Rrespiratory Block

PATHOLOGY OF TUBERCULOSIS

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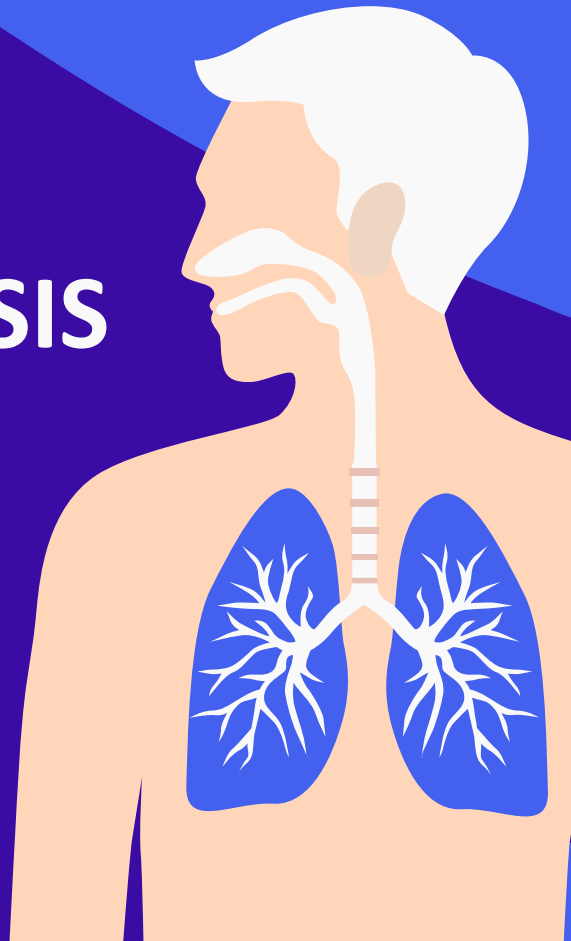


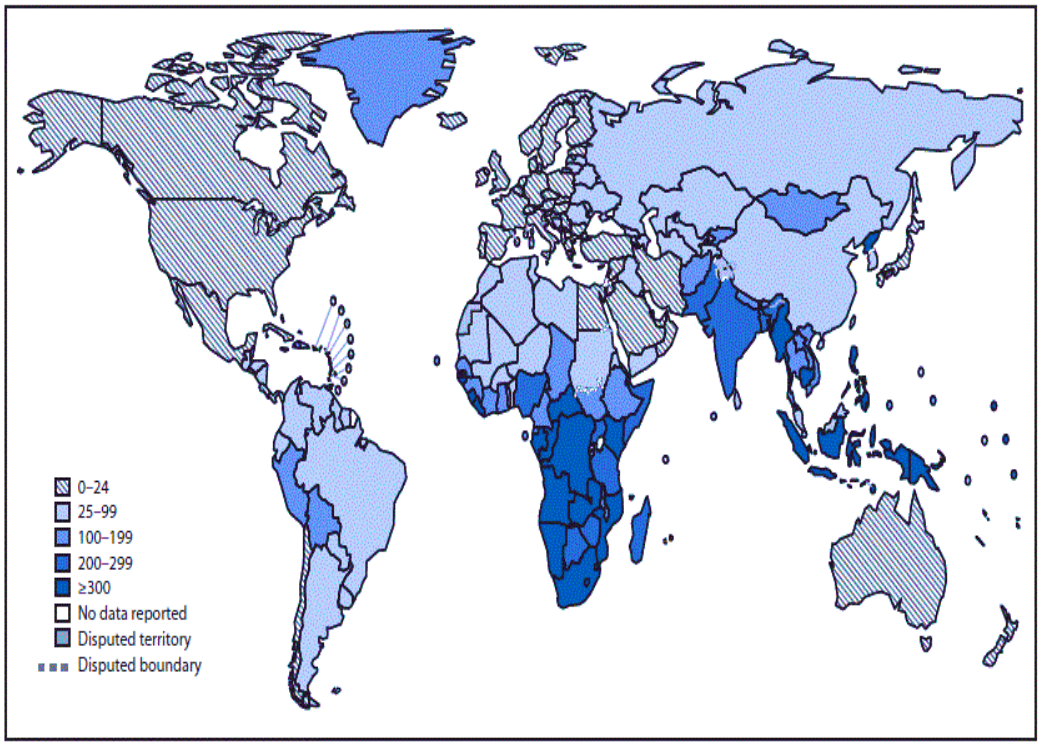
Objectives

- Define tuberculosis
- Know the epidemiology of tuberculosis (TB)
- List conditions associated with increased risk of Tuberculosis
- Recognize the morphology of Mycobacteria and its special stain (the Ziehl-Neelsen) as well as the morphology of granulomas in TB (tubercles).
- Know the Pathogenesis of tuberculosis
- In regard to Mycobacterial lung infection: Compare and contrast the following in relation to their gross and histologic lung pathology:
  - Primary tuberculosis (include a definition of the Ghon complex).
  - Secondary or reactivation tuberculosis.
  - Miliary tuberculosis.
- List organs other than lung that are commonly affected by tuberculosis.
- Know the basis and use of tuberculin skin (Mantoux) test.
- List the common clinical presentation of tuberculosis.
- List the complication and prognosis of tuberculosis.

Tuberculosis is a communicable chronic granulomatous disease caused by Mycobacterium tuberculosis. It usually involves the lungs but may affect any organ or tissue in the body

Epidemiology

- Contracted by inhalation of Mycobacterium tuberculosis (TB)
- TB bacilli are strict aerobe, acid-fast (due to mycolic acid in cell wall)
- It is estimated that 1.7 billion individuals are infected by tuberculosis worldwide, with 8 to 10 million new cases and 1.5 million deaths per year
- Tuberculosis flourishes under conditions of poverty, crowding, and chronic debilitating illness



Epidemiology

- Certain disease states also increase the risk, such as:
  1. diabetes mellitus
  2. Hodgkin lymphoma
  3. chronic lung disease (particularly silicosis)
  4. chronic renal failure
  5. malnutrition, alcoholism, and immunosuppression

- In areas of the world where HIV infection is prevalent, HIV infection is the dominant risk factor for the development of tuberculosis

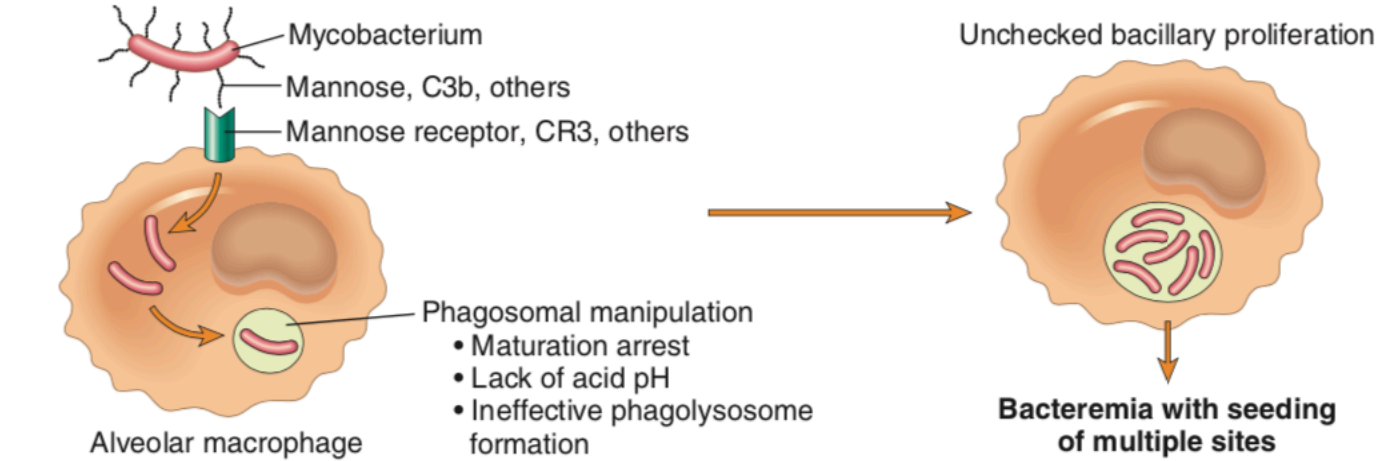
Etiology and Pathogenesis

- Mycobacteria are slender rods that are acid-fast (i.e., they have a high content of complex lipids that readily bind the Ziehl-Neelsen stain
- **M. tuberculosis hominis** is responsible for most cases of tuberculosis
- Transmission usually is direct, by inhalation of airborne organisms in aerosols generated by expectoration or by exposure to contaminated secretions of infected individual
- Oropharyngeal and intestinal tuberculosis contracted by drinking milk contaminated with **Mycobacterium bovis** infection
- Other mycobacteria, particularly **Mycobacterium avium complex**, they cause disease in 10% to 30% of patients with AIDS

