Appropriateness of Lyme Disease Serologic Testing

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ABSTRACT

BACKGROUND Although rapid diagnosis of Lyme disease is essential for effective treatment, there is concern about inappropriate testing. We conducted a prospective, cross-sectional survey of clinicians to assess the use and appropriateness of Lyme disease serologic tests (LDSTs).

METHODS LDSTs performed at 2 large Wisconsin reference laboratories were systematically sampled for 12 consecutive months. A standardized questionnaire was used to gather data about the submitting clinician and the patient tested. Tests were categorized as appropriate, inappropriate, or discretionary, and associations were assessed using logistic regression analysis. A test was defined as inappropriate if the patient was asymptomatic, had erythema migrans, or was treated empirically, or if the test was ordered as a test of cure.

RESULTS We surveyed 303 clinicians regarding 356 LDSTs: 72 tests (20%) were appropriate, 95 (27%) were inappropriate, and 189 (53%) were discretionary. Tests were more likely to be inappropriate if they were ordered by an emergency or urgent care physician compared with other specialists (adjusted odds ratio [AOR] 5.2, 95% confidence interval [CI], 1.3–20.6), or if preceded by a known tick bite (AOR 6.8, 95% CI, 2.6–17.6). The patient rather than the clinician requested 26% of tests, which were more likely to be inappropriate than clinician-requested tests (crude odds ratio [COR] 5.8, 95% CI, 2.5–13.6). Tests were more likely to be patient-requested if they were ordered by an internist (AOR 2.6, 95% CI, 1.4–4.8) or if the patient was ≥40 years old (AOR 2.2, 95% CI, 1.3–3.9).

CONCLUSIONS Many LDSTs are ordered inappropriately, often influenced by patient demand. Education of clinicians and patients about testing indications and contraindications is needed to reduce the number of inappropriate LDSTs.

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INTRODUCTION

Lyme disease is a multisystem tick-borne infection caused by the spirochete *Borrelia burgdorferi*.[1,2] Erythema migrans, the characteristic expanding rash of early localized Lyme disease, is present in at least 80% of cases, and joint, neurologic, cardiac and other manifestations may develop.[3] In the absence of erythema migrans, antibodies to *B burgdorferi* are generally required to diagnose Lyme disease.[3,4] Approximately 2.8 million Lyme disease serologic tests (LDSTs) are performed each year in the United States according to a 1995 estimate.[4] At $40 per test, a conservative figure, the annual direct medical expenditure for LDSTs would exceed $100 million.

There is persisting concern that LDSTs are used inappropriately by clinicians.[5-7] Early serologic testing based only on tick bite or potential exposure to ticks has low sensitivity and specificity and is not recommended.[8] For patients who live in areas where Lyme disease is endemic, and who have erythema migrans, serologic testing is not routinely recommended. The likelihood that these patients have Lyme disease exceeds the positive

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predictive value of serologic testing, and the negative predictive value of serologic testing of these patients is exceedingly low.[9,10]

To assess factors contributing to appropriate and inappropriate use of LDSTs, we conducted a prospective, cross-sectional survey of clinicians ordering LDSTs.

METHODS

We surveyed clinicians who submitted specimens for Lyme disease serologic testing (enzyme immunoassay or immunofluorescence assay) to 2 large clinical reference laboratories in Wisconsin. Up to 30 consecutive tests per month were selected from each laboratory during October 1999 through September 2000. No more than 2 tests per clinician were sampled during the study.

Consenting clinicians or other providers with access to the medical record completed a standardized survey questionnaire by telephone. Data gathered pertained to clinician characteristics and clinical circumstances related to each test.

Tests were classified as appropriate, inappropriate, or discretionary (indeterminate appropriateness) using clinical criteria based on published recommendations.[3,4,8-10] A test was defined as appropriate if the patient had any objective findings consistent with disseminated Lyme disease, including joint, neurologic, or cardiac symptoms, such as arthritis, lymphocytic meningitis, cranial neuritis, or atrioventricular conduction defects. A test was defined as inappropriate if the patient was asymptomatic, had clinician-diagnosed erythema migrans, or was treated empirically with antibiotics, or the test was ordered as a test of cure (Table 1). Because evidence-based practice guidelines do not address Lyme disease testing for other clinical symptoms (eg, arthralgias, myalgias, malaise, or fatigue), the test was defined as discretionary if it met none of these criteria.

