

Mucormycosis

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دیفنسی ← مادرزادی ایمنی ↓
کسپرمایت ← ایمنی ↓

Opportunistic Systemic Mycoses

- ❑ These are fungal infections that occur almost exclusively in patients whose normal defense mechanisms are impaired (immunocompromised people).
- ❑ Weakened immune function may occur due to inherited immunodeficiency diseases, drugs that suppress the immune system (cancer chemotherapy, corticosteroids, drugs to prevent organ transplant rejection), radiation therapy, infections (e.g., HIV), cancer, diabetes, advanced age, and malnutrition.

The most **common infections** are:

Disease	Causative organisms	Incidence
Aspergillosis	<i>Aspergillus</i> spp. : <i>A. fumigatus</i> , <i>A. flavus</i> , <i>A. terreus</i> etc.	Common
Mucormycosis * میکو مایکوسس *	Order Mucorales: <i>Rhizopus</i> , <i>Mucor</i> , <i>Rhizomucor</i> , etc.	Rare
Cryptococcosis	<i>Cryptococcus</i> spp. : <i>C. neoformans</i> , <i>C. gattii</i>	Rare
Candidiasis کھدرا اندوزون	<i>Candida</i> spp. : <i>C. albicans</i> , non- <i>albicans Candida</i> <u><i>Candida auris</i></u>	The most Common invasive IFI

← فوگنڈ ، فلو رینال سین سے مزید صدری انڈوزون مینا / گرائس سے نہ معائنہ دہ بہ داروحا

Recent global outbreaks of mucormycosis during the COVID-19 pandemic highlighted the importance of host immune and metabolic factors such as diabetes and corticosteroid use.”

↓
↑↑ خطر مرگ

Introduction



اسی کا اسباب
اسم لذائذ سے بہت علائم دہکتے ہیں
ہیالین

Prevention of black fungus disease



Avoid going to the dusty area or construction sites, wear N95 mask if not able to avoid going to area with a lot of dust.



Clean the skin injuries with warm water and antiseptic liquid to avoid having skin infection. Maintain personal hygiene including thorough scrub bath.



If you have had a stem cell transplant or organ transplant talk to your doctor for antifungal medication to prevent fungal infections.



Avoid activities that has direct contact with dust or soil. Wear shoes, long trousers, long sleeve shirts, gloves while handling soil (gardening), moss or manure.



- Control high blood sugar and monitor blood glucose level post COVID-19 discharge
- Use steroid as per prescribed dosage and duration.
- Use clean sterile water for humidifiers during oxygen therapy
- Use antibiotics / Antifungals wisely
- Watch out warning signs of black fungus disease that need immediate medical attention and don't delay in case of any warning signs and symptoms.



T: 0404848688
Hyderabad, Telangana, India.

Warning signs of black fungus disease



Patients showing symptoms including a swollen eyelid is when either the lower or upper eyelid (or both) become enlarged, discharge from the eyes, paralysis of eyelid muscles, fever, nausea, vomiting, facial pain, nasal congestion and identified as black fungus infection that can affect sinus and can spread to the brain but wherein infection spreads through the bloodstream and can affect other body parts and organs such as heart, spleen and skin.



Swollen Eyes, Redness around Eyes & Nose



Facial pain, numbness and tingling sensation



Fever and Headache



Coughing



Chest Pain & Shortness of Breath



Bloody vomiting



Altered mental Status



Infected skin area turning black

Past

Global incidence rate 0.005 to 1.7 per million population

Prevalence in India is around 140 per million population (80 times that of developed countries)

Around 46% patients with the disease reportedly die with 68% risk with disseminated and 31% with cutaneous mucormycosis

Present

Current data (May 5-July 12, 2021) reports 41,512 cases and 3,554 deaths due to mucormycosis in India

Around 80% of patients with COVID-19 associated mucormycosis have diabetes

- ❑ Mucormycosis has been regarded as a relatively **rare** mold infection, but recent reports suggest its incidence may increase.
- ❑ Mucormycosis (zygomycosis) is the most **acute** and **aggressive** fungal infection known.
- ❑ Historically, these infections have been seen in immunocompromised hosts in particular, patients being treated for haematological malignancies, where it is the second most common **invasive** **mold** **infection** after invasive aspergillosis.

از نظر آماری دیر سے اول



Clinically relevant species of Mucorales →

فادریغہ سائی

Human
pathogenic
Mucorales

✓ 12 genera: 39 species → در اسان ای ر ساری

Family	Genus	Clinically Relevant Species
Rhizopodaceae	Rhizopus ~50%	<i>R. arrhizus</i> (including var. <i>arrhizus</i> and var. <i>delemar</i>) → <i>R. homothallicus</i> <i>R. microsporus</i> <i>R. schipperae</i>
Saksenaeaceae	Saksenaea	<i>S. erythrospora</i> <i>S. loutrophoriformis</i> <i>S. trapezispora</i> <i>S. vasiformis</i>
Syncephalastraceae	Syncephalastrum	<i>S. racemosum</i>
Lichtheimiaceae	Thamnostylum	<i>T. lucknowense</i>
Mucoraceae	Actinomucor	<i>A. elegans</i>
Saksenaeaceae	Apophysomyces	<i>A. mexicanus</i> <i>A. ossiformis</i> <i>A. trapeziformis</i> <i>A. variabilis</i>
Mucoraceae	Cokeromyces	<i>C. recurvatus</i> <i>C. arunalokei</i>
Cunninghamellaceae	Cunninghamella	<i>C. bertholletiae</i> <i>C. blakesleeana</i> <i>C. echinulata</i> <i>C. elegans</i>
Lichtheimiaceae	Lichtheimia ~13%	<i>L. corymbifera</i> <i>L. ornata</i> <i>L. ramosa</i>

سپین



Rhizopus arrhizus (oryzae) remains the most common cause, responsible for approximately **70% of cases**.

