

Improved Diagnosis of *Histoplasma* Meningitis by Testing for Antigen and IgG and IgM Antibody in CSF

ANSWER: *Histoplasma* antigen was detected in the urine at 1.7 ng/ml.

BACKGROUND: *Histoplasma* meningitis often goes unrecognized, delaying diagnosis and treatment, resulting in neurologic complications or death. It occurs in 5% to 10% of patients with disseminated histoplasmosis, including 29% who were not immunocompromised and 58% who presented with illnesses of less than one month (LJ Wheat et al, <https://www.ncbi.nlm.nih.gov/pubmed/29595679>). Despite clinical suspicion, laboratory confirmation can be challenging. Diagnosis is critically important, as these patients require more intensive treatment for ≥ 1 year.

DISCUSSION: A retrospective multicenter study was conducted to evaluate improvements in antigen detection combined with a new IgG and IgM antibody enzyme immunoassay (KC Bloch et al, <https://www.ncbi.nlm.nih.gov/pubmed/29020213>).

Combined testing improved the sensitivity over antigen testing and antibody testing using immunodiffusion (ID) and complement fixation (CF) (table, KC Bloch et al. 2018). Cross reactions for IgG and IgM antibodies occurred in 1 patient each with blastomycosis and cryptococcosis and 3 with histoplasmosis not involving the CNS. Cross-reactions were at much lower levels than the true positive results, facilitating accurate diagnosis.

Cross reactions for antigen detection are common in blastomycosis, at levels like those in histoplasmosis. The correct diagnosis can usually be established by comparison of endemicity patterns, clinical features and IgG and IgM levels. Cross-reactivity is less common in coccidioidomycosis and can be differentiated by endemicity patterns and antigen concentrations. Cross reactions do not occur in cryptococcal meningitis.

CONCLUSIONS: Testing CSF for antigen and IgG and IgM antibodies provides the highest diagnostic yield. Antibody testing by ID also is recommended, identifying additional patients with negative IgG and IgM results. Antigen and antibody testing of blood and antigen detection of urine and serum identify additional cases.

Histoplasma Diagnostic Testing in Cerebrospinal Fluid

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Culture	9/47 (19)	119/119 (100)	100	91.8
Antigen	39/50 (78)	140/145 (96)	71.8	97.5
IgG or IgM antibody	37/45 (82)	142/153 (92)	52.1	97.9
Antigen or IgG or IgM antibody	48/49 (98)	139/153 (90)	54.7	100
ID antibody	19/43 (44)	13/13 (100)	100	94.1
CF antibody	5/10 (50)	13/14 (93)	43.9	94.4
Antigen or antibody ID or CF	44/50 (88)	139/145 (96)	70.9	98.6

Information about the tests available at <http://miravistalabs.com/>

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