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Lifespan Lyme Disease Center

CONTROVERSIES IN LYME TESTING EXPLAINED

Take Home Message:

We understand that testing for Lyme is complicated and can be very frustrating at times. It is important to evaluate your symptoms with your doctor and discuss the best treatment options for you, whether that be antibiotics or lifestyle changes. Please see our wellness section about the power of non-pharmaceutical Lyme treatment for persistent long-term symptoms.

The non-specific symptoms of Lyme disease often make it difficult for doctors to determine a proper diagnosis. Many diseases, illnesses, or conditions have similar symptoms to Lyme disease. Additionally, patients do not always remember or notice an attached tick to report to the doctor. Even if patients are able to confirm a tick bite, this does not necessarily indicate Lyme disease because most ticks do not carry *B. Burgdorferi* bacteria. Your care provider may treat you with antibiotics for Lyme disease at times even if the Lyme antibody tests is equivocal or not fully positive. The length of the therapy is usually the same; typically, 21 to 28 days. Patients must also be wary of getting an incorrect Lyme diagnosis and treatment in case their symptoms are being caused by an undiscovered illness. Serological lab testing can be helpful in diagnosing Lyme disease. However, the accuracy of these tests is often debated because serological testing is imperfect. The diagnosis for Lyme is based on the clinical picture as well as serological testing

Immunological background for understanding serological testing:

When the immune system encounters foreign substances within the body such as *B. Burgdorferi*, it begins releasing specialized antibodies to fight the infection. These antibodies attack foreign matter and are produced by immune cells. The specificity of the antibodies released is dependent on the illness contracted. For example, you have different antibodies that recognize Lyme disease versus the common cold. However, serological testing (testing of bodily fluids) has limitations to its capacity to differentiate between antibody specificity. So while the antibodies may be very specific, the immune system is so complex that sometimes our tests cannot distinguish between two very similar antibodies. For example, having syphilis, periodontal disease, rheumatoid arthritis, systemic lupus erythematosus, mononucleosis, and other autoimmune diseases can result in a false positive test for Lyme disease.

The presence of these antibodies also varies as the disease progresses. It takes the immune system a while to register an infection with *B. Burgdorferi*, so antibodies will not be detected in the blood in the first few weeks of the disease, and serological testing can result in a false negative. These are also different classes of antibodies (IgM and IgG antibodies in particular) that rise, then

ebb independently at certain times. To make matters even more complicated, antibiotic treatment will affect antibodies, as will a previous but resolved Lyme infection. Regardless of these complexities, the medical community tries its best to serve patients as accurately and effectively as possible. Here are examples of commonly used Lyme tests:

Two-Tiered Testing using EIA (Enzyme Immunoassay, also called Lyme reflex) And Immunoblot

The CDC and many health professionals accept two-tiered testing as the most effective method for Lyme testing. Here is a link to the CDC's official statement about these tests in 1994 (still current recommendations): http://www.cdc.gov/mmwr/preview/mmwrhtml/00038469.htm First, a Lyme reflex will determine whether you have antibodies that could be specified for Lyme. If you have Lyme, you should have a positive Lyme reflex result. However, this test will also be positive for a variety of other illnesses. Thus, a second test called an Immunoblot test (Western Blot) should be completed in order to confirm that the infection is Lyme, rather than these other illnesses. This test is specific for antibodies produced against *B. Burgdorferi.* It measures IgM and IgG antibodies. The CDC describes the reason for this as such, "IgM antibodies are made sooner, so testing for them can be helpful for identifying patients during the first few weeks of infection. The downside of testing for IgM antibodies is that they are more likely to give false positive results. Tests for IgG antibodies are more reliable, but can take 4 to 6 weeks for the body to produce in large enough quantities for the test to detect them". Here is a chart of common immunoblot results and what they can mean:

IgM Antibody	IgG Antibody	Western Blot	Likely Interpretation
Positive	Positive	Positive	Likely Lyme disease if consistent with other signs and symptoms
Positive	Negative	Negative	Early infection or false-positive IgM test due to cross reactive antibodies
Negative	Positive	Positive	Latent or previous infection
Negative	Negative	(usually not performed if IgM and IgG are negative	No infection present; symptoms may be due to another cause or antibody levels are too low to detect
Negative	Positive	Negative	Patient has recovered from prior infection or false-positive IgG test due to cross reactive antibodies

Source: https://labtestsonline.org/understanding/analytes/lyme/tab/test#how

The CDC states that a positive Lyme diagnosis with immunoblot will have at least 5 out of 10 IgG bands present on the test. These "bands" mark the presence of a certain IgG antibody specific for Lyme.

These tests are commonly done on blood, but they can also be conducted on cerebrospinal fluid if the patient shows severe neurological symptoms and *B. Burgdorferi* is suspected in the Central Nervous System.

C6 Peptide ELISA

This test is an IgG ELISA on the C6 region of the VIsE lipoprotein. Studies have shown that it has a similar accuracy to the two-tiered test, but two-tiered testing still has slightly better specificity for Lyme in early diagnosis. Here is a link to that study: http://cid.oxfordjournals.org/content/47/2/188.short
However, C6 ELISA has slightly better sensitivity and specificity in the later stages of the disease. It is recommended that the C6 ELISA be used as a second-tier test after an initial positive ELISA screen to improve its accuracy. A C6 ELISA test eliminates the need for and confusion of IgM testing.

CD57 Test

This Lifespan Lyme Disease Center sees some patients who have had a CD57 test done by a previous doctor. The basis for this test follows a study conducted in the 1980s which concluded that Lyme patients have abnormally low numbers of CD57 Natural Killer (NK) cells. CD57 NK cells are immune system attackers, not taggers such as the antibodies explained in the two-tiered test section. (CD57 T cell tests are different and do not indicate Lyme, so be aware of the differentiation). A link to that study is here: http://www.ncbi.nlm.nih.gov/pubmed/11222912
Granted, other studies have not found a significant difference in CD57 NK cells in patients with Lyme. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725528/pdf/0167-09.pdf. As a result, the conflicting information has facilitated debate between patients, scientists, and health professionals.

Efficacy of Lyme Tests after Antibiotic Treatment

We mentioned before that antibodies rise and ebb throughout the course of the illness. However, this does not mean that they are an indicator of the disease progression. Having more or less of an antibody does not mean you have more or less of an infection. In addition, antibodies stick around long after the infection is gone; sometimes for the rest of your life. This is how the immune system works and it is a very good thing. By retaining a small number of antibodies against Lyme disease (or any illness), your body will mount a faster and more efficient immune response the next time it encounters the pathogen.

What does this mean for subsequent Lyme testing? Since Lyme tests detect the presence of antibodies, you may test positive for Lyme antibodies for the rest of your life, even when *B. Burgdorferi* has been successfully eliminated. Be assured, this does not mean you have Lyme disease. It simply means that you have a normal and healthy immune system.

Work Cited

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