Technical Brief

Syphilis Serological Testing

Background Information

Syphilis testing can be divided into two categories. Treponemal assays (FTA, syphilis IgG) measure antibodies that directly react with the syphilis-causing organism *T. pallidum*, while non-treponemal assays (RPR, VDRL) measure antibodies against non-specific cardiolipin antigens released during treponemal infections.

In the past, the traditional algorithm for diagnosing syphilis was to screen initially with a non-treponemal test, followed by confirmation with a more specific treponemal test. This was largely due to the technical ease of the RPR relative to FTA or EIA testing. However, because the RPR test does not recognize treponemal-specific antibodies, a number of clinical situations can result in false-positive RPR results, including autoimmune disease, acute viral infection, recent immunizations or drug addiction. Most importantly, because RPR reactivity is a feature of active infection, the test can give false negative results in latent or late syphilis.

The CDC now recommends screening the patient using a specific treponemal test and confirming with a non-treponemal test. The algorithm below represents Cleveland Clinic's recommended screening for syphilis serology testing.

Clinical Indications

A reactive syphilis IgG result indicates that a person has been exposed to *T. pallidum* at some point in his/her life. However, this testing may remain reactive for life in the majority of people who have had syphilis, even if they have been treated properly. Therefore, a positive result does not indicate that the person currently has untreated syphilis and should be confirmed with a non-treponemal test such as RPR to assess disease activity.

If the non-treponemal test is reactive in the absence of a clinical history of treatment, it generally can be assumed that the patient has syphilis and should receive treatment. Most people become seronegative on non-treponemal tests following adequate treatment; however, some patients have a low RPR titer for life when they present with untreated late, latent or tertiary disease, despite being adequately treated. These patients are referred to as being “serofast.”

- VDRL (CSF) is used for diagnosis of tertiary or neurosyphilis.
- Samples tested reactive in the initial syphilis IgG screening test will be further tested by RPR. If the RPR tested positive, it will be followed with quantitative RPR with titer, then no further testing is required.
- When the initial syphilis IgG is weakly positive (<0.9-5.9) and RPR is negative, then the syphilis IgG results of <0.6 will automatically be confirmed by FTA EIA test.

Results Reporting

Syphilis IgG

- Nonreactive: ≤ 0.8 Al
- Weakly reactive: 0.9 - 5.9 A
- Reactive: ≥ 6.0 A1

RPR, FTAABS, VDRL (CSF) are all reported as Reactive or Nonreactive.
Limitations of the Assay

- Infants up to 15 months with reactive syphilis IgG and/or RPR probably have a maternal antibody. Testing for IgM antibody should be performed.
- Samples with very high antibody concentrations may produce false negative results for the RPR test due to the prozone effect.

Methodology

Multiplex immunoassay (EIA) method for syphilis IgG. Flocculation method for RPR and VDRL (CSF). EIA for FTA Antibody.

References


Test Overview

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Syphilis IgG with Confirmation</th>
<th>RPR with Titer</th>
<th>VDRL (CSF) (Venereal Disease Research Laboratory)</th>
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<tbody>
<tr>
<td>Reference Range</td>
<td>Nonreactive: ≤ 0.8 AI</td>
<td>Nonreactive</td>
<td>Nonreactive</td>
</tr>
<tr>
<td></td>
<td>Weakly reactive: 0.9-5.9 AI</td>
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<tr>
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<td>Reactive: ≥ 6.0 AI</td>
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<tr>
<td>Patient Preparation</td>
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<td>None</td>
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<tr>
<td>Specimen Requirements</td>
<td>1.0 mL serum</td>
<td>1.0 mL serum or EDTA plasma</td>
<td>0.5 mL CSF</td>
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<td>Test Ordering Information</td>
<td>SYPHGX</td>
<td>RPRT</td>
<td>VDRLCF</td>
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<tr>
<td>Reflex Information</td>
<td>If Syphilis IgG is weakly reactive, RPRT and FTAABS are ordered and billed.</td>
<td>If RPR is reactive, RPRQNT (RPR Titer) is ordered and billed.</td>
<td>If reactive, titer is performed.</td>
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