Respiratory System
RS

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6. Chronic Pneumonia

- Chronic pneumonia most often is a **localized** lesion in an **immunocompetent** individual.

- In **immunocompromised** patients, the usual presentation is **widespread** disease due to systemic dissemination of the organism.

- There is typically **granulomatous inflammation.**

1. Bacteria, TB

2. Fungi

1. Tuberculosis (TB):

•Caused by Mycobacterium Tuberculosis (acid-fast +).

Epidemiology:

- Common among **medically & economically deprived persons** (e.g. crowding, elderly people, diabetes, and HIV).

Infection VS *disease*

-Infection: seeding of a focus with organisms may or may not cause clinically significant tissue damage (i.e., disease).

-Leads to the development of **delayed hypersensitivity,** can be detected by the **Tuberculin (Mantoux) test**

Pathogenesis:

- Centered on the development of **cell-mediated immunity**, which confers resistance to the organism and results in the development of tissue hypersensitivity to tubercular antigens.
- The pathologic features of tuberculosis (caseating granulomas and cavitation) are the result of the **destructive tissue hypersensitivity that is part of the host immune response**.
- The appearance of tissue hypersensitivity also signals the **acquisition of immunity to the organism**

The sequence of events from inhalation of the organism (in non-sensitized individuals) before activation of cell-mediated immunity:

- Mycobacteria enters the macrophage endosomes ⟹ inhibits normal microbicidal responses by preventing the fusion of the lysosomes with the phagocytic vacuole, allowing the mycobacterium to persist and proliferate within the pulmonary alveolar macrophages & airspaces with resulting bacteremia & seeding in multiple sites.

- Despite the bacteremia the patients are asymptomatic or have a mild flu-like illness.

❖ The cell-mediated immunity develops 3 weeks after exposure.

- Processed mycobacterial Ag is presented to CD4 T cells by dendritic cells and macrophages.

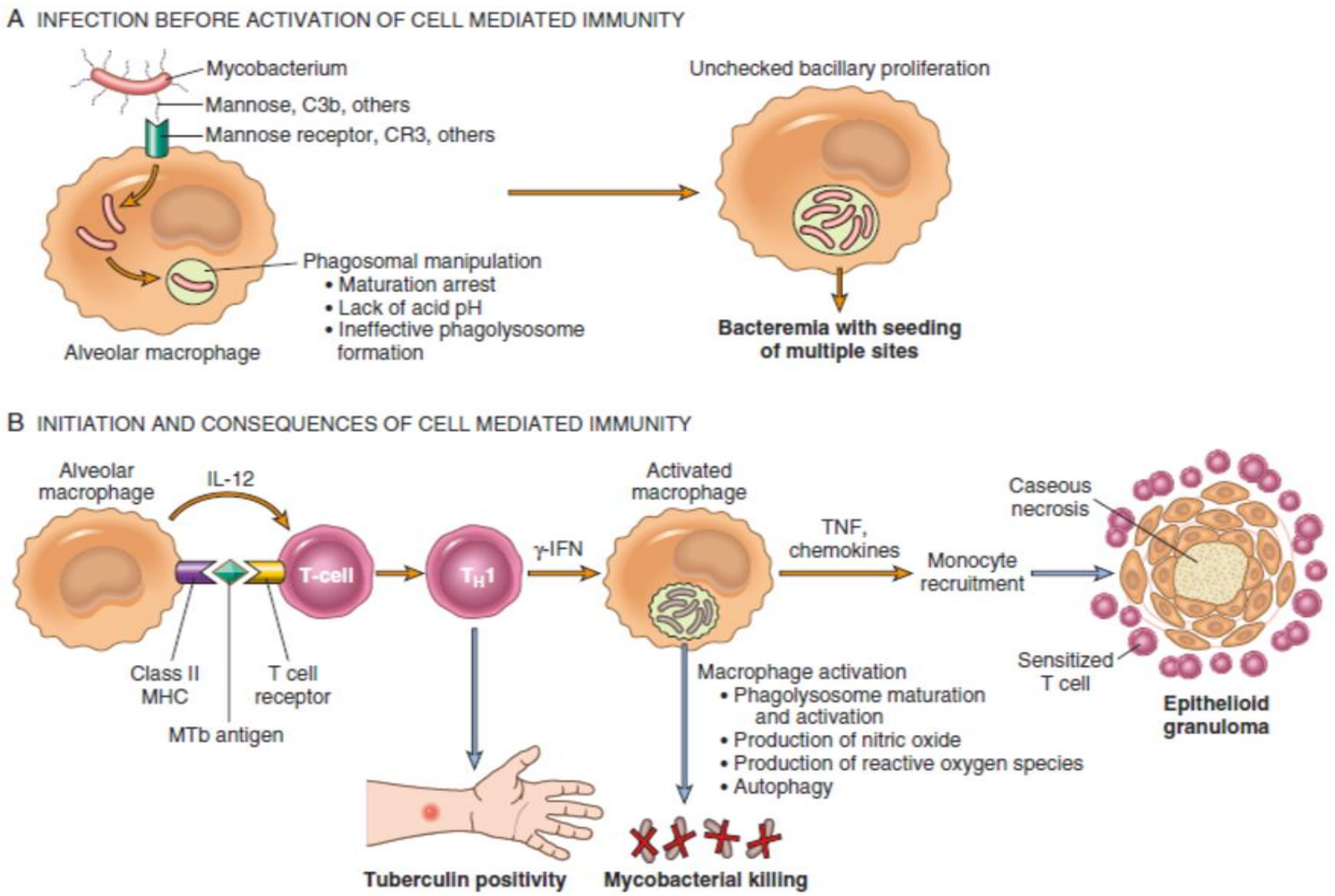
- Macrophages → **IL-12** → **CD4+ T cells** (**TH1** subset) → **secreting IFN Y which activates macrophages.**

- **Activated macrophages** release a variety of mediators like:

✓ **TNF leads to** the activation of monocytes and then differentiation into epithelioid histiocytes that characterize **the granulomatous reaction**

✓ **Nitric oxide (NO) is** a powerful **bactericidal agent** & ROS that has antibacterial activity**.**

✓ **Anti-microbial peptides (defensins)**.

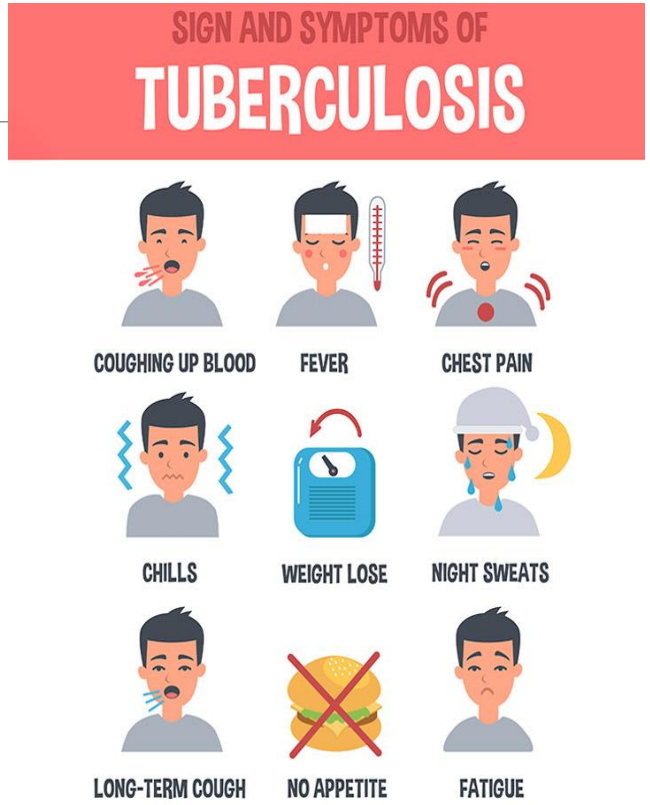


The sequence of events in the natural history of primary pulmonary tuberculosis:
(A) Events occurring in the first 3 weeks after exposure.
(B) Events there after

Clinically:

- May be asymptomatic.

- Malaise, anorexia, weight loss, fever (low grade), sputum, hemoptysis & night sweats.



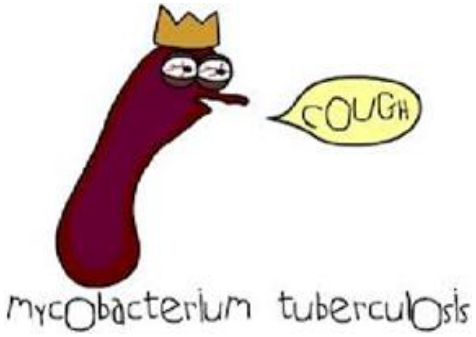
Diagnosis:

- Clinical picture

-X-ray picture

- Sputum

- Skin test: Tuberculin test



- The most common method is the demonstration of acid-fast bacilli in the **Ziehl Neelsen stain**.

Types:

Primary Tuberculosis:

- In a previously **un**exposed & **un**sensitized person.
- The source of the organism is **exogenous.**
- In most individuals, the only consequence is the foci of scarring. However, these foci may harbor viable bacilli and thus serve as a nidus for disease reactivation later if host defenses wane.

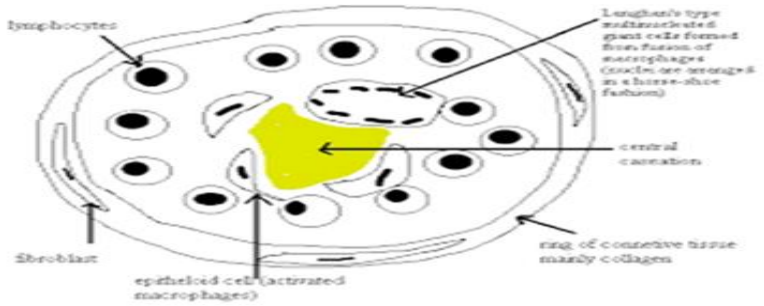
Morphology:

- Mostly in the **lower part of the upper lobe & upper part of the lower lobe, usually close to the pleura.**
- Area of inflammatory consolidation emerges **(the Ghon focus);** in most cases, the center of this focus undergoes caseous necrosis.
- TB bacilli drained to **the regional lymph nodes** which also caseate.
- This combination of the **parenchymal lesion and nodal involvement** is referred to as the **Ghon complex**

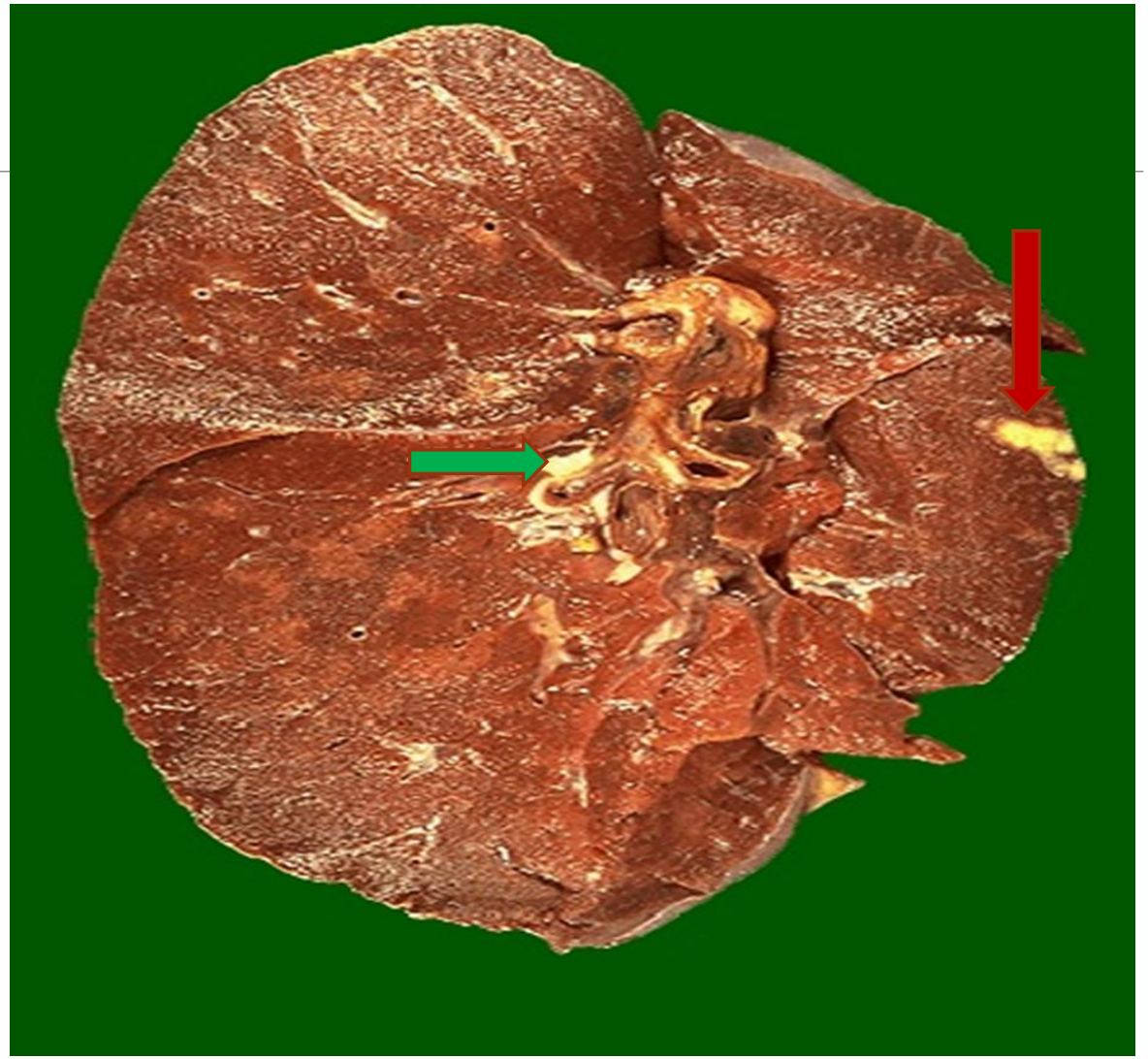
- In 95% of cases, the development of cell-mediated immunity controls the infection.
- The Ghon complex undergoes progressive fibrosis, often followed by radiologically detected calcification (Ranke complex) & despite dissemination to other organs, no lesion develops**.**
- Sometimes ,progressive primary disease develops

Histologically :

