Long-term Outcomes of Persons With Lyme Disease

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Although Lyme disease is the most common vector-borne illness in the United States, there are few data about the long-term outcomes of patients treated for it. Reports have appeared in both the lay press and the medical literature of persons who were diagnosed as having Lyme disease and subsequently developed either recurrent or persistent, non-specific symptoms (such as fatigue or arthralgia) attributed to Lyme disease (sometimes even if they were treated with antimicrobial therapies). Such patients occasionally receive either repeated or prolonged parenteral courses of antimicrobial therapy despite statements by the American College of Rheumatology, the Infectious Diseases Society of America, and others that such treatment is not warranted. Some of these reports are about highly selected samples of patients, many of whom developed symptoms months to years before Lyme disease was diagnosed and were not treated from months to years after the onset of their symptoms. These patients are not comparable to most patients who currently are being diagnosed as having Lyme disease and being treated for it.

In both 1984 and 1985, the Connecticut State Department of Public Health offered to test, free of charge, serum samples of patients suspected of having Lyme disease for antibodies against *Borrelia burgdorferi* if the practitioner would submit information about the patient. Since 1987, all cases of Lyme disease in Connecticut are required to be reported to the Department of Public Health. To assess the long-term outcomes of patients diagnosed as having Lyme disease, we conducted a 2-part study: a community-based, longitudinal cohort study of a random sample of persons with Lyme disease from approximately 1 to 11 years after diagnosis (range, 15-135 months). An increased frequency of symptoms (eg, pain, fatigue) or of difficulty with daily activities (eg, performing housework, exercising) was reported by 69% of the patients, although few (19%) of these problems were attributed to Lyme disease. Whenever there was a statistically significant difference in the frequencies of either increased symptoms or increased difficulties with typical activities between those who did or did not meet the surveillance case definition, in all instances the greater frequency of problems was in the group that did not meet the case definition. The frequencies of reports of both increased symptoms and increased difficulties with typical activities among patients who had been diagnosed as having Lyme disease were similar to those among age-matched controls without Lyme disease.

Conclusions: In this cohort, although many patients reported increases in symptoms and/or increased difficulties with typical daily activities between 1 and 11 years after diagnosis of Lyme disease, the frequencies of these reports were similar to the frequencies of such reports among age-matched controls without Lyme disease.
LONG-TERM OUTCOMES OF LYME DISEASE

years earlier, reported to the Connecticut Department of Public Health, and a matched cohort study in which the outcomes of a randomly selected subsample of the patients reported to have had Lyme disease from the larger study were compared with those of controls without Lyme disease, matched to the patients by age and area of residence.

METHODS

Selection of Patients for the Longitudinal Cohort Study
From all reports submitted to the Connecticut State Department of Public Health from 1984 through 1991 of patients with suspected Lyme disease, a random sample (identified with the use of a table of random numbers) was selected. If a physician submitted a report to the Department of Public Health, she or he was contacted and asked for permission to contact the patient. If the physician consented, potential patients were contacted by telephone, and informed consent to participate in the study was obtained. Patients were excluded if they reported that they had never had Lyme disease, if they did not speak English, or if they resided outside of Connecticut at the time of diagnosis of Lyme disease.

Selection of Patients and Controls for the Matched Cohort Study
A random subsample of patients enrolled in the longitudinal cohort study was selected using a table of random numbers. For each patient in the subsample, 1 control without a history of Lyme disease, matched for age and area of residence, was identified by sequential-digit dialing. Controls without Lyme disease were matched to patients reported to have had Lyme disease (by age ±1 year for those younger than 2 years, ±2 years for those aged 2 to 10 years, ±3 years for those aged 11 to 17 years, and ±5 years for those aged 18 years or older). Each telephone number was called 3 times before advancing to the next number: once during the daytime, once during the evening, and once during the weekend. Respondents at telephone numbers that were not residences, those who did not speak English, and those who said they had been diagnosed as having Lyme disease were excluded.

Interviews
Both patients and controls were interviewed via telephone. If the subject was a child, a parent was interviewed. Interviews were conducted by a trained research assistant who used a standardized questionnaire. Patients were asked whether they believed they were cured of Lyme disease, whether they experienced increased frequency of certain symptoms, and whether they noted increased difficulty in their abilities to perform certain typical daily activities since being diagnosed as having Lyme disease. For example, they were asked: “Since you were diagnosed with Lyme disease, have you experienced episodes of joint pain more frequently, less frequently, or with no change in frequency?” In addition, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), a standardized survey that measures health-related quality of life, and the Center for Epidemiologic Studies-Depression (CES-D) questionnaire (developed for use in studies of the epidemiology of depression in the general population) were administered only to adults (persons aged ≥18 years).

