Introduction

Mucormycosis

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Mucormycosis is a severe fungal infection, primarily affecting immunocompromised individuals and those with diabetes mellitus.

It manifests in various syndromes, with devastating rhino-orbital-cerebral and pulmonary infections being the most common.

Risk Factors

Predisposing Conditions

Diabetes Mellitus

Especially with ketoacidosis.

Immunosuppression

From glucocorticoids, hematologic malignancies, or organ transplantations.

Iron Overload

Often linked to deferoxamine treatment.

Recent COVID-19

A newly recognized risk factor.

Epidemiology

Malignancy

Hematologic Malignancies

More frequently associated with mucormycosis than solid tumors. Pulmonary infection is common. Incidence is less than 1% in this group.

Epidemiology

Diabetes and Mucormycosis

Diabetes is a common predisposing condition, particularly for rhino-orbital-cerebral infections. While reported cases in the US have declined, possibly due to statin use, this trend is not seen globally.

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Epidemiology

COVID-19 Associated

COVID-19 Associated

Numerous reports, especially in diabetic patients receiving steroids. Rhino-orbital-cerebral mucormycosis is most frequent, with symptoms appearing 5-14 days post-admission.

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Pathophysiology

Mucorales fungi are ubiquitous but primarily affect immunocompromised individuals, especially those with diabetes mellitus.

Inhalation

Fungal spores enter through inhalation or trauma.

Vascular Invasion

Spores lodge in blood vessels, forming thrombi.

Ischemic Necrosis

Compromised blood supply leads to tissue death and characteristic blackening.

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Clinical Presentation

Rhino-Orbital-Cerebral Mucormycosis

This is the most common presentation, starting in paranasal sinuses. It progresses rapidly, causing tissue necrosis and vascular invasion.

1 Symptoms

Fever, nasal congestion, purulent discharge, headache, sinus pain, facial swelling, decreased vision.

2 Progression

Palatal eschars, turbinate destruction, perinasal swelling, black eschar in nasal mucosa or skin.

3 Complications

Orbital involvement (proptosis, blindness), facial numbness, cranial nerve palsies, cavernous sinus thrombosis.

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Treatment Overview

Antifungal Therapy

Initiate empiric antifungal therapy promptly upon suspicion.

Surgical Debridement

Aggressive surgical removal of infected tissues when feasible.

Early treatment and reversal of predisposing factors (e.g., ketoacidosis, neutropenia) significantly improve patient outcomes.

Algorithm for Management of Patients with Mucormycosis

Suspicion of mucormycosis in patients with predisposing factors or a history of COVID-19 and one of the following:

- Symptoms suggestive of sinusitis
- Facial edema/pain
- Numbness or paresthesia
- Visual loss, diplopia, orbital pain
- Frozen eye
- Headache or focal neurological signs without specific cause
- Prolonged fever

local nasal endoscopy

Pale mucosa or obvious necrosis

Mucosal swelling / relatively normal mucosa

- If pale/ischemic mucosa → take biopsy (send for pathology)
- If relatively normal mucosa → perform PNS CT

If **CT** shows involvement of sinuses + (orbit ± brain) → MRI with contrast (Gadolinium).

CT scan Findings:

- No suspicious involvement (In cases with normal mucosa / normal endoscopy) → unlikely mucormycosis
- Suspicious involvement (In cases that the sinuses show evidence of involvement on CT scan, endoscopic debridement and biopsy of the involved tissues is recommended) → mucormycosis probable

Aggressive Surgical Debridement

Surgical debridement is crucial for improved survival in mucormycosis.

It allows for tissue collection for culture and histopathology, confirming diagnosis and assessing resection margins.

Repeat debridement is often necessary for maximal resection.

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Antifungal Therapy: Initial Approach

Early antifungal therapy significantly improves outcomes. Liposomal amphotericin B is the preferred initial treatment.

Monotherapy for Most

Use lipid formulation of amphotericin B (liposomal or lipid complex) for suspected or diagnosed mucormycosis.

Combination Therapy

For disseminated infection and severe immunosuppression, some experts start with combination therapy (e.g., amphotericin B plus posaconazole).

Avoid Deoxycholate

Avoid amphotericin B deoxycholate due to nephrotoxicity, unless other options are unavailable or for isolated renal mucormycosis.

