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Review Article

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Ixodes Ticks – Carriers of Pathogens of Vector-Borne Infections (Review)

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ABSTRACT

Ixodes ticks are known as carriers of pathogens of many infectious diseases with natural foci. The purpose of the study is to analyze the literature on the infection of Ixodes ticks with pathogens of infectious diseases with natural foci in the territory of the Russian Federation. RSCI, Cyberleninka, PubMed, WoS, and Scopus are just a few of the electronic databases that contain information on Ixodes ticks as natural foci for infectious disease pathogens. This information served as the foundation for the analysis and scientific approach, which employed analytical, comparative, and systematic study techniques. 12 species of Ixodes ticks carrying the virus of Crimean-Congo hemorrhagic fever and lumpy skin disease (dermatitis nodulares) of cattle were found in the foothill zone of Kabardino-Balkaria. In the Republic of Dagestan, Hyalomma plumbeum ticks are the carriers of pathogens of taileriosis of cattle (13.6%), and the incidence of animals is 24.4%. In the Kaluga region, infection with Ixodes ricinus Borrelia reaches 16.9%, and with Dermacentor reticulatus, it is at 12.3%. In the Omsk region, mixed infection with pathogens of infectious diseases with natural foci was found in 16.5% of Ixodes ticks. In the south of Eastern Siberia, the infection rate of taiga ticks with tick-borne encephalitis virus ranged from 0.5-4.5%, and on average it was about 1.2%. Infection of taiga ticks with Borrelia ranges from 10-34%, on average reaching 19%, of which 2.5% cases are with a high degree of infection. In Khabarovsk, 18.3% of ticks were infected with Borrelia, and the tick-borne encephalitis virus was found in 2.4% of ticks. In the south of Primorsky Krai, 13.3% of Ixodes persulcatus ticks have pathogens of viral and bacterial infections. In the Republic of Sakha (Yakutia), the virulence of ticks was 5.7-9.8%. The biological type of tick development does not change the fundamental side of brucella reservation and transmission of infection to healthy animals.

Keywords: *Human, Animals, Ixodes ticks, Vectors, Infection rate, Infections*

INTRODUCTION

Ixodes ticks are the most common parasites in the world, capable of inducing dangerous diseases in humans and animals. Ticks of the Ixodidae family are found everywhere, even on the coasts of the Arctic and Antarctic (*Ixodes uriae*). From the very beginning of studying (the end of the XIX century), they were objects of purely zoological research; later physicians and veterinary specialists started looking into this topic since blood-sucking parasites turned out to be carriers and reservoirs for pathogens of bacterial, viral and protozoal diseases of animals and humans [1].

Intensive anthropogenic impact on natural complexes against the background of climatic changes impacts the boundaries of habitat, the number of *Ixodes* ticks, and manifestations of epidemiological activity. The present state of anthropogenic landscape modification is one of increasing attenuation or removal of infection foci or, on the other hand, progressive growth and expansion of these foci.

The number of biotopes that are conducive to tick growth varies depending on environmental and socioeconomic conditions. The habitats of vector-borne disease carriers are typically far larger than the areas where these illnesses are most commonly disseminated. This is due to the pathogen's essential activity needing more than just the vectors. The past 25 years have seen changes in the climate and weather, including high humidity, and an increase in spring, summer, fall, and even wintertime average air temperatures, which have all contributed to an enhancement in *Ixodes* tick populations and activity periods in natural biotopes [1]. The primary types of wild feeders are birds, reptiles, and occasionally even amphibians; tiny animals, particularly rodents like hares, squirrels, chipmunks, mice, shrews, and hedgehogs; big ungulates and predatory mammals, including moose, roe deer, wild boars, badgers, foxes, and wolves. Among anthropogenically adapted animals, ticks can parasitize and transmit infectious agents to cattle and small cattle, sheep, rabbits, horses, dogs, and cats [2, 3].

