Mucormycosis
(zygomycosis)

GGRID

JOHNS HOPKINS
CENTER FOR CLINICAL
GLOBAL HEALTH EDUCATION

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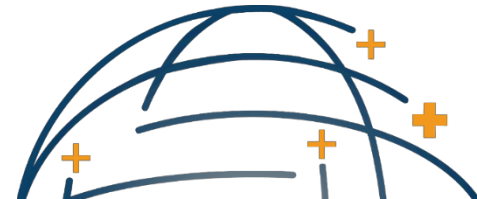
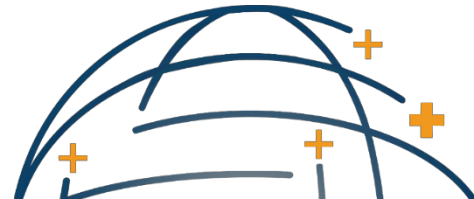
No Disclosures



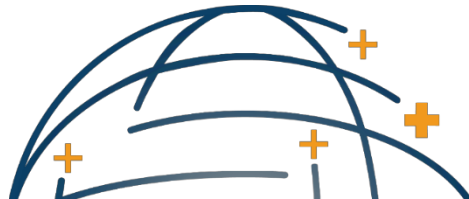
Mucormycosis

- Clinical syndrome
- Risk factors
- Diagnosis
- Management
- Prevention



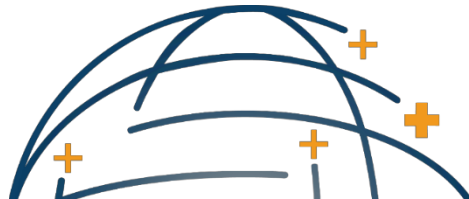
Mucorales

- *Rhizopus*
- *Apophysomyces*
- *Mucor*
- *Rhizomucor*
- *Cunninghamella*
- *Absidia* (Reclassified as *Lichtheimia*)
- *Saksenaea*



Clinical Syndrome

- Rhinocerebral ~40%
- Pulmonary ~25%
- Skin ~20%
- Disseminated ~20%
- Other: GI, bone/joint, heart valve

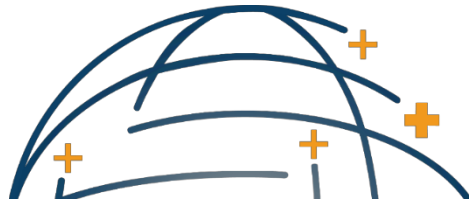


Risk Factors

- Diabetes, hyperglycemia, acidosis
- Immunosuppression: BMT, SOT, Heme malignancies
- Malnutrition
- Iron overload, deferoxamine
- Steroids
- Burns, IDU,
- Environmental/Nosocomial
- Epi and association with COVID-19
- Voriconazole prophylaxis

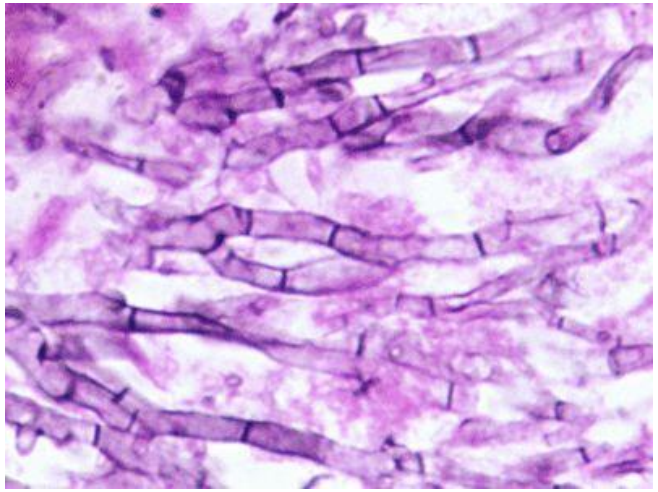
High Mortality

- DM 40-50%
- Cancer 60-70%
- No underlying condition ~35%
- Pulmonary ~75%
- GI ~85%
- Disseminated ~100%



