

## Overview

### Useful For

Aid for the diagnosis of infection with *Treponema pallidum* using an algorithmic approach

Routine prenatal screening

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

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

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
RRPRS	RPR Screen w/ Reflex to Titer, S	No	No
RTPPA	Syphilis Ab, TP-PA, S	Yes, (Order TPPA)	No
RRPRQ	RPR Titer, S	No	No

### Testing Algorithm

If the syphilis IgG result is reactive or equivocal, then the rapid plasma reagin (RPR) screen will be performed at an additional charge.

If the RPR screen is positive, then the RPR titer will be performed at an additional charge.

If the RPR screen is negative, then syphilis antibody *Treponema pallidum* particle agglutination testing will be performed at an additional charge.

For more information see:

[-Syphilis Serology Algorithm](#)

[-Meningitis/Encephalitis Panel Algorithm](#)

### Special Instructions

- [Syphilis Serology Algorithm](#)
- [Meningitis/Encephalitis Panel Algorithm](#)

### Highlights

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

Syphilis screening at Mayo Clinic and Mayo Clinic Laboratories is performed using the reverse screening algorithm.

### Method Name

SYPH1: Enzyme Immunoassay (EIA)  
RRPRS, RRPRQ: Flocculation/Agglutination  
RTPPA: Particle Agglutination

**NY State Available**

Yes

**Specimen****Specimen Type**

Serum

**Specimen Required****Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)**Collection Container/Tube:****Preferred:** Serum gel**Acceptable:** Red top**Submission Container/Tube:** Plastic vial**Specimen Volume:** 1.5 mL Serum**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.**Forms**[If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:](#)[-Kidney Transplant Test Request](#)[-Infectious Disease Serology Test Request \(T916\)](#)[-General Test Request \(T239\)](#)**Specimen Minimum Volume**

Serum: 0.6 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	

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## 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 nontreponemal 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 infections. 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 antibody by EIA	RPR result	TP-PA result	Interpretation	Follow-up
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-T pallidum particle agglutination

### Reference Values

SYPHILIS IgG SCREEN

Nonreactive

RAPID PLASMA REAGIN SCREEN

Negative

RAPID PLASMA REAGIN TITER

Negative

SYPHILIS ANTIBODY, *Treponema pallidum*-PARTICLE AGGLUTINATION

Negative

Reference values apply to all ages

### Interpretation

Nonreactive:

No serologic evidence of infection to *Treponema pallidum* (syphilis). Repeat testing may be considered in patients with suspected acute or primary syphilis in 2 to 4 weeks.

Equivocal:

Rapid plasma reagin has been ordered to help distinguish between infection with *T pallidum* (syphilis) versus a falsely reactive treponemal antibody result.

Reactive:

Rapid plasma reagin has been ordered to help distinguish between infection with *T pallidum* (syphilis) versus a falsely reactive treponemal antibody result.

### 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 for syphilis may be negative.

In cases of untreated, late or latent syphilis, the result of rapid plasma reagin may be negative. However, the syphilis screening by enzyme immunoassay and *Treponema pallidum* particle agglutination 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. MMWR Morb Mortal Wkly Rep. 2011;605):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; 2020:2865-2892
- 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;50(1):148-150

### Performance

### Method Description

Syphilis IgG

Microtitration wells, coated with whole-cell sonicated *Treponema pallidum* (Nichols strain) antigens are incubated with

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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 during a second incubation period. Following a second wash cycle, the enzyme conjugate on bound secondary antibodies is detected following addition of TMB (tetramethylbenzidine). 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 Biotech; 800-970-29 Rev H, 10/2013)

**Rapid Plasma Reagin Screen and Titer:**

The rapid plasma reagin titer test is a macroscopic screening assay done with unheated serum. Reagin reacts with nontreponemal antigen containing colloidal charcoal particles. This reaction results in a visual flocculation of the black particles against the white card background. The test yields a positive or negative result, and all positive samples are titered to determine the highest positive dilution. (Huber TW, Storms S, Young P, et al. Reactivity of microhemagglutination, fluorescent treponemal antibody absorption, Venereal Disease Research Laboratory, and rapid plasma reagin tests in primary syphilis. *J Clin Microbiol.* 1983;17[3]:405-409; Kaur G, Kaur P. Syphilis testing in blood donors: an update. *Blood Transfus.* 2015;13[2]:197-204)

**Syphilis Antibody, *Treponema pallidum*- Particle Agglutination**

The Serodia *Treponema pallidum* particle agglutination (TP-PA) test is based on the agglutination of colored gelatin particle carriers sensitized with *T 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.; 05/2024)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday, Sunday

**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-Syphilis IgG Screen

86592-Syphilis Rapid Plasma Reagin Screen (if appropriate)

86593-Rapid Plasma Reagin Titer (if appropriate)

86780-Syphilis Antibody by TP-PA (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
SYPH1	Syphilis IgG w/ Reflex, EIA, S	47238-1

Result ID	Test Result Name	Result LOINC® Value
SYPH1	Syphilis IgG w/ Reflex, EIA, S	47238-1