Lyme Disease in Minnesota: 
Epidemiologic and Serologic Findings 

MICHAEL T. OSTERHOLM, Ph.D., M.P.H., JAN C. FORFANG, M.P.H., 
KAREN E. WHITE, M.P.H., AND JOEL N. KURITSKY, M.D. 

Acute Disease Epidemiology Section, Minnesota Department of Health, 
Minneapolis, Minnesota 

Received December 8, 1983

During the four years, 1980 to 1983, 83 Minnesota residents have been diagnosed with Lyme disease. Sixty-five of the patients were male. The median age of patients was 39 years with a range from one to 77 years. Seventy-five (90 percent) had onset in 1982 and 1983. Of these latter cases, 56 (75 percent) recalled a tick bite three to 27 days prior to the development of erythema chronicum migrans. Patients experienced possible exposure to Ixodes dammini in at least 24 (28 percent) of the 87 Minnesota counties; however, over 50 percent had reported exposure in one of eight east-central counties near or immediately west of the Wisconsin border. Serologic studies for antibody against the Ixodes dammini spirochete were completed on 30 patients with onset in 1982 and 1983. Of 28 patients with paired acute and convalescent serum samples, only two (7 percent) had fourfold rises in antibody titers. Lyme disease is an emerging public health problem in Minnesota. Additional studies are needed to define the risk of disease by geographic area within the state. Physicians statewide should be alert to the possibility of Lyme disease among their patients, since only 39 percent of patients with onset in 1982 and 1983 were exposed in their county of residence.

Our understanding of the natural history of Lyme disease has progressed significantly since its first recognition in 1975 and the first reports in the medical literature by Steere et al. in 1977 [1,2]. Lyme disease, with typical onset during the summer months, begins most often with the unique skin lesion, erythema chronicum migrans (ECM). It may be accompanied by headache, stiff neck, fever, myalgias, arthralgias, malaise, fatigue, or lymphadenopathy [1,3]. Latter manifestations of the disease may include arthritis, neuropathies, myocarditis or atrioventricular-node block, migratory musculoskeletal pain, and meningoencephalitis [2,4–6].

Subsequent studies have shown that penicillin or tetracycline given early in the illness have shortened the duration of ECM and attenuated or completely prevented arthritis; that a spirochete transmitted by the newly identified tick Ixodes dammini, or by related ixodid ticks, is the agent responsible for Lyme disease; and that by indirect immunofluorescence assay (IFA), human serologic responses to the spirochete can be documented [3,7–11].

Patients with Lyme disease report confirmed or possible tick exposures in at least 14 states, Europe, and Australia [4,11–16]. Despite increasing interest in this newly described disease, there is only limited data on incidence of it throughout the world and, in particular, in many areas of the United States. We report here on the epidemiologic and serologic findings of our studies of Lyme disease in Minnesota.
Our surveillance effort for Lyme disease has primarily been an epidemiologically defined passive system. That is, the Minnesota Department of Health (MDH) personnel did not routinely survey physicians in the state for case assessment. Since 1980, as part of our passive surveillance system, we have published an article regarding Lyme disease each spring in the MDH Disease Control Newsletter, a publication received by more than 6,000 state health professionals. Physicians and other health professionals were encouraged in these articles to report cases of Lyme disease to local health agencies or the Acute Disease Epidemiology Section of the MDH. In April 1982, we collaborated with three local physicians in the publication of an article on Lyme disease in the state medical journal [12]. In the spring of 1983 we also publicized, to the medical community, the availability through MDH of serologic testing for patients with possible Lyme disease.

A patient was considered to have Lyme disease if there was presence of ECM and a physician's diagnosis of Lyme disease; or if the patient did not experience ECM but had systemic illness characteristic of Lyme disease and an indirect immunofluorescence assay titer for *Ixodes dammini* spirochete greater than or equal to 1:256. Information regarding travel to a known endemic area for Lyme disease or a history of tick bite was not required to fulfill the case criteria.

Reports of possible Lyme cases taken by telephone were noted on a standard Lyme disease surveillance form; it included information on patient demographic data, history of exposure to ticks and tick bites, recent travel history, detailed clinical and laboratory findings, and antibiotic treatment history. Following initial reports, review of the available clinical and laboratory data was conducted. Interviews of patients were conducted by the local health agency, MDH epidemiologists, or the patient's physician. All clinical data were confirmed with the patient's physician. Antibody titers against the *Ixodes dammini* spirochete were determined by indirect immunofluorescence assay at the Centers for Disease Control (CDC) [17].

