are indicated to determine the true incidence of melioidosis in Central America, South America, and the Caribbean.

Finally, I must correct some factual inaccuracies. First, the patient originally described by Whitmore and Krishnaswami [7] was 40 years old, not 10 years old as stated by Dorman et al. [1]. Second, the longest incubation period for melioidosis has recently been increased to 29 years [8]. Last, the case reported by Lee et al. [2] is not, as they state, the first reported case of mycotic aneurysm caused by B. pseudomallei; an earlier case was reported in 1996 [9].

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References

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Controlled Trials of Amphotericin B Lipid Complex and Other Lipid-Associated Formulations

Str—In their report of an uncontrolled study of amphotericin B lipid complex (ABLC; Liposome, Princeton, NJ) for invasive fungal infections, Walsh et al. [1] emphasize the importance of randomized, controlled trials for assessing comparative antifungal efficacy. We participated in 2 randomized, controlled trials of ABLC therapy for neutropenic patients that were not mentioned in this report.

The first trial was a randomized study comparing the efficacy and safety of ABLC and fluconazole as prophylaxis for fungal infections in bone marrow transplant recipients. Unfortunately, this trial was prematurely discontinued because of unacceptable nephrotoxicity when ABLC prophylaxis was used for patients receiving cyclosporine treatment. Patients who received ABLC prophylaxis also had frequent chills and fever; these toxicities were not observed in patients who received fluconazole prophylaxis. In a second multicenter, randomized trial, ABLC was compared with amphotericin B as empirical antifungal therapy for febrile neutropenic patients. Despite objections from investigators, this trial was also prematurely discontinued by the study sponsor, the Liposome Company. Nonetheless, analysis of patients from our center who participated in this trial showed that the incidence of nephrotoxicity (defined as doubling of the baseline serum creatinine level) and fever or chills among ABLC recipients was not different from the incidence among amphotericin B recipients. The rates of clinical response to amphotericin B and ABLC were similar.

Randomized, double-blind, controlled trials evaluating the efficacy and safety of other lipid-associated formulations of amphotericin B as empirical antifungal therapy have also been performed. The efficacy of amphotericin B colloidal dispersion (ABCD) was found to be comparable with the efficacy of amphotericin B as empirical antifungal therapy for febrile neutropenic patients [2]. ABCD was associated with less renal dysfunction but more infusion-related hypoxia and chills. Similarly, liposomal amphotericin B (AmBisome; Vestar, San Dima, CA) and amphotericin B were equally effective as empirical antifungal treatment of persistently febrile neutropenic patients [3]. However, nephrotoxicity, fever, chills, and cardiopulmonary events were less frequently associated with liposomal amphotericin B.

Therefore, when choosing an agent for antifungal therapy for neutropenic patients, physicians will need to consider not only the difference in toxicity between the lipid-associated formulations and amphotericin B, but also possible differences in the toxicity of the different lipid-associated preparations of amphotericin B.

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minocycline versus doxycycline in the Treatment of Lyme Neuroborreliosis

Str—Dotevall and Hagberg [1] from Göteborg University (Göteborg, Sweden) deserve praise for their well-done study on oral doxycycline treatment of Lyme disease–associated facial palsy and meningitis. This study confirms that oral doxycycline is equivalent to parenteral ceftriaxone in the treatment of Lyme disease–associated palsy and/or meningitis. Experience indicates 21 days of oral doxycycline therapy is equivalent to 14 days of ceftriaxone therapy [3], and Swedish investigators have demonstrated that equivalent results are achieved with doxycycline therapy for \( \approx 2 \) weeks (median, 10.8 days).

Dotevall and Hagberg correctly point out that there has been some reluctance to use oral antibiotics in the treatment of Lyme neuroborreliosis because of fear of inadequate CSF and/or CNS penetration [2, 3]. Doxycycline is preferred over conventional tetracycline for this purpose because of its lipid solubility characteristics [4–6], as stated by Dotevall and Hagberg.

Doxycycline is 5 times more lipid soluble than conventional tetracycline, which is an important determinant of permeability of the blood-brain barrier [7, 8]. Dotevall and Hagberg showed that most patients had highly elevated CSF protein levels, which is the best index of antibiotic permeability of the blood-brain barrier. Aside from emphasizing a shorter duration of therapy, these researchers stressed the use of high dosages of doxycycline (e.g., 400 mg/d) for treatment of Lyme neuroborreliosis.

It is not commonly appreciated that ill patients treated with doxycycline (e.g., patients with legionnaires’ disease) should be given a loading regimen of 200 mg iv q12h for the first 72 h, because of doxycycline’s lipid solubility characteristics and long half-life. Since 5 serum half-lives are usually required to achieve steady-state serum concentrations, and early therapeutic effect, a loading regimen rather than a loading dose permits rapid saturation of the serum. If doxycycline is administered in the usual dosage of 100 mg q12h, then it takes 4–5 days to achieve steady-state kinetics and an observable therapeutic response. In Lyme neuroborreliosis, rapid saturation of the CNS compartment is

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**References**


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**Minocycline versus Doxycycline in the Treatment of Lyme Neuroborreliosis**

Str—Dotevall and Hagberg [1] from Göteborg University (Göteborg, Sweden) deserve praise for their well-done study on oral doxycycline and minocycline after multiple 100-mg oral doses given twice daily. Data are from [11].