**Langzeit – Antibiosen , Mono – Therapie, Kombination – Therapie**
**Long time - antibiosis, mono - therapy, combination - therapy**

**Long-term treatments with antibiotics are standard procedures for tuberculosis, leprosy, Whipple's disease, acne vulgaris pustulosa et conglobata, chronic bacterial prostatitis, chronic obstructive pulmonary disease (COPD), malaria and some other chronic infectious diseases.**

**Langzeit-Behandlungen mit Antibiotika sind Standard - Behandlungen bei Tuberkulose, Lepra, Morbus Whipple, Akne vulgaris pustulosa et conglobata, bei chronischer bakterieller Prostatitis, chronischer obstruktiver Lungen-krankheit (COPD), bei der Malaria und auch bei einigen anderen chronisch verlaufenden Infektionskrankheiten.**

**Prove that, for a chronic Lyme disease and Co-infections, the pathogen had disappeared within a 2 - or 4-week treatment with antibiotics, were never shown.**

**Beweise, dass bei einer chronischen Lyme-Borreliose und Ko-Infektionen der Krankheits-erreger nach einer 2- oder 4-wöchiger Antibiotika-Behandlung verschwunden sei, wurden nie erbracht.**

**Evidence about whether chronic Lyme disease and co-infections with long-term antibiotic treatment only the placebo effect is effective or that the remaining symptoms cannot be correlated with the infection were also never produced, partly for ethical reasons.**

**Beweise dazu, ob bei einer chronischen Lyme-Borreliose und Ko-Infektionen unter Langzeitantibiose nur der Plazebo-Effekt wirksam ist, oder dass bleibende Symptome nicht mit der Infektion korreliert sein können, wurden z.T. aus ethischen Gründen ebenfalls nie erbracht.**

**Antibiotics reduce the host-specific pathogen load. Thus, the host's own immune system is assisted in its function. The host's own immune system is not weakened by Antibiotics.**

**Antibiotika vermindern die Erregerlast. Dadurch wird das wirtseigene Immunsystem in seiner Funktion unterstützt. Durch Antibiotika wird das Immunsystem des Wirtes nicht geschwächt.**

**But by the use of antibiotics** the bacterial colonization of the intestine can be disturbed, a mitochondriopathy could be strengthened.
**Durch die Anwendung von Antibiotika** kann aber die Bakterienbesiedlung des Darmes gestört und eine Mitochondriopathie deutlicher werden.

**Cortisone in therapeutic doses or heavy metals such as e.g. Gold or specific immune suppressive drugs such as MTX, Azathioprim or other cytostatic drugs or the so called biologicals weaken the host's own immune system, however lasting.**

**Cortison in therapeutischen Dosen oder Schwermetalle wie z.B. Gold oder spezielle Immun-Suppressiva wie z.B. MTX, Azathioprim, oder andere Zytostatika und sog. Biologicals schwächen das wirtseigene Immunsystem dagegen nachhaltig.**

DOUBLE BLIND PLACEBO CONTROLLED STUDIES ON THE TREATMENT OF BORRELIOSIS are **prohibited for ethical reasons**. I remind the disaster with the **Tuskee study**. http://en.wikipedia.org/wiki/Tuskegee_syphilis_experiment
http://www.cdc.gov/tuskegee/timeline.htm

Doppelblind, placebo-kontrollierte Studien zur Behandlung einer Borreliose sind **aus ethischen Gründen verboten**. Ich erinnere an die Katastrophe mit der **Tuskee Studie**.
http://de.wikipedia.org/wiki/Tuskegee-Syphilis-Studie

BILL NUMBER: A7558A (2013) **S T A T E  O F  N E W  Y O R K. An act to amend the public health law, in relation to authorizing long term antibiotic treatment for certain patients with Lyme disease**.
http://assembly.state.ny.us/leg/?default_fld=&bn=A07558&term=2013&Summary=Y&Actions=Y&Votes=Y&Memo=Y&Text=Y

## Plazebo Effekt


Breidert M, Hofbauer K (2009) Placebo: Missverständnisse und Vorurteile. Dt. Ärztebl. 106(46), 751-5 http://www.aerzteblatt.de/archiv/66733/Placebo-Missverstaendnisse-und-Vorurteile

Macauda MM, Erickson P, Miller J et al. (2011) Long-term Lyme disease antibiotic therapy beliefs among New England residents. Vector borne and zoonotic diseases (Larchmont, N.Y.) 11(7), 857-62. DOI:10.1089/vbz.2010.0116 http://www.ncbi.nlm.nih.gov/pubmed/21417921

Enck P, Bingel U, Schedlowski M et al. (2013) The placebo response in medicine: minimize, maximize or personalize? Nat Rev Drug Discov. 12(3), 191-204. doi: 10.1038/nrd3923. http://www.ncbi.nlm.nih.gov/pubmed/23449306


## Immunsuppression ohne oder mit Antibiose,
## Immunosuppression with or without antibiotics


Kollikowski HH, Schwendemann G, Schulz M, Wilhelm H, Lehmann HJ. (1988) Chronic borrelia encephalomyeloradiculitis with severe mental disturbance: immunosuppressive versus antibiotic therapy. J Neurol 235, 140-142.

Massengo SA et al (2005) Severe neuroborreliosis: The benefit of prolonged highdose combination of antimicrobial agents with steroids- - an illustrative case. Department of Neurology, Centre Hospitalier de Mont de Marsan, 40000 Mont de Marsan, France Diagn Microbiol Infect Dis 51(2), 127-30. http://www.ncbi.nlm.nih.gov/pubmed/15698718

Saviola G et al. (2013) Clarithromycin in rheumatoid arthritis: the addition to methotrexate and low-dose methylprednisolone induce a significant additive value-a 24 month single-blind pilot studie. Rheumatol Int. 33(11),2833-8. doi: 10.1007/s00296-013-2822-0 http://www.ncbi.nlm.nih.gov/pubmed/23864141


## Antibiose,
## Antibiosis


Sigal LH (1990) **Summary of the first 100 patients seen at a Lyme disease referral center**. Am J Med 88, 577-81.

Steere AC, Taylor E, McHugh GL, Logigian EL. (1993) **The overdiagnosis of Lyme disease**. JAMA 269, 1812-26.

Reid MC, Schoen RT, Evans J, Rosenberg JC, Horwitz RI (1998) **The consequences of overdiagnosis and overtreatment of Lyme disease: an observational study**. Ann Intern Med 128, 354-62.