Diagnosis

A



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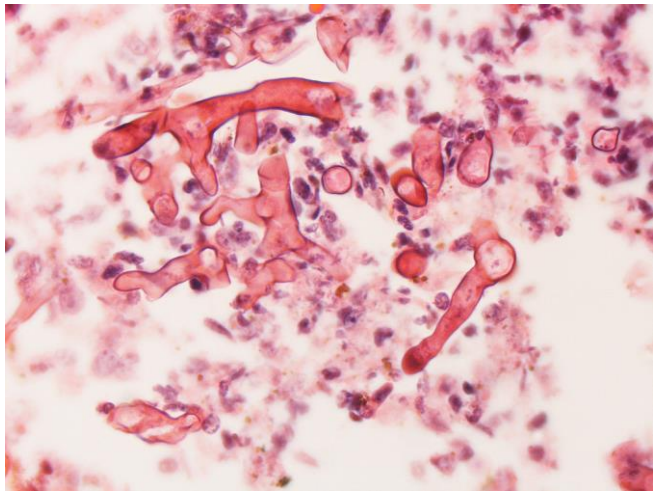

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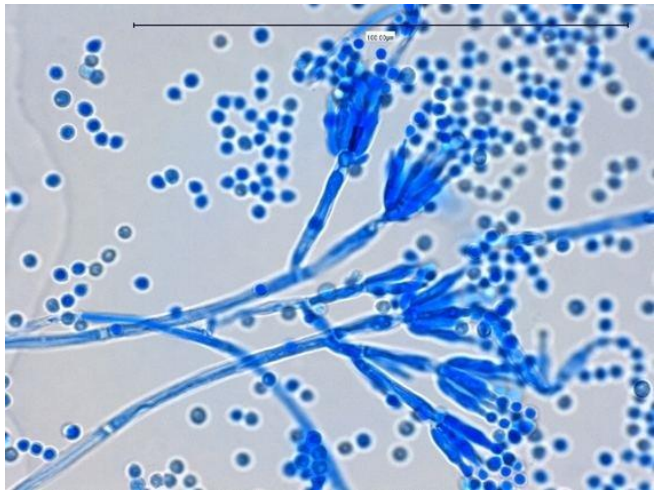

D

https://www.flickr.com/photos/pulmonary_pathology/5390897069

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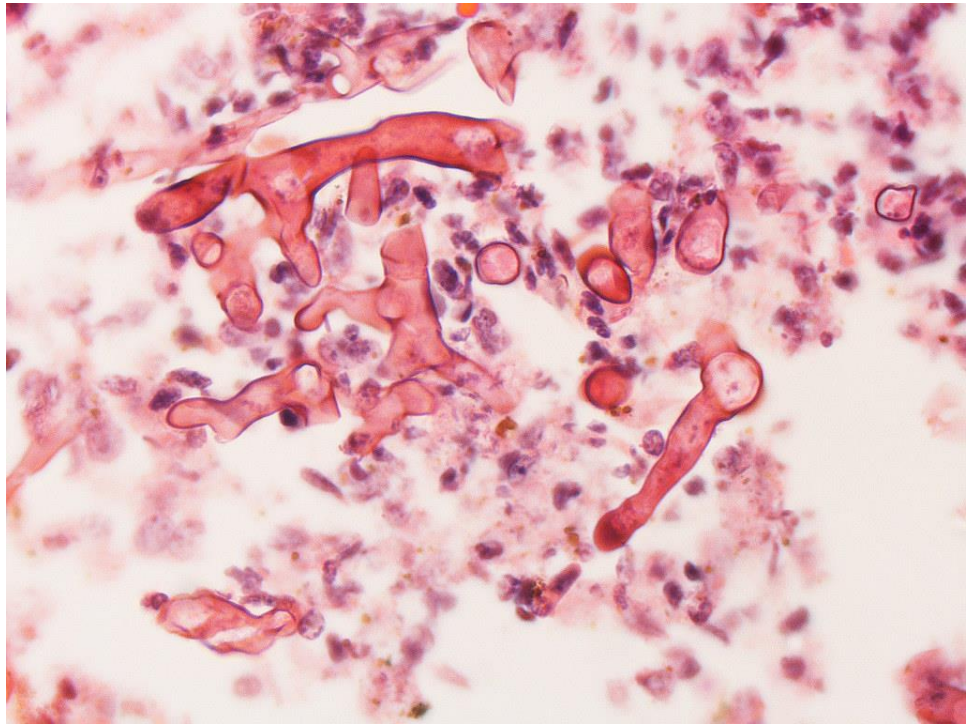
https://upload.wikimedia.org/wikipedia/commons/e/e6/Candida_albicans_2.jpg

