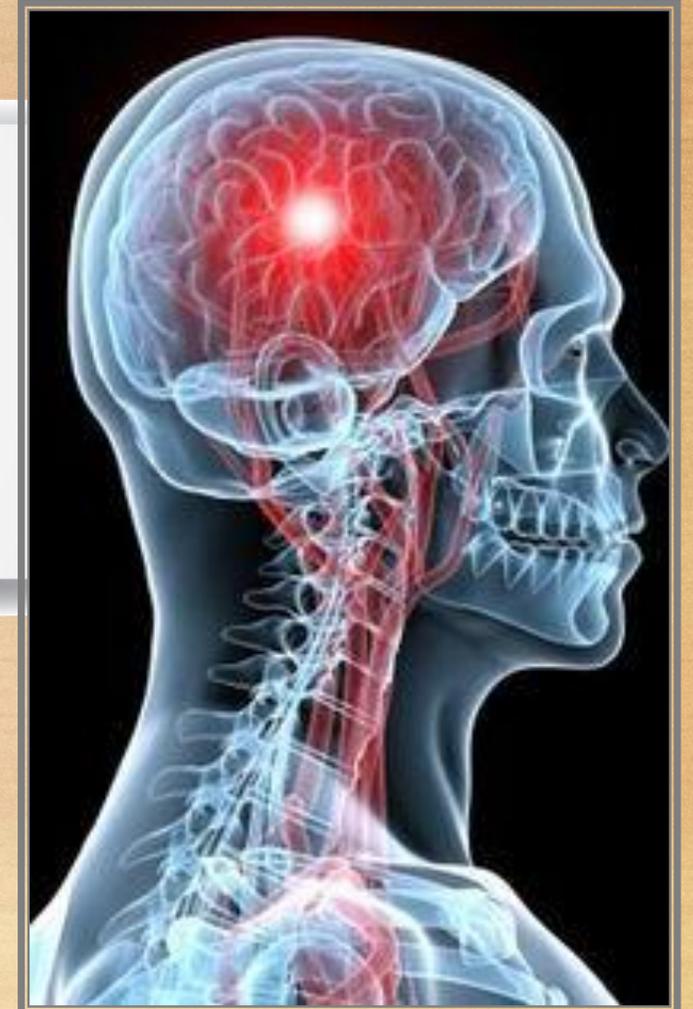


Fungal Encephalitis



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Learning outcomes

At the end of the lecture, the students should be able to:

- List causes of fungal encephalitis
- Identify the laboratory diagnosis of candida and aspergillus species.
- Describe etiology, virulence factors, clinical diseases and laboratory diagnosis of mucormycosis.

Causes of fungal encephalitis

1. **Cryptococcus neoformans**: This **encapsulated** yeast is a leading cause of fungal meningitis and encephalitis.
 2. **Candida species**: **Candida albicans** and other Candida species, especially in **neonates**, **elderly** individuals, **diabetics** or prolonged **antibiotic** use.
 3. **Aspergillus species**: Aspergillus **fumigatus** and other Aspergillus particularly those with **hematological malignancies** or recipients of solid organ **transplants**.
 4. **Histoplasma capsulatum**:
 5. **Blastomyces dermatitidis**:
 6. **Coccidioides immitis**:
 7. **Mucormycetes**:
- particularily in **immunocompromised** individuals or those residing in **endemic** areas.

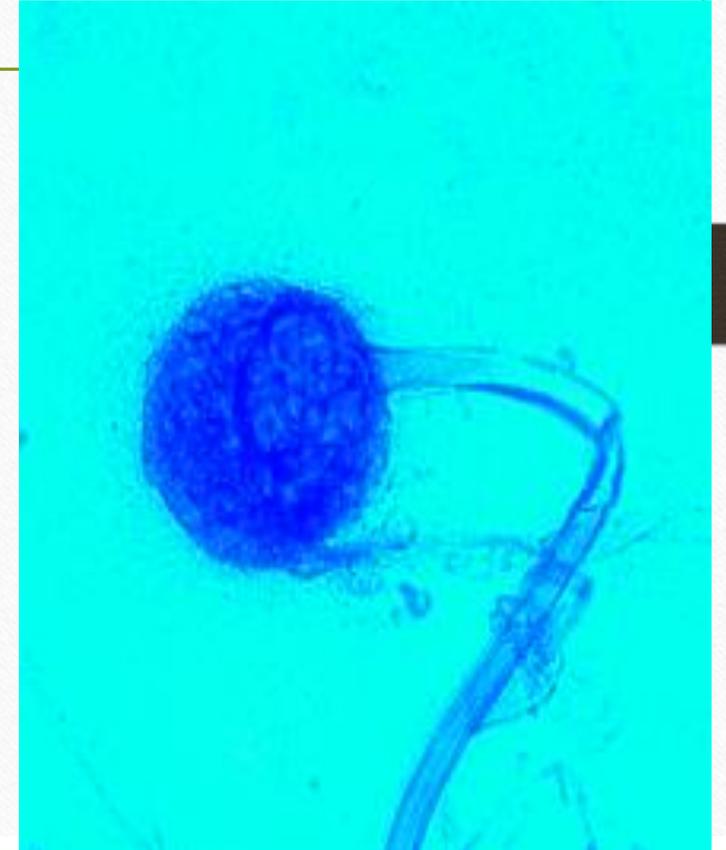


Diagnosis of fungal infections



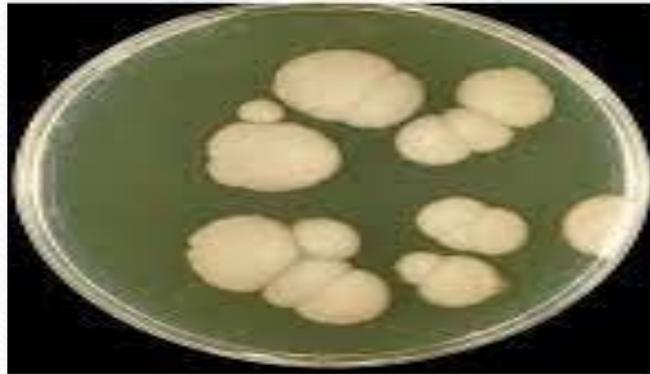
1-Sample

- **Sample:**
 - According to the site of infection * skin, hair & nail
- **1. Direct Microscopic Preparation:**
 - a) Unstained preparation: KOH (10 – 30%).
 - b) Stained preparation: Lactophenol cotton blue stain.



