hemoglobin levels, in our view, is the clinical significance of any toxicity. The abnormalities were reversible. In the patients for whom 4-week values were available, median creatinine and hemoglobin values were the same for patients in both trial arms. Of the 5 patients in the high-dose arm who discontinued study drugs early, 4 were alive and well and receiving antiretroviral therapy at 6 months, and 1 died of culture-proven tuberculosis.

For settings in developed countries, the current Infectious Diseases Society of America guidelines [3] for treatment of HIV-associated cryptococcal meningitis suggest a dose range for AmB of 0.7–1 mg/kg per day combined with flucytosine. The updated guidelines will retain this dose range (J. R. Perfect, personal communication). Our study [2] provides the first comparative data for making a choice of dose within this range. At the higher dose, clinicians will know that they can achieve more-rapid clearance of infection. In addition, complementary data on the toxicity of AmB at 1 mg/kg per day for a larger number of patients will be available from a trial in Vietnam in which all patients received the higher dose [4].

In the many settings in which flucytosine is not yet generally available—and resource limitations may make a full 2 weeks of induction treatment difficult—toxicity issues may be reduced, and the importance of more-rapid initial clearance, in the absence of flucytosine, is increased. In such settings, our study [2] and an earlier study [5] provide evidence to support the use of the 1 mg/kg dose of AmB. Thus, South African guidelines advocate AmB at 1 mg/kg per day for 7–14 days [6].

Routine, frequent monitoring and saline fluid loading during administration of AmB, at any dose, are essential. In Kampala, Uganda, with use of AmB at 0.7 mg/kg per day in 2 observational study cohorts in 2001 and 2006, 2-week mortality was reduced from 42% in 2001 to 20% in 2006, a reduction that may have been associated, at least in part, with more-frequent monitoring (3 times weekly vs. once weekly) and routine fluid loading in the later cohort [7]. Indeed, in settings in which frequent routine monitoring and transfusion, if occasionally needed, are not available, it is possible that an optimized oral treatment regimen could give results comparable to the results of treatment with AmB. In response to specific questions, none of our patients were excluded on the basis of previous adverse reactions to AmB, saline preloading was given for all doses, and AmB infusions were over 4 h.

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Serologic Tests for Lyme Disease: More Smoke and Mirrors

To the Editor—The article by Steere et al. describing serologic testing for Lyme disease contains the following conclusion: “the sensitivity of 2-tier testing in patients with later manifestations of Lyme disease was 100%, and the specificity was 99%” [1, p. 192]. This conclusion is both disingenuous and misleading.

Steere et al. [1] classified 44 patients as having disseminated (stage 2) or persistent (stage 3) infection due to Borrelia burgdorferi, the spirochetal agent of Lyme disease. The mandatory inclusion criteria for these categories were neurologic, cardiac, or joint involvement and a serologic result positive for B. burgdorferi by ELISA and Western blot [2]. Thus, by definition, all patients with disseminated or persistent Lyme disease were required to have a positive serologic test result. It is disingenuous to define a condition by a positive test result and then state that the test has 100% sensitivity. The true sensitivity of the 2-tier test system has been estimated to be 44%–56% when standard commercial Lyme testing was evaluated in clinical practice [3–5]. In fact, on the basis of a recent molecular diagnostic study, the sensitivity of this testing approach may be as low as 7.5% [6]. Thus, the sensitivity data presented by Steere et al. [1] is not realistic.

In the study by Steere et al. [1], 14 pa-
patients were classified as having “post–Lyme disease symptoms,” with persistent symptomatic manifestations after receiving “recommended antibiotic therapy” for Lyme disease. Among these patients, 36% had serologic evidence of persistent infection due to B. burgdorferi, as defined by the Centers for Disease Control and Prevention criteria of positive results of ELISA and IgG Western blot [2]. Recent studies have revealed that “post–Lyme disease symptoms” may represent failure of short-course antibiotic therapy and persistent infection due to the Lyme spirochete, and this chronic illness may respond to a longer duration of antibiotic treatment [7–11]. Thus, the test results in patients with “post–Lyme disease symptoms” may reflect the true sensitivity of 2-tier testing for persistent Lyme disease, and the 36% sensitivity reported by Steere et al. [1] is consistent with the poor results of previous studies [3–5]. The VlsE C6 peptide ELISA was not significantly better, with a test sensitivity of only 43% for patients with persistent Lyme disease symptoms.

In summary, the sensitivity data presented by Steere et al. [1] reflect both circular reasoning in the context of disseminated infection and poor results in the context of persistent Lyme disease. Better tests are needed for diagnosis of this elusive tick-borne illness.

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Reply to Stricker and Johnson

To the Editor—Stricker and Johnson [1] maintain that the frequency of seropositivity among patients with disseminated or persistent Lyme disease is lower than the frequency reported in our prospective study of serologic testing for this infection. As stated in our article [2], it is problematic to determine the frequency of seroreactivity among patients with neurologic, cardiac, or joint manifestations of Lyme disease, because serologic confirmation is a part of the case definition [3]. However, it has not been possible to confirm Borrelia burgdorferi infection by other methods, such as culture or PCR, in all patients with the aforementioned manifestations of Lyme disease. Nevertheless, B. burgdorferi DNA can be detected by PCR of joint fluid specimens obtained before antibiotic therapy for the majority of patients with Lyme arthritis [4, 5], and it has been detected by culture or PCR in some patients with neuroborreliosis [6, 7]. In our experience, all such patients have had samples that were seropositive for B. burgdorferi. Moreover, in animal models of Lyme disease, spirochetes have been seen in and cultured from CNS, heart, or joint lesion specimens, and animals with spirochetes were seropositive for B. burgdorferi [8, 9]. Therefore, on the basis of current knowledge, all patients with objective neurologic, cardiac, or joint abnormalities of Lyme disease have serologic responses to B. burgdorferi.

Serologic testing for Lyme disease is insensitive during the first several weeks of infection in patients with the initial skin lesion erythema migrans, but the frequency of seropositivity is low during this period only [10, 11]. In our study, 29% of patients with erythema migrans had acute-phase samples with positive IgM or IgG antibody responses to B. burgdorferi, and 64% had convalescent-phase samples with positive responses 3–4 weeks later [2]. After that time, the sensitivity of 2-tier testing (ELISA and Western blot) for patients with disseminated or persistent Lyme disease was 100%, and the specificity was 99% [2]. Others have reported similar results [11], and similar results were found with a newer serologic test, the VlsE C6 peptide ELISA [2, 11, 12].

In our study, 36 (47%) of the 76 patients with erythema migrans had blood samples obtained during the acute phase of the illness that were positive for B. burgdorferi by PCR [2]. Other researchers have found similar results of blood cultures for patients with erythema migrans [13]. After this early period, results of culture and PCR testing of blood samples for B. burgdorferi DNA are almost always negative.

Finally, 10 (71%, not 36%) of 14 patients with post–Lyme disease symptoms...