Family	Genus	Clinically Relevant Species
Mucoraceae	Mucor ~14%	<i>M. amphibiorum</i> <i>M. circinelloides</i> * <i>M. griseocyanus</i> * <i>M. indicus</i> <i>M. irregularis</i> <i>M. janssenii</i> * <i>M. lusitanicus</i> * <i>M. plumbeus</i> <i>M. racemosus</i> <i>M. ramosissimus</i> * <i>M. variicolumellatus</i> * <i>M. velutinosus</i> *
Lichtheimiaceae	Rhizomucor	<i>R. miehei</i> <i>R. pusillus</i>
Mycotyphaceae	<i>Mycotypha</i>	<i>M. microspora</i>



❑ Agents of mucormycosis are **ubiquitous** and **thermotolerant** organisms that usually grow and sporulate abundantly on any carbohydrate-containing source in decaying matter, including bread, vegetables, fruits, and seeds. → خاک

❑ They can also be recovered from soil, compost piles, and animal excreta. → براہی مہل

❑ The spores are easily **airborne**, and mucorales are readily recovered as contaminants in laboratory cultures. → آلودہ نشہ شایع
میکس آرماسٹافس

❑ **COVID-associated mucormycosis (CAM)** became an important concern in 2020–2022.



(خطرِ حَرِیر) ← حتی با استخوان
↑

Risk factors

❑ Uncontrolled diabetes mellitus and other forms of metabolic acidosis

لے دیا بت سیرینی نہ بہ لگو اسیدز می رسہ

نمونہ ادراری نہ با ریش لہا جمی کرینہ سور اٹا ملہ اسیریل است
↓
ارزش در حد CSF

❑ Immunosuppressive therapy especially high-dose corticosteroids

❑ Experienced trauma or burns سوجنی
لے دارد های نورینی ↑

❑ Malignant hematologic disorders بیماری های بد خیم نسیم خون ساز

❑ Recently COVID-19 particularly among those with diabetes.

➤ Only rare case reports of invasive mucormycosis in apparently normal hosts have been described.

فقط در صورتی نہ علامت
پاسخ سیرینہ نور
↑
خلع سلاح در برابر مولود ویا بلورین!

➤ Allergic pulmonary disease does occur in immunocompetent hosts and reflects an acute hypersensitivity immune response illness rather than an invasive disease.

لے نسیم ایسی نر نہ ہیزہا ہی نہ نیاید پاسخ سیرینہ در حد . خود بدل ہم می رسہ

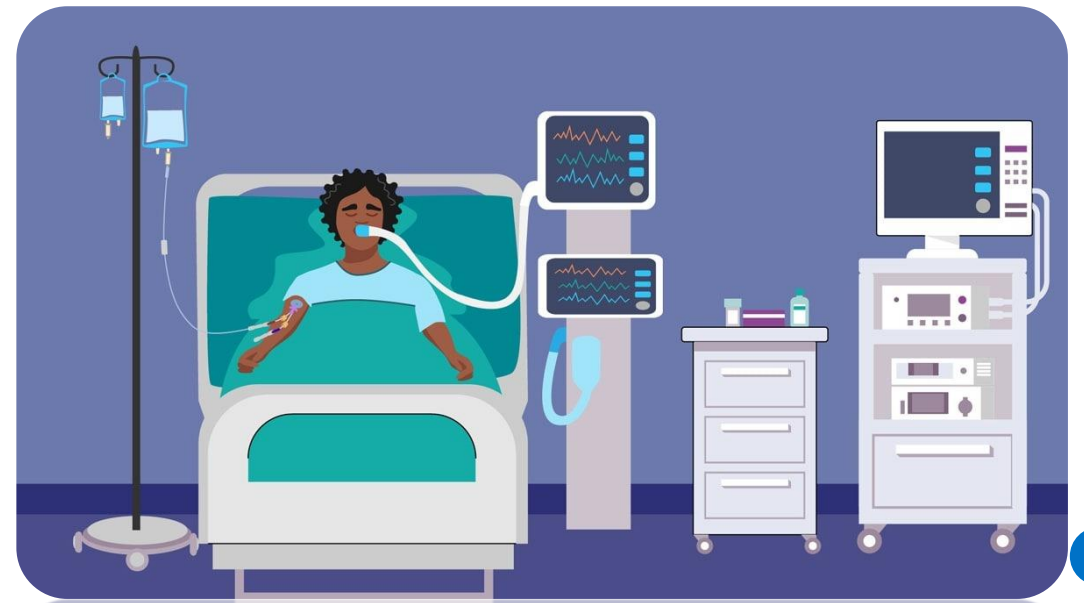
Pathogenesis

❑ The ability of **inhaled spores** to **germinate** and form hyphae in the host is critical for establishing infection.

❑ Findings suggest that **neutrophils**, but not necessarily T lymphocytes, are critical for inhibiting fungal spore proliferation. تاریخ کے متعلقہ تاریخی حقائق بھی تونہ سنئے

❑ Both mononuclear and polymorphonuclear phagocytes of normal hosts **kill mucorales** by generating oxidative metabolites and the cationic peptides, defensins.

❑ **High glucose**, **acidic pH**, and **elevated free iron levels** promote fungal growth via the **CotH** protein-mediated endothelial adhesion (**GRP78**).