The purpose of the study is to analyze the literature on the infection of *Ixodes* ticks with pathogens of infectious diseases with natural foci in the territory of the Russian Federation.

MATERIALS AND METHODS

RSCI, Cyberleninka, PubMed, WoS, and Scopus are just a few of the electronic databases that contain information on *Ixodes* ticks as natural foci for infectious disease pathogens. This information served as the foundation for the analysis and scientific approach, which employed analytical, comparative, and systematic study techniques. Keywords such as: "human", "animals", "*Ixodes* ticks", "vectors", "infection rate", and "infections" were utilized. The scientific publications were chosen based on how valuable they were to the study question from a scientific standpoint. After an analysis of over 150 articles, information on the infection of *Ixodes* ticks with pathogens of infectious illnesses with natural foci was found in 53 of them. Preference was given to publications from the Elibrary database since the review is focused on research in the Russian Federation.

RESULTS AND DISCUSSION

Data on *Ixodes* ticks as vectors and pathogens of infectious diseases with natural foci can be found in several countries. So, Gilbert [4] conducted research on the impact of climate change on ticks and the risk of tick-borne diseases; Yang *et al.* [5] studied the proliferation of ticks in China in the context of climate change and changes in the land use; Gray *et al.* [6] and Voyiatzaki *et al*. [7] researched the occurrence of Lyme borreliosis and tick-borne encephalitis in Europe; Bush and Vazquez-Pertejo [8] conducted research on Lyme disease in the United States; Grochowska *et al.* [9] on the pathogens carried by ticks *Ixodes ricinus* (*I. ricinus*) and *Dermacentor reticulatus* (*D. reticulatus*), including coinfection; Diarra *et al.* [10] studied tick-borne diseases of humans and animals in West Africa; Hussain *et al*. [11] examined symbiotic continuum inside ticks: ability to fight disease; Namina *et al*. [12] made study of the pathogens from ticks collected from dogs, Latvia, 2011-2016 [12]; Kocoń *et al*. [13] and Telmadarraiy *et al*. [14] published a study on ticks as vectors of the Crimean Kong hemorrhagic fever virus in Iran; Wang *et al*. [15] studied diseases of humans and animals in China.

Currently, there is an increase in the incidence of people who have been attacked by *Ixodes* ticks, which are carriers of many vector-borne infections **(Figure 1)**. The study of this phenomenon and the identification of those changes in the development of the vector (*Ixodes* ticks) due to increasing anthropogenic load on the habitat of parasites, globalization, and the observed climate changes require increasing attention and further study [16, 17].

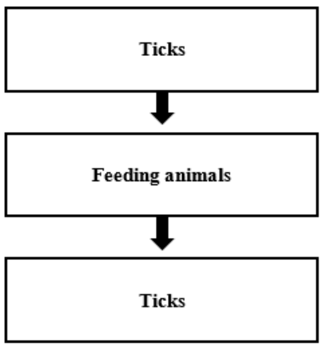

Figure 1. Virus circulation in natural conditions

One factor contributing to the extension of the epidemic season is the rise in the quantity and length of tick activity throughout the spring-autumn season. Because the natural areas of ticks' habitats are so large, infections spread by tick bites necessitate ongoing epidemiological and epizootological surveillance and infestation management.

Ixodes persulcatus have the greatest epidemiological significance as the main carriers of infectious agents in the central, and eastern regions and partially in the forest zone of the European part of Russia, and *I. ricinus* ticks show prevalence in the western territories. In addition, the widespread mixed infection of people after being attacked by forest and taiga ticks, which are simultaneously infected with pathogens of various infections, has been proven **(Figure 2)**. For the population of the southern European part of Russia, Crimean hemorrhagic fever is a serious threat – a particularly dangerous arbovirus infection, multiple cases of which were registered annually in the endemic territory of the Southern and North Caucasian Federal Districts over the past twenty years. *Hyalomma marginatum* ticks are the main vector of the Crimean-Congo hemorrhagic fever virus [18].

