

Borrelien Behandlung mit Antibiotika bei Menschen
Lyme disease treatment with antibiotics in humans
Bei Tieren. In Animals: <http://www.erlebnishaft.de/trotzantibiosetier.pdf>

[Adeolu M, Gupta RS.](#) (2014) **A phylogenomic and molecular marker based proposal for the division of the genus Borrelia into two genera:** the emended genus Borrelia containing only the members of the relapsing fever Borrelia, and the genus Borreliella gen. nov. containing the members of the Lyme disease Borrelia (Borrelia burgdorferi sensu lato complex). [Antonie Van Leeuwenhoek.](#) <http://www.ncbi.nlm.nih.gov/pubmed/24744012>

„The genus Borrelia contains two groups of organisms: the causative agents of Lyme disease and their relatives and the causative agents of relapsing fever and their relatives. These two groups are morphologically indistinguishable and are difficult to distinguish biochemically. In this work, we have carried out detailed comparative genomic analyses on protein sequences from 38 Borrelia genomes to identify molecular markers in the forms of conserved signature inserts/deletions (CSIs) that are specifically found in the Borrelia homologues, and conserved signature proteins (CSPs) which are uniquely present in Borrelia species. Our analyses have identified 31 CSIs and 82 CSPs that are uniquely shared by all sequenced Borrelia species, providing molecular markers for this group of organisms. In addition, our work has identified 7 CSIs and 21 CSPs which are uniquely found in the Lyme disease Borrelia species and eight CSIs and four CSPs that are specific for members of the relapsing fever Borrelia group. Additionally, 38 other CSIs, in proteins which are uniquely found in Borrelia species, also distinguish these two groups of Borrelia. The identified CSIs and CSPs provide novel and highly specific molecular markers for identification and distinguishing between the Lyme disease Borrelia and the relapsing fever Borrelia species. We also report the results of average nucleotide identity (ANI) analysis on Borrelia genomes and phylogenetic analysis for these species based upon 16S rRNA sequences and concatenated sequences for 25 conserved proteins. These analyses also support the distinctness of the two Borrelia clades. On the basis of the identified molecular markers, the results from ANI and phylogenetic studies, and the distinct pathogenicity profiles and arthropod vectors used by different Borrelia spp. for their transmission, we are proposing a division of the genus Borrelia into two separate genera: an emended genus Borrelia, containing the causative agents of relapsing fever and a novel genus, Borreliella gen. nov., containing the causative agents of Lyme disease.“

[Huismans BD](#) (2014) **Defense and escape mechanisms of Borrelia against the human immune system and against antibiotics and chemotherapeutics.** http://www.xerlebnishaft.de/escape_eng.pdf

[Maloney EL](#) (2016) **Controversies in Persistent (Chronic) Lyme Disease.** *J Infus Nurs.* 39(6), 369-375. <https://www.ncbi.nlm.nih.gov/pubmed/27755213>
« This paper discusses the medical controversies related to posttreatment manifestations and their potential impact on infusion nurses. »

[Stone BL, Tourand Y, Brissette CA](#) (2017) **Brave New Worlds: The Expanding Universe of Lyme Disease.** *Vector Borne Zoonotic Dis.* 17(9), 619-629. doi: 10.1089/vbz.2017.2127. Epub 2017 Jul 20. <https://www.ncbi.nlm.nih.gov/pubmed/28727515>

[Bernard Q, Smith AA, Yang X et al](#) (2018) **Plasticity in early immune evasion strategies of a bacterial pathogen.** *PNAS.* 201718595; published ahead of print April 2, 2018. <https://doi.org/10.1073/pnas.1718595115> <http://www.pnas.org/content/early/2018/03/28/1718595115>

Borrelia burgdorferi sensu lato strains

NCBI Taxonomy Borrelia (2014) <http://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=138>

- ➔ **Immunitaet** http://www.erlebnishaft.de/danger_model.pdf
- ➔ **Gen Dynamik** http://www.xerlebnishaft.de/gen_dynamik.pdf
- ➔ **Bakterielle Stressvarianten** <http://www.erlebnishaft.de/stressvar1.pdf>
- ➔ **Borrelien Populationsdynamik** <http://www.erlebnishaft.de/stressvar2.pdf>
- ➔ **Henle-Koch Postulate erweitert** http://www.xerlebnishaft.de/expand_koch_post.pdf

