The case for mandatory reporting of Lyme disease cases in Connecticut to fuel scientific discovery

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Viewpoints on the 2002 Connecticut Department of Public Health's decision to discontinue mandatory laboratory seem to represent two diametrical extremes: those shifting from counting cases to devising and testing methods of prevention,[1] and those that feel that counting cases remains necessary for understanding the disease.

The CDC has historically considered reporting of cases of infectious diseases a vital step "in controlling and preventing disease, provision of appropriate therapy, and planning and evaluating prevention and control programs."[2] As of January 1, 1999, a total of 58 infectious disease were designated as notifiable to the CDC.[2]

The number of cases reported to the CDC from Connecticut dropped dramatically from 4,631 (up to 46,000 assuming a ten-fold underreporting) to 1,403 (up to 14,000 assuming underreporting) following the Connecticut Department of Public Health's decision to discontinue mandatory laboratory.

There are a number of reasons to argue for a reinstatement of the mandatory reporting of Lyme disease (LD).

Evidence for mandatory reporting

Connecticut remains hyperendemic for Lyme disease

Connecticut remains hyperendemic for LD. The number of cases of LD has grown fourfold from 1,192 (up to 11,000 assuming underreporting) in1991 to more than 4,631 (up to 46,000 assuming underreporting in 2003. There is no evidence that the marked drop in cases of LD to 1,403 (up to 14,000 assuming underreporting) is due to any other reason than the Connecticut Department of Public Health's decision to discontinue mandatory laboratory.

Severity of LD documented

Recent IDSA guidelines likened the post-treatment symptoms to the "aches and pains of daily living" without highlighting the poor quality of life of subsets of LD patients.[3]

The IDSA panel did not reconcile these conclusions with quality of life of LD patients enrolling in two NIH sponsored clinical trials.[4] The quality of life of subjects enrolling in the Klempner et al. trials was worse than that of the average type II diabetic or patient recovering from a heart attack, and as poor as that of subjects suffering from congestive heart failure.[4] The quality of life was equally as poor for LD patients enrolling in a third randomized clinical trial.[5]

Poor outcome of treatment

The view that chronic LD is not a problem assumes essentially all LD patients are successfully treated with a single course of 10 to 30 days of antibiotics.[3] The quality of life of LD patients to support this view cites a Connecticut cohort study by Seltzer and colleagues based on self report or parents' reports.[6]

The contrasting view that chronic LD remains a problem considers the Connecticut cohort study failed to appreciate the problems by not examining the patients. [6] Shadick and colleagues from the Department of Rheumatology-Immunology, Brigham and Women's Hospital, Boston Massachusetts found 34% of LD subjects remained ill a mean of 6.2 year after treatment by using a "standardized physical examination, health status measure (Short Form 36), psychometric test battery, and serologic analysis". [7] They concluded that "thirteen of 38 patients with previous LD (34%; CI, 19% to 49%) had evidence for musculoskeletal, neuropathic, or neurocognitive impairment likely caused by LD because all had earlier classic manifestations of LD, a positive serologic test result, and no other disease to explain their symptoms"[7](See Table 1).

The poor outcome was reinforced on follow-up examination of a cohort of LD patients by the Department of Medicine, New York Medical College, Valhalla, New York. LD patients were seen at a mean of 3.2 years after initial treatment.[8] The investigators reported "a history of relapse with major organ involvement had occurred in 28% and a history of reinfection in 18%. Anti-Borrelia antibodies, initially present in all patients, were still positive in 32%. At follow-up, 82 (38%) patients were asymptomatic and clinically active LD was found in 19 (9%). Persistent symptoms of arthralgia, arthritis, cardiac or neurologic involvement with or without fatigue were present in 114 (53%) patients."[8]

Weaknesses of the overdiagnosis hypothesis

Steere introduced the overdiagnosis hypothesis in 1993.[9] Over half of the patients referred to his LD clinic were diagnosed with fibromyalgia or chronic fatigue. The LD clinic did not report the outcome of treatment when changing the diagnosis to fibromyalgia or chronic fatigue. In a separate study of Lyme patients who were told they had fibromyalgia, 14 of 15 patients continued to have symptoms despite 2 ½ years of antidepressant and exercise.[10]

Diagnostically, the overdiagnosis hypothesis leaves clinicians and patients with unanswered questions. How can a clinician be sure a LD patient has

fibromyalgia? How can a patient diagnosed as fibromyalgia prove they do not have LD? What are the consequences of diagnosing a patient with fibromyalgia only to discover later the patient has LD?

