

Epidemiologic Features of Lyme Disease in New York

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During 1982, surveillance identified 207 cases of Lyme disease in New York State. Cases were clustered in two geographic areas, eastern Long Island and northern Westchester counties. Symptoms and signs of Lyme disease in cases were consistent with previous reports, with erythema chronicum migrans (ECM) being the most frequently (77 percent) reported sign of disease. Facial palsy was reported in a surprisingly high 18 percent of cases. Of 160 cases whose sera were submitted for Lyme spirochete specific IgG antibody testing, 112 (70 percent) had titers ≥ 64 , while 88 (55 percent) had titers ≥ 128 . Positive titers were not associated with any single sign or symptom of disease, but were significantly associated with symptom onset or tick bite occurring during the three-month period of June, July, and August. We conclude that the incidence of Lyme disease in New York is much higher than previously recognized. In addition, our data suggest that a serologic test for Lyme-spirochete IgG antibody lacks sensitivity, but can be useful in confirming the diagnosis of Lyme disease when antibody titers are high.

Since Lyme disease (LD) was initially recognized in southern Connecticut in 1975 [1], its geographic distribution has expanded to include much of the northeastern seaboard and at least 15 states [2]. A spirochete present in *Ixodes dammini* ticks is now known to be the etiologic agent of the disease [3,4]. During 1980 and 1981 the New York State Department of Health received numerous reports of cases of LD from physicians and county health departments. In 1982, we initiated heightened passive surveillance to better define the distribution and epidemiologic features of LD in New York, and to assess serologic response to the Lyme spirochete in persons with the disease. We report here data on cases of Lyme disease occurring in 1982.

MATERIALS AND METHODS

Case Ascertainment and Reporting

Reporting of LD cases was encouraged by several mechanisms. First, practitioners were urged to report cases by articles on LD in the Health Department's Communicable Disease Newsletter, a monthly public health advisory sent statewide to all

practicing physicians. Second, individual letters were sent to more than 300 primary care physicians in areas where previous case reports originated. Finally, serologic testing for antibodies to the Lyme spirochete was offered free of charge to any practitioner submitting sera from patients with suspected LD.

Information on reported cases was collected on a form which elicited demographic information, tick exposure histories, and symptoms associated with the disease.

For the purposes of this study, we defined a case as any person reported by a physician to have Lyme disease with symptoms beginning in 1982 and who had at least one of the following disease manifestations: erythema chronicum migrans (ECM), aseptic meningitis (fever, headache, and stiff neck), facial nerve palsy, and/or large joint arthritis.

Serologic Assay

Stock cultures of the *I. dammini* spirochete maintained in modified Kelly's medium [5] were fixed to the wells of microtiter slides in a method previously described [4]. Sera from persons with suspected LD were tested in pairs when two or more specimens were obtained, or singly when one specimen was available. Both positive and negative control specimens were tested simultaneously. Indirect immunofluorescence was performed using fluorescein isothiocyanate-(FITC) labeled goat anti-human IgG serum (Cappel Laboratories, Cochranville, PA). Sera reactive at $\geq 1:16$ were titered to endpoint dilution.

Control Sera

As control sera, we utilized specimens obtained for premarital syphilis screening from 329 persons who lived in two upstate counties, located more than 200 miles from any area known to be endemic for LD. All specimens were submitted to the New York State Department of Health Laboratories between July and September 1982. None were reactive when tested by automated reagin test (ART). Clinical histories of LD or other illnesses on these patients were not known.

Analysis of Data

Data from case report forms and serologic results were computerized. Data from seropositive and seronegative persons were compared, using Pearson's chi-square contingency test. This comparison was conducted twice. Seropositives were first defined as persons with convalescent sera collected more than two weeks after first symptoms of LD with titers ≥ 64 . These cases were compared with seronegative persons having convalescent titers < 64 . Seropositives were defined in the second comparison as persons with titers ≥ 256 , who were again compared to seronegative persons with titers < 64 .

Persons with paired sera who demonstrated a fourfold rise in IgG antibody titer were also compared to persons with paired sera demonstrating no fourfold rise and no single titer ≥ 64 . In this comparison, the acute serum specimen was required to be collected within two weeks of symptom onset.

