TABLE 11–2
Arthropod Species in Which *Borrelia burgdorferi sensu lato* Has Been Confirmed

SPECIES	GEOGRAPHIC LOCATION	COMMON NAME	*Bb SENSU LATO* GENOSPECIES ISOLATED	VECTOR COMPETENCE FOR *B. BURGDORFERI*
Ixodes scapularis	N. America	Deer tick	*B.b.s.s., B. andersonii B. bissettii*	Efficient
Ixodes pacificus	N. America	Western black-legged tick	*B.b.s.s., B. andersonii, B. bissettii*	Efficient
Ixodes ricinus	Europe	Sheep tick	*B. garinii, B. afzelii, B.b.s.s., B. valaisiana, B. lusitaniae*	Efficient
Ixodes persulcatus	Asia	Taiga tick	*B. garinii, B. afzelii, B. valaisiana, B. lusitaniae, B. miyamotoi*	Efficient
Ixodes dentatus	N. America	Rabbit tick	*B.b.s.l., B. andersonii*	Efficient
Ixodes neotomae	N. America	Woodrat tick	*B.b. B. bissettii, B.b.s.l.*	Efficient
Ixodes angustus	N. America		*B.b.*	
Ixodes cookei	N. America		*B.b.*	Poor
Ixodes spinipalpis	N. America	Mexican woodrat tick	*B.b.*	Efficient
Ixodes hexagonus	Europe	Hedgehog and fox tick	*B.b.s.l.*	Efficient
Ixodes canisuga	Europe	Fox tick	*B.b.s.l.*	?
Ixodes frontalis	Europe	Bird tick	*B.b.s.l.*	?
Ixodes ovatus	Asia	Oriental and Palearctic tick	*B. japonica*	?
Ixodes granulatus	Asia		*B.b.*	?
Ixodes uriae	Subarctic and subantarctic islands	Seabird tick	*B. garinii*	Efficient
Ixodes rangtangensis	Asia		*B.b.*	?
Ixodes columnae	Asia		*B.b.* Am501	?
Ixodes tanuki	Asia		*B. tanukii*	
Ixodes turdus	Asia		*B. turdae*	
Amblyomma americanum	N. America	Lone Star tick	*B.b.s.s., B.b.s.l., B. lonestarii*	Poor
Amblyomma maculatum	N. America	Gulf Coast tick	*B.b.*	?
Dermacentor variabilis	N. America	Dog tick	*B.b.*	Poor
Dermacentor albipictus	N. America		*B.b.*	
Dermacentor occidentalis	N. America	Pacific Coast tick	*B.b.*	Poor
Dermacentor parumapertus	N. America	Rabbit tick	*B.b.*	?
Dermacentor marginatus	Europe		*B.b.*	?
Rhipicephalus sanguineus	N. America	Dog tick	*B.b.*	?
Haemaphysalis leporispalustris	N. America	Rabbit tick	*B.b.*	?
Haemaphysalis punctata	Europe		*B.b.*	?
Haemaphysalis concinna	Asia		*B.b.s.l.*	?
Haemaphysalis bispinosa	Asia		*B.b.s.l.*	?
Haemaphysalis longicornis	Asia		*B.b.s.l.*	?
Ctenocephalides felis	N. America	Cat flea	*B.b.*	?
Chrysops and *Hybomitra* spp.	N. America	Tabanid (Deer and horse) flies	*B.b.*	Poor
Aedes spp. and *Culex* spp.	N. America, Europe	Mosquitoes	*B.b.*	Poor

Data obtained from references 53, 59, 61, 64–70, 73, 74, 77, 100, 153–158, 163–166, 170, 180, 336, 344, 350, 351, 355, 362, 365, 376–381, 382–389, 405, 412, 420, 438, 449, 621, 878, 884, and additional references noted in text.

ences in vector competence of *I. scapularis* and *I. ricinus* for different genospecies of *B. burgdorferi*, and even for different strains within the same genospecies,[878] which may be related to differential susceptibility to bacteriolysis of various *B. burgdorferi* genospecies by complement of different host species.[294]

In North America, *I. scapularis* has also been reported to be the vector of the agent of human babesiosis, *Babesia microti*,[394] and of the agent of human granulocytic ehrlichiosis (HGE) (which is closely related to *Ehrlichia equi/phagocytophila*)[395–398]; presumably, *I. pacificus* in the western United States[398] and *I. ricinus* in Europe[398–400]

act in the same capacity. In North America, *Amblyomma americanum* is the vector of the agent of human monocytic ehrlichiosis (HME), *Ehrlichia chaffeensis* (initially incorrectly reported as *Ehrlichia canis*), and has also been considered a possible secondary vector of *B. burgdorferi*; the European vector of HME is not known. The vector of the *Babesia* species piroplasm WA1, which causes human infection in California, is not known.[401] Co-infections of ticks with *B. burgdorferi* and *Ehrlichia* or *Babesia* have been reported.

Enzootic Cycles: Tick Vector Life Cycles and Reservoir Animal Hosts

The *Ixodes ricinus* complex ticks are all three-host ticks with a 2- to 3-year life cycle, and each of the three stages of the tick feeds once (Table 11–3): Larvae feed on small rodents, reptiles, and birds; nymphs feed on small or medium-sized mammals; and adults feed on large mammals.* Eggs laid by infected adult female ticks usually hatch into uninfected larvae, as the rate of transovarial transmission of the spirochete is very low,[352–356] and larvae acquire the spirochete by feeding on *B. burgdorferi* spirochetemic–competent reservoir hosts. The infection is maintained in the larvae through the transstadial molt and is passed from the larval to the nymphal stage. The infected nymphs transmit the infection to reservoir-competent hosts by feeding, maintain the infection through the transstadial molt, and pass it to the adult stage of the tick, which then mates while feeding on a large mammalian host. The prevalence of *B. burgdorferi* infection in a tick population is determined by the frequency of feeding of larvae and nymphs on infected reservoir-competent hosts. The infection rate in adult ticks is higher than in nymphal ticks.[161, 396, 409, 410] Larval ticks have been found to acquire *B. burgdorferi* even after only partial feeding.[357]

For *B. burgdorferi* infection to be maintained in nature, there must be horizontal transmission of infection from infected nymphs to a competent reservoir host to larvae, which requires that nymphs feed before larvae on the same reservoir-competent host.[347] The white-footed mouse, *Peromyscus leucopus*, and other *Peromyscus* species mice are reservoir-competent for *B. burgdorferi*, are easily infected by a single infected tick bite, develop persistent spirochetemia, are able to infect feeding ticks, and are almost universally infected in endemic areas.[411] Humans are accidental hosts of all stages of *I. scapularis* and *I. ricinus*, and of the adult ticks of *I. pacificus*, *I. persulcatus*, and *I. ovatus*. Some animal hosts of *I. ricinus* complex ticks, such as North American catbirds, western fence lizards, and European blackbirds, have a zooprophylactic effect, and decrease the force of *B. burgdorferi* transmission by eliminating infectious spirochetes within feeding ticks, thus removing these ticks from the enzootic cycle.[173]

The life cycle of *I. scapularis* has been the most extensively studied.[138, 154, 167, 168, 182, 390, 407, 408] Eggs laid on the ground in the spring hatch into larvae in mid- to late summer. In late summer, July and August, larvae become

*See references 138, 167, 168, 182, 336, 346, 347, 390, 407, and 408.

