GARY SMITH, DPHIL ■ E. PAUL WILEYTO, PHD MS ROBERT B. HOPKINS ■ BRYAN R. CHERRY, VMD JOHN P. MAHER, MD MPH

Risk Factors for Lyme Disease in Chester County, Pennsylvania

Dr. Smith, Dr. Wileyto, and Mr. Hopkins are with the Section of Epidemiology and Public Health, University of Pennsylvania School of Veterinary Medicine, Kennett Square, Pennsylvania. Dr. Smith is Professor of Population Biology and Epidemiology, Dr. Wileyto is a Research Specialist, and Mr. Hopkins is a Research Technician. Dr. Cherry is a Public Health Veterinarian, New York City Department of Health. Dr. Maher is County Health Director, Chester County Health

SYNOPSIS

Objective. To identify factors associated with increased or decreased risk of infection for Lyme disease in Chester County, Pennyslvania.

Methods. The authors designed an unmatched case-control study involving 294 incident cases reported to the Chester County Health Department in 1998 and 449 controls selected by random digit dialing. All case and control participants were interviewed by telephone.

Results. Age is a risk factor for Lyme disease for groups aged 10–19 years old and 50 years or older. Sex was not a risk factor. Incidence of Lyme disease in a rural setting was three times the incidence in an urban setting. Increased risk also was associated with living in single family homes, homes with yards or attached land, woods on the land, signs of tick hosts seen on the land, and homes within 100 feet of woodland. Gardening for more than four hours per week was also a risk factor, but most other outdoor activities were not. Twice as many participants took protective measures against tick bites before outdoor employment than those who merely ventured into the yard or land associated with the home. Only checking for ticks during outdoor activity and the use of repellents prior to outdoor activities outside the yard were unequivocally associated with a reduced risk of Lyme disease.

Conclusions. It is important to increase public awareness about the risk of acquiring Lyme disease from ticks in the immediate environment of the home.

Address correspondence to:

Dr. Smith, 382 West Street Rd., New Bolton Center, Kennett Square PA 19348; tel. 610-444- 5800, x 2312; fax 610-925-8123; e-mail <garys@vet.upenn.edu>.

yme disease is caused by infection with the spirochete Borrelia burgdorferi, which in the eastern United States is transmitted to humans by infected Ixodes scapularis ticks. I. scapularis, commonly called the black-legged or deer tick, has a characteristic arrowhead shape (rounded behind, pointed in front) and when unfed, these ticks appear to vary in color from reddish brown to black. They are easily distinguished from dog ticks (and some others) because they have no white markings dorsally. Although much is made of the small size of *I. scapularis*, in our experience even unfed I. scapularis nymphs and adults (the stages which present most risk to people) are easily seen by the naked eye. The ticks get bigger as they feed. Engorged nymphs are about the size of peppercorns and engorged adults are about the size of a pea. Female adult ticks are commonly found feeding on white tailed deer. As they feed, they can exhibit a wide range of colorations, from beige with pink tones to the dark, gunmetal gray of fully engorged adult females. Feeding females are frequently found with small, dark, unengorged adult males. This array of colors and sizes leads to much confusion among hunters, for example, who often claim that there are several different species of tick present.

The black-legged tick is common throughout much of the eastern United States, and is most easily found in wooded areas, although it occurs in a variety of habitats, including lawns. Its wide host range includes people, which accounts for the zoonotic nature of Lyme disease. The largest focus of Lyme disease in the eastern United States encompasses the north and north central states. Lyme disease is common in the state of Pennsylvania, for example, with 13,020 cases reported from 1992 to 1998.¹ In 1999, the crude annual incidence of Lyme disease in the 10 Health Planning Districts of Chester County, Pennsylvania, ranged from 80.4 to 397.8 cases per 100,000 people.²

The US Food and Drug Administration approved the first human vaccine against Lyme disease in 1998.³⁻⁶ However, Sigal, *et al.*, recommended that vaccination "should never be the main strategy of personal precaution" for individuals at high risk of tick bite³ because vaccine efficacy is less than 100% and its efficacy and safety have been tested so far in only a restricted range of people.³⁻⁶ Also, the vaccine is directed against *B. burgdorferi* sensu stricto only, and cross protection against other strains is unlikely.⁶ In addition, the ixodid ticks which transmit *B. burgdorferi* in the eastern and mid-western US also transmit other serious pathogens.⁶ The clear implication is that in high-risk areas, even those who are

vaccinated should continue to practice measures to lessen their risk of tick bites. We can best advise those at risk if we can discover where most cases of Lyme disease are acquired and what activities are associated with an increased or decreased risk of infection. This was the objective of the study reported here.

