MAYO CLINIC LABORATORIES

Test Definition: HIBC

Histoplasma/Blastomyces Panel, Spinal Fluid

Overview

Useful For

Aiding in the diagnosis of histoplasmosis or blastomycosis meningitis

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
HICSF	Histoplasma Ab CompFix/ImmDiff, CSF	Yes	Yes
CBL	Blastomyces Ab Immunodiffusion, CSF	Yes	Yes

Testing Algorithm

For more information see Meningitis/Encephalitis Panel Algorithm

Special Instructions

- Meningitis/Encephalitis Panel Algorithm

Method Name

HICSF: Complement Fixation (CF)/Immunodiffusion (ID)

CBL: Immunodiffusion (ID)

NY State Available

Yes

Specimen

Specimen Type

CSF

Specimen Required

Container/Tube: Sterile vial

Specimen Volume: 1.5 mL

Collection Instructions: Submit specimen from collection vial 1.

Specimen Minimum Volume

1 mL

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Histoplasma

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.

Blastomyces

Blastomyces dermatitidis is endemic throughout the Midwestern, south central, and Southeastern United States, particularly in regions around the Ohio and Mississippi river valleys, the Great Lakes, and the Saint Lawrence River. It is also found in regions of Canada. *Blastomyces* species are dimorphic fungi, preferring moist soil and decomposing organic matter, which produces fungal spores that are released and inhaled by humans. At body temperature, spores mature into yeast, which may remain in the lungs or disseminate through the bloodstream to other parts of the body. Through phylogenetic analysis, *B. dermatitidis* has been separated into 2 distinct species: *B dermatitidis* and *Blastomyces gilchristii,* both able to cause blastomycosis. *B dermatitidis* infections are frequently associated with dissemination, particularly in older patients, smokers, and immunocompromised hosts, while *B gilchristii* has primarily been associated with pulmonary and constitutional symptoms. Additional species of *Blastomyces* have recently been discovered and characterized, however the performance characteristics of this assay for these species are unknown.

Approximately half of patients infected with *Blastomyces* will develop symptoms, which are frequently nonspecific, including fever, cough, night sweats, myalgia or arthralgia, weight loss, dyspnea, chest pain, and fatigue. Symptoms may appear anywhere from 3 weeks to 3 months following infection. Diagnosis of blastomycosis relies on a combination of assays, including culture and molecular testing performed on appropriate specimens, and serologic evaluation for both antibodies to and antigen released from *Blastomyces.* Although culture remains the gold standard method and is highly specific, the organism can take several days to weeks to grow and sensitivity is diminished in cases of acute or localized disease. Similarly, molecular testing offers high specificity and a rapid turnaround time, however sensitivity is imperfect. Detection of an antibody response to *Blastomyces* offers high specificity, however results may be falsely negative in patients who are acutely ill or are immunosuppressed.

Reference Values

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

BLASTOMYCES ANTIBODY IMMUNODIFFUSION
Negative

Interpretation

Histoplasma:
-Any positive serologic result in spinal fluid is significant.
-Simultaneous appearance of the H and M precipitin bands suggests active histoplasmosis.
-The M band alone indicates active or chronic disease or a recent skin test for histoplasmosis.

Blastomyces:
A positive result is suggestive of infection, but the results cannot distinguish between active disease and prior exposure. Furthermore, detection of antibodies in cerebrospinal fluid (CSF) may reflect intrathecal antibody production or may occur due to passive transfer or introduction of antibodies from the blood during lumbar puncture.

Routine fungal culture of clinical specimens (eg, CSF) is recommended in cases of suspected blastomycosis involving the central nervous system.

Cautions

Histoplasma:
-Antibody levels may be low in spinal fluid in cases of *Histoplasma* meningitis.
-Histoplasmin skin tests yield specific antibodies in titratable quantity, and may cause difficulties in interpretation.
-Cross-reacting antibodies with coccidioidomycosis or blastomycosis may cause false-positive results for histoplasmosis.

Blastomyces:
-A negative result does not rule out blastomycosis.
-Patients with histoplasmosis may have low-titered cross reactions.

Clinical Reference

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

Blastomyces
The ID test is a qualitative test employed for the detection of precipitating antibodies present in the specimen. Soluble antigens of the fungus are placed in wells of an agarose gel-filled Petri dish, and the patient's specimen and a control (positive) are placed in adjoining wells. If present, specific precipitate antibody will form precipitin lines between the wells. Their comparison to the control establishes the results. When performing the ID test, only precipitin bands of

identity with the reference bands are significant.(Kaufman L, McLaughlin DW, Clark MJ, Blumer S: Specific immunodiffusion test for blastomycosis. Appl Microbiol. 1973;26:244-247, Williams JE, Murphy R, Standard PG, Phan JP: Serologic response in blastomycosis: diagnostic value of double immunodiffusion assay. Am Res Resp Dis. 1981;123:209-212; Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020)

Performance

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 7 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

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
86612

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value

HIBC	Histoplasma/Blastomyces Panel,CSF	91683-3

Result ID	Test Result Name	Result LOINC® Value
15134	Blastomyces Immunodiffusion (CSF)	51741-7
621217	Histoplasma Yeast CompFix, CSF	27209-6
621218	Histoplasma Immunodiffusion, CSF	91682-5