Primary TB

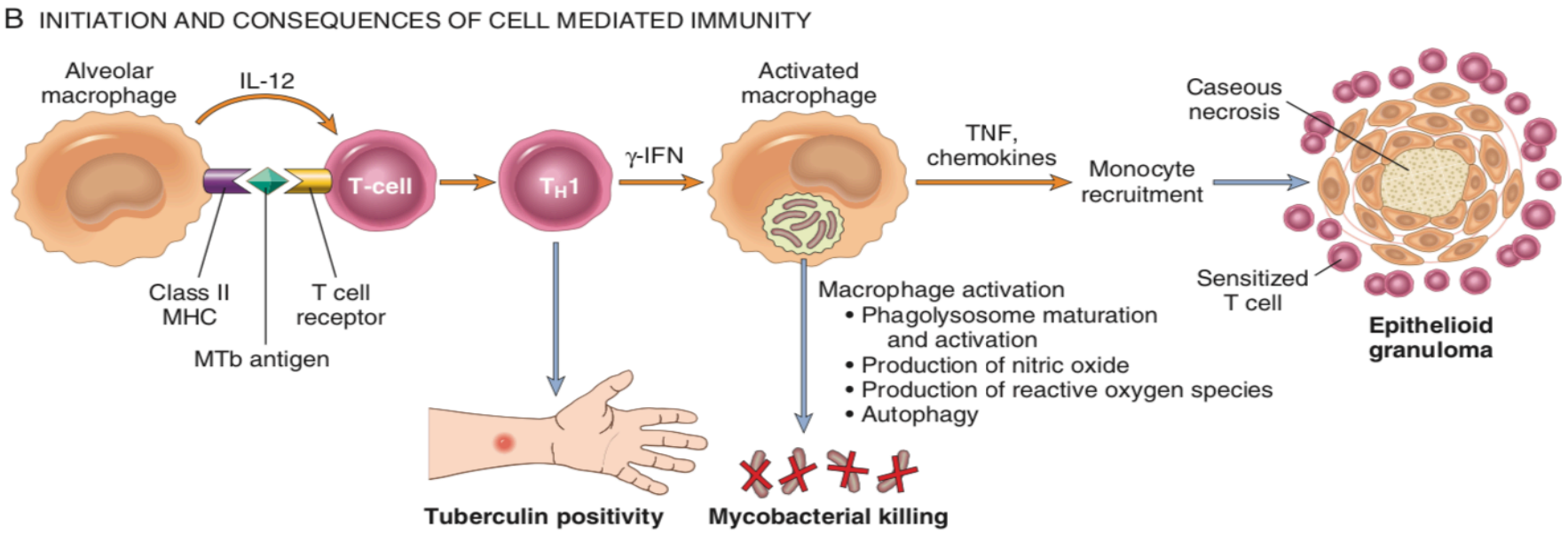
Events occurring in the first 3 weeks after exposure

Organism resides in phagosomes of alveolar macrophages



Produces a protein (cord factor) that prevents fusion of lysosomes with phagosome

Primary TB



The development of resistance to the organism is accompanied by conversion to a positive result on tuberculin skin testing. Cells and bacteria are not drawn to scale. *IFN-γ,* Interferon γ; *iNOS,* inducible nitric oxide synthase; *MHC,* major histocompatibility complex; *MTb, Mycobacterium* tuberculosis; *TNF,* tumor necrosis factor

Pathogenesis

- **Immunity to a tubercular infection is primarily mediated by T_H1 cells, which stimulate macrophages to kill mycobacteria**
- This immune response, while largely effective, comes at the cost of hypersensitivity and the accompanying tissue destruction
- Defects in any of the steps of a T_H1 T cell response (including IL-12, IFN-γ, TNF, or nitric oxide production) result in poorly formed granulomas, absence of resistance, and disease progression
- Reactivation of the infection or reexposure to the bacilli in a previously sensitized host results in rapid mobilization of a defensive reaction but also increased tissue necrosis

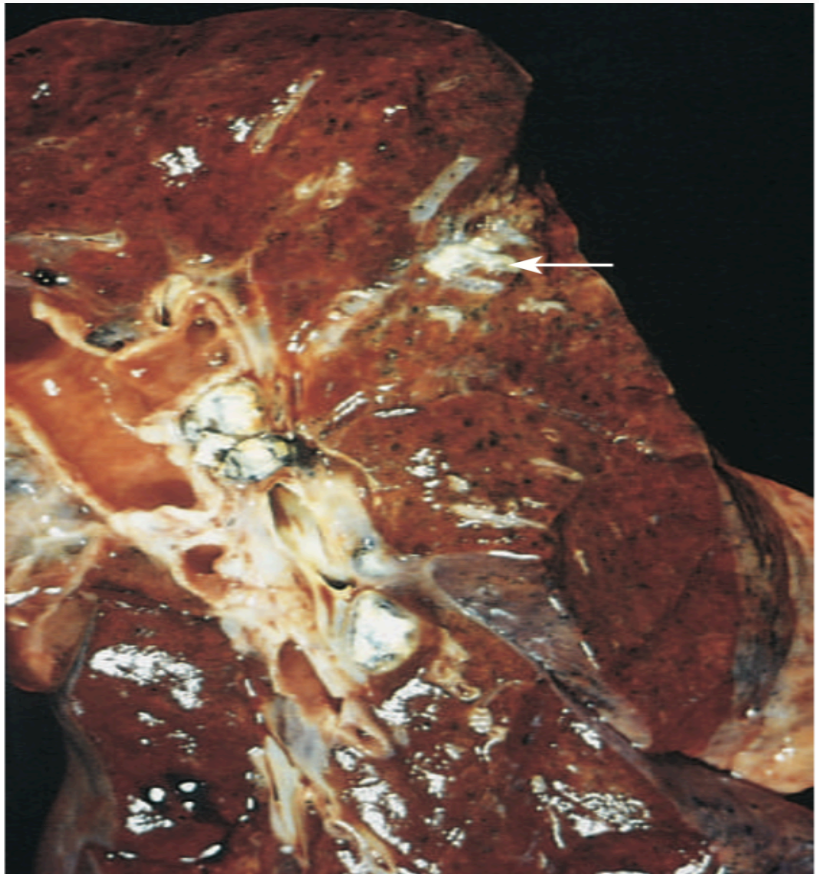
Primary Tuberculosis	Secondary Tuberculosis (Reactivation Tuberculosis)
Form of disease that develops in a previously unexposed and therefore unsensitized patient (1st time exposure). About 5% of those newly infected acquire significant disease.	Pattern of disease that arises in a previously sensitized host (2nd time exposure). It may appear shortly after primary tuberculosis.
Method of infection: inhalation, ingestion	Endogenous due to reactivation of dormant primary lesions many decades after initial infection (specially in immunocompromised individuals or exogenous due to reinfection
lower part of the upper lobe or in the upper part of the lower lobe.	Apex of lungs or upper part of lower lobe
Ghon focus, Ghon complex	Associated with cavitation
Noninfectious	Highly infectious in +ve patients

MORPHOLOGY

1ry TB: Gross morphology

Ghon complex:

