Test Definition: LNBAB

Lyme Central Nervous System Infection IgG with Antibody Index Reflex, Serum and Spinal Fluid

Overview

Useful For

Aiding in the diagnosis of neuroinvasive Lyme disease or neuroborreliosis due to *Borrelia* species associated with Lyme disease (eg, *Borrelia burgdorferi, Borrelia garinii, Borrelia afzelli*)

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
LNBAC	Lyme CNS Infection IgG Screen, CSF	No	Yes
LNBAS	Lyme CNS Infection IgG, S	No	No

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
LNBAI	Lyme CNS Infection IgG, Ab Index	No	No

Testing Algorithm

This test begins with IgG screening of the spinal fluid (CSF) specimen. If the screen is negative, no additional testing will be performed.

If the screen is positive, the paired CSF and serum specimens will be used to establish the antibody index. In order to establish the antibody index, the paired serum and CSF samples (collected within 24 hours of each other) are tested on the same run using quantitative assays to determine levels for the following analytes:
1. Anti-*Borrelia* species IgG levels in CSF and serum
2. Total IgG in CSF and serum
3. Albumin in CSF and serum

These additional tests are necessary in order to normalize the level of anti-*Borrelia* antibodies to total IgG and albumin in the CSF and establish the antibody index ratio of anti-*Borrelia* antibodies in CSF-to-serum. This testing is performed at an additional charge.

The following algorithms are available:
-Lyme Neuroborreliosis Diagnostic Algorithm
-Acute Tick-borne Disease Testing Algorithm
-Meningitis/Encephalitis Panel Algorithm

Special Instructions

- Acute Tick-borne Disease Testing Algorithm

- Lyme Neuroborreliosis Diagnostic Algorithm
- Meningitis/Encephalitis Panel Algorithm

Highlights

Although a small percentage of patients with neuroinvasive Lyme disease may be seronegative, it is recommended that all patients test by the Lyme Antibody Index assay also have standard 2-tiered testing for Lyme disease performed on serum.

This test compares the level of IgG antibodies to Lyme disease-causing *Borrelia* species in spinal fluid (CSF) and serum. The level of anti-*Borrelia* species IgG is normalized to total IgG and albumin in CSF and serum.

This test can help identify whether the presence of IgG to *Borrelia* species in the CSF is due to true intrathecal antibody synthesis, suggesting neuroinvasive Lyme disease, versus antibody presence due to passive diffusion through the blood-brain barrier or, possibly, due to blood contamination of the CSF as a result of a traumatic lumbar puncture.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

CSF
Serum

Ordering Guidance

This test should be ordered in patients with suspected neuroinvasive Lyme disease. It is preferred for diagnosis of neuroinvasive Lyme disease over testing of spinal fluid (CSF) by immunoblot for IgM and IgG class antibodies to *Borrelia* species associated with Lyme disease. This test can help distinguish true intrathecal synthesis of antibodies to Lyme disease in the CSF, indicating neuroinvasive infection, versus antibody presence due to passive diffusion through the blood-brain barrier or, possibly, due to blood contamination of the CSF as a result of a traumatic lumbar puncture.

For Lyme testing on serum, order LYME / Lyme Disease Serology, Serum.

Additional Testing Requirements

Although a small percentage of patients with neuroinvasive Lyme disease may be seronegative, it is recommended that all patients tested by this assay also have standard 2-tiered testing for Lyme disease performed (LYME / Lyme Disease Serology, Serum).

Specimen Required

Both spinal fluid (CSF) and serum are required for this test. CSF and serum must be collected within 24 hours (maximum) of each other.

Specimen Type: Spinal fluid
Container/Tube: Sterile vial
Specimen Volume: 1.2 mL
Collection Instructions:
1. A 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.

Forms

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

Specimen Minimum Volume

See Specimen Required

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
CSF contaminated	Reject

with blood	

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Refrigerated (preferred)	11 days	
	Frozen	35 days	
Serum	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.

NLD 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.

Spinal fluid (CSF) should not be tested for the presence of antibodies to Bbsl using the current 2-tiered testing algorithm as there are 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 infection antibody index is performed as a reflex and 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

Negative

Reference values apply to all ages.

Interpretation

Negative:
No antibodies to Lyme disease causing *Borrelia* species detected in spinal fluid. A negative result in a patient with appropriate exposure history and symptoms consistent with neuroinvasive Lyme disease should not be used to exclude infection. Testing for antibodies to Lyme disease-causing *Borrelia* species in serum should be performed.

Reactive:
Supplemental testing to determine a Lyme central nervous system antibody index has been ordered. Diagnosis of neuroinvasive Lyme disease should not be established solely based on a reactive screening result.

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 for Disease Control and Prevention recommended standard 2-tiered testing algorithm should be performed (LYME / Lyme Disease Serology, Serum).

False-negative results may be acquired in patients tested soon after infection, prior to the development of a detectable level of antibodies in the spinal 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 spinal fluid samples are compared against a 6-level calibration curve to quantitatively determine the relative anti-*Borrelia* IgG antibody titers.(Unpublished Mayo method)

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.

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
86618 x2-(if appropriate)
82040-(if appropriate)
82042-(if appropriate)
82784 x2-(if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LNBAB	Lyme CNS Infection IgG w/ AI Reflex	92815-0

Result ID	Test Result Name	Result LOINC® Value
LNB1	Lyme CNS Infection IgG, CSF	92813-5
LNB2	Lyme CNS Infection IgG Interp	69048-7
LNBAS	Lyme CNS Infection IgG, S	92814-3