THE YALE JOURNAL OF BIOLOGY AND MEDICINE 62 (1989), 253-262

Epidemiological and Clinical Features of 1,149 Persons with Lyme Disease Identified by Laboratory-Based Surveillance in Connecticut

LYLE R. PETERSEN, M.D.,[a] ANNE H. SWEENEY, M.P.H.,[b] PATRICIA J. CHECKO, M.P.H.,[c] LOUIS A. MAGNARELLI, Ph.D.,[d] PATRICIA A. MSHAR,[c] ROBERT A. GUNN, M.D., M.P.H.,[a] AND JAMES L. HADLER, M.D., M.P.H.[c]

[a]Division of Field Services, Epidemiology Program Office, Centers for Disease Control, Atlanta, Georgia; [b]Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut; [c]Preventable Diseases Division, State of Connecticut Department of Health Services, Hartford, Connecticut; [d]Department of Entomology, Connecticut Agricultural Experiment Station, New Haven, Connecticut

Received May 15, 1989

Laboratory-based surveillance of Lyme disease in Connecticut during 1984 and 1985 identified 3,098 persons with suspected Lyme disease; 1,149 were defined as cases. Lyme disease incidence in Connecticut towns ranged from none to 1,407 cases per 100,000 population in 1985. A comparison of 1985 data with data from 1977 epidemiologic studies indicated that incidence increased by 129 percent to 453 percent in towns previously known to be endemic for Lyme disease and that Lyme disease had spread northward into towns thought to be free of Lyme disease in 1977. Children aged five to 14 years had the highest incidence. Of persons with Lyme disease, 83 percent had erythema migrans, 24 percent had arthritis, 8 percent had neurologic sequelae, and 2 percent had cardiac sequelae. The distribution of symptoms was age-dependent: case-persons <20 years old were almost twice as likely to have arthritis than older case-persons (35 percent versus 18 percent). Of persons with arthritis, 92 percent of those <20 years of age, compared to 68 percent of older persons, did not have antecedent erythema migrans. We conclude that Lyme disease is increasing in incidence and geographic distribution in Connecticut. Of those with Lyme disease, children may be more likely than adults to develop arthritis and have it as their first major disease manifestation.

Lyme disease, discovered in 1975 in Connecticut, is now endemic in at least 19 countries and 24 states and is the most commonly reported anthropod-related disease in the United States [1,2]. It is caused by a spirochete, *Borrelia burgdorferi*, that is transmitted to humans by ixodid ticks [3,4]. Three clinical stages can occur. The first stage typically begins three to 32 days after a tick bite with a characteristic skin lesion, erythema migrans [5–7]. Nonspecific symptoms, such as myalgias, headache, fever, fatigue, and arthralgias, often accompany the skin lesions. The second stage begins weeks to months later with the development of neurologic [8,9] or cardiac manifestations [10,11]. The third stage is characterized by arthritis weeks to years after the

Abbreviations: ELISA: enzyme-linked immunosorbent assay IFA: immunofluorescence assay

Address reprint requests to: Lyle R. Petersen, M.D., AIDS Program, Mailstop G-29, Centers for Disease Control, 1600 Clifton Rd., Atlanta, GA 30333

initial tick bite [4,5]. The second and third stages may occur without the clinical manifestations of the earlier stage.

