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The Biological and Social Phenomenon of Lyme Disease

Alan G. Barbour and Durland Fish

Lyme disease, unknown in the United States two decades ago, is now the most common arthropod-borne disease in the country and has caused considerable morbidity in several suburban and rural areas. The emergence of this disease is in part the consequence of the reforestation of the northeastern United States and the rise in deer populations. Unfortunately, an accurate estimation of its importance to human and animal health has not been made because of difficulties in diagnosis and inadequate surveillance activities. Strategies for prevention of Lyme disease include vector control and vaccines.

Lyme disease is a zoonosis, an inadvertent infection of humans with an animal pathogen. In temperate regions of the Northern Hemisphere, ticks transmit the etiologic bacterium *Borrelia burgdorferi* from its usual wildlife reservoirs to humans and domestic animals (*1*, *2*). In the United States, Lyme disease occurs primarily in suburban and rural areas (*3*). Early infection of humans is usually a self-limited, flu-like illness with a skin rash where the tick imbeds itself (*4*) (Fig. 1). After a few weeks to several months, as many as 70% of untreated, infected patients suffer the effects of bacterial invasion of one or more distant organs or systems, including the brain, nerves, eyes, joints, and heart (*5*). These late manifestations, particularly the dysfunction of the central nervous system and chronic arthritis, are disabling but rarely fatal (*5*).

In the United States during 1991, 9465 cases of Lyme disease were formally reported, making it by far the most common arthropod-borne disease (*6*). The rising incidence and geographic spread of this zoonosis have interested the general public (*7*). Lyme disease probably ranks only behind acquired immunodeficiency syndrome in media coverage of infectious diseases in the United States over the last decade. News, public health programs, and patient advocacy groups have informed the public of the symptoms of Lyme disease and of ways to avoid infection (*8*). A less salubrious consequence of the attention has been the attribution to *B. burgdorferi* of a number of ills, only a fraction of which are likely to be Lyme disease (*9*, *10*). Wisconsin had 545 reported cases of Lyme disease in 1989; in the same year, 94,000 serum samples were received by reference laboratories in the state for Lyme disease testing (*11*). Georgia reported hundreds of cases of Lyme disease until it was documented that there were few ticks bearing *B. burgdorferi* in the state (*12*).

A provisional diagnosis of Lyme disease is often acceptable to patients with vexing, undefined illnesses, not only because there is hope for a cure with antibiotics but also because Lyme disease is acquired through what are generally perceived to be wholesome activities, such as hiking and working out-of-doors (*7*). The full extent to which people are being inappropriately treated with antibiotics cannot be estimated at present, but it is likely that a large minority, if not a majority, of the health care dollars expended on therapy for Lyme disease are for inaccurate diagnoses of *B. burgdorferi* infection (*9*, *10*). Some of these resources would better benefit the community if directed toward methods of disease prevention, such as vector control. A zoonosis can be characterized with respect to the microbiology of the agent, the ecology in relation to vectors and reservoir hosts, and the epidemiology of human disease. Full description of the phenomenon of Lyme disease will also require consideration of behavioral and economic factors in the response to the disease's emergence. These social factors are still poorly understood.

The Origins of Lyme Disease in North America

The clinical syndrome of *B. burgdorferi* infection had been described in Europe (*13*) more than six decades before Steere and colleagues in 1975 investigated an unusual cluster of childhood arthritis in the coastal community of Lyme, Connecticut (*14*). Soon after the Connecticut investigation, the relation between the arthritis and a prior episode of the characteristic skin rash, erythema migrans (Fig. 1), common in Europe, was noted (*15*). The search for an etiologic agent implicated a tick, *Ixodes scapularis* (*I. dammini*), as the vector on epidemiological grounds (*16*). The bite of a related species, *I. ricinus*, was known to cause erythema migrans in Europe (*17*). Identity between the two tick-borne conditions was established when *B. burgdorferi* was first isolated from *I. scapularis* and *I. ricinus* and then from patients in the United States and Europe with Lyme disease and erythema migrans (*18*).

The events leading to an epidemic of arthritis in residents of Lyme began several centuries earlier. Infections from *B. burgdorferi* probably occurred in North America before the first waves of European colonization. Erythema migrans, the hallmark of *B. burgdorferi* infection, was already present in midwestern and Pacific states at the time Lyme disease was first described in Connecticut (*19*). Early descriptions of colonial forests, the abundance of deer, and ticks annoying explorers suggest that the condi-

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tions for *B. burgdorferi* transmission were present in the Northeast hundreds of years ago (*20, 21*). The generally benign nature of acute *B. burgdorferi* infection relative to the debilitating and fatal effects of diseases plaguing North Americans through the 19th century may have contributed to its obscurity until a cluster of cases of childhood arthritis first brought it to wider attention on this continent.

The ecological changes in the northeastern and midwestern United States during this century are responsible for the recent emergence of Lyme disease as a public health problem (*1, 22*). The establishment of an endemic focus of *B. burgdorferi* in these areas is primarily dependent on ecological conditions favorable for deer. The white-tailed deer is a keystone host for *I. scapularis* populations, and the maintenance of *B. burgdorferi* is in turn dependent on the presence of *I. scapularis* (*23, 24*). Deforestation of much of the Northeast during the 18th and 19th centuries resulted in the near total elimination of deer, and presumably also of deer ticks (*20, 21*). However, deer were never totally eliminated from a few isolated areas, such as Long Island, New York (*20*). Both entomological collection records and polymerase chain reaction analysis of museum specimens document the presence of *B. burgdorferi* and *I. scapularis* on Long Island 50 years ago (*25*).

The abandonment of farms in New England and in suburban metropolitan areas elsewhere in the Northeast resulted in a change in the landscape through natural succession from open fields to eastern deciduous forests. As the forests returned, so did the deer. The invasion by *I. scapularis* of the increasingly reforested mainland from island refuges initiated the current epidemic of Lyme disease in the Northeast; the closest mainland community from Long Island's northernmost tip is Lyme. There is evidence that several independent mainland invasions by *I. scapularis* took place, resulting in early Lyme disease foci in central New Jersey, mainland Westchester County, New York, southeastern Connecticut, and eastern Massachusetts (*26, 27*). The population of *I. scapularis* in north-central states appears to be expanding its range independently from an indigenous relict population (*28*).

The threat of Lyme disease in wooded, suburban residential communities such as Westchester County (*29, 30*) has resulted in a new sense of conflict between humans and nature. Because the extremely small nymphs of *I. scapularis* commonly transmit *B. burgdorferi* to people, relatively few cases of Lyme disease are associated with recognized tick bites (*4*). The resulting fear of nymphal *I. scapularis* in residential yards, school grounds, and nature preserves has had a negative impact on public attitudes about deer and nature in some of the most desirable residential areas of the Northeast (*31*).

Maintenance of *Borrelia burgdorferi* in Nature

Lyme disease occurs in environments where the distributions of competent vectors, *B. burgdorferi*, and wildlife reservoir hosts overlap. Among *Borrelia* species, *B. burgdorferi* is remarkable in the variety of tick and vertebrate hosts it can infect; the several species that cause relapsing fever have much more limited ranges of hosts and vectors (*32*). Competent vectors involved in the transmission of *B. burgdorferi* to humans are members of the *I. persulcatus* group of ticks, including *I. scapularis* and *I. pacificus* in eastern and western North America, respectively, and *I. ricinus* and *I. persulcatus* of Europe and Eurasia, respectively (*33, 34*). Some species outside this group have also been shown as competent enzootic vectors (*35*).

The northern form of *I. scapularis*, which is responsible for more than 80% of the Lyme disease cases in North America, was described as a separate species, *I. dammini*, in 1979 (*36*). Although the northern and southern forms have distinguishable morphological and ecological characteristics, the species status of *I. dammini* has recently been rejected because of mating compatibility and genetic similarity between the two forms (*37*). The immature stages, larvae and nymphs, of the northern form feed on all terrestrial mammal species and on as many as half of the bird species that occur in the eastern deciduous-forest ecosystem (*38, 39*). Many mammalian and avian species are reservoir-competent and capable of infecting larvae with *B. burgdorferi* during their 4-day feeding event. The white-footed mouse, *Peromyscus leucopus*, is of primary importance as a reservoir species throughout the northern range of *I. scapularis*, but other small and medium-sized mammals, as well as birds, can also be important locally (*27, 38, 40, 41*). Engorged larvae molt and overwinter as nymphs, which seek hosts again the following summer. Infected nymphs transmit spirochetes to reservoir-competent hosts just before the maximum host-seeking activity of the next generation's larvae. The exploitation of reservoir hosts for the transmittal of spirochetes between tick generations in the near absence of inherited (transovarial) transmission results in infection rates that average 25% in unfed nymphs (*1, 41, 42*). Spirochete prevalence in adult ticks averages 50%, in part because an adult has two chances of acquiring an infectious blood meal, having fed as both a larva and a nymph. The prevalence of *B. burgdorferi* infection in vector-competent ticks varies geographically and is a good predictor of Lyme disease incidence.

The endemic cycle of *B. burgdorferi*, and the consequent epidemiology of Lyme disease, varies among geographic locations. In the southern United States, immature *I. scapularis* feeds primarily on lizards, which are reservoir-incompetent (*43*). Consequently, nymphal and adult infection rates are <1%, about the expected rate for transovarial passage (*44*). Spirochete infection rates are also 1 to 5% in *I. pacificus*. Although transovarial passage contributes to this infection rate, it is not sufficient to explain the maintenance of endemic foci in the western United States (*45*). A transmission cycle involving *I. neotomae* and the dusky-footed woodrat *Neotoma fuscipes* was found responsible for the maintenance of endemic foci in California. Because *I. neotomae* is host-specific and not anthropophilic, the few larval and nymphal *I. pacificus* that feed on reservoir-competent mammals rather than lizards are responsible for transmitting *B. burgdorferi* to humans (*33, 46*).

In Europe *I. ricinus* and in the former Soviet Union *I. persulcatus* have feeding

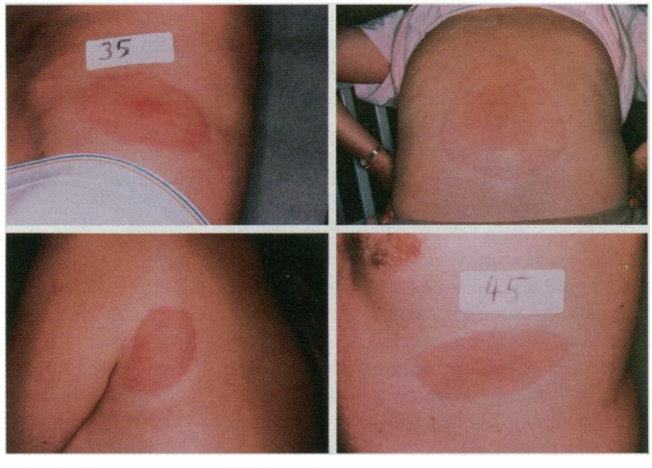

Fig. 1. Erythema migrans of the skin of patients at the Lyme Disease Diagnostic Center, Westchester County Medical Center, New York [Photograph courtesy of G. P. Wormser]

ecologies similar to that of northern *I. scapularis*: immatures feed primarily on mammals and birds (*47*). Consequently, spirochete infection rates in these tick species can be as high as that found in *I. scapularis* of the northeastern United States (*48*). Reservoir-competent hosts reported for *I. ricinus* include the mice *Apodemus flavicollis* and *A. sylvaticus* as well as a vole, *Clethrionomys glareolus* (*49*). The epizootiology of Lyme disease is more complex in Europe and Asia than in the United States because of the greater diversity of landscapes and ecology. Enzootic cycles involving the hedgehog tick, *I. hexagonus*, in Switzerland and the avian tick, *I. uriae*, in Sweden have been described (*50*). Recovery of organisms like *B. burgdorferi* from *I. ovatus* in Japan and *Haemaphysalis longicornis* in China (*51*), both of which primarily parasitize man and domestic animals, indicates even greater diversity of endemic cycles and vectors in Asia. A tick-associated disease similar to Lyme disease has been described in Australia (*52*), but the agent has not yet been successfully isolated from ticks, wildlife, or patients. There have been reports of *B. burgdorferi* in other tick species in North America, including *Dermacentor variabilis*, *I. cookei*, and *Amblyomma americanum* (*53*). Although borrelias can be acquired by these species during feeding, these ticks have not been shown to be competent for transmission of the borrelias to other hosts (*54*). The presence of spirochetes similar to *B. burgdorferi* in *A. americanum* in areas where competent vectors are absent is inexplicable.

Biology of *Borrelia burgdorferi*

Like other spirochetes, *B. burgdorferi* has a wavy shape and flagella that lie between the outer and inner membranes of the cell (*32*). All *Borrelia* sp. are host-associated bacteria and usually shuttle between a vertebrate and a hematophagous arthropod. They do not live in water, soil, or plants and are not transmitted by aerosols or fecal contamination. Although spirochetes are predominantly extracellular pathogens, they invade endothelial layers to pass into tissues, including the brain (*55*). Species of *Borrelia* differ from other spirochetes in that they have a chromosome and several extrachromosomal elements that are linear rather than circular (*56, 57*).

Most U.S. isolates, as well as some strains from western Europe, are still included under the original species designation *B. burgdorferi* (*58*). Other strains, such as those from northern and eastern Europe, Russia, and Asia, represent two other genomic groups, on the basis of DNA relatedness and ribosomal RNA sequences (*58*). A further justification for the division of extant *B. burgdorferi* strains into two or more species would be consistent differences between strains in their associated diseases. The most compelling evidence for this difference appears in the infrequency of joint swelling and inflammation as sequelae of acute infection in northern and eastern Europe as compared to the United States (*59*). This difference does not seem to result from acquisition bias. The absence of "arthritogenic" strains may help to explain the rarity of chronic arthritis after erythema migrans in regions of Europe and Russia. Aside from its taxonomic value, this difference in disease expression may provide insight into the pathogenesis of other chronic arthritides, such as rheumatoid arthritis, for which an etiologic agent is not known (*60*).

Two major contributors to antigenic distinctness of *B. burgdorferi* in North America are the surface-exposed lipoproteins OspA, the focus of vaccine efforts, and OspB (*61*). They or other lipoproteins are anchored in an outer membrane that is more fluid than that of Gram-negative bacteria (*62*). In the least variable of the two proteins, OspA (*63*), there are three major groups that differ from each other in their primary sequences by 21 to 23% (*64*). Both OspA and OspB are cotranscribed from an operon located on linear plasmids of about 50 kilobases (*56*). The ends of the linear plasmids are hairpins that most closely resemble in structure and sequence the telomeres of poxviruses and the iridovirus that causes African swine fever (*65*). The African swine fever virus and a related *Borrelia* species, *B. duttoni*, live in the same tick vector, *Ornithodorus moubata*, in Africa. The unusual genomic structure and organization of *Borrelia* sp. may be the result of a trans-kingdom genetic exchange in the past (*65*).

Dilemmas in Diagnosis and Case Management

In an area where there is a high incidence of Lyme disease, such as Westchester County, the presentation in July of a patient with low-grade fever, muscle aches, and erythema migrans (Fig. 1) poses few diagnostic or therapeutic problems (*66, 67*). On clinical and epidemiologic grounds, this condition would likely be early *B. burgdorferi* infection, and in most instances prompt treatment with oral antibiotics such as amoxicillin or doxycycline would be curative (*65, 68*). However, if a skin lesion is absent, a situation that may occur in 10% or more of infections (*4, 5*), nothing in the clinical presentation can clearly distinguish early Lyme disease from other acute, febrile summer illnesses of temperate latitudes. Later manifestations of Lyme disease, such as arthritis or carditis, can be attributed to other disorders. Neurologic symptoms, especially those involving changes in cognitive functions, are especially difficult to interpret (*69–71*). Moreover, factors such as the premorbid personality and a tendency to somatization may determine the length of convalescence and the response to postinfection fatigue and joint aches (*71, 72*). Even if the original diagnosis of Lyme disease is undisputed, lingering or recurrent symptoms, many of which are also characteristic of chronic fatigue syndrome or fibromyalgia, may not be attributable to persistent infection (*9, 10, 70, 73*).

In cases in which the hallmark skin rash is not observed, laboratory assays assume a more important role in diagnosis (*66, 67*). A tentative diagnosis would be validated by isolation of the agent from the patient, but this standard is seldom achieved in practice (*7*). After a few weeks of infection, *B. burgdorferi* is rarely if ever present in the blood; in other involved tissues, such as joints or nerves, organisms are scarce (*74*). The more commonly performed diagnostic procedure is a serologic test, usually an enzyme-linked immunosorbent assay at a commercial laboratory, for antibodies to *B. burgdorferi* at a single point in time. However, a positive serology result may be incidental to the patient's disorder. In areas without Lyme disease, 1 to 2% of residents have antibodies that sufficiently cross-react with *B. burgdorferi* antigens to give a false-positive test result (*75*). In some endemic areas, 10% of healthy residents have serologic evidence of past infection with *B. burgdorferi* (*75*). Skepticism about serologic assays has also been raised by surveys that show unacceptably high variation in results between different diagnostic laboratories (*76*). Test irreproducibility is attributable in part to lack of a standardized assay. In the absence of leadership by the federal government in standardizing assays and assessing proficiency, a cottage industry for Lyme disease testing has developed (*7*).

When opportunities or resources to confirm the presence of an infection by specific laboratory tests are nonexistent or limited, antibiotics are often used empirically (*77*). An inherent problem, though, for this empirical approach is the lack of a clear endpoint for treatment. Late Lyme disease is not likely to show a clear improvement within the time frame of the therapy, at least not for the standardly recommended period. Not surprisingly, there is controversy about whether the appropriate treatment duration for chronic Lyme disease is measured in weeks or months (*5, 68, 78*). When antibiotics are given parenterally for weeks, the direct and indirect costs of administration of drugs are considerable for patients and third-party payers (*79*). Studies of antibiotics for Lyme disease therapy have often been funded by pharmaceutical companies; the emphasis in these studies has been on antibiotics still under patent protection (*80*).

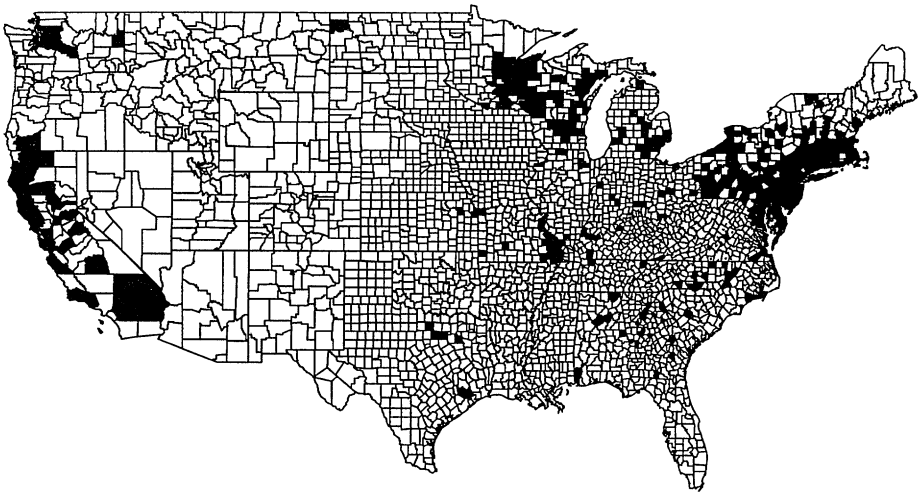

Fig. 2. Human cases of Lyme disease in the United States in 1990 by county. Counties with two or more cases of Lyme disease by criteria of the Centers for Disease Control (*83*) are shown in black. The map was produced by W. Paul and J. Montenieri, Centers for Disease Control, Fort Collins, Colorado.

Decisions on diagnostic criteria, treatment strategies, research-funding allocation, and insurance reimbursement are being made. Policy-makers are under pressure from some health professionals and lay persons who believe that the spectrum of *B. burgdorferi* disease is broader than the limits accepted by most peer-reviewed medical journals. The conditions in this larger set include degenerative, inflammatory, and neuropsychiatric conditions not previously thought to be ameliorated by antibiotics (*81*). Alternative views of diagnostic criteria and treatment strategies have been presented primarily at regional meetings sponsored by patient advocacy groups and in newsletters devoted to Lyme disease. More recently, the influence of these points of view on the last international scientific meeting on Lyme disease was such that several additional abstracts, which had originally been rejected, were permitted presentation (*82*).

Surveillance for Lyme Disease

Misdiagnosis and inappropriate treatment could be lessened by improved surveillance of known and emerging endemic foci. Clinical case distributions in the United States often do not coincide with the known geographic distribution of endemic foci (*83*). Travel to endemic foci accounts for only a small fraction of the disparities. As with other vector-borne diseases, a history of exposure to Lyme disease in an endemic area is an important consideration in diagnosis. Unfortunately, the need for active surveillance of Lyme disease comes at a time when state and local governmental budget cuts have reduced or eliminated many vector surveillance activities (*84*).

Current estimates of Lyme disease distribution are made principally from reports of human cases (Fig. 2). However, inasmuch as humans are not involved in the natural maintenance cycle of *B. burgdorferi*, the endemic status of this infection is not dependent on human involvement. Spirochetes are far more frequent in wildlife and in ticks than in humans (*67, 85*). In terms of surveillance, efforts to isolate the spirochete from ticks or reservoir hosts are more efficacious than isolation attempts from patients (*86*). Reservoir mice are particularly useful for surveillance because *B. burgdorferi* can be cultured from their internal organs or ear punch biopsies, and they are generally infected for life (*87*). Polymerase chain reaction analysis will most likely replace the use of cultures for this purpose (*88*).

Better knowledge of the geographic distribution and local abundance of vectors would improve assessments of human risk. Although a national tick survey is only now under way in this country (*12*), distribution maps for *I. ricinus* and *I. persulcatus* have been available for nearly 20 years in Europe and Russia (*89*). Methods for quantitative assessment of vector abundance and the application of remote sensing technology for the mapping of tick-borne disease distributions are more advanced in central Europe and the former Soviet Union than in the United States (*28, 90*). Decades of experience with and study of tick-borne viral encephalitis in Europe and Asia have resulted in accurate knowledge of the geographic distributions of *I. ricinus* and *I. persulcatus*.

The changing nature of the distribution and abundance of *I. scapularis* in the northern United States complicates the surveillance of this vector. Invasions into areas previously free of *I. scapularis* continue to occur (*91*), and establishment in new areas can be rapid and unpredictable (*92*); the ultimate limits of its distribution are uncertain. A steady increase in vector abundance at a single location in Westchester County has been observed over a period of 5 years (*27*). Such changes in vector abundance can cause difficulties in the prediction of risk and in the assessment of the efficacy of preventive measures, whether interventional or educational.

Prevention Through Immunization

Until recently there was no consensus that a human vaccine against Lyme disease was a realistic prevention strategy, let alone profitable for a company to produce. A vaccine for a more frequently fatal tick-borne disease, Rocky Mountain spotted fever, was taken off the market for lack of use (*93*). Moreover, human and animal studies indicate that the pathologic changes in Lyme disease are determined in part by the host's immune response (*94*). Until disease pathogeneis and immunity are better understood, the risk of provoking disease through vaccination cannot be accurately predicted. Because Lyme disease is rarely fatal, societal tolerance of untoward reactions from the vaccine would probably be low.

Despite these discouraging considerations, demand for preventive measures against Lyme disease has prompted efforts to develop a human vaccine for the disease (*95*). One justification for this effort is the accumulated evidence over the last decade that the morbidity from *B. burgdorferi* infection in highly endemic areas is considerable; in some areas, 10% of the population has been infected (*96*). Some patients with Lyme disease involving the joints or nervous system do not improve substantially even after parenteral antibiotic therapy (*69–71, 97*). Although doubts remain about many diagnoses of chronic Lyme disease, the specter of a large number of persons with unrelieved disabilities prompts further consideration of a *B. burgdorferi* vaccine for high-risk populations, such as outdoor workers and residents of endemic areas.

The feasibility of a human vaccine was demonstrated with experimental infections of animals. Passive and active protection against homologous challenge was obtained in hamsters immunized with killed *B. burgdorferi* cells (*98*). These findings were the basis for the commercially developed vaccine for dogs, which in an experimental infection study provided evidence of protection (*99*). However, because of concerns about the safety of whole-cell vaccines, the initial focus for a human vaccine has been on recombinant DNA products. Most work has been done on the OspA lipoprotein.

The ability of recombinant OspA to induce an immune response against *B. burgdorferi* was first demonstrated with rabbits and subsequently with mice and hamsters (*100, 101*). Mice immunized with recombinant OspA were protected against challenge from borrelias that were delivered by syringe and by tick (*101, 102*). The lipid moiety of OspA is necessary for protection in mice when no adjuvants or adjuvants approved for human use are used (*103*). Phase I human trials of recombinant OspA lipoprotein have begun (*104*).

Prevention Through Vector Control

Most vector-borne diseases are prevented through vector control and not by vaccines for humans. However, relatively few methods to control ticks that influence public health have been developed, in contrast to measures of mosquito control, for instance. Consequently, reduction of the risk of Lyme disease through reduction of tick exposure has been limited to insecticide use and personal protection measures. In regions where tick infection rates are low or where exposure is elective and occasional, personal protection measures may be adequate to minimize risk. However, in regions where tick infection rates are high and exposure is unavoidable, as in many suburban environments in the northeastern United States, the use of insecticides is the only effective means available to lower the risk of Lyme disease.

Ticks are susceptible to several chemical insecticides that are suitable for use in the environment or on hosts. Application of an insecticide directly to a tick-infested area is the most common method of control. However, because of the tick's life cycle of two or more years and the redistribution of ticks between each host-feeding event, several applications of an insecticide over a large area are necessary to suppress significantly tick populations of the *I. persulcatus* complex (*105*). Large area applications of DDT were successfully used to reduce morbidity from tick-borne encephalitis in Siberia (*106*), but only insecticides with the persistence of DDT provide long-term control. Although single insecticide applications reduced the abundance of nymphal *I. scapularis* on high-risk residential properties in Westchester County and Lyme, acceptance by the public and health agencies of such well-targeted insecticide use has been slow because of environmental concerns (*107*). Nevertheless, because of the prevalence of Lyme disease in suburban areas of the Northeast, the benefit of reduced tick abundance through annual insecticide application to lawns may outweigh potential environmental costs.

A novel approach to reduce the risk of Lyme disease through insecticides includes a self-delivery system for mice (*108*). Cotton, treated with permethrin insecticide and provided in paper tubes, is used for nesting material by the white-footed mouse. The application system is designed to render mice tick-free during the entire enzootic transmission season and, thus, prevent immature *I. scapularis* from either transmitting or acquiring *B. burgdorferi*. Although this technique was effective in one study in Massachusetts, it did not reduce risk measurably in three field tests in Connecticut and New York (*109*). The diversity of reservoir-competent host species that help to maintain endemic foci of Lyme disease may limit the usefulness of any method that targets a single reservoir species. An imaginative strategy, not yet evaluated in the field, to reduce the prevalence of infected ticks and wildlife through vaccination of reservoir hosts against *B. burgdorferi* may suffer from the same limitation (*102*). A host-targeted insecticide applied to deer may be more effective in reducing the incidence of Lyme disease (*108*). Because of the narrow host range of adult *I. scapularis*, topical applications of an insecticide to deer would limit tick reproduction and eventually reduce the total tick population in the affected area. However, identification of appropriate insecticides, provision of effective delivery systems, and better knowledge of deer behavior in suburban environments are problems to be solved before a deer-targeted strategy can be put into practice.

The potential for biological means of tick control through natural enemies is relatively unexplored. Few natural predators or pathogens are known for ticks (*110*). The obligatory blood-feeding nature of ticks suggests that there may be limited opportunities for the acquisition of pathogens or parasites directly from the environment. An insect parasite of *I. scapularis* has been found in the Elizabeth Islands, Massachusetts (*109*), but its impact on risk has not been determined. Laboratory colonies of the parasite appear to be easily established, and sustained releases from colonized stock may ultimately help to reduce risk in isolated situations.

The total nutritional dependency of ticks on vertebrate hosts affords an opportunity to reduce the abundance of Lyme disease vectors through limits in the availability of hosts. Such restriction can be accomplished either directly by affecting host abundance or indirectly by making hosts unavailable for tick feeding through topical application of repellents or insecticides or by vaccination against ticks (*108, 111*). Again, deer would be the most suitable target. An attempt to reduce the population of *I. scapularis* on a Massachusetts island by the removal of deer was only successful when nearly all the deer were eliminated (*24*). Thus, traditional deer management practices alone are not likely to decrease significantly the risk of Lyme disease. Any alternative to the elimination of deer would probably also have to approach 100% effectiveness. A combination of host reduction, habitat modification, and area insecticide application was successfully used in a control program for a pest tick, *A. americanum* (*112*), but the general suitability of such integrated control techniques for Lyme disease prevention remains to be determined.

Personal protection measures are the most frequent recommendation provided by public health agencies to reduce the risk of Lyme disease (*3*). These measures include the wearing of light-colored clothing, taping the tops of socks over trouser cuffs, and the use of insect repellents on clothing and exposed skin. Such recommendations are easy to make because they place responsibility for prevention on the individual. However, personal protection measures may actually have limited effectiveness in suburban areas with high tick density. Clearly, public health agencies will have to take a more active role in prevention than providing simple cautions if their efforts are to reduce the incidence of *B. burgdorferi* infection.

Conclusion

Ironically, the emergence of Lyme disease as a health problem is attributable in part to the "greening" of the United States: forests are regaining those lands formerly devoted to agriculture. Citizens value ever more highly the propinquity of wildlife to their residences. Deer, once close to elimination in many parts of the United States, are now as commonly noted as squirrels in some suburban communities. A cost of this otherwise welcomed development is Lyme disease. Living close to nature may have more public health consequences in the future as other known zoonotic diseases expand their ranges, and as perhaps others are discovered (*113*). The history of Lyme disease also shows that a newly recognized disease may be defined as much by individuals and groups outside of academic and governmental institutions as by those within them. Consequently, a mix of opinion has formed about what Lyme disease is and how it should be managed.

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