2. Culture for isolation of fungi

Media: **Sabouraud`s dextrose agar (SDA)**



Candida albicans in SDA

Source: Wikipedia



Trichophyton terrestre in SDA

Source: Wikipedia

3-Histopathology

detect Fungi in tissue

4- Woods light

- Helps in clinical diagnosis.
- Ultraviolet rays which when come in contact with mycotic areas of skin and hair produce fluorescent colours.



Infectious organisms glowing under Wood's lamp illumination

Q4

- The appropriate media for the recovery of fungi is

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

a) Sabouraud dextrose agar.

Opportunistic mycoses can cause encephalitis

- The opportunistic mycoses are those that affect debilitated and or **immunocompromised** individuals and are rare in normal individuals.
- 1- candida infection
- 2- Aspergillosis

Predisposing factors

Extreme of age.

Immunosuppression:

- Pregnancy and diabetes.
- Prolonged use of antibiotics, steroids or immunosuppressive drugs.

Traumatic conditions such as catheter.

Factors that can increase your risk of a yeast infection



Antibiotics,
birth control pills and
certain steroids.



Being pregnant.



A weakened
immune system.



Unmanaged
diabetes.

Candida Infection

- **Source of infection**

- **Endogenous:** (autoinfection): 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 is more than 200 species of Candida





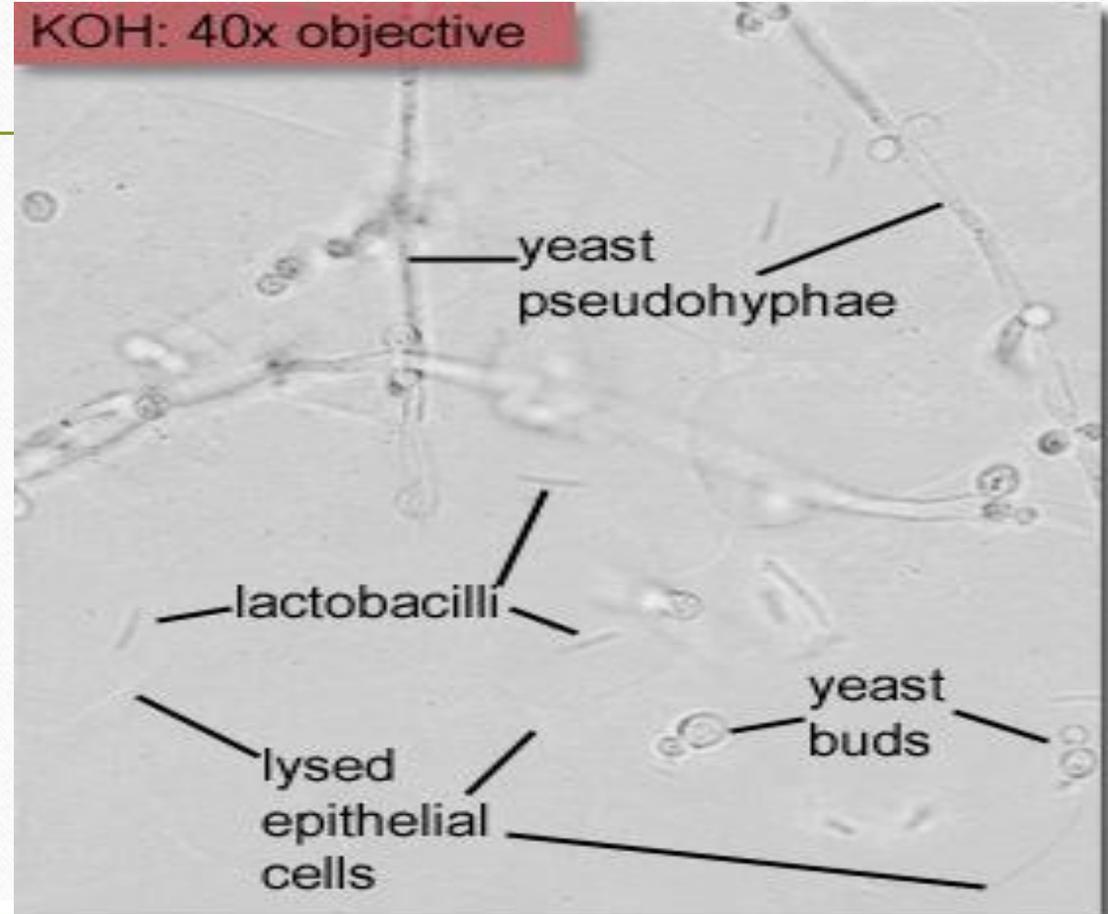
Laboratory diagnosis of Candidiasis



A. Direct:

1. Microscopic examination:

- Unstained preparation (**KOH**)
- Stained preparation **lactophenol-cotton blue** stains.
- For detection of yeast cells and **pseudohyphae**



Adapted with permission from Seattle STD/HIV Prevention & Training Center, Washington State Dept. of Health