TABLE 11–3
Preferred Hosts for Different Stages of *Ixodes ricinus* Complex Ticks That Transmit Lyme Borreliosis to Humans[a, b]

TICK	LARVAL AND NYMPHAL STAGES	ADULT STAGE	TOTAL NO. HOSTS			
			Mammal	Bird	Reptile	All
I. scapularis						
(northern U.S.)	White-footed mouse, *Peromyscus leucopus*	White-tailed deer, *Odocoileus virginianus*	31	49	0	80
(southern U.S.)	Lizards and skinks Cotton mouse, *Peromyscus gossypinus* Cotton rat, *Sigmodon hispidus*	White-tailed deer, *Odocoileus virginianus* Black-tailed deer, *Odocoileus hemionus columbianus*	39	11	6	53
I. pacificus	Fence lizard, *Sceloporus occidentalis*	Black-tailed deer, *Odocoileus hemionus columbianus*, cattle, horses, bears	54	19	7	80
I. ricinus	Woodmouse, *Apodemus sylvaticus*, and Yellow-necked mouse, *Apodemus flavicolus* Bank vole, *Cletbrionomys glareolus* Black rat, *Rattus rattus*, and Norway rat, *Rattus norvegicus*	Deer, *Capreolus capreolus* Deer, canids, cattle, hares, sheep	91	132	14	237
I. persulcatus	Woodmouse, *Apodemus speciosus* Red-backed vole, *Cletbrionomys rutilus* Black-faced bunting, *Emberiza spodocephala* Red-bellied thrush, *Turdus chrysolaus*	Deer, canids, cattle, hares	89	121	2	212

[a]Data from references 163, 164, 167–169, 182, 336, 348, 378, 413, and 419–421.
[b]Humans are incidental hosts of all stages of the ticks.

infected with *B. burgdorferi* by feeding for 3 to 5 days on small rodents such as the white-footed mouse, which are amplifying reservoirs for *B. burgdorferi* infection; the fed larvae then fall to the ground. The infection persists in the larvae throughout the winter and through the transstadial molt the following spring into the nymphal stage. The nymphs are voracious and feed in the spring and early summer (May, June, and early July) for 4 to 7 days on a variety of hosts, including small rodents such as the white-footed mouse, birds, wild and domestic animals, and occasionally, humans; the fed nymphs fall to the ground. Because transovarial passage of *B. burgdorferi* infection is rare, horizontal transmission is necessary to maintain the tick infection, and it occurs because infected nymphs feed earlier in the season on the same hosts as the larvae and infect the hosts, which then infect the larvae. The nymphs molt into adults by late summer or fall, and the spirochete is passed transstadially to the adult form. The adults quest for vegetation, especially at edges between lawns and forests,[336] and for medium-sized to large mammalian hosts, such as white-tailed deer, in the fall (mid-October through November), warm days in winter, and the following spring (April and early May); they mate while the females are feeding on these hosts. Questing adult field-collected infected ticks contain a median of 1500 to 1900 spirochetes per tick.[412] Because tick mating occurs on these large mammalian hosts, particularly deer, these hosts are needed for tick survival but not for maintenance of the *B. burgdorferi* infection.[411] The females then feed for 8 to 11 days, fall to the ground, lay eggs in the spring, and die; the eggs hatch in 45 to 53 days into larvae in the summer. The prevalence of *B. burgdorferi* infection increases from the nymphal to the adult stage because the ticks feed on amplifying reservoir-competent hosts.

In northeastern and upper midwestern North America, the preferred small rodent host of *I. scapularis* is the white-footed mouse, *Peromyscus leucopus*, which is also the primary reservoir of *B. burgdorferi* infection in nature,[167, 182, 346, 411] and the preferred large mammal host is the white-tailed deer, *Odocoileus virginianus*, which is the host of the reproductive stage of the tick[346, 408]; however, larvae and nymphs have been found attached to 80 different species of mammals and birds, but not reptiles, and adult ticks to 13 species of medium-sized to large mammals.[167, 168, 336, 337, 413] The mice remain chronically spirochetemic but asymptomatic. The deer are occasionally spirochetemic with *B. burgdorferi* but are also asymptomatic.[169, 407, 408, 413] The deer are responsible for the geographic expansion of Lyme-endemic areas because the infected *I. scapularis* adult females overwinter and mate on the deer, and the deer travel widely but are not considered reservoirs for *B. burgdorferi* maintenance in nature. The geographic distribution of North American Lyme disease and *I. scapularis* correlates with that of the white-tailed deer.[408]

Other reservoir-competent small mammal hosts may be involved in the maintenance of *B. burgdorferi* infection in nature[182] in certain geographic areas, or at times in which the population of the usual reservoir host, the white-footed mouse, is low or absent. The deer mouse, *Peromyscus maniculatus*, has been shown to be a competent reservoir host for *I. scapularis* on an offshore island in Maine with no resident *P. leucopus*, and may also be an important alternate reservoir host in the northern forests of Maine.[414] The eastern chipmunk, *Tamias striatus*, is an important reservoir-competent alternate host for immature *I. scapularis*, which can feed on either mice or chipmunks in hardwood forests of the Upper Midwest, including Wisconsin[416] and northwestern Illinois[417]; the meadow vole *Microtus pennsylvanicus* is a secondary, less important, small mammal reservoir host of *I. scapularis* in some areas of eastern North America.[168] A parallel cycle involving the cottontail rabbit, *Sylvilagus floridanus*, *I. scapularis*, and the rabbit tick *Ixodes dentatus*[169, 170] occurs either in areas where the enzootic *I. scapularis*–white footed mouse cycle of maintenance of *B. burgdorferi* infection is inefficient or does not occur, or in areas such as Nantucket Island, Massachusetts, New York,[100] and other parts of the northeastern United States[70] where the *I. scapularis*–mouse cycle occurs but the *I. dentatus*–rabbit cycle functions as an independent complementary cycle.[170] The *I. dentatus*–rabbit cycle is silent with respect to human Lyme disease as *I. dentatus* rarely bites humans; *I. scapularis* rarely feeds on rabbits,[170] but may be important in the spread of *B. burgdorferi* to new geographic areas because immature *I. dentatus* also feeds on birds.[157]