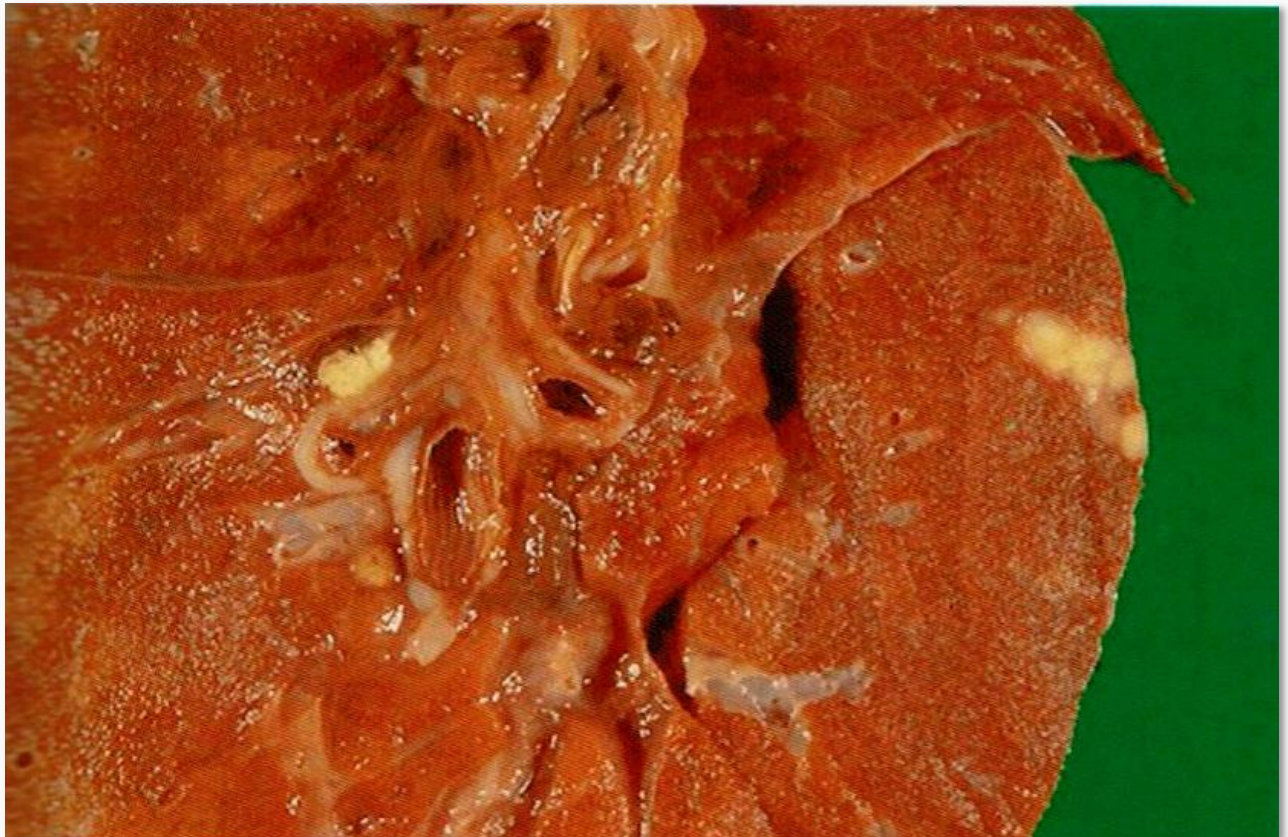
- Subpleural location
- Upper part of the lower lobes or lower part of the upper lobes
- Ghon focus (caseous necrosis) in periphery
- Ghon complex (caseous necrosis) in hilar lymph nodes
- Hilar lymph nodes with caseation



1ry TB: Gross morphology

Primary tuberculosis, Ghon complex

he gray-white parenchymal focus is under the pleura Hilar lymph nodes with caseation are seen *(left).*