The authors know of only four previous case-control studies that reported on risk factors for Lyme disease in the US. The first dealt with Lyme disease acquired in California, matching cases with controls on the basis of age, sex, and neighborhood.7 A case was defined in that study as a physician-diagnosed instance of erythema migrans (the characteristic rash) and, thus, excluded those cases in which this pathognomonic feature was absent. Despite many suggestive associations, the only statistically clear associations with an increased incidence of Lyme disease were those pertaining to the observation of deer and lizards around the home, a history of exposure to ticks, and the use of maintained trails for more than five hours per week. The second study⁸ used geographical information system technology to compare the exterior residential environments of Lyme disease cases reported in 1990 in Baltimore County, Maryland, with randomly selected control residences. In that study, the case definition met the Centers for Disease Control and Prevention (CDC) surveillance definition for 1989-90 (erythema migrans or laboratory confirmation of infection plus one or more of the late stage skeletomuscular, neurological, or cardiac manifestations). The findings indicated that the risk of disease decreased in relation to the increasing distance of a home from the forest edge, and that highly developed neighborhoods, such as those with multiunit residences, tended to be associated with a reduced risk of disease. In the third study, the presence of both deer ticks and moist humus and leaf litter in the yard were found to elevate the risk of acquiring physiciandiagnosed Lyme disease in children in Delaware.9 The fourth study of Lyme disease, conducted in Hunterdon County, New Jersey, matched 51 physician-diagnosed cases with 51 controls on the basis of age and sex.¹⁰ The risk factors identified were living in a rural residence, clearing brush in the yard during spring and summer, the presence of rock walls, and bird feeders or deer on a residential property.

The interpretation of the results of these studies was hampered by small sample sizes. The large number of incident cases reported in Chester County, in contrast, afforded us an opportunity to improve upon the statistical power of previous case-control studies. We were particularly interested in (a) testing the consistency of previously identified risk factors, including living in a rural residence in a low density development near a forest edge, and observation of ticks and tick hosts on residential property; (b) determining if, and which type of, outdoor activities elevate the risk of disease; and (c) determining which, if any, of the recommended protective behaviors reduce the risk of acquiring Lyme disease (using insect repellents, wearing long pants, or using compounds that kill ticks, for example.)

METHODS

We used an unmatched case-control study design based on telephone interviews with 294 incident cases and 449 controls to identify risk factors associated with acquiring Lyme disease. The research protocol was approved by the University of Pennsylvania Committee on Studies Involving Human Beings.

Population and recruitment. The source population consisted of all residents of Chester County from January 1 through December 31, 1998. Chester County is a largely rural part of the greater Philadelphia area. It occupies 760 square miles and in 1998 had an estimated population of 421,686.¹¹

A case was defined as any person reported to the Chester County Department of Health (CCHD) as having been diagnosed in 1998 with Lyme disease under the current CDC surveillance case definition (erythema migrans or laboratory confirmation of infection plus one or more of the late stage skeletomuscular, neurological, or cardiac manifestations). To maintain the privacy of those who did not wish to participate in the study and to ensure compliance with applicable laws governing reportable diseases and confidentiality, the CCHD mailed letters to all residents (including parents of children) infected with Lyme disease as reported by the CCHD data base for 1998. Of 778 reported cases, 334 respondents returned signed consent forms to the CCHD, which then released to the authors the name, address, and telephone number of each respondent. The authors began confirming participation in July 1998, continuing the recruitment process through March 1999 in order to accommodate reporting lags.

A control was defined as anyone resident in Chester County during all of 1998 not reported as having Lyme disease between November 1, 1997, and December 31, 1998. Telephone calls were made to the three-digit prefix codes for which there was a greater than 90% probability that the corresponding home addresses were in Chester County. A commercial company that specializes in random digit dialing techniques generated a list of 554 potential controls.

Strategies to encourage participation. In the weeks preceding the recruitment of cases and controls, and at intervals thereafter, the authors issued a series of press releases to newspapers and radio stations serving the Chester County area. These publicized the objectives of the study to encourage participation and to establish legitimacy for the initial contact. All recruitment letters and consent forms were printed in Spanish and English. We sent one or two additional letters to those not responding to the initial letter from the CCHD.

Beginning in April 1999, everyone on the list of eligible controls was called to verify the telephone number and to arrange a time for a telephone interview. The conversations were conducted in Spanish whenever necessary. If participation could not be confirmed in two successive telephone calls (due to no reply or an ambiguous response), the eligible control was sent one last formal letter of request. Some cases and controls were minors (defined as less than 18 years of age) for whom we received written agreement to participate from the appropriate adult caretaker.

Data collection. We used a telephone interview with a standard questionnaire to collect data on putative risk factors for Lyme disease. Interviews were conducted by two of the authors and by six part-time workers who were employed on the basis of a good telephone manner and the ability to make calls outside office hours. The parttime interviewers were trained during real telephone conversations with the principals to adhere to a predefined script and to accurately record responses on prepared data sheets. The first few actual interviews were supervised by one of the principals. The interviewers knew when they were speaking to a case or a control but were required to adhere to a strict protocol (script) prior to and during the administration of the questionnaire to avoid bias. Spanish-speaking interviewers were available at all times to administer the questionnaire. Minors were questioned directly if that seemed reasonable and the adult caretaker had no objections; otherwise, we relied on surrogate responses from the caretaker. The questionnaire contained 205 questions and took from 17 to 30 minutes to complete. The interviewers were directed to make it clear that responses should pertain to the calendar year 1998. All interviewers were knowledgeable about Lyme disease and were encouraged to continue conversing after completing the questionnaire if the interviewee had questions. Case interviews took place from October 1, 1998, through March 31, 1999; control interviews were conducted from April 1 through October 31, 1999.