Epidemiologic studies of Lyme disease have been difficult to conduct, in part because erythema migrans is the only unique clinical manifestation of Lyme disease and, consequently, accurate case ascertainment can be difficult to establish based on clinical criteria alone for persons with cardiac, neurologic, or arthritic manifestations, especially without antecedent erythema migrans. Indirect immunofluorescence assays (IFA) and enzyme-linked immunosorbent assays (ELISA) now exist for detecting antibodies to *Borrelia burgdorferi* [12,13]. Because these tests have a sensitivity approaching 100 percent during the secondary and tertiary stages of Lyme disease, stages when the disease can be the most difficult to diagnose, more complete case ascertainment is now possible [13,14]. The specificities of the IFA and ELISA tests are high: of ten healthy controls and 30 persons with rheumatoid arthritis, systemic lupus erythematosus, or infectious mononucleosis who were tested by ELISA [13], and of 40 healthy controls and 51 persons with unknown febrile illness tested by both ELISA and IFA [14], none were positive for antibodies to *Borrelia burgdorferi*. Although cross-reactivity occurs with tick-borne relapsing fever, louse-borne relapsing fever, syphilis, yaws, and Rocky Mountain spotted fever [15], these diseases are usually easily distinguished from Lyme disease on the basis of clinical or epidemiologic findings.

From July 1984 to March 1986, we studied Lyme disease in Connecticut using a laboratory-based surveillance system. Our objectives were to determine the frequencies of the most common clinical manifestations, the descriptive epidemiology of Lyme disease in Connecticut, especially its geographic distribution, and the sensitivity of the serologic test during early Lyme disease as determined by a surveillance system. The findings of this study are the subject of this report.

METHODS

Case Ascertainment and Reporting

Serologic testing for Lyme disease has been available to patients of Connecticut physicians since 1983 from the Connecticut Agricultural Experiment Station. In the spring of 1984, three announcements from the Connecticut State Department of Health Services were mailed to all general internists, internal medicine subspecialists, general pediatricians, pediatric subspecialists, family practitioners, and neurologists licensed to practice in Connecticut to inform them about Lyme disease and to spread the word further about the availability of free serologic testing for all suspected Lyme disease cases. Physicians were required to complete a case report form with all specimens submitted for testing from July 1, 1984, to March 1, 1986. In addition, physicians were asked to report voluntarily suspected cases of Lyme disease from whom serologic testing was not sought. The case report form included information about the patient's demographic characteristics, detailed clinical history, and history of tick bite. Information about the patient's race, number and size of erythema migrans lesions, constitutional symptoms, and specific joint involvement, and the specialty of the referring physician was obtained only for persons reported in 1984.

Only Connecticut residents with onset of illness in 1984 or 1985 were included in the analyses reported here. To meet the case definition, a resident had to have either erythema migrans or to have neurologic [8,9], cardiac [10,11], or arthritic [4,5] manifestations consistent with Lyme disease and at least one positive serologic test

result. Persons with erythema migrans who had reported neurologic, cardiac, or arthritic symptoms and a negative serologic test result were considered to have erythema migrans as their only Lyme disease manifestation. This distinction was primarily made to minimize misclassifying arthralgia as arthritis. Arthralgia frequently occurs in early Lyme disease when the serology is often negative, whereas arthritis, which occurs later, is almost always accompanied by a positive serology. Persons with a positive serologic test but without erythema migrans, and without cardiac, neurologic, or arthritic manifestations were not counted as cases.

Although information submitted on the case report form was not systematically validated, the medical charts of 72 persons with erythema migrans and 29 persons with arthritis reported as part of this surveillance study in 1984 were reviewed in 1987. Ninety-four percent of patients with erythema migrans and 93 percent of patients with arthritis had sufficient information recorded in the medical chart to confirm these diagnoses [16].

Long-term changes in Lyme disease incidence were assessed by comparing 1977 incidences for residents of nine towns west of the Connecticut River (Chester, Clinton, Deep River, Essex, Haddam, Killingworth, Madison, Old Saybrook, and Westbrook) [17] and three towns east of the Connecticut River (East Haddam, Lyme, and Old Lyme) [17] to the 1985 incidences found in this study. The study conducted in 1977 utilized an active surveillance system where all physicians in the study communities were contacted in person and by telephone. Although the case definition used in the 1977 study was similar to that used in 1984–1985, serologic testing was not available in 1977 to confirm the diagnosis of Lyme disease in those with neurologic, cardiac, or arthritic manifestations. Misclassification of patients with arthritis in 1977 was minimized, however, because patients were required to have laboratory and clinical evidence that should have excluded other causes of arthritis.

