

Lyme Disease

Borrelia burgdorferi C6 PEPTIDE ANTIBODY DETECTION BY ELISA, A SENSITIVE AND SPECIFIC ALTERNATIVE TO THE STANDARD TWO-TIER TESTING ALGORITHM

Introduction

Lyme disease, caused by *Borrelia burgdorferi*, is a multisystem disease that is transmitted by ticks of the genus Ixodes.⁵ In 2000, the CDC reported 17,730 cases of Lyme disease, 94 percent of which occurred in New York, Connecticut, Pennsylvania, Massachusetts, Rhode Island, New Jersey, Maryland, Delaware, Wisconsin, and Minnesota.² It is estimated that Lyme disease cases are under reported and that the actual incidence of Lyme disease is more than 100,000 cases per year.³ Lyme disease is also endemic in Europe and Asia, although caused by different *Borrelia* species.

Clinical Significance

Patients with Lyme disease generally present with erythema migrans, a skin lesion that resembles a “bull’s-eye” pattern. Systemic complications involving the heart, joints, and nervous system occur shortly thereafter. The initial skin lesion is often absent from the patient and, since symptoms can be general and nonspecific, other medical conditions such as arthritis, lupus, or syphilis may resemble Lyme disease.

Laboratory Diagnosis

- In 1995, the CDC recommended a two-tier approach when testing for antibodies against *B. burgdorferi*. First, serum is tested using a sensitive ELISA and, if the sample is positive or equivocal, it is then retested by Western immunoblot.¹ False positive ELISA results often cause overdiagnosis in Lyme disease. In fact, samples from 55 percent of normal donors,³ 70 percent of patients with antibodies against *Treponema pallidum*,³ 64 percent of patients with tick-borne relapsing fever,⁸ and 98 percent of patients who lived in a tropical country where Lyme disease is endemic,⁴ had positive whole-cell Lyme ELISA results. Additionally, samples from patients who have been vaccinated against Lyme disease may have false positive results.⁹ While most of these false positive results are identified when the sample is tested by the Western blot, the Western blot is not 100 percent specific.
- The C6 Peptide ELISA is formatted using a synthetic peptide, the sequence of which is antigenically conserved among *B. burgdorferi* sensu lato complex strains and species.⁷ **The assay is both sensitive and specific, and appears to lack many of the problems with false positive results that are seen in whole-cell extract-based ELISA test systems.⁷**

- While it has been suggested that the C6 Peptide ELISA replace the standard two-tier testing algorithm,² the CDC has not made any recommendations in this respect and the C6 ELISA is offered as an alternative to the current whole-cell extract ELISA. **In this capacity, the ImmuneC6 Peptide ELISA has been approved by the FDA for testing serum samples.**

Methodology

The C6 *B. burgdorferi* (Lyme) ELISA uses a standard enzyme immunossay format. Diluted samples are incubated in microwells coated with synthetic C6 peptide antigen. Antibodies specific to the C6 peptide bind to the antigen, and unbound antibodies are removed by a wash step. Horseradish peroxidase-conjugated goat antihuman IgG/IgM conjugate is added to the wells, followed by an enzyme-based substrate. The enzymatic reaction is quenched with the addition of sulfuric acid. If C6 peptide-specific antibodies are present in the well, a yellow color will be present and then measured spectrophotometrically.

Limitations

- The C6 Peptide ELISA has been approved by the FDA for serum samples as an alternative to the whole-cell extract ELISA in the current two-tiered testing algorithm for Lyme disease. The C6 Peptide ELISA is both sensitive and specific, and appears to lack many of the problems with false positive results that are seen in whole-cell extract-based ELISA test systems.⁷
- Results from this test should be used with correlation to clinical history. Because co- and triple- infections with the parasites that cause Babesiosis and human granulocytic ehrlichiosis may occur, serologic testing specific for these agents is recommended.⁶

Related Tests

- *Borrelia burgdorferi* C6 Peptide Antibodies, Total by ELISA (CSF) (0051046)
- *Borrelia burgdorferi* C6 Peptide Antibodies, Total by ELISA with Reflex to IgG by Western Blot (0051045)
- *Borrelia burgdorferi* C6 Peptide Antibodies, Total by ELISA (0051044)

References

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4. Burkot TR, Schriefer ME, and Larsen SA. Cross-reactivity to *Borrelia burgdorferi* proteins in serum samples from residents of a tropical country nonendemic for Lyme disease. J Infect Dis 1997; 175:466-469.
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6. Krause PJ, et al. Concurrent Lyme disease and babesiosis. Evidence for increased severity and duration of illness. JAMA 1996; 275:1657-60.
7. Liang, FT, et al. Sensitive and specific serodiagnosis of Lyme disease by enzyme-linked immunosorbent assay with a peptide based on an immunodominant conserved region of *Borrelia burgdorferi* vIsE. J Clin Microbiol 1999; 37:3990-6.
8. Magnarelli LA, Anderson JF, and Johnson RC. Cross-reactivity in serological tests for Lyme disease and other spirochetal infections. J Infect Dis 1987; 156:183-8.
9. Marques AR, Martin DS, and Phillip MT. Evaluation of the C6 peptide enzyme-linked immunosorbent assay for individuals vaccinated with the recombinant OspA vaccine. J Clin Microbiol 2002; 40:2591-3.

Test Information

0051043

***Borrelia burgdorferi* C6 Peptide Antibodies, Total by ELISA with Reflex to IgG & IgM Western Blot**

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.