Lyme Disease: The ABCs

I spent all of 2003 and the first months of 2004 researching and writing a book-length report on Lyme disease. The Lyme Disease Association (LDA), a national not-for-profit organization whose mission includes educating the public and government about Lyme and its associated tick-borne diseases, published the report in paperback this spring. Titled the Lyme Disease Update: Science, Policy & Law, it dwells on chronic and recurrent incidence.

Why update clinical research and political developments in Lyme disease? According to a late 1990s estimate, Lyme directly affects 6 out of every 100,000 Americans. Since it was first described as a distinct medical condition in the mid-1970s, in patients clustered around the town of Lyme, Connecticut, virtually every state has reported Lyme cases. Lyme has become the most prevalent vector-borne infection in the US, with the national incidence continuing to climb steeply. At the millennium, the number of cases annually reported to the Center for Disease Control & Prevention (CDC) had risen 33-fold since the CDC began surveillance in 1982. Between 2001 and 2002, the CDC recorded a 40% increase in national incidence.

The CDC, though, has estimated that its surveillance data for Lyme represent a fraction of the number of Americans infected. Independent estimates suggest that for every case reported, ten meeting the CDC case definition aren’t recorded. Further, an unknown number of cases not meeting the CDC surveillance criteria go unreported. Probable bottom line on the number of Americans who actually contract Lyme: 250,000 to 300,000 per year.

Several factors account for the steady rise in Lyme. Additional factors contribute to the uncertainty about its true incidence. These all involve complex explanations beyond the length of this column. One of the purposes of the LDA in publishing the Lyme Disease Update is to give the public a fuller understanding of the interplay of these factors as they affect diagnosis and treatment of chronic Lyme.

Lyme Disease & the Politics of Therapeutic Evaluation

The Lyme Disease Update identifies and explains these factors and their interplay as “objectively” as possible. Chronic Lyme and its treatment, however, have set off a debate in mainstream medicine between Lyme specialists. One side has come to believe that Lyme is overdiagnosed, questions whether manifestations persisting after a relatively short course of antibiotics represents active infection or an auto-immune reaction, and considers long-term antibiotic therapy proven and inappropriate. The other side is concerned that Lyme is underdiagnosed, maintains that clinical data indicate persistent or recurrent disease in a small but significant percentage of patients, and finds that many of these patients respond to extended antibiotic treatment.

In writing the Lyme Disease Update, the LDA and I offered scientific evidence and discussed public health issues raised by persistent Lyme in a way that is mostly free of conscious partisanship; however, as we proceeded in our selection of information for the Update, an article analyzing the evaluation of cancer treatment, which appeared in the journal Social Science in 1988, hovered in the back of my mind. The title of this article reads, “The Politics of Therapeutic Evaluation: The Vitamin C and Cancer Controversy.” The author Dr. Evileen Richards, is an Australian social scientist. Her main insights into therapeutic evaluation are that it “is inherently a social and political process,” and that “the idea of neutral appraisal is a myth.”

Expanding on these insights, Richards turns to their broad ramifications: “The randomized controlled clinical trial, no matter how tightly organized and evaluated, can neither guarantee objectivity nor definitively resolve disputes over contentious therapies or technologies.... These conflicts must be treated as essentially political issues where there are no impartial experts. The medical expert must be seen as a necessarily ‘partisan participant’ in a political debate, not as an apolitical arbiter of medical truth.”

The perception that conflicts arising from disagreements in therapeutic approach “must be treated as essentially political issues where there are no impartial experts” leads Richards to make two major projections. “This implies,” she says in the first projection, “a radical review of the expert’s role in therapeutic evaluation.” Her second projection follows as a corollary: “It also opens the way to an active and acknowledged evaluative role for non-experts, for patients and public at large, in the process of assessment and decision making.”

Richards predicated both projections on a “revised view of medical knowledge,” which presumably will evolve out of “the current widespread dissatisfaction with modern scientific medicine.” She concludes in a cautionary tone: “The institution of medicine has a great deal invested in the perpetuation of the myth of objective evaluation. It underpins the cognitive and social authority of its practitioners and legitimizes powerful vested interests, not only in medicine, but in society at large.”

Roughly 15 years after Richards ventured that politics is an inseparable component of the therapeutic assessment, and that medical experts are unavoidably partisans in political debates, dissatisfaction with modern scientific medicine has yet to reach a level that might force the radical changes she projects.

