Performance of Treponemal Tests for the Diagnosis of Syphilis

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Background. Treponemal immunoassays are increasingly used for syphilis screening with the reverse sequence algorithm. There are few data describing performance of treponemal immunoassays compared to traditional treponemal tests in patients with and without syphilis.

Methods. We calculated sensitivity and specificity of 7 treponemal assays: (1) ADVIA Centaur (chemiluminescence immunoassay [CIA]); (2) Bioplex 2200 (microbead immunoassay); (3) fluorescent treponemal antibody absorption test (FTA-ABS); (4) INNO-LIA (line immunoassay); (5) LIAISON CIA; (6) Treponema pallidum particle agglutination assay (TPPA); and (7) Trep-Sure (enzyme immunoassay [EIA]), using a reference standard combining clinical diagnosis and serology results. Sera were collected between May 2012–January 2013. Cases were characterized as: (1) current clinical diagnosis of syphilis: primary, secondary, early latent, late latent; (2) prior treated syphilis only; (3) no evidence of current syphilis, no prior history of syphilis, and at least 4 of 7 treponemal tests negative.

Results. Among 959 participants, 262 had current syphilis, 294 had prior syphilis, and 403 did not have syphilis. FTA-ABS was less sensitive for primary syphilis (78.2%) than the immunoassays or TPPA (94.5%–96.4%) (all P ≤ .01). All immunoassays were 100% sensitive for secondary syphilis, 95.2%–100% sensitive for early latent disease, and 86.8%–98.5% sensitive in late latent disease. TPPA had 100% specificity.

Conclusions. Treponemal immunoassays demonstrated excellent sensitivity for secondary, early latent, and seropositive primary syphilis. Sensitivity of FTA-ABS in primary syphilis was poor. Given its high specificity and superior sensitivity, TPPA is preferred to adjudicate discordant results with the reverse sequence algorithm over the FTA-ABS.

Keywords. syphilis; immunoassay; treponemal; diagnostic performance.

Syphilis is currently increasing at epidemic rates among men and women in the United States, with the largest increases observed among men who have sex with men, women of reproductive age, and newborns [1]. Diagnosis of syphilis has traditionally involved use of nontreponemal serology (eg, rapid plasma reagin [RPR], Venereal Disease Research Laboratory [VDRL]) directed against lipoidal antigens including lecithin, cardiolipin, and cholesterol. Confirmation of reactive results is performed with a treponemal test (eg, Treponema pallidum particle agglutination assay [TPPA]). While nontreponemal tests are inexpensive and useful for monitoring response to treatment, they require significant hands-on time by laboratory personnel. One study found lower sensitivity of nontreponemal tests (RPR and VDRL) compared to TPPA in primary disease [2]. Nontreponemal tests are also associated with biologic false-positive results among injection drug users and in various chronic diseases, including autoimmune conditions and human immunodeficiency virus (HIV) [3].

In the past decade, a shift has occurred in the syphilis testing paradigm; high-volume laboratories are increasingly utilizing treponemal immunoassays for syphilis screening and diagnosis, including the enzyme immunoassay (EIA), chemiluminescence immunoassay (CIA), and microbead immunoassay (MBIA), among others. These assays can be automated, reducing labor and turnaround time. Employing a reverse sequence algorithm, a treponemal immunoassay is performed first, followed by reflex nontreponemal testing (eg, RPR) on initially reactive specimens [4]. It is unclear whether this algorithm is more sensitive than the traditional algorithm for detection of early syphilis, as some immunoassays have demonstrated poorer sensitivity than RPR for detection of primary disease [5].
Patients with discordant serology (eg, EIA-reactive, RPR-nonreactive) present diagnostic and treatment challenges for clinicians, because these results may reflect either a false-positive treponemal EIA, prior syphilis, or very early syphilis prior to development of a reactive RPR [6–9]. Analyses including early-generation EIAs demonstrated that 31% of reactive EIA specimens were nonreactive when tested with TPPA. These isolated EIA-reactive specimens could reflect false-positive results, but definitive interpretation is difficult without a laboratory gold standard [10]. Currently the Centers for Disease Control and Prevention (CDC) recommends performance of a TPPA to adjudicate discordance between the immunoassay and RPR [4]. There are few studies comparing head-to-head performance of treponemal tests in clinically characterized sera, stratified by stage of syphilis [11, 12].