Questionnaire responses were handwritten on prepared forms during the telephone interview and then coded for transcription into a Microsoft Access database.

Data analysis. Almost all of the odds ratios presented in this paper have been adjusted for age of subject and residential setting. This removes the effect of these potential confounding influences from the estimate of the odds ratio associated with the factor of interest. With this exception (and those few instances where we considered several levels of the same risk factor), what we present here is a univariate, rather than a multivariate, analysis of the data. It is conventional to perform a univariate analysis prior to a multivariate analysis in order to screen those variables that might be useful in the final model. We cover in this paper only a fraction of all the potential risk factors considered in our study; we have postponed a multivariate analysis until the univariate screen of the entire data set is complete.

Selected items from the questionnaire are grouped in the following categories: age, type (apartment, single family home) and setting (urban, suburban, or rural, as specified by respondent) of the respondent's residence; proximity of respondent's home to woodland; direct sightings of and markers for tick host activity in the land immediately around the respondent's residence; domestic activities (indices of gardening); outdoor employment; outdoor recreation; and behaviors intended to prevent infection.

We performed the analysis using statistical tools available in STATA.¹² A Mantel-Haenszel odds ratio was calculated for each potential risk factor.¹³ We also calculated the appropriate nested (80%, 95%) confidence intervals, as well as the associated P-value, in order to provide a broad set of criteria for evaluating the importance of the factor under study.¹⁴ Only the 95% confidence interval is reported in the main text. Continuous variables were categorized into exposure levels *a posteriori*, based upon their distribution. The actual grouping used depended upon what was intuitively reasonable for the given factor and the requirement that no single level should contain a particularly small number of people. Mantel-Haenszel tests for trend were calculated for all factors with more than two levels.

RESULTS

Recruitment of cases and controls. Interviews were completed for 294 of 778 cases reported to the Chester

County Health Department in 1998, and for 449 of the 554 potential controls made known to us by the random digit dialing procedure. We define the refusal rate as the proportion of people we were not able to interview, for whatever reason. The refusal rate among cases (59%) was significantly greater than the refusal rate among controls (19%) $\chi^2 = 206.9$, df = 1, P <0.001). The ratio of interviewed cases to interviewed controls was 1:1.5. The mean age of cases (n = 294) with completed interviews was 40.8 (standard deviation ± 21.7). The mean age of cases (n = 39) who actively declined our invitation to participate was 45.2 (standard deviation ± 24.3), whereas the mean age of case subjects who did not respond to recruitment attempts (n = 350) was 34.2 (standard deviation ± 21.1).

There were some specific differences, too, in the observed ratios by sex. The percentage of men among cases with completed interviews was 48.3%, whereas the percentage of men among the cases who did not respond to recruitment attempts was about 10% higher, or 59.2%. We also were able to examine differences in age and sex ratios for the various groups of candidate controls. The mean age of controls with completed interviews was 37.8 years (standard deviation \pm 20.6). The mean age of controls that declined the initial approach was 50.5 (standard deviation \pm 26.9), the mean age of controls who declined the subsequent approach by our staff at the University of Pennsylvania was 40.4 (standard deviation \pm 27.3), and the mean age of controls who later proved to be unreachable or evasive was 36.7 years (standard deviation ± 22.3). There were no noteworthy differences in the sex ratios for any of the candidate groups of controls.

Given the high refusal rate among cases, we examined the distribution of symptoms and manifestations reported to the CCHD for all cases in 1998 (Table 1). None of those who actively declined our invitation to participate (n = 39) had any of the more serious long term symptoms usually associated with Lyme disease in Chester County. Those who neglected our invitation to participate (n = 350) reported proportionately more arthritis than those we interviewed (46% compared with 41%) and fewer instances of erythema migrans, the "bull's-eye" rash (58% compared with 66%). Those who were unreachable or evasive after having initially agreed to participate (n = 33), or those for whom we could not complete an interview (n = 7) reported proportionally less arthritis than interviewed cases (27% compared with 41%), and higher occurrences of Bell's palsy (15% compared with 5%), radiculoneuropathy (6% compared with 3%), and encephalitis (6% compared with 2%). In short, the prevalence of late manifestations of Lyme disease was