- ➔ **Zytoskelett** <http://www.xerlebnishaft.de/zytoskelett.pdf>
- ➔ **Symbiogenese** <http://www.erlebnishaft.de/symbiogenese.pdf>

Chronische Krankheitsverläufe, chronic diseases:

Levy Körper – [M. Parkinson](#)

Amyloide Plaques – [M. Alzheimer](#)

Elementarkörper (EK) – [Chlamydia pneumoniae](#) und [Arteriosklerose](#)

Spheroide neuronale Einschlusskörper * – [Amyotrophe Lateralsklerose](#)

Bakterien – Granulate Stau ? – [Chronische Borreliose](#) ([Huismans dt.](#), [engl.](#), 2007, 2014)

Karzinome und Sarkome, neoplasms:

Blasen und Granulate – [Karzinome und Sarkome](#) ([Enby E.](#) 1984, 1989)

Nicole Ch, Lebailly Ch (1919) **l'étude des infections inapparentes**, comme le typhus de certains cobayes ou du rat. **Untersuchung von inapparenten Infektionen** wie dem Typhus bestimmter Meerschweinchen oder Ratten.

Steere AC, Malawista SE, Hardin JA; Ruddy S (1977) **Erythema chronicum migrans and Lyme arthritis. The enlarging clinical spectrum.** Annals of Internal Med, 86, 685-98

« We remain skeptical that antibiotic therapy helps... Eight of our patients received penicillin, erythromycin, or cephalexin before Askenase PW; entering the study because of the skin lesion. In one of them, the lesion persisted for 2 months despite therapy, longer than in Andiman WA. any of the other study patients, and seven of the eight patients still developed joint, neurologic, or cardiac abnormalities.“

[Holt SC](#) (1978) **Anatomy and chemistry of spirochetes.** *Microbiol Rev.* 42(1), 114–160. PMID: PMC281421 PMID: [379570](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC281421/) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC281421/>

Schmidli J, Hunziker T, Moesli Pet al. (1988) **Cultivation of Borrelia burgdorferi from joint fluid three months after treatment of facial palsy due to Lyme borreliosis.** J Inf Dis, 158, 905-906

“This positive culture strongly suggests that the spirochetes were not eradicated by the initial antimicrobial regimens [12 days amoxicillinclavulanate followed by two weeks of doxycycline, 200 mg/d].“

Preac-Mursic V, Weber K, Pfister HW, Wilske B et al. (1989) **Survival of Borrelia burgdorferi in antibioticly treated patients with Lyme borreliosis.** Infection, 17(6), 355-9

“However, some patients later developed symptoms of the disease despite antibiotic treatment Because of these observations it has become questionable if a definite eradication of B. burgdorferi with antibiotics is possible. ... It seems appropriate to treat patients with substantially larger doses of antibiotics and/or longer than is provided in present treatment Regimens. ... As shown, negative antibody-titers do not provide evidence for successful therapy; antibody-titers may become negative despite persistence of B. burgdorferi.”

Logigian EL, Kaplan RF; **Steere AC** (1990) **Chronic neurologic manifestations of Lyme disease.** NEJM, 323(21), 1438-44

« The likely reason for relapse is failure to eradicate the spirochete.....This is reminiscent of far advanced neurosyphilis..... This last article is one of many studies that show continuing symptoms are most likely due to persistence of the spirochete.”

MacDonald AB, Berger BW; Schwan TG (1990) **Clinical implications of delayed growth of the Lyme borreliosis spirochete Borrelia burgdorferi.** Borrelia Acta Trop, 48(2), 89-94

“ 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.”

Harden VA (1990) Rocky Mountain spotted fever: history of a twentieth century disease, The Henry E. Sigerist Series in the History of Medicine, Baltimore and London, The Johns Hopkins University Press, 8vo, pp. xvi, 375, illus.

Pfister HW, Preac-Mursic V, Wilske B, Schielke E, Sorgel F, Einhaupl KM (1991) **Randomized comparison of ceftriaxone and cefotaxime in Lyme neuroborreliosis.** J Inf Dis, 163(2), 311-8

«The authors conclude that “a prolongation of therapy may be necessary.”