The objective of this study was to compare the sensitivity and specificity of newer automated treponemal tests (eg, EIA, CIA, MBIA) and manual treponemal tests (eg, fluorescent treponemal antibody absorption test [FTA-ABS], TPPA) in patients with a clinical diagnosis of syphilis (by stage), and in those without evidence of syphilis. The findings from this study will help inform the selection of the most appropriate second treponemal test for patients with initially discordant treponemal and nontreponemal serology, and selection of an automated treponemal test when the reverse sequence algorithm is used for a laboratory diagnosis of syphilis.

MATERIALS AND METHODS

Study Population

A convenience sample of de-identified remnant serum samples (n = 1995) prospectively collected between May 2012 and March 2013 were frozen and sent to the CDC Syphilis Reference Laboratory for testing. Samples were from Kaiser Permanente Northern California (KPNC), Kaiser Permanente Southern California (KPSC), and the San Francisco Department of Public Health (SFDPH).

KPNC and KPSC are large managed healthcare organizations, each with approximately 4 million members [13]. Both KPNC and KPSC regional laboratories utilized reverse sequence screening: KPNC utilized the LIAISON CIA and KPSC utilized the Trep-Sure EIA as the initial screening test and reflex-tested all reactive CIA or EIA specimens with the RPR. Seroprevalence has previously been reported as approximately 2% at each institution [10]. Specimens from KPNC and KPSC were a combination of screening and diagnostic specimens and included specimens from each of the following categories: (1) EIA/CIA nonreactive; (2) EIA/CIA reactive, RPR reactive; (3) EIA/CIA reactive, RPR nonreactive, TPPA reactive; (4) isolated EIA/CIA reactive (RPR nonreactive, TPPA nonreactive).

Specimens from SFDPH were from consecutive patients presenting to the city’s municipal sexually transmitted disease clinic with reactive serology and diagnosed with primary or secondary syphilis. SFDPH utilizes a point-of-care RPR in the clinical setting; all specimens are tested with the VDRL test followed by the TPPA (if the initial VDRL is reactive) in the laboratory. TPPA may also be ordered together with VDRL if the clinician suspects primary syphilis and the point-of-care RPR is negative. SFDPH specimens were remnant sera from another study, and met current case definitions for primary and secondary syphilis (see Case Definitions below), but initial serology results were not available.

Treponemal Testing

All participants’ sera were tested with 7 treponemal assays. CDC investigators were blinded to clinical characteristics or original serologic results when performing the laboratory testing. Assays were performed on the same freeze–thaw cycle. Testing was performed according to the manufacturer’s instructions in package inserts. A more complete description of the assays and testing methods for this study has been published previously [14].

1. ADVIA Centaur Syphilis (Siemens Healthcare Diagnostics, Newark, Delaware) is a CIA that measures immunoglobulin G (IgG).
2. Bioplex 2200 Syphilis IgG (Bio-Rad Laboratories, Hercules, California) is a CIA that measures IgG.
3. INNO-LIA (Fujirebio, Malvern, Pennsylvania) is a manual line immunoassay that measures IgG.
4. The FTA-ABS DS (Zeus Scientific, Pomona, New York) is a manual indirect fluorescence assay that measures IgG and immunoglobulin M (IgM).
5. LIAISON Treponema Screen (Diasorin, Stillwater, Minnesota) is a CIA that measures IgG and IgM.
6. The TPPA (Fujirebio) is a manual agglutination assay that measures IgG and IgM.
7. Trep-Sure EIA (Trinity Biotech, Mississauga, Ontario, Canada) is an EIA that measures IgG and IgM.

Of the 7 assays, Bioplex 2200-MBIA, Centaur CIA, LIAISON CIA, and Trep-Sure EIA are automated immunoassays typically used for initial screening with the reverse sequence algorithm. The TPPA and FTA-ABS are manual treponemal tests typically used to confirm reactive nontreponemal tests or for adjudication of discordant serology. INNO-LIA is a manual line immunoassay used by some laboratories to adjudicate discordant results with the reverse sequence algorithm (eg, EIA reactive, RPR nonreactive).

