TUBERCULOSIS

Ghadeer Hayel, M.D.
Assistant Professor of Pathology
Consultant Pathologist/Hematopathologist
10/21/2025

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
- The World Health Organization (WHO) considers tuberculosis (TB) to be the most common cause of death resulting from an endemic infectious agent.
- Tuberculosis flourishes under conditions of poverty, crowding, and chronic debilitating illness

TRANSMISSION AND RISK FACTORS

- Certain diseases also increase the risk: diabetes, Hodgkin lymphoma, chronic lung disease (particularly silicosis), chronic renal failure, malnutrition, alcohol use disorder, and immunosuppression.
- In areas of the world where HIV infection is prevalent, HIV infection is a dominant risk factor for the development of TB.
- Mycobacteria are slender rods that are acid fast (i.e., they have a high content of complex lipids that bind tightly to the Ziehl-Neelsen [carbol fuchsin] stain).
- M. tuberculosis hominis is responsible for most cases of TB, which is spread by individuals with **active disease**.
- Transmission is primarily through inhalation of airborne organisms in aerosols generated by expectoration or by exposure to contaminated secretions.

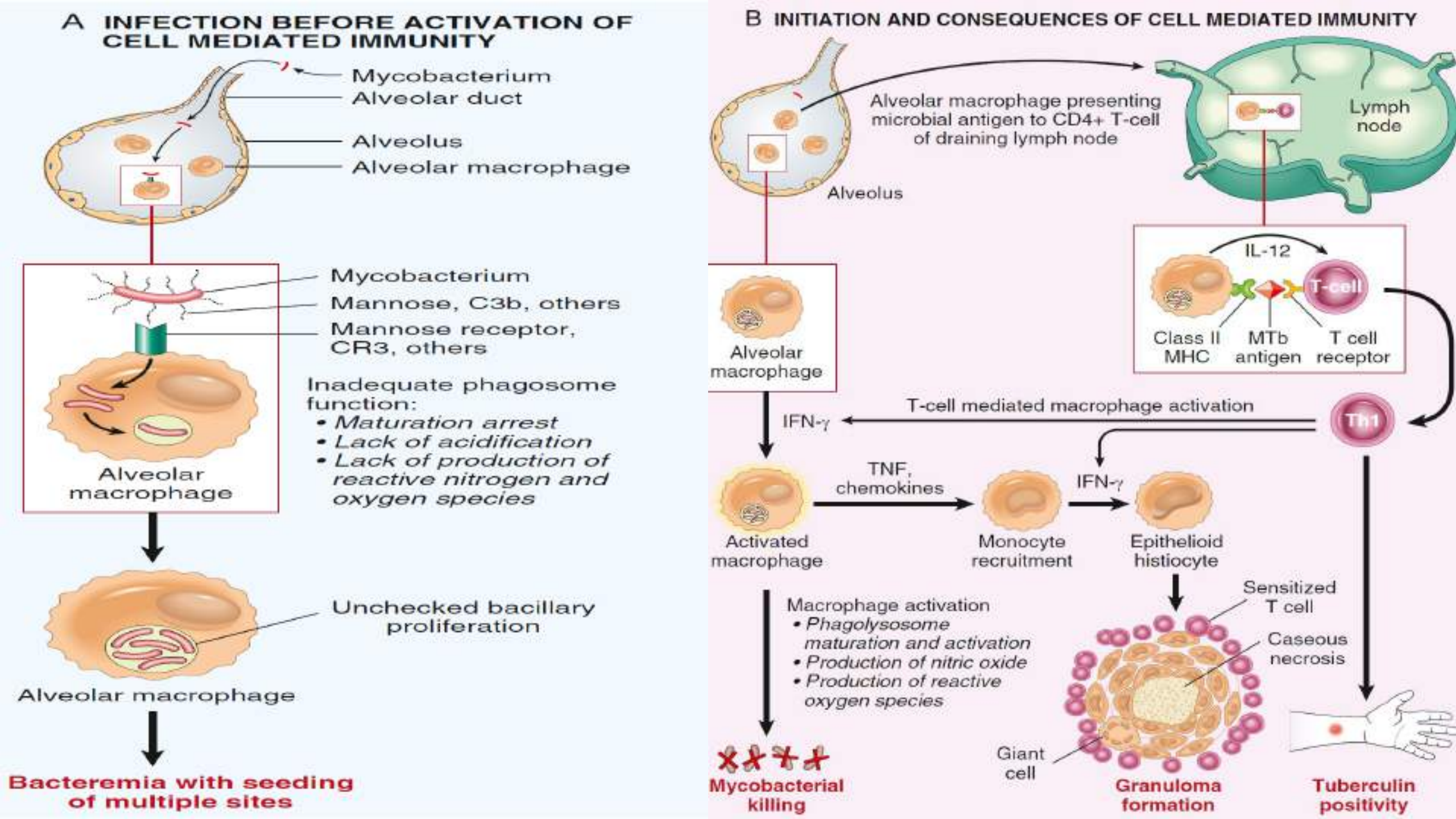
INFECTION VS DISEASE

- Infection implies seeding of a focus with organisms, acquired by direct person-to-person transmission of organisms in airborne droplets from individual with **active Disease to a susceptible host.**