Serological Assay

All serum samples were tested by IFA or ELISA with a polyvalent conjugate using methods described elsewhere [15,18–20]. Serum samples received before July 1985 were tested by IFA; sera received later were analyzed by ELISA. In a preliminary study of 139 patients with erythema migrans reported in 1984, both tests had 95 percent concordance when identical paired sera were tested [20]. For this study, a titer of $\geq$1:128 by IFA or $\geq$1:160 by ELISA was considered positive. Because as many as three serum samples were submitted for some patients, persons were considered to have a positive serologic test result if any sample was positive.

Data Analysis

The data were analyzed using the Statistical Analysis System program [21]. Univariate analyses were performed using the chi-square test. Age-specific population estimates were derived from 1984 data in the Connecticut *Annual Registration Report of Vital Statistics, 1985* [22]. Because the *Registration Report* did not contain yearly population estimates by town of residence, data from the 1980 U.S. Census were used for computation of 1984 and 1985 Lyme disease incidence by town of residence.

RESULTS

Of the 3,098 persons reported with possible Lyme disease, 1,149 (37 percent) were defined as cases. Of these, 460 had onset of symptoms in 1984 and 689 in 1985. The percentages of persons reported with possible Lyme disease who met our case

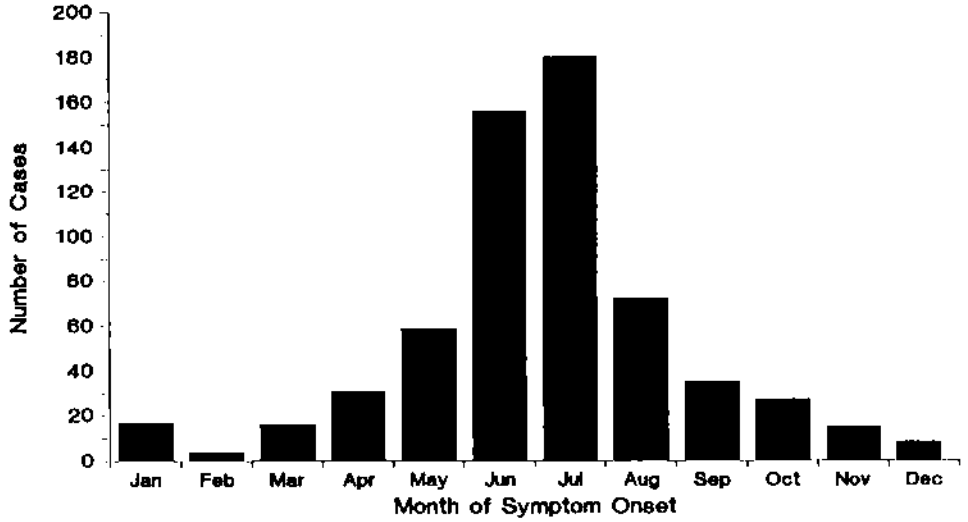

FIG. 1. Lyme disease cases by month of initial symptom onset: Connecticut, 1985.

definition were similar in 1984 (36 percent; 460/1,290) and 1985 (38 percent; 689/1,808). In 1984, over 75 percent of case-persons were reported by primary care physicians: family practice (40 percent), internal medicine (20 percent), and pediatrics (16 percent). The remainder were reported by specialists in rheumatology (9 percent), dermatology (3 percent), infectious disease (2 percent), neurology (1 percent), or other fields (7 percent).

Epidemiologic Features

In 1985, the first complete year of reporting, 66 percent (408) of 619 case-persons with known month of onset had onsets in June, July, and August (Fig. 1). When comparisons in Lyme disease incidence were limited to those with onset of symptoms from July to December, time periods during both reporting years when serologic testing was equally available, a 24 percent increase was observed from 1984 (397) to 1985 (492).

