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MAYO CLINIC LABORATORIES

# Test Definition: LNBAI

Lyme Central Nervous System Infection IgG, Antibody Index, Spinal Fluid

## Overview

### Useful For

Providing antibody index information to aid in the diagnosis of neuroinvasive Lyme disease or neuroborreliosis due to *Borrelia* species associated with Lyme disease (eg, *Borrelia burgdorferi, Borrelia garinii, Borrelia afzelli*)

### Method Name

Only orderable as part of a profile. For more information see LNBAB / Lyme Central Nervous System Infection IgG with Antibody Index Reflex, Serum and Spinal Fluid.

Enzyme-Linked Immunosorbent Assay (ELISA)

### NY State Available

Yes

## Specimen

### Specimen Type

CSF

### Specimen Required

Only orderable as part of a profile. For more information see LNBAB / Lyme Central Nervous System Infection IgG with Antibody Index Reflex, Serum and Spinal Fluid.

**Both cerebrospinal fluid (CSF) and serum are required for this test. CSF and serum must be collected within 24 hours maximum of each other. CSF specimens with blood contamination will be rejected.**

**Specimen Type:** Spinal fluid
**Container/Tube:** Sterile vial
**Specimen Volume:** 1.2 mL
**Collection Instructions:**
1. A spinal fluid (CSF) sample of 1.2 mL needs to be collected within 24 hours of the serum specimen, preferably at the same time.
2. Label vial as spinal fluid or CSF.
3. 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**.
4. Band specimens together.

**Specimen Type:** Serum

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:**
**Preferred:** Serum gel
**Acceptable:** Red top
**Submission Container/Tube:** Plastic vial
**Specimen Volume:** 1.2 mL
**Collection Instructions:**
1. A serum sample of 1.2 mL needs to be collected within 24 hours of the spinal fluid specimen, preferably at the same time.
2. Centrifuge and aliquot serum into a plastic vial.
3. Label as serum.
4. Band specimens together.

### Specimen Minimum Volume

See Specimen Required

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| CSF contaminated with blood | Reject |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| CSF | Refrigerated (preferred) | 11 days | |
| | Frozen | 35 days | |

## Clinical & Interpretive

### Clinical Information

Lyme disease is a multisystem and multistage tick-transmitted infection caused by spirochetal bacteria in the *Borrelia burgdorferi* sensu lato (Bbsl) complex. Nearly all human infections are caused by 3 Bbsl species; *B burgdorferi* sensu stricto (hereafter referred to as *B burgdorferi*) is the primary cause of Lyme disease in North America, while *Borrelia afzelii* and *Borrelia garinii* are the primary causes of Lyme disease in Europe and parts of Asia.

Lyme disease is the most commonly reported tick-borne infection in North America and Europe, causing an estimated 300,000 cases in the United States each year and 85,000 cases in Europe. The clinical features of Lyme disease are broad and may be confused with various immune and inflammatory disorders. The classic presenting sign of early localized Lyme disease caused by *B burgdorferi* is erythema migrans, which occurs in approximately 80% of individuals. Other

early signs and symptoms include malaise, headache, fever, lymphadenopathy, and myalgia. Arthritis, cardiac disease, and neurological disease may be later stage manifestations.

Neuroinvasive Lyme disease (NLD) can affect either the peripheral or central nervous system, with patients classically presenting with the triad of lymphocytic meningitis, cranial neuropathy (especially facial nerve palsy) and radiculoneuritis, which can affect the motor or sensory nerves, or both. These symptoms can occur in any combination or alone. Some patients may present with Bannwarth syndrome, which includes painful radiculoneuritis with variable motor weakness.

Neuroinvasive Lyme disease should be considered in individuals presenting with appropriate symptoms who have had exposure to ticks in a Lyme endemic region of the United States, Europe, or Asia. Patients meeting these criteria should be evaluated for the presence of anti-Bbsl antibodies in serum using the standard 2-tiered testing algorithm (LYME / Lyme Disease Serology, Serum) as recommended by the Centers for Disease Control and Prevention. Briefly, the LYME test includes testing of serum specimens by an anti-Bbsl antibody enzyme-linked immunosorbent assay, followed by supplemental testing of all reactive samples using an immunoblot or western blot for detection of IgM- and IgG- class antibodies to Bbsl. Notably, the majority of patients with NLD, will be seropositive in serum. Therefore, it is recommended that all patients tested by this assay also have LYME / Lyme Disease Serology, Serum performed. Results from these assays, alongside appropriate exposure history and clinical presentation, may be used to establish a diagnosis of NLD.

Cerebrospinal fluid (CSF) may also be tested for the presence of antibodies to Bbsl using the current 2-tiered testing algorithm as defined for serum samples. However, there are currently no interpretive criteria for assessment of anti-Bbsl IgM and IgG immunoblot banding patterns in CSF. Additionally, while the presence of antibodies to Bbsl in CSF may be due to true intrathecal antibody synthesis, thus indicating central nervous system (CNS) infection, antibodies may alternatively be present as a result of passive diffusion through the blood-brain barrier or due to blood contamination of CSF during a traumatic lumbar puncture.

The Lyme CNS antibody index quantitatively measures the level of anti-Bbsl antibodies in CSF and serum, ideally collected within 24 hours of each other, and normalizes those levels to total IgG and albumin in both specimen sources. A positive Lyme CNS AI indicates true intrathecal antibody synthesis of antibodies to Bbsl, which alongside clinical and exposure history can be used to establish a diagnosis of NLD.