In some parts of North America, *B. burgdorferi* is present in areas that are not endemic for human Lyme disease because *B. burgdorferi* is maintained in nature by enzootic cycles that produce endemic foci that are silent with respect to human transmission of Lyme disease. One such cycle is the *I. spinipalpus–Mexican woodrat* cycle in Colorado; this tick has a broad host range, including rodents, rabbits, and ground-dwelling birds, but humans are rarely bitten because questing ticks are found only in woodrat nests; therefore, this cycle does not contribute to transmission of human Lyme disease.[362]

In the southern United States, the enzootic cycles that maintain *B. burgdorferi* in nature have been less fully described, are more complex and less efficient than those in the North, and result in lower *B. burgdorferi* tick infection rates.[156, 167, 361] The most common reservoir hosts for maintenance of *B. burgdorferi* infection in nature are the cotton mouse, *Peromyscus gossypinus*, and the cotton rat, *Sigmodon hispidus*; however, the life cycle of southern *I. scapularis* is less synchronized, so that nymphal feeding does not always precede larval feeding, thereby reducing the acquisition of infection by feeding larvae.[361] The southern *I. scapularis* is able to feed on 53 species of hosts, including mammals, birds, and reptiles, but the preferred hosts for immature *I. scapularis* are lizards and skinks (which are incompetent hosts incapable of maintaining and amplifying *B. burgdorferi* infection)[336, 348, 418]; the large mammal hosts for adult *I. scapularis* are white- and black-tailed deer, *Odocoileus virginianus* or *hemionus columbianus*. Reptiles exert a zooprophylactic effect on Lyme disease transmission, with a decrease in transmission in areas where reptiles predominate: South of the 38 degrees North latitude boundary, which runs from Virginia through Missouri, reptiles make up over 10% of the total *I. scapularis* hosts available (reptile index is greater than 10), and questing

ticks are significantly diverted away from reservoir-competent amplifying hosts, such as the cotton mouse and the cotton rat, leading to lower tick infection rates.[156, 348, 418] *B. burgdorferi* in Missouri, and probably in Georgia, appears to be maintained in a cottontail rabbit–*I. dentatus* enzootic cycle, and *I. scapularis* and possibly *A. americanum* have been proposed as bridge vectors from rabbits to humans.[153, 361] *I. cookei* has been reported to bite humans in West Virginia, where it is considered a possible human Lyme disease vector; its immature forms feed on small and medium-sized carnivores, and its adults only on medium-sized carnivores.[363] *I. affinis* may enhance enzootic *I. scapularis*–cotton mouse/rat cycles, and *I. minor* may be involved in parallel enzootic cycles with the eastern woodrat, *Neotoma floridana*, or birds; these cycles maintain *B. burgdorferi* infection in nature in Georgia and South Carolina.[361]

Ixodes pacificus,[167, 180, 182, 336, 419, 420] in the far western United States, has a life cycle similar to that of *I. scapularis* but with some differences in hosts, reservoirs, and seasonality of feeding. Although *I. pacificus* is able to feed on a wide variety of hosts, including 80 different species of mammals, birds, and reptiles, its immature stages feed preferentially on lizards,[421] which are not competent *B. burgdorferi* reservoirs and cannot infect feeding ticks[336, 347, 348]; its larval feeding peaks before nymphal feeding,[336, 421] leading to the relatively low tick infection rates reported for adult ticks.[420] The black-tailed deer, *Odocoileus hemionus columbianus*, is the host of the adult tick, which feeds mostly in fall and winter, and to a lesser degree of the immature stages; in one study, all three stages were present simultaneously on deer.[421] *B. burgdorferi* infection is maintained in nature by a parallel enzootic cycle involving the competent reservoir host, the dusky-footed woodrat *Neotoma fuscipes*, and a non–*I. ricinus* complex tick, *I. neotomae* (now *I. spinipalpis*),[378] which rarely bites humans. *I. pacificus* is responsible for human transmission and acts as a bridging vector between the *I. neotomae*–woodrat cycle and man. In 1995, in California, the nymphal tick infection rate was found to be 14%, compared with the adult rate of 4%, and the possibility of a borreliacidal factor in lizard hosts was raised.[173, 180]

There are some differences between the life cycles of European *I. ricinus* and North American *I. scapularis* ticks.[167–169, 182, 336] *I. ricinus* has a 2- to 3-year life cycle (occasionally, 5 to 6 years in far northern latitudes), less coherent seasonal activity, and all three tick stages have feeding activity at the same time, particularly from mid-May to early July[181]; it has a broader host range, which includes 237 to 317 species of mammals, birds, and reptiles. *I. ricinus* abundance correlates with that of deer,[181] but *I. ricinus* occurs in some geographic areas even in the absence of deer because it can use cattle as well as deer as the large mammalian host.[168] The geographic distribution of Lyme borreliosis in Europe correlates with the geographic distribution of *I. ricinus* ticks,[11] particularly the distribution of *B. burgdorferi*–infected ticks,[181, 402] and even more with the distribution of highly infected ticks[422] and of deer,[168, 181] as in North America. The hedgehog *Erinaceus europaeus*–*I. hexagonus* cycle is involved in maintenance of *B. burgdorferi* infection in nature in Europe and Asia, but *I. hexagonus* rarely bites humans and is not considered important in the transmission of human Lyme disease.[182] In some areas, such as an urban park in Magdeburg, Germany, Norway rats, *Rattus norvegicus*, and *I. ricinus* are involved in maintenance of *B. burgdorferi* in nature in a cycle that occurs in addition to the mouse cycle.[423]

I. persulcatus[167, 169, 182] is responsible for human Lyme disease transmission in Asia; it has a similar life cycle to *I. ricinus* but a greater host range, which includes 212 to 241 different species of mammals, birds, and reptiles, although deer, canids, cattle, and hares are particularly important hosts.[344] The life cycle is usually 2 to 3 years, but in extreme northern latitudes it may be 5 to 6 years. The geographic distribution of Lyme disease and the genospecies of *B. burgdorferi* isolated from human Lyme disease patients in China, Japan, and eastern Russia correlate with the geographic distribution of, and genospecies isolated from, *I. persulcatus*.[163, 164, 374] There appear to be two separate enzootic cycles involving larvae and nymphs in Japan—the *I. persulcatus*–rodent cycle involving mainly the woodmouse (and sometimes the vole), and the *I. persulcatus*–bird cycle[163]; adult ticks feed mainly on large animals.