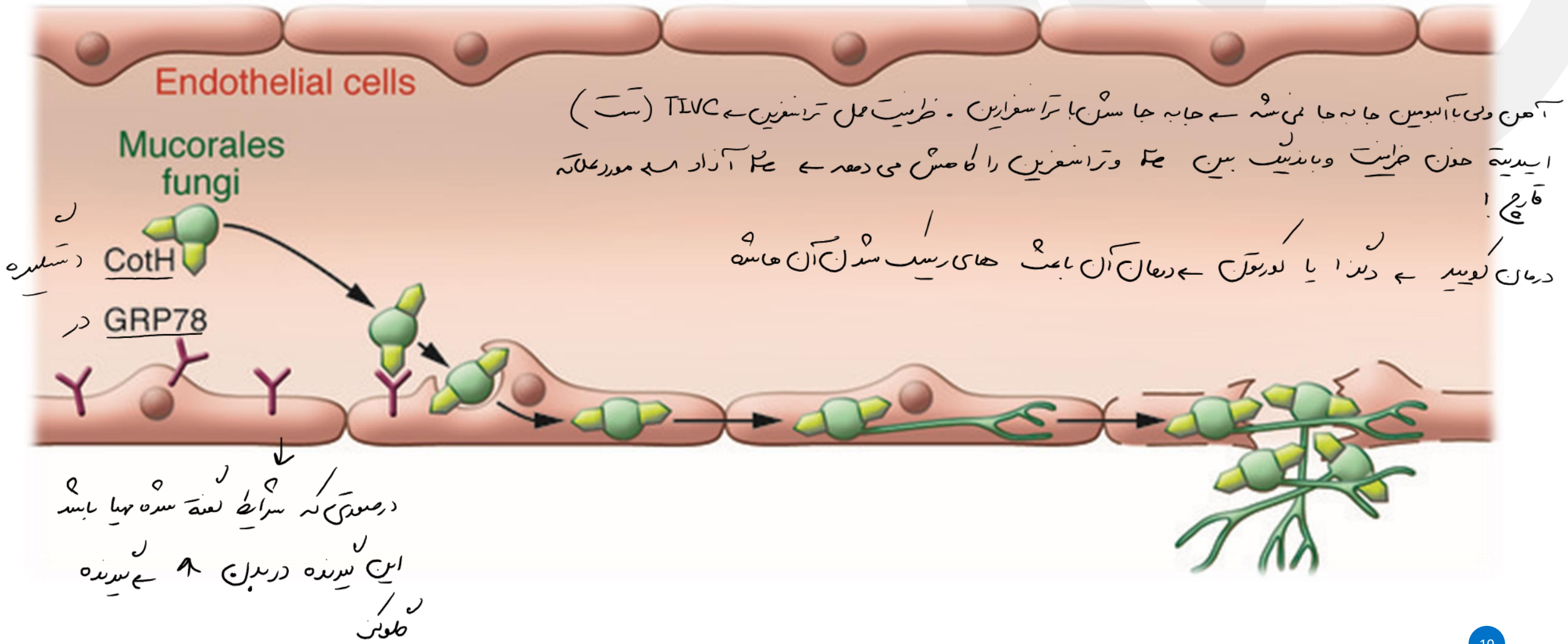


کموٹا کسی سے ٹرائس طویل های سفید

تند وزن ↑ سے کموٹا کسی ↑ سے طویل سفید (نوروسل) غیرو صبی

Pathogenesis

چرا اسیدز سره کھنا؟ سید آسن دست pro غالب فلن؟ کموٹین صبی؟ آلفا ایو بریش سے دصدی در بربک سال ↑ سے فرد دارای Cancer
له حکم اسب فلن ما



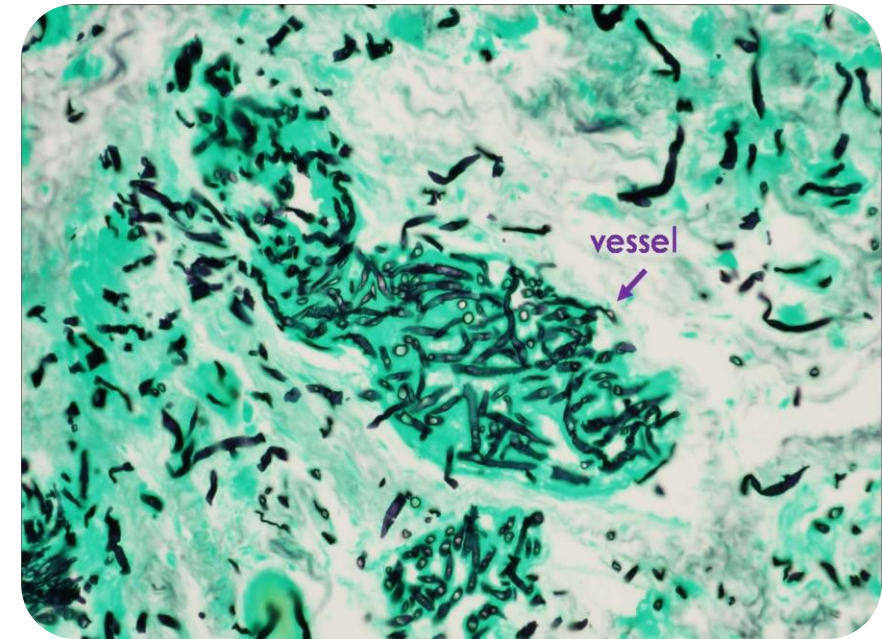
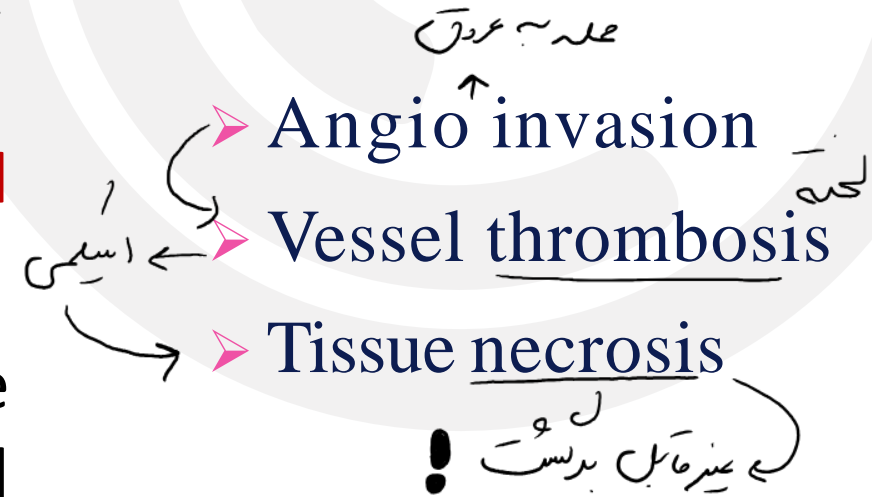
Pathophysiology

