Borrelia burgdorferi in Ixodidae Tick around Asia

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Lyme disease (LD) is a common arthropod-borne inflammatory disorder prevalent in the northern hemisphere. LD is caused by a spirochete named *Borrelia burgdorferi* s.l., which is transmitted to humans by ticks. Climate, environment, and other factors affect land use; recreational-behavior changes affect human contact with infected ticks. *Ixodes*, *Haemaphysalis* and *Dermacentor* may be the most common tike of *B. burgdorferi*-positive in Asia.

Keywords: Lyme disease ; Borrelia burgdorferi ; tick ; Ixodes

1. Introduction

Lyme disease (LD) is a tick-borne inflammatory disease caused by infection with *Borrelia burgdorferi* sensu lato (*B. burgdorferi* s.l.) complex. LD is of public-health importance in moderate-climate regions of the northern hemisphere, such as North America, Europe, North Africa, and Northern Asia. As landscapes have altered, the number of reported cases have revealed obvious differences in many regions such as *Ixodes ricinus*, *Ixodes persulcatus*, etc.

The clinical symptoms of LD can be divided into three stages. Erythema migrans (the most common clinical manifestation) is a typical sign of early acute infection [1]. It is an expanding skin redness that usually develops at the site of a tick bite. Often, several weeks to months after the tick bite, followed by early dissemination and development, *B. burgdorferi* s.l. can spread to other tissues and organs, and untreated infections can progress to neurologic abnormalities or heart dysfunction [2][3]. Usually, late LD manifests as arthritis or acrodermatitis chronica atrophicans, and is associated with spirochete invasion of joints [4][5][6]. A fatal outcome from LD is extremely rare.

There are several *B. burgdorferi* s.l. genospecies, and not all strains/genotypes cause LD in humans. *B. burgdorferi sensu stricto, Borrelia afzelii*, *Borrelia garinii,* and *Borrelia bavariensis* are considered to be of pathogenic relevance to humans. Despite cases of LB caused by *Borrelia valaisiana*, *Borrelia lusitaniae*, and *Borrelia bissettiae* have been described, their pathogenic ability has been questioned and their description is occasional. *Borrelia mayonii* has been recently incorporated in the Americas [7][8]. Globally, three genospecies of *B. burgdorferi* are principally pathogenic to humans. *Borrelia burgdorferi sensu stricto* (hereafter referred to as *B. burgdorferi*) is distributed mainly in the Americas. *Borrelia afzelii* and *Borrelia garinii* infections are predominant in LD cases in Europe. *B. garinii* is the primary cause of LD in Asia [9]. Other species, such as *Borrelia bissettii*, *Borrelia lusitaniae*, and *Borrelia valaisiana*, are also considered to cause human LD, but the prevalence of infections is low and so they are not considered to be major pathogens [10][11]. Interestingly, the genotype of pathogens seems to be the main factor causing the diversity of clinical symptoms of LD. For example, *B. afzelii* most frequently leads to skin lesions, *B. burgdorferi* is especially arthritogenic, and *B. garinii* is linked to neuroborreliosis [12][13].

Different *B. burgdorferi* s.l. genospecies are transmitted by different genera of ticks, and some ticks can be infected with multiple genospecies of *B. burgdorferi* s.l. The main vectors transmitting LD-associated spirochetes to humans are *Ixodes ricinus* in Europe, *Ixodes persulcatus* in Asia, *Ixodes scapularis* in eastern North America, and *Ixode pacificus* in Western North America [14]. These vectors have four life stages (egg, larva, nymph, and adult). In the last three feeding stages, ticks require a blood meal from a variety of mammals, birds, and lizards [13]. The lifecycle of spirochetes in nature is dependent upon horizontal transmission between an infected tick and vertebrate host. Typically, tick larvae acquire spirochetes from infectious hosts via a blood meal. Spirochetes are carried in the midgut of ticks, and transmitted to susceptible host populations through injection of tick saliva during tick feeding. *B. burgdorferi* replicates in the mammalian dermis, and then disseminates to distant cutaneous sites and other organs, including joints [15].

The risk to humans of infection with *Borrelia* depends on outdoor recreational activity, on the density of tick populations, and on the infection of the ticks with *Borrelia* [16]. *I.persulcatus* is the prevalent vector in the southern forest zone on the Asian side of Eurasis, from the western border of Russia to its far eastern frontier bordering China, Korea, and Japan. However, on the Western sade of Eurasia, most European countries and North Africa harbor *I. ricinus*. *I. ricinus*, which is

the most common tick species that bites humans in the study area and in most European countries. The jury is still out on the main spirochete transmission tick in Asia [17].

