incident enteric infections and malnutrition. Compared with exclusive breastfeeding, it seems biologically plausible that premasturbation may be an incremental HIV risk factor for a substantial number of infants given mixed feedings. Future studies should account for this potentially decisive covariate [23, 24]. On the other hand, pending more quantitative controlled data, counseling nursing mothers against prechewing their babies’ food during weaning might potentially cause more harm than good [14, 25].

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Mark J. DiNubile
Merck Research Laboratories, North Wales, Pennsylvania

References


Reprints or correspondence: Dr Mark DiNubile, Merck Research Laboratories, PO Box 1000, UG3C-06, North Wales, PA 19454 (mark_dinubile@merck.com).

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Underestimating the Real Burden of Invasive Fungal Infections in Hematopoietic Stem Cell Transplant Recipients?

To the Editor—We read the article by Kontoyiannis et al [1] with great interest because the authors found a comparatively low invasive fungal infection (IFI) rate of 3.4% among 15,820 patients who underwent at least 1 hematopoietic stem cell transplant (HSCT). When interpreting the results of the study; however, 3 considerations should be taken into account.

First, the rate of galactomannan testing performed is not reported. A low rate of routine weekly galactomannan testing of serum samples and low rates of testing of bronchoalveolar lavage specimens, which has recently been shown to be superior to serum testing in terms of sensitivity [2], may have led to significant underestimation of the burden of invasive aspergillosis. Many probable cases may have been considered to be possible IFIs because they lacked fulfillment of the microbiological criteria. Consequently, the number of possible IFIs would be of considerable interest, but this number is not reported.

Second, the rate of invasive diagnostic procedures performed in the patient population of the study by Kontoyiannis et al [1] would be of great interest. Regarding the intensity of diagnostic measures performed, the authors reported variability...
between the sites, which may have led to the strong variation in IFI incidence (ranging by site from 0.9% to 13.2%) [1]. However, we do not know the overall rate of bronchoscopies, autopsies, and other invasive diagnostic procedures, or the rate of chest computed tomography scans performed in the patient population. Knowledge of these rates would be essential to interpret the incidence rates correctly.

Third, no data regarding antifungal prophylaxis are presented in the article. The authors report, however, that the incidence of IFIs did not decrease over the study period despite common practice of antifungal prophylaxis [1]. Possible explanations for the high rates and lack of decrease in invasive aspergillosis could be the broad usage of fluconazole as prophylactic treatment. In contrast to posaconazole, which has been shown to possess superior activity against molds, compared withitraconazole, fluconazole is lacking activity against molds. In a prospective single-center evaluation of IFIs in patients with hematologic malignancies (including patients undergoing HSCT) performed at our institution, we observed that yeasts have outpaced molds as the primary cause of probable and proven IFI [3]. The broad prophylactic use of posaconazole may have contributed to that finding in our patient population.

Despite these concerns, we would like to underline the significant impact of the groundbreaking prospective, multicenter study performed by Kontoyiannis et al [1], which brings new insights into the epidemiology of IFIs in patients who have undergone HSCT.

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Martin Hoenigl, Thomas Valentin, Helmut J. F. Salzer, Ines Zollner-Schwetz, and Robert Krause
Section of Infectious Diseases, Division of Pulmonology, Medical University of Graz, Graz, Austria

References


Reprints or correspondence: Dr Robert Krause, Sect of Infectious Diseases, Div of Pulmonology, Medical University of Graz, Graz, Austria (robert.krause@muedingraz.at).

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Reply to Hoenigl et al

To the Editor—We thank Hoenigl et al for their comments [1] and for their interest in our work, which represents the first national prospective multicenter surveillance for the burden of fungal disease in hematopoietic transplant recipients [2]. All the points raised by Hoenigl et al are both relevant and complex. We agree that analyzing risks, frequency, and type of fungal infection in the context of intensity of Aspergillus galactomannan testing, invasive procedures, and antifungal prophylaxis is important; however, these are complicated issues that were beyond the scope of our first manuscript. A key challenge of this analysis was the heterogeneity of the prophylactic, diagnostic, and management approaches among the different participating centers. This makes it very difficult to “dissect” the relative contribution of each entity (eg, timing and intensity of prophylaxis, diagnostic work-up) to the incidence of invasive fungal infections in our cohorts. Specifically, the lack of a uniform approach to diagnosis, differences in the net state of immunosuppression and comorbidities, and the lack of detailed data regarding the effects of prior, concomitant, and subsequent antifungal exposure(s) create complex scenarios and necessitate careful analysis in future publications. We plan to explore host-specific (eg, type of transplant, age, and comorbidities) and fungus-specific (eg, Zygomyces) risk factors in future publications. However, it must be recognized that the true prevalence of many invasive mycoses will remain uncertain given the decreasing autopsy rates in many major transplant centers. For example, at The University of Texas M.D. Anderson Cancer center, <10% of patients with hematological malignancies now undergo autopsy (R. E. Lewis, K. Leventakos, G. Chamilos, R. Ben-Ami, P. Tamboli, J. Tar rand, I. I. Raad, G. P. Bodey, M. Luna, and D.P.K., unpublished data). In conclusion, we feel that such analyses are important but quite complicated, and we will attempt to address some of these important issues as they relate to specific infections and hosts in future publications.

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Dimitrios P. Kontoyiannis,1 Benjamin J. Park,2 Kathleen A. Wannemuehler,3 Tom M. Chiller,2 and Peter G. Pappas2
1The University of Texas MD Anderson Cancer Center, Houston, Texas; 2Mycotic Diseases Branch, Centers for Diseases Control and Prevention, Atlanta, Georgia; and 3Division of Infectious Diseases, Department of Medicine, University of Alabama at Birmingham Medical Center, Birmingham, Alabama

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