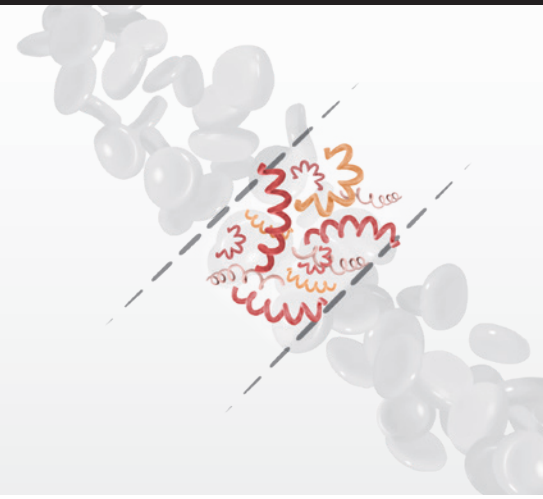


Syphilis Assay

Increased testing and treatment for syphilis is essential to global elimination efforts



Introduction

Syphilis is a disease caused by the gram-negative bacterium, *Treponema pallidum*, subspecies *pallidum* (*T. pallidum*), a spirochete with humans as the only known host. Infection results principally from sexual contact. Vertical transmission can occur in pregnancy, producing the often-serious complication of congenital syphilis (CS).¹⁻³

Antibiotic therapy remains highly effective, and timely treatment in pregnancy can significantly reduce fetal infection and harm.²⁻⁶

Goal: syphilis elimination

Syphilis continues to afflict millions of people worldwide, with many regions experiencing a resurgence of the disease, including significant increases in the U.S. over the last decade.^{2,5-8}

The World Health Organization (WHO) and partners have launched a triple-elimination campaign focused on mitigating mother-to-child transmission of syphilis, HIV, and HBV with testing and treatment key pillars.^{6,9-11} Syphilis reduction targets have also been announced by the Pan-American Health Organization (PAHO).⁹ **Table 1.**

Table 1. Goals for syphilis reduction/elimination include:⁹⁻¹¹

Congenital syphilis: 2030 reduction goal	Pregnancy targets include:	2030 reduction targets for syphilis
WHO: ≤50 cases of CS per 100,000 live births in 80% of countries	Achieve ≥95% coverage of syphilis testing for pregnant women. Ensure ≥95% treatment coverage for syphilis-positive pregnant women.	WHO: 90% reduction from 2020 rates (7.1 million cases) in those aged 15–49
PAHO: Reduce the incidence of CS to less than 0.5 cases per 1,000 live births.	95% of pregnant women receive prenatal care; 95% of pregnant women are tested for syphilis; and 95% of pregnant women with syphilis receive treatment.	PAHO: A 90% reduction in cases (compared to 2018)

NEW!

Updated CDC syphilis testing algorithm¹²

Increased testing and linkage to treatment is recommended and essential to achieving meaningful reductions in syphilis eradication efforts.^{5,9-11} In 2024, the U.S. CDC updated its syphilis testing algorithm recommendations.¹² This updated guidance highlights the importance of serology in the diagnosis of syphilis and aligns with testing guidance outside the U.S.¹³ **Importantly, the CDC now also recommends use of the reverse testing algorithm as an alternative to the traditional method.**¹²

Syphilis background

Infection with the bacterium *T. pallidum* subspecies *pallidum* causes syphilis.^{1,8,12,13} Left untreated, systemic infection can lead to serious sequelae that can vary with the organs systems impacted and the stage of disease.

Figure 1. High rates of vertical transmission can occur in pregnancy and result in serious fetal complications including stillbirths and neonatal death.^{12,14}

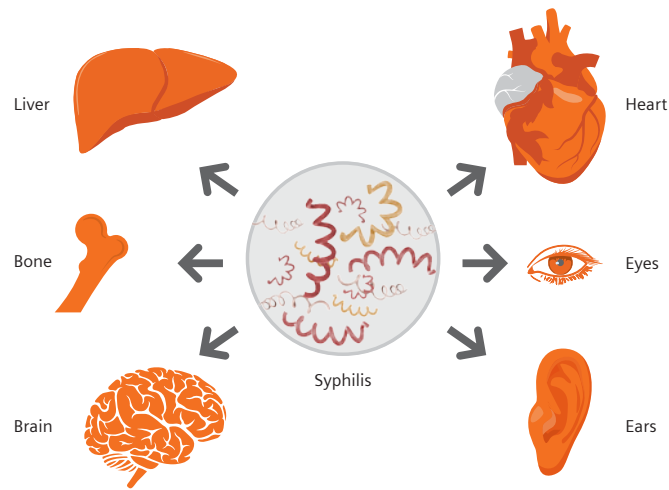


Figure 1. Syphilis can damage multiple organ systems including the liver, heart, brain, bones, eyes, and ears.

Stages of syphilis

Infection occurs when *T. pallidum* penetrates mucosal membranes or through epithelial breaks in the skin, followed by bacterial dissemination.^{15,16}

In adults (non-congenital), clinical features of untreated infection are characterized in progressive stages.^{1,12,15}

Figure 2.

Stage	Timing
Primary	3–4 weeks after exposure
Secondary	4–8 weeks after appearance of primary chancre
Latent	Early: <1 year after infection Late: >1 year after infection
Tertiary	1–10 years after infection

Figure 2. Stages of untreated syphilis.

Primary syphilis is clinically typified by a usually painless ulcer known as a chancre at the point of entry. Resolution occurs typically within 2–6 weeks. Chancres may go unnoticed, especially in women.^{1,7,12,15}

Secondary syphilis may present with a rash, often on palms or soles, that also resolves.^{1,7,12} Other indications can include lymphadenopathy, alopecia, and organ damage (in about 10% of cases) among other signs or symptoms.¹² Asymptomatic disease progression may also occur.

Latent syphilis is normally asymptomatic and can be divided into **early latent** (<1 year) and **late latent** (>1 year). Up to 25% of early-latent case may revert to symptoms characteristic of secondary before again becoming asymptomatic.⁷ Latency in untreated infection can be lifelong, with as many as one out of three progressing in ~10–30 years to **tertiary** syphilis.^{7,12}

Tertiary syphilis can be highly variable depending on the organ system(s) affected, but often involves the nervous system, heart, or liver. Neurosyphilis, otosyphilis, ocular syphilis, or liver infection may occur at any point (including in early stages).^{7,12,18}

Congenital syphilis (CS)

Rates of CS have risen significantly in some regions in recent years.^{16,17} In the U.S., data show a steep rise in syphilis-associated stillbirths and neonatal deaths over the last several years.¹⁶ **Figure 3.**

More than 1 in 20 pregnancies complicated by CS may result in stillbirths.¹⁷ Early stages of syphilis are associated with high rates of vertical transmission (~60–100%), although latent transmission can also occur.¹⁴

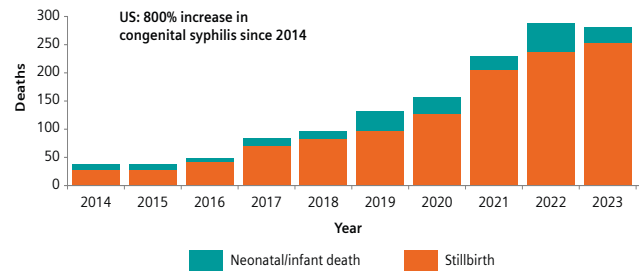


Figure 3. Congenital syphilis (CS)—Reported stillbirths and neonatal/infant deaths by year, United States, 2014–2023.¹⁶

While many pregnancies are screened as recommended in the first trimester for syphilis, data indicate many cases (up to 50%) may be missed due to late maternal infection where no subsequent repeat testing was done.^{5,19,20}



Testing for syphilis

Who should be tested for syphilis?

Syphilis testing is recommended in targeted populations, including those presenting with other sexually transmitted infections (STI) and those with suspected syphilis exposure or infection.^{6,12,13,29} Testing is recommended regardless of risk in each pregnancy at least once (ideally in the first trimester), with subsequent testing in at-risk pregnancies.^{3,12,13}

Serology testing for syphilis

Serology remains the mainstay of testing for syphilis and requires two different types of antibody test results (treponemal and nontreponemal) to support a diagnosis.^{5,12,13} While manual versions of both types of assays have been available for decades, recent years have seen the introduction of sensitive and automated treponemal testing options.^{5,12,13}

An understanding of the different antibody assays used, and what they indicate when reactive, is essential when selecting an algorithm and interpreting test results.

Types of antibody assays in syphilis testing

Nontreponemal tests

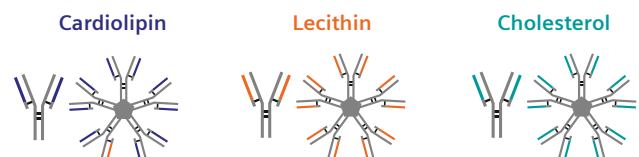
These assays recognize antibodies (IgM and IgG) formed to lipoidal antigens released with damage to both the human host cell and the invading spirochete.^{5,12,13} **Figure 4.** Nontreponemal testing can be run qualitatively or quantitatively using serial dilutions.

Clinical applications of nontreponemal testing in syphilis

If starting with a nontreponemal assay, international guidelines,^{12,13} recommend that reactive results should be followed up with treponemal testing to aid in the diagnosis of syphilis.

Nontreponemal titers rise in syphilis and decline with successful treatment, usually becoming nondetectable over a period of months.¹² Without treatment, titers typically remain elevated though can wane or disappear over time.

Changes in nontreponemal test titers are useful in monitoring the response to treatment and in detecting reinfection. In most labs, nontreponemal tests are manual assays (labor-intensive and time-consuming), with the process being highly dependent on the skill of the technician to run and interpret test results.



- Detects one or more nontreponemal antibodies associated with cell damage and released antigens (commonly cardiolipin, lecithin, and cholesterol)
- Detects both IgM and IgG
- Can be run qualitatively or quantitatively (using serial dilutions)

Figure 4. Nontreponemal antibodies and their antigens include cardiolipin, lecithin, and cholesterol.¹²

Nontreponemal reactivity is not specific to syphilis

While detection of these antibodies can indicate active cellular damage is occurring, these antibodies are not specific to syphilis. Reactivity can be associated with multiple other disease states, producing cellular damage and antigen release, ultimately resulting in biologic false positives.^{12,21,22}

Biologic false positives with nontreponemal testing

Reactive tests associated with other conditions are known as biologic false positives (BFP), since nontreponemal antibodies form from alternate causes of cell damage.²² **Table 2.**

Data suggest up to 11% of reactive nontreponemal tests may be a BFP versus syphilis, although higher and lower rates have been observed.^{12,22,23}

This lack of specificity for syphilis is why a second antibody test, specific for the treponeme, should be conducted before reporting results.^{12,13}

Table 2. Alternate causes for elevated or non-detectable nontreponemal antibodies include:^{12,21,22}

Biologic false nontreponemal results for syphilis can include:	Analytical false positive nontreponemal results can include:	False-negative nontreponemal results can include:
Viral infections, recent vaccinations, injection drug use, serofast state from prior infection, autoimmune disease, age, pregnancy	Errors in interpretation (requires visual assessment for evidence of flocculation) Errors in handling (including pipetting or rotor speed), humidity, or waiting too long to interpret results	Early or late-latent infection, prozone or postzone reactions, analytical/process errors, subjective interpretation (e.g., non-reactive vs. low reactive)

Qualitative versus quantitative nontreponemal testing

Nontreponemal assays can be run qualitatively or quantitatively using serial dilutions, and testing recommendations include use of both.^{12,13} Benefits of quantitative titers include assessing therapeutic response, or testing in those with a prior history of syphilis, as higher titers are linked with reinfection. Guidelines incorporate and recommend quantitative testing prior to result reporting.^{12,13}

If using an algorithm that starts with a nontreponemal test, guidance recommends either a quantitative test be used initially, or following a reactive qualitative result.^{12,13} When starting with a treponemal assay, reactive results should be followed up with quantitative nontreponemal testing.^{12,13}

Other clinical considerations with nontreponemal testing

• **Serofast state**

A subset of successfully treated infections may produce a serofast state where a typically lower titer of nontreponemal antibodies persists.^{5,12,13,24} Serofast states are more common in patients with repeated syphilis infections or in patients with HIV.^{12,25}

• **Loss of nontreponemal reactivity over time despite ongoing infection**

In as many as one in three non-treated patients, nontreponemal reactivity can significantly wane over time, often starting around two years after infection. **Figure 5.** Approximately 30% of untreated infections may become non-reactive >10–30 years.^{12,24} As these infections can still lead to tertiary syphilis, detection remains clinically important.

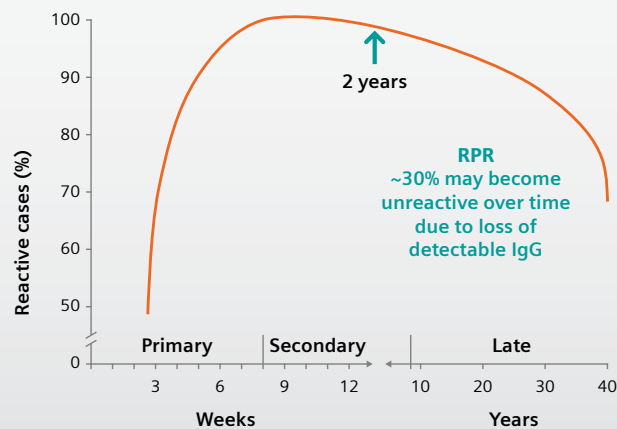


Figure 5. Loss of nontreponemal detection over time despite ongoing infection.²⁴

Treponemal tests

Treponemal assays offer specificity for the cause of infection as they recognize antibodies (most assays detect both IgM and IgG) exclusive to treponemal antigens, indicating infection has occurred. **Figure 6.** Treponemal assays may provide earlier detection of infection compared to nontreponemal assays.^{5,12,13}

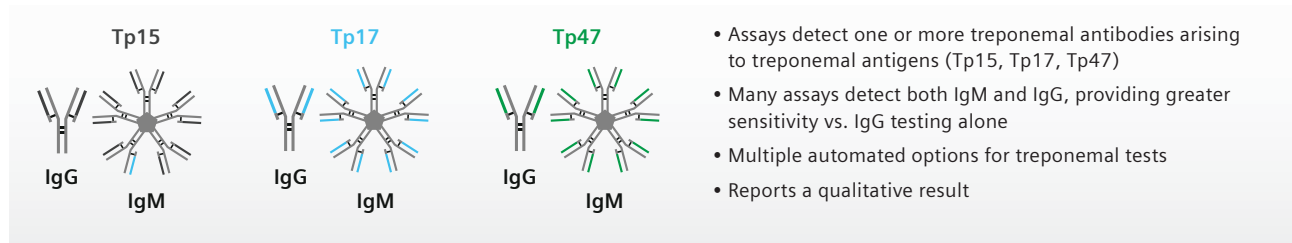


Figure 6. Antibodies to treponemal antigens.¹²

Clinical applications of treponemal testing in syphilis

While treponemal reactivity indicates infection with the bacterium has occurred at some point, reactivity is seen with existing and prior treated infections.

If starting with a treponemal test, reactive treponemal results should be followed by nontreponemal testing as the combined reactivity indicates a likelihood of current infection.^{5,12,13} Treponemal assays are reported qualitatively. Many treponemal assays are fully automated.

Resolving discordance

As with all assays, false-positive results can occur with treponemal testing.^{5,12,26-28} To resolve discordant samples (treponemal positive, nontreponemal negative) the CDC recommends confirmation using an alternate treponemal assay, preferably TP-PA.¹²

- Patients who confirm for treponemal reactivity but are non-reactive with nontreponemal testing should be clinically assessed for benefit of treatment, especially if lacking a history of treated infection.¹²
- For patients with a known prior history of infection and treatment, use of a quantitative nontreponemal test can aid assessment for reinfection.

Serologic profiles of nontreponemal and treponemal antibodies with infection

Figure 7 depicts the antibody profiles for both types of testing.¹² Treponemal antibodies form early and usually remain positive for life (with or without treatment). Nontreponemal reactivity can vary with treatment, progression to late-latent disease, or a development of a serofast state.

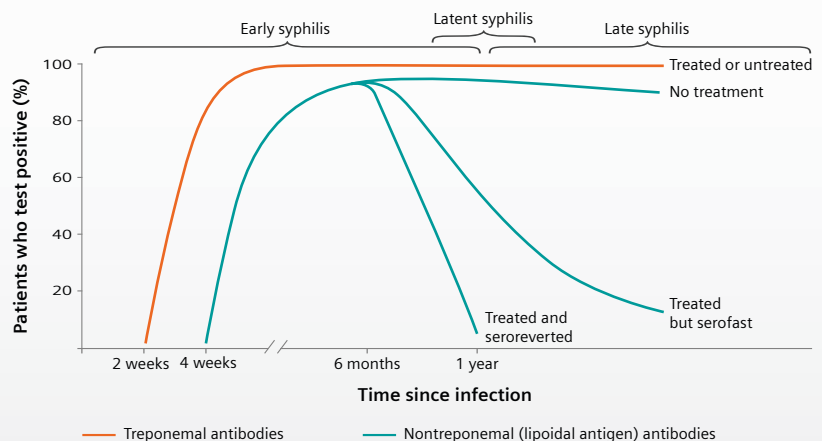


Figure 7.¹²

Manual versus automated assays

Most nontreponemal assays are run manually, although automation to support RPR testing is becoming available.⁵ In contrast, automation on widely used immunoassay analyzers is available for multiple treponemal assays. **Table 3** lists some assays used, including manual and automated treponemal options.

Table 3. Nontreponemal and Treponemal assays include:

Nontreponemal assays	Treponemal assays
<ul style="list-style-type: none"> • RPR (Rapid Plasma Reagin) • VDRL (Venereal Disease Research Laboratory) • TRUST (Toluidine Red Unheated Serum Test) 	<p>Manual:</p> <ul style="list-style-type: none"> • FTA-ABS (Fluorescent Treponemal Antibody Absorption) • TP-PA (Treponema pallidum particle agglutination) • TPHA (Treponema pallidum Hemagglutination Assay) <p>Automated:</p> <ul style="list-style-type: none"> • EIA (enzyme immunoassay—some can be automated) • CLIA (chemiluminescent immunoassay-available from multiple manufacturers), and multiplex immunoassay

Interpreting test results

Results of both tests are required to support a diagnosis. Reactive treponemal and nontreponemal tests, along with a relevant clinical history and findings, are important to rule in a likelihood of syphilis.

- Treponemal antibodies indicate infection with the treponeme (at some point).
- Nontreponemal antibodies suggest infection may be current and need to be treated.
- Because false positives and false negatives can occur with both assays (as with all assays), the clinical picture is important.

Point-of-care (POC) and nucleic acid testing (NAT) testing for syphilis

The 2024 CDC guidance Includes updates on expanded testing modalities and discusses POC and molecular testing for *T. pallidum* DNA (although lab-based serology remains the primarily recommended method).¹²

- POC assays for syphilis are currently more broadly available outside the U.S. and may offer an advantage in some settings.^{5,12} These can include outreach programs for those facing barriers to traditional healthcare facilities or for same day testing and treatment to reduce loss of patients for follow-up care.
- While no molecular testing for syphilis in the U.S., some lab-developed NAT’s are available.^{5,12} These may be useful for samples from a primary lesion or in seronegative early syphilis.⁵

Automating syphilis testing

While testing with both antibody assays is important to identify and treat cases of syphilis, most populations return a high percentage of (appropriately) negative results, even in many higher prevalence populations. Use of an automated initial immunoassay that supports early detection while offering a high negative predictive value (NPV) is desirable, improving workflow and providing clinically reliable results.³⁰⁻⁴⁰ Some benefits to automated treponemal testing are shown in **Figure 8**.

Clinical

Can identify cases missed by nontreponemal tests, e.g., early primary syphilis, late-latent syphilis

Workflow

- Can reduce labor time and costs
- Automation allows increased test volume with faster TAT
- Decreased opportunity for human error/subjective interpretation

Ratman S. Can J Infect Dis Med Microbiol. 2005 Jan/Feb;16:(1):45-51.
Larsen SA. ClinMicrobial Rev.1995 Jan;8(1):1-21.



Atellica IM Analyzer

Figure 8. Automated Treponemal Assay advantages.

Testing algorithms to support a syphilis diagnosis

While serologic assessment for syphilis incorporates use of both treponemal and non-treponemal assays, the order in which the tests are conducted can vary.

Two approaches are widely recommended for syphilis testing.^{12,13}

• Traditional testing algorithm

- The traditional algorithm begins with a nontreponemal test, with non-reactive samples ruling out. Quantitative testing should either be performed initially or following a reactive qualitative result.^{12,13}
- Reactive samples are confirmed for syphilis using a treponemal assay.^{5,12,13}
- This algorithm was established decades ago, when all testing (both treponemal and nontreponemal) was manual, with nontreponemal assays often considered less expensive and easier to conduct.

• Reverse testing algorithm

- The reverse algorithm starts with a treponemal assay, with non-reactive samples ruling out.^{5,12,13}
- Reactive samples are confirmed using a nontreponemal assay.^{5,12,13}
- This algorithm evolved with the availability of EIA and clinically validated automated CLIA treponemal assays.

Figure 9 shows the syphilis testing algorithms defined by the U.S. CDC. Both approaches are recommended, with choice of algorithm based in part on sample number, lab resources, and population tested.¹²

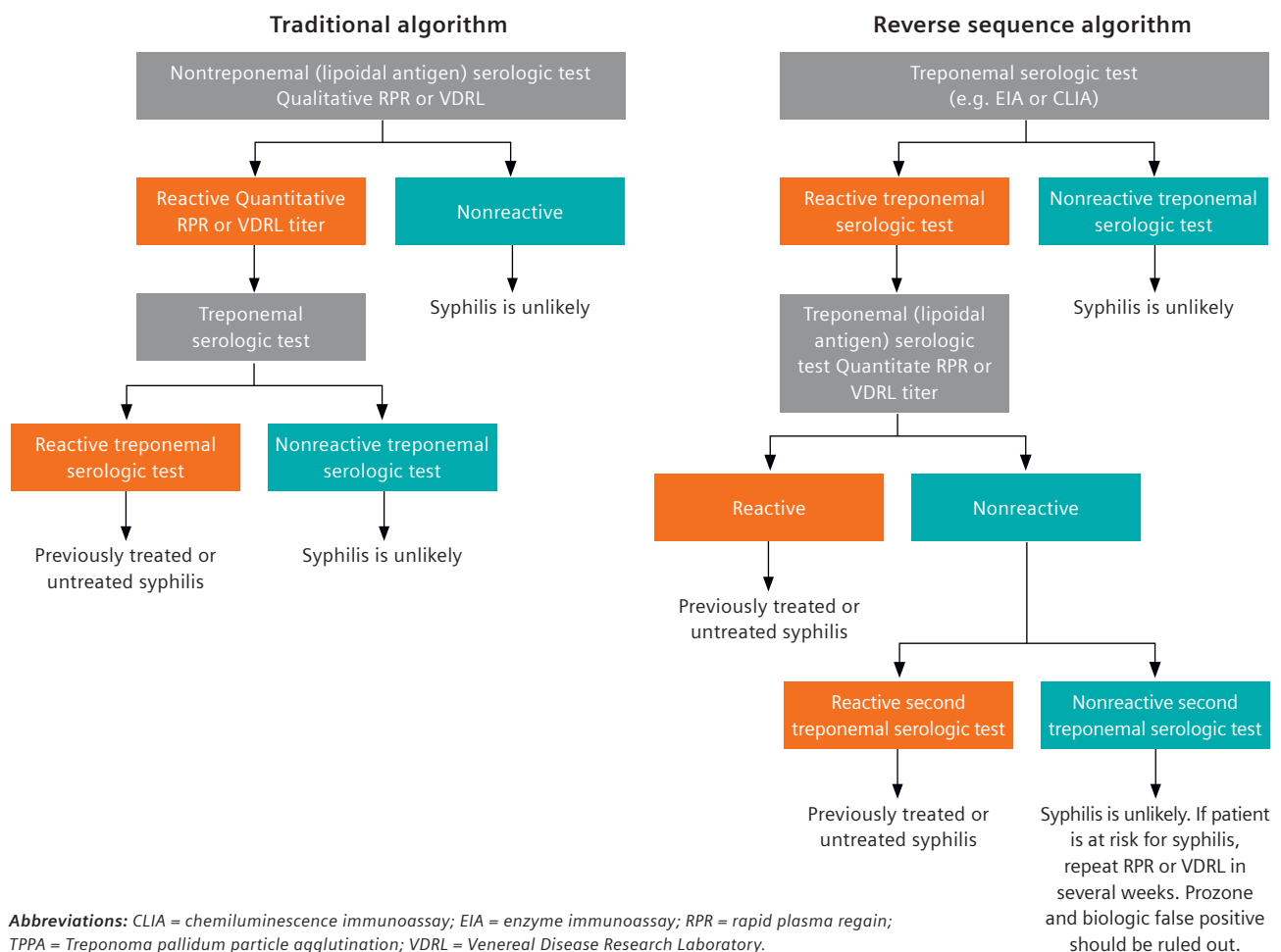


Figure 9. Updated guidance for syphilis testing from the CDC (U.S.)¹²

European recommendations for syphilis testing algorithms

Similar testing recommendations to the CDC exist outside the U.S. The 2020 European guidelines support both traditional and reverse testing, but comment that reverse testing may provide both earlier primary and increased late latent disease detection.¹³

Quantitative nontreponemal testing is recommended if using a nontreponemal assay in a traditional algorithm or following a reactive treponemal result if using the reverse algorithm.¹³ If qualitative nontreponemal testing is used initially in a traditional algorithm, the assay should then be run quantitatively to determine titer.^{12,13}

Clinical and operational advantages of a reverse testing algorithm*

Multiple studies have indicated that a reverse screening algorithm may improve detection of syphilis, including early primary and late-latent disease compared to nontreponemal assays.^{12,13,36,39}

While concerns have been raised over a higher initial reactive rate if using the reverse algorithm, abundant data supports routine use of reverse testing, including in lower and higher prevalence populations.^{5,12,13,30,31,36,39}

An elevated rate of initial reactives with reverse testing that do not confirm for current infection may occur in populations with rates of syphilis (due to persisting levels of treponemal antibody in treated infection).¹² However, a study that explored automated treponemal testing in a very high prevalence population (24%) found good performance for the reverse algorithm (using the ADVIA Centaur syphilis assay).³⁰

Findings for acceptable false-positive rates in a general population were observed in a large (>1.6 million samples) study exploring performance of the reverse algorithm (also using the ADVIA Centaur syphilis assay).³⁶

This study additionally observed a significant number of late infections detected by the reverse algorithm that likely would have been missed if using the traditional, highlighting the clinical value of adopting this algorithm.³⁶ See Table 4.

Sample number (testing with the ADVIA Centaur syphilis assay)	Late latent cases detected that would likely have been missed by RPR
1,631,519	4,693

“The reverse algorithm had a low false-positive rate and very few equivocal screening results but did identify previously undiagnosed late latent syphilis cases.”³⁶

Table 4. Reverse testing identifies late-latent infections likely missed if using the traditional algorithm.³⁶

*The statements and findings of the peer-reviewed studies described herein are based on results that were achieved in the customer’s unique setting using the Siemens Healthineers syphilis assay. Because there is no “typical” hospital or laboratory and many variables exist (e.g., hospital size, samples mix, case mix, level of IT, and/or automation adoption) there can be no guarantee that other customers will achieve the same results.

Comparative performance amongst automated treponemal assays

Multiple studies have explored the performance of available treponemal assays, including automated CLIA.³⁰⁻⁴⁰ Some performance data from peer-reviewed studies is shown in **Table 5** for the Siemens Healthineers syphilis assay, indicating its good comparative performance.

Table 5. Publications comparing the performance of the Siemens Healthineers syphilis assay include:*

Saw et al. ¹³⁵	Gios et al. ³⁰	Park et al. ³⁴
ADVIA Centaur compared to Abbott ARCHITECT syphilis assays relative to patient clinical status Reported sensitivity/specificity	ADVIA Centaur compared to TP-PA Reported sensitivity/specificity	Included ADVIA Centaur, Roche COBAS, Abbott ARCHITECT syphilis assays compared to FTA-ABS Reported sensitivity/specificity
ADVIA Centaur: 100%/95.5%	ADVIA Centaur: 99.7%/99.4%	ADVIA Centaur and Roche COBAS (both): 99.4%/100%
Abbott ARCHITECT: 100%/93.9%	TP-PA: 99.7%/99.4%	Abbott ARCHITECT: 96.8%/100%

**The statements and findings of the peer-reviewed studies described herein are based on results that were achieved in the customer's unique setting using the Siemens Healthineers syphilis assay. Because there is no "typical" hospital or laboratory and many variables exist (e.g., hospital size, samples mix, case mix, level of IT, and/or automation adoption) there can be no guarantee that other customers will achieve the same results.*

†Samples were preselected on ARCHITECT then tested on ADVIA Centaur.

Testing with the Siemens Healthineers syphilis assay on ADVIA Centaur and Atellica

The ADVIA Centaur and Atellica IM analyzers utilize the same set of reagents for syphilis testing, and data show a high correlation between the analyzers.⁴¹

The Siemens Healthineers syphilis assay detects both IgM and IgG

The Siemens Healthineers syphilis assay detects both IgM and IgG treponemal antibodies, with confirmed detection in IgM-only samples from early infections.⁴²

Conclusion:

Increased testing and linkage to care is critical in mitigating rising rates of syphilis, including congenital, and in driving elimination efforts. Automated treponemal testing for syphilis, like the Atellica IM Syphilis assay, offers workflow and clinical advantages in both low and higher prevalence populations. Guideline endorsement of the reverse algorithm using automated treponemal assays allows labs to readily scale as test demand grows.

For more information on the Siemens Healthineers Syphilis or other ID assays available on the Atellica IM and CI Systems please visit [siemens-healthineers.com](https://www.siemens-healthineers.com) or contact your local representative.

References

1. Tudor ME et al. Syphilis. [Updated 2024 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534780/>
2. Gilmour LS, Walls T. Congenital Syphilis: a Review of Global Epidemiology. *Clin Microbiol Rev.* 2023 Jun 21;36(2):e0012622.
3. <https://www.cdc.gov/std/treatment-guidelines/syphilis-pregnancy.htm> Accessed June 3, 2025.
4. Jaiswal, AK et al. The Critical Role of Penicillin in Syphilis Treatment and Emerging Resistance Challenges. *Diseases* 2025, 13, 41.
5. Treger, RS. et al. Advances in Syphilis Diagnostics to Address the 21st-Century Epidemic, *Clinical Chemistry*, 2025; hvaf072.
6. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Geneva: World Health Organization; 2022. License:CC BY-NC-SA 3.0 IGO.
7. Nyatsanza F, Tipple C. Syphilis: presentations in general medicine. *Clin Med (Lond).* 2016 Apr;16(2):184-8.
8. Fatima, Z. et al. Unraveling the resurgence of syphilis: a deep dive into the epidemic sweeping across the United States; a mini review. *Annals of Medicine & Surgery* (2025) 87:641–649.
9. Guidance for the Elimination of Syphilis and Congenital Syphilis in the Americas [https://iris.paho.org/handle/10665.2/61824#:~:text=The%20countries%20of%20the%20Americas%20have%20made,of%20syphilis%20cases%20\(as%20compared%20to%202018](https://iris.paho.org/handle/10665.2/61824#:~:text=The%20countries%20of%20the%20Americas%20have%20made,of%20syphilis%20cases%20(as%20compared%20to%202018)
10. Introducing a framework for implementing triple elimination of mother-to-child transmission of HIV, syphilis and hepatitis B virus. <https://iris.who.int/bitstream/handle/10665/375893/9789240086784-eng.pdf?sequence=1>
11. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Geneva: World Health Organization; 2022. License: CC BY-NC-SA 3.0 IGO.
12. Papp, JR et al. CDC Laboratory Recommendations for Syphilis Testing, United States, 2024. *MMWR. Recommendations and Reports / February 8, 2024 / 73(1)*:1–32.
13. Janier, M. et al. 2020 European guideline on the management of syphilis. *JEADV* 2020. <https://iusti.org/wp-content/uploads/2020/11/2020-Syphilis-guideline.pdf>
14. Sankaran, D. et al. Congenital Syphilis—An Illustrative Review. *Children* 2023, 10, 1310.
15. Syphilis. <https://www.who.int/news-room/fact-sheets/detail/syphilis>
16. <https://www.cdc.gov/sti-statistics/annual/index.html>
17. Machefsky, A. et al. Rising Stillbirth Rates Related to Congenital Syphilis in the United States From 2016 to 2022. *Obstetrics & Gynecology* 144(4):p 493-500, October 2024.
18. Ha T. et al. Neurosyphilis. [Updated 2024 Apr 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK540979/>
19. McDonald R. et al. Vital signs: missed opportunities for preventing congenital syphilis—United States, 2022. *MMWR Morb Mortal Wkly Rep* 2023;72: 1269–74.
20. Sykes, KJ et al. Using surveillance data to respond to an outbreak of congenital syphilis in Arizona through third-trimester screening policies, 2017–2018. *Public Health Rep* 2021;136:61–9.
21. Ahmed Ismail et al. Evaluating chemiluminescent immunoassays for syphilis detection: A comparative analysis, *Journal of Infection and Public Health*, Volume 18, Issue 6, 2025, 1 02731, ISSN 1876-0341.
22. Matthias J. et al. 2019. Frequency and Characteristics of Biological False-Positive Test Results for Syphilis Reported in Florida and New York City, USA, 2013 to 2017. *J Clin Microbiol* 57:10.1128/jcm.00898-19.
23. Ismail, A. et al. Evaluating chemiluminescent immunoassays for syphilis detection: A comparative analysis, *Journal of Infection and Public Health*, Volume 18, Issue 6, 2025, 102731, ISSN 1876-0341.
24. Larson, SA et al. Laboratory Diagnosis and Interpretation of Tests for Syphilis. *Clinical Microbiology Reviews.* Jan. 1995, p. 1–21.
25. Paul, G. et al. Predictors of serofast state after treatment for early syphilis in HIV-infected patients. *HIV Med.* 2021 Mar;22(3):165-171.
26. Morshed MG, Singh AE. 2015. Recent trends in the serologic diagnosis of syphilis. *Clin Vaccine Immunol* 22:137–147.
27. Wang, W. et al. (2025) Clinical characteristics and cause analysis of false-positive results in treponemal testing among patients, *Annals of Medicine*, 57:1, 2454327.
28. Li Z. et al. Screening for antibodies against *Treponema pallidum* with chemiluminescent microparticle immunoassay: analysis of discordant serology results and clinical characterization. *Annals of Clinical Biochemistry.* 2015;53(5):588-592.
29. <https://www.cdc.gov/sti/testing/index.html>
30. Gios, L. et al. A multi-country comparative study of two treponemal tests for the serodiagnosis of syphilis amongst men who have sex with men (MSM): Chemo-luminescent assay vs Treponema *pallidum* particle agglutination assay. *BMC Infect Dis* 24 (Suppl 1), 313 (2024).
31. Arcot, PJ et al. Comparative evaluation of ADVIA Centaur® XP chemiluminescence system for screening of HBV, HCV, HIV and syphilis in Indian blood donors, *Transfusion and Apheresis Science*, Volume 61, Issue 2, 2022, 103318, ISSN 1473-0502.
32. Park, IU et al. Performance of treponemal tests for the diagnosis of syphilis. *Clin Infect Dis.* 2019 Mar 5;68(6):913-918.
33. Lee, S. et al. Evaluation of the Elecsys Syphilis electrochemiluminescence immunoassay as a first-line screening test in the reverse algorithms for syphilis serodiagnosis. *International Journal of Infectious Diseases.* 80 (2019); 98–104.
34. Park, BG et al. Comparison of Six Automated Treponema-Specific Antibody Assays. *J Clin Microbiol.* 2016 Jan;54(1):163-7.
35. Saw, S. et al. Evaluation of the automated ADVIA centaur® XP syphilis assay for serological testing. *Diagn Microbiol Infect Dis.* 2017 May;88(1):7-11.
36. Morshed, M. et al. 2022. British Columbia's Experience after Implementation of the Treponema *pallidum* Reverse Algorithm and PCR Detection, 2015 to 2020. *Microbiol Spectr* 10:e00686-22.
37. Donkers, A. et al. Syphilis detection using the Siemens ADVIA Centaur Syphilis treponemal assay. *Clin Chim Acta.* 2014 Jun 10;433:84-7.
38. Ortiz, DA et al. The Traditional or Reverse Algorithm for Diagnosis of Syphilis: Pros and Cons. *Clinical Infectious Diseases*, Volume 71, Issue Supplement_1, 1 July 2020, Pages S43–S51.
39. Buono SA et al. 2017. Comparing three treponemal tests for syphilis screening. *Diagn Microbiol Infect Dis* 89: 173–177.
40. Fakile YF et al. Correlation of Treponemal Immunoassay Signal Strength Values with Reactivity of Confirmatory Treponemal Testing. *J Clin Microbiol.* 2017 Dec 26;56(1):e01165-17 .
41. Comparison of Atellica IM Analyzer Assays to the ADVIA Centaur System Assays White Paper. Siemens Healthcare Diagnostics Inc August 2018.
42. Data on file with Siemens Healthineers.

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