- In most newly infected individuals, an asymptomatic focus of pulmonary infection appears that is self-limited and, upon resolution, leaves (if anything) a tiny, fibrocalcific nodule.
- Bacteria spread from the primary focus to various other sites in the body but the infection remains latent. Viable organisms may remain dormant in such foci for decades & possibly for the life of the host. Such individuals are infected but do not have active disease (No transmission)
- if immune defenses are lowered, the infection may reactivate to produce communicable and potentially life threatening disease

IGRAS VS PPD

Infection with M. tuberculosis typically leads to the development of delayed hypersensitivity, can be detected by either IFN-gamma release assays (IGRAs) or the tuberculin (purified protein derivative [PPD], or Mantoux) skin test

Feature	PPD (Tuberculin Skin Test)	IGRA (Interferon-Gamma Release Assay)
Principle	In vivo skin reaction to tuberculin (PPD)	In vitro IFN-γ release by patient's T cells exposed to TB-specific antigens
Antigens	Shared mycobacterial proteins (cross-react with BCG & NTM)	Specific antigens - not affected by BCG
Procedure	Intradermal injection → read induration at 48–72 hrs	Blood test → lab measures IFN-γ level
Advantages	Simple, cheap, widely available	High specificity, single visit, objective, not affected by BCG
Limitations	False positives (BCG, NTM), false negatives (immunosuppressed), needs 2 visits	Costly, needs lab, indeterminate results in low immunity
Best Use	Unvaccinated, low-resource settings	BCG-vaccinated adults, healthcare workers, developed settings