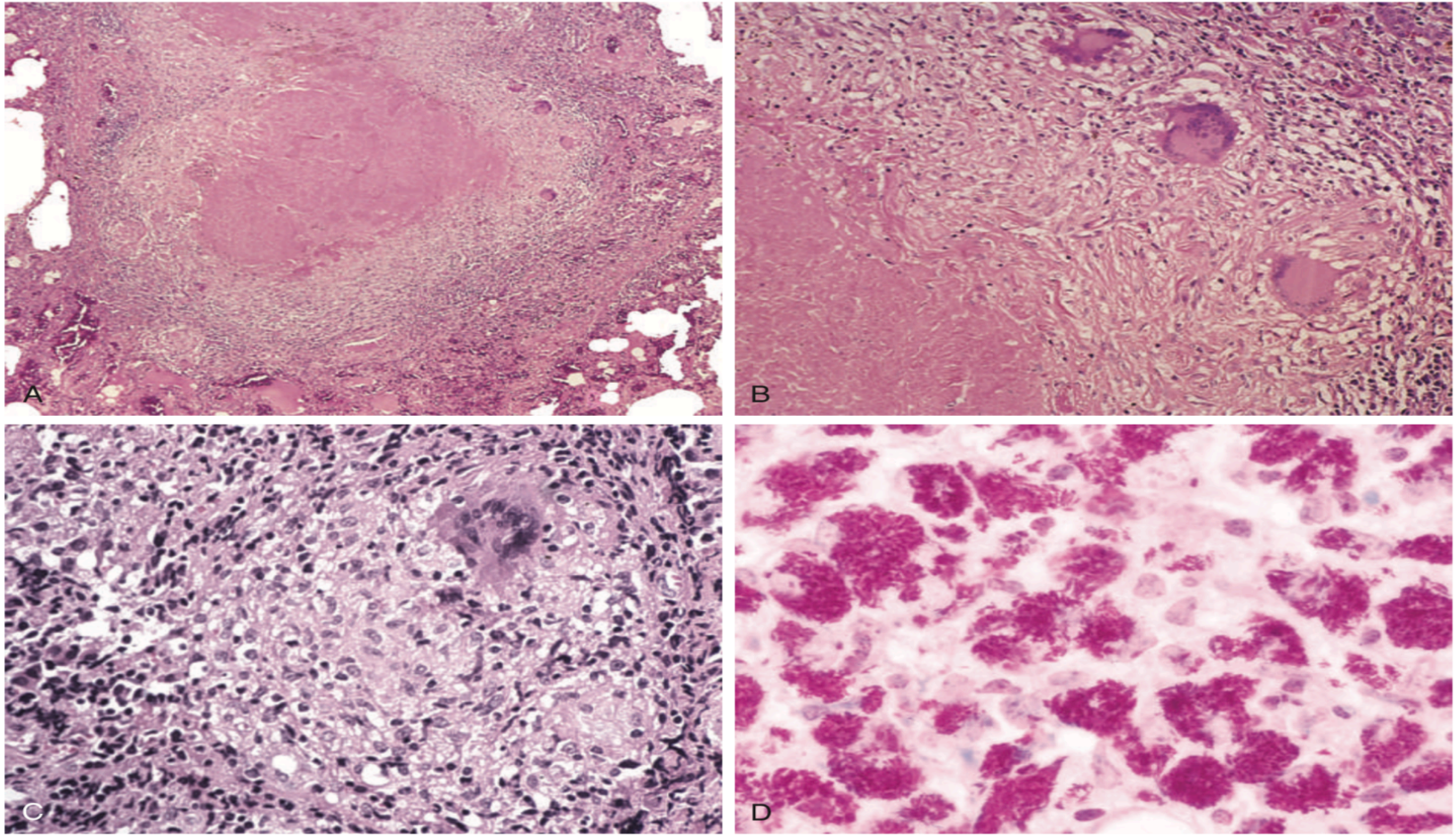
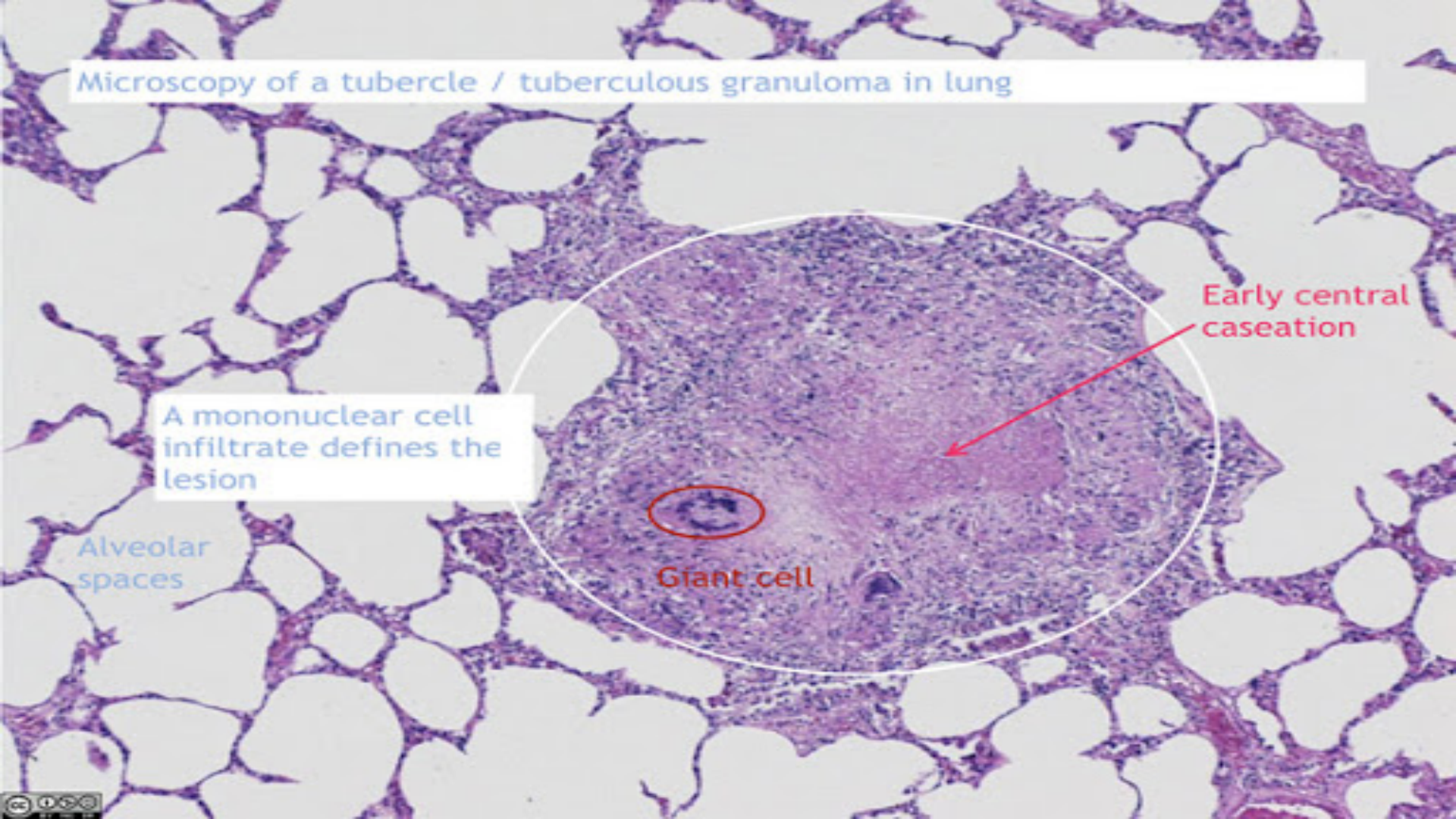
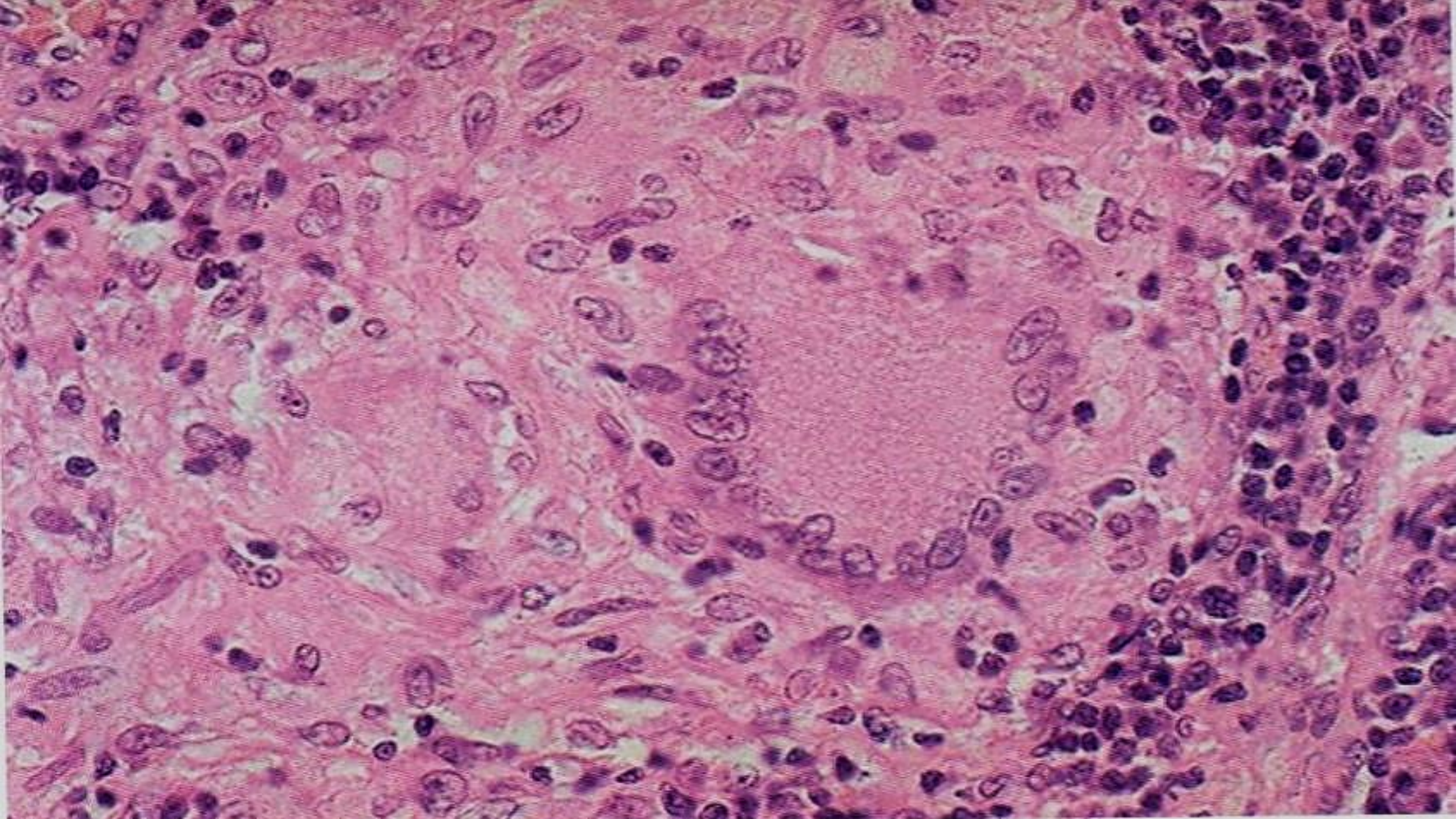


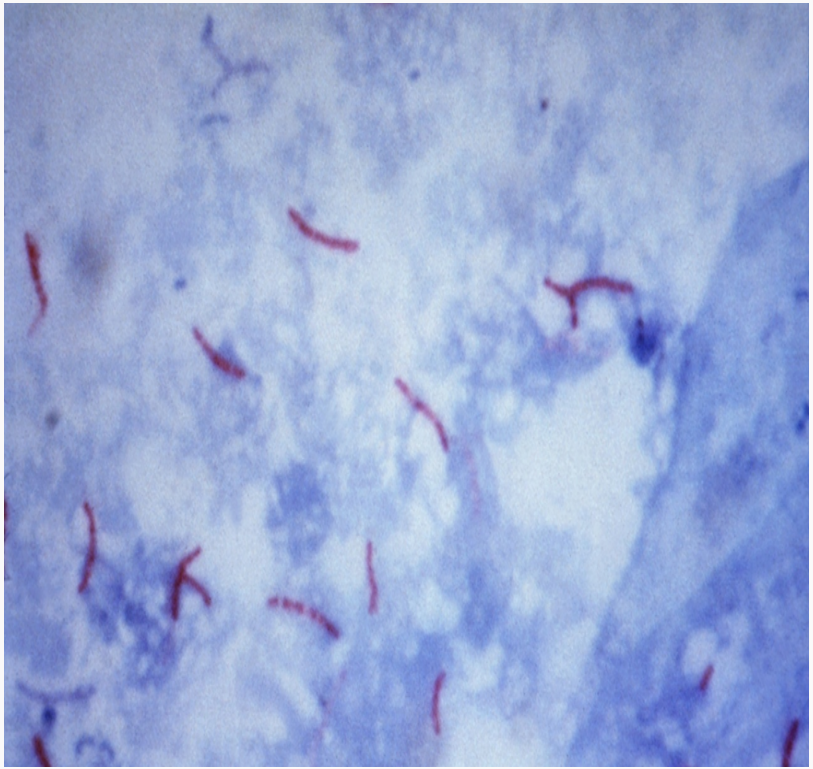
Fig. 13.35 The morphologic spectrum of tuberculosis. A characteristic tubercle at low magnification (A) and at higher power (B) shows central granular caseation surrounded by epithelioid and multinucleate giant cells. This is the usual response in individuals who develop cell-mediated immunity to the organism. (C) Occasionally, even in immunocompetent patients, tubercular granulomas may not show central caseation; hence, irrespective of the presence or absence of caseous necrosis, use of special stains for acid-fast organisms is indicated when granulomas are present. (D) In this specimen from an immunosuppressed patient, sheets of macrophages packed with mycobacteria are seen (acid-fast stain).


