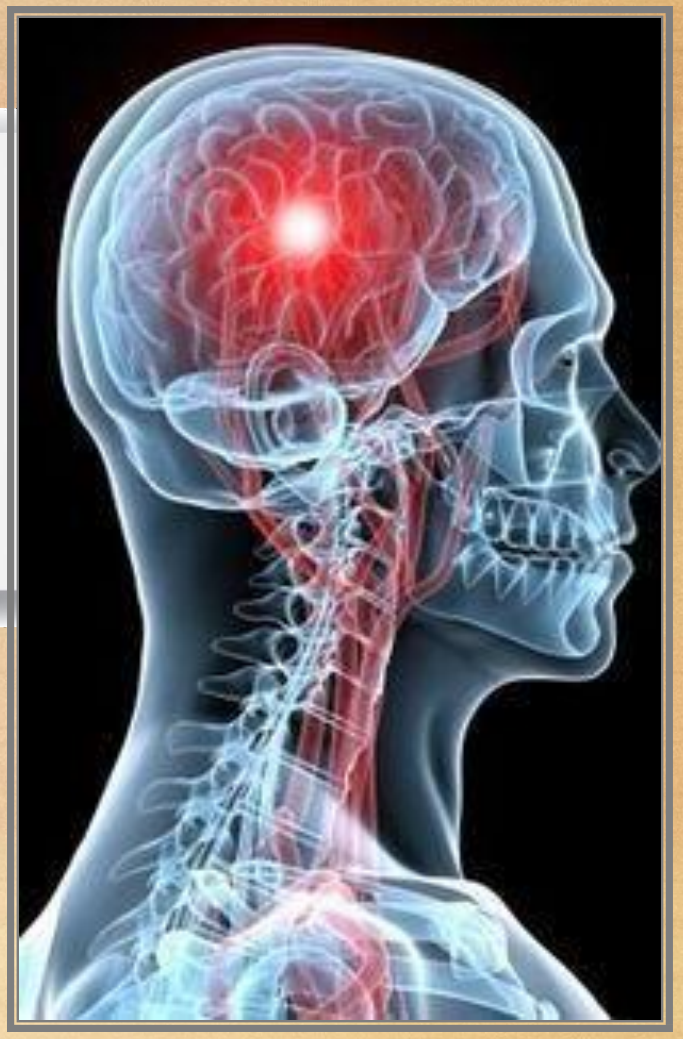
Fungal Encephalitis



Contact	Official email
Prof. Niveen Adel Mohamed El-wakeel	niveen10@gmail.com
Dr.Amany Elmatbouly Elsayed	amanielmatbouly@gmail.com
Dr.Aya Ahmad Elnegery	ayaelnegery@mans.edu.eg
Dr. Nada Hamid Qandeel	nadahamid@mans.edu.eg
Dr. Lamis Mohamed Taha	Lamis_mohamed@mans.edu.eg
Dr. Aya Gamal Borham	ayagamalborham@mans.edu.eg
Dr. Azza Mohamed Mamon	Azzam2010@mans.edu.eg

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

الاشهر الل بتعمل
Meningitis

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**:

particularly in **immunocompromised** individuals or those residing in **endemic** areas.

Diagnosis of fungal infections

1-Sample

- **Sample:**

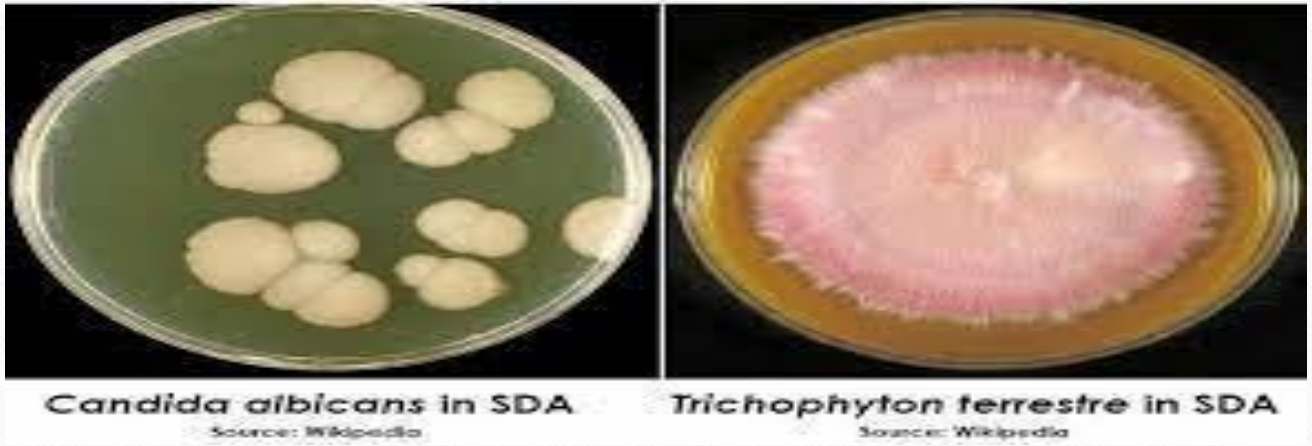
- According to the site of infection * skin, hair & nail

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

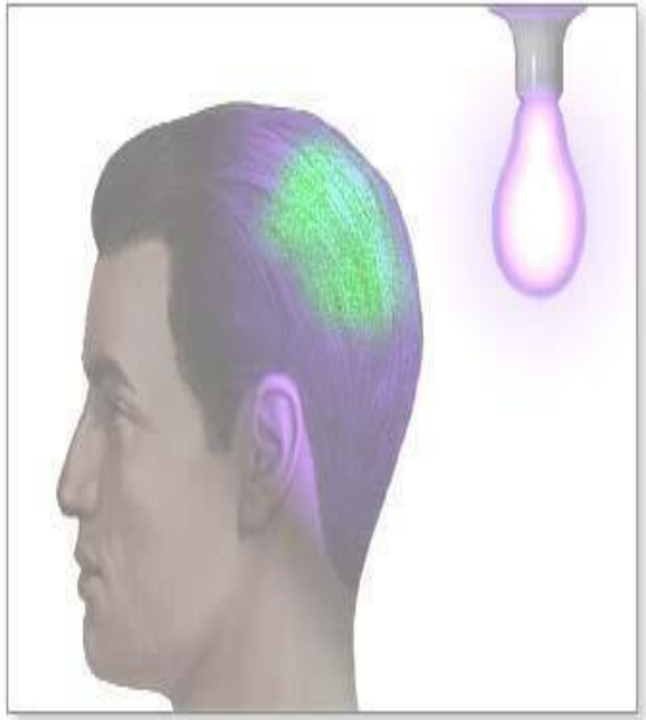
Trichophyton terrestre in SDA
Source: Wikipedia

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

ADAM.