Georgilis K, Peacocke M, Klempner MS (1992) Fibroblasts protect the Lyme disease spirochete, *Borrelia burgdorferi*, from ceftriaxone in vitro. *J Infect Dis* 166, 440-444

<http://www.ncbi.nlm.nih.gov/pubmed/1634816>

“The Lyme disease spirochete, *Borrelia burgdorferi*, can be recovered long after initial infection, even from antibiotic-treated patients, indicating that it resists eradication by host defense mechanisms and antibiotics. .. Fibroblasts protected *B. burgdorferi* for at least 14 days of exposure to ceftriaxone. .. Thus, several eukaryotic cell types provide the Lyme disease spirochete with a protective environment contributing to its long-term survival. »

Liegner KB, Shapiro JR, Ramsay D et al. (1993) **Recurrent erythema migrans despite extended antibiotic treatment with minocycline in a patient with persisting *Borrelia burgdorferi* infection.** *JAMACAD Dermatol* 28, 312-4

«Further treatment with minocycline led to resolution of erythema migrans.»

Brett Finlay B, McFadden G (2006) **Anti-Immunology: Evasion of the Host Immune System by Bacterial and Viral Pathogens.** *Cell* 124, 767-782

<https://www.hu.liu.se/lakarprogr/t2/t2-filer/1.260321/LottaDahleGrupp13och18ImmunevasionCellReviewJE.pdf>

“In this review, we highlight and compare some of the many molecular mechanisms that bacterial and viral pathogens use to evade host immune defenses.”

Kroun M (2007) **Microscopy, Culture or PCR-verified cases of persistent [seronegative] Lyme Borreliosis.** <http://lymerick.net/persistent-borreliosis.htm>

Phillips S (2009) **Active Infection: Clinical Definitions and Evidence of Persistence in Lyme Disease—Contesting the Underlying Basis for Treatment Limitations for Early and Late Lyme Disease, as well as Chronic Lyme Disease, Alternatively Known as “Post-Lyme Disease Syndrome”.**

<https://www.semanticscholar.org/paper/Active-Infection%3A-Clinical-Definitions-and-Evidenc-Phillips-Phillips/e0e7b325043fa56ecf0c40e46aa110eb1c983>

Huismans BD (2011) **Diagnosis and Treatment of Lyme Disease and Co-Infections in terms of Eberth-Koch's bacterial variants (L-forms, Cell Wall Defective forms, CWD's) and bio-films.** *Medical hypotheses.* <http://www.wv.wvarchiv.de/wwwarchiv/anfang/texte/Eberth%20Biofilme%20eng.pdf>
http://www.xerlebnishaft.de/eberth_biofilme.pdf

Embers ME, Barthold SW, Borda JT, Bowers L, Doyle L, Hodzic E et al. (2012) *LoS One*, 7(1), e29914. 2012.

“[Our] results challenge prevailing dogma about [the] effectiveness of antibiotics for eliminating *B. burgdorferi* infection... spirochetes persisted in sites where they encountered the antibiotic.”

Embers M (2012) **The Pathogenic Spirochetes: strategies for evasion of host immunity and persistence.** http://books.google.de/books?id=peL0ZM7wu3MC&pg=PA190&lpg=PA190&dq=Tick-borne+Relapsing+Fever+and+Borrelia+hermsii,+Los+Angeles+County,+California,+USA&source=bl&ots=D3oBp4Bq14&sig=A19huo-u8ia9YsOzYDKq6o6Stic&hl=de&sa=X&ei=VasrVMazl42sOv_2gOgP&ved=0CDQQ6AEwAg#v=onepage&q=Tick-borne%20Relapsing%20Fever%20and%20Borrelia%20hermsii%2C%20Los%20Angeles%20County%2C%20California%2C%20USA&f=false

<http://www.amazon.de/The-Pathogenic-Spirochetes-strategies-persistence/dp/1461454034>

“This book explores the many mechanisms by which the most prevalent Spirochetal pathogens persist in a healthy immune-competent host. Among them are the direct and indirect suppression of host immune signals, phase and antigenic variation, escaping recognition by host complement proteins, and seclusion into immune privileged sites. We also explore antibiotic therapy for control of infection, a baffling topic that lends itself to exalted interpretation. »