Klempner MS, Hu LT, Evans J, et al. (2001) Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. N Engl J Med. 345, 85-92

Berghoff W (2012) **Infektiologische Differentialdiagnose der chronischen Lyme-Borreliose und sogenannte Coinfektionen.** http://www.praxis-berghoff.de/dokumente/berghoff30062014/Kapitel_4_Infektiologische_Differentialdiagnose_der_chronischen_LB_und_sogenannte_Coinfektionen.pdf

Berghoff W (2014) Antibiotische Behandlung der Lyme-Borreliose im **Frühstadium**. Literaturübersicht. http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-f_Antibiotische_Behandlung_der_LB_im_Fruehstadium_Literaturuebersicht.pdf

Cox LM et al. (2014) **Altering the intestinal microbiota during a critical developmental window has lasting metabolic consequences.** Cell doi:10.1016/j.cell.2014.05.052. http://www.cell.com/cell/pdf/S0092-8674%2814%2900821-6.pdf

Berghoff W (2014) **Versagerquote bei antibiotischer Behandlung nach Standard (IDSA) der LB im Früh- und Spätstadium**. http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-2_Versagerquote_bei_antibiotischer_Behandlung_nach_Standard.pdf

Berghoff W (2014) **Seronarbe.** http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_22-5_Seronarbe.pdf

Berghoff W (2014) **Literaturübersicht Antibiotische Behandlung Lyme-Borreliose Stadium III** http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-d_Literaturuebersicht_Antibiotische_Behandlung_LB_III.pdf

Berghoff W (2014) **Antibiotische Langzeitbehandlung, Effizienz und Legalisierung.** http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-3_Antibiotische_Langzeitbehandlung_Effizienz_und_Legalisierung.pdf

Cameron D (2015**) B. burgdorferi persister cells survive attacks by antibiotics and may contribute to chronic illness in Lyme disease patients.** http://danielcameronmd.com/b-burgdorferi-persister-cells-survive-attacks-by-antibiotics-and-may-contribute-to-chronic-illness-in-lyme-disease-patients/

Tseng Y-J, Cami A, Goldmann DA et al. (2015) **Incidence and Patterns of Extended-Course Antibiotic Therapy in Patients Evaluated for Lyme Disease**. Clinical Infectious Diseases, http://doi.org/10.1093/cid/civ636 http://www.prohealth.com/library/showarticle.cfm?libid=20922
**«Insurance claims data suggest that the use of extended courses of antibiotics and multiple antibiotics in the treatment of Lyme disease has increased in recent years. «**

Raymond F, Deraspe M, Boissinot M, Bergeron MG, Corbeil J (2016) **Partial recovery of microbiomes after antibiotic treatment.** Gut Microbes. 2016 Aug 5:0. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/27494088#
**„Recovery of gut microbiomes three months after antibiotherapy was characterized by the emergence of new genome sequences not observed prior to antibiotic exposure. Participants with low initial gut microbiome diversity had an increased amount of sequences related to antibiotic resistance. Therefore, we suggest that while the taxonomical composition of microbiomes is partially affected by the antibiotic, the genomic content and population structure of bacterial communities is noticeably impacted.“**

Berende A, ter Hofstede HJ, Vos FJ, van Middendorp H, Vogelaar ML, Tromp M, van den Hoogen FH, Donders AR, Evers AW, Kullberg BJ (2016) **Randomized Trial of Longer-Term Therapy for Symptoms Attributed to Lyme Disease.** N Engl J Med. 374(13), 1209-20. doi: 10.1056/NEJMoa1505425. https://www.ncbi.nlm.nih.gov/pubmed/27028911#cm27028911_26797
**Comment: Raphael Stricker** 2016 Sep 04 05:28 a.m.
**Study Conclusion is Incorrect This study did not have a true control group because all chronic Lyme disease patients received an additional two weeks of intravenous ceftriaxone therapy. The study clearly shows that this additional antibiotic treatment was associated with significant improvement in the SF-36 quality of life scale in all patient groups (see Figure 2). Thus the conclusion that additional antibiotic therapy was ineffective for chronic Lyme disease is incorrect.**

Berghoff W (2016) **Lyme Borreliose : Lehrbuch.** https://www.amazon.de/Lyme-Borreliose-Lehrbuch-Walter-Berghoff/dp/3981770501

Huismans BD (2016) **Ko-Erreger und Toxine bei Lyme – Borreliose, Multi-System – Multi-Infektions – Krankheiten und bei Cavete Diagnosen** http://www.xerlebnishaft.de/ko-erreger.pdf

Huismans BD (2016) **Co-pathogens and toxins in Lyme disease, Multi-system – Multi-infektion – diseases and in Cavete diagnoses** http://www.kabilahsystems.de/ko-erreger_eng.pdf

Marks CM, Nawn JE, Caplow JA (2016) **Antibiotic treatment for chronic Lyme disease—say no to DRESS.** JAMA Intern Med 176, 1745-46.

Steere AC, Strie F, Wormser GP, et al. (2016) Primer: Lyme borreliosis. Nat Rev Dis Primers. 2, 1-18

Arvikar SL, Crowley JT, Sulka KB, et al. (2017) Autoimmune arthritides, rheumatoid arthritis, psoriatic arthritis, or peripheral spondyloarthritis following Lyme disease. Arthritis & Rheumatology. 69, 194-202.

Tamma PD et al. (2017) **Association of adverse events with antibiotic use in hospitalized patients.** JAMA Intern Med [e-pub]. http://dx.doi.org/10.1001/jamainternmed.2017.1938 https://www.ncbi.nlm.nih.gov/pubmed/28604925

Shapiro ED, Baker PJ, Wormser GP (2017) **False and Misleading Information About Lyme Disease.** Am J Med. 130(7), 771-772. doi: 10.1016/j.amjmed.2017.01.030. Epub 2017 Feb 16. https://www.ncbi.nlm.nih.gov/pubmed/28216447
**"…results of multiple clinical trials that show that patients with well-documented Lyme disease who have residual nonspecific symptoms after treatment do not benefit from additional treatment, even with extended courses of IV antibiotics."**

Huismans BD (2017) **Chronic Inflammatory Disorders. Multisystem diseases caused by pathogens.** http://www.kabilahsystems.de/ko-erreg_eupd1.pdf

- ➔ **Archaeen** http://www.erlebnishaft.de/archaeae.pdf

- ➔ **Mitochondrien** http://www.xerlebnishaft.de/mitochondrien.pdf
- ➔ **Zytoskelett** http://www.xerlebnishaft.de/zytoskelett.pdf
- ➔ **RNA, DNA** http://www.xerlebnishaft.de/rna.pdf http://www.xerlebnishaft.de/endo_reticulum.pdf
- ➔ **Peptide** http://www.kabilahsystems.de/biogeneamineundpeptide.pdf
- ➔ **Fettsäuren** http://www.kabilahsystems.de/ungesaettfetts.pdf
- ➔ **Elektrolyte, pH-Wert, Spurenelemente** http://www.xerlebnishaft.de/elektro_spur_ph.pdf
- ➔ **Vitamine** http://www.xerlebnishaft.de/vitamine.pdf
- ➔ **Zytokine, Chemokine** http://www.kabilahsystems.de/antizyt-chem.pdf

- ➔ **Chronic Inflammatory Disorders. Multisystem diseases caused by pathogens** http://www.kabilahsystems.de/ko-erreg_eupd1.pdf

