Epidemiology of Candidemia

We read with great interest the article by Colombo et al. (1). The findings are very interesting and very useful for Brazilian doctors, especially with respect to the frequency of antifungal resistance. We have some questions on the clinical methodology. The authors reported that the identification of included patients was by the isolation of *Candida* spp. from a blood sample and that the investigators then collected the patients' clinical data. This means that the start point of the study was the blood culture result and not the clinical suspicion of infection. A clinical incidence study must begin with the patient's data instead of a laboratory result. If there is no standard clinical protocol for fungal infection suspicion across the medical centers participating in the surveillance, many cases will be missed, and therefore, the reported incidence will be undervalued.

We reported the results of a prospective study of clinical protocols associated with the suspicion and treatment of neonatal fungal infection over a 5-year period in one neonatal intensive care unit, and we showed that the incidence of isolation of *Candida* spp. in blood cultures changes according to different clinical practices, decreasing from 1.1 to 0.4% (2).

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Authors' Reply

We thank Dr. Procianoy and Dr. Silveira for their interest in our paper (1).

They suggested that our study probably underestimated the burden of candidemia in Brazil because of the study design (laboratory-based survey). They cited a study in which they reported that the rates of candidemia in their neonatal intensive care unit varied widely according to different standards of clinical suspicion (4). It is important to highlight that the mentioned papers are examples of different studies with different objectives and designs.

Surveillance studies of candidemia can be categorized into population-based and sentinel surveillance programs. Of note, both sentinel and population-based studies use a laboratory-based methodology for the identification of patients with can-

didemia, since an incident case of candidemia starts with the growth of *Candida* species from blood cultures. Laboratory-based sentinel surveillance studies may be criticized because they potentially miss data from patients with hematogenous candidiasis, from which positive blood cultures will never be obtained, thus underestimating the burden of disease. Nevertheless, their approach represents the most reliable and accurate methodology for conducting surveillance studies of candidemia (2). On the other hand, close monitoring of patients at risk, as in the study by Procianoy et al., is feasible only if performed with selected high-risk populations, such as premature neonates. It is hard to imagine such a strategy applied in a large hospital. Furthermore, as shown in our study, a substantial number of candidemic patients have coexisting exposures that are risk factors for candidemia, including prior colonization, the use of central venous catheters, the use of broad-spectrum antimicrobials, mucosal surface disruption, and neutropenia. While the exposure to multiple risk factors may occur in a large proportion of hospitalized patients, the vast majority will never develop candidemia. For example, in a study of 2,890 critically ill adults patients admitted to intensive care units of nine hospitals in the United States and Brazil, among 303 patients at high risk for candidemia identified by a prediction rule, only 9.9% developed invasive candidiasis (3). Invasive candidiasis presents a major challenge to clinicians, and the conductance of epidemiologic studies with different designs that may help to understand its epidemiology, risk factors, natural history, and predictors of outcome is very useful and welcome.

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