Validation of Reverse Sequence Screening for Syphilis

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 nontreponemal 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 the Treponema pallidum particle agglutination (TP-PA) test (1).

Recently, the availability of automatable treponemal enzyme and chemiluminescence immunoassays (EIA/CIA) has reduced the 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 nontreponemal test—a reverse sequence. As of late, the CDC has offered 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 nontreponemal 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 the chemiluminescent microparticle immunoassay (CMIA) (Architect Syphilis TP; Abbott, Wiesbaden, Germany) and the 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 (Microslymph-TP; Axis-Shield Diagnostics, Dundee, Scotland) as a confirmatory treponemal test.

Our data indicate a 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 and RPR) and the confirmatory test (TP-PA) (Table 1).

The data demonstrate false positives in the CMIA. 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 was shown in previous studies (3, 4). False-positive results were also obtained in the RPR test. None of the 65 specimens that showed RPR reactive results and CMIA nonreactive results were confirmed by the 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 the CMIA 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 was effective in the identification of true negative samples, which constituted the majority of the samples in a low-prevalence population.

Replacing manual work with automation able to overcome obstacles related to manual procedures saves time (CMIA Architector produces 200 results/hour and RPR produces 20 results/hour) and consequently reduces labor costs.

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

REFERENCES

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Published ahead of print 18 January 2012
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doi:10.1128/JCM.06286-11