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

SAQ

- The opportunistic mycoses are those that affect debilitated and or **immunocompromised** individuals and are rare in normal individuals.

- 1- candida infection

- 2- Aspergillosis

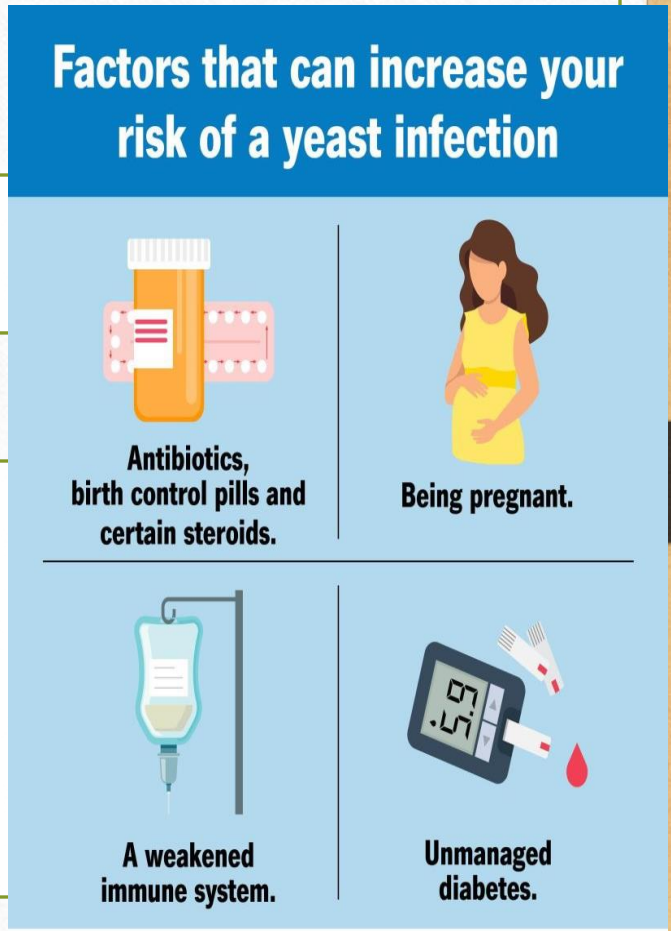
Predisposing factors

Extreme of age.

Immunosuppression:

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

Traumatic conditions such as catheter.



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

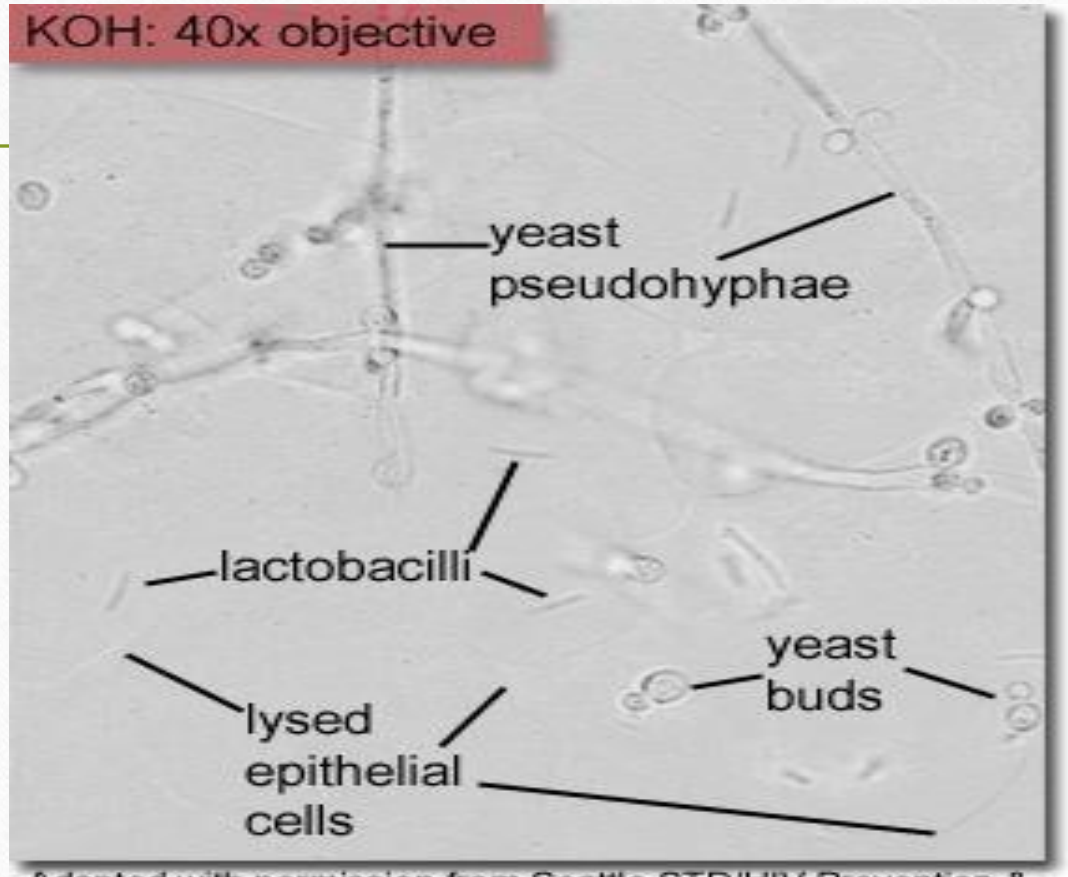
- Candidiasis caused by the **yeast like** *Candida* ***albicans***, and other candida species
- There is more than 200 species of Candida

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

Mcq

2. Culture

- On Sabouraud`s dextrose agar (SDA)