Associations were assessed using univariate unconditional logistic regression analysis with calculation of odds ratios (OR) and 95% confidence intervals (CI). Variables associated with inappropriate tests ($P \leq .10$) were entered into a multivariate unconditional logistic regression model using forward stepwise selection, followed by backward elimination. Discretionary tests were excluded from this analysis. All reported P values are 2-sided and $P \leq .05$ was considered statistically significant. Statistical analyses were done with SAS version 6.12 (SAS Institute, Cary, NC).

Table 1. Appropriate and Inappropriate Indications For Lyme Disease Serologic Testing in Lyme-Endemic Regions

Appropriate	Inappropriate
Patient with oligoarticular arthritis	Patient is asymptomatic
Patient with cranial neuritis	Patient with clinician-diagnosed erythema migrans
Patient with lymphocytic meningitis	Patient treated empirically with antibiotics
Patient with atrioventricular block	Serologic test ordered as a test of cure
Patient with carditis	

Note: If patient does not meet any of the above criteria for appropriateness, the decision to order a Lyme disease serologic test is left to the discretion of the clinician.

RESULTS

We sampled 408 LDST requests, and 356 (87%) survey questionnaires were completed; 250 clinicians completed 1 questionnaire, and 53 completed 2 questionnaires. Forty clinicians refused to participate, and 12 could not be reached.

Of the 356 LDST requests, 20% were classified as appropriate, 27% inappropriate, and 53% discretionary. Reasons for classifying tests as inappropriate were not mutually exclusive and included absence of symptoms (55%), empiric antibiotic treatment (27%), test of cure (27%), and diagnosis of erythema migrans (24%). Stratified by specialty, family physicians, internists, and emergency and urgent care physicians ordered 70% of all tests and 75% of inappropriate tests (Table 2).

Patients initiated 27% of LDST requests (Table 2). Factors associated with patient-initiated testing included submission by a general internist (adjusted odds ratio [AOR] 2.6, 95% CI, 1.4–4.8) and patient age of 40 years and older (AOR 2.2, 95% CI, 1.3–3.9).

Patient-initiated tests were more likely to be inappropriate than tests initiated by clinicians (Table 3). Other characteristics significantly associated with inappropriate tests by univariate analysis included known or suspected tick bite within 30 days of illness onset, test ordered by an emergency or urgent care physician, and test done during the summer. Patient referral from another clinician and patient hospitalization were associated with a reduced likelihood of inappropriate testing.

Two factors were independently associated with inappropriate testing in the multivariate analysis: known or suspected tick bite within 30 days of illness onset, and test ordered by an emergency or urgent care clinician (Table 3). The reasons for inappropriate testing by emergency or urgent care physicians were not significantly different from those for other physicians.

DISCUSSION

Our study results show that only 20% of LDST requests were appropriate, and at least 27% were inappropriate. Inappropriate Lyme disease serologic testing represents an inefficient use of health care resources and may con-

Table 2. The Number of Appropriate, Inappropriate and Discretionary Lyme Disease Serologic Test Requests by Clinical Specialty and by Source of Test Initiation

Characteristic	No.	Appropriate No. (%)	Inappropriate No. (%)	Discretionary No. (%)
Clinical specialty				
Family practice	151	30 (20)	35 (23)	86 (57)
Internal medicine	67	12 (18)	21 (31)	34 (51)
Emergency or urgent care	32	4 (13)	15 (47)	13 (41)
Pediatrics	23	2 (9)	5 (22)	16 (70)
Neurology	19	6 (32)	2 (11)	11 (58)
Rheumatology	8	6 (75)	1 (13)	1 (13)
Others	56	12 (21)	16 (29)	28 (50)
Total	356	72 (20)	95 (27)	189 (53)
Initiation of testing				
Clinician initiated	218	60 (28)	47 (22)	111 (51)
Patient initiated	95	8 (8)	37 (39)	50 (53)
Not clear	43	4 (9)	11 (26)	28 (65)
Total	356	72 (20)	95 (27)	189 (53)

Table 3. Results of Univariate and Stepwise Multivariate Unconditional Logistic Regression Model Analysis for Factors Associated With Inappropriate Lyme Disease Serologic Testing

Variable	Univariate COR (95% CI)	Multivariate AOR (95% CI)
Known or suspected tick bite within 30 days of symptom onset	6.9 (2.9-16.5)	6.8 (2.6-17.6)
Test ordered by emergency or urgent care physician	3.7 (1.2-11.4)	5.2 (1.3-20.6)
Test initiated by patient request	5.8 (2.5-13.6)	
Test done during summer	2.5 (1.3-4.7)	
Patient age less than 40 years	1.6 (0.8-3.0)	
Initial evaluation of problem for which test was ordered	1.5 (0.8-3.1)	
Test done at Laboratory A	1.1 (0.4-2.9)	
Test ordered by physician	0.9 (0.4-2.3)	
Clinician in practice less than 10 years	1.0 (0.5-1.8)	
Tick habitat exposure during last 30 days	0.6 (0.1-3.1)	
Patient hospitalized	0.3 (0.1-1.0)	
Patient referred from another clinician	0.3 (0.1-0.6)	

COR = crude odds ratio; AOR = adjusted odds ratio; CI = confidence interval.

Note: discretionary tests were excluded from this analysis.

tribute to both underdiagnosis (eg, negative serologic findings in patients with erythema migrans) and overdiagnosis (eg, patients with nonspecific constitutional symptoms) of Lyme disease.[5,11-13] False-positive tests can result in unnecessary antibiotic treatment, which in turn may be associated with adverse events and contribute to the spread of antimicrobial resistance.[14,15] False-negative tests may result in delayed treatment and increase the risk of spirochete dissemination.[12]

In this study, more than one half of the inappropriate tests were for asymptomatic patients. Compared with family physicians and internists, physicians in emergency or urgent care were significantly more likely to order inappropriate tests. The reason for this finding is unclear, but we speculate that physicians in these settings may use testing as a temporizing measure, delaying final treatment decisions until the patient can follow up with his or her primary care physician. A known or suspected preceding tick bite was also strongly associated with inappropriate testing, suggesting a need for more clinician education on the risk of Lyme disease after a tick bite. A controlled study has shown that single-dose doxycycline given prophylactically can reduce the risk of Lyme disease after tick attachment in an endemic region,[16] but there is no benefit to serologic testing regardless of the treatment decision. Interventions should be focused on educating providers about indications for Lyme disease testing, particularly that the absence of symptoms with or without a known or suspected recent tick bite obviates the need for testing.

We found 53% of all tests could not be classified as either appropriate or inappropriate based on published recommendations. The existing diagnostic guidelines base testing decisions on the pretest probability of Lyme disease as calculated by an expert panel.[4] From a practical standpoint, clinicians and others might have difficulty calculating the pretest probability of Lyme disease; hence, the high proportion of discretionary tests.

We also found that patients requested a large number of tests, which is consistent with previous findings.[6] Nearly 40% of these tests were inappropriate, although most inappropriate tests were initiated by physicians.

A limitation of this study is that clinical information was provided by clinicians without validation by medical record review, although respondents often used the medical record to complete the interview. In addition,

sampling from 2 laboratories in Wisconsin might not be representative of all clinicians ordering LDSTs.

We conclude that inappropriate Lyme disease serologic testing is common in Wisconsin, and patients initiate many of these tests. Expanded education for clinicians and patients about testing indications and contraindications may reduce the number of inappropriate LDST requests. Clarification of existing testing guidelines is needed to promote optimal use of LDSTs.

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