EXTRACORPOREAL NEPHROLOGY GROUP [ECNG]

RENAL TRANSPLANT
ASPERGILLOSIS / MUCOR MYCOSIS

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INTRODUCTION

- **Timing after transplant** : <1 month: hospital exposure , 1–6 months: peak immunosuppression , >6 months: rejection/CMV.
- **Risk factors** : Diabetes , rejection , pulse steroids , ATG , Leukopenia and long ICU stay.
- **Galactomannan** : A polysaccharide cell wall antigen released during growth of Aspergillus species. Detected in serum and BAL fluid. Negative in mucor.
- **Algorithm** : Suspicion → Imaging → Biomarkers → BAL/Biopsy → Therapy. Do not wait for biopsy and culture reports. Start therapy early.
- **Mortality** : high. Medical management and early surgical debridement.

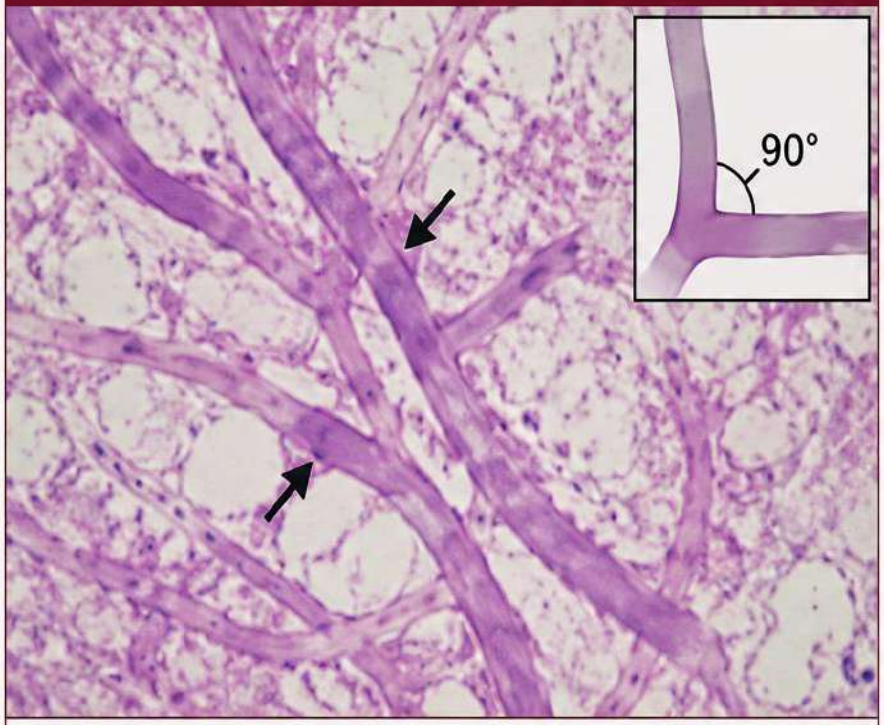
Mucor vs Aspergillus

Feature	Mucormycosis	Aspergillosis
Clinical pattern	Rapidly progressive, often **rhino-orbital-cerebral** disease with tissue necrosis	Predominantly **pulmonary** disease with nodules and hemoptysis
Angioinvasion	**Marked angioinvasion** causing thrombosis, infarction, and black eschar	Angioinvasive, but usually less extensive
Biomarkers	Galactomannan and β-D-glucan usually **negative**	Galactomannan often **positive**
Histopathology	Broad, pauciseptate hyphae with **90° branching**	Thin, septate hyphae with **45° branching**
Treatment	**Liposomal amphotericin B** first-line; **posaconazole/isavuconazole** for salvage or step-down; surgery often essential	**Voriconazole** first-line; **posaconazole/isavuconazole** alternatives or salvage therapy

