Reply

Str—Lazzarini and Luzzati [1] agree with our analysis [2] of the mortality for patients with candidemia; in particular, they agree that (1) the impact of central venous catheter (CVC) removal in their study was modest, (2) the prognosis is dominated by host factors, (3) inherent bias exists in retrospective studies, and (4) the lack of correlation between mortality and severity of illness in their study probably resulted from limitations of the scoring system they used.

Lazzarini and Luzzati [1] also state that we have misinterpreted the results of their study [3] with regard to mortality rates by site of care, stating that a higher mortality rate was observed among patients in the intensive care unit (ICU). However, data presented in table 5 of their manuscript [3] show that patients who received care in a non-ICU setting had the highest chance of dying (OR, 2.06). If the authors intended to show that the mortality rate was higher among patients in the ICU (OR, 2.06), the order in the variable “hospitalization ward” should have been “ICU vs. surgical” and not “surgical/medical vs. ICU,” as presented. For example, the variable “antifungal therapy (adequate vs. none/inadequate)” correctly indicates that adequate therapy was associated with a lower risk of 30-day mortality from candidemia.

Lazzarini and Luzzati also question a conclusion of ours, that, “because most candidemic episodes have an intestinal source, the removal of CVC is likely to have a limited impact on the outcome” [1]. In their study, 75% of the evaluable nonneutropenic patients with a CVC in place had CVC-related candidemia (defined as recovery of the same *Candida* species from blood specimens and from the CVC tip) [3]. However, this finding does not necessarily mean that the CVC was the source of candidemia, because the CVC tip may have been contaminated during a bloodstream candidal infection that originated from another site. Indeed, the literature strongly suggests that most episodes of candidemia originate in the gut [4]. In addition, *Candida* species have great genotypic diversity [5], indicating that recovery of the same species from different sites does not necessarily imply recovery of the same organism.

Finally, the authors raise concern about whether the proposed prospective, randomized study of removal of CVCs from patients with candidemia would be ethical, because CVC removal was reportedly beneficial in 3 of the 4 studies cited [3, 6, 7] in our original article [2]. However, the benefit of CVC removal was marginal in 2 of these studies [3, 6] and in our original article [2], and, in all 4 studies included [2], host factors were far more important for outcome than CVC removal. In addition, CVC removal is associated with serious complications (pain, bleeding, pneumothorax, and death), particularly in patients with a short life expectancy for whom CVC removal is considered to be futile therapy. Finally, reestablishing venous access after CVC removal may not be possible in a significant proportion of patients who still need to receive intravenous therapy. Thus, concern about whether a prospective study of CVC removal in patients with candidemia is ethical must be weighed against the potential harm that could result from CVC removal. Until such a randomized study is conducted, we submit that our risk-adjusted approach to CVC removal represents a reasonable attempt at making this decision in an individual patient when concerns about serious complications or lack of venous access preclude CVC removal. Furthermore, data from controlled studies focused on answering the question of whether to remove CVCs from patients with candidemia are lacking, despite the availability of data from numerous retrospective studies, which gives strong support to the need for randomized trials—the “gold standard” for testing scientific hypotheses.

Central Venous Catheters as a Risk Factor for Disseminated Phaeohyphomycosis?

Str—We read with interest the article by Revankar et al. [1] and were surprised that the presence of a central venous catheter (CVC) was not considered to be a risk factor for disseminated phaeohyphomycosis. We recently encountered a patient with *Wangiella dermatitidis* fungemia, which we believe was related to her CVC.

A 61-year-old woman was receiving chemotherapy through a totally implanted central venous access device (Port-a-Cath;
Sims Deltec) for metastatic breast cancer when she developed fullness on the left side of her neck and low-grade fever. Physical examination was remarkable for left supraventricular swelling and jugular venous distension. Warmth and swelling were noted over the CVC reservoir in the left chest wall. An ultrasound study revealed complete occlusion of the left internal jugular vein. Empiric antibacterial therapy for neutropenic fever and systemic anticoagulation were started. Neutropenia resolved but blood culture yielded a fungus that was subsequently identified as W. dermatitidis. The CVC was removed but was not submitted to the laboratory for culture, and all additional culture results were negative. There was no evidence of metastatic fungal infection, although an infiltrate visible on a chest radiograph slowly resolved with concurrent antibacterial therapy. The patient received a course of amphotericin B (total dose, 1260 mg) followed immediately by itraconazole (200 mg po q.d. for 8 weeks). She did well for several months but subsequently died of progressive metastatic breast cancer.

Although W. dermatitidis grew in only 1 culture, we believe that this was a true CVC-associated infection, as opposed to specimen contamination or central venous line colonization. This organism is rarely recovered from blood (it did not occur at all among >6000 fungal blood isolates recovered during a 20-year period at one institution [2]), and there were clinical signs of infection associated with the CVC.

CVC-related W. dermatitidis fungemia has been reported previously in 4 patients [3–6], and reports of infection involving other dematiaceous fungi also implicate the presence of a CVC as a predisposing condition for fungemia. Walsh et al. [7] reported a case of Bipoloris spicifera fungemia in which the Hickman catheter “demonstrated 1–3 mm brown colonies of hyphae along the luminal surfaces” (p. 903). Nucci et al. [8] described 23 patients with fungemia due to Exophiala jeaneselmei and Rhinocladiella species (including 18 patients with CVCs in place), 1 of whom is mentioned in the review by Revankar et al. [1]. This latter patient died of disseminated E. jeaneselmei infection after an earlier episode of fungemia with the same organism; during that first episode, the only positive culture results were for blood obtained through her Hickman catheter. In their review, Revankar et al. [1] also included information regarding 3 patients for whom the original reports [9–11] noted that CVCs were in place at the time that fungemia occurred and that infection was limited to the blood alone, with no other source or foci of infection.

Many cases of CVC-related dematiaceous fungemia seem to be mild in nature, as opposed to the fulminant clinical picture characteristic of persons with disseminated disease, as reviewed by Revankar et al. [1]. Nevertheless, it is difficult to understand how the CVC can play a role in simple fungemia but not merit discussion to be associated with fungemia due to dematiaceous fungi in several cases in the literature. In our review, there was 1 patient with a malignancy for whom a central venous line was noted to have been a possible risk factor in the clinical summary (see table 1 in [2]), but this was not mentioned in the list of underlying diseases and risk factors (see table 3 in [2]). This was an oversight. However, none of the immunocompetent patients we described had the presence of a CVC as a possible risk factor.

If one looks closely at the cases men-