RESULTS

During the four years, 1980 to 1983, 83 Minnesota residents have been diagnosed with Lyme disease (see Fig. 1). Seventy-five (90 percent) had onset in 1982 and 1983. Our results will specifically address these 75 patients. They had onset of illness between the months of March and October, with 69 percent of the onsets in June or July (Fig. 2). Fifty-six patients (75 percent) recalled a tick bite three to 27 days prior to the development of ECM. In particular, two cases, one with onset in late March and the other with onset in mid-April, remember bites by a small and unusual "wood tick" prior to illness. The description provided by the patients of the two biting ticks supports the conclusion that they were *Ixodes dammini*.

Fifty-six (75 percent) of the patients were exposed within the state of Minnesota (i.e., no travel history outside the state). Thirteen (17 percent) residents had exposure in Wisconsin, one (1 percent) in Michigan, one (1 percent) in Georgia, and four (5 percent) with probable exposure locations unknown (i.e., travel history outside of the state but no documented tick bite). Of the patients with exposure in the state, 27 patients (37 percent of all 1982 and 1983 patients) had exposure within the state but in a different county from their home residence and 29 (39 percent of all 1982 and 1983 patients) had exposure in the same county as their home residence.

Forty-nine (65 percent) of the 75 patients were male. The median age of patients was 39 years, with a range from one to 77 years. The ages of the patients appear to reflect the approximate age of Minnesota residents (Table 1).
Patients had tick bite exposures in at least 24 (28 percent) of the 87 Minnesota counties (Fig. 3). In particular, over 50 percent of the cases reported exposure in one of eight east-central counties, near or immediately west of the Wisconsin border. However, some patients recorded exposure in counties as far as 150 miles from this eight-county area.
Serologic studies were completed on 30 patients, eight with onset in 1982 and 22 with onset in 1983. Twenty patients (66 percent) had ECM only, eight patients (27 percent) had ECM and systemic illness (i.e., fever, arthralgias, myalgias), and two patients (7 percent) had ECM with eventual cardiac or neuralgic complications. Twenty-eight patients provided acute (1 to 14 days after onset of ECM) and con-
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TABLE 2
Relationship Between Interval from Onset of Erythema Chronicum Migrans to Appropriate Antibiotic Therapy* and Indirect Immunofluorescence Antibody (IFA) Titer for *Ixodes dammini* Spirochete among Patients with Lyme Disease, Minnesota, 1982 and 1983

| IFA Titer | ≤ 10 Days Number (%) | > 10 Days or None Number (%) |
|-----------|----------------------|------------------------------|
| ≥ 1:256   | 2 (20)               | 8 (42)                       |
| <1:256    | 8 (80)               | 11 (58)                      |
| Total     | 10 (100)             | 19 (100)                     |

*Appropriate antibiotic therapy included use of penicillin and tetracycline as outlined by Steere et al. [8].

*p = 0.18 (titer for ≤ 10 days vs. titer for > 10 days).

valescent (30 to 60 days after onset of ECM) serum samples. One patient had a single serum obtained 42 days after onset and a second patient had a single serum obtained four days after onset. Of the 28 patients with paired samples, only two (7 percent) had fourfold rises in antibody titers. Of the 29 patients with at least one serum sample obtained between 30 and 60 days after onset, 17 (59 percent) had an antibody titer ≥ 1:128 and only 10 (34 percent) had an antibody titer ≥ 1:256. Twenty-eight of these 29 patients (97 percent) had ECM.

Two (20 percent) of 10 patients who received appropriate antibiotic therapy for Lyme disease within ten days after onset of ECM had a convalescent titer ≥ 1:256, while eight (42 percent) of 19 patients who did not receive appropriate therapy within ten days had a convalescent titer ≥ 1:256 (*p* = 0.18) (Table 2).