## Monotherapie Langzeit – Antibiose, Monotherapy Longterm – Antibiosis

| Studie Jahr | Krankheit bis Therapie | Pat. Zahl | Antibiotika | Behand-lungs Dauer | Behandlungs-Ergebnis und -Aussagen |
|---|---|---|---|---|---|
| Wahlberg 1994 | - | 100 | Ceftriaxon<br>Amoxicillin<br>Cefadroxil | 14 Tage<br>100 Tage<br>100 Tage | "Titres of IgG antibodies to B. burgdorferi flagella declined significantly after 6 and 12 months in the patients who had successful treatments". |
| Donta 1997 | - | 277 | Tetrazyklin | 2 Monate<br>3 Monate<br>~4 Monate | 20% geheilt, 70% gebessert,<br>10% unverändert<br>"These results support the use of longer courses of treatment in the management of patients with chronic Lyme disease". |
| Oksi 1998 | - | 30 | Cefixime +<br>+ Probenicid<br>Ceftriaxon,<br>Amoxicillin | 3 bis 4 Monate | "The general outcomes of infection in patients with disseminated Lyme borreliosis after 3-4 months of therapy indicate that prolonged courses of antibiotics may be beneficial in this setting, since 90% of the patients showed excellent or good treatment responses". |
| Oksi 1999 | - | 165 | Oral Antib.<br>Ceftriaxon | 3 Monate<br>1 ½ Monate | Rückfälle. Gute Ergebnisse<br>"We conclude that the treatment of Lyme borreliosis with appropriate antibiotics for even more than 3 |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | months may not always eradicate the spirochete". |
| Fallon 1999 | - | 18 | i.v., i.m. i.v. doxycycline, minocycline, amoxacillin, penicillin, azithromycin, clarithromycin, cefuroxime, cefixime | 4 Monate | This uncontrolled study suggests that repeated antibiotic treatment can be beneficial, even among patients who have been previously treated and even among patients who are currently Western blot negative, with the intravenous route of treatment being the most effective. A double-blind placebo-controlled study is needed to confirm these results. |
| Klempner 2001 | ~4,7 Jahre | 129 | Ceftriaxon Doxycyclin | 1 Monat 2 Monate | "Antibiotic treatment is highly effective for the acute and late septic manifestations of Lyme disease, which is caused by the tick-borne bacterium Borrelia burgdorferi". "During the six-month evaluation period, we observed improvement in health status in 36 percent of patients, worsening health status in 39 percent, and no significant change in 25 percent". "There is considerable impairment of health-related quality of life among patients with persistent symptoms despite previous antibiotic treatment for acute Lyme disease. However, in these two trials, treatment with intravenous and oral antibiotics for 90 days did not improve symptoms more than placebo". |
| Krupp 2003 | - | 55 | Ceftriaxon | 1 Monat | 64% Besserung der Erschöpfung,<br>keine Besserung des Bewusstseins<br>"Patients assigned to ceftriaxone showed improvement in disabling fatigue compared to the placebo group (rate ratio, 3.5; 95% CI, 1.50 to 8.03; *p* = 0.001)" |
| Fallon 2008 | ~9 Jahre | 23 | Ceftriaxon | 2 bis 6 Monate | Signifikante Besserung<br>"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". |
| Cameron 2008 | ~7,1 Mon. | 52 | Amoxicillin | 3 Monate | 2/3 der Patienten gebessert |
| Klemann 2009 | ~9 Jahre | 105 | Ceftriaxon Tetrazykline Makrolide Linkosamide Nitroimidazol Lysosomo-tropika | 6 Monate bis 3 Jahre | 38,8% beschwerdefrei, symptom-free<br>56,7% gebessert, improved<br>5,5% unverändert, unchanged |
| Stricker 2010 | - | 200 | i.v. | ~4 Monate | "Prolonged intravenous antibiotic therapy is associated with low morbidity and no IVD-related mortality in patients referred for treatment of neurologic Lyme disease. With proper IVD care, the risk of extended antibiotic therapy in these patients appears to be low". |
| Kuhn 2012 | - | - | Amoxycillin | 6 Monate | "The assessors also reported anecdotal data of improved speech, eye contact, sleep behaviors, and a reduction of repetitive behaviors". |
| DeLong 2012 | - | - | Ceftriaxon | 3 bis 6 Monate | "This biostatistical review reveals that retreatment can be beneficial. Primary outcomes originally reported as statistically insignificant were likely underpowered". |


Cimmino MA, Accardo S. (1992) Long term treatment of chronic Lyme arthritis with benzathine penicillin. Ann Rheum Dis. 51(8), 1007-8 (two cases) http://www.ncbi.nlm.nih.gov/pubmed/1417107

**Wahlberg P**, Granlund H, Nyman D, Panelius J, Seppala I. (1994) Treatment of late Lyme borreliosis. J Infect 29(3), 255-61. http://www.ncbi.nlm.nih.gov/pubmed/7884218

Gasser R, Reisinger E, Eber B, Pokan R, Seinost G, Bergloff J, Horwarth R, Sedaj B, Klein W (1995) Cases of Lyme borreliosis resistant to conventional treatment: improved symptoms with **cephalosporin plus specific beta-lactamase inhibition**. Microb Drug Resist 1(4), 341-4. http://www.ncbi.nlm.nih.gov/pubmed/9158807 http://www.benbrew.com/lb/lactamase.pdf

Cimmino MA, Moggiana GI, Parisi M, Accardo S. (1996) Treatment of Lyme arthritis. Infection 24(1), 91-3.

Ziska MH, Donta ST, Demarest FC, (1996) Physician preferences in the diagnosis and treatment of Lyme disease in the Unites States. Infection 24(2) 182-186

**Donta ST** (1997) Tetracycline therapy for chronic Lyme disease. Clin Infect Dis 25(Suppl 1), S52-6. PMID 9233665. http://cid.oxfordjournals.org/content/25/Supplement_1/S52.abstract

Dattwyler RJ et al. (1997) Clarithromycin in treatment of **early Lyme disease**: a pilot study. Antimicrob Agents Chemother 40, 468-469 http://www.ncbi.nlm.nih.gov/pubmed/8834900 [41 Patienten, Erythema migrans, Behandlungsdauer 21 Tage]

**Oksi J**, Nikoskelainen J, Viljanen MK. (1998) Comparison of oral cefixime and intravenous ceftriaxone followed by oral amoxicillin in disseminated Lyme borreliosis. Eur J Clin Microbiol Infec Dis 17 (10), 715-9. PMID 9865985. http://www.ncbi.nlm.nih.gov/pubmed/9865985

**Oksi J**, Marjamaki M, Nikoskelainen J, Viljanen M. (1999) Borrelia burgdorferi detected by culture and PCR in clinical relapse of disseminated Lyme borreliosis. Ann Med 31(3), 225-32 http://www.ncbi.nlm.nih.gov/pubmed/10442678

**Fallon BA**, Tager F, Fein L, Liegner K, Keilp J, Weiss N, Liebowitz M. (1999) Repeated antibiotic treatment in chronic Lyme disease. J Spirochet Tick-Borne Dis 6(3), 94-102. http://www.theoneclickgroup.co.uk/documents/Borreliosis/Repeated%20Antibiotic%20Treatment%20in%20Chronic%20Lyme%20Disease.htm

Seltzer EG, Gerber MA, Cartter ML, Freudigman K, Shapiro ED. (2000) Long-term outcomes of persons with Lyme disease. JAMA. 283(5), 609-616

**Klempner MS**, Hu LT, Evans J, et al. (**2001**). Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. N Engl J Med 345 (2), 85–92. http://www.nejm.org/doi/full/10.1056/NEJM200107123450202#t=articleDiscussion http://www.ncbi.nlm.nih.gov/pubmed/11450676

Bransfield R, Brand S, Sherr V. (2001) Treatment of patients with persistent symptoms and a history of Lyme disease. N Engl J Med. 345(19), 1424-5 http://www.ncbi.nlm.nih.gov/pubmed/11794179

**Krupp L.** et al. (2003) Study and treatment of post-Lyme disease (STOP-LD) a randomised double-masked clinical trial. Neurology 60, 1923-1930 http://www.neurology.org/content/60/12/1923.abstract

Nowakowski J, Nadelman RB, Sell R, McKenna D, Cavaliere LF, Holmgren D, Gaidici A, Wormser GP. (2003) Long-term follow-up of patients with culture-confirmed Lyme disease.Am J Med. 1,115(2) 91-6.