I. holocyclus, the most common tick in Australia, is not competent for *B. burgdorferi*.[392] So far, no competent vector or reservoir host has been identified in Australia. The mammalian hosts of *B. burgdorferi* in the northern hemisphere are all placental animals, and none of these are present in Australia, where the small mammals are mostly marsupial.[375]

A migratory seabird–*I. uriae* enzootic cycle has been described in high-latitude subarctic and subantarctic circumpolar areas, in which the seabirds maintain *B. burgdorferi* (*B. garinii*) infection in nature without the involvement of mammalian hosts.[152, 165, 166] The geographic distributions of *I. uriae* and *I. ricinus* overlap on islands in the Bothnian Gulf at the northern end of the Baltic Sea, and bridging may occur between the two enzootic cycles.[13, 152] It has been proposed that the migratory seabird is the reservoir for *B. burgdorferi* in the southern hemisphere, is responsible for the transhemispheric and global spread of *B. burgdorferi*, and may be important for the spread of Lyme disease to Australia and South Africa.[165]

In addition to *I. uriae*, other ixodid ticks, including the human Lyme disease vectors, *I. ricinus*, *I. scapularis*, *I. pacificus*, and *I. persulcatus*, and the rabbit-feeding ticks, *I. dentatus*, *I. spinipalpus*, and *H. leporispalustris*, are able to feed on birds as alternate hosts in addition to mammalian hosts[157, 163, 167, 182, 362]; therefore, they presumably have an opportunity to be transported by migratory birds to new geographic areas,[425, 426] and also to acquire *B. burgdorferi* from birds that may be reservoir-competent. The potential epidemiologic impact of migratory birds as transporters of infected ticks is great because an estimated 100 million birds migrate into Sweden each spring, carrying 6.8 million new ticks, 1.8 million of which carry *B. burgdorferi*; also, 4.7 million ticks, 1.3 million of which harbor *B. burgdorferi*, are transported out of Sweden toward the South every fall.

Small mammals, including mice and rabbits, and their

ticks may be important in establishment and maintenance of new cryptic *B. burgdorferi* endemic foci in nature by providing reservoir-competent hosts for infected ticks carried to new sites by migratory birds.[170, 171]

Seasonality of Human Tick Bites/ Transmission of *Borrelia burgdorferi* Infection

Humans acquire Lyme borreliosis by being used as the incidental host of a *B. burgdorferi*–infected tick. Table 11–4 shows the seasonality of human tick bites and the time of onset of Lyme borreliosis by geographic region.

In North America, humans are incidental hosts of all stages of *I. scapularis*,[337] and in the Northeast and Upper Midwest, they are usually infected by voracious host-seeking *I. scapularis* nymphs during the spring and early summer (in May and June); the peak incidence of Lyme disease with erythema migrans occurs 1 month later during June and July.[336, 428] In mid-Atlantic states such as Maryland, the onset of most cases of Lyme disease is from May through September.[429] Epidemiologic studies have found that the tick infectivity rate increases from less than 1% of larvae, to 20 to 74% of nymphs, to 57 to 87% of adult ticks.[411] Nymphs are responsible for transmission of almost 90% of cases of Lyme disease.[347] Because the nymphs are so small, and because the tick injects saliva containing anti-inflammatory, analgesic, antihemostatic, and immunosuppressive components while feeding,[168] the bites are not painful and often go unnoticed long enough to allow *B. burgdorferi* transmission, which usually takes 2 to 3 days.[430] However, there are rare European reports of transmission after less than 24 hours[430, 431] and within 2 hours.[9] Human infection is less often caused by adult female *I. scapularis*, which feeds in late fall through early winter (from October through May), with a peak in October, even though *B. burgdorferi* infection rates among adults are higher than for nymphs, because the adults are larger and more easily detected and can be removed before transmission of *B. burgdorferi* infection occurs.[336, 430]

The *I. scapularis* tick takes a long time to feed; during a 5-day feeding period, the female tick ingests 3.5 ml of blood and injects or regurgitates 2.5 ml of fluid secretions into the host.[270] The blood meal triggers multiplication of the *B. burgdorferi* associated with the tick's gastrointestinal tract, which disseminate to the hemolymph by the third day of feeding and then spread to the host either by injection of *B. burgdorferi*–containing tick saliva or by regurgitation of *B. burgdorferi*–containing tick gut contents into the dermal feeding cavity created by the tick.[341, 342] These immunosuppressive salivary secretions and other factors related to the spirochete and its acquisition of host extracellular matrix digestive enzymes[144] result in host-specific immune evasion by the tick, which modifies the tick attachment site so that *B. burgdorferi* deposited in the skin may be in an immunologically privileged site and may be protected against attack by the host immune system.[168]

In the Pacific Northwest, along the Pacific Coast, humans are also incidental hosts of both the adult and immature stages of *I. pacificus*, which is one of the most common ticks biting humans[336, 420]; it is responsible for 59% of human tick bites[180] (66% of bites by adult ticks, and 44% by nymphs). The incidence of *B. burgdorferi* infection in nymphal ticks is much higher than in adult ticks, possibly because of the zooprophylactic effect of the reptile hosts of the immature stages.[180] The peak onset of Lyme disease with EM (March through August) corresponds to the nymphal feeding season (March through September), rather than to the adult tick feeding season (October through June, with peaks in December and March).[180] Because the incidence of *B. burgdorferi* infection of *I. pacificus* is lower than that of the northeastern *I. scapularis*, the rate of human infection following *I. pacificus* bites is also lower.[378, 420]

In Europe, humans are incidental hosts for all stages of the *I. ricinus* tick—which is the most common tick in Europe,[336] the most frequent cause of human tick bites in Central Europe, and the main vector for *B. burgdorferi* transmission to humans in Europe.[181, 336] The feeding activities of the three stages of *I. ricinus* overlap throughout Europe, especially from April through July,[181, 409, 422,

TABLE 11–4
Seasonal Risk of Human Tick Bites and Development of Lyme Borreliosis (LB[a])

GEOGRAPHIC LOCATION	*B. BURGDORFERI* TICK VECTOR	MONTHS OF TICK FEEDING ACTIVITY, BY STAGE			MOST COMMON MONTHS OF ONSET OF LB
		Larvae	Nymphs	Adults	
North America					
Northeast, Atlantic, Midwest	*I. dammini/scapularis*	July–Sept.	May–July[b]	Oct.–May	May–Sept. (peak June–July)
Pacific Northwest	*I. pacificus*	Mar.–Sept.	Mar.–Sept.[b]	Oct.–June (peaks Dec. and Mar.)	Mar.–Aug.
Europe	*I. ricinus*	Mar.–Nov.	Mar.–Nov.	Mar.–Nov.	May–Oct.
Asia	*I. persulcatus*			May–June[c]	May–June

[a]Data from references 23, 180, 243, 251, 336, 344, 347, 358, 371, 428, 434, 460, 463, 464, 466–469, 596, and 637.
[b]Nymphal ticks feeding during this time are responsible for most *B. burgdorferi* transmission to humans.
[c]Adult ticks feeding during this time are responsible for most *B. burgdorferi* transmission to humans.

