Published in final edited form as:

Sex Transm Dis. 2015 January ; 42(1): 48–52. doi:10.1097/OLQ.0000000000000222.

Point of Care Treponemal Tests for Neurosyphilis Diagnosis

Emily L. Ho, MD, PhD, Lauren C. Tantalo, BS, Trudy Jones, MN, ARNP, Sharon K. Sahi, BS, and Christina M. Marra, MD

Department of Neurology, University of Washington, Seattle, WA, USA

Abstract

Background—The laboratory diagnosis of neurosyphilis rests upon identifying cerebrospinal fluid (CSF) abnormalities, including CSF-Venereal Disease Research Laboratory (VDRL) reactivity. The CSF-VDRL may not be available in the parts of the world where neurosyphilis is most common. Treponemal immunochromatographic strip tests (ICSTs) have been developed as point of care tests on blood for syphilis diagnosis in resource-limited settings.

Methods—We optimized three commercial ICSTs for performance on CSF and tested CSF samples from 217 patients with syphilis. The Syphichek-WB test (Qualpro Diagnostics, Goa, India; “Syphichek”) was chosen for further study based on agreement with CSF-VDRL test results. We determined CSF-Syphichek titers for 152 samples. We modified the CSF-Syphichek for point of care testing in a US sexually transmitted diseases clinic and compared results on 102 paired centrifuged and uncentrifuged CSF samples obtained in the laboratory to the results obtained at point of care; results of samples diluted 1:4 were compared in a subset.

Results—The diagnostic sensitivity of a reactive CSF-Syphichek (62–64%) and the diagnostic specificity of a CSF-Syphichek titer at or above 1:4 (79–81%) were equivalent to the CSF-VDRL (54–69% sensitivity, 73–75% specificity) for laboratory and clinical neurosyphilis diagnoses. The CSF-Syphichek normalized after neurosyphilis therapy similarly to the CSF-VDRL. The modified CSF-Syphichek performed well at the point of care, albeit with better performance on cell-free compared to uncentrifuged CSF.

Conclusions—CSF Treponemal ICSTs hold promise for point of care neurosyphilis diagnosis in regions where the CSF-VDRL is not available. Further study should address the performance of CSF ICSTs in resource-limited settings.

Keywords

syphilis; neurosyphilis; diagnosis; cerebrospinal fluid; Venereal Disease Research Laboratory test; resource limited settings

Address correspondence to: Christina M. Marra, MD, Harborview Medical Center Box 359775, 325 9th Avenue, Seattle, WA 98104, Phone: 206-897-5400, Fax: 206-897-5401, cmarra@uw.edu.

The authors report no conflicts of interest relevant to this work.

Portions of this work were presented at the 16th Conference on Retroviruses and Opportunistic Infections, February 8–11, 2009, Montreal, Canada.

INTRODUCTION

The World Health Organization estimates that at any point in 2008, 36.4 million adults 15–49 years of age worldwide had syphilis, with 10.6 million incident cases (<http://www.who.int/reproductivehealth/publications/rtis/stisestimates/en/>). Seventy-three percent of the prevalent and 60% of the incident syphilis cases came from Africa and Southeast Asia, regions of the world in which HIV is also highly prevalent and incident (1), and in which diagnostic resources may be limited. Neurosyphilis is a serious complication of syphilis that can be asymptomatic or symptomatic; when symptomatic, it can cause vision and hearing loss, meningitis, stroke and cognitive impairment. Neurosyphilis may be more common in HIV-infected individuals than in those who are not infected with HIV (2).

The laboratory diagnosis of neurosyphilis rests upon identifying cerebrospinal fluid (CSF) abnormalities, including CSF pleocytosis and reactivity of the CSF-Venereal Disease Research Laboratory (VDRL) test (3). A reactive CSF-VDRL confirms the diagnosis of neurosyphilis, but the test can be nonreactive in individuals with neurosyphilis (4). Treponemal tests such as the fluorescent treponemal antibody-absorption (FTA-ABS) have been used on CSF for neurosyphilis diagnosis; they are more sensitive than the CSF-VDRL, particularly in asymptomatic neurosyphilis, but they are less specific (5). Both the CSF-VDRL and the CSF-FTA-ABS are logistically complicated to perform. The CSF-VDRL requires specialized glass plates and a light microscope, and the CSF-FTA-ABS requires a fluorescent microscope (6). In addition, the reagents for the FTA-ABS must be refrigerated (6). As a consequence, these tests may not be available in the parts of the world where syphilis and neurosyphilis are most common.