Case Definitions

Investigators performed a review of the electronic medical record to characterize patient specimens as having current syphilis, prior syphilis only, or not having syphilis. Two investigators (I. U. P., J. M. C.) were aware of CDC laboratory testing.
results, as one of the case definitions required ≥4 of 7 negative treponemal tests. All other investigators performing records review/data abstraction and staging were blind to CDC laboratory results. Among the 1995 specimens, 1036 (52%) either had insufficient information to clinically characterize the cases, or insufficient serum volume for testing with all of the assays.

Patients with current syphilis included those with a diagnosis of primary, secondary, early latent, or late latent disease. Syphilis stage was determined through combined analysis of serology results from the initial visit (plus past results, if available), physical findings, clinical presentation, plus darkfield microscopy findings (for SFDPH patients). Records review included determination of symptoms/signs on the day of testing, gender of sex partners, HIV status, serologic test results, recent contact to a case of early syphilis, past history of treated syphilis, and clinical diagnosis associated with initial visit. Data were also collected on alternative diagnoses accounting for positive test results (eg, endemic treponematoses, autoimmune conditions).

**Primary Syphilis**
Primary syphilis was defined as presence of an anogenital chancre or lesions and (1) presence of spirochetes on darkfield microscopy plus reactive nontreponemal or treponemal serology, or (2) negative darkfield (or darkfield not performed) with reactive treponemal and nontreponemal serology.

**Secondary Syphilis**
Secondary syphilis was defined as mucocutaneous lesions including presence of a rash (trunk, scrotum, palms/soles) and/or patchy alopecia, mucous patches, and/or condyloma lata with reactive nontreponemal and treponemal serology.

**Early Latent Syphilis**
Early latent syphilis was defined as absence of symptoms and either (1) reactive nontreponemal and treponemal serology, or (2) 2 reactive treponemal tests (eg, EIA reactive, RPR nonreactive, TPPA reactive), no prior history of syphilis AND prior sexual contact to a case of early syphilis within the past 12 months, OR prior nonreactive serology within the past 12 months.

**Late Latent Syphilis**
Late latent syphilis was defined as absence of symptoms and (1) reactive nontreponemal and treponemal serology, or (2) 2 reactive treponemal tests (eg, EIA reactive, RPR nonreactive, TPPA reactive), no prior history of syphilis, no serologic test results in the prior 12 months, and no sexual contact to a case of early syphilis in the prior 12 months.

**Prior Treated Syphilis Only**
Prior treated syphilis was defined as syphilis history documented in the patient chart, but no signs or symptoms of syphilis on the day of specimen collection and no subsequent diagnosis of syphilis in the 6 months after the day of specimen collection. This also includes patients with a known history of serofast RPR titer.

**No Syphilis**
No syphilis was defined as no diagnosis of syphilis on the day of testing or in the 6 months after the day of specimen collection, no syphilis in the past medical history, no reactive prior syphilis serology (all available laboratory records reviewed), and a negative result in at least 4 of 7 treponemal tests (after testing by the CDC reference laboratory).

**Data Analysis**
Sensitivity and specificity by stage of syphilis were calculated with 95% confidence intervals (CIs) using the binomial distribution. The t test was used to compare means, the χ² test was used to compare proportions, and a P value of <.05 was considered statistically significant.

The institutional review boards at the California Department of Public Health, KPSC, KPNC, the University of California, San Francisco, and the CDC approved this study.

**RESULTS**
Of 959 patients included in the analysis, 262 had current syphilis (all stages), 294 had prior syphilis only, and 403 did not have syphilis. No patients had a history of endemic treponematoses (eg, yaws, pinta, bejel). The demographic characteristics of all patients and a comparison of patients with current syphilis and those who did not have syphilis are included in Table 1. Patients with current syphilis were older, more likely to be male, a man who has sex with men, and HIV-positive compared to those who did not have syphilis (all P < .05).

The sensitivity and specificity of the assays associated with a clinical diagnosis of syphilis is included in Table 2. For syphilis (all stages combined), all assays demonstrated >95% sensitivity, with the exception of FTA-ABS (90.8% [95% CI, 86.7%–94.0%]), which was significantly less sensitive than TPPA (P = .038) and the other immunoassays (all P < .001).