Each case was given a clinical index score ranging from 0-25, based upon their reported symptoms. Index scores were derived from the presence of the following symptoms: ECM (10 points), fever (2), aseptic meningitis (3), large joint arthritis (5), facial palsy (3), and palpitations (2). Index scores were compared for seropositive and seronegative cases.

RESULTS

During 1982, 207 cases of LD meeting the case definition were reported. Cases ranged in age from one to 79 years, with a mean age of 28 years. Forty-eight percent were men, and 52 percent were women. Cases were reported from 11 upstate counties and New York City, but 84 percent were residents of either Suffolk (56 percent) or Westchester (28 percent) counties (Fig. 1). Of 152 cases with tick bite information recorded, 130 (86 percent) reported a tick bite prior to illness. Of these, 102 (79 percent) occurred in Suffolk county, 25 (19 percent) in Westchester county, and 3 (2 percent) in other counties close to Suffolk or Westchester. Tick bites and ECM were reported to occur in every month except March, but 90 (71 percent) of 126 bites and 115 (75 percent) of 154 persons with ECM reported bite or ECM onset in the three-month period of June, July, and August (Fig. 2). In the 156 cases who had at least one serum specimen collected and who reported a precise date of onset, symptoms began in every month except February and March. Again, however, 101 (65 percent) had symptoms beginning in June, July, or August (Fig. 2).

Forty-six (23 percent) of 201 cases reported hospitalization as a result of LD. Length of stay ranged from 1-21 days, with a mean of 7.5 days. Antibiotic treatment was reported to have been given to 169 (82 percent) of 205 cases. Most frequently administered antibiotic therapy was penicillin (72.5 percent), followed by tetracycline (14.4 percent) and erythromycin (2.4 percent). Other antibiotics or antibiotic combinations accounted for the remaining 10.7 percent.

Symptoms and signs seen most commonly in cases included: ECM (77 percent), myalgias (72 percent), fever (65 percent), and headache (61 percent) (Table 1). Although joint pain was noted in 62 percent of cases, demonstrable joint swelling was reported in only 31 percent. The knee was affected more than twice as frequently

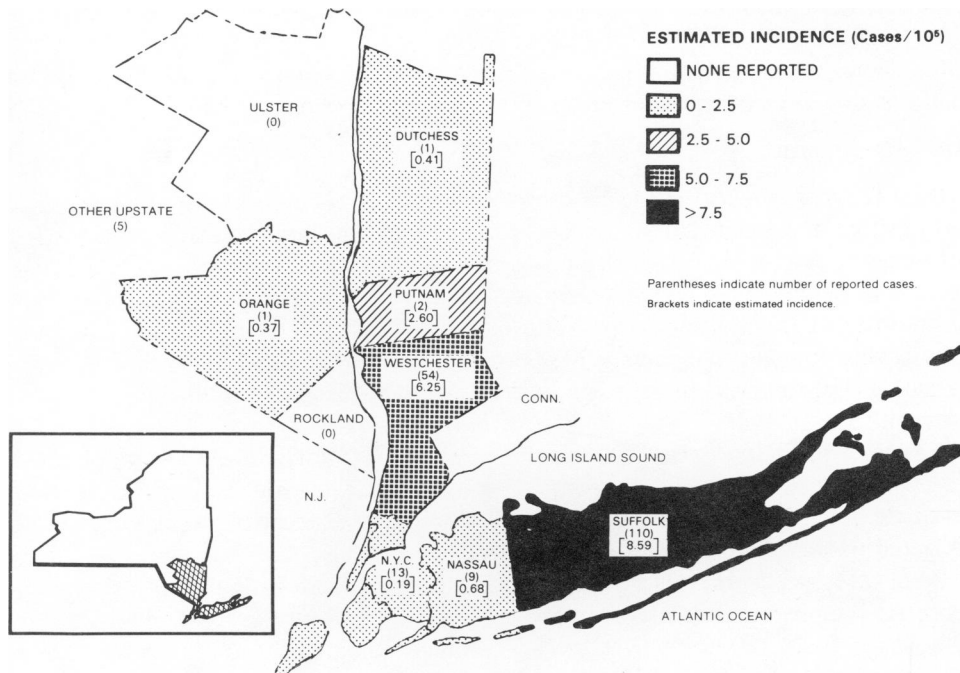


FIG. 1. Lyme disease in New York—1982: Cases by county of residence.

