

Opinion

Lyme Disease: Call for a “Manhattan Project” to Combat the Epidemic

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Lyme disease is the most common tick-borne illness in the world today. Until recently, the Centers for Disease Control and Prevention (CDC) reported an average of only 30,000 cases of Lyme disease per year in the United States. Three preliminary CDC studies, however, have indicated that the true incidence of Lyme disease may be greater than 300,000 cases and as high as one million cases per year in the United States. A majority of these cases occur in women and children. Based on this new information, Lyme disease should be recognized as a virulent epidemic that is at least six times more common than HIV/AIDS. In response to these alarming statistics, we review the ongoing problems with diagnosis and treatment of Lyme disease. We propose the need for an HIV/AIDS-style “Manhattan project” to combat this serious epidemic that threatens the physical and mental health of millions of people around the world.

Almost from the moment of its discovery, Lyme disease has been a controversial illness [1,2]. The disease is caused by a spirochete, *Borrelia burgdorferi*, that is transmitted to humans by the bite of an *Ixodes* tick [3,4]. Following the discovery in 1982 that a spirochete was the agent of the disease, numerous reports described the protean clinical manifestations of the tick-borne illness, and laboratory testing for the disease was implemented in a haphazard fashion. This poorly directed approach to Lyme disease resulted in the perception in the early 1990s that the disease was being “overdiagnosed and overtreated” [5,6]. This perception in turn led to a backlash, culminating in the development of stringent diagnostic and therapeutic criteria for Lyme disease [7,8]. As a result, the diagnosis and treatment of Lyme disease has been limited by a surveillance case definition formulated by the Centers for Disease Control and Prevention (CDC) and supported by the Infectious Diseases Society of America (IDSA) [9,10]. Use of this stringent case definition has restricted CDC reporting of the disease to about 30,000 cases per year in the United States.

In response to this limited view of Lyme disease, a number of practitioners felt that the diagnostic criteria embraced by CDC/IDSA, such as the need for at least five antibodies against a laboratory strain of *B. burgdorferi*, geographical and seasonal restriction of the disease, and the presence of severe objective symptoms, were too restrictive and excluded many sick patients with tick-borne diseases. They also saw treatment failure with the short-term antibiotic regimens recommended by CDC/IDSA guidelines, and they recognized that Lyme disease may be complicated by infection with other tick-borne agents such as *Babesia*, *Anaplasma*, *Ehrlichia*, *Rickettsia*, and *Bartonella*. These practitioners formed the International Lyme and Associated Diseases Society (ILADS), an organization whose viewpoint is that Lyme disease is much more prevalent and complex than the CDC/IDSA criteria allow [11,12]. Based on the ILADS clinical perspective, it follows that the successful treatment of tick-borne diseases is more challenging than the limited recommendations of CDC/IDSA [3,12]. The contrasting CDC/IDSA and ILADS perspectives have given rise to the “Lyme Wars,” with sick patients stuck between the “overdiagnosed/overtreated” and “underdiagnosed/undertreated” camps [13,14]. The controversial nature of Lyme disease, coupled with the relatively small number of cases reported by the CDC, has stunted progress in combatting this illness.

All of this has suddenly changed. Three preliminary reports from the CDC have drastically altered our view of Lyme disease [15–17]. The first report, by Hinckley et al., examined laboratory test results for Lyme disease in 2008. The

authors concluded that the true annual rate of diagnosed Lyme disease was on the order of 312,000 cases, more than ten times the official number reported by the CDC [15]. The second report, by Hook et al., examined self-reported cases of Lyme disease in the years 2009, 2011, and 2012. The study found that in 2012, Lyme disease was diagnosed in 0.3% of respondents during the previous year; extrapolating from a population of >300 million, as many as one million people would have been diagnosed with Lyme disease in that timeframe. Furthermore, 42% of Lyme disease patients remained ill after 6 months, 12% were ill for more than 3 years, and 36% were treated with antibiotics for more than 8 weeks. Based on these results, the authors concluded that “a very large number of individuals in the US have been diagnosed with Lyme disease” [16].

