TABLE 240-2 TREATMENT OF MUCOCUTANEOUS CANDIDAL INFECTIONS

Disease	Preferred Treatment	Alternatives
Cutaneous	Topical azole	Topical nystatin
Vulvovaginal	Oral fluconazole (150 mg) or azole cream or suppository	Nystatin suppository
Thrush	Clotrimazole troches	Nystatin, fluconazole
Esophageal	Fluconazole tablets (100–200 mg/d) or itraconazole solution (200 mg/d)	Caspofungin, micafungin, or amphotericin B

challenging aspect of diagnosis is determining which patients with *Candida* isolates have hematogenously disseminated candidiasis. For instance, recovery of *Candida* from sputum, urine, or peritoneal catheters may indicate mere colonization rather than deep-seated infection, and *Candida* isolation from the blood of patients with indwelling intravascular catheters may reflect inconsequential seeding of the blood from or growth of the organisms on the catheter. Despite extensive research into both antigen and antibody detection systems, there is currently no widely available and validated diagnostic test to distinguish patients with inconsequential seeding of the blood from those whose positive blood cultures represent hematogenous dissemination to multiple organs. Many studies are under way to establish the utility of the β-glucan test; at present, its greatest utility is its negative predictive value (~90%). Meanwhile, the presence of ocular or macronodular skin lesions is highly suggestive of widespread infection of multiple deep organs. Although extensive research is being conducted on other tests for infection, such as PCR, none of these tests is fully validated or widely available at present.

TREATMENT *CANDIDA* INFECTIONS

MUCOCUTANEOUS *CANDIDA* INFECTION

The treatment of mucocutaneous candidiasis is summarized in Table 240-2.

CANDIDEMIA AND SUSPECTED HEMATOGENOUSLY DISSEMINATED CANDIDIASIS

All patients with candidemia are treated with a systemic antifungal agent. A certain percentage of patients, including many of those who have candidemia associated with an indwelling intravascular catheter, probably have "benign" candidemia rather than deep-organ seeding. However, because there is no reliable way to distinguish benign candidemia from deep-organ infection, and because antifungal drugs less toxic than amphotericin B are available, antifungal treatment for candidemia—with or without clinical evidence of deep-organ involvement—has become the standard of practice. In addition, if an indwelling intravascular catheter is present, it is best to remove or replace the device whenever feasible.

The drugs used for the treatment of candidemia and suspected disseminated candidiasis are listed in Table 240-3. Various lipid formulations of amphotericin B, three echinocandins, and the azoles fluconazole and voriconazole are used; no agent within a given class has been clearly identified as superior to the others. Most institutions choose an agent from each class on the basis of their own specific microbial epidemiology, strategies to minimize toxicities, and cost considerations. Unless azole resistance is considered likely, fluconazole is the agent of choice for the treatment of candidemia and suspected disseminated candidiasis in nonneutropenic, hemodynamically stable patients. Initial treatment in the context of likely azole resistance depends, as mentioned above, on the epidemiology of the individual hospital. For example, certain hospitals have a high rate of recovery of *C. glabrata*, while others do not. At institutions where non-*albicans Candida* species are frequently recovered, therapy with an echinocandin is typically started while the results of sensitivity testing are awaited. For hemodynamically unstable or neutropenic patients, initial treatment with broader-spectrum agents is desirable; these drugs include polyenes, echinocandins, or later-generation azoles such as voriconazole. Once the clinical response has been assessed and the pathogen specifically identified, the regimen can be altered accordingly. At present, the vast majority of *C. albicans* isolates are sensitive to fluconazole. Isolates of *C. glabrata* and *C. krusei* are less sensitive to fluconazole and more sensitive to polyenes and echinocandins. *C. parapsilosis* is less sensitive to echinocandins in vitro; however, this lesser sensitivity is considered nonsignificant.

Some generalizations exist regarding the management of specific *Candida* infections. Recovery of *Candida* from sputum is almost never indicative of underlying pulmonary candidiasis and does not by itself warrant antifungal treatment. Similarly, *Candida* in the urine of a patient with an indwelling bladder catheter may represent colonization only rather than bladder or kidney infection; however, the threshold for systemic treatment is lower in severely ill patients in

TABLE 240-3 AGENTS FOR THE TREATMENT OF DISSEMINATED CANDIDIASIS

Agent	Route of Administration	Dose[a]	Comment
Amphotericin B deoxycholate	IV only	0.5–1.0 mg/kg daily	Being replaced by lipid formulations
Amphotericin B lipid formulations			Not FDA approved as primary therapy, but used commonly because less toxic than amphotericin B deoxycholate
Liposomal (AmBiSome, Abelcet)	IV only	3.0–5.0 mg/kg daily	
Lipid complex (ABLC)	IV only	3.0–5.0 mg/kg daily	
Colloidal dispersion (ABCD)	IV only	3.0–5.0 mg/kg daily	Associated with frequent infusion reactions
Azoles[b]			
Fluconazole	IV and oral	400 mg/d	Most commonly used
Voriconazole	IV and oral	400 mg/d	Multiple drug interactions
			Approved for candidemia in nonneutropenic patients
Echinocandins			Broad spectrum against *Candida* species; approved for disseminated candidiasis
Caspofungin	IV only	50 mg/d	
Anidulafungin	IV only	100 mg/d	
Micafungin	IV only	100 mg/d	

[a]For loading doses and adjustments in renal failure, see Pappas PG et al: Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 48:503, 2009. The recommended duration of therapy is 2 weeks beyond the last positive blood culture and the resolution of signs and symptoms of infection. [b]Although ketoconazole is approved for the treatment of disseminated candidiasis, it has been replaced by the newer agents listed in this table. Posaconazole has been approved for prophylaxis in neutropenic patients and for oropharyngeal candidiasis. FDA, U.S. Food and Drug Administration.