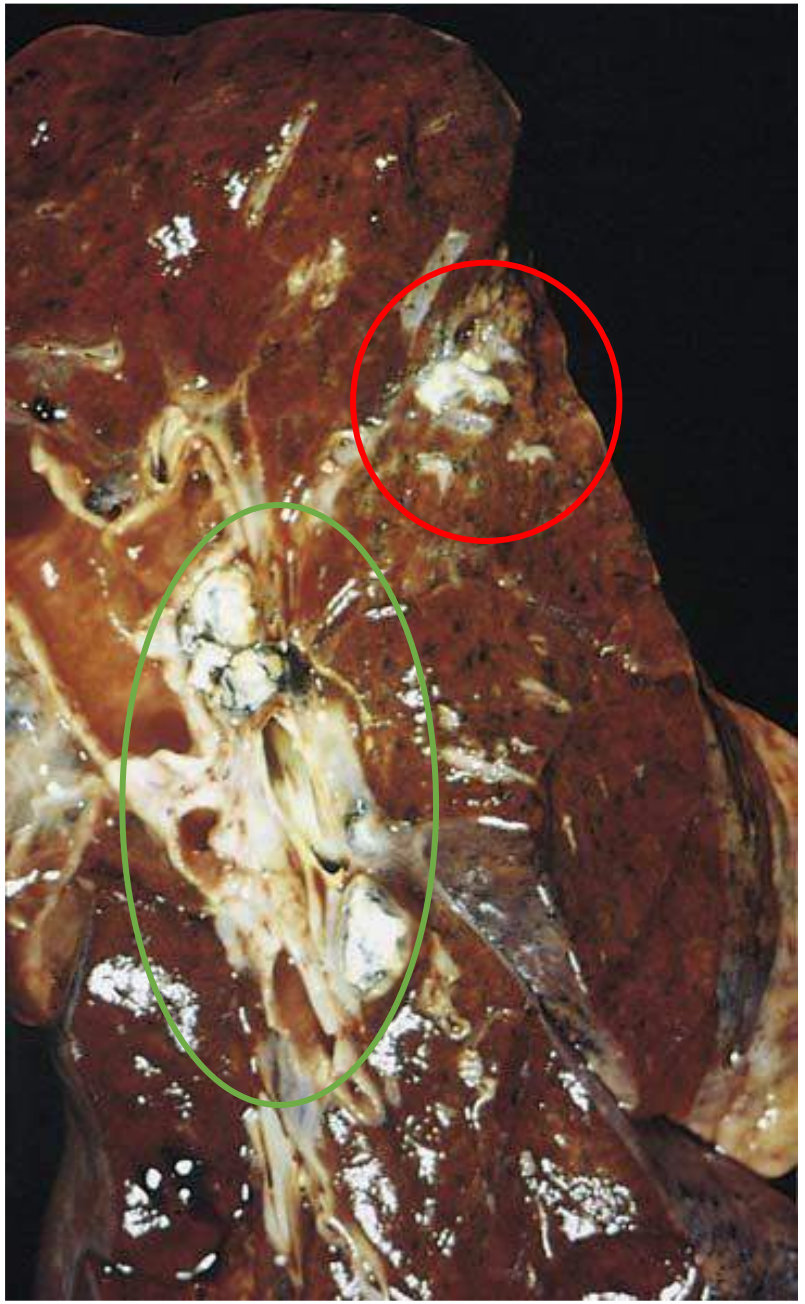

A INFECTION BEFORE ACTIVATION OF CELL MEDIATED IMMUNITY
Mycobacterium
Alveolar duct
Alveolus
Alveolar macrophage
Mycobacterium
Mannose, C3b, others
Mannose receptor, CR3, others
Inadequate phagosome function:
• Maturation arrest
• Lack of acidification
• Lack of production of reactive nitrogen and oxygen species
Alveolar macrophage
Unchecked bacillary proliferation
Alveolar macrophage
Bacteremia with seeding of multiple sites
B INITIATION AND CONSEQUENCES OF CELL MEDIATED IMMUNITY
Alveolar macrophage presenting microbial antigen to CD4+ T-cell of draining lymph node
Lymph node
Alveolus
IL-12
T-cell
Class II MHC
MTb antigen
T cell receptor
Alveolar macrophage
T-cell mediated macrophage activation
IFN-γ
Th1
TNF, chemokines
IFN-γ
Activated macrophage
Monocyte recruitment
Epithelioid histiocyte
Macrophage activation
• Phagolysosome maturation and activation
• Production of nitric oxide
• Production of reactive oxygen species
Sensitized T cell
Caseous necrosis
Giant cell
Mycobacterial killing
Granuloma formation
Tuberculin positivity

PRIMARY TB

- Primary TB is the form of disease that develops in a previously unexposed (unsensitized) patient.
- In the large majority of otherwise healthy individuals, the only short-term consequence of primary TB is a focus of pulmonary scarring
- 5% of those newly infected develop significant disease.
- Infection leads to progressive primary tuberculosis in patients who are overtly immunocompromised or or who have subtle defects in host defenses (severe acute malnutrition.
- The incidence of progressive primary TB is particularly high in patients who are HIV positive with significant immunosuppression (i.e., CD4+ T cell counts below 200 cells/mL).