2. Culture

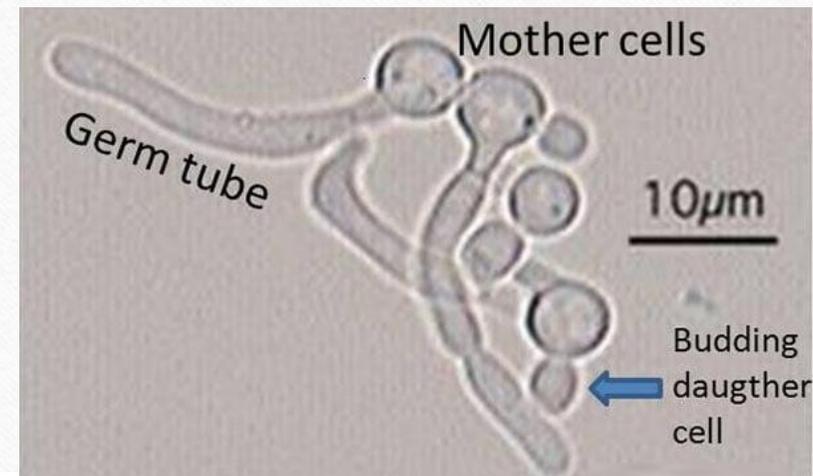
- On Sabouraud`s dextrose agar (SDA)

White creamy colonies



3-Germ tube formation

- Filamentation in the serum (Germ tube formation): When Candida is grown on human serum at 37°C for 4 hours, show **filamentous** outgrowth.



Q3

- The common source of infection in candidiasis is the
- a) Surrounding environment.
- b) Other patients.
- c) Patient's own flora

a) Patient's
own flora

Q4

- A female complains of a white vaginal discharge & itching. Laboratory examination of the discharge reveals yeasts & pseudohyphae, what is the most likely diagnosis?
 - a) Aspergillosis.
 - b) Candidiasis.
 - c) Cryptococcosis.
 - d) Histoplasmosis

Antifungal Treatment

Systemic antifungal

- Polyenes e.g Amphotericin-B
- Azoles e.g Itraconazole, fluconazole, Voriconazole.
- 5- Flucytosine.
- Terbinafine, Griseofulvin, Caspofungin.

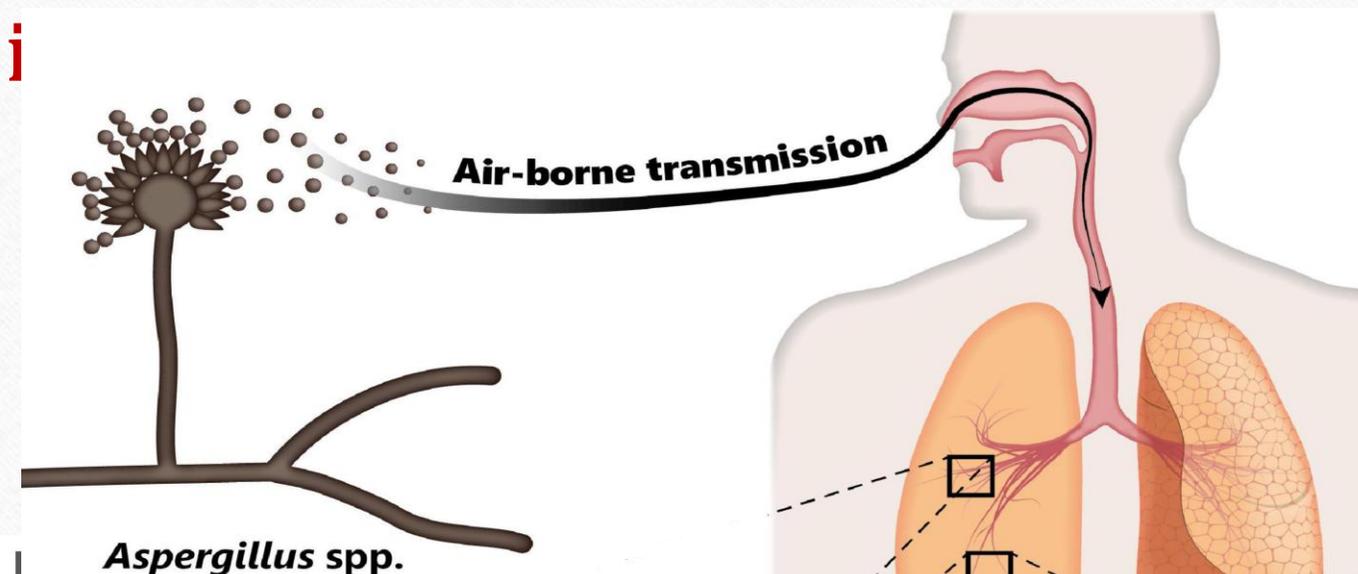


Aspergillus



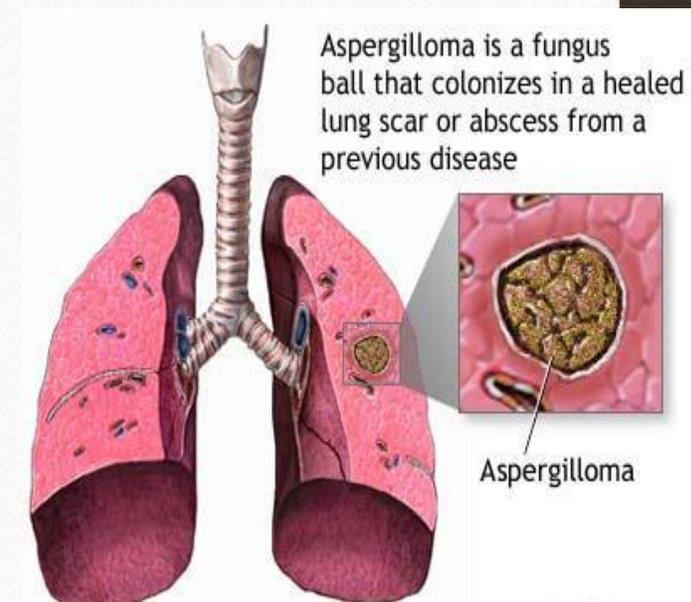
Aspergillosis

- Fungal infection by *Aspergillus* spp.
- **Mode of transmission:** Environmentally by