Symptoms and manifestations	Completed interview (n = 294)	Declined invitation to participate (n = 39)	Ignored invitation to participate (n = 350)	Other (n = 40)
	Percent			
Erythema migrans (diameter >5cm)	66.3	57.4	58.4	63.6
Arthritis (brief attacks or swelling)	40.8	40.4	45.9	27.3
Bell's palsy	5.1	6.4	7.4	15.2
Radiculoneuropathy	3.4	0.0	4.2	6.1
ymphocytic meningitis	2.7	0.0	1.1	3.0
ncephalitis/encephalomyelitis	1.7	0.0	1.1	6.1
nd or 3rd degree atrioventricular block	0.7	0.0	0.0	0.0
Required hospitalization	3.7	0.0	4.5	0.0

Table 1. Symptoms and manifestations of Lyme disease among cases reported to the Chester County (PA) Health Department in 1998, distributed by responses to requests for participation in study (N = 723)

higher among those cases that initially agreed to participate than among cases that actively declined to participate or simply ignored our approach.

Age, sex, and residential setting. Age is a risk factor for Lyme disease. There were proportionately more cases than controls in the age groups 10–19 and 50 years or older (Figure). A chi-square test of homogeneity showed a significant difference between the age distribution of interviewed controls and interviewed cases ($\chi^2 = 18.16$, df = 8, *P* = 0.02). Crude odds ratios calculated using the group 0-9 years of age as the comparison were: 10–19 years (odds ratio = 1.90; confidence interval 1.02, 3.54); 20–49 years (odds ratio = 1.04; confidence interval 0.64, 1.67); 50 years or older (odds ratio = 1.70; confidence interval 1.03, 2.79).

Previous studies have found that the reported incidence of Lyme disease for men was higher than for

women, especially for ages 5–19 and 60 or older.¹ There was no evidence of this difference in our study. The sex of interviewed cases and controls was almost identical (48.30% of the cases were men and 48.88% of the controls were men). We examined the relationship between sex and Lyme disease after stratification by age of participant (grouped by decade). In most age groups, the sex ratios in cases and controls did not differ from expected values. Although there were proportionately more females than males among the cases at ages 30-39 (odds ratio = 2.45; confidence interval 1.08, 5.55), this is the reverse of the usually reported association.1 The Breslow-Day test of homogeneity ($\chi^2 = 12.14$, P = 0.096) indicated that while the odds of Lyme disease might vary by sex for ages 30-39, we could not reject the hypothesis that the odds ratios were, in fact, the same for all age groups (Mantel-Haenszel combined estimate for being male as a risk factor, odds ratio = 1.05; confidence interval 0.77, 2.05).



Residential setting was important. Only 39 (5.25%) of those interviewed said that they lived in an urban setting; 563 (75.77%) said that they lived in a suburban environment and 141 (19.98%) said they lived in a rural environment. The incidence of Lyme disease among those who lived in a suburban setting was more than twice that of those who lived in an urban setting (odds ratio = 2.29; confidence interval 1.03, 5.10, adjusted for age). The incidence of Lyme disease among those who lived in a rural setting was three times that of those who lived in a rural setting (odds ratio = 3.09; confidence interval 1.30, 7.27, adjusted for age).

In summary, age and residential setting appeared to be risk factors for Lyme disease, but sex was not. There were good *a priori* reasons to hypothesize that both age and residential setting also would be associated with other variables, such as gardening and occupation, examined in this study. Therefore, we stratified by age and residential setting.^{13,15} For that reason, all odds ratios presented below have been adjusted for the effect of both age and residential setting, without formally testing the hypothesis of confounding (or interaction) by age and residential setting for each variable.

Univariate analysis. The odds ratios associated with each risk factor are given in Tables 2–4. In summary, residence in a single family home increased the risk of Lyme disease between two and three times (odds ratio = 2.48; confidence interval 1.57, 3.90). Oddly, occupancy of a house in a residential setting in which nearby houses were of mixed ages was a lower risk than if the nearby houses were all older, younger, or of the same age as the affected residence (see Table 2). Respondents who had occupied their homes for more than 15 years had almost

Risk factor	Odds ratio	80% CI	95% CI	Р
Single family home ^a	2.48	1.84, 3.33	1.57, 3.90	<0.001
Urban ^b (n = 39)	1.00			
Suburban ^b (n = 563)	2.20	1.30, 3.73	0.98, 4.94	0.049
Rural ^b (n = 141)	2.96	1.66, 5.29	1.22, 7.18	0.012
Age of home ^c	1.99	1.04, 2.51	0.82, 3.18	0.158
Relative age of nearby housing [®]				
Younger	2.67	1.66, 4.29	1.28, 5.52	0.006
Same	1.76	1.30, 2.38	1.11, 2.79	0.015
Older	2.67	1.52, 4.67	1.13, 6.28	0.019
Mixed	1.00			
Number of years lived in home ^a				
0-4	1.00			
5–9	1.53	1.15, 2.03	1.00, 2.37	0.045
10–14	1.11	0.77, 1.51	0.66, 1.86	0.683
>15	1.75	1.20, 2.28	1.07, 2.84	0.022

Table 2. Residential risk factors for Lyme disease among cases reported to the Chester County (PA) Health Department in 1998 (N = 743)

NOTE: A Mantel-Haenszel odds ratio, weighted for differences in the distribution of numbers among strata where applicable

^aAdjusted for age and urban setting

^bAdjusted for age. Different sample totals in different tables reflect differences in the number of usable responses. ^cAdjusted for age (40–49 years compared with 0–9 years) of case subject and urban setting

twice the risk of Lyme disease than those who lived in their homes for shorter periods (odds ratio = 1.75; confidence interval 1.07, 2.84). This was true even after adjustment for age of respondent and residential setting.

A yard or land attached to the home (odds ratio = 4.53; confidence interval 1.12, 18.21), or woods within 100 feet of the home (odds ratio = 4.26; confidence interval 1.71, 10.59), increased the risk of Lyme disease by a striking four to five times. This was true even after adjustment for residential setting. Having woods in a yard or land attached to the home increased the risk even further (odds ratio = 2.62; confidence interval 2.11, 3.26). If tick hosts (deer or mice) were sighted on the land attached to the home, or if there were rock walls or woodpiles that might provide suitable habitat for *Peromyscus leucopus* (the white footed mouse), the risk of Lyme disease

increased two to three times over yards or land with no obvious host habitat or host sightings (see Table 3).

Indices of gardening activity or yard work also were associated with an increased risk of Lyme disease (Table 4). In particular, the risk almost doubled if the respondent engaged in gardening activities for more than four hours per week (odds ratio = 1.83; confidence interval 1.21, 2.54).

Most indices of outdoor activity outside the yard or land attached to the home, including employment, showed no increase in risk of disease, with some exceptions (see Table 4). Risk increased by about half for parents with children who participated in outdoor sports (odds ratio = 1.64; confidence interval 1.12, 2.41) and for respondents who picnicked either in the countryside outside of parks or within parks but outside designated pic-

D:1 C	Odds ratio	80% CI	95% CI	Р
Risk factor				
Proximity of home to woods				
0–99 feet (n = 334)	4.26	2.34, 7.72	1.71, 10.59	<0.001
100-299 feet (n = 152)	2.37	1.27, 4.41	0.91, 6.13	0.068
300 feet–1 mile (n = 212)	2.00	1.09, 3.66	0.79, 5.04	0.135
>1 mile (n = 38)	1.00			
A yard or land attached to home ^a	4.53	1.83, 11.25	1.12, 18.21	0.020
Does having woods in the yard increase risk? ^a	2.62	2.11, 3.26	1.88, 3.65	<0.001
Does using woods in or near the yard for recreation				
or play increase the risk? ^a	1.63	1.21, 2.20	1.03, 2.57	0.032
For homes with a yard				
Leave feed for mammals	1.70	1.28, 2.26	1.10, 2.63	0.016
Leave feed for birds	1.58	1.28, 1.95	1.15, 2.19	0.005
Deer observed	2.71	2.18, 3.38	1.94, 3.79	< 0.001
Deer damage to trees	1.46	1.14, 1.88	1.00, 2.14	0.046
Deer damage to shrubs	2.43	1.99, 3.02	1.73, 3.40	< 0.001
Mice observed	1.97	1.59, 2.45	1.42, 2.75	<0.001
Rock walls on property	1.97	1.60, 2.41	1.44, 2.68	< 0.001
Woodpiles on property	2.84	2.28, 3.54	2.03, 3.98	< 0.001

Table 3. Periresidential risk factors for Lyme disease among cases reported to the Chester County (PA)

NOTE: A Mantel-Haenszel odds ratio was used, weighted for differences in the distribution of numbers among strata where applicable.