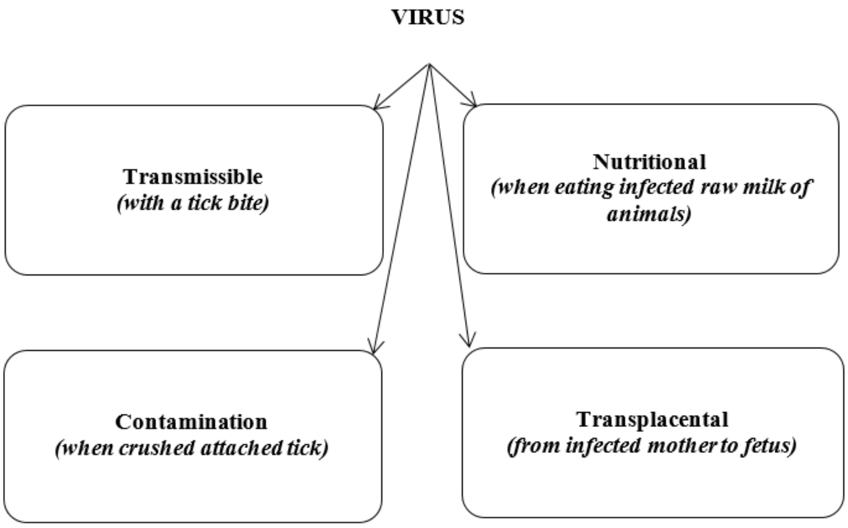

Figure 2. Routes of human infection with tick-borne infections

DNA of pathogens of borreliosis, granulocytic anaplasmosis, and ehrlichiosis were found in ticks collected in various landscape zones of the Crimean Peninsula from 2012 to 2014. *Borrelia monoinfected* were detected in 9 cases, and *Ehrlichia* and *Anaplasma* infected ticks in 7 cases each. In other cases, *Borrelia* and *Ehrlichia* (5 cases), *Borrelia* and *Anaplasma* (2 cases) were detected simultaneously, and there were isolated cases of all three pathogens together. The genome of *B. burgdorferi* was found most frequently in ticks of four species: *I. ricinus* in 54.1%, *H. punctata* in 14.2%, *Rhipicephalus sanguineus* in 14.2%, and *H. inermis* in 14.2% of samples. The ticks were collected in Central, and Eastern Crimea, and in Alushta (broad-leaved forests of the southern slope). The genome of *Ehrlichia chaffeensis/muris* only was found in *Rh. sanguineus* – 28.6%, *Rh. Bursa* – 28.6%, *D. reticulatus* – 28.6%, *I. ricinus* in 14.2% of samples. The *Anaplasma phagocytophilum* genome was found in *H. punctata* ticks in 42.8%, *H. marginatum* in 28.6%, *Rh. bursa* and *D. reticulatus* in 14.2% each [19].

In the Central Fore-Caucasus in 2016-2019, 4,908 specimens of *D. marginatus* (616 pools), 4,208 specimens of *D. reticulatus* (566 pools), and 43 specimens of *D. niveus* (18 pools) were studied for infection with the causative agent of Ku fever. To assess the presence of *Coxiella burnetii* in ticks, depending on the physiological age, 3048 specimens of *D. reticulatus* (381 pools) and 2319 specimens of *D. marginatus* (366 pools) were studied. As a result, it was established that the infection of *Ixodes* ticks with Coxiella in natural populations of *D. reticulatus* and *D. marginatus* varies by year and does not exceed 1% [20].