2. *Borrelia burgdorferi* in Ixodidae Tick around Asia

LD occurs most frequently in the Northern Hemisphere, where some ticks of the Ixodidae family are present. Each year, ~300,000 people in the USA and ≤85,000 people in Europe are infected with *B. burgdorferi* s.l. and suffer LD [18][19]. Although the true incidence of LD in Asian populations is not known, its distribution appears to be widening.

Ticks are ectoparasites that carry multiple pathogens. They transmit these pathogens to humans and animals. Persistent and relapsing infection as well as long-term sequelae caused by tick-borne pathogens worsen human health further. As the infection rate is very high, animal husbandry is a global economic burden. [20][21].

One of the most notable functions of ticks is that they serve as vectors of LD. In LD, there is a dynamic interplay between spirochetes, vectors, and reservoir hosts. The spirochetes involved in LD hold a wide range of reservoir hosts, so clarifying the distribution of infected ticks in Asia could help for estimating the prevalence of *B. burgdorferi* s.l. and improve the prevention and control of LD.

Ticks transmit a wide range of pathogens into humans and animals. In North America, *I. scapularis* and *I. pacificus* have been shown to be vectors of the major LD-causing spirochete *B. burgdorferi* s.l. *I. ricinus* and *I. persulcatus* have been confirmed experimentally to be the carriers of LD-causing spirochetes in Eurasia [22][23]. Due to the genetic diversity of ticks, the relative abundance of certain pathogens is quite different across different tick genera [24]. None of the eight tick species from three genera (one species from the genus *Amblyomma*, five from *Dermacentor*, and two from *Haemaphysalis*) evaluated to date have been unequivocally and experimentally confirmed to be vectors of *B. burgdorferi* s.l. spirochetes [22][25][26]. The host specialization and/or vector compatibility of LD spirochetes may affect the distribution of spirochetes of different genospecies.

The genetic structure and pathogen composition of different tick genera are affected mainly by ecologic and geographic factors. For example, *H. longicornis* is a widely distributed tick species indigenous to eastern Asia, whereas *Hyalomma asiaticum* prefers to live in desert or semi-desert environments, *I. ricinus* is distributed widely at high altitudes [27][28][29]. Within an endemic area, the risk of infection by *B. burgdorferi* s.l. in humans is determined by the local abundance and infection rate of vector ticks, and by human behavior that affects the likelihood of being bitten. Research on tick genera infected with spirochetes helps public-health agencies make strategies to prevent LD.

With a total area of land and population, China is the largest country in Asia. China has a total area of ~9.6 million km^2, which is almost the size of Europe. Due to influencing factors such as the size of geographic area and number of reports on infected ticks, data were concentrated mainly in East Asia (especially China). With tick activity, LD shows relatively constant regional characteristics and seasonal peaks. The habitat types of ticks and local microclimate determine the abundance of infected ticks, which affects LD prevalence. Numerous tick species are expanding beyond their historical distribution range and invading new regions, and the increase in the number of human cases of tick-borne disease is concomitant with such an expansion [30][31]. It showed that the typical habitats of uninfected/infected ticks were woodlands and grasslands in regions with mild climates, which tallies with the geographic range of LD transmission. These habitats provide sufficient humidity for the development and survival of ticks and vertebrate hosts. It demonstrated that ticks usually become active from spring to late summer, which is consistent with the peak incidence of LD in humans. LD in humans is also correlated with meteorological conditions that influence tick feeding and human behavior, such as temperature, humidity, and rainfall [27][32][33]. Ticks usually feed on blood meals in the summer, which is the same time that recreation by humans increases. In areas with a high incidence of ticks, the annual average temperature is stable at 6.85–16.85 °C, and spring vegetation is lush [27].

Understanding the distribution of ticks spcies can help in the prevention and diagnosis of LD. Equally important, differences among genospecies of *B. burgdorferi* s.l. are thought to cause variability in the clinical symptoms of LD in different geographic areas. *I. persulcatus* and *I. granulatus* were the most numerous and had a higher infection rate. Consistent with previous research, *I.persulcatus* is the prevalent vector in the southern forest zone on the Asian side of Eurasis, from the western border of Russia to its far eastern frontier bordering China, Korea, and Japan. In Southeast Asia and West Asia, tick infection rates are low and data collection is low, and more studies should be added.

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