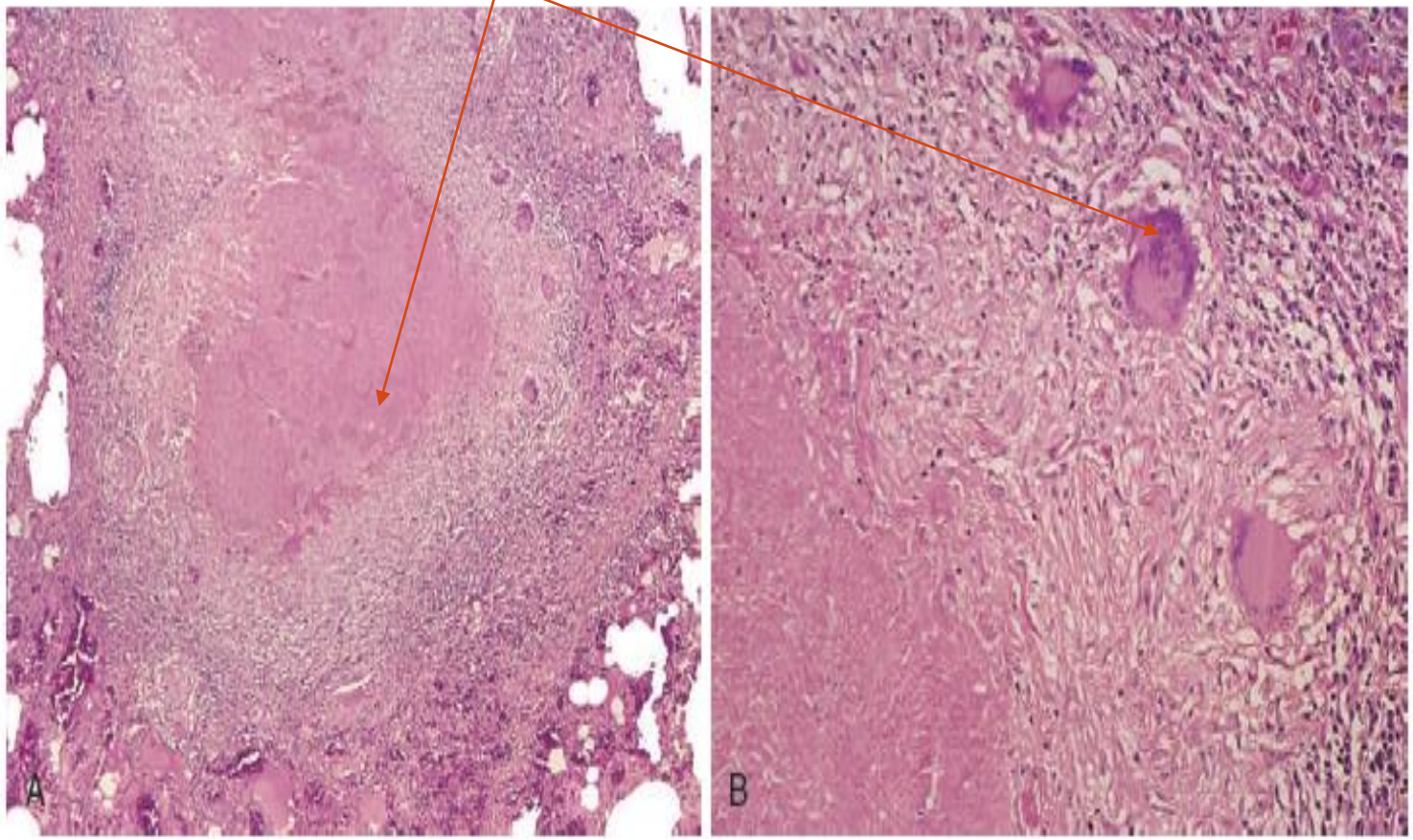
- Inflammatory reaction marked by the presence of **caseating (necrotizing) and noncaseating granulomas**, which consist of epithelioid histiocytes and multinucleate giant cells.



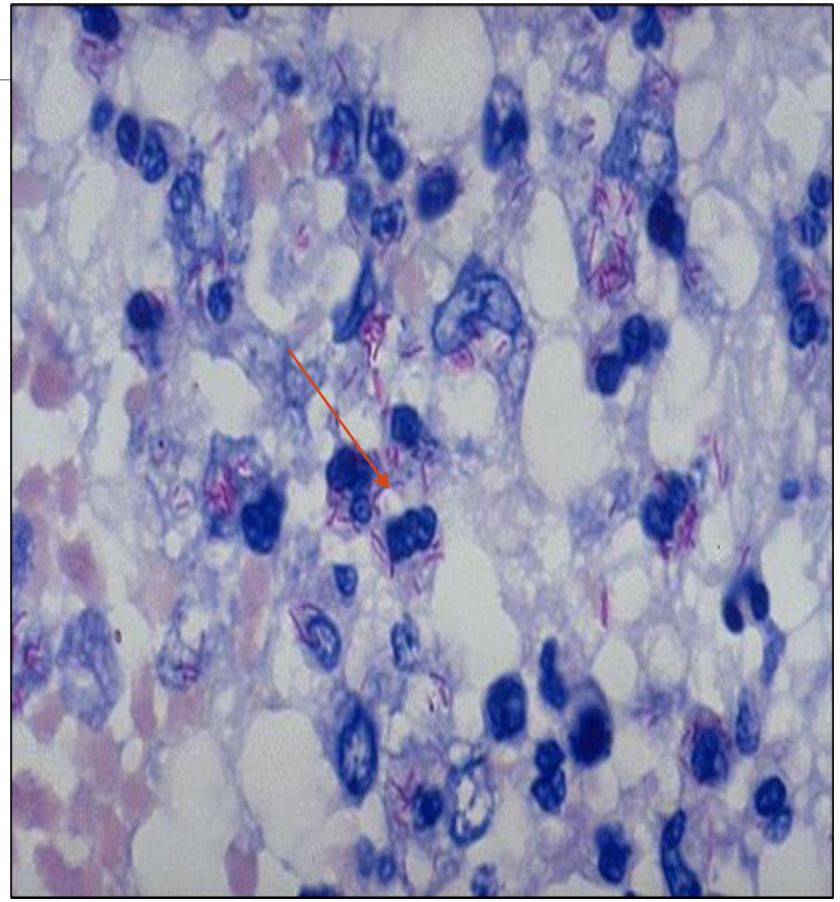
There is a small tan-yellow **subpleural granuloma** in the mid-lung field on the right. In the hilum is a small yellow tan **granuloma in a hilar lymph node** next to a bronchus. This is the **"Ghon complex".**



A characteristic tubercle at low magnification (A) and at higher power (B) shows central granular caseation surrounded by epithelioid and multinucleate giant cells.



In this picture, mycobacteria are seen (acid-fast stain).



Secondary TB (Reactivation TB):

- Arises in a **previously sensitized** host.

- It may appear shortly after primary TB or more commonly arises from the reactivation of dormant primary lesions many decades after initial infection.
- **Only a few patients (<5%) with the primary disease develop secondary tuberculosis**.
- Classically in **apex of one or both lobes**
- Because of the preexistence of hypersensitivity, the bacilli excite **marked tissue responses**.
- The **regional lymph nodes are LESS prominently** involved early in the disease than in primary TB.
- **Cavitation** occurs readily.

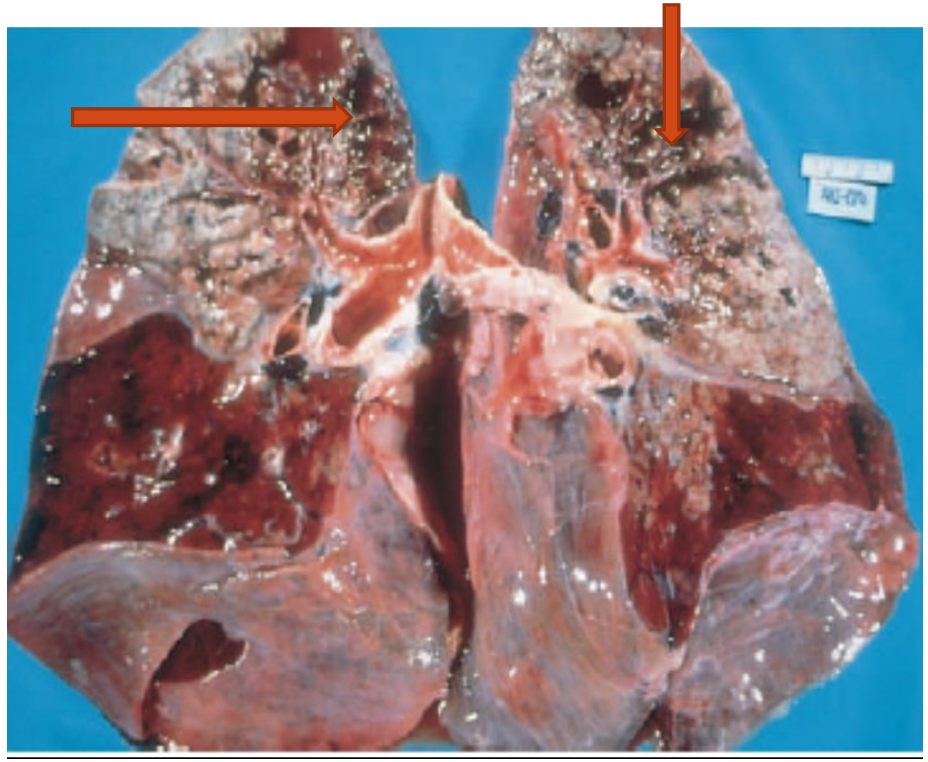
Morphology:

- A focus of consolidation in the apical pleura with a variable amount of caseous necrosis.
- In favorable cases, the focus becomes fibrotic.