There was greater variability in specificity among the 7 assays. The Trep-Sure EIA demonstrated significantly lower specificity than the other assays (82.6% [95% CI, 78.4%–86.1%]; P < .0001). TPPA had 100% specificity (95% CI, 99.0%–100%).

In this analysis, there were 41 patients who were classified as not having syphilis after chart review and had 1, 2, or 3 out of 7 reactive treponemal tests. Among these patients, Trep-Sure EIA was most likely to be reactive (85%), followed by Centaur CIA (61%), LIAISON CIA (37%), INNO-LIA (25%), and Bioplex (20%). TPPA and FTA-ABS were least likely to be reactive (2%).

In examining sensitivity by stage of syphilis (Table 2), FTA-ABS had the lowest sensitivity among the 7 assays for primary syphilis (all P ≤ .01). It was also significantly less sensitive for secondary syphilis (P = .007). All other assays demonstrated...
sensitivity ranging between 94.5% and 96.4% for primary syphilis and sensitivity of 100% for secondary syphilis.

Among patients with early latent syphilis (n = 41), all 7 assays demonstrated high sensitivity, ranging from 95% to 100%, with no statistically significant differences. Sensitivity for those with late latent disease (n = 68) was lower, ranging from 86.8% to 98.5%. TPPA was significantly less sensitive than Trep-Sure EIA (86.8% vs 98.5%; P = .009); there were no other statistically significant differences.

Persistence of treponemal antibody in patients with prior treated syphilis is described in Table 3. Reactivity of FTA-ABS and TPPA were both <95% and were not statistically different from each other (P > .05), but FTA-ABS was less likely to be persistently reactive than the immunoassays (P < .001). The immunoassays all demonstrated reactivity of 95.9%–99.3%.

**DISCUSSION**

This study demonstrates that the 4 immunoassays routinely used for screening (LIAISON CIA, ADVIA Centaur CIA, Trep-Sure EIA, Bioplex 2200 MBIA) all demonstrated high sensitivity for primary, secondary, and early latent syphilis, with sensitivities comparable to traditional manual tests such as TPPA. The FTA-ABS demonstrated poor sensitivity, particularly for primary syphilis. The FTA-ABS was previously used as the gold standard in studies of syphilis test performance in the 1990s [15, 16]. During this time, the CDC conducted quality control on FTA-ABS reagents manufactured in the United States. These quality control activities are no longer being performed. FTA-ABS also produces subjective results and thus requires microbiologist expertise for optimal performance/interpretation. The current data call into question whether FTA-ABS should continue to be used, particularly given the availability of immunoassays and/or TPPA that demonstrate better performance and provide objective results. Of note, our findings only apply to use of FTA-ABS for serology; FTA-ABS on cerebrospinal fluid continues to play a role in the diagnosis of neurosyphilis [4].

Specificity was high for both the traditional treponemal tests and most immunoassays. In particular, the TPPA demonstrated 100% specificity, which supports the current recommendation for its use as a second test to adjudicate discordant specimens (eg, EIA reactive, RPR nonreactive) [4]. The exception was the Trep-Sure EIA, which demonstrated significantly lower specificity than the other assays.

**Table 2. Sensitivity and Specificity of Treponemal Assays for Detection of Syphilis, by Stage and Overall**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Sensitivity by Stage</th>
<th>Specificity</th>
<th>Overall</th>
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<tbody>
<tr>
<td></td>
<td>Primary (n = 55)</td>
<td>Secondary (n = 98)</td>
<td>Early Latent (n = 41)</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>78.2% (95.0–88.2)</td>
<td>92.8% (85.7–97.0)</td>
<td>100 (90.7–100)</td>
</tr>
<tr>
<td>TPPA</td>
<td>94.5% (84.9–96.9)</td>
<td>100 (96.2–100)</td>
<td>100 (90.7–100)</td>
</tr>
<tr>
<td>Centaur CIA</td>
<td>94.5% (84.9–96.9)</td>
<td>100 (96.2–100)</td>
<td>100 (90.7–100)</td>
</tr>
<tr>
<td>Trep-Sure EIA</td>
<td>94.5% (84.9–96.9)</td>
<td>100 (96.2–100)</td>
<td>100 (90.7–100)</td>
</tr>
<tr>
<td>LIAISON CIA</td>
<td>96.4% (94.5–98.2)</td>
<td>100 (96.2–100)</td>
<td>976 (874–99.9)</td>
</tr>
<tr>
<td>Bioplex MBIA</td>
<td>96.4% (94.5–98.2)</td>
<td>100 (96.2–100)</td>
<td>95.1 (83.8–99.4)</td>
</tr>
<tr>
<td>INNO-LIA</td>
<td>96.4% (94.5–98.2)</td>
<td>100 (96.2–100)</td>
<td>90 (90.7–100)</td>
</tr>
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</table>

