

## Overview

### Useful For

Diagnosing syphilis

### Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
RPRT4	RPR, Titer, S	No	No
TPPA	Syphilis Ab, TP-PA, S	Yes, (Order TPPA)	No

### Testing Algorithm

If this test is positive, then the rapid plasma reagin titer will be performed at an additional charge.

If this test is negative, then the *Treponema pallidum* particle agglutination test will be performed at an additional charge.

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

### Special Instructions

- [Syphilis Serology Algorithm](#)

### Highlights

This test is for the diagnosis of syphilis infection.

### Method Name

RPRT3, RPRT4: Flocculation/Agglutination

TPPA: Particle Agglutination

### NY State Available

No

## Specimen

### Specimen Type

Serum

### Ordering Guidance

This assay should only be used following an initial reactive treponemal antibody assay result as part of the reverse syphilis testing algorithm.

**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:** 0.3 mL

**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

**Forms**

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

**Specimen Minimum Volume**

See Specimen Required

**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 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

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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.

Patients with primary or secondary syphilis are typically tested by RPR to monitor response to treatment. Typically, RPR titers decrease following successful treatment, but this may occur over a period of months to years. Additionally, testing of maternal and neonate serum, collected concurrently, by RPR can be used as an aid to diagnose congenital syphilis.

## Reference Values

Negative

Reference values apply to all ages.

## Interpretation

Negative:

Non-treponemal antibodies not detected. Testing on a new specimen collected in 2 to 3 weeks is recommended if acute infection is suspected. Sample reflexed for detection of *Treponema pallidum* specific antibodies by the *T pallidum* particle agglutination assay.

Positive:

Specimen reflexed to determine rapid plasma reagin titer.

## Cautions

Biological false-positive reactions with cardiolipin-type antigens have been reported in diseases such as infectious mononucleosis, leprosy, malaria, lupus erythematosus, vaccinia, and viral pneumonia.

Pregnancy, autoimmune diseases, and narcotic addictions may give false-positive results. Pinta, yaws, bejel, and other treponemal diseases may also produce false-positive results with this test.

## Clinical Reference

1. Tuddenham S, Katz SS, Ghanem KG. Syphilis Laboratory Guidelines: Performance characteristics of nontreponemal antibody tests. *Clin Infect Dis*. 2020;71(Suppl 1):S21-S42. doi:10.1093/cid/ciaa306
2. Park IU, Tran A, Pereira L, Fakile Y. Sensitivity and specificity of treponemal-specific tests for the diagnosis of syphilis. *Clin Infect Dis*. 2020;71(Suppl 1):S13-S20. doi:10.1093/cid/ciaa349
3. Theel ES, Katz SS, Pillay A. Molecular and direct detection tests for *Treponema pallidum* subspecies *pallidum*: A review of the literature, 1964-2017. *Clin Infect Dis*. 2020;71(Suppl 1):S4-S12. doi:10.1093/cid/ciaa176

4. Ortiz DA, Shukla MR, Loeffelholz MJ. The traditional or reverse algorithm for diagnosis of syphilis: Pros and cons. *Clin Infect Dis*. 2020;71(Suppl 1):S43-S51. doi:10.1093/cid/ciaa307

## Performance

### Method Description

If the rapid plasma reagin (RPR) screen is reactive, the RPR titer is performed. 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 Mar;17[3]:405-409; [Kaur G, Kaur P: Syphilis testing in blood donors: an update. \*Blood Transfus\*. 2015 Apr;13\[2\]:197-204](#))

### PDF Report

No

### Day(s) Performed

Monday through Saturday

### Report Available

Same day/1 to 4 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Mayo Clinic Jacksonville Clinical 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**

86592

86593- (if appropriate)

86780- (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
RPRT3	RPR w/ Reflex to TP-PA, S	20507-0

Result ID	Test Result Name	Result LOINC® Value
616970	RPR w/ Reflex to TP-PA, S	20507-0