Lyme Disease Diagnosis

Lyme disease is a clinical diagnosis–based on your medical history, symptoms and exposure to ticks. Because the typical diagnostic tests for Lyme are so insensitive, a negative test result does not mean you don't have Lyme. There are many reasons why someone who actually has Lyme may have a negative test result. There may not have been time for antibodies to develop; the immune system may be suppressed; or the person may be infected with a strain the test doesn't measure.

Lyme disease is known to inhibit the immune system and 20-30% of patients have falsely negative antibody tests.

Did You Know?

- LLMDS consider the specificity of the particular bands that test positive for a patient.
- Although the CDC requires 5 of 10 bands for IgG surveillance purposes, 2 of 5 bands have specificity of 93-96% and a sensitivity of 100%. (Engstrom 1995).
- 56% of patients with Lyme disease test negative using the two-tiered testing system recommended by the CDC. (Stricker 2007)
- The CDC case surveillance definition allows single-tier IgG immunoblot seropositivity using established criteria. (CDC 2011; www.cdc.gov/nndss/conditions/lyme-disease/case-definition/2011/)
- The CDC states: "This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis." (www.cdc.gov/nndss/conditions/lyme-disease/case-definiti

on/2011/)

- The College of American Pathologists (CAP) found that ELISA tests do not have adequate sensitivity to be used for screening purposes. (Bakken 1997)
- 52% of patients with chronic disease are negative by ELISA but positive by Western blot. (Donta 2002)

Tests can not only help to diagnose a disease, but also to manage an illness. A good test can help a doctor assess the severity of disease, estimate the patient's prognosis, monitor the course of disease progression, stability or resolution, detect relapse, and select drugs or adjust therapy. Unfortunately, a test with this capability does not exist for Lyme disease.

LymeDisease.org has developed a Lyme disease symptom checklist to help you document your exposure to Lyme disease and common symptoms for your healthcare provider. You will receive a report that you can print out and take with you to your next doctor's appointment.

CHECK YOUR SYMPTOMS

Two-tier Testing

The most common diagnostic tests for Lyme disease are indirect ones. They measure the patient's antibody response to the infection, not the infection itself. The two most-used antibody tests are the enzyme-linked immunosorbent assay (ELISA) and the Western blot. The CDC recommends that doctors first order an ELISA to screen for the disease and then confirm the disease with a Western blot.

During the first four-to-six weeks of Lyme infection, these tests are unreliable because most people have not yet developed the antibody response that the test measures. Even later in the illness, the two-tiered testing is highly insensitive missing roughly half of those who have Lyme

disease.

Two-tiered testing uses two tests. The first is a screening test that should detect anyone who might have the disease. Tests that do this well have are regarded as having high sensitivity. This test is followed by a second test that is intended to make sure that only people with the disease are diagnosed. Tests that do this well have high specificity.

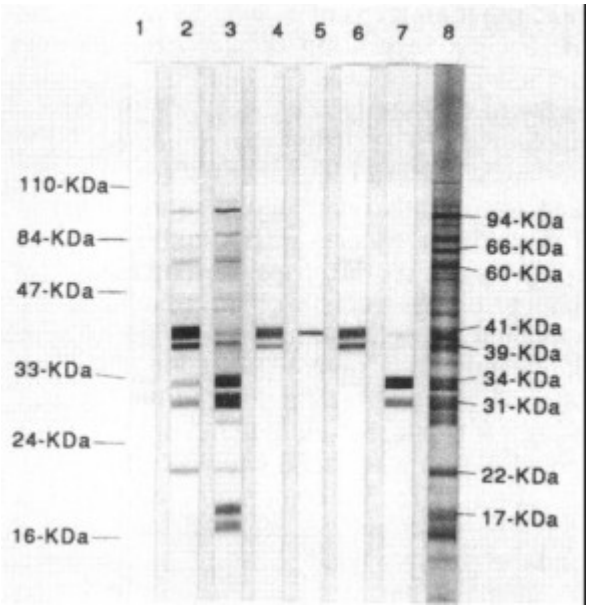
HIV/AIDS is diagnosed with tests that are both highly sensitive and highly specific. They are accurate more than 99% of the time. In Lyme disease, the second test is highly specific. So there are few false positives. Unfortunately, the screening test is highly insensitive and fails to accurately identify patients who have Lyme disease. The two-tiered test system misses roughly 54% of patients. (Stricker Minerva 2010)

Sensitivity/specificity of commercial two tier testing for convalescent/late stage Lyme disease in the US*			
Study/Year	**Patients/Controls**	**Sensitivity**	**Specificity**
Schmitz (1993)	25/28	66%	100%
Engstrom (1995)	55/159†	55%	96%
Ledue (1996)	41/53	44%	100%
Tilton (1997)	23/23	45%	100%
Trevejo (1999)	74/38	29%	100%
Bacon (2003)	106/559	67%	99%
Binnicker (2008)	35/5	49%	100%
Steere (2008)	76/86††	18%	99%
TOTAL	435/951	46%	99%
*Limited to studies from the US that included negative controls; †Non-commercial ELISA and Western blot; ††Non-commercial ELISA			

Because of this, LDo recommends the patients and physicians skip the ELISA and go straight to the Western blot.