Data are presented as % (95% confidence interval).
Abbreviations: CIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; FTA-ABS, fluorescent treponemal antibody absorption test; LIA, line immunoassay; MBIA, microbead immunoassay; TPPA, Treponema pallidum particle agglutination assay.

*FTA-ABS was less sensitive than other assays for primary syphilis (all P ≤ .01) and secondary syphilis (P = .007). Combining all stages, FTA-ABS was less sensitive than TPPA (P = .038) or the immunoassays (all P < .001).

**Table 1. Demographic Characteristics of Patients With Current Clinical Diagnosis of Syphilis, With Prior Treated Syphilis, or Without Syphilis (N = 959)**

| Characteristic          | Current Syphilis (n = 262) | Prior Treated Syphilis Only (n = 294) | No Syphilis (n = 403) | P Value*
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<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>43.3 (13.7)</td>
<td>47.7 (12.6)</td>
<td>40.5 (18.4)</td>
<td>.03</td>
</tr>
<tr>
<td>Male sex</td>
<td>233 (88.9)</td>
<td>248 (84.4)</td>
<td>204 (50.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>MSM</td>
<td>172 (65.6)</td>
<td>145 (48.3)</td>
<td>51 (12.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pregnant</td>
<td>3 (1.2)</td>
<td>6 (2.0)</td>
<td>11 (2.7)</td>
<td>.16</td>
</tr>
<tr>
<td>HIV infected</td>
<td>136 (51.9)</td>
<td>181 (61.6)</td>
<td>12 (3.0)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Abbreviations: HIV, human immunodeficiency virus; MSM, men who have sex with men; SD, standard deviation.

aComparing patients with current syphilis vs those without syphilis.
Prior studies of Trep-Sure's specificity have yielded mixed results. In studies by Wong et al and Busse et al (using TPPA and FTA-ABS as the reference standard), Trep-Sure demonstrated 99% and 94% specificity, respectively [17, 18]. Prior analyses by the CDC in both high- and low-prevalence populations demonstrated that 18.6%–25.2% of Trep-Sure EIA-reactive specimens were subsequently TPPA nonreactive, possibly reflecting false-positive results [10]. The specificity estimate of 82.8% in this study using a clinical reference standard is in line with this prior CDC analysis. Further studies with clinically well-characterized specimens would better define Trep-Sure EIA's performance. Presently, given mixed results regarding Trep-Sure's specificity and evidence of poor sensitivity in primary syphilis, Trep-Sure would not be a preferred immunoassay for syphilis diagnosis [5].

Clinicians and laboratories utilizing reverse sequence screening with immunoassays should ensure that a highly specific treponemal test such as TPPA be performed on all EIA-reactive, RPR-nonreactive specimens. This is key in prenatal screening of populations with low rates of syphilis among women of reproductive age and low rates of congenital syphilis. Another option to discern true-positive vs false-positive results would be INNO-LIA, a manual line immunoassay [19]. Although it is not US Food and Drug Administration (FDA) cleared, it has been validated to meet Clinical Laboratory Improvement Amendments (CLIA) and is used by some commercial laboratories in the United States. In this analysis, specificity of INNO-LIA was 98.5%; Centaur CIA and Bioplex MBIA demonstrated specificities of >95%. Any of these could be a reasonable alternative to TPPA as a second treponemal test in high-risk populations such as men who have sex with men.

In populations with a low prevalence of syphilis, using tests with lower specificity may lead to false-positive results, which could cause harm and emotional distress due to an incorrect syphilis diagnosis [20]. Larger studies are needed to better define the specificity of treponemal tests in high- and low-prevalence populations. Until then, this study supports use of TPPA as the most specific, FDA-cleared test available to adjudicate discordant treponemal/nontreponemal results, especially in low-prevalence populations.

