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LYME BORRELIOSIS IN THE SOUTHERN UNITED STATES: A REVIEW

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ABSTRACT: Lyme borreliosis (Lyme disease) is the most often reported arthropod transmitted disease in humans in the U.S.A. Although it has been reported from 43 states, cases are especially abundant in the mid-Atlantic and northeastern regions. *Borrelia burgdorferi*, the etiologic agent, is transmitted primarily by the western blacklegged tick (*Ixodes pacificus*) in far western North America, and by the blacklegged tick (*Ixodes scapularis*) in eastern North America. Although Lyme disease cases have been reported from southern states, some researchers doubt the presence of *B. burgdorferi* or of human Lyme disease in the south. However, new data show that *B. burgdorferi* is widely distributed in the south and that strains are genetically more varied than in the north. Moreover, *B. burgdorferi* enzootic cycles appear to be more complex and more tick species are identified as vectors of the spirochete in the southern states.

Lyme borreliosis (LB) or Lyme disease (LD) is caused by the spirochete *Borrelia burgdorferi* sensu lato and is transmitted to humans and other animals primarily by ticks in the *Ixodes ricinus* species complex. This borreliosis is known to occur in endemic foci throughout the Northern Hemisphere (Lane et al., 1991; Anderson and Magnarelli, 1993; Barbour and Fish, 1993) and is the most frequently reported vector-borne disease in the U.S.A. More than 13,000 human cases were reported from 43 states to the Centers for Disease Control and Prevention (CDC) in 1994 (Herrington, 1995). Lyme borreliosis is probably the most frequently reported tick-borne disease of humans in the world. In the U.S.A. most of the human cases are reported from the mid-Atlantic–northeastern area followed by cases in the north central and northern California coastal areas.

Clinical symptoms of LD affect all age groups and may involve the skin, joints, nervous system, and heart. Some of the symptoms of the disease were described in Europe as early as 8 decades ago (Afzelius, 1910; Lipschutz, 1913), but it was not recognized in North America until 1975 (Steere et al., 1978). There was an unusual cluster of childhood arthritis cases in Lyme, Connecticut, which subsequently were shown to be related to prior episodes of the characteristic skin rash of LD, erythema migrans (Mast and Burrows, 1976; Steere et al., 1977). Although clinical symptoms were described in Europe and the U.S.A., the etiologic agent and its mode of transmission were unknown. Epidemiologic evidence suggested that the disease was transmitted by a tick (Steere et al., 1978), but it was not until later that the spirochete *B. burgdorferi* was isolated from *Ixodes scapularis* (*I. dammini*) (Burgdorfer et al., 1982). The antiquity of *B. burgdorferi* is unknown, but it is probably ancient. It has been demonstrated in North America in archived ticks collected in the 1940s (Persing et al., 1990) and in museum specimens of mice collected in 1894 (Marshall et al., 1994). It has also been documented in European ticks preserved since 1884 (Matuschka et al., 1995).

Lyme borreliosis exists as zoonoses among vertebrate hosts and certain species of ticks. Rodents appear to be the principal reservoir hosts, although other mammals and birds are known to harbor *B. burgdorferi* (Anderson and Magnarelli, 1993). The principal vectors of the spirochetes to humans in North America are the ticks *I. scapularis* and *Ixodes pacificus* in the eastern and western parts, respectively; *I. ricinus* is the chief vector in Europe and *Ixodes persulcatus* in Asia. These ticks feed on an extremely wide variety of mammals, birds, and reptiles and may become abundant if adequate vertebrate hosts and appropriate climatic conditions exist (Lane et al., 1991; Anderson and Magnarelli, 1993, 1994). Ecologic requirements for the ticks include temperatures between −10 and 35 C, with tolerance to the extremes for only brief periods, and a constant relative humidity in the air of no lower than 80% and near saturation in the soil (Burgdorfer, 1989). The typical enzootic cycle involves larval or nymphal ticks becoming infected with *B. burgdorferi* while feeding on infected reservoir hosts. The tick subsequently passes the spirochetes transstadially to the next developmental stage, whereupon they are transmitted to the next host during feeding. Transovarial transmission from infected female ticks to larvae sometimes occurs, but it is uncommon (Piesman, Donahue et al., 1986; Lane and Burgdorfer, 1987; Magnarelli et al. 1987; Schoeler and Lane, 1993).

Adult ticks in the *I. ricinus* species complex usually feed on large mammals and to a lesser extent on medium-sized ones; larvae and nymphs usually feed on small, medium-sized, and large mammals, birds, and reptiles (Balashov, 1972; Piesman and Spielman, 1979; Piesman et al. 1979; Anderson et al., 1987). In the northeastern U.S.A., mice, particularly the white-footed mouse, *Peromyscus leucopus*, are the most frequently parasitized hosts of larval and nymphal *I. scapularis* and are also extremely competent reservoir hosts of *B. burgdorferi*, remaining infective throughout life (Levine et al., 1985; Spielman et al., 1985; Magnarelli et al., 1988; Mather et al., 1989; Lane et al., 1991; Anderson and Magnarelli, 1993). White-tailed deer (*Odocoileus virginianus*) serve as the principal hosts for adult *I. scapularis*, but appear to be incompetent (Telford et al., 1988) or perhaps marginally competent (Bosler et al., 1983, 1984; Oliver et al., 1992) as reservoir hosts for *B. burgdorferi*. The enzootic cycle of the spirochete is extremely efficient in certain foci in the northeastern U.S.A. where the spirochete overwinters in vertebrate reservoir hosts, and in fed larvae or unfed nymphs. The peak of nymphal questing (host-seeking) is usually in May and June and precedes the peak of larval questing, which occurs in August and September (Piesman and Spielman, 1979; Main et al., 1982; Wilson and Spielman, 1985). The earlier feeding of nymphs, some of which are infected, ensures that many juvenile rodents will be infected prior to larval feeding. Natural infection rates of questing nymphs are approximately 25% (Anderson et. al., 1983; Bosler et al., 1983; Piesman, Mather et al., 1986; Schulze et al., 1986; Piesman et al., 1987; Falco and Fish, 1988; Magnarelli and Anderson, 1988);

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in hyperendemic areas up to 100% of adults have been reported to be infected (Burgdorfer, 1984). This allows for great efficiency of the enzootic cycle and the perpetuation of the infection from year to year (Spielman et al., 1985).

There have been several dominant tenets in the past concerning Lyme borreliosis in the U.S.A. One of these was that *B. burgdorferi* was endemic only in the northeastern, north central, and northern Pacific coastal areas (Lane et al., 1991), and, therefore, only those areas were potential risk sites for acquiring infection with this spirochete. Another was that *I. pacificus* was the main vector in the west and a relatively new species, *I. dammini,* was the vector in the north central and northeastern areas (Lane et al., 1991). Moreover, *I. scapularis* from the southern U.S.A. was shown to be a competent laboratory vector of the spirochete (Burgdorfer and Gage, 1986; Piesman and Sinsky, 1988), but it was not thought to be commonly infected in nature. A fourth tenet was that the white-footed mouse (*P. leucopus*) and the white-tailed deer (*O. virginianus*) were the only 2 hosts of real importance in maintaining the vector tick populations in the north, and *P. leucopus* was the only significant reservoir for the spirochete in the eastern half of the U.S.A. (Lane et al., 1991). Finally, it was believed that *B. burgdorferi* was quite homogeneous with little variation in North America compared to significant variation among the spirochete populations in Europe (Barbour et al., 1984; Anderson et al., 1989; LeFebvre et al., 1990; Anderson, 1991; Wilske et al., 1992). Data obtained during the last few years provide evidence that some of these presumptions must be altered and these are discussed below.

GEOGRAPHIC DISTRIBUTION OF *B. BURGDORFERI* IN THE SOUTHERN U.S.A.

Contrary to dogma, *B. burgdorferi* is present and widely distributed in the south. It is cycling enzootically in foci located in several southern states. Isolates of *B. burgdorferi* have been obtained from mammals, birds, and ticks in Barbour–Stoenner–Kelly (BSK) culture medium from Georgia (Oliver, Chandler et al., 1993), Florida (Oliver, Chandler et al., 1995; Sanders and Oliver, 1995), South Carolina (J. H. Oliver, Jr., K. L. Clark, A. M. James, C. W. Banks, unpubl. obs.), North Carolina (Levine et al., 1993; Ouellette et al., 1993), Virginia (Sonenshine et al., 1993, 1995), Missouri (J. H. Oliver, Jr., T. M. Kollars, F. W. Chandler, Jr., A. M. James, unpubl. obs.), Oklahoma (Kocan et al., 1992), and Texas (Teltow et al., 1991; Rawlings and Teltow, 1994). Serum antibodies to *B. burgdorferi* have been found in deer from North Carolina (Magnarelli et al., 1986); in deer, or raccoons, or both, from Maryland, North Carolina, Georgia, and Florida (Magnarelli et al., 1991); deer from Georgia (Mahnke et al., 1993), Alabama (Luckhart et al., 1992, 1993), Oklahoma (Barker and Kocan, 1993), Texas (Rawlings, 1986); and in rodents from Virginia (Sonenshine et al., 1995), Kentucky (Duobinis-Gray et al., 1993), and several counties in North Carolina, South Carolina, Georgia, Florida, Alabama, and Mississippi (Magnarelli et al., 1992).

GENETIC DIVERSITY OF *B. BURGDORFERI*

As noted above, it is often reported that *B. burgdorferi* is rather homogeneous in North America compared to much greater heterogeneity in Europe (Barbour et al., 1985; Wilske et al., 1988; Anderson et al., 1989; LeFebvre et al., 1990; Anderson, 1991; Wilske et al., 1992). That generalization must now be modified. Discovery and analysis of new *B. burgdorferi* isolates from the southern U.S.A. (Oliver, Chandler et al., 1993; Oliver, 1995, 1996; Oliver, Chandler et al., 1995; Sanders and Oliver, 1995; Mathiesen et al., 1996), Colorado (Craven and Dennis, 1993), and California (Lane and Pascocello, 1989; Brown and Lane, 1992; Zingg et al., 1993) now indicate considerable genetic heterogeneity among the isolates from North America. In Europe, *B. burgdorferi* sensu lato has been separated into at least 5 genospecies: *B. burgdorferi* sensu stricto, *Borrelia garinii, Borrelia afzelii,* group VS116, and group PotiB2. In the U.S.A., *B. burgdorferi* sensu stricto was thought to be the only genospecies present. However, recently group DN127 from California (Assous et al., 1993; Postic et al., 1994) and *Borrelia andersonii* from New York (Marconi et al., 1995) have been recognized as belonging to different genospecies. There is also an unusual strain from a veery songbird (Barbour et al., 1985; Anderson et al., 1986) and 1 (25015) from *I. scapularis* from Millbrook, New York (Anderson et al., 1988; Fikrig et al., 1992). Even greater genetic heterogeneity is found among *B. burgdorferi* sensu lato isolates from the southern U.S.A., most of which have yet to be thoroughly analyzed. Currently, the medical significance of the genetically diverse strains is unclear, but information that is available will be discussed later in this paper under the heading of human cases.

VECTORS AND RESERVOIRS OF *B. BURGDORFERI* IN THE SOUTHERN U.S.A.

The earlier literature states that the main tick vector of *B. burgdorferi* in the eastern half of North America is *I. dammini* (Spielman et al., 1985; Lane et al., 1991). However, recent results based on hybridization, assortative mating, morphometrics, chromosome analysis, isozymes, and life cycle data indicate that *I. dammini* is not a separate species distinct from *I. scapularis.* Because the name *I. scapularis* has priority, *I. dammini* has been relegated to a junior subjective synonym of *I. scapularis* (Oliver, Owsley et al., 1993). Confirmatory evidence based on rDNA (Wesson et al., 1993; McLain et al., 1995), chromosomes (Chen et al., 1994), and multivariate morphometric discrimination analysis (Hutcheson et al., 1995) corroborates that *I. scapularis* is a polytypic species with a widespread geographic distribution throughout much of the eastern U.S.A. The report dealing with multivariate morphometric analysis sampled populations from Georgia, North Carolina, Maryland, Massachusetts, Missouri, and Minnesota, and laboratory hybrids between ticks from Georgia and Massachusetts; analysis of the morphometric data indicated north–south and east–west morphologic clines (Hutcheson et al., 1995). Most medical entomologists and LD researchers accept the species synonomy, but a dwindling number of researchers still defend the separateness of *I. dammini* (Rich et al., 1995; Caporale et al., 1996). The latter authors analyzed nucleotides from 16S mtDNA and suggest that cross-contamination of laboratory colonies accounts for the successful results on hybridization and the general lack of assortative mating. Contamination seems unlikely for several reasons. If it occurred in the laboratory colonies from Massachusetts and Georgia that were used in hybridization and other experiments (Oliver, Owsley et al., 1993), it

would have been revealed as inconsistences in the Massachusetts and Georgia groups during the multivariate morphometric analyses of nymphs and adults (Hutcheson et al., 1995) and larvae (Hutcheson and Oliver, 1996) that were conducted soon after the hybridization and mating experiments. Instead, Massachusetts and Georgia morphotypes were recognized in the respective laboratory colonies, and F_1 hybrids were morphologically intermediate. Analyses of ticks not maintained in laboratory colonies, but from several geographic sites, revealed gradual north–south and east–west morphologic clines. In the paper devoted to discriminating between *Ixodes* ticks by means of mtDNA sequences and in which the authors suggest possible contamination of laboratory tick colonies (Caporale et al., 1996), the authors failed to mention that mtDNA is useful for establishing phylogenetic history of maternal lineages, but not for amounts of gene flow in the nuclear genome. Moreover, in the abstract they incorrectly included *Ixodes angustus, Ixodes cookei, Ixodes hexagonus,* and *Ixodes muris,* along with the accurate inclusion of *I. pacificus, I. persulcatus, I. ricinus,* and *I. scapularis* in the *I. ricinus* complex (Keirans, Needham et al., 1996). *Ixodes angustus, I. cookei,* and *I. hexagonus* are not only *not* in the *I. ricinus* complex, they are not even in the subgenus *Ixodes* (Clifford et al., 1973; Robbins and Keirans, 1992; Keirans, Hutcheson et al., 1996; Keirans, Needham et al., 1996).

Interestingly, Rich and Caporale and their coworkers (Rich et al., 1995; Caporale et al., 1996) also failed to acknowledge that most of the confirmatory data indicating a single species are not based on laboratory colonies, but on field-collected ticks. Moreover, a much more extensive genetic investigation than those of Rich et al. (1995) and Caporale et al. (1996), which utilizes many more ticks (198 samples) from a greater number of geographic sites, provides evidence for continuous gene flow among the 2 mitochondrial clades that were described among *I. scapularis* populations (Norris et al., 1996). Norris et al. (1996) provided an analysis of 880 nucleotides of the same region of the 16S mitochondrial rDNA gene studied by Rich et al. (1995) and Caporale et al. (1996), plus an additional portion of the 12S gene, and random amplified polymorphic DNA (RAPD) markers in *I. scapularis* from throughout the range of the species and the results support conspecificity of northern and southern populations. Furthermore, analysis suggests that *I. scapularis* arose in the south and subsequently moved northward, not the reverse that is sometimes stated. The genetically more varied southern *I. scapularis* is also reflected in the morphologically more variable southern specimens (Hutcheson et al., 1995; Hutcheson and Oliver, 1996). Finally, the curators of the U.S. National Tick Collection and other authors, after reviewing all the data available and extensive museum specimens, have recently redescribed *I. scapularis* to include populations in the north (Keirans, Hutcheson et al. 1996).

Although *I. scapularis* appears to be the main vector of *B. burgdorferi* in the south as well as in the north, several other tick species have been found to be infected naturally with the spirochete. A closely related species in the *I. ricinus* species complex, *I. affinis,* is naturally infected and can experimentally transmit the spirochete (J. H. Oliver, Jr., A. M. James, C. W. Banks, unpubl. obs.). This tick does not usually bite humans, but it probably serves as a vector in the enzootic cycle of *B. burgdorferi* in Georgia, South Carolina, and possibly other areas in which the tick is distributed. Thus far, all species in the *I. ricinus* complex worldwide that have been tested under laboratory conditions can transmit the spirochete.

There are other species of *Ixodes* not included in the *I. ricinus* complex that are also vectors of *B. burgdorferi* in nature. These include *I. hexagonus* in Europe (Gern et al., 1991), *Ixodes ovatus* in Japan (Saito, 1977; Kawabata et al., 1993; Nakao and Miyamoto, 1993), *Ixodes uriae* in Northern and Southern Hemisphere seabird colonies (Olsén et al., 1995; Bunikis et al., 1996), *Ixodes neotomae* and *Ixodes spinipalpis* in California (Brown and Lane, 1992; R. S. Lane and J. E. Keirans, unpubl. obs.) and Colorado (Craven and Dennis, 1993), *Ixodes dentatus* in New York (Anderson et al., 1989), Nantucket (Telford and Spielman, 1989), Missouri (J. H. Oliver, Jr., T. M. Kollars, F. W. Chandler, Jr., A. M. James, unpubl. obs.), and Georgia (Oliver et al., 1996), and *Ixodes minor* in Georgia and South Carolina (J. H. Oliver, Jr., C. W. Banks, K. L. Clark, A. M. James, unpubl. obs.).

Borrelia burgdorferi has also been detected and/or isolated from several non-*Ixodes* tick species in the U.S.A. It was isolated from *Dermacentor variabilis* (Anderson et al., 1985) and detected in *Dermacentor albipictus* (Magnarelli et al., 1986) in Connecticut. It was also isolated from the latter species in Oklahoma (Kocan et al., 1992). Evidence of *Borrelia* spirochetes in *Amblyomma americanum* exists from New Jersey (Schulze et al., 1984), North Carolina (Levine et al., 1989), Georgia (J. H. Oliver, Jr., H. J. Hutcheson, A. M. James, J. F. Anderson, unpubl. obs.), Alabama (Luckhart et al., 1992), Missouri (Feir et al., 1994), Oklahoma (Kocan et al., 1992), and Texas (Rawlings and Teltow, 1994). Recently, we isolated *B. burgdorferi* sensu lato from cultures of *A. americanum* from Missouri and we are in the process of further characterizing them (J. H. Oliver, Jr., T. M. Kollars, F. W. Chandler, A. M. James, unpubl. obs.). In spite of the association of *B. burgdorferi* with *D. variabilis* and *A. americanum,* attempts to transmit the spirochete by these species in the laboratory have failed (Piesman and Sinsky, 1988; Mather and Mather, 1990; Mukolwe et al., 1992; Ryder et al., 1992), even when 2 different *B. burgdorferi* strains from the south were used (Oliver, Chandler et al., 1993; Sanders and Oliver, 1995). The recent report of an uncultivable *Borrelia* species different from *B. burgdorferi* and other described species from approximately 2% of *A. americanum* ticks from Texas and New Jersey further complicates an understanding of enzootic cycles of *B. burgdorferi* and Lyme disease in the southern U.S.A. (Barbour et al., 1996).

There is a variety of vertebrate hosts of ticks that may serve as reservoir hosts for *B. burgdorferi* sensu lato. In the U.S.A., the white-footed mouse (*P. leucopus*) is best known and is the chief reservoir in the hyperendemic northeastern region (Lane et al., 1991; Barbour and Fish, 1993; Anderson and Magnarelli, 1993, 1994). Other species of *Peromyscus* are capable of serving as reservoirs if the spirochetes, vectors, and ecologic conditions are conducive to enzootic cycles (Rand et al., 1993). In general, rodents appear to be the most common reservoir hosts, but other small to medium-sized mammals and birds may also function as reservoirs (Anderson and Magnarelli, 1993). In the south, the cotton mouse (*Peromyscus gossypinus*) and cotton rat (*Sigmodon hispidus*) appear to be 2 of the most common reservoir hosts (Oliver, Chandler et al., 1993, 1995), but the eastern woodrat (*Neotoma floridana*) and cottontail rabbit (*Syl-*

vilagus floridanus) are also naturally infected in some areas and probably serve as reservoirs (J. H. Oliver, Jr., C. W. Banks, T. M. Kollars, A. M. James, unpubl. obs.). Several species of birds, including the cardinal, Carolina wren, and rufous-sided towhee in Georgia and South Carolina, are also naturally infected with *B. burgdorferi* and may serve as reservoirs for the spirochete (J. H. Oliver, Jr., R. G. McLean, L. A. Durden, A. M. James, C. W. Banks, unpubl. obs.).

ENZOOTIC CYCLES OF *B. BURGDORFERI* IN THE SOUTHERN U.S.A.

There appear to be several enzootic transmission cycles operating for *B. burgdorferi* in the south and the interrelationships among them are currently unknown. The typical *I. scapularis* vector and *P. leucopus* reservoir cycle that is most common in the northeast appears to be modified by replacement of *P. leucopus* with *P. gossypinus* (cotton mouse) and *S. hispidus* (cotton rat) as major reservoir hosts in some areas of the south. That enzootic cycle is probably the dominant one in the south based on the widespread distribution and large numbers of infected *I. scapularis, P. gossypinus,* and *S. hispidus* (Oliver, Owlsey et al., 1993; Oliver, Chandler et al., 1993, 1995; Sanders and Oliver, 1995; Oliver, 1996; and J. H. Oliver, Jr., F. W. Chandler, A. M. James, C. W. Banks, F. H. Sanders, G. N. Vogel, unpubl. obs.). The cycle is probably enhanced by *Ixodes affinis* in areas where that species also occurs (J. H. Oliver, Jr., unpubl. obs.). The roles of *I. minor,* the eastern woodrat (*N. floridana*), and several species of birds in enzootic cycles have yet to be determined. There may be several separate parallel cycles operating or there may be overlapping cycles. For example, there might be a separate woodrat and *I. minor* cycle or a bird and *I. minor* cycle. Alternatively, because *I. minor* feeds on birds, woodrats, cotton mice, cotton rats, gray squirrels, spotted skunks, and other small mammals, the 2 cycles might not be separate and there might be a weblike overlap. *Ixodes scapularis* also feeds on all of these hosts. *Ixodes minor* usually does not bite humans; however, it probably functions as a maintenance vector in the enzootic cycle (J. H. Oliver, Jr., unpubl. obs.). Because *I. scapularis* also feeds on these hosts and bites humans, it could be a "bridge" vector that infects humans. An analogous example is seen in California where nonanthropophilic *I. neotomae* ticks function as maintenance vectors of *B. burgdorferi* among dusky-footed woodrats (*Neotoma fuscipes*). When *I. pacificus* feeds on the woodrats it may subsequently bite and transmit the spirochetes to humans (Brown and Lane, 1992; Clover and Lane, 1995).

Another enzootic cycle involving *Ixodes dentatus* and the cottontail rabbit (*S. floridanus*) operates in Georgia, Missouri (J. H. Oliver, Jr., T. M. Kollars, F. W. Chandler, Jr., A. M. James, pers. obs.; Oliver et al., 1996), and perhaps other parts of the south, in a manner similar to the *I. dentatus* and rabbit cycle in New York (Anderson et al., 1989). *Ixodes dentatus* only occasionally bites humans, but *I. scapularis* feeds on rabbits and also bites humans, so theoretically it might transmit the spirochete to humans if the spirochetes are infective to humans. The *B. burgdorferi* sensu lato isolates from *I. dentatus* are genetically different from other strains of southern and northern isolates (Mathiesen et al., 1996; Oliver, 1996; Oliver et al., 1996) and the ones from New York have recently been described as a new genospecies, *B. andersonii* (Marconi et al., 1995). It is unknown whether the *I. dentatus* isolates can infect hosts other than rabbits.

Enzootic cycles in the south are more complex and in some respects less efficient than those in the north. In the south, the life cycle of *I. scapularis* is less regulated and synchronized and does not ensure that infected overwintered nymphs feed and infect hosts prior to larval feeding (Rogers, 1953; Durden and Oliver, 1996; Lavender and Oliver, 1996). Moreover, ticks in the south feed on a greater number of host species, some of which may be reservoir incompetent, and there appears to be a lower percentage of infected ticks and hosts.

Published data on prevalence of *B. burgdorferi* isolates in ticks in the south are lacking, but unpublished data based on spirochete isolates suggest approximately 2–8% of *I. scapularis* and *I. affinis* adults are infected (J. H. Oliver, Jr., F. W. Chandler, Jr., A. M. James, C. W. Banks, pers. obs.). It should be emphasized that prevalence data based on spirochete isolates in laboratory culture is probably the most conservative measure of prevalence; however, clearly the infection rate is much lower than in the hyperendemic areas of the north. Prevalence rates of *B. burgdorferi* based on spirochete isolates from tick hosts in the south are unavailable, but prevalence data based on antibodies to *B. burgdorferi* in animals from that region are known. Serologic surveys of antibodies to *B. burgdorferi* in mice indicate prevalence to be 35.7 and 27.3% in 56 *P. leucopus* and 535 *P. gossypinus,* respectively, collected in Connecticut, North Carolina, South Carolina, Georgia, Florida, Alabama, and Mississippi (Magnarelli et al., 1992). Percent positive prevalence varied from 0 to 90 depending on the particular geographic site in Georgia and Florida. In raccoons the percent positive sera was 15 for Connecticut, 79 for Maryland, 38 for North Carolina, and 33 for Florida (Magnarelli et al., 1991).

HUMAN CASES OF LYME BORRELIOSIS

As noted in the introduction, most of the human cases of Lyme disease in the U.S.A. are concentrated in the hyperendemic mid-Atlantic and northeastern regions. Cases reported from New York and Connecticut increased 318% and 190%, respectively, from 1985 to 1994 (Herrington, 1995). The number of reported cases in the U.S.A. declined slightly from 1994 (13,043) to 1995 (11,603), but still was the second highest annual number reported since 1982 (*Morbidity and Mortality Weekly Report* [*MMWR*]; Centers for Disease Control and Prevention, 1996). Eight states (Connecticut, Rhode Island, New York, New Jersey, Pennsylvania, Maryland, Wisconsin, and Minnesota) accounted for 92% of reported cases in 1995. Nevertheless, illness due to *B. burgdorferi* is not confined to those areas (Herrington, 1995). Zoonotic diseases such as LD exist in foci in nature by cycling among wild animals and usually only become of concern when they spill over into the human population. Thus, *B. burgdorferi* could be cycling silently among wild animals and might be endemic, yet not recognized, unless humans become ill and are accurately diagnosed. Lyme disease cases were reported to the CDC by 43 states and the District of Columbia in 1995. Lyme disease is endemic in many foci over large areas of the southern U.S.A., yet relatively small numbers of human cases are reported. This apparent contradiction is worthy of further discussion and investigation.

Because competent tick vectors and the spirochete are present in many areas of the south, why are more human cases not reported? This enigma has yet to be solved; however, several possible explanations can be offered. The true number of cases in the south is really not known because surveillance for LD in the southern U.S.A. is so poor that it is difficult to have confidence in the statistics. The prevailing dogma about Lyme disease has been that it does not occur, or rarely occurs there. Also, although LD is a reportable disease, it seems likely that many physicians probably do not report suspected cases. Moreover, diagnosis of LD is complicated and there is no single "gold standard" diagnostic test yet available. Controversy surrounds the reliability of tests and of patient symptoms, especially early in the disease; false negative and false positive results from tests may be obtained. The single criterion that is irrefutable is the isolation of the spirochete in culture medium from biopsy of the patient. Unfortunately, this is difficult, expensive, impractical, and not attempted by most physicians. A characteristic rash (erythema migrans) is present in most LD patients (estimates vary from 60 to 90%) and is probably the single most used diagnostic sign, especially if the patient has a history of tick exposure in an endemic area. Unfortunately, many LD patients do not recognize the rash, or do not seek treatment for it, or both, and not all physicians recognize it even if it is a typical erythema migrans rash. These potential pitfalls are exacerbated in regions where the public and physicians have been told that LD does not occur.

Although the CDC reports LD cases in the *Morbidity and Mortality Weekly Report* (*MMWR*) that it receives from state health departments, the editor of the *MMWR* states that LD is not endemic in Georgia and Missouri (Centers for Disease Control and Prevention, 1996), and by implication other southern states. Several CDC scientists concluded that a series of patients with suspected LD in Missouri did not have LD, but instead a Lymelike disease (Campbell et al., 1995). Two LD researchers in Missouri, one of whom is the state epidemiologist, strongly disagree with that conclusion and declined authorship of that paper (Masters and Donnell, 1995). It seems prudent to maintain an open mind regarding this controversy. The working hypothesis in my laboratory is that human infection with *B. burgdorferi* in the southern U.S.A. is significantly greater than reported. However, many cases are probably mild and perhaps some are asymptomatic. If this hypothesis is correct, it is easy to understand that many patients do not seek medical attention, and, when they do seek help, some physicians may misdiagnose cases. It is known, even among the less genetically variable *B. burgdorferi* strains from the northeastern U.S.A., that some are more infective than others and some appear to infect but cause little pathogenesis to Lewis strain rats (Barthold et al., 1990). Also, infectivity to laboratory mice varied significantly between the MI-6 strain from Florida cotton rats and the SH2-82 strain from New York *I. scapularis* ticks (Sanders and Oliver, 1995). Finally, some physicians may treat patients for erythema migrans lesions and not report the disease to the state health departments or the CDC. Clearly, there are fewer physicians and the public is less concerned about LD in the largely rural southern U.S.A. compared to the northeastern region.

Data indicate that typical northern strains of *B. burgdorferi* sensu stricto plus other genetically variable strains occur in the south (Oliver, Chandler et al., 1993, 1995; Sanders and Oliver, 1995; Mathiesen et al., 1996; Oliver, 1996). A continuation of our working hypothesis is that the typical northern strains similar to strain B-31 cause LD symptoms in the south similar to those observed in the north, whereas some other strains may be infective but produce low pathogenicity, and some may not be infective to humans. For example, 3 strains from cottontail rabbits in Missouri do not appear to be infective to laboratory mice (J. H. Oliver, Jr., A. M. James, C. W. Banks, T. M. Kollars, unpubl. obs.). Also, as noted above, Barthold et al. (1990) and Sanders and Oliver (1995) indicated variation in strain pathogenesis and infectivity. Thus, the role of *B. burgdorferi* in producing human disease may be more varied in the south than in the north.

In Europe, 3 of the 5 described genospecies of *B. burgdorferi* sensu lato have been associated with Lyme borreliosis in humans. There are indications that the different genospecies are associated with distinct clinical manifestations of Lyme borreliosis in Europe (Assous et al., 1993; van Dam et al., 1993; Balmelli and Piffaretti, 1995). These authors indicated that the genotypes have different pathogenic potentials. Other authors have also suggested that variation in disease presentation may be associated with variants of *B. burgdorferi* (Dressler et al., 1994; Wienecke et al., 1994). Although not demonstrated, it seems likely that differences in clinical symptoms may be correlated with spirochete strain differences in the south. This view is consistent with the common theme demonstrated among some other bacterial pathogens, in which analyses indicate that distinct bacterial clones are responsible for disease outbreaks and increases in infection frequency (Musser, 1996). Some of the clones contain unique combinations of virulence genes or alleles of virulence genes.

Even if there are more cases of human LD than are reported in the southern U.S.A., clearly the disease is not of the magnitude observed in the hyperendemic regions of the north. There is a vastly different human population density between the northeast and southeast and the ecologic conditions are different. For example, in Westchester County, New York (where there is an extremely high prevalence of Lyme disease) people, deer, and rodents are in much closer contact with each other than in most areas. Lyme disease is often peridomestic in such places as Westchester County. The area from Boston to Washington, D.C., is a megalopolis and that is where the highest prevalence of Lyme disease is recorded.

There are also several other circumstances that perhaps account for the profound difference in the number of human cases reported in the south as compared to the north. As noted in the previous section on enzootic cycles, the less regulated and synchronized life cycle of *I. scapularis* in the south does not ensure that infected overwintered nymphs feed and infect a new cohort of mice or other reservoir hosts prior to larvae feeding on them. This does occur in the northeast. Moreover, immature *I. scapularis* feed on a wider variety of hosts, especially lizards, in the south and thus there is a reduced probability of feeding on an infected host. The fact that immature *I. scapularis* in the northeast feed largely on *P. leucopus* and that a high percentage of these mice are infected with *B. burgdorferi* compounds the probability of high tick and reservoir infection rates. Lizards are the most frequently and heavily parasitized hosts of immature *I. scapularis* in the south (Rogers, 1953; Apperson et al., 1993; Oliver, Cummins et al., 1993; Durden and Oliver,

1996). Based on data obtained from the field, one might presume that southern immature *I. scapularis* prefer lizards to other hosts, but laboratory results dispute that presumption. Larval and nymphal *I. scapularis* (from Georgia and Massachusetts) and *I. pacificus* (from California) were exposed to laboratory mice, lizards, and chickens to determine comparative feeding success, molting success, and so on, and ticks from all 3 geographic origins generally responded similarly (James and Oliver, 1990). When the ticks were allowed to choose among the hosts, larvae of all 3 populations showed a preference for mice and for mice or lizards compared to chickens. Nymphs displayed no preference between mice and lizards, but preferred both host species over chickens. Nevertheless, many also readily fed on the birds. It appears that northern and southern *I. scapularis* and *I. pacificus* immatures are opportunistic feeders, and that climate, ecologic conditions, and potential host availability determine the "preferred" host species in nature. *Ixodes scapularis* has been recovered from 125 species of native hosts, including immature ticks from 41 mammal species, 57 bird species, and 14 lizard species, and adults from 27 mammal species (Keirans, Hutcheson et al., 1996).

The notion that lizards are incompetent reservoirs to *B. burgdorferi,* and indeed serve as a "sink" to reduce the number of ticks that might otherwise feed on competent reservoirs, seemed to fit the overall dogma advanced regarding the epizootiology of this spirochete. This notion was based on supposition and also on some experimental data that indicated the western fence lizard, *Sceloporus occidentalis* (Lane and Loye, 1989; Lane, 1990; Manweiler et al., 1992), and the European sand lizard, *Lacerta agilis* (Matuschka et al., 1991), were reservoir incompetent for *B. burgdorferi.* However, a recent paper indicated that the southeastern five-lined skink, *Eumeces inexpectatus,* is reservoir competent and remains so for at least 5 wk (Levin et al., 1996). More than 20% of xenodiagnostic larvae fed on infected skinks acquired spirochetes. A smaller proportion of ticks feeding on infected green anoles, *Anolis carolinensis,* became infected. It seems prudent not to make a generalization regarding the role of all lizard species as being either reservoir-competent or -incompetent; rather, the reservoir capacity of each species should be evaluated. Clearly, *E. inexpectatus* can maintain *B. burgdorferi* for 5 wk and remain infective to ticks, is somewhat efficient at transmission, is abundant in the coastal southeast, has an activity period that coincides with that of larval and nymphal *I. scapularis,* and is heavily parasitized by them. Also, *B. burgdorferi* recovered from infected *E. inexpectatus* retained infectivity for mammalian hosts (Levin et al., 1996).

Another point that requires evaluation regarding *B. burgdorferi* transmission to humans in the south involves feeding behavior of nymphal *I. scapularis.* The importance of nymphal feeding in human LD cases has been documented for cases in the north (Lane et al., 1991; Barbour and Fish, 1993) and in the far west (Clover and Lane, 1995). It is claimed that nymphs do not bite or rarely bite humans in the south and that this characteristic is a biological difference between northern and southern populations of *I. scapularis.* That claim may be accurate, but more data are needed to prove that assertion. It is mentioned anecdotally that there are no data indicating nymphal feeding on humans in the south. Clearly, the absence of data is not negative data when experiments are not reported. The argument that if the nymphs were biting humans they would be reported and at least more anecdotal evidence would be available is flawed. Most LD patients in the hyperendemic areas of the north, where the public and physicians are quite aware of the dangers of contracting LD, do not recall tick bites (Barbour and Fish, 1993). It is unreasonable to expect people in the south, where the current information is that LD does not occur, where fewer physicians per 100,000 people practice, and where rural sociologic and economic conditions are less likely to result in personal alarm about tick bites, to recognize a tiny tick attached to them. Bites by adult *I. scapularis* are reported in the south, especially if announcements are made warning of the dangers associated with tick bites (Felz et al., 1996). On the other hand, there may be real proportional differences between the numbers of human attacks by nymphal *I. scapularis* in the north and south. In many localities in the north, Lyme disease is peridomestic, whereas there is no such report in the south. If differences do exist and human attack by nymphs is proportionately greater in the north, data suggest that it is not due to innate differences in host preferences between northern and southern ticks based on experiments in which mice, lizards, and chickens were offered to ticks (James and Oliver, 1990). Perhaps it might be due to ecologic conditions that provide a greater variety of hosts in milder climates and somewhat different sociological activities of the human populations.

Finally, some scientists are not convinced that true LD occurs in the south. For instance, the LD cases reported in Missouri involving appearance of characteristic erythema migrans rash and other symptoms of LD (Masters et al., 1994) are rejected by some researchers who claim that those cases are due to a Lymelike disease (Campbell et al., 1995). The absence of human isolates of *B. burgdorferi* from patients in the south is cited as 1 reason to reject LD as a diagnosis, although interpreting absence of data as negative data is premature. As noted, the report of an uncultivable *Borrelia* species in the tick *A. americanum,* which has not been demonstrated to transmit *B. burgdorferi* but has been epidemiologically associated with LD or Lymelike disease, further complicates understanding of LD in the south, at least temporarily (Barbour et al., 1996).

CONCLUSIONS

Lyme borreliosis or Lyme disease is a zoonotic infection that occurs in enzootic cycles among wildlife and affects humans when they are bitten by infected ticks. It is the most frequently reported arthropod transmitted disease in humans in the U.S.A. The primary tick vectors of the etiologic agent, *B. burgdorferi,* to humans are the western blacklegged tick, *I. pacificus,* in the coastal northern Pacific region and the blacklegged tick, *I. scapularis,* in the eastern half of the country. Until recently, the prevailing dogma was that the deer tick, *I. dammini,* was the vector of the spirochete in the north central and northeastern U.S.A.; that *B. burgdorferi* was antigenically and genetically uniform in North America compared to Europe; that *B. burgdorferi* did not occur in the southern part of the U.S.A.; and thus, Lyme borreliosis did not occur in wildlife and humans did not acquire Lyme disease in the south. Data generated during the last 5 yr are causing a reevaluation of the previously held

concepts about Lyme borreliosis in the U.S.A., particularly in the southern U.S.A.

The blacklegged tick, *I. scapularis,* is the main vector of *B. burgdorferi* in the eastern half of the U.S.A., both in the northern and southern parts. Dammin's northeastern deer ixodid, *I. dammini,* is not a separate species distinct from *I. scapularis* and it has been relegated to a junior subjective synonym of *I. scapularis.* A closely related tick, *I. affinis,* is also in the same *I. ricinus* species complex as *I. scapularis* and *I. pacificus* and is naturally infected with *B. burgdorferi* in Georgia and South Carolina. Although it rarely bites humans, it probably plays a role in maintaining the enzootic cycle of the spirochete in the southeastern U.S.A. Other species of *Ixodes* known to be naturally infected and to transmit *B. burgdorferi* among wildlife include *I. neotomae* and *I. spinipalpis* in the western U.S.A. and *I. dentatus* and *I. minor* in the eastern U.S.A. The 2 western species serve as maintenance vectors and *I. pacificus* is the "bridge" vector to humans. Perhaps the 2 eastern species function similarly and *I. scapularis* is the "bridge" vector. Alternatively, *I. dentatus* and *I. minor* may operate in parallel and nonoverlapping enzootic cycles and not play a role in human Lyme borreliosis. Their role is yet to be determined.

It is now known that *B. burgdorferi* occurs in many parts of the U.S.A. where it was not previously thought to occur. In the south, isolates have been obtained from ticks, vertebrate hosts, or both, from Virginia south to mid-coastal Florida, Missouri, Oklahoma, and Texas; immunologic data exist that are based on serum antibodies to *B. burgdorferi* from tick hosts in many other southern states. Moreover, immunologic and genetic analyses confirm a much greater degree of heterogeneity among *B. burgdorferi* sensu lato isolates, particularly in the south, than heretofore suspected for North America. It is hypothesized, but not supported, that the diversity among *B. burgdorferi* sensu lato strains might produce different levels of infectivity and pathogenicity and produce a greater variety of clinical symptoms in infected humans. A substantial amount of the new data mentioned in this review is in the process of publication or is recently published and, therefore, not widely known among parasitologists and biomedical scientists. The newly discovered data raise many questions and likely will stimulate productive research.

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LITERATURE CITED

AFZELIUS, A. 1910. Verhandlungen der Dermatologischen Gesellschaft zu Stockholm. Archives of Dermatology and Syphilology **101:** 404–407.

ANDERSON, J. F. 1991. Epizootiology of Lyme borreliosis. Scandinavian Journal of Infectious Diseases **77(Supplement):** 23–34.

———, R. C. JOHNSON, L. A. MAGNARELLI, AND F. HYDE. 1985. Identification of endemic foci of Lyme disease: Isolation of *Borrelia burgdorferi* from feral rodents and ticks (*Dermacentor variabilis*). Journal of Clinical Microbiology **22:** 36–38.

———, ———, ———, AND ———. 1986. Involvement of birds in the epidemiology of the Lyme disease agent *Borrelia burgdorferi.* Infection and Immunity **51:** 394–396.

———, AND L. A. MAGNARELLI. 1993. Natural history of *Borrelia burgdorferi* in vectors and vertebrate hosts. *In* Ecology and environmental management of Lyme disease, H. S. Ginsberg (ed.). Rutgers University Press, New Brunswick, New Jersey, p. 11–24.

———, AND ———. 1994. Lyme disease: A tick-associated disease originally described in Europe, but named after a town in Connecticut. American Entomologist **40:** 217–227.

———, ———, W. BURGDORFER, AND A. G. BARBOUR. 1983. Spirochetes in *Ixodes dammini* and mammals from Connecticut. American Journal of Tropical Medicine and Hygiene **32:** 818–824.

———, ———, R. B. LEFEBVRE, T. G. ANDREADIS, J. B. MCANINCH, G. C. PERNG, AND R. C. JOHNSON. 1989. Antigenically variable *Borrelia burgdorferi* isolated from cottontail rabbits and *Ixodes dentatus* in rural and urban areas. Journal of Clinical Microbiology **27:** 13–20.

———, ———, AND J. B. MCANINCH. 1987. *Ixodes dammini* and *Borrelia burgdorferi* in northern New England and upstate New York. Journal of Parasitology **73:** 419–421.

———, ———, AND ———. 1988. New *Borrelia burgdorferi* antigenic variant isolated from *Ixodes dammini* from upstate New York. Journal of Clinical Microbiology **26:** 2209–2212.

APPERSON, C. S., J. F. LEVINE, T. L. EVANS, A. BRASWELL, AND J. HELLER. 1993. Relative utilization of reptiles and rodents as hosts by immature *Ixodes scapularis* (Acari: Ixodidae) in the coastal plain of North Carolina, USA. Experimental and Applied Acarology **17:** 719–731.

ASSOUS, M. V., D. POSTIC, G. PAUL, P. NEVOT, AND G. BARANTON. 1993. Western blot analysis of sera from Lyme borreliosis patients according to the genomic species of the *Borrelia* strains used as antigens. European Journal of Clinical Microbiology and Infectious Disease **12:** 261–268.

BALASHOV, YU. S. 1972. Bloodsucking ticks (Ixodoidea)—Vectors of diseases of man and animals. Miscellaneous Publications of the Entomological Society of America **8:** 167–376.

BALMELLI, T., AND J.-C. PIFFARETTI. 1995. Association between different clinical manifestations of Lyme disease and different species of *Borrelia burgdorferi* sensu lato. Research in Microbiology **146:** 329–340.

BARBOUR, A. G., AND D. FISH. 1993. The biological and social phenomenon of Lyme disease. Science **260:** 1610–1616.

———, R. A. HEILAND, AND T. R. HOWE. 1985. Heterogeneity of major proteins in Lyme disease borreliae: A molecular analysis of North American and European isolates. Journal of Infectious Diseases **152:** 478–484.

———, G. O. MAUPIN, G. J. TELTOW, C. J. CARTER, AND J. PIESMAN. 1996. Identification of an uncultivable *Borrelia* sp. in the hard tick *Amblyomma americanum*: Possible agent of a Lyme disease-like illness. Journal of Infectious Diseases **173:** 403–409.

———, S. L. TESSIER, AND S. F. HAYES. 1984. Variation in a major surface protein of Lyme disease spirochetes. Infection and Immunity **45:** 94–100.

BARKER, R. W., AND A. A. KOCAN. 1993. Lyme disease research in Oklahoma. *In* Proceedings of the 2nd Workshop on Lyme Disease in the Southeast, C. S. Apperson, J. F. Levine, and E. L. Snoddy (eds.). North Carolina State University, Raleigh, North Carolina, p. 6–7.

BARTHOLD, S. W., K. D. MOODY, AND D. S. BECK. 1990. Susceptibility of laboratory rats to isolates of *Borrelia burgdorferi* from different geographic areas. American Journal of Tropical Medicine and Hygiene **42:** 596–600.

BOSLER, E. M., J. L. COLEMAN, J. L. BENACH, AND D. A. MASS. 1983. Natural distribution of the *Ixodes dammini* spirochete. Science **220:** 321–322.

———, B. G. ORMISTON, J. L. COLEMAN, J. P. HANRAHAN, AND J. L. BENACH. 1984. Prevalence of the Lyme disease spirochete in pop-

ulations of white-tailed deer and white-footed mice. Yale Journal of Biology and Medicine **57:** 651–659.

BROWN, R. N., AND R. S. LANE. 1992. Lyme disease in California: A novel enzootic transmission cycle of *Borrelia burgdorferi*. Science **256:** 1439–1442.

BUNIKIS, J., B. OLSÉN, V. FINGERLE, J. BONNEDAHL, B. WILSKE, AND S. BERGSTRÖM. 1996. Molecular polymorphophism of the Lyme disease agent *Borrelia garinii* in northern Europe is influenced by a novel enzootic *Borrelia* focus in the North Atlantic. Journal of Clinical Microbiology **34:** 364–368.

BURGDORFER, W. 1984. The New Zealand white rabbit: An experimental host of infecting ticks with Lyme disease spirochetes. Yale Journal of Biology and Medicine **57:** 609–612.

———. 1989. Vector/host relationships of the Lyme disease spirochete, *Borrelia burgdorferi*. Rheumatic Diseases Clinics of North America **15:** 775–787.

———, A. G. BARBOUR, J. L. BENACH, J. P. DAVIS, E. GRUNWALDT, AND S. F. HAYES. 1982. Lyme disease—A tick borne spirochetosis? Science **216:** 1317–1319.

———, AND K. L. GAGE. 1986. Susceptibility of the black-legged tick, *Ixodes scapularis*, to the Lyme disease spirochete, *Borrelia burgdorferi*. Zentralblatt für Bakteriologie Mikrobiologie und Hygiene, Series A **263:** 15–20.

CAMPBELL, G. L., W. S. PAUL, M. E. SCHRIEFER, R. B. CRAVEN, K. E. ROBBINS, AND D. T. DENNIS. 1995. Epidemiologic and diagnostic studies of patients with suspected early Lyme disease, Missouri, 1990–1993. Journal of Infectious Diseases **172:** 470–480.

CAPORALE, D. A., S. M. RICH, A. SPIELMAN, S. R. TELFORD III, AND T. D. KOCHER. 1996. Discriminating between *Ixodes* ticks by means of mitochondrial DNA sequences. Molecular Phylogenetics and Evolution **4:** 361–365.

CENTERS FOR DISEASE CONTROL AND PREVENTION. 1996. Lyme disease—United States, 1995. Morbidity and Mortality Weekly Report **45:** 481–484.

CHEN, C., U. G. MUNDERLOH, AND T. J. KURTTI. 1994. Cytogenetic characteristics of cell lines from *Ixodes scapularis* (Acari: Ixodidae). Journal of Medical Entomology **31:** 425–434.

CLIFFORD, C. M., D. E. SONENSHINE, J. E. KEIRANS, AND G. M. KOHLS. 1973. Systematics of the subfamily Ixodinae (Acarina: Ixodidae), 1. The subgenera of *Ixodes*. Annals of the Entomological Society of America **66:** 489–500.

CLOVER, J. R., AND R. S. LANE. 1995. Evidence implicating nymphal *Ixodes pacificus* (Acari: Ixodidae) in the epidemiology of Lyme disease in California. American Journal of Tropical Medicine and Hygiene **53:** 237–240.

CRAVEN, R., AND D. DENNIS. 1993. Isolation of *Borrelia burgdorferi* from *Ixodes spinipalpis* ticks in California and Colorado. Lyme Disease Surveillance Summary **4**(4): 1–2.

DRESSLER, F., R. ACKERMAN, AND A. C. STEERE. 1994. Antibody responses to the three genomic groups of *Borrelia burgdorferi* in European Lyme borreliosis. Journal of Infectious Diseases **169:** 313–318.

DUOBINIS-GRAY, L., J. STUART, E. ZIMMERER, S. WHITE, Z. WANG, R. A. SEIFERT, S. WITT, E. SNODDY, J. COONEY, AND S. BLOEMER. 1993. Lyme disease surveillance in western Kentucky. *In* Proceedings of the 2nd Workshop on Lyme Disease in the Southeast, C. S. Apperson, J. F. Levine, and E. L. Snoddy (eds.). North Carolina State University, Raleigh, North Carolina, p. 5–6.

DURDEN, L. A., AND J. H. OLIVER, JR. 1996. Ecology of *Ixodes scapularis* and Lyme disease in coastal Georgia, USA. *In* Acarology IX, G. R. Needham, D. J. Horn, and W. C. Welbourn (eds.). Ohio Biological Survey, Columbus, Ohio (in press).

FALCO, R. C., AND D. FISH. 1988. Prevalence of *Ixodes dammini* near the homes of Lyme disease patients in Westchester County, New York. American Journal of Epidemiology **127:** 826–830.

FEIR, D., C. R. SANTANELLO, B.-W. LI, C.-S. XIE, E. MASTERS, R. MARCONI, AND G. WEIL. 1994. Evidence supporting the presence of *Borrelia burgdorferi* in Missouri. American Journal of Tropical Medicine and Hygiene **51:** 475–482.

FELZ, M. W., L. A. DURDEN, AND J. H. OLIVER, JR. 1996. Ticks parasitizing humans in Georgia and South Carolina. Journal of Parasitology **82:** (in press).

FIKRIG, E., S. W. BARTHOLD, D. H. PERSING, X. SUN, F. S. KANTOR, AND R. A. FLAVELL. 1992. *Borrelia burgdorferi* strain 25015: Characterization of outer surface protein A and vaccination against infection. Journal of Immunology **148:** 2256–2260.

GERN, L., L. N. TOUTOUNGI, C. M. HU, AND A. AESCHLIMANN. 1991. *Ixodes* (*Pholeoixodes*) *hexagonus*, an efficient vector of *Borrelia burgdorferi* in the laboratory. Medical and Veterinary Entomology **5:** 431–435.

HERRINGTON, J. E., JR. 1995. An update on Lyme disease. Health and Environment Digest **9:** 29–32.

HUTCHESON, H. J., AND J. H. OLIVER, JR. 1996. Multivariate morphometrics of larvae of the blacklegged tick (*Ixodes scapularis*), principal vector of the agent of Lyme disease in eastern North America, with notes on nomenclature. Journal of Parasitology **82:** (in press).

———, ———, M. A. HOUCK, AND R. E. STRAUSS. 1995. Multivariate morphometric discrimination of nymphal and adult forms of the blacklegged tick (Acari: Ixodidae), a principal vector of the agent of Lyme disease in eastern North America. Journal of Medical Entomology **32:** 827–842.

JAMES, A. M., AND J. H. OLIVER, JR. 1990. Feeding and host preference of Immature *Ixodes dammini*, *I. scapularis*, and *I. pacifus* (Acari: Ixodidae). Journal of Medical Entomology **27:** 324–330.

KAWABATA, H., T. MASUZAWA, AND Y. YANAGIHARA. 1993. Genomic analysis of *Borrelia japonica* sp. nov. isolated from *Ixodes ovatus* in Japan. Microbiology and Immunology **37:** 843–848.

KEIRANS, J. E., H. J. HUTCHESON, L. A. DURDEN, AND J. S. H. KLOMPEN. 1996. *Ixodes* (*Ixodes*) *scapularis* (Acari: Ixodidae): Redescription of all active stages, distribution, hosts, geographic variation, and medical and veterinary importance. Journal of Medical Entomology **33:** (in press).

———, G. R. NEEDHAM, AND J. H. OLIVER, JR. 1996. The *Ixodes* (*Ixodes*) *ricinus* complex worldwide: Diagnosis of the species in the complex, hosts and distribution. *In* Acarology IX, G. R. Needham, D. J. Horn, and W. C. Welbourn (eds.). Ohio Biological Survey, Columbus, Ohio (in press).

KOCAN, A. A., S. W. MUKOLWE, G. L. MURPHY, R. W. BARKER, AND K. M. KOCAN. 1992. Isolation of *Borrelia burgdorferi* (Spirochaetales: Spirochaetaceae) from *Ixodes scapularis* and *Dermacentor albipictus* ticks (Acari: Ixodidae) in Oklahoma. Journal of Medical Entomology **29:** 630–633.

LANE, R. S. 1990. Suspectibility of the western fence lizard (*Sceloporus occidentalis*) to the Lyme borreliosis spirochete (*Borrelia burgdorferi*). American Journal of Tropical Medicine and Hygiene **42:** 75–82.

———, AND W. BURGDORFER. 1987. Transovarial and transstadial passage of *Borrelia burgdorferi* in the western blacklegged tick, *Ixodes pacificus* (Acari: Ixodidae). American Journal of Tropical Medicine and Hygiene **37:** 188–192.

———, AND J. E. LOYE. 1989. Lyme disease in California: Interrelationship of *Ixodes pacificus* (Acari: Ixodidae), the western fence lizard (*Sceloporus occidentalis*), and *Borrelia burgdorferi*. Journal of Medical Entomology **26:** 272–278.

———, AND J. A. PASCOCELLO. 1989. Antigenic characteristics of *Borrelia burgdorferi* isolates from ixodid ticks in California. Journal of Clinical Microbiology **27:** 2344–2349.

———, J. PIESMAN, AND W. BURGDORFER. 1991. Lyme borreliosis: Relation of its causative agent to its vectors and hosts in North America and Europe. Annual Review of Entomology **36:** 587–609.

LAVENDER, D. R., AND J. H. OLIVER, JR. 1996. Ticks (Acari: Ixodidae) in Bulloch County, Georgia. Journal of Medical Entomology **33:** 224–231.

LEFEBVRE, R. B., R. S. LANE, G. C. PERNG, J. A. BROWN, AND R. C. JOHNSON. 1990. DNA and protein analysis of tick-derived isolates of *Borrelia burgdorferi* from California. Journal of Clinical Microbiology **28:** 700–707.

LEVIN, M. L., J. F. LEVINE, S. YANG, P. B. HOWARD, AND C. S. APPERSON. 1996. Reservoir competence of the southeastern five-lined skink (*Eumeces inexpectatus*) and the green anole (*Anolis carolinensis*) for *Borrelia burgdorferi*. American Journal of Tropical Medicine and Hygiene **54:** 92–97.

LEVINE, J. F., C. S. APPERSON, AND W. L. NICHOLSON. 1989. The occurrence of spirochetes in ixodid ticks in North Carolina. Journal of Entomological Science **24:** 594–602.

———, ———, J. B. STRIDER, JR., M. LEVIN, J. R. RYAN, P. HOWARD,

W. COUGHLIN, M. KNIGHT, AND S. YANG. 1993. Ticks, their hosts, and *Borrelia burgdorferi* on the outer banks of North Carolina. *In* Proceedings of the 2nd Workshop on Lyme Disease in the Southeast. C. S. Apperson, J. F. Levine, and E. L. Snoddy (eds.). North Carolina State University, Raleigh, North Carolina, p. 7–8.

———, M. L. WILSON, AND A. SPIELMAN. 1985. Mice as reservoirs of the Lyme disease spirochete. American Journal of Tropical Medicine and Hygiene **34:** 355–360.

LIPSCHUTZ, B. 1913. Über eine seltene Erythemform (Erythema chronicum migrans). Archives of Dermatology and Syphilology **118:** 349–356.

LUCKHART, S., G. R. MULLEN, L. A. DURDEN, AND J. C. WRIGHT. 1992. *Borrelia* sp. in ticks recovered from white-tailed deer in Alabama. Journal of Wildlife Diseases **28:** 449–452.

———, ———, AND J. C. WRIGHT. 1993. Etiologic agent of Lyme disease, *Borrelia burgdorferi*, detected in ticks (Acari: Ixodidae) collected at a focus in Alabama. Journal of Medical Entomology **28:** 652–657.

MAGNARELLI, L. A., AND J. F. ANDERSON. 1988. Ticks and biting insects infected with the etiologic agent of Lyme disease, *Borrelia burgdorferi*. Journal of Clinical Microbiology **26:** 1482–1486.

———, ———, C. S. APPERSON, D. FISH, R. C. JOHNSON, AND W. A. CHAPPELL. 1986. Spirochetes in ticks and antibodies to *Borrelia burgdorferi* in white-tailed deer from Connecticut, New York State, and North Carolina. Journal of Wildlife Diseases **22:** 178–188.

———, ———, AND D. FISH. 1987. Transovarial transmission of *Borrelia burgdorferi* in *Ixodes dammini* (Acari: Ixodidae). Journal of Infectious Diseases **156:** 234–236.

———, ———, K. E. HYLAND, D. FISH, AND J. B. MCANINCH. 1988. Serologic analyses of *Peromyscus leucopus*, a rodent reservoir for *Borrelia burgdorferi* in northeastern United States. Journal of Clinical Microbiology **26:** 1138–1140.

———, J. H. OLIVER, JR., H. J. HUTCHESON, AND J. F. ANDERSON. 1991. Antibodies to *Borrelia burgdorferi* in deer and raccoons. Journal of Wildlife Diseases **27:** 562–568.

———, ———, ———, J. L. BOONE, AND J. F. ANDERSON. 1992. Antibodies to *Borrelia burgdorferi* in rodents in the eastern and southern United States. Journal of Clinical Microbiology **30:** 1449–1452.

MAHNKE, G. L., D. E. STALLKNECHT, C. E. GREENE, V. F. NETTLES, AND M. A. MARKS. 1993. Serologic survey for antibodies to *Borrelia burgdorferi* in white-tailed deer in Georgia. Journal of Wildlife Diseases **29:** 230–236.

MAIN, A. J., A. B. CAREY, M. G. CAREY, AND R. H. GOODWIN. 1982. Immature *Ixodes dammini* (Acari: Ixodidae) on small animals in Connecticut, USA. Journal of Medical Entomology **19:** 655–664.

MANWEILER, S. A., R. S. LANE, AND C. H. TEMPELIS. 1992. The western fence lizard *Sceloporus occidentalis*: Evidence of field exposure to *Borrelia burgdorferi* in relation to infestation by *Ixodes pacificus* (Acari: Ixodidae). American Journal of Tropical Medicine and Hygiene **47**(3): 328–336.

MARCONI, R. T., D. LIVERIS, AND I. SCHWARTZ. 1995. Identification of novel insertion elements, restriction fragment length polymorphism patterns, and discontinuous 23S rRNA in Lyme disease spirochetes: Phylogenetic analyses of rRNA genes and their intergenic spacers in *Borrelia japonica* sp. nov. and genomic group 21038 (*Borrelia andersonii* sp. nov.) isolates. Journal of Clinical Microbiology **33:** 2427–2434.

MARSHALL, W. F., S. R. TELFORD III, P. N. RYS, B. J. RUTLEDGE, D. MATHIESEN, S. E. MALAWISTA, A. SPIELMAN, AND D. H. PERSING. 1994. Detection of *Borrelia burgdorferi* DNA in museum specimens of *Peromyscus leucopus*. Journal of Infectious Diseases **170:** 1027–1032.

MAST, W. E., AND W. M. BURROWS. 1976. Erythema chronicum migrans in the United States. Journal of the American Medical Association **236:** 859–860.

MASTERS, E. J., AND H. D. DONNELL. 1995. Lyme and/or Lyme-like disease in Missouri. Missouri Medicine **92:** 346–353.

———, ———, AND M. FOBBS. 1994. Missouri Lyme disease: 1989 through 1992. Journal of Spirochetal and Tick-Borne Diseases **1:** 12–17.

MATHER, T. N., AND M. E. MATHER. 1990. Intrinsic competence of three ixodid ticks (Acari) as vectors of the Lyme disease spirochete. Journal of Medical Entomology **27:** 646–650.

———, M. L. WILSON, S. I. MOORE, J. M. C. RIBEIRO, AND A. SPIELMAN. 1989. Comparing the relative potential of rodents as reservoirs of the Lyme disease spirochete (*Borrelia burgdorferi*). American Journal of Epidemiology **130:** 143–150.

MATHIESEN, D. A., J. H. OLIVER, JR., C. P. KOLBERT, E. D. TULLSON, B. J. B. JOHNSON, G. L. CAMPBELL, P. D. MITCHELL, K. D. REED, S. R. TELFORD III, J. F. ANDERSON, R. S. LANE, AND D. H. PERSING. 1996. Genetic heterogeneity of *Borrelia burgdorferi* in the United States. Journal of Infectious Diseases (in press).

MATUSCHKA, F.-R., P. FISCHER, K. MUSGRAVE, D. RICHTER, AND A. SPIELMAN. 1991. Hosts on which nymphal *Ixodes ricinus* most abundantly feed. American Journal of Tropical Medicine and Hygiene **44**(1): 100–107.

———, A. OHLENBUSCH, H. EIFFERT, D. RICHTER, AND A. SPIELMAN. 1995. Antiquity of the Lyme-disease spirochaete in Europe. Lancet **346:** 1367.

MCLAIN, D.-K., D. M. WESSON, J. H. OLIVER, JR., AND F. H. COLLINS. 1995. Variation in ribosomal DNA internal transcribed spacers 1 among eastern populations of *Ixodes scapularis* (Acari: Ixodidae). Journal of Medical Entomology **32:** 353–360.

MUKOLWE, S. W., A. A. KOCAN, R. W. BARKER, K. M. KOCAN, AND G. L. MURPHY. 1992. Attempted transmission of *Borrelia burgdorferi* (Spirochaetales: Spirochaetaceae) (JDI strain) by *Ixodes scapularis* (Acari: Ixodidae), *Dermacentor variabilis*, and *Amblyomma americanum*. Journal of Medical Entomology **29:** 673–677.

MUSSER, J. M. 1996. Molecular population genetic analysis of emerged bacterial pathogens: Selected insights. Emerging Infectious Diseases **2:** 1–17.

NAKAO, M., AND K. MIYAMOTO. 1993. Long-tailed shrew, *Sorex unguiculatus*, as a potential reservoir of the spirochetes transmitted by *Ixodes ovatus* in Hokkaido, Japan. Japanese Journal of Sanitary Zoology **44:** 237–245.

NORRIS, D. E., J. S. H. KLOMPEN, J. E. KEIRANS, AND W. C. BLACK IV. 1996. Population genetics of *Ixodes scapularis* (Acari: Ixodidae) based on mitochondrial 16S and 12S genes. Journal of Medical Entomology **33:** 78–89.

OLIVER, J. H., JR. 1995. Arthropod research in the southeastern U.S. Journal of Agromedicine **2:** 79–84.

———. 1996. Importance of systematics to public health: Ticks, microbes, and disease. Annals of the Missouri Botanical Garden **83:** 37–46.

———, F. W. CHANDLER, JR., M. P. LUTTRELL, A. M. JAMES, D. E. STALLKNECHT, B. S. MCGUIRE, H. J. HUTCHESON, G. A. CUMMINS, AND R. S. LANE. 1993. Isolation and transmission of the Lyme disease spirochete from the southeastern United States. Proceedings of the National Academy of Sciences U.S.A. **90:** 7371–7375.

———, ———, A. M. JAMES, L. O. HUEY, G. N. VOGEL, AND F. H. SANDERS, JR. 1996. Unusual strain of *Borrelia burgdorferi* isolated from *Ixodes dentatus* in central Georgia. Journal of Parasitology **82:** (in press).

———, ———, ———, F. H. SANDERS, JR., H. J. HUTCHESON, L. O. HUEY, B. S. MCGUIRE, AND R. S. LANE. 1995. Natural occurrence and characterization of the Lyme disease spirochete, *Borrelia burgdorferi*, in cotton rats (*Sigmodon hispidus*) from Georgia and Florida. Journal of Parasitology **81:** 30–36.

———, G. A. CUMMINS, AND M. S. JOINER. 1993. Immature *Ixodes scapularis* (Acari: Ixodidae) parasitizing lizards from the southeastern U.S.A. Journal of Parasitology **79:** 684–689.

———, M. R. OWSLEY, H. J. HUTCHESON, A. M. JAMES, C. CHEN, W. S. IRBY, E. M. DOTSON, AND D. K. MCLAIN. 1993. Conspecificity of the ticks *Ixodes scapularis* and *Ixodes dammini* (Acari: Ixodidae). Journal of Medical Entomology **30:** 54–63.

———, D. E. STALLKNECHT, F. W. CHANDLER, JR., A. M. JAMES, B. S. MCGUIRE, AND E. W. HOWERTH. 1992. Detection of *Borrelia burgdorferi* in laboratory-reared *Ixodes dammini* (Acari: Ixodidae) fed on experimentally inoculated white-tailed deer. Journal of Medical Entomology **29:** 980–984.

OLSÉN, B., D. C. DUFFY, T.G.T. JAENSON, A. GYLFE, J. BONNEDAHL, AND S. BERGSTRÖM. 1995. Transhemispheric exchange of Lyme disease spirochetes by seabirds. Journal of Clinical Microbiology **33:** 3270–3274.

OUELLETTE, J. R., P. HOWARD, J. F. LEVINE, T. L. EVANS, AND C. S. APPERSON. 1993. Tick-raccoon associations in the Coastal Plain of

North Carolina. *In* Proceedings of the 2nd Workshop on Lyme Disease in the Southeast. C. S. Apperson, J. F. Levine, and E. L. Snoddy (eds.). North Carolina State University, Raleigh, North Carolina, p. 9–10.

PERSING, D. H., S. R. TELFORD III, P. N. RYS, D. E. DODGE, T. J. WHITE, S. E. MALAWISTA, AND A. SPIELMAN. 1990. Detection of *Borrelia burgdorferi* DNA in museum specimens of *Ixodes dammini* ticks. Science **249:** 1420–1423.

PIESMAN, J., J. G. DONAHUE, T. N. MATHER, AND A. SPIELMAN. 1986. Transovarially acquired Lyme disease spirochetes (*Borrelia burgdorferi*) in field-collected larval *Ixodes dammini* (Acari: Ixodidae). Journal of Medical Entomology **23:** 219.

———, T. N. MATHER, G. J. DAMMIN, S. R. TELFORD III, C. C. LASTAVICA, AND A. SPIELMAN. 1987. Seasonal variation of transmission risk of Lyme disease and human babesiosis. American Journal of Epidemiology **126:** 1187–1189.

———, ———, J. G. DONAHUE, J. LEVINE, J. D. CAMPBELL, S. J. KARAKASHIAN, AND A. SPIELMAN. 1986. Comparative prevalence of *Babesia microti* and *Borrelia burgdorferi* in four populations of *Ixodes dammini* in eastern Massachusetts. Acta Tropica **43:** 263–270.

———, AND R. J. SINSKY. 1988. Ability of *Ixodes scapularis*, *Dermacentor variabilis*, and *Amblyomma americanum* (Acari: Ixodidae) to acquire, maintain, and transmit Lyme disease spirochetes (*Borrelia burgdorferi*). Journal of Medical Entomology **25:** 336–339.

———, AND A. SPIELMAN. 1979. Host-associations and seasonal abundance of immature *Ixodes dammini* in southeastern Massachusetts. Annals of the Entomological Society of America **72:** 829–832.

———, ———, P. ETKIND, T. K. RUEBUSH II, AND D. D. JURANEK. 1979. Role of deer in the epizootiology of *Babesia microti* in Massachusetts, USA. Journal of Medical Entomology **15:** 537–540.

POSTIC, D., M. V. ASSOUS, P. A. D. GRIMONT, AND G. BARANTON. 1994. Diversity of *Borrelia burgdorferi* sensu lato evidenced by restriction fragment length polymorphism of rrf(5S) rrl(23S) intergenic spacer amplicons. International Journal of Systematic Bacteriology **44:** 743–752.

RAND, P. W., E. H. LACOMBE, R. P. SMITH, S. M. RICH, C. W. KILPATRICK, C. A. DRAGONI, AND D. CAPORALE. 1993. Competence of *Peromyscus maniculatus* (Rodentia, Cricetidae) as a reservoir host for *Borrelia burgdorferi* (Spirochaetares, Spirochaetaceae) in the wild. Journal of Medical Entomology **30:** 614–618.

RAWLINGS, J. A. 1986. Lyme disease in Texas. Zentralblatt für Bakteriologie Mikrobiologie und Hygiene, Series A **263:** 483–487.

RAWLINGS, J. A., AND G. J. TELTOW. 1994. Prevalence of *Borrelia* (Spirochaetaceae) spirochetes in Texas ticks. Journal of Medical Entomology **31:** 297–301.

RICH, S. M., D. CAPORALE, S. R. TELFORD III, T. D. KOCHER, D. L. HARTL, AND A. SPIELMAN. 1995. Distribution of the *Ixodes ricinus*-like ticks of eastern North America. Proceedings of the National Academy of Sciences U.S.A. **92:** 6284–6288.

ROBBINS, R. G., AND J. E. KEIRANS. 1992. Systematics and ecology of the subgenus *Ixodiopsis* (Acari: Ixodidae: *Ixodes*). Thomas Say Foundation Monographs **14:** 1–159.

ROGERS, A. J. 1953. A study of the ixodid ticks of northern Florida, including the biology and life history of *Ixodes scapularis* Say (Ixodidae: Acarina). Ph.D. Dissertation. University of Maryland, College Park, Maryland, 183 p.

RYDER, J. W., R. R. PINGER, AND T. GLANCY. 1992. Inability of *Ixodes cookei* and *Amblyomma americanum* nymphs (Acari: Ixodidae) to transmit *Borrelia burgdorferi*. Journal of Medical Entomology **29:** 525–530.

SAITO, Y. 1977. Preliminary report of first detection of *Borrelia* sp. from *Ixodes ovatus* in Japan. Japanese Journal of Sanitary Zoology **28:** 58. [In Japanese.]

SANDERS, F. H., JR., AND J. H. OLIVER, JR. 1995. Evaluation of *Ixodes scapularis*, *Amblyomma americanum*, and *Dermacentor variabilis* (Acari: Ixodidae) from Georgia as vectors of a Florida strain of the Lyme disease spirochete, *Borrelia burgdorferi*. Journal of Medical Entomology **32:** 402–406.

SCHOELER, G. B., AND R. S. LANE. 1993. Efficiency of transovarial transmission of the Lyme disease spirochete, *Borrelia burgdorferi*, in the western blacklegged tick, *Ixodes pacificus* (Acari: Ixodidae). Journal of Medical Entomology **30:** 80–86.

SCHULZE, T. L., G. S. BOWEN, E. M. BOSLER, M. F. LAKAT, AND W. E. PARKIN. 1984. *Amblyomma americanum*: A potential vector of Lyme disease in New Jersey. Science **224:** 601–603.

———, M. F. LAKAT, W. E. PARKIN, J. K. SHISLER, D. J. CHARETTE, AND E. M. BOSLER. 1986. Comparison of rates of infection by the Lyme disease spirochete in selected populations of *Ixodes dammini* and *Amblyomma americanum* (Acari: Ixodidae). Zentralblatt für Bakteriologie Mikrobiologie und Hygiene, Series A **263:** 72–78.

SONENSHINE, D. E., R. E. RATZLAFF, J. TROYER, S. DEMMERLE, E. R. DEMMERLE, W. E. AUSTIN, S. TAN, B. A. ANNIS, AND S. JENKINS. 1995. *Borrelia burgdorferi* in eastern Virginia: Comparison between a coastal and inland locality. American Journal of Tropical Medicine and Hygiene **53:** 123–133.

———, R. RATZLAFF, J. M. TROYER, S. M. DEMMERLE, E. DEMMERLE, S. JENKINS, AND B. ANNIS. 1993. Tick–host associations and maintenance of *Borrelia burgdorferi* in Virginia. *In* Proceedings of the 2nd Workshop on Lyme Disease in the Southeast. C. S. Apperson, J. F. Levine, and E. L. Snoddy (eds.). North Carolina State University, Raleigh, North Carolina, p. 8–9.

SPIELMAN, A., M. L. WILSON, J. F. LEVINE, AND J. PIESMAN. 1985. Ecology of *Ixodes dammini*-borne human babesiosis and Lyme disease. Annual Review of Entomology **30:** 439–460.

STEERE, A. C., T. F. BRODERICK, AND S. E. MALAWISTA. 1978. Erythema chronicum migrans and Lyme arthritis: Epidemiologic evidence for a tick vector. American Journal of Epidemiology **108:** 312–321.

———, S. E. MALAWISTA, J. A. HARDIN, S. RUDDY, P. W. ASKENASE, AND W. A. ANDIMAN. 1977. Erythema chronicum migrans and Lyme arthritis: The enlarging clinical spectrum. Annals of Internal Medicine **86:** 685–698.

TELFORD, S. R. III, T. N. MATHER, S. I. MOORE, M. L. WILSON, AND A. SPIELMAN. 1988. Incompetence of deer as reservoirs of the Lyme disease spirochete. American Journal of Tropical Medicine and Hygiene **39:** 105–109.

———, AND A. SPIELMAN. 1989. Enzootic transmission of the agent of Lyme disease in rabbits. American Journal of Tropical Medicine and Hygiene **41:** 482–490.

TELTOW, G. J., P. V. FOURNIER, AND J. A. RAWLINGS. 1991. Isolation of *Borrelia burgdorferi* from arthropods collected in Texas. American Journal of Tropical Medicine and Hygiene **44:** 469–474.

VAN DAM, A. P., H. KUIPER, K. VOS, A. WIDJOJOKUSUMO, B. M. DE JONGH, L. SPANJAARD, A. C. P. RAMSELAAR, M. D. KRAMER, AND J. DANKERT. 1993. Different genospecies of *Borrelia burgdorferi* are associated with distinct clinical manifestations of Lyme borreliosis. Clinical Infectious Diseases **17:** 708–717.

WESSON, D. M., D. K. MCLAIN, J. H. OLIVER, JR., J. PIESMAN, AND F. H. COLLINS. 1993. Investigation of the validity of species status of *Ixodes dammini* (Acari: Ixodidae) using rDNA. Proceedings of the National Academy of Sciences U.S.A. **90:** 10221–10225.

WIENECKE, R., N. ZOCHLING, U. NEUBERT, E.-M. SCHLUPEN, M. MEURER, AND M. VOLKENANDT. 1994. Molecular subtyping of *Borrelia burgdorferi* in erythema migrans and acrodermatitis chronica atrophicans. Journal of Investigative Dermatology **103:** 19–22.

WILSKE, B., V. PREAC-MURSIC, U. B. GOBEL, B. GRAF, S. JAURIS, E. SOUTSCHEK, E. SCHWAB, AND G. ZUMSTEIN. 1992. An OspA serotyping system for *Borrelia burgdorferi* based on reactivity with monoclonal antibodies and OspA sequence analysis. Journal of Clinical Microbiology **31:** 340–350.

———, ———, G. SCHIERZ, R. KUHBOCK, A. G. BARBOUR, AND M. KRAMER. 1988. Antigenic variability of *Borrelia burgdorferi*. Annals of the New York Academy of Sciences **539:** 126–143.

WILSON, M. L., AND A. SPIELMAN. 1985. Seasonal activity of immature *Ixodes dammini* (Acari: Ixodidae). Journal of Medical Entomology **22:** 408–414.

ZINGG, B. C., R. N. BROWN, R. S. LANE, AND R. B. LEFEBVRE. 1993. Genetic diversity among *Borrelia burgdorferi* isolates from woodrats and kangaroo rats in California. Journal of Clinical Microbiology **31:** 3109–3114.