Lyme disease despite treatment with antibiotics in humans:

Serum and CSF findings.

1. Serum

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<th>Authors</th>
<th>Text – Quotes</th>
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<tr>
<td>Duray PH, Steere AC. (1988) <a href="http://www.ncbi.nlm.nih.gov/pubmed/2847622">http://www.ncbi.nlm.nih.gov/pubmed/2847622</a></td>
<td>“All of these histologic derangements suggest immunologic damage in response to persistence of the spirochete, however few in number”.</td>
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<td>Preac-Mursic V, Weber K, Pfister HW, Wilske B, Gross B, Baumann A, Prokop J. (1989) <a href="http://www.ncbi.nlm.nih.gov/pubmed/2613324">http://www.ncbi.nlm.nih.gov/pubmed/2613324</a></td>
<td>“Patients may have subclinical or clinical disease without diagnostic antibody titers to B. burgdorferi. We conclude that early stage of the disease as well as chronic Lyme disease with persistence of B. burgdorferi after antibiotic therapy cannot be excluded when the serum is negative for antibodies against B. burgdorferi”.</td>
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<td>Cimmino MA, Azzolini A, Tobia F, Pesce CM. (1989) <a href="http://www.ncbi.nlm.nih.gov/pubmed/2910019">http://www.ncbi.nlm.nih.gov/pubmed/2910019</a></td>
<td>“Borrelia-like spirochetes were identified histologically in the spleen; this finding was consistent with persistence of B. burgdorferi organisms in inner organs in chronic Lyme disease”.</td>
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<td>Logigian EL, Kaplan RF, Steere AC. (1990) <a href="http://www.ncbi.nlm.nih.gov/pubmed/2172819">http://www.ncbi.nlm.nih.gov/pubmed/2172819</a></td>
<td>“At the time of examination, chronic neurologic abnormalities had been present from 3 months to 14 years, usually with little progression”.</td>
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<td>MacDonald AB, Berger BW, Schwan TG (1990) <a href="http://www.ncbi.nlm.nih.gov/pubmed/1980573">http://www.ncbi.nlm.nih.gov/pubmed/1980573</a></td>
<td>“The latency and relapse phenomena suggest that the Lyme disease spirochete is capable of survival in the host for prolonged periods of time. Some patients with Lyme borreliosis may require more than the currently recommended two to three week course of antibiotic therapy to eradicate strains of the spirochete which grow slowly”.</td>
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<td>Wahlberg P, Granlund H, Nyman D, Pannius J, Seppälä I. (1994) <a href="http://www.ncbi.nlm.nih.gov/pubmed/7884218">http://www.ncbi.nlm.nih.gov/pubmed/7884218</a></td>
<td>“Short periods of treatment were not generally effective.” “To conclude, we have shown that long-term treatments beginning with intravenous ceftriaxone and continuing with amoxycillin plus probenecid or with cephalorod in the treatment of late Lyme borreliosis.” (pp. 260-1)</td>
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<td>Lawrence C, Lipton RB, Lowy FD, Coyle PK (1995) <a href="http://www.ncbi.nlm.nih.gov/pubmed/7796837">http://www.ncbi.nlm.nih.gov/pubmed/7796837</a></td>
<td>“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&quot;. &quot;We believe this to be an example of a patient with chronic relapsing Bb infection&quot;.</td>
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<td>Sala-Lizarraga JA, Salcede-Vivo J, Ferris J, Lopez-Andreu JA (1995)</td>
<td><a href="http://www.lymeinfo.net/medical/LDPersist.pdf">http://www.lymeinfo.net/medical/LDPersist.pdf</a></td>
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<td>Preac Mursic V, Marjet B, Busch U, Pleterski Rigler D, Hagi S. (1996)</td>
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<td>Petrovic M, Vogelaers D, Van Reuck J, Afschrift M. (1998)</td>
<td><a href="http://www.ncbi.nlm.nih.gov/pubmed/9701852">http://www.ncbi.nlm.nih.gov/pubmed/9701852</a></td>
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<td>Mikkilä H, Karma A, Viljanen M, Seppälä I. (1999)</td>
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<td>Oksi J, Marjamäki M, Nikoskelainen J, Viljanen MK (1999)</td>
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<td>Honegr K (2001)</td>
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<td>Grignolo MC, Buffrini L, Monteforte P, Rovetta G. (2001)</td>
<td><a href="http://www.ncbi.nlm.nih.gov/pubmed/11317136">http://www.ncbi.nlm.nih.gov/pubmed/11317136</a></td>
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<td>Tylewska-Wierzbanska S, Chmielewski T.</td>
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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”.