Donta ST (2003) Macrolide therapy of chronic Lyme disease. Med Sci Monit 9, I-136–I-142.

Wormser GP, Ramanathan R, Nowakowski J, McKenna D, Holmgren D, Visintainer P, Dornbush R, Singh B, Nadelman RB. (2003) Duration of antibiotic therapy for early Lyme disease. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 6, 138(9), 697-704.

Fallon BA. (2004) Laboratory findings in chronic Lyme disease and results of the controlled treatment study. Lyme & Other Tick-Borne Diseases:Technology Leading the Way Conference; Rye Town, NY.

Cameron D, Gaito A, Harris N, et al. (2004) Evidence-based guidelines for the management of Lyme disease. Expert Rev Anti-Infect Ther 2(1 Suppl), 1-13.

Stricker RB, Lautin A, Burrascano JJ. (2005) Lyme disease: point/counterpoint. Expert Rev Anti Infect Ther. 3(2), 155-65,

Stricker RB, Johnson L, Harris N, Burrascano JJ. (2005) Inaccurate information about Lyme disease on the Internet. Pediatr Infect Dis J 24, 577-8.

Dinser R, Jendro MC, Schnarr S, Zeidler H. (2005) Antibiotic treatment of Lyme borreliosis: what is the evidence? Ann Rheum Dis 64, 519-523 doi:10.1136/ard.2004.027367

Fallon BA et al. (2007) A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. Neurology. 70(13), 992-1003. Epub 2007 Oct 10. http://www.ncbi.nlm.nih.gov/pubmed/17928580

Stricker R.B. (2007) Kontrapunkt: Langzeit-Antibiotika-Therapie verbessert die persistierenden, mit Lyme-Borreliose verbundenen Symptome. in Antibiotic Therapy and Lyme Disease 45, 149-157

Stricker, R. B. (2007) Counterpoint: long-term antibiotic therapy improves persistent symptoms associated with lyme disease. In: Clin Infect Dis 45 Nr. 2, 149–157.

Oksi J., Nikoskelainen J., Kiekkanen et al. (2007) Duration of antibiotic treatment in disseminated Lyme borreliosis: a double-blind, randomized, placebo-controlled, multicenter clinical trial. Eur J Clin Microbiol Infect Dis 26, 571-581

Cameron DJ. (2008) An appraisal of ‘‘chronic Lyme disease”. N Engl J Med 358, 429-30.

**Cameron D**. (2008) Severity of Lyme disease with persistent symptoms. Insights from a double blind placebo controlled clinical trial. Minerva Med 99, 489-96. http://www.ncbi.nlm.nih.gov/pubmed/18971914

**Fallon BA**, Keilp JG, Corbera KM et al. (2008) A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. Neurology 70, 992-1003. http://www.ncbi.nlm.nih.gov/pubmed/17928580

**Huismans BD,** Klemann W. (2008) Langzeitbehandlung mit Antiinfektiva bei persistierender Borreliose mit Borrelien-DNA-Nachweis durch PCR. Mit Hinweisen auf Antiinfektiva – Kombinationen im Anhang. Grin Verlag ISBN 978-3-640-19384-4 http://www.hausarbeiten.de/faecher/vorschau/117294.html

**Klemann W**, Huismans B.D. (2009) Patienten mit Erreger-Direktnachweis bei chronischer Lyme-Borreliose: Klinik, Labordiagnostik, Antibiotika-Therapie und Krankheitsverlauf. Eine retrospektive Studie. Umwelt-medizin-gesellschaft 22 (2) 132-138 http://www.umg-verlag.de/umwelt-medizin-gesellschaft/209_kh_z.pdf

Clarissou J, Song A, Bernede C, Guillemot D, Dinh A, Ader F, Perronne C, Salomon J. (2009) Efficacy of a long-term antibiotic treatment in patients with a chronic Tick Associated Poly-organic Syndrome (TAPOS). Med Mal Infect. 39(2), 108-15. Epub 2009 Jan 4.

BCA (2009) Langzeit-Antibiotika-Therapie verbessert die persistierenden, mit Lyme-Borreliose verbundenen Symptome. http://www.b-c-a.de/fileadmin/img/bca/StrickerLangzeitbehandlungAntibiotikaIDSALecture110309deutsch.pdf

Clarissou J, Song A, Bernede C, et al. (2009) Efficacy of a long-term antibiotic treatment in patients with a chronic Tick Associated Poly-organic Syndrome (**TAPOS**). Med Mal Infect 39(2), 108-15. Abstract

**Stricker**, R. B.; Green, C. L.; Savely, V. R. Chamallas, S. N.; Johnson, L. (2010) Safety of intravenous antibiotic therapy in patients referred for treatment of neurologic Lyme disease. In: Minerva Med 101 Nr. 1, S. 1–7. http://www.ncbi.nlm.nih.gov/pubmed/20228716

**Klemann W** et al. (2011) Prolonged antibiotic therapy in PCR confirmed persistent Lyme disease Scientific Study, 20 Pages Grin Verlag http://www.grin.com/en/e-book/166179/prolonged-antibiotic-therapy-in-pcr-confirmed-persistent-lyme-disease

Shor S. (2011) Retrospective analysis of a cohort of internationally case defined chronic fatigue syndrome patients in a lyme epidemic area. Bulletin of the IACFS/ME 18(4), 109-123 http://www.iacfsme.org/BULLETINWINTER2011/Winter2011ShorABSTRACT/tabid/459/Default.aspx

Kullberg BJ, Berende A, van der Meer JW. (2011) The challenge of Lyme disease: tired of the Lyme wars. Neth J Med 69, 98-100.

Stricker RB, Delong AK, Green CL, Savely VR, Chamallas SN, Johnson L. (2011) **Benefit of intravenous antibiotic therapy in patients referred for treatment of neurologic Lyme disease.** Int J Gen Med. 639-46. doi: 10.2147/IJGM.S23829. Epub 2011 Sep 6. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177589/ http://www.ncbi.nlm.nih.gov/pubmed/21941449
**« For the purpose of this study, only patients receiving intravenous ceftriaxone were included in the analysis. … Prolonged intravenous antibiotic therapy is associated with improved cognition, fatigue, and myalgias in patients referred for treatment of neurologic Lyme disease. Treatment for 25-52 weeks may be necessary to obtain symptomatic improvement in these patients".**

Macauda MM, Erickson P., Miller J. et al. (2011) Long-Term Lyme Disease Antibiotic Therapy Beliefs Among New England Residents. Vector-Borne and Zoonotic Diseases, Vol. 11, No. 7, 857-862.