Microscopy of a tubercle / tuberculous granuloma in lung
Early central caseation
A mononuclear cell infiltrate defines the lesion
Alveolar spaces
Giant cell

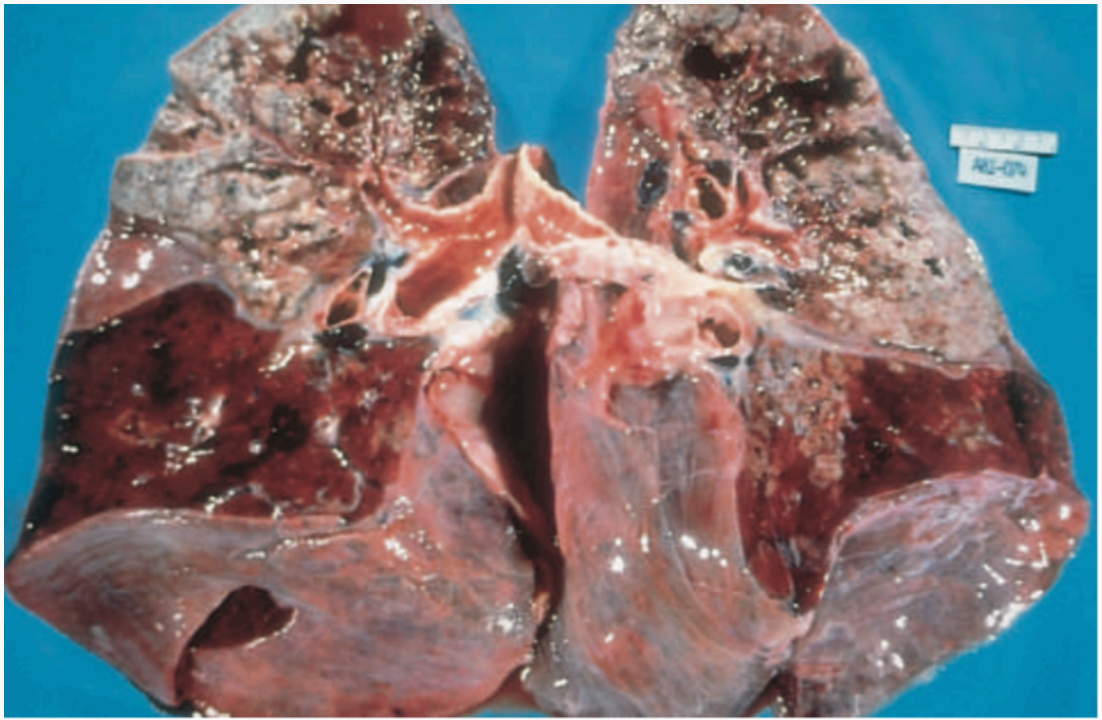


Morphology

Use of special stains for acid-fast organisms (Zeil-Neilson stain) is indicated when granulomas are present (red/pink)



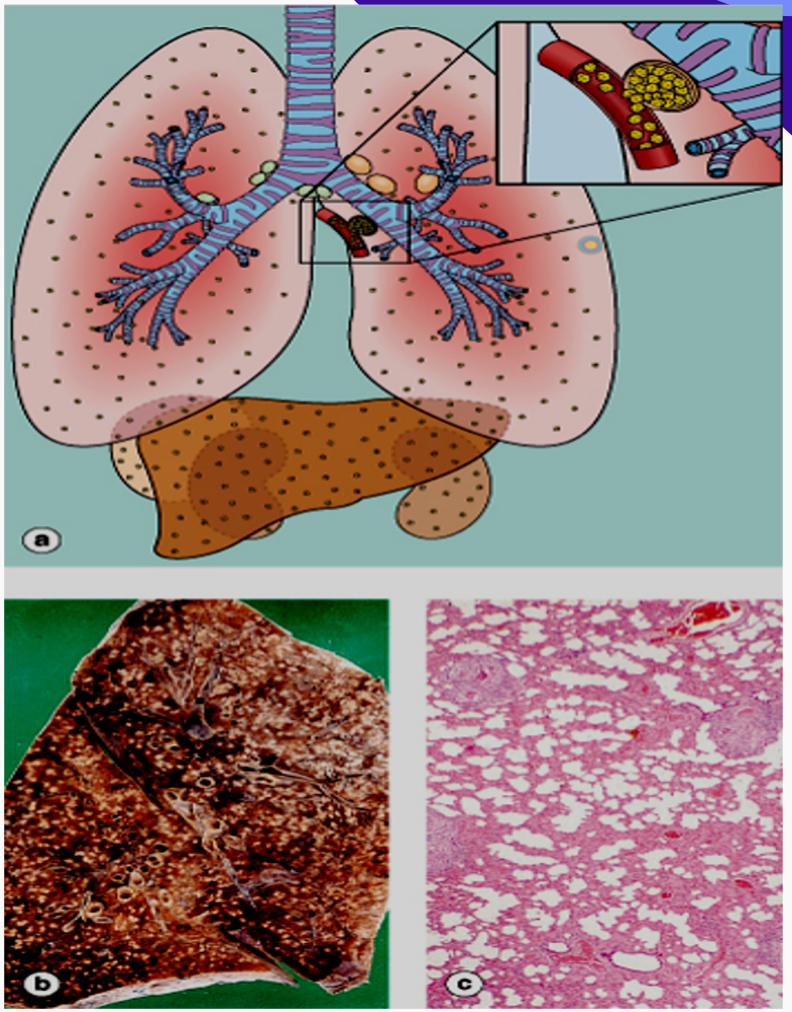
Secondary pulmonary TB



The apex of one or both upper lobes are affected with cavitation leading to erosion into and dissemination along airways, patient become infective

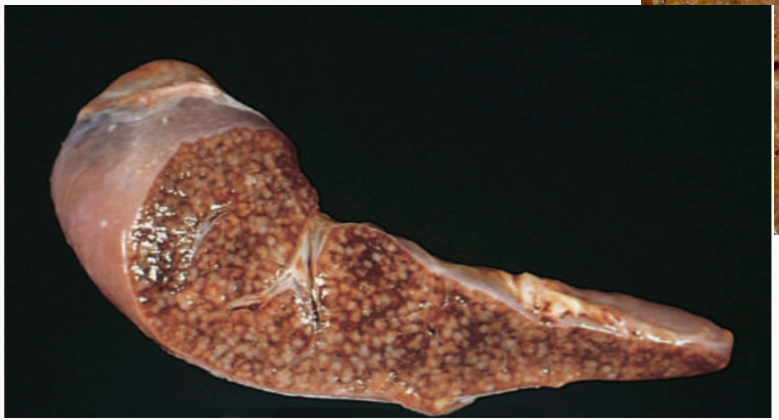
Miliary pulmonary disease

- Haematogenous spread of TB organism throughout the body
- When bacteria in the lungs enters the pulmonary venous return to the heart; the organisms subsequently disseminate through the systemic arterial system and the lymphatic channels