Diagnosis



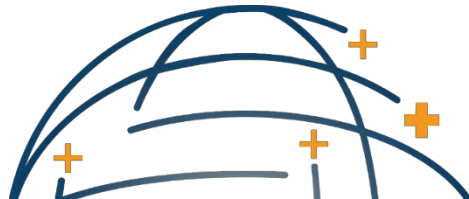
Broad hyphae (5-15 micron diameter)
Irregularly branched
Rare septations

- Hard to culture
- Blood cultures are never positive
- BD-glucan and galactomannan negative
- PCR in development, not yet routine

https://www.flickr.com/photos/pulmonary_pathology/5390897069

Mucormycosis Management

- Control hyperglycemia and acidosis
- Taper steroids
- Aggressive surgical debulking
- Drug of choice: Liposomal (l-AmB) or Amphotericin B (deoxycholate)
- Azoles for step-down: Itraconazole, Posaconazole, Isavuconazole
- No data for echinocandins



Amphotericin B

- Typical regimen: L-AmB 5mg/kg IV q24 hours for >6 weeks
- Could use higher dose in an intermittent (non-daily) schedule as opposed to reducing dosing. (see Brazilian reference)
- Poor tolerability (nephrotoxicity) of dAmB at high dosing
- L-AmB has a longer tissue half-life enabling a step-down type of approach if you're forced to spare drug (ex: 5 mg/kg/day x 3 days then every other day may be a reasonable approach).
- Although we frequently dose-increase out of desperation, we've never documented benefits. D-AmB does not have as long tissue half-life and typically gets more drug into blood.
- You can also spare L-AmB by using the azole quickly in course – ex. 1-2 weeks AmB then transition to azole. If you do this, overlap drugs for about 3 days to achieve azole levels.

Source: Dr. Kieren Marr, Johns Hopkins School of Medicine

Azoles

- Options:
  - Itraconazole: Liquid formulation > capsules for better absorption
  - Posaconazole: Oral suspension is not highly bioavailable and requires fatty food for absorption, watch renal function.
  - Isavuconazole: Limited data
- If available, obtain culture and MIC for azoles to guide choice.
- If cultures not available, organisms causing rapid progression are likely Rhizopus species (mainly arrhizus). Others (eg Apophysomyces) are more likely to cause insidious GI disease, local necrotic skin disease, etc.
- Check levels
- Step down, maintenance therapy
- Potential preventative therapy
- Azoles inhibit dexamethasone metabolism → higher steroid levels. So, decrease the steroid dosing if giving azole concurrently.