➔ **Persistence of Lyme Disease Despite Antibiotic Treatment. 77 Peer-Reviewed Studies, 1977-2012**

https://www.google.de/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwiq9Jfd_bPZAhUoKcAKHRIHBpUQFggzMAA&url=http%3A%2F%2Fwww.kentuckyindianalymesupport.org%2Fwp-content%2Fuploads%2F2012%2F11%2FLDPersist77studies.pdf&usq=AOvVaw2c-aM74KAd0MsTJ5AwGII6

Berndtson K (2013) **Review of evidence for immune evasion and persistent infection in Lyme disease.** *Int J. Gen Med.* 6, 291-306. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3636972/>

„This review describes known and suspected mechanisms by which spirochetes of the *Borrelia* genus evade host immune defenses and survive antibiotic challenge. Accumulating evidence indicates that

Lyme disease spirochetes are adapted to persist in immune competent hosts, and that they are able to remain infective despite aggressive antibiotic challenge. »

Berghoff W (2014) **Abwehrmechanismen von Borrelia burgdorferi (Bb) gegenüber dem humanen Immunsystem.** http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-b_Abwehrmechanismen_von_Bb.pdf

Berghoff W (2014) **Abwehr der Antibiose durch Bb.** http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-a_Abwehr_der_Antibiose_durch_Bb.pdf

Marques A, Hu LT et al. (2014) **Xenodiagnosis to detect Borrelia burgdorferi infection: a first-in-human study.** Clin Infect Dis. 58(7), 937-45.

Huismans BD (2014) **Abwehr- und Escape- Mechanismen der Borrelien gegen das menschliche Immunsystem und gegenüber Antibiotika und Chemotherapeutika.** Warum Borrelien infektiös bleiben trotz intensiver antibiotischer Behandlung. <http://www.xerlebnishaft.de/escape.pdf>

Huismans BD (2014) **Defense and escape mechanisms of Borrelia against the human immune system and against antibiotics and chemotherapeutics. Why Borrelia remains infectious despite intensive antibiotic treatment.** http://www.xerlebnishaft.de/escape_eng.pdf

Perronne C (2014) **Lyme and associated tick-borne diseases: global challenges in the context of a public health threat. Global challenges of Lyme disease.** Front. Cell. Infect. Microbiol. 4, 74. doi: 10.3389/fcimb.2014.00074 <http://journal.frontiersin.org/Journal/10.3389/fcimb.2014.00074/full>

Stricker RB, **Johnson** L (2014) **Lyme Disease: Call for a “Manhattan Project” to Combat the Epidemic.** PLoS Pathog 10(1): e1003796. doi:10.1371/journal.ppat.1003796 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3879353/>

Shapiro ED (2015) **Repeat or persistent Lyme disease: persistence, recrudescence or reinfection with Borrelia Burgdorferi?** F1000Prime Rep. 7, 11. doi: 10.12703/P7-11. eCollection 2015. [http://www.ncbi.nlm.nih.gov/pubmed/25705394?log\\$=activity](http://www.ncbi.nlm.nih.gov/pubmed/25705394?log$=activity)

«There continues to be no evidence that viable B. burgdorferi persist in humans after conventional treatment with antimicrobials. «

PubMed Commons :

Stricker B (2015) [http://www.ncbi.nlm.nih.gov/pubmed/25705394?log\\$=activity](http://www.ncbi.nlm.nih.gov/pubmed/25705394?log$=activity)

« In summary, this one-sided opinion piece will only add to the confusion and misinformation surrounding Lyme disease. With better testing and novel treatments, a solution to this tickborne disease will someday be found. Shapiro's muddled article fails to contribute to this solution.“

Rescigno M (2015) **Dendritic cell functions: Learning from microbial evasion strategies.** Semin Immunol. 27(2), 119-24 <https://www.ncbi.nlm.nih.gov/pubmed/25843245>

„In this review we will mention several mechanisms employed by pathogens to evade [Dendritic celle] DCs patrolling function.“

Baker PJ, **Wormser GP** (2017) **The Clinical Relevance of Studies on Borrelia burgdorferi Persisters,** The American Journal of Medicine, doi: 10.1016/j.amjmed.2017.04.014.

