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Physician Preferences in the Diagnosis and Treatment of Lyme Disease in the United States

Summary: To assess physician preferences in the diagnosis and treatment of Lyme disease, questionnaires were sent to physicians in various Lyme disease endemic areas in the U. S. Seventy-eight responses were analyzed. Both ELISA and Western blot were ordered by 86% of responders. Fifty percent of responders believed that 25% or more of patients who have Lyme disease were seronegative. The treatment was influenced by physician specialty. Antibiotic treatment for tick bite was prescribed by 20% of responders. Erythema migrans rash was treated by all responders without serologic confirmation. The median treatment duration of erythema migrans was 4 weeks. For post-erythema migrans Lyme disease, 43% of responders treat 3 months or more; for chronic Lyme disease, 57% of responders treat 3 months or more. Our survey documents significant differences between published recommendations and actual practices. Physician education and clinical trials are needed to clarify the reasons for these differences.

Introduction

Lyme disease is a multi-systemic infection caused by a spirochete, *Borrelia burgdorferi* [1]. In 1994, more than 11,000 cases of Lyme disease were reported to the Centers for Disease Control and Prevention, accounting for the most common tick-borne disease in the U.S. [2]. Physicians practicing in Lyme endemic areas are likely to diagnose patients with Lyme disease. Many rely on a clinical diagnosis due to documented problems with the reliability of serological assays [3] and the possibility of seronegative Lyme disease [4, 5]. This approach has been criticized by some as leading to overdiagnosis and overtreatment [6, 7].

In the area of treatment, the appropriate type and duration of antibiotic therapy to effect clinical improvement or resolution of the disease after the initial infection has disseminated is unclear. Therefore, it is understandable that physician practices, habits, beliefs, and attitudes toward Lyme disease in endemic areas vary [8-10]. To further delineate the physician opinions and preferences in diagnosis and treatment of Lyme disease, a survey was conducted.

Materials and Methods

A questionnaire was developed addressing areas of clinical and laboratory diagnoses, and treatment of various stages of Lyme disease. It was mailed to 200 randomly selected physicians practicing in Lyme endemic areas of northeastern U. S. Ninety-two physicians responded in August 1994; 14 responses were incomplete and could not be included in the analysis. Using Quattro Pro, 78 questionnaires (39% response rate) were analyzed as a group, according to medical specialties and number of patients seen with Lyme disease. The statistical analysis was performed using Statistica (Statsoft, Tulsa, OK, USA) program.

Results

A summary of the results is shown in Tables 1, 2 and 3. The percentages are relative to the number of responses to each particular question. In several cases the total is more than 100% due to multiple responses.

Table 1: Laboratory diagnosis of Lyme disease (LD).

Laboratory tests ordered by physicians			
ELISA	94%		
Western blot	91%		
ELISA + Western blot only	31%		
PCR	39%		
More than 1 test	99%		
More than 2 tests	61%		
CSF analyses	No: 17%	Yes: 17%	Sometimes: 70%
Reliability of ELISA tests			
Percent positive	Early LD	Post-erythema migrans LD	Chronic LD
< 25%	49%	25%	24%
25%-50%	34%	17%	28%
50%-75%	9%	35%	23%
> 75%	9%	23%	24%
Frequency of seronegative Lyme disease			
Percent seronegative			
< 20%	47%		
21%-40%	24%		
41%-60%	19%		
61%-80%	10%		
Median = 25%	Mean = 28%	SD = 22%	
Reliability of diagnosis			
	Most	Least	
Clinical	80%	12%	
Western blot	47%	18%	
Epidemiology	33%	25%	
ELISA/IFA	31%	24%	
Disease exclusion	31%	31%	
PCR	27%	25%	
Urine antigen	11%	40%	

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Table 2: Clinical Diagnosis of Lyme disease (LD).

Percent of patients with no known tick bite		
<26	19%	
26-50	49%	
51-75	23%	
> 75	9%	
Median = 50%	Mean = 49%	SD = 21%
Percent of patients with erythema migrans		
<26	45%	
26-50	34%	
51-75	15%	
> 75	5%	
Median = 30%	Mean = 35%	SD = 23%
Frequency of symptoms/signs		
	Median	Mean
Fatigue	90%	81%
Arthralgias	80%	73%
Headache	70%	62%
Cognitive	50%	47%
Behavioral	50%	46%
Paresthesias	40%	38%
Arthritis	25%	33%
Sweats	10%	20%
Sore throat	20%	26%
Cardiac	10%	16%
Recurring rash	10%	16%
Ocular	10%	22%
Fibromyalgia, Chronic fatigue, and Lyme disease		
	Fibromyalgia	Chronic fatigue
Separate entity	26%	27%
Result of LD	25%	25%
Possibly both	67%	66%

Laboratory Diagnosis (Table 1)

ELISA and Western blot are almost universally used. Thirty-one percent of responders used only the ELISA and Western blot tests. Western blot was the most reliable laboratory test; the ELISA was thought to be unreliable in over 50% of all cases. Seronegative Lyme disease was thought to occur in 25% of cases. Ninety-nine percent of physicians ordered more than one test; 61% ordered more than two tests. CSF analyses were not routinely ordered.