Clinical Form

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



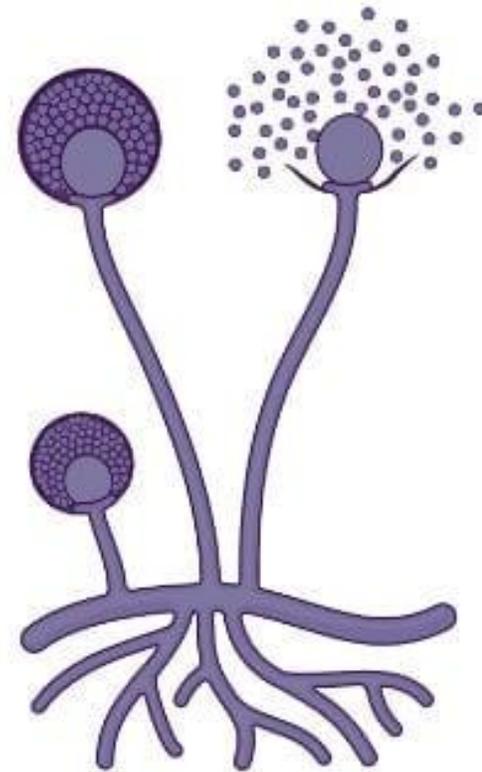
Diagnosis

- **Film stained by lactophenol blue: septated mycelium and Aspergillus head.**
- **Culture:**
 - On SDA incubated at room temperature for 24-48 hr.
 - **Hairy** colonies different in color according to the species



Mucormycosis (The black fungus)

- What is Mucormycosis?
- Habitat of order Mucorales
- Etiology of Mucormycosis
- Virulence Factors of Mucorales
- Mode of Transmission of Mucormycosis
- Pathogenesis of Mucormycosis
- Types or Forms of Mucormycosis
- Laboratory Diagnosis of Mucormycosis
- Treatment of Mucormycosis
- Prevention and Control of Mucormycosis
- Mucormycosis and COVID-19



WHY BLACK FUNGUS

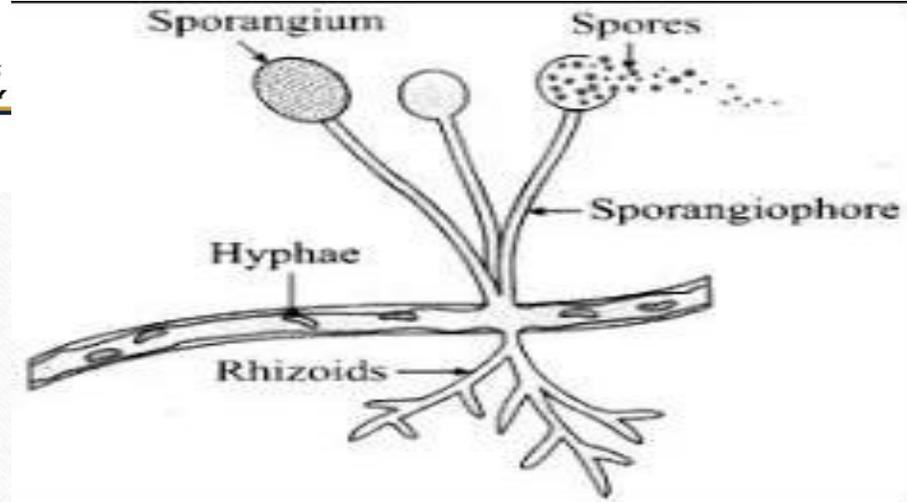


The fungal hyphae invade **blood vessels**, leading to tissue **necrosis** and potentially causing the affected tissue to turn black or dark in color. Mucorales fungi bind to **glucose-regulated protein 78** on endothelial cells, promoting angiogenesis and tissue necrosis.

Habitat

Habitat: commonly found in **soil**, decaying **organic** matter, and various **environmental** substrates.

Reproduction



A) Asexual :

1-primarily through the production of spores.