The third study, by Nelson et al., analyzed private insurance claims related to Lyme disease between 2001 and 2010. The study found that a large number of Lyme disease cases not formally reported are nevertheless diagnosed and treated by healthcare providers. Among inpatients, children aged 5–9 years had the highest rate of Lyme disease diagnosis, while women were diagnosed with Lyme disease more often than men in the outpatient setting. The reason for this gender discrepancy is unclear [17]. In summary, these CDC studies indicate that Lyme disease is far more prevalent than official reporting statistics indicate, with at least 300,000 new Lyme disease cases and as many as one million cases (a majority of them women and children) diagnosed each year in the United States. In

Citation: 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

Editor: Glenn F. Rall, The Fox Chase Cancer Center, United States of America

Published: January 2, 2014

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Funding: The authors received no specific funding for this study.

Competing Interests: The authors have declared that no competing interests exist.

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comparison to HIV/AIDS, which is diagnosed at a rate of 55,000 new cases per year, Lyme disease appears to be at least six times more common in the United States.

How did Lyme disease reach these epidemic proportions? Three major factors play a role. First, the clinical diagnostic criteria for Lyme disease are too stringent, with only objective signs of the disease, such as an erythema migrans rash, arthritis, meningitis, or carditis, considered relevant [7]. Many patients with late Lyme disease (up to 90%) will only display subjective symptoms of the disease such as fatigue, musculoskeletal pain, and neurocognitive problems, and these patients will often fail to be diagnosed and treated for the disease [3,18]. Second, commercial laboratory testing for Lyme disease yields poor results, with a sensitivity of only 46% in patients who have been infected for more than 4–6 weeks. Thus, these tests miss more than half of Lyme disease cases [4,19]. In contrast, testing for HIV/AIDS has a sensitivity of >99.5% and misses less than one in 200 HIV/AIDS cases [3,4]. Third, treatment for Lyme disease is very restrictive, with CDC/IDSA clinging to the use of monotherapy with questionably effective short courses of antibiotics. This outdated approach contrasts with other serious infectious diseases such as tuberculosis and HIV/AIDS, where long-term combination antimicrobial therapy is the norm [4,20].

Controversy also persists over the existence of chronic Lyme disease due to

persistent infection with *B. burgdorferi* in patients who are untreated or undertreated for the spirochetal illness [8,21,22]. While some researchers continue to insist that there is no “credible scientific evidence” for chronic Lyme disease, a growing body of clinical and research evidence supports persistent symptomatic infection with the Lyme spirochete [21–24]. Recognition of the 10-fold greater magnitude of the Lyme disease epidemic and persistence of symptoms for more than 3 years supports the concept of chronic Lyme disease [15,16]. It remains to be determined how the chronic form of the disease is related to the ability of *B. burgdorferi* to penetrate tissue sites, evade the immune response and survive antibiotic therapy.

What needs to be done to combat the growing Lyme disease epidemic? As suggested by others [25], we need to establish a “Manhattan project” along the lines of the approach to the HIV/AIDS epidemic. First, an inclusive panel of clinicians, researchers, patients, and government officials should be established to determine the new approach to Lyme disease using the type of panel balancing recommended by government guidelines for controversial diseases [26]. This panel should revoke the archaic and ineffective IDSA Lyme guidelines and establish new clinical parameters for Lyme disease diagnosis [27,28]. Second, a uniform standard for Lyme disease testing should be established, with emphasis on a “gold standard” culture and/or PCR test for

the spirochete [29–31]. This effort would mirror the government-supervised approach to HIV/AIDS that was used to ensure high test sensitivity for that disease, as described above [3,4]. Third, further trials of antibiotic therapy should be conducted once the “gold standard” testing is in place, with emphasis on combination antimicrobial therapy and encouragement of pharmaceutical industry participation [4,32,33]. Although development of a safe and effective Lyme vaccine would be desirable, the failure of a previous Lyme vaccine and the inability over 30 years to develop an effective HIV/AIDS vaccine should serve as a cautionary note that vaccine-based prevention of Lyme disease may not be feasible in the near future [34–36].

In summary, preliminary studies from the CDC indicate that the Lyme disease epidemic has reached an unprecedented level with at least 300,000 people and as many as one million people, a majority of them women and children, diagnosed with Lyme disease each year in the United States. The staggering magnitude of the epidemic should prompt the CDC to show leadership in developing new guidelines for the diagnosis and treatment of Lyme disease. A coordinated “Manhattan project” similar to the attack mounted against the HIV/AIDS epidemic is urgently needed to address the serious worldwide threat of Lyme disease.

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