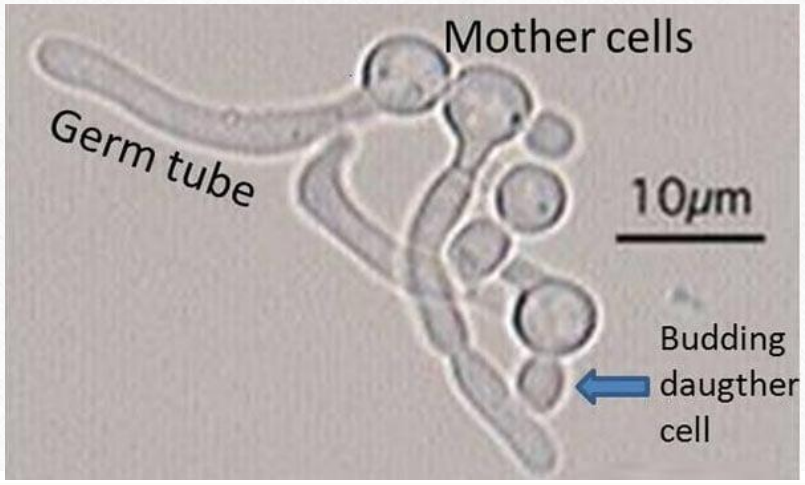
White creamy colonies

3-Germ tube formation

SAQ

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

يفرق بين الكانددا البيكان و بين باقية الانواع



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

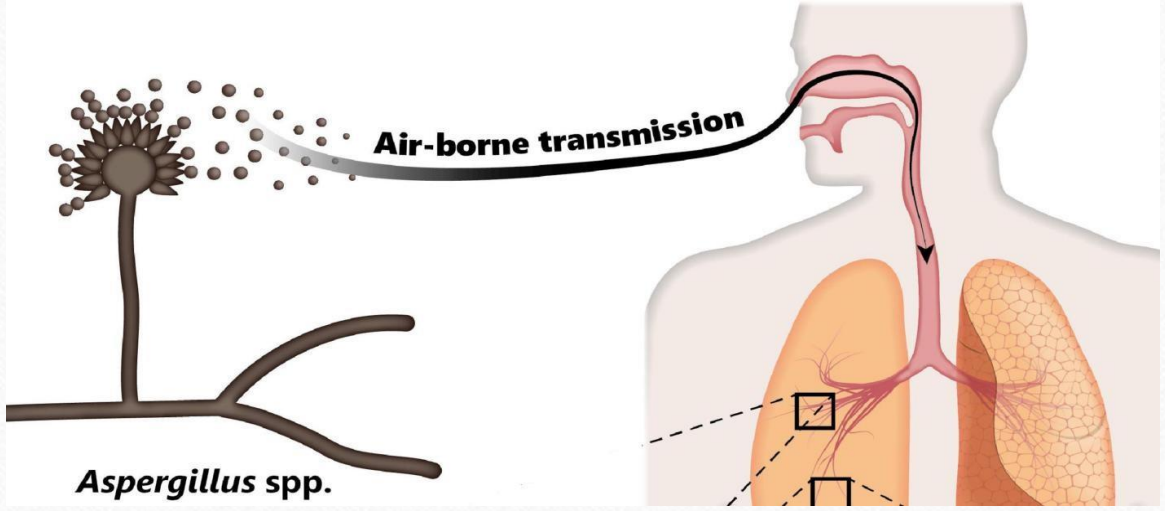
Systemic antifungal

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

Aspergillus

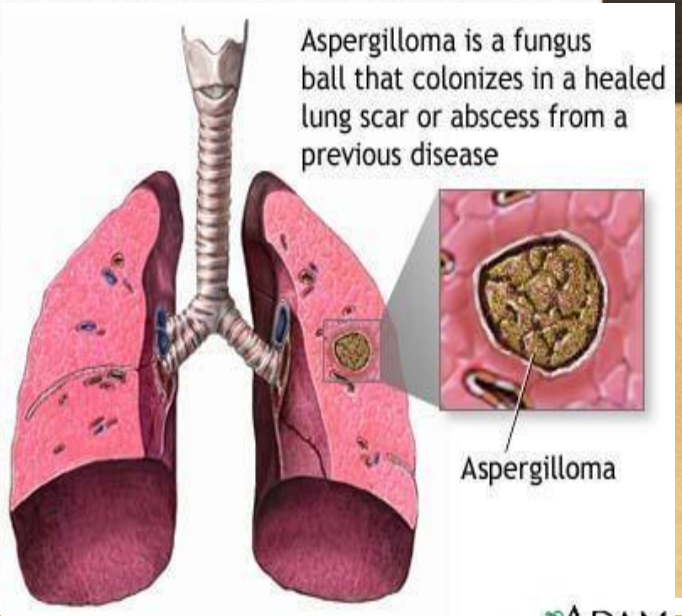
Aspergillosis

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



Clinical Form

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



Diagnosis

Mcq

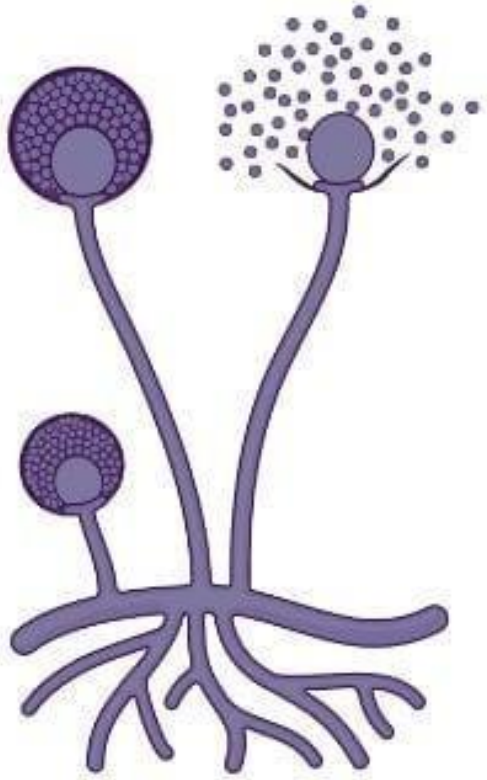
- **Film stained by lactophenol blue: septated** mycelium and Aspergillus **head**.