All patients were asked about medical problems in the following manner: “Do you have any medical problems? Specifically, do you have any problems with heart disease, kidney disease, liver disease, etc.” Controls were asked the same questions, except questions that directly related to having had Lyme disease in the past. Instead of asking controls about changes in either symptoms or difficulties with typical daily activities since they were diagnosed as having Lyme disease, controls were asked about changes during the same time interval as the matched patient with Lyme disease (eg, “During the past 5 years, have you experienced episodes of joint pain more frequently, less frequently, or with no change in frequency?”).

Review of Medical Records
Medical records of each patient, from as early as 1975 to the most recent visit, were reviewed by research assistants. Information was recorded about clinical and laboratory data at the time of diagnosis of Lyme disease, about the treatment for Lyme disease, and about office visits, hospitalizations, and underlying medical conditions both before and after the onset of Lyme disease. Records of the reporting physician and of any other physicians who treated the patient for Lyme disease were reviewed. Although occasionally there were discrepancies between a patient’s reports in the interview and the medical records, the results were not significantly different regardless of which data we used.

This study was approved by the human investigation committees of the Yale School of Medicine and the Connecticut State Department of Public Health.

Classification of Patients With Lyme Disease
An abstract of the clinical and laboratory information at the time of diagnosis of each patient reported to have had Lyme disease was prepared by research assistants who were blinded to the long-term outcomes of the patients. These forms were reviewed by investigators who also were blinded to the outcomes. Patients were classified by the stage of Lyme disease at the time of diagnosis and by whether they met the national surveillance case definition for Lyme disease of the Centers for Disease Control and Prevention.14 This classification was made independent of the classification done by the health department at the time of the report and was based on additional information gathered for this study.

Patients with a single erythema migrans lesion at least 5 cm in diameter (with or without concurrent symptoms of fever, malaise, or arthralgia) that was documented by a physician were classified as having early localized disease. Because there were no significant differences in the results if they were excluded from the analyses or
were included with the cohort of patients who did not meet the case definition, 98 patients who had an erythema migrans rash the size of which was not documented by a physician or was not at least 5 cm in diameter were included in the cohort of patients with early localized disease who met the case definition. Patients with multiple erythema migrans lesions were classified as having early disseminated Lyme disease. Patients with either early neurologic disease (eg, cranial nerve palsy, aseptic meningitis, peripheral neuropathy) or cardiac disease (eg, acute atrioventricular block) and serologic evidence of infection with *B burgdorferi* (a positive test result as defined by the laboratory that did the test; confirmation by Western immunoblot was not required) also were classified as having early disseminated Lyme disease. Patients with arthritis, encephalopathy, or polyneuropathy and serologic evidence of infection with *B burgdorferi* were classified as having late-stage Lyme disease. Patients who had only nonspecific symptoms (eg, arthralgia, fatigue), with or without serologic evidence of infection with *B burgdorferi*, and patients who had objective signs consistent with Lyme disease other than erythema migrans (eg, arthritis) but with no serologic evidence of infection with *B burgdorferi*, were classified as not meeting the surveillance case definition for Lyme disease.

**Statistical Methods**

The data were analyzed using standard statistical techniques. The 95% confidence intervals (CIs) for proportions were calculated using statistical software. Relative risks (RRs), associated 95% CIs, and their statistical significance also were calculated. Logistic regression was used to adjust RRs for the effects of potential confounders (results reported are unadjusted, except where noted). All *P* values are 2-tailed.

**RESULTS**

**Longitudinal Cohort Study**

A random sample of 1325 patients (15%) reported as having Lyme disease was selected from the 8764 reports of Lyme disease received by the health department from 1984 through 1991. Of these, 16 were not contacted at the request of the reporting physician, 17 were deceased, 80 refused to participate, 82 reported that they had never had Lyme disease, 85 lived outside of Connecticut at the time of diagnosis, and 367 could not be located (for most of these, addresses were not available from the report form or from the physician or the laboratory that submitted the report). The remaining 678 patients (median age, 36 years) were enrolled in the study. The median age of the 445 adults was 46 years (range, 18-86 years) and of the 233 children was 8 years (range, 6 months to 17 years). There were 350 females (51.6%) and 670 whites (98.8%). The median time from the diagnosis of Lyme disease to the follow-up interview was 51 months (range, 15-133 months). The signs and symptoms of the patients at the time they presented to the reporting physician, stratified by age and by whether they met the surveillance case definition for Lyme disease, are shown in Table 1.