^aAdjusted for age and urban setting

Health Department in 1998				
Risk factor	Odds ratio	80% CI	95% CI	Р
Indices of gardening activity				
Use one or more electrical tools	1.51	1.22, 1.88	1.08, 2.11	0.014
Use one or more gasoline tools	1.39	1.12, 1.71	1.01, 1.91	0.043
Unpowered hand tools				
No tools (n = 220)	1.00			
I-4 tools (n = 170)	1.34	1.01, 1.76	0.87, 2.04	0.181
5–9 tools (n = 181)	1.61	1.18, 2.19	1.00, 2.58	0.047
10–15 tools (n = 106)	2.00	1.40, 2.85	1.16, 3.44	0.011
>15 tools (n = 51)	2.63	1.67, 4.13	1.32, 5.25	0.004
Hours per week spent doing yard work in spring and summer				
None (n = 215)	1.00			
I–4 hours (n = 272)	1.28	0.99, 1.67	0.92, 1.79	0.216
5–9 hours (n = 139)	1.83	1.33, 2.54	1.21, 2.78	0.014
>10 hours (n = 101)	1.73	1.20, 2.48	1.09, 2.75	0.049
Employment				
Have an outdoor job	0.73	0.55, 0.97	0.45, 1.13	0.156
Have a job that takes you into woods	0.53	0.32, 0.88	0.15, 2.16	0.104
Have a job that takes you into woody margins	0.67	0.43, 1.02	0.34, 1.28	0.226
Being a parent (parental age >20 years)				
A parent	1.36	1.06, 1.75	0.92, 2.01	0.116
Have children who participate in outdoor sports	1.64	1.28, 2.11	1.12, 2.41	0.011
Outdoor recreation				
Engage in any outdoor recreation	1.26	0.84, 1.88	0.68, 2.32	0.468
Visit parks	0.51	0.39, 0.68	0.34, 0.79	0.002
Fish	0.84	0.66, 1.08	0.58, 1.22	0.371
Hunt	0.80	0.51, 1.27	0.40, 1.62	0.542
Ride horses	1.23	0.84, 1.82	0.68, 2.22	0.476
Camp in a tent	0.67	0.51, 0.89	0.44, 1.03	0.068
Camp in an RV	0.96	0.64. 1.44	0.52, 1.77	0.916
Walk or jog outdoors	1.36	1.05, 1.76	0.92, 2.01	0.121
Walk or jog in woods				
0-9 years of age	3.19	1.76. 5.79	1.29, 7.87	
10–19 years of age	2.30	1.27, 4.15	0.93, 5.66	
20-49 years of age	0.88	0.64, 1.20	0.54, 1.41	
>50 years of age	1.84	1.31, 2.61	1.08, 3,13	
All ages	1.48	1.21, 1.90	1.09, 2.00	0.012
Picnic in designated areas in parks	1.17	0.96, 1.42	0.86, 1.59	0.313
Picnic outside parks or in non-designated areas in parks	1.47	1.16, 1.88	1.02. 2.12	0.039

Table 4. Outdoor activities as risk factors for Lyme disease among cases reported to the Chester County (PA)

NOTE: A Mantel-Haenszel odds ratio was used, weighted for differences in the distribution of numbers among strata where applicable.

nic areas (odds ratio = 1.47; confidence interval 1.02, 2.12). Walking or jogging in woodland also was associated with increased risk for ages younger than 10 (odds ratio = 3.19; confidence interval 1.29, 7.87) or older than 50 (odds ratio = 1.84; confidence interval 1.08, 3.13). This was the only instance in which the Mantel-Haenszel test of homogeneity indicated the odds of disease differed by age strata. We found it baffling that respondents who preferred to visit particular parks on a regular basis were at lower risk than those who had no preference (odds ratio = 0.51; confidence interval 0.34, 0.70).

We asked respondents if they had used insect repellents, worn long pants, worn light colored clothing, tucked pants legs into sock tops, and used compounds that kill ticks (acaricides). Only one of these strategies appeared to reduce the risk of Lyme disease (use of insect repellents before work or recreation outdoors away from home, odds ratio = 0.70; confidence interval 0.56, 0.95). Using acaricides before working or playing in the yard was actually associated with an increased risk of Lyme disease (odds ratio = 1.76; confidence interval 1.03, 3.01). We also found that a greater proportion of respondents took protective action before outdoor recreational activities or employment than before simply venturing into the yard or land near home. For example, 44% of all respondents reported using insect repellents before recreational activities or employment outside the yard, whereas only 22% reported using insect repellents before yard work. Similarly, 17% used acaricides before recreational activities or employment outside the yard, whereas only 9% used acaricides before yard work.

The most common preventive measure was checking for ticks: 82% of respondents reported checking for ticks either during outdoor activity (n = 13) or after outdoor activity (n = 267), or both during and after outdoor activity (n = 324). Only respondents who reported checking for ticks *during* outdoor activity were at lower risk for Lyme disease than those who did not check for ticks (odds ratio = 0.59; confidence interval 0.43, 0.80); respondents who checked for ticks *after* outdoor activity did not alter their risk. Those who reported finding ticks on their person while checking had similar risk to those who reported never finding ticks while searching (Table 5).

County, Pennsylvania, 1998				
Risk factor	Odds ratio	80% CI	90% CI	Р
Before working or playing in your yard, you:				
Apply insect repellents	1.16	0.91, 1.47	0.81, 1.67	0.419
Wear long pants.	1.23	1.03, 1.54	0.92, 1.72	0.140
Wear light colored clothing	1.03	0.84, 1.26	0.76, 1.40	0.852
Tuck pants leg into socks	1.50	1.06, 2.10	0.89, 2.52	0.124
Use acaricides	1.76	1.24, 2.50	1.03, 3.01	0.035
Before work or recreation outdoors away from home, you:				
Apply insect repellents	0.70	0.57, 0.86	0.56, 0.95	0.022
Wear long pants	0.78	0.64, 0.97	0.78, 1.07	0.118
Wear light colored clothing	0.88	0.72, 1.07	0.65, 1.19	0.396
Tuck pants leg into socks	0.83	0.64, 1.08	0.56, 1.24	0.361
Use acaricides	1.14	0.88, 1.20	0.77, 1.68	0.510
Check for ticks during outdoor activities	0.59	0.80, 1.31	0.48, 0.72	<0.001
Check for ticks after outdoor activities	1.02	0.99, 1.59	0.70, 1.50	0.898
Finding ticks during a search	1.26	0.43, 0.80	0.87, 1.81	0.223

Table 5. Case and control respondents' use of measures intended to prevent B. burgdorferi infection, Chester County, Pennsylvania, 1998

NOTE: A Mantel-Haenszel odds ratio was used, weighted for differences in the distribution of numbers among strata where applicable.

