See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/311575626

The Case for the Persistence of Lyme Disease After Antibiotic Therapy

Article ·	December 2016		
CITATIONS	S	READS	
0		586	
1 autho	r:		
0	Christine Heidt		
	University of Alberta		
	1 PUBLICATION 0 CITATIONS		
	SEE PROFILE		

The Case for the Persistence of Lyme Disease After Antibiotic Therapy

Christine Heidt
BSC Engineering

Never has there been so much controversy over a bacterial infection as there has been over Lyme disease (LD). On one side of the fence is the Infectious disease Society of America (IDSA) and on the other side is the International Lyme and Associated Diseases Society (ILADS). The IDSA claims that Lyme disease is easy to diagnose and easy to treat. ILADS, on the other hand claims that Lyme disease is not easy to diagnose nor is it easy to treat.

The Canadian government sides with the IDSA and concludes that "Some people who were treated for Lyme disease continue to have symptoms months to years after treatment. This condition is known as post-treatment Lyme disease syndrome (PTLDS). Its symptoms should be managed and treated appropriately." and "There is no definitive evidence that persistent symptoms represent ongoing infection. Post-infectious inflammation due to damage from the infectious process may respond to antiinflammatory drugs." (28) This information is not exactly correct, unless the only research that is allowed to be considered comes from the IDSA, who maintains that the proof of residual symptoms comes from the results of four clinical trials where antibiotic failures occurred.(1,2,3) Because administration of either doxycycline or ceftriaxone did not result in symptom reduction, members of the IDSA conclude that treatment for PTLDS with any and all antibiotics is pointless. The problem here is that only one of two different antibiotics were administered in these trials.(1,2,3) This is just one example of the IDSA's "expert opinion" regarding Lyme disease and is the basis of their claim that any symptom that lingers after antibiotic treatment must be residual in nature, in other words not caused by ongoing infection. The IDSA calls this version of chronic Lyme disease "Post Treatment Lyme Disease Syndrome" (PTLDS). This version is based solely on the IDSA's "expert opinion" AND is in no way based on solid facts. The fact is that these three studies do support current research, which demonstrates that both doxycycline and ceftriaxone are ineffective at addressing lingering symptoms. (5,6,9,10,11,12,13,14,15,16) While the IDSA team spends their days promoting their PTLDS model and patting themselves on the back, many fact seeking scientists are not content with the IDSA's "expert opinions" and continue to search for the cause of these so called "residual" symptoms.

The fact is that when scientists and researchers actually do look for the LD bacteria in the tissues and blood of antibiotic treated subjects, they tend to find them.(4,5,6,7,8,15) What has been observed in both in-vitro and in-vivo studies includes drug tolerant persisters, round bodies, cysts, biofilm communities and granules.(4,5,6,7,8,9,10,11,12,13,14,15,16) Biofilm communities and persisters are not a new concept. It is a well-known fact in the medical profession that both morphologies are considered to signal the onset of chronic infection.(19,20) By admitting that these bacteria do form biofilm colonies or persisters, the IDSA would be forced to acknowledge the chronic nature of Lyme disease.

In a study published over 20 years ago, it was reported that "Antibiotic therapy with penicillin, doxycycline, and ceftriaxone has proven to be effective for the treatment of Lyme borreliosis. In some patients, however, it was noticed that borreliae can survive in the tissues in spite of seemingly adequate therapy." (14) Interestingly, recent studies support this same conclusion. Additionally, researchers have observed that either of the two antibiotics that were administered in the IDSA studies were found to initiate the transformation of the LD spirochete into treatment resistant persister cells and other

bacterial forms.(5,6,9,10,11,12,13,14,15,16) Ironically, the four clinical trials meant to support the IDSA's PTLDS model actually serve to support this recent research, which in turn supports ILADS assertion of reversion to persistent bacteremia causing ongoing symptoms, rather than the IDSA's expert opinion that the infection has been eradicated and residual symptoms remain indefinitely.

