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Antiscience and ethical concerns associated with advocacy of Lyme disease

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Contributors

EMcS prepared the first draft, worked on subsequent drafts, and helped with the literature search. JSB participated in the construction of the paper and reviewed the final draft. PGA, JJH, RBN, SO'C, SKS, ACS, AW, GPW contributed to the writing of the article, and RJD, JSD, EDS contributed to the writing and editing of the paper. JSD, JJH, SO'C, GPW contributed to the literature search, and EDS, ACS, AW, GPW contributed to the data interpretation.

Conflicts of interest

PGA has served as a consultant for Oxford Diagnostics and has participated in expert testimony in two medicolegal suits about possible Lyme disease. He has equity interest in Johnson & Johnson, no products of which are referred to in this article. RJD is part owner of and has stock in Biopeptides Corporation, no product of which is referred to in this article, has received payment for providing expert testimony in malpractice cases and holds patents on vaccine and diagnostic technology with SUNY at Stony Brook Biopeptides. JSD has received support for travel to meetings from DiaSorin and has licence of US patent 5,955,359 to Focus Diagnostics; none of these declarations are directly related to the contents of this article. JJH has served as an expert witness in several medicolegal cases concerning Lyme disease and has equity in Abbott, Bristol-Myers Squibb, Johnson & Johnson, and Merck; no products from these companies are referred to in this article. EMcS was a former programme officer for Lyme disease at the US NIH. RBN has served as an expert witness in malpractice litigation involving Lyme disease. EDS is a board member of the American Lyme Disease Foundation, for which no compensation is received. He has reviewed medical records for the Metropolitan Life Insurance Company and has provided medicolegal testimony. GPW is a board member of the American Lyme Disease Foundation for which no compensation is received, has served as an expert witness in malpractice cases involving Lyme disease, has research grants from the NIH/Immunitics, BioRad, DiaSorin, and BioMerieux to study diagnostic tests for Lyme disease, none of which is mentioned in the manuscript, and has equity in Abbott, a company not known to have any approved product for Lyme disease. JSB, RJD, JSD, JJH, RBN, EDS, ACS, and GPW have served on the panel for the 2006 IDSA Lyme disease guidelines. JSB, SO'C, SKS, ACS, and AW declare that they have no conflicts of interest.

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Abstract

Advocacy for Lyme disease has become an increasingly important part of an antiscience movement that denies both the viral cause of AIDS and the benefits of vaccines and that supports unproven (sometimes dangerous) alternative medical treatments. Some activists portray Lyme disease, a geographically limited tick-borne infection, as a disease that is insidious, ubiquitous, difficult to diagnose, and almost incurable; they also propose that the disease causes mainly non-specific symptoms that can be treated only with long-term antibiotics and other unorthodox and unvalidated treatments. Similar to other antiscience groups, these advocates have created a pseudoscientific and alternative selection of practitioners, research, and publications and have coordinated public protests, accused opponents of both corruption and conspiracy, and spurred legislative efforts to subvert evidence-based medicine and peer-reviewed science. The relations and actions of some activists, medical practitioners, and commercial bodies involved in Lyme disease advocacy pose a threat to public health.

Introduction

For much of its history, medicine has endured an often justifiable degree of public scorn and suspicion for its many faults, including ignorance and ineffectiveness, elitism and exclusivity, unyielding dogma and fashionable quackery, and a certain laissez-faire commercialism. But the profession of medicine has evolved, embracing scientific and statistical methods to establish theories and practices that revolutionised the effectiveness of medical care in the 20th century. Medicine's critics, however, have also evolved. Today, there are diverse groups of activists many of whom share a common suspicion of modern medicine.

In his book, *Denying AIDS*,¹ the psychologist Seth Kalichman wrote of such activists: "They are deeply skeptical of science and untrusting of government and big business. Some are surely misguided and others seem to foolishly believe that they understand everything there was to know...". He was writing about people who deny the viral cause of AIDS. He could just as easily have been writing about other antiscience movements, including ardent antivaccine activists and those who promote unproven alternative medical therapies.

Aspects of Lyme disease advocacy are an important example of this antiscience movement. For the purposes of this Personal View, we will define this antiscience outlook to also include the promotion of pseudoscience and science that has weak credibility or validity because of fundamental flaws in its design or poor reproducibility. For two decades, many Lyme disease activists have portrayed Lyme disease, a tick-borne infection, as an insidious, ubiquitous, difficult to diagnose, and often incurable disease, which causes mainly non-specific symptoms such as chronic fatigue, musculoskeletal pain, and neurocognitive dysfunction that can be treated only through the use of antibiotics for months or years (panel 1).² As with other antiscience groups, some Lyme disease activists have created a parallel universe of pseudoscientific practitioners, research, publications, and meetings, arranged

public protests and made accusations of corruption and conspiracy, used harassment and occasional death threats, and advocated legislative efforts to subvert evidence-based medicine and peer-reviewed science. Politicians, the media, and the public have been left trying to discern the scientific facts from the pseudoscientific ones, with many regarding both as equally valid as they try to be fair and balanced. When such inappropriate and uncritical weighting occurs, public and government officials unknowingly come to accept or even endorse highly unconventional and sometimes dangerous theories and therapies.

The infection that launched a thousand protests

Lyme disease is a bacterial infection caused by *Borrelia burgdorferi* sensu lato (which includes *B burgdorferi*, *B afzelii*, *B garinii*, and other species) and transmitted by *Ixodes* species ticks. The infection is non-fatal, non-communicable from person-to-person, is responsive to antibiotics, and is limited in range both geographically and seasonally. The most common clinical manifestation is a characteristic skin lesion (erythema migrans) that occurs at the site of the tick bite. Within weeks, some untreated patients might develop nervous system abnormalities (eg, meningitis or facial nerve palsy) or cardiac symptoms (eg, heart block); within months, arthritis can develop, most commonly affecting the knee. In addition to these objective clinical manifestations, some patients have several subjective complaints that are usually most prominent early in the infection. These symptoms include fatigue, arthralgia, myalgia, headache, stiff neck, and impaired concentration; symptoms that are common in many infectious and non-infectious disorders.

The Infectious Diseases Society of America (IDSA), a professional organisation of more than 9000 infectious disease physicians, has published evidence-based treatment guidelines for the various manifestations of Lyme disease³ and for many other infectious diseases. On the basis of published, peer-reviewed studies, the IDSA guidelines recommend antibiotic treatment for Lyme disease for 10–28 days, depending on the disease manifestation.³ The recommendations are similar to others developed independently by European societies and expert groups.⁴ The objective clinical manifestations typically resolve (eg, erythema migrans) or show improvement (eg, arthritis) during the course of antibiotic treatment. Additional treatment is usually not needed, but a second course of therapy might be given in a few cases.³

Panel 1: Concepts* about Lyme disease that are unsubstantiated or proven to be inaccurate

Epidemiology

- Sexually transmitted
- Not restricted geographically

Clinical features and outcome

- Most patients have only subjective symptoms
- Incurable illness when not treated very early

- Causes autism, Morgellons disease, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, homicidal behaviour ("Lyme rage"), immune dysfunction, birth defects, and Alzheimer's disease
- Patients usually have several co-infections, such as from *Bartonella*, *Babesia*, *Mycoplasma*, *Chlamydia*, and *Anaplasma* species

Pathobiology

- *Borrelia burgdorferi* is an intracellular pathogen, forms antibiotic-resistant cysts, and produces a neurotoxin

Diagnostic testing

- Serological testing is of no value in the diagnosis of extracutaneous manifestations of Lyme disease
- IgM testing is appropriate for assessment of patients with illness of long duration
- Serology is less sensitive for detection of Lyme disease in women than in men

Treatment

- Usual doses and durations of antibiotics are insufficient; open-ended treatment with multiple antibiotics is needed
- Combinations of antibiotics are needed to eradicate *B burgdorferi*

*Obtained from popular Lyme disease websites, and from public statements and presentations made by some "Lyme literate medical doctors" and chronic Lyme disease activists.

The accompanying subjective manifestations, such as fatigue, are often improved but not completely resolved at the conclusion of antibiotic treatment. Evidence from clinical trials shows that prolonging the initial course of antibiotic treatment does not accelerate the rate of resolution of such symptoms.^{3,5-7} Four National Institutes of Health (NIH)-sponsored, double-blind, randomised, placebo-controlled treatment trials have been done to examine whether persistent (for 6 months) subjective symptoms were improved by retreatment with antibiotics after standard courses of oral or intravenous treatment for Lyme disease.^{3,8-10} Data from the two largest studies indicated no benefit from re-treatment with 90 days of additional antibiotic therapy.⁸ Results from the other two studies reported at most equivocal evidence for benefit. None of the investigators of the four studies concluded that the possible and unconfirmed benefits of additional antibiotic treatment outweighed their risks, which were substantial in the two smaller trials (eg, admission to hospital for intravenous catheter sepsis).⁸⁻¹⁰ Consistent with these findings, there was also no microbiological evidence for persistence of *B burgdorferi* despite rigorous examination of several body fluid samples, including culture and molecular diagnostic assays.^{3,8,10} Nevertheless, many activists believe that patients whose objective manifestations of Lyme disease have resolved after antibiotic treatment are still chronically infected with *B burgdorferi*.