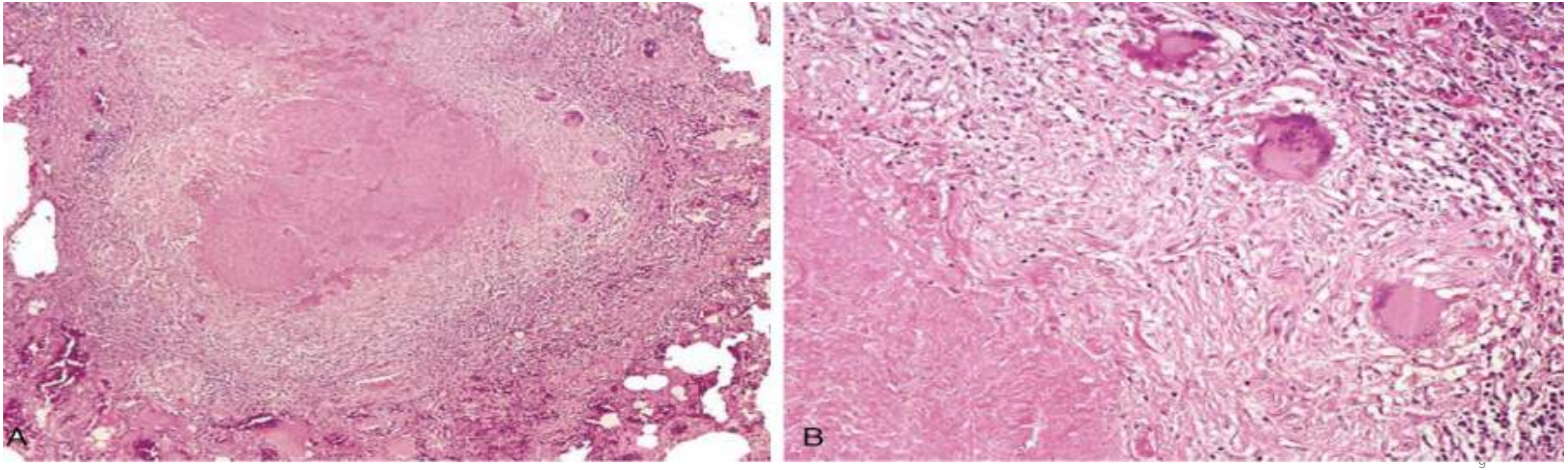
PRIMARY TB -MORPHOLOGY

- A 1-cm to 1.5-cm area of gray-white inflammatory consolidation emerges, called the Ghon focus, with caseous necrosis in the center.
- Tubercle bacilli, either free or within phagocytes, travel via the lymphatic vessels to the regional lymph nodes.
- This combination of parenchymal and nodal lesions is called the Ghon complex.
- Lymphatic and hematogenous dissemination to other parts of the body also occurs during the first few weeks.



