

Persistence of Borrelia and sero-negativity

Testing:

- 1.15 EIA Antibody Test may be sero-negative & yet culture, immune complex tests, WB or PCR prove that borrelia is present

Results of studies using direct antigen detection suggest that seronegative Lyme borreliosis is not rare and support the hypothesis that Borrelia antigens can persist in humans (Hulínská et al. 1993)

In the case of ELISA, positive or borderline results were observed in only 24 patients (53.3%)...Therefore using only ELISA as a screening test or for diagnosing Lyme borreliosis seems debatable (Wojciechowska-Koszko et al. 2011)

Source:

- 1) Although the patient never had detectable free antibodies to *B. burgdorferi* in serum or spinal fluid, the CSF was positive on multiple occasions for complexed anti-*B. burgdorferi* antibodies, *B. burgdorferi* nucleic acids and free antigen (Lawrence et al. 1995)
- 2) 50% of the PCR positive results, obtained with serum and cerebrospinal fluid samples corresponded to patients who were true positives at clinical examination but negatives at serologic tests (Grignolo et al. 2001)
- 3) Lyme borreliosis patients who have live spirochetes in body fluids have low or negative levels of borrelial antibodies in their sera. This indicates that an efficient diagnosis of Lyme borreliosis has to be based on a combination of various techniques such as serology, PCR and culture, not solely on serology (Tylewska-Wierzbanowska & Chmielewski 2002)
- 4) Polymerase chain reaction analysis of serum and synovial fluid may be of significant diagnostic value in Lyme disease, especially in the absence of a serologic response in early, partially treated and seronegative chronic disease (Mouritsen et al. 1996)
- 5) Seronegative Lyme arthritis was diagnosed based on the classic clinical manifestations. DNA of *Borrelia garinii* was repeatedly detected in the synovial fluid and the tissue of the patient. At the same time, antigens or parts of spirochaetes were detected by electron microscopy in the synovial fluid, the tissue and the blood of the patient (Dejmková et al. 2002)
- 6) These results show that antibodies to *B. burgdorferi* may be present in low levels or even absent in patients with culture- or PCR-proven late LB. In this study, multiple organs were frequently involved. Recurrent fever episodes were seen in nearly half of the patients, neurological symptoms were seen in more than half of the patients, and musculoskeletal manifestations were seen in three-fourths of the patients. Moreover, most of these manifestations were long-lived. In spite of this, several patients were seronegative and most seropositive patients had only weakly positive antibody levels (Oksi et al. 1995)

References:

Dejmková, H. et al., 2002. Seronegative Lyme arthritis caused by *Borrelia garinii*. *Clinical rheumatology*, 21(4), pp.330-4. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12189466>

Grignolo, M.C. et al., 2001. [Reliability of a polymerase chain reaction (PCR) technique in the diagnosis of Lyme borreliosis]. *Minerva medica*, 92(1), pp.29-33. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/11317136>

Hulínská, D. et al., 1993. Electron microscopy and the polymerase chain reaction of spirochetes from the blood of patients with Lyme disease. *Central European journal of public health*, 1(2), pp.81-5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8004045>

Lawrence, C. et al., 1995. Seronegative chronic relapsing neuroborreliosis. *European neurology*, 35(2), pp.113-7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/7796837>

Mouritsen, C.L. et al., 1996. Polymerase chain reaction detection of Lyme disease: correlation with clinical manifestations and serologic responses. *American journal of clinical pathology*, 105(5),

pp.647-54. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/8623775>

Oksi, J. et al., 1995. Antibodies against whole sonicated *Borrelia burgdorferi* spirochetes, 41-kilodalton flagellin, and P39 protein in patients with PCR- or culture-proven late Lyme borreliosis. *Journal of clinical microbiology*, 33(9), pp.2260-4. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=228390&tool=pmcentrez&rendertype=abstract>.

Tylewska-Wierzbanska, S. & Chmielewski, T., 2002. Limitation of serological testing for Lyme borreliosis: evaluation of ELISA and western blot in comparison with PCR and culture methods. *Wiener klinische Wochenschrift*, 114(13-14), pp.601-5. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/12422608>

Wojciechowska-Koszko, I. et al., 2011. Serodiagnosis of Borreliosis: Indirect Immunofluorescence Assay, Enzyme-Linked Immunosorbent Assay and Immunoblotting. *Archivum immunologiae et therapeuticae experimentalis*. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21258869>

JOD