

# Syphilis

## Lab Interpretation

### Quick Reference



This reference guide will assist in interpretation of syphilis testing results. It is not a comprehensive or exhaustive guide to diagnosing or staging syphilis. Accurate syphilis diagnosis requires a thorough sexual and medical history, a detailed physical exam, and interpretation of current and previous laboratory data. For further information, please see the CDC's [2021 STI Treatment Guidelines](#) and/or utilize the [STD Clinical Consultation Network \(CCN\)](#) for specific patient questions.

## TESTING FOR SYPHILIS INVOLVES TWO TYPES OF TESTS

	<b>① Treponemal</b>	<b>② Non-treponemal</b>
<b>Test Description</b>	<ul style="list-style-type: none"> <li>Measures antibodies the immune system makes in response to a syphilis infection</li> </ul>	<ul style="list-style-type: none"> <li>Measures antibodies to lipoidal antigens released from damaged host tissues</li> <li>Not specific to <i>T. pallidum</i> <ul style="list-style-type: none"> <li>» A positive result may be due to other conditions. Examples include autoimmune disease, injection drug use, &amp; pregnancy.</li> </ul> </li> </ul>
<b>Examples of Tests</b>	<ul style="list-style-type: none"> <li>Fluorescent treponemal antibody absorption (FTA-ABS)</li> <li>Micro hemagglutination test for antibodies to <i>T. pallidum</i> (MHA-TP)</li> <li><i>T. pallidum</i> Particle Agglutination Assay (TPPA)</li> <li><i>T. pallidum</i> Enzyme Immunoassay (TP-EIA)</li> <li>Chemiluminescence Immunoassay (TP-CIA)</li> </ul>	<ul style="list-style-type: none"> <li>Rapid Plasma Reagins (RPR)</li> <li>Venereal Disease Research Lab (VDRL) <ul style="list-style-type: none"> <li>» The two tests above are NOT interchangeable.</li> </ul> </li> </ul>
<b>Test Results</b>	<ul style="list-style-type: none"> <li>Generally reported as "Positive or Negative" or "Reactive or Nonreactive"</li> </ul>	<ul style="list-style-type: none"> <li>Reported as a ratio (or titer) reflecting number of times the sample can be diluted and still test positive <ul style="list-style-type: none"> <li>» i.e. 1:1, 1:2, 1:4, 1:8...</li> </ul> </li> <li>Titers reflect disease activity and are used to monitor treatment response or for reinfection.</li> </ul>

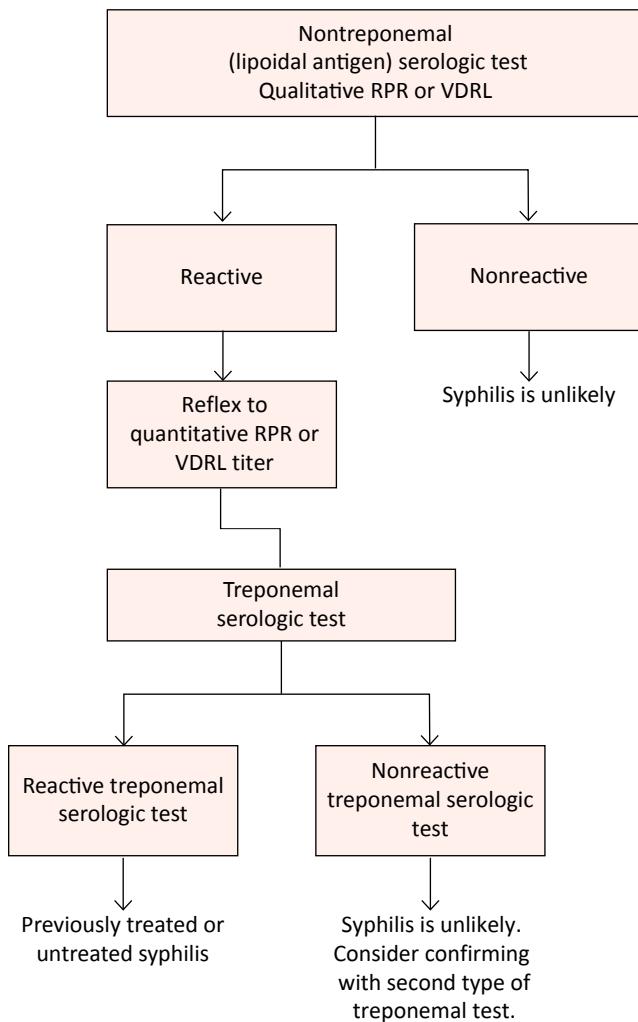
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	<b>① Treponemal</b>	<b>② Non-treponemal</b>
<b>Result Interpretation</b>	<ul style="list-style-type: none"> <li>Generally, once a patient's treponemal test is positive, it will remain so for life.</li> <li>Treponemal tests are not useful for determining current infection in a patient with known history of a previous infection.</li> </ul>	<ul style="list-style-type: none"> <li>Titers are measured by serial dilutions of blood specimens to determine the amount of non-treponemal antibody. There is significant variability between labs and technicians.</li> <li>Each dilution change represents a two-fold change in titer.</li> </ul> <div style="background-color: #fce4ec; padding: 10px; margin-top: 10px;"> <p>1:2048 1:1024 1:512 1:256 1:128 1:64 1:32 1:16 ← 2 dilution (ie, fourfold) rise in tier =clinically significant change 1:8 1:4 1:2 1:1 ("minimally reactive") Nonreactive</p> </div> <ul style="list-style-type: none"> <li>Clinicians should measure a patient's titer at the time of treatment to determine the pretreatment baseline.</li> <li>Following treatment, repeat non-treponemal titers at 6 and 12 months for individuals treated for primary or secondary syphilis and again at 24 months for individuals treated for latent syphilis.<sup>7</sup> <ul style="list-style-type: none"> <li>» Individuals living with HIV should be retested at 3, 6, 12, and 24 months after treatment.</li> </ul> </li> <li>By 12 months, the patient should have a four-fold decrease in titer (i.e., 1:16 --&gt;1:4). The response may take up to 24 months after treatment of latent syphilis. Reasons for the titer to not decrease by fourfold could include treatment failure, new infection, slow response, or serofast state.</li> <li>While most patients who are treated for syphilis will revert to a non-reactive non-treponemal titer over time, some individuals may have persistent low-level titers (known as "serofast").<sup>7</sup></li> <li>Individuals with serofast titers who experience a fourfold increase in titer (i.e., 1:1 --&gt; 1:4 or greater) should be evaluated for possible reinfection.<sup>7</sup></li> <li>For pregnant patients who are tested and treated at or prior to 24 weeks gestation, do not repeat testing for at least 8 weeks (until at least 32 weeks gestation) and again at delivery.<sup>1</sup></li> <li>For pregnant patients who are tested and treated after 24 weeks gestation, repeat titers at delivery.<sup>1</sup></li> </ul>

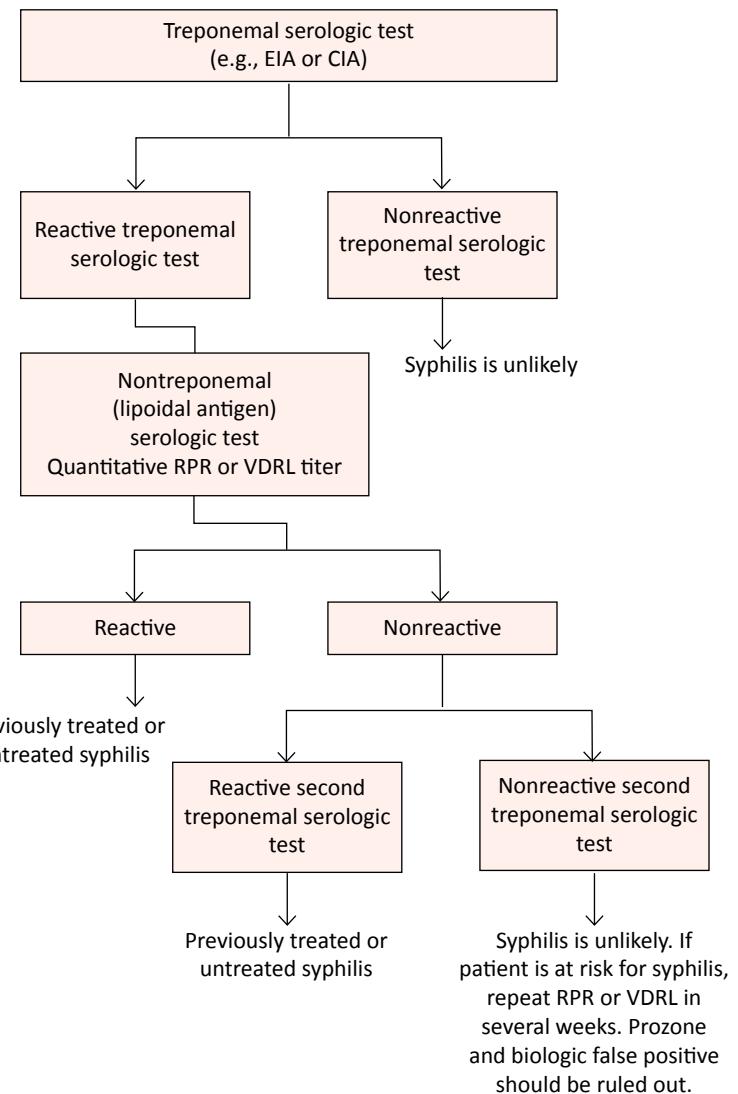
# THERE ARE TWO SYPHILIS TESTING ALGORITHMS

The “traditional” algorithm starts with a non-treponemal test and uses a treponemal test for confirmation. Conversely, the “reverse” algorithm starts with a treponemal test and uses a non-treponemal test for confirmation.

## ① Traditional algorithm



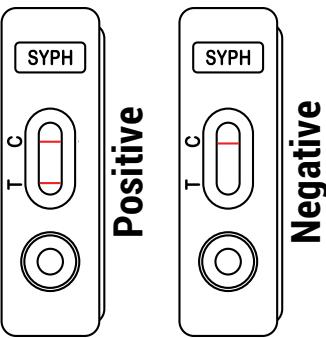
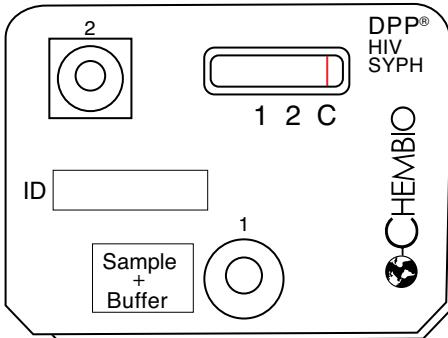
## ② Reverse Sequence algorithm



## POINT OF CARE (POC) SYPHILIS TESTS

Note that all currently FDA-approved POC syphilis tests are treponemal tests.

Advantages	Disadvantages
<ul style="list-style-type: none"><li>Results available in minutes compared to hours or days</li><li>Useful in non-traditional settings where blood draw is difficult or privacy is limited</li></ul>	<ul style="list-style-type: none"><li>Not helpful for individuals with prior history of syphilis treatment (does not distinguish current vs prior infection)</li><li>Positive predictive value varies based on local epidemiology (i.e., may have false positives in settings with low prevalence)<sup>2,4,5</sup></li><li>Still requires blood draw for RPR/VDRL which is needed to monitor treatment response</li></ul>

	Test	Test Considerations
Syphilis Health Check®		<ul style="list-style-type: none"> <li>• Uses finger stick whole blood</li> <li>• Results in 10 minutes</li> </ul>
Chembio DPP® HIV-Syphilis System (a.k.a. Chembio)		<ul style="list-style-type: none"> <li>• First HIV AND syphilis POC test</li> <li>• Detects antibodies to HIV-1, HIV-2, and T. pallidum</li> <li>• Uses finger stick or venous whole blood or plasma</li> <li>• Results in 15 minutes</li> </ul>
Over the Counter (OTC) Syphilis Tests <i>NOTE: Not all OTC tests are point of care. Some at-home tests require patients to mail in self-collected samples.</i>	Examples include First to Know®, Everlywell®, others	<ul style="list-style-type: none"> <li>• Refer to specific product's package insert</li> <li>• While this may be a great option to increase access to testing, follow-up is uncertain.</li> </ul>

## References

1. Centers for Disease Control and Prevention (2024). Screening recommendations and considerations referenced in treatment guidelines and original sources. *CDC.gov*. <https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm>
2. Fakile, Y.F., Markowitz, N., Zhu, W., Mumby, K., Dankerlui, D., McCormick, J.K., Ham, D.C., Hopkins, A., Manteuffel, J., Sun, Y., Huang, Y.A., Peters, P.J., Hoover, K.W. (2019). Evaluation of a rapid syphilis test in an emergency department setting in Detroit, Michigan. *Sexually Transmitted Diseases*, 46(7): 429-433.
3. New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections. (2019). Figure 4: Example of quantitative nontreponemal titers that indicate a clinically significant change [Image]. *Publichealth.Columbia.edu*. <https://www.publichealth.columbia.edu/file/15568/download?token=exDNYpJ>
4. New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections. (2019). The diagnosis, management, and prevention of syphilis: An update and review. *Publichealth.Columbia.edu*. <https://www.publichealth.columbia.edu/file/15568/download?token=exDNYpJ>
5. Obafemi, O., Wendel, K., Anderson, T.S., Scott, T.E., Rowan, S.E., Travanty, E.A., Rietmeijer, C.A. (2019). Rapid syphilis testing for men who have sex with men in outreach settings: Evaluation of test performance and impact on time to treatment. *Sexually Transmitted Diseases*, 46(3): 191-195.
6. Papp, J.R., Park, I.U., Fakile, Y., Pereira, L., Pillay, A., & Bolan, G.A. (2024). Figure 3: Algorithms that can be applied to screening for syphilis with serologic tests – CDC laboratory recommendations for syphilis testing in the United States, 2024 [Image]. *Morbidity and Mortality Weekly Report*, 73(1): 1-24. <https://www.cdc.gov/mmwr/volumes/73/rr/pdfs/rr7301a1-H.pdf>
7. Workowski, K.A., Bachman, L.H., Chan, P.A., Johnston, C.M., Muzny, C.A., Park, I., Reno, H., Zenilman, J.M., & Bolan, G.A. (2021). Sexually transmitted infections treatment guidelines, 2021. *Morbidity and Mortality Weekly Report*, 70(4): 1-192. <https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf>