Test Definition: SLFA

Cryptococcus Antigen Screen with Titer, Serum

Overview

Useful For

Aiding in the diagnosis of cryptococcosis

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

This test **should not be used** as a screening procedure for the general populations.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLFAT	Cryptococcus Ag Titer, LFA, S	Yes	No

Testing Algorithm

If result is positive, *Cryptococcus* titer will be performed at an additional charge.

Method Name

Lateral Flow Assay (LFA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

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

Specimen Minimum Volume
0.5 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
Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *Cryptococcus gattii*. *C neoformans* has been isolated from several sites in nature, particularly weathered pigeon droppings. *C gattii* was previously only associated with tropical and subtropical regions. More recently, however, this organism has been found to be endemic in British Columbia and the Pacific Northwestern US 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 higher predilection for infection of healthy individuals.(1,2)

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

Reference Values
Negative

Interpretation
The presence of cryptococcal antigen in any body fluid (serum or cerebrospinal fluid) is indicative of cryptococcosis. Specimens that are positive by the lateral flow assay screen are automatically repeated with the same method utilizing dilutions to generate a titer value.

Disseminated infection is usually accompanied by a positive serum test.

Higher *Cryptococcus* antigen titers appear to correlate with more severe infections. 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 the resolution of infection.(3)

Cautions

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

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

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

Testing hemolyzed serum specimens may lead to false-negative results due to the high background color on the lateral flow assay strip.

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

There were 634 serum specimens (632 prospective and 2 archived) tested in a blinded fashion by the IMMY *Cryptococcus* antigen lateral flow assay (LFA), the Meridian latex agglutination (Meridian Bioscience Inc) assay, and the Meridian *Cryptococcus* antigen enzyme immunoassay (EIA) within a 24-hour period. Specimens with discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. The results are summarized in Table 1 and Table 2 below:

Table 1. Comparison of the IMMY LFA to the Meridian latex agglutination assay

	Meridian latex agglutination		
IMMY LFA	Positive	Negative	Total
Positive	9	1*	10
Negative	0	624	624
Total	9	625	634

*This sample showed 1+ reactivity by the Meridian latex agglutination assay upon screening but was interpreted as negative according to the package insert requirement for 2+ reactivity.
Sensitivity: 100% (9/9); 95% CI: 65.5%-100%
Specificity: 99.8% (624/625); 95% CI: 99.0%-99.9%
Overall Percent Agreement: 99.8% (633/634); 95% CI: 99.0%-99.9%

Table 2. Comparison of the IMMY LFA to the Meridian *Cryptococcus* antigen EIA

	Meridian EIA		
IMMY LFA	Positive	Negative	Total

Positive	5	5*	10
Negative	0	624	624
Total	5	629	634

*These 5 samples were positive by the Meridian latex agglutination assay
Sensitivity: 100% (5/5); CI: 51.7%-100%
Specificity: 99.2% (624/629); CI: 98.1%-99.7%
Overall Percent Agreement: 99.2% (629/634); CI: 98.1%-99.7%

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):28-34
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):499-505. doi:10.1086/313992
3. 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
4. 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
5. 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 [published correction appears in Lancet Infect Dis. 2024 Aug;24(8):e485. doi:10.1016/S1473-3099(24)00426-2]. Lancet Infect Dis. 2024;24(8):e495-e512. doi:10.1016/S1473-3099(23)00731-4
6. 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, anti-*Cryptococcus* antigen monoclonal antibodies and gold-conjugated control antibodies deposited on the test membrane. If *Cryptococcus* antigen is present in the specimen, it binds to the gold-conjugated, anti-*Cryptococcus* antigen antibodies. This complex wicks up the membrane and interacts with the test line, which has immobilized anti-*Cryptococcus* 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 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
87899

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SLFA	Cryptococcus Ag Screen w/Titer, S	29903-2

Result ID	Test Result Name	Result LOINC® Value
62075	Cryptococcus Ag Screen w/Titer, S	29903-2