

RESPIRATORY SYSTEM

HA4AT BATCH



SUBJECT : Pathology

LEC NO. : 7

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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 +**). بسبب ال lipid الموجود في ال cell wall

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** الفحص موجودة بالتفصيل بالمايكرو

Infection vs. Disease:

- **Infection:** TB infection occurs when a person inhales *M. tuberculosis* bacteria, which then establish a focus of infection within the body. This may or may not cause clinically significant tissue damage or symptoms. In many cases, the immune system is able to contain the infection, leading to latent tuberculosis infection (LTBI), where the bacteria remain dormant within granulomas in the lungs.
- **Disease:** TB disease occurs when the infection progresses to active disease, causing symptomatic illness and tissue damage. Factors such as a weakened immune system (e.g., due to HIV infection) or other medical conditions can increase the risk of progression from TB infection to TB disease.

Delayed Hypersensitivity and the Tuberculin (Mantoux) Test:

- **Delayed Hypersensitivity:** Following exposure to *M. tuberculosis*, the body mounts a delayed hypersensitivity response, characterized by the activation of T cells and the release of inflammatory cytokines. This immune response is responsible for the formation of granulomas and helps contain the infection.
- **Tuberculin (Mantoux) Test:** The Mantoux test is a diagnostic test used to detect TB infection. It involves injecting a small amount of purified protein derivative (PPD), a substance derived from *M. tuberculosis*, into the skin of the forearm. A positive reaction, characterized by induration (swelling) at the injection site, indicates a delayed hypersensitivity response to the PPD antigen, suggesting TB infection. However, the Mantoux test cannot distinguish between latent TB infection and active TB disease.

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**

This destructive tissue hypersensitivity is a double-edged sword—it helps contain the infection but can also contribute to tissue damage

اول مرة يتعرض لل 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.


لما ال Mycobacteria يدخل عن طريق ال inhalation إلى ال lung يدخل لل macrophage

و رح يعمل preventing the fusion of the lysosomes with the phagocytic vacuole و بعدها رح يتكاثر جوا

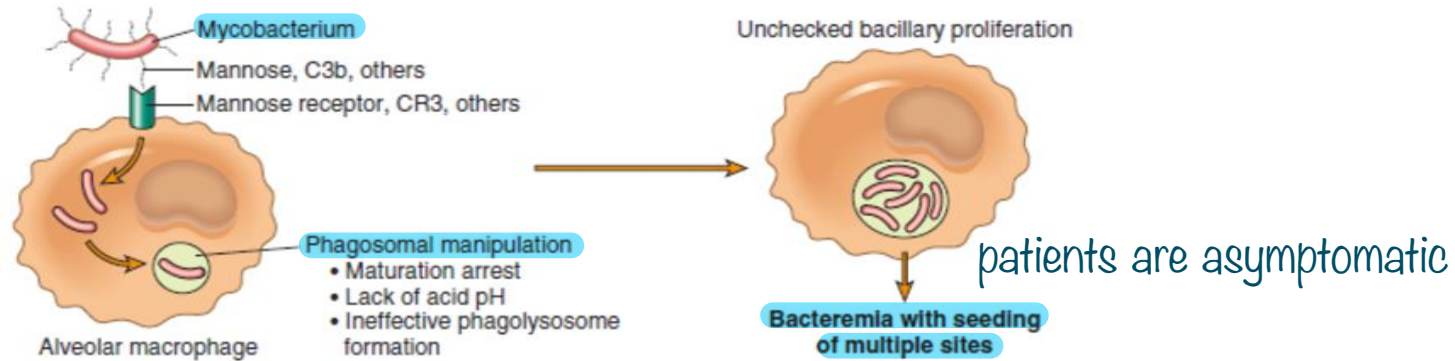
ال macrophage في ال lung و ممكن يعمل bacteremia

كل هاد بدون ما يكون عندي اي symptoms

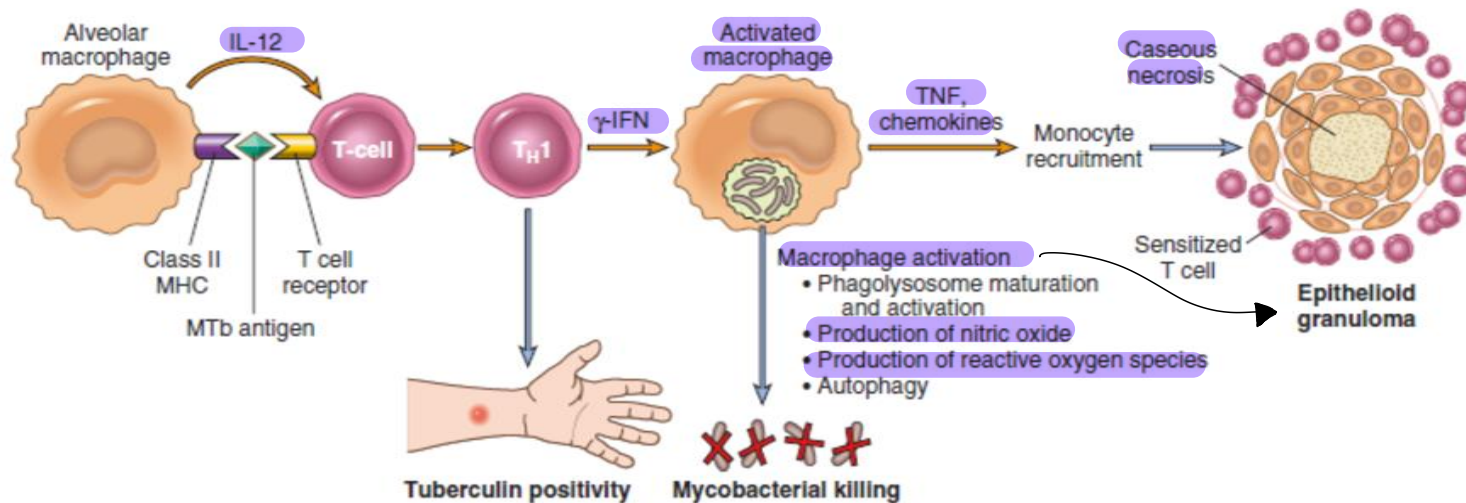
❖ The cell-mediated immunity develops **3 weeks after exposure.**

- 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.**
ال macrophages تفرز IL-12 و T cells ينشط T cells و IFN ينشط ال 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).**

A INFECTION BEFORE ACTIVATION OF CELL MEDIATED IMMUNITY



B INITIATION AND CONSEQUENCES OF CELL MEDIATED IMMUNITY 3w



The sequence of events in the natural history of primary pulmonary tuberculosis:

(A) Events occurring in the first 3 weeks after exposure.

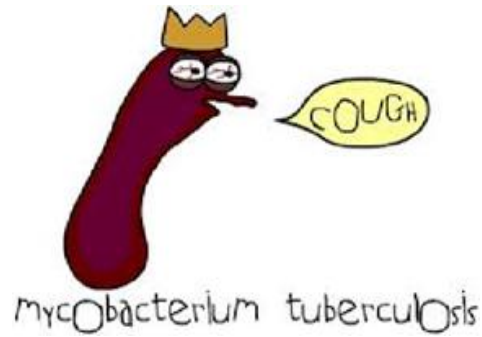
(B) Events there after

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**.