Current studies are focused on finding effective treatments that not only eradicate the spirochetal form of the LD bacteria but also target persister bacteria, round bodies, cysts and biofilm communities.(10,11,12,13,14,16,17,18) A recent research article co-authored by, Dr Paul Auwaerter (Presidentelect of the IDSA), entitled "Drug Combinations against Borrelia burgdorferi Persisters In Vitro: Eradication Achieved by Using Daptomycin, Cefoperazone and Doxycycline" suggests that perhaps even the IDSA's own members are not fully convinced of the IDSA's version of chronic Lyme disease. (10) While Auwaerter asserts that the cause of PTLDS is unknown, he admits that "findings that suggest the continued presence of B. burgdorferi in some form indicate that current Lyme disease treatment may not sufficiently eliminate B. burgdorferi persisters or that the immune system fails to clear persisting organisms or bacterial debris, which may be the underlying cause for those who suffer from unresolved Lyme disease symptoms." Prior to this publication, Dr Auwaerter co-authored a publication with IDSA LD Guidelines members entitled "Antiscience and ethical concerns associated with advocacy of Lyme disease" where he and the other authors attempt to discredit any research that does not support the IDSA's PTLDS theories, with statements such as "Some activists portray Lyme disease, a geographically limited tick-borne infection, as a disease that is insidious, ubiquitous, difficult to diagnose, and almost incurable; they also propose that the disease causes mainly non-specific symptoms that can be treated only with long-term antibiotics and other unorthodox and unvalidated treatments. Similar to other antiscience groups, these advocates have created a pseudoscientific and alternative selection of practitioners, research, and publications and have coordinated public protests, accused opponents of both corruption and conspiracy, and spurred legislative efforts to subvert evidence-based medicine and peer-reviewed science."(21) The truth is that over 50% of the IDSA's guidelines are based on "expert opinion" rather than "evidence-based medicine" as their publication suggests. A further 31% of the IDSA guidelines are based on observational studies. Only a meagre 29% of the IDSA Guidelines fit into "evidence-based medicine".(22,23,24,25,27) Importantly, the IDSA's own research supports these very findings.(22) Furthermore, various IDSA members that co-authored the "Antiscience and ethical concerns" publication(21) were also involved with the creation of the Lyme Guidelines although they, themselves hold competing interests. Some members hold patents for LD products, some own shares in companies that have vested interests with the diagnosis and treatment of LD and some act as "expert witnesses in malpractice litigation" against any Dr that dares to question their "expert opinion".(22,26) Rather than sharing information and learning from others, the IDSA continues to belittle, publicly attack and/or attempt to jail any Dr or researcher that does not endorse their Lyme disease Guidelines and policies.(22)

To prove their "anti-science" and PTLDS theories, one would expect the IDSA to quickly follow up the research of Dr Auwaerter with clinical trials utilizing the daptomycin, cefoperazone, doxycycline combination in either animal or human subjects. If, as they assert, no benefit is derived from this treatment combination, such a clinical trial would serve not only to establish their "evidence based-medicine" claim, it would also provide actual evidence for their PTLDS assumptions. Instead it appears that there has been no commitment by the IDSA to undertake such an activity, which further raises suspicion of flaws in their theories.

In his editorial, Powers discusses "expert opinion" and concludes "history has shown that this type of evidence can be misleading, sometimes with major adverse consequences for patients", "We would do well to remember Voltaire's admonition that "opinion has caused more trouble on this little earth than plagues or earthquakes".(25) Ironically, Guideline recommendations that are meant to subvert "adverse consequences" often end up being the cause of catastrophic consequences for many, which could very well be the case with Lyme disease.

