MAYO CLINIC LABORATORIES

Test Definition: ELYMI

Lyme Disease European Immunoblot, Serum

Overview

Useful For

Aiding in the diagnosis of Lyme disease caused by infection with *Borrelia* species endemic to Europe and Asia, including *Borrelia garinii* or *Borrelia afzelii*

This test is only intended for use in patients with recent travel to and exposure to ticks in Europe or regions of Asia who are suspected to have Lyme disease caused by *Borrelia* species endemic to Europe/Asia

This test **should not be used** to screen the general population.

Testing Algorithm

Only orderable as a reflex. For more information see ELYME / Lyme Disease European Antibody Screen, Serum.

If antibody screen is positive or equivocal, then this test will be performed at an additional charge.

For more information see Acute Tick-Borne Disease Testing Algorithm.

Special Instructions

- Acute Tick-Borne Disease Testing Algorithm

Method Name

Only orderable as a reflex. For more information see ELYME / Lyme Disease European Antibody Screen, Serum.

Immunoblot Microarray

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

Patients who are suspected to have Lyme disease who have **not** traveled to Europe should be tested by the LYME / Lyme Disease Serology, Serum assay for detection of antibodies specifically to *Borrelia burgdorferi*, the most common agent of Lyme disease in North America.

Specimen Required

Only orderable as a reflex. For more information see ELYME / Lyme Disease European Antibody Screen, Serum.

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Pediatric: 0.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume

0.2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	10 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Lyme disease (LD) is caused by infection with a member of the *Borrelia burgdorferi* sensu lato complex. Among the genospecies within this complex, *B burgdorferi* sensu stricto (*B burgdorferi*) is the primary agent causing LD in North America. While *B burgdorferi* is also found abroad, *Borrelia garinii* and *Borrelia afzelii* are more prevalent in Europe and regions of Asia. These spirochetes are transmitted to humans through the bite of *Ixodes* species ticks, primarily *Ixodes ricinus* and, to a lesser extent, *Ixodes persulcatus*, both of which are found throughout Europe, the Baltic regions, and parts of Asia. Therefore, residents of or travelers to these areas who are bitten by ticks are at increased risk for LD caused by a European *Borrelia* species.

Transmission of LD-associated *Borrelia* requires at least 36 hours of tick attachment. Approximately 80% of infected individuals will develop a unique, expanding skin lesion with a central zone of clearing, referred to as erythema migrans (EM; stage 1). In the absence of treatment, patients may progress to early disseminated disease (stage 2), which is characterized by neurologic manifestations (eg, meningitis, cranial neuropathy, radiculoneuropathy) and is often associated with *B garinii* infection. Patients with late LD often present with intermittent or persistent arthralgia, most often associated with *B burgdorferi* infection, or with acrodermatitis chronica atrophicans, typically due to infection with *B afzelii*.

Diagnosis of LD is currently based on a 2-tiered serologic testing algorithm to detect antibodies to LD-associated *Borrelia* species. Importantly, patients may be seronegative until 2 weeks post onset of symptoms. An IgM-class antibody response usually peaks 3 to 6 weeks after infection but may persist for years in some cases. IgG-class antibodies to *Borrelia* spirochetes are detectable 2 to 3 weeks postinfection and may remain elevated for years after resolution of symptoms. In patients with EM, culture of skin biopsies obtained near the margins of the rash, are frequently positive, though this technique is not commonly available. In late (chronic) stages of the disease, serology is often positive and is the diagnostic method of choice. Polymerase chain reaction testing may also be of use in these late stages if performed on synovial fluid or tissue.

Early antibiotic treatment of Lyme disease can resolve clinical symptoms and prevent progression of the disease to later stages. Also, if provided early in disease, treatment may suppress the immune response to the bacteria leading to negative serologic results.

