Letter to the Editor

Screening for Syphilis: validation of the reverse sequence screening

Syphilis, which is caused by Treponema pallidum, is a chronic bacterial infection that remains a public health concern worldwide. Serologic testing is the method most often used, as the bacterium cannot be cultured.

Syphilis serological tests are divided into nontreponemal and treponemal tests and neither is sufficient alone for diagnosis, as each type of test has limitations, including the possibility of false-positive results.

For many years the CDC has been recommending syphilis serologic screening with a non-treponemal test, such as the rapid plasma reagin (RPR) test or the Venereal Disease Research Laboratory (VDRL) test, followed by confirmation using one of several treponemal tests such as Treponema pallidum particle agglutination (TP-PA) (1).

Recently, the availability of automatable treponemal enzyme and chemiluminescence immunoassays (EIA/CIA) has reduced time and labor required for syphilis testing. This new technology has led laboratories to validate such automated treponemal methods for use as syphilis screening tests, with confirmation of positive results by a non-treponemal test –reverse sequence. As of late, the CDC offers the reverse sequence algorithm in addition to the traditional screening algorithm for syphilis (2). Specimens with reactive EIA/CIA results should be reflexively tested with a quantitative non-treponemal test (e.g., RPR or VDRL). If test results are discordant, the specimen should be tested reflexively using the TP-PA test as a confirmatory treponemal test. To validate the impact of the reverse sequence screening on the outcome diagnosis in our population, we retrospectively analyzed data obtained in our laboratory during 2009. During this period, 12,235 patients have been tested by both, CMIA test (Architect-syphilis
TP; Abbott, Wiesbaden, Germany) and RPR test (Macro-Vue™; Becton Dickinson, Sparks, MD). If one or both of these tests showed a reactive result, the specimen was reflexively tested using the TP-PA test (Microsyph-TP; Axis-Shield Diagnostics, Dundee, Scotland) as a confirmatory treponemal test.

Table 1. Results of syphilis screening by treponemal CMIA test and non-treponemal RPR test followed by confirmatory treponemal TP-PA test (n=12235)

<table>
<thead>
<tr>
<th>Reactive CMIA test &amp; reactive RPR test</th>
<th>No. of specimens (%)</th>
<th>No. of specimens Reactive in TP-PA test</th>
<th>% Agreement with TP-PA test</th>
</tr>
</thead>
<tbody>
<tr>
<td>157 (1.3)</td>
<td>155</td>
<td>98.7</td>
<td></td>
</tr>
<tr>
<td>Reactive CMIA test &amp; nonreactive RPR test</td>
<td>334 (2.7)</td>
<td>197</td>
<td>58.9</td>
</tr>
<tr>
<td>Nonreactive CMIA test &amp; reactive RPR test</td>
<td>65 (0.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nonreactive CMIA test &amp; nonreactive RPR test</td>
<td>11679 (95.5)</td>
<td>ND&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ND</td>
</tr>
</tbody>
</table>

<sup>a</sup>ND, not done

Our data indicate low incidence of syphilis in our population (low prevalence population). Of 12,235 patients who were tested for syphilis 155 (1.3%) had reactive results in both screening tests (i.e., CMIA & RPR) and confirmatory test (TP-PA) (Table 1).

The data demonstrate false positives in CMIA assay. Of 334 patients who had reactive CMIA results and nonreactive RPR results, 197 (59%) had reactive TP-PA results (Table 1). The high percentage of false positives obtained by the CMIA test was shown in previous studies (3, 4). False positive results were also obtained in the RPR test. All 65 specimens that showed RPR reactive results and CMIA nonreactive results were not confirmed by TP-PA test. It should be noted that of 157 specimens which had RPR and CMIA reactive results, 155 (98.7%) also had TP-PA reactive results.

To summarize our data, screening with CMIA assay did not miss any positive results that would have been obtained by screening with RPR; the "reverse screening" approach maintains RPR screening sensitivity. The CMIA assay was effective in the identification of true negative samples which constituted the majority of samples in a low prevalence population.
Replacing manual work by automation able to overcome obstacles related to manual procedure, saves time (CMIA-Architect 200 results/hour vs. RPR 20 results/hour) and consequently reduces labor cost.

Our results, obtained from a large cohort, support the new approach of reverse screening sequence for Syphilis serology screening in a low prevalence population.

achemiluminescent microparticle immunoassay

REFERENCES


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