Of the 678 patients, 70.9% (95% CI, 67.3%-74.3%) believed they were cured of Lyme disease, 9.0% (95% CI, 7.0%-11.4%) believed they were not cured, and 20.1% (95% CI, 17.1%-23.3%) were unsure whether they were cured of Lyme disease. Most patients who reported that they were unsure if they were cured said they were unsure whether Lyme disease was curable. Patients who believed they were cured of Lyme disease were less likely to have underlying comorbid illnesses than were patients who believed they were not cured of Lyme disease (32% vs 46%; RR, 0.69; 95% CI, 0.51-0.94; *P* = .04). Fifteen percent of adults and 5% of children believed they were not cured of Lyme disease (RR, 3.0; 95% CI, 1.3-5.7; *P* < .001). Patients who met the surveillance case definition for Lyme disease were more likely to believe that they were cured of Lyme disease than were patients who did not meet the case definition (75% vs 63%; RR, 1.2; 95% CI, 1.1-1.3; *P* = .001).

**Reported Increases in Symptoms and in Difficulties With Typical Daily Activities.** The proportions of patients that reported increases in symptoms and in difficulties with typical daily activities are shown in Tables 2 and 3, respectively. The proportions of patients that attributed these increases to Lyme disease also are shown. Overall, 31% of patients reported no increases either in symptoms or in difficulties with typical daily activities since having Lyme disease, 16% reported increases either in symptoms or in difficulties with typical activities in 1 category, 10% reported increases in 2 categories, 9% reported increases in 3 categories, 7% reported increases in 4 categories, and 27% reported increases in 5 or more categories. However, overall, only 19% of the increases either in symptoms or in difficulties with typical daily activities were attributed to Lyme disease; most

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**Table 1. Presenting Signs and Symptoms of Patients Reported to Have Lyme Disease**

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Adults (n = 445)</th>
<th>Children (n = 233)</th>
<th>Met Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single erythema migrans</strong></td>
<td>200 (44.9)</td>
<td>97 (41.6)</td>
<td>297 (68.1)</td>
</tr>
<tr>
<td><strong>Multiple erythema migrans</strong></td>
<td>46 (10.3)</td>
<td>42 (18.0)</td>
<td>88 (20.2)</td>
</tr>
<tr>
<td><strong>Facial nerve palsy/neuritis</strong></td>
<td>16 (3.6)</td>
<td>8 (3.4)</td>
<td>16 (3.7)</td>
</tr>
<tr>
<td><strong>Arthritis</strong></td>
<td>25 (5.6)</td>
<td>26 (11.2)</td>
<td>33 (7.6)</td>
</tr>
<tr>
<td><strong>Carditis</strong></td>
<td>4 (0.9)</td>
<td>0 (0)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td><strong>Nonspecific symptoms only</strong></td>
<td>143 (32.1)</td>
<td>53 (22.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>No data available</strong></td>
<td>11 (2.5)</td>
<td>7 (3.0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Percentages in this and other tables may not add to 100% due to rounding.*

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patients attributed the increases either to aging or to a comorbid illness, such as a stroke. There was a statistically significant association between whether patients believed they were not cured of Lyme disease and increases in symptoms or in difficulties with typical daily activities for each of the categories reported.

The proportions of patients that reported increases in symptoms and in difficulties with typical daily activities, stratified by whether they met the surveillance case definition for Lyme disease, are also shown in Tables 2 and 3, respectively. In all instances in which there were statistically significant differences between those who did and those who did not meet the surveillance case definition, the higher proportion of reported problems was in the group who did not meet the surveillance case definition. Among the patients who did not meet the surveillance case definition for Lyme disease and presented with only nonspecific symptoms, there was no significant difference in the reported frequencies of any specific symptom, of difficulty with any typical daily activity, or of whether they believed they were cured of Lyme disease when they were stratified by whether they had test results positive for antibodies to *B. burgdorferi*. If the results for the categories reported in Table 2 are summed and then averaged, there is a statistically significant linear trend in the proportion of patients who believed they were not cured (patients who were unsure whether they were cured of Lyme disease were excluded) after stratification by whether they met the case definition: patients who met the case definition and did not report increased symptoms (5.9%), patients who did not meet the case definition and did not report increased symptoms (10.4%), patients who met the case definition and reported increased symptoms (26.4%), and patients who did not meet the case definition and reported increased symptoms (34.6%) (*P*<.001). A similar trend was found among the categories reported in Table 3: patients who met the case definition and did not report increased difficulties with typical daily activities (8.1%), patients who did not meet the case definition and did not report increased difficulties with typical daily activities (11.1%), patients who met the case definition and reported increased difficulties with typical daily activities (26.6%), and patients who did not meet

