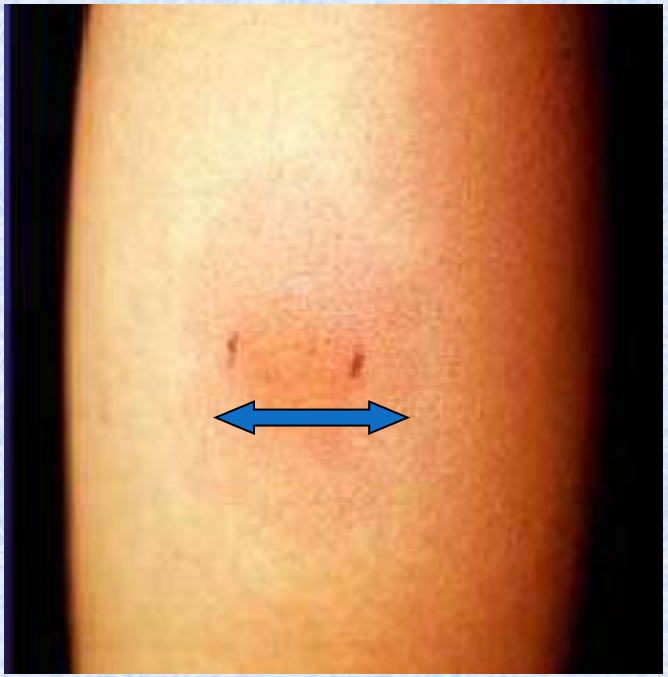
Sure diagnosis of TB depends on detection of the bacilli by Ziehl Neelsen stain in:

- In smears prepared from sputum
- In culture of sputum
- In tissue sections

Tuberculosis

- **Tuberculin test:**
  - A delayed hypersensitivity of skin after injection of TB protein product called PPD (purified protein derivative)





- Intradermal injection of 0.1ml of PPD.
- The reaction develops within 48-72 hours after injection.
- Positive reaction: a wheal of 6-10 mm in diameter.

Thank you