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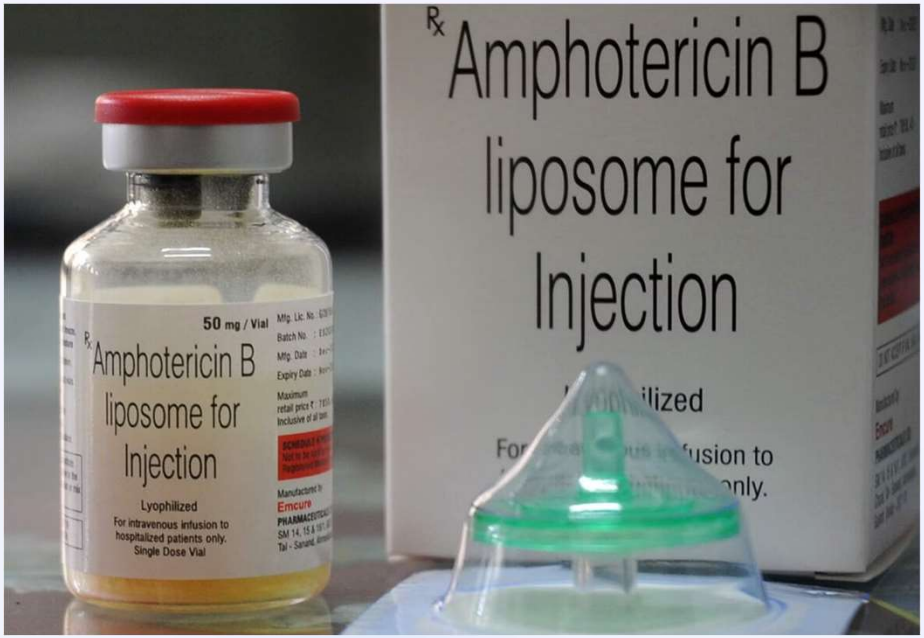
Antifungal Dosing & Duration

Dosing Guidelines

- Standard: 5 mg/kg liposomal amphotericin B daily
- CNS involvement/transplant recipients: 10 mg/kg daily.
- Increase to 10 mg/kg daily if no improvement after one week of standard dose.

Duration of Initial Therapy

Continue lipid formulation amphotericin B until clinical improvement, typically several weeks.



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Monitoring & Managing Side Effects

1

Frequent Monitoring

Regular lab tests and hydration to prevent or correct amphotericin B side effects (nephrotoxicity, electrolyte abnormalities).

2

Nephrotoxicity

Kidney injury is a serious side effect, though mitigated by liposomal formulations. Risks are tolerated due to high mortality.

3

Kidney Compromise

Continue liposomal amphotericin B if kidney function is compromised but infection hasn't improved, justifying the risk of replacement therapy.

4

Switching Therapy

If acute kidney injury develops with clinical improvement, switch to posaconazole or isavuconazole.

Rationale for Antifungal Choice

Amphotericin B is preferred due to clinical experience and its high in vitro activity against Mucorales, followed by posaconazole and isavuconazole.

Ineffective Agents

- Itraconazole has variable activity.
- Voriconazole, fluconazole, flucytosine, and echinocandins are not effective against Mucorales.

Combination Therapy

Not routinely recommended due to lack of convincing efficacy data.

Assessing Response to Therapy

01

Radiographic Imaging

Repeat after 1-2 weeks of initial therapy to check for progression or recurrence.

02

Endoscopic Assessment

For sinus disease, repeat endoscopy and biopsies within two weeks of antifungal initiation.

03

Switch to Maintenance

Once clinically improved and no further debridement is planned, switch to posaconazole or isavuconazole.

04

Re-evaluate Worsening

If clinical worsening occurs after one week, re-evaluate for debridement, optimize underlying conditions, and intensify antifungal therapy.

Maintenance Therapy

For patients who have improved on amphotericin B, switching to posaconazole is suggested for maintenance. Isavuconazole is an alternative if posaconazole is not tolerated.

Overlap Period

Maintain a one-week overlap of both drugs to ensure therapeutic azole concentrations before discontinuing amphotericin B.

Route of Administration

Oral route is preferred for maintenance, but IV azole formulations are used for impaired GI function or critical illness.

Agent Preference

Posaconazole is preferred over isavuconazole due to lower minimum inhibitory concentrations for most Mucor species.

Orbital Exenteration in Sino-Orbito-Cerebral Mucormycosis (2025 Updates)

When to Strongly Consider ***Exenteration*** ?

- Blind, painful eye (no light perception) with central retinal/ophthalmic artery occlusion

- Diffuse orbital apex involvement ± superior ophthalmic vein thrombosis

- Rapid progression despite amphotericin B + sinonasal/skull base debridement

- Threatened intracranial spread (cavernous sinus involvement) if patient is operable

- Extensive orbital necrosis not amenable to limited debridement

When to Avoid / Defer Exenteration?

- Preserved vision (partial or intact)

- Limited anterior/medial orbital disease

- Good response to systemic amphotericin B + local therapy

- Salvageable cases with retrobulbar amphotericin or local orbital debridement

Globe-Sparing Approaches

- Endoscopic orbital decompression / limited debridement
- Transcutaneous retrobulbar amphotericin B (TRAMB)
- Local catheter irrigation with amphotericin
- Aggressive metabolic control, repeat sinonasal clearance