DISCUSSION

We studied the ways in which people differ in their risks of acquiring Lyme disease. Most of what we know about this area is derived from ecological studies.¹⁶⁻²⁰ These correlative studies, however, are subject to the ecological fallacy¹⁴ that individual and group characteristics are the same. As they may not be, it is sensible to buttress this considerable literature with methodologies that take explicit account of individual (rather than group) attributes. This is one advantage of the case-control study design.

Most of the previous case control studies of Lyme disease in the US7-10 were hampered by the small number (<101) of cases considered, which decreases their statistical power, especially after stratification. Despite the examination of dozens of plausible risk factors, only a few statistically significant associations were reported between the factors and an increased risk of Lyme disease. The larger number of cases and controls in our study enabled us to confirm previous findings and establish the validity of several associations that previously were merely suggestive. Most notably, we have confirmed the association between an increased incidence of Lyme disease and having woods or woodland near the home,^{8,10} and demonstrated that this manifests a "dose-response" effect in that the risk decreases with increasing distance between home and woods. Furthermore, unlike previous studies, every one of our direct and indirect indices of having potential tick hosts in the yard or land associated with the home was a significant risk factor for an increased risk of Lyme disease.7,9,10 We found no evidence that outdoor employment was a risk factor. On the other hand, activities in the yard surrounding the home, especially gardening, did increase the risk of Lyme disease. Ecological studies have provided good evidence that periresidential (infection acquired near the home) transmission is the principal mode of transmission of Lyme disease in the US.¹⁶⁻²⁰ The contrasting methodology of our case-control study provides independent confirmation of that assumption.

Ineffectiveness of protective measures? A perplexing result is the apparent inefficacy of the protective measures. We are not the first to find that the recommended protective measures appear not to be associated with odds ratios significantly less than one (which would signify a protective effect). Neither Ley⁷ nor Orloski¹⁰ and their colleagues found any significant protective effect. Indeed, Ley, *et al.*, found that those who wore long pants

almost all the time when outdoors apparently had an approximately four- to five-fold greater risk of infection (odds ratio = 4.83; confidence interval 1.04, 22.41). In our study, we interviewed almost three times the number of participants questioned by Ley, et al.,⁷ and almost six times the number questioned by Orloski, et al.¹⁰ Therefore, the finding is not due to lack of statistical power. We could explain the apparent lack of protective effect if those employing preventive measures were doing so because they know or suspect that they are entering a particularly high-risk environment. If the respondents in our study who used preventive measures were guided by educational campaigns that delineated where one might expect to find ticks, then we might expect that their use of preventive measures could have acted as a marker for some environmental risk factor. In such a case, the protective effect might be masked by exposure to the correspondingly high-risk environment.

Potential sources of bias. While we have no evidence that selection bias has compromised our results, the disparity of 7 years in mean age between interviewed cases (age 41) and eligible but non-responding cases (age 34) raises the possibility of some variance in relationships between at least one exposure (age) and disease.¹⁴ There were differences, too, in the symptoms of Lyme disease reported by different groups of cases. Because we know there were at least some systematic differences between the case participants we interviewed and those we did not, we cannot be certain our case population was fully representative for all risk factors of Lyme disease.

For administrative and financial reasons, we did not begin interviewing controls until five months after we interviewed our first case. It is possible this delay created a recall bias, especially in surrogate responses from adult caretakers of minors. For example, the age adjusted odds ratios for walking or jogging in the woods were significantly different from each other, with greatest risk (odds ratio = 3.19; confidence interval 1.29, 7.8) for children under 10 years old. Parents of infected children may have recalled more clearly than the parents of controls, due to the sometimes dramatic manifestations of Lyme disease in children (Bell's palsy), occasions when their children played or strayed into environments where they were at greater risk.

In doing only the univariate analyses now, we run the risk that unrecognized confounding between associated risk factors may have inflated the reported odds ratios of the univariate analysis in some instances.

CONCLUSIONS

In Chester County, those at highest risk for Lyme disease lived in single family homes with partially wooded land (or yard) attached to the home. Those who gardened, in both wooded and non-wooded yards, were at increased risk of disease compared with those who did not garden. The risk of Lyme disease increased with the proximity of the home to woodland. Outdoor recreational activities outside the yard, and outdoor employment were generally not associated with an increased risk of Lyme disease among residents of Chester County, although spectators at children's sporting events may need to exercise care, and picnicking outside designated areas is ill-advised.

