Overview

Useful For
Supporting the diagnosis of Lyme disease in conjunction with serologic testing

Specific indications including testing skin biopsies when a rash lesion is not characteristic of erythema migrans and testing synovial fluid or synovium to support the diagnosis of Lyme arthritis

This test should not be used to screen asymptomatic patients.

Testing Algorithm
The following algorithms are available:
- Acute Tick-Borne Disease Testing Algorithm
- Meningitis/Encephalitis Panel Algorithm

Special Instructions
- Acute Tickborne Disease Testing Algorithm
- Meningitis/Encephalitis Panel Algorithm

Method Name
Real-Time Polymerase Chain Reaction (PCR)/DNA Probe Hybridization

NY State Available
Yes

Specimen

Specimen Type
Varies

Ordering Guidance
This assay does not detect Borrelia miyamotoi. If infection with this organism is suspected, order BMIPB / Borrelia miyamotoi Detection, PCR, Blood or BMIYC / Borrelia miyamotoi Detection, PCR, Spinal Fluid.

Necessary Information
Specimen source is required.

Specimen Required
Submit only 1 of the following specimens:
Test Definition: LYMPV
Lyme Disease, Molecular Detection, PCR, Varies

Specimen Type: Spinal fluid
Container/Tube: Sterile vial
Specimen Volume: 1 mL
Collection Instructions: Label specimen as spinal fluid.

Specimen Type: Synovial fluid
Container/Tube: Sterile vial
Specimen Volume: 1 mL
Collection Instructions: Label specimen as synovial fluid.

Specimen Type: Tissue (fresh only)
Sources: Skin or synovial biopsy
Container/Tube: Sterile container with normal saline
Specimen Volume: Approximately 4 mm(3)
Collection Instructions:
1. Submit only fresh tissue.
2. Skin biopsies:
   a. Wash biopsy site with an antiseptic soap. Thoroughly rinse area with sterile water. Do not use alcohol or iodine preparations. A local anesthetic may be used.
   b. Biopsy specimens are best taken by punch biopsy to include full thickness of dermis.
3. Label specimen with source of tissue.

Forms
If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume
Spinal Fluid, Synovial Fluid: 0.3 mL; Tissue: See Specimen Required

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

<table>
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<tr>
<th>Specimen Type</th>
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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. (1) 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. In 2012, *Borrelia mayonii* was identified as a less common cause of Lyme disease in the upper Midwestern United States. (2,3) This organism has only been detected in patients with exposure to ticks in Minnesota and Wisconsin and has not been detected in over 10,000 specimens from patients in other states, including regions of northeast where Lyme disease is endemic.

Lyme disease is the most commonly reported tick-borne infection in Europe and North America, causing an estimated 300,000 cases in the United States each year and 85,000 cases in Europe. (4,5) 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 (EM), which occurs in approximately 80% of individuals. Other early signs and symptoms include malaise, headache, fever, lymphadenopathy, and myalgia. Arthritis, neurological disease, and cardiac disease may be later stage manifestations. EM has also been seen in patients with *B mayonii* infection, but diffuse rashes are more commonly reported. (2) The chronic skin condition, acrodermatitis chronicum atrophicans, is also associated with *B afzelii* infection.

The presence of EM in the appropriate clinical setting is considered diagnostic for Lyme disease; no confirmatory laboratory testing is needed. In the absence of a characteristic EM lesion, serologic testing is the diagnostic method of choice for Lyme disease. (6) However, serology may not be positive until 1 to 2 weeks after onset of symptoms and may show decreased sensitivity for detection of infection with *B mayonii*. Therefore, detection of BbsI DNA using polymerase chain reaction (PCR) may be a useful adjunct to serologic testing for detection of acute disease. PCR has shown utility for detection of *Borrelia* DNA from skin biopsies of Lyme-associated rashes and can be used to detect *Borrelia* DNA from synovial fluid and synovium biopsies. Less commonly, *Borrelia* DNA can be detected in cerebrospinal fluid. (7) Lyme PCR should always be performed in conjunction with US Food and Drug Administration-approved serologic tests, and the results should be correlated with serologic and epidemiologic data and clinical presentation of the patient. (8) The Mayo Clinic Lyme PCR test detects and differentiates the main causes of Lyme disease in North America (*B burgdorferi* and *B mayonii*) and Europe (*B afzelii* and *B garinii*). (2,7)

**Reference Values**

Negative

Reference values apply to all ages.

**Interpretation**

A positive result indicates the presence of DNA from *Borrelia burgdorferi*, *Borrelia mayonii*, *Borrelia afzelii*, or *Borrelia garinii*, the main agents of Lyme disease.

A negative result indicates the absence of detectable target DNA in the specimen. Due to the clinical sensitivity limitations of the polymerase chain reaction assay, a negative result does not preclude the presence of the organism or active Lyme disease.

