

Overview

Useful For

An aid to resolve discrepant results between screening treponemal (eg, enzyme immunoassay [EIA], multiplex flow immunoassay) and non-treponemal (eg, rapid plasma regain) 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

See [Syphilis Serology Algorithm](#) in Special Instructions.

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 specimens 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.

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.5 mL

Forms

If not ordering electronically, complete, print, and send a [Microbiology Test Request](#) (T244) 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 and Interpretive
Clinical Information

Syphilis is a disease caused by infection with the spirochete *Treponema 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 non-treponemal 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.

For prenatal syphilis screening, the syphilis IgG test (SYPGN / Syphilis Total Antibody, Serum) is recommended. Testing for IgM-class antibodies to *T pallidum* should not be performed during routine pregnancy screening unless clinically indicated.

Historically, the serologic testing algorithm for syphilis included an initial non-treponemal screening test, such as the RPR or the venereal disease research laboratory (VDRL) tests. Because these tests measure the host's antibody response to non-treponemal antigens, they may lack specificity. Therefore, a positive result by RPR or VDRL requires confirmation by a treponemal-specific test, such as fluorescent treponemal antibody absorption (FTA-ABS) or *T pallidum* particle agglutination (TP-PA). Although the FTA-ABS and TP-PA are technically simple to perform, they are labor intensive and require subjective interpretation by testing personnel.

Due to the low prevalence of syphilis in the United States, the increased specificity of treponemal assays, and the objective interpretation of automated treponemal enzyme immunoassay (EIA) and multiplex flow immunoassay (MFI), 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 assay (eg, EIA or MFI). Specimens testing positive by these assays are then reflexed to the RPR assay to provide an indication of the patient's disease state and history of treatment. Recently, the Centers for Disease Control and Prevention recommended that specimens testing positive by a screening treponemal assay and negative by RPR be tested by a second treponemal test (eg, TP-PA). 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 multiplex flow immunoassay (MFI).(1) IgG 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 IgG 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*.(2) 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 (syphilis IgG) and RPR may be discordant (eg, syphilis IgG positive and RPR negative). To discriminate between a falsely reactive screening result and past syphilis, the Centers for Disease Control and Prevention recommends performing a second treponemal-specific antibody test using a method that is different from the initial screening test (eg, *T pallidum* particle agglutination; TP-PA).(2)

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 titers, 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 1).

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 1). If syphilis remains clinically suspected, a second specimen should be submitted, order SYPHT / Syphilis Total Antibody with Reflex, Serum.

Table 1. Interpretation and follow-up of reverse screening results

Patient history	Test and result			Interpretation	Follow-up
	EIA/CIA/MFI	RPR	TP-PA		
Unknown history of syphilis	Non-reactive	N/A	N/A	No serologic evidence of syphilis	None, unless clinically indicated (eg, early syphilis)
Unknown history of syphilis	Reactive	Reactive	N/A	Untreated or recently treated syphilis	See CDC treatment guidelines
Unknown history of syphilis	Reactive	Non-reactive	Non-reactive	Probable false-positive screening test	No follow-up testing, unless clinically indicated
Unknown history of syphilis	Reactive	Non-reactive	Reactive	Possible syphilis (eg, early or latent) or previously treated syphilis	Historical and clinical evaluation required

Known history of syphilis	Reactive	Non-reactive	Reactive or N/A	Past, successfully treated syphilis	None
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CIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; MFI, multiplex flow 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 (eg, enzyme immunoassay [EIA] or multiplex flow immunoassay; MFI) 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*.

Supportive Data

Accuracy:

The *Treponema pallidum* particle agglutination (TP-PA) assay was compared to the BioPlex 2200 syphilis IgG multiplex flow immunoassays (MFI) assay using 1200 serum specimens (1100 prospective and 100 previously characterized sera). The results are summarized in Table 2:

Table 2. Comparison of the BioPlex 2200 syphilis IgG and TP-PA assays using serum samples (n=1,200)

		BioPlex syphilis IgG MFI assay		
		Positive	Negative	No result

Fujirebio TP-PA	Positive	101	3	0
	Negative	11	1083	1
	Indeterminate	0	1	0

Sensitivity = 90.18%; (95% CI, 83.15%-94.61%)

Specificity = 99.6%; (95% CI, 99.0%-99.9%)

Overall percent agreement = 98.7%; (95% CI, 96.3%-100%)

All discrepant samples tested negative by rapid plasma reagin (RPR)

Precision:

For interassay precision, 1 negative (TP-PA titer <1:80), 1 low-positive (1:80), 1 mid-positive (1:320), and 1 high-positive (1:1280) serum specimen were tested by TP-PA over 10 separate days and showed 100% agreement with the expected result for each category of results.

For intraassay precision, a negative, low-positive, and high-positive serum specimen were tested 20 times in a single run and showed 100% agreement for each category of results.

Reference Range:

The expected result is negative for this test. To validate reference range, testing of sera collected from 50 healthy blood donors showed a reactive rate of 2% (1/50) by TP-PA. The positive sample was also determined to be positive by the BioPlex syphilis IgG assay.

Reportable Range:

The TP-PA is reported as positive, negative, or indeterminate.

Analytic Specificity:

Testing of sera (n=58) known to be positive for antibodies to other microorganisms/conditions (n =30) or from pregnant females (n=28) showed a positive rate of 0% (0/58) by TP-PA. See Table 3 for a list of samples included in the cross-reactivity panel.

Table 3. Cross-reactivity panel tested by TP-PA to assess analytical specificity

Antibody or condition tested:	Number of samples tested by TP-PA
Epstein Barr VCA IgG	5
Epstein Barr VCA IgM	5
HSV IgG	5
HSV IgM	2
Lyme IgM/IgG	5
Heterophile antibody	5
Rheumatoid factor	3
Pregnancy	28

Clinical Reference

1. 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
2. Center of Disease Control and Prevention (CDC): Discordant results from reverse sequence syphilis screening-five laboratories, United States, 2006-2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(5):133-137
3. 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; 2020:2865-2892

Performance

Method Description

The Serodia 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 nonagglutinated particles characterizes negative reactions. The agglutination patterns are read visually to determine interpretation. (Package insert: Serodia TP-PA. Fujirebio Diagnostics, Inc; 8/13/2017)

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

Rochester

Fees and 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 Regional Manager. 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