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The Truth About Lyme Disease

Part 2 of a 3 Part Series

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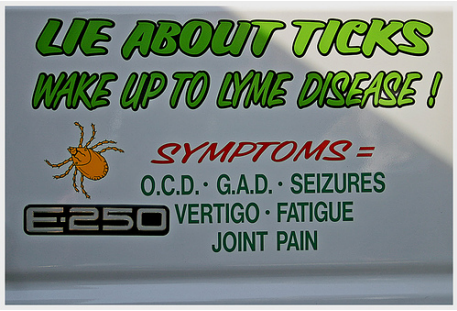


After years of endless suffering, pain, confusion and despair the search for an answer is beginning to seem bleak. The body aches, lack of energy, feelings of depression have not relented, in fact they are worse. Specialists after specialists have consistently concluded that you are perfectly "normal", "it is all in your head" and "it is just anxiety". By now your internal monitor has begun to question everything, are they right? Then you are introduced to something called Lyme and you immediately do what everyone does, you Google it. While reading through the symptom list and you begin to feel a small spark of excitement, you found it. Finally, there is a name to what you have and there are others who are suffering like you; you have Lyme! Having a diagnosis can be very empowering however little did you know, you are now embarking into the tangled web of Lyme.

Introduction

The new self-diagnosed patient, charged with the exciting news, will take the subsequent step and enter their doctors office to share their eureka moment. The physician, following the Canadian Health guidelines, orders the ELISA (Enzyme-linked immunosorbent assay) lab test for Lyme disease and despairingly the results are negative.

This article is the second installment of the three part series The Truth About Lyme Disease. The first paper focused on the background information on Lyme, ticks, signs and symptoms. The second paper will centre on the politics surrounding Lymes and diagnostic testing. Finally, the last section will emphasize treatments. Please note that Part 2 does contain diplomatic views on facts, Lyme guidelines and certain medical parties that could be perceived as an expose. The technical nature of the article may contain information you have experienced or maybe the piece you need to show your physician.

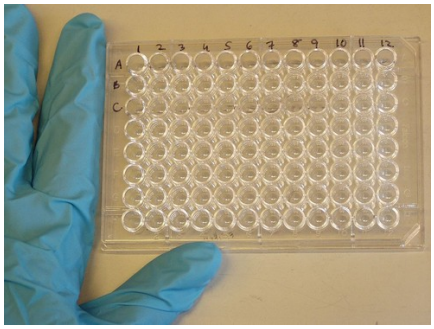
The political controversy surrounding Lyme revolves around three central points. First, the testing procedures used for diagnosing the condition and their subsequent contribution to a timely treatment. Second, the clinical guidelines used by physicians. In Canada, the established guidelines have created a conflict with two main medical parties, the Infectious Diseases Society of America (IDSA) and the International Lyme and Associated Diseases Society (ILADS). Third, is the acknowledgement of Chronic Lyme and the debate over the length of antibiotic use. Ultimately, the disagreement exists over treatment of the patient; is it even necessary to treat and how long to treat? Unfortunately, it is the patient who suffers and who continues to suffer while the argument endures.

Diagnosis of Lyme Disease

According to the Public Health Agency of Canada, diagnosis of Lyme requires three criteria;

1. Doctor's assessment of the patient
2. Evidence or history that the patient could have encountered blacklegged tics which carry Lyme disease
3. **The results of laboratory testing**

Figure 1: ELISA Microtiter plate



The Labs

The National Microbiology Laboratory (NML) diagnoses Lyme disease using a two-tiered testing method, an ELISA (Enzyme-linked immunosorbent assay) screening test followed by a confirmatory Western blot test. The two-tiered approach is considered the gold standard for blood testing Lyme and is recommended by both the US and the Canadian public health organizations. The ELISA is used to detect antibodies against the *Borrelia burdgorferi* bacteria however the ELISA test produces up to **90%** false negatives! If the ELISA test produces a positive result only then will the more accurate Western blot test be performed. The Western blot test is the preferred test for Lyme. There have been numerous cases where the patient has had a negative test with the ELISA and a positive with the more accurate Western blot. Physicians are ordering a lab test with a 90% failure rate! Therefore, if a patient has Lyme disease the chance of being diagnosed with the two-tier approach is extremely low. The patient will not receive necessary treatment and the condition will inevitably worsen. One of the most important considerations in the management of Lyme is timing and duration. The sooner treatment is initiated after infection, the higher the success rate. Doctors who are unfamiliar with Lyme disease, follow the guidelines set out by the medical boards and are horrifically missing approximately 90% of cases. Medical physicians who are "Lyme literate" realize that Lyme is a **clinical** diagnosis, that the ELISA is a useless test and consequently order the Western blot.

Sensitivity vs. Specificity

In order to understand why the ELISA is not the preferred choice of testing for the diagnosis of Lyme disease, one must understand the difference between **sensitivity** and **specificity** of a lab test. A highly **sensitive** test will be able to correctly identify those individuals having the condition being tested for; this is known as a true positive and produces a low rate of false negative (an individual who has the condition but the test gives a false negative). A highly **specific** test will be able to correctly identify those patients who truly do not have the condition; known as a true negative and has a low rate of false positives (an individual who does not have the condition but the test result came back positive, a false positive). Laboratory diagnosis of Lyme in Canada has focused on diagnostic specificity and thus reducing false positives, instead of focusing on a highly sensitive test which would focus on true positives. This emphasis creates a high rate of false negatives, hence the patient suffering with Lymes will have a negative ELISA result **90%** of the time. Further testing through the Western blot will produce a positive result although this test is only performed if the ELISA test is positive. Interestingly, according to the Canadian Public Health Guidelines, **"the ELISA test presently in use lack the specificity necessary to base a diagnosis of Lyme disease",** however it continues to be recommended with the two step approach.

In Canada, "the sensitivity of ELISA is considered to be close to 100% for tests performed **4 weeks post tick bite"** (Barker and Lindsay 2000; Forward 2005; Zaretsky 2006; CPHLN 2007; CPS 2009). The majority of individuals fail to realize that they have been bitten because the tick saliva contains an anaesthetic. Therefore even if the above statement is correct, the probability of the patient presenting to the physician's office 4 weeks post bite is highly unlikely. Lymes disease will be considered as a differential diagnoses once **all tests and specialists have been exhausted**. Months or years may pass before testing for Lyme is considered. The travesty of the situation is that Lyme "illiterate" doctors ordering the ELISA test and following the guidelines are completely unaware of the potential for such high false negatives especially in late disease.

Western blot

The Western blot detects antibodies that are specific to different parts of the *Borrelia burdgorferi* bacteria. The Western blot for Lyme disease detects two different classes of antibodies: IgM and IgG and the reaction of these immunofactors to different components of the bacteria. The interaction appears as bands as seen in Figure 2.

Unfortunately, the CDC require that for a "positive" result to occur there must be at least 2 of the 3 bands (23-25, 39, 41) for IgM and 5 of the 10 bands (18, 23-25, 28, 30, 39, 41, 45, 58, 66, 83-93) for IgG. Other bands have been excluded by the CDC, such as IgM for both OspA (bands 31) and OspB (band 34) (Outer surface proteins A and B respectively) as well as OspB for IgG. These bands are highly diagnostic for Lymes and yet have been excluded. It is also important to realize that the diversity of species and strains of *Borrelia* is not completely understood. There are approximately 5 subspecies of *Borrelia burgdorferi*, over 100 strains in the US and 300 strains worldwide. The diagnostic kits utilized by the CDC and Canada were developed using the B31 strain of *B. burgdorferi s.s*.

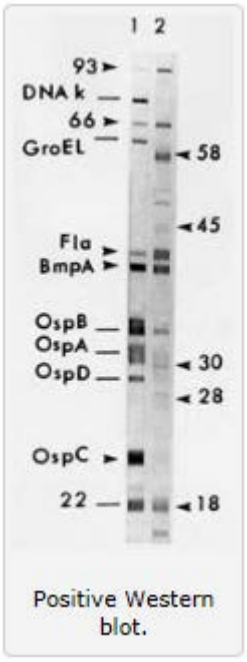


Figure 2: Positive Western Blot for Lyme Disease. www.cdc.gov/lyme/diagnosistreatment/LabTest/TwoStep/WesternBlot/

Canadian Public Health Laboratory Network Recommendations

1. The appearance of a typical EM (Erythema Migrans) rash occurring in season and with a history of exposure to ticks should be considered an indication for antibiotic treatment, irrespective of the results of serological testing.
2. An EM- like rash occurring out of season and/or after exposition in Lyme nonendemic area where ticks are not known to be established should be investigated with antibody testing
    a. Initial negative serological tests in patients with skin lesions suggestive of EM should have testing repeated after four weeks.
3. Patients with symptoms and signs suggestive of early disseminated or late Lyme disease should be tested for antibodies to B. burgdorferi.
    a. Initial testing should include an ELISA commercially available and approved for use in Canada.
    b. Sera (blood serum) that are positive or indeterminate by an ELISA should be subjected to Western blot confirmatory
    c. Sera that are screened negative for antibodies using an ELISA should not be subjected to Western blot testing.
4. Western blot tests should be interpreted using **criteria set forth by the CDC Working Group.**
    a. Western blot tests that fail to meet all of the criteria set out by the CDC Working should be reported as negative; testing may be repeated when it is appropriate to do so.
    b. The specific banding patterns seen on Western blots should not be reported
    c. When serological testing is requested for Lyme borreliosis, and when the initial screening test is positive and the subsequent Western blot confirmatory test is negative, specimens should be reported as 'negative for antibodies to *B. burgdorferi*".

5. Culturing for *B burgdorferi* is a low yield procedure and is not encouraged; if performed, it should be done only on biopsies from EM lesions and synovial or spinal fluid
6. There is inadequate evidence to support the use of *B burgdorferi* antigen testing as an adjunct to the diagnosis of Lyme borreliosis.
    a. The role of Nucleic acid AmplificationTesting (eg.PCR) is limited, and its use should be restricted to patients with objective, evidence of joint or central nervous system infection.
    b. There is inadequate evidence to recommend PCR testing of blood and urine for the diagnosis of Lyme disease
7. Patients without objective finding suggestive of *B burgdorferi* infection should not be 'screened' for *B burgdorferi* antibodies.
    a. The diagnosis of Lyme borreliosis should not be based on positive serological tests in the absence of objective findings of infection and a credible epidemiological link to infected ticks.
    b. **Bypass of laboratories that apply the two-step testing procedure (initial ELISA followed by Western blot testing) is strongly discouraged**
    c. Patients should be made aware that antibody testing is subject to false-positive results, and that a positive test in the absence of objective findings and credible exposure histories usually represent false-positive results.
8. The role of antibody testing to monitor the results of therapy has not been established and is therefore not recommended.
9. The role of the microbiology laboratory in the assessment of patients with the persistence of symptoms following antibiotic treatment has not yet been established.
10. In patients in whom tick exposure occur outside of North America, physicians should seek diagnostic advice on testing from a Canadian laboratory with expertise in the diagnosis of Lyme disease
11. Testing patients suspected of Lyme disease for other tick-associated diseased should not be routinely performed; instead, testing should be based on risk exposure and clinical symptoms.

Guidelines

In 1994 the Infectious Disease Society of America (IDSA) established a two tiered test protocol incorporating the ELISA test and the Western blot at Centers for Disease Control meeting in Dearborn, Michigan. In 2000 the IDSA published its first set of guidelines for the treatment of Lymes. These guidelines have served as a basis for the Canadian government policy on Lyme. The Canadian Public Health Laboratories Network guidelines of 2007 align themselves exclusively with the IDSA's guidelines, in addition with their provincial counterparts, the medical licensing authorities and the provincial Colleges of Physicians and Surgeons.

"Bypass of laboratories that apply the two-step testing procedure (initial ELISA followed by Western blot testing) is strongly discouraged!"

So what are the guidelines?

According to the Canadian Medical Association:

Clinical practice guidelines (CPGs) are defined as "systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances." The systematic process of developing CPGs is meant to ensure that they are based on the best available evidence, supplemented by clinical expertise and patient preferences.

The purpose of guidelines is to:

- **Improve the quality of patient care and health care outcomes**
- Summarize research findings and make clinical decisions more transparent
- Reduce inappropriate variation in practice
- Promote efficient use of resources
- Identify gaps in knowledge and prioritize research activities
- **Provide guidance for consumers and inform and empower patients**
- Inform public policy
- Support quality control, including audits of clinicians' or hospitals' practices.

Clinical practice guidelines are **not intended to**:

- Provide a "menu-driven" or "cookbook" approach to medicine **where the clinician has no discretion**
- Provide guidance in all circumstances and for all patients
- Provide in-depth background clinical knowledge, such as information related to etiology, epidemiology and prognosis, which is usually covered in medical textbooks
- **Be a legal resource in malpractice cases;** their more general nature renders them insensitive to the particular circumstances of individual cases.

Financial and other biases

In many cases, the funding of CPG development or adaptation has come from **industry, in particular pharmaceutical companies that have links with members of the CPG working group.** The authors of clinical practice guidelines published between 1991 and 1999 which have been endorsed by North American and European societies, were surveyed and it was found that **87%** of the authors had some form of interaction with the **pharmaceutical industry; 58%** had received **financial support** to perform research; and **38% had been an employee of or a consultant for a pharmaceutical company.**

Discussion

It is questionable whether the interest of the patient is truly considered by the guidelines set by the IDSA. The IDSA ascertains a considerable amount of power over the medical and pharmaceutical fields. They are recognized as the preeminent infections disease specialty society in the US, they publish two of the three most influential infectious disease journals, their members have strong influence on peer reviewed medical journals by serving as peer reviewers and editors and finally they have a tremendous amount of power over antibiotic treatment protocols in hospitals. Needless to say when the IDSA produce a guideline, people listen, doctors listen and the government listens.

Following the Lyme guidelines published in 2000, a number of physicians were subjected to review for failure to comply with the new recommendations. Insurance companies were denying patient reimbursement for treatment that was not in compliance with the approved regulations. Moreover, patients were having a difficult time finding physicians willing to treat their illness. Johnson and Stricker capture this unfortunate paradigm best in The Infectious Diseases Society of America Lyme Guidelines: a cautionary tale about the development of clinical practice guidelines, "guidelines may either be **used as a shield against liability** by those who comply with their protocols, or **as a sword against** those who do not comply. In the case of Lyme disease, **IDSA guidelines have been used as a sword against physicians** who do not conform to the IDSA protocols guidelines".

In October of 2006, a revised Lyme guideline which is even more restrictive was published by IDSA. In fact nineteen members of the U.S. Congress sent a letter to the Centers for Disease Control and Prevention (CDC) requesting a review of guidelines that 'had the potential to effectively shut down' treatment of chronic Lyme disease. In November 2006, the Attorney General of Connecticut launched a ground breaking antitrust investigation into the development of the Lyme disease treatment guidelines by IDSA. The investigation found **significant indiscretions in the IDSA Lyme guideline** development process such as significant conflicts of interest and bias among the guidelines panel members and suppression of competing viewpoints. If these guidelines that are apparently produced by a respected and influential medical society are obediently abided and remain quite restrictive, how does the patient benefit? Have we as doctors gotten to the point where we have forgotten what medicine is all about? It is about the patient, we are here to provide this service to the patient and must endeavor to push through the politics and make the decision that is in the best interest of the patient.

Table 1 introduces some of the problems found with the IDSA Lyme Disease Guidelines.

Weakness or Flaw	IDSA Guidelines
Conflict of interest[1]	Key panel members had financial interests related to Lyme disease patents, diagnostic tests, pharmaceutical (vaccines) interests, and insurance consulting fees.[2] Citation by panel members of their own research was high (40%).
Overreliance on expert opinion[1]	38 of the 71 recommendations in the guidelines depend on the weakest Level III evidence, namely 'expert opinion'.[3]
Artificial unanimity of recommendations[1]	The panel excluded competing viewpoints voiced by community physicians and members of its rival, ILADS.[2]
Specialty society self-publication[1]	The guidelines were published in an IDSA journal and were not submitted to normal peer review that would include divergent viewpoints. Letters to the editor critical of the guidelines were not published.
Failure to acknowledge legitimate controversy[1]	The controversy over Lyme disease was well known, but physicians with divergent viewpoints were excluded from participation on the panel and the guidelines failed to mention that other treatment approaches exist.[2]
Limitations on the exercise of clinical judgment and failure to provide treatment options[4]	The guidelines impose severe restrictions on the exercise of clinical judgment and fail to provide treatment options despite a weak evidence base.
Academic researchers setting medical protocols[5]	The IDSA panel consisted almost exclusively of academic researchers.[6]

Table 1: Problems with IDSA Lyme Disease Guidelines.
Lorraine Johnson, Raphael B Stricker; *The Infectious Diseases Society of America Lyme Guidelines: a cautionary tale about the development of clinical practice guidelines.*

ISDA vs ILADS

Over the past decade, a small battle has aroused between the two groups over Lymes. They have disagreed on the treatment length and of the recognition of Chronic Lymes. The IDSA, does not recognize the existence of Chronic Lymes, they feel that Lymes can be treated with short courses of antibiotics. The International Lyme and Associated Diseases Society (ILADS) represent the opposition, which disagrees with the IDSA Lyme's guideline and strongly feel that short courses of antibiotics are ineffective. A prolonged course of antibiotic therapy is necessary especially for Chronic Lymes. Therefore one organization acknowledges Chronic Lymes and the need for a prolonged treatment course. However since the established guidelines for the treatment of Lyme, have been created by ILADS it is evident which school of thought is enforced and ultimately it is the patient who suffers.

At NaturoMedic.com, we hope that this second installment of Truth About Lyme Disease Series have been able to shed some light into the murky waters of Lyme. It is our intention to educate and inform the patient thereby allowing them to make an informed decision about their health.

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