

FDA Medical Bulletin * Summer 1999 * **Final Issue**

Lyme Disease Test Kits: Potential for Misdiagnosis

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The Food and Drug Administration (FDA) is concerned about the potential for misdiagnosis of Lyme disease based on the results of commonly marketed tests for detecting antibodies to *Borrelia burgdorferi*, the organism that causes Lyme disease. It is important that clinicians understand that a positive test result **does not** necessarily indicate current infection with *B. burgdorferi*, and a patient with active Lyme disease may have a negative test result. (1-5)

The tests should be used only to support a clinical diagnosis of Lyme disease and should **never** be the primary basis for making diagnostic or treatment decisions. Diagnosis should be based on a patient history, which includes symptoms and exposure to the tick vector and physical findings. The most definitive diagnostic procedure is biopsy and isolation of *B. burgdorferi* in culture.

Assays for anti-*Borrelia burgdorferi* (anti-Bb) can provide evidence of previous or current infection, but to improve reliability FDA supports the Centers for Disease Control and Prevention (CDC) recommendation for two-step testing and interpretation of results (1).

The first step is to perform an assay that detects either total or class-specific antibodies (IgM or IgG) by using enzyme-linked immunosorbent technology ("ELISA" or "EIA") or indirect immunofluorescence microscopy ("IFA"). IgM levels usually peak 3 to 6 weeks after infection. IgG antibodies begin to be detectable several weeks after infection and may continue to develop for several months and generally persist for years.

- A negative result indicates only that there was no serologic evidence of infection with *B. burgdorferi*. **It should not be used as the basis for excluding *B. burgdorferi* as the cause of illness**, especially if the blood was collected within 2 weeks of when symptoms began.
- A positive or equivocal result is presumptive evidence of the presence of anti-Bb. **It should always be followed by second-step testing and should not be reported until the second step testing is completed.**

The second step is to perform a Western-blot (immunoblot) assay, a more specific assay than that used for the first step

- A negative result indicates that no reliable serologic evidence of *B. burgdorferi* infection was present. **A negative result should not be used as the sole basis for excluding *B. burgdorferi* as the cause of illness.** If Lyme disease is suspected, a second specimen collected 2 to 4 weeks after the first specimen should be tested. If retesting, do the first step and if the result is positive or equivocal, do the second step.
- A positive result provides serologic evidence of past or current infection with *B. burgdorferi*. **Because the presence of even specific antibodies to *B. burgdorferi* does not always indicate current infection, a positive result can support, but not establish, a clinical diagnosis of Lyme disease.**

Even using the two-step approach, the sensitivity and specificity of the combined test results are inadequate. Because assays for anti-*Bb* should be used only for supporting a clinical diagnosis of Lyme disease and not for "screening" asymptomatic individuals, the result of the first-step assay is best described as "initial" rather than "screening." Likewise, the second-step Western-blot assay is best described as "supplemental" rather than "confirmatory", because of the low specificity for detecting IgM anti-*Bb*. **Thus, a positive IgM anti-*Bb* result alone is not adequate for supporting a diagnosis of Lyme disease in persons with illness of greater than one-month duration.**

Several factors contribute to the limitations of using ELISA, IFA, or Western blot tests for supporting a diagnosis of Lyme disease. The stage of disease in which the specimen was taken is critical. Many patients with active or recent infections do **not** have detectable anti-*Bb* in a single specimen. This happens because such antibodies often develop after manifestations of early infection or because detectable anti-*Bb* may diminish or never develop in patients treated with antibiotics. Further, a positive test result can be true evidence of previous infection with *B. burgdorferi* and unrelated to a current illness. Assays for anti-*Bb* may yield false-positive results, because antibodies to *B. burgdorferi* antigens may cross react with antigens associated with autoimmune diseases or from infection with other spirochetes, rickettsia, ehrlichia, or other bacteria such as *Helicobacter pylori*. (6,7)

In summary, serologic testing is not useful early in the course of Lyme disease, because of the low sensitivity of tests in early disease. Serologic testing may be more useful in later disease at which time sensitivity and specificity of the test is improved.

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