Connecticut patient values

The IDSA guidelines described LD patients who are "symptomatic for many months to years after completion of appropriate antibiotic therapy" only to conclude that there is "considerable confusion and controversy exist over the frequency and cause of this process and even over its existence".[3]

The IDSA guideline authors did not consider the outcry of LD patients who remain ill despite recommended treatment.[3] The guideline authors did not reconcile these conclusions with the poor outcomes for 34% to 62% of LD patients described in the Shadick[7] and Asch[8] papers respectively. Instead the IDSA guideline authors dismissed most patients as having nothing more than the "aches and pains of daily living rather than to either LD." [3]

Weaknesses of testing

The IDSA guidelines stressed the need for epidemiologic criteria and/or positive serologic tests.[3] The epidemiologic criteria are restricted to an erythema migrans rash, Bell's palsy, meningitis, arthritis, and/or heart block. Positive serologic tests are restricted to a positive ELISA or IFA confirmed by a positive IgM or IgG test. There are no guidelines for the clinical diagnosis of Lyme disease in the absence of epidemiologic criteria and/or the two-tier diagnostic approach. Dr. Mead, medical epidemiologist, testified January 29, 2004 before the Connecticut Department of Public Health and the Connecticut Attorney General's Office that Lyme disease is "a clinical diagnosis is made for the purpose of treating an individual patient and should consider the many details associated with that patient's illness."[1]

The epidemiologic definition of LD has remained relatively stagnant and has not kept pace with dramatic advances in clinical presentations in LD. Like other infections, definitions of LD need to be periodically updated. The IDSA panel dismissed the results of patients of a Meta analysis of 504 LD patients[11] as not meeting strict epidemiologic and serologic criteria. [3] The IDSA panel did not mention that these five studies were published by leading institutions in *JAMA*[6], *Ann Intern Med*[7, 12], *Pediatrics*[13], and the *J. Rheum.*[13]

Recommendation

Mandatory Lyme testing should be reinstated. Follow-up studies should be added to measure the burden of illness.

Testing the recommendation

The hypothesis is fairly straightforward and should be simple to test. Vazquez and colleagues from Yale and the State of Connecticut Department of Health have already demonstrated that 65% of reported cases of LD had definite LD and

16% had probable LD.[14] The Shadick and colleagues cohort study would be a particularly good model to test concerns Connecticut residents have raised regarding the diagnosis and treatment of LD.[7] Neurologic LD is an example of a clinical presentation not included in the CDC epidemiologic definition that should be included in follow-up. Neurologic Lyme as described by Dr. Steere and colleagues includes symptoms of fatigue, headaches, memory and concentration problems, and sleep disturbances.[15]

Summary

Mandatory reporting coupled with follow-up studies in the treatment of LD would return the health department to its historic role of "controlling and preventing disease, provision of appropriate therapy, and planning and evaluating prevention and control programs."

Reference

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Table 1. Six of the cases of LD with long term sequelae described by Shadick and colleagues in their population-based retrospective cohort study

"Four patients reported persistent memory or concentration difficulties. Each patient had verbal memory deficits (neurocognitive test result). Each of these patients had had prominent headache or meningismus during acute Lyme disease; and two had lymphocytic meningitis. Patients 10 and 11 had previously diagnosed neuroborreliosis with meningeal symptoms and spinal fluid pleocytosis that was treated with antibiotics. Although their symptoms improved after therapy, they still had residual encephalopathy with verbal memory deficits."[7]

"Patient 12 had had high fever, meningeal symptoms, and subsequent arthritis in 1982. She was noted to have a positive serologic test result for Lyme disease 4 years later and was treated with 2 weeks of parenteral penicillin. She later developed a progressive speech disorder, bradykinesia, and abnormal ocular motor function. Magnetic resonance imaging of the brain showed scattered white matter lesions in the hemispheres and pons, and she was diagnosed with supranuclear palsy. Lumbar puncture showed no selective concentration of antibody in the spinal fluid. Nevertheless, she was re-treated with 2 weeks of parenteral ceftriaxone in 1989 that had no effect on her neurologic symptoms. During the time of observation, this patient died. At autopsy, lymphoid mononuclear cells were observed surrounding the intracerebral vessels in one section. Using Dieterle silver stain, a spirochete was present in the cortex and another was exterior to a leptomeningeal vessel."[7]

"Patient 13 had recently diagnosed late neuroborreliosis with intrathecal IgA production and had been treated with 6 weeks of intravenous ceftriaxone 1 year before our study. His neurocognitive test results showed improvement compared with his pretreatment scores, but he still had residual verbal memory deficits."[7]