DISCUSSION

Lyme disease is emerging as a new public health problem in Minnesota, as it is elsewhere in the country. We have documented a ninefold increase in reported cases for 1982 and 1983 when compared to the two previous years. This raises an important question of whether this increase reflects a rapidly growing number of cases or is the result of an increased awareness and reporting of the disease by the Minnesota medical community. Our surveillance efforts to date for Lyme disease would be classified as passive, although there was an effort in 1982 and 1983 to heighten physician awareness of the disease and to report cases to the MDH. The impact of different intensities and types of surveillance efforts on disease reporting has been shown [18–23]. In particular, there can be a significant increase in case reports for a disease that suddenly gains national importance and whose natural history is initially unclear [22,23]. However, it is possible that there has been a significant increase in the number or range of the *Ixodes* tick in Minnesota. It is also possible to speculate that the *Ixodes dammini* spirochete has only recently become prevalent among the *Ixodes* ticks in the state. Last, a less likely possibility, is that Minnesota residents are now participating in more outdoor activities and therefore coming into contact with the ticks more often than in the past.

Although a marked increase in the incidence of Lyme disease may have recently occurred, without a regional or possibly even a statewide extensive retrospective
medical chart review for patient diagnoses suggestive of Lyme disease, we will not be able to comment further on the reason(s) for this increase. Regardless of reason(s), Lyme disease is now an important public health problem in the state.

Of particular importance is the finding that only 75 percent of our patients had their tick exposures in Minnesota and that only 37 percent had their exposures in the same county as their home residence. This has important implications with respect to the timely and accurate diagnosis of Lyme disease patients and the need to determine the location of a tick exposure rather than the location of a patient’s residence for the purposes of epidemiologic study. With at least 14 states now reporting cases of Lyme disease, it is possible to be bitten by an *Ixodes* tick while traveling and subsequently develop illness days and miles from the geographic location of the exposure. If physicians in the non-endemic areas do not obtain sufficient travel histories from these patients or are not familiar with the clinical presentation of the disease, it is unlikely that appropriate antibiotic therapy will be administered in a timely manner. It is important that federal, state, and local public health agencies make an effort to define those regions of the country with endemic Lyme disease and those regions where a person could possibly be exposed to an infected *Ixodes* tick. This information should be made known to practitioners nationwide.

One finding of our surveillance effort that differs from the experience by Steere et al. is the gender and age distribution of patients. While 49 (65 percent) of 75 Minnesota patients are male, only 164 (52 percent) of 314 patients seen at Yale are male (risk ratio = 1.7, *p = 0.04*) [3]. Also, the median age of Minnesota patients is 39 years, while those seen at Yale is 28 years. One possible explanation for this apparent difference is the difference in the completeness of case reporting in Minnesota compared to the studies in the New England states.

The CDC has suggested that a titer of 1:256 or greater to the *Ixodes dammini* spirochete in a patient with ongoing systemic illness is supportive of the diagnosis of Lyme disease. They also indicate that similar serologic findings may not be helpful in patients with only ECM. In our studies, of the 29 patients with uncomplicated Lyme disease who had a serum sample obtained between 30 and 60 days after onset of ECM, only 10 (34 percent) had an antibody titer ≥1:256. Also, of the 28 patients with paired serum samples, only two (7 percent) had fourfold rises in antibody titers. While there was some suggestion in our study that receiving appropriate antibiotic therapy for Lyme disease within ten days after onset of ECM would abort an antibody response, only 42 percent of patients with more than ten days from onset of ECM to therapy or no inappropriate therapy, had a titer ≥1:256.

For the patient without recognizable ECM and not living in, or exposed to, a known endemic area, the diagnosis of Lyme disease may be difficult. In particular, a history of tick bite, or the lack of it, may be misleading because patients with Lyme disease do not always remember a tick bite, and such bites are common in endemic areas. A sensitive, specific, and standardized serologic test to assist in the diagnosis of Lyme disease is clearly needed. Perhaps a single serum tested for the presence of a specific IgM antibody against the *Ixodes dammini* spirochete will provide such a test. Steere and colleagues found that, among 40 patients who had only ECM, 90 percent had IgM specific antibody between the ECM phase and convalescence [10].

Until a sensitive and specific serologic assay is available, Lyme disease epidemiologic surveillance and studies in areas with sporadic cases, or on the border of endemic areas, will be difficult. Such studies are necessary to define the incidence of Lyme disease and, more specifically, to assist the physician in regions of the coun-
try not yet known to have the infected \textit{Ixodes} ticks, in appropriately diagnosing and treating these patients.

\section*{ACKNOWLEDGEMENTS}

We would like to acknowledge the assistance of Lynne Pierson and Juanita Heiser in the preparation of the manuscript, the physicians and public health personnel of the state for their assistance in reporting and investigating possible Lyme disease cases, and Drs. Jacquelyn Sampson and Hazel Wilkinson of the Centers for Disease Control for providing serologic testing.

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