<table>
<thead>
<tr>
<th>Table 2. Reported Increase in Symptoms Since Diagnosis of Lyme Disease*</th>
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</thead>
<tbody>
<tr>
<td>Symptom</td>
</tr>
<tr>
<td>Joint or muscle pain</td>
</tr>
<tr>
<td>Memory problems</td>
</tr>
<tr>
<td>Numbness</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Swollen joints</td>
</tr>
<tr>
<td>Headaches</td>
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<tr>
<td>Neck pain</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval.  †The comparison is for met case definition vs did not meet case definition.

<table>
<thead>
<tr>
<th>Table 3. Reported Increase in Difficulties With Typical Daily Activities Since Diagnosis of Lyme Disease*</th>
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</thead>
<tbody>
<tr>
<td>Activity</td>
</tr>
<tr>
<td>Word finding</td>
</tr>
<tr>
<td>Naming objects</td>
</tr>
<tr>
<td>Sleeping</td>
</tr>
<tr>
<td>Exercise</td>
</tr>
<tr>
<td>Housework</td>
</tr>
<tr>
<td>Ability formulating ideas</td>
</tr>
<tr>
<td>Attending gym class</td>
</tr>
<tr>
<td>Falling asleep</td>
</tr>
<tr>
<td>Attending school or work</td>
</tr>
<tr>
<td>Appetite</td>
</tr>
<tr>
<td>Judgment</td>
</tr>
</tbody>
</table>

*Denominators differ because not all activities applied to all subjects (eg, not all subjects did housework). CI indicates confidence interval.  †The comparison is for met case definition vs did not meet case definition.
the case definition and reported increased difficulties with typical daily activities (42.4%) (P < .001).

**Antimicrobial Treatment.** Overall, 85.6% of patients were treated with antimicrobial agents for Lyme disease, 6.7% were not treated, and for 7.7% the data on antimicrobial therapy were unavailable. Among subjects for whom information about treatment was available, the proportions of adults and of children who had received antimicrobial treatment were similar (93% vs 91%; RR, 1.1; 95% CI, 0.9-1.4; P = .41). The frequencies of reports of any increased symptom or increased difficulty with a typical daily activity were similar when patients were stratified by whether they had received antimicrobial therapy, except for the category of joint or muscle aches (32% of those who had received antimicrobial therapy vs 48% of those who had not; RR, 0.7; 95% CI, 0.5-0.9; P = .04). The proportions of patients who received antimicrobial treatment were similar among patients who did and did not believe they were cured of Lyme disease (93% vs 90%; RR, 1.04; 95% CI, 0.95-1.1; P = .54). Patients who met the surveillance case definition for Lyme disease were more likely to have received antimicrobial therapy for Lyme disease than were subjects who did not meet the surveillance case definition (98% vs 82%; RR, 1.2; 95% CI, 1.1-1.3; P < .001).

**Differences Between Adults and Children.** A higher proportion of children than of adults met the surveillance case definition for Lyme disease (71.7% vs 60.5%; RR, 1.2; 95% CI, 1.1-1.3; P < .005). Adult patients were more likely to report increased frequencies of every symptom since being diagnosed as having Lyme disease than were children (eg, numbness [RR, 6.6; 95% CI, 3.5-12.3; P < .001] or memory problems [RR, 5.3; 95% CI, 3.0-9.2; P < .001]). Likewise, the proportion of adult patients that reported increased difficulties with each activity was significantly higher than the proportion of children (eg, exercise [21.1% vs 5.2%; RR, 4.1; 95% CI, 2.3-7.3; P < .001], falling asleep [9.7% vs 4.7%; RR, 2.0; 95% CI, 1.1-3.9; P = .02], and ability to formulate ideas [10.8% vs 3.0%; RR, 3.6; 95% CI, 1.7-7.8; P < .001]).

