Test Definition: CLFAT

Cryptococcus Antigen Titer, Lateral Flow Assay, Spinal Fluid

Overview

Useful For

Monitoring *Cryptococcus* antigen titers in cerebrospinal fluid

Aiding in the diagnosis of cryptococcosis

This test **should not be used** as a test of cure or to guide treatment decisions.

Method Name

Lateral Flow Assay (LFA)

NY State Available

No

Specimen

Specimen Type

CSF

Specimen Required

Container/Tube: Sterile vial

Specimen Volume: 0.5 mL

Collection Instructions: Submit specimen from collection vial 2 (preferred), 3, or 4.

Forms

If not ordering electronically, complete, print, and send Infectious Disease Serology Test Request (T916) with the specimen.

Specimen Minimum Volume

0.3 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container

CSF	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *Cryptococcus gattii*. *C neoformans* has been isolated from several environmental sources, especially weathered pigeon droppings. Historically, *C gattii* was associated with tropical and subtropical regions. More recently, it has been recognized as endemic in British Columbia and the Pacific Northwestern United States and is associated with several different tree species.

Infection is usually acquired via the pulmonary route. Patients are often unaware of any exposure history. Approximately half of the patients with symptomatic disease have a predisposing immunosuppressive condition such as AIDS, steroid therapy, lymphoma, or sarcoidosis. Symptoms may include fever, headache, dizziness, ataxia, somnolence, and cough. While the majority of *C neoformans* infections occur in immunocompromised patient populations, *C gattii* is has a greater predilection for infection in healthy individuals.(1,2)

In addition to the lungs, cryptococcal infections often involve the central nervous system (CNS), especially in patients with HIV infection. Mortality among patients with CNS cryptococcosis may approach 25% despite antifungal therapy. Untreated CNS cryptococcosis is invariably fatal. Disseminated disease may involve any organ system and usually occurs in immunosuppressed individuals.

Reference Values

Negative

Reference values apply to all ages.

Interpretation

The presence of cryptococcal antigen in any body fluid (serum or cerebrospinal fluid [CSF]) is indicative of cryptococcosis.

Disseminated infection is usually accompanied by a positive serum test.

Declining titers may indicate regression of infection. However, monitoring titers to cryptococcal antigen should not be used as a test of cure or to guide treatment decisions. Low-level titers may persist for extended periods of time following appropriate therapy and resolution of infection.(3,4)

According to the College of American Pathologists (CAP, IMM.41840), CSF specimens submitted for initial diagnosis that test positive by the lateral flow assay, should also be submitted for routine fungal culture. Culture can aid in differentiating between the 2 common *Cryptococcus* species causing disease (*Cryptococcus neoformans* and *Cryptococcus gattii*) and can be used for antifungal susceptibility testing, if necessary. CSF specimens submitted to monitor antigen levels during treatment do not need to be cultured.

Cautions

A traumatic lumbar puncture and contamination of the cerebrospinal fluid (CSF) specimen with serum may lead to a positive *Cryptococcus* antigen result from CSF in patients without neuroinvasive cryptococcosis.

Cryptococcus antigen titers acquired by the lateral flow assay may be higher than titers achieved by other *Cryptococcus* antigen assays. Titers acquired by different assay methods are not interchangeable. *Cryptococcus* antigen titers should be followed using the same assay.

A positive result is indicative of cryptococcosis; however, all test results should be reviewed considering other clinical findings.

A negative result does not preclude diagnosis of cryptococcosis, particularly if only a single specimen has been tested and the patient exhibits symptoms consistent with cryptococcosis.

Testing should not be performed as a screening procedure for the general population and should only be performed when clinical evidence suggests the diagnosis of cryptococcal disease.

Although rare, extremely high concentrations of cryptococcal antigen can result in weak test lines and in extreme instances, yield negative test results.

This assay has not been evaluated for cross-reactivity in patients with trichosporonosis.

Supportive Data

Endpoint titers between the IMMY LFA and the Meridian latex agglutination test were compared for 18 cerebrospinal fluid (CSF) samples positive for *Cryptococcus* antigen. While the overall qualitative correlation was good, these data indicate that the endpoint titer achieved by the IMMY LFA was at least 2-fold higher than that achieved by the Meridian latex agglutination assay in 15 of 17 (88%) serum samples. (Table 1) Therefore, *Cryptococcus* antigen titers should be monitored by using the same method on serially-collected samples; titers acquired by different methods are not interchangeable.

Table. Reciprocal Endpoint Titer

CSF Sample	Meridian latex agglutination	IMMY LFA
1	>256	5,120
2	2	80
3	128	40
4	64	640
5	2	10
6	>256	5,120
7	128	40
8	>256	640
9	>256	5,120
10	32	256
11	256	10,240
12	64	640
13	64	2,560

14	>256	10,240
15	32	640
16	>256	10,240
17	64	2,560
18	1	5

Clinical Reference

1. Speed B, Dunt D. Clinical and host differences between infections with the two varieties of Cryptococcus neoformans. Clin Infect Dis. 1995;21(1):28-36
2. Chen S, Sorrell T, Nimmo G, et al. Epidemiology and host- and variety-dependent characteristics of infection due to Cryptococcus neoformans in Australia and New Zealand. Australasian Cryptococcal Study Group. Clin Infect Dis. 2000;31(2):499-508. doi:10.1086/313992
3. Lu H, Zhou Y, Yin Y, Pan X, Weng X. Cryptococcal antigen test revisited: significance for cryptococcal meningitis therapy monitoring in a tertiary Chinese hospital. J Clin Microbiol. 2005;43(6):2989-2990
4. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis. 2010;50(3):291-322
5. Perfect JR. Cryptococcosis (Cryptococcus neoformans and Cryptococcus gattii). In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020:3146-3161
6. Chang CC, Harrison TS, Bicanic TA, et al. Global guideline for the diagnosis and management of cryptococcosis: an initiative of the ECMM and ISHAM in cooperation with the ASM. Lancet Infect Dis. 2024;24(8):e495-e512
7. Perfect JR, Bicanic T. Cryptococcosis diagnosis and treatment: What do we know now. Fungal Genet Biol. 2015;78:49-54. doi:10.1016/j.fgb.2014.10.003

Performance

Method Description

The *Cryptococcus* antigen (CrAg) lateral flow assay is a sandwich immunochromatographic assay. Specimens and diluent are added to a test tube and the lateral flow device is added. The test uses specimen wicking to capture gold-conjugated, anticryptococcal antigen monoclonal antibodies and gold-conjugated control antibodies deposited on the test membrane. If cryptococcal antigen is present in the specimen, it binds to the gold-conjugated, anticryptococcal antigen antibodies. This complex wicks up the membrane and interacts with the test line, which has immobilized anticryptococcal antigen monoclonal antibodies. The antigen-antibody complex forms a sandwich at the test line causing a visible line to form. A valid test shows a visible line at the control line. Positive test results create 2 lines (control and specimen), while negative results form only the control line.(Package insert: CrAg Lateral Flow Assay. IMMY; Rev 06/27/2019)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available
Same day/1 to 2 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Jacksonville Clinical Lab

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
87899

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CLFAT	Cryptococcus Ag Titer, LFA, CSF	9817-8

Result ID	Test Result Name	Result LOINC® Value
62076	Cryptococcus Ag Titer, LFA, CSF	9817-8