the patients were not vaccinated during this period, the authors attributed this low incidence to hospital practices and good vaccine coverage of health care workers (HCWs) and family caregivers.

Worldwide HCW compliance with influenza vaccination recommendations has been disappointing, varying from 2% to 36% [2]. At the Clinical Hospital of the University of São Paulo, Brazil, we observed a compliance rate of 34.4% in a recent survey of HCWs who manage high-risk patients. Since 2000, Brazil has showed influenza vaccine coverage rates similar to those of many countries in western Europe [3], which reflects the successful efforts of the Brazilian Health Ministry in vaccination campaigns among elderly patients (82.1% coverage in 2003) but not in other high-risk populations [4].

The authors reported 30%–60% rates of HCW compliance with influenza vaccination recommendations during the study period. Hats off to the Fred Hutchinson Cancer Research Center if their present rates are closer to 60% than to 30%. Recently, the Centers for Disease Control and Prevention reported 51.1% coverage among persons aged ≥65 years and 34.2% coverage among HCWs in the United States [5].

In the article by Nichols et al. [1], no cases of influenza pneumonia or flu-related death were observed among the 9 patients who had been treated with oseltamivir. We have previously reported our experience in treating 41 episodes of influenza in 39 patients during 1 year [6]. We observed a much higher rate of influenza infection (22%) in our study, probably because influenza B virus circulated with great activity in Brazil that year. Second, most of the patients in our study were observed at the outpatient clinic, where only part of the recommended infection-control measures could be implemented. Thus, transmission between patients may have occurred. Third, we also evaluated patients after the sixth month after HSCT, when they became eligible to receive influenza vaccination. The high rate of influenza in our study obviously raised concerns about vaccine efficacy and patients’ compliance with yearly vaccination recommendations. Reviewing the vaccination records, we found an 80% rate of vaccine efficacy but a surprisingly low compliance with seasonal influenza vaccine recommendations [7]. Unfortunately, this question could not be addressed in the study of Nichols et al. [1].

In our study, only 2 (5.1%) of the 39 patients who had been treated with oseltamivir developed pneumonia [6]. Compared with pneumonia rates previously reported in different bone marrow transplant centers (up to 75%), it seems that early introduction of oseltamivir substantially helped to control the development of influenza-related complications in the patients in our study.

In conclusion, good coverage of influenza vaccine must be assured for transplant recipients and HCWs. Patients who are not eligible to receive influenza vaccination because they are within the first 6 months after HSCT are natural candidates for controlled studies evaluating preemptive treatment versus prophylactic treatment with oseltamivir during this period.

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Diagnosis and Treatment of Fungal Endophthalmitis: A Reassessment

Sir—We read with interest the recent report by Sarria et al. [1] on the treatment of Candida glabrata endophthalmitis with caspofungin. We agree that endogenous fungal endophthalmitis would be one of the differential diagnoses for the patient they described. However, the authors do not present any firm evidence for a proven case of C. glabrata endophthalmitis [2]. Without a positive microscopy for fungal elements or culture of vitreous or retina, the case cannot be confirmed.

The funduscopy images demonstrate a white fundal lesion with no signs of significant vitritis, which is normally common in Candida endophthalmitis [3]. Other causes need to be considered, such as non–infection-related processes or lesions due to pathogens, including Staphylococcus aureus, Enterobacter species, or Candida albicans, all of which caused previous episodes of bacteremia in this patient. Clinically, it is impossible to differ-
Evidence about the efficacy of caspofungin treatment for fungal endophthalmitis remains very poorly documented. Caspofungin is a large molecule with a high molecular weight (1213 Da) and is not known to penetrate the blood-ocular barrier, which, under normal conditions, only allows smaller particles (300–500 Da) to penetrate. The drug is lipophobic, with a protein binding value of 97%, which makes it difficult to penetrate tissue. Sarria et al. [1] provide data about the penetration and efficacy of caspofungin and other related echinocandins for the successful treatment of Candida infection in the brain. However, the blood-brain barrier cannot necessarily be assumed to be the same as the blood-ocular barrier, which can be defined as the barrier between the vascular endothelial cells of the retinal capillaries and the retinal epithelial cells. In endogenous endophthalmitis, blood-borne pathogens cross this blood-ocular barrier at the choroid-retina interface, causing infection and damage of the inner eye. During inflammation, the blood-ocular barrier may become “leakier,” allowing larger molecules to pass. However, we feel that clinically significant inflammation or “leakiness” of the retinal vessels was not demonstrated by the authors. A simple angiography with fluorescein dye (376.7 Da) or indocyanine green dye (775 Da), a procedure normally performed to confirm inflammation in the retina or choroids, respectively, would have been helpful to suggest the penetration of a large molecule such as caspofungin into the eye. To our knowledge, there are no published data on the detection of caspofungin in the vitreous or retina tissue, and we await further studies to demonstrate the efficacy of this new drug in the treatment of fungal endophthalmitis. Other antifungal agents, such as voriconazole, which can be detected in human vitreous fluid at concentrations greater than the MIC90 for many fungal pathogens, should be considered for the treatment of fungal endophthalmitis [5, 6].

The choice of antifungal agents for the treatment of fungal endogenous endophthalmitis greatly depends on the drug susceptibility of the fungus and the pharmacokinetic and efficacy of the drug. Unfortunately, because of the rareness of the infection, there is a lack of controlled or comparative studies, and recommendations for the treatment of fungal endophthalmitis are often based on single case reports or case series.

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References


Reply to Schelenz and Watson

Sir—We appreciate the comments on our recent article [1] by Schelenz and Watson [2] and would like to address their concerns. First, the authors state that endogenous endophthalmitis in our patient was likely the result of a bloodstream infection he had had previously, not a concurrent Candida glabrata infection. This seems highly speculative, because the patient’s earlier infections were transient, preceded ocular involvement by ≥6 weeks, were not associated with concurrent abnormal funduscopic findings, and resolved with ≤2 weeks of antimicrobial therapy. Additionally, endophthalmitis occurred in our patient during an episode of persistent candidemia caused by C. glabrata that improved during and resolved after a 28-day course of intravenous caspofungin therapy. Second, examination of the posterior segment of the patient’s left eye revealed an exudative retinal lesion and mild vitreitis. These findings confirm the presence of intraocular inflammation.

Third, we concur that microbiologic confirmation of ocular involvement should be sought to prove causation. However, sampling of the vitreous or retina is not always feasible and, in fact, may not be warranted for patients who are minimally symptomatic or who respond rapidly to treatment aimed at the systemic infection causing endogenous spread to the eye [3], as in our case.