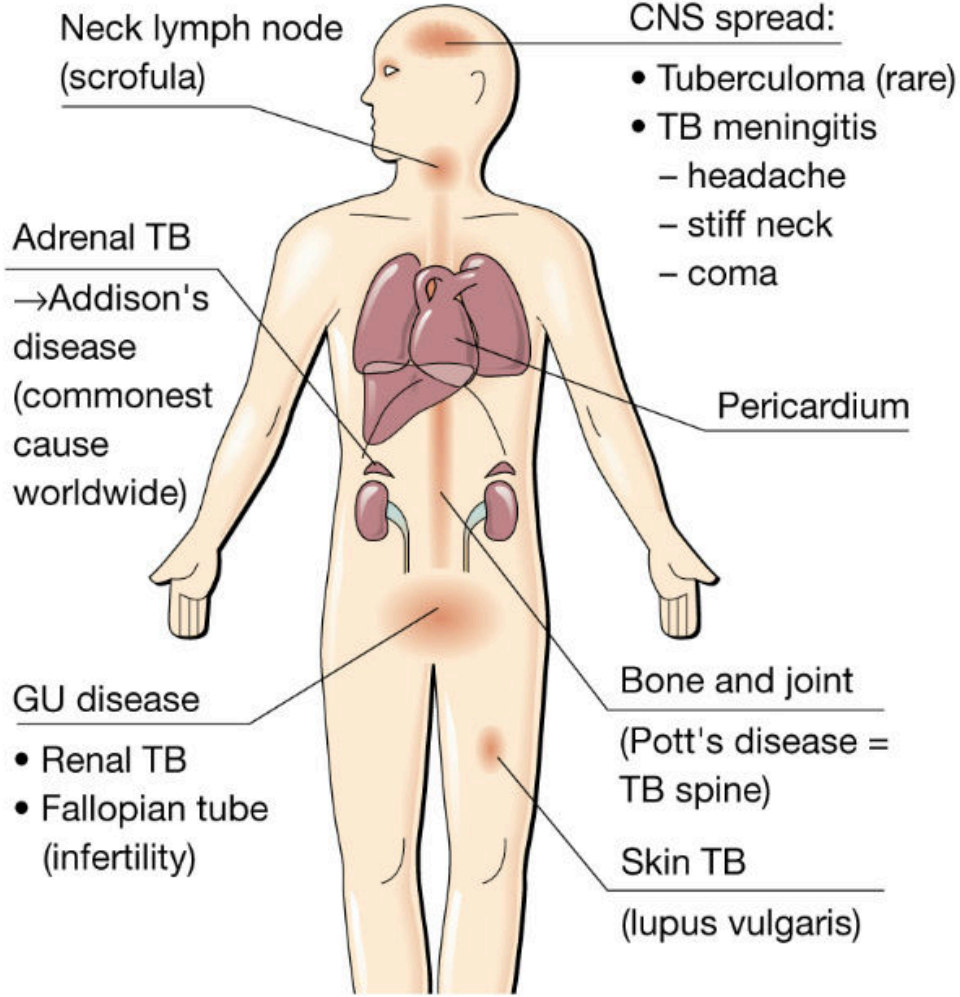
Miliary pulmonary disease

- It produces multiple small yellow nodular lesions in several organs. Almost every organ in the body may be seeded. Lesions resemble those in the lung.
- In the lungs, there multiple lesions either microscopic or small, visible (2-mm) foci of yellow-white consolidation scattered through the lung parenchyma.



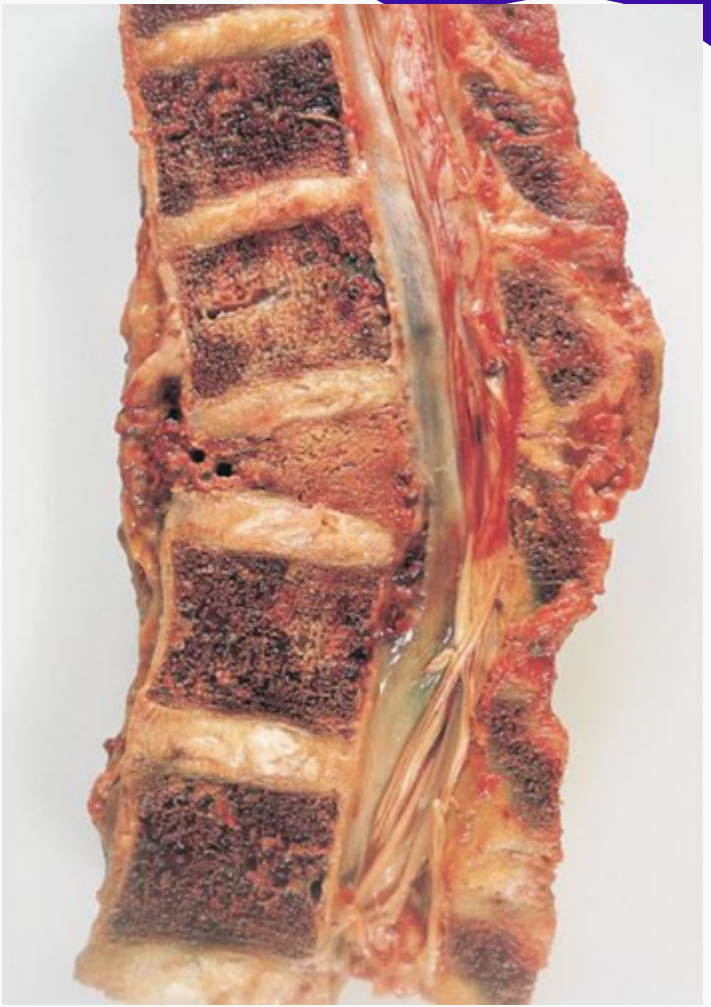
Extrapulmonary tuberculosis

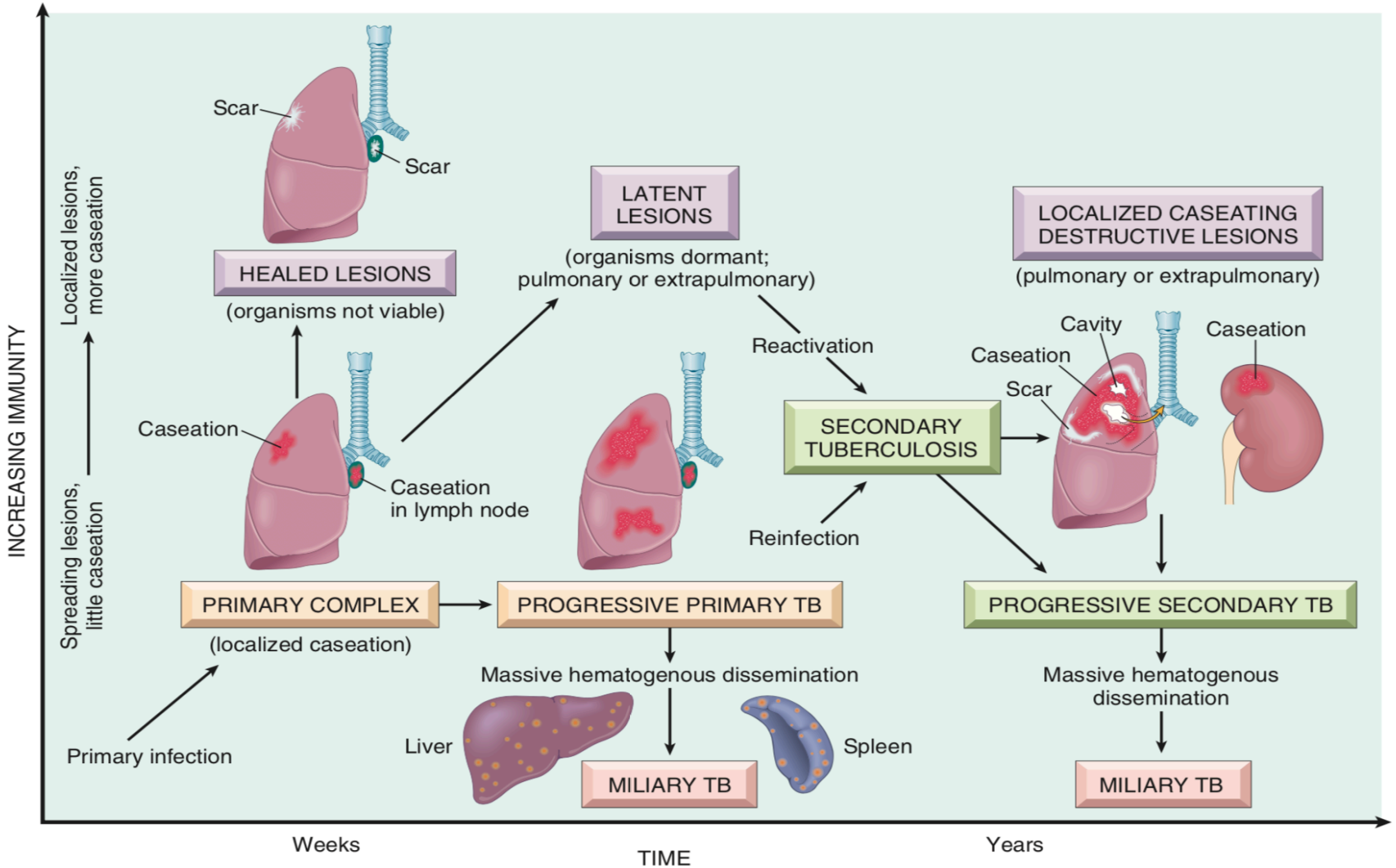
- Lymph nodes (tuberculous llymphadenitis): are the most frequent form of extrapulmonary tuberculosis esp. in the cervical region
- Pleura with pleural effusion (exudate)
- Liver and spleen
- adrenals
- fallopian tube and endometrium
- Epididymis and prostate
- kidneys
- meninges around the base of the brain (tuberculous meningitis),
- Bone marrow
- Vertebrae (Pott's disease)
- Intestinal tuberculosis