« It cannot be over emphasized that the complete elimination of infection is seldom used as the benchmark for success in the treatment of other infectious diseases. Resolution of the objective manifestations of the infection and lack of relapse, rather than the complete elimination of viable bacteria, are of primary concern. Experience with latent tuberculosis has been highly instructive in providing evidence that persistence per se causes no symptoms, and if latent disease becomes active it is associated with a site of inflammation. »

Freyberg Z, Harvill ET (2017) **Pathogen manipulation of host metabolism: A common strategy for immune evasion.** PLoS Pathog 13(12): e1006669. <https://doi.org/10.1371/journal.ppat.1006669> <http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006669>

„The manipulation of the host's metabolic state may not only affect the immune response to the respective causative pathogen but also to additional opportunistic infections, further compounding morbidity and mortality associated with infection. On the other hand, treating the metabolic manifestations of infection, including hyperinsulinemia and hypoglycemia, may potentially blunt or ameliorate the disease course of these pathogens and could be implemented relatively quickly, safely, and inexpensively to make a difference in the lives of many affected people globally. »

Huismans BD (2018) **Chronic Inflammatory Disorders. Multisystem diseases caused by pathogens.** http://www.kabilahsystems.de/ko-erreg_eupd1.pdf

- ➔ **Borrelien Populations – Dynamik** <http://www.erlebnishaft.de/stressvar2.pdf>
- ➔ **Gen – Dynamik** http://www.xerlebnishaft.de/gen_dynamik.pdf
- ➔ **Bakterielle Stressvarianten** <http://www.erlebnishaft.de/stressvar1.pdf>

Serum und Liquor. Serum and CSF findings.

1. Serum

Gelb. Yellow IDSA Autoren. IDSA Autors
Grün. Green ILADS Autoren. ILADS Autors

Autoren	Text – Aussagen
Duray PH, Steere AC. (1988) http://www.ncbi.nlm.nih.gov/pubmed/2847622	“All of these histologic derangements suggest immunologic damage in response to persistence of the spirochete, however few in number”.
Dattwyler RJ, Volkman DJ, Luft BJ, Halperin JJ, Thomas J, Golightly MG. (1988) http://www.ncbi.nlm.nih.gov/pubmed/2847622	„We conclude that the presence of chronic Lyme disease cannot be excluded by the absence of antibodies against B. burgdorferi and that a specific T-cell blastogenic response to B. burgdorferi is evidence of infection in seronegative patients with clinical indications of chronic Lyme disease”.
Preac-Mursic V, Weber K, Pfister HW, Wilske B, Gross B, Baumann A, Prokop J. (1989) http://www.ncbi.nlm.nih.gov/pubmed/2613324	“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”.
Cimmino MA, Azzolini A, Tobia F, Pesce CM. (1989) http://www.ncbi.nlm.nih.gov/pubmed/2910019	“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”.
Logigian EL, Kaplan RF, Steere AC. (1990) http://www.ncbi.nlm.nih.gov/pubmed/2172819	“At the time of examination, chronic neurologic abnormalities had been present from 3 months to 14 years, usually with little progression”.
MacDonald AB, Berger BW, Schwan TG (1990) http://www.ncbi.nlm.nih.gov/pubmed/1980573	“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”.
Pfister HW, Preac-Mursic V, Wilske B et al. (1991) http://www.ncbi.nlm.nih.gov/pubmed/1988514	“In this prospective, randomized, open trial, 33 patients with Lyme neuroborreliosis were assigned to a 10-day treatment with either ceftriaxone, 2 g intravenously (iv) every 24 h (n = 17), or cefotaxime, 2 g iv every 8 h (n = 16). Of the 33 patients, 30 were eligible for analysis of therapeutic efficacy.... In one patient Borrelia burgdorferi was isolated from the cerebrospinal fluid (CSF) 7.5 months after ceftriaxone therapy. CSF antibiotic concentrations were above the MIC 90 level for B. burgdorferi in nearly all patients examined. ...However, as 10 patients were symptomatic at follow-up and borreliae persisted in the CSF of one patient, a prolongation of therapy may be necessary”.
Banyas GT. (1992) http://www.ncbi.nlm.nih.gov/pubmed/1583267	“At present, seronegativity in persons strongly suspected of having Lyme disease does not necessarily exclude the diagnosis of Lyme disease. The clinician must recognize this in patients who may have Lyme disease or a recurrence of the disease”.
Liegner KB, Shapiro JR, Ramsay D, Halperin JJ, Hogrefe W, Kong L. (1993) http://www.ncbi.nlm.nih.gov/pubmed/8436647	“The patient was seronegative by Lyme enzymelinked immunosorbent assay but showed suspicious bands on Western blot. Findings of a Warthin-Starry stain of a skin biopsy specimen of the eruption revealed a Borrelia-compatible structure”.