- **Culture:**
  - On SDA incubated at room temperature for 24-48 hr.
  - **Hairy** colonies different in color according to the species

Mcq

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

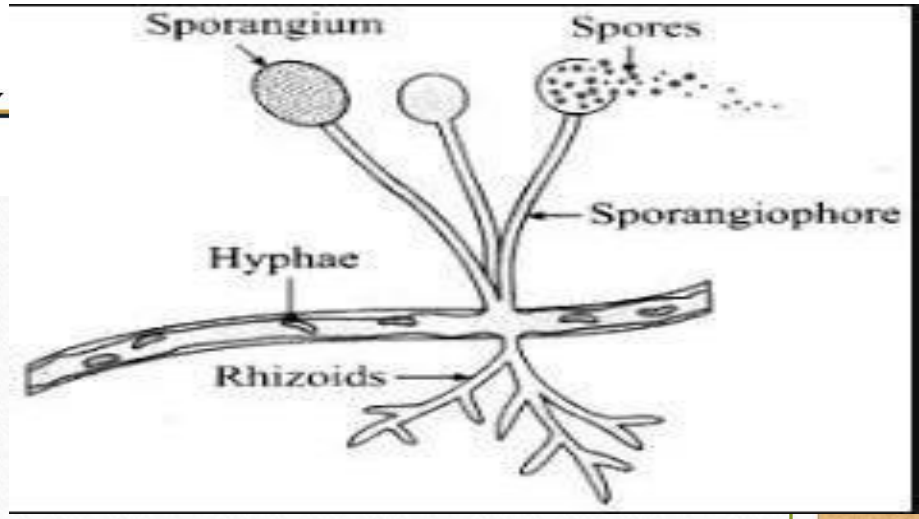
The fungal hyphae invade blood vessels, leading to tissue necrosis and potentially causing the affected tissue to turn black or dark in color. Mucorales fungi bind to glucose-regulated protein 78 on endothelial cells, promoting angioinvasion and tissue necrosis.

Mcq

Habitat

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

Reproduction



A)Asexual :

1-primarily through the production of spores.

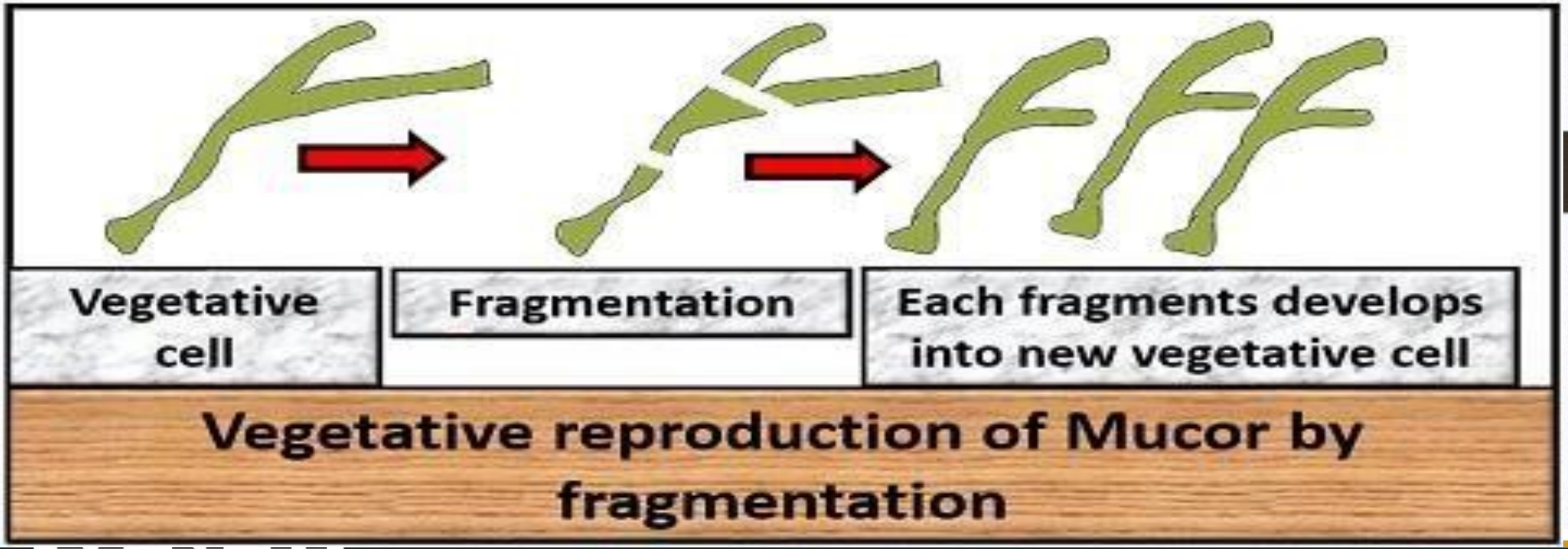
These spores are formed at the ends of specialized hyphal structures called sporangiophores.

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.