Although unsupported by scientific evidence, a belief system has emerged for some activists over the past 20 years—that Lyme disease can cause disabling subjective symptoms even in the absence of objective signs of disease, that diagnostic tests for extracutaneous manifestations of Lyme disease are often falsely negative, and that treatment with antibiotics for months or years is necessary to suppress the symptoms of the disease, which often recur despite prolonged antibiotic therapy. Consequently, some individuals with medically unexplained symptoms¹¹ and others with more well defined conditions (panel 1) were diagnosed with, or themselves attributed their symptoms to, Lyme disease in the absence of supportive laboratory data. Believing that they were chronically infected, these individuals formed support groups and sought treatment from “Lyme literate medical doctors” (LLMDs)—physicians who specialise or claim to be experts in the diagnosis and treatment of patients with what has been called chronic Lyme disease.^{12,13} The overall result is that many patients who receive long-term treatment have no convincing evidence of ever having had *B burgdorferi* infection, by history (sometimes including having never been exposed to ticks, never having been in an endemic area, and never having had objective clinical findings suggestive of Lyme disease), physical examination, or laboratory test results.^{12,13} Even children with autism are thought by some LLMDs to have persistent *B burgdorferi* infection as the cause of the disorder.¹⁴

By the early 1990s, some activist groups and LLMDs were accusing university scientists and public health officials of intentionally under-reporting and under-diagnosing cases of Lyme disease. If medical insurance companies denied payment for long-term treatment, this refusal was often blamed on academic physicians being in the pay of insurance companies, rather than on the absence of credible medical evidence to support either the diagnosis or a beneficial role for such treatment. Other researchers were accused of financial conflicts created by patent applications, federal grants, or funding from pharmaceutical companies.¹⁵

The accusations eventually drew the attention of the US Congress. During a 1993 Senate hearing on Lyme disease, one LLMD accused “a core group of university-based Lyme disease researchers and physicians...of act[ing] unscientifically and unethically. They work with government agencies to bias the agenda of consensus meetings, and have worked to exclude...those with alternate opinions. They behave this way for reasons of personal or professional gain, and are involved in obvious conflicts of interest”.¹⁶ However, no evidence to substantiate the charges was offered nor was any requested by the senators serving on the committee. In 2000, activists persuaded a few congressmen to investigate the federal Lyme disease research programmes of the Centers for Disease Control and Prevention (CDC) and the NIH. The General Accounting Office (GAO-01-787R, GAO-01-755)^{17,18} found no evidence of conflicts of interest, retaliation, physician harassment, or controlled science.

More recently, Richard Blumenthal, the then Attorney General of Connecticut in the USA and a long-time supporter of chronic Lyme disease activism and adviser to the support group Time for Lyme, threatened IDSA with antitrust litigation after the release of updated Lyme disease treatment guidelines.^{19,20} The fact that these practice guidelines, essentially unchanged from the 2000 IDSA guidelines,²¹ are voluntary measures was ignored. Blumenthal asserted that the authors of the guidelines were “rife with conflicts of interest”, but declined to identify any of those conflicts or explain how they might have affected the

recommendations.²² His actions were widely denounced by physicians and lawyers alike,^{23,24} because federal courts had earlier ruled that professional guidelines are a medical, not a legal, concern. The Blumenthal investigation resulted in the convening of an independent scientific panel (vetted for potential conflicts of interest by an ethicist and physician) to review the appropriateness of the IDSA recommendations. After an extensive review of the scientific evidence, the new panel unanimously concluded that the Lyme disease guidelines by IDSA were accurate and appropriate.²⁵

Proven or alleged unethical activities of some LLMDs

Some LLMDs, advocacy organisations for patients, and certain diagnostic laboratories have interconnections, presenting potential conflicts of interest for these LLMDs in their multiple roles as advisors, personal physicians, and recipients of grants from activist organisations. Many of these physicians are represented by the International Lyme and Associated Diseases Society (ILADS), located in Maryland, USA. Two of the most vocal patient-activist organisations are the Lyme Disease Association (LDA) in New Jersey, and the California Lyme Disease Association (CALDA), USA.

Several physician members of ILADS—including current and former officers—have been sanctioned by state medical licensing boards or reprimanded by federal agencies (panel 2).^{26–33} Other LLMDs have been convicted in state and federal courts raising concerns about ethics and professional credibility (panel 2).^{34–41} For example, a doctor in Kansas served a prison sentence for causing the death of a patient he treated for Lyme disease with injections of bismuth.³⁵ An LLMD in Georgia was charged with allegedly treating patients for Lyme disease with injections of dinitrophenol, a toxic substance banned from medicinal consumption in the USA for more than 50 years.³⁶ He was suspended by the state medical board after his indictment in 2005, and was sentenced to 5 years' probation for defrauding insurance companies of US\$650 000.³⁶ In 2007, an LLMD in New Jersey was sentenced to 41 months in federal prison for tax evasion related to his two Lyme disease clinics.³⁹ In Connecticut, a physician and adviser to the Lyme group Turn The Corner Foundation was reprimanded, fined, and placed on 2 years' probation for diagnosing Lyme disease in children without examining them and for improperly prescribing antibiotics.⁴¹ He is appealing the case using funds provided by Lyme activists.

Panel 2: Examples of professional and legal issues of LLMDs

Current or former ILADS officers

- Scientific misconduct; barred from receiving NIH research funding²⁶
- University employment terminated²⁷
- Disciplinary actions by state medical boards^{28–33}

Other LLMDs

- Sentenced for selling medical equipment and drug treatments for a non-existent Lyme disease epidemic³⁴

- Imprisonment for causing the death (manslaughter) of a patient by treating Lyme disease with injections of bismuth³⁵
- Sentenced for health-care fraud³⁶
- Conviction for conspiracy, mail fraud, wire fraud, and money laundering³⁷
- Disciplinary action by state medical board for infusing patients with H₂O₂³⁸
- Imprisonment for tax evasion related to two Lyme disease clinics³⁹
- FDA warning letter for using veterinary drugs in people⁴⁰
- Disciplinary action by state medical board for diagnosing and treating patients for Lyme disease without examining them⁴¹

ILADs=International Lyme and Associated Diseases Society. LLMD=Lyme literate medical doctor. NIH=US National Institutes of Health. FDA=US Food and Drug Administration. Additional information is available at <http://www.casewatch.org>.

Unvalidated laboratory testing

Despite warnings from the US Food and Drug Administration and the CDC about the potential unreliability of unvalidated diagnostic tests for Lyme disease,⁴² many LLMDs continue to use such assays (panel 3).^{42–46} Lyme specialty laboratories are favoured by some activists and LLMDs because their nonstandard testing methods and interpretation criteria often lead to more positive results than other laboratories that rely on validated methods.⁴⁷ An owner of one such diagnostic company is an ILADS director and an adviser to three Lyme organisations. He was one of the authors of the treatment guidelines by ILADS, although his company affiliation is not disclosed in that document.⁴⁸ This laboratory was investigated by Medicare; in 2001, the US Federal Office of the Inspector General placed it on a list of non-compliant laboratories, resulting in fines totalling \$48 000. The laboratory is now compliant.⁴⁹ In 2009, several residents in Kansas won a \$30 million suit against another Lyme disease specialty laboratory for incorrectly diagnosing these individuals with Lyme disease.⁵⁰

By use of an unconventional culture method, a former president of ILADS reported positive blood cultures for *B burgdorferi* in more than 90% of a group of patients who had previously received antibiotic treatment for Lyme disease.⁵¹ His work could not be replicated by others,⁵² and the novel culture medium was shown to be lethal for *Borrelia* species.⁵² Two immunological tests favoured by some LLMDs to indicate the presence of *B burgdorferi* infection include a T-cell assay and measurement of the CD57 cell count; both of these tests are considered to be unreliable.^{44,46}

Ethics of propaganda and persuasion

In 2005, representatives of the LDA in New Jersey, USA, and CALDA in California, USA, wrote to the Director of the CDC, criticising the information about Lyme disease on the organisation's website and its warning about improper diagnostic tests.⁴² In December, 2006, a New Jersey congressman complained that it was “inappropriate for CDC to

highlight IDSA's findings—to the exclusion of others".⁵³ Lost in these political discussions was the absence of scientific merit in the arguments raised by activists. ILADS leaders claim their practice guidelines are evidence-based and peer-reviewed, but they were not subjected to an external peer-review process by the journal in which they were published as a supplement.⁵⁴ Moreover, the support they cite for their guidelines, consisting mainly of anecdotes, studies of animal systems of questionable relevance to human disease, and uncontrolled studies of long-term antibiotic treatment, does not meet accepted criteria for evidence-based medicine.^{3,12,48,55–57} The ILADS guidelines were funded by two activist organisations, the LDA in New Jersey and the Turn The Corner Foundation.⁴⁸