SIGN AND SYMPTOMS OF **TUBERCULOSIS**



Types:



Primary Tuberculosis:

- In a previously **un**exposed & **un**sensitized person. اول مرة يتعرض للorganism
- 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.

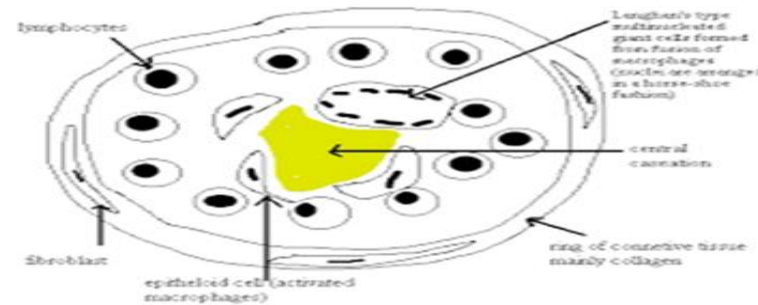
Morphology:

- Mostly in the **lower part of the upper lobe & upper part of the lower lobe, usually close to the pleura.** Middle lung
- 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 :

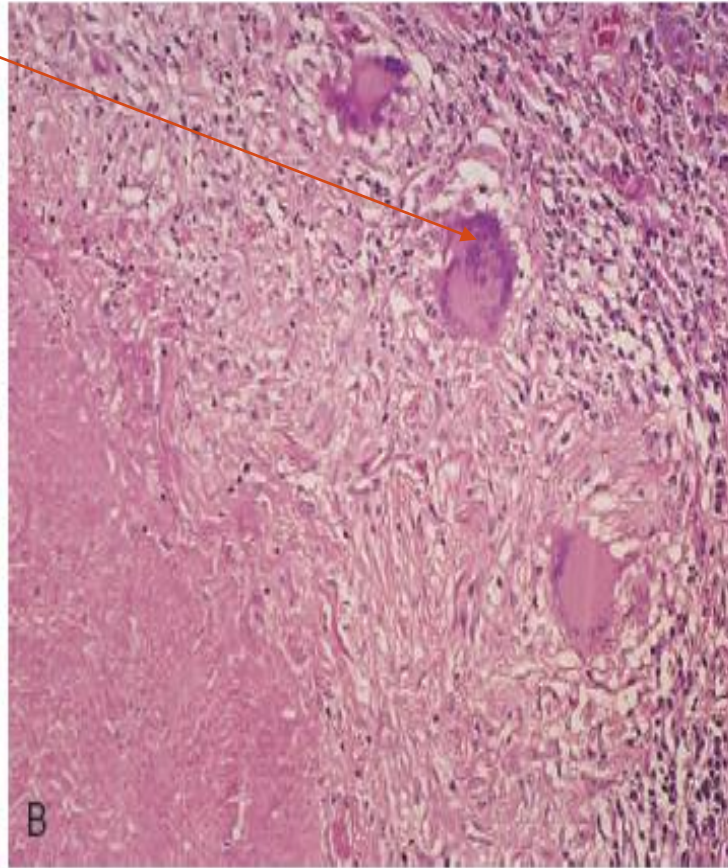
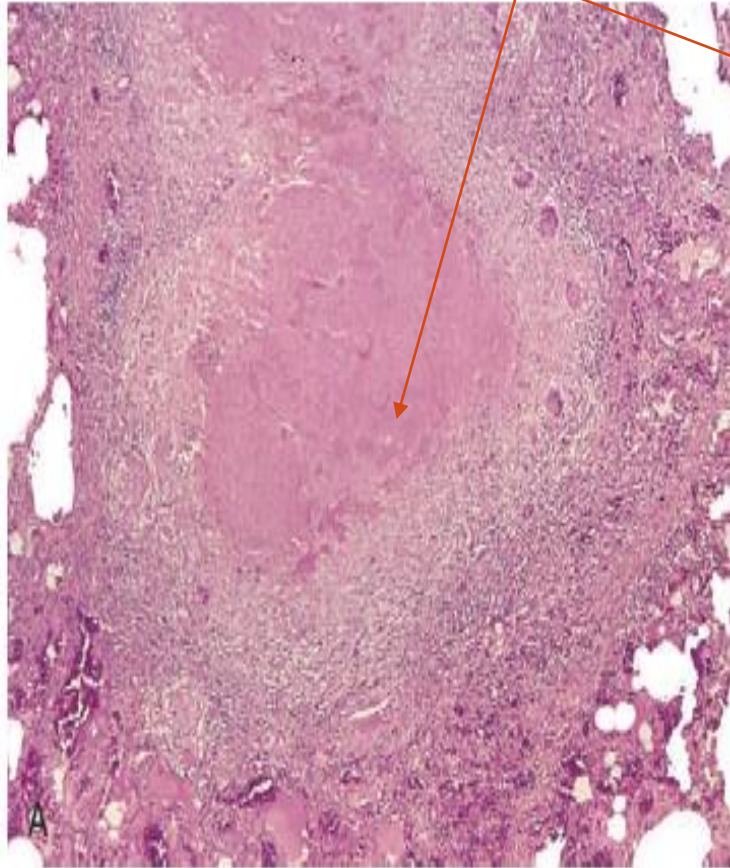
- Inflammatory reaction marked by the presence of **caseating (necrotizing) and noncaseating granulomas**, which consist of epithelioid histiocytes and multinucleate giant cells.



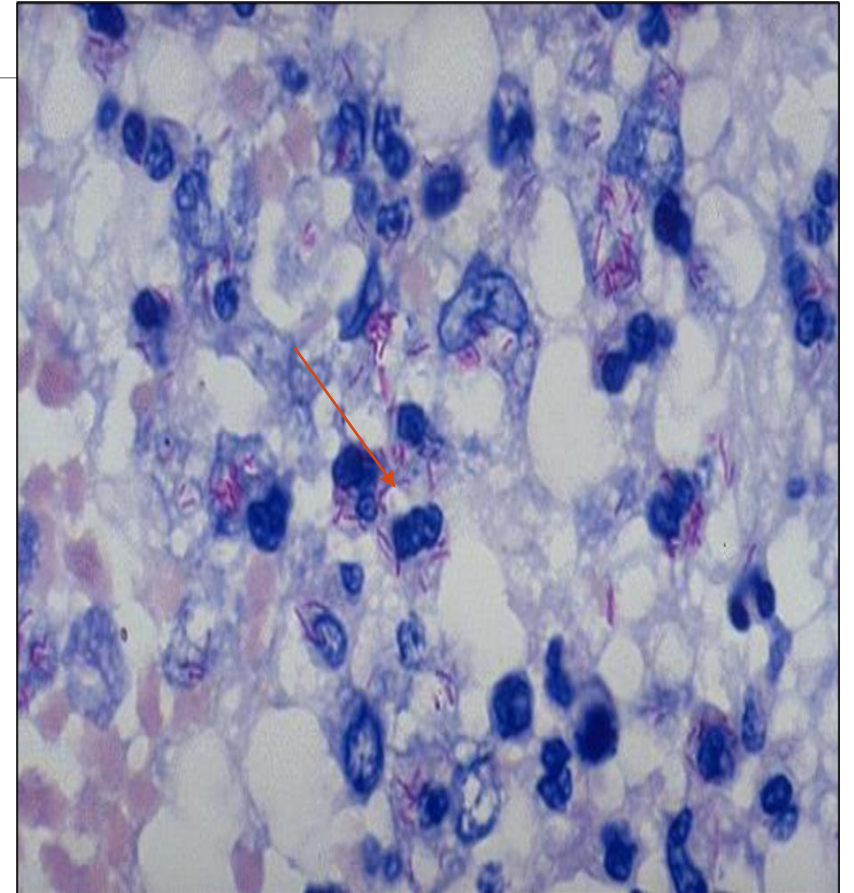
There is a small tan-yellow **subpleural granuloma** in the mid-lung field on the right. In the hilum is a small yellow tan **granuloma in a hilar lymph node** next to a bronchus. This is the **"Ghon complex"**.