**Cautions**

Serologic tests are recommended for diagnosis of Lyme disease. Polymerase chain reaction (PCR) may play an adjunctive role but may not detect *Borrelia burgdorferi* DNA from cerebrospinal fluid (CSF) in cases of active or chronic disease. The presence of inhibitory substances may also cause a false-negative result. If clinical features of illness are highly indicative of Lyme neuroborreliosis, serologic testing on CSF is warranted. PCR test results should be used as an aid in diagnosis and not considered diagnostic by themselves. These results should be correlated with serologic and epidemiologic data and clinical presentation of the patient.
Testing of CSF by PCR in patients with suspected Lyme neuroborreliosis should be requested only on patients with positive *B burgdorferi* antibody in serum confirmed by Western blot assay (LYWB / Lyme Disease Antibody, Immunoblot, Serum) and with abnormal CSF findings (elevated protein and WBC >10 cells/high-power field).

Concurrent infections with multiple tick-borne pathogens, including *Ehrlichia muris eauclairensis, Anaplasma phagocytophilum, Babesia microti*, and *Borrelia miyamotoi* (a relapsing fever *Borrelia*) have been reported in United States, and consideration should be given to testing for other pathogens, if clinically indicated.

This assay detects most members of the *Borrelia burgdorferi* sensu lato (Bbsl) complex, including *Borrelia andersonii, Borrelia americana*, and *Borrelia bissettii*, which have been rarely detected in humans. Detection of DNA from these organisms would be reported as an atypical result and prompt additional laboratory testing to further identify the DNA present. The sensitivity of this assay for detecting these organisms has not been determined.

This assay also detects some members of the Bbsl complex that are not considered to be human pathogens but may be found in ticks and other animals. Therefore, this assay should not be used to test nonhuman specimens.

**Supportive Data**
The following validation data supports the use of this assay for clinical testing.

**Analytical Sensitivity/Limit of Detection:**
The lower limit of detection (LOD) is approximately 300 to 1000 genomic copies/mL in cerebrospinal fluid (CSF), tissue, blood, and synovial fluid.

**Accuracy/Diagnostic Sensitivity and Specificity:**
Spiking studies of whole organism in fresh tissue, synovial fluid, and CSF (spiked near the approximate LOD) showed 100% recovery.

**Analytical Specificity:**
No polymerase chain reaction signal was obtained from the extracts of 22 bacterial, viral, parasitic, and fungal isolates that can cause symptoms similar to Lyme disease, including *Rickettsia rickettsii, Rickettsia typhi, Ehrlichia canis, Babesia microti, Plasmodium falciparum, Plasmodium vivax, Bartonella henselae, Bartonella quintana*, herpes simplex virus, and *Toxoplasma gondii*. Relapsing fever borreliae (including *Borrelia miyamotoi*) are also not detected with this assay.

**Precision:**
Interassay precision was 100%, and intra-assay precision was 100%.

**Reference Range:**
The reference range for this assay is negative. This assay is only to be used for patients with a clinical history and symptoms consistent with Lyme disease and must be interpreted in the context of serologic tests, which are the gold standard for diagnosis of Lyme disease.

**Reportable Range:**
This is a qualitative assay, and the results are reported as negative or positive for targeted *Borrelia burgdorferi, Borrelia*
**Test Definition: LYMPV**
Lyme Disease, Molecular Detection, PCR, Varies

*afzelii, Borrelia garinii, or Borrelia mayonii.*

**Clinical Reference**

**Performance**

**Method Description**
Nucleic acid is extracted from clinical specimens using the automated MagNA Pure LC instrument system. The extract is then transferred to individual wells of a 96-well plate for amplification. The LightCycler is an automated instrument that amplifies and monitors the development of target nucleic acid (amplicon) after each cycle of polymerase chain reaction (PCR). The DNA target for PCR assay is the 283-base pairs plasminogen-binding protein gene (*OppA2*), which is present at a frequency of 1 copy per organism in all 4 confirmed pathogenic species of the *Borrelia burgdorferi* sensu lato genogroup (*B burgdorferi* sensu stricto, *Borrelia afzelii*, *Borrelia garinii*, and *Borrelia mayonii*). A specific base pair DNA target sequence is amplified by PCR. The detection of amplicon is based on fluorescence resonance energy transfer, which utilizes 1 hybridization probe with a donor fluorophore, fluorescein, at the 3’ end, and a second hybridization probe with an acceptor fluorophore, LC-Red 610, at the 5’ end. When the target amplicon is present, the LC-Red 610 emits a measurable and quantifiable light signal at a specific wavelength. Presence of the specific organism nucleic acid may be confirmed by performing a melting curve analysis of the amplicon. Using features of the melting curve analysis, the assay primers and specific hybridization probes are able to detect and differentiate *B burgdorferi* sensu stricto from *B mayonii*, *B afzelii*, and *B garinii*, although the melting curve analysis cannot differentiate between *B afzelii* and *B garinii*. Each assay run can be completed within 60 minutes.(Unpublished Mayo method)

**PDF Report**
No

**Day(s) Performed**

Test Definition: LYMPV
Lyme Disease, Molecular Detection, PCR, Varies

June through November: Monday through Saturday
December through May: Monday through Friday

Report Available
Same day/ 1 to 4 days

Specimen Retention Time
1 week

Performing Laboratory Location
Rochester

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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
87476
87798 x 2
87999 (if appropriate for government payers)

LOINC® Information

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