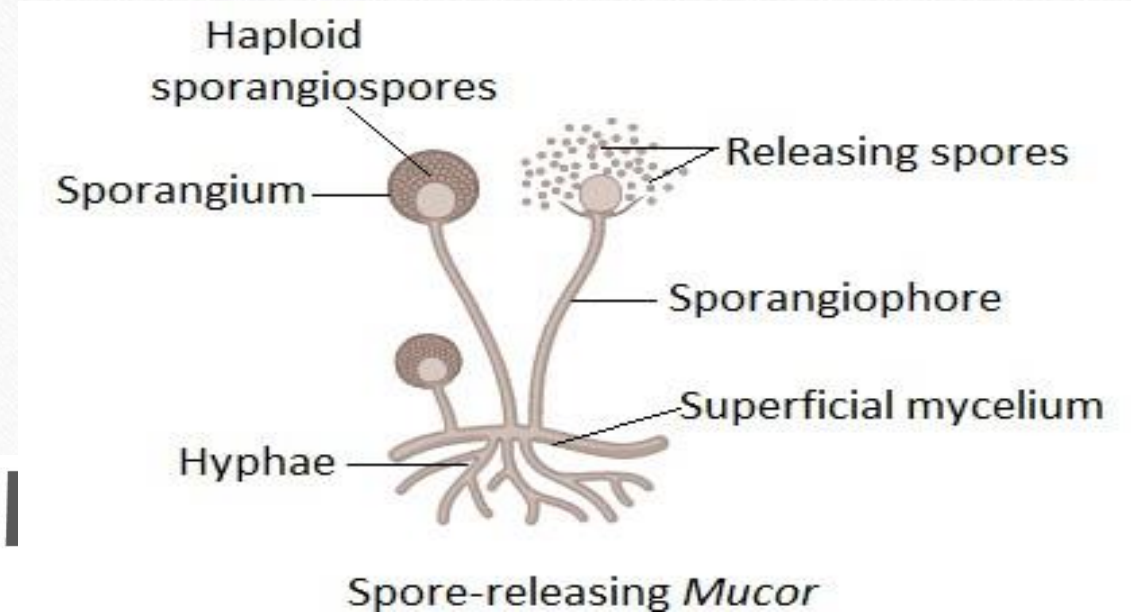


B) Sexual reproduction:

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.

Mcq



Spore-releasing *Mucor*

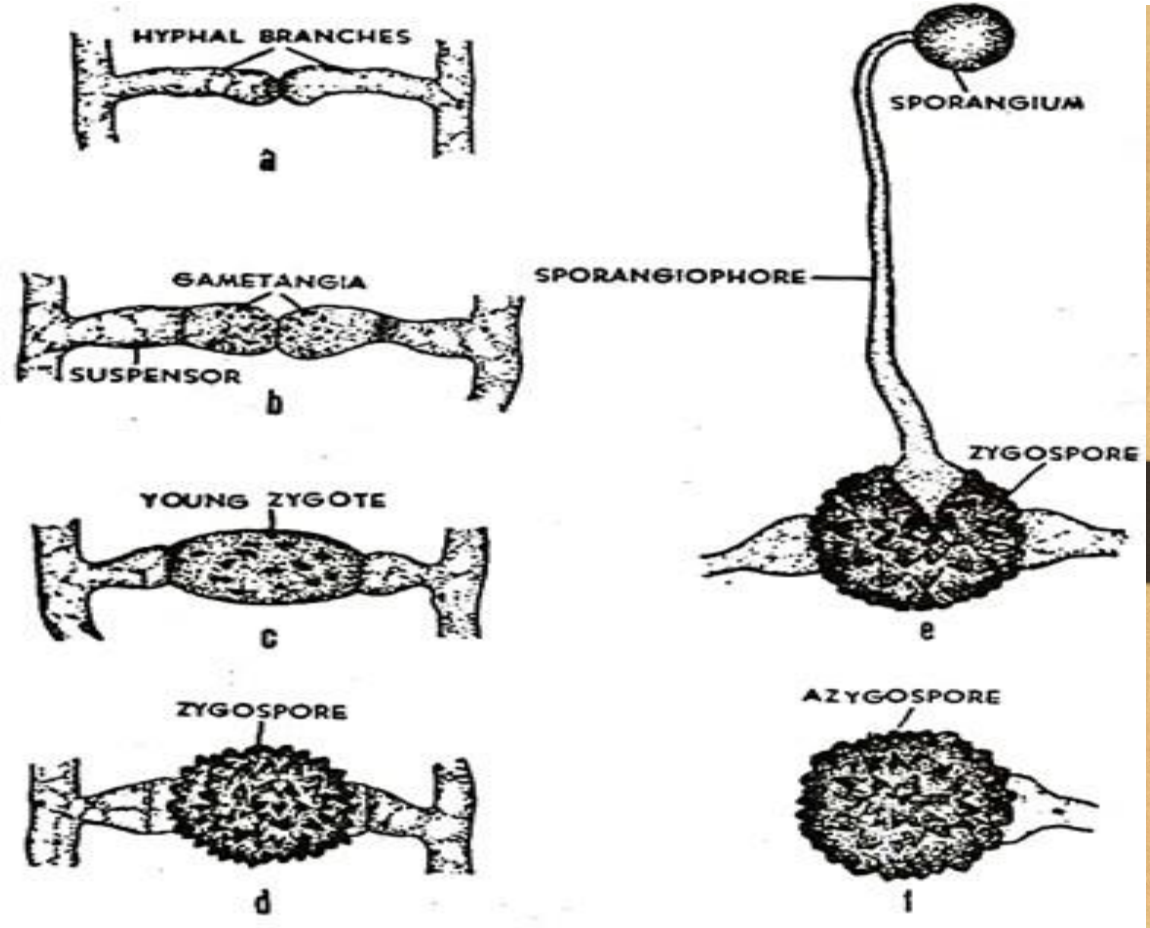


Fig. 194. *Mucor* : a-d—stages in the formation of Zygospore; e—zygospore germinating; f—an Azygospore.

Virulence factors of Mucorales fungi

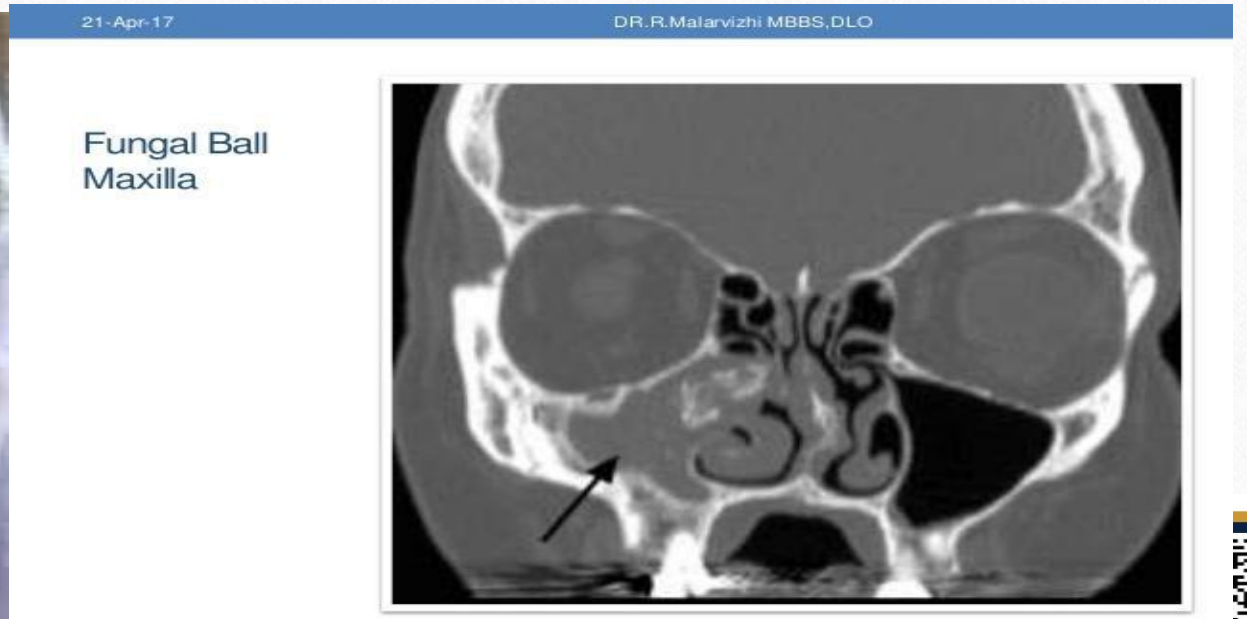
1. **Thermotolerance:** thrive in a wide range of temperatures.
2. **Rapid growth:** allowing them to quickly colonize and invade host tissues.
3. **Ability to penetrate tissues:** rhizoids and sporangiophores, which aid in the penetration and invasion of host tissues.
4. **Iron acquisition:** have high 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