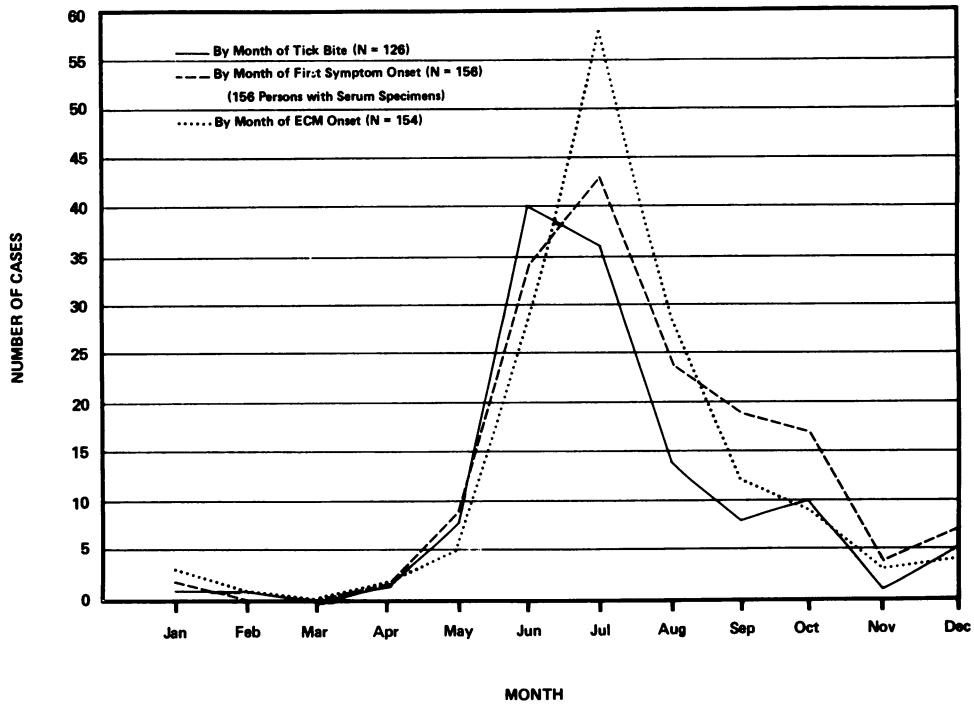


FIG. 2. 1982 Lyme disease cases.

TABLE 1
Lyme Disease in New York—1982:
Frequency of Symptoms/Signs of Lyme Disease

Symptom/Sign	Number Reporting/Total	%
ECM	155/201	77
Malaise	150/198	76
Myalgias	143/198	72
Fever	129/198	65
Headache	120/197	61
Stiff neck	82/191	43
Nausea	36/198	18
Facial palsy	34/191	18
Palpitations	20/183	11
Temporomandibular joint pain	16/201	8
Large joint pain	124/201	62
Knee	101/201	50
Elbow	43/201	21
Hip	40/201	20
Ankle	33/201	16
Shoulder	32/201	16
Wrist	30/201	15
Large joint swelling	63/201	31
Knee	46/201	23
Elbow	14/201	7
Hip	7/201	4
Ankle	12/201	6
Shoulder	11/201	5
Wrist	11/201	5

as any other joint. Less commonly reported symptoms included facial palsy (18 percent) and palpitations (11 percent).

Of 160 cases who had at least one serum specimen collected more than two weeks after onset of symptoms, 112 (70 percent) had anti-spirochete IgG antibody titers of $\geq 1:64$, 88 (55 percent) had titers $\geq 1:128$, and 57 (36 percent) $\geq 1:256$. Of the 329 control serum specimens, 11 (3.3 percent) had anti-spirochete titers of $\geq 1:64$. Of these, ten were reactive at 1:64 and one at 1:128. No control specimens were positive at a dilution of 1:256. Of the 46 persons with paired sera and first specimen collected within two weeks of symptom onset, 35 (76 percent) had fourfold rises in antibody titer.