References:

- 1. Klempner MS, Hu LT, Evans J, Schmid CH, Johnson GM, Trevino RP, Norton D, Levy L, Wall D, McCall J, Kosinski M, Weinstein A., Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. New Eng. J. Med. 345:85-92, 2001).
- 2. Krupp LB, Hyman LG, Grimson R, Coyle PK, Melville P, Ahnn S, Dattwyler R, Chandler B., Study and treatment of post Lyme disease (STOP-LD): a randomized double masked clinical trial. Neurology. (2003) Jun 24;60(12):1923-30.
- 3. Fallon BA, Keilp JG, Corbera KM, Petkova E, Britton CB, Dwyer E, Slavov I, Cheng J, Dobkin J, Nelson DR, Sackeim HA., A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. Neurology. 2008 Mar 25;70(13):992-1003. Epub (2007) Oct 10.
- 4. Straubinger RK, Summers BA, Chang YF, Appel MJ., Persistence of Borrelia burgdorferi in experimentally infected dogs after antibiotic treatment. J Clin Microbiol, 35(1), 111-116 (1997).
- 5. Yrjänäinen, Hytönen J, Hartiala P, Oksi J, Viljanen MK., Persistence of borrelial DNA in the joints of Borrelia burgdorferi-infected mice after ceftriaxone treatment., APMIS. (2010) Sep 1;118(9):665-73. doi: 10.1111/j.1600-0463.2010.02615
- 6. Embers ME, Barthold SW, Borda JT, Bowers L, Doyle L, et al. (2012) Persistence of Borrelia burgdorferi in Rhesus Macaques following Antibiotic Treatment of Disseminated Infection. PLoS ONE 7(1): e29914. doi:10.1371/journal.pone.0029914
- 7. Miklossy J, Kasas S, Zurn AD, McCall S, Yu S, McGeer PL, Persisting atypical and cystic forms of Borrelia burgdorferi and local inflammation in Lyme neuroborreliosis., Journal of Neuroinflammation (2008), 5:40 doi:10.1186/1742-2094-5-4
- 8. Sapi E , Balasubramanian K , Poruri A , Maghsoudlou JS, Socarras KM , Timmaraju AV , Filush KR , Gupta K , Shaikh S , Theophilus PAS, Luecke DF, MacDonald A, Zelger B, (2016). Evidence of in vivo existence of Borrelia biofilm in borrelial lymphocytomas. European Journal of Microbiology and Immunology. Published online Feb. 9, 2016. doi: 10.1556/1886.2015.00049
- 9. Meriläinen L., Characterization and immunological aspects of Borrelia burgdorferi pleomorphic round bodies., Jyväskylä: University of Jyväskylä, (2015), 64 p., ISSN 1456-9701; 307, ISBN 978-951-39-6334-7, ISBN 978-951-39-6335-4

- Feng J, Auwaerter PG, Zhang Y (2015), Drug Combinations against Borrelia burgdorferi Persisters In Vitro: Eradication Achieved by Using Daptomycin, Cefoperazone and Doxycycline. PLoS ONE 10(3): e0117207. doi:10.1371/journal. pone.0117207
- 11. Feng J, Wang T, Shi W, Zhang S, Sullivan D, Autwaerter PG, (2014) Identification of Novel Activity against Borrelia burgdorferi Persisters Using an FDA Approved Drug Library. Emerg Microb Infect July 2, 2014: 3, e49.
- 12. Brorson O, Brorson SH, Scythes J, MacAllister J, Wier A, et al. (2009) Destruction of spirochete Borrelia burgdorferi round-body propagules (RBs) by the antibiotic tigecycline. Proc Natl Acad Sci U S A 106:18656–18661. doi: 10.1073/pnas.0908236106 PMID: 19843691
- 13. Feng J, Zhang S, Shi W and Zhang Y (2016) Ceftriaxone Pulse Dosing Fails to Eradicate Biofilm-Like Microcolony B. burgdorferi Persisters Which Are Sterilized by Daptomycin/ Doxycycline/Cefuroxime without Pulse Dosing. Front. Microbiol. 7:1744. doi: 10.3389/fmicb.2016.01744
- 14. Kersten A, Poitschek C, Rauch S, Aberer E, Effects of Penicillin, Ceftriaxone, and Doxycycline on Morphology of Borrelia burgdorferi., Antimicrobial Agents and chemotherapy 39(5), May (1995), p. 1127–1133 0066-4804/95
- 15. Hodzic E, Imai D, Feng S, Barthold SW (2014) Resurgence of Persisting Non-Cultivable Borrelia burgdorferi following Antibiotic Treatment in Mice. PLoS ONE 9(1): e86907. doi:10.1371/journal.pone.0086907
- 16. Sharma B, Brown AV, Matluck NE, Hu LT, Lewis K. (2015). Borrelia burgdorferi, the causative agent of Lyme disease, forms drug-tolerant persister cells., Antimicrob Agents Chemother 59:4616 4624. doi:10.1128/AAC.00864-15.
- 17. Sapi E, Kaur N, Anyanwu S, Lueke DF, Datar A, Patel S, Rossi M, Stricker RB, Evaluation of in-vitro antibiotic susceptibility of different morphological forms of Borrelia burgdorferi., Infection and Drug Resistance (2011):4 97–11, DOI:10.2147/IDR.S19201
- 18. Theophilus PAS, Victoria MJ, Socarras KM, Filush KR, Gupta K, Luecke DF, Sapi E, Effectiveness of Stevia Rebauiana whole leaf extract against various morphological forms of Borrelia burgdorferi in vitro., (2015) European Journal of Microbiology and Immunology 5 (2015) 4, pp. 268–280, ISSN 2062-8633, DOI: 10.1556/1886.2015.00031
- 19. Bjarnsholt T1., The role of bacterial biofilms in chronic infections., APMIS Suppl. 2013 May;(136):1-51. doi: 10.1111/apm.12099, PMID: 23635385, DOI:10.1111/apm.12099
- 20. Fauvar M, De Groote V, Michiels J, Role of persister cells in chronic infections: clinical relevance and perspectives on anti-persister therapies., Journal of Medical Microbiology (2011), 60, 699–709, DOI: 10.1099/jmm.0.030932-0
- 21. Auwaerter PG, Bakken JS, Dattwyler RJ, Dumler S, Halperin JJ, McSweegan E, Nadelman RB, O'Connell S, Shapiro ED, Sood SK, Steere AC, Weinstein A, Wormser GP, Antiscience and ethical concerns associated with advocacy of Lyme disease., Lancet Infect Dis. 2011 September; 11(9): 713–719. doi:10.1016/S1473-3099(11)70034-2.

- 22. Khan AR, Khan S, Zimmerman V, Baddour LM, Tleyjeh IM, Quality and Strength of Evidence of the Infectious Diseases Society of America Clinical Practice Guideliines., Clinical Infectious Diseases (2010); 51(10):1147–1156, DOI: 10.1086/656735
- 23. Keller DM, Infectious Disease Treatment Guidelines Weakened By Paucity of Scientific Evidence, Infectious Diseases Society of America (IDSA) 47th Annual Meeting: Abstract 1324. Presented November 1, 2009; Abstract LB-31, presented October 31, 2009
- 24. Lee DH, MD; Vielemeyer O, Analysis of Overall Level of Evidence Behind Infectious Diseases Society of America Practice Guidelines, Arch Intern Med. 2011;171(1):18-22, PMID:21220656 DOI: 10.1001/archinternmed.2010.482
- 25. Powers JH, Practice Guidelines: Belief, Criticism and Probability, Arch Intern Med. 2011;171(1):15-17. doi:10.1001/archinternmed.2010.453
- 26. Johnson L, Stricker RB, The Infectious Diseases Society of America Lymeguidelines: a cautionary tale about the development of clinical practice guidelines, Philosophy, Ethics, and Humanities in Medicine 2010, 5:9
- 27. Chowhury M, Lee D, Solari P, O Vielemeeyer, IDSA Guidelines: What Evidence Are They Based On?, Conference: Infectious Diseases Society of America 2009 Annual Meeting
- 28. Government of Canada Website: http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/lyme/professionals-professionnels/index-eng.php