Persistence of Lyme Disease

The following references for persistence of Lyme disease (Lyme borreliosis) are listed alphabetically and chronologically:

1. Aalto A, Sjowall J, Davidsson L, Forsberg P, Smedby O. Brain magnetic resonance imaging does not contribute to the diagnosis of chronic neuroborreliosis. Acta Radiol 2007; 48: 755-762. [white matter hyperintensities or basal ganglia lesions].
knee for seven years, despite multiple antibiotic trials and synovectomies. Bb documented in synovium and synovial fluid.

19. Bayer ME, Zhang L, Bayer MH. *Borrelia burgdorferi* DNA in the urine of treated patients with chronic Lyme disease symptoms. A PCR study of 97 cases. Infection 1996; 24: 347-353. [97 patients who had been treated with antibiotics for extended periods of time and had symptoms of chronic Lyme were PCR-positive.]


25. Breier F, Khanakah G, Stanek G, Aberer E, Schmidt B, and Tappeiner G. Isolation and polymerase chain reaction typing of *Borrelia afzelii* from a skin lesion in a seronegative patient with generalized ulcerating bullous lichen sclerosus et atrophicus. Br J Dermatol 2001; 144: 387-392. [Despite treatment with four courses of ceftriaxone, “*s’pirochetes were isolated from skin cultures obtained from enlarging LSA lesion...[S]erology ...was repeatedly negative.”]


27. Brorson O and Brorson S-H. Transformation of cystic forms of *Borrelia burgdorferi* to normal mobile spirochetes. Infection. 1997; 25: 240-246. [change in physical characteristics; change of spirochetes to other pleomorphic forms, i.e., cell wall deficient forms, namely cysts.]

28. Brorson O and Brorson S. *In vitro* conversion of *Borrelia burgdorferi* to cystic forms in spinal fluid, and transformation to mobile spirochetes by incubation in BSK-H medium. Infection. 1998; 26: 144-150. [change in physical characteristics; change of spirochetes to other pleomorphic forms, i.e., cell wall deficient forms, namely cysts.]


44. Chmielewski T, Tylewlska-Wierzanowska S. Inhibition of fibroblast apoptosis by Borrelia afzelii, Coxiella burnetii and Bartonella henselae. Poll Microbiol 2011; 60(3); 269-272.


46. Cleveland CP, Dennler PS, Duray PH. Recurrence of Lyme disease presenting as a chest wall mass: Borrelia burgdorferi was present despite five months of IV ceftriaxone 2 g, and three months of oral cefixime 400 mg BID. The presence of Borrelia burgdorferi confirmed by biopsy and culture. Poster presentation at V Lyme Disease Foundation International Scientific Conference. Stamford, CT, April 10-11, 1992.


95. Häupl T, Hahn G, Rittig M, Krause A, Schoerner C, Schonherr U, Kalden JR, and Burmester GR. Persistence of *Borrelia burgdorferi* in ligamentous tissue from a patient with chronic Lyme borreliosis. Arthritis Rheum 1993; 36(11): 1621-1626. [Repeated antibiotic treatment necessary to stop the progression of disease but did not completely eliminate Bb from all sites of infection. Bb cultured from ligament sample; intracellular sanctuaries for Bb]


117. Lawrence C, Lipton RB, Lowy RD, and Coyle PK. Seronegative chronic relapsing neuroborreliosis. Eur Neurol 1995; 35(2): 113-117. [Patient’s CSF was positive for complex anti-Bb antibodies, B. burgdorferi nucleic acids and free antigen despite aggressive antibiotic therapy.]


122. Liegner KB, Shapiro JR, Ramsay D, Halperin AJ, Hogrefe W, and Kong L. Recurrent erythema migrans despite extended antibiotic treatment with minocycline in a patient with persisting Borrelia burgdorferi infection. J Am Acad Dermatol 1993; 28: 312-314. [Eleven months following treatment, T-cell stimulation test with Bb antigens were strongly positive; a year later, paired serum and CSF samples were strongly positive.]


127. Lawrence C, Lipton RB, Lowy RD, and Coyle PK. Seronegative chronic relapsing neuroborreliosis. Eur Neurol 1995; 35(2): 113-117. [Patient’s CSF was positive for complex anti-Bb antibodies, B. burgdorferi nucleic acids and free antigen despite aggressive antibiotic therapy.]


132. Liegner KB, Shapiro JR, Ramsay D, Halperin AJ, Hogrefe W, and Kong L. Recurrent erythema migrans despite extended antibiotic treatment with minocycline in a patient with persisting Borrelia burgdorferi infection. J Am Acad Dermatol 1993; 28: 312-314. [Eleven months following treatment, T-cell stimulation test with Bb antigens were strongly positive; a year later, paired serum and CSF samples were strongly positive.]


134. Livengood JA and Gilmore RD, Jr. Invasion of human neuronal and glial cells by an infectious strain of *Borrelia burgdorferi*. Microbes and Infection. 2006; 8: 2832-2840. [intracellular sanctuaries of Bb]


143. Lyme Disease Foundation. The controversies surrounding Lyme disease diagnosis and treatment and why it is not uncommon for patients to experience persistent symptoms despite receiving conventional (short-term) antibiotic therapy for Lyme disease. www.lyme.org/lymelight/trtcontrov.html


152. MacDonald AB. Alzheimer’s neuroborreliosis with trans-synaptic spread of infection and neurofibrillary tangles derived from intraneuronal spirochetes. Med Hypotheses 2007; 68: 822-825. [7 of 10 cases of Alzheimer’s disease had *B. burgdorferi* in their brains].