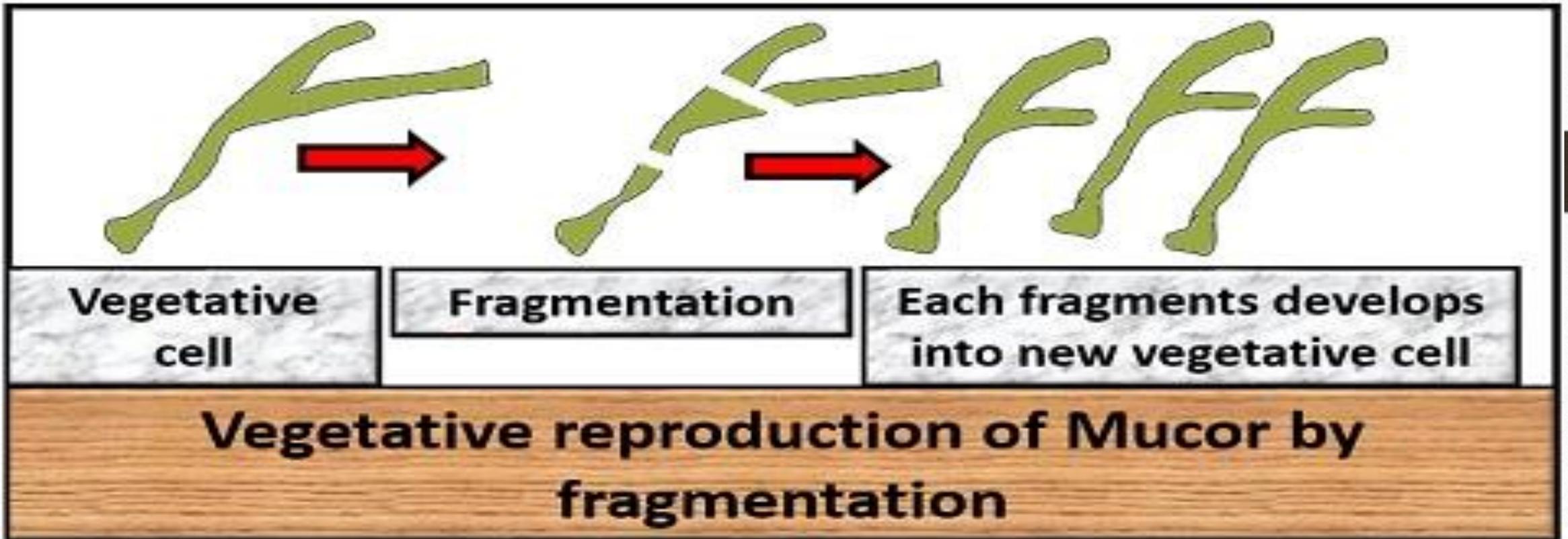
These spores are formed at the ends of specialized hyphal structures called **sporangiophores**.

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.

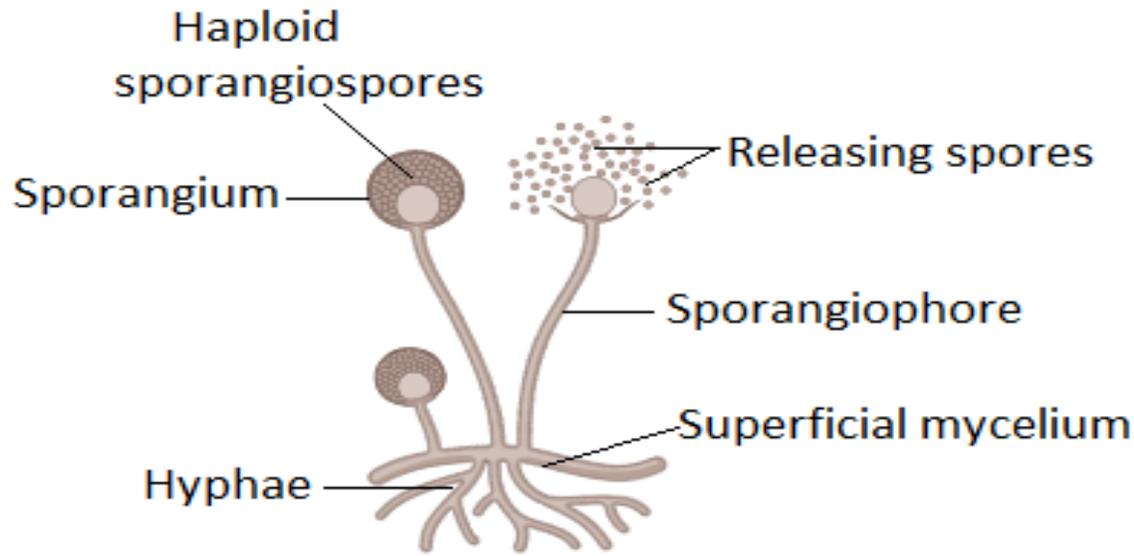
2-The fragmentation of hyphae.



B) Sexual reproduction:

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.



