Test Definition: PLFA

Cryptococcus Ag Screen, LFA, PF

Overview

Useful For

Diagnosis of infection with *Cryptococcus* species

Highlights

This test can be used as an adjunct for diagnosis of pulmonary infection with *Cryptococcus* species. Positive results are indicative of infection; however, cryptococcal antigen may remain detectable for prolonged periods of time following disease resolution.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
PLFAT	Cryptococcus Ag Titer, LFA, PF	No	No

Testing Algorithm

If this screen is positive, the antigen titer will be performed at an additional charge.

Method Name

Lateral Flow Assay (LFA)

NY State Available

Yes

Specimen

Specimen Type

Pleural Fluid

Additional Testing Requirements

Pleural fluid testing for cryptococcal antigen should also be submitted for routine fungal culture.

Specimen Required

Container/Tube: Sterile vial

Specimen Volume:0.5mL

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume

0.25

Reject Due To

Hemolysis	NA

Lipemia	NA
Icterus	NA
Other	NA

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Pleural Fluid	Refrigerated (preferred)	21 days	
	Frozen	30 days	

Clinical and Interpretive

Clinical Information

Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *C 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; however, more recently this organism has also been found to be endemic in British Columbia, along the Pacific Northwest, and in the Southeastern United States. 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* has a higher predilection for infection of healthy hosts. 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 pleural fluid is indicative of infection with *Cryptococcus* species.

Monitoring cryptococcal antigen levels as a means to determine response to therapy is discouraged, as antigen levels may persist despite adequate treatment and disease resolution.

A negative result indicates lack of infection; however, rare cases of false-negative results have been reported. Fungal culture should always be ordered alongside antigen testing.

Cautions

A negative result does not preclude diagnosis of cryptococcal infection, particularly if the patient is at risk for cryptococcosis and shows symptoms consistent with this disease.

False-positive results may occur in patients with trichosporonosis or infection with *Capnocytophaga* species.

Supportive Data

Sixty pleural fluid samples, including 30 specimens collected from patients without microbiologic testing ordered and 30 specimens spiked at various dilutions with *Cryptococcus* antigen (CrAg)-positive specimens, were evaluated by both the IMMY CrAg LFA and the Meridian CALAS assays. The results are summarized in Table 1.

Table 1. Comparison of the IMMY CrAg LFA and the Meridian CALAS assays

		Meridian CALAS Result		Positive Agreement (95% CI)	Negative Agreement (95% CI)	Overall Agreement (95% CI)
		Positive	Negative	81% (65.4-90.8)	100% (86.5-100)	89.5% (79.6-95.1)
IMMY LFA Result	Positive	23	7(a)			
	Negative	0	30			

(a)Details for these 7 discordant samples are provided in Table 2. All 7 specimens were pleural fluid spiked with CrAg-positive material and were expected to be positive by both assays.

Table 2. Comparison of discordant specimens between the IMMY CrAg LFA and Meridian CALAS Assays

Sample	Meridian Qualitative Result	LFA Qualitative Result	LFA Quantitative Result
1	Negative	Positive	1:10
2	Negative	Positive	1:2
3	Negative	Positive	1:10
4	Negative	Positive	1:2
5	Negative	Positive	1:5
6	Negative	Positive	1:160
7	Negative	Positive	1:80

The IMMY CrAg LFA has been shown to be significantly more sensitive in both serum and CSF specimens in prior studies.(1) Our findings in pleural fluid are consistent with these previous studies.

The reportable range for this assay is 1:2 to 1:2560 and the reference range is negative. Cross-reactivity was not observed with specimens positive for *Histoplasma capsulatum* or *Aspergillus* species antigens.

Clinical Reference

1. Binnicker MJ, Jespersen DJ, Bestrom JE, Rollins LO: Comparison of four assays for the detection of cryptococcal antigen. J Clin Micro 2012;19(12):1988-1990

2. Howell SA, Hazen KC, Brandt ME: *Candida, cryptococcus,* and other yeast of medical importance. In Manual of Clinical Microbiology. 11th edition. Washington, DC. ASM Press, 2015, pp 1984-2014

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, Norman, OK, Rev 2012)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 1 p.m. and 8 p.m.

Saturday, Sunday; 11 a.m.

Analytic Time

Same day/1 day

Maximum Laboratory Time

2 days

Specimen Retention Time

7 days/1 week

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification

This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

87899-*Cryptococcus* Ag Screen, LFA, PF

87899-*Cryptococcus* Ag Titer, LFA, PF (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PLFA	Cryptococcus Ag Screen, LFA, PF	29533-7

Result ID	Test Result Name	Result LOINC Value
42396	Cryptococcus Ag Screen, LFA, PF	29533-7