MUCORMYCOSIS vs ASPERGILLOSIS

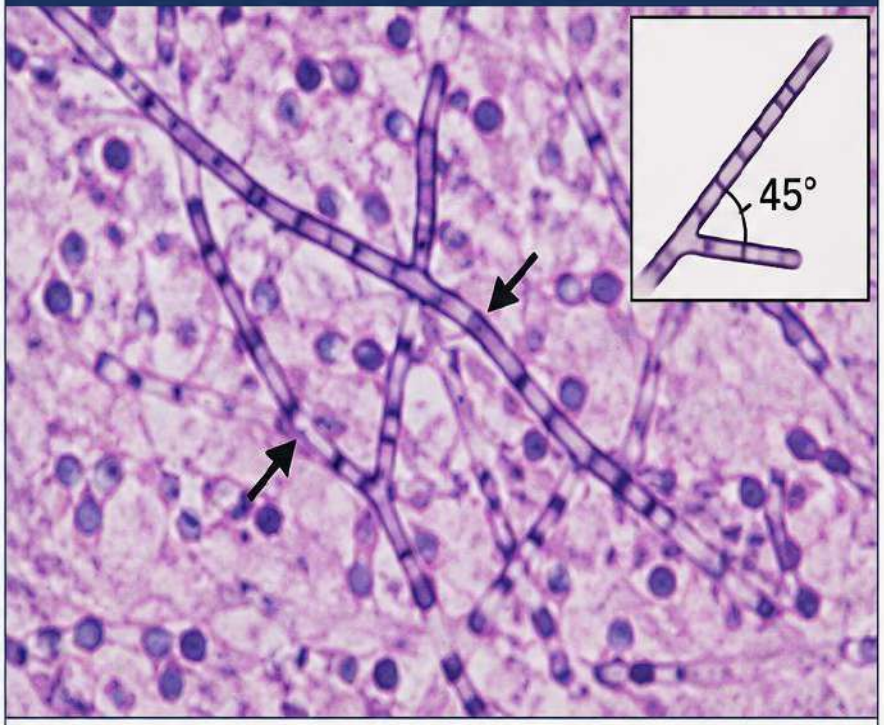
Hyphae on Histopathology (H&E/PAS/GMS)

MUCORMYCOSIS



- Broad (5–20 µm)
- Pauciseptate or aseptate
- Irregular, ribbon-like hyphae
- Branching at right angles (≈ 90°)

ASPERGILLOSIS



- Thin (3–6 µm)
- Septate hyphae with regular septations
- Uniform, tubular hyphae
- Branching at acute angles (≈ 45°)

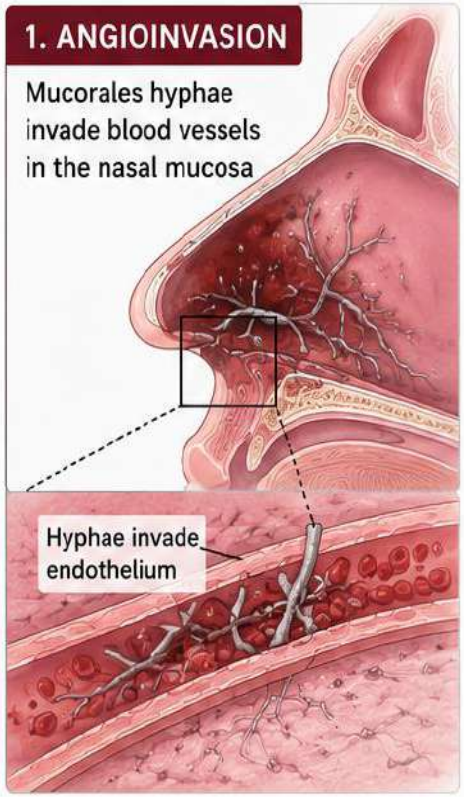
Key Point: Broad, aseptate, 90° branching → **Mucorales (Mucormycosis)**
Thin, septate, 45° branching → **Aspergillus**

WHY BLACK ESCHAR IN MUCORMYCOSIS?