Mcq

- **Etiology:** *Rhizopus (R. oryzae), Rhizomucor & Mucor.*



Clinical Diseases

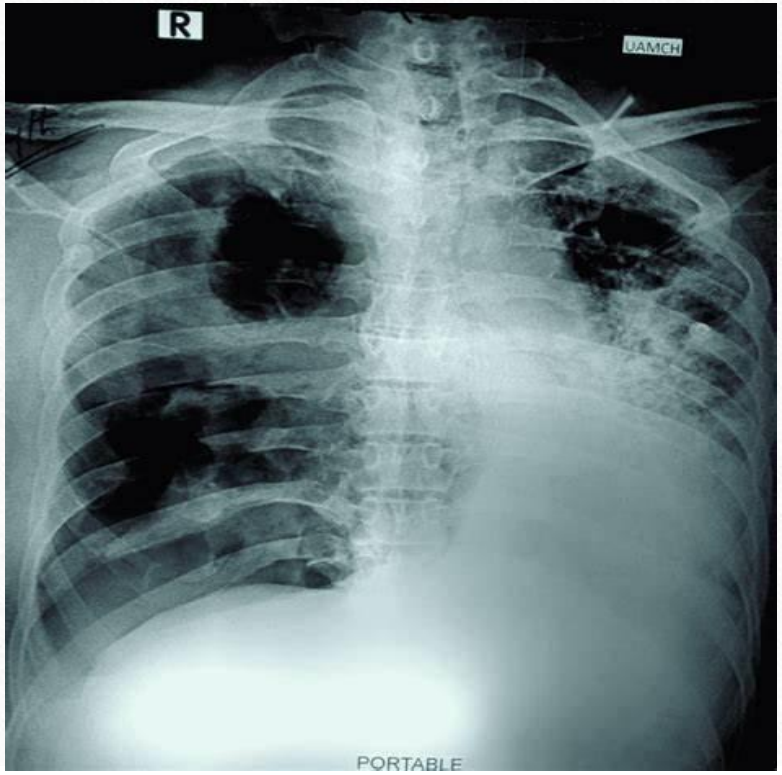
1. Rhinocerebral mucormycosis:

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.



