# Articles

# Lyme Disease in Northwestern Coastal California

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**To determine the incidence of physician-diagnosed Lyme disease in an endemic area of California, an active surveillance program was implemented in Lake, Mendocino, Sonoma, and southern Humboldt counties. More than 200 medical care providers were called monthly for their list of suspected cases of Lyme disease. Pertinent information was abstracted from the medical record of each patient.**

**Of 153 cases of possible early Lyme disease ascertained from July 1991 to December 1992, 37% consisted of physician-diagnosed erythema migrans. Only 58% of erythema migrans rashes were at least 5 cm in diameter. An additional 43 patients had suspicious rashes not classified as erythema migrans. Of 166 patients with possible late-stage Lyme disease, 31% had specific clinical symptoms and 75% had a positive serologic test.**

**With an incident case defined as physician-diagnosed erythema migrans of at least 5 cm in diameter, the annual incidence of Lyme disease in northwestern coastal California according to active surveillance only was 5.5 per 100,000. The rate of Lyme disease in California is substantially lower than that in the Atlantic northeastern United States. Many suspected cases of Lyme disease in this endemic area do not meet surveillance criteria, which are intentionally restrictive. Although some of the illnesses not meeting surveillance criteria may be due to infection with *Borrelia burgdorferi*, it appears that Lyme disease is being overdiagnosed in this area.**

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*Borrelia burgdorferi* causes Lyme disease, a multisystem illness with dermatologic, musculoskeletal, neurologic, or cardiac manifestations.[1-3] In the Pacific northwestern United States, this spirochete is transmitted by the western black-legged tick, *Ixodes pacificus*; an average of 1% to 2% of these ticks are infected in northern California.[4]

Difficult to grow in culture from humans and requiring special media,[5] *B burgdorferi* has been identified in only three patients in California to date (G. L. Campbell, MD, PhD, MPH, Centers for Disease Control and Prevention, Fort Collins, Colorado, oral communication, August 1993). Furthermore, because the available serologic tests for antibodies to *B burgdorferi* are not standardized, vary widely in sensitivity and specificity, and typically give negative results early in the course of infection, they are not useful as diagnostic tools.[6-8] Thus, Lyme disease remains a clinical diagnosis. Unfortunately, many of the signs and symptoms associated with Lyme disease are nonspecific, and there is ongoing controversy about the clinical criteria that define a case.

For surveillance purposes only, the Centers for Disease Control and Prevention defines a case of Lyme disease as any patient with a physician-diagnosed erythema migrans rash at least 5 cm in diameter or specific musculoskeletal, cardiac, or neurologic manifestations and a serologic test positive for *B burgdorferi*.[9] During the five-year period 1983 to 1987, a passive surveillance system in California identified 399 autochthonous cases of Lyme disease meeting these criteria (unpublished data). These cases were reported primarily from the northwestern coastal counties of the state. To determine a more accurate incidence of Lyme disease in this endemic region, we implemented an active surveillance program in July 1991. We present here the characteristics of all patients suspected of having Lyme disease who were identified in the active surveillance area during the 18-month period from July 1, 1991, to December 31, 1992.

## Patients and Methods

The region covered by the active surveillance program is located in northwestern coastal California. It occupies

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18,710 km² (7,224 sq mi) in total area and includes Lake, Mendocino, Sonoma, and the southern half of Humboldt counties. The area includes a variety of habitats but generally forms a patchwork of Mediterranean chaparral, redwood forest, and cultivated lands. *Ixodes pacificus* is focally abundant throughout the region (J. Clover, California Department of Health Services, oral communication, October 1992). Most of the 531,366 inhabitants live in rural areas and are involved primarily in agriculture, forestry, government, and the retail and service industries.[10]

All medical care professionals in the area thought likely to diagnose and treat cases of Lyme disease were invited to participate in the surveillance program. These included general practitioners, internists, dermatologists, rheumatologists, medical staff at primary and tertiary care centers, and other physicians specializing in the diagnosis and treatment of Lyme disease. They were identified through medical societies, previous reporting to the California Department of Health Services, and commercial listings. All enrolled professionals were telephoned monthly to list any patients who were suspected of having or who had been treated for presumptive Lyme disease during the previous month.