Fanelli M, Kupperman E, Lautenbach E. et al. (2011) Antibiotics, Acne, and Staphylococcus aureus Colonization, Arch Dermatol. 147(8), 917-921. doi:10.1001/archdermatol. 67

Stricker RB, Johnson L. (2011) Lyme Disease diagnosis and treatment: lessons from the aids epidemic. Minerva Med. 101, 419-425 http://www.ncbi.nlm.nih.gov/pubmed/21196901

Stricker RB, Johnson L. (2011) Lyme disease: The next decade. Infect Drug Resist 4, 1-9. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108755/

Johnson L, Aylward A, Stricker RB. (**2011**) Healthcare access and burden of care for patients with Lyme disease: a large United States survey. Health Policy.102(1), 64-71 http://www.ncbi.nlm.nih.gov/pubmed/21676482

**Kuhn M**, Grave a S, Bransfield R, Harris S. (2012) Long term antibiotic therapy may be an effective treatment for children co-morbid with Lyme disease and Autism Spectrum Disorder. Medical Hypotheses 78(5) 606-15. Epub 2012 Feb 22. http://www.ncbi.nlm.nih.gov/pubmed/22361005 http://www.sciencedirect.com/science/article/pii/S0306987712000485

Doernberg SB, Winston LG, Deck DH, Chambers HF (2012) Does doxycycline protect against development of Clostridium difficile infection? Clin Infect Dis. doi: 10.1093/cid/cis457 http://cid.oxfordjournals.org/content/early/2012/05/02/cid.cis457

Fallon BA, Petkova E, Keilp JG, Britton CB. (2012) A reappraisal of the U.S. clinical trials of post-treatment Lyme disease syndrome. Open Neurol J 6(Suppl. 1-M2), 79–87. http://www.ncbi.nlm.nih.gov/pubmed/23091568

**DeLong AK**, Blossom B, Maloney E, Phillips SE. (2012) Antibiotic retreatment of Lyme disease in patients with persistent symptoms: A biostatistical review of randomized, placebo-controlled, clinical trials. Contemp Clin Trials epub ahead of print. http://dx.doi.org/10.1016/j.cct.2012.08.009

Stricker RB, DeLong A, Johnson L. (2012) Correspondence. Outpatient parenteral antibiotic therapy for Lyme borreliosis: a 'real world' view. QJM Advance Access published December 6, 1-2 http://qjmed.oxfordjournals.org/content/early/2012/12/06/qjmed.hcs227.extract

Halperin JJ.(2013) Nervous system lyme disease: diagnosis and treatment. Curr Treat Options Neurol. 15(4), 454-64. doi: 10.1007/s11940-013-0240-y.

Klempner MS, Baker PJ, Shapiro ED et al. (2013) Treatment trials for post-lyme disease symptoms revisited. Am J Med. 126(8), 665-9. doi: 10.1016/j.amjmed.2013.02.014. Epub 2013 Jun 10. http://www.ncbi.nlm.nih.gov/pubmed/23764268
**"On the basis of this analysis, the conclusion that there is a meaningful clinical benefit to be gained from retreatment of such patients with parenteral antibiotic therapy cannot be justified".**

Stricker RB, Johnson L. (2013) Borrelia burgdorferi aggrecanase activity: **more evidence for persistent infection in Lyme disease**. Front Cell Infect Microbiol. 3, 40. doi: 10.3389/fcimb.2013.00040. eCollection 2013. http://www.ncbi.nlm.nih.gov/pubmed/23967405

Stricker RB, Johnson L. (2013) **Chronic lyme disease**: liberation from lyme denialism. Am J Med. 126(8), e13-4. doi: 10.1016/j.amjmed.2013.01.030. http://www.ncbi.nlm.nih.gov/pubmed/23885681

Berndtson K. (2013) **Review of evidence for immune evasion and persistent infection in Lyme disease.** Int J Gen Med. 6, 291-306. doi: 10.2147/IJGM.S44114. Print 2013. http://www.ncbi.nlm.nih.gov/pubmed/23637552
**„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. Advancing understanding of the survival mechanisms of the Lyme disease spirochete carry noteworthy implications for ongoing research and clinical practice."**

Borgemans L, Goderis G, Vandevoorde J et al. (2014) Relevance of Chronic Lyme Disease to Family Medicine as a Complex Multidimensional Chronic Disease Construct: A Systematic Review. International Journal of Family Medicine. Volume 2014 (2014), Article ID 138016, 10 pages http://dx.doi.org/10.1155/2014/138016 http://www.hindawi.com/journals/ijfm/2014/138016/

Jares TM, Mathiason MA, Kowalski TJ. (2014) Functional outcomes in patients with Borrelia burgdorferi reinfection. Ticks Tick Borne Dis. 5(1), 58-62. doi: 10.1016/j.ttbdis.2013.09.002. http://www.ncbi.nlm.nih.gov/pubmed/24215678

Berende A, ter Hofstede HJM, Donders ART et al (2014) Persistent Lyme Epidemic Antibiotic Study Europe (**PLEASE**) – design of randomized controlled trial of prolonged antibiotic treatment in patients with persistent symptoms attributed to Lyme borreliosis. BMC Infectious Diseases. 14, 543 http://www.biomedcentral.com/1471-2334/14/543

Huismans BD (2014) **Antibiotika Langzeit-Therapie bei chronischer Lyme-Borreliose mit Borrelien Dna-Nachweis durch Pcr: Intensivbehandlung, Kombinationsbehandlung, Langzeitbehandlung.** http://www.amazon.de/Antibiotika-Langzeit-Therapie-chronischer-Lyme-Borreliose-Dna-Nachweis/dp/3956842588

Merit E Cudkowicz ME, Sarah Titus S, Marianne Kearney M et al. (2014) **Safety and effi cacy of ceftriaxone for amyotrophic lateral sclerosis: a multi-stage, randomised, double-blind, placebo-controlled trial**Lancet Neurol 13, 1083–91
http://www.thelancet.com/journals/laneur/article/PIIS1474-4422%2814%2970222-4/abstract
http://www.researchgate.net/publication/266561222_Safety_and_efficacy_of_ceftriaxone_for_amyotrophic_lateral_sclerosis_a_multi-stage_randomised_double-blind_placebo-controlled_trial
**« Despite promising stage 2 data, stage 3 of this trial of ceftriaxone in amyotrophic lateral sclerosis did not show clinical effi cacy. The adaptive design allowed for seamless transition from one phase to another, and central venous catheter use in the home setting was shown to be feasible"**

Berende A, ter Hofstede HJM, A Rogier A et al. (2014) **Persistent Lyme Empiric Antibiotic Study Europe (PLEASE) - design of a randomized controlled trial of prolonged antibiotic treatment in patients with persistent symptoms attributed to Lyme borreliosis.** BMC Infectious Diseases, 14, 543 http://www.biomedcentral.com/1471-2334/14/543 http://www.ncbi.nlm.nih.gov/pubmed/25318999

Melia MT, Auwaerter PG (2016) **Time for a different approach to Lyme disease and long-term symptoms**. N Engl J Med. 374, 1277-1278.
**« Though prolonged antibiotic therapy is not the answer, we do not know what is truly helpful. … Future research efforts should continue to explore such different strategies that may lead to proven options for helping our patients. »**

- ➔ **Klemann W** http://www.dr-w-klemann.de/htmldocs/neuigkeiten-erfahrungen-mit-langzeitantibiose-erkenntnisse-ueber-biofilme.php