Estimated Lyme disease incidence for all Connecticut residents was 22/100,000 in 1985. Because the geographic location where the tick bite occurred was often unknown, town-specific incidences were computed by town of residence. Lyme disease was sharply demarcated in geographic distribution. In 1985, Lyme disease incidence for Connecticut towns ranged from zero to 1,156/100,000, and every town with an incidence >300/100,000 population was located within 40 kilometers of another town where Lyme disease was not reported (Fig. 2). High-incidence towns were located in southeastern Connecticut and in the lower Connecticut River Valley. Almost half (48 percent) of towns with an incidence of 1–49/100,000 had only one case-resident. Compared to 1977 data, the 1985 incidence increased by 129 percent (280/100,000 to 650/100,000) in three towns east of the Connecticut River, and by 453 percent (13/100,000 to 73/100,000) in eight towns west of the River.

Fifty-one percent (585/1,149) of persons with Lyme disease were male. All but one of the 372 case-persons reported in 1984 whose race was specified were white. Age-specific Lyme disease incidence was tabulated by five-year age groups for those

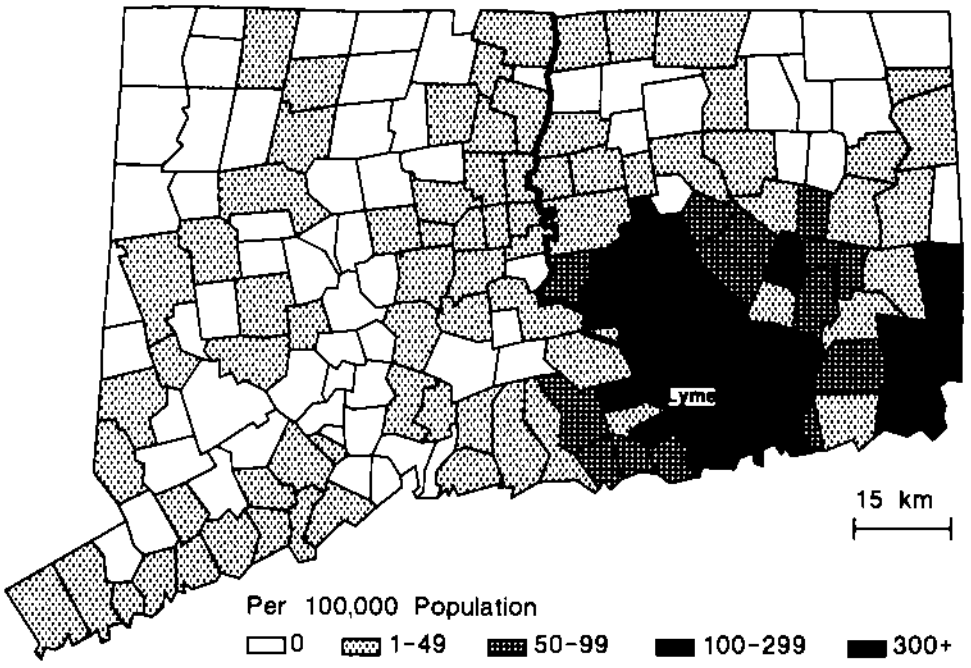

FIG 2. Lyme disease incidence by town of residence: Connecticut, 1985.

with symptom onset in 1985. Incidence ranged from 11/100,000 for persons aged 20 to 24 years to 39/100,000 for those aged five to nine years (Fig 3).

Clinical Features

Overall, 911 (83 percent) of those with Lyme disease had erythema migrans, 252 (24 percent) had arthritis, 84 (8 percent) had neurologic manifestations, and 22 (2 percent) had cardiac involvement (Table 1). Data about the number and size of erythema migrans skin lesions were available for 285 persons reported in 1984: 31 percent (89/285) had two or more erythema migrans lesions; the median size of the largest lesion was 10 centimeters, with a range of 1 to 45 centimeters. Information about specific joint involvement was available for 44 of 49 persons with arthritis reported during 1984. Affected joints were the knee (89 percent), hip (9 percent), shoulder (9 percent), ankle (7 percent), and elbow (2 percent).