Data collected either over the telephone or by chart review at the medical office included, for each patient, the following: demographic information; presenting symptom(s); history of recent tick bite(s), with the geographic location where the bite occurred; all signs and symptoms, particularly dermatologic, musculoskeletal, neurologic, and cardiac manifestations; laboratory test results, if any; treatment regimen, if given; and the classification of the condition by the medical care professional as a probable, possible, or unlikely case of Lyme disease.

For surveillance purposes, all incident cases were assumed to have received exposure in the previous 30 days, as they resided in a known endemic area. An incident or early case of Lyme disease was defined as any patient with physician-diagnosed erythema migrans. This criterion was chosen to allow the comparison of incidence rates in California with those in other areas of the United States. As the size of the rash was not available for many suspected cases, estimates of incidence were calculated using three different numerators:

- Only those cases meeting national surveillance case criteria—that is, patients with physician-diagnosed erythema migrans of at least 5 cm in diameter (minimum number of cases)[9];
- All cases of physician-diagnosed erythema migrans regardless of rash size (maximum number of cases);
- All cases meeting national surveillance case criteria plus a proportion of those cases missing information on rash size. We defined this proportion of additional cases as equal to the number of patients with erythema migrans of at least 5 cm in diameter over the total number of persons with erythema migrans of a known size.

A case of prevalent or late-stage Lyme disease that met national surveillance criteria was defined as any patient with specific musculoskeletal, cardiac, or neurologic manifestations and with a serologic test positive for antibodies to *B burgdorferi*.[9]

## Results

A total of 205 medical care professionals participated in the surveillance program, of whom 94% were enrolled in 1991. From July 1, 1991, through 1992, Lyme disease presumed to have been contracted in California was suspected in 319 persons through the active surveillance program. Of these patients, 49% resided in Mendocino County, 29% in Sonoma County, 15% in southern Humboldt County, 6% in Lake County, and 3% in adjacent counties (cases from adjacent counties were excluded from the calculation of rates). The ages of patients with suspected Lyme disease ranged from 1 to 86 years (median, 41), and 55% were female.

### *Incident Cases*

Of the 57 patients diagnosed with erythema migrans by a physician, 42 had information on the rash size (Table 1). Of these 42 cases, 33 (78%) reported a rash size of 5 cm or greater in diameter and thus met national surveillance case criteria for incident Lyme disease. We assumed that this same proportion, 78%, of the 15 cases lacking information on erythema migrans size also met national surveillance case criteria. Excluding the one patient who lived in an adjacent county, the annual incidence of physician-diagnosed erythema migrans, estimated using different numerators as outlined earlier, ranged from 4.0 to 7.0 cases per 100,000 population (Table 2). Of the 57 cases of erythema migrans, 43 had a history of a recent tick bite; of these 43 patients, 14 were bitten at least three days before the onset of the rash (24 unspecified). Of the 57 patients, 43 were classified by a physician as probable or possible cases of Lyme disease; 54 were treated with antibiotics. Although cases occurred throughout the year, Lyme disease was diagnosed most often in the spring and summer months (Figure 1). Of all the cases of physician-diagnosed erythema migrans regardless of rash size, the age-specific annual incidence ranged from 1.9 to 11.9 cases per 100,000 population (Table 3). The county-specific annual incidence, again using all cases of physician-diagnosed erythema migrans, ranged from 2.1 to 65.7 cases per 100,000 population (Table 4).

A total of 43 patients were diagnosed with a suspicious rash not defined by the physician as erythema migrans (Table 1). Of these 43 patients, 33 recalled a recent tick bite (4 unspecified); 8 had a rash greater than 5 cm in diameter (21 unspecified); and the rash had occurred more than three days after the known bite for 8 patients (15 unspecified). Of these 43 patients, 27 were classified by the physician as probable or possible cases of Lyme disease, and 40 patients were treated with antibiotics. These cases were not included in any of the estimates of incidence.

