Letters to the Editor
Detection of Circulating Capsular Polysaccharide Antigen from Cryptococcus neoformans

In their paper entitled “Comparison of the PREMIER Cryptococcal Antigen Enzyme Immunoassay and the Latex Agglutination Assay for Detection of Cryptococcal Antigens” (1), Gade et al. compare a new enzyme immunoassay (EIA) for the detection and quantification of circulating capsular polysaccharide antigen from Cryptococcus neoformans with the latex agglutination (LA) test performed with a commercially available kit, the CALAS LA test (Meridian Diagnostics). In the Discussion, the authors conclude that “PREMIER appears to have a 12-fold sensitivity advantage over LA,” which is indeed supported by their experimental data.

In our opinion, this sentence should be modified to read as follows: “PREMIER appears to have a 12-fold sensitivity advantage over the CALAS LA test,” since it is well known that the sensitivity of the LA test varies from one kit to another.

In their comparative study, the authors have chosen a latex kit which, in our experience, is much less sensitive than, e.g., the IMMY kit from Immuno-Mycologics. In our laboratory, the IMMY has been used for years on several hundreds of specimens. It is also our standard for the evaluation of the value of other antigen detection kits. We would like to suggest that they compare their new EIA kit, which possibly is better than any latex kit, with a more sensitive LA test, such as the IMMY kit from Immuno-Mycologics.

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Author’s Reply

We agree that the performance characteristics (i.e., sensitivity and specificity) of the commercially available kits vary between manufacturers. The conclusions expressed in our manuscript (1) followed a direct comparison of the PREMIER EIA with the CALAS latex agglutination kit (both kits by Meridian Diagnostics, Cincinnati, Ohio). The term LA was used throughout the article and was clearly defined as referring to the CALAS test in the Materials and Methods section. As the market leader with over 60% of the market share, the CALAS kit seems an appropriate choice for comparisons with any new cryptococcal antigen product.

A more complete and independent study comparing the EIA with several latex kits would certainly be even more informative.

The sensitivity issue raised by Swinne and De Vroey concerns whether the EIA is approximately 12-fold more sensitive than latex assays in general or only the CALAS kit. We did not directly compare the analytical or clinical sensitivities of other latex kits, since the manuscript was intended to describe the new EIA. Thus, it is quite possible that another kit is more sensitive than the CALAS kit. The IMMY package insert (Immuno-Mycologics, Inc.) claims a range of detection limits of 5 ng/ml to 25 μg/ml, which is slightly more sensitive than the 7.6 ng/ml for CALAS stated in the manuscript.

Only one comparison of several latex products and the EIA has been published (2). In this study, the CALAS, IMMY, and PREMIER EIA kits all detected antigen in 21 of 21 (100%) true positives. Two other commercial latex kits missed two positives each. The specificity of the EIA (99%) was superior to those of all latex kits, and the CALAS kit (92%) was more specific than the IMMY kit (89%). In this investigation, 17 of 155 negative specimens were incorrectly detected as positives by the IMMY kit, compared with 12 false positives for the CALAS and only 2 for the EIA.

Thus, any evaluation of various diagnostic kits should compare all of the performance characteristics. Although Meridian plans no additional clinical evaluations of this product, we would certainly encourage a thorough evaluation of both the EIA and CALAS LA test by independent investigators.

REFERENCES

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