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):

المشكلة هون لو ال organism بعده موجود في منطقة ال fibrosis

- 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.



Characteristic	Primary Tuberculosis	Secondary Tuberculosis
Host Exposure	unsensitized person	Preciously sensitized
Source of Organism	Exogenous	Reactivation of dormant primary lesions
Location of Lesions	Lower part tupper lobe upper part of lower lobe	Apex of one or both lobes
Lymph Node Involvement	Prominent	Less prominent
Histological Features	Caseating and noncaseating granulomas	Granulomas with TB bacilli demonstrated

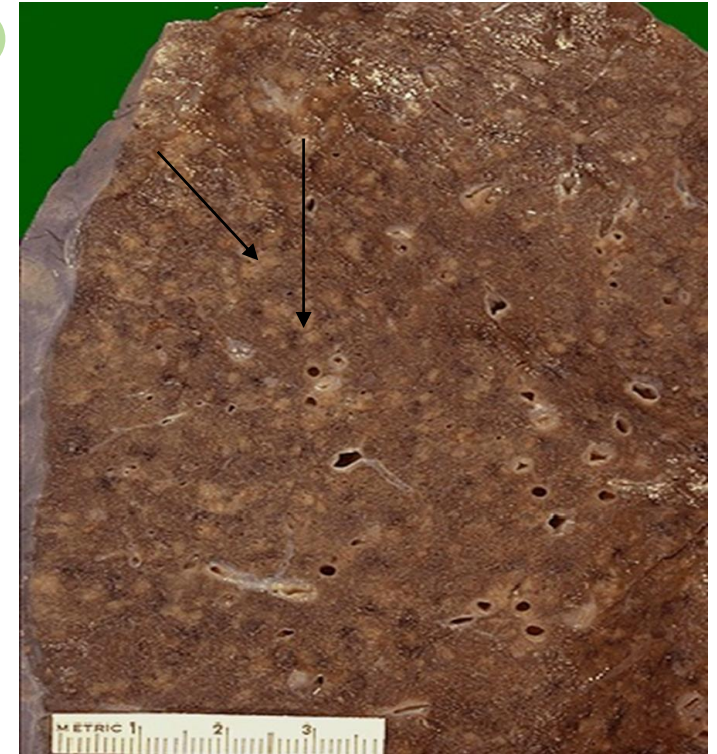
➡ The apical lesion may heal with fibrosis or may extend along different pathways :

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. غالباً يكون ال spleen

6- Isolated Organ TB:

Vertebral TB → POTT's Disease

Tuberculous lymphadenitis (Scrofula)



2. Histoplasmosis, Coccidioidomycosis, and Blastomycosis

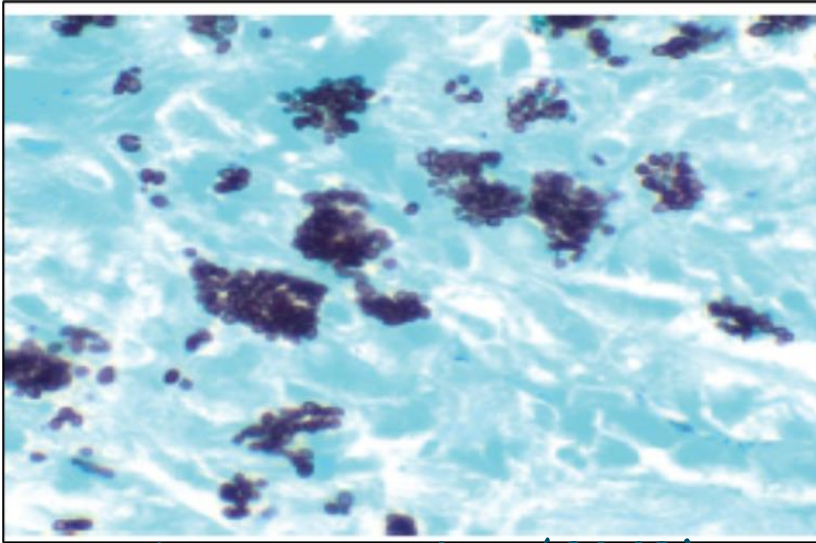
The primary nodules are composed of aggregates of macrophages filled with organisms. These lesions evolve into small granulomas with giant cells and may develop central necrosis and later fibrosis and calcification.

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

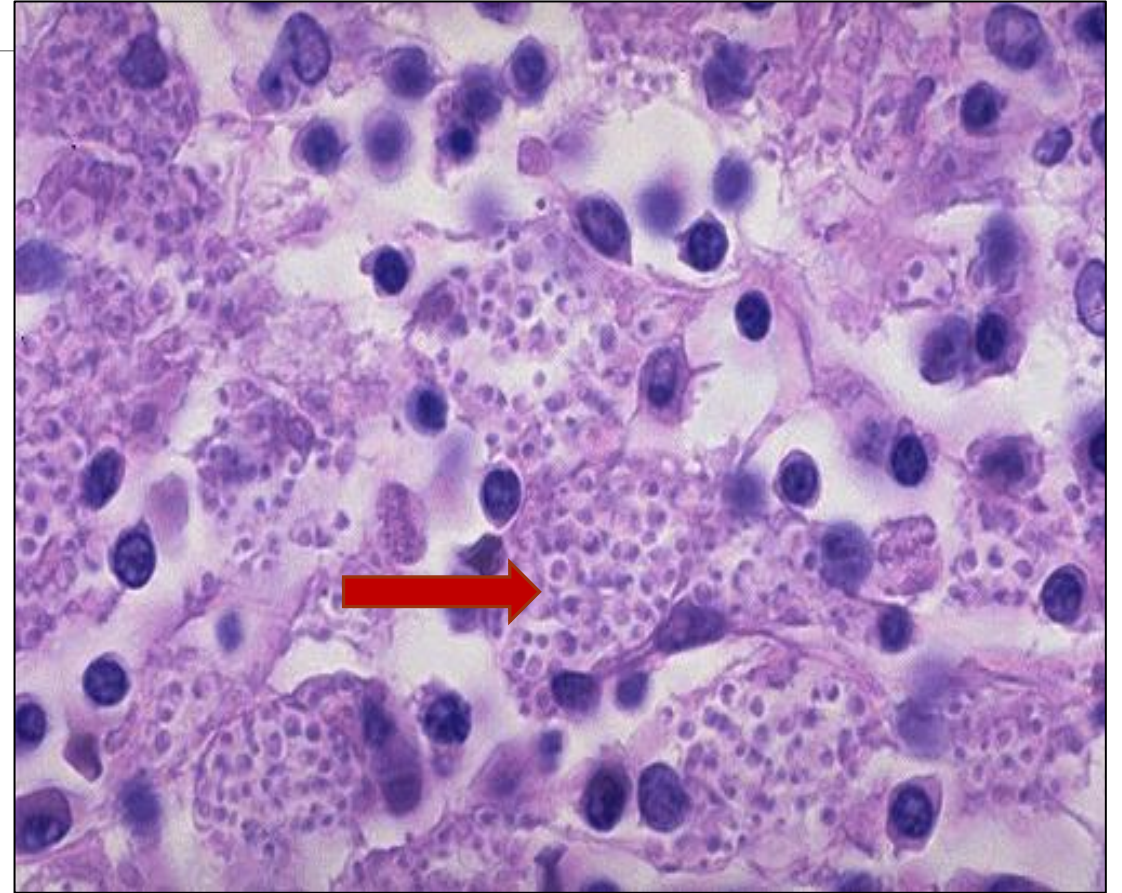
كلهم فيهم granuloma / macrophage
فلازم نشوف ال organism داخلهم حتى احدد
***مهم ال Morphology الهم

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.