Treponemal immunochromatographic strip tests, or ICSTs, have been developed as point of care tests for syphilis diagnosis. These can be used to test whole blood, plasma or serum, do not require special equipment or refrigeration, are simple to perform and have high diagnostic sensitivity and specificity (7). We investigated whether such tests could be used on CSF to diagnose neurosyphilis.

MATERIALS AND METHODS

Clinical Methods

Samples used in this study were collected from individuals with syphilis enrolled in a study of CSF abnormalities conducted in Seattle, WA, USA (8). All participants underwent a structured history and neurological examination that included assessment of cranial nerves, motor strength, sensation, coordination, reflexes and gait; lumbar puncture; and venipuncture. Individuals with CSF abnormalities who were treated for neurosyphilis underwent follow-up lumbar punctures at 3 months after therapy. Those with persistent CSF abnormalities at 3 months underwent repeat CSF examinations at 6 months after therapy; if CSF was abnormal at 6 months, the study was repeated at 12 months after therapy. The study protocol was reviewed and approved by the University of Washington Institutional Review Board, and all participants provided written informed consent.

Standard Laboratory Methods

Cerebrospinal fluid VDRL tests and enumeration of CSF white blood cells (WBCs) were performed in a Clinical Laboratory Improvement Amendments (CLIA)-approved hospital clinical laboratory. Cerebrospinal fluid-FTA-ABS was performed in a single research laboratory according to standard methods (6), except that unheated cell-free CSF (centrifuged at 1000 rpm for 10 minutes at room temperature) was used rather than serum.

Optimization of Treponemal ICSTs for CSF

CSF samples were centrifuged at 1000 rpm for 10 minutes at room temperature, frozen, and thawed once before testing. Three commercial treponemal ICSTs were chosen for study: the Bioline SD Syphilis 3.0 test (Standard Diagnostics, Inc., Kyonggi-do, Korea; hereafter referred to as “Bioline”), the Visitect Syphilis test (Omega Diagnostics, Scotland, UK; hereafter referred to as “Visitect”) and the Syphichek-WB test (Qualpro Diagnostics, Goa, India; hereafter referred to as “Syphichek”). We used a panel of 19 CSF samples from patients with syphilis to optimize the three tests: 10 positive CSF controls (CSF-VDRL-reactive with titers ranging from 1:1 to 1:64) and 9 negative CSF controls (VDRL and FTA-ABS nonreactive, WBCs < 5/μl). We reasoned that the optimal conditions for each test on blood, plasma or serum might not be optimal for CSF because the concentration of treponemal antibodies in CSF would be lower. We thus increased the amount of CSF and decreased the amount of diluent buffer, maintaining the total volume consistent with the manufacturer’s recommendation. We also varied the incubation times for each test compared to the manufacturer’s instructions for blood, plasma or serum. The Bioline test recommends use of a standard laboratory pipette for measurement of sample and diluent volumes. The Visitect and Syphichek tests use a proprietary disposable dropper for application of sample and diluent buffer on each test device. For these test kits, we determined the volume in microliters of one drop from each test dropper device by weighing the volume in one drop of water ten times, and averaging the results. We identified the optimal volumes and incubation times that provided the fewest false positive and false negative results and were judged by the operator as “easiest to read” using our defined panel of 19 samples. A single operator performed all the tests and was blinded to the participants’ clinical and laboratory data.

Determination of the “Best” CSF Treponemal ICST for Neurosyphilis Diagnosis

CSF samples from 217 individuals with syphilis were tested using all three tests employing the optimal conditions as identified in the studies described above. Test results were compared to the result of the CSF-VDRL using the kappa statistic. Serial 2-fold dilutions of CSF in normal saline from 152 individuals with syphilis were tested using the optimized Syphichek method (the test that was ultimately deemed “best”); the highest reactive dilution was defined as the test titer. A receiver operator characteristic curve was derived using the CSF-VDRL as the gold standard and the optimal test titer was determined. Sensitivity and specificity for a laboratory definition of neurosyphilis (CSF WBCs > 20/ul regardless of clinical findings) and a clinical definition of neurosyphilis (vision or hearing loss regardless of CSF findings) was determined for the optimal test, the optimal test titer, the CSF-VDRL and the CSF-FTA-ABS.

Normalization of the CSF ICST After Neurosyphilis Therapy

Cerebrospinal fluid was collected from 53 individuals after neurosyphilis therapy. Normalization for the CSF Syphicheck and the CSF-VDRL was defined as a four-fold decline in titer or reversion to nonreactive. Time to normalization of the CSF-Syphicheck and of the CSF-VDRL was estimated by Kaplan-Meier analysis.

Modification and Performance of the CSF ICST for the Point of Care

We optimized the three tests in a research laboratory using centrifuged CSF delivered by laboratory pipettes, methods that may not be feasible at the point of care settings in which the tests might ultimately be used. As such, we investigated agreement between the CSF-Syphicheck conducted as above compared to modifying the method by measuring the CSF and diluent volumes using a tuberculin syringe (0.3ml, with graduated markings indicating 10 ul increments; the needle was removed) on centrifuged and uncentrifuged CSF samples from 107 consecutive patients, 95 undergoing initial evaluation for possible neurosyphilis and 12 undergoing a follow-up visit after neurosyphilis treatment. For 15 centrifuged and 14 uncentrifuged CSF samples, we also compared agreement between results obtained with CSF diluted 1:4 in saline using pipettes or syringes in the laboratory. Finally, in parallel with the laboratory studies described above, the study clinician tested 102 centrifuged and uncentrifuged undiluted CSF samples, and 11 centrifuged and 9 uncentrifuged samples diluted 1:4 in saline at the point of care (a US sexually transmitted diseases clinic). The clinician performed the centrifugation and dilution of their sample aliquots in the clinic. Results were compared to the results obtained using the syringe method in the laboratory.

Statistical Methods

SPSS version 19 (IBM Company, Armonk, NY, USA) was used to calculate Kappa statistics and to perform Kaplan-Meier analysis. Sensitivity and specificity were calculated using standard formulas and expressed as percent (95% confidence intervals); statistical differences between them were assessed using Stata version 11.2 (StataCorp, College Station, TX). Log rank test was used to compare normalization of CSF-Syphicheck and CSF-VDRL titers using Prism 5 for Mac OS X (GraphPad Software Inc., San Diego, CA).

RESULTS

Optimization of Treponemal ICSTs for CSF

For all three tests, we varied the incubation times for the assays from 5 to 30 minutes in 5 minute increments. For the Bioline test, we varied the CSF volume from 10–130 ul in a total volume of 130 ul including diluent (at the highest CSF volume, no diluent was added for all tests). For the Visitect, we varied the CSF volume from 36–90 ul in a total volume of 90 ul, and for the Syphicheck, we varied the CSF volume from 38–142 ul in a total of 142 ul. Table 1 shows the manufacturers' recommended conditions and the conditions that we determined to be optimal for CSF as defined above for each of the three tests. As expected, higher volumes of CSF than recommended for blood, plasma or serum improved the performance of each test on CSF.

CSF Treponemal ICSTs for Neurosyphilis Diagnosis

We compared agreement between the results of the three optimized ICSTs on CSF and results of the CSF-VDRL test in a convenience sample of CSF from 217 individuals with syphilis. In keeping with the demography of syphilis in Seattle, these individuals were predominantly white (n=145, 67%), HIV-infected (n=152, 70%) men (n=197, 91%). One hundred thirty-seven (63%) had early syphilis and 80 (37%) had late latent or unknown duration syphilis; CSF-VDRL was reactive in 54 (25%). Agreement with the results of the CSF-VDRL was moderate for all three ICSTs and was highest for the Syphichek test (Bioline kappa 0.40, Visitect kappa 0.45, Syphichek kappa 0.54). Compared to the CSF-VDRL, the diagnostic specificity of the CSF-Syphichek was 79% (73–85%) and the sensitivity was 83% (73–93%).

In order to determine the reproducibility of the CSF-Syphichek, we subsequently repeated the tests on 104 of the 217 samples using kits from a different lot. Agreement between the results was good (kappa 0.69): 5 (11%) of 44 samples that were negative on the first assessment were positive on the second assessment, and 11 (18%) of 60 that were positive on the first assessment were negative on the second.

One study showed that the specificity and sensitivity of a treponemal test on CSF (the *Treponema pallidum* hemagglutination assay or TPHA) for diagnosis of neurosyphilis was high if a titer threshold was used to define a positive result rather than simply considering the test to be reactive vs. nonreactive (9). Accordingly, we pursued whether the performance of the CSF-Syphichek could be improved by identifying a titer cut-off in a convenience sample of 152 patients that included 104 previously tested. As with the analysis of the best test samples, most participants were white (n=116, 76%), HIV-infected (n=123, 81%) men (n=147, 97%). One hundred three (68%) had early syphilis and 49 (32%) had late latent or unknown duration syphilis; CSF-VDRL was reactive in 56 (37%). Using a ROC curve (not shown), we determined that a titer at or above 1:4 vs. below 1:4 yielded 93% (95% CI, 88–98%) specificity and 59% (99% CI, 46–72%) sensitivity using the CSF-VDRL as the diagnostic gold standard.

We then compared the diagnostic performance of the CSF Syphichek with and without the titer cut-off to the CSF-VDRL using the laboratory and clinical definitions of neurosyphilis (see Methods) in the same 152 patients (Table 2). For purposes of comparison, we also determined the specificity and sensitivity of the CSF-FTA-ABS; results for this test were missing for three patients (Table 2). Sixty-three patients (41%) had CSF WBCs >20/ul and 36 (25%) of 145 individuals without preexisting abnormalities had vision or hearing loss. The diagnostic specificity of the CSF-Syphichek was significantly poorer than the CSF-VDRL, but using the titer cut-off of below vs. at or above 1:4, the specificity was equivalent to the CSF-VDRL for both neurosyphilis definitions. The diagnostic sensitivity for the CSF-Syphichek was equivalent to the CSF-VDRL, but was significantly lower for the CSF-Syphichek 1:4 for the clinical neurosyphilis definition, and bordered on being significantly lower for the laboratory definition of neurosyphilis. The diagnostic sensitivity and specificity of the CSF-FTA-ABS was similar to the CSF-Syphichek for both neurosyphilis definitions (Table 2). The specificity of the CSF-FTA-ABS was significantly

lower and the sensitivity significantly higher than the CSF-Syphicheck 1:4 for both neurosyphilis definitions ($p < 0.005$ for all comparisons). As expected, the diagnostic specificity of the CSF-FTA-ABS was significantly lower than the CSF-VDRL for both neurosyphilis definitions; the diagnostic sensitivity for the clinical definition of neurosyphilis was equivalent to the CSF-VDRL, and it bordered on being better than the CSF-VDRL for the laboratory definition of neurosyphilis.

Normalization of the CSF-Syphicheck After Neurosyphilis Therapy

Follow-up CSF samples were obtained for 53 patients treated for neurosyphilis. Median pre-treatment CSF WBCs was 38/ul (IQR, 13–66) and median pre-treatment CSF-Syphicheck and CSF-VDRL titers were 1:4 (IQR, 1:2–1:8) and 1:1 (IQR, nonreactive [$n = 15$]-1:4). The median estimated time to normalization of the CSF-Syphicheck after neurosyphilis therapy was 4.2 months (95% CI, 3.8–4.5 months). This compared favorably to the CSF-VDRL (median time to normalization 3.7 months, 95% CI, 3.5–3.8 months). Figure 1 shows Kaplan-Meier curves for normalization of the two tests; there was no statistically significant difference between them.

Modification and Performance of the CSF-Syphicheck for the Point of Care

We modified the optimized CSF-Syphicheck for use at the point of care by employing a tuberculin syringe (with the needle removed) for sample delivery. In the research laboratory, we found that agreement between the results of the test using a laboratory pipette or using the syringe on 107 consecutive samples was very good for centrifuged (kappa 0.87) and uncentrifuged (kappa 0.80) CSF. We also compared the results of the CSF-Syphicheck with a sample diluted 1:4 in saline in the laboratory using a pipette or syringe on 15 consecutive cell-free and 14 consecutive uncentrifuged samples. Agreement was good (kappa 0.73) for cell-free CSF and was moderate for uncentrifuged CSF (kappa 0.58).

We made similar comparisons between results of tests conducted in the laboratory and by the study clinician at the point of care, both using a tuberculin syringe for CSF and diluent delivery, on 102 undiluted cell-free and uncentrifuged CSF samples, and 11 cell-free and 9 uncentrifuged CSF samples diluted 1:4 in saline. Agreement between results obtained in the laboratory and at the point of care for the undiluted CSF samples was very good for cell-free CSF (kappa 0.80) and was good for uncentrifuged CSF (kappa 0.63). Agreement between results of the diluted samples obtained in the laboratory and at the point of care for the cell-free CSF samples was moderate (kappa 0.46) but was only fair for uncentrifuged CSF (kappa 0.36).

DISCUSSION

The CSF-VDRL is considered the gold standard test for diagnosis of neurosyphilis. However, it is logistically complicated and is not available in many parts of the world. Several studies have examined whether the Tolidine Red Unheated Serum Test (TRUST) or the Rapid Plasma Reagin (RPR) test, nontreponemal tests that use the same antigen as the VDRL but do not require specialized glass plates or a light microscope, can be used in place of the CSF-VDRL (10–13). These studies have used different diagnostic criteria for

neurosyphilis and overall have shown as good or better diagnostic specificity, but generally lower sensitivity, than the CSF-VDRL. Although these tests are less logistically complicated to read than the CSF-VDRL, like the CSF-VDRL, they require a mechanical rotator and a centrifuge, and the reagents for the RPR must be refrigerated (6). As yet, these tests have not been applied to point of care testing.

The goal of this study was to determine if a commercially available syphilis ICST, which requires no specialized equipment, could be adapted for use on CSF as an alternative to the CSF-VDRL to diagnose neurosyphilis. We optimized three ICSTs for CSF and chose one, the CSF-Syphicheck, with the best performance relative to the CSF-VDRL for further study. We found that the diagnostic sensitivity of a reactive CSF-Syphicheck and the diagnostic specificity of a CSF-Syphicheck titer at or above 1:4 were equivalent to the CSF-VDRL. We further show that the CSF-Syphicheck normalized after neurosyphilis therapy similarly to the CSF-VDRL. We modified the CSF-Syphicheck to be performed at the point of care, and showed that it performed well, albeit with better performance on cell-free compared to uncentrifuged CSF. Better performance on cell-free CSF might be expected. The method for the CSF-VDRL and CSF-FTA-ABS both specify that cell free CSF should be used (6), presumably because red or white blood cells or debris can inhibit the antigen-antibody reaction.

Several factors should be considered in interpreting our data. Most of our study participants were HIV-infected, consistent with the demographics of syphilis in the US. Although there is no evidence that, compared to HIV-uninfected persons, HIV-infected individual have impaired antibody responses to treponemal or nontreponemal antigens in serum (3), it is possible that these antibody responses are impaired in CSF. The number of HIV-uninfected individuals in our study was too small to allow for meaningful comparisons by HIV status. Our goal was to replace the CSF-VDRL, which is specific but lacks sensitivity for neurosyphilis diagnosis. While we were not able to improve on this drawback of the CSF-VDRL, we reasoned that being able to replace the CSF-VDRL with an equivalently specific test would be a vast improvement over the situation in which the test is simply not available. Our definition of laboratory neurosyphilis was regardless of symptoms or signs, and our definition of clinical neurosyphilis was regardless of CSF abnormalities. These definitions recapitulate clinical care scenarios. Although we tested agreement between the results of the CSF-Syphicheck performed in the laboratory and at the point of care, our point of care, which was an air conditioned US sexually transmitted diseases clinic, may not be relevant to point of care conditions in other parts of the world. Moreover, we were only able to test the performance of the titer cut-off in the clinic in a small number of cases, limiting the accuracy of our kappa estimates.

The CSF-Syphicheck, particularly employing a titer cut-off, shows promise for neurosyphilis diagnosis. However, before the CSF-Syphicheck or any other CSF ICST can be used for point of care neurosyphilis diagnosis, further studies are required to determine test performance, including CSF dilution and use of uncentrifuged CSF samples, at the point of care in resource-limited point of care settings.

Acknowledgments

This work was supported by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health [grant numbers NS34235 and NS52135].