In all, 41 patients presented with flulike symptoms that included fever, headache, and arthralgias, myalgias, or both (Table 1). Of these patients, 28 recalled a tick bite,

**TABLE 1.—*Characteristics of Suspected Cases of Incident Lyme Disease in Northwestern Coastal California, July 1991 to December 1992***

| Characteristic | Patients, No. (%) | | | | | |
|---|---|---|---|---|---|---|
| | *Erythema Migrans* | | *Suspicious Rash Not Diagnosed as Erythema Migrans* | | *Flulike Symptoms Without Rash or Tick Bite* | |
| | n=57* | 95% CI | n=43 | 95% CI | n=53 | 95% CI |
| Size of skin lesion | | | | | | |
| ≥5 cm | 33 (58) | 44-70 | 8 (19) | 9-34 | NA | |
| <5 cm | 9 (16) | 8-29 | 14 (33) | 20-49 | | |
| Unspecified | 15 (26) | 16-40 | 21 (49) | 34-64 | | |
| Meets national surveillance case criteria† | | | | | | |
| Yes | 33 (58) | 44-70 | NA | | NA | |
| No | 9 (16) | 8-29 | | | | |
| Insufficient information | 15 (26) | 16-40 | | | | |
| Known tick bite | | | | | | |
| Yes | 43 (75) | 62-85 | 33 (77) | 61-88 | 40 (75) | 61-85 |
| No | 12 (21) | 5-24 | 6 (14) | 6-29 | 9 (17) | 9-30 |
| Unspecified | 2 (4) | 1-14 | 4 (9) | 3-23 | 4 (8) | 3-20 |
| Time from known bite to rash onset | | | | | | |
| ≥3 days | 14 (33) | 22-47 | 8 (15) | 7-30 | 12 (30) | 19-44 |
| <3 days | 5 (12) | 5-24 | 10 (30) | 18-46 | 14 (35) | 23-49 |
| Unspecified | 4 (45) | 16-40 | 15 (45) | 30-61 | 14 (35) | 23-49 |
| Treated with antibiotics | | | | | | |
| Yes | 54 (95) | 85-99 | 40 (93) | 80-98 | 51 (96) | 86-99 |
| No | 0 (0) | | 2 (5) | 1-18 | 1 (2) | 0-12 |
| Unspecified | 3 (5) | 1-15 | 1 (2) | 0-13 | 1 (2) | 0-12 |
| *Borrelia burgdorferi* serologic results | | | | | | |
| Positive | 11 (19) | 10-32 | 10 (23) | 12-39 | 18 (34) | 22-43 |
| Borderline | 4 (7) | 2-18 | 2 (5) | 1-18 | 4 (8) | 3-20 |
| Negative | 10 (18) | 10-31 | 11 (26) | 14-42 | 12 (23) | 13-37 |
| Not tested or unknown | 32 (56) | 42-69 | 20 (47) | 32-63 | 19 (36) | 24-50 |
| Classification by physician | | | | | | |
| Probable case | 27 (47) | 34-61 | 4 (9) | 3-23 | 14 (26) | 15-40 |
| Possible case | 16 (28) | 17-42 | 23 (53) | 37-68 | 17 (32) | 20-46 |
| Unlikely case | 2 (4) | 1-14 | 11 (26) | 14-42 | 15 (28) | 17-42 |
| Unspecified | 12 (21) | 12-34 | 5 (12) | 5-26 | 7 (13) | 6-26 |

CI = confidence interval, NA = not applicable

*One patient resided in an adjacent county.
†Rash size ≥5 cm; exposure occurred in an endemic county.

and the symptoms began at least three days after the bite in 12 patients (13 unspecified). Of these 41 patients with flulike symptoms, 29 were classified by their physicians as probable or possible cases of Lyme disease; 40 patients were treated with antibiotics. Again, these cases were not included in any of the estimates of incidence.

The incidence using alternative criteria to national surveillance criteria may be calculated from these data. For example, 27 patients with erythema migrans, 4 with suspicious rashes, and 14 with flulike symptoms were classified as probable cases of Lyme disease by their physician (Table 1). Using these 45 cases of suspected incident Lyme disease, we estimated the annual incidence of probable Lyme disease as 5.6 cases per 100,000 population.

Twelve patients who were asymptomatic presented with a history of a tick bite during the previous two days. One of these patients was treated with antibiotics because the tick had been identified as positive for *B burgdorferi;* the attachment time of this tick was not known. The other 11 patients were treated with a course of antibiotics at their own request.

### *Prevalent Cases*

The remaining 166 patients presented with symptoms considered by their physicians as consistent with a diagnosis of prevalent or late Lyme disease (Table 5). Of these, 51 patients presented with specific symptoms, including 37 patients with arthritis. Of these 51 suspected cases, 37 were classified as probable and possible cases of Lyme disease (Table 6); all 51 patients were treated with antibiotics. Only 34 of these 51 patients met national surveillance case criteria for Lyme disease.