[432, 433] and the peak incidence of Lyme borreliosis occurs between May and October.[251, 371, 405, 409, 422, 432, 434–436] Similar seasonality has been demonstrated historically in a retrospective study of museum ticks from Great Britain over the past 100 years, in which *B. burgdorferi* PCR–positive museum specimens of *I. ricinus* ticks were found mainly from May through October, the overall PCR positivity rate was 20%, and the nymphal positivity rate was 38%.[340] The seasonality was particularly well defined in the migratory seabird tick, *I. uriae*, because ticks of this species were found only from April through August, and the PCR positivity rate was 98%.[340] The frequency with which *I. uriae* bites humans is not known, but one of the British museum *I. uriae* was involved in a human bite.[340]

In Asia, the adult stage of *I. persulcatus*, the most common tick in the Lyme-endemic areas of China and Japan, feeds in May and June and commonly bites humans, but larvae and nymphs rarely bite humans. The *B. burgdorferi* infection rate of the adult ticks is high in endemic regions, and the seasonality of EM, which peaks in May and June, correlates with that of human *I. persulcatus* tick bites.[349, 351, 374, 437, 438] *I. ovatus* is also frequently found in Japan, and has been demonstrated to be infected with *B. japonicus*, but no human cases of Lyme disease have been associated with it[163, 374]; *B. burgdorferi* isolates from Japanese patients with EM have been strains transmitted by *I. persulcatus* ticks.[164, 374, 439]

The risk of transfusion-acquired Lyme borreliosis was zero in a large study of 149 recipients of 601 units of packed red blood cells, and 48 recipients of 371 units of platelets, in a Lyme-endemic area of Connecticut; one patient developed transfusion-acquired babesiosis during this study.[440]

In North America, seasonal peaks of other tickborne infections that share vectors with Lyme disease are similar to those of Lyme disease: HME peaks in May through July,[398] HGE in May through July and in October through December,[397, 398] and babesiosis in the summer.[394] In Europe, the seasonality of tickborne encephalitis (TBE) is similar to that of Lyme borreliosis, which shares tick vectors.[402]

Geographic Distribution of Tick Vectors

The focus here is on the vectors involved in human transmission. The *Ixodes ricinus* complex ticks are widely distributed in the northern hemisphere,[182] require an environment with high humidity and temperature between −10° C and 35° C, and are therefore not found at high elevations because they are susceptible to the desiccation that occurs in unprotected, high windy areas.[181, 336] *I. scapularis* inhabits heavily forested and brushy areas, particularly the brushy areas at junctions between cleared and forested areas,[336, 407] but it has also been found on well-manicured lawns in hyperendemic areas such as Westchester County, New York, at densities as high as one tick per square meter of lawn.[441] *I. pacificus* is found only at elevations less than 2100 feet in coastal California.[420] *I. ricinus* inhabits dense heterogeneous deciduous forests with dense undergrowth,[181] as well as pastures below 1000 meters of elevation, is rare between 1000 and 1500 meters, and is not found above 1500 meters of elevation.[167, 336, 352] There is uneven distribution of these ticks even within their geographic range as a result of local microniche differences in elevation, foliage, humidity, temperature, and host populations.[181]

The evolution of distinct tick species and their *B. burgdorferi* genospecies has resulted in unique geographic ranges of both ticks and *B. burgdorferi* genospecies.[7, 13, 54, 63, 74]

The geographic distribution of the northern *I. scapularis* includes the northeastern and upper midwestern United States from Maine to Virginia, from the Atlantic Coast to Minnesota and Iowa, and from southern Ontario along coastal Lake Erie through Illinois and Indiana; small numbers of *I. scapularis* have also been found in Canada as far north as 50 degrees North latitude in Ontario, and in all provinces from Manitoba east to the Gulf of St. Lawrence and the Atlantic coast; the southern *I. scapularis* is found in the Southeast from Virginia to Florida, from the Atlantic coast to Texas and Oklahoma, and from the Midwest to the Gulf Coast.[167, 182, 348, 419, 445, 447] These areas include most of the Atlantic and Gulf Coasts, the Mississippi Valley, and forested areas of Missouri, Arkansas, Louisiana, Oklahoma, and Texas; *I. scapularis* is not found west of the 100th meridian, which runs midway through Texas and beyond which annual rainfall decreases.[348]

The distribution of *I. pacificus* extends from British Columbia to Baja California, from the Pacific coast to the Cascade and Sierra Nevada Mountains, and from Nevada to the Wasatch Range in Utah; it also includes some pockets of higher humidity within arid regions in eastern Oregon, northwestern Arizona, southern Nevada and Utah, and Idaho.[167, 348, 419] *I. pacificus* is well established in localized areas of southern British Columbia around the Fraser Delta, the Gulf Islands, and Vancouver Island.[445] *Ixodes angustus*, also suspected to be a potential *B. burgdorferi* vector for humans in Washington State,[364] has a wide geographic range that overlaps with that of *I. pacificus* and extends along the Pacific from California to Alaska[336, 364]; *B. burgdorferi* has also been found in *I. angustus* in British Columbia. It is the most common tick in some parts of coastal Oregon.[364]

Several tick species involved in enzootic cycles also overlap geographically with human Lyme disease tick vectors but are rarely or never related to human Lyme disease transmission as they rarely bite humans.[348, 378] These include *I. neotomae*,[348, 378] *I. dentatus*,[100, 170, 348, 363] *I. cookei*,[129] *I. affinis*, and *I. minor*;[361] as well as *I. spinipalpis*[362] in North America, and *I. hexagonus*[182, 381] in Europe and Asia.

Although the status of *A. americanum* as a human vector of Lyme disease has not been proved, it has been suspected as a secondary vector in some mid-Atlantic, southeastern, and southern states[153–155, 158, 359, 360, 366–369]; it occurs from Rhode Island to Florida, and from the Atlantic Coast to central Texas.[73] A *Borrelia* identified as *B. burgdorferi* has been found in *A. americanum* in New Jersey, Missouri, Texas, Oklahoma, Virginia, North Carolina, and Alabama.[153–158, 386] Also, an uncultivable *Borrelia*, *Borrelia lonestarii*, which may be related to the

Lyme-like disease in the southern states,[73] was found in *A. americanum* from New York, New Jersey, Missouri, and North Carolina.

The geographic distribution of *I. ricinus* extends from Algeria, Tunisia, and Egypt in North Africa to 65 degrees North latitude in Europe to southern Norway, Sweden, and Finland, and from the United Kingdom to 50 to 55 degrees East longitude in Turkey, Iran, and Russia to the Caspian Sea west of the Ural Mountains.[11, 167, 181, 182, 336, 448] It also includes southern Italy, the Balkans, and subtropical Madeira Island. *I. ricinus* is the most common tick in Europe.[336] *I. ricinus* occurs in northern but not southern Spain.[90]

The distribution of *I. persulcatus* extends east from the Ural Mountains[448] in eastern Europe to Asia and Japan and, at its western margin, overlaps somewhat with that of *I. ricinus*[167, 344]; it extends south to include the Hokkaido and Nagano districts in northern Japan, but does not occur in southern Japan.[351] *I. persulcatus* was the predominant tick in the Lyme-endemic areas of northeastern (Heilongjiang, Jilin, Liaoning, and Hebei Provinces), north central (Inner Mongolia), and northwestern (Xinjiang Province) China,[344, 350, 437, 438, 449] and in the Lyme-endemic areas, Hokkaido and Nagano districts, and Saitama Prefecture of Japan.[163, 351, 450]

So far, no ticks of the *I. ricinus/persulcatus* complex have been found to occur in Australia.[375]

In South America, there are ixodid ticks but it is unknown whether they harbor *B. burgdorferi*[453]; there are no *Ixodes* ticks in Chile.[454]

I. ricinus is prevalent in northern Africa, including Tunisia,[455] but does not occur farther south. In most of Africa, the Middle East, Asia, South America, and Central America, there are ticks that transmit human non-Lyme borrelial relapsing fever.[342]

I. uriae has a large high-latitude bi- and circumpolar marine ecologic geographic distribution[13, 152, 165, 166]; migratory seabirds congregate to breed on subarctic and subantarctic islands and peninsulas; they make transequatorial migrations to overwinter in northern parts of the Atlantic and Pacific, and in southern waters around South America and South Africa.[165, 166] Migratory seabirds and their *I. uriae* ticks are thought to be involved in transhemispheric spread of *B. burgdorferi* to the southern hemisphere, and possibly to be involved in the occurrence of Lyme disease in the southern hemisphere in areas without known *I. ricinus* complex vector ticks, such as Australia and South Africa. *I. uriae* have occasionally been found to bite humans.[165, 340] Migratory birds are able to bring potentially *B. burgdorferi*–infected ticks into contact with humans in geographic areas in which they would otherwise have no tick contact.[182, 425]

Geographic Distribution of Lyme Borreliosis

GEOGRAPHIC DISTRIBUTION OF LYME DISEASE IN NORTH AMERICA

The earliest cases of Lyme disease in the United States were recognized retrospectively to have occurred in the small New England communities of Great Island, Massachusetts, in 1962[334] and in and around Lyme, Connecticut, in 1965.[335] The earliest recognized case of EM in the United States occurred in 1969 in the Upper Midwest, in north central Wisconsin,[333] and the earliest recognized case in the Pacific Northwest, which followed an *I. pacificus* tick bite,[341] was reported in 1978 from Sonoma County, California.

To monitor trends and determine endemic geographic areas, the CDC and the Council of State and Territorial Epidemiologists began a national Lyme disease surveillance program in 1982 and established Lyme disease as a nationally notifiable disease in 49 states and the District of Columbia in 1990.[3] In addition to the increased reporting of cases of Lyme disease since then, there has been a true increase in the incidence of Lyme disease because of spread of the *I. scapularis* tick vector and its large mammalian host, the white-tailed deer, into larger geographic areas. If nymphal tick infection rates are high, as in some endemic areas of the northeastern United States, small variations in the tick population can significantly change the risk of Lyme disease exposure, and this will be reflected in the annual incidence of Lyme disease cases.[459]

A comparison of Lyme disease cases reported to the CDC from 1982 through 1998 shows impressive increases in both the number of cases reported (see Fig. 11–3) and the number of states reporting cases (see Fig. 11–2).[460, 461] The original northeastern focus of endemic Lyme disease in Connecticut[15] and Massachusetts[334, 462] in the late 1970s progressively expanded[463] to the mid-Atlantic states, and by 1982 it included Rhode Island, New York,[464–466] and New Jersey[155, 467, 468]; by 1987, Ohio, Pennsylvania, Maryland,[469, 470] and Virginia[358]; by 1992, New Hampshire; and by 1998, it extended to Vermont.[4] The original upper midwestern focus in Wisconsin[271, 471–473] expanded to include Minnesota[272] by 1982. By 1987, cases of Lyme disease were reported from Texas,[382] and by 1992, from the majority of the southeastern,[359, 360, 474] south central,[369] and midwestern[366, 368, 473, 475, 476] states. In the northwestern states between 1982 and 1987, Lyme disease began to be reported from California, Oregon, and Washington State.[364] As of 1998, ten states—New York, Connecticut, New Jersey, Pennsylvania, Wisconsin, Rhode Island, Maryland, Massachusetts, California, and Minnesota—accounted for 90%, and the first four states accounted for 75%, of all cases of Lyme disease reported to the CDC from 1982 through 1998.[4, 461] Endemic areas have become established in many other states.

Although Lyme disease now has been reported from all states except Montana,[3, 4, 461] some states such as the Mountain states (Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, and Nevada), the Dakotas, Louisiana, Mississippi, South Carolina, Maine, Vermont, Hawaii, and Alaska reported very few or no cases in 1992, and most cases continue to be reported from the highly endemic areas of the northeastern, mid- and south Atlantic, and upper midwestern states. By region, in 1992 and 1998, there were approximately 5300 and 6900 cases of Lyme disease reported from the mid-Atlantic states, 2300 and 4500 from the northeastern

states, 1100 and 1165 from the north central states, 700 and 900 from the south Atlantic states (over 75% from the northern part of this area—Maryland, Delaware, and Virginia), 200 and 100 from the south central states, 300 and 200 from the Pacific states, and only 16 and 25 cases from the Mountain states. Cases reported from nonendemic areas but acquired in endemic areas may explain the reporting of some cases from nonendemic states. Variation in tick and reservoir host population density, application of more stringent case definitions, and Lyme disease educational programs may be related to decreases in incidence of cases in some areas in 1998 compared with 1992.

The existence of Lyme disease in southern United States has been controversial,[361, 477] although there is general agreement about the existence of a Lyme-like illness with erythema migrans in the South.[367, 368, 477] The presence of *B. burgdorferi* in *I. scapularis* and small mammals in the South has been established,[386, 477] but it has been suggested that genospecies of *B. burgdorferi* other than *sensu stricto* and tick vectors other than *I. scapularis*, such as *I. dentatus* or *A. americanum*, might be involved in enzootic cycles in nature and in transmission of this disease to humans.[153, 158, 359, 360, 366–368] This issue has been complicated by misdiagnosis, as was the case in Georgia in 1989 when more than 700 cases were suddenly reported in 1 year, the majority of which were later considered not to be Lyme disease.[461]

Yearly incidences of Lyme disease cases occurring per 100,000 population have been calculated for different geographic areas of the United States, and are designated as follows: low incidence, 10 cases per 100,000 population (0.01% annually); moderate, 100 cases per 100,000 (0.1% annually); high, 1000 cases per 100,000 (1% annually); and very high, 3000 cases per 100,000 (3% annually).[478] Very high, hyperendemic areas are Westchester County, New York, with a 2.6 to 3% annual incidence and a 17% cumulative incidence; Great Island, Massachusetts, with a 3% annual incidence and a 16% cumulative incidence; and Fire Island, New York, with a 1 to 3% annual incidence and a 7.5% cumulative incidence.[478]

In Canada, southern British Columbia (the Fraser Delta area, Vancouver Island, and the Gulf Islands) and Ontario (Long Point Peninsula and coastal areas of Lake Erie) are now considered Lyme-endemic areas,[376, 445, 479] with established tick vector populations (*I. pacificus* and *I. angustus* in British Columbia, and *I. scapularis* in Ontario)[376, 445]; there are limited focal, established populations of *I. scapularis* and *I. pacificus* in other areas of Canada at risk to become endemic foci if *B. burgdorferi* is introduced into these populations.[445] *I. pacificus* is established in southern British Columbia in the Fraser Delta area, the Gulf Islands, and Vancouver Island; *I. scapularis* is established in Ontario in coastal Lake Erie, and has also been reported in Manitoba, Quebec, Nova Scotia, New Brunswick, Newfoundland, and Prince Edward Island; its occasional appearance in other provinces has been thought to be due to introduction by migratory birds.[445] Between 1977 and 1989, 30 cases of Lyme disease were reported to the Canadian Laboratory Centre for Disease Control; Lyme disease is now notifiable in 8 of 12 provinces; between 1987 and 1997, 333 cases were reported, half acquired in Canada, mostly from southern Ontario (71% of autochthonous cases), British Columbia, Ontario, Quebec, Manitoba, and New Brunswick near Lyme-endemic areas in the United States.[479] In 1993, *B. burgdorferi* was found in *I. pacificus* and *I. angustus*, as well as deer mice, in British Columbia.[376] A serosurvey of residents of Alberta, Canada, in 1993 found no seropositivity by ELISA or Western blot assays, and a tick survey found *I. angustus* and *H. leporispalustris* but no *I. scapularis*[479]; in 1995, *B. burgdorferi* was isolated from an *H. leporispalustris* tick removed from a rabbit in Alberta, near the border with British Columbia, establishing its presence in Alberta.[479] In 1993, *B. burgdorferi* was found in *I. scapularis* from a dog in Ontario, at 50 degrees North latitude near the Manitoba border, just north of the endemic areas of Minnesota.[446]

EXPANSION OF LYME-ENDEMIC AREAS IN NORTH AMERICA

B. burgdorferi–infected ticks may be transported from Lyme-endemic areas into nonendemic areas, which may establish new Lyme-endemic foci.[165, 168, 169, 336, 408, 462, 490] Infected *I. ricinus* complex ticks (including *I. scapularis*) and infected *I. uriae* have been found on migratory birds and along migratory "flyways"; they may be transported into new areas by these birds as they travel between endemic and nonendemic areas, including counties, states, countries, continents, and even hemispheres.[13, 63, 157, 165, 167–169, 171, 376] Rodents, hunting dogs, household pets,[454] domestic animals, wide-ranging wild animals such as coyotes and foxes, and campers, hunters, and other people[13] traveling between endemic and nonendemic areas may also transport infected ticks from one area to another; deer hunters may transport deer or other game animals[63] with infected ticks still attached. If the newly arrived tick finds its necessary hosts, or if it arrives together with a population of its hosts, a new endemic focus of infected ticks and Lyme disease will be established.[460, 470, 492] *I. scapularis* and other *I. ricinus* complex ticks, along with the rabbit ticks *I. dentatus* and *H. leporispalustris*, are able to feed on birds as well as mammals,[157, 163, 167, 362] and could provide a bridging vector between hosts.[167]

In North America, the incidence of Lyme disease has been found to correlate with the population density and geographic distribution of *I. scapularis*[335, 442, 443, 490, 491] and white-tailed deer.[335] Because deer are the reproductive hosts of adult *I. scapularis* and they determine the success rate of tick mating, the population density of *I. scapularis* correlates with the population density of deer, and an *I. scapularis* focus may enlarge geographically as the geographic distribution of deer expands.[408] Even infrequent visits by deer to an area may be sufficient to sustain a small population of *I. scapularis*.[492]

The deer populations in North America have changed dramatically over the past 400 years.[168, 394] Particularly since the 1970s, there has been a deer population explosion, and deer have regained their original widespread North American distribution as forests have replaced farmland and federal programs have protected deer. Hu-

man contact with deer has been increasing as residence or recreation in rural and suburban forested areas has become increasingly popular.[6, 7, 168, 336, 390, 394]

The expansion of the Lyme-endemic areas has been particularly impressive in New England, the mid-Atlantic states, and Wisconsin, where this has been extensively studied epidemiologically. In Ipswich, Massachusetts, the emergence of a new focal epidemic of Lyme disease was associated with a 35% Lyme disease attack rate overall for residents living near the deer-populated nature preserve considered to be the focus, and 66% for those living closest to the preserve.[462] Among permanent residents of Great Island, Massachusetts, the Lyme seropositivity rate was 8%, the history positivity rate was 16%, and the incidence of Lyme disease was 7% over a 2-year period.[334] Among middle and high school students in an endemic area of Connecticut, the physician-diagnosed Lyme disease history positivity and seropositivity rates were 7 and 3%, respectively; during the 1990–1992 tick season, 2% developed clinical physician-diagnosed Lyme disease and 1% experienced asymptomatic seroconversion.[493] The incidence of Lyme disease increased steadily between 1991 and 1996 from rates of 36 to 94 cases per 100,000 population annually overall for Connecticut, and from 340 to 450 cases per 100,000 annually for a hyperendemic 12-town area along the Connecticut River and the Atlantic Coast; the increase in the 12-town area was found to correlate with the abundance and *B. burgdorferi* infection rate of *I. scapularis* in this area; nymphal tick infection rates increased from 14 to 24% during this time in the 12-town area.[490]

In the mid-Atlantic United States, in New York and New Jersey, the geographic distribution of the *I. scapularis* tick vector has expanded annually outside of the original Long Island focus, and there has been a corresponding increase in both the number of counties reporting Lyme disease and the number of cases reported per county.[465, 494–497]

In Wisconsin, the Lyme-endemic area has expanded southward from the original northwestern region,[271, 416] and the seropositivity rate is 6 to 11%,[471, 473] which is similar to the 7% seropositive rate in Minnesota. In southern and southwestern United States, where the reported incidence of Lyme disease is low, seroprevalence studies have been less frequent; the rate of seropositivity was 23 to 26% in Texas,[382] and 0% in a nonendemic area of Arizona.[473] In western United States, the deer population is more stable than in eastern United States and in Europe, and apparent increases in Lyme disease may be related more to reporting than to actual increased incidence.[394]