REFERENCES

1. Murray CJ, Ortblad KF, Guinovart C, Lim SS, Wolock TM, Roberts DA, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014
2. Taylor MM, Aynalem G, Olea LM, He P, Smith LV, Kerndt PR. A consequence of the syphilis epidemic among men who have sex with men (MSM): neurosyphilis in Los Angeles, 2001–2004. *Sex Transm Dis*. 2008; 35(5):430–434. [PubMed: 18446083]
3. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep*. 59(RR-12):1–110.
4. Larsen, SA.; Hambie, EA.; Wobig, GH.; Kennedy, EJ. Cerebrospinal fluid serologic test for syphilis: treponemal and nontreponemal tests. In: Morisset, R.; Kurstak, E., editors. *Advances in sexually transmitted diseases*. Utrecht, The Netherlands: VNU Science Press; 1986. p. 157–162.
5. Harding AS, Ghanem KG. The performance of cerebrospinal fluid treponemal386 specific antibody tests in neurosyphilis: a systematic review. *Sexually transmitted diseases*. 2012; 39(4):291–297. [PubMed: 22421696]
6. Larsen, SA.; Pope, V.; Johnson, RE.; Kennedy, EJ, Jr. *A Manual of Tests for Syphilis*. 9th ed.. Washington, DC: American Public Health Association; 1998. p. 361
7. Tucker JD, Bu J, Brown LB, Yin YP, Chen XS, Cohen MS. Accelerating worldwide syphilis screening through rapid testing: a systematic review. *Lancet Infect Dis*. 2010; 10(6):381–386. [PubMed: 20510278]
8. Marra CM, Maxwell CL, Smith SL, Lukehart SA, Rompalo AM, Eaton M, et al. Cerebrospinal fluid abnormalities in patients with syphilis: association with clinical and laboratory features. *J Infect Dis*. 2004; 189(3):369–376. [PubMed: 14745693]
9. Luger AF, Schmidt BL, Kaulich M. Significance of laboratory findings for the diagnosis of neurosyphilis. *Int J STD AIDS*. 2000; 11(4):224–234. [PubMed: 10772085]
10. Gu W, Yang Y, Wu L, Yang S, Ng LK. Comparing the performance characteristics of CSF-TRUST and CSF-VDRL for syphilis: a cross-sectional study. *BMJ Open*. 2013; 3(2)
11. Zhu L, Gu X, Peng RR, Wang C, Gao Z, Zhou P, et al. Comparison of the cerebrospinal fluid (CSF) toluidine red unheated serum test and the CSF rapid plasma reagin test with the CSF venereal disease research laboratory test for diagnosis of neurosyphilis among HIV-negative syphilis patients in China. *J Clin Microbiol*. 2014; 52(3):736–740. [PubMed: 24335955]
12. Castro R, Prieto ES, da Luz Martins Pereira F. Nontreponemal tests in the diagnosis of neurosyphilis: an evaluation of the Venereal Disease Research Laboratory (VDRL) and the Rapid Plasma Reagin (RPR) tests. *J Clin Lab Anal*. 2008; 22(4):257–261. [PubMed: 18623120]
13. Marra CM, Tantalo LC, Maxwell CL, Ho EL, Sahi SK, Jones T. The rapid plasma reagin test cannot replace the venereal disease research laboratory test for neurosyphilis diagnosis. *Sexually transmitted diseases*. 2012; 39(6):453–457. [PubMed: 22592831]

SHORT SUMMARY

A point of care treponemal test was modified for use on cerebrospinal fluid (CSF). The diagnostic sensitivity of a reactive test and the diagnostic specificity of a titer at or above 1:4 were equivalent to the CSF-VDRL for neurosyphilis diagnosis.

Figure 1.

Normalization of CSF-Syphicheck and CSF-VDRL tests after neurosyphilis therapy.

Normalization was defined as a four-fold decline in titer or reversion to nonreactive. The two curves do not differ significantly by Log-rank test.

Table 1

Optimization of the three ICSTs tests for CSF

Test	Method	Sample volume	Diluent volume	Incubation time (minutes)
Bioline	Standard	10	120	10
	Optimized	60	70	20
Visitect	Standard	36	54	15
	Optimized	60	30	15
Syphichack	Standard	38	104	15
	Optimized	90	52	15

Standard, method recommended by the manufacturer for blood, plasma or serum; Optimized, method determined to provide best results for CSF.

Table 2
Sensitivity and specificity of CSF tests for neurosyphilis diagnosis with comparison to the CSF-VDRL

Test									
CSF-VDRL		CSF-Syphicheck		CSF-Syphicheck titer 1:4		CSF-FTA-ABS			
Neurosyphilis Definition	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
	%, (95% Confidence Interval), P-value Compared to CSF-VDRL								
Laboratory (CSF WBC > 20/ μ l), n=152	75 (66-84)	54 (42-66)	57 (47-67) P=0.01*	62 (50-74) P=NS	81 (73-89) P=NS	37 (25-49) P=0.06*	54 (43-65) P=0.004*	70 (59-81) P=0.06**	
Clinical (vision or hearing loss), n=145	73 (65-81)	69 (54-84)	53 (44-62) P=0.002*	64 (48-80) P=NS	79 (71-87) P=NS	44 (28-60) P=0.03*	51 (42-61) P=0.001*	81 (68-94) P=NS	

* CSF, cerebrospinal fluid; VDRL, Venereal Disease Research Laboratory; FTA-ABS, fluorescent treponemal antibody-absorption; NS, P>0.10; * indicates lower value than for CSF-VDRL,
** indicates higher value than CSF-VDRL