In the Republic of Dagestan, the main carriers of pathogens of bovine taileriosis are *H. plumbeum ticks* - 13.56%. The dynamics of the incidence of animals with taileriosis show that the incidence among cattle in the lowland belt is high – 220 cases per 900 heads (24.4%). It should be noted that teileriosis was registered in the livestock of animals that did not have preventive anti-tick treatments. At the summer peak of the invasion, the number of sick animals was the largest among all age groups – 86 heads (28.6% of the total number – 220). In animals that were not subjected to acaricide treatment, the number of ticks of *H. A. anatolicum*, *H. punctata* varies from 87 to 350 specimens, *H. plumbeum* and *H. scupense* at different stages of development, and the rest at the nymph and imago stages. In addition, in the conditions of the republic, 3 species of *Ixodes* ticks are capable of transmitting brucella to farm animals both transovarially and by actively attacking their hosts. The most frequent culture secretions were noted from ticks taken from animals with a fresh course of infection. This confirms the assumption that the frequency of brucella excretion depends on the presence of blood cultures in donors. The eggs laid by infected females and their generations turned out to be overwhelmingly affected by brucella, which can be both a reservoir of brucella and an agent of their transmission in natural conditions. The biological type of tick development does not change the fundamental side of brucella reservation and transmission of infection to healthy animals. *Ixodes* ticks can swallow any type of brucella when saturating. Pathologically, brucella microbes reduce virulence when have pass through the body of ticks in natural conditions [21, 22].

In the Stavropol Territory, the general rate of spontaneous infection of *H. marginatum ticks* with Crimean-Congo hemorrhagic fever amounts to 10.4%. The analysis of samples derived from nymphs showed the greatest infection rates (20%). In pools formed by men, the infection rate was 11%, but in pools formed by females, the infection rate was only 8.5%. It has been proven that the virus is circulating throughout the majority of the region. Between 2012 and 2018, the population of *H. marginatum* ticks had an average infection rate of 1.54%; this rate varied annually, ranging from 0.23% in 2014 to 2.97% in 2017. It was discovered that the occurrence of Crimean hemorrhagic fever in the Stavropol Territory is unaffected by the tick infection rate. It is likely that the overall number of infected ticks in the community, rather than their proportion, determines the occurrence of Crimean hemorrhagic fever [23].

On the territory of 12 urban municipalities of the Rostov region, acarological collections and accounting of *Ixodes* ticks were carried out. The conducted monitoring established that 8 species of ticks of the Ixodidae family live in the cities of the Rostov region. Molecular genetic analysis by PCR found the genetic material of the causative agent of Crimean-Congo hemorrhagic fever in tick samples collected on the territory of 5 out of 12 urban municipalities of the Rostov region. The genetic material of the causative agents of babesiosis in animals was revealed in the samples of ticks collected on the territory of 5 urban districts [24].

12 species of *Ixodes* ticks congesting the virus of Crimean-Congo hemorrhagic fever and lumpy skin disease (dermatitis nodulares) were found in the foothill zone of Kabardino-Balkaria [25].

In four districts of the Republic of Karelia, 733 specimens of the imago of hungry *I. persulcatus* ticks collected from vegetation on a flag were examined by PCR analysis. The infection rate with *Borrelia* in ticks averaged 18.3 ± 3.4% in Karelia. The tensest situation is in the Kondopoga district of the republic, where a high number of ticks is combined with a high incidence of *Borrelia* [26].

In the Kaluga region, *D. reticulatus* and *I. ricinus* are the most common species of *Ixodes* ticks. *I. persulcatus* has not been found in this region. Of the 1,545 ticks collected on humans, 164 (10.6%) had *Borrelia burgdorferi s.l.* and 48 (3.1%) had the causative agent of human granulocytic anaplasmosis (*Anaplasma phagocytophilum*); these indicators were 235; 31 (13.2%) and 15 (6.4%), respectively found in biotopes of ticks. Infection with Ixodid *Borrelia* and *A. phagocytophilum* in biotopes was 2.6 and 3.3% higher, respectively than in ticks collected on humans. 38 cases of borreliosis were registered, with infection of *I. ricinus* with *Borrelia* amounting to 16.9%, and *D. reticulatus* – 12.3% [27].

