To the Editor—We read the article by Maertens et al [1] with great interest. In a series of 58 patients who received a diagnosis of proven or probable invasive aspergillosis (IA), the authors confirmed previous work that the diagnostic performance of galactomannan antigen levels in bronchoalveolar lavage (BAL) fluid samples is good and that the procedure is safe in critically ill hematology patients.

However, the article leaves both the readers of Clinical Infectious Diseases and the treating physicians of patients who have a high risk of IA with the burning question whether performance of BAL has additional diagnostic yield in comparison with serum galactomannan testing. The most convincing argument to persuade hematologists and pulmonologists to perform BAL would be that determination of galactomannan levels in BAL fluid samples has a higher sensitivity without a loss of specificity. In addition, for patients with a positive serum galactomannan level, attempts to make a culture-positive diagnosis can be done by performing BAL, which is increasingly important in the context of recent data on emerging azole resistance in Aspergillus fumigatus [2]. Furthermore, patients might be diagnosed with a mixed (bacterial and/or fungal) infection.

To our surprise, the authors did not provide any data on the sensitivity of galactomannan in BAL in comparison with in serum samples. As an explanation, they state that such a comparison is not possible, because a positive serum galactomannan test result was part of the gold standard for the diagnosis of IA. Although this argument is true for probable cases of IA, incorporation of a positive serum galactomannan test result as a criterion for case classification is unnecessary for proven cases.

Therefore, we hope that Maertens et al [1] can provide us the data on the sensitivity of BAL galactomannan measurements for the substantial subset of patients with proven pulmonary IA (31 of 58 patients). We are particularly interested in the data for patients with proven pulmonary IA and not other molds, because other molds will not be detected by means of galactomannan testing. Therefore, even if galactomannan levels in BAL samples would yield 100% sensitivity, a negative BAL sample test result should always be followed by tissue diagnostics to exclude other invasive fungal infections. In addition, data on mixed infections, which were diagnosed after BAL performance but were unrecognized before, would also be valuable, to serve as another argument in favor of BAL performance.

Acknowledgments


Bart J. A. Rijnders and Lennert Slobbe
Departments of Medical Microbiology and Internal Medicine, Section of Infectious Diseases, Erasmus Medical Centre, Rotterdam, the Netherlands

References


Galactomannan Detection and Diagnosis of Invasive Aspergillosis

To the Editor—The article on bronchoalveolar lavage (BAL) galactomannan enzyme immunoassay (EIA) for diagnosis of invasive aspergillosis of patients with hematologic diseases raises some important points [1]. The authors, like others before them, seem not to have fully appreciated the fact that, with such a high prior probability of disease—35% in their series—the galactomannan EIA is being used to confirm the diagnosis. Thus, the posterior probability for a positive test result (ie, the positive predictive value [PPV]) should be the highest possible. Their data show that the highest PPV was 80.4% and was associated with a threshold optical density (OD) index of 1.5–2. One cannot confirm and exclude a diagnosis using the same threshold without paying a price in terms of false-positive and false-negative results, respectively. This is shown clearly in this article and also in a recent meta-analysis of serum and plasma galactomannan [2]. These effects are displayed in Table 1 for 2 hypothetical populations of 100 patients: one with a prior probability (prevalence) of IA of 8% for whom serum and plasma specimens are tested once or twice weekly for galactomannan, and the other with a prevalence of 35% in which a BAL fluid specimen was tested for the same antigen. It is clear that one needs to choose a low threshold in both