The sensitivity of the manual treponemal tests (FTA-ABS, TPPA, and MHA-TP) ranged from 94.4% to 100% for the diagnosis of early latent syphilis; a wider range for late latent syphilis than early latent syphilis (84.5%–100%) has been reported (*113*,*115*,*116*,*118*,*120*,*124*) (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/138288). Among the treponemal immunoassays, sensitivity ranged from 95% to 100% for early latent syphilis and from 91.7% to 100% for late latent syphilis (*115*,*119*,*120*,*136*) (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/138288). Although the sensitivity of treponemal tests is generally high for early latent and late latent syphilis, the range of sensitivities identified in these studies suggests that additional studies are needed in larger samples where the duration of infection is better characterized. The duration of latency is often difficult to pinpoint; certain patients staged as late latent could have unknown latency duration, whereas other patients classified as late latent could have recently acquired their syphilis infection. This misclassification of duration of infection could falsely elevate the syphilis test performance sensitivity in patients with late latent syphilis.

The sensitivity of nontreponemal (lipoidal antigen) tests decreases during latent syphilis of longer duration because the antibody detected by these test titers diminishes over time. Typically, treponemal tests remain reactive during latent syphilis.

Sensitivity of Serologic Tests for Tertiary Syphilis

Because tertiary syphilis is rare in the postantibiotic era, published data are very limited on the performance of serologic tests for diagnosis of tertiary syphilis (e.g., gummatous disease, late neurosyphilis, and cardiovascular syphilis); further studies are unlikely to be done. One study estimated the sensitivities of the FTA-ABS and VDRL at 70.6% and 47%, respectively, in 17 patients with tertiary syphilis (*133*), although the criteria for the stage of diagnosis were not stated. There were several studies that examined sensitivity of treponemal tests (Liaison CIA, Captia EIA, and FTA-ABS) for detection of cardiovascular syphilis. All studies estimated sensitivity to be 100%; however, sample sizes were extremely small (n = 1–21 cases) (*119*,*120*,*123*,*137*,*138*). The largest study of cardiovascular syphilis included 21 patients and found sensitivities of the MHA-TP and FTA-ABS were 89.5% and 100%, respectively (*114*). The sensitivity of nontreponemal (lipoidal antigen) tests varies from 47% to 64% during tertiary syphilis (*21*), whereas treponemal tests remain reactive.

Specificity of Serologic Tests

Reference standards for specificity analyses varied widely and included apparently healthy volunteers, antenatal patients, syphilis-negative blood donors who were not living with HIV infection, and patients clinically characterized as not having syphilis (from serum banks or on the basis of previous test results or chart review). Certain studies of treponemal test specificity also used results from a different treponemal test or a consensus of a panel of treponemal tests as the reference standard.

Few head-to-head studies compared the specificity of RPR with VDRL specificity on well-characterized specimens. A study of 500 antenatal serum samples found little difference in specificity between VDRL and RPR (two versus one false positive, respectively) (*139*). Another study among 200 blood donors found VDRL was slightly less specific than RPR (98.5%, with RPR as the gold standard) (*140*).

For manual treponemal tests, one study found the specificity of FTA-ABS to be 87% (n = 128 patients) (*141*), whereas the specificity ranges of FTA-ABS and TPPA (95%–100% and 94%–100%, respectively) were similar in older studies (*102*,*113*–*115*,*117*,*118*,*122*–*127*). The specificity of the FTA-ABS test can be limited by laboratory expertise and quality control measures. For these reasons and on the basis of the recent high-quality, head-to-head study demonstrating superior TPPA test performance characteristics, the manual serologic TPPA test is preferred over the serologic FTA-ABS test. However, the CSF FTA-ABS can still help in excluding a neurosyphilis diagnosis because of its negative predictive value when performed in a laboratory experienced in the off-label use of this test. The immunoassays demonstrated specificity ranging from 94.5% to 100% (*119*–*121*,*137*,*142*–*149*); however, Trep-Sure was 82.6% (95% CI = 78.4%–86.1%) specific, significantly lower than the other immunoassays evaluated in a single head-to-head study of 959 patients (*115*).

Recommendation for serologic syphilis testing. Nontreponemal (lipoidal antigen) tests (e.g., RPR or VDRL) are not interchangeable when used to determine antibody titers; testing on follow-up samples must be performed with the same type of test (Box). The TPPA test is the preferred manual treponemal test.

Comment and evidence summary. Sensitivity and specificity estimates of RPR and VDRL were similar but not exact in head-to-head studies and studies that used similar reference standards (*95*–*99*,*101*–*104*,*106*–*108*,*111*,*112*,*139*). When assessing changes in antibody titers using nontreponemal (lipoidal antigen) tests, it is critical that the same test be used because titers are used by clinicians to classify the infection status of a patient and follow treatment response (*55*). A recent study with 959 patients estimated the sensitivity of FTA-ABS and TPPA to be 78.2% and 94.5%, respectively, when testing specimens from patients with primary syphilis (*115*). Two studies that tested specimens from patients with secondary