The distribution of some symptoms was age-dependent. Among those with Lyme disease, persons <20 years old were almost twice as likely to have arthritis as those ≥20 years old (Table 2). There was, however, no corresponding increase in frequency of neurologic or cardiac manifestations in case-persons <20 years old (Table 2). Of case-persons with arthritis, only 10 percent (11/113) of those <20 years of age had antecedent erythema migrans, compared to 32 percent (41/129) of those ≥20 years of age ($p < 0.001$).

Information about tick bites within 30 days of onset of illness was collected from 1,940 of the persons reported with Lyme disease. Persons defined as cases were almost twice as likely to have a history of tick bite (54 percent, 417/779) than those not defined as cases (31 percent, 360/1,161). Among case-persons, 60 percent (333/552)

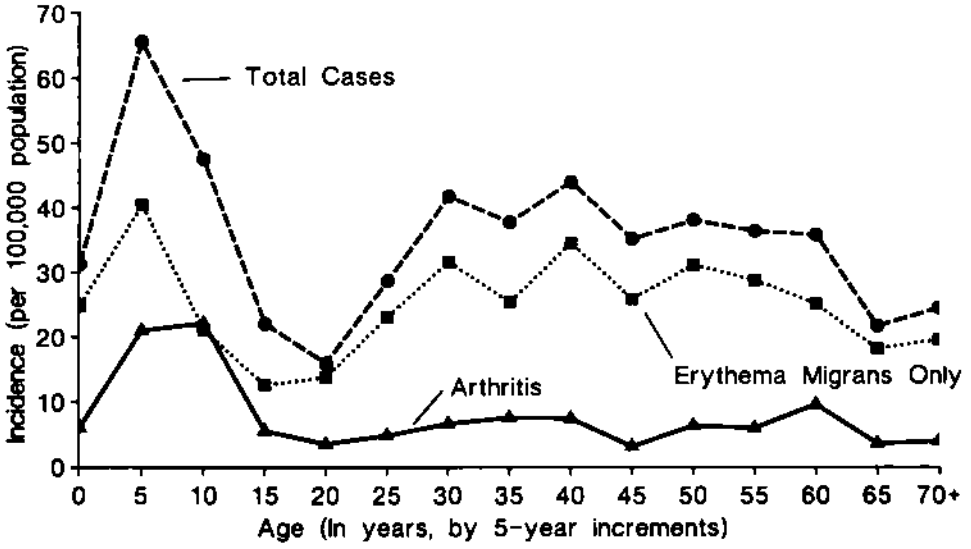

FIG. 3. Lyme disease incidence by age of patient: Connecticut, 1985.

of those with only erythema migrans, 64 percent (41/64) of those with erythema migrans and arthritic, neurologic, or cardiac manifestations, and 26 percent (43/163) of those with arthritic, neurologic, or cardiac involvement but without erythema migrans, had a history of tick bite. The species of ticks were not identified.

Information about antibiotic therapy was available for 391 case-persons reported in 1984. Three hundred thirty-two persons (85 percent) were treated with tetracycline, penicillin, or erythromycin, nine persons (2 percent) received other antibiotics, and 50 persons (13 percent) had received no antibiotics as of the date of submission of the initial case report form.

Serologic Study

Seventy-two persons were reported without a request for serologic testing in 1984; therefore, 3,026 (98 percent) of 3,098 reported persons had at least one serologic test. Of those with serologic tests, 37 percent (1,117) had two specimens and 3 percent (86) had three specimens submitted for testing. Specimens from 1,447 persons were analyzed by IFA, and specimens from 1,579 persons were analyzed by ELISA.

