CRITICAL REVIEW
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Indirect Immunofluorescence (IFA) for Lyme Disease

Method

The IFA for Lyme disease is performed by incubating serum at 37°C for 30 minutes with Ixodes dammini spirochetes fixed to microtiter wells. After washing with phosphate-buffered saline, the slides are stained with fluoresceinated antihuman IgM or IgG, washed with distilled water, and read with a fluorescent microscope. The end point is the highest titer at which all organisms fluoresce faintly.

Clinical Applications

Lyme disease is caused by a spirochete transmitted by Ixodes ticks (1). It is prevalent in Lyme, Connecticut, many states including California (2), Europe and Australia. It is postulated that after the tick bite, immune complexes are formed and cause disease or are cleared without causing symptoms (3). A hallmark of the disease is the characteristic skin rash, erythema chronicum migrans (ECM). This is an evanescent, erythematous, papular, expanding annular lesion (that may be pruritic) with central clearing. Periorbital edema and diffuse erythema may be present. Other symptoms may include headache, stiff-neck, photophobia, sore throat, fever, myalgias, arthralgias, malaise, fatigue, lymphadenopathy, testicular swelling, splenomegaly and abdominal pain (4). Weeks or months later, some patients may develop neurologic symptoms such as cranial or peripheral neuropathies, meningoencephalitis, as well as myocarditis or AV-node block. Later in the course of the disease arthritis can develop which may recur for years, or may become chronic with destruction of bone and cartilage. Rarely, the spirochetes are isolated from blood (5), the skin or CSF (1).

Antibodies against the Ixodes dammini spirochete are not found in healthy controls or in patients prior to the onset of symptoms (1). IgM antibody titers appear one week after symptoms, peak between the third and sixth week after the onset of ECM and subsequently decline. In some patients the IgM titers were greater than or equal to 1:128 during later stages of the disease. IgG titers may also appear within one week of initiation of symptoms, but usually peak months later when arthritis is evident. IgG titers greater than or equal to 1:128 were observed in 95 patients with CNS, heart or joint involvement (1). Similar titers were observed in serum from all 60 patients with arthritis. Forty patients with ECM, alone, were treated with antibiotics. An IgM titer greater than or equal to 1:128 was observed in 36 (90%) of these individuals. After treatment, both IgM and IgG titers eventually return to undetectable levels.

Fourfold or more rises in IgM or IgG antibody titers were observed in patients with ECM who subsequently developed CNS, heart, or joint involvement. These changes occurred between the early ECM phase and subsequent disease months or years later. An IgM or IgG titer greater than or equal to 1:128 was observed in 98% of
these individuals. A fourfold decrease in IgM titers and a concomitant increase in IgG titers was observed in most patients. The IgG titers remained elevated in those individuals with recurrent arthritis. Thirty-eight percent of patients with ECM and sequelae received antibiotics. Their antibody responses were similar to those observed in untreated patients if their disease progressed.

**Technical and Clinical Limitations**

Acute and convalescent IgM and IgG titers are useful in the proper clinical setting, i.e., a person living in an endemic area with a tick bite, rash, or other clinical manifestations of Lyme disease. Although some patients do not notice a bite, almost all patients develop a characteristic rash. The other clinical symptoms may be nonspecific. Patients with infectious mononucleosis may have falsely elevated IgM titers (1). Therefore, both IgM and IgG titers should be followed. Treatment and timing of the samples may affect the results as discussed above.

**References**


