



Test Definition: NSYPH

Syphilis IgG Enzyme Immunoassay, Serum

Overview

Useful For

An aid in the diagnosis of infection with *Treponema pallidum*

Routine prenatal screening

This test is **not useful** for diagnosis of congenital syphilis.

This test is **not offered** as a screening or confirmatory test for blood donor specimens.

Highlights

This testing should be used to assess for recent or past infection with *Treponema pallidum* or for routine prenatal screening.

Testing for syphilis is performed using the reverse screening algorithm at Mayo Clinic and Mayo Clinic Laboratories.

Method Name

Enzyme Immunoassay (EIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 0.6 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial.

Forms

If not ordering electronically, complete, print, and send [Infectious Disease Serology Test Request](#) (T916) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Syphilis is caused by infection with the spirochete *Treponema pallidum* subspecies *pallidum*. The infection is systemic, and the disease is characterized by periods of latency. These features, together with the fact that *T pallidum* cannot be isolated in culture, mean that serologic techniques play a major role in the diagnosis and follow-up of treatment for syphilis.

Historically, the serologic testing algorithm for syphilis included an initial non-treponemal screening test, such as the rapid plasma reagin (RPR) or the VDRL tests. Because these tests measure the host's immune response to nontreponemal antigens, they lack specificity. Therefore, a positive result by RPR or VDRL requires confirmation by a treponemal-specific test, such as the fluorescent treponemal antibody-absorption (FTA-ABS) or microhemagglutination (MHA-TP) assay. Although the FTA-ABS and MHA-TP assays are technically simple to perform, they are labor intensive and require subjective interpretation by testing personnel.

As an alternative to the traditional syphilis screening algorithm, many laboratories utilize the reverse syphilis screening algorithm. This algorithm starts with an automated treponemal assay to detect antibodies specific to *T pallidum*. If this screening assay is positive, the sample is reflexed for testing by RPR, which, if positive, is reported with a titer and is indicative of active or recent syphilis infection. If the RPR is negative, the sample is reflexed to a second treponemal assay, such as the *T pallidum* particle agglutination (TP-PA) assay. If the TP-PA is positive, this would indicate previously treated or late-stage syphilis infection. Alternatively, if the TP-PA is negative, the initial positive screen is interpreted as a false-positive result.

Syphilis screening at Mayo Clinic is performed using the reverse algorithm, which first tests sera for *T pallidum* specific IgG antibodies using an automated enzyme immunoassay. A positive treponemal test suggests infection with *T pallidum* but does not distinguish between recent, past, treated, or untreated infection. This is because treponemal tests may remain reactive for life, even following adequate therapy. Therefore, the results of a nontreponemal assay, such as RPR, are needed to provide information on a patient's disease state and history of therapy.(Table)

In some patients, the results of the treponemal screening test and RPR may be discordant (eg, syphilis IgG positive and RPR negative). To discriminate between a falsely reactive screening result and past syphilis, a second

treponemal-specific antibody test is recommended using a method that is different from the initial screen test (eg, TP-PA).

In the setting of a positive syphilis IgG screening result and a negative RPR, a positive TP-PA result is consistent with either 1) past, successfully treated syphilis, 2) early syphilis with undetectable RPR, or 3) late/latent syphilis in patients who do not have a history of treatment for syphilis. Further historical evaluation is necessary to distinguish between these scenarios.(Table)

In the setting of a positive syphilis IgG screening result and a negative RPR, a negative TP-PA result is most consistent with a falsely reactive syphilis IgG screen.(Table) If syphilis remains clinically suspected, a second specimen should be submitted for testing.

Table. Interpretation and follow-up of reverse screening results:

Patient history	Syphilis IgG Ab by EIA	Test and result		Interpretation	Follow-up
		RPR	TP-PA		
Unknown history of syphilis	Nonreactive	NA	NA	No serologic evidence of syphilis	None, unless clinically indicated (eg, early/acute/primary syphilis)
Unknown history of syphilis	Reactive	Reactive	NA	Untreated or recently treated syphilis	See Centers for Disease Control and Prevention treatment guidelines
Unknown history of syphilis	Reactive	Nonreactive	Nonreactive	Probable false-positive screening test	No follow-up testing, unless clinically indicated (eg, acute/primary syphilis)
Unknown history of syphilis	Reactive	Nonreactive	Reactive	Possible syphilis (eg, early or latent) or previously treated syphilis	Historical and clinical evaluation required
Unknown history of syphilis	Equivocal	NA	NA	NA	Unknown history of syphilis
Known history of syphilis	Reactive	Nonreactive	Reactive or NA	Past, successfully treated syphilis	None

EIA, enzyme immunoassay; NA, not applicable; RPR, rapid plasma reagin; TP-PA, *Treponema pallidum* particle agglutination

Reference Values

Nonreactive

Reference values apply to all ages

Interpretation

Nonreactive:

No serologic evidence of exposure to *Treponema pallidum* (syphilis). Repeat testing may be considered in patients with suspected acute or primary syphilis.

Equivocal:

Recommend follow-up testing in 10 to 14 days if clinically indicated.

Reactive:

Results suggest infection with *T pallidum* at some point in time. Results do not distinguish between recent or past infection, or between treated and untreated syphilis as treponema-specific IgG may remain elevated despite appropriate therapy. Falsely reactive treponemal results may occur; additional testing by a non-treponemal assay is recommended if not previously performed on this sample.

Cautions

Despite active syphilis, serologic tests may be negative in severely immunosuppressed patients such as those with AIDS.

In very early cases of primary syphilis, serology tests may be negative.

In cases of untreated, late or latent syphilis, the result of rapid plasma reagin may be negative. However, the syphilis screening enzyme immunoassay (EIA) and *Treponema pallidum* particle agglutination (TP-PA) should be positive. A thorough clinical and historical evaluation should be performed to determine if treatment for latent syphilis is required.

Results should be considered in the context of all available clinical and laboratory data.

Clinical Reference

- Centers for Disease Control and Prevention (CDC): Discordant results from reverse sequence syphilis screening-five laboratories, United States, 2006-2010. *Morb Mortal WKLY Rep.* 2011 Feb 11;60(5):133-137
- Radolf JD, Tramont EC, Salazar JC: Syphilis (*Treponema pallidum*). In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 9th ed. Elsevier; 2020:2865-289291
- Binnicker MJ, Jespersen DJ, Rollins LO: Direct comparison of the traditional and reverse syphilis screening algorithms in a population with a low prevalence of syphilis. *J Clin Microbiol.* 2012 Jan;50(1):148-150

Performance

Method Description

[Microtitration wells, coated with whole-cell sonicated *Treponema pallidum* \(Nichols strain\) antigens, are incubated with serum specimens which may contain specific antibodies to *T pallidum*. After incubation, unbound components in the test sample are washed away. IgG antibodies from the specimen that bound to *T pallidum* antigens are detected using monoclonal anti-human IgG secondary antibodies conjugated to horseradish peroxidase \(HRP\) during a second incubation period. Following a second wash cycle, the enzyme conjugate on bound secondary antibodies is detected](#)

[following addition of tetramethylbenzidine \(TMB\). The enzymatic reaction is stopped using 1 N sulfuric acid. The assay is measured spectrophotometrically to indicate the presence or absence of IgG treponemal antibodies relative to a cut-off calibrator.\(Package insert: CAPTIA Syphilis \(*T Pallidum*\)-G. Trinity Biotek USA; 800-970-29 Rev H, 10/2013\)](#)

PDF Report

No

Day(s) Performed

Monday through Friday, Sunday

Report Available

Same day/1 to 3 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

86780

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NSYPH	Syphilis IgG EIA, S	47238-1

Result ID	Test Result Name	Result LOINC® Value
NSYPH	Syphilis IgG EIA, S	47238-1