Overview

Useful For
An aid in the diagnosis of cryptococcosis

Reflex Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLFAT</td>
<td>Cryptococcus Ag Titer, LFA, S</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

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
Container/Tube:
Preferred: Serum gel
Acceptable: Red top

Specimen Volume: 1 mL

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

Specimen Minimum Volume
0.5 mL

Reject Due To

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
</tr>
</tbody>
</table>

Specimen Stability Information
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 gatti* was previously only associated with tropical and subtropical regions; however, more recently this organism has also been found to be endemic in British Columbia and among the Pacific Northwest United States, and is associated with several different trees 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 gatti* is has a higher predilection for infection of healthy hosts.(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 in order 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, as 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 in light of 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; Norman, OK), the Meridian Latex Agglutination (Meridian Bioscience Inc, Cincinnati, OH) assay, and the Meridian Cryptococcus Antigen 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 below:

| Table 1. Comparison of the IMMY LFA to the Meridian Latex Agglutination Assay |
|-------------------------------|-----------------|-----------------|-----------------|
|                               | IMMY LFA        |                  | Meridian Latex Agglutination |
| 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% Confidence Interval (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 |
|-------------------------------|-----------------|-----------------|-----------------|
|                               | IMMY LFA        |                  | Meridian EIA    |
| 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%
Test Definition: SLFA
Cryptococcus Ag Screen w/Titer, S

Overall Percent Agreement: 99.2% (629/634); CI: 98.1%-99.7%

Clinical Reference

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, 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
14 days
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 cleared, approved or is exempt by the U.S. 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

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tbody>
<tr>
<td>SLFA</td>
<td>Cryptococcus Ag Screen w/Titer, S</td>
<td>29903-2</td>
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<table>
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<tbody>
<tr>
<td>62075</td>
<td>Cryptococcus Ag Screen w/Titer, S</td>
<td>29903-2</td>
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