Histologically:

- The active lesion shows granuloma.
- TB bacilli can be demonstrated in early lesions

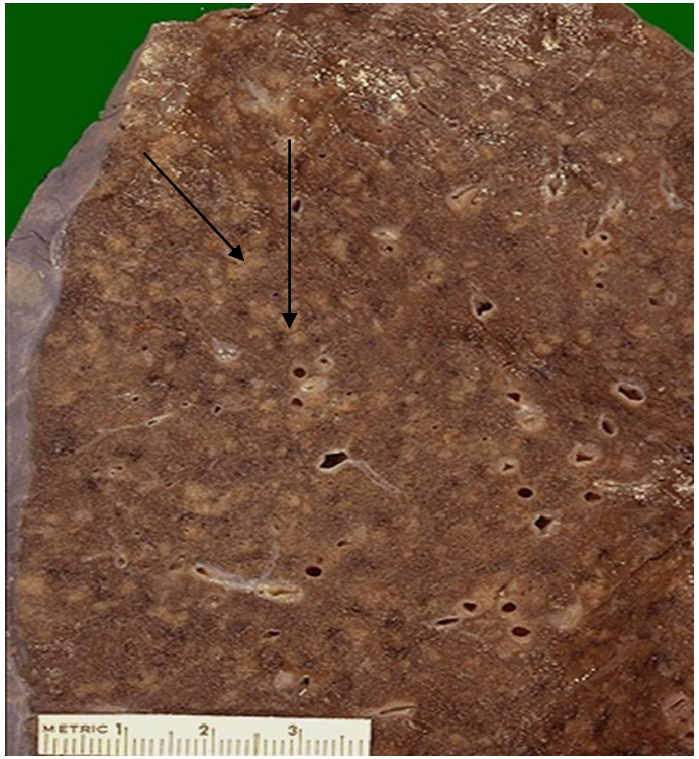
The upper parts of both lungs are riddled with gray-white caseation areas with multiple cavitations.



⟹ The apical lesion may heal with fibrosis or may extend along different pathways :

1- Progressive pulmonary TB :

- The apical lesion enlarges with the expansion of the area of caseation.
- Erosion into the bronchus evacuates the caseous center, creating an irregular cavity.



- ### 2- Miliary pulmonary TB :

- Small foci of yellow-white consolidation scattered through the lung parenchyma

3- TB Pleurisy :

- May involve the pleura.

4- Endobronchial, endotracheal & laryngeal TB

5- Systemic miliary TB;

- When infection seeds, and the organism is disseminated through the systemic arterial system.

6- Isolated Organ TB:

Vertebral TB → POTT's Disease

Tuberculous lymphadenitis (Scrofula)

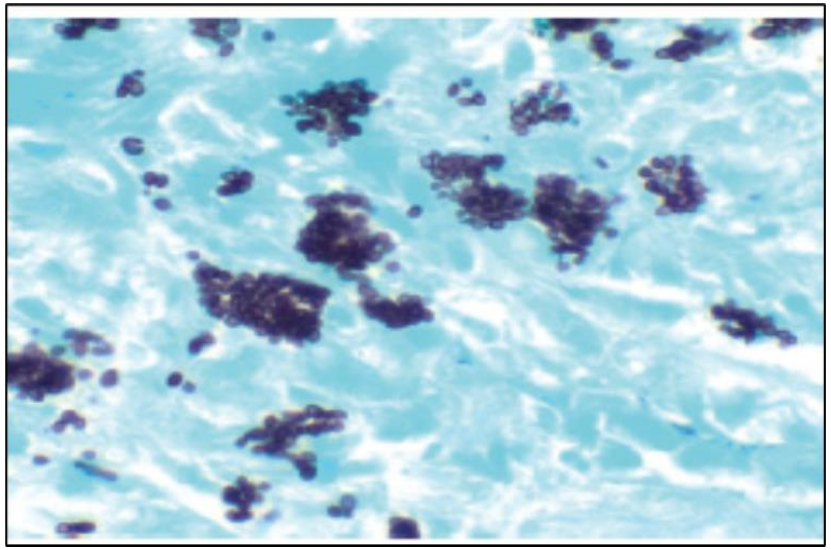
2. Histoplasmosis, Coccidioidomycosis, and Blastomycosis

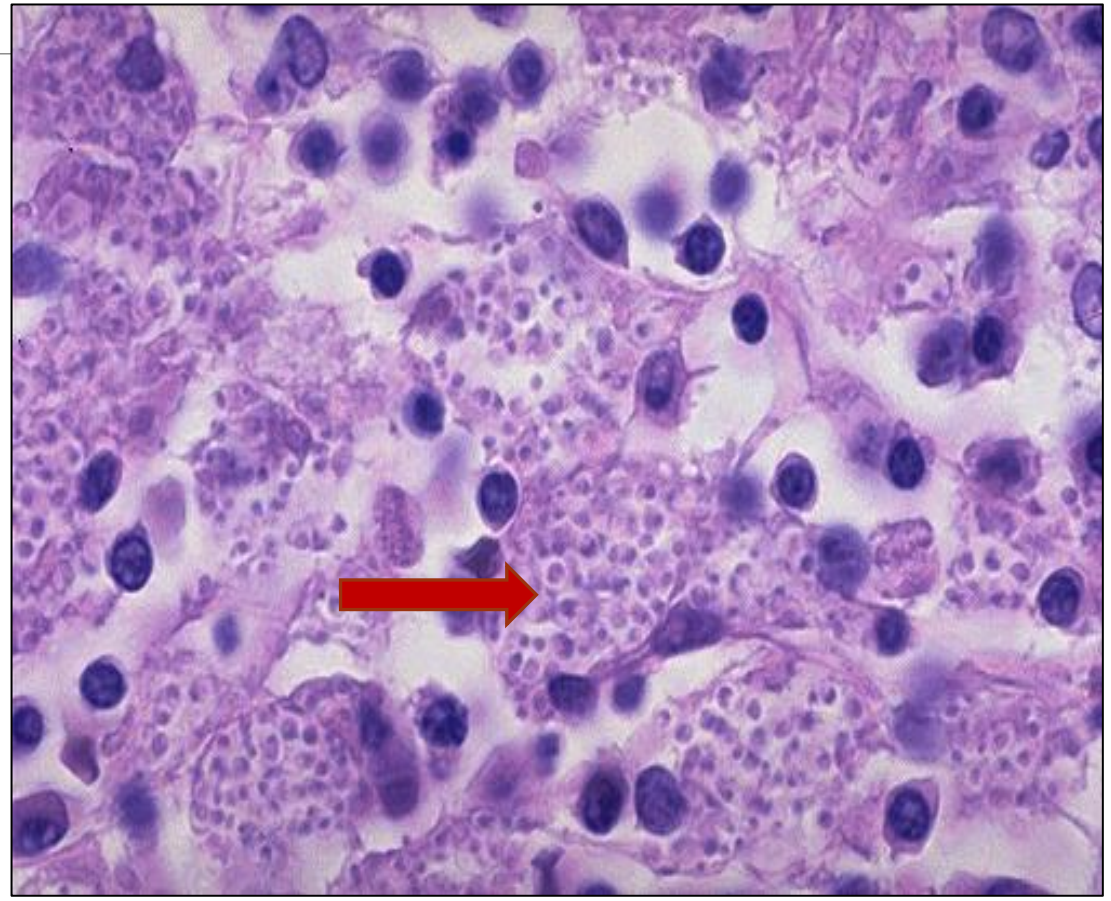
The primary nodules are composed of aggregates of macrophages filled with organisms. These lesions evolve into small granulomas with giant cells and may develop central necrosis and later fibrosis and calcification.

- In immunocompromised adults, disseminated disease develops, and there are no well-formed granulomas. Instead, focal collections of phagocytes containing yeast forms are present.

