

The pain of “chronic Lyme disease”: moving the discourse in a different direction

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ABSTRACT About 30% of the population of the United States suffers from acute or chronic pain, often of unknown cause. Among this group might be included patients with symptoms claimed to be caused by a poorly defined condition called “chronic Lyme disease” in which chronic pain is a major contributor. Since there is no evidence to indicate that chronic Lyme disease is due to a persistent infection and that extended antibiotic therapy is beneficial and safe, this condition should not be viewed solely as an infectious disease problem. Rather, it should be considered within the context of a broad-based, multidisciplinary approach to determining the cause of chronic pain *per se* and developing more effective strategies for its treatment as outlined in a recent report on pain issued by the Institute of Medicine.—Baker, P. J. The pain of “chronic Lyme disease”: moving the discourse in a different direction. *FASEB J.* 26, 11–12 (2012). www.fasebj.org

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THE INSTITUTE OF MEDICINE (IOM) recently issued a comprehensive and perceptive report on pain in the United States. It asserts that “Acute and chronic pain affect large numbers of Americans with at least 116 million U.S. adults—~30% of the population—burdened by chronic pain alone. The annual economic cost associated with chronic pain is estimated to be \$560–635 billion” (1). The report sadly notes that the personal experiences of some of those seeking relief from such pain can be torturous, and frustrating; they often go from one physician to another, unable to find anyone who can identify the cause of their symptoms or suggest a remedy for temporary—let alone lasting—relief.

It is reasonable to assume that patients with symptoms claimed to be caused by a poorly defined condition called “chronic Lyme disease” might be included in this large group of 116 million Americans. Published reports note that they indeed suffer from significant impairment of health-related quality of life in which chronic pain is a major contributor; in some patients, the deficits in physical health status are equivalent to those of patients with congestive heart failure or osteoarthritis (2). Some patients may consult as many as seven different physicians in search of a cause and treatment, often to no avail. Eventually, they are persuaded by Lyme disease support group members to believe that they have chronic Lyme disease and are told that only a Lyme-literate physician (LLMD), that is, a primary care physician who “specializes” in the diagnosis and treatment of Lyme disease, has the unique clinical insights to help them.

Despite the fact that the results of a validated, Food and

Drug Administration (FDA)-approved serological test for Lyme disease were negative based on criteria established by the Centers for Disease Control and Prevention (CDC), the LLMD likely will order additional tests. However, this time, the tests will be done by a Lyme disease specialty laboratory using nonvalidated tests and nonstandard diagnostic criteria, inconsistent with the criteria established by the CDC. The LLMD is convinced that the tests performed by this specialty laboratory are more sensitive because they reveal antibodies not detected by other FDA-approved tests. What seems to be lacking in this thought process is that even the most sensitive test imaginable is not going to give a positive result if one does not have Lyme disease, and that the additional antibodies detected by nonvalidated tests are of unproven relevance to the diagnosis of Lyme disease. What is not appreciated is that the evaluation criteria established by the CDC are based on hundreds of independent comparative assays of well-characterized specimens from patients known to have Lyme disease at different stages of development; they are designed to provide maximum sensitivity without compromising specificity. And so, based on a falsely positive test result, the patient is told—and is greatly relieved to learn—that he or she has chronic Lyme disease. Here the take home lesson is that only validated FDA-approved tests, evaluated by criteria established by the CDC, should be used for the diagnosis of Lyme disease. As of this date, there are 46 such tests (<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfivd/index.cfm>).