DeLong AK, Blossom B, Maloney E, Phillips SE. (2012) http://www.ncbi.nlm.nih.gov/pubmed/22922244 “This biostatistical review reveals that retreatment can be beneficial. Primary outcomes originally reported as statistically insignificant were likely underpowered. The positive treatment effects of ceftriaxone are encouraging and consistent with continued infection, a hypothesis deserving additional study. Additional studies of persistent infection and antibiotic treatment are warranted”.

2. CSF (Commentary: http://www.praxis-berghoff.de/dokumente/Liquordiagnostik_bei_LNB.pdf)

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| Pfister HW (1989) http://www.ncbi.nlm.nih.gov/pubmed/2668788 | “Borrelia burgdorferi, the etiologic agent of Lyme borreliosis, was isolated from the CSF of a patient with elevated serum IgG antibody titers against B burgdorferi and a history of multiple tick bites. The absence of concurrent inflammatory signs of CSF as well as intrathecal antibody production indicates a phase of latent Lyme neuroborreliosis in which no tissue infection or reaction has yet occurred”.

| Steere AC (1990) http://www.ncbi.nlm.nih.gov/pubmed/2345301 | “Intrathecal antibody determinations are the most specific diagnostic test currently available for Lyme neuroborreliosis, but local antibody production in CSF is an inconsistent finding in American patients with late neurologic manifestations of the disorder”.

| Kaiser R (1993) http://www.ncbi.nlm.nih.gov/pubmed/8411090 | “Intrathecal synthesis of IgM antibodies to B. burgdorferi was demonstrated in patients with neuroborreliosis by sonicate ELISA in 20 of 35 samples, by flagellin ELISA in 16 of 35 samples and by 14-kDa ELISA in 9 of 35 samples”.

| Peter O. (1993) http://www.ncbi.nlm.nih.gov/pubmed/8421774 | “Isolation of Borrelia burgdorferi from the CSF is relatively rare. The present report describes the first three isolations in Switzerland. In neither of the two CSF could intrathecal synthesis of specific antibodies be demonstrated. In the third case, however, immunofluorescence showed IgG antibody titers of 1/128 in the CSF and 1/512 in serum”.

| Coyle PK (1995) http://www.ncbi.nlm.nih.gov/pubmed/7501150 | “B burgdorferi antigen can be detected in CSF that is otherwise normal by conventional methodology, and can be present without positive CSF antibody. Since CSF antigen implies intrathecal seeding of the infection, the diagnosis of neurologic infection by B burgdorferi should not be excluded solely on the basis of normal routine CSF or negative CSF antibody analyses”.

| Oksi J (1996) http://www.ncbi.nlm.nih.gov/pubmed/9010017 | “We conclude that cerebral lymphocytic vasculitis and multifocal encephalitis may be associated with B. burgdorferi infection. The presence of B. burgdorferi DNA in tissue samples from areas with inflammatory changes indicates that direct invasion of B. burgdorferi may be the pathogenetic mechanism for focal encephalitis in LNB”.

| Logigian EL et al. (1999) http://www.ncbi.nlm.nih.gov/pubmed/10395852 | “Months to years after classic manifestations of Lyme disease, the 18 patients presented with memory difficulty, minor depression, somnolence, or headache. Sixteen (89%) had abnormal memory scores; 16 (89%) had cerebrospinal fluid (CSF) abnormalities, and all 7 patients tested had frontotemporal perfusion defects on single photon emission computed tomographic (SPECT) imaging…. We conclude that Lyme encephalopathy can be treated successfully with ceftriaxone”.

