LYME BORRELIOSIS: GUIDELINES TO A SPECIFIC DIAGNOSIS

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DIRECT DETECTION

CULTURE

The most important instrument for the identification of a specific case is knowledge of the clinical presentations of Lyme Borreliosis. Ideally, this should be supported by the isolation of the infectious agent. However, the success of isolation and cultivation procedures in Lyme Borreliosis depends on the clinical manifestation of Lyme Borreliosis. Laboratories with long experience in the isolation and cultivation of borrelia from human specimens may achieve isolation rates of 80% from skin biopsies and of 30% from cerebrospinal fluid samples taken from patients with erythema migrans and meningoradiculitis, respectively. Consequently, only positive results are of value, but negative ones do not exclude Lyme Borreliosis.

STAINING TECHNIQUES

Non-specific stains are the Steiner method as well as Bosma Steiner, Warthin Starry, Dieterle, and their modifications. These histochemical techniques may work well in the hands of experienced technicians. However, the results are not specific and additional methods are required to identify a case.

Specific methods include immunohistochemical technique. This uses modifications of the immunoperoxidase method as developed by Steiner and involves a substitution of avidin-biotin and biotinylated secondary and tertiary antibodies in place of horse radish peroxidated conjugates. Both cryostat and paraffin embedded tissue sections can be used but frozen sections seem to work best for immunohistochemical detection of borrelia. With respect to the large number of subtypes of *Borrelia burgdorferi* sensu lato it would be a very complicated and time consuming process to identify a strain on the species level. Again, these techniques cannot be recommended for routine diagnostic procedures.

POLYMERASE CHAIN REACTION

The polymerase chain reaction (PCR) provides the possibility to detect specific sequences of borrelial nucleic acids in human specimens. PCR may be potentially helpful, however, protocols remain essentially non-standardized or their use in a clinical context is not fully evaluated. There is no general agreement on the most appropriate genomic targets for amplification and whether the presence or absence of borrelia DNA is clinically significant in some manifestations of Lyme Borreliosis.

INDIRECT DETECTION

Detection of specific antibodies in serum and other body fluids is currently the method widely

used to confirm the clinical diagnosis. Physicians who are experienced in the diagnosis of Lyme Borreliosis are well aware of the fact that in early localized manifestations the proportion of seropositives is low. Even in clearly identified and culture proven cases of erythema migrans, specific serum antibodies may be present in only 30%. Further, serum antibodies alone cannot support the diagnosis of neuroborreliosis. Samples of cerebrospinal fluid and serum, simultaneously taken, are necessary in order to demonstrate the production of intrathecal specific antibodies.

Serology includes now a variety of techniques: immunofluorescence, hemagglutination, ELISA using whole cell supernatant sonicate or recombinant antigens. The heterogeneity of European borrelia strains may cause an additional problem. Although the test systems have been improved during the last years some problems have yet not been solved. These are

i) seroprevalence in the healthy population which may exceed 40% in certain subpopulations,

ii) highly sensitive IgM in commercially available test systems, and

iii) the interpretation of test results.

Finally, the results from a single sample may not allow to draw conclusions; the minimal standard is paired samples within 4 to 8 weeks.

Presently, no consensus exists for the identification of immunoblot results in order to discriminate between early and late infection, or for confirmatory testing.

Thus, currently serodiagnosis of Lyme Borreliosis should be left to reference laboratories.

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