★ نابت نمره صفاً باید خارج شود
سریع

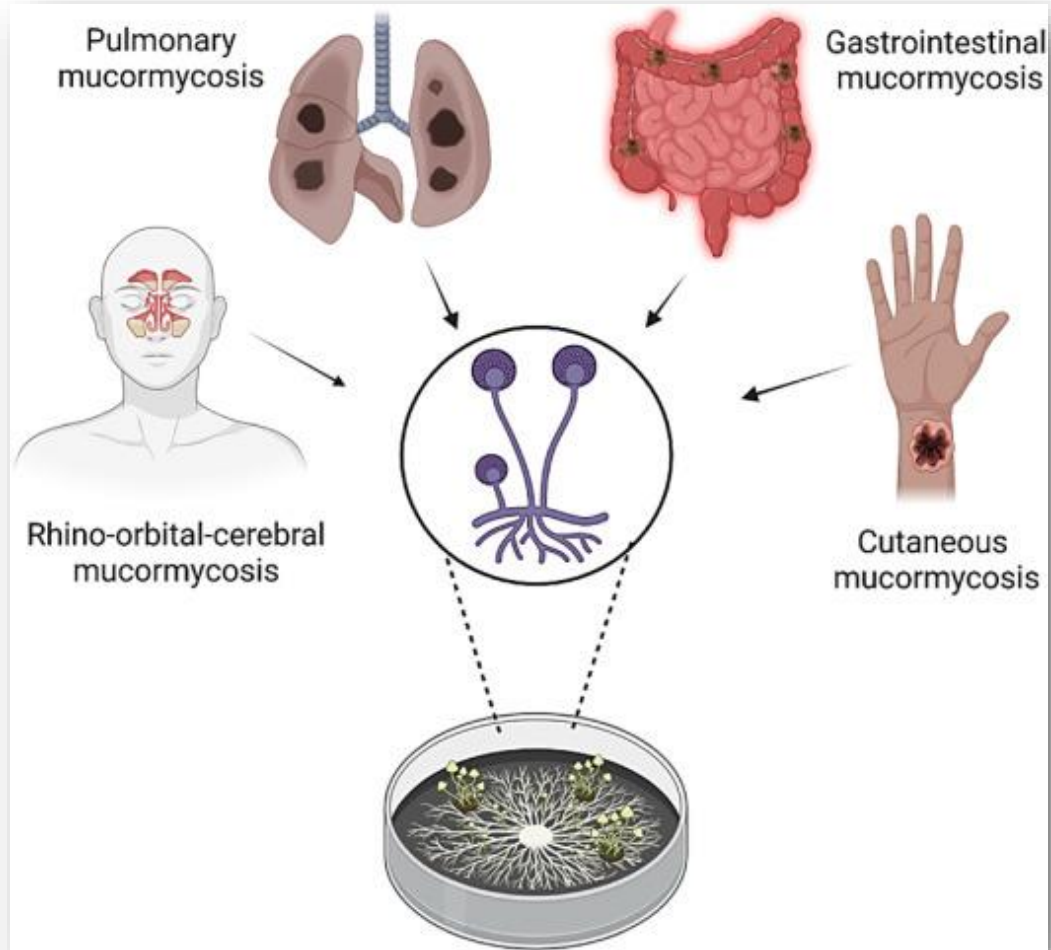
عمله با سی

- ❑ The clinical hallmark of mucormycosis is the rapid onset of tissue necrosis, with or without fever.
- ❑ This necrosis is the result of invasion of blood vessels and subsequent thrombosis.
- ❑ Unfortunately, the aggressive nature of the infection often means that delayed diagnosis and erroneous treatment decisions often result in significantly higher patient morbidity and mortality.
- ❑ As mucoraceous moulds have no septa in their hyphae, allowing more rapid nutrient transport, they can grow faster than many other moulds.

