soil organisms), can cause clinical syndromes identical to mucormycosis. Histopathologic examination usually allows distinction of the Mucorales from these other organisms, and a positive culture permits definitive species identification. As stated above, it is important to distinguish the Mucorales from these other fungi, as the preferred antifungal treatments differ (i.e., polyenes for the Mucorales vs. expanded-spectrum triazoles for most septate molds). The entomophthoromycoses caused by *Basidiobolus* and *Conidiobolus* also can cause identical clinical syndromes. These fungi may appear similar to the Mucorales on histopathology and can be reliably distinguished from the latter only by culture.

In a patient with sinusitis and proptosis, orbital cellulitis and cavernous sinus thrombosis caused by bacterial pathogens (most commonly *Staphylococcus aureus*, but also streptococcal and gram-negative species) must be excluded. *Klebsiella rhinoscleromatis* is a rare cause of an indolent facial rhinoscleroma syndrome that may appear similar to mucormycosis. Finally, the Tolosa-Hunt syndrome causes painful ophthalmoplegia, ptosis, headache, and cavernous sinus inflammation; biopsies and clinical follow-up may be needed to distinguish the Tolosa-Hunt syndrome from mucormycosis by the lack of progression of the former entity.

TREATMENT MUCORMYCOSIS

GENERAL PRINCIPLES

The successful treatment of mucormycosis requires four steps: (1) early diagnosis; (2) reversal of underlying predisposing risk factors, if possible; (3) surgical debridement; and (4) prompt antifungal therapy. Early diagnosis of mucormycosis is critical, since early initiation of therapy is associated with improved survival rates. It is also crucial to reverse (or prevent) underlying defects in host defense during treatment (e.g., by stopping or reducing the dosage of immunosuppressive medications or by rapidly restoring euglycemia and normal acid-base status). Finally, iron administration to patients with active mucormycosis should be avoided, as iron exacerbates infection in animal models. Blood transfusion typically results in some liberation of free iron due to hemolysis, so a conservative approach to red blood cell transfusions is advisable.

Blood vessel thrombosis and resulting tissue necrosis during mucormycosis can result in poor penetration of antifungal agents to the site of infection. Therefore, debridement of all necrotic tissues is critical for eradication of disease. Surgery has been found (by logistic regression and in multiple case series) to be an independent variable for favorable outcome in patients with mucormycosis. Limited data from a retrospective study support the use of intraoperative frozen sections to delineate the margins of infected tissues, with sparing of tissues lacking evidence of infection. A multidisciplinary team, including an internist, an infectious disease specialist, and surgical specialists whose expertise is relevant to the sites of infection, is typically required for the management of mucormycosis.

ANTIFUNGAL THERAPY

Primary therapy for mucormycosis should be based on a polyene antifungal agent (Table 242-2), except perhaps for mild localized infection (e.g., isolated suprafascial cutaneous infection) that has been eradicated surgically in an immunocompetent patient. Amphotericin B (AmB) deoxycholate remains the only licensed antifungal agent for the treatment of mucormycosis. However, lipid formulations of AmB are significantly less nephrotoxic, can be administered at higher doses, and are probably more effective than AmB deoxycholate for this purpose. Liposomal amphotericin B (LAmB) is preferred to amphotericin B lipid complex (ABLC) for management of CNS infection on the basis of retrospective survival data and superior brain penetration; there is no clear advantage of either agent for non-CNS infections.

TABLE 242-2 FIRST-LINE ANTIFUNGAL OPTIONS FOR THE TREATMENT OF MUCORMYCOSIS[a]

Drug	Recommended Dosage	Advantages and Supporting Studies	Disadvantages
Primary Antifungal Therapy			
AmB deoxycholate	1.0–1.5 mg/kg qd	• >5 decades of clinical experience • Inexpensive • Only licensed agent for treatment of mucormycosis	• Highly toxic • Poor CNS penetration
LAmB	5–10 mg/kg qd	• Less nephrotoxic than AmB deoxycholate • Better CNS penetration than AmB deoxycholate or ABLC • Better outcomes than with AmB deoxycholate in murine models and a retrospective clinical review	• Expensive
ABLC	5 mg/kg qd	• Less nephrotoxic than AmB deoxycholate • Murine and retrospective clinical data suggest benefit of combination therapy with echinocandins	• Expensive • Possibly less efficacious than LAmB for CNS infection
Primary Combination Therapy[b]			
Caspofungin plus lipid polyene	70-mg IV loading dose, then 50 mg/d for ≥2 weeks 50 mg/m^2 IV in children	• Favorable toxicity profile • Synergistic in murine disseminated mucormycosis • Retrospective clinical data suggest superior outcomes for rhino-orbital-cerebral mucormycosis.	• Very limited clinical data on combination therapy
Micafungin or anidulafungin plus lipid polyene	100 mg/d for ≥2 weeks Micafungin: 4 mg/kg qd in children Micafungin: 10 mg/kg qd in low-birth-weight infants Anidulafungin: 1.5 mg/kg qd in children	• Favorable toxicity profile • Synergistic with LAmB in murine model of disseminated mucormycosis	• No clinical data

[a]Primary therapy should generally include a polyene. Non-polyene-based regimens may be appropriate for patients who refuse or are intolerant of polyene therapy or for relatively immunocompetent patients with mild disease (e.g., isolated suprafascial cutaneous infection) that can be surgically eradicated. [b]Prospective randomized trials are necessary to confirm the suggested benefit (from animal and small retrospective human studies) of combination therapy for mucormycosis. Dose escalation of any echinocandin is not recommended because of a paradoxical loss of benefit of combination therapy at echinocandin doses of ≥3 mg/kg qd.

Abbreviations: ABLC, AmB lipid complex; AmB, amphotericin B; CNS, central nervous system; LAmB, liposomal AmB.

Source: Modified from B Spellberg et al: Clin Infect Dis 48:1743, 2009.