Studies on the use of alternatives to mainstream health care published in the mid-1990s indicate that perhaps one in three Americans has tried some form of non-standard treatment. Bear in mind that these studies tend to include among the alternatives many modalities that psychologically support standard therapy, or “complement” standard treatments in ways not intended in themselves to produce therapeutic effects.

As for the “institution of medicine”: There’s marginal disillusionment in the profession with the therapies it currently prescribes, considerable agreement on the need for better, less invasive treatment for many conditions, but no sign of near-future divestment in the belief in objective therapeutic evaluation. In all the debates, among experts over appropriate treatment, few members of either side question their ability to assess contentious therapies objectively.
Several pieces I’ve published in Townsend quote a recent opinion in the case of Dr. Joseph Burrascano, an infectious disease specialist charged by the New York Health Department’s Office of Professional Medical Conduct with inappropriately treating persistent Lyme with long-term antibiotics. Quoting part of this opinion again in connection with Richards is illuminating:

“...The Hearing Committee recognizes the existence of the current debate within the medical community over issues concerning management of patients with recurrent or long term Lyme disease. This appears to be a highly polarized and politicized conflict, as was demonstrated to this Committee by expert testimony from both sides, each supported by numerous medical journal articles, and each emphatic that the opposite position was clearly incorrect.... We are also acutely aware that it was not this Committee’s role to resolve this medical debate.” [emphasis added]

Perceiving that the dispute over Lyme had intensely polarized and politicized, the hearing panel in Burrascano declined a role in resolving the treatment issues. Whose role is it, then, to resolve the therapeutic issues in Lyme? The panel opinion doesn’t specify, but it intimates that it is the role of peer review.

And what essentially is peer review? A customary process involving (1) publication of findings about contending therapies in peer-reviewed journals, and (2) presentation of additional data at medical conferences, in expectation that “truth” about efficacy, safety, and indications for proper use will emerge: all this is grounded and perpetuated, as a matter of course, on the “myth” of “neutral appraisal.”

I’ve brought up Richards’ paper partly to account for the selection of scientific material in the Lyme Disease Update. From Richards’ perspective, has she been analyzing the controversy over chronic Lyme and long-term antibiotics to control it instead of the controversy over vitamin C and cancer, she would have attached the label “necessarily partisan” to all the scientific evidence on Lyme chosen, all the medical experts cited as authorities.

In other words, political bias is inescapable in the selection process; but in that process one can still strive for a balanced choice among “partisan” evidence, “partisan” authorities. That’s what the Update concentrated on achieving – the inclusion of significant evidence on Lyme regardless of the side in the debate from which it originated.

My chief reason, though, for bringing up Richards here is to expose the underlying political nature of the Lyme debate, and to suggest (with Richards) that political action will assist in ultimately settling it, not the peer review process alone.

Lyme Disease: Cause, Transmission, Manifestations & Incidence

The heading for this column promises basic information on Lyme disease. Here, then, are some of the salient “ABC’s.”

Lyme disease is caused by spirochetes, small spiral-shaped bacteria, that belong to the genus Borrelia. One species is responsible for septicaemia in chickens. A second species causes relapsing fevers. A third species, named Borrelia burgdorferi (Bb) after its identification in the US in 1982, which is parasitic in warm-blooded mammals, is the causative agent in humans bitten by one of several strains of Ixodes ticks. These ticks become infected with Bb after a blood meal on Lyme’s main animal reservoirs, white-footed mice and white-tailed deer.

Another species of tick, the Lone Star tick, co-existent with Ixodes ticks in many US regions, is believed by the CDC to transmit a “Lyme-like illness” (the CDC’s term) to humans in much of the American midwest and southwest. The spirochete responsible seems related to the Borrelia species that causes relapsing fevers.

Two slightly different genomic groups of the spirochetes in the US that cause Lyme Borreliosis (the technical name for Lyme Disease), are native to Europe and Asia. Because of this genomic variation, European Lyme in particular can manifest in ways that differ from the North American counterpart.

Ixodes ticks go through larval, nymph, and adult stages, feeding at each stage; larvae in summer, nymphs the following spring and summer, adults in autumn. Compared to the common dog tick, Ixodes ticks are much smaller, their legs black, and the nymphs tinier than a grain of sand.

While their blood meals can last many days, the time it takes for ticks to transmit the infectious agent to humans ranges from 12 to 72 hours, and there are documented cases where transmission occurred in less than half a day. Lyme Borreliosis is transmitted to fetuses; also, Bb DNA has recently been discovered in human breast milk.