**Results of Standardized Tests.** The results of the SF-36 survey are shown in Table 4 (the optimal score in each category is 100%). Except for the category “bodily pain,” the mean scores of patients who did and did not meet the surveillance case definition for Lyme disease were similar. The mean scores on the CES-D scale among patients who did and did not meet the surveillance case definition for Lyme disease also were similar (Table 4). Although a higher proportion of patients who did not meet the case definition had scores of at least 16 (a score ≥ 16 on the CES-D questionnaire suggests that the subject experiences depression), the difference was not statistically significant (RR, 1.7; 95% CI, 0.97-2.8; P = .06). When patients who had presented with only nonspecific symptoms were stratified by whether they had positive serologic test results for antibodies to *B burgdorferi*, the mean scores for the groups were similar on both the SF-36 and the CES-D scale.

**Matched Cohort Study**

Controls without a history of Lyme disease were selected for 212 randomly selected patients diagnosed as having Lyme disease. Using sequential-digit dialing, 2731 telephone numbers were called to enroll the 212 age-matched controls. Of the numbers called, there were no eligible persons at 1588 numbers, there was no answer or the line was busy on 3 separate attempts at 705 numbers, the respondent refused at 205 numbers, the respondent did not speak English at 18 numbers, and there was no adult available to give consent at 3 numbers.

Of the 212 patients diagnosed as having Lyme disease, 151 were adults (median age, 45 years) and 61 were children (median age, 8 years); 59% met the surveillance case definition for Lyme disease. Patients and controls were similar with respect to race and frequency of underlying illnesses. A higher proportion of controls than of patients was female (66% vs 49%; P < .001). The proportions of patients and controls who reported increased symptoms and/or increased difficulties with typical daily activities are shown in Table 5. Although many patients who had been diagnosed as having Lyme disease reported increased symptoms or increased difficulties with typical daily activities, the proportions were similar to those reported by the matched controls, except that there were statistically significant differences between the groups in the

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**Table 4. Adults’ Scores on Standardized Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Subjects, %</th>
<th>Met Case Definition</th>
<th>Did Not Meet Case Definition</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 category</td>
<td></td>
<td>(n = 269)</td>
<td>(n = 176)</td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>87.4</td>
<td>86.8</td>
<td>.73</td>
<td></td>
</tr>
<tr>
<td>Role limitations from physical problems</td>
<td>87.2</td>
<td>82.5</td>
<td>.13</td>
<td></td>
</tr>
<tr>
<td>Social functioning</td>
<td>89.8</td>
<td>89.1</td>
<td>.79</td>
<td></td>
</tr>
<tr>
<td>Bodily pain</td>
<td>81.2</td>
<td>76.9</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>General mental health</td>
<td>80.7</td>
<td>79.3</td>
<td>.35</td>
<td></td>
</tr>
<tr>
<td>Role limitations from emotional problems</td>
<td>89.3</td>
<td>86.5</td>
<td>.16</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>68.7</td>
<td>64.0</td>
<td>.39</td>
<td></td>
</tr>
<tr>
<td>General health perceptions</td>
<td>73.8</td>
<td>72.0</td>
<td>.38</td>
<td></td>
</tr>
</tbody>
</table>

* SF-36 indicates the Medical Outcomes Study 36-Item Short-Form Health Survey. CES-D, Center for Epidemiologic Studies-Depression scale. All data are percentages except the mean CES-D scores. The optimal score in each category of the SF-36 is 100%, and a score ≥ 16 on the CES-D questionnaire suggests that the subject suffers from depression.

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categories of “joint or muscle pain” and “ability formulating ideas.” Likewise, there were no significant differences in the entire cohort between the cases and the controls in the results of the SF-36 or the CES-D. The results of these tests for the 88 adults who met the surveillance case definition for Lyme disease and for their matched controls are shown in Table 6. There were no significant differences in any of the results when conditional logistic regression was used to adjust for differences in potential confounders such as sex, race, and the presence of 1 or more underlying comorbid illnesses.

