

Increasing Early Syphilis Cases in Illinois – Syphilis Laboratory Tests

Syphilis is a sexually transmitted disease (STD) caused by the *Treponema pallidum* bacterium.

Syphilis testing should be performed on patients with signs or symptoms of infection, as well as asymptomatic patients at high risk for infection or for transmitting to others, as described in the Part 1 of this series. Diagnosis of syphilis is made using both non-treponemal and treponemal serologic tests and should not be made on the basis of a single test result. Further, clinical history and symptoms must be taken into consideration when diagnosing and staging individuals.

Serologic Diagnostic Tests:

Non-treponemal tests, also called screening tests (RPR and VDRL), do not detect antibodies specific for syphilis and are based upon the reactivity of serum from infected patients to a cardiolipin-cholesterol-lecithin antigen (regain). RPR and VDRL results should have a quantitative titer reported with them (1:2, 1:4, 1:8, etc.). A reactive RPR must also have a reactive treponemal test to be considered a case of syphilis as false positives are possible. Changes in titer are followed after treatment to detect a therapeutic response and to assess for new infection. With adequate treatment, most individuals will return to a non-reactive RPR. Some individuals may maintain a low titer RPR for life despite adequate treatment (serofast). False negatives can also occur with this test, most often during early acute infection.

Treponemal tests, also called confirmatory tests (FTA, TP-PA, EIA), detect antibodies specific to syphilis. Treponemal antibodies will appear earlier after acute infection than non-treponemal antibodies. The antibodies detected in these tests usually remain detectable for life even after successful treatment. Thus, a reactive treponemal test can indicate current or past syphilis infection.

Common Syphilis Serologic Tests

Test	Full Name	Type	Target	Notes
RPR	Rapid Plasma Reagin	Non-treponemal	Cardiolipin Antibodies	Quantitative results reported as a titer.
VDRL	Veneral Disease Research Laboratory	Non-treponemal	Cardiolipin Antibodies	Quantitative results reported as a titer. Only test approved for CSF (cerebrospinal fluid) specimens.
FTA-ABS	Fluorescent Treponemal Antibody-Absorption	Treponemal	<i>T. pallidum</i> Antibodies	
TP-PA	<i>Treponema pallidum</i> -particle agglutination	Treponemal	<i>T. pallidum</i> Antibodies	
MHA-TP	Microhemagglutination- <i>Treponema pallidum</i>	Treponemal	<i>T. pallidum</i> Antibodies	
EIA	Enzyme immunoassay	Treponemal	<i>T. pallidum</i> Antibodies	May be initial test in reverse sequencing algorithm.
CIA	Chemiluminescent immunoassay	Treponemal	<i>T. pallidum</i> Antibodies	May be initial test in reverse sequencing algorithm.

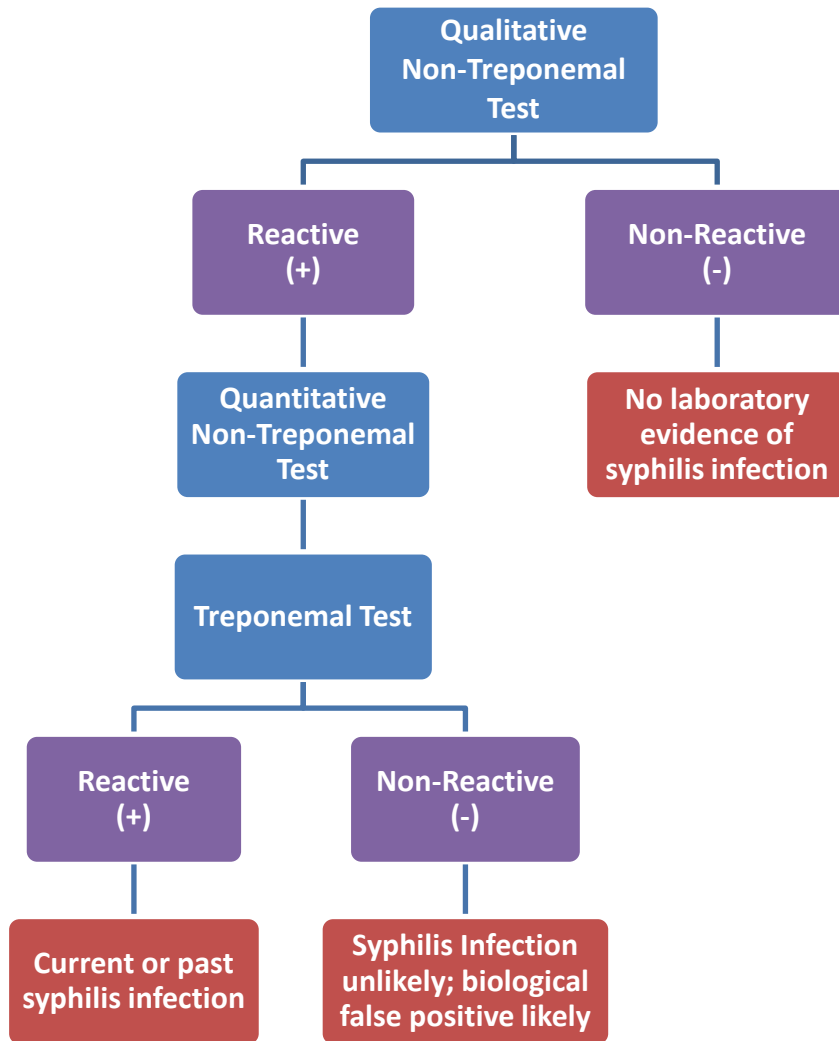
Note: This table is not exhaustive of all the tests available for diagnosing syphilis.

Testing Algorithms:

Traditional Testing Algorithm

The traditional testing algorithm for syphilis begins testing with the non-treponemal test. If the non-treponemal test is reactive, a treponemal test is then used to confirm syphilis infection. This algorithm has been in use for many years and may be most familiar for interpretation of results.

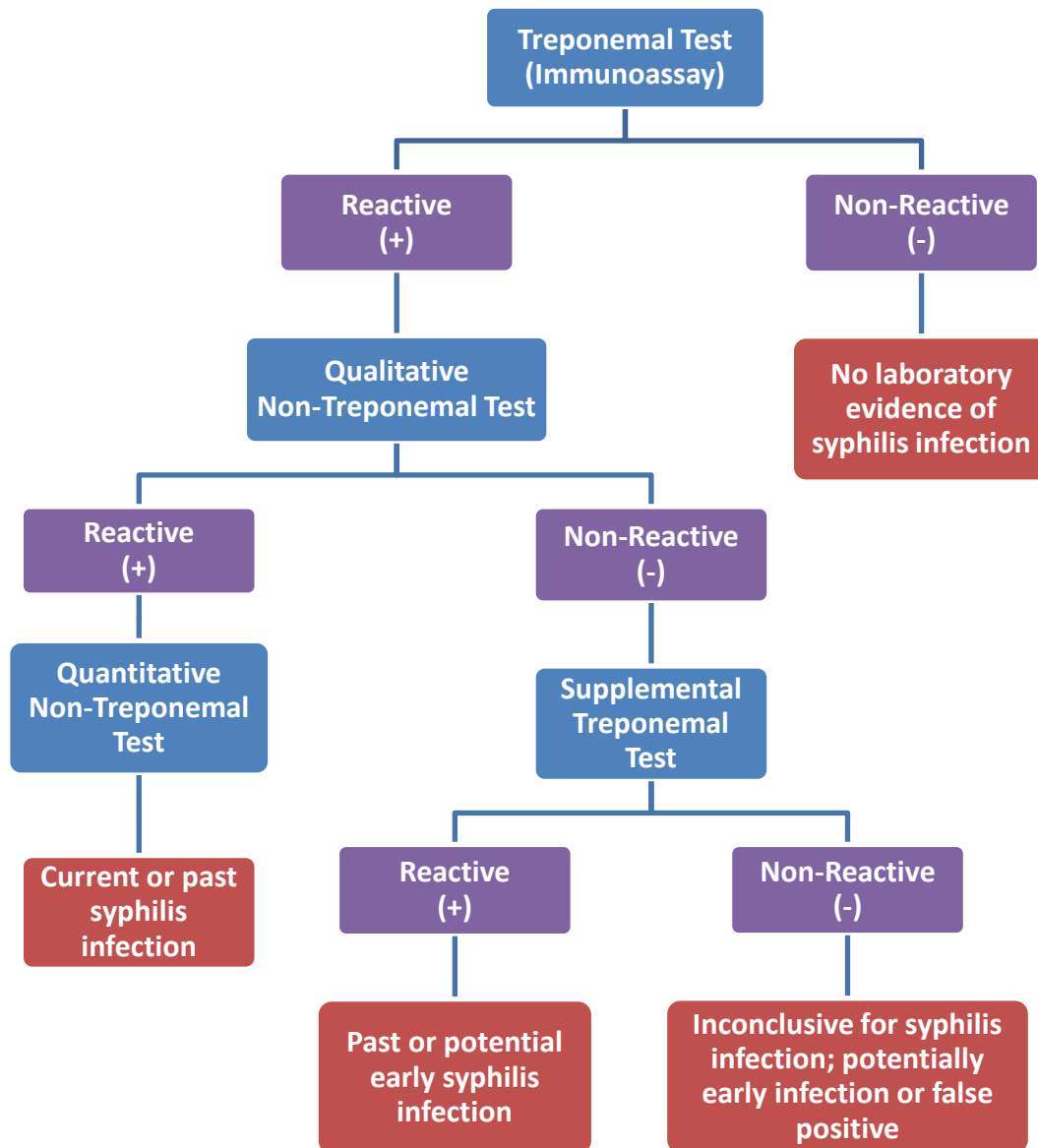
Traditional Syphilis Testing Algorithm



Reverse Testing Algorithm

The reverse testing algorithm for syphilis begins testing with a treponemal test. If this test is reactive, a non-treponemal test is performed. When the non-treponemal test is non-reactive, a second treponemal test is performed to determine if the first treponemal test was a false positive. The second treponemal test performed must be different than the initial treponemal test. The reverse testing algorithm has been in place since 2009. This algorithm is attractive to laboratories that have a high testing volume because it reduces the amount of manual labor conducted for the non-treponemal tests. The reverse algorithm will detect past infections that were previously undetected by the traditional testing method (reactive treponemal test with a non-reactive non-treponemal test).

Reverse Syphilis Testing Algorithm



Syphilis Re-infection

Because the antibodies detected in treponemal tests usually remain detectable for life, even after successful treatment, the non-treponemal titer (RPR or VDRL) must be used to monitor for a re-infection with syphilis. An increase in titer of two dilutions represents re-infection with *Treponema pallidum*. For example, a titer increase from 1:1 to 1:4 would indicate a re-infection.

Neurosyphilis

Further testing is required for persons with clinical signs of neurosyphilis (headache, cognitive dysfunction, difficulty coordinating muscle movements, sensory deficits, meningitis, dementia, or ophthalmic findings), with evidence of active tertiary disease affecting other parts of the body, or with treatment failure. The diagnosis of neurosyphilis depends on a combination of cerebrospinal fluid (CSF) tests (CSF leukocyte count, CSF protein, or CSF-VDRL) in the presence of reactive serologic test results and neurologic signs and symptoms.

Interpretation of Syphilis Test Results

Traditional Testing Algorithm		
Non-Treponemal Assay	Treponemal Assay	Interpretation
Non-Reactive	Not Indicated*	No laboratory evidence of syphilis infection
Reactive	Non-Reactive	Syphilis Infection unlikely; biological false positive likely
Reactive	Reactive	Current or past syphilis infection

*If there is high clinical suspicion for early acute disease, then serologic testing should be repeated in 2-4 weeks, or patient should be presumptively treated.

Reverse Testing Algorithm			
Treponemal Assay	Non-Treponemal Assay	Treponemal Assay	Interpretation
Non-Reactive	Not Indicated	Not indicated	No laboratory evidence of syphilis infection
Reactive	Non-Reactive	Non-Reactive	Inconclusive for syphilis infection; potentially early infection or false positive. If recent exposure, recommend re-screening in 2-4 weeks.
Reactive	Non-Reactive	Reactive	Past or potential early syphilis infection
Reactive	Reactive	Not indicated	Current or past syphilis infection

Additional Resources:

- Suggested Reporting Language for Syphilis Serology Testing
https://www.aphl.org/AboutAPHL/publications/Documents/ID_Suggested_Syphilis_Reporting_Lang_122015.pdf
- CDC Syphilis Detailed Fact Sheet <https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm>
- CDC 2015 Sexually Transmitted Diseases Treatment Guidelines
<https://www.cdc.gov/std/tg2015/syphilis.htm>