Neither the IFA nor the ELISA was sensitive during the early stages of disease. The positivity rate for the first serum specimen for those with erythema migrans was only 30 percent by IFA and 24 percent by ELISA (Table 3). The sensitivity of both the IFA and the ELISA improved if the serum sample was drawn ≥21 days after the onset of illness.

DISCUSSION

Our data indicate that Lyme disease is spreading geographically in Connecticut. In 1977, epidemiologic studies in Connecticut showed that Lyme disease occurred almost exclusively in towns located near the shoreline and east of the Connecticut River [15,23], areas where the tick vector, *I. dammini,* was abundant [24]. By 1983, entomologic and serologic studies suggested that the geographic distributions of *I.*

TABLE 1
Clinical Characteristics of Lyme Disease
Connecticut, 1984–1985

Symptom/Sign	No. Reporting[a]	%
Constitutional		
Fever	214	57
Myalgia	181	49
Headache	164	44
Arthralgia	126	34
Stiff neck	75	20
Sore throat	39	11
Nausea/vomiting	38	10
Skin rash	938	86
Erythema migrans	911	83
Other rash	94	9
Neurologic	84	8
Bell's palsy	29	3
Encephalitis	14	1
Meningitis	14	1
Cardiac	22	2
Conduction defect	15	1
Arthritic	252	24

[a]Denominator totals range from 367 to 378 for constitutional symptoms and from 1,070 to 1,111 for other symptoms and signs because of persons with unknown symptom history. Constitutional symptom information was gathered only in 1984.

dammini and human *B. burgdorferi* infections had extended northward in the Connecticut River Valley and into northeastern Connecticut [25,26]. By 1985, Lyme disease was endemic in nearly all towns in southeastern Connecticut; four of these towns were located >25 kilometers from the shoreline and had incidences >300 per 100,000 population.

Our surveillance data also suggest that the incidence of Lyme disease is increasing in Connecticut. From 1984 to 1985, the incidence increased by 24 percent. This increase was probably a conservative estimate, because surveillance was stimulated by physician notification only in 1984. Physicians may have also realized by 1985 that the serologic test had low sensitivity during the early stages of Lyme disease and may have ordered the test less frequently. The percentage of case-persons with erythema migrans

TABLE 2
Lyme Disease Clinical Characteristics by Age of Patient
Connecticut, 1984–1985

Characteristic	Age <20 Years Reported/Total (%)	Age ≥20 Years Reported/Total (%)	RR[a]	95% C.I.
Neurologic	27/319 (8)	51/744 (7)	1.2	0.8–2.0
Cardiac	3/210 (1)	17/566 (3)	0.5	0.1–1.7
Arthritic	113/326 (35)	129/701 (18)	1.9	1.5–2.3

[a]Relative risk (RR): risk of characteristic for persons aged <20 years compared to those aged ≥20 years

TABLE 3
Detection of Total Immunoglobulin to *B. burgdorferi* in Initial Serum Samples, by Time After the Onset of Erythema Migrans
Connecticut, 1984–1985

Time After Onset of Erythema Migrans[a]	IFA *n*/Total (%)	ELISA *n*/Total (%)
<21 days	59/236 (25)	72/317 (23)
≥21 days	31/67 (46)	20/63 (32)
Total	90/303 (30)	92/380 (24)

[a]The time after symptom onset was unknown for 192 persons, and 36 persons had no serology obtained.

did not change over both reporting years, suggesting that reporting patterns did not change overall. Nevertheless, the observed annual rate of increase is consistent with the 129 percent to 453 percent increases in incidence observed from 1977 to 1985 in southeastern Connecticut. It is doubtful that the magnitude of this increase could be accounted for by different surveillance methodologies or case definitions. In fact, the 1977 study may have had greater case ascertainment because physicians were telephoned to report cases [17]. Anecdotal reports received by us from physicians with long-standing practices in Lyme and surrounding communities also suggest that Lyme disease markedly increased in incidence from 1977 to 1985.