| Honegr K (2001) http://www.ncbi.nlm.nih.gov/pubmed/11233667 | “In 18 patients with Lyme borreliosis the authors proved the persistence of Borrelia burgdorferi sensu lato by detection of the causal agent by immune electron microscopy or of its DNA by PGR in plasma or cerebrospinal fluid after an interval of 4-68 months. Clinical
manifestations common in Lyme borreliosis were present in only half the patients, in the remainder non-specific symptoms were found. In nine subjects with confirmed Borrelia burgdorferi sensu lato in the cerebrospinal fluid the cytological and biochemical finding was normal. Examination of antibodies by the ELISA method was negative in 7 of 18 patients during the first examination and in 12 of 18 during the second examination**.


Keller TL et al. (1992) PCR detection of Borrelia burgdorferi DNA in cerebrospinal fluid of Lyme neuroborreliosis patients. Neurology. 43, 32-42


Luft BJ et al. (1992) Invasion of the CNS by Bb in acute disseminated infection. JAMA 267, 1364-1367


Fallon BA et al. (1995) LateStage Neuropsychiatric Lyme Borreliosis. Case Reports. Psychosomatics. 36, 295-300


Bujak et al. (1996) Clinical and neurocognitive features of the post Lyme syndrome. J. Rheumatol 23, 1392-1397


Girschick HJ et al. (1996) Intracellular persistence of Borrelia burgdorferi in human synovial cells. Rheumatol Int. 16(3), 125-132


Donta ST (1997) Tetracycline therapy in chronic Lyme diseases. 25 (Suppl1) 552-556


Commentary: http://www.praxis-berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf


Steere et al. (2001) **Autoimmune mechanisms** in antibiotic treatment-resistant Lyme arthritis JAI. 16, 263-266


Raveche et al. (2005) Evidence of Borrelia **autoimmunity**-induced component of Lyme carditis and arthritis. J Clin Mikro 43, 850-856


„Bei der chronischen Lyme-Borreliose mit Encephalopathie sind die Liquorveränderungen selten und wenig ausgeprägt. Die Liquoruntersuchung in dieser Situation (chronische LB mit Encephalopathie) ist daher diagnostisch nicht hilfreich und somit nicht indiziert“.

Wormser GP, Shapiro ED, Halperin JJ et al. (2009) Analysis of a flawed double-blind, placebo-controlled, clinical trial of patients claimed to have persistent Lyme disease following treatment. Minerva Med 100(2), 171-172


Greco Jr TP, Conti-Kelly AM, Greco TP (2011) Antiphospholipid antibodies in patients with purported ‘chronic Lyme disease' Lupus 0, 1–6 [http://lup.sagepub.com/content/early/2011/07/05/0961203311414098](http://lup.sagepub.com/content/early/2011/07/05/0961203311414098)


Stricker R. (2012, pers. Mitteilung) “One of the benefits of doing C3a and C4a testing in a Lyme patient with positive ANA is that if the C3a is normal prior to antibiotic treatment, the patient is unlikely to have an autoimmune disease no matter how high the ANA titer is. Like the ANA, C4a is an inflammatory marker that can be high in any condition that involves inflammation.”


http://benthamscience.com/open/toneuj/articles/V006/SI0078TONEUJ/79TONEUJ.htm

Stricker RB, Johnson L (2012) Spirochetal 'debris' versus persistent infection in chronic Lyme disease: from semantics to science. Future Microbiol. 7(11), 1243–1246


"It is unclear whether our findings can be extrapolated to B. burgdorferi infections in vivo. It has been suggested that B. burgdorferi may be sequestered in protective niches during animal infection such that antibiotics might be less effective."

Unbound MEDLINE results for: borrelia persistence AND human  
http://www.unboundmedicine.com/medline?in=kw%257Cborrelia%2520persistence&in=jn%257C&in=au%257C

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