Test Definition: RRPRS

Rapid Plasma Reagin Screen with Reflex to Titer, Serum (Non-Orderable)

Overview

Useful For

Only orderable as a reflex. For more information see SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum.

Aid for the diagnosis of infection with *Treponema pallidum*

Rapid plasma reagin testing following a positive treponemal antibody test

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

Testing Algorithm

If the rapid plasma reagin (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.

Special Instructions

- Syphilis Serology Algorithm

Method Name

Only orderable as a reflex. For more information see SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum.

Flocculation/Agglutination

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Only orderable as a reflex. For more information see SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top

Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL Serum
Collection Information: Centrifuge and aliquot serum into plastic vial.

Specimen Minimum Volume

Serum: 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	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 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:

		Test and result			
Patient history	**Syphilis IgG antibody by EIA**	**RPR**	**TP-PA**	**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	Positive	NA	Untreated or recently treated syphilis	See Centers for Disease Control and Prevention treatment guidelines
Unknown history of syphilis	Reactive	Negative	Negative	Probable false-positive screening test	No follow-up testing, unless clinically indicated (eg, acute/ primary syphilis)
Unknown history of syphilis	Reactive	Negative	Positive	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	Negative	Positive 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

Only orderable as a reflex. For more information see SYPH1 / Syphilis IgG with Reflex, Enzyme Immunoassay, Serum.

Negative
Reference values apply to all ages

Interpretation

Negative:
Treponema pallidum-particle agglutination has been ordered to distinguish between infection with *T pallidum* (syphilis) versus a falsely reactive treponemal antibody result.

Positive:
Specimen reflexed to determine rapid plasma reagin titer value.

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 using a treponemal assay, including the *Treponema pallidum* particle agglutination test, 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

1. 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
2. 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
3. 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. doi:10.1128/JCM.05636-11

Performance

Method Description

If the IgG result is equivocal or reactive, a rapid plasma reagin (RPR) screen is performed manually. If the RPR screen is positive the RPR titer is performed manually. The RPR 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)

If the RPR screen is negative, the Serodia *Treponema pallidum* particle agglutination (TP-PA) test is performed. The 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; 04/2015)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

Same day/1 to 2 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

86592-Rapid Plasma Reagin Screen
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
RRPRS	RPR Screen w/ Reflex to Titer, S	20507-0

Result ID	Test Result Name	Result LOINC® Value
616866	RPR Screen w/ Reflex to Titer, S	20507-0