162. Masters EJ, Lynxwiler P, and Rawlings J. Spirochetemia after continuous high-dose oral amoxicillin therapy. Infect Dis Clin Practice 1995; 3: 207-208. [Following six months of treatment, patient relapsed and Bb was cultured from blood.]

163. Mattman LH. Cell wall deficient forms: stealth pathogens. 2nd edition. CRC Press, Inc., Boca Raton, FL. 1993. [change in physical characteristics; change of spirochetes to other pleomorphic forms, i.e., cell wall deficient forms, namely cysts.]


167. Miklossy J, Gern L, Darekar P, Janzer RC, Loos H. Senile plaques, neurofibrillary tangles and neuropil threads contain DNA? J Spirchetal and Tick-borne Dis 1995; 2: 1-5. [Spirochetes were observed in the


174. Miklossy, J. 2011. Alzheimer's disease—a neurospirochetosis. Analysis of the evidence following Koch's and Hill's criteria. Journal of Neuroinflammation 8:90. [Spirochetes were observed in the
brain in more that 90% of Alzheimer’s disease. Persistence occurs when spirochetes change physical characteristics by converting to dormant cysts.]

176. Miklossy, J. 2011. Alzheimer’s disease – a neurospirochetosis. Analysis of the evidence following Koch’s and Hill’s criteria. 2011; 8: 90 (http://www.jneuroinflammation.com/content/8/1/90) [91% of Alzheimer’s patients sampled were positive for spirochetes; 25% of Alzheimer’s patients analyzed had B. burgdorferi spirochetes in their brains]


191. Oksi J, Marjamäki M, Nikoskelainen J, and Viljanen MK. Borrelia burgdorferi detected by culture and PCR in clinical relapse of disseminated Lyme borreliosis. Ann Med 1999; 31(3): 225-232. [40% (13% of 32) patients had clinical relapses that were PCR or culture-fonfirmed.]


202. Pfister HW, Preac Mursic V, Wilske B, Schielke E, Sorgel F, Einhaupl KMJ. Randomized comparison of ceftriaxone and cefotaxime in Lyme neuroborreliosis. Infect Dis 1991; 163(2): 311-318. [In one patient, Bb as isolated from the cerebrospinal fluid 7.5 months after ceftriaxone therapy and, thus, showing that extended therapy is necessary.]


205. Phillips SE, Burrascano JJ, Wilske B, Schier G, Sorgel F, Ehinaulp KMJ. Randomized comparison of ceftriaxone and cetoaxime in Lyme neuroborreliosis. Infect Dis 1991; 163(2): 311-318. [In one patient, Bb as isolated from the cerebrospinal fluid 7.5 months after ceftriaxone therapy and, thus, showing that extended therapy is necessary.]


212. Preac Mursic V, Marjet W, Busch U, Rigler DP, Hagl S. Kill kinetics of *Borrelia burgdorferi* and bacterial findings in relation to the treatment of Lyme borreliosis. *Infection* 1996; 24(1): 9-16. [Bb was isolated by culture in five patients, four of whom had previously tested antibody-negative.]

213. Priem S, Burmester GR, Kamradt T, Wolbart K, Rittig MG, and Krause A. Detection of *Borrelia burgdorferi* by polymerase chain reaction in synovial membrane, but not in synovial fluid from patients with persisting Lyme arthritis after antibiotic therapy. *Ann Rheum Dis* 1998; 57(2): 118-121. [After antibiotic treatment, synovial membrane still demonstrates spirochetes.][Although PCR was negative in synovial fluid and urine, PCR confirmed Bb in synovial membrane of four previously treated patients with Lyme arthritis; intracellular sanctuaries of Bb]


239. Straubinger RK, Straubinger AF, Jacobson RH, Chang Y, Summers BA, Erb HN, and Appel MJG. Two lessons from the canine model of Lyme disease: migration of *Borrelia burgdorferi* in tissues and persistence after antibiotic treatment. J Spiir Tick-Borne Dis 1997; 4: 24-31. [In dogs: 30-day treatment diminished but failed to eliminate persistent infection in dogs. Antibody titers fell, but after antibiotic treatment was discontinued antibody levels began to rise again, presumably in response to proliferation of the surviving pool of spirochetes.]


242. Straubinger RK. PCR-based quantification of *Borrelia burgdorferi* organisms in canine tissues over a 500-day postinfection period. J Clin Microbiol 2000; 38: 2191-2199. [All 8 infected dogs previously treated with 30-day antibiotics were PCR positive from tissue samples after necrosis; 25 tissue samples per dog were used.]


271. Yrjänäinen H, Hytönen J, Hartiala P, Oksi J, Viljanen MK. APMIS 2010;118(9): 665-673. [Borrelia burgdorferi DNA in joints and tissue adjacent to the joint is the niche of persisting B. burgdorferi in ceftriaxone-treated mice.]


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