Having been incorrectly diagnosed, the patient then is placed on either extended antibiotic therapy or some other unproven and potentially harmful unorthodox treatment regimen; this is usually done at the patient’s own considerable expense, because most health insurance companies refuse coverage for treatments not shown to be beneficial and safe. Although the patient might begin to feel better after several months of treatment, it is not possible to determine whether improvement is due to the therapeutic regimen *per se* or a placebo effect; this is an important consideration, because a placebo effect as high as 38% has been reported in prior clinical trials on the benefit of

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extended antibiotic therapy for the treatment of chronic Lyme disease (2). It is entirely possible that the patient might have gotten better in time, without treatment; that happens. Sadly, there is no guarantee that the therapy proposed is not a complete waste of time and money, as well as one that places the patient at great risk. To ensure that their physician is treating in accordance with the results of evidence-based research, patients should ask about the results of published studies showing that the therapeutic regimen proposed is both beneficial and safe before consenting to treatment; this is especially important if they expect the costs to be covered by health insurance. Solicited and selective testimonials by previously treated patients—regardless of the number obtained—do not constitute proof of efficacy.

It is important also to note that if the therapy was truly beneficial, one would expect to see significant and lasting improvement in a large percentage (>90%) of all patients treated in the same manner; that is, benefit would be noted in a percentage well beyond the 38% attributable to a placebo effect. No evidence has ever been presented to document anything near such impressive results in patients given extended antibiotic therapy for the treatment of chronic Lyme disease; in fact, all of the evidence obtained thus far is to the contrary and indicates no significant benefit as well as serious safety problems (2–4). Although some patients may show improvement, far too many do not; some patients experience “relapses” that prompt them to believe that they must undergo additional rounds of treatment or that chronic Lyme disease is a hopeless and permanent condition that can never really be cured. Although it is always better to do so, all is not lost if one does not begin antibiotic therapy as soon as possible after a correct diagnosis of Lyme disease. Late manifestations are also responsive to 3–4 wk of oral antibiotic therapy (5), and a recent case report indicates that a patient was cured with two short courses of oral antibiotics, as late as 4 yr after correct diagnosis (6).

The signs associated with seventh nerve facial palsy are a good example of the fact that neurological symptoms associated with Lyme disease often persist beyond the completion of effective antibiotic therapy. Although short-term antibiotic therapy does indeed cure the infection, facial paralysis may persist for several weeks or months after the completion of therapy, largely because damaged nerves are slow to heal; however, these neurological signs eventually will vanish in time, without the need for additional antibiotic therapy. In view of these considerations, recommending that one continue to treat until all symptoms disappear is not justified and may even be harmful. It is also important to note that Lyme disease is not a permanent condition that ebbs and flows, nor is it a lethal, life-threatening disease as some falsely portray it to be (7).

A major source of confusion and misunderstanding is the failure to distinguish between Lyme disease *per se* and chronic Lyme disease; the two are not the same, and the terms, which are often and carelessly used interchangeably, suggest different things to different people. Lyme disease should be viewed only in the context of an infection caused by *Borrelia burgdorferi sensu lato* (8); much is known about its cause, prevention, diagnosis, and treatment (5, 8). That is not the case for chronic Lyme disease, which remains to be defined as a distinct clinical entity and is indistinguishable from other medical conditions with similar conditions, for

example, fibromyalgia and chronic fatigue syndrome (5). There is no evidence to indicate that chronic Lyme disease is due to a persistent *B. burgdorferi* infection, and the published results of four rigorously reviewed NIH-supported clinical trials provide no evidence that extended antibiotic therapy is beneficial and safe for patients suspected of having chronic Lyme disease (2–4).

In view of these considerations, it is time to discard the unproven view that chronic Lyme disease is due to persistent *Borrelia* infection and begin to examine alternative causes and therapeutic approaches, if we truly wish to help these and other patients who experience chronic pain associated with this undefined condition. The IOM report provides a detailed and multidisciplinary blueprint for transforming pain prevention, care, education, and research and provides opportunities for dealing with that aspect of chronic Lyme disease in a constructive and noncontentious manner (1). Since the average primary care physician living in an endemic area surely must see many patients who believe that they have chronic Lyme disease, he or she would welcome new insights on how best to manage and treat this condition in an effective manner. The issue of cost also is of no small concern because the government is seeking ways to reduce unnecessary medical costs without compromising on the delivery of essential care in accordance with the Patient Protection and Affordable Care Act. Implementation of the blueprint outlined in the IOM report would be an excellent first step in achieving these worthy goals. FJ

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