**Kombinationstherapie Langzeit – Antibiose, Kombination- Longterm – Antibiosis**

| Studie Jahr | Krankheits-Dauer | Pat. Zahl | Antibiotika | Behand-lungs Dauer | Behandlungs-Ergebnis |
|---|---|---|---|---|---|
| Gasser 1990 Gasser 1996 | - | 18 | Roxythromycin + Cotrim | - | 76% of the patients recovered completely. These results show that oral therapy of co-trimoxazole and roxithromycin in combination provides similar results as i.v. antibiotics in earlier studies. |
| Gasser 1995 | - | - | Penicillin G Cephalosporin e + Sulbactam | - | - |
| Aygen 1996 | - | 10 | Ceftriaxon + Rifampicin + Doxycyclin | 2 bis 6 Wochen | - |
| Donta 2003 | - | 235 | Macrolide + +Hydroxy-chloroquine | 2 Monate 3 Monate | ->20% gebessert, prolonged therapy ->45% gebessert. “These results support the hypothesis… that the use of a lysosomotropic agent augments the clinical activity of macrolide antibiotics in the treatment of patients with chronic Lyme Disease”. |
| Schardt 2004 | - | 11 | Antibiotika, im Anschluss daran Fluconazol | nach erfolgloser Antibiose 25 Tage lang | At the end of treatment eight patients had no borreliosis symptoms and remained free of relapse in a follow-up examination one year later. In the remaining four patients, symptoms were considerably improved. |
| Sparing 2004 | - | - | Makrolide, Tetracycline, Fluoro-chinolone | - | - |
| Hartmann 2010 | - | 5000 | Actos+Cholestyramin+Minocyclin+Quensyl, anschließend Metronidazol | Ca 4 Jahre, entspr. der Sympto-matik | - |


**Gasser R**, Dusleag J, (1990) Oral treatment of late lyme borreliosis with roxythromycine plus co-trimoxazole, Lancet, 1189-90 http://www.lancet.com/journals/lancet/article/PII0140-6736%2890%2992801-N/fulltext

**Gasser, R** et al (1995) Cases of Lyme borreliosis resistant to conventional treatment: improved symptoms with cephalosporin plus specific beta-lactamase inhibition, Microb Drug Resist, 1, 341-4 http://online.liebertpub.com/doi/abs/10.1089/mdr.1995.1.341

**Gasser R**, et al. (1996) Oral treatment of late Lyme Borreliosis with a combination of roxithromycine and cotrimazole – a pilot study on 18 patients. Acta Med Austria 23, 99-101 http://www.ncbi.nlm.nih.gov/pubmed/8798283

**Aygen B**, Sümerkan B, Mirza M et al. (1996) Treatment of neurobrucellosis with a combination of ceftriaxone, rifampicin and doxycycline (a study on ten cases) Médecine et Maladies Infectieuses, Volume 26, Issue 12, Pages 1199-1201 http://www.sciencedirect.com/science/article/pii/S0399077X96801247

**Donta ST**. (2003) Macrolide therapy of chronic Lyme Disease. Med Sci Monit 9(11), 136-42. PMID 14586290. http://www.ncbi.nlm.nih.gov/pubmed/14586290

**Schardt WF** (2004) Clinical effects of Fluconazole in patients with neuroborreliosis. Eur J Med Res 9(7) 334-336 http://www.ncbi.nlm.nih.gov/pubmed/15337633

**Sparing R**. (2004) Kombitherapie stoppt Mykoplasmen-Enzephalitis. Makrolide, Tetrazykline und Fluorchinolone töten Mykoplasmen / Betalaktame sind gegen die Erreger unwirksam. Der Nervenarzt 10, 16, Ärzte Zeitung http://www.aerztezeitung.de/medizin/fachbereiche/allgemeinmedizin/article/341932/kombitherapie-stoppt-mykoplasmen-enzephalitis.html

Stricker, RB (2007) Counterpoint – Long-term antibiotic therapy improves persistent symptoms associated with lyme disease. Clin Infect Dis 45, 149–157.http://-dx.doi.org/10.1086/518853

Donta ST (2007) Lyme disease guidelines--it's time to move forward. Clin Infect Dis 44(8), 1134-5; author reply 1137-9. Full Citation

Stricker RB, Johnson L (2010) Lyme disease diagnosis and treatment: lessons from the AIDS epidemic. Minerva Med 101(6), 419-25. Abstract

**Hartmann F, Müller-Marienburg H**. (2010) Zur Entstehung und Behandlung der BORRELIOSE. hansadruck, Kiel http://www.bfbd.de/media/literaturdownloads/Hartmann%20Borreliose%2071.pdf

Waag DM (2012) **Q Fever**. Medical Aspects of Biological Warfare * Microbiologist, Division of Bacteriology, US Army Medical Research Institute of Infectious Diseases, 1425 Porter Street, Fort Detrick, Maryland 21702 http://www.bordeninstitute.army.mil/published_volumes/biological_warfare/BW-ch10.pdf
"Q fever endocarditis patients generally receive **18 months** of therapy with doxycycline, 100 mg twice daily, and chloroquine, 200 mg three times daily.107 Quinolones can also be used for those who cannot tolerate chloroquine. For these patients, **3 years** of therapy with doxycycline, 100 mg twice daily, and ofloxacin, 200 mg three times daily, is recommended. **The long duration is recommended because relapses have occurred when the latter regimen was stopped**".

Hashemi S., Gachkar L., Keramat F. et al. (2012) Comparison of doxycycline–streptomycin, doxycycline–rifampin, and ofloxacin–rifampin in the treatment of **brucellosis**: a randomized clinical trial☆ International Journal of Infectious Diseases Volume 16, Issue 4 , Pages e247-e251
http://www.ijidonline.com/article/S1201-9712%2812%2900015-X/abstract?elsca1=etoc&elsca2=email&elsca3=1201-9712_201204_16_4&elsca4=infectious_diseases#article-footnote-1

DeLong AK (2012) Study reports flaws in design, analysis, and interpretation of Lyme disease. Medical Research News.
http://www.news-medical.net/news/20120831/Study-reports-flaws-in-design-analysis-and-interpretation-of-Lyme-disease.aspx

Stricker RB, Johnson L (2013) Borrelia burgdorferi **aggrecanase activity**: more evidence for persistent infection in Lyme disease. Front Cell Infect Microbiol. 2013; 3: 40. Published online 2013 August 14. doi: 10.3389/fcimb.2013.00040 PMCID: PMC3743303
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3743303/
**"Discovery of the spirochetal aggrecanase raises many questions about the pathogenesis of Lyme arthritis and lends support to the concept of persistent B. burgdorferi infection in patients with chronic Lyme disease symptoms".**

Barten DG, Delsing CE, Keijmel SP et al. (2013) **Localizing chronic Q fever**: a challenging query. BMC Infect Dis. 13(1), 413. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/24004470
**"CONCLUSIONS: If chronic Q fever is diagnosed, 18F-FDG PET/CT is a helpful imaging technique for localization of vascular infections due to chronic Q fever. Patients with proven chronic Q fever were diagnosed significantly more often with mycotic aneurysms than in previous case series. Definite endocarditis due to chronic Q fever was less frequently diagnosed in the current study. Chronic Q fever often occurs in patients without a known episode of acute Q fever, so clinical suspicion should remain high, especially in endemic regions."**

Hermans T, Jeurissen L, Hackert V, Hoebe C (2014) Land-Applied Goat Manure as a Source of Human Q-Fever in the Netherlands, 2006-2010. PLoS ONE 9(5), e96607. doi:10.1371/journal.pone.0096607
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0096607

