Test Definition: CLFA
Cryptococcus Ag Screen w/Titer, CSF

Overview

Useful For
Aids 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>CLFAT</td>
<td>Cryptococcus Ag Titer, LFA, CSF</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.

See Meningitis/Encephalitis Panel Algorithm in Special Instructions.

Special Instructions
- Meningitis/Encephalitis Panel Algorithm

Method Name
Lateral Flow Assay (LFA)

NY State Available
Yes

Specimen

Specimen Type
CSF

Specimen Required
Container/Tube: Sterile vial

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

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
</tr>
</thead>
</table>

Specimen Stability Information
Test Definition: CLFA
Cryptococcus Ag Screen w/Titer, CSF

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
<td></td>
</tr>
</tbody>
</table>

**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 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. gattii* 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.

**Note:** According to the College of American Pathologists (CAP, IMM.41840), cerebrospinal fluid (CSF) samples submitted for initial diagnosis, which test positive by the lateral flow assay, should also be submitted for routine fungal culture. Fungal cultures are not required for CSF samples that are submitted to monitor *Cryptococcus* antigen titers during treatment.

**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. Specimens that are positive by the lateral flow assay (LFA) screen are automatically repeated by the same method utilizing dilutions in order to generate a titer value. CSF specimens submitted for initial diagnosis, which test positive by LFA, should also be submitted for routine fungal culture. Culture can aid to differentiate between the 2 common *Cryptococcus* species causing disease (*C. neoformans* and *C. 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.

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 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.

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.

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

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

**Supportive Data**

Cerebrospinal fluid (CSF) retrospective specimens (111) were tested in a blinded fashion by the IMMY *Cryptococcus* Antigen Lateral Flow Assay (LFA; Normon, OK) and the Meridian Latex Agglutination (Meridian Bioscience Inc, Cincinnati, OH) assay within a 24-hour period. Of these 111 specimens, 45 were also tested by the Meridian *Cryptococcus* Antigen EIA also within a 24-hour period. Samples with discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. The results are summarized below in Table 1 and Table 2:

| Table 1. Comparison of the IMMY LFA to the Meridian Latex Agglutination Assay in CSF |
|---------------------------------|-----------------|-----------------|-------------|
|                                | Meridian Latex Agglutination |
|                                | Positive | Negative | Total |
| LFA IMMY                       |          |          |       |
| Positive                       | 18       | 0        | 18    |
| Negative                       | 0        | 93       | 93    |
| Total                          | 18       | 93       | 111   |

Sensitivity: 100% (18/18); 95% Confidence Interval (95% CI): 81.2%-100%

Specificity: 100% (93/93); 95% CI: 96.0%-100%

Overall Percent Agreement: 100% (111/111); 95% CI: 99.0%-100%

| Table 2. Comparison of the IMMY LFA to the Meridian Cryptococcus Antigen EIA Assay in CSF |
|---------------------------------|-----------------|-----------------|-------------|
|                                | Meridian EIA    |
|                                | Positive | Negative | Total |
| LFA IMMY                       |          |          |       |
| Positive                       | 12       | 0        | 12    |
### Test Definition: CLFA
Cryptococcus Ag Screen w/Titer, CSF

<table>
<thead>
<tr>
<th></th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>45</td>
</tr>
</tbody>
</table>

Sensitivity: 100% (12/12); 95% CI: 72.2%-100%

Specificity: 100% (33/33); 95% CI: 87.8%-100%

### 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, anticytrococcal 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, anticytrococcal antigen antibodies. This complex wicks up the membrane and interacts with the test line, which has immobilized anticytrococcal 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-Cryptococcus screen
87899-Cryptococcus titer (if appropriate)

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLFA</td>
<td>Cryptococcus Ag Screen w/Titer, CSF</td>
<td>29896-8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>62074</td>
<td>Cryptococcus Ag Screen w/Titer, CSF</td>
<td>29896-8</td>
</tr>
</tbody>
</table>