Treponemal test positivity generally persists after prior treated infection, although positivity may wane for patients treated in the primary stage of syphilis as well as those with advanced HIV disease [21–23]. Among patients with prior treated syphilis, assay positivity was >90% overall, and the immunoassays were significantly more likely to remain reactive compared to the FTA-ABS. In this study, stage of disease at the time of prior diagnosis/treatment was not known, so it is possible that further differences in reactivity would be observed if the population with a history of treated syphilis could be further stratified by stage. Given the high proportion of reactivity of the immunoassays among patients with a prior history of treated syphilis, laboratories in high-seroprevalence settings (eg, sexually transmitted disease clinics) would likely have to perform greater numbers of costly confirmatory tests under a reverse sequence screening algorithm compared to the traditional screening algorithm [10].

There are several limitations to this study. Testing was performed on frozen samples that were subjected to a single freeze–thaw cycle. According to the manufacturers' inserts for the 7 treponemal tests, it is recommended that fresh samples (serum or plasma) be used for testing. It is unclear if use of frozen specimens affects test performance. Additional treponemal immunoassays are FDA approved and commercially available for syphilis screening (Abbot Architect CIA, Lumipulse G-TP CIA); the current results are not generalizable to these assays. Although sensitivity of the immunoassays was similar, our study was underpowered to find differences of <4% in overall sensitivity and specificity. Finally, all patients with primary syphilis included in this study had reactive serologies when they were diagnosed; however, both treponemal and nontreponemal tests can be negative early in the course of primary syphilis. Therefore, the true sensitivity of these treponemal assays in primary syphilis is likely lower than what was observed in this study.

Serology alone is not sufficient for diagnosis of syphilis. Serology results must be interpreted in the context of the patient's sexual history, prior syphilis history, and current symptoms/findings. The CDC guidelines recommend presumptive treatment for patients with syphilis-related symptoms and risk factors for syphilis even before serology results are available [4].

In conclusion, treponemal immunoassays and TPPA demonstrated excellent sensitivity for seropositive primary syphilis, secondary syphilis, and early latent syphilis. Sensitivity of FTA-ABS for diagnosis of syphilis was inferior, particularly in primary and secondary syphilis. Other treponemal tests (EIA, CIA, MBIA, TPPA) would be preferred for confirming nontreponemal tests using the traditional algorithm. TPPA is preferred to adjudicate cases of discordant serology with the reverse sequence algorithm in populations with both low and

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**Table 3. Persistent Reactivity of Treponemal Assays Among Patients With Prior Syphilis (n = 294)**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Reactive</th>
<th>Nonreactive</th>
<th>Indeterminate</th>
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<tbody>
<tr>
<td>FTA-ABS</td>
<td>258 (87.8)</td>
<td>33 (11.2)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>TPPA</td>
<td>272 (92.5)</td>
<td>22 (7.5)</td>
<td>0</td>
</tr>
<tr>
<td>Bioplex MBIA</td>
<td>282 (95.9)</td>
<td>12 (4.1)</td>
<td>0</td>
</tr>
<tr>
<td>LIAISON CIA</td>
<td>283 (96.3)</td>
<td>8 (2.7)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>INNO-LIA</td>
<td>284 (96.6)</td>
<td>1 (0.3)</td>
<td>9 (3.1)</td>
</tr>
<tr>
<td>Trep-Sure EIA</td>
<td>289 (98.3)</td>
<td>5 (1.7)</td>
<td>0</td>
</tr>
<tr>
<td>ADVIA Centaur CIA</td>
<td>292 (99.3)</td>
<td>2 (0.7)</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as No. (%).

Abbreviations: CIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; FTA-ABS, fluorescent treponemal antibody absorption test; LIA, line immunoassay; MBIA, microbead immunoassay; TPPA, Treponema pallidum particle agglutination assay.

*FTA-ABS was more likely to revert to nonreactive than the immunoassays (P < .001) but not significantly different from TPPA (P > .05).
high prevalence of syphilis. If CLIA validation and appropriate quality assurance were in place, INNO-LIA would be an acceptable alternative. Centaur CIA and Bioplex MBIA would also be acceptable alternatives to TPPA as a second treponemal test in high-prevalence populations.

Notes

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Disclaimer. The findings and conclusions in this manuscript are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

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References