Histoplasma Capsulatum

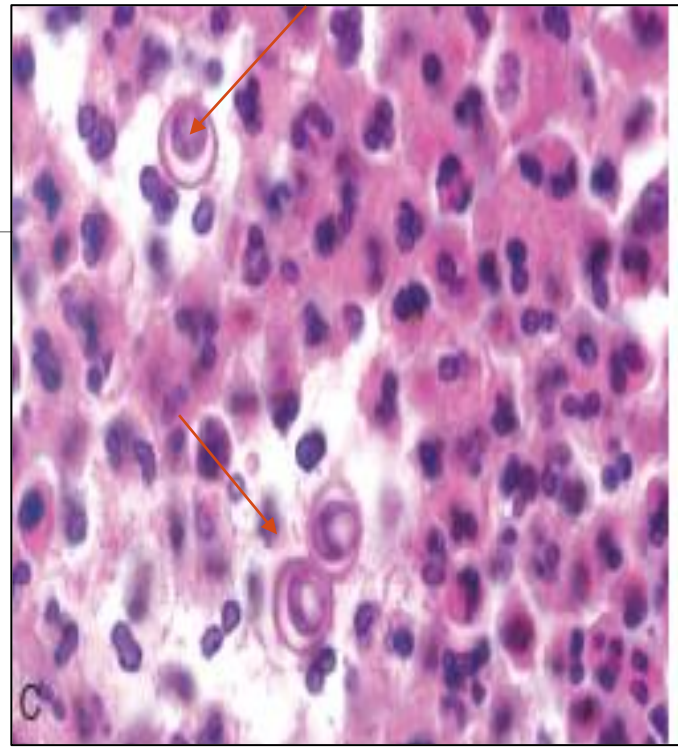
Each macrophage is filled with numerous **small round yeast organisms** having a clear zone around a central blue nucleus which gives the cell membrane the appearance of a capsule.

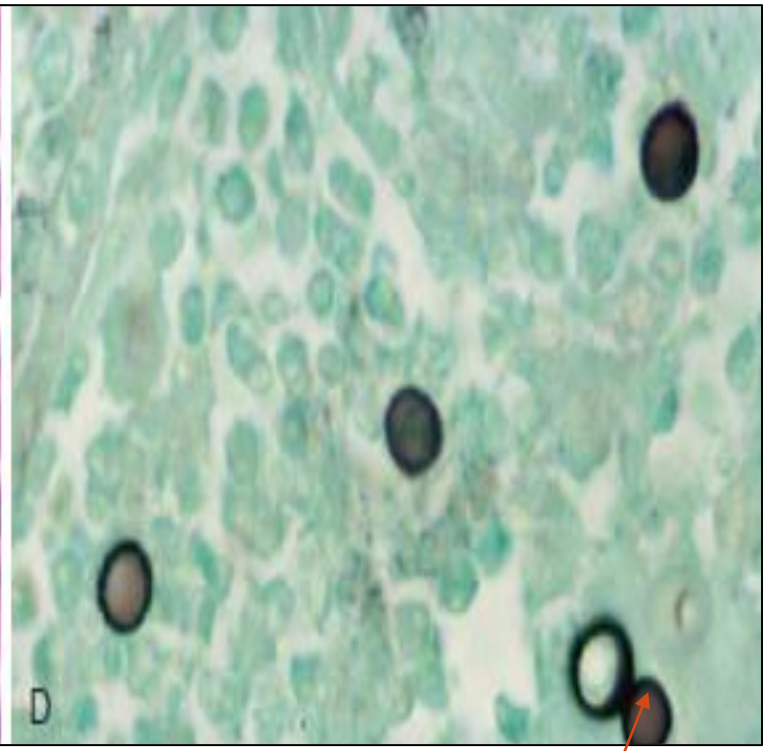




Blastomycosis

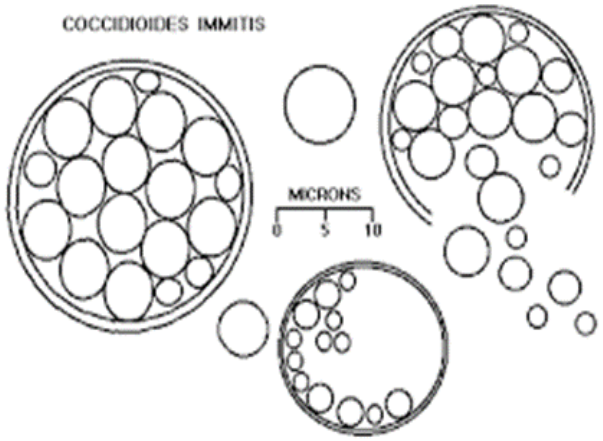
(C)Blastomycosis, with rounded budding yeasts with characteristic thick wall, and (D) Silver stain highlights the broad-based budding.

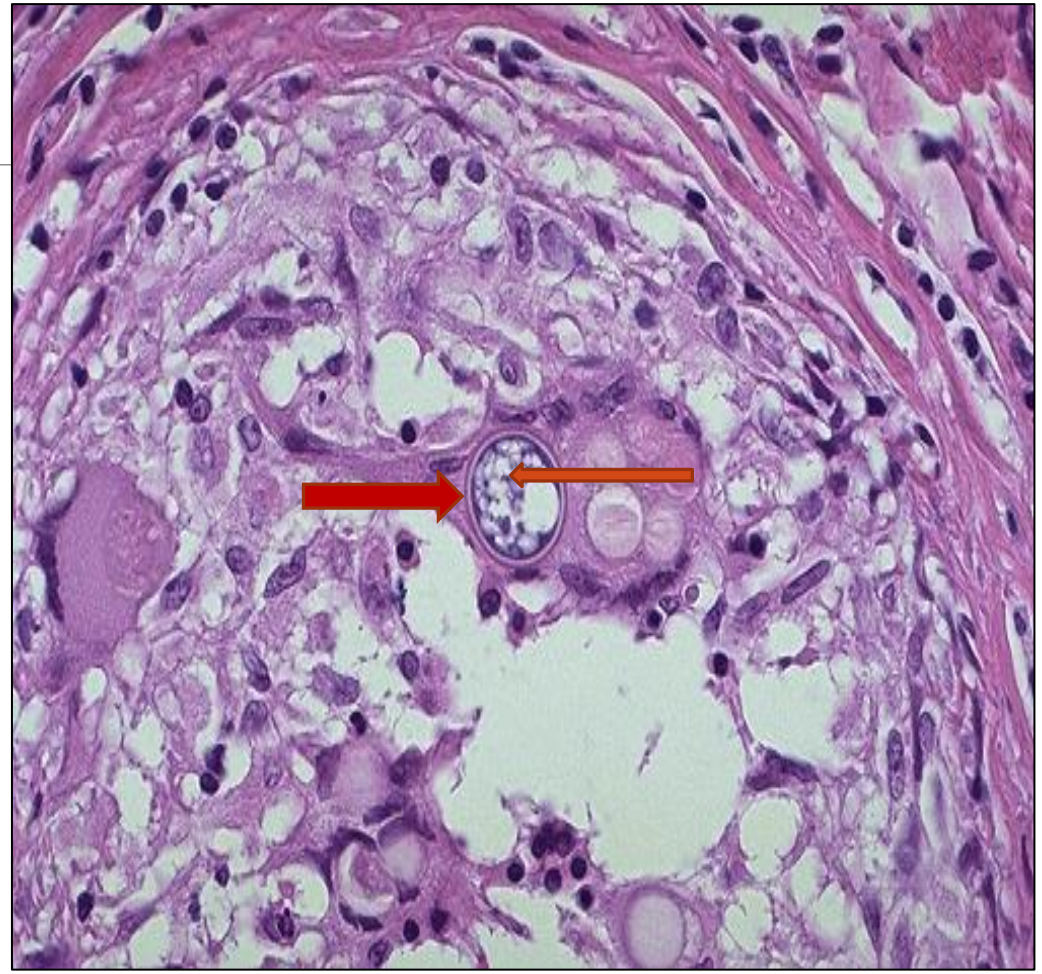




Granuloma with coccidioidomycosis immitis

The **thick wall** of the *C. immitis* spherule is seen in a giant cell in the center of this image. The spherule contains **endospores.**