No single symptom of LD was significantly associated with positive IgG titers, either at a level of $\geq 1:64$ or at $\geq 1:256$ (Table 2). In addition, reported cases with high clinical index scores (many symptoms or signs suggestive of LD) were no more likely than persons with lower scores to have had positive titers, either at $\geq 1:64$, or $\geq 1:256$. Similarly, cases with positive titers were no more likely to have reported

TABLE 2
Lyme Disease in New York—1982: Features of Lyme Disease vs. Anti-Spirochete IgG Titers

Disease Feature (Number Reporting)		No. of Cases with Titers			<i>p</i> ^a
		< 64	≥ 64	≥ 256	
ECM (155)	Present	33	80	43	NS
	Absent	14	28	13	
Large joint pain (160)	Present	33	65	34	NS
	Absent	15	47	23	
Large joint swelling (160)	Present	12	39	22	NS
	Absent	36	73	35	
Knee pain (160)	Present	29	50	26	NS
	Absent	19	62	51	
Knee swelling (160)	Present	10	27	17	NS
	Absent	38	85	40	
Facial palsy (155)	Present	7	25	15	NS
	Absent	40	83	39	
Palpitations (148)	Present	7	10	8	NS
	Absent	35	96	47	
Antibiotic therapy (158)	Yes	35	91	48	NS
	No	12	20	7	
Hospitalization (159)	Yes	12	27	12	NS
	No	36	84	45	
Tick bite (116)	Yes	32	60	26	NS
	No	5	19	10	
Month of bite (102)	Jun, Jul, Aug	18	54	45	$\geq 64: X^2 = 6.43;$ $p < 0.02$ $\geq 256: X^2 = 7.12;$ $p < 0.01$
	Other	16	14	10	
Month of symptom onset (139)	Jun, Jul, Aug	17	76	62	$\geq 64: X^2 = 21.4;$ $p < 0.0001$ $\geq 256: X^2 = 24.7;$ $p < 0.0001$
	Other	27	19	11	

^aCases with titers ≥ 64 and ≥ 256 are compared to those with titers < 64 .

tick bites, to have been hospitalized, or to have received antibiotics. Time delay between first symptoms of LD and start of antibiotic therapy was also not found to be associated with positive titers or with development of joint pain or swelling. Thirty-four persons whose sera demonstrated a fourfold titer rise were no more likely than 11 non-converters to have had any single symptom or sign of Lyme disease, to have had higher clinical index scores, to have been treated with antibiotics or hospitalized, or to have reported a tick bite.

Cases with positive titers more frequently reported tick bites in June, July, or August than persons with negative titers ($X^2 = 6.43$; $p < 0.02$, for cases with titers $\geq 1:64$; $X^2 = 7.12$, $p < 0.01$ for $\geq 1:256$.) Cases with positive titers also more frequently reported symptom onset in these three months ($X^2 = 21.4$; $p < 0.0001$, for cases with titers $\geq 1:64$, $X^2 = 24.7$; $p < 0.0001$, for $\geq 1:256$).

DISCUSSION

Our findings lend further support to the accumulating evidence that LD is considerably more common than previously recognized. During 1980, when organized nationwide surveillance for LD was first initiated by the Centers for Disease Control (CDC), 226 cases from 13 states were reported, 11 of which were from New York [6]. In 1982, CDC received 487 Lyme disease case reports, with 179 from New York [7]. The increase in New York state cases can be attributed to three factors. First, case reports were more intensively solicited from physicians and county health departments. Second, serologic testing for Lyme spirochete antibodies was offered as a free service to practitioners, which served as an adjunct to case ascertainment. Finally, LD is probably being better recognized and diagnosed by physicians in endemic areas.

It is unclear if the rise in reported cases of LD represents any real increase in incidence or expansion of the endemic distribution of the *Ixodes* tick vector. However, nearly all cases reported tick bites in areas previously known to be endemic, suggesting that most of the 1982 cases resulted from better recognition of the disease.

Wherever it occurs, LD appears to be highly focal in its distribution. New York cases occurring in 1982 also followed this pattern, being clustered in two areas: the south shore and eastern forks of Long Island, and parts of northern Westchester County. Both areas share several features which contribute to the substantial incidence of LD: they have plentiful deer populations, they are endemic areas for *Ixodes dammini* ticks, and they have sufficient population densities to allow humans to serve as alternate tick hosts with some frequency. While other areas of New York have greater deer population density, *I. dammini* does not occur in areas farther north and west, accounting for the absence of cases reported from these areas.