Source: Dr. Kieren Marr, Johns Hopkins School of Medicine

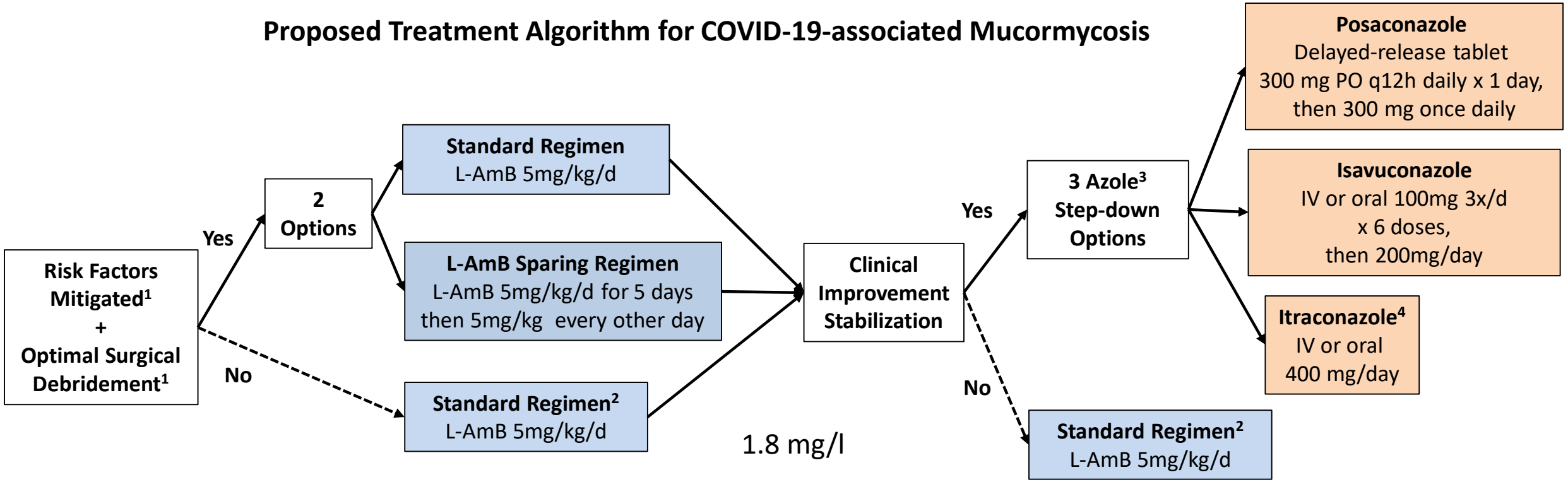
Mucormycosis Prevention

- Rapid correction of hyperglycemia and acidosis
- Avoid routine use of steroids for COVID-19 (only if hypoxic)
- Taper steroids

1.8 mg/l

- Consider saline sinus irrigation (safe amphotericin for treatment)
- Utility of iron chelators is mixed
- Limited data on azoles: Itraconazole, Posaconazole, Isavuconazole

Proposed Treatment Algorithm for COVID-19-associated Mucormycosis



[1]Glucose normalized, acidosis resolved, steroids tapered, etc. In the absence of optimal surgical debridement and risk factor mitigation, anti-fungal therapy has limited effectiveness.

[2]Although higher dose L-AmB has been used in practice for some patients, there are no data clearly demonstrating that it improves survival. But there are data suggesting high dosing of L-Amb triggers accelerated blood clearance of subsequent doses. Higher dose of lipid also leads to higher rates of complement-mediated infusion reactions. There are no data clearly demonstrating improved survival with addition of azoles or echinocandins to L-AmB.

[3]Consider azole step-down after 1-2 weeks of L-AmB in clinical stable/improving patients. Overlap azoles with L-AmB for at least 3 days to achieve adequate levels. Adjust azole dose based on trough serum concentration and organism MIC, to optimize efficacy and avoid toxicity. Depending on organism MIC and drug, target trough concentrations range of 0.5-3mg/l is typical.

[4]Itraconazole has been used successfully in some patients in the past Best to confirm susceptibility with culture/MIC. Historically some effectiveness with *Rhizopus, Apophysomyces, Rhizomucor, Absidia* (Reclassified as *Lichtheimia*) and *Saksenaea, but l*ess effective for *Mucor* and *Cunninghamella*.

Draft RCB 30 May 2021

Sources

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Minimum concentration of Amphotericin B in serum according to the formulation, dose, and daily or prolonged intermittent therapeutic regimen.
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