In the Republic of Mordovia, *Ixodes* ticks are most often infected with tick-borne borreliosis. Among *I. persulcatus*, 1.4% were infected with *Borrelia*, and 0.03% were infected with *I. ricinus*. *Granulocytic anaplasmosis* is the second disease in terms of the frequency of infection in *Ixodes* ticks in the region. Among *I. persulcatus*, 0.1% was infected with granulocytic anaplasmosis, and 0.2% was infected with *I. ricinus*. Tick-borne encephalitis was recorded in isolated cases only in 2015 in *I. persulcatus, and I. ricinus*. The proportion of *D. reticulatus* and *D. marginatus* as disease vectors is minimal in the region. It was found that *I. persulcatus* (38.9%) and *D. reticulatus* (32.1%) enjoyed numerical dominance over the entire period of research [28].

In the Omsk region, a molecular genetic analysis of *Ixodes* ticks collected on humans showed mixed infection with pathogens of infectious diseases with natural foci (encephalitis, borreliosis, anaplasmosis, ehrlichiosis, Siberian tick-borne rickettsiosis, tularemia, bartonellosis) in 16.5%. The genetic material of two pathogens at once was detected in 84.5% of all mixed-infected ticks, three in 14.3%, and four in 1.2%. Among the mixed-infected ticks, combinations of Siberian tick-borne rickettsiosis + tularemia (42.9%), borreliosis + Siberian tick-borne rickettsiosis (20.2%), borreliosis + Siberian tick-borne rickettsiosis + tularemia (8.3%) were most common [29].

In the Altai Territory, the leading role in encephalitis and borreliosis belongs to the *I. persulcatus* tick. Ticks of the Dermacentor *(D. marginatus*, *D. reticulatus*, *D. silvarum*, and *D. nuttali*) and Hemofisalis genera are the main vectors of Siberian tick-borne rickettsiosis. They are capable of more or less long-term preservation of the pathogens of these human diseases, their trans-phase, and transovarial transmission to offspring [30].

The ecosystems of the south of Eastern Siberia and the north of Mongolia are optimal for the existence of a variety of vectors and pathogens of vector-borne tick infections. There are at least 4 species of *Ixodes* ticks living here, which are of high epidemiological importance. The causative agents of vector-borne tick-borne infections are encephalitis virus, *Borrelia*, *Rickettsia*, possibly *Ehrlichia*, and other pathogens. The infection rate of taiga ticks with tick-borne encephalitis virus ranged from 0.5-4.5%, and on average it was about 1.2%. The infection rate of taiga ticks with *Borrelia* in the South of East Siberia ranges from 10-34%, on average reaching 19%, of which 2.5% are with a high degree of infection. Infection with borreliosis pathogens of ticks collected in natural foci of Northern Mongolia varies every year: in the Khentiyskiy aimag, it goes from 7.1 to 16.1%, in the Selenga — from 32.8-36.1%, in the Central – 32.8%. The average infection of female and male ticks with *Borrelia* differs slightly (2-6%). Mixed infection was observed in 2.4% of taiga ticks, while the majority of individuals (over 70%) contained a small amount of virus and *Borrelia* [31].

In 2014, a study of tick infestation with the causative agent of a poorly studied tick-borne vector-borne infection caused by *B. miyamotoi* was launched in the Khabarovsk Territory. In the study of ticks removed after suction from residents of the Khabarovsk Territory in 2014-2016, *B. miyamotoi* DNA was detected in 4.9 ± 1.9%, 3.35 ± 1.8%, and 4.72 ± 2.1% of samples, respectively. In comparison to *D. silvarum* ($P < 0.01$) and *Haemaphysalis* spp. ($P < 0.05$), the infection rates of *B. burgdorferi* s.l. in *I. persulcatus* were substantially greater. There were statistically minor differences in the infection rates of *B. miyamotoi* across the various species. Note that in 2017, combined infection of ticks with *B. miyamotoi* and *B. burgdorferi* s.l. was found in 10 instances (27.8 ± 7.47%). In this case, the Ct values (the value of the threshold reaction cycle) of *B. burgdorferi* s.l. DNA in most cases significantly exceeded the Ct *B. miyamotoi* DNA, which indicates higher concentrations of *B. burgdorferi* s.l. DNA in the studied material, and, consequently, a higher level of infection of the tick with this pathogen compared to *B. miyamotoi* [32].

