Test Definition: TLYME

Lyme IgM and IgG, Whole Cell Sonicate, ELISA, Serum

Overview

Useful For

Supplemental testing for samples with positive or equivocal first-tier test results for antibodies to Lyme disease causing *Borrelia* species

This test **should not be used** as a screening procedure for the general population.

Testing Algorithm

For more information see Acute Tick-Borne Disease Testing Algorithm

Special Instructions

- Acute Tickborne Disease Testing Algorithm

Highlights

Lyme disease serology positive results by the modified 2-tier testing algorithm are supportive evidence for the presence of antibodies and exposure to *Borrelia burgdorferi*, the cause of Lyme disease.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

No

Specimen

Specimen Type

Serum

Ordering Guidance

This test should only be ordered on specimens that have tested positive or equivocal by a first tier Lyme disease antibody test.

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: 0.6 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

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Heat inactivated	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, which includes *B burgdorferi* sensu stricto (herein referred to as *B burgdorferi*), *Borrelia afzelii,* and *Borrelia garinii.* Among these species, *B burgdorferi* is the most frequent cause of LD in North America. These tick-borne spirochetes are transmitted to humans through the bite of *Ixodes* species ticks. Endemic areas for LD in the United States correspond with the distribution of 2 tick species, *Ixodes scapularis* (Northeastern and Upper Midwestern US) and *Ixodes pacificus* (West Coast US).

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 either the standard or modified 2-tiered serologic testing algorithm (STTTA or

MTTTA, respectively). For the STTTA, see LYME / Lyme Disease Serology, Serum.

The MTTTA starts with an initial enzyme immunoassay (EIA) screen for detection of total antibodies against the *Borrelia* Vlse/pepC10 proteins. Samples that screen positive or equivocal by this first tier EIA are subsequently reflexed for supplemental assessment using 2 separate EIAs for detection of IgM and IgG antibodies against *B burgdorferi* whole cell sonicate material.

Importantly, while serologic assessment for LD may be negative in the early weeks following infection, over 90% of patients with later stages of infection are seropositive by serology, which remains the diagnostic method of choice for this disease.

Reference Values

Negative
Reference values apply to all ages.

Interpretation

Tier 1	Tier 2 IgM result	Tier 2 IgG result	Interpretation
Positive/equivocal	Negative	Negative	Negative for antibodies to the *Borrelia* (*Borreliella)* species causing Lyme disease. Antibodies detected by the first-tier test were not confirmed. Negative results may occur in recently infected (< or =14 days) patients. If recent infection is suspected, repeat testing on a new sample collected in 7 to 14 days is recommended.
Positive/equivocal	Positive/equivocal	Negative	IgM-class antibodies to the *Borrelia* (*Borreliella)* species causing Lyme disease were detected, suggesting acute or recent infection. IgM enzyme immunoassay (EIA) results should only be considered as indicative of recent infections in patients presenting within 30 days of symptom onset. Consideration of IgM EIA results in patients with symptoms lasting more than 30 days is discouraged due to the risk of false-positive IgM results and/or prolonged IgM seropositivity following disease resolution. If both first and second tier IgM results are equivocal consider repeat testing in 7 to 14 days if clinically warranted.
Positive/equivocal	Negative	Positive/equivocal	IgG-class antibodies to the *Borrelia* (*Borreliella)* species causing Lyme disease were detected, suggesting infection in the recent or remote past. IgG-class antibodies may remain detectable for months to years following resolution of infection. Results should not be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical

			symptoms; additional laboratory testing should not be performed.
Positive/equivocal	Positive/equivocal	Positive/equivocal	IgM and IgG-class antibodies to the *Borrelia* (*Borreliella)* species causing Lyme disease were detected, suggesting infection in the recent or remote past. Antibodies may remain detectable for months to years following resolution of infection. Results should not be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing should not be performed. If both first and second tests are equivocal consider repeat testing in 7 to 14 days if clinically warranted.

For specimens that did not have first tier testing performed at Mayo Clinic Laboratories, the results will also include the comment: "Interpretation assumes first tier Lyme disease causing *Borrelia* species antibody test was performed and resulted as positive or equivocal."

Cautions

The modified 2-tiered serologic testing (MTTT) study was conducted using the ZEUS ELISA *Borrelia* VlsE1/pepC10 IgG/IgM Test System as the first-tier assay and the ZEUS ELISA *Borrelia burgdorferi* IgM and IgG Test System as the second-tier assay with testing performed in that order. The performance characteristics of the device are not established for changing the order of testing or for substituting other enzyme immunoassay (EIA) in the MTTT (2-EIA) procedure.

Sera from patients with other spirochetal diseases (syphilis, yaws, pinta, leptospirosis, and relapsing fever), or infectious mononucleosis and systemic lupus erythematosus may give false-positive results. In cases where false-positive reactions are observed, extensive clinical epidemiologic, and laboratory workups should be carried out to determine the specific diagnosis. False-positive sera from syphilis patients can be identified by running a rapid plasma reagin and a treponemal antibody assay on such specimens. True *B burgdorferi* disease-positive sera will be negative in these assays.

False-negative results may be obtained if serum specimens are collected too early after onset of disease before antibody levels have reached significant levels. Also, early antibiotic therapy may abort an antibody response to the spirochete.

Interpret all data in conjunction with clinical symptoms of disease, epidemiologic data, exposure in endemic areas, and results of other laboratory tests.

Do not perform screening of the general population. The positive predictive value depends on the pretest likelihood of infection. Only perform testing when clinical symptoms are present, or exposure is suspected.

The performance characteristics of the ZEUS ELISA *B burgdorferi* IgM and IgG Test Systems are not established with specimens from individuals vaccinated with *B burgdorferi* antigens.

Rheumatoid factor may cause false-positive results with the *B burgdorferi* IgM Test System.

Clinical Reference

1. Theel ES: The past, present and (possible) future of serologic testing for Lyme disease. J Clin Microbiol. 2016 May;54(5):1191-1196. doi: 10.1128/JCM.03394-15
2. Dattwyler RJ: Lyme borreliosis: an overview of clinical manifestations. Lab Med. 1990 May;21(5):290-292. doi: 10.1093/labmed/21.5.290
3. Schwan TG, Burgdorfer W, Rosa PA: *Borrelia*. In: Murray PR, ed: Manual of Clinical Microbiology. 7th ed. ASM Press; 1999:746-758
4. Centers for Disease Control and Prevention (CDC): Recommendation for test performance and interpretation from second national conference on serological diagnosis of lyme disease. MMWR Morb Mortal Wkly Rep. 1996;45:481-484

Performance

Method Description

The ZEUS *Borrelia burgdorferi* IgM and IgG ELISA Test Systems are designed to detect anti-*B burgdorferi* IgM and IgG antibodies, respectively, in human serum from patients suspected of Lyme disease. A positive result in IgM and/or IgG demonstrates that one or both classes of antibodies for *B burgdorferi* are present within the test sample.

The wells of the plastic microwell strips provided in each respective kit have been prepared by the passive adsorption of *B burgdorferi* whole cell antigen. The test procedure involves 3 incubations steps. First, test sera (properly diluted) 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. Second, peroxidase conjugated goat anti-human IgM (mu chain specific) and IgG (Fc chain specific) are added to their respective wells and incubated. The conjugate will react with IgM and/or IgG antibody immobilized on the solid phase in step 1. The wells are washed to remove unbound conjugate. Third, the microwells containing immobilized peroxidase conjugate are incubated with peroxidase substrate solution. Hydrolysis of the substrate by peroxidase produces a color change. After a period of time 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 sample.(Package inserts: *B burgdorferi* IgM Test System and *B burgdorferi* IgG Test Systems. ZEUS Scientific, Inc; Rev Date 01/2020)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

Same day/1 to 5 days

Specimen Retention Time

14 days

Performing Laboratory Location

Test Definition: TLYME

Lyme IgM and IgG, Whole Cell Sonicate, ELISA, Serum

Mayo Clinic Jacksonville Clinical Lab

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 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

86617 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TLYME	Lyme IgM/IgG, WCS, EIA, S	34942-3

Result ID	Test Result Name	Result LOINC® Value
LYMEM	Lyme Ab, IgM, S	40612-4
LYMEG	Lyme Ab, IgG, S	16480-6
LYMEI	Lyme Ab Interpretation	46248-1