TABLE 238-1 TREATMENT OF BLASTOMYCOSIS[a]

Disease	Primary Therapy	Alternative Therapy
Immunocompetent Patient/Life-Threatening Disease		
Pulmonary	Lipid AmB, 3–5 mg/kg qd, *or* AmB deoxycholate, 0.7–1.0 mg/kg qd (total dose: 1.5–2.5 g)	Itraconazole, 200–400 mg/d (once patient's condition has stabilized)
Disseminated		
CNS	Lipid AmB, 3–5 mg/kg qd, *or* AmB deoxycholate, 0.7–1.0 mg/kg qd (total dose: at least 2 g)	Fluconazole, 800 mg/d (if patient is intolerant to full course of AmB)
Non-CNS	Lipid AmB, 3–5 mg/kg qd, *or* AmB deoxycholate, 0.7–1.0 mg/kg qd (total dose: 1.5–2.5 g)	Itraconazole, 200–400 mg/d (once patient's condition has stabilized)
Immunocompetent Patient/Non-Life-Threatening Disease		
Pulmonary or disseminated (non-CNS)	Itraconazole, 200–400 mg/d, *or* Lipid AmB, 3–5 mg/kg qd, *or* AmB deoxycholate, 0.5–0.7 mg/kg qd (in patients intolerant to itraconazole or whose disease progresses despite therapy)	Fluconazole, 400–800 mg/d, *or* Ketoconazole, 400–800 mg/d
Immunocompromised Patient[b]		
All infections	Lipid AmB, 3–5 mg/kg qd, *or* AmB deoxycholate, 0.7–1.0 mg/kg qd (total dose: 1.5–2.5 g)	Itraconazole, 200–400 mg/d (non-CNS disease, once clinically improved)

[a]Therapy is generally given for 6–12 months. For bone and joint disease, a 12-month course is usually necessary. [b]Suppressive therapy with itraconazole may be considered for patients whose immunocompromised state continues. Fluconazole (800 mg/d) may be useful for patients who have CNS disease or cannot tolerate itraconazole.

Abbreviations: AmB, amphotericin B; CNS, central nervous system.

its good penetration of cerebrospinal fluid—CNS disease. Posaconazole has also been used for refractory pulmonary disease. The echinocandins have variable activity against *B. dermatitidis* and therefore are not used in the treatment of blastomycosis.

PROGNOSIS

Cure rates are 90–95% among compliant immunocompetent patients given itraconazole for mild to moderate pulmonary and extrapulmonary disease without CNS involvement. Bone and joint disease usually requires 12 months of therapy. The fewer than 5% of infections that relapse after an initial course of itraconazole usually respond well to a second treatment course.

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239 Cryptococcosis

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DEFINITION AND ETIOLOGY

Cryptococcus, a genus of yeast-like fungi, is the etiologic agent of cryptococcosis. Both species, *C. neoformans* and *C. gattii*, can cause cryptococcosis in humans. The two varieties of *C. neoformans—grubii* and *neoformans*—correlate with serotypes A and D, respectively. *C. gattii*, although not divided into varieties, also is antigenically diverse, encompassing serotypes B and C. Most clinical microbiology laboratories do not routinely distinguish between *C. neoformans* and *C. gattii*, or among varieties, but rather identify and report all isolates simply as *C. neoformans*.

EPIDEMIOLOGY

Cryptococcosis was first described in the 1890s but remained relatively rare until the mid-twentieth century, when advances in diagnosis and increases in the number of immunosuppressed individuals markedly raised its reported prevalence. Although serologic evidence of cryptococcal *infection* is common among immunocompetent individuals, cryptococcal *disease* (cryptococcosis) is relatively rare in the absence of impaired immunity. Individuals at high risk for disease due to *C. neoformans* include patients with hematologic malignancies, recipients of solid organ transplants who require ongoing immunosuppressive therapy, persons whose medical conditions necessitate glucocorticoid therapy, and patients with advanced HIV infection and CD4+ T lymphocyte counts of <200/μL. In contrast, *C. gattii*–related disease is not associated with specific immune deficits and often occurs in immunocompetent individuals.

Cryptococcal infection is acquired from the environment. *C. neoformans* and *C. gattii* inhabit different ecologic niches. *C. neoformans* is frequently found in soils contaminated with avian excreta and can easily be recovered from shaded and humid soils contaminated with pigeon droppings. In contrast, *C. gattii* is not found in bird feces. Instead, it inhabits a variety of arboreal species, including several types of eucalyptus tree. *C. neoformans* strains are found throughout the world; however, var. *grubii* (serotype A) strains are far more common than var. *neoformans* (serotype D) strains among both clinical and environmental isolates. The geographic distribution of *C. gattii* was thought to be largely limited to tropical regions until an outbreak of cryptococcosis caused by a new serotype B strain began in Vancouver in 1999. This outbreak has extended into the United States, and *C. gattii* infections are being encountered increasingly in several states in the Pacific Northwest.

The global burden of cryptococcosis was recently estimated at ~1 million cases, with >600,000 deaths annually. Thus cryptococci are important human pathogens. Since the onset of the HIV pandemic in the early 1980s, the overwhelming majority of cryptococcosis cases have occurred in patients with AIDS (Chap. 226). To comprehend the impact of HIV infection on the epidemiology of cryptococcosis, it is instructive to note that in the early 1990s there were >1000 cases of cryptococcal meningitis each year in New York City—a figure far exceeding that for all cases of bacterial meningitis. With the advent of effective antiretroviral therapy, the incidence of AIDS-related cryptococcosis has been sharply reduced among treated individuals. Thus most cases of cryptococcosis now occur in resource-limited regions of the world. The disease remains distressingly common in regions where antiretroviral therapy is not readily available (e.g., parts of Africa and Asia); in these regions, up to one-third of patients with AIDS have cryptococcosis. Among HIV-infected persons, those with a decreased percentage of memory B cells expressing IgM may be at greater risk for cryptococcosis.