MAYO CLINIC LABORATORIES

Test Definition: ELYME

Lyme Disease European Antibody Screen, 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* and *Borrelia afzelii*

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

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
ELYMI	Lyme Disease European Immunoblot, S	No	No

Testing Algorithm

If this test is positive or equivocal, then immunoblot testing 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

Highlights

The first-tier screening assay detects antibodies to the VlsE protein. C6 is a conserved epitope in the VlsE protein. Therefore, this assay will detect antibodies to C6, in addition to other epitopes on VlsE and pepC10.

This test should be ordered for evaluation of possible Lyme disease in individuals who have recently traveled to Europe or Asia and who have been exposed to or bitten by a tick.

This panel includes a screening test capable of detecting antibodies to the most common Lyme disease causing *Borrelia* species found in Europe and Asia. Specimens with positive or equivocal results by the screening assay will be reflexed to a supplemental immunoblot able to detect antibodies to *Borrelia afzelii* or *Borellia garinii*, both Lyme disease-causing *Borrelia* species endemic to Europe and regions of Asia.

The immunoblot does not distinguish between infection with *B afzelli* or *B garinii*.

Patients infected with *B afzelii* or *B garinii* may be serologically negative by diagnostic assays used in North America, which are designed to detect antibodies to the *Borrelia burgdorferi* B31 strain.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Ordering Guidance
This test should **only** be ordered for patients who present with Lyme disease symptoms **and** who have recently returned from travel to Europe or Asia. These patients may be infected with Lyme disease causing *Borrelia* species endemic to Europe (eg, *Borrelia afzelii*, *Borrelia garinii*), which may not be detected using diagnostic tests in North America. The North American serologic assays for Lyme disease are developed specifically for detection of antibodies to *Borrelia burgdorferi* (strain B31), the most commonly encountered species.

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 *B burgdorferi*, the most common agent of Lyme disease in North America.

Specimen Required
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.

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

Specimen Minimum Volume
0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	10 days	
	Frozen	30 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 the ability to detect antibodies to the European *Borrelia* species, immunoblot tests designed to detect IgM- and 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

Negative

Interpretation

Negative result:
No antibodies to Lyme disease *Borrelia* species (eg, *Borrelia afzelii*, *Borrelia burgdorferi*, *Borrelia garinii*) detected. Repeat testing on a new specimen collected in 2 to 3 weeks should be considered if acute Lyme disease due to one of these *Borrelia* species is suspected.

Equivocal result:
Not diagnostic. Supplemental immunoblot testing has been ordered by reflex.

Positive result:
Not diagnostic. Supplemental immunoblot testing has been ordered by reflex.

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*.

A positive result is not definitive evidence of infection with Lyme disease-associated *Borrelia* species. Supplemental testing of all specimens that result as positive or equivocal by the Lyme disease screening enzyme-linked immunosorbent assay (ELISA) require supplemental testing by immunoblot for IgM- and IgG-class antibodies to *Borrelia* species endemic in Europe and regions of Asia.

False-reactive screening ELISA results may occur in patients with other disease conditions, including syphilis, periodontal disease, rheumatoid arthritis, systemic lupus erythematosus, and other autoimmune diseases.

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

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 first-tier Lyme disease screening enzyme-linked immunosorbent assay (ELISA) used is the Zeus ELISA *Borrelia* VlsE1/pepC10 IgG/IgM test system. This test system is designed to detect IgG- and IgM-class antibodies (not differentiated) in human sera to VlsE1 and pepC10 antigens. Diluted test sera are incubated in antigen coated microwells. Any antigen-specific antibody in the sample will bind to the immobilized antigen. The plate is washed to remove unbound antibody and other serum components. Peroxidase conjugated goat antihuman IgG and IgM are added to the wells and the plate is incubated. The conjugate will react with IgG and IgM antibodies immobilized on the plate. The wells are washed to remove unreacted conjugate. The microwells containing immobilized peroxidase conjugate are incubated with peroxidase substrate solution. Hydrolysis of the substrate by peroxidase produces a color change. After the incubation period, the reaction is stopped, and the color intensity of the solution is measured photometrically. The color intensity of the solution depends upon the antibody concentration in the original test sample.(Instruction manual: *Borrelia* VlsE1/pepC10 IgG/IgM Test System. Zeus Scientific, Inc; Rev. 05/25/2021)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 to 4 days

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 Definition: ELYME

Lyme Disease European Antibody Screen, Serum

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

86618
86617 x 2-Lyme Disease European Immunoblot, S (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ELYME	Lyme Disease European Ab Screen, S	57916-9

Result ID	Test Result Name	Result LOINC® Value
ELYME	Lyme Disease European Ab Screen, S	57916-9