Finally, 115 patients presented with only one or more nonspecific symptoms, including arthralgias, myalgias, fatigue, paresthesias, and confusion, depression, or both. These patients were classified into two groups: those who

TABLE 2.—*Annual Incidence of Physician-Diagnosed Erythema Migrans (EM) in Northwestern Coastal California, July 1991 to December 1992*

| *Numerator of EM Cases* | *Patients (n=57), No.* | *Annual Incidence/ 100,000* (95% CI)* |
|---|---|---|
| Physician-diagnosed EM in persons residing in the study area | 56† | 7.0 (6.77-7.22) |
| Information on size available | 41 | |
| Meets national surveillance case criteria‡ | 32 | 4.0 (3.83-4.17) |
| Proportion of cases with information on size meeting national surveillance case criteria | 0.78 | |
| Missing information on size | 15 | |
| Proportion with missing information on size assumed to meet national surveillance case criteria | 0.78 | |
| Missing information assumed to meet national surveillance case criteria | 12 | |
| Both meets and assumed to meet national surveillance case criteria | 44 | 5.5 (5.30-5.70) |

CI = confidence interval

*From the Bureau of the Census.[10]
†Excludes the 1 patient living in an adjacent county.
‡Rash size ≥5 cm; exposure occurred in an endemic county.

presented with arthralgias as the predominant complaint, and those who presented with other nonspecific symptoms. Of the 83 patients with arthralgias, 64 were seropositive for *B burgdorferi* (Table 5). These patients were classified as having probable (38), possible (35), or unlikely (7) cases of Lyme disease (3 unspecified), and all were treated with antibiotics. Of the 32 patients presenting with nonspecific symptoms other than arthralgias, including fatigue, depression, confusion, or paresthesias, 26 were seropositive. In all, 13 patients were considered probable cases, and 14 were considered possible cases of Lyme disease; 20 were treated with a course of antibiotics.

## Discussion

Using active surveillance in an area of California considered endemic for Lyme disease, we ascertained the occurrence of 153 suspected incident and 166 suspected prevalent cases during the 18-month period July 1991 through December 1992. Of these 319 suspected cases, 94% were treated with antibiotics. Only 21% met national surveillance case criteria for Lyme disease, however.

For surveillance purposes, the most sensitive and specific criterion for incident Lyme disease is physician-diagnosed erythema migrans.[11] In this study, 57 patients were diagnosed with erythema migrans by a medical care professional; of these cases, however, only 33 of 42 with information on rash size met national surveillance case criteria. When we assumed that the same proportion, 78%, of the remaining 15 cases lacking information on erythema size also met national surveillance case criteria, the cumulative annual incidence of physician-diagnosed erythema migrans was estimated to be 5.5 cases per 100,000 population in this area of northwestern coastal California.

TABLE 3.—*Age-Specific Incidence Rates of Erythema Migrans in Northwestern Coastal California, July 1991 to December 1992*

| *Age, years* | *Patients, No.* | *Population Size** | *Annual Incidence/ 100,000 (95% CI)* |
|---|---|---|---|
| 0-9 | 11 | 78,607 | 9.3 (8.6-10.0) |
| 10-19 | 7 | 68,053 | 6.9 (6.3-7.6) |
| 20-29 | 2 | 70,146 | 1.9 (1.6-2.3) |
| 30-39 | 7 | 94,593 | 4.9 (4.5-5.4) |
| 40-49 | 14 | 78,501 | 11.9 (11.2-12.7) |
| 50-59 | 5 | 43,690 | 7.6 (6.8-8.5) |
| 60-69 | 4 | 45,566 | 5.9 (5.2-6.7) |
| 70+ | 6 | 52,120 | 7.7 (7.0-8.5) |
| Total | 56 | 531,276 | |

CI = confidence interval

*From Bureau of the Census.[10]

TABLE 4.—*County-Specific Annual Incidence of Erythema Migrans in Northwestern Coastal California, July 1991 to December 1992*

| *County* | *Patients, No.* | *Population Size* | *Annual Incidence/ 100,000 (95% CI)* |
|---|---|---|---|
| Humboldt, southern half | 12 | 12,168 | 65.7 (61.4-70.3) |
| Lake | 3 | 50,631 | 4.0 (3.5-4.6) |
| Mendocino | 29 | 80,345 | 24.1 (23.1-25.5) |
| Sonoma | 12 | 388,222 | 2.1 (2.0-2.3) |
| Total | 56 | 531,366 | |