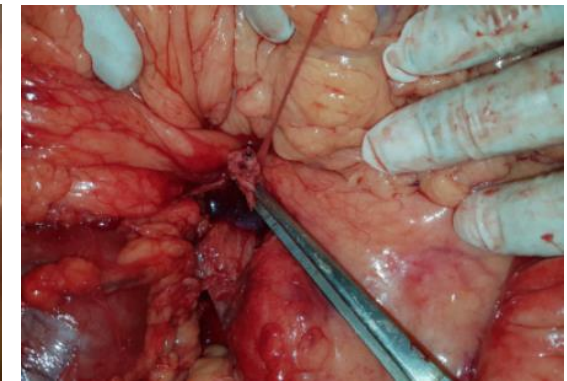
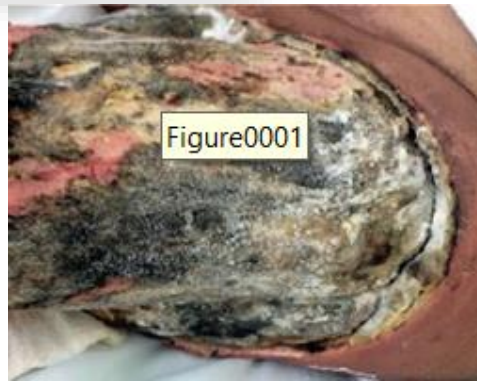
چرا مغز O₂ سیره از رمان دیدن نابت نمره صفاً کم است



Clinical Manifestations



- ☐ Rhino-Orbital-Cerebral (ROCM)
- ☐ Pulmonary
- ☐ Cutaneous
- ☐ Gastrointestinal
- ☐ Disseminated



Major route of infection:

☐ Inhalation

Both ROCM and pulmonary mucormycosis are acquired through inhalation.

☐ Ingestion

Ingestion of contaminated food, which leads to gastrointestinal mucormycosis in highly immunocompromised patients and premature neonates.

☐ Traumatic inoculation

Other routes of infection include direct implantation into skin, causing local cutaneous infection.

استنشاق

کرم های نابالغ

Rhino-Orbital-Cerebral (ROCM)

Clinical Manifestations

- ❑ ROCM is the most common form of the disease, representing between one-third to one-half of all cases.
- ❑ 70% of cases of ROCM are found in DKA. → ديابت كيتواسيدوز
- ❑ The most clinical form observed in COVID-19.
- ❑ Beyond classic diabetic ketoacidosis, ROCM now frequently presents in patients on high-dose corticosteroids (for autoimmune conditions or transplant) and those with hematological malignancies.



Clinical Manifestations

❑ ROCM may present as paranasal sinusitis. ← علامت سینس

❑ Delayed recognition and diagnosis may result in rapid progression to involve the orbit, retro-orbital tissues, and brain, with devastating consequences.

❑ Common Symptoms: Headache, sinus pain, facial swelling, fever, and visual impairment (Ptosis, ophthalmoplegia,...). ← محدود شدن حرکت چشم ← بدون توضیح ←

❑ Early Warning Signs: Unexplained toothache, loosening of teeth, or facial numbness, often appearing before the development of a black eschar. ← لوز سین در دندان ←

❑ A black eschar may appear on the hard palate or nasal mucosa. ← مثل ارجاع به آرماسیفاه اسفان سبوع در حال آستی فانتان ←



اول نمره 4 سی

Pulmonary mucormycosis

- ❑ Pulmonary mucormycosis occurs most commonly in patients with profound and prolonged **neutropenia** such as that noted in patients with **leukemia** or recipients of a **hematopoietic stem cell** transplant.
- ❑ Patients with DKA can also develop pulmonary mucormycosis.
- ❑ Pulmonary mucormycosis may develop as a result of **inhalation** or by hematogenous or lymphatic spread.
- ❑ In immunocompromised or neutropenic patients, pulmonary mucormycosis may mimic **invasive aspergillosis**; differentiation requires histopathology or molecular confirmation

Clinical Manifestations

عمر مری درگیری امراض سانس کر
با درصد در بیمار !!
است این
با درصد
۱۰۰۰ - ۴۰۰۰ نوترون
طول سفید ←

ولی خط سبز

صافیت غیر امتصاص ← با تصویر رادی می سه



Cutaneous mucormycosis

□ Primary

This form occurs following the direct traumatic implantation of the fungus into the skin, such as in burn injuries, motor vehicle accidents, or contamination of surgical or catheter sites. It can affect immunocompetent individuals if the trauma is severe or the inoculum is large.

□ Secondary →

This form results from hematogenous dissemination from a distant primary infection site (e.g., lungs, sinuses) to the skin. It typically occurs in severely immunocompromised patients, such as those with uncontrolled diabetes, hematologic malignancies, or organ transplantation, and signals widespread, disseminated disease.

Clinical Manifestations

تخلع برداشت

حالت ناصیه
↑



استارازولون

مسح عفونت های دینه

سرولوژی آنتی بادی دانه های داریم
له



نوی بدین داره می خورم

Gastrointestinal mucormycosis

Clinical Manifestations

❑ Mucormycosis of the gastrointestinal tract is rare, but it is increasingly encountered in nosocomial settings occurs mostly in premature infants or malnourished individuals.

سرگزشتہ نغزار نارس

❑ It is thought to arise from ingestion of the fungi.

بلع

❑ The diagnosis is notoriously challenging and is often made only post-mortem, during autopsy.

شخص !

❑ This delay occurs because symptoms are non-specific (e.g., abdominal pain, distension, bleeding) and can mimic more common conditions like bowel infarction or bacterial sepsis.