Angioinvasion → Thrombosis → Ischemia → Tissue Necrosis → Black Eschar

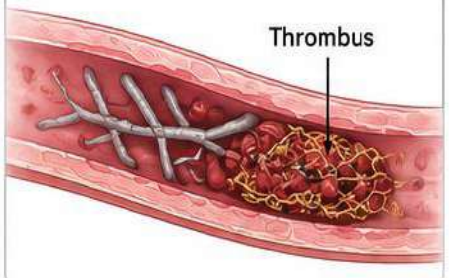
1. ANGIOINVASION

Mucorales hyphae invade blood vessels in the nasal mucosa



2. VASCULAR THROMBOSIS

Endothelial damage triggers platelet aggregation and thrombus formation

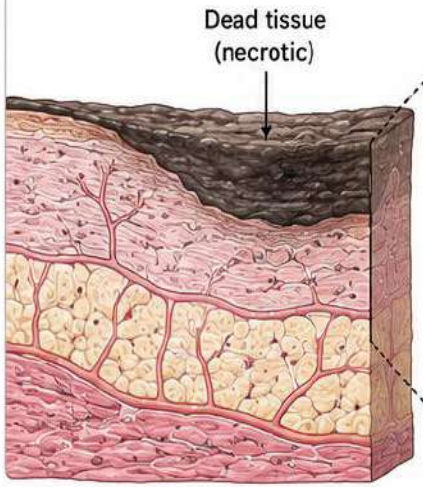


3. ISCHEMIA

Vessel blockage → cessation of blood flow → tissue ischemia

4. TISSUE NECROSIS

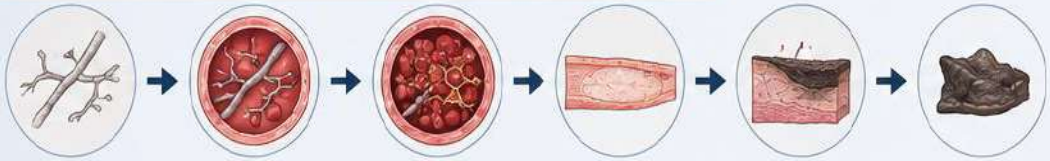
Prolonged ischemia causes coagulative necrosis of overlying mucosa and submucosa



5. BLACK ESCHAR

Necrotic tissue dries and turns black due to hemoglobin breakdown (deoxyhemoglobin, sulfhemoglobin) and devitalized tissue

PATHOPHYSIOLOGIC SEQUENCE



CLINICAL PEARLS

- Black eschar is a hallmark of tissue necrosis from angioinvasion.
- It is not just superficial – it represents underlying vascular thrombosis and devitalized tissue.
- Urgent diagnosis and debridement are crucial to remove necrotic tissue and control spread.

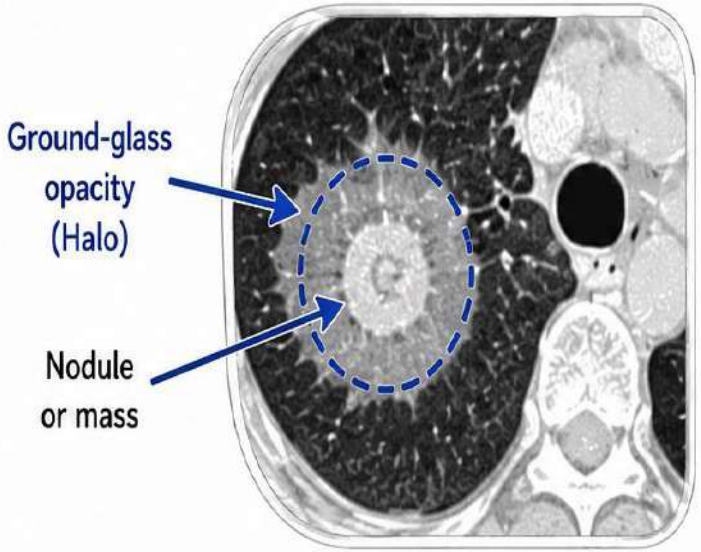
KEY POINT: BLACK ESCHAR = DEAD TISSUE DUE TO VASCULAR THROMBOSIS AND NECROSIS CAUSED BY ANGIOINVASIVE FUNGI (MUCORALES)