The 2-tiered testing algorithm for LD involves an initial screening assay for detection of total antibodies to LD-causing *Borrelia* species. For this algorithm, the C6 enzyme-linked immunosorbent assay (ELISA) is used to screen all specimens and those with positive or equivocal results are reflexed for supplemental testing by immunoblot for detection of IgM and IgG antibodies to LD-causing *Borrelia* species. Importantly, while most screening ELISAs detect antibodies to all major LD-associated *Borrelia* species, the immunoblot assays used for supplemental testing in North America are specifically designed to detect antibodies to the *B burgdorferi* B31 strain. Despite similarity between the genospecies, the North America immunoblot tests have a reported sensitivity of approximately 50% for LD caused by the European *Borrelia* species (eg, *B afzelii* and *B garinii*). In order to improve upon our ability to detect antibodies to the European *Borrelia* species, immunoblot tests designed to detect IgM and/or IgG-class antibodies *B garinii*, *B afzelii*, and *B burgdorferi* are used for supplemental testing of all specimens with positive or equivocal results by the LD screening ELISA.

Reference Values

Only orderable as a reflex. For more information see ELYME / Lyme Disease European Antibody Screen, Serum.

IgG: Negative
IgM: Negative
Reference values apply to all ages.

Interpretation

Immunoglobulin M:
The interpretation of IgM immunoblots for Lyme disease caused by *Borrelia* species endemic to Europe differs from the interpretive criteria for IgM immunoblot tests used for evaluation of Lyme disease caused by *Borrelia burgdorferi* in North America. The European Lyme disease IgM immunoblot interpretive criteria is as follows:
Positive: The presence of a band at **1 or more** of the following 5 proteins-p39, OspC, Osp17 (DbpA), VlsE, and/or p41 (high intensity)
-Interpretation: Specific antibodies against Lyme disease associated *Borrelia* species detected suggesting recent infection.
Negative: No distinct bands
-Interpretation: No specific antibodies against Lyme disease-associated *Borrelia* species were detected. If infection remains suspected, repeat testing on a new specimen collected in 2 to 3 weeks is suggested.

IgM-class antibodies to *Borrelia* species that cause Lyme disease, including *Borrelia afzelii* and *Borrelia garinii*, may be

detectable as early as 1 to 2 weeks following a tick bite, however, they typically peak during the third to sixth week postinfection. IgM-class antibodies to these agents may persist for months following disease resolution and antimicrobial treatment. Results of the IgM immunoblot should only be interpreted and considered during the first 4 to 6 weeks after disease onset.

Patients tested soon after disease onset may be negative for IgM-class antibodies to Lyme disease-associated *Borrelia* species. Repeat testing should be performed in 2 to 3 weeks if infection with a European species of *Borrelia* continues to be suspected.

Immunoglobulin G:
The interpretation of IgG immunoblots for Lyme disease caused by *Borrelia* species endemic to Europe differs from the interpretive criteria for IgG immunoblot tests used to for evaluation of Lyme disease caused by *B burgdorferi* in North America. The European Lyme disease IgG immunoblot is interpreted as follows:
Positive: The presence of a band at **2 or more** of the following 10 proteins: p38, p58, p43, p39, p30, OspC, p21, Osp17(DbpA), p14, VlsE
-Interpretation: Specific antibodies against Lyme disease associated *Borrelia* species were detected, suggesting infection at some point in the recent or remote past. Clinical correlation required.
Equivocal: One distinct band at the VlsE protein only
-Interpretation: Specific antibodies to the VlsE protein of Lyme disease associated *Borrelia* species were detected, suggesting possible infection. Repeat testing on a new specimen collected in 2 to 3 weeks is recommended to confirm infection.
Negative: One or no distinct bands (except VlsE)
-Interpretation: No specific antibodies against Lyme disease-associated *Borrelia* species were detected. If infection remains suspected, repeat testing on a new specimen collected in 2 to 3 weeks is suggested.

IgG-class antibodies to Lyme disease causing *Borrelia* species may remain detectable for months to years following resolution of disease and/or antimicrobial treatment.

Cautions

The predictive value of the assay is a function of the pretest probability of Lyme disease in the population tested. Hence, only patients with clinical symptoms of Lyme disease with recent travel to or residence in Europe or parts of Asia should be tested for Lyme disease caused by *Borrelia* species endemic to Europe.

A negative result does not exclude the possibility of infection with Lyme disease-associated *Borrelia* species, including *Borrelia afzelii* or *Borrelia garinii*. Specimens collected soon after infection (less than 2 weeks) may be negative for IgM- and IgG-class antibodies to Lyme disease-associated *Borrelia* species. Repeat testing on a new specimen collected 2 to 3 week following tick bite and exposure is recommended in cases of suspected acute Lyme disease due to infection with *Borrelia* species endemic to Europe and regions of Asia.

This assay does not differentiate between infection with *B afzelii* or *B garinii*.

Test results should be used in conjunction with exposure history, travel history, clinical presentation, and other clinical findings.

False-positive reactions may occur with patients with other spirochetal diseases (syphilis, yaws, pinta, relapsing fever, or

leptospirosis), influenza, autoimmune disorders, multiple sclerosis, or amyotrophic lateral sclerosis.

Clinical Reference

1. Branda JA, Strle F, Strle K, Sikand N, Ferraro MJ, Steere AC: Performance of United States serologic assays in diagnosis of Lyme borreliosis acquired in Europe. Clin Infect Dis. 2013 Aug;57(3):333-340
2. Liang FT, Steere AC, Marques AR, Johnson BJ, Miller JN, Philipp MT: Sensitive and specific serodiagnosis of Lyme disease by enzyme-linked immunosorbent assay with a peptide based on an immunodominant conserved region of Borrelia burgdorferi VlsE. J Clin Microbiol. 1999 Dec;37(12):3990-3996

Performance

Method Description

The European *Borrelia* IgM and IgG immunoblot tests are based on an enzyme-immunoassay in a microarray format, carrying highly purified, specific native antigens from *Borrelia afzelii* (Pko strain) and *Borrelia burgdorferi* sensu stricto, as well as recombinant VlsE at defined position on a solid-phase nitrocellulose membrane in triplicate. The positions of these antigen "spots" are well defined and are reliably identifiable using customized software. Each microarray also has spots for a negative control, serum controls, conjugate controls, and 6 calibrators.

One microarray is fixed at the bottom of each well in a standard microtiter plate (MTP). For each test to be performed, the diluted patient serum is added to each microarray (note: the *Borrelia* IgM and IgG microarrays are in separate wells). If specific antibodies recognizing a *Borrelia* antigen are present, they will bind to the specific antigens on the microarray. After incubation, the microarray is washed to remove unbound antibodies. Alkaline-phosphatase-antihuman IgG or antihuman IgM (conjugate) is then added to the well and incubated. If antibodies are present, the conjugate will bind to those respective antibodies, and, after a washing step to remove unbound conjugate, substrate solution is added. If the antibody/conjugate complex is present, the substrate will undergo precipitation and color change. After an incubation period, the reaction is stopped, and the presence of precipitated substrate is visualized at specific locations on the microarray. The presence of a colored precipitation at various locations on the microarray is an indirect measurement of *Borrelia* specific antibodies in the patient specimen. Visualized spots from the reaction are compared for intensity with the integrated calibrator controls for evaluation. The IgM-analyte spots serve to detect antibodies against p41, p39, OspC, Osp17, and VlsE. The IgG-analyte spots serve to detect antibodies against p83, p58, p43, p39, p30, p21, OspC, DbpA/Osp17, p14, and VlsE.(Package insert: Borrelia ViraChip IgM and IgG Test kits. ViraMed; 11/2018)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 day

Specimen Retention Time

14 days

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 Regional Manager. 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

86617 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ELYMI	Lyme Disease European Immunoblot, S	87274-7

Result ID	Test Result Name	Result LOINC® Value
48569	Euro Lyme IgG Immunoblot Result	87275-4
48570	Euro Lyme IgG Band(s) Detected	87276-2
48571	Euro Lyme IgM Immunoblot Result	87277-0
48572	Euro Lyme IgM Band(s) Detected	87278-8
48573	Euro Lyme Interpretation	69048-7