Lyme Disease

Diagnosis of Lyme disease (B. burgdorferi infection) is best made on the basis of a history of exposure to the tick vector or tick environment and clinical findings. Although biopsy with isolation of B. burgdorferi in culture is definitive, culture is often impractical and rarely available. Since the sensitivity and specificity of anti-B. burgdorferi antibody tests are less than desired, a two-step algorithm has been recommended by the CDC/ASTPHLD Second National Conference on Serologic Diagnosis of Lyme Disease: the first step is performance of either total or immunoglobulin-specific (IgG and IgM) antibody assays using EIA technology; the second step involves measurement of antibodies with the Western blot technology on specimens having a positive or equivocal EIA result. For early stage disease (<1 month duration), IgM Western blot testing is recommended, whereas both IgG and IgM testing are recommended for late-stage disease.

IgM antibodies may be present within a few weeks of disease onset (early stage); however, IgG antibodies are produced later in the disease. Both IgM and IgG antibodies may persist for many months or years. IgM antibody testing is most sensitive between 1 and 2 months following onset, whereas IgG antibody testing is most sensitive 3 months after onset. Patients who are on antibiotic therapy and who have early stage disease may have low or negative antibody titers. Thus, negative results may indicate lack of infection or lack of seroconversion (due to the time of specimen collection relative to disease onset or to suppression of antibody production subsequent to therapy, etc.) If Lyme disease is still suspected following a negative antibody result, testing a second specimen collected 2 to 4 weeks after the first specimen is recommended.

Positive antibody results may be due to current or previous B. burgdorferi infection as well as other spirochete-caused diseases such as syphilis, yaws, pinta, leptospirosis, and relapsing fever. Syphilis and Lyme disease may be differentiated by VDRL and RPR tests, both of which are negative in Lyme disease and positive in syphilis. Patients with autoimmune disorders (e.g., lupus erythematosus and rheumatoid arthritis), mononucleosis, rickettsia, Ehrlichia, and bacterial infections (e.g., Helicobacter pylori) may also have a positive antibody test. A positive IgM result, in conjunction with a negative IgG result, is presumptive evidence of early infection, unless obtained on a specimen collected more than 1 month following onset. A positive IgM result on a specimen collected more than 1 month following onset is likely to be a false-positive when the IgG result is negative. A positive IgG result with a positive or negative IgM result is presumptive evidence of late infection.

Expression of cerebrospinal fluid (CSF) and serum EIA antibody results as a ratio may help correct for passive diffusion of antibodies across the blood-brain barrier and thus can be used to further support a clinical diagnosis of Lyme neuroborreliosis. Red cell contamination of CSF specimens as well as xanthochromia and turbidity interfere with test results. Collection of the serum and CSF specimen should be within 24 hours of each other; both specimens should be assayed simultaneously. An index less than 0.76 is deemed negative and indicative of passive blood-brain antibody diffusion, while an index greater than 1.13 is deemed positive and is supportive of Lyme neuroborreliosis.

The interpretation of Western blot antibody assays is based on the number and pattern of band positivity: 2 of 3 bands (23, 39, 41kDa) for IgM positivity and 5 of 10 bands (18, 23, 28, 30, 39, 41, 45, 58, 66, or 93kDa) for IgG positivity. The Western blot is to be used only following initial EIA testing.
A positive PCR test result may be obtained prior to or following seroconversion, and, although it is associated with active disease, it does not necessarily prove the presence of active disease because PCR cannot distinguish between live and dead organisms. A negative PCR test is suggestive of the absence of *B. burgdorferi* infection; however, a negative PCR result does not exclude the diagnosis due to transient spirochetemia, inadequate spirochete numbers in the sample, or DNA sequence variances in different *B. burgdorferi* strains. Although whole blood specimens are clinically indicated under rare circumstances during acute or early infection, such specimens are generally not recommended since transient spirochetemia renders negative results useless. PCR tests are most useful in patients with Lyme arthritis and Lyme neuroborreliosis; the specimens of choice are synovial fluid and CSF, respectively. Test results should be interpreted in context with clinical findings.

Continued presence or absence of antibodies during treatment does not imply therapeutic failure or success; however, PCR-detected *B. burgdorferi* DNA may be of use. Following adequate therapy, PCR results are generally negative, while in cases of therapeutic failure, evidenced by ongoing or worsening symptoms, PCR results are usually positive.