

Life After Lyme Disease

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(See the Brief Report by Wormser et al on pages 244–7.)

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William James, the noted physician and philosopher, was among the thought leaders in the late 19th and early 20th centuries who popularized the term “Americanitis,” considered to be a condition brought on by the harried and demanding economic lifestyle of modern society [1]. He took dedicated interest in describing cases without chiding or condemning people who had become suddenly ill and bedridden, whose lives appeared to change overnight with complaints both physical and mental. He was perhaps most struck by the intelligent nature of these men and women who were abandoned by family and friends owing to problems of fatigue, nervousness, gastrointestinal problems, and the like [2]. James was among the first who sought to provide an extrinsic, environmental explanation for conditions that changed people’s lives—

changed who they were with, frustratingly, no remedy apparent.

This intense yearning to try to label and understand the cause of problems under control of neither patients nor physicians may be rooted in human nature; more modern study suggests that the brain may well be preconditioned in this regard [3]. Since James’s time, various infections, including brucellosis, chronic Epstein-Barr virus, candidal overgrowth, and, more recently, chronic Lyme disease, have been advocated by some as a universal explanation for fatiguing conditions. Alternative, descriptive, and ultimately syndromic explanations for problems without true biological understanding, such as fibromyalgia or chronic fatigue syndrome (CFS), are understandably unpalatable for some and are even considered pejorative; a recent Institute of Medicine panel suggested a new term and definition for CFS, systemic exertional intolerance syndrome [4].

There has been limited headway in modern medicine’s ability to alleviate chronic fatigue, pain, and other incapacitating symptoms. For those seeking explanations, Lyme disease remains a popular consideration. A difficult dynamic often emerges in medical offices wherein evaluations and conversations center on whether there is sufficient evidence to implicate Lyme disease or whether the vaguely defined entity of chronic Lyme disease has no solid scientific grounding [5]. Moreover, the 20th-century

miracle of antibiotics, while relieving the objective findings of authentic *Borrelia burgdorferi* infection, leaves some still suffering from residual Lyme disease symptoms that do not appear to respond to additional treatment courses for what has been proposed as posttreatment Lyme disease syndrome (PTLDS) [6–8]. In essence, a responsible clinician using best available evidence often appears to be removing hope and therefore a pathway to improvement. This often further exacerbates the fear and anxiety of having disabling symptoms that may not improve—no matter how they are labeled.

In this issue of *Clinical Infectious Diseases*, Wormser and colleagues have contributed valuable information that should help allay the common distress that Lyme disease is routinely life-altering for the long term. They have followed an extremely well-characterized cohort of patients with treated early Lyme disease (ie, erythema migrans), who had their infection unquestionably confirmed by isolation of *B. burgdorferi* in culture. One hundred of the original 283 (35%) patients followed for an average of approximately 15 years had recent application of the widely used 36-Item Short Form General Health Survey version 2 (SF-36v2) self-administered instrument to inventory their state of functionality including both physical and mental health. Compared to norms in the general US population,

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these patients fared no worse and even better than average in all 8 measured spheres, suggesting that Lyme disease did not have an ongoing impact on their health at that time. Additionally, because the normalized SF-36v2 values reflect the entire country, where Lyme disease is not endemic in most parts, the lack of a signal implicating worse health in this New York-based study is conceivably more meaningful.

Important caveats regarding this study are that it did not specifically include patients with extracutaneous manifestations of *B. burgdorferi* infection such as neuroborreliosis or late Lyme arthritis. Such patients could answer survey questions differently in the long term. Although loss to follow-up is not surprising in a study of this duration, those lost compared with those studied were more likely to be male, to be younger, and to have 1 additional symptom at initial presentation; how this potential selection bias might have affected results is unclear. The SF-36v2 instrument is perhaps the most widely used of such functional surveys in evaluating group comparisons and therefore the health impact of conditions such as back pain, cancer, human immunodeficiency virus, and the like; however, its significance is greater when administered serially [9]. This long-term study's findings would therefore be strengthened by additional survey administrations in subsequent years. Regardless, given the relative paucity of such longitudinal outcome data for patients with Lyme disease, this study is an important contribution.

This group performed an earlier analysis of long-term follow-up of patients with culture-confirmed Lyme disease and found that 10% of patients experienced persistent symptoms >1 year after antibiotic therapy and 4% had symptoms at each follow-up visit [10]. For many other studies examining both short- and longer-term impact of *B. burgdorferi* infection, a common confounder is that preexisting symptoms were not carefully assessed, making it difficult to precisely attribute symptoms to Lyme disease or

other factors. Perhaps the most carefully constructed longitudinal study to date, by Aucott et al, only enrolled patients carefully examined to exclude those with preexisting health problems. They found that 8 of 74 (11%) patients met the definition for PTLDS [11]. So, although Wormser et al's SF-36v2-based quality of life study takes a snapshot in the second decade after erythema migrans, it does not describe how patients may respond in the initial months or early years following diagnosis and treatment. It does offer a view, through a public health lens, of the impact of Lyme disease upon longer-term health, and the study does not strongly suggest that it is significant.