Pott’s disease

- Vertebrae (Pott's disease). It collapses the spine and leads to pparaspinal "cold" abscesses
- In these patients, infected material may track along the tissue planes to present as an abdominal or pelvic mass




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
Caseation
Scar
Caseation
Caseation in lymph node
SECONDARY TUBERCULOSIS
Reinfection
PRIMARY COMPLEX
(localized caseation)
PROGRESSIVE PRIMARY TB
PROGRESSIVE SECONDARY TB
Massive hematogenous dissemination
Massive hematogenous dissemination
Primary infection
Liver
Spleen
MILIARY TB
MILIARY TB
Weeks
TIME
Years

SYMPTOMS OF THE DISEASE

Cough

Hemoptysis

Fever

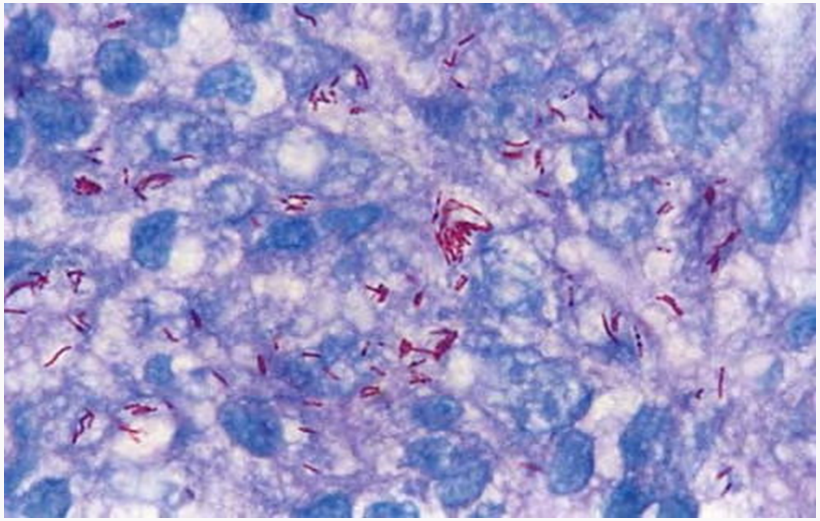
Low grade, night sweating

General

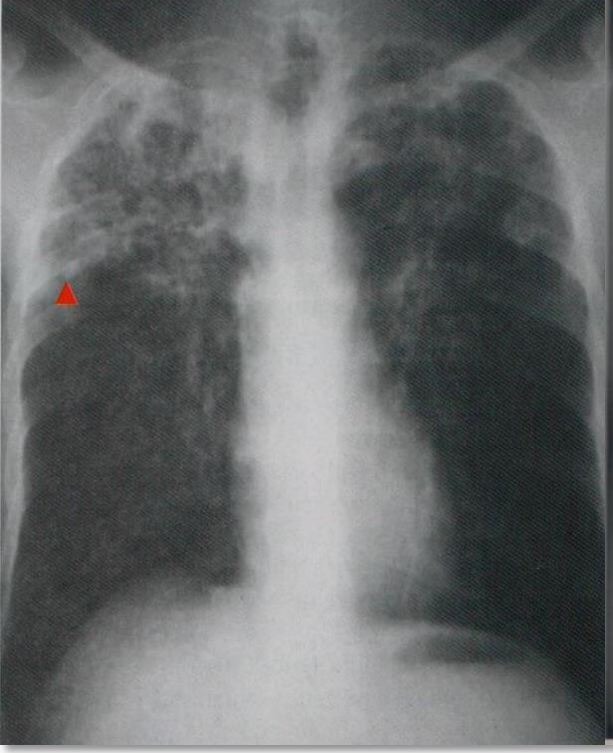
Malaise, wt. loss, anorexia

Diagnosis of TB

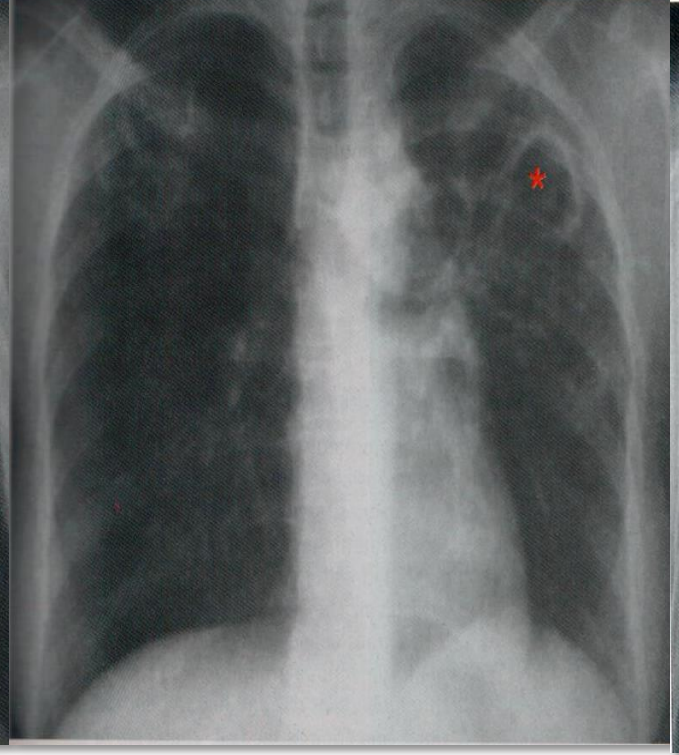
- Based on the history ,physical and radiographic findings of consolidation or cavitation in the apices of *the lungs*.
- Ultimately, *tubercle bacilli must be identified by:*
  1. Radiology
  2. Mantoux skin test
  3. Zeil-Neilson stain→ the organism stains red/pink.
  4. Culture
  5. **PCR** amplification of *M. tuberculosis* DNA allows for rapid diagnosis.
- Culture remains the **gold standard**



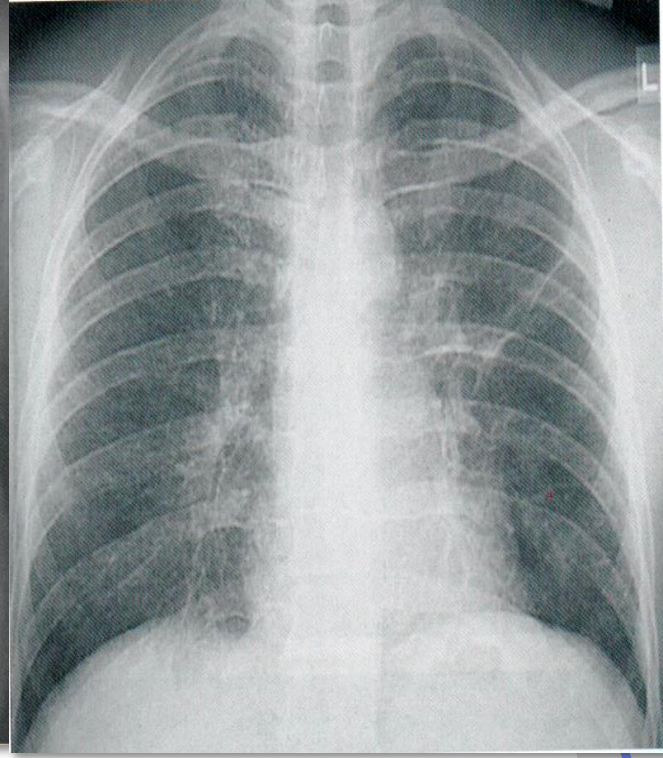
Ziehl-Neelsen stain shows red acid-fast staining M. tuberculi



