

Overview

**Useful For**  
Aid in the diagnosis of neuroinvasive syphilis as part of a profile

**Method Name**  
Only orderable as a reflex. For more information see NSAIP / Neurosyphilis IgG Antibody Index with VDRL, Serum and Spinal Fluid.

Flocculation/Agglutination

**NY State Available**  
Yes

Specimen

**Specimen Type**  
CSF

**Specimen Required**  
Only orderable as a reflex. For more information see NSAIP / Neurosyphilis IgG Antibody Index with VDRL, Serum and Spinal Fluid.

**Specimen Type:** Spinal fluid

**Container/Tube:** Sterile vial

**Specimen Volume:** 2.2 mL

**Collection Instructions:**

- 1. The spinal fluid (CSF) specimen **must be** collected within 24 hours of the serum specimen, preferably at the same time.
- 2. The CSF aliquot should be from the second, third, or fourth CSF vial collected during the lumbar puncture. **Do not submit CSF from the first vial due to the possibility of blood contamination, which will cause specimen rejection.**
- 3. Label vial as spinal fluid or CSF.
- 4. Band CSF specimen together with the serum sample.

**Specimen Minimum Volume**  
1.5 mL

Reject Due To

Gross hemolysis	Reject
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Gross lipemia	Reject
Spinal fluid (CSF) contaminated with blood	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Neurosyphilis (NS) caused by the spirochete *Treponema pallidum* can occur at any stage of syphilis. Currently the Center for Disease Control estimates that approximately 2% of patients with syphilis will develop neuroinvasive syphilis if untreated. Early stages of NS may be asymptomatic or symptomatic, with patients typically exhibiting classic meningitis symptoms. Patients with late-stage NS patients may present with dementia paralytica or tabes dorsalis. Other manifestations of neuroinvasive syphilis include ocular or otologic syphilis, which can occur at any stage, however are more common during early NS.

The diagnosis of NS is challenging due to a number of factors, including the lack of consensus on the relevance of abnormal cerebrospinal fluid (CSF) findings in patients who are seropositive for syphilis but neurologically asymptomatic. With respect to diagnostic testing, numerous treponemal and non-treponemal (lipoidal) assays have been evaluated, alongside CSF protein and pleocytosis findings, however direct comparisons of these assays are limited. The Venereal Diseases Research Laboratory (VDRL) assay is currently the only assay with US Food and Drug Administration (FDA) clearance as an aid in the diagnosis of NS, however the sensitivity and specificity of this non-treponemal (lipoidal) assay is highly variable, ranging from 66.7% to 85.7% and 78.2% to 86.7%, respectively. Although no treponemal assay has FDA clearance as an aid for diagnosis of NS, studies evaluating the fluorescent treponemal antibody absorption (FTA-ABS) assay performed in CSF from patients with definitive NS was associated with a sensitivity of 90.9% to 100%. Specificity of this approach ranged from 55% to 100% however, primarily due to the issue of passive diffusion of serum antibodies across the blood-brain barrier.

The NS antibody index assay corrects for passive diffusion across an inflamed blood-brain barrier by measuring quantitative levels of anti-*T. pallidum* antibodies in serum and CSF and normalizing those to total IgG and albumin in both specimen sources. A positive NS antibody index indicates true intrathecal antibody synthesis of antibodies to *T. pallidum*, which alongside clinical and exposure history can be used to establish a diagnosis of NS. All NS antibody index positive samples are also reflexed for testing by the VDRL assay to acquire a semi-quantitative titer. The NS antibody index should only be ordered in patients who are seropositive for antibodies to *T. pallidum* in blood, who also present with neurologic manifestations suspicious for NS or who are at risk for asymptomatic NS.

Reference Values

Only orderable as a reflex. For more information see NSAIP / Neurosyphilis IgG Antibody Index with VDRL, Serum and

Spinal Fluid.

Negative

Reference values apply to all ages.

Interpretation

Negative:

No non-treponemal (lipoidal) antibodies to syphilis (*T. pallidum*) detected. Discordant results between the neurosyphilis antibody index and the VDRL result may be due to increased sensitivity of the antibody index assay.

Positive:

Results are consistent with neurosyphilis.

Cautions

VDRL testing on spinal fluid may be falsely-negative due to lower sensitivity and testing too soon following infection.

Clinical Reference

1. Miller JN. Value and limitations of nontreponemal and treponemal tests in the laboratory diagnosis of syphilis. Clin Obstet Gynecol. 1975;18(1):191-203

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

Performance

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

2 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

86593

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VDSFT	VDRL Titer,CSF	31146-4

Result ID	Test Result Name	Result LOINC® Value
621959	VDRL Titer,CSF	31146-4