Clinical Diagnosis (Table 2)

Over 80% consider the clinical signs and symptoms to be the most reliable criteria for the clinical diagnosis. The most frequent symptoms were fatigue, arthralgias, headache and cognitive changes. Erythema migrans was thought to occur in only 30% of cases. Fifty percent of patients reported no known tick bite. Fibromyalgia and chronic fatigue syndrome were thought to be a result of Lyme disease in 25% of cases; only 26% of respondents thought they were separate entities.

Treatment (Table 3)

The duration of treatment is influenced by the physician's specialty and number of new Lyme disease patients seen in a week. One third of respondents prophylactically treated tick bites. Amoxicillin and doxycycline were the most frequently used antibiotics in the treatment of erythema migrans. The mean duration of treatment was 4 weeks, although 31% treated for more than 4 weeks. Seventy-two percent of respondents did not require a laboratory confirmation for treatment of post-erythema migrans and chronic Lyme disease. Intravenous ceftriaxone, amoxicillin, doxycycline and macrolides were the antibiotics of choice in the treatment of post-erythema migrans and chronic Lyme disease. The mean duration of therapy was 3-6 months.

Discussion

Lyme disease was first described in the U.S. in 1977 by Steere et al. as Lyme arthritis [11]. The subsequent reports suggested that arthritis might not be the most representative clinical manifestation of Lyme disease; rather, the disease is of a multi-systemic character [12]. Even though major progress has been made in the past 20 years, many questions regarding pathogenesis, diagnosis and optimal clinical management of Lyme disease remain to be answered [13]. It is therefore understandable that physician approaches toward the management of this disease are subject to change.

The diagnosis of Lyme disease is based on clinical symptoms, laboratory results and epidemiological data [14]. The ultimate diagnosis, isolation of the organism, is difficult to achieve. Laboratory diagnosis relies on serological testing. The performance of routinely used serological assays is variable. Standardization is needed, as false-positives and false-negatives occur [15, 16]. Even though the exact extent of this problem is not known, there are some reports alleging the overdiagnosis of Lyme disease, based on the lack of serological confirmation [6, 7]. A lack of confidence in the performance reliability of serological tests was confirmed by our survey. Also, the general recommendation to confirm every positive and equivocal ELISA by Western blot is not being followed. The majority of physicians order ELISA and Western blots concurrently. They also send testing samples to multiple laboratories, further showing limited confidence in the test results. There are a few explanations for this discrepancy. The reliability of serologic tests may depend on the laboratory where the test was performed [17, 18]. The antibody response of the tested individual may vary. Patients might lack an antibody response, for example due to the formation of circulating complexes and/or early antibiotic treatment [4, 5].

In the view of most respondents, the diagnosis of Lyme disease is based primarily on clinical signs and symptoms. The presence of erythema migrans is considered pathognomonic by the majority of experts [19]. Unfortunately,

Table 3: Treatment of Lyme disease (LD).

Treatment of tick bites						
	ALL (n = 75)	IM (n = 12)	ID (n = 15)	RH (n = 11)	<1 (n = 19)	>1 (n = 55)
No	33%	8%	60%	36%	68%	20%
Yes	20%	25%	0%	9%	5%	25%
Sometimes	33%	58%	27%	45%	26%	36%
On request	16%	8%	20%	9%	0%	22%
At risk	17%	33%	7%	9%	5%	22%

IM = internist; ID = infectious disease; RH = rheumatologist; <1 = <1 new patient/week; >1 = 1 or more new patient/week.

Antibiotic therapy of erythema migrans	
Amoxicillin	86%
Doxycycline	82%
Azithromycin	28%
Cefuroxime	24%
Clarithromycin	24%
Cefixime	18%
Tetracycline	16%
IV ceftriaxone	14%
Minocycline	11%
IV cefotaxime	8%

Duration of therapy: median, mean = 4 weeks; > 4 weeks = 31%;
symptoms post therapy: median = 15%, mean = 25%.

Antibiotic therapy of post-erythema migrans LD			Duration of Antibiotic therapy of post-erythema migrans LD					
Basis	Yes	No	ALL (n = 71)	IM (n = 11)	ID (n = 14)	RH (n = 12)	<1 (n = 15)	>1 (n = 54)
Clinical diagnosis	66%	34%						
Require lab confirmation	28%	72%						
Treatment			<2 weeks	1%	0%	0%	7%	0%
IV ceftriaxone	81%		2-4 weeks	35%	0%	50%	53%	30%
Amoxicillin	72%		1-3 months	30%	36%	29%	27%	31%
Doxycycline	65%		3-6 months	23%	45%	14%	7%	28%
Clarithromycin	43%		>6 months	24%	36%	29%	0%	28%
Azithromycin	41%		Median: 1-3 months					
Cefuroxime	38%		IM = internist; ID = infectious disease; RH = rheumatologist;					
IV cefotaxime	32%		<1 = <1 new patient/week; >1 = 1 or more new patient/week.					
Cefixime	24%							
Penicillin	14%							
Others	<10%							
Combination therapy: yes: 40%								

Antibiotic therapy of chronic LD		Duration of antibiotic therapy of chronic LD			
		ALL (n = 69)	IM (n = 11)	ID (n = 14)	RH (n = 12)
IV ceftriaxone	79%	<2 weeks	1%	0%	0%
Amoxicillin	61%	2-4 weeks	28%	0%	43%
Doxycycline	60%	1-3 months	25%	18%	29%
Azithromycin	46%	3-6 months	19%	45%	7%
Clarithromycin	43%	>6 months	38%	55%	29%
IV cefotaxime	34%	Median = 3-6 months			
Cefuroxime	30%	IM = internist; ID = infectious disease; RH = rheumatologist.			
Cefixime	25%				
Others	<20%				
Combination therapy: yes: 42%					
Repeat testing: yes: 16%, no: 32%, sometimes: 52%, % patients symptom-free: median = 50%, % patients retreated: median = 30%, mean = 39%.					

our respondents thought erythema migrans occurred in only 30% of cases. The most commonly seen symptoms are nonspecific and difficult to objectify [20]. Whether

these symptoms represent "active" Lyme disease, or non-infectious, so called "post-Lyme" syndrome [21] is a point of disagreement at this time. Some suggest that a favora-

ble response to antibiotics is an important clue in the determination of the presence of active infection [22]. Clinical studies are needed to bring a clearer and more comprehensive view.

Current treatment recommendations are inconclusive for most parts of Lyme disease. It is, therefore, not surprising that treatment preferences are most variable. Even though some reports do not recommend antibiotic treatment for a tick bite [23, 24], a considerable percentage of physicians elect to treat [8]. Lengths of therapy for post-erythema migrans and chronic Lyme disease exceed the recommended 4 weeks [25]. Some reports have suggested that longer and/or repeated treatment might be needed in individual cases to eradicate the persistent organism [26-29]. Only double-blind, randomized, controlled, prospective treatment trials can answer these questions with any certainty. Of interest was the fact that treatment choices were influ-

enced by both the specialty of the treating physician and the number of new Lyme disease patients seen in a week. This shows biases unrelated to the true character of Lyme disease.

The results of our survey document that the current recommendations for the diagnosis and treatment of Lyme disease and physicians' actual choices vary markedly. A possible bias due to estimated responses is acknowledged. The detected trends are so striking, however, that further investigation is warranted to clarify whether current recommendations, or physicians' choices, should be changed. Until then, physicians' education, scientific data and open-mindedness are the best approaches.

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Zusammenfassung: Bevorzugte Methoden in der Diagnostik und Therapie der Lyme-Borreliose bei amerikanischen Ärzten. Zur Erhebung von Daten zur Präferenz amerikanischer Ärzte in der Diagnostik und Therapie der Lyme-Borreliose wurden in verschiedenen endemischen Gebieten der USA Fragebogen an Ärzte verschickt. 78 Antworten wurden ausgewertet. 86% der Befragten forderten eine Untersuchung mittels ELISA und Western Blot. 50% der Befragten gaben an, daß ihrer Ansicht nach 25% der Patienten mit Lyme-Borreliose seronegativ sind. In der Therapiewahl ist ein Einfluß der Spezialisierung der Ärzte zu erkennen. 20% der Befragten

verordnen nach Zeckenstich ein Antibiotikum. Alle Ärzte gaben an, das Erythema migrans auch ohne serologische Bestätigung mit Antibiotika zu behandeln. Die mediane Behandlungsdauer bei Erythema migrans betrug 4 Wochen. Eine nach Erythema migrans auftretende Lyme Borreliose wurde von 43% der Befragten 3 Monate oder länger behandelt. Die von uns durchgeführte Umfrage deckte erhebliche Unterschiede zwischen publizierten Empfehlungen und der Praxis auf. Es ist erforderlich, die Gründe für diese Unterschiede aufzuklären und den Ärzten Fortbildung anzubieten.

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