Hulínská D, Krausová M, Janovská D, Roháčová H, Hancil J, Mailer H. (1993) http://www.ncbi.nlm.nih.gov/pubmed/8004045	"Results of studies using direct antigen detection suggest that seronegative Lyme borreliosis is not rare and support the hypothesis that <i>Borrelia</i> antigens can persist in humans".
Preac-Mursic V, Pfister HW, Spiegel H, Burk R, Wilske B, Reinhardt S, Böhmer R. (1993) http://www.ncbi.nlm.nih.gov/pubmed/8106639	"Persistence of <i>B. burgdorferi</i> cannot be excluded when the serum is negative for antibodies against it."
Battafarano DF, Combs JA, Enzenauer RJ, (1993) http://www.ncbi.nlm.nih.gov/pubmed/8242938	"... A patient had chronic septic Lyme arthritis of the knee for seven years despite multiple antibiotic trials and multiple arthroscopic and open synovectomies. Spirochetes were documented in synovium and synovial fluid (SF). Polymerase chain reaction (PCR) analysis of the SF was consistent with <i>Borrelia</i> infection. Persistent infection should be excluded with silver stains and cultures in any patient with chronic monoarticular arthritis and a history of Lyme disease".
Haupt T, Hahn G, Rittig M et al. (1993) http://www.ncbi.nlm.nih.gov/pubmed/8240439	"... Despite antibiotic therapy, there was progression to a chronic stage, with multisystem manifestations. ... Viable spirochetes were identified. Ultramorphologically, the spirochetes were situated between collagen fibers and along fibroblasts, some of which were deeply invaginated by these organisms. The cultured bacteria were identified as <i>B. burgdorferi</i> by reactions with specific immune sera and monoclonal antibodies, and by polymerase chain reaction amplification and Southern blot hybridization techniques".
Nocton JJ, Dressler F, Rutledge BJ et al. (1994) http://www.ncbi.nlm.nih.gov/pubmed/8272083	"Of 73 patients with Lyme arthritis that was untreated or treated with only short courses of oral antibiotics, 70 (96 percent) had positive PCR results. In contrast, of 19 patients who received either parenteral antibiotics or long courses of oral antibiotics (> or = 1 month), only 7 (37 percent) had positive tests ($P < 0.001$)".
Shadick NA, Phillips CB, Logigian EL, Steere AC, Kaplan RF, Berardi VP, Duray PH, Larson MG, Wright EA, Ginsburg KS, Katz JN, Liang MH (1994) http://www.ncbi.nlm.nih.gov/pubmed/8085687	"Persons with a history of Lyme disease have more musculoskeletal impairment and a higher prevalence of verbal memory impairment when compared with those without a history of Lyme disease. Our findings suggest that disseminated Lyme disease may be associated with longterm Morbidity".
Wahlberg P, Granlund H, Nyman D, Panelius J, Seppälä I. (1994) http://www.ncbi.nlm.nih.gov/pubmed/7884218	"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 cephadroxil were useful in the treatment of late Lyme borreliosis." (pp. 260-1)
Lawrence C, Lipton RB, Lowy FD, Coyle PK (1995) http://www.ncbi.nlm.nih.gov/pubmed/7796837	"Although the patient never had detectable free antibodies to <i>B. burgdorferi</i> in serum or spinal fluid, the CSF was positive on multiple occasions for complexed anti- <i>B. burgdorferi</i> antibodies, <i>B. burgdorferi</i> nucleic acids and free antigen". "We believe this to be an example of a patient with chronic relapsing <i>Bb</i> infection".
Waniek C, Prohovnik I, Kaufman MA, (1995) http://www.ncbi.nlm.nih.gov/pubmed/7580195	"LD must be considered even in cases with purely psychiatric presentation, and prolonged antibiotic therapy may be necessary".
Sala-Lizarraga JA, Salcedo-Vivo J, Ferris J, Lopez-Andreu JA (1995) http://www.lymeinfo.net/medical/LDPersist.pdf	"We add, however, in accord with the advice of others that antibiotics should be continued in the long term, until we achieve cure or delay the progression of the disease."
Nanagara R, Duray PH, Schumacher HR Jr. (1996) http://www.ncbi.nlm.nih.gov/pubmed/8892586	"Electron microscopy [...] adds further evidence for persistence of spirochetal antigens in the joint in chronic Lyme disease. Spirochaetes may elude host immune response and antibiotic treatment. High-dose parenteral antibiotics, or combination therapies with long duration may be needed to kill the living spirochetes." (p.1032)
Preac Mursic V, Marget W, Busch U, Pleterski Rigler D, Hagl S. (1996) http://www.ncbi.nlm.nih.gov/pubmed/8852456	"Furthermore, the persistence of <i>B. burgdorferi</i> s.l. and clinical recurrences in patients despite seemingly adequate antibiotic treatment is described. The patients had clinical disease with or without diagnostic antibody titers to <i>B. burgdorferi</i> ".
Bayer ME, Zhang L, Bayer MH. (1996) http://www.ncbi.nlm.nih.gov/pubmed/8923044	The presence of <i>Borrelia burgdorferi</i> DNA was established by PCR from urine samples of 97 patients clinically diagnosed as presenting with symptoms of chronic Lyme