Wormser et al have also recently published helpful companion studies examining whether these same patients with Lyme disease were more prone to developing fibromyalgia or chronic fatigue. Only 1 of 100 (1%) studied subjects met criteria for fibromyalgia, with the single patient developing it 19 years after Lyme disease diagnosis; this value is lower than the 2%–8% fibromyalgia prevalence in the United States [12]. Severe fatigue was identified in 9% of 100 studied subjects, but in most was attributable to other factors, with less severe fatigue possibly linked to Lyme disease in 3%, well within the frequency of fatigue experienced by adults generally [13].

Whether Lyme disease causes problems of a persistent but nonspecific nature remains uncertain. Given the poorly understood pathophysiology of such chronic problems such as fatigue, pain, and diminished mental acuity, there are likely many potential contributors in life; moreover, the background common prevalence of these symptoms increases especially as people age (perhaps why PTLDS seems uncommon in children), and there is the potential tendency of an anchoring bias to ascribe symptoms to Lyme disease or even just tick bites by patients and physicians alike [14].

How might this study inform physicians and patients seeking care or explanation of problems that may or may not be related to Lyme disease? Given the

high rates of nonspecific, subjective symptoms such as pain and fatigue in the general population, for those with erythema migrans, it should help suppress concerns that the effects of early Lyme disease are likely to cause lifelong debilitation. For patients with difficult-to-resolve, less well-understood problems without good evidence of *B. burgdorferi* infection, this study offers evidence that treated erythema migrans is not likely a significant driver of chronic health problems in the United States. For this latter group, this study offers little solace and, much like William James more than a century ago, thoughtful physicians are left listening to patients without a clear understanding of mechanisms or effective solutions.

Note

Potential conflict of interest. The author receives support from the Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases, Johns Hopkins University School of Medicine. He has also participated in medical-legal expert testimony regarding tick-borne diseases.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

- Richardson RD. William James: in the maelstrom of American modernism: a biography. New York: Houghton Mifflin, 2007:311.
- James W. Varieties of religious experiences: a study in human nature. Washington, DC: Library of Congress, 2010 (originally published 1902).
- Whitson JA, Galinsky AD. Lacking control increases illusory pattern perception. *Science* 2008; 322:115–7.
- Institute of Medicine. Beyond myalgic encephalomyelitis/chronic fatigue syndrome. Redefining an illness. Report guide for clinicians. Available at: http://www.iom.edu/~/media/Files/Report%20Files/2015/MECFS/MECFS_cliniciansguide.pdf. Accessed 9 March 2015.
- Feder HM Jr, Johnson BJ, O'Connell S, et al. A critical appraisal of "chronic Lyme disease." *N Engl J Med* 2007; 357:1422–30.
- Klempner MS, Baker PJ, Shapiro ED, et al. Treatment trials for post-Lyme disease symptoms revisited. *Am J Med* 2013; 126:665–9.
- Oksi J, Nikoskelainen J, Hiekkänen H, et al. Duration of antibiotic treatment in disseminated Lyme borreliosis: a double-blind, randomized, placebo-controlled, multicenter clinical study. *Eur J Clin Microbiol Infect Dis* 2007; 26:571–81.

8. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* **2006**; 43: 1089–134.
9. Ware JE. User's manual for the SF-36v2 Health Survey. 2nd ed. Lincoln, RI: QualityMetric, **2007**:27–33.
10. Nowakowski J, Nadelman RB, Sell R, et al. Long-term follow-up of patients with culture-confirmed Lyme disease. *Am J Med* **2003**; 115:91–6.
11. Aucott JN, Crowder LA, Kortte KB. Development of a foundation for a case definition of post-treatment Lyme disease syndrome. *Int J Infect Dis* **2013**; 17:e443–9.
12. Wormser GP, Weitzner E, McKenna D, et al. Long-term assessment of fibromyalgia in patients with culture-confirmed Lyme disease. *Arthritis Rheum* **2014**; doi:10.1002/art.38972.
13. Wormser GP, Weitzner E, McKenna D, Nadelman RB, Scavarda C, Nowakowski J. Long-term assessment of fatigue in patients with culture-confirmed Lyme disease. *Am J Med* **2015**; 128:181–4.
14. Halperin JJ. Lyme disease: neurology, neurobiology, and behavior. *Clin Infect Dis* **2014**; 58:1267–72.