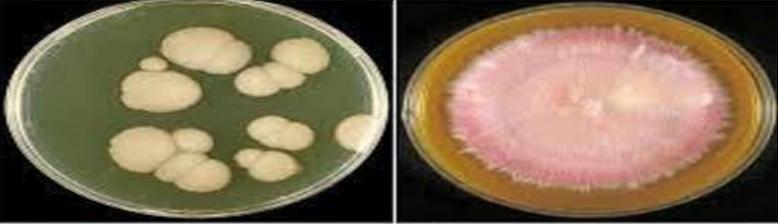


Fungal Encephalitis

Causative organisms of fungal encephalitis

<i>Cryptococcus neoformans</i>	This encapsulated yeast is a leading cause of fungal meningitis and encephalitis.
<i>Candida species</i>	<i>Candida albicans</i> and other <i>Candida</i> species, especially in neonates, elderly individuals, diabetics or prolonged antibiotic use .
<i>Aspergillus species</i>	<i>Aspergillus fumigatus</i> and other <i>Aspergillus</i> particularly those with hematological malignancies or recipients of solid organ transplants .
<i>Histoplasma capsulatum</i>	Particularly in immunocompromised individuals or those residing in endemic areas.
<i>Blastomyces dermatitidis</i>	
<i>Coccidioides immitis</i>	
<i>Mucoromycetes</i>	

Diagnosis of fungal infections

a) Sample	b) Culture
<p>According to the site of infection.</p> <p>1. Direct Microscopic Preparation:</p> <p>a) Unstained preparation: KOH (10 – 30%).</p> <p>b) Stained preparation: Lactophenol cotton blue stain</p>	<p>Media: Sabouraud's dextrose agar (SDA)</p>  <p><i>Candida albicans</i> in SDA <small>Source: Wikipedia</small> <i>Trichophyton terrestre</i> in SDA <small>Source: Wikipedia</small></p>
c) Histopathology	d) Woods Light
<p>Detect Fungi in tissue</p> 	<p>Helps in clinical diagnosis.</p> <p>Ultraviolet rays when comes in contact with mycotic areas of skin and hair produce fluorescent colors.</p> 

Opportunistic mycoses that cause encephalitis

- The opportunistic mycoses are those that affect debilitated and or immunocompromised individuals and are rare in normal individuals.
- They are:
 - a) Candidal infections
 - b) Aspergillosis

Predisposing factors:

- Extremes of age.
- Immunosuppression as in:
 - Pregnancy & Diabetes
 - Prolonged use of antibiotics, steroids or immunosuppression drugs.
- Traumatic conditions such as catheter.

a) Candida infections:

Source of infection:

- Endogenous (auto-infection): Present as normal flora in oral cavity, GIT, female genital tract and skin which is the major source of infection.
- Exogenous: Contact.

Causative agents:

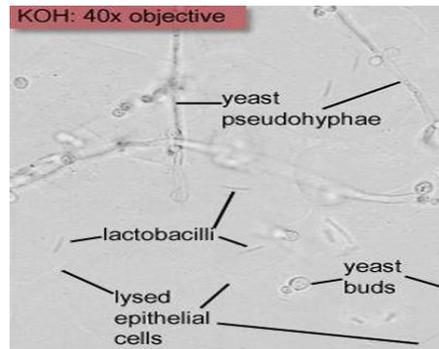
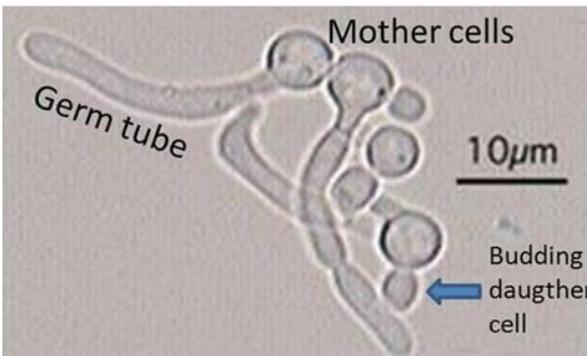
- Candidiasis caused by the yeast like *Candida albicans*, and other candida species.
- There are more than 200 species of Candida.

Lab diagnosis:

- Microscopic: **Unstained** preparation (KOH) / **Stained** preparation lactophenol-cotton blue stains. / **Detection** of yeast cells and pseudo-hyphae.
- Culture: On SDA → **White creamy colonies**.
- **Germ tube formation in serum** when grown at 37°C for 4 hours.

Anti-fungal treatment:

- Polyenes (Amphotericin-B)
- 5- Flucytosine.
- Azoles (Itraconazole, fluconazole, Voriconazole).
- Terbinafine, Griseofulvin, Caspofungin



b) Aspergillosis:

Mode of transmission:

- Environmentally by **inhalation of spores**.

Clinical form:

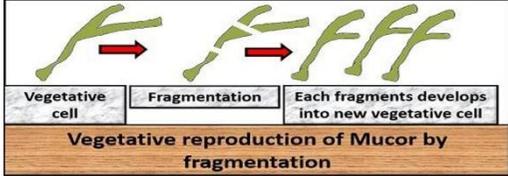
- **Fungal ball** in old TB cavity (Aspergilloma).
- **Allergic** type: Asthma.
- **Acute pneumonia** and **Disseminated encephalitis**

Diagnosis:

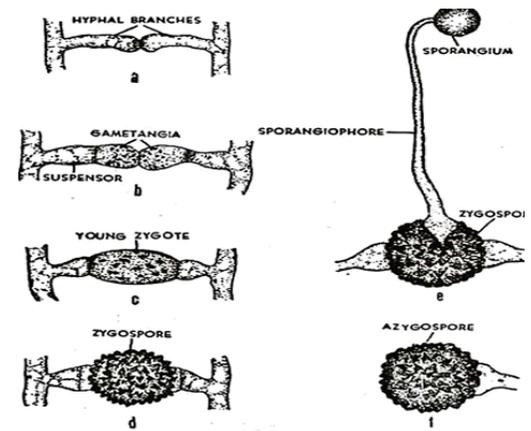
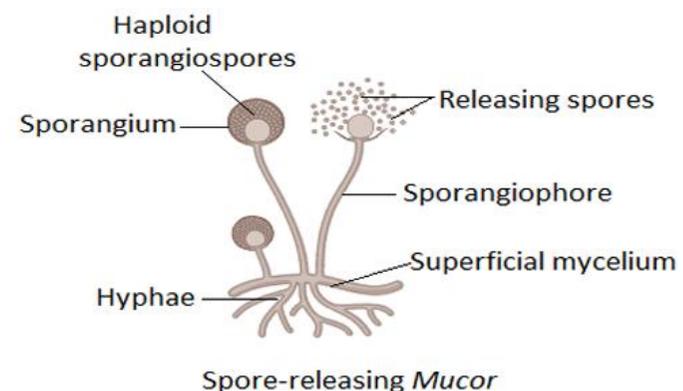
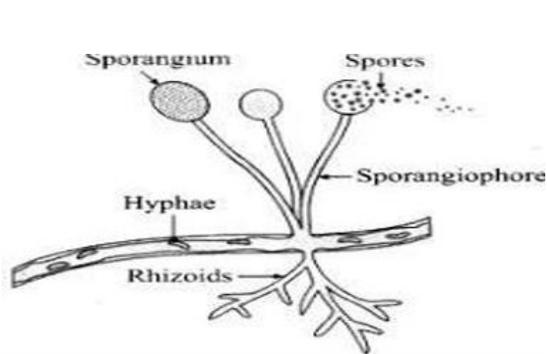
- Film stained by **lactophenol blue**: septated mycelium and Aspergillus head
- Culture: on SDA at room temperature for 24-48h → **Hairy colonies**



Mucormycosis (Zygomycosis) (The black fungus)

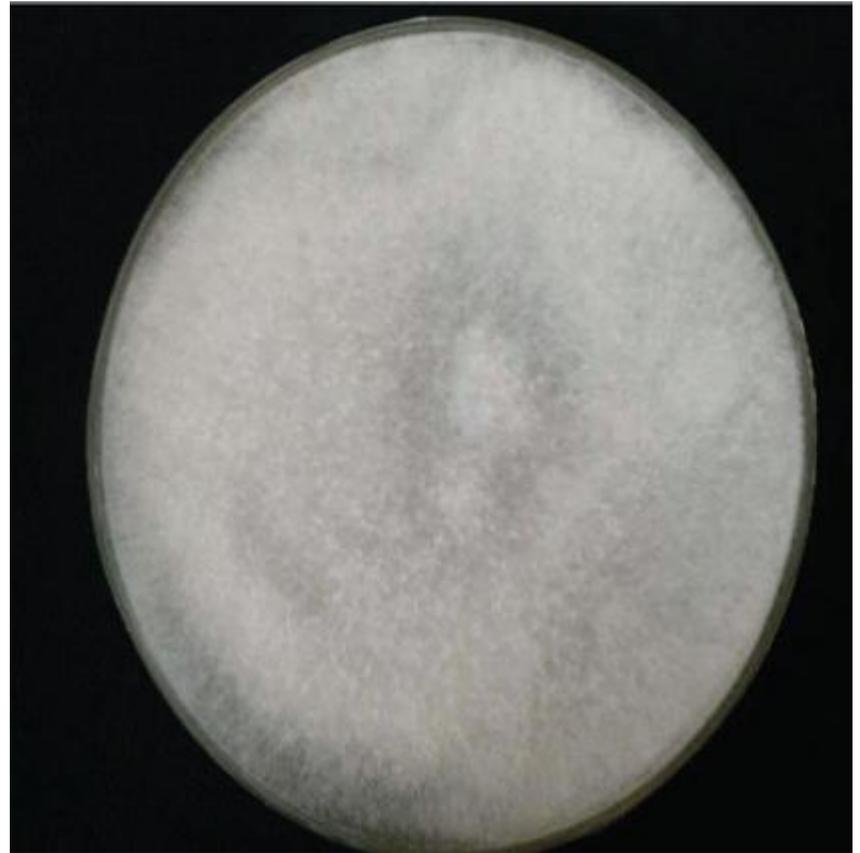
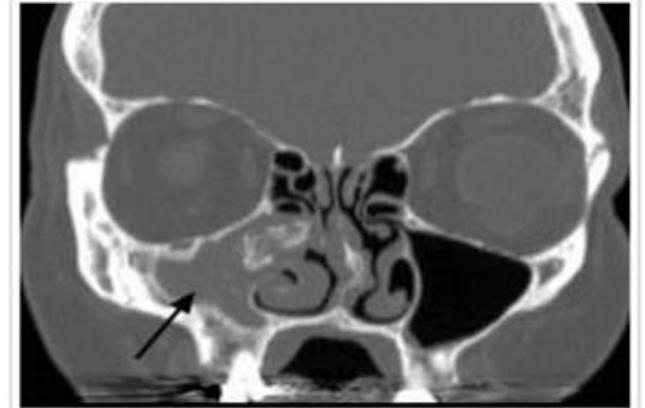
Description	Habitat	Reproduction	
<p>The fungal hyphae invade blood vessels, leading to tissue necrosis and potentially causing the affected tissue to turn black or dark in color. Mucorales fungi bind to glucose-regulated protein 78 on endothelial cells, promoting angioinvasion and tissue necrosis.</p> 	<p>Commonly found in soil, decaying organic matter, and various environmental substrates.</p>	<p>Asexual:</p> <p>a) Spores (primarily): These spores are formed at the ends of specialized hyphal structures called sporangiophores. The sporangia, which contain the spores, are often spherical or elongated structures that develop at the tips of the sporangiophores. When conditions are favorable, the sporangia rupture, releasing the spores into the surrounding environment. These spores can then germinate under suitable conditions to form new hyphae.</p> <p>b) Fragmentation (Picture)</p>  <p>Sexual: Hyphae from different mating types come into contact and fuse. Results in the formation of a zygospore, which contains the genetic material from both mating types.</p>	
Virulence factors	High-risk factor patients	Etiology	Clinical Diseases
<ul style="list-style-type: none"> a) Thermotolerance (wide ranges) b) Rapid growth (quick colonization) c) Tissue penetration (rhizoids and sporangiophores) d) Iron acquisition (↑ iron affinity) e) Proteolytic enzymes 	<ul style="list-style-type: none"> Diabetes with acidosis Corticosteroids treatment Sever burn Debilitating diseases 	<ul style="list-style-type: none"> Rhizopus (<i>R. oryzae</i>) Rhizomucor Mucor 	<p>a) Rhino-cerebral mucormycosis: Results from germination of the spores in nose & invasion of the hyphae into blood vessels (angiotrophic), causing thrombosis & infarction. The disease progress rapidly with invasion of sinuses, eye, cranial bone & brain. Blood vessels & nerves are damaged.</p> <p>b) Thoracic mucormycosis: Follows inhalation of the spores with invasion of lung parenchyma & vasculature, causing ischemic & massive tissue destruction</p>

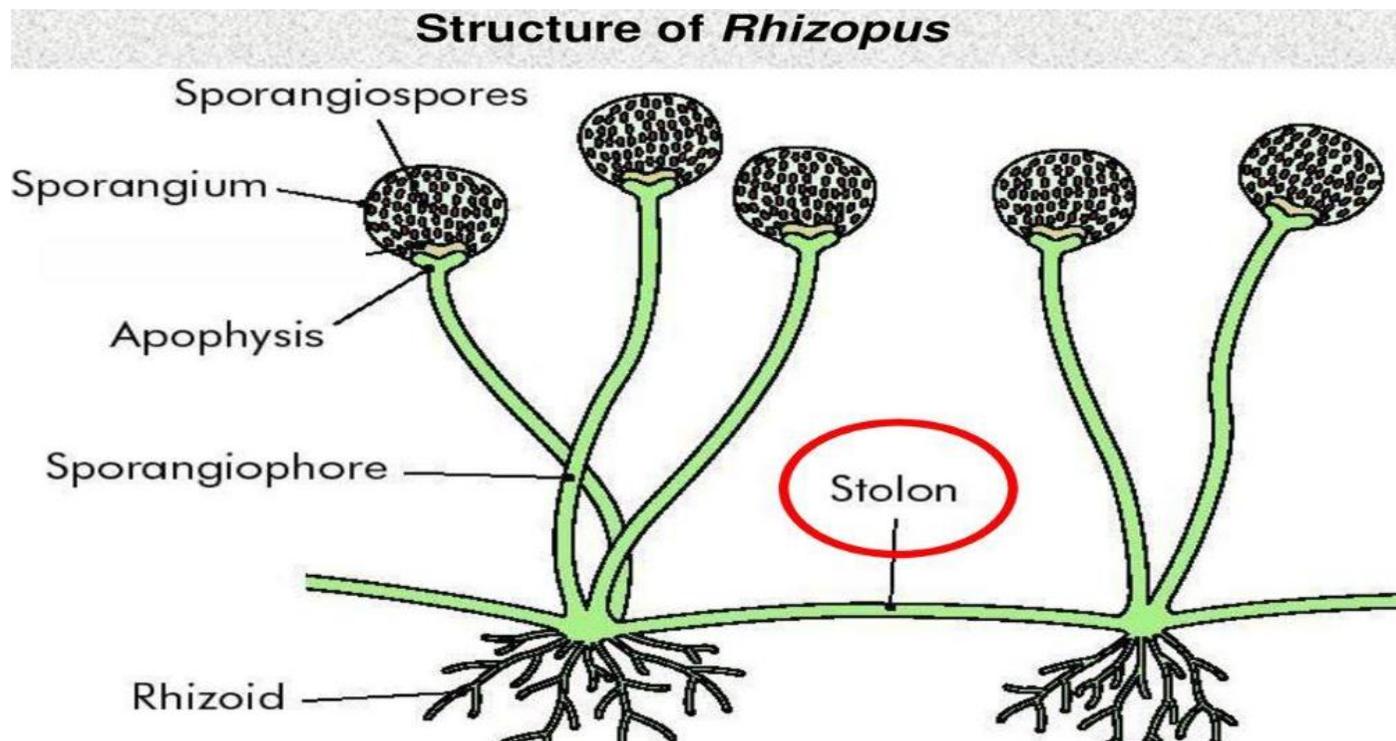
N.B.	Lab Diagnosis	Treatment	Recurrence
<p>Mucorales have very low β-glucan content in their cell wall, making echinocandins (which target β-glucan synthesis) ineffective.</p> <p>Acidosis leads to increased free iron levels, which promotes <i>Rhizopus</i> growth since Mucorales require iron for pathogenesis</p>	<p>a) Specimen: Nasal discharge, tissue or sputum</p> <p>b) Direct examination: 10% KOH mount of sample: irregular branching broad hyphae & non-septated or sparse septations, hyphae are hyaline (They lack pigmentation) with sporangia containing sporangiospores.</p> <p>c) Culture (SDA without cycloheximide): Rapidly growing cottony white to-gray or black colonies. Colony gray to black appearance like dirty snow.</p>	<p>Mucormycosis causes extensive vascular thrombosis and tissue necrosis, preventing antifungal penetration, making surgical debridement essential. Aggressive removal of all necrotic and infected tissue, even if disfiguring, improves survival.</p> <p>Mucormycosis is rapidly progressive, and waiting for biopsy confirmation can be fatal. The infection often spreads before necrosis is clinically evident. Early empirical liposomal amphotericin B therapy is crucial, as delayed treatment significantly worsens survival. Liposomal amphotericin B is nephrotoxic due to direct damage to renal tubular cells.</p>	<p>It often results from:</p> <p>a) Uncontrolled diabetes or persistent immunosuppression, allowing fungal regrowth.</p> <p>b) Incomplete surgical debridement, leaving residual fungal elements.</p> <p>c) Iron overload or metabolic abnormalities (e.g., persistent acidosis).</p> <p>d) Delayed immune reconstitution (common in post-COVID or transplant patients)</p>





Fungal Ball
Maxilla





■ **Quiz:**

1. **The appropriate media for the recovery of fungi is**

- a) MacConkey agar.
- b) Nutrient agar.
- c) Sabouraud's dextrose agar.
- d) CLED agar

Answer: C

2. *The common source of infection in candidiasis is the*

- a) Surrounding environment.
- b) Other patients.
- c) Patient's own flora

Answer: C

3. *A female complains of a white vaginal discharge & itching. Laboratory examination of the discharge reveals yeasts & pseudo-hyphae, what is the most likely diagnosis?*

- a) Aspergillosis.
- b) Candidiasis.
- c) Cryptococcosis
- d) Histoplasmosis

Answer: B

4. *Which of the following statements about the hyphae of Mucorales fungi is true?*

- a) They are heavily septate
- b) They are narrow and branched
- c) They are pigmented
- d) They are unicellular
- e) They are broad and non-septate

Answer: E

5. *Which of the following structures is most commonly observed in histopathological examination of tissues affected by mucormycosis?*

- A) Yeast cells
- b) Pseudo-hyphae
- c) Hyphal fragments
- d) Cystic structures
- e) Sporangia

Answer: E

A 45-year-old diabetic male presents to the emergency room with severe facial pain, fever, and black necrotic lesions on the palate and nasal mucosa. He reports a recent history of sinusitis that did not respond to antibiotics. On examination, there is extensive tissue necrosis in the affected areas, and nasal endoscopy reveals black eschars. A biopsy confirms the presence of broad, non-septate hyphae consistent with Mucorales fungi.

Q: What is the probable diagnosis?