On the territory of Khabarovsk, every year people report cases of suction of *Ixodes* ticks. The distribution of six species of *Ixodes* ticks of the Ixodidae family belonging to three genera: *Ixodes* (*I. persulcatus*, *I. pavlovsky*), *Haemaphysalis* (*H. japonica*, *H. concinna*), and *Dermacentor* (*D. silvarum*, *D. reticulatus*) were found in the natural and anthropogenically transformed biocenoses of Khabarovsk and the suburbs. The highest rates of abundance and infection with tick-borne vector-borne infections were found in the species of *I. persulcatus*. Thus, the infection rate of ticks with pathogens of *Ixodes* tick-borne borreliosis was 18.3% (95%, confidence interval: 15.1-21.5%). The antigen of the tick-borne encephalitis virus was detected in 23 tick specimens (2.4%; 95%, confidence interval: 1.42-3.38%) [33, 34].

The results of the 2013–2020 research on the DNA content of pathogenic *Borrelia* in *Ixodes* ticks (n = 3714) from natural foci of the Baikal region (the Republic of Buryatia and the Irkutsk region) showed that, on average, *Borrelia* markers were detected in 40.9% of samples, with fluctuations over the years ranging from 32-55%. The dynamics over the long period show an increasing tendency toward infection. The highest infection rates were seen during the tick activity period at the end of the season (60%) and the lowest at the start of the season (28.6%), as well as during the height of the vector population (36-39%). There were notable variations in Ixodid *Borrelia* infection by age, species, and geography. The primary vector, the taiga tick, and its nymphs were shown to harbor *Borrelia* DNA far more frequently than adults did. The infection rates of men and females, as well as ticks retrieved from humans and animals and gathered from plants, were identical. These are the species that make up the genotyped *Borrelia*: of these were *B. garinii*, accounting for 64.2%, *B. afzelii* for 21.7%, and *B. miyamotoi* for 14.2% [35].

It was discovered that 91.9% of *Ixodes* persulcatus ticks infected with diseases associated with bacterial and viral tick-borne illnesses were found in the southern region of the Primorsky Territory, which includes the Khasansky district. However, different pathogens were present in 13.3% of ticks. 1.1-3.0% of samples had tick-borne encephalitis virus RNA, 12.5-26.6% had *Borrelia burgdorferi* sensu lato DNA, 0.6% had *Borrelia miyamotoi* DNA, 4% had *Anaplasma phagocytophillum* DNA, and 1.6-7.0% had Ehrlichia chaffeensis/Erlichia muris DNA. In 8% of cases, *Rickettsia* DNA was found; 12 of those cases included *Rickettsia heilongjiangensis*. There were seven instances of mixed infections involving two diseases and different tick species. Combinations of borreliosis + anaplasmosis were more often detected, less often – of borreliosis + ehrlichiosis [36, 37].

The epizootological examination of Popov Island (Primorsky Krai) recorded four species of *Ixodes* ticks during collection from vegetation: *I. pavlovsky* Pomerantsev, 1946 (77.5% of the total of all individuals), *I. persulcatus* Schulze, 1930 (15.3%), *Haemaphysalis concinna* Koch, 1844 (4.5%) and *H. japonica douglasi* Nuttall et Warburton, 1915 (2.7%). An area known as Cape Lycander was discovered to have up to 100 ixodids per flag hour. Only 346 of the 487 ticks in the research had RNA or DNA pathogens found in them, and those samples were from the genus *Ixodes*. In representatives of this genus, RNA of tick-borne encephalitis virus was found in

0.9 ± 0.50% of ticks, *Borrelia* DNA in 37.0 ± 2.6%, the genetic material of *Ehrlichiosis* pathogens in 9.0 ± 1.5%, and *Anaplasmosis* in 7.2 ± 1.39% of ticks [38].