مجموعاً موت کی وجہ سے شخص کے معموں میں مار رہے ہیں۔
بایوپسی دارہ۔



Disseminated mucormycosis →

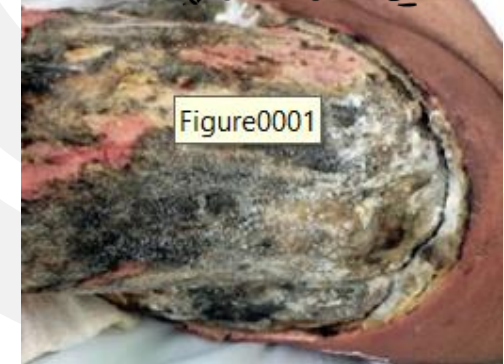
انتشار

حرب صلي

Clinical Manifestations

- ❑ Hematogenously disseminated mucormycosis may originate from any primary site of infection. Pulmonary mucormycosis in severely neutropenic patients has the **highest incidence** of dissemination.
- ❑ Disseminated infection has a **high mortality rate** (often >90%), especially with CNS involvement.
- ❑ Symptoms are **non-specific** and depend on the organs involved, often including fever, altered mental status, and multi-organ failure.
- ❑ Common Sites of Spread: **Brain** (most common) - often presenting with abscesses or infarcts, Spleen, Heart, Skin

چرا Fe ردیویدیم از بدن؟ (دیپولسایمن) ← تجمع برای ادرار و ادرار
آهن حاد از ترانسفوزین جلوی کبد می‌گیرند و حودش و تعدیم مولود می‌ند.



Host Factor	Associated Clinical Syndrome
Diabetes mellitus, particularly with ketoacidosis	ROCM
Corticosteroid use	ROCM
Haematologic malignancies	Pulmonary or disseminated infection
COVID-19	<u>ROCM</u>
Haematopoietic cell transplantation	Pulmonary
Solid organ transplantation	Disseminated infection
HIV/AIDS	Disseminated infection
Treatment with deferoxamine	ROCM
Iron overload	<u>ROCM</u>
Injection drug use	Isolated cerebral
Major trauma	Cutaneous
Burns	Cutaneous

بسترین مریال ها

1. Clinical material:

Skin scrapings from cutaneous lesions; sputum and needle biopsies from pulmonary lesions; nasal discharges, scrapings, and aspirates from sinuses in patients with rhinocerebral lesions; and biopsy

2. Direct Microscopy:

(a) Scrapings, sputum, and exudates should be examined using **10% KOH** & Parker ink or Calcofluor mounts; and (b) Tissue sections should be stained with **H&E** and **GMS**. → دریا تیلوری

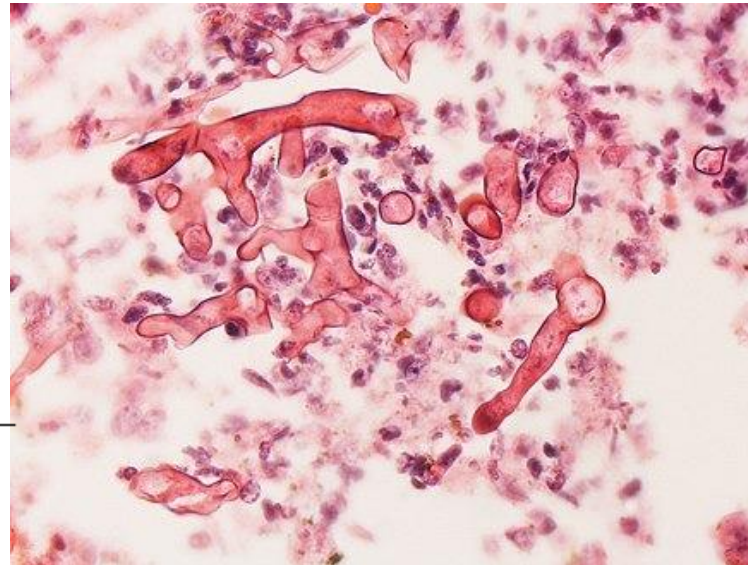
با بران شد است

Examine specimens for **wide, ribbon-like, coenocytic (mostly aseptate)** hyphae that branch at right angles.

معمولاً مانت

- ❖ As a rule, positive direct microscopy, especially from a sterile site, should be considered significant.

