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Low-Positive *Histoplasma* Antigen Results in the MVista Assay Should Not Be Assumed To Be False Positive

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We read with interest the paper by Theel and Ramanan in the September issue of the Journal of Clinical Microbiology on the clinical significance of low-positive *Histoplasma* urine antigen results (1). The authors report that *Histoplasma* antigen below the limit for quantification (BLQ) in the MVista immunoassay may be falsely positive. Of 57 patients with BLQ results at their hospital, 12 (21%) were classified as false positive. However, 10 of the 12 results cannot be classified as false positive with certainty.

Five were from patients with blastomycosis or coccidioidomycosis, mycoses that produce cross-reactive antigens (2, 3). At least two of these five patients appear to have been treated on the basis of a positive antigen result. Positive results caused by the detection of a cross-reacting fungal antigen should not be disregarded as false-positive results, as the indications for treatment and regimens are similar.

Two of these results were for patients with sarcoidosis, both with positive anti-*Histoplasma* antibody results. Histoplasmosis causes a chronic inflammatory condition similar to that of sarcoidosis (4), and death has occurred as a result of corticosteroid treatment in patients who had undiagnosed histoplasmosis.

Three were for patients with unknown diagnoses. Antibody tests were not performed, and one of the patients was treated with fluconazole. That the other two recovered without therapy was used to indicate that the results were falsely positive. Thirty percent of patients with subacute pulmonary histoplasmosis have similar results, and most recover without therapy (3).

We would like to expand on their experience by an analysis of results from a multicenter study that used the MVista assay. Positive results occurred in 171 (78%) of 218 patients with histoplasmosis, including 92% of disseminated, 83% of acute pulmonary, and 88% of chronic pulmonary cases. Twenty (9%) were BLQ, including 11 (7%) of 158 disseminated cases. False-positive results occurred in 2 (1%) of 199 controls, and both were BLQ (3).

In conclusion, we agree with the authors that a BLQ result may be falsely positive or truly positive and must be evaluated carefully before it is used as the basis for a diagnosis of histoplasmosis or disregarded as falsely positive. A reasonable approach would be to repeat the antigen test with urine and serum, perform antibody tests, carefully review histopathology and/or cytology findings with a pathologist skilled in recognition of fungal organisms, and obtain cultures if this has not already been done. Consultation with an expert should also be considered. If the result is considered to be falsely positive, careful follow-up with repeat testing is recommended, especially for immunocompromised patients, including those beginning or undergoing intensified immunosuppressive therapy for sarcoidosis or another inflammatory condition.

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