Huismans BD, Klemann W (2014) **Antibiotika Langzeit-Therapie bei chronischer Lme-Borreliose mit Borrelien DNA-Nachweis durch PCR. Intensivbehandlung, Kombinationsbehandlung, Langzeitbehandlung.** Bachelor Master publishing.
http://www.diplomica-verlag.de/gesundheitswissenschaften_94/antibiotika-langzeit-therapie-bei-chronischer-lyme-borreliose-mit-borrelien-dna-nachweis-durch-pcr-intensivbehandlung-kombinationsbehandlung-langzeitbehandlung_159733.htm

Huismans BD, Klemann W, Heyl S (2014**) Prolonged antibiotic therapy in PCR confirmed persistent Lyme disease**. Anchor Academic Publishing.
http://www.amazon.de/Prolonged-antibiotic-therapy-confirmed-persistent/dp/3954892413

Klemann W, Huismans B-D (2014) **Etude rétrospective sur la maladie de Lyme** (French Edition) Paperback GRIN Verlag GmbH. ISBN-10: 3656732833 ISBN-13: 978-3656732839 http://www.hausarbeiten.de/faecher/vorschau/279155.html

Berende A, Hadewych JM, ter Hofstede HJM,Voss FJ et al. (2016) **Randomized Trial of Longer-Term Therapy for Symptoms Attributed to Lyme Disease. The New England Journal of Medicine.** N Engl J Med 374, 1209-1220 March 31, 2016DOI: 10.1056/NEJMoa1505425 http://www.nejm.org/doi/full/10.1056/NEJMoa1505425
**„In patients with persistent symptoms attributed to Lyme disease, longer-term antibiotic treatment did not have additional beneficial effects on health-related quality of life beyond those with shorter-term treatment." „12-week oral course of doxycycline, clarithromycin plus hydroxychloroquine, or placebo. All study groups received open-label intravenous ceftriaxone for 2 weeks before initiating the randomized regimen".**

Feng J, Zhang Sh, Shi W, Zhang Y (2017) **Activity of Sulfa Drugs and Their Combinations against Stationary Phase B. burgdorferi in vitro. Running title: Sulfa drugs and their combinations against B. burgdorferi persisters.** bioRxiv preprint http://dx.doi.org/10.1101/112607 doi: bioRxiv preprint first posted online Mar. 3, 2017
**„Four drug combinations dapsone+minocycline+cefuroxime+azithromycin and dapsone+minocycline+cefuroxime+rifampin showed best activity against stationary phase B. burgdorferi in these sulfa drug combinations. However, these 4-sulfa drug containing combinations still had considerably less activity against B. burgdorferi stationary phase cells than the daptomycin+cefuroxime+doxycycline used as a positive control which completely eradicated B. burgdorferi stationary phase cells."**

Lacout A, Marcy PY, El Hajjam M, Thariat J, Perronne C (2017) **Dealing with Lyme disease treatment**. Am J Med, 2017; doi:10.1016/j.amjmed.2016.12.039 http://www.amjmed.com/article/S0002-9343(17)30103-1/fulltext
**„This explain why Lyme disease treatment can be challenging, particularly in the chronic form of the disease. The importance of the bacterial load and the deep bacterial location may require long-term antibiotherapy by combining different therapeutic molecules."**

- **Borrelien Direkt – Nachweis, Direct Detection of Borrelia** http://www.erlebnishaft.de/borrelien_direktnachweis.pdf
- **Antibiosetherapie** www.kabilahsystems.de/antibiosetherapieplan.pdf
- **Phytotherapie** http://www.kabilahsystems.de/phytotherapie.pdf
- **Begleit-Therapie allgemein** www.kabilahsystems.de/kommentmedbegleittherapie.pdf
- **Salutogenese und Resilenz** www.xerlebnishaft.de/salutogenese.pdf
- **Klemann W** http://www.dr-w-klemann.de/htmldocs/neuigkeiten-erfahrungen-mit-langzeitantibiose-erkenntnisse-ueber-biofilme.php
- **Interview with Prof. Ying Zhang at the NorVect Conference 2015** https://www.youtube.com/watch?v=krXSFmkwXxo&feature=youtu.be&app=desktop
- **Antibiotika Pulstherapie, pulsed antibiotic therapy** http://www.kabilahsystems.de/antibiotika_pulse.pdf
- **Management nach Zeckenkontakt** www.xerlebnishaft.de/management_nach_zeckenkontakt_en.pdf www.xerlebnishaft.de/management_nach_zeckenkontakt.pdf

**Therapie – Komplikationen,**
**Therapy complications**

**1. Gallenblasen – Komplikationen bei Infusionstherapie mit Ceftriaxon**
**2. Sepsis bei liegendem Katheter (Fremdkörper)**
**3. Candida – Sepsis**
**4. Chlostridium difficile – Sepsis**
**5. Allergische und pseudoallergische Reaktionen (Jarisch-Herxheimer – Reaktion)**
**6. evtl. bakterielle Hypermutation (Anlass zu häufigerem Medikamenten – Wechsel)**
**7. DRESS = Drug reaction with eosinophilia and systemic syndroms**


Nadelman RB, Arlin Z, Wormser GP (1991). Life-threatening complications of empiric ceftriaxone therapy for `seronegative Lyme disease'. South Med J 84, 1263-5. CrossRefMedlineWeb of Science Search Google Scholar

Centers for Disease Control and Prevention (CDC) (1993) Ceftriaxone-associated biliary complications of treatment of suspected disseminated Lyme disease–New Jersey, 1990-1992. MMWR Morb Mortal Wkly Rep. 42(2), 39-42.

Ettestad PJ, Campbell GL, Welbel SF et al. (1995) **Biliary complications** in the treatment of unsubstanciated Lyme disease. J Infect Dis 171, 356-361 Abstract/FREE Full Text

Maloy AL, Black RD, Segurola RJ Jr. (1998) Lyme disease complicated by the **Jarisch-Herxheimer** reaction.J Emerg Med. 16(3), 437-8.

Bonnet JP, Abid L, Dabhar A, Lévy A, Soulier Y, Blangy S. (2000) Early biliary **pseudolithiasis** during **ceftriaxone** therapy for acute pyelonephritis in children: a prospective study in 34 children. Eur J Pediatr Surg. 10(6):368-71

Patel R., Grogg KL., Edwards WD., et al. (2000) **Death** from inapproprate therapy for Lyme disease. Clin Infect Dis 31, 1107-1109 http://cid.oxfordjournals.org/content/31/4/1107.short
**[Cefotaxime, Venenkatheter, Candida, Sepsis]**

**Stricker** RB, Green CL, Savely VR, Chamallas SN, Johnson L (2010) Safety of intravenous antibiotic therapy in patients referred for treatment of neurologic Lyme disease. In: Minerva Med 101(1), 1–7. http://www.ncbi.nlm.nih.gov/pubmed/20228716

Holzbauer S, Kemperman M, Lynfield R (2010) **Death** due to community-associated **Chlostridium difficile** in a woman receiving prolonged antibiotic therapy for suspected Lyme disease. CID 51, 369-70 http://www.ncbi.nlm.nih.gov/pubmed/20597684

Jolivet-Gougeon A, Kovacs B, Le Gall-David S, (2011) Bacterial **hypermutation:** clinical implications. Journal of Medical Microbiology 60, 563–573 http://jmm.sgmjournals.org/content/60/5/563.abstract http://www.ncbi.nlm.nih.gov/pubmed/21349992 **[methyl-directed mismatch repair (MMR) system]**

