SHC Clinical Pathway: Candidemia

Background:

- Infectious Diseases consultation is strongly recommended for all cases of candidemia and invasive candidiasis.
- Yeast in the blood is not always *Candida spp.* see FAQ for more detail.
- *Candida* isolated from blood warrants treatment and should never be considered a contaminant.
- Candidemia is the most common manifestation of invasive candidiasis. Management of other clinical manifestations of invasive candidiasis such as meningitis and endocarditis/endovascular infection is outside the scope of this document.
- *C. albicans* is the most commonly isolated species at SHC, followed by *C. glabrata* and *C. parapsilosis*.
- Non-*Candida* opportunistic yeasts such as *Cryptococcus* are excluded from this document.

	Fluconazole	Voriconazole [1]	Caspofungin [2]	L-AmB
Candida albicans	+	+	+	+
Candida auris [3]	-	+/-	+	+/-
Candida dubliniensis	+	+	+	+
Candida glabrata (Nakaseomyces glabrata) [4]	+/-	+/-	+	+
Candida guilliermondii (Meyerozyma guilliermondii)	+	+	+	+
Candida krusei (Pichia kudriavzevii) [5]	-	+	+	+
Candida lusitaniae (Clavispora lusitaniae) [6]	+	+	+	-
Candida parapsilosis [7]	+	+	+	+
Candida tropicalis	+	+	+	+

+ Reliably active; +/- variably active; - resistant. L-AmB = Liposomal amphotericin B (Ambisome).

[1] Isavuconazole, itraconazole, and posaconazole are also active in vitro against voriconazole-susceptible *Candida spp*.
[2] Susceptibilities apply to all echinocandins including micafungin, anidulafungin, and rezafungin.
[3] Emerging multidrug-resistant organism. Caspofungin is the preferred initial treatment. ID consultation is strongly recommended.
[4] Reduced susceptibility to azoles, i.e., dose dependent.
[5] Intrinsically resistant to fluconazole. Itraconazole generally not recommended.
[6] Intrinsically resistant to L-AmB.
[7] Higher MICs for echinocandins, although the clinical significance of this is unknown.

Diagnosis:

- Routine aerobic/anaerobic blood cultures easily recover *Candida*, and fungal blood cultures are unnecessary.
- *Candida spp*. often take longer than bacterial pathogens to grow. *C. albicans* is typically detected from blood at >24 hours, whereas *C. glabrata* is typically detected at >48-72 hours.
- (1,3)-Beta-D-glucan cannot accurately identify candidemia, and routine testing should generally be avoided.

Initial Treatment:

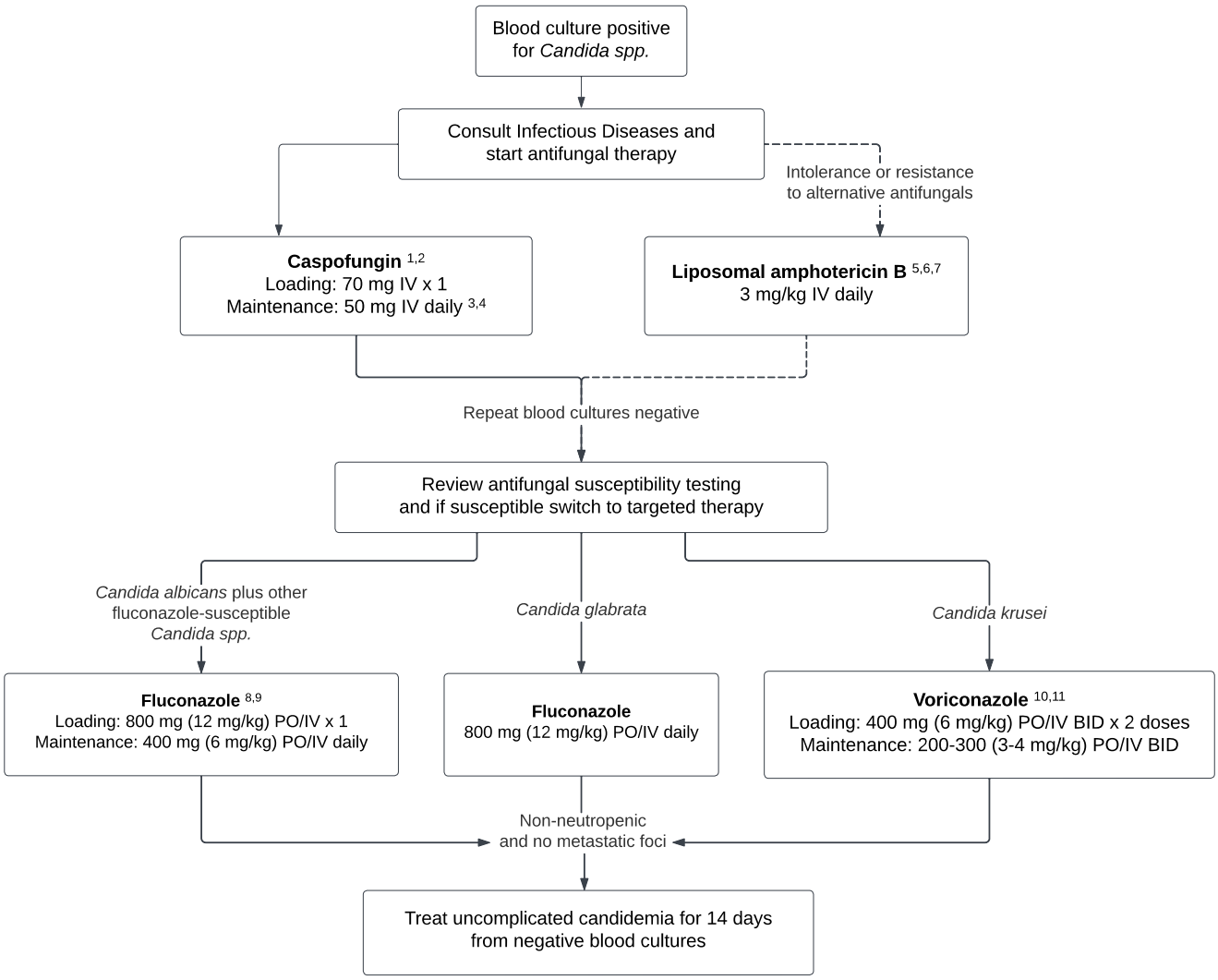
- Caspofungin is first-line initial therapy for candidemia at SHC and generally well tolerated.
- Liposomal amphotericin B is recommended if there is resistance or intolerance to alternative antifungal agents.

Targeted Treatment:

- De-escalation to azoles is safe and effective, and azoles are highly orally bioavailable. If a patient is tolerating oral therapy, their isolate is susceptible, and there are no clinically significant drug-drug interactions, the patient should be switched to an oral azole.
- Antifungal susceptibility testing may be difficult to interpret, and questions should be discussed with ID.

SHC Treatment Guideline for Candidemia

This algorithm does not apply to Candida meningitis or endocarditis/endovascular infection.



[1] Fluconazole is an alternative initial therapy for non-neutropenic, clinically stable patients.
[2] Echinocandins including caspofungin do not treat *Cryptococcus* and concentrate poorly in the eye, CSF, and urine.
[3] Caspofungin 70 mg IV daily is recommended for patients on strong enzyme inducers, e.g., rifampin or phenytoin. Additional information here.
[4] Caspofungin 70 mg IV daily may be considered in critically ill obese patients ≥75 kg. Additional information here.
[5] L-AmB is the preferred antifungal agent in pregnancy.
[6] L-AmB is the preferred antifungal agent for patients with suspected cryptococcal infection.
[7] *C. lusitaniae* is intrinsically resistant to L-AmB.
[8] Fluconazole requires renal dosing. Additional information here.
[9] Recommend using total body weight (TBW) for obese patients with BMI ≥30. Additional information here.
[10] Recommend using adjusted body weight (ABW) for obese patients with BMI ≥30. Additional information here.
[11] Information about therapeutic drug monitoring for voriconazole may be found here.

Frequently Asked Questions

Is isolating Candida from blood ever considered a contaminant? What about other sites?
You should always assume that isolating *Candida* from blood warrants treatment and is NOT a contaminant. That said, *Candida* species are normal respiratory and skin flora. *Candida* isolated from non-sterile sites such as sputum or BAL, urine, and indwelling drains are generally considered colonizers and do not require targeted antifungal therapy. If there is concern for symptomatic *Candida* cystitis, pyelonephritis, or fungal ball, ID consultation is recommended.

Is isolating yeast from blood culture the same as isolating Candida?
Although yeast in blood culture most commonly refers to *Candida*, other forms of yeast such as *Cryptococcus* can also be isolated from blood. In this sense, yeast is NOT synonymous with *Candida*, and if there is high suspicion for cryptococcal infection, initial therapy with liposomal amphotericin B is recommended.

What is the utility of (1-3)- beta-D-glucan and when is it useful?
The clinical utility of (1-3)-beta-D-glucan (Fungitell) and non-invasive *Candida* species PCRs in diagnosing invasive candidiasis is unknown. Particularly for (1,3)-beta-D-glucan, a negative test does not rule out infection and a positive result has poor specificity and does not indicate invasive disease. Neither test should be used alone to diagnose invasive candidiasis.

Antifungal susceptibility testing indicates that caspofungin is "intermediate" but micafungin and anidulafungin are "susceptible." Is caspofungin still an appropriate therapy?
Yes. Caspofungin susceptibility testing for *Candida spp*. is laboratory dependent, and resistance may be falsely reported. In the absence of mutations causing resistance, caspofungin is still recommended. Additional questions about interpreting antifungal susceptibility results should be discussed with ID.

When should I consider empiric antifungal therapy?
The EMPIRICUS[7] trial showed no benefit to empiric antifungal therapy in critically ill patients at high risk for candidemia with persistent sepsis despite broad-spectrum antibiotic treatment. This finding was consistent across various subgroups including surgical patients and those with elevated (1-3)-beta-D-glucan results. Notably, the EMPIRICUS trial excluded neutropenic patients, those receiving high-dose corticosteroids, and transplant recipients. Except in these immunocompromised patient groups, empiric antifungal therapy is not evidence based and should be considered only on a case by case basis.

References

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