MAYO CLINIC LABORATORIES

Test Definition: HISER

Histoplasma Antibody Complement Fixation and Immunodiffusion, Serum

Overview

Useful For
Aiding in the diagnosis of active histoplasmosis

Testing Algorithm
For information see Meningitis/Encephalitis Panel Algorithm.

Special Instructions
- Meningitis/Encephalitis Panel Algorithm

Method Name
Complement Fixation (CF)/Immunodiffusion (ID)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1.1 mL Serum
Collection Instructions: Centrifuge and aliquot serum into plastic vial.

Forms
If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Kidney Transplant Test Request
-Infectious Disease Serology Test Request (T916)

Specimen Minimum Volume
Serum: 0.6 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Histoplasma capsulatum is a dimorphic fungus endemic to the Midwestern United States, particularly along the Mississippi River and Ohio River valleys. Infection occurs following inhalation of fungal microconidia, and subsequent clinical manifestations are largely dependent on the fungal burden at the time of exposure and the patient's underlying immune status. While the vast majority (>90%) of exposed individuals will remain asymptomatic, individuals seeking medical attention can present with a diverse set of symptoms ranging from a self-limited pulmonary illness to severe, disseminated disease. Individuals at risk for severe infection include those with impaired cellular immunity, who have undergone organ transplantation, who are HIV positive, or who have a hematologic malignancy.

The available laboratory methods for the diagnosis of *H capsulatum* infection include fungal culture, molecular techniques, serologic testing, and antigen detection. While culture remains the gold standard diagnostic test and is highly specific, prolonged incubation is often required, and sensitivity decreases (9%-34%) in cases of acute or localized disease. Similarly, molecular methods offer high specificity but decreased sensitivity. Serologic testing likewise offers high specificity; however, results may be falsely negative in immunosuppressed patients or those who present with acute disease. Also, antibodies may persist for years following disease resolution, thereby limiting the clinical specificity.

Reference Values

Anti-Yeast Antibody by Complement Fixation:
Negative (positive results reported as titer)

Antibody by Immunodiffusion:
Negative (positive results reported as band present)

Interpretation

Complement fixation (CF) titer results of 1:32 or higher indicate active disease. A rising CF titer is associated with progressive infection.

Patients infected with *Histoplasma capsulatum* demonstrate a serum antibody with a rising titer within 6 weeks of infection. A rising titer is associated with progressive infection. Specific antibody persists for a few weeks to a year, regardless of clinical improvement.

The presence of H and/or M bands on immunodiffusion tests is considered a positive result for the presence of antibodies to *Histoplasma*. Presence of an H band suggests recent infection.

Cautions

Recent histoplasmosis skin tests must be avoided because the test causes a misleading rise in complement fixation titer, as well as an M precipitin band, in approximately 17% of patients having previous exposure to *Histoplasma capsulatum.*

Cross-reacting antibodies sometimes present interpretive problems in patients having blastomycosis or coccidioidomycosis.

Clinical Reference

1. Kaufman L, Kovacs JA, Reiss E. Clinical immunomycology. In: Rose NR, de Macario ED, Folds JD, Lane HC, Nakamura RM, eds. Manual of Clinical and Laboratory Immunology. 5th ed. ASP Press; 1997
2. Deepe GS. *Histoplasma capsulatum* histoplasmosis. In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020:3162-3176
3. Theel ES, Kus JV, Grys TE, Ampel NM, Schwartz IS, Zhang SX. Practical Guidance for Clinical Microbiology Laboratories: Antibody and antigen detection methods for dimorphic fungal infections.Clin Microbiol Rev. 2025;38(2):e0000520. doi:10.1128/cmr.00005-20

Performance

Method Description

Both immunodiffusion and complement fixation (CF) tests are used to detect antibodies to *Histoplasma capsulatum*. For immunodiffusion, the antigen used is a culture filtrate. Histoplasmin H and M precipitins can be identified by the assay. For the CF test, antigens are histoplasmin and a yeast form antigen of *Histoplasma capsulatum*; the latter is more sensitive.(Roberts GD. Fungi. In: Washington II JA, ed. Laboratory Procedures in Clinical Microbiology. 2nd ed. Springer-Verlag, 1985; Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 to 7 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

86698 x2

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HISER	Histoplasma Ab CompFix/ImmDiff, S	90227-0

Result ID	Test Result Name	Result LOINC® Value
621214	Histoplasma Yeast CompFix, S	20574-0
621215	Histoplasma Immunodiffusion, S	90232-0