← حالت های رودانی شکل



3. Culture: → اگر کوئی قارچی (اسپی) ۱۲ روزہ کی داری صند قارچی

اگر راپیٹ (-) سست (+) احتمال آلودگی در راه ردی و صیم !!
↓

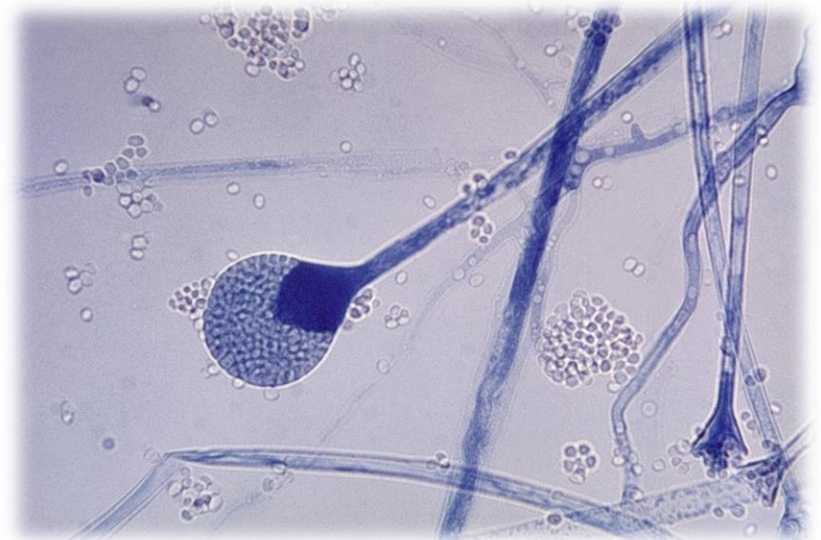
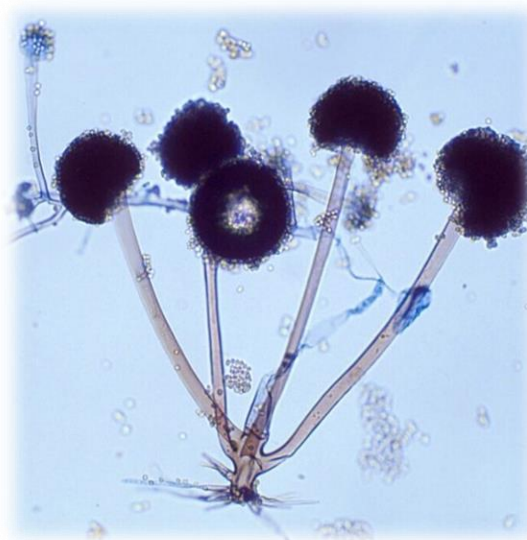
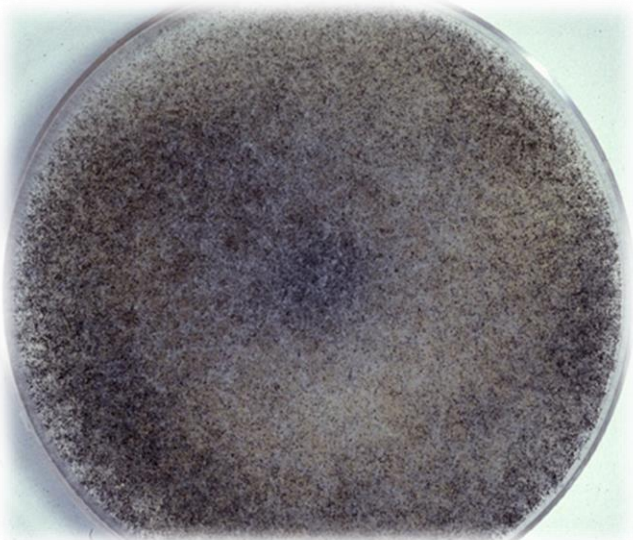
Clinical specimens should be inoculated onto SDA.

Look for fast-growing, white to grey or brownish, downy colonies.

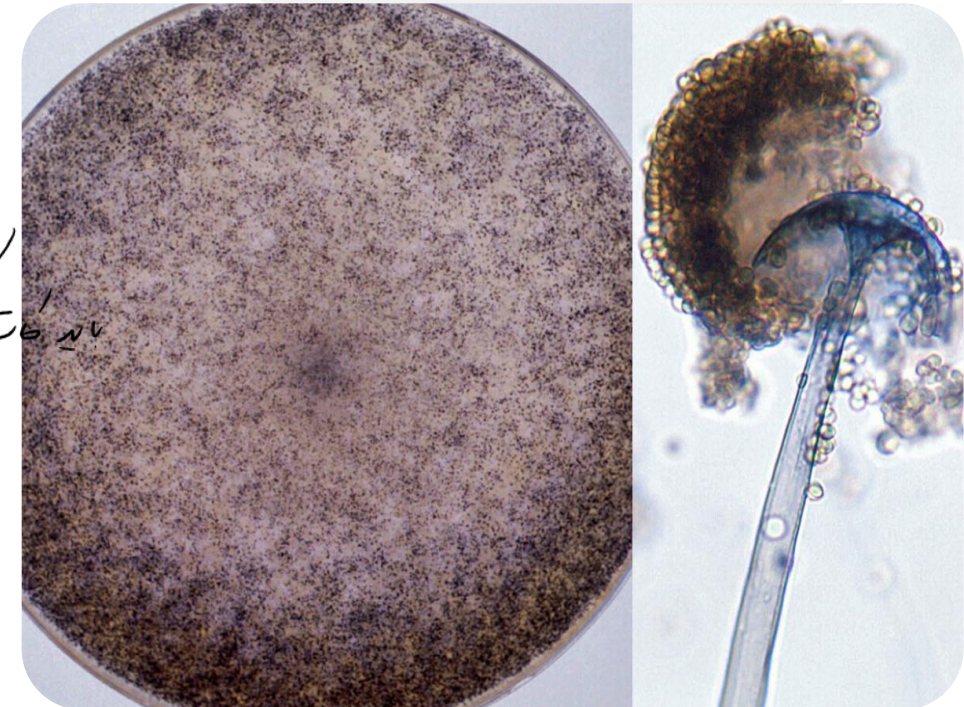
Because the Mucorales are environmental isolates, establishing a definitive diagnosis requires a positive culture from a **sterile site** obtained by a needle aspirate or a tissue biopsy, or histopathologic evidence of invasive disease.

4. Serology:

There are currently no commercially available serological procedures for the diagnosis of mucormycosis.