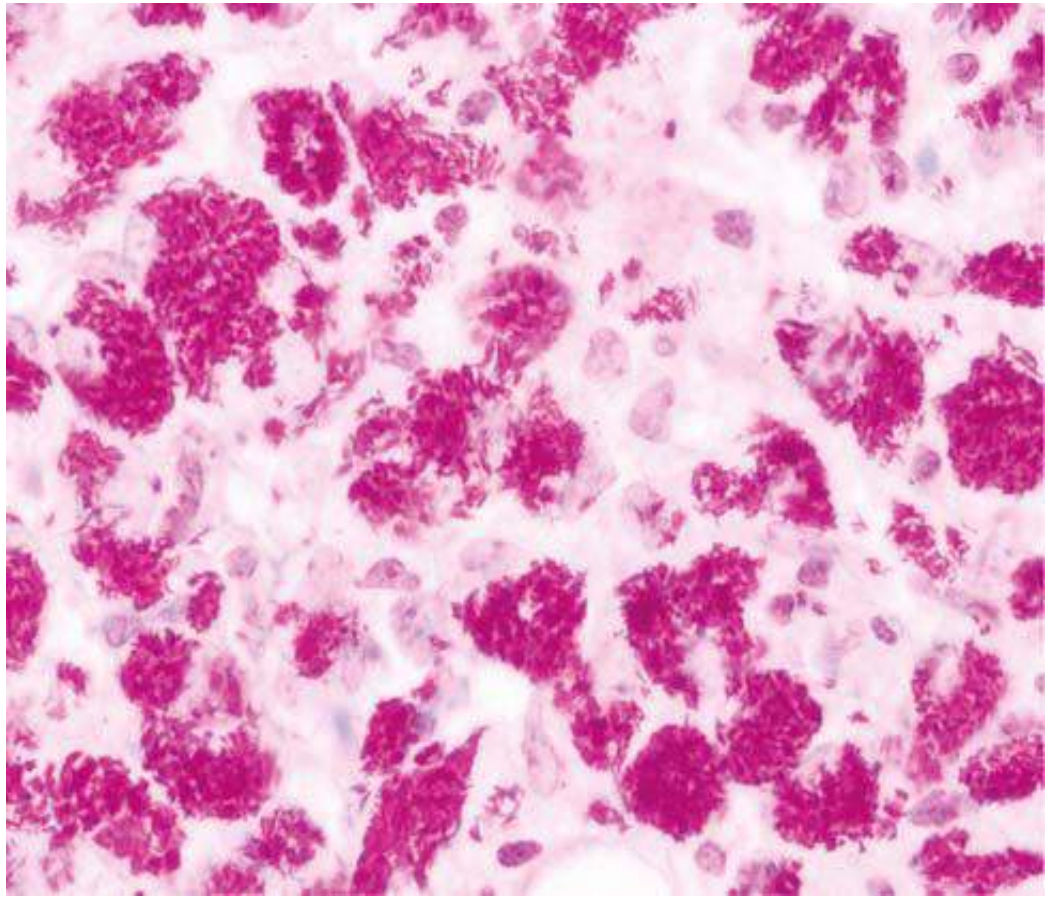
PRIMARY TB -MORPHOLOGY

- Histologically, sites of overt infection are involved by inflammatory reaction marked by the presence of caseating and noncaseating granulomas: epithelioid macrophages & multinucleate giant cells.



PRIMARY TB -MORPHOLOGY

- In those who do not mount an effective immune response due to immunocompromise, progressive primary tuberculosis may develop. Lesions in such individuals often lack granulomas and instead consist of sheets of macrophages containing numerous bacilli



SECONDARY TUBERCULOSIS (REACTIVATION TUBERCULOSIS)

The pattern of disease that arises in a previously sensitized host.

- It may appear shortly after primary tuberculosis, but more commonly arises from reactivation of dormant primary lesions many decades after initial infection.
- Only a few patients (<5%) with primary disease subsequently develop secondary tuberculosis.
- CAUSES: Host resistance is weakened, Reinfection(either because the protection afforded by the primary disease has waned or because of exposure to a large inoculum of virulent bacilli)

SECONDARY TUBERCULOSIS (REACTIVATION TUBERCULOSIS)