Spore-releasing *Mucor*

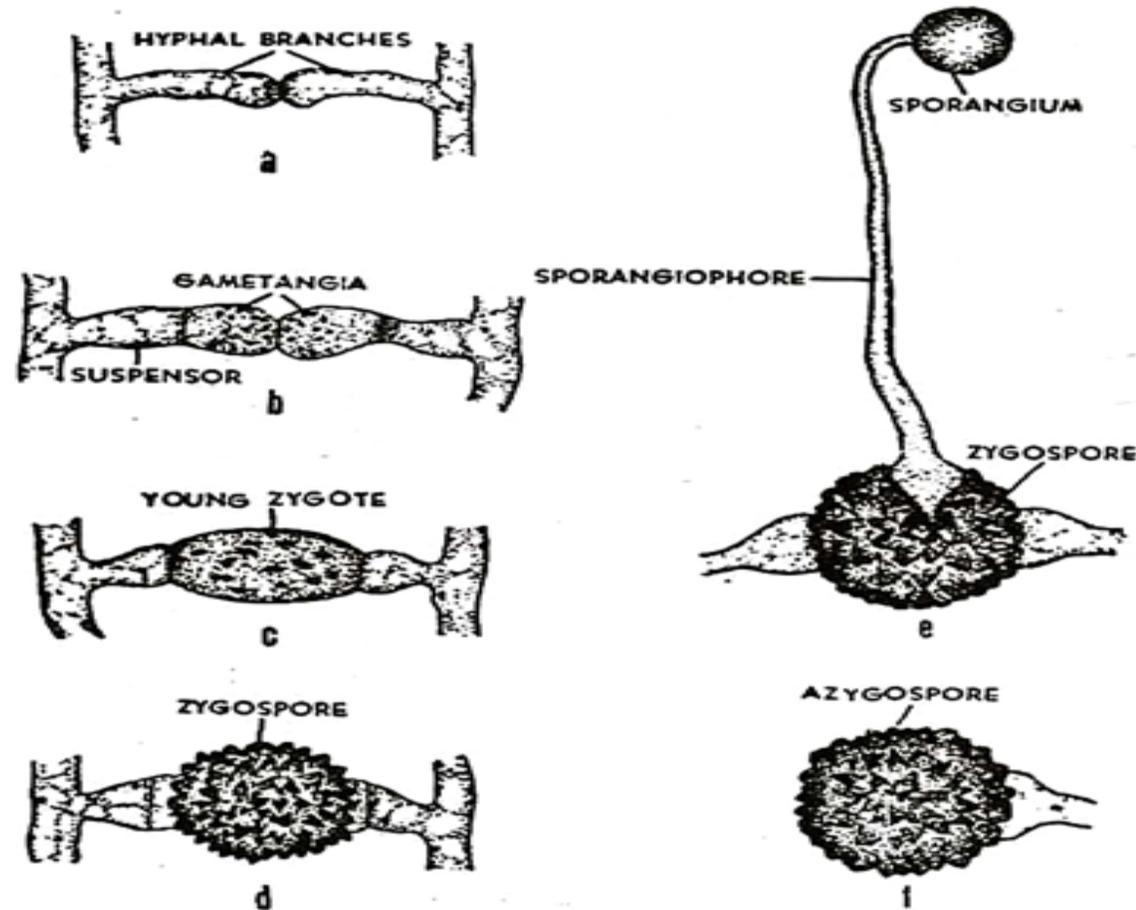


Fig. 194. *Mucor* : a-d—stages in the formation of Zygospore; e—zygospore germinating; f—an Azygospore.



Virulence factors of Mucorales fungi

- 1. Thermotolerance:** thrive in a wide range of temperatures.
- 2. Rapid growth:** allowing them to quickly colonize and invade host tissues.
- 3. Ability to penetrate tissues:** rhizoids and sporangiophores, which aid in the penetration and invasion of host tissues.
- 4. Iron acquisition:** have high affinity for iron and can acquire iron from host tissues, allowing them to grow and proliferate within the host.
- 5. Production of proteolytic enzymes:** degrade host tissues, facilitating tissue invasion and damage.



Mucormycosis (Zygomycosis)

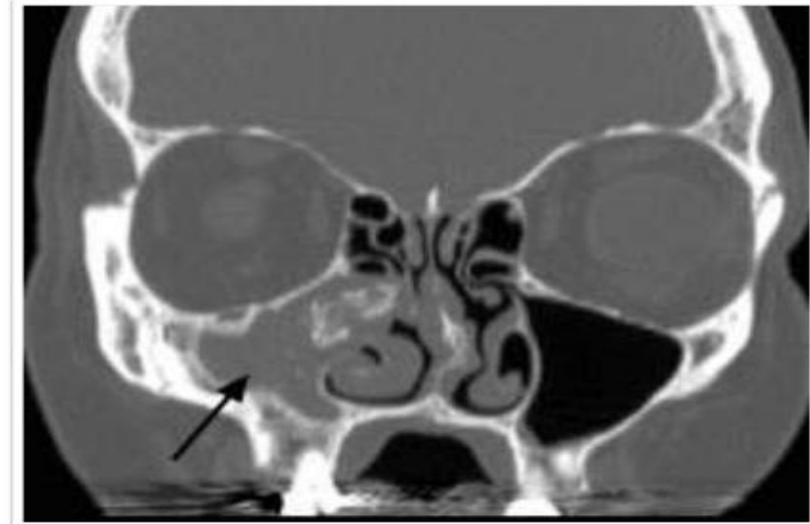
- **habitat:** The fungal species belonging to the order Mucorales can be found throughout the environment in different sources ranging from soil to vegetables.
- **Patients:** with acidosis associated with diabetes mellitus, corticosteroids treatment, sever burn & other debilitating diseases
- **Etiology:** *Rhizopus (R. oryzae), Rhizomucor & Mucor.*



21-Apr-17

DR.R.Malarvizhi MBBS,DLO

Fungal Ball
Maxilla



Clinical Diseases

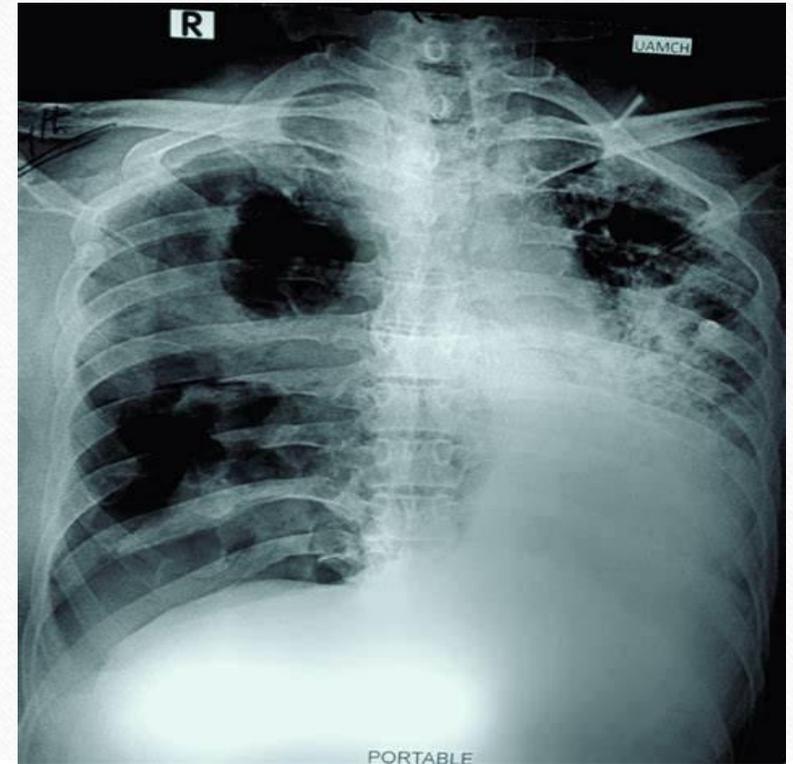
1. Rhinocerebral mucormycosis:

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.

2. Thoracic mucormycosis:

Follows **inhalation** of the spores with invasion of lung **parenchyma** & **vasculature** causing ischemic necrosis & massive tissue destruction.

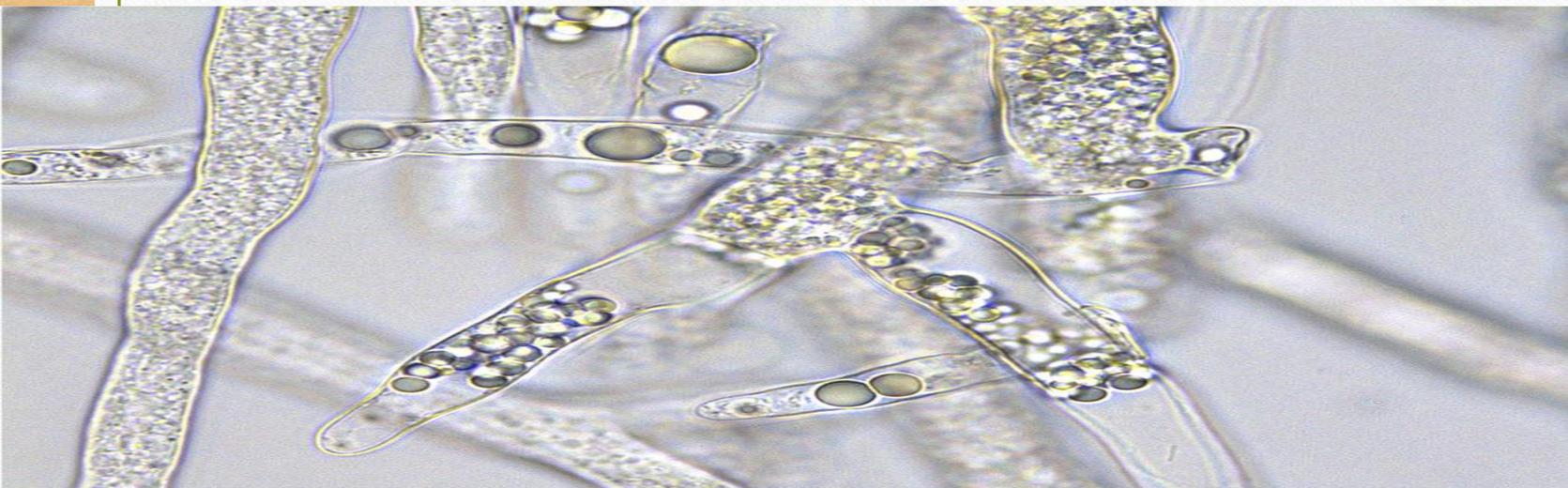




Mucorales have very low β -glucan content in their cell wall, making echinocandins (which target β -glucan synthesis) ineffective. Acidosis leads to increased free iron levels, which promotes *Rhizopus* growth since Mucorales require iron for pathogenesis.

Laboratory Diagnosis

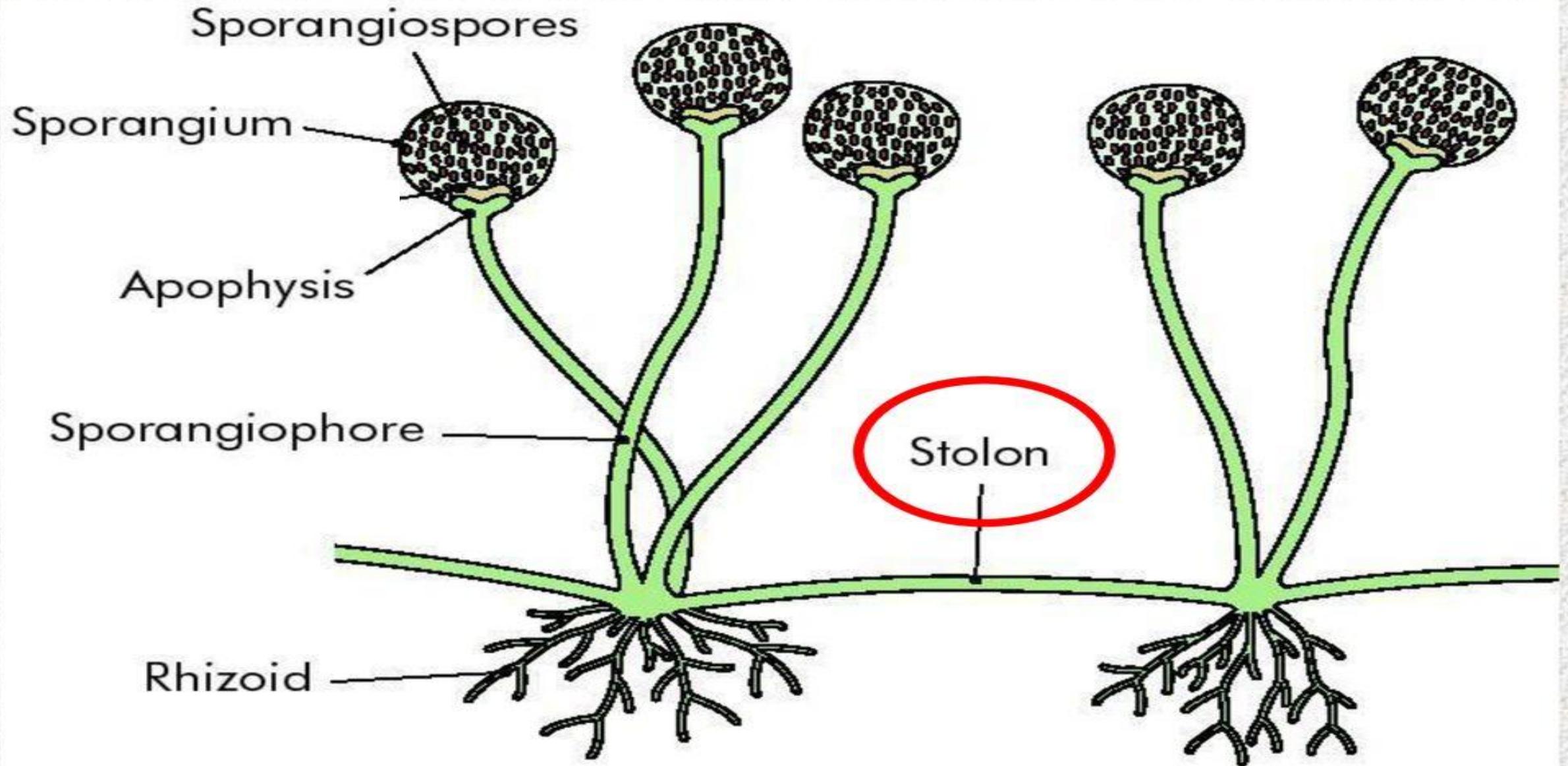
- **Specimen:** nasal discharge, tissue or sputum.
- **Direct examination:** 10% KOH mount of sample: **irregular branching broad** hyphae & **non-septated** or **sparse** septations, hyphae are **hyaline** (the translucent or colorless appearance. they lack pigmentation) with sporangia containing sporangiospores.





Hyaline hyphae with sporangia containing sporangiospores.

Structure of *Rhizopus*



Question

- 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

E) They are broad and non-septate

Question

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

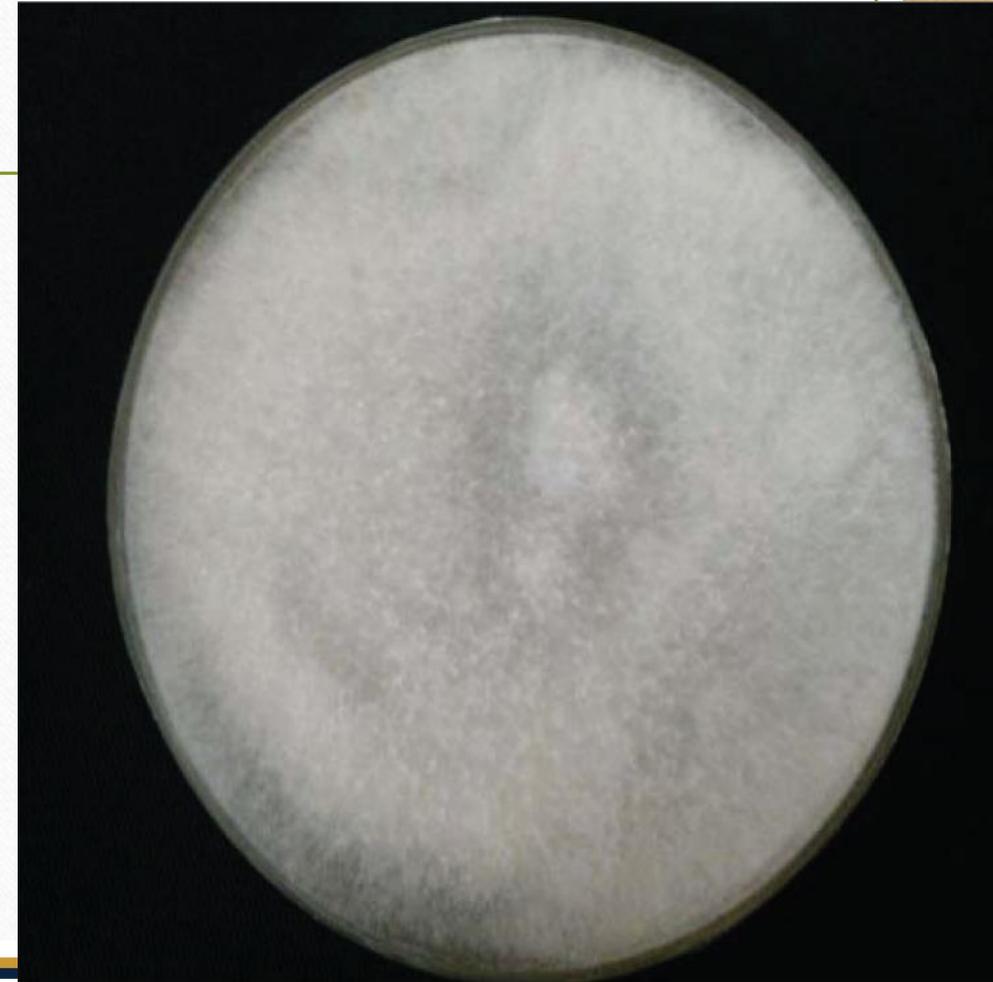
- A) Yeast cells
- b) Pseudohyphae
- c) Hyphal fragments
- d) Cystic structures
- e) Sporangia

e) Sporangia

Culture on SDA without cyclohexamide to show:

Rapidly growing **cottony white-to-gray or black** colonies

Colony gray to black appearance like **dirty snow**.



Treatment

- 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.
- 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.

Recurrent mucormycosis often results from:

- Uncontrolled **diabetes** or persistent immunosuppression, allowing fungal regrowth.
- **Incomplete surgical debridement**, leaving residual fungal elements.
- **Iron overload** or metabolic abnormalities (e.g., persistent acidosis).
- **Delayed immune reconstitution** (common in post-COVID or transplant patients).

Case scenario

- 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.
- **What is the probable diagnosis?**



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THANK
YOU

Akbarian

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Thank You!

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