SEROPREVALENCE OF TICK-BORNE DISEASES IN THE NORTHWEST FEDERAL DISTRICT OF THE RUSSIAN FEDERATION

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СЕРОПРЕВАЛЕНТНОСТЬ КЛЕЩЕВЫХ ЗАБОЛЕВАНИЙ В СЕВЕРО-ЗАПАДНОМ ФЕДЕРАЛЬНОМ ОКРУГЕ РОССИЙСКОЙ ФЕДЕРАЦИИ

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Abstract

Introduction: Knowledge about tick-borne disease (TBD) distribution is necessary to improve prevention, whereas detection of human serum IgG antibodies against relevant pathogens is a method for monitoring TBD prevalence in local population. The study objective was to estimate seroprevalence of IgG antibodies against tick-borne encephalitis virus (TBEV), *Borrelia burgdorferi sensu lato, Coxiella burnetii, Anaplasma phagocytophilum,* and *Ehrlichia chaffeensis/E.muris* in healthy residents from the five territories of the Northwestern Federal District of the Russian Federation (Arkhangelsk Oblast, Leningrad Oblast, Pskov Oblast, the Republic of Komi and the Republic of Karelia). Materials and methods: in 2017-2019, a total of 1244 serum samples from healthy residents, not vaccinated against TBDs or other flavivirus-caused infections was studied by ELISA. Results: 21.7% of the sera samples contained IgG antibodies against a single TBD pathogen, whereas 2.1% showed signs of coinfection with two or more pathogens. The most common were IgG antibodies against TBEV (5 territories, 12.2%), followed by *Borrelia burgdorferi sensu* lato (5 territories, 3.5%), *C. burnetii* (4 territories, 2.9%), *Anaplasma phagocytophilum* (3 territories, 1.6%), *E. chaffeensis /E. muris* (5 territories, 1.5%). The IgG antibodies were more common in men (55.2%) than in women (44.8%), being found virtually evenly in age- independent manner (from juniors under 18 to seniors over 60). Conclusion: The results of this first comprehensive serosurveillance study in the Northwestern Federal District of the Russian Federation assessing serum IgG antibodies against tick-borne diseases indicate a wide distribution of such pathogens. Moreover, infections caused by *C. burnetii, Anaplasma phagocytophilum*, and *Ehrlichia chaffeensis /E.muris* might be highly underdiagnosed.

Keywords: seroprevalence; antibodies; tick-borne encephalitis; Lyme disease; human granulocytic anaplasmosis; human monocytic ehrlichiosis; Q fever; European North of Russia

Резюме.

Введение: Знание распространения клещевых заболеваний необходимо для улучшения их профилактики, а выявление IgG-антител к их возбудителям в сыворотках крови человека является методом мониторинга распространенности клещевых заболеваний среди местного населения. Цель исследования: изучение серопревалентности практически здорового населения Архангельской, Ленинградской, Псковской, областей, Республик Коми и Карелии, расположенных на европейском Севере России, в отношении вируса КЭ, *Borrelia burgdorferi sensu lato, Coxiella бurnetiid*, *Anaplasma phagocytophilum,* and *Ehrlichia chaffeensis /E.muris*. Материалы и методы*:* всего было исследовано 1244 сыворотки крови практически здоровых лиц, постоянно проживающих на данной территории, не вакцинированных против клещевого энцефалита и других инфекций, вызываемых флавивирусами, профессия которых не связана с риском заражения клещевыми инфекциями. Сыворотки крови доноров исследовали методом ELISA. Результаты: установлено, что в 21,7% образцах исследованных сывороток, полученных от жителей всех анализируемых территорий, обнаружены антитела класса IgG к возбудителям различных инфекций, передающихся клещами, в том числе в 26 пробах одновременно к двум и более патогенам. В сыворотках жителей Республик Коми и Карелия, а так Ленинградской области выявлены антитела ко всем исследованным антