



Test Definition: SYPHT

Syphilis Total Antibody with Reflex, Serum

Overview

Useful For

Aiding in the diagnosis of recent or past *Treponema pallidum* infection

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
RTPPA	Syphilis Ab, TP-PA, S	Yes, (Order TPPA)	No
RRPRQ	RPR Titer, S	No	No
SYPNB	Syphilis Total Ab Bill Only 1	No, (Bill Only)	No
RRPRS	RPR Screen w/ Reflex to Titer, S	No	No

Testing Algorithm

If the syphilis total antibody result is nonreactive, billing will be captured under SYPNB.

If the syphilis total antibody result is reactive or equivocal, then the rapid plasma reagin (RPR) screen will be performed, and billing will be captured under SYPNB.

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.

Highlights

This testing should be used to assess for recent or past 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

SYPHT: Multiplex Flow Immunoassay

RRPRQ, RRPRS: Flocculation/Agglutination

RTPPA: Particle Agglutination

NY State Available

No

Specimen**Specimen Type**

Serum

Specimen Required**Collection Container/Tube:** 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.**Specimen Minimum Volume**

0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Heat-inactivated specimen	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*. 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 antibody response to non-treponemal 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, such as an enzyme immunoassay and multiplex flow immunoassay (MFI), to detect antibodies specific to *T pallidum*. If the screening assay is positive, the sample is reflexed to a RPR assay, 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 by using the reverse algorithm, which first tests sera for *T pallidum* specific IgG/IgM antibodies using an automated MFI. 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/IgM 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/IgM 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)

In the setting of a positive syphilis IgG/IgM screening result and a negative RPR, a negative TP-PA result is most consistent with a falsely reactive syphilis IgG/IgM 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 total antibody by MFI	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	Reactive	Nonreactive	Nonreactive	Probable	No follow-up

history of syphilis				false-positive screening test	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
MFI - multiplex flow immunoassay NA - not applicable RPR - rapid plasma reagin TP-PA - <i>T pallidum</i> particle agglutination					

Reference Values

SYPHILIS TOTAL ANTIBODY

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

Reactive:

RPR 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 test multiplex flow immunoassay (MFI) 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. MMWR Morb Mortal Wkly Rep. 2011;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; 2020:2865-2892
- 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; Jan;50(1):148-150

Performance**Method Description**

The BioPlex 2200 Syphilis Total kit employs *Treponema pallidum* fusion protein (rTP47/rTP17) and cardiolipin antigen-coated fluoromagnetic beads with unique fluorescent signatures to identify the presence of IgG and IgM antibodies to *T pallidum* and non-treponemal reagin antibodies in a 2-step assay format. Dyed beads are coated with recombinant *T pallidum* rTP47/rTP17 fusion protein or cardiolipin antigen. The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel. The mixture is incubated at 37 degrees C. After a wash cycle, a mixture of murine monoclonal antihuman IgG and murine monoclonal antihuman-IgM antibody conjugated to phycoerythrin (PE) is added to the dyed beads, and this mixture is incubated at 37 degrees C. The excess conjugate is removed in another wash cycle, and the beads are resuspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of antibody captured by the antigen is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity (RFI). (Package insert: BioPlex 2200 Syphilis Total and RPR. Bio-Rad; 06/2017)

If the total antibody result is reactive, a rapid plasma reagin (RPR) screen is performed. If the RPR screen is reactive, the RPR titer test is performed manually.

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 4 days

Specimen Retention Time

7 days

Performing Laboratory Location

Mayo Clinic- Scottsdale Lab

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

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

86593-Rapid Plasma Reagin Titer (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SYPHT	Syphilis Total Ab w/ Reflex, S	47236-5

Result ID	Test Result Name	Result LOINC® Value
SYPHT	Syphilis Total Ab w/ Reflex, S	47236-5