Studies of the seroprevalence of antibody to *B. burgdorferi*, *Babesia microti*, *E. chaffeensis*, and the agent of HGE have been done in various geographic areas. In Wisconsin, the frequency of co-infection in patients with Lyme disease was 5.2% for HGE, 2.1% for *B. microti*, and 2.1% for both; the frequency of co-infection in patients with HGE was 5.3% for *B. burgdorferi*, 5.3% for *B. microti*, and 5.3% for both.[486] In Minnesota, one third of HGE patients had seropositivity to *B. burgdorferi*.[498] In Westchester County, New York, 22% of HGE patient sera were also seropositive for *B. burgdorferi*.[488] Twenty percent of patients from Minnesota, New York, New Jersey, and Connecticut with early Lyme disease had serologic evidence of previous or current HGE.[498] In Rhode Island and Connecticut, 11% of patients with Lyme disease were co-infected with *B. microti*, 72% of patients with babesiosis were co-infected with *B. burgdorferi*, and seroprevalence was 7% for *B. burgdorferi* compared with 5% for *B. microti*.[481] In Connecticut in 1994, the rates of co-infection with other tickborne infections in patients with serologically confirmed Lyme disease were 10% for HME, 7.5% for HGE, 7.5% for babesiosis, and 5% for more than two infections.[487] In eastern Long Island, 66% of Lyme disease sera were also positive for *B. microti* antibody, and 54% of babesiosis sera were positive for *B. burgdorferi* antibody.[485]

The earliest reported major inland focus of *I. scapularis* was on Long Point Peninsula, which extends into Lake Ontario from the southern coast of Ontario.[394] Lyme disease is notifiable in 8 of 12 provinces in Canada, and its incidence has gradually increased from 30 cases reported to the Canadian Laboratory Centre for Disease Control between 1977 and 1989, predominantly from southern parts of the provinces Ontario and Manitoba (with single cases reported from the provinces of Alberta, British Columbia, and Quebec), to 333 cases (half acquired within Canada) between 1987 and 1997,[479] predominantly from the endemic areas in southern British Columbia, Vancouver Island, the Gulf Islands, Ontario along coastal Lake Erie, and other provinces such as Manitoba, Quebec, and New Brunswick, which are near Lyme-endemic areas of the United States. The presence of *B. burgdorferi* has been confirmed in ticks in the endemic provinces[376, 446] and Alberta,[479] but because of the existence of established vector tick populations in other parts of Canada, spread to these areas may occur if *B. burgdorferi* is introduced into these tick populations by dog and human travelers, or by migratory birds.[445]

Several studies have been done[442, 443, 491, 499] to try to develop predictors of geographic risk by using satellite photographs of vegetation, as well as data on *I. scapularis* population density and infection rate (acarologic index), deer population density, mouse reservoir population density, *B. burgdorferi* seroprevalence in resident dog populations, and human Lyme disease incidence; correlations have been found with vegetation, wetness, residence in less developed areas outside of towns, deer density, tick density, tick infection rates, mouse population density, dog seroprevalence rates, and even with the abundance of acorns. The abundance of acorns as a food source for white-footed mice determines their survival through the winter and resulting mouse population density; abundant acorns also attract deer, resulting in increased *I. scapularis* population density brought by the deer; the combination of increases in mouse, deer, and tick population densities is expected to increase the risk of Lyme disease acquisition about 2 years after a bumper crop of acorns.[500]

GEOGRAPHIC DISTRIBUTION OF LYME BORRELIOSIS IN EUROPE, ASIA, AND OTHER CONTINENTS

The true worldwide country-by-country incidence of Lyme borreliosis is impossible to determine because

only a few countries other than the United States have mandatory reporting of Lyme borreliosis, and because clinical and serologic criteria for definition and reporting of the disease vary in different countries.[11, 12, 501] Efforts are being made by the EUCALB to improve reporting and to standardize European case definitions.[8, 10, 502]

Lyme borreliosis has been reported from six continents—North and South America, Europe, Asia, northern Africa, and Australia—but the majority of cases have originated in North America, Central Europe, and Asia (see Fig. 11–1; Table 11–5).[4, 8–13, 504] The existence of indigenous Lyme borreliosis in South America[452, 453, 505, 506] and Australia is still uncertain.[391, 392]

In Europe, as of 1998, *B. burgdorferi sensu lato* had been isolated from either arthropod vectors, animal hosts, or human patients in the following European countries (Table 11–6): Austria, Belarus, Belgium, Croatia, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Great Britain, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Moldavia, the Netherlands, Norway, Poland, Portugal, Russia, Slovakia, Slovenia, Spain, Sweden, Switzerland, and the Ukraine.[10, 54, 405] A large study by the EUCALB of over 2000 patients with Lyme borreliosis in 15 European countries during 12 months in 1994 found that the incidence of Lyme borreliosis per 100,000 population increased from western to eastern Europe, with higher incidences east of the Netherlands, France, and Italy.[10]

The number of European cases of Lyme borreliosis (LB) through 1998, since reporting has improved, has been estimated to be over 60,000 annually, based on *B. burgdorferi*–seropositive cases reported voluntarily to the World Health Organization (WHO) by Public Health Administrations of WHO European Region countries, and to the EUCALB by member countries, as well as cases reported in the medical literature through 1998.[9] Most of these cases were from central Europe (see Table 11–5).

In Asia, cases have been reported from China and Japan, as well as from eastern parts of Russia. In 1981, one case of EM was reported from Japan following an *Ixodes persulcatus* bite in the mountainous district of the Nagano Prefecture, across the Sea of Japan from Vladivostock, and as of 1998, 100 cases of Lyme disease had been reported, mainly from Hokkaido and Nagano Prefectures.[169, 374, 439] *I. persulcatus* is considered the major

TABLE 11–5
Incidence of Lyme Borreliosis (LB) in Europe, by Country[a]

RELATIVE RISK[b]	COUNTRY	LB/100,000 POPULATION PER YEAR	LB/YEAR	REGION
High	Austria	150	14,000	
	Slovenia	120	2000	Central
	Poland	120		
	Sweden	69	>2000	South, Southeast
	Bulgaria	50–55	3500	
Medium	Denmark[c]	50		
	Hungary	50	1000	
	Netherlands	43	6500	North, East, Coast
	Czech Republic	40	6300	
	Finland	40	2000	Southeast, Southwest, Aland Islands
	France	40	7200	Northwest, East
	Switzerland	30	2000	
	Germany	25	20,000	
	Italy	17		North, North Central
Low	Belgium	<5	50–100	East
	Yugoslavia (former)		400	
	Croatia		200	Northwest
	U.K.		200	South, Southwest England, Scottish Highlands
	Lithuania		350	
	U.S.S.R. (former)		6000–11,000	Kaliningrad, Leningrad, Kirov, Perm, Kurgan, Omsk, Tomsk, Khabarovsk, and Northwestern areas
Very low	Norway		<50	
	Ireland		<50	
	Spain		<50	North, Northeast
	Luxembourg		<100	
	Greece		~0	
	Romania		<100	

[a]Estimated or reported LB cases.
[b]LB/100,000 population/year: High: >50; Medium: 5–50; Low: <5; Very low: Only a few cases reported.
[c]As only neuroborreliosis is reported in Denmark, this is an underestimate of total LB cases in Denmark.
Data obtained from 9–12, 90, 162, 251, 268, 352, 370, 371, 402, 404, 405, 409, 432–434, 448, 501, 503, 504, 507, 511, 515, 517, 519, 525, 532, 534, 535, 539,