White B, Seaton RA, Evans TJ (2012) Management of suspected Lyme borreliosis: experience from an outpatient parenteral antibiotic therapy service. QJM Advance Access. 1-6 http://www.ncbi.nlm.nih.gov/pubmed/23070203 **[Ceftriaxon 21-23 Tage, maximal 43 Tage, Venenkatheter, 40% Nebenwirkungen]**

Rashid MU, Lozano HM, Weintraub A et al. (2013) In vitro activity of **cadazolid against Clostridium difficile strains** isolated from primary and recurrent infections in Stockholm, Sweden. Anaerobe. pii: S1075-9964(13)00023-1. doi: 10.1016/j.anaerobe.2013.02.003. http://www.ncbi.nlm.nih.gov/pubmed/23454525

Pena-Miller R, Laehnemann D, Jansen G, Fuentes-Hernandez A, Rosenstiel P, Schulenburg H, Beardmore R (2013) Research Article: **When the Most Potent Combination of Antibiotics Selects**

**for the Greatest Bacterial Load: The Smile-Frown Transition**. PLOS Biology 11(4), e1001540, 1-13 [**in vitro**]
http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.1001540?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+plosbiology%2FNewArticles+%28Ambra+-+Biology+New+Articles%29

Kalghatgi S et al. (2013) **Bactericidal antibiotics induce mitochondrial dysfunction and oxidative damage in mammalian cells. Science** Translational Medicine, 5, 192ra85
http://stm.sciencemag.org/content/5/192/192ra85.short

Berghoff W (2014) **Literaturübersicht Antibiotische Behandlung Lyme-Borreliose Stadium III**
http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-d_Literaturuebersicht_Antibiotische_Behandlung_LB_III.pdf

Nelson C, Elmendorf S, Mead P (2015) Neoplasms misdiagnosed as "chronic Lyme disease. JAMA Intern Med. 175, 132–133. 36.

Marks CM, Nawn JE, Caplow JA (2016) Antibiotic treatment for chronic Lyme disease-Say no to the DRESS. JAMA Intern Med. 176(12), 1745-1746. . **[Drug reaction with eosinophilia and systemic syndroms]**
https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2571617?redirect=true

Marzec NS, Nelson C, Waldron PR et al. (2017) **Serious Bacterial Infections Acquired During Treatment of Patients Given a Diagnosis of Chronic Lyme Disease - United States.** MMWR Morb Mortal Wkly Rep. 66(23), 607-609. doi: 10.15585/mmwr.mm6623a3.
https://www.ncbi.nlm.nih.gov/pubmed/28617768#cm28617768_69799

De Wilde M, Speeckaert M, Callens R, Van Biesen W (2017) **Ceftriaxone-induced immune hemolytic anemia as a life-threatening complication of antibiotic treatment of 'chronic Lyme disease'.** Acta Clin Belg. 72(2), 133-137. doi: 10.1080/17843286.2016.1180829.

➔ **Herxheimer** http://kabilahsystems.de/herx.pdf

## Verlaufs – Muster, course pattern

Petersen LR, Sweeney AH, Checko PJ, Magnarelli LA, et al. (1989) Epidemiological and clinical features of 1,149 persons with Lyme disease identified by laboratory-based surveillance in Connecticut Yale J Biol Med 62, 253–62 http://www.ncbi.nlm.nih.gov/pubmed/2683415

Fahrer H, Sauvain MJ et al. (1998) Longterm survey (7 years) in a population at risk for Lyme borreliosis: what happens to the seropositive individuals? Eur J Epidemiol 14(2), 117-23
http://www.unboundmedicine.com/medline/citation/9556169/Longterm_survey_%287_years%29_in_a_population_at_risk_for_Lyme_borreliosis:_what_happens_to_the_seropositive_individuals?

Nowakowski J, Nadelman RB, Sell R, et al. (2003) Long-term follow-up of patients with culture-confirmed Lyme disease 115(2), 91-6.
http://www.ncbi.nlm.nih.gov/sites/entrez?filters=&orig_db=PubMed&db=pubmed&cmd=Search&term=12893393[uid]

Hassler D. (2006) **Phasengerechte Therapie der Lyme-Borreliose**. Chemother J 15, 106-11.
http://www.dieterhassler.de/fileadmin/PDF/CTJ806.pdf
„Je nach Region zeigen Seroprävalenzstudien, dass bis zu 20 % der Probanden Antikörper gegen Borrelia burgdorferi sensu lato aufweisen. Diese hohe Rate von Seropositiven hat die Annahme begründet, dass der Nachweis von Immunglobulin-G-Antikörpern (IgG-Antikörpern) in vielen Fällen lediglich auf eine früher durchgemachte Infektion zu interpretieren wäre. Diese Ansicht wird noch heute vielfach publiziert. In einer Langzeituntersuchung des genannten Kollektivs konnten wir dann aber zeigen, dass alle seropositiven Probanden irgendwann auch klinisch symptomatisch werden. Die maximale Latenzzeit bis zum Auftreten von Krankheitssymptomen betrug acht Jahre. **Daher kann heute als geklärt gelten, dass die Lyme-Borreliose eine primär chronisch verlaufende Infektionskrankheit ist, bei der es in Analogie zur Syphilis keine Spontanheilung gibt. Die These eines „Durchseuchungstiters" im Sinne einer durchgemachten, spontan überstandenen Infektion konnte nie belegt werden und sollte heute obsolet sein."**

**In English now: Therefore, it can be said today that Lyme borreliosis is a primarily chronically infectious disease in which there is no spontaneous healing in analogy to syphilis. The thesis of a "penetration titrix" in the sense of a spontaneously surrendered infection could never be proven and should be obsolete today.**

Lyme disease.org http://www.lymedisease.org/resources/handouts5.html
**Relapses and Failure Rates Using Short Term Approaches**
http://www.lymedisease.org/resources/Relapses%20and%20Failure%20Rates.pdf
**"This listing of peer-reviewed, published articles illustrates the high failure rates, ranging from 26% to 50%, using short term antibiotic approaches."**

Berghoff W (2014) **LNB Verlaufsbeobachtungen nach antibiotischer Behandlung**. Literaturübersicht. http://www.praxis-berghoff.de/dokumente/berghoff150714/Kapitel_23-e_LNB_Verlaufsbeobachtungen_nach_antibiotischer_Behandlung_Literaturuebersicht.pdf

Cadavid D, Auwaerter PG, Rumbaugh J, Gelderblom H. (2016) **Antibiotics for the neurological complications of Lyme disease. Cochrane Database of Systematic Reviews** Issue 12. Art. No.: CD006978. DOI: 10.1002/14651858.CD006978.pub2. View/save citation
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006978.pub2/abstract
**"None of the trials revealed any between-group differences in symptom resolution in response to active treatment". "There is mostly low- to very low-quality clinical evidence from a limited number of mostly small, heterogeneous trials with diverse outcome measures, comparing the relative efficacy of central nervous system-penetrant antibiotics for the treatment of LNB. The few existing randomized studies have limited power and lack consistent and well-defined entry criteria and efficacy endpoints. It is not possible to draw firm conclusions on the relative efficacy of accepted antibiotic drug regimens for the treatment of LNB."**

- ➔ **Borrelien Populationsdynamik** http://www.erlebnishaft.de/stressvar2.pdf
- ➔ **Bakterielle L-Formen** http://www.erlebnishaft.de/stressvar1.pdf
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