



## FEATURED ARTICLE

# Diagnosis of *Histoplasma* Meningitis by Combined Testing for Antigen and IgG & IgM Antibody in Cerebrospinal Fluid

### BACKGROUND:

Central nervous system (CNS) histoplasmosis often goes unrecognized, delaying diagnosis and treatment, resulting in neurologic complications or death. It occurs in 5% to 10% of patients with disseminated histoplasmosis, and despite clinical suspicion of CNS involvement, laboratory confirmation can be challenging. Diagnosis is critically important, as these patients require longer courses and higher doses of liposomal amphotericin B than patients with disseminated disease not involving the CNS and longer monitoring after stopping treatment.

### DISCUSSION:

A retrospective multicenter study was conducted with 50 cases and 157 controls to evaluate the sensitivity and specificity of a new anti-*Histoplasma* antibody enzyme immunoassay (EIA) for the detection of IgG and IgM antibody in the CSF for diagnosis of CNS histoplasmosis and to determine the effect of improvements in the *Histoplasma* galactomannan antigen detection EIA on the diagnosis of *Histoplasma* meningitis.

### HISTOPLASMA DIAGNOSTIC TESTING IN CEREBROSPINAL FLUID

Test	Sensitivity <sup>1</sup>	Specificity <sup>2</sup>	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, IgG or IgM antibody	48/49 (98) <sup>3</sup>	139/153 (90) <sup>4</sup>	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, ID or CF antibody	44/50 (88) <sup>3</sup>	139/145 (96) <sup>4</sup>	70.9	98.6

<sup>1</sup>TRUE POSITIVE/TOTAL (%), <sup>2</sup>TRUE NEGATIVE/TOTAL (%), <sup>3</sup>P VALUE = 0.121, <sup>4</sup>P VALUE = 0.073

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(continued)

Combined testing of *Histoplasma* antigen or anti-*Histoplasma* antibodies by EIA in CSF improve the sensitivity over antigen testing and antibody testing by older methods (table). The negative predictive value for combined antigen and antibody testing by EIA was 100%, and specificity for antigen detection in CSF was 97%. Specificity was high (table). Cross reactivity of antigens was seen in patients with meningitis caused by blastomycosis or cryptococcosis.

### CONCLUSIONS:

Fungal infection should be considered in all patients with subacute or chronic meningitis. Histoplasmosis has also occurred in patients with CNS findings of less than two weeks, and should be considered in patients with persistent clinical findings if another diagnosis has not been established. Testing CSF for antigen and IgG and IgM antibodies by EIA provides the highest diagnostic yield. Antibody testing by ID also is recommended. Antigen and antibody testing of blood and antigen detection of urine may identify cases in which all CSF studies are negative of coccidioidomycosis.

The full article can be obtained at: <https://www.ncbi.nlm.nih.gov/pubmed/29020213>. Information about the tests is available at [www.miravistalabs.com](http://www.miravistalabs.com)