There was a study of ticks for infection with the causative agent of borreliosis in the regions of the south of Sakhalin Island over the spring and summer periods of 2019-2020. In 2019, the peak of infection of ticks with pathogens of borreliosis was recorded in June. At an average temperature of 11.9 °C, the infection rate was 27.3% of the total number of studied individuals. During the same period in 2020, the peak infection of ticks with borreliosis pathogens was in July and at an average temperature of 16.9 °C, the infection rate was 100.0% of the studied individuals. In 2019, the increase in infection of ticks with borreliosis pathogens was observed twice during the spring and summer period and was recorded in May, when at an average temperature of 6.7 °C the infection rate was 50.0% of the total number of studied individuals, and in July, when at an average temperature of 18.5 °C, the infection rate was 40.0% of the total number of studied individuals. In 2020, the peak infection rate (borreliosis) was in May, at an average temperature of 9.7 °C, it amounted to 80.0% of the total number of studied individuals and continued to remain at this level until June at an average temperature of 14.3 °C. During the spring-summer period of 2019, the largest number of ticks infected with encephalitis pathogens was observed in May, when, at an average temperature of 5.2 °C, 2 out of 58 ticks were infected (3.4%) and in August, when, at an average temperature of 21.0 °C, 2 out of 68 ticks were infected (2.9%). During the spring-summer period of 2020, the largest number of ticks infected with encephalitis pathogens was observed in May, when, at an average temperature of 9.1 °C, 7 out of 87 individuals were infected (8%) and in August, when, at an average temperature of 20.1 °C, 1 out of 20 individuals was infected (5%). The largest number of ticks infected with borreliosis pathogens was detected in May when 9 individuals out of 51 specimens were infected (17.6%) at an average temperature of 5.2 °C, and in September, when 6 out of 18 individuals were infected at an average temperature of 14.4 °C, which makes 33.3%. During the spring-summer period of 2020, the largest number of ticks infected with borreliosis pathogens was observed in April, when, at an average temperature of 4.6 °C, 1 of the 4 studied ticks was infected, that is 25.0%. In August as well: 3at an average temperature of 20.0 °C, 4 out of 19 ticks were infected, that is 21.1% [39].

There is no official tick-borne encephalitis endemic in the Republic of Sakha (Yakutia). This is the first place where the human morbidity and tick infection rates have been determined. In 2013, ticks infected with the tick-borne encephalitis virus were identified for the first time in all the years of surveillance: out of 105 studied ticks removed from humans, 6 were positive (5.7%). In 2014, in a laboratory study of 183 specimens of ticks collected from humans, 18 were infected (9.8%) [40].

CONCLUSION

Ixodes ticks are known as carriers of pathogens of many infectious diseases with natural foci. The infection rate of ticks ranges from 0.5-34%. At the same time, the infection rate of *I. ricinus* with *Borrelia* was 16.9–18.3%, and *D. reticulatus* – 12.3%, infection rate of taiga ticks with tick-borne encephalitis virus was from 0.5-4.5%, averaged 1.2%. Infection of *I. persulcatus* with *Borrelia* ranges from 10-34%, on average reaching 19%, of which 2.5% of cases show a high degree of infection. 16.5% of *Ixodes* ticks showed mixed infection with pathogens of infectious diseases with natural foci. The main carriers of pathogens of bovine taileriosis are *H. plumbeum* ticks (13.56%).

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CONFLICT OF INTEREST: None

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ETHICS STATEMENT: The investigation was carried out in compliance with global ethical guidelines. Neither people nor animals were used in the investigation.

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