Western Blot

Labs performing a Western blot use electricity to separate proteins called antigens into bands. The read-out from the Western blot looks like a bar code. The lab compares the pattern produced by running the test with your blood to a template pattern representing known cases of Lyme disease. If your blot has bands in the right places, and the right number of bands, it is positive.



The CDC requires 5 out of 10 bands for a positive test result. However, because some bands on the Western blot are more significant than others your doctor may decide you have Lyme disease even if your Western blot does not have the number of bands or specific bands recommended by the CDC. Different laboratories use different methods and criteria for interpreting the test, so you can have a positive test result from one lab and a negative test result from another.

For a comprehensive explanation of the western blot test, download this PDF.

The chart below will help you understand how to interpret the western blot test.

Interpretation of the Western blot—More is not necessarily better.

		IgG	IgG	IgM	IgM
Band kDa	Band importance	Ma et al. 2 of 6	CDC 5 of 10	Ma et al 2 of 5	CDC 2 of 3
18	Thought to be specific				
22	Thought to be specific				
23-25	OSP-C highly specific				
28	Not specific				
30	Thought to be specific				
31	OSP-A highly specific				
34	OSP-B highly specific				
37	Thought to be specific				
39	Thought to be specific				
41	Non-specific flagella				
45	Non-specific				
58	Non-specific				
66	Non-specific				
73	Non-specific				
88	Thought to be specific				
93	Thought to be specific				

Engstrom found 2 of 5 bands to be highly sensitive and specific for Lyme disease (Engstrom 1995), while 46 of 66 symptomatic pediatric patients with a history of bulls eye rash and tick bite were negative by CDC criteria (Fawcett 1995 Rheumatology Symposia Abstract #1254.) The CDC criteria are intended only for surveillance purposes, not diagnosis. Many physicians interpret the Western blot based on the number and specificity of the patient's bands. See also (Ma et al. 1989).

Other tests

Three other tests that may be used to diagnose Lyme disease are polymerase chain reaction (PCR), antigen detection and culture testing. They are called "direct" tests because they detect the bacteria, not just your immune response to it.

PCR multiplies a key portion of DNA from the Lyme bacteria so that it can be detected. While PCR is highly accurate when the Lyme DNA is detected, it produces many false negatives. This is because the Lyme bacteria are sparse and may not be in the sample tested.

Antigen detection tests look for a unique Lyme protein in fluid (e.g. blood, urine, joint fluid). Sometimes people whose indirect tests are negative are positive on this test.

Culture is the “gold standard” test for identifying bacteria. The lab takes a sample of blood or other fluid from the patient and attempts to grow Lyme spirochetes in a special medium.

Although culture tests are generally accepted as proof of infection, the CDC has advised caution on the only commercially available culture test developed by Advanced Laboratory Services. LDo recognizes that the test is new and requires further validation in other studies. However, we believe that informed patients should be able to choose the test if they prefer. Choice is particularly important given the low quality of Lyme disease tests generally.

Recommended labs

Although the CDC recommends that patients use “FDA-approved” tests, LDo does not support this restriction because there are no FDA-approved test for Lyme disease. Instead, the the FDA has “cleared” certain lab tests, but these test are not required to demonstrate that they are effective or safe, they are only required to be “equivalent” to test previously cleared. The current FDA cleared tests have poor sensitivity and miss more than 50% of patients with Lyme disease. The US Centers for Medicare & Medicaid Services (CMS) requires tests without FDA approval to undergo a rigorous certification process. CMS regulates all laboratory testing (except research) performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA). CLIA certification is designed to ensure quality laboratory testing. All clinical laboratories must be properly certified to receive Medicare or Medicaid payments. CLIA covers approximately 244,000 laboratory entities.

Two highly specific bands (OspA and OspB) are not included in the CDC bands because they were used for vaccine development. Your doctor may want to know if you have antibodies directed towards those proteins. A few labs test for them.

LDo recommends that you use a CLIA-approved lab that specializes in testing for tick-borne diseases and reports all bands on the Western blot. The healthcare professional ordering the test must ask the lab to report all bands except in the case of IGeneX, which automatically reports all bands. Blots may still vary in sensitivity.

- IGeneX: 800-832-3200
- StonyBrook: 631-444-3824
- MDL: 877-269-0090