Only two recommended preventive measures—checking for ticks *during* outdoor activity and the use of repellents prior to outdoor activities *outside* the yard—were unequivocally associated with a reduced risk of Lyme disease. Surprisingly, those who reported checking for ticks after outdoor activity were at no less risk of contracting Lyme disease than those who did not check for ticks at all. People are much less likely to employ preventive measures when they are inside the confines of their yards than when they are elsewhere, but it is clear that yards containing areas of woodland, especially yards in which there have been sightings or signs of tick hosts, are associated with substantial increases in the risk of Lyme disease.

It is important that educational programs designed to reduce Lyme disease incidence stress the risk of acquiring the disease in your own back yard. It is equally important that future research clearly establish whether or not the recommended personal protective measures that we espouse actually do reduce the risk of infection. While it might be reasonable to recommend avoiding tick habitats in parks and the countryside at large, it is not reasonable to expect that people will avoid entering their own back yards. We must be confident, therefore, that the personal protective measures we recommend are, indeed, effective.

This study was supported by Grant number U50/CCU314861, National Center for Infectious Diseases, Centers for Disease Control and Prevention.

The authors wish to acknowledge the technical assistance of Inese Benks, Kim Beson, Irma Campos, Vic Zittle, Mia Griffin, Nicorina Navarette, and Catherine Smith. Dr. Kathy Orloski (CDC) provided valuable commentary throughout the study.

References-

- Orloski KA, Hayes EB, Campbell GL, Dennis, DT. Surveillance for Lyme disease—United States, 1992–1998. In: CDC surveillance summaries, 2000 April 28. MMWR 2000;49(SS-3):1-11.
- Chester County (PA) Health Department. Lyme disease summary report 1988-2000. West Chester (PA): The Department; 2000.
- Sigal LH. Borrelia burgdorferi outer-surface protein A vaccine: importance, role, value. J Pediatr 1999;135:539-41.
- Sigal LH, Zahradnik JM, Lavin P, et al. A vaccine consisting of recombinant Borrelia burgdorferi outer-surface protein A to prevent Lyme disease. New Engl J Med 1998;339:216-22.
- Steere AC, Sikand VK, Meurice F, et al. Vaccination against Lyme disease with recombinant Borrelia burgdorferi outer-surface lipoprotein A with adjuvant. New Engl J Med 1998;339:209-15.
- Thanassi WT, Schoen RT. The Lyme disease vaccine: conception development and implementation. Ann Intern Med 2000;132:661-8.
- Ley C, Olshen EM, Reingold AL. Case-control study of risk factors for incident Lyme disease in California. Am J Epidemiol 1995;142:S39-S47.
- Glass GE, Schwartz BS, Morgan JM, et al. Environmental risk factors for Lyme disease identified with geographic information systems. Am J Public Health 1995;85:944-8.
- Klein JD, Eppes SC, Hunt P. Environmental and lifestyle risk factors for Lyme disease in children. Clin Pediatr 1996;35:359-63.
- Orloski KA, Campbell GL, Genese CA, Beckley JW, Schhriefer ME, Spitalny KC, et al. Emergence of Lyme disease in Hunterdon County, New Jersey, 1993: a case-control study of risk factors and evaluation of reporting patterns. Am J Epidemiol 1998;147:391-7.

- Bureau of Health Statistics. Chester county health profile 2000, H200.215P Harrisburg Department of Health (PA); Rev. 9/2000.
- Statcorp. Stata Statistical Software. Release 6. College Station (TX): Stata Corporation; 1999.
- Breslow NE, Day NE. Statistical methods in cancer research. Vol. I. The analysis of case-control studies. Lyon, IARC Scientific Publications No. 32; 1980.
- Rothman KJ, Greenland S. Modern epidemiology. 2nd ed. Philadelphia (PA): Lippincott Williams and Wilkins; 1998.
- Hosmer DW, Lemeshow S. Applied logistic regression. New York: John Wiley and Sons; 1989.
- Frank DH, Fish D, Moy FH. Landscape features associated with Lyme disease risk in a suburban residential environment. Landscape Ecol 1998;13:27-36.
- Mather TN, Nicholson MC, Donnelly EF, Matyas BT. Entomological index for human risk of Lyme disease. Am J Epidemiol 1996;144:1066-9.
- Dister SW, Fish D, Bros SM, Frank DH, Wood BL. Landscape characterization of peridomestic for Lyme disease using satellite imagery. Am J Trop Med Hyg 1997;57:687-92.
- Adler GH, Telford SR, Wilson ML, Spielman A. Vegetation influences the burden of immature *lxodes dammini* on its main host, *Peromyscus leucopus*. Parasitol 1992;105:105-10.
- Ostfeld RS, Cepeda OM, Hazler KR, Miller MC. Ecology of Lyme disease: habitat associations of ticks (*lxodes scapularis*) in a rural land-scape. Ecol Appl 1995;5:353-61.