Both upper lobes are affected

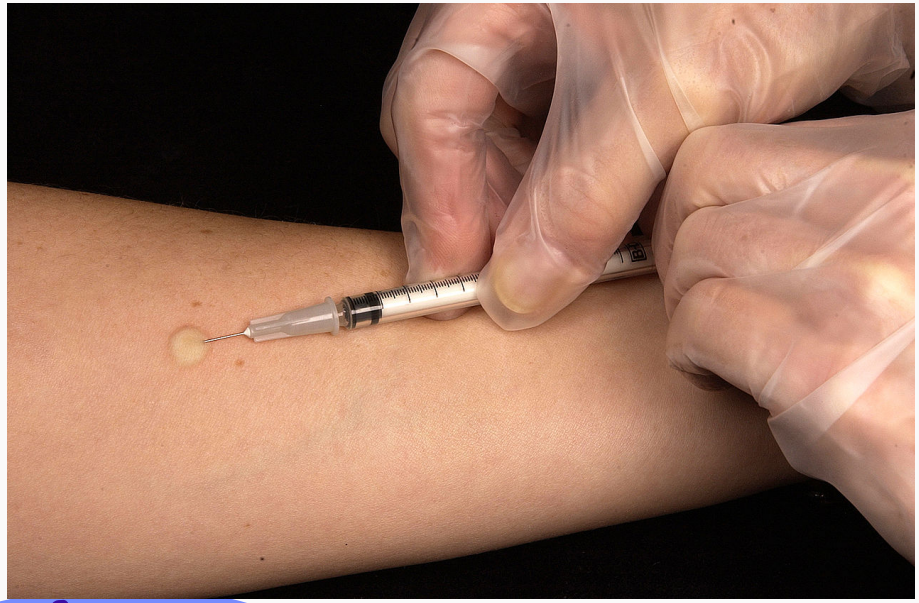


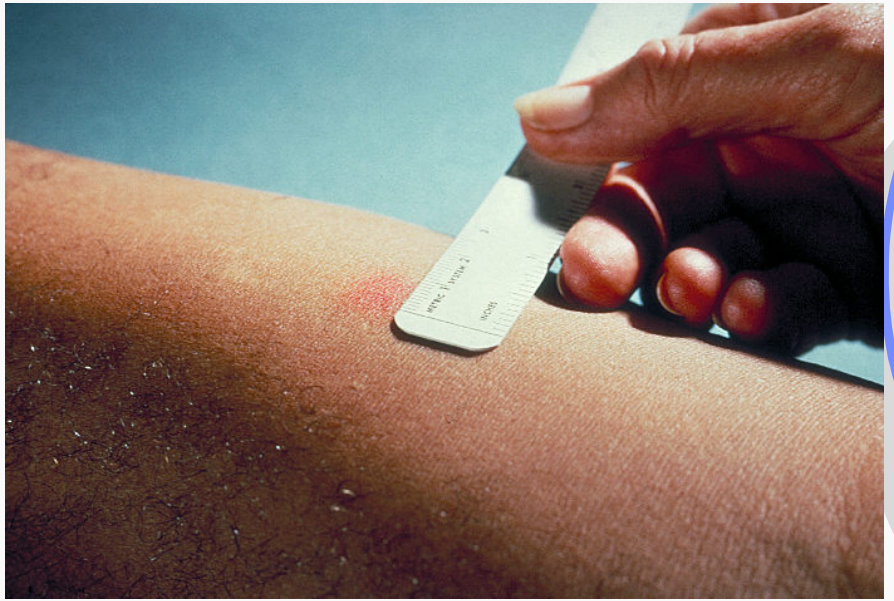
Cavity formation



Miliary tuberculosis

Mantoux skin test

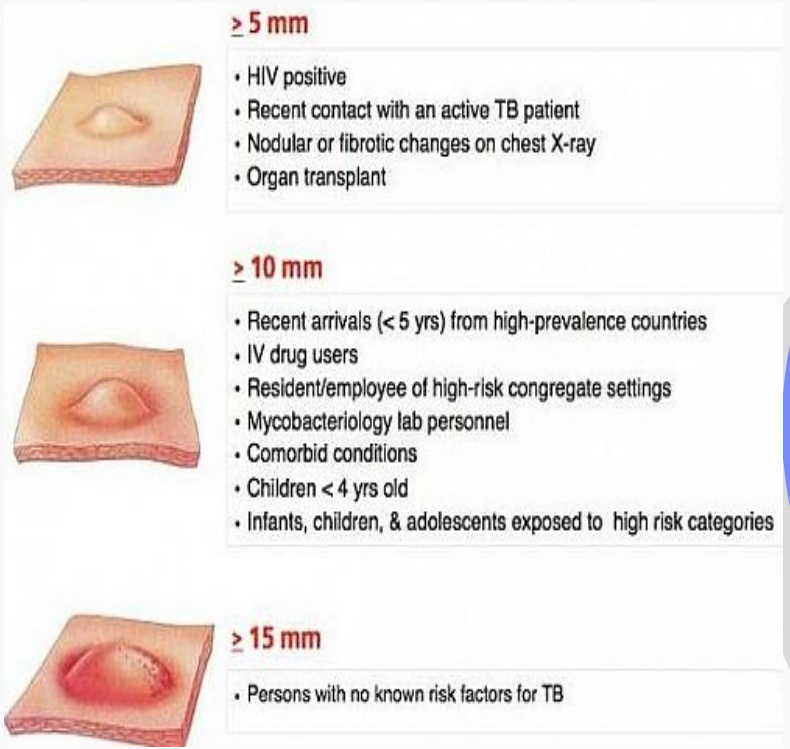




Mantoux skin test

- A positive tuberculin skin test result signifies cell-mediated hypersensitivity to tubercular antigens but does not differentiate between infection and disease.
- The size of induration is measured 48–72 hours later
- Positive results: induces a visible and palpable induration (at least 5 mm in diameter)

- False-negative reactions may be produced by certain viral infections, sarcoidosis, malnutrition, Hodgkin lymphoma, immunosuppression and AIDS.
- False-positive reactions may result from infection by atypical mycobacteria



Prognosis

- The prognosis with proper treatment is generally good if infections are localized to the lungs, except when they are caused by drug-resistant strains or occur in aged debilitated, or immunosuppressed persons, who are at high risk for developing miliary TB
- The outcome depends on the adequacy of the host immune response and treatment

Summery

- Tuberculosis is a chronic granulomatous disease caused by *M. tuberculosis,* usually affecting the lungs, but virtually any extra- pulmonary organ can be involved.
- • Initial exposure to mycobacteria results in development of a cellular immune response that confers resistance and leads to hypersensitivity (as determined by a positive result on the tuberculin skin test).
- The TH1 subset of CD4+ T cells has a crucial role in cell- mediated immunity against mycobacteria; mediators of inflammation and bacterial containment include IFN-γ, TNF, and nitric oxide.
- The histopathologic hallmark of host reaction to tuberculosis in immunocompetent individuals is the presence of granulomas, usually with caseous necrosis.
- Primary pulmonary tuberculosis in immunocompetent individuals is asymptomatic and results only in healed lesions, typically in a sub-pleural focus and a draining lymph node.
- Secondary (reactivation) tuberculosis arises in previously exposed individuals when host immune defenses are compromised, and usually manifests as cavitary lesions in the lung apices.
- Both progressive primary tuberculosis and secondary tuberculosis can result in systemic seeding, causing life-threatening forms of disease such as miliary tuberculosis and tuberculous meningitis.
- HIV-seropositive status is an important risk factor for development or recrudescence of active tuberculosis.

Protect your self