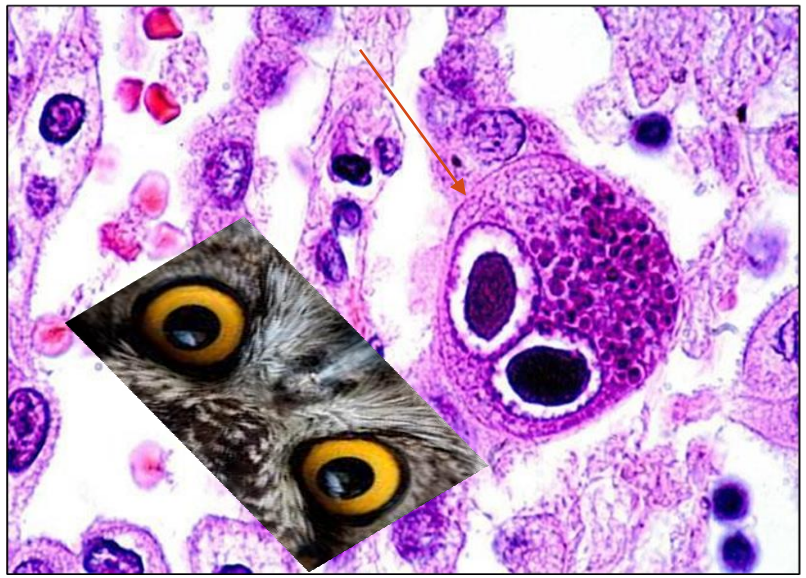


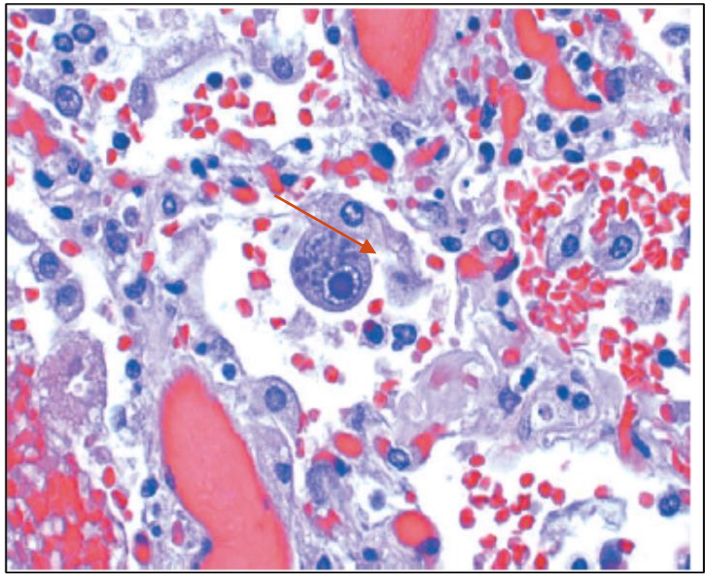
7. Pneumonia in the immunocompromised patients

1. Cytomegalovirus Infections :

Morphology:

- Interstitial mononuclear cells infiltrate with foci of necrosis, accompanied by the typical viral inclusion.
- Cells infected by the virus exhibit gigantism of both the nucleus & cytoplasm; within the nucleus, a basophilic inclusion surrounded by a clear halo giving an owl-eye appearance and cytoplasmic inclusions.



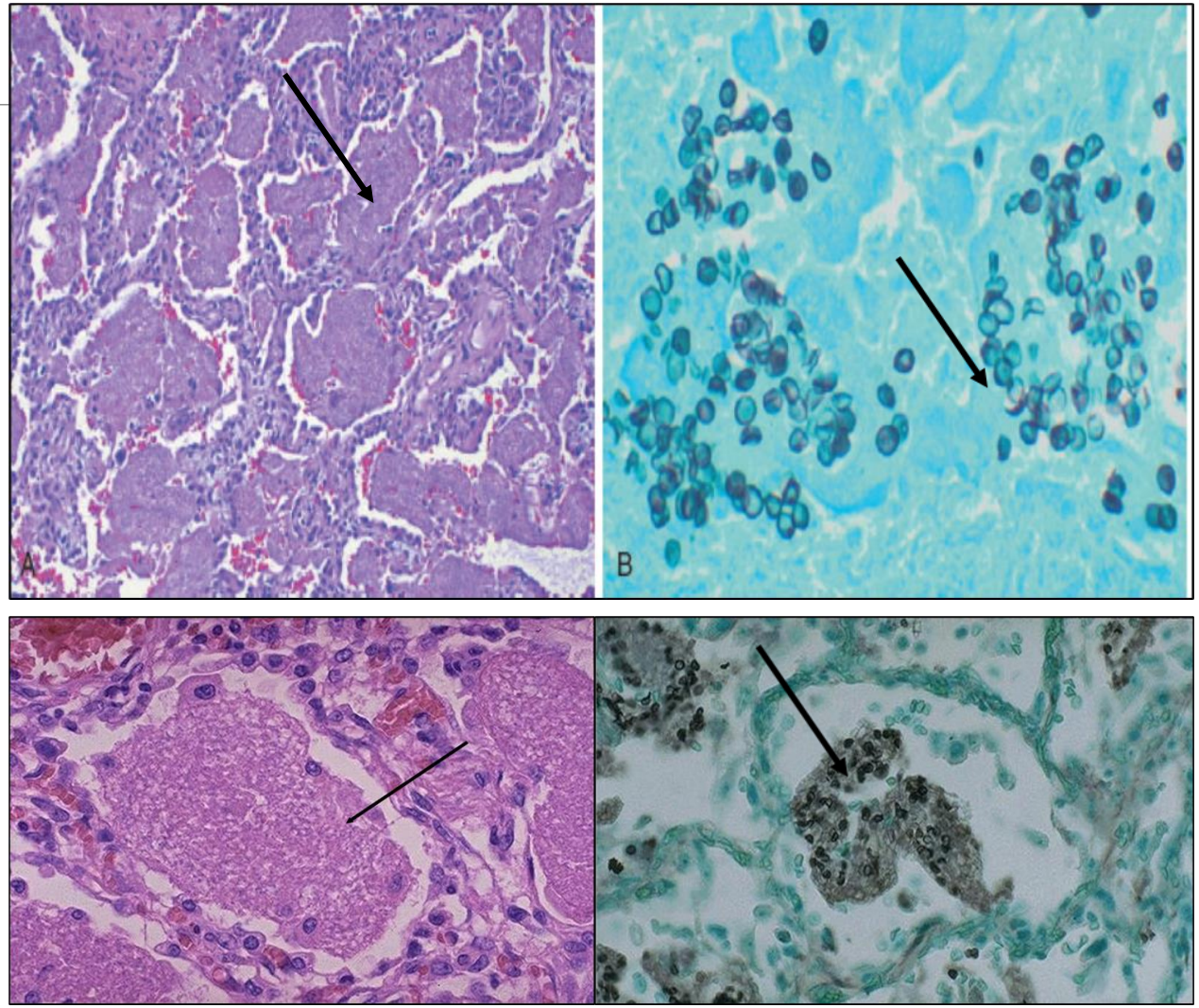


2. Pneumocystis Pneumonia :

- Pneumocystis jeroveci is closely related to fungi.
- It is extremely common in patients with AIDS.

Microscopically :

- Intra-alveolar foamy pink-staining exudate **("cotton candy" exudate),** the septa are thickened by edema & minimal mononuclear cells infiltrate.
- Silver stain demonstrates the organism as a round to cup-shaped cyst wall.