CI = confidence interval

For the 26 cases of physician-diagnosed erythema migrans with data available, the median time from a known bite to the appearance of erythema was seven days. This compares with a median of seven to nine days for cases of erythema migrans diagnosed in the endemic Atlantic northeastern United States.[11,12] It is possible that some rashes classified by physicians as erythema migrans were, in fact, allergic reactions to tick bites that occur immediately after the bite. Including allergic reactions as cases of erythema migrans would inflate its estimated incidence in this area.

Few studies have examined risk factors for Lyme disease in California.[13,14] *Ixodes pacificus* is focally endemic throughout the northwestern coastal counties and is active throughout most of the year. Most cases of erythema migrans reported actively from the surveillance area in 1992 occurred in the spring and summer months, when nymphal ticks are most common, suggesting that this immature stage, small and easily overlooked, is important in transmitting Lyme disease. Children aged 1 to 9 years were at high risk of erythema migrans, suggesting that exposure to ticks may occur primarily around the home. Al-

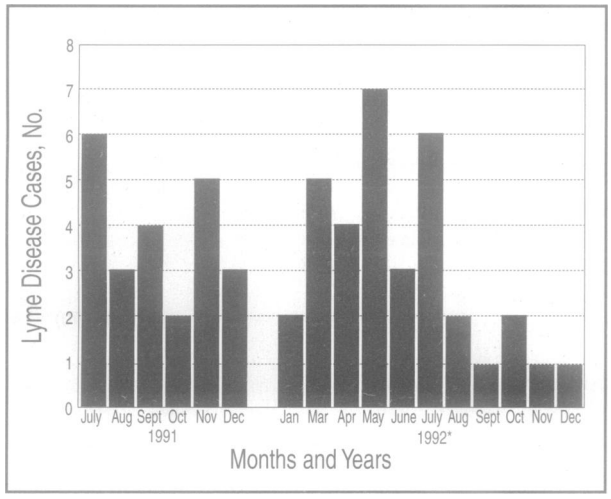


**Figure 1.**—The graph shows the temporal distribution of cases of physician-diagnosed erythema migrans as ascertained by active surveillance in northwestern coastal California, July 1991 through December 1992. *No cases of erythema migrans were diagnosed in February 1992.

ternatively, however, given the high infection rate in persons aged 40 to 49, exposure may also occur in the work environment.

In this study, 63% of patients with suspected incident cases had only nonspecific symptoms, including flulike symptoms or a suspicious rash not classified by a physician as erythema migrans. Most of these patients (60%) were classified as having probable or possible Lyme disease and treated with antibiotics as a precautionary measure. Because such patients are excluded by the surveillance criteria, the actual incidence of Lyme disease in this area may be seriously underestimated.

Antibiotics were prescribed to 12 patients with a history of a tick bite but no signs or symptoms of Lyme disease. The prophylactic treatment of tick bites is not routinely indicated, as treatment after symptoms of Lyme disease develop is sufficient to resolve an initial infection.[15] Furthermore, in California the risk of Lyme disease following a single tick bite is probably less than 1%, because the prevalence of *B burgdorferi* infection in the tick vector is on the order of 1% to 2%,[4] and an infective tick most probably must be attached to its animal host for 24 to 48 hours before *B burgdorferi* is to be transmitted.[16,17] It is important that persons in the surveillance area understand the extremely low probability of contracting Lyme disease in California after a single tick bite.[18]

Only 34 (20%) of 166 patients suspected of having prevalent or late-stage Lyme disease in this study met national surveillance case criteria; 25 of these 34 cases (74%) were diagnosed with arthritis. Most of the remaining 115 patients who did not have any of the specific musculoskeletal, neurologic, or cardiac manifestations of late Lyme disease presented with nonspecific symptoms, and it appears that many were diagnosed with Lyme disease based primarily on their positive serologic test results. Most of these patients were treated with antibiotics, and several received long-term therapy. Based on these findings, we think that some patients in this region may be treated unnecessarily for suspected Lyme disease. Other diseases, such as fibromyalgia and chronic fatigue syndrome, produce nonspecific symptoms similar to those of Lyme disease and should be considered as possible diagnoses.[3]