DRUG INTERACTIONS OF ANTIFUNGALS IN KIDNEY TRANSPLANT RECIPIENTS

Drug	Tacrolimus	Cyclosporine	Sirolimus/Everolimus	Key Message
Voriconazole	↑Major increase	↑	↑ Massive increase	Most important interaction
Posaconazole	↑ Major increase	↑↑	↑ Massive increase	Close monitoring needed
Isavuconazole	↑ Moderate increase	↑ Moderate increase	↑ Moderate increase	Less interaction than voriconazole
Fluconazole	↑ Moderate increase	↑	↑	Dose adjustment often needed
Liposomal Amphotericin B	No CYP interaction	No CYP interaction	No CYP interaction	But nephrotoxicity may worsen CNI toxicity

HALO vs REVERSE HALO

HALO SIGN (Aspergillosis)



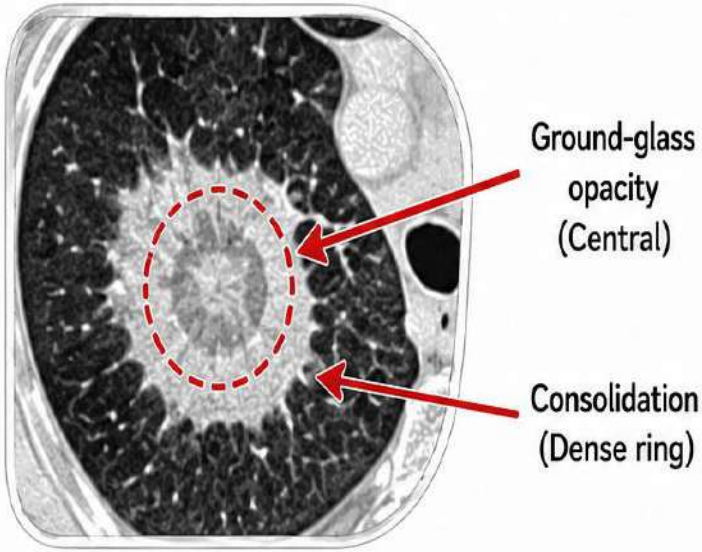
DEFINITION

Nodule or mass surrounded by ground-glass opacity

SEEN IN

Invasive Aspergillosis

REVERSE HALO SIGN (Mucormycosis)



DEFINITION

Central ground-glass opacity surrounded by consolidation

SEEN IN

Mucormycosis

REMEMBER:

HALO = NODULE with a **HAZY** halo

REVERSE HALO = **HAZY** center with a **DENSE** ring

TREATMENT

Mucor Mycosis :

- **Liposomal Amphotericin B :** First-line treatment Dose Usually IV 5 mg/kg/day CNS disease: Up to 10 mg/kg/day.
- **Posaconazole** : step down treatment. 300 mg PO twice daily on Day 1, then 300 mg PO once daily from Day 2 onwards.
- **Isavuconazole** **: first line alternative to amphotericin B.**

Apergillosis :

IV Voriconazole - 6 mg/kg q12h × 2 doses, then 4 mg/kg q12h.

Oral Voriconazole - 200 mg BID. **Isavuconazole can also be given.**

LIPOSOMAL VS CONVENTIONAL AMPHOTERICIN B

Feature	Liposomal Amphotericin B (L-AmB)	Conventional Amphotericin B Deoxycholate (AmB-D)
Dose (Mucormycosis)	**5 mg/kg/day IV** (up to 10 mg/kg/day for CNS disease)	**1–1.5 mg/kg/day IV**
	★	★★★
Cost	~ Rs 30000-50000/- per day	~ Rs 500 per day
Infusion reactions	Less fever, chills, rigors	Frequent fever, chills, rigors
Use in transplant patients	Preferred	Avoid if possible
CNS penetration	Better at high doses	Less favorable
Mortality benefit	Similar efficacy with better tolerability	Effective but limited by toxicity