	disease. All patients had shown erythema chronica migrans following a deer tick bite. Most of the patients had been antibiotic-treated for extended periods of time.
Petrovic M, Vogelaers D, Van Renterghem L, Carton D, De Reuck J, Afschrift M (1998) http://www.ncbi.nlm.nih.gov/pubmed/9701852	"Difficulties in diagnosis of late stages of Lyme disease include low sensitivity of serological testing and late inclusion of Lyme disease in the differential diagnosis. Longer treatment modalities may have to be considered in order to improve clinical outcome of late disease stages. Several aspects of late borreliosis: false negative serology due to narrow antigen composition of the used ELISA format, the need for prolonged antibiotic treatment in chronic or recurrent forms".
Mikkilä H, Karma A, Viljanen M, Seppälä I. (1999) http://www.ncbi.nlm.nih.gov/pubmed/10090586	"For efficient diagnosis of ocular Lyme borreliosis, immunoblot analysis and PCR should be used in addition to ELISA. A positive PCR seems to be associated with a negative immunoblot".
Oksi J, Marjamäki M, Nikoskelainen J, Viljanen MK (1999) http://www.ncbi.nlm.nih.gov/pubmed/10442678	"The response to retreatment was considered good in nine patients. We conclude that the treatment of Lyme borreliosis with appropriate antibiotics for even more than 3 months may not always eradicate the spirochete".
Phillips SE, Mattman LH, Hulínská D, Moayad H. (1998) http://www.ncbi.nlm.nih.gov/pubmed/9861561	"This new method for culturing B. burgdorferi from patients with chronic Lyme disease certainly defines the nature of the illness and establishes that it is of chronic infectious etiology".
Logigian EL et al. (1999) http://www.ncbi.nlm.nih.gov/pubmed/10395852	"We conclude that Lyme encephalopathy can be treated successfully with ceftriaxone". Kommentar: http://www.praxis-berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf
Breier F, Khanakah G, Stanek G, Kunz G, Aberer E, Schmidt B, Tappeiner G (2001) http://www.ncbi.nlm.nih.gov/pubmed/11251580	"Despite treatment with four courses of ceftriaxone with or without methylprednisone for up to 20 days, progression of LSA was only stopped for a maximum of 1 year. Spirochaetes were isolated from skin cultures obtained from enlarging LSA lesions. These spirochaetes were identified as Borrelia afzelii by sodium dodecyl sulphate-polyacrylamide gel electrophoresis and polymerase chain reaction (PCR) analyses. However, serology for B. burgdorferi sensu lato was repeatedly negative. These findings suggest a pathogenetic role for B. afzelii in the development of LSA and a beneficial effect of appropriate antibiotic treatment".
Klempner MS, Hu LT, Evans J, et al. (2001) http://www.ncbi.nlm.nih.gov/pubmed/11450676	Kommentar: http://www.praxis-berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf
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 PCR 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".
Grignolo MC, Buffrini L, Monteforte P, Rovetta G. (2001) http://www.ncbi.nlm.nih.gov/pubmed/11317136	"..true positives at clinical examination but negatives at serologic tests. The obtained results suggested a good reliability of positive results obtained with the PCR technique used in this study".
Tylewska-Wierzbanowska S, Chmielewski T. (2002) http://www.ncbi.nlm.nih.gov/pubmed/12422608	"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 ".
Kaplan R et al. (2003)	Kommentar: http://www.praxis-berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf

http://www.ncbi.nlm.nih.gov/pubmed/12821733	berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf
Krupp LB, Hyman LG, Grimson R, et al. (2003) http://www.ncbi.nlm.nih.gov/pubmed/12821734	Kommentar: http://www.praxis-berghoff.de/dokumente/Behandlungsparameter_der_Neuroborreliose.pdf
Diterich I, Rauter C, Kirschning CJ, Hartung T. (2003) http://www.ncbi.nlm.nih.gov/pubmed/12819085	„It was recently reported that Borrelia suppresses the host's immune response, thus perhaps preventing the elimination of the pathogen (I. Diterich, L. Härter, D. Hassler et al, Infect. Immun. 69:687-694, 2001)“
Kroun M. Microscopy, Culture or PCR-verified cases of persistent [seronegative] Lyme Borreliosis (2007) http://lymerick.net/persistent-borreliosis.htm	“... In this I focus on collecting cases where late (seronegative) and or persistent borrelia despite "curative" antibiotic treatment were confirmed by direct detection methods”.
Fallon BA (2008) http://www.ncbi.nlm.nih.gov/pubmed/17928580	“IV ceftriaxone therapy results in short-term cognitive improvement for patients with posttreatment Lyme encephalopathy, but relapse in cognition occurs after the antibiotic is discontinued”.
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. Liquor (Kommentar: http://www.praxis-berghoff.de/dokumente/Liquordiagnostik_bei_LNB.pdf)

Autoren	Text – Aussagen
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”
Pfister HW (1991) http://www.ncbi.nlm.nih.gov/pubmed/1988514	“In one patient Borrelia burgdorferi was isolated from the cerebrospinal fluid (CSF) 7.5 months after ceftriaxone therapy. ...Patients with Lyme neuroborreliosis may benefit from a 10-day treatment with ceftriaxone or cefotaxime. However, as 10 patients were symptomatic at follow-up and borreliae persisted in the CSF of one patient, a prolongation of therapy may be necessary. ”
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”.
Nocton JJ, Bloom BJ, Rutledge BJ et al. (1996) http://www.ncbi.nlm.nih.gov/pubmed/8769624	“A polymerase chain reaction (PCR) assay that detects <i>Borrelia burgdorferi</i> DNA in cerebrospinal fluid (CSF) was evaluated as a diagnostic test for acute or chronic Lyme neuroborreliosis. In one laboratory, 102 samples were tested blindly, and 40 samples were retested in a second laboratory. In the first laboratory, <i>B. burgdorferi</i> DNA was detected in CSF samples in 6 (38%) of 16 patients with acute neuroborreliosis, 11 (25%) of 44 with chronic neuroborreliosis, and none of 42 samples from patients with other illnesses”.
Oksi J (1996) http://www.ncbi.nlm.nih.gov/pubmed/9010017	“We conclude that cerebral lymphocytic vasculitis and multifocal encephalitis may be associated with <i>B. burgdorferi</i> infection. The presence of <i>B. burgdorferi</i> DNA in tissue samples from areas with inflammatory changes indicates that direct invasion of <i>B. burgdorferi</i> 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 <i>Borrelia burgdorferi</i> sensu lato by detection of the causal agent by immune electron microscopy or of its DNA by PCR 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 <i>Borrelia burgdorferi</i> 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”.

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<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3636972/> **"This review describes known and suspected mechanisms by which spirochetes of the Borrelia genus evade host immune defenses and survive antibiotic challenge. Accumulating evidence indicates that Lyme disease spirochetes are adapted to persist in immune competent hosts, and that they are able to remain infective despite aggressive antibiotic challenge".**

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Accessed November 26, 2017. « **ILADS is grateful to Drs. Robert Bransfield, Bernt-Dieter Huismans, Steven Phillips, John Scott and Raphael Stricker for help with compiling this list of references.** »

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