**COMMENT**

Only 64% of the patients met the surveillance case definition for Lyme disease. Among the patients who met the definition, 88.3% presented with either single or multiple erythema migrans. This is similar to the proportions of patients with single or multiple erythema migrans in other reports of community-based, prospective studies of Lyme disease and supports the validity of how our patients were classified.18-20

There has been a great deal of controversy about the consequences of infection with *B burgdorferi*. Some patient advocacy groups and physicians believe that Lyme disease is a very serious and difficult-to-treat illness. Others believe that the majority of patients with Lyme disease remain relatively healthy, regardless of the stage of the illness at the time they present, and suggest that in many of the patients who have either persistent or recurrent subjective complaints, Lyme disease either was a misdiagnosis or was not the cause of the symptoms.2,5,18,21-30

Our data indicate that the outcomes of most persons diagnosed as having Lyme disease who are treated with antimicrobial agents are excellent. Although at the follow-up interview (a median of 51 months after diagnosis of Lyme disease) many of the patients diagnosed as having Lyme disease reported increased frequencies of some symptoms, increased difficulties with typical daily activities, or both, relatively few of the patients attributed these problems to Lyme disease. Moreover, the frequencies of such complaints among patients since the diagnosis of Lyme disease were similar to those of controls (when asked about changes during the same period) who had been matched to the patients by age and area of residence. Among adults reported to have had Lyme disease, scores on standardized tests of health-related quality of life and on the CES-D scale were similar to those of other generally healthy populations, and in the matched cohort study, among adults who met the surveillance case definition for Lyme disease, the scores on these standardized tests were similar to the scores of matched controls.

Among the patients reported to have had Lyme disease who did not meet the surveillance case definition, three quarters had only nonspecific symptoms.
(such as fatigue, arthralgia, or headache). In these patients, the diagnosis was based primarily on positive serologic test results. Because of the poor specificity of serologic tests and the low probability that a patient with only nonspecific symptoms has Lyme disease, it is likely that the diagnosis of Lyme disease was inaccurate in many of these patients. 31-36 The frequencies of reported increases in symptoms and of increased difficulties with typical daily activities were consistently lower (statistically significantly lower in a number of specific categories) among the patients who met the surveillance case definition for Lyme disease than among those who did not meet this case definition. In the matched cohort study, even though patients who did not meet the case definition were included, there were few significant differences between the patients and matched controls in reported increases in symptoms or in difficulties with typical activities. Patients did report increased joint or muscle pain and difficulties in their abilities to formulate ideas more frequently than did matched controls. However, the magnitude of these differences was relatively small, and if a correction in the P value considered to be statistically significant had been made to compensate for the effect of making multiple comparisons (the more comparisons made, the greater the likelihood that, by chance alone, 1 or more of them will be statistically significant), these differences would not be statistically significant. 37 Moreover, it is likely that there is some degree of reporting bias that occurs after a patient is diagnosed as having Lyme disease (ie, patients who have been told they have Lyme disease may be more likely than the general population to report minor joint or muscle pains).

This study has some potential limitations. Although the controls reported that they had not had Lyme disease, we did not confirm this serologically. However, the prevalence of seropositivity in the general population of the area is relatively low (<5%), so that it is unlikely that the results of the study would be significantly affected by misclassification as a control of someone who previously had been infected with Borrelia burgdorferi. 38 Moreover, the significance of asymptomatic infection with Borrelia burgdorferi is unknown. We were unable to enroll a substantial number of the potential patients who had been randomly selected from among all patients who had been reported to the Connecticut Department of Public Health. However, in most instances we were unable to contact the patients because the report form did not have adequate contact information available. It is unlikely that this introduced a systematic bias into the study. Finally, we relied on reports from patients (or their parents, in the case of children); we did not examine the patients. However, we did carefully review the medical records and reported functional outcomes of all patients to confirm their reports. Moreover, the results of the SF-36 were consistent with our other results that indicated that outcomes of patients reported to have had Lyme disease generally are excellent. The results of a recently published study of the outcomes of persons on Nantucket Island who previously were treated for Lyme disease are similar to ours. 39 This study does not indicate that all patients with Lyme disease have favorable outcomes. Indeed, there is good evidence that in rare instances they may experience complications—particularly recurrent arthritis in patients who are not treated promptly and who have a genetic predisposition to develop an autoimmune-mediated arthritis. 40-42 However, the large size of our sample and the generally excellent overall outcomes of the patients should reassure both patients and physicians that the prognosis for most patients with Lyme disease who receive conventional antimicrobial treatment is excellent.

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LONG-TERM OUTCOMES OF LYME DISEASE


Nature—that is, biological evolution—has not fitted man to any specific environment. . . . Among the multitude of animals which scamper, fly, burrow, and swim around us, man is the only one who is not locked into his environment. His imagination, his reason, his emotional subtlety and toughness, make it possible for him not to accept the environment but to change it. And that series of inventions by which man from age to age has remade his environment is a different kind of evolution—not biological, but cultural evolution. I call that brilliant sequence of cultural peaks The Ascent of Man.
—Jacob Bronowski (1908–1974)