The case definition we employed in this surveillance study was not as rigid as that required by the CDC and utilized in previous case series. Specifically, ECM was not required for inclusion in our case count. We purposely employed a less stringent case definition for two reasons. First, some cases of LD may occur without ECM, or where this sign is not recognized. We sought to quantitate the proportion of cases which were suspected by physicians on clinical grounds to be LD, who had signs or symptoms associated with the disease, but did not have ECM. Second, we wished to assess whether or not any particular sign or symptom in persons suspected of having LD, including ECM, was significantly associated with a serologic response. While some cases may have been included in our case count who did not have LD, we feel the number of non-cases is probably small. If we used a stricter case definition

demanding ECM, a fourfold rise in IgG titer, or a single IgG titer of ≥ 128 , 179 (86 percent) of the 207 cases would continue to be included.

Most symptoms or signs of LD were reported with frequencies consistent with that noted in previous reports [8,9]. However, myalgias (72 percent) and facial palsy (18 percent) occurred more frequently in our cases. The higher proportion of persons with facial palsy is in part due to inclusion of persons with palsy but without recognized ECM. Nonetheless, 21 (13.5 percent) of 155 persons with ECM reported palsy, a figure still substantially higher than previous reports [8,10]. Thirty (88 percent) of 34 persons with palsy had either ECM, a fourfold titer rise, or a single titer ≥ 128 , suggesting that 17 percent of our cases demonstrated this sign even when a stricter case definition is used.

Large joint swelling developed in 31 percent of patients, which is consistent with the 35–43 percent of patients treated with antibiotics who developed arthritis in previous reports [10,11]. Overall, more than 80 percent of our cases received antibiotic therapy.

The lack of association between IgG anti-spirochete titers and the individual symptoms or signs of LD suggests that each, considered separately, may be an unreliable predictor of Lyme spirochete infection. The absence of association between positive titers and ECM, the clinical sign used previously to define cases of LD, further suggests the serologic IgG assay may not be adequately sensitive to detect a high proportion of cases. This possibility was first noted by Steere et al. [3], who found only 22 (55 percent) of 40 persons with ECM as the only symptom of LD developed fourfold IgG titer rises.

Because no single symptom of LD was associated with positive titers, it is not surprising that high clinical index scores were also not associated with positive titers. A potential confounding variable, the presence or absence of antibiotic therapy, did not correlate with positive titers, nor did the length of time between start of symptoms and initiation of antibiotic therapy. These data should be viewed with caution, however, as cases were reported by more than 50 physicians. No attempt was made to verify clinical diagnoses, as surveillance was the primary purpose of the study. The usefulness of a clinical index score in predicting positive titers can perhaps best be determined in clinical trials, where diagnosis is uniform and verifiable, and where confounding variables such as type and timing of antibiotic therapy can be strictly controlled.

Although the serologic test for Lyme-spirochete IgG antibody is not sensitive, our data support previous evidence [3] that an IgG titer of ≥ 128 is a specific marker of Lyme spirochete exposure. Only one (0.3 percent) of 329 control sera had positive titers at this level, compared to 88 (55 percent) of 160 reported cases.

The significant association between persons with reactive sera and tick bite and/or symptoms beginning in June, July, and August may imply that cases reported during these months are more likely to have LD. Previous reports have established that nymphal *Ixodes dammini* are the tick stage most frequently found during these three months [12], and that this stage is commonly infected with the Lyme spirochete [13]. Data from our study may indicate that nymphal *Ixodes* ticks are the most important stage involved in human transmission of LD, as tick bite history without respect to month was not associated with positive titers.

We conclude that the incidence of LD in certain areas of New York is much higher than previously appreciated. Although LD remains a clinical diagnosis, our data suggest that high titers of Lyme spirochete-specific IgG antibody in patients with

symptoms of LD can be helpful in confirming the diagnosis. However, a laboratory test sufficiently sensitive to diagnose all cases of LD must await future refinements or developments.

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