Like other spirochetal infections (syphilis, for example), Lyme Borreliosis can affect numerous organ systems, may proceed through several stages, and can present acutely in any stage. Shortly after a tick bite, many patients develop erythema migrans (EM), a slightly raised or flat reddish rash at the site, often resembling a “bull’s eye” in appearance. EM rashes usually disappear in three or four weeks. Between 20% to 50% of the time, though, no rash develops, or it appears where infected persons don’t spot it, or it presents in an uncharacteristic, equivocal form. About a third of patients with confirmed Lyme don’t even recall a tick bite.

Major references divide Lyme into early-stage disease (which may manifest weeks or months after infection), and later, persistent or recurrent disease (the manifestations of which can appear many months or years after infection). During early and later periods, Lyme mainly affects the musculoskeletal system, the central nervous system, and skin.

Signs and symptoms of early Lyme include chills, fatigue, a flu-like illness with fever, muscle pain (myalgia), and migratory pains in joints. About 50% of patients with early disease develop secondary skin lesions, not directly associated with tick bites. Except for the fatigue, most of these frequent early manifestations are intermittent or brief.

Not promptly diagnosed and treated, up to 20% of patients may develop neurological disease, which can be acute. Bell’s Palsy is the most frequent neurological sign. Eczematitis, with forgetfulness and changes in personality, and aseptic meningitis with headache and stiff neck are also common early neurological manifestations.

Between 5 to 10% of patients may suffer cardiac involvement, leading to arrhythmias and atrophicventricular heart block. Like the neurological manifestations, the heart problems in early Lyme can also be acute.

Later Lyme again presents mostly as a musculoskeletal or neurological involvement. More than half the patients with later disease complain of chronic arthritis (mainly of the large joints), or pain in joints or surrounding tissue (for which there are no objective findings), or inflammation of synovial membranes (which can be permanently disabling).

Frequent central and peripheral nervous system manifestations of later Lyme include axonal polyneuropathy, encephalomyelitis, and encephalopathy. Radical pain and distal sensory paresthesia are the chief signs of axonal polyneuropathy. Subacute encephalopathy in Lyme often produces loss of memory, or changes in mood, or sleep disturbances.

Psychiatric signs and symptoms in Lyme disease can range broadly, manifesting as anorexia nervosa, bipolar disorder, dementia, major depression, obsessive-compulsive disorder, panic attacks, paranoia, and schizophrenia.
Lyme Disease

I've noted that the true national incidence of Lyme is not accurately known. What is certain is that all states save Montana have reported cases. Northeastern, mid-Atlantic, and north-central states have reported the great majority of new cases. Case reports from California, Florida, and Texas suggest that Lyme Borreliosis has a firm foothold in these states.

One factor limiting better incidence data is the CDC case definition, developed for surveillance, not for clinical diagnosis and treatment. It is much narrower than clinical criteria for diagnosing Lyme. The CDC requires, for instance, a physician-diagnosed EM rash, which never appears in a substantial percentage of cases, or positive serology and major system involvement.

Another instance: The CDC guidelines for interpreting Lyme Western blots (the more accurate of two antibody tests for confirming Lyme), require five of ten specific bands to be positive; however, there are patients with confirmed active infection whose Western blots don’t evidence the CDC’s requisite bands.

Several factors appear to account together for the sharply rising number of US Lyme cases: the spread of suburbs into rural areas, an “explosion” of the white-tailed deer population resulting in their closer proximity to humans; and the migration of the tick carriers (such as birds) to new geographic regions.

Lyme Disease: Diagnosis & Treatment

Guidelines for Lyme Borreliosis recommend that physicians make a clinical diagnosis. This involves basing the diagnosis either on a history of exposure in an area endemic for Lyme-transmitting ticks and identification by a physician of EM, or recognition of characteristic clinical signs with confirmation by lab findings. Complicating diagnosis, certain signs and symptoms may manifest in one stage, others may present in sequence through early and later stages, and stages can overlap. Moreover, like syphilis, Lyme manifestations are numerous, very varied, and can mimic the signs and symptoms of many other conditions.

The usual serologic tests for confirming Lyme, the ELISA, and Western blot, provide indirect evidence for the presence of Bb. In a Lyme ELISA, the methodology basically involves looking for antibodies in the patient’s serum that react to antigens present in Bb. These antibodies indicate probable exposure to the Lyme pathogen.