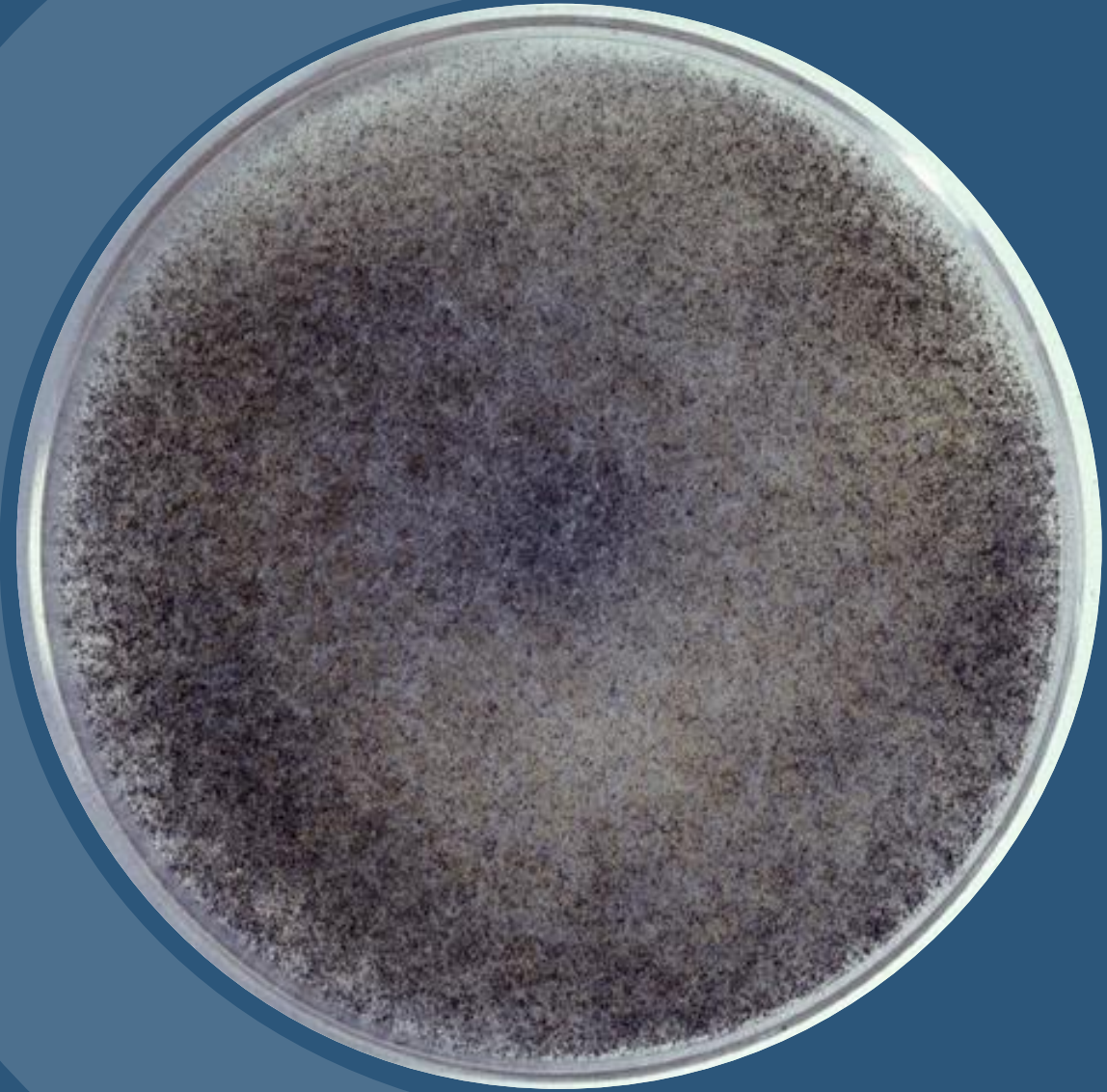
- Despite the fact that the mucorales grow **quite quickly** on laboratory culture media, cultures may be negative in up to half of patients with mucormycosis.
- Due to various factors such as sample collection, storage at 4 °C, and tissue grinding. → تدریس →
- Fungal culture is an essential diagnostic modality for **Mucorales identification** to genus and species level and **antifungal sensitivity** testing.



- First-line liposomal amphotericin B 5–10 mg/kg per day
- high dose with less **nephrotoxicity**
- Posaconazole (delayed-release tablets) or isavuconazole can be used for oral **step-down** therapy.
- **Echinocandins** (e.g., caspofungin) have no *in vitro* activity against the agents of mucormycosis!
- **Adjunctive Surgical Intervention**: "Early, aggressive, and repeated **surgical debridement** of all necrotic tissue is a cornerstone of successful management and is critical for survival."
- "Despite aggressive therapy, mortality remains high (40–80%). **Early diagnosis** and combined medical–surgical management significantly improve survival."



- Gullì, S.P.; Hallur, V.; Kale, P.; Menezes, G.A.; Russo, A.; Singla, N. From Spores to Solutions: A Comprehensive Narrative Review on Mucormycosis. *Diagnostics* **2024**, *14*, 314.
- Wang, W.; Yao, Y.; Li, X.; Zhang, S.; Zeng, Z.; Zhou, H.; Yang, Q. Clinical Impact of Metagenomic Next-Generation Sequencing of Peripheral Blood for the Diagnosis of Invasive Mucormycosis: A Single-Center Retrospective Study. *Microbiol. Spectr.* **2024**, *12*, e0355323.
- Özbek, L.; Topçu, U.; Manay, M.; Esen, B.H.; Bektas, S.N.; Aydın, S.; Özdemir, B.; Khostelidi, S.N.; Klimko, N.; Cornely, O.; et al. COVID-19-Associated Mucormycosis: A Systematic Review and Meta-Analysis of 958 Cases. *Clin. Microbiol. Infect.* **2023**, *29*, 722–731.
- Brandt ME, Warnock DW. Taxonomy and Classification of the Fungi | Taxonomy, Classification, and Nomenclature of Fungi. *Manual of Clinical Microbiology.* **2023**.
- Hallur, V.; Prakash, H.; Sable, M.; Preetam, C.; Purushotham, P.; Senapati, R.; Shankarnarayan, S.A.; Bag, N.D.; Rudramurthy, S.M. *Cunninghamella arunalokei* a New Species of *Cunninghamella* from India Causing Disease in an Immunocompetent Individual. *J. Fungi* **2021**, *7*, 670.
- Prakash, H.; Chakrabarti, A. Global Epidemiology of Mucormycosis. *J. Fungi* **2019**, *5*, 26.



THANK YOU