### Reference Values

Only orderable as part of a profile. For more information see LNBAB / Lyme Central Nervous System Infection IgG with Antibody Index Reflex, Serum and Spinal Fluid.

0.6-1.2

### Interpretation

Negative (Lyme CNS antibody index [AI] 0.6 to <1.3): Results indicate lack of intrathecal antibody synthesis to Lyme disease associated *Borrelia* species. This suggests the absence of neuroinvasive Lyme disease. The initial screen reactive result may be due to anti-*Borrelia* species antibodies present in the cerebrospinal fluid (CSF) due to increased permeability of the blood-brain barrier or transient introduction during lumbar puncture.

Equivocal (Lyme CNS AI 1.3 to 1.5): Low level of intrathecal antibody synthesis to Lyme disease associated *Borrelia* species detected. Results should be correlated with exposure history and clinical presentation to establish a diagnosis of neuroinvasive Lyme disease.

Positive (Lyme CNS AI >1.5): Results indicate the presence of intrathecal antibody synthesis to Lyme disease associated *Borrelia* species, suggesting neuroinvasive Lyme disease. Results should be correlated with exposure history and clinical presentation to establish the diagnosis.

Invalid (Lyme CNS AI <0.6): Result is due to abnormally elevated total IgG levels in CSF. This may be due to passive diffusion through the blood-brain barrier or contamination of the CSF with blood during a traumatic lumbar puncture. Repeat testing may be considered

### Cautions

A single negative result should not be used to exclude the diagnosis of neuroinvasive Lyme disease in a patient with appropriate exposure history and symptoms suggestive of infection. Testing of serum samples using the Centers of Disease Control and Prevention recommended Standard 2-Tiered Testing Algorithm should be performed.

False-negative results may be acquired in patients tested soon after infection, prior to the development of a detectable level of antibodies in the cerebrospinal fluid.

False-reactive results may occur in patients with syphilis or *Leptospira* infections. Patient management decisions should not be made on a single reactive result.

### Clinical Reference

1. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2006;43(9):1089-1134
2. Halperin JJ, Shapiro ED, Logigian E, et al. Practice parameter: treatment of nervous system Lyme disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2007;69(1):91-102
3. Halperin JJ. Neuroborreliosis: J Neurol. 2017;264(6):1292-1297
4. Theel ES. The Past, present and (possible) future of serologic testing for Lyme disease. J Clin Microbiol. 2016;54(5):1191-1196
5. Theel ES, Aguero-Rosenfeld ME, Pritt B, Adem PV, Wormser GP. Limitations and confusing aspects of diagnostic testing for neurologic Lyme disease in the United States. J Clin Microbiol. 2019;57(1): e01406-18. doi:10.1128/JCM.01406-18

## Performance

### Method Description

The test uses microtiter strips with break-off reagent wells coated with a mix of *Bb* sl antigens (whole antigen extracts of *Borrelia burgdorferi* sensu stricto, *Borrelia afzelii*, *Borrelia garinii* and recombinant VlsE of *B burgdorferi* sensu stricto). In

the first reaction step, diluted patient samples are incubated in the wells. In the case of positive samples, *Borrelia*-specific IgG antibodies will bind to the antigens. To detect the bound antibodies, a second incubation is carried out using an enzyme-labelled antihuman IgG (enzyme conjugate), followed by a third incubation using chromogen/substrate, which catalyzes a color reaction that is then measured for optical density (OD) using spectrophotometry. The obtained OD values of the paired patient serum and cerebrospinal fluid samples are compared against a 6-level calibration curve to quantitatively determine the relative anti-*Borrelia* IgG antibody titers.(Unpublished Mayo method)

The quantitative test results obtained on paired serum and CSF specimens using the *Borrelia* IgG enzyme-linked immunosorbent assay are expressed as relative units (U/mL) and must be used along with the total IgG and albumin levels in the patient's paired serum and CSF samples to calculate the anti-*Borrelia* antibody index (AI), which determines the absence or presence of intrathecal anti-*Borrelia* IgG antibody synthesis. Total IgG and albumin testing on serum and CSF is performed using the Siemens BN II nephelometric testing system.(Instruction manual: Siemens Nephelometer II Operations. Siemens V 2.3, 2008; Addendum to the Instruction Manual 2.3, 08/2017)

To detect an infection of the central nervous system, it is necessary to differentiate between intrathecally produced antibodies and antibodies passed from blood into the CSF. The AI is the value of intrathecal pathogen-specific antibody production. This AI value represents the portion of pathogen-specific antibodies in total IgG of CSF and the portion of pathogen-specific antibodies in total IgG of serum. The patient's AI is calculated using the Reiber and Lange method.(Reiber H, Lange P. Quantification of virus-specific antibodies in cerebrospinal fluid and serum: sensitive and specific detection of antibody synthesis in brain. Clin Chem. 1991;37(7):1153-1160)

### PDF Report
No

### Day(s) Performed
Monday, Wednesday, Friday

### 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.

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## Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

## CPT Code Information

86618 x 2
82040
82042
82784 x 2

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| LNBAI | Lyme CNS Infection IgG, Ab Index | 92812-7 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| LNB3 | Lyme CNS IgG Ab Index Value | 92811-9 |
| LNB4 | Lyme CNS IgG Ab Index Interp | 69048-7 |