Although the observed Lyme disease incidence was considerable in some towns, our surveillance system probably underestimated the actual incidence for several reasons: *(1)* the system was laboratory-based, so that many persons with erythema migrans, a unique clinical marker of Lyme disease, may not have had serologic testing; *(2)* persons with stage one disease who had atypical skin rashes or nonspecific symptoms would not have been defined as cases, regardless of the serologic test results; *(3)* the diagnosis of Lyme disease may not have been considered for those with atypical presentations; and *(4)* sera from some Connecticut residents may have been tested at Yale University. Although the actual number tested at Yale was unknown, a record review of all patients tested there from July to December 1984 found only seven additional Connecticut residents who would have met the case definition for this study.

Our data also indicate that there is age-specific variation in Lyme disease incidence and clinical response to *Borrelia burgdorferi* infection. Children five to 14 years of age had the highest Lyme disease incidence. It is unknown if they had the greatest exposure to ticks, were more likely to develop symptoms after infection, or were simply more likely to be reported. A previous serologic study of a defined island population suggested that adults were less likely to develop symptoms after infection than children [27]. We also found that persons with Lyme disease who were <20 years of age were more likely to have arthritis as the first manifestation of Lyme disease than were persons ≥20 years of age. This finding is supported by the longitudinal study of an island population that also found that children were more likely to present with arthritis alone [27].

Serologic tests for Lyme disease have generally been reported to have low or moderate sensitivity during stage-one Lyme disease [12–14,28]. In a preliminary study of 139 patients with erythema migrans, ELISA and IFA tests had comparable sensitivities, regardless of whether class-specific IgM or polyvalent conjugates were

used [20]. In our study, the ELISA with a polyvalent conjugate had an overall sensitivity of only 24 percent. This low value could be due to delayed immune response or to previous antibiotic treatment [28]. In view of the low sensitivities of serologic tests during early Lyme disease, it is particularly important for physicians to re-evaluate clinical data when antibodies are not detected. If necessary, a second or third serum sample should be obtained to monitor a rise in antibody levels. Serologic testing, however, remains a valuable diagnostic tool for patients with secondary or tertiary stages of Lyme disease [13].

ACKNOWLEDGEMENT

The authors thank Carmelle Kennedy for technical assistance with data management; Clifford Snow III, Pat Trzcinski, and Deborah Shea for assistance in performing serologic tests; and Matt Cartter for his editorial suggestions.

REFERENCES

1. Ciesielski CA, Hightower AW, Horsley R, Russell H, Markowitz LE, Broome CV: The epidemiology of Lyme disease in the United States. In Abstracts, International Conference on Lyme Disease and Related Disorders. New York, New York Academy of Sciences, 1987
2. Schmid GP: The global distribution of Lyme disease. Rev Infec Dis 7:41–50, 1985
3. Burgdorfer W, Barbour AG, Hayes SF, Peter O, Aeschlimann A: Lyme disease—a tick-borne spirochetosis? Science 216:1317–1319, 1982
4. Johnson RC, Schmid FW, Hyde FW, Steigerwalt AG: *Borrelia burgdorferi* sp. nov.: Etiologic agent of Lyme disease. Int J Syst Bacteriol 34:496–497, 1984
5. Steere AC, Bartenhagen NH, Craft JE, Hutchinson GJ, Newman JH, Rahn DW, Sigal LH, Spieler PN, Stenn KS, Malawista SE: The early clinical manifestations of Lyme disease. Ann Int Med 99:76–82, 1983
6. Steere AC, Malawista SE, Bartenhagen NH, Spieler PN, Newman JH, Rahn DW, Hutchinson GJ, Green J, Snydman DR, Taylor E: The clinical spectrum and treatment of Lyme disease. Yale J Biol Med 57:453–461, 1984
7. Pachner AR, Steere AC: Neurological findings of Lyme disease. Yale J Biol Med 57:481–483, 1984
8. Pachner AR, Steere AC: The triad of neurologic manifestations of Lyme disease: Meningitis, cranial neuritis, and radiculoneuritis. Neurology 35:47–53, 1985
9. Reik L, Burgdorfer W, Donaldson JO: Neurologic abnormalities in Lyme disease without erythema chronicum migrans. Am J Med 81:73–78, 1986
10. Steere AC, Batsford WP, Weinberg M: Lyme carditis: Cardiac abnormalities of Lyme disease. Ann Int Med 93:8–16, 1980
11. Marcus LC, Steere AC, Duray PH, Anderson AE, Mahoney EB: Fatal pancarditis in a patient with coexistent Lyme disease and babesiosis. Ann Int Med 103:374–376, 1985
12. Russell H, Sampson JS, Schmid GP, Wilkinson HW, Plikaytis B: Enzyme-linked immunosorbent assay and indirect immunofluorescence assay for Lyme disease. J Infect Dis 149:465–470, 1984
13. Craft JE, Grodzicki RL, Steere AC: Antibody response in Lyme disease: Evaluation of diagnostic tests. J Infect Dis 149:789–795, 1984
14. Wilkinson HW: Immunodiagnostic tests for Lyme disease. Yale J Biol Med 57:567–572, 1984
15. Magnarelli LA, Anderson JF, Johnson RC: Cross-reactivity in serologic tests for Lyme disease and other spirochetal infections. J Infect Dis 156:183–188, 1987
16. Rhodes VJ: An epidemiologic study of morbidity in Lyme disease (Dissertation). Storrs, CT, University of Connecticut, 1988, 58 pp
17. Steere AC, Broderick TF, Malawista SE: Erythema chronicum migrans and Lyme arthritis; epidemiologic evidence for a tick vector. Am J Epidemiol 108:312–321, 1978
18. Magnarelli LA, Meegan JM, Anderson JF, Chappell WA: Comparison of an indirect fluorescent-antibody test with an enzyme-linked immunosorbent assay for serological studies of Lyme disease. J Clin Microbiol 20:181–184, 1984
19. Anderson JF, Magnarelli LA, Burgdorfer W, Barbour AG: Spirochetes in *Ixodes dammini* and mammals from Connecticut. Am J Trop Med Hyg 32:818–824, 1983

20. Magnarelli LA, Anderson JF: Early detection and persistence of antibodies to *Borrelia burgdorferi* in persons with Lyme disease. Zbl Bakt Hyg 263:392–399, 1988
21. SAS Institute Inc: SAS User's Guide: Statistics, version 5 edition. Cary, NC, SAS Institute Inc, 1985
22. State of Connecticut Department of Health Services: Annual Registration Report of Vital Statistics, 1984. Hartford, CT, State of Connecticut Department of Health Services, 1985
23. Kaslow RA, Samples CL, Simon DG, Lewis JN: Occurrence of erythema chronicum migrans and Lyme disease among children in two noncontiguous Connecticut counties. Arthritis Rheum 24:1512–1516, 1981
24. Wallis RC, Brown SE, Kloter KO: Erythema chronicum migrans and Lyme arthritis: Field study of ticks. Am J Epidemiol 108:322–327, 1978
25. Magnarelli LA, Anderson JF, Shaw E, et al: Borreliosis in equids in northeastern United States. Am J Vet Res 49:359–362, 1988
26. Magnarelli LA, Anderson JF, Chappell WA: Geographic distribution of humans, racoons, and white-footed mice with antibodies to Lyme disease spirochetes in Connecticut. Yale J Biol Med 57:619–626, 1984
27. Steere AC, Taylor E, Wilson ML, Levine JF, Spielman A: Longitudinal assessment of the clinical and epidemiological features of Lyme disease in a defined population. J Infect Dis 154:295–300, 1986
28. Shrestha M, Grodzicki RL, Steere AC: Diagnosing early Lyme disease. Am J Med 78:235–240, 1985