Panel 3: Noted problems with diagnostic tests that are or have been advocated by some LLMDs and chronic Lyme disease activists

Lyme urine antigen test

Unreliable⁴³

CD57 cell count

No specific association with *Borrelia burgdorferi* infection⁴⁴

PCR

Variable sensitivity in the plasma, urine, and CSF; no clinical validation⁴⁵

Flow cytometry

No clinical validation⁴²

Lymphocyte transformation

Low specificity; no clinical validation⁴⁶

Immunofluorescence for L-forms of *Borrelia*

No clinical validation⁴²

Urine reverse western blot

No clinical validation⁴²

Urine dot blot

No clinical validation⁴²

Support groups for Lyme disease originated as information sources for patients and the public. Many have devolved into partisan organisations, promoting unproven therapies and the clinical services of their LLMD advisers. Their leaders lobby for legislation to promote their perception of chronic Lyme disease and to protect LLMDs from licensing boards, and they work to raise defence funds for those who face legal complaints. Activists have organised their own scientific meetings, published their own journal, and funded research by LLMDs.^{58,59} All this activity has led to the creation of a cadre of doctors and activists with their own institutions, research, and conferences, a dedicated pool of patients, and unorthodox, alternative views of microbiology, immunology, and pharmacology.

Belief in a chronic, insidious Lyme disease epidemic hidden from the public by a cabal of public health officials, academic scientists, and insurance companies has sometimes led to bizarre and dangerous behaviour among activists. Some have stalked and threatened scientists⁶⁰ or tried to sue others.⁶¹ Employers and deans have received anonymous phone calls alleging misdeeds by employees and faculty. One activist was confined to a psychiatric ward after threatening a state's attorney.⁶² The latest promotional technique by activists is through the cinema. One well publicised film, entitled *Under Our Skin*, was criticised in a previous issue of *The Lancet Infectious Diseases* as partisan, manipulative, and prone to conspiracy⁶³ and by another reviewer as “full of suspicions, assertions, and anecdotes; it's low on science and objectivity”.⁶⁴

Conclusions

Many individuals who represent themselves as Lyme disease activists and LLMDs hold and promote views of a tick-borne infectious disease that is inconsistent with credible scientific evidence. Although relatively small in number, their effect should not be underestimated. Their unorthodox perspectives and resulting practices have contributed to injury and even deaths of patients.^{35,65} Millions of dollars have been spent refuting their claims, and thousands of hours have been spent responding to false allegations, legal threats, congressional queries, and other harassments. At a time when unnecessary health-care expenditures are being scrutinised and widespread bacterial resistance has been linked to overuse of antibiotics, it is particularly important that unsubstantiated treatments be avoided.⁶⁶

This situation is not likely to end anytime soon. As with other antisience groups, many Lyme disease activists are well funded and often connected to influential political and media sources. Treatment of Lyme disease with long-term antibiotics is profitable for LLMDs and can be falsely reassuring to patients, who believe that they have a debilitating chronic infection and thus do not seek diagnosis and treatment for other disorders. There is no deficiency of either new patients or activists. The medical anthropologist Sharon Kaufman wrote that “Information technology has transformed the way trust and knowledge are produced”.⁶⁷ Most people now find medical information on the internet, and the websites of LLMDs and activists are often viewed as legitimate and reliable sources of information, which they may not be.^{68,69} Such misplaced trust has also contributed to a similar situation in Europe, with increasing pressure being brought on authorities there to sanction the use of prolonged antibiotic treatment for patients without credible evidence of Lyme disease by groups such as the German Borreliosis Society and Dutch Lyme Association. This ill-founded advocacy is being extended to other, less common, tick-borne infections (and to non-*Ixodes* tick-transmitted pathogens such as *Bartonella*).^{48,70}

In conclusion, activists, through public appeal and political lobbying, have managed to divert attention away from existing evidence-based medicine in their quest to redefine Lyme disease. There is a serious concern that they will further endanger the public's health unless responsible physicians, scientists, government leaders, and the media firmly stand up for an evidence-based approach to this infection that is based on high-quality scientific studies. Many patients who have been labelled as having chronic Lyme disease arrive at this

diagnosis as a consequence of inadequate or frustrating previous medical care for symptoms that are difficult to define. Patients who suspect or who have been diagnosed with chronic Lyme disease should consider seeking a comprehensive assessment from an empathetic physician. This physician should objectively look at all elements of history, physical examination, and laboratory data to guide assessment and management based on the best available clinical evidence.

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