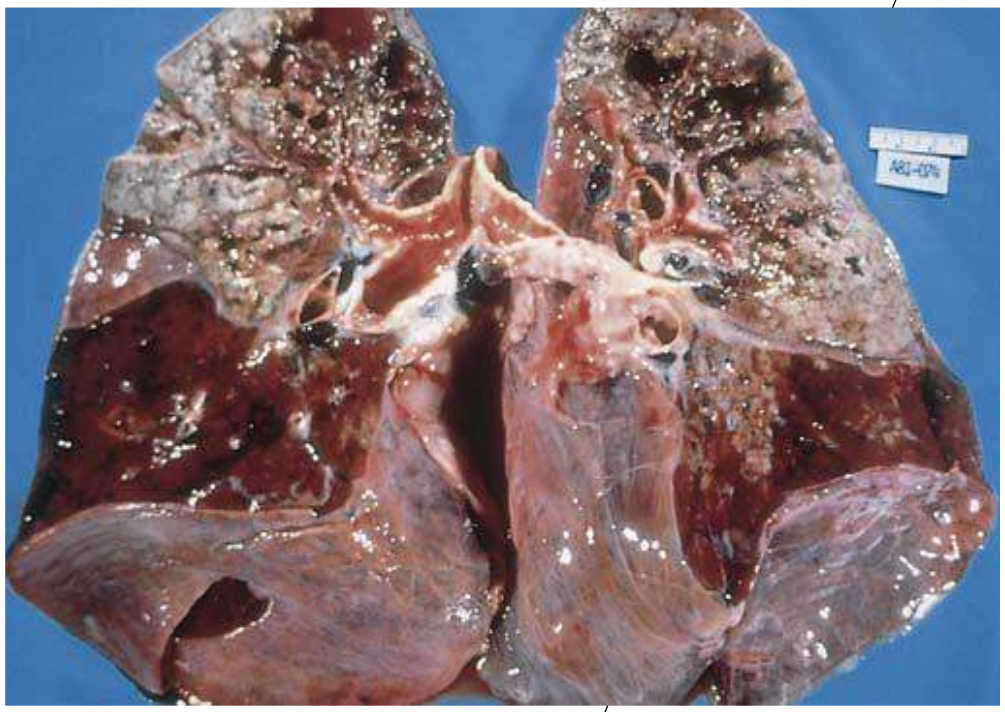
- Secondary pulmonary tuberculosis is classically localized to the apex of one or both upper lobes, may relate to high oxygen tension in the apices.
- The regional lymph nodes are less prominently involved early in the disease .
- Cavitation is common in the secondary form, leading to erosion into and dissemination along airways → Changes are an important source of infectivity, as affected patients produce sputum containing the bacilli

SECONDARY PULMONARY TUBERCULOSIS CONSEQUENCES

Localized, apical, secondary pulmonary TB may heal with fibrosis either spontaneously or after therapy.

Or the disease may progress and extend along several different pathways:

1. Progressive pulmonary TB: the apical lesion and the caseation expands. Erosion into a bronchus evacuates the caseous center, creating a ragged, irregular cavity lined by caseous material that is poorly walled off by fibrous tissue.



SECONDARY PULMONARY TUBERCULOSIS CONSEQUENCES

2. Miliary pulmonary disease: occurs when organisms reach the bloodstream through lymphatic vessels and then recirculate to the lung via the pulmonary arteries.

The lesions appear as small (2-mm) foci of yellow-white consolidation scattered through the lung parenchyma (the word miliary is derived from the resemblance of these foci to millet seeds).

SECONDARY PULMONARY TUBERCULOSIS CONSEQUENCES

3. **Pleural involvement:** Pleural effusions, tuberculous empyema, or obliterative fibrous pleuritis may develop.

4. **Systemic miliary tuberculosis:** When the organisms disseminate hematogenously throughout the body.

Systemic miliary tuberculosis is most prominent in the liver, bone marrow, spleen, adrenal glands, meninges, kidneys, fallopian tubes, and epididymis

CLINICAL FEATURES

- Localized secondary tuberculosis may be :

1. Asymptomatic.
2. Cytokines-related (TNF, IL-1) symptoms: malaise, anorexia, weight loss, and fever. Mucoid and later purulent-bacilli containing sputum.
3. Hemoptysis.
4. Pleuritic pain.

THANK YOU