

Test Definition: TPPA

Syphilis Antibody, Treponema pallidum
Particle Agglutination, Serum

Overview

Useful For

An aid to resolve discrepant results between screening treponemal and non-treponemal assays

This test is **not recommended for** general screening purposes for syphilis.

This test should **not be used** to evaluate response to therapy.

This test is **not intended for** medical-legal use.

Testing Algorithm

For more information see [Syphilis Serology Algorithm](#).

Special Instructions

- [Syphilis Serology Algorithm](#)

Method Name

Particle Agglutination

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This assay is recommended by the Centers for Disease Control and Prevention for sera testing positive by a screening treponemal assay and negative by rapid plasma reagin (RPR). The results of this assay assist in determining whether the results of a screening treponemal test are truly or falsely positive.

For prenatal syphilis screening, the syphilis IgG test (SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum) is recommended. Testing for IgM-class antibodies to *T pallidum* should not be performed during routine pregnancy screening.

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)

Collection Container/Tube:

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- Preferred:** Serum gel
- Acceptable:** Red top
- Submission Container/Tube:** Plastic vial
- Specimen Volume:** 0.5 mL
- Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

Forms

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

Specimen Minimum Volume

0.3 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Syphilis is a disease 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.

Syphilis is categorized by an early primary infection in which patients may have nonspecific symptoms and, potentially, genital lesions. Patients tested by serology during the primary phase may be negative for antibodies, especially if testing is performed during the first 1 to 2 weeks after symptom onset. As the disease progresses into the secondary phase, antibodies to *T pallidum* reach peak titers and may persist indefinitely regardless of the disease state or prior therapy. Therefore, detection of antibodies to nontreponemal antigens, such as cardiolipin (a lipoidal antigen released by host cells damaged by *T pallidum*) may help to differentiate between active and past syphilis infection. Non-treponemal antibodies are detected by the rapid plasma reagin (RPR) assay, which is typically positive during current infection and negative following treatment or during late/latent forms of syphilis.

Historically, the serologic testing algorithm for syphilis included an initial nontreponemal screening test, such as the RPR

or VDRL tests. Because these tests measure the host's antibody response to nontreponemal antigens, they may lack specificity. Therefore, a positive result by RPR or VDRL requires confirmation by a treponemal-specific test, such as the *T pallidum* particle agglutination (TP-PA) assay. Although technically simple to perform, the TP-PA assay is labor intensive and requires subjective interpretation by testing personnel.

Due to the increased specificity of treponemal assays and the objective result interpretation of automated treponemal immunoassays, many large clinical laboratories have switched to screening for syphilis using a reverse algorithm. Per this algorithm, serum samples are first tested by an automated treponemal immunoassay, and positive samples are reflexed to the RPR assay to provide an indication of the patient's disease state and history of treatment. For specimens testing positive by the screening treponemal assay and negative by RPR, a second treponemal test (eg, TP-PA) is performed. The results of TP-PA assist in determining whether the results of a screening treponemal test are truly or falsely positive.

Reference Values

Negative

Interpretation

Syphilis screening at Mayo Clinic is performed by using the reverse algorithm, which first tests sera for *Treponema pallidum* specific IgG antibodies using an automated immunoassay. Antibodies to syphilis can remain elevated despite appropriate antimicrobial treatment and a reactive result does not distinguish between recent or past infection. To further evaluate disease and treatment status, samples that are reactive by the syphilis screening test are reflexed to the rapid plasma reagin (RPR) assay, which detects antibodies to cardiolipin, a lipoidal antigen released from host cells damaged by *T pallidum*. Unlike treponemal-specific antibodies, RPR titers decrease and usually become undetectable following appropriate treatment and can be used to monitor response to therapy.

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 screening test (eg, *T pallidum* particle agglutination: TP-PA).

In the setting of a positive syphilis IgG screening result and a negative RPR, a positive TP-PA result is consistent with one of the following:

- 1. Past, successfully treated syphilis
 - 2. Early syphilis with undetectable RPR titers
 - 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, order SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum.

Table. Interpretation and follow-up of reverse screening results

Patient history	Test and result			Interpretation	Follow-up
	EIA/CIA/MF I	RPR	TP-PA		

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Unknown history of syphilis	Nonreactive	N/A	N/A	No serologic evidence of syphilis	None, unless clinically indicated (eg, early/acute/primary syphilis)
Unknown history of syphilis	Reactive	Reactive	N/A	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
Known history of syphilis	Reactive	Nonreactive	Reactive or N/A	Past, successfully treated syphilis	None

CIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; N/A, not applicable; RPR, rapid plasma reagin; TP-PA, *Treponema pallidum* particle agglutination.

Cautions

Testing by only *Treponema pallidum* particle agglutination (TP-PA) is not recommended for general screening purposes for syphilis. TP-PA should only be requested when:

1. The results of a treponemal screening test and rapid plasma reagin (RPR) are discordant (eg, syphilis IgG-positive, RPR-negative).
2. A laboratory screens for syphilis using RPR and is in need of a treponemal confirmatory test.

Interpretation of results obtained with the Serodia TP-PA syphilis antibody test must be used in conjunction with the patient's clinical symptoms, medical history, and other clinical and laboratory findings.

Serodia TP-PA assay is less sensitive than the fluorescent treponemal antibody absorption (FTA-ABS) test in untreated primary syphilis but compares favorably in all other stages of syphilis.

Serodia TP-PA assay should not be used to evaluate response to therapy since treponemal tests tend to remain reactive following treatment for syphilis.

Serodia TP-PA assay may be reactive in a small percentage (<1%) of normal or healthy persons. These false-positive

results are often transient with unknown cause. False-positive results may occur in association with other underlying illnesses.

Serodia TP-PA may be reactive in persons from areas endemic for yaws or pinta.

Serodia TP-PA performs best in populations at risk for *T pallidum* infection.

False-positive or inconclusive results for this assay may be seen in patients with HIV, leprosy, toxoplasmosis, or *Helicobacter pylori*.

Clinical Reference

1. Park IU, Tran A, Pereira L, Fakile Y. Sensitivity and specificity of treponemal-specific tests for diagnosis of syphilis. *Clinical Infectious Diseases*. 2020;71:S13-S20
2. Tuddenham S, Katz SS, Ghanem KG. Syphilis laboratory guidelines: performance characteristics of nontreponemal antibody tests. *Clinical Infectious Diseases*. 2020;71:S21-S42
3. Ortiz DA, Shukla MR, Loeffelholz MJ. The traditional or reverse algorithm for diagnosis of syphilis: pros and cons. *Clinical Infectious Diseases*. 2020;71:S43-S51

Performance

Method Description

The Serodia *Treponema pallidum* particle agglutination (TP-PA) test is based on the agglutination of colored gelatin particle carriers sensitized with *Treponema pallidum* (Nichols Strain) antigen. Serum samples are serially diluted in microplate wells. Sensitized gelatin particles are added to respective wells and the contents of the plate mixed. The mixture is incubated for 2 hours at ambient temperature. Serum containing specific antibodies will react with the antigen-sensitized colored gelatin particles to form a smooth mat of agglutinated particles in the microplate well. A compact button formed by the settling of the non-agglutinated particles characterizes negative reactions. The agglutination patterns are read visually to determine interpretation. (Package insert: Serodia TP-PA. Fujirebio Diagnostics, Inc; 08/2017)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 to 4 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
TPPA	Syphilis Ab by TP-PA, S	24312-1

Result ID	Test Result Name	Result LOINC® Value
61480	Syphilis Ab by TP-PA, S	24312-1