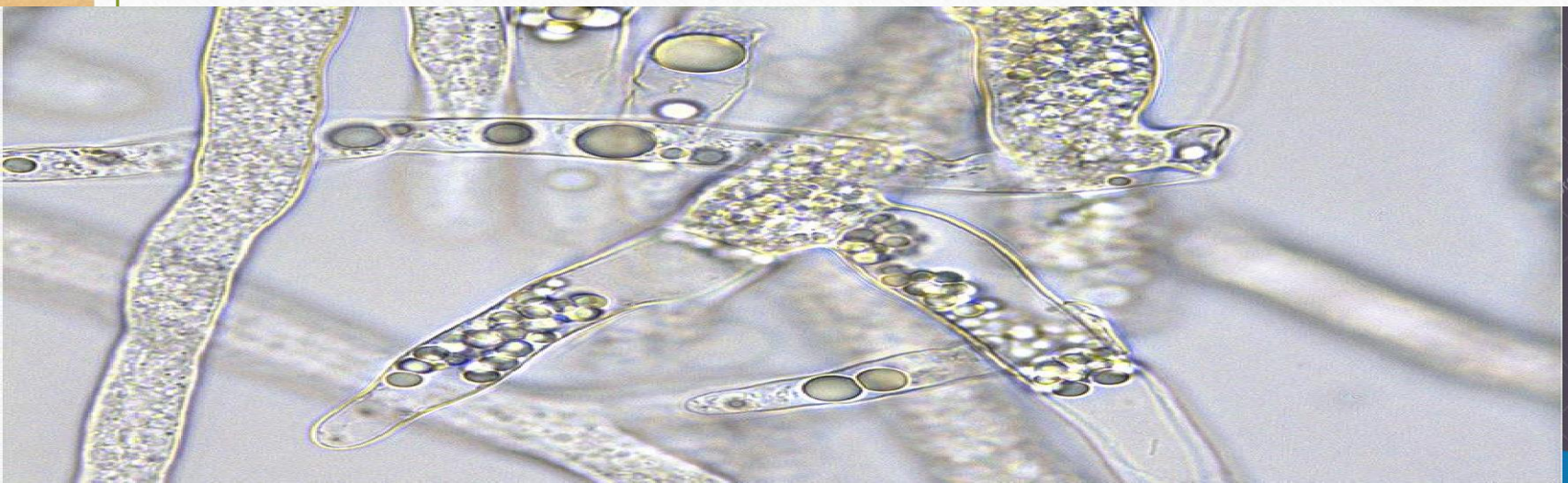
Mcq

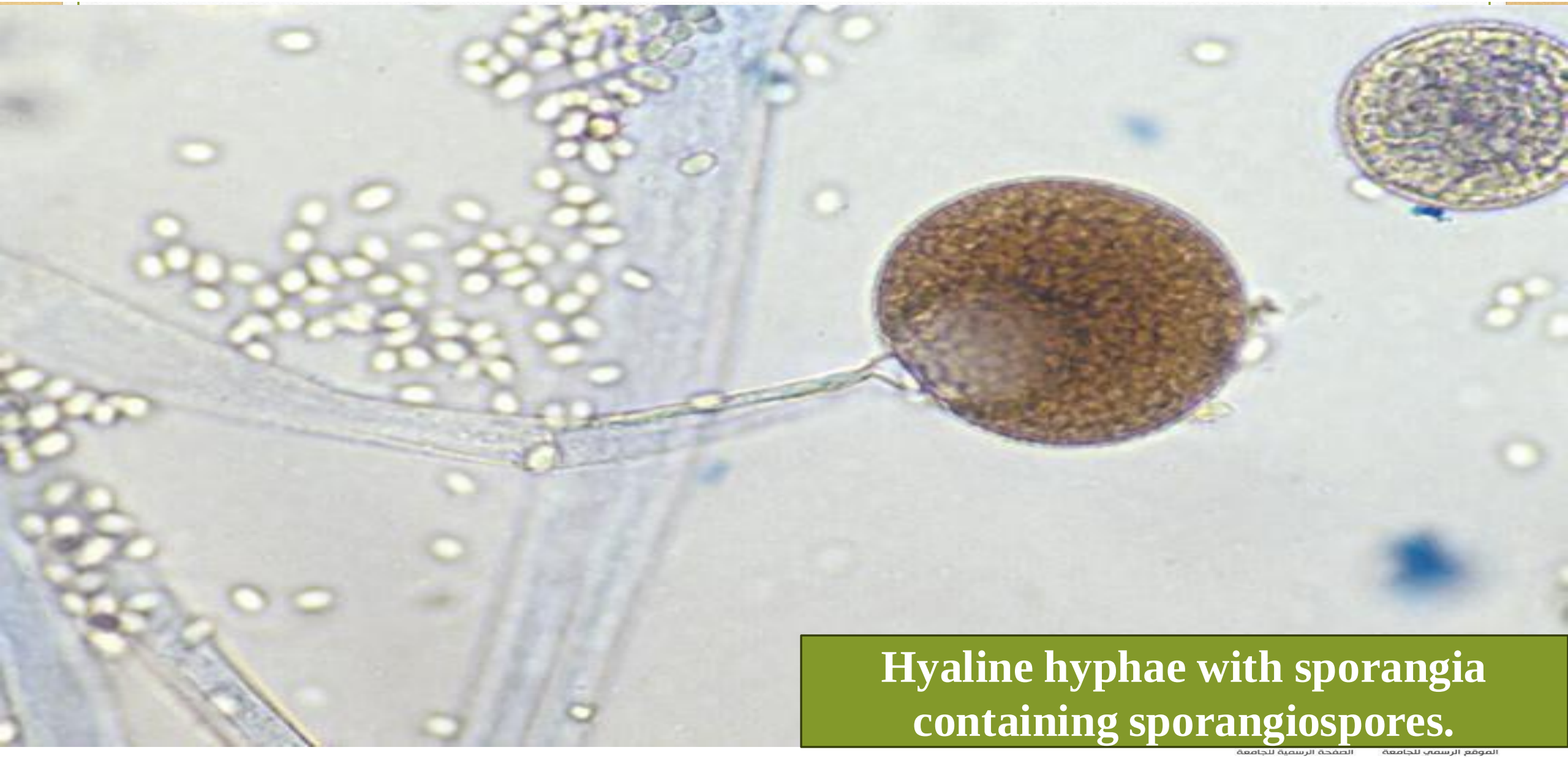
Mcq

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

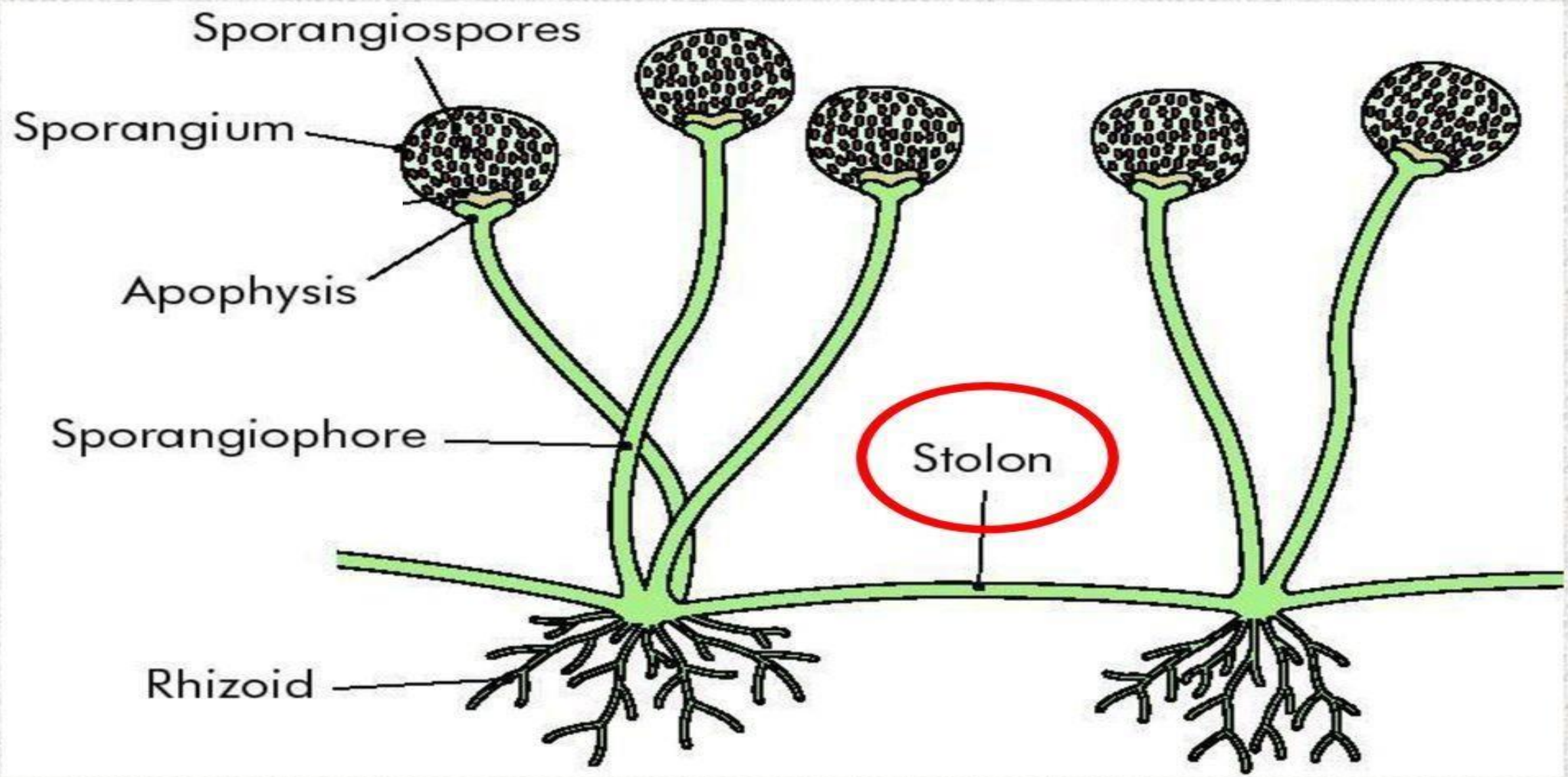
- **Specimen:** nasal discharge, tissue or sputum.
- **Direct examination:** 10% KOH mount of sample: irregular branching broad hyphae & non-septated or sparse septations, hyphae are hyaline (the translucent or colorless appearance. they lack pigmentation) with sporangia containing sporangiospores.