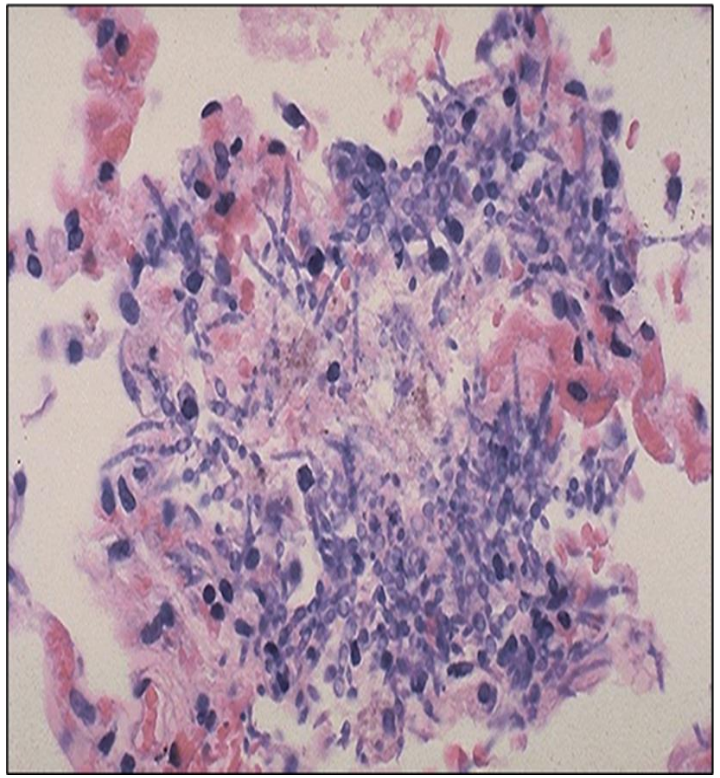


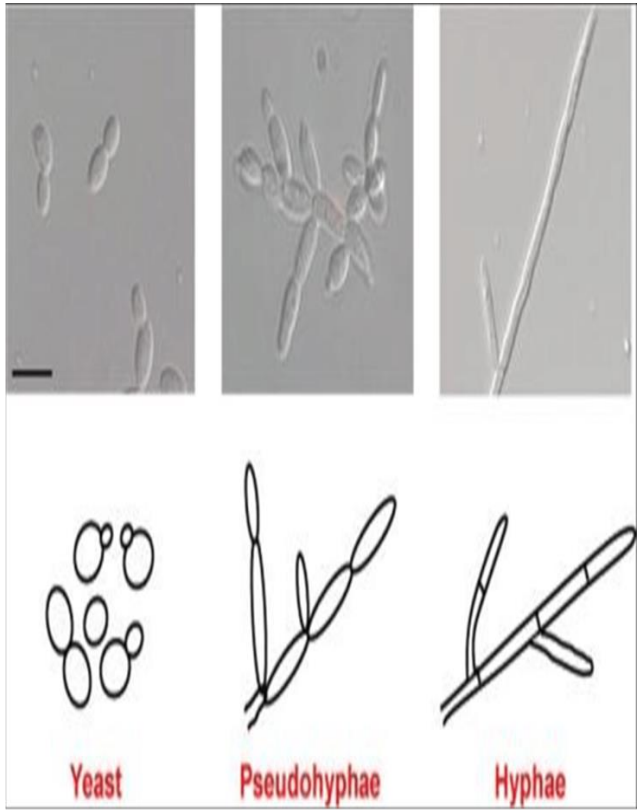
3. Candidiasis :

Morphology:

- It demonstrates yeast, pseudo & true hyphae forms.

➢The organisms are positive for GMS and PAS stains.



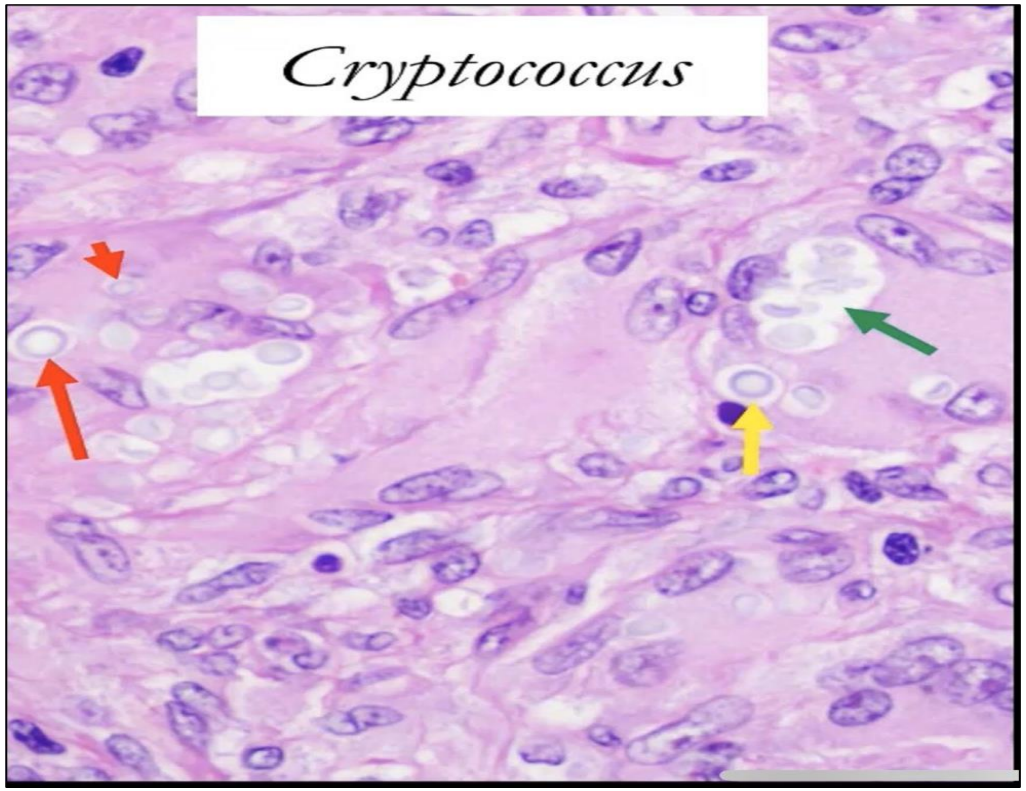


4.Cryptococcosis : (krip-toh-ko-koh-sis)

Morphology

- A yeast has a thick, gelatinous capsule.

- In H&E stains, the capsule is not visible, but a clear “halo” representing the area of the capsule can be seen.



5. Aspergillosis :

1- Invasive pulmonary aspergillosis:

- Immunocompromised host:

  - Multifocal necrotizing pneumonia

2-Aspergilloma:

- (Fungus ball) growing in existing cavities, especially in TB & bronchiectasis.

3-Allergic bronchopulmonary aspergillosis:

- Occurs in patients with asthma who develop an exacerbation of symptoms caused by hypersensitivity against the fungus growing in the bronchi.

6. Mucormycosis:

- Caused by the class of fungi known as *Zygomycetes*.

- Immunocompromised host.

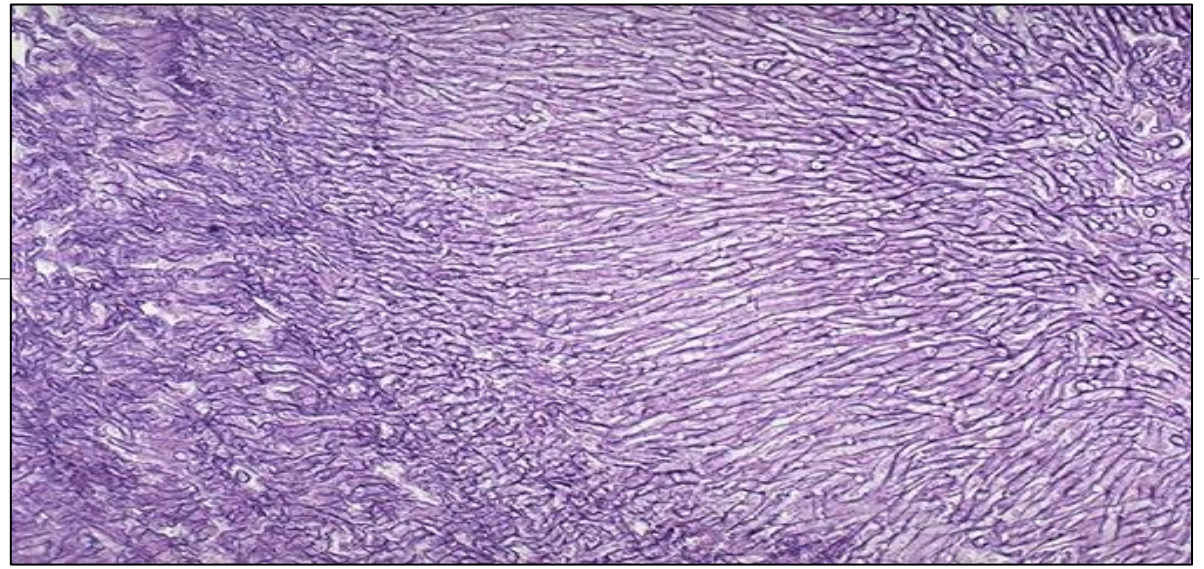
Morphology:

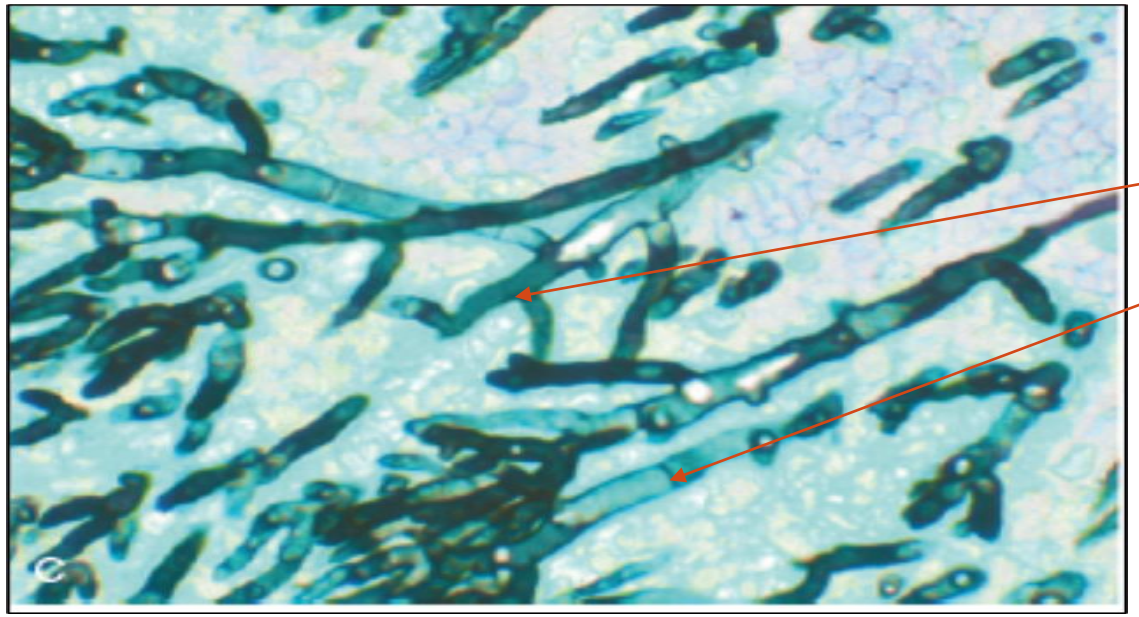
Mucor: Hyphae are **non-septate** and branch at **right** angles.

Aspergillus*:* Hyphae are **s**eptate and branch at more **A**cute angles.

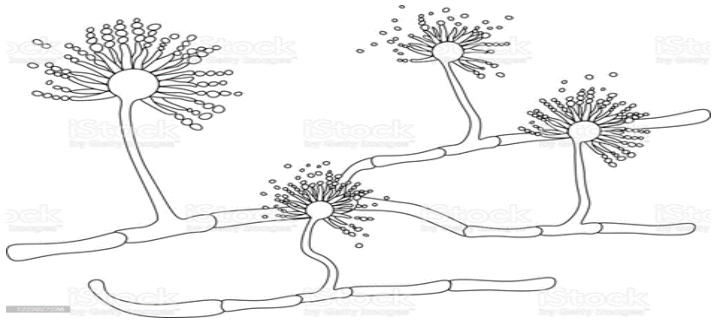
- Both cause a suppurative, sometimes granulomatous reaction **with a predilection for invading blood vessel walls,** causing hemorrhage, vascular necrosis, and infarction.

Aspergillus



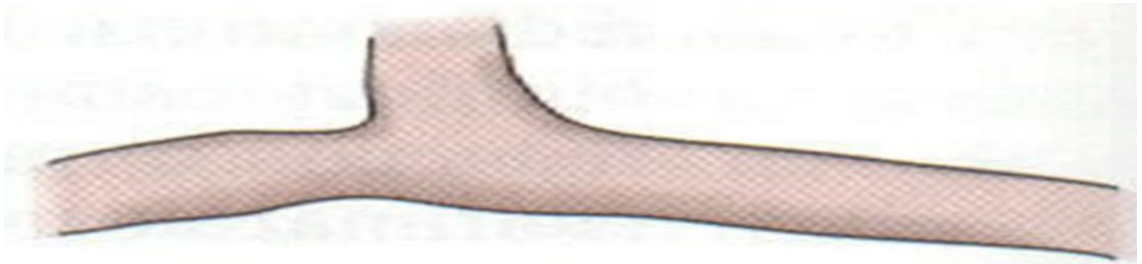


(GMS) stain shows septate hyphae with acute-angle branching, consistent with Aspergillus

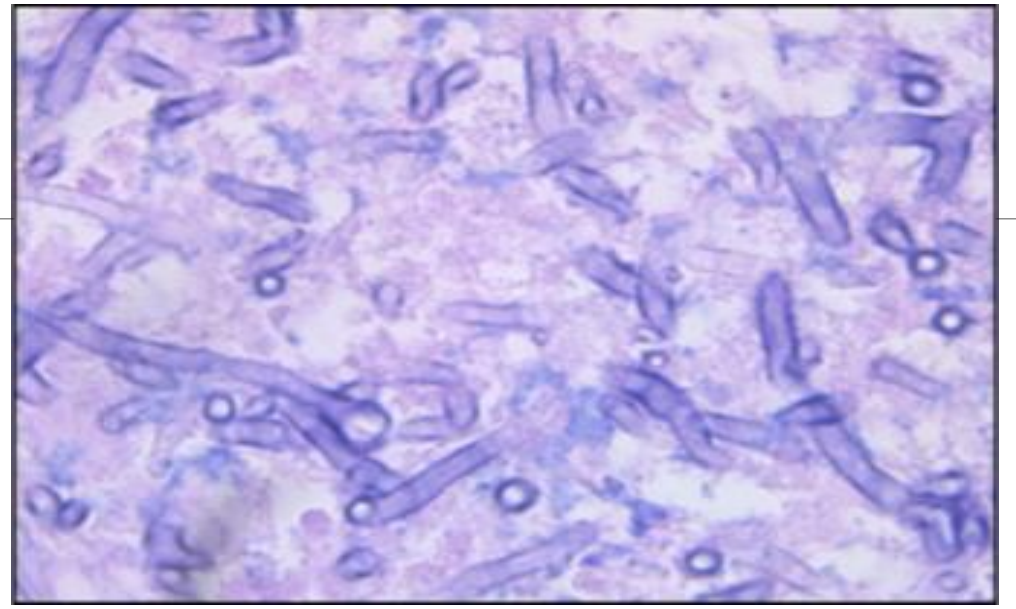


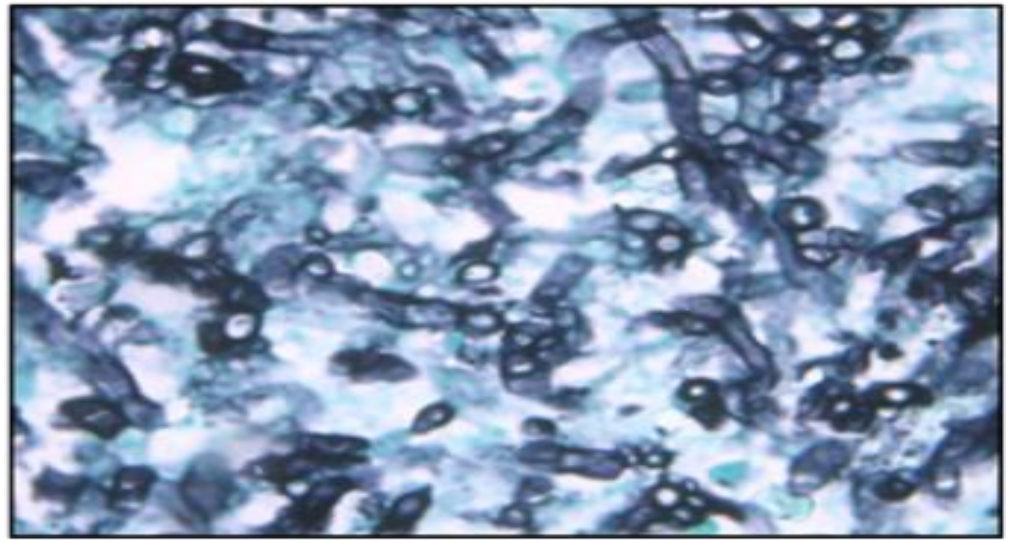
Mucormycosis

Broad non-septate hyphae with right-angled branching characteristic for *Mucor* in H&E and GMS stains.



Mucor has nonseptate hyphae with right-angle branching.





Thank you