Several limitations are inherent in any study involving active surveillance. First, results are not comparable to those of passive surveillance. At least one other active surveillance program for Lyme disease has been implemented, in a hyperendemic area of Connecticut; the incidence of Lyme disease there was shown to be 560 cases per 100,000 population in 1992 (M. Cartter, MD, Connecticut Health Division, oral communication, October 1993). This comparison of rates using the same criteria suggests that Lyme disease in California, although endemic, is most probably present at a substantially lower rate than in the Atlantic northeastern United States. Second, the active surveillance program did not encompass all medical care professionals practicing in the northwestern coastal counties. Any case of Lyme disease diagnosed by a physician not included in the program or reported by passive surveillance would be missed, leading to an un-

TABLE 5.—*Characteristics of Suspected Cases of Lyme Disease, July 1991 to December 1992*

| Characteristics | Patients, No. | Serologic Borrelia burgdorferi Test Results | | |
|---|---|---|---|---|
| | | Positive | Borderline | Negative |
| Specific symptoms | | | | |
| Arthritis | 37 | 25 | | 11 |
| Facial palsy | 8 | 4 | 3 | 1 |
| Atrioventricular block | 1 | 1 | | |
| Meningoencephalitis | 2 | 2 | | |
| Facial palsy and arthritis | 1 | 1 | | |
| Encephalitis | 1 | 1 | | |
| Atrioventricular block | 1 | 1 | 1 | |
| Nonspecific symptoms | | | | |
| Arthralgia | 83 | 64 | 10 | |
| Myalgia | 15 | | | |
| Other complaints | 32 | 26 | | 4 |
| Total | 166 | 124 | 14 | 16 |
| Meet CDC surveillance case criteria | 34 | 34 | | |

CDC = Centers for Disease Control and Prevention

TABLE 6.—*Classification by the Physician of Patients With Suspected Lyme Disease by Presence of Specific or Nonspecific Symptoms*

| Classification | Patients, No. | |
|---|---|---|
| | Specific Symptoms* | Nonspecific Symptoms |
| Probable Lyme disease | 25 | 51 |
| Possible Lyme disease | 12 | 49 |
| Unlikely Lyme disease | 2 | 11 |
| Unspecified | 12 | 4 |
| Total | 51 | 115 |

*Specific symptoms include arthritis, facial palsy, atrioventricular block, and meningitis.

derestimate of the incidence in this area. If we include the 21 cases ascertained by passive surveillance from the surveillance area, the annual incidence of physician-diagnosed erythema migrans was 8.2 cases per 100,000 population. Third, only cases that come to medical attention will be included in an estimate of incidence. It is not possible to determine the proportion of patients with Lyme disease in this area of California who did not seek medical care. Fourth, because physicians and patients were not called when information was missing from the medical record, data may be incomplete, leading to unreliable estimates of incidence. Most important, a diagnosis of Lyme disease is difficult to substantiate by medical record review. Given these limitations, the true incidence of Lyme disease in these northwestern coastal counties of California may be higher than the estimate calculated in this study.

Surveillance criteria for Lyme disease are designed for high specificity and thus have lower sensitivity. Although persons who do not have the disease are more likely to be correctly excluded from the calculated rates, actual cases of disease are also more likely to be excluded. These criteria are not intended to be used as a guide for clinical diagnosis and treatment. Instead, they provide a systematic method of assessing the effects of Lyme disease in an area and allow a comparison of rates between years and between geographic areas. Although the use of alternative criteria to those used by the Centers for Disease Control and Prevention for surveillance purposes may produce a different estimate of incidence, it does not allow the comparison of the rate of Lyme disease in California with that of other areas of the United States.

In conclusion, surveillance criteria for Lyme disease appear to exclude a large proportion of cases of Lyme disease diagnosed in California from July 1991 through 1992. An argument could be made to expand the surveillance criteria so that more patients with nonspecific symptoms are included, but we do not think they should be changed, as it is possible that most of these cases are misdiagnosed.[19,20] Until a standardized, highly sensitive and specific laboratory test is available for national surveillance purposes, many patients in California presenting with nonspecific signs and symptoms who are currently diagnosed with suspected Lyme disease will be excluded from any measures of incidence or prevalence.

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