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LYME DISEASE SEROLOGY TEST UPDATE

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SUMMARY

Effective May 8, 2013, the Division of Laboratory Medicine will make the following changes regarding the serological diagnosis of Lyme Disease (LD):

1) The LYME ANTIBODY SCREEN, EARLY and LYME ANTIBODY SCREEN, LATE reflex panels will be replaced with a single reflex panel, LYME DISEASE SEROLOGY, SERUM. This panel will include the following tests:
   a) Lyme Antibody EIA, always performed;
   b) Lyme IgM & IgG Immunoblots, performed only when the Lyme EIA is positive or equivocal.

2) Requests for immunoblots on Lyme EIA-negative sera will no longer be honored.

(For more information and rationale on these changes see Diagnosis below.)

BACKGROUND

LD, caused by the spirochete bacterium *Borrelia burgdorferi*, is the most common tick-borne illness in our region. *B. burgdorferi* is a zoonosis of deer and various small mammals, primarily the white-footed mouse and the chipmunk, spread by the hard-bodied tick *Ixodes scapularis* (aka deer tick). Humans are incidentally infected by a tick bite, usually the second stage nymph. Because of the tiny size of the nymph, most humans do not recall being bitten, even though the tick will typically stay attached for up to several days.

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Phases of LD may be broken into three groups:

1) The Local Early phase, arising within several days to several weeks after the tick bite. Manifestations typically include mild non-specific flu-like symptoms and the characteristic annular red skin lesion at the site of the tick bite, known as *erythema migrans* (EM). EM is seen in approximately 80% of cases but is not always of the typical appearance.
2) The Disseminated Early phase begins within several days to several weeks of the primary EM lesion's appearance. Secondary EM lesions are common, denoting a spread of the organism, and the various constitutional symptoms become progressively worse. Without treatment, frank neurologic and/or cardiac symptoms will develop within about 20% of untreated patients. Other organ systems can also be affected.
3) Late LD develops in untreated patients weeks to years (average six months) after the initial tick bite. Reoccurring, intermittent attacks of arthritis, usually of the large joints and especially the knees, occur in about 60% of patients with late LD. Joint effusions with a leukocytic cytosis of up to 110,000 cells/mcL are common. Additionally, chronic neurologic manifestations may rarely occur.

DIAGNOSIS

Serological studies are the cornerstone of LD diagnosis. The CDC recommends that all previously undiagnosed possible LD cases be tested by a two-tier algorithm:

1) All sera are to be initially tested with an anti-*B. burgdorferi* antibody enzyme immunoassay (EIA).
2) All EIA positive or equivocal sera are then confirmed with *B. burgdorferi* antibody immunoblot (IB) assays.
   a) IgM & IgG IBs in first month of infection (i.e., during the EM period), or
   b) IgG only thereafter.

The sensitivity of the CDC two-tier algorithm ranges from 40% in the first weeks of infection to nearly universal seropositivity in untreated Late LD. The IgM IB is necessary to maximize sensitivity early in the infection, but is prone to false positive results; a positive IgM/negative IgG IB result after the first 1 – 2 months of illness is most likely a false positive result. When reviewing LD serology results, it is important to remember two things:

1) LD patients can remain seropositive for months or years, even after successful treatment. Repeat testing when reinfection is suspected is therefore of little clinical utility.
2) There are no published data that support the appearance and disappearance of individual bands on IBs as a tool in diagnosis. It is thus more useful to rely on the interpretation of an IB, and not on the individual bands reported.

The change to a single reflex panel composed of both IgM & IgG IBs was made in order to simplify test selection and reduce delays in diagnosis. *It is important to note that IgM IB data will now always be provided when the EIA is positive or equivocal regardless of the stage of infection. The clinician should therefore be highly cautious of a positive IgM/negative IgG IB result in cases clearly beyond the Local Early phase.*

Please be aware that IBs will no longer be performed on EIA-negative sera. This decision was made in consultation with our infectious disease specialists, is fully endorsed by the Laboratory Compliance Committee, and follows CDC recommendations. LD IBs, when interpreted using the CDC criteria of

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≥2 out of 3 IgM bands and ≥5 out of 10 IgG bands as a positive result, are no more sensitive than modern EIA assays. Furthermore, interpreting LD IBs as positive when fewer bands are present, while possibly correctly identifying additional cases of LD, will also lead to incorrect diagnoses of LD, cause unnecessary antimicrobial treatment, and in some cases lead to a missed true diagnosis. When Local Early LD is suspected and the LD antibody screen test is negative, retesting once in 2-4 weeks is recommended. Beyond the Local Early phase, a negative EIA result confidently rules out LD in the immunocompetent patient.

It is important to remember that serological testing is not 100% accurate. The diagnosis of LD is thus largely a clinical one that requires a thorough history & physical exam by the clinician, as well as careful consideration of the diagnostic study results.

TEST INFORMATION -

TEST NAME:
Lyme Disease Serology, Serum

ORDERING CODES:
Clinical Order Manager: Lyme Disease Serology, Serum
Centricity: Lyme Disease Serology, Serum

LAB TEST CODE:
LYMPAN

SPECIMEN REQUIREMENTS:
1.0 mL serum (Red Top Tube preferred, Serum Separator Tube acceptable)

MINIMUM VOLUME:
0.5 mL serum

REJECTION CRITERIA:
Bilirubinemic, hemolyzed, lipemic and turbid sera are unacceptable
CSF is unacceptable

AVAILABILITY:
Lyme Antibody Screen (EIA) performed Sunday through Thursday
Lyme Confirmatory Immunoblot performed Monday, Wednesday, Friday during summer and Friday during off season.

REFERENCE VALUE:
Negative

ADDITIONAL INFORMATION:

Test Name	CPT Code	Description
Lyme Disease Serology, Serum		
Lyme Antibody Screen	86618	EIA
Lyme Confirmatory Immunoblot	86617x2	Immunoblot (if needed)

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QUESTIONS

Please contact Dr. Thomas Novicki or Dr. Thomas Fritsche with clinical and interpretive questions regarding this test, or Dr. Joyce Flanagan with technical questions at extension 1-6700 or 800-222-5835.

REFERENCES

1) Centers for Disease Control. *Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease.* Morb Mortal Wkly Rep. 1995. 44:1.
2) Engstrom, SM et al. *Immunoblot interpretation criteria for serdiagnosis of early Lyme disease.* J. Clin. Microbiol. 1995. 33:419.
3) Dressler, F et al. *Western blotting in the serodiagnosis of Lyme disease.* J. Infect. Dis. 1993. 167:392.