Lyme ELISAs, however, have two crucial deficiencies: a relative lack of specificity (ability to exclude people without Lyme Borreliosis) and sensitivity (inclusion of patients with Lyme). Thus, they can produce false positive results among patients infected by other illness.

To distinguish between false and true positives on ELISAs, physicians follow with a Western blot, which “detects” antibodies for a wide range of Bb proteins. In a patient having antibodies to a specific Bb protein, a “band” will form at a specific place on the Western blot. Reading the “band” patterns formed by the full range of antibodies specific to Bb, labs can determine with greater sensitivity whether a patient’s immune response is specific for Lyme.

Western blots contain two parts that show two immunoglobins (antibody proteins), IgM and IgG; the IgM “band” pattern appears shortly after infection, the IgG several weeks afterward (sometimes peaking months or years later). Most labs doing Western blots report these immunoglobulin patterns separately, and the criteria for a positive result differ for IgM and IgG.

Indirect antibody detection of Lyme has several notable limitations. Infected patients can vary considerably from individual to individual in their serologic responses. Patients with early Lyme may test negative because of the time needed to develop detectable levels of antibodies. It can take up to six weeks for IgM and/or IgG antibodies to be measurable.

Further, antibodies can form complexes with antigens, but currently marketed antibody response tests can only detect free antibodies.

Patients treated with antibiotics during the early period of disseminated Lyme also may have negative or equivocal serologies. (The therapy presumably nullified their immune response.) In other patients, antibodies may be detectable well beyond antibiotic therapy, making it difficult to distinguish between past or active illness.

Detection of the Bb DNA through polymerase chain reaction (PCR) and detection of pieces of the spirochete through antigen assays both supply better indications of the presence of the Lyme pathogen; but neither test conclusively proves that the spirochete is alive.

Diagnosed and adequately treated early, most Lyme patients respond to short-term antibiotic therapy (14 to 28 days) without recurrence. Optimal therapy for late Lyme, however, remains an unsettled question. Diagnosed later, when disseminated, Lyme appears less responsive to antibiotics or may be controllable only when antibiotics are given in repeated longer courses or for extended periods.

Chronic Lyme patients usually receive an initial course of antibiotics, lasting for a month to six weeks. If they experience a relapse or symptoms persist, longer courses may be required. Certain “features” of the Lyme pathogen spirochete suggest why: Bb grows slowly. It can invade intracellular sites, “hiding” in areas where antibiotic penetration is minimal. In vitro studies indicate it can remain dormant for long periods or assume atypical forms that enable it to avoid immune detection and destruction or eradication by antibiotics.

Note: Ticks serving as vectors for Lyme transmit other microorganisms that infect humans, most importantly: Babesiosis, Bartonella, Ehrlichiosis, and Rocky Mountain Spotted Fever. Serologic and other lab tests to confirm these co-infections exhibit the same major inadequacies as in Lyme diagnostic tests. Because of these diagnostic problems, and because many physicians are unacquainted with the signs and symptoms of the tick-borne conditions associated with Lyme, an unknown number of Americans are not diagnosed and/ or treated for such co-infections, especially since they can be asymptomatic. As a result, people suffering from Lyme disease and one of its co-infections may remain inexplicably sick or fail to benefit from standard treatment for Lyme alone.

Lyme Disease: The Chronic Patient’s Perspective

A passage from a 1992 paper on neuropsychiatric Lyme Borreliosis in the Psychiatric Quarterly best conveys the concerns of patients with persistent disease: “Many patients have felt abandoned by their medical doctors when the diagnosis was uncertain and the treatment not fully curative. Others have had to see many different doctors before one was able to put together the diversity of their symptoms and come up with a diagnosis. Several patients have said that the hardest thing to bear — even more than the pain and disability — had been the feeling that they were somehow inexplicably altered, in their emotions and personality and ability to function, with hope of finding a cause or a cure, and without a doctor who could honor their difficulty, whether or not he or she could solve it. For some patients then, the ambiguities surrounding diagnosis and treatment and the consequent sense of abandonment by medical professionals were among the most distressing aspects of the illness experience.”

This depiction remains valid a dozen years later. Additional research is vitally needed to answer open questions about the pathogenesis of Lyme, to improve therapy for persistent or recurrent disease. Townsend readers can expect more on these and related matters in future columns...
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