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

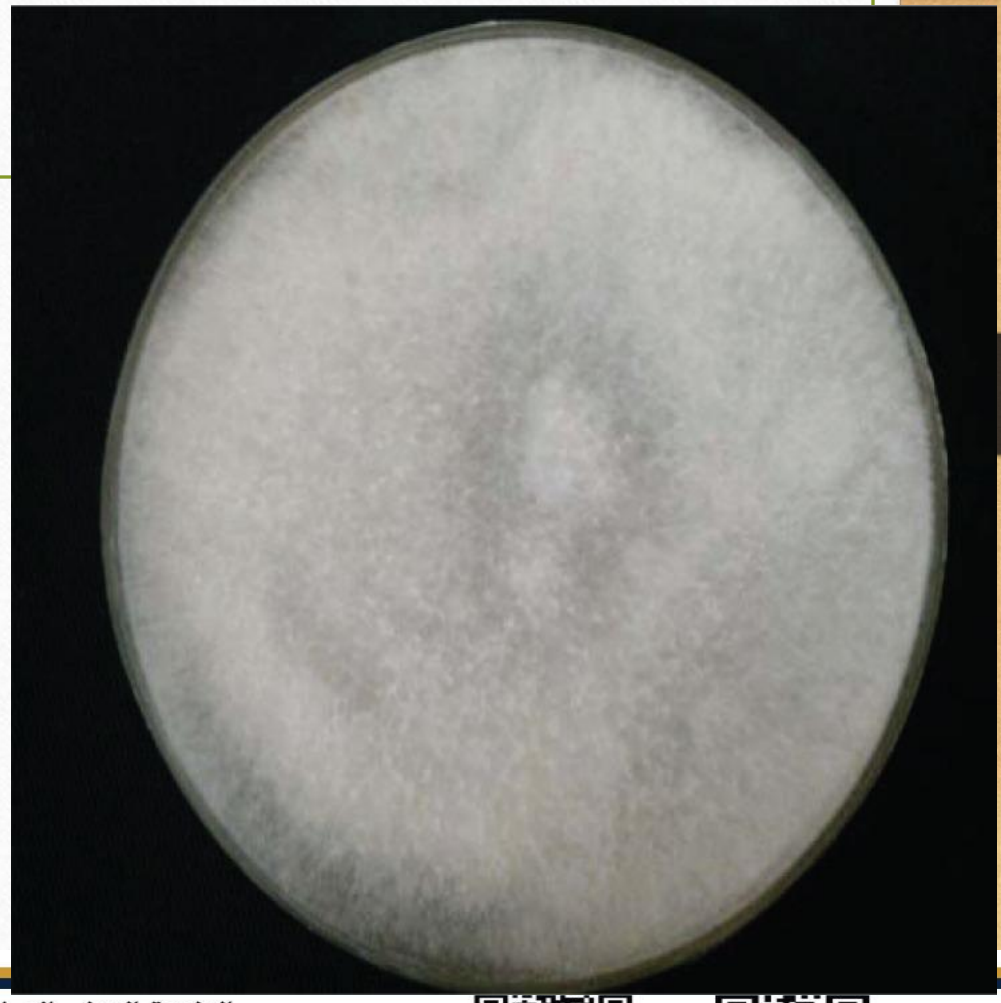
e) Sporangia

Culture on SDA without cyclohexamide to show:

Rapidly growing cottony white-to-gray or black colonies

Colony gray to black appearance like dirty snow.

Mcq



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?**

الطريق الدولي الساحلي - منطقة 15 مايو - مدينة جمصة - محافظة الدقهلية
International Coastal Road - 15th of May District - Gamasa City - Dakahlia Governorate
medic@mansnu.edu.eg

الصفحة الرسمية للجامعة
الموقع الرسمي للجامعة

References

- **Textbook of Medical Microbiology and Immunology 2019-2020: Textbook by staff members of medical Microbiology and Immunology Department.**
- **Jawetz, Melnick, & Adelberg's Medical Microbiology, 28e. Riedel S., Hobden J.A., Miller S., Morse S.A., Mietzner T.A., Detrick B. et al. McGraw-Hill, 2019.**
- **https://www.ncbi.nlm.nih.gov/books/NBK470162/**
- **https://www.sciencedirect.com/topics/immunology-and-microbiology/arbovirus**
- **https://www.ncbi.nlm.nih.gov/books/NBK8618/**
- **https://www.cdc.gov/fungal/diseases/mucormycosis/index.html**
- **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3286196/**


Thank You!