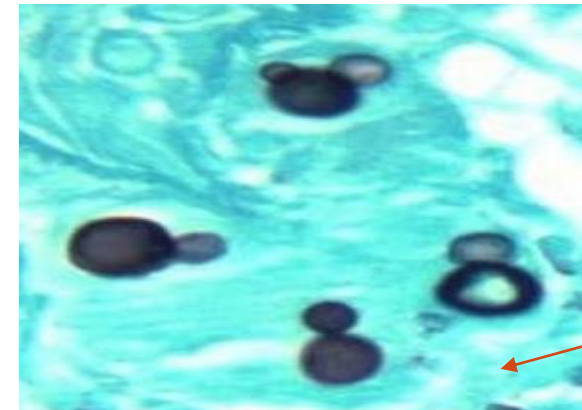
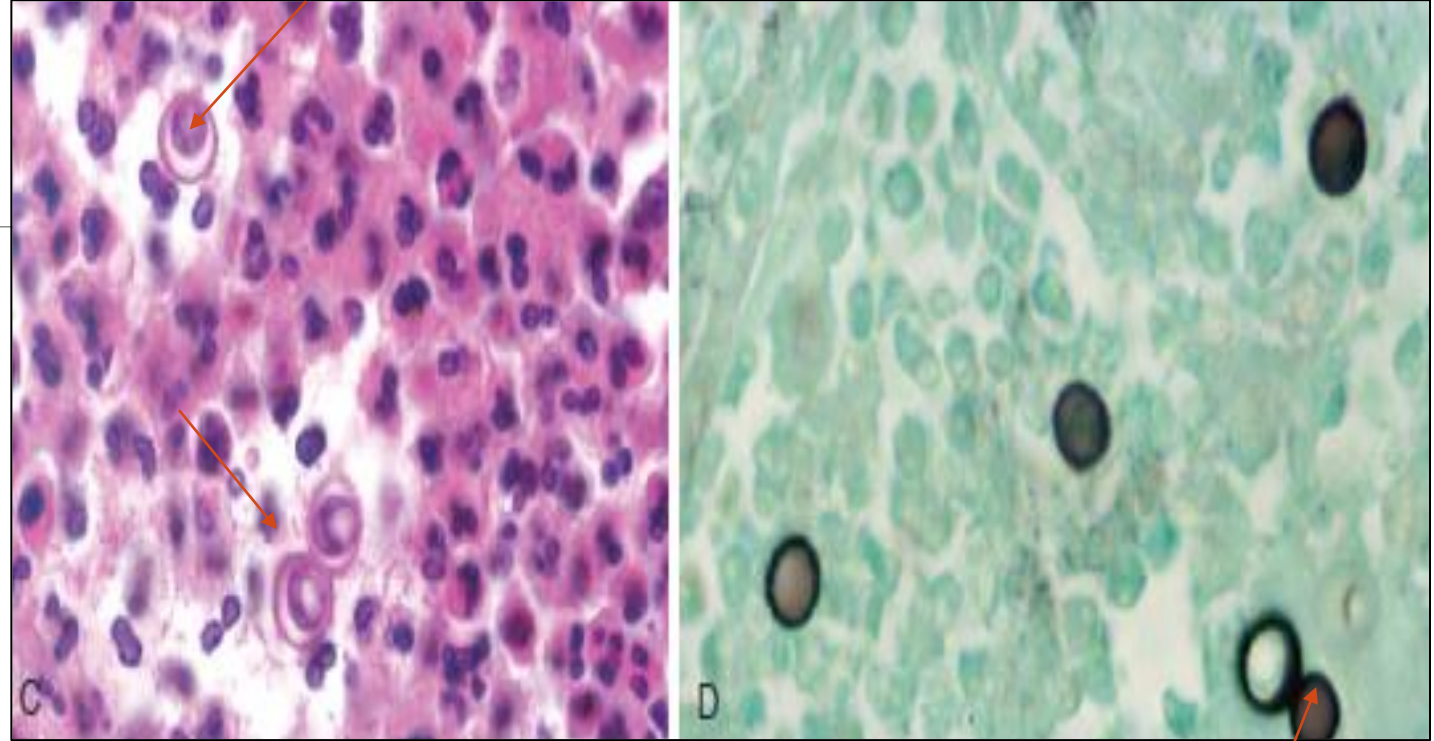
Gomori methenamine silver (GMS) stain.



Blastomycosis

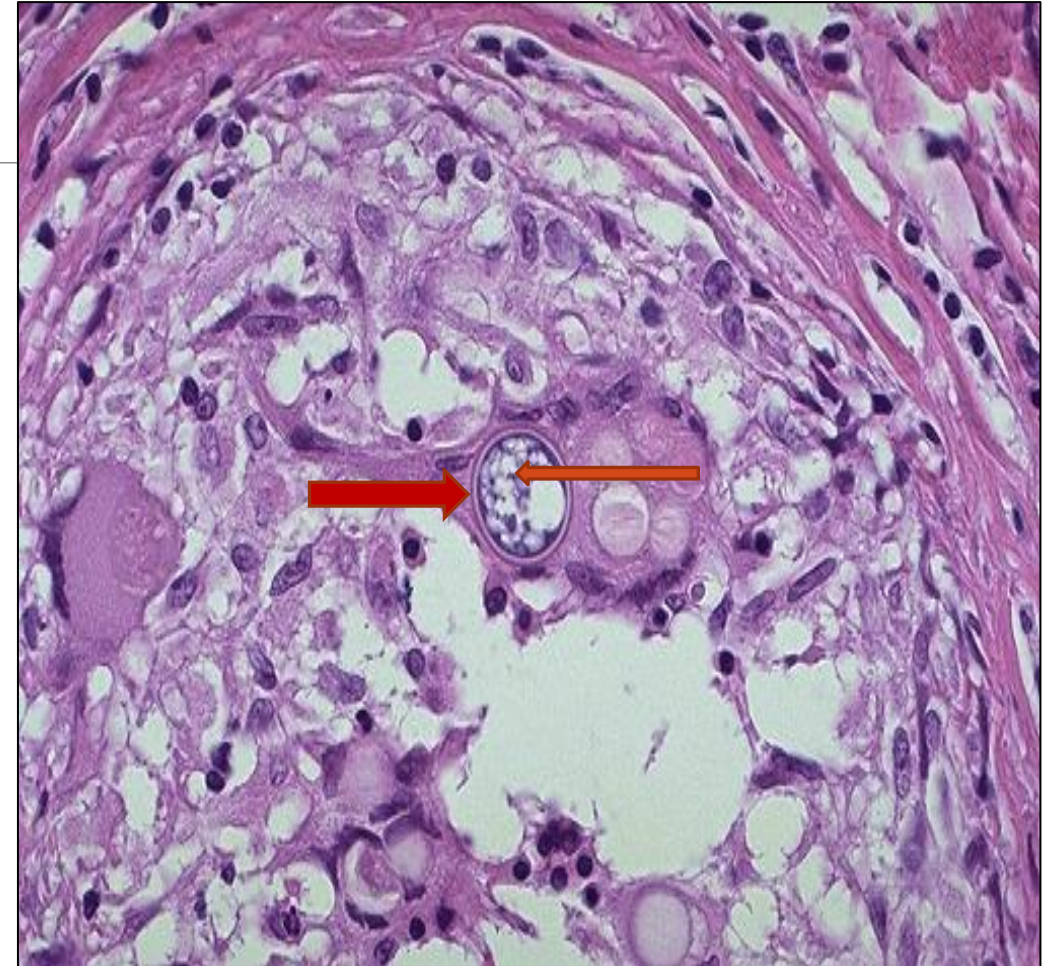
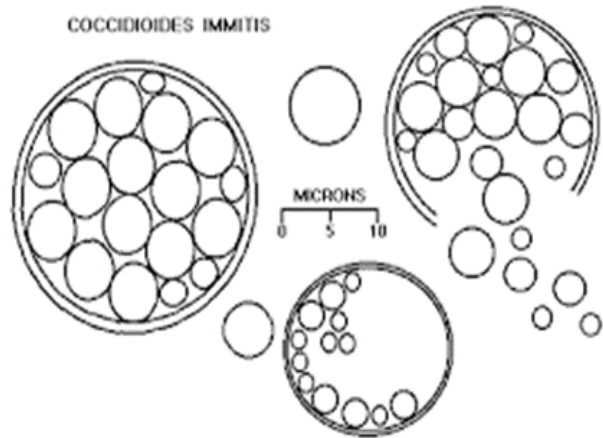
(C) Blastomycosis, with rounded budding yeasts with characteristic thick wall, and (D) Silver stain highlights the broad-based budding.

Positive to Gomori methenamine silver (GMS) stain.



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**.

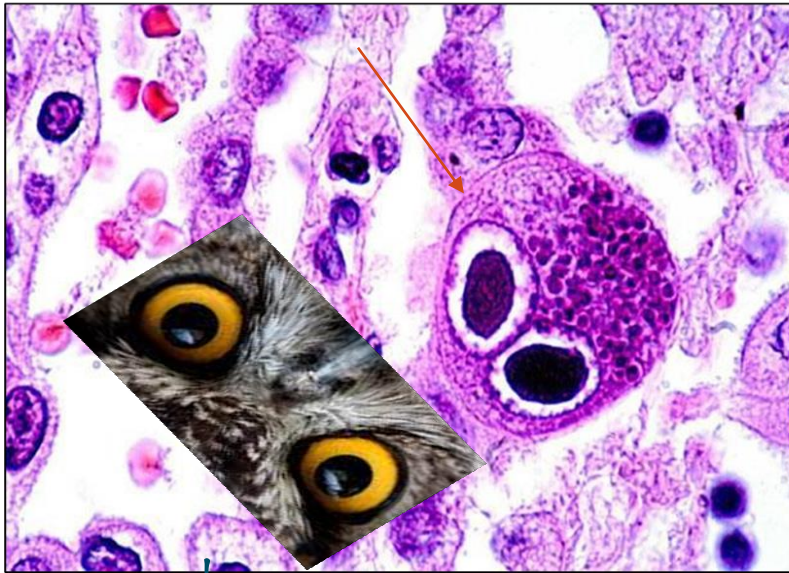


7. Pneumonia in the immunocompromised patients

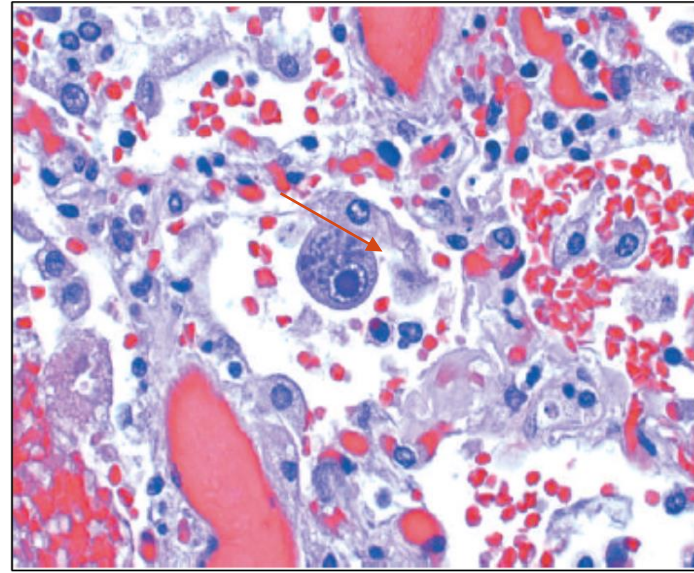
1. Cytomegalovirus Infections :

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**.



owl-eye appearance

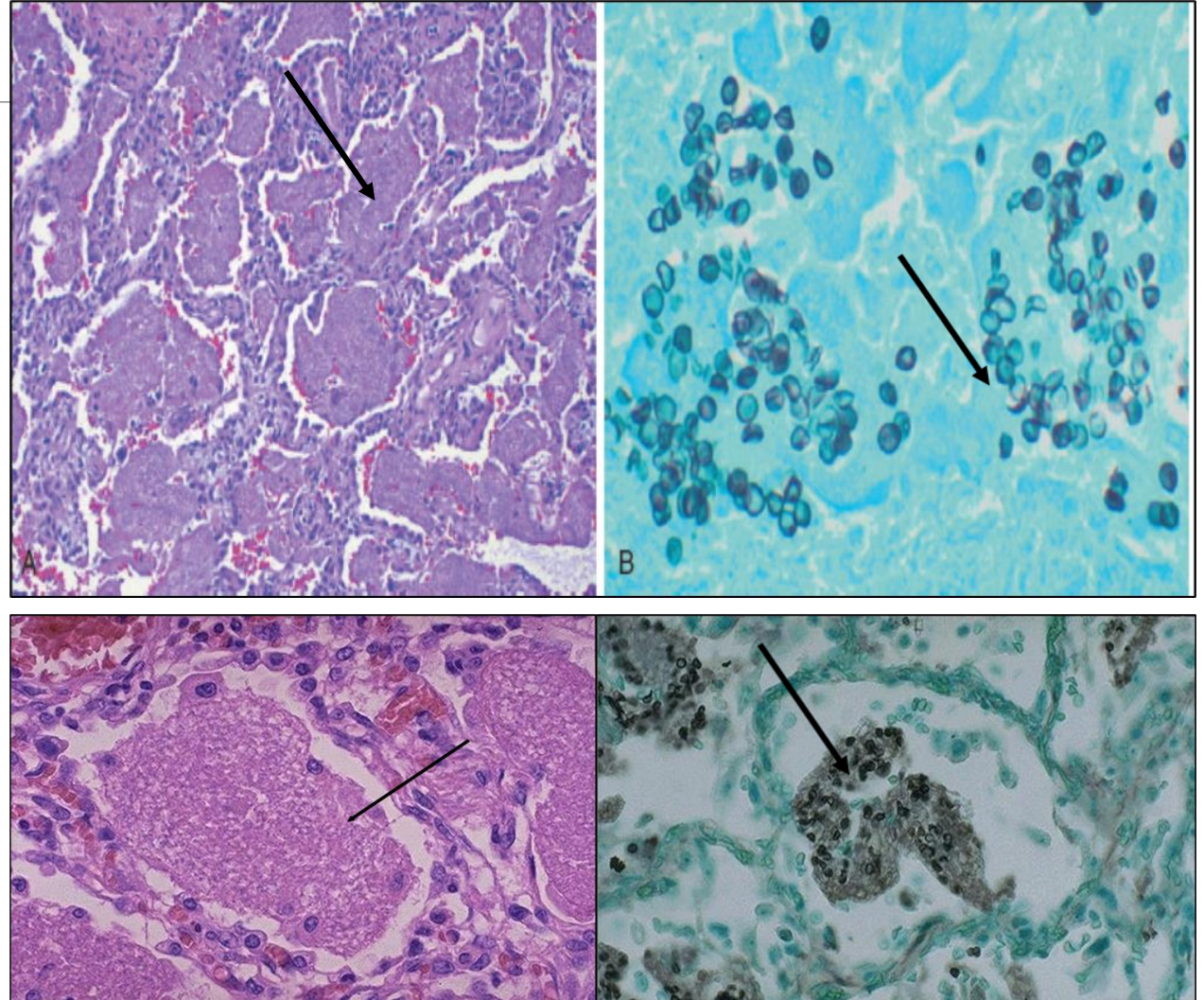


2. Pneumocystis Pneumonia :

- ▶ Pneumocystis jirovecii 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 :

بتكون على شكل Yeast + filamentous

Yeast are round to oval-shaped

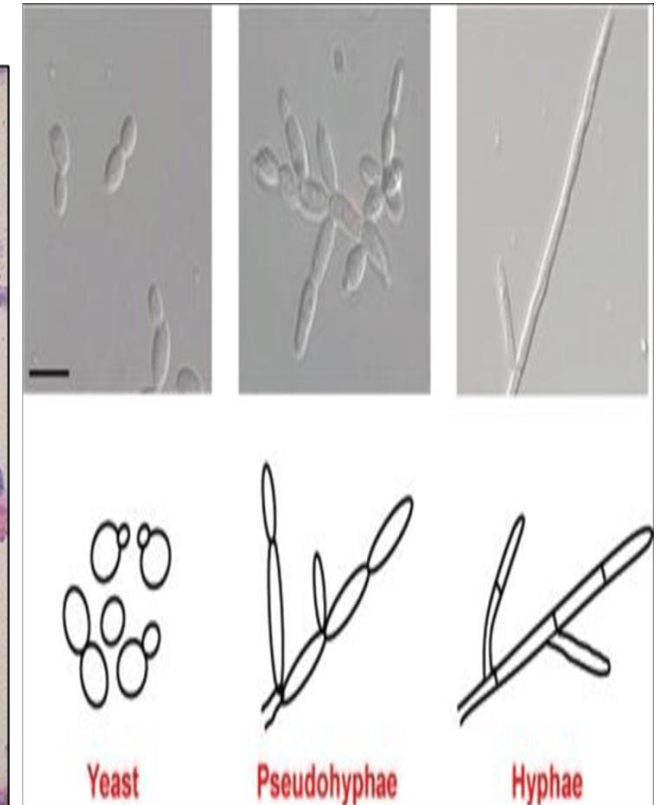
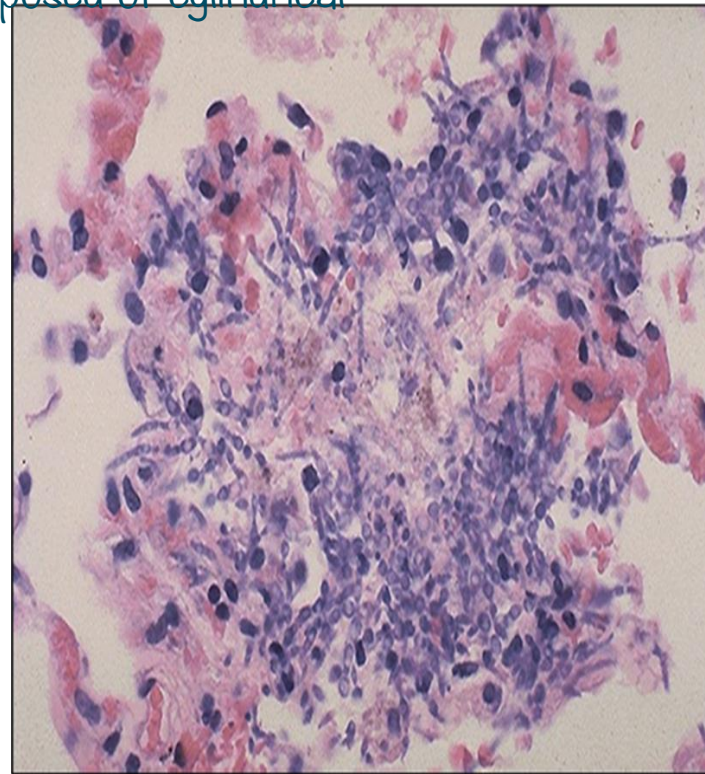
Pseudohyphae are chains of elongated yeast cells that remain attached to each other.

True hyphae are long, branching, filamentous structures composed of cylindrical cells.

Morphology:

► It demonstrates yeast, pseudo & true hyphae forms.

⊗ ➤ The organisms are positive for GMS and PAS stains.

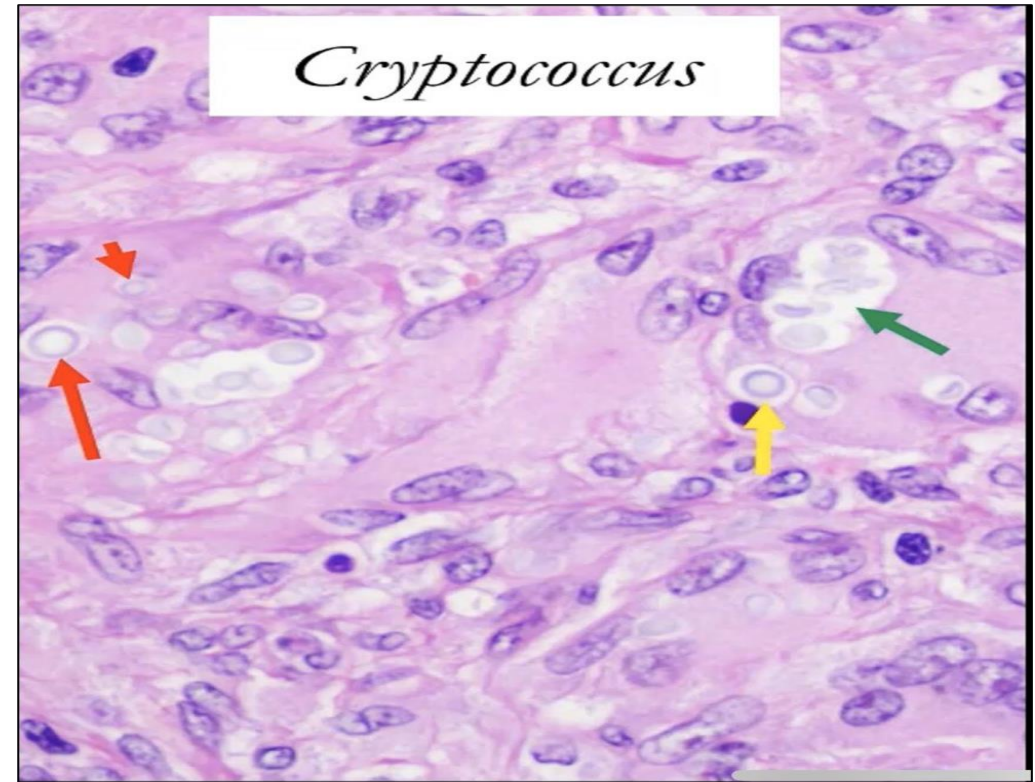


4.Cryptococcosis : (krip-toh-ko-koh-sis)

بتكون على شكل yeast بس

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.



Fungal infection

5. Aspergillosis :

بتكون بس على شكل filamentous

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:

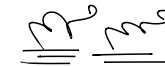
بتكون بس على شكل filamentous

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

❑ Immunocompromised host.

Morphology:

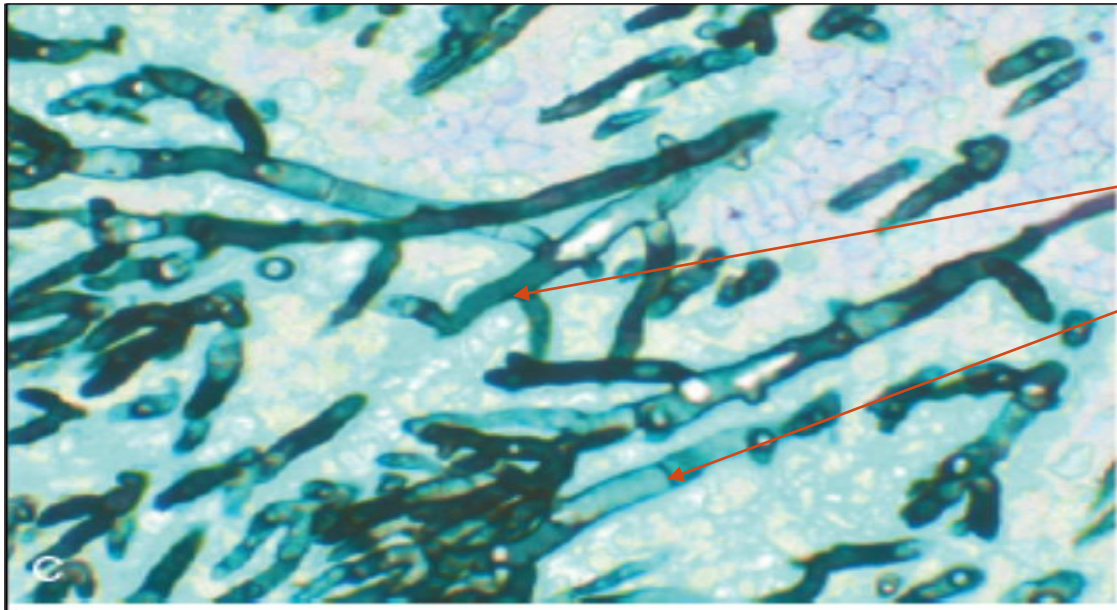
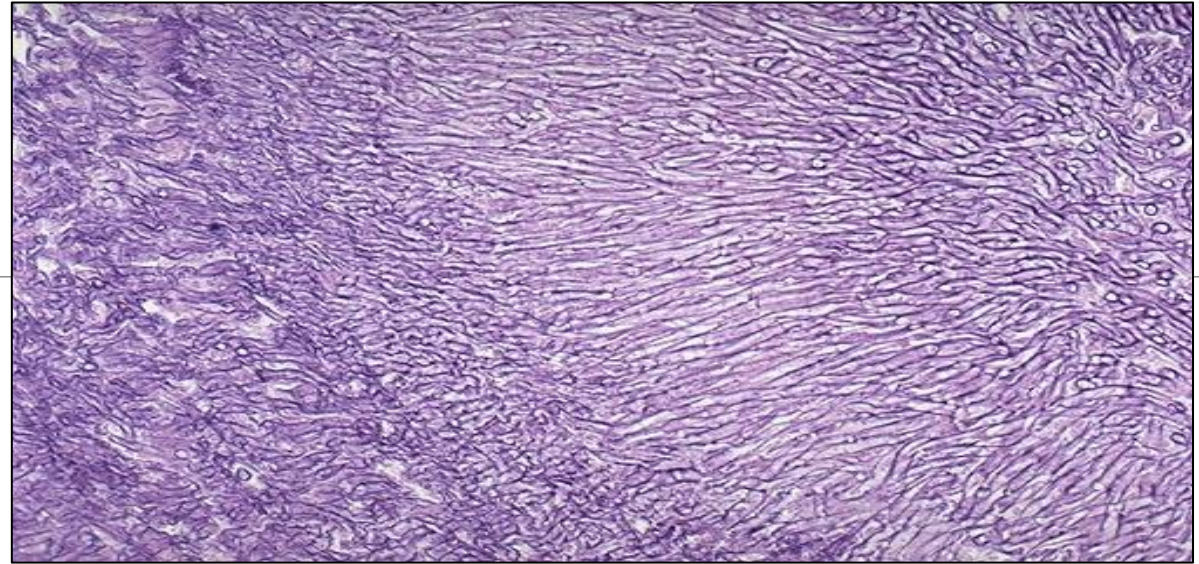
Mucor: Hyphae are **non-septate** and branch at **right** angles.



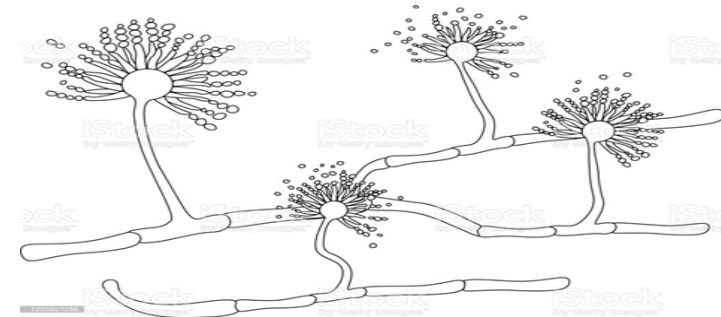
Aspergillus: Hyphae are **septate** and branch at more **Acute** angles.

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

Aspergillus

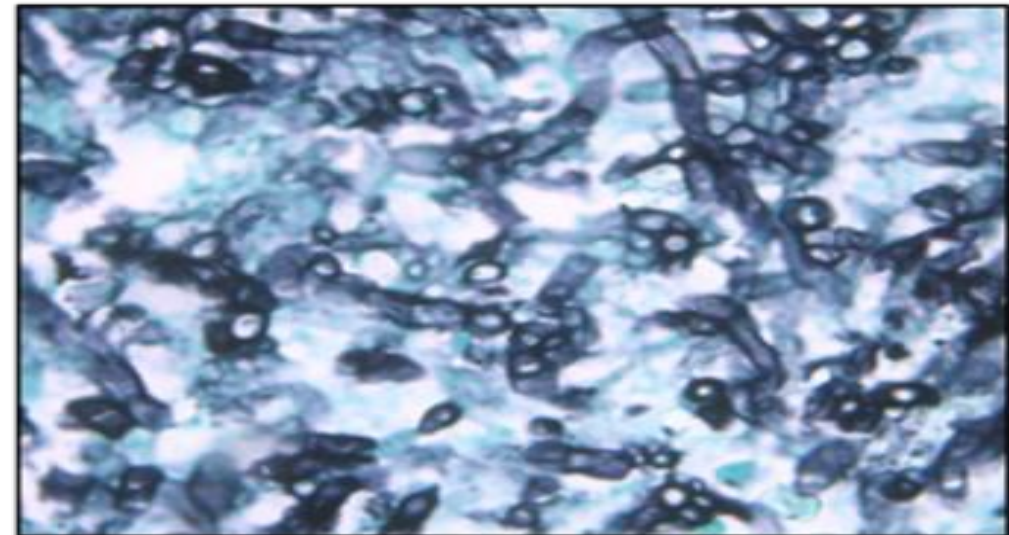
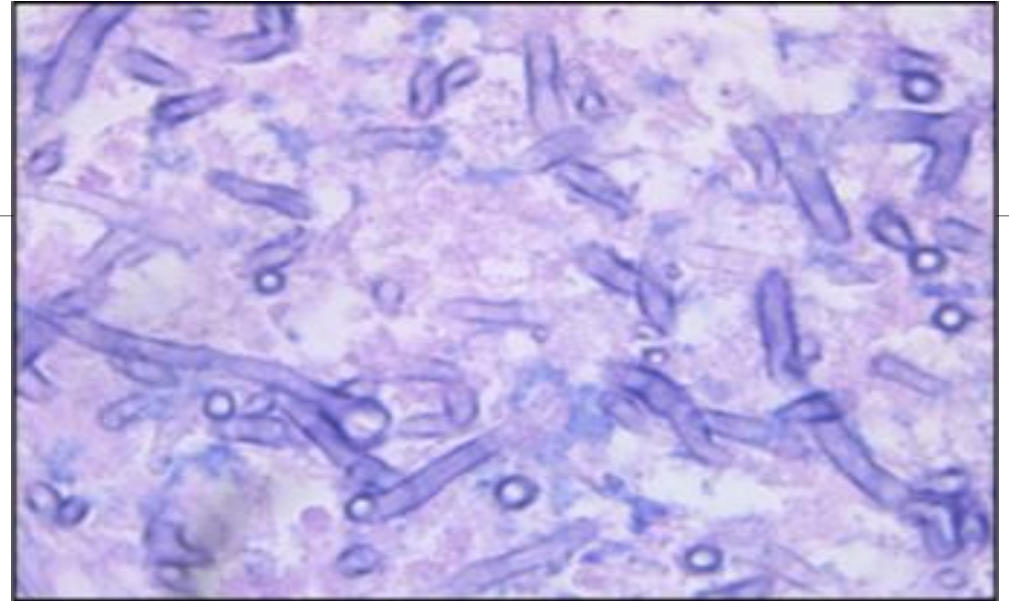
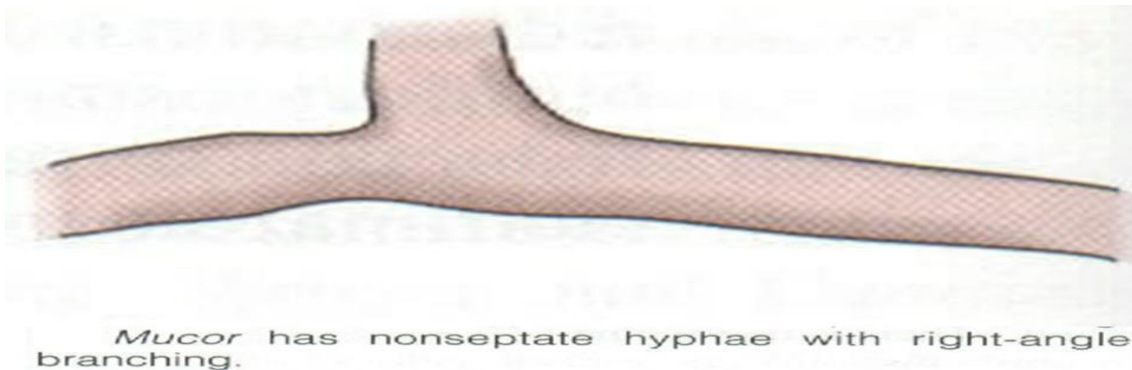


(GMS) stain shows septate hyphae with acute-angle branching, consistent with Aspergillus



Mucormycosis

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



ضفنا لكم على خانة ال Guidance جداول بتحتوي على فيديوهات بتساعدكم بفهم مواضيع

الباثو بشكل أكبر ولتسهل عليكم الحفظ بتلاقوهم من

(دفعه حياة .. Rs .. باثو .. Guidance)

اضغط على الكلام المكتوب باللون الازرق لتنتقل مباشرة الى المحاضرة

الموضوع	الفديوهات المطلوبة 1	الفديوهات المطلوبة 2	الفديوهات المطلوبة 3
Upper Respiratory Tract Pathology lec1	Nasopharyngeal Carcinoma video 1 video 2	Vocal Cord Nodules and Polyps	neoplasia Laryngeal Papilloma and Carcinoma Of The Larynx
lower Respiratory Tract Pathology lec1	شوية هستو لازم تعرفوهم video	Atelectasis	Acute Respiratory distress syndrome 1. medicosis 2. osmosis
Obstructive Lung diseases 1 lec2	Emphysema video 1 video 2	Chronic Bronchitis Chronic Bronchitis VS Emphysema (Comparison)	Chronic Obstructive Pulmonary Diseases (COPD)
Obstructive Lung diseases 2 lec3	Asthma video 1 video 2	Bronchiectasis	
Restrictive Lung Diseases lec 4	1.Obstructive VS Restrictive Lung Disease	2. Introduction	
Restrictive Lung Diseases: 1.fibrosing diseases lec 4	1.Idiopathic Pulmonary Fibrosis 2.Nonspecific Interstitial Pneumonia (NSIP) 3 -Cryptogenic Organizing Pneumonia (COP)	4. Pneumoconiosis: 1. Coal- workers pneumoconiosis and Silicosis 2. Asbestosis and asbestos-related diseases	هذه الالموضوعين كل واحد عنهم سلايد قمش عتاهل احطاهم فيديوهات 4. "Collagen" Vascular Diseases 5. Drug- and Radiation-Induced Pulmonary Disease
Restrictive Lung Diseases: 2.Granulomatous diseases lec 5	1. Sarcoidosis: video1 video2	2.Hypersensitivity Pneumonitis	Hypersensitivity Pneumonitis VS Sarcoidosis
Restrictive Lung Diseases: 3.Smoking Related diseases lec 5	smoking related interstitial diseases	Pulmonary diseases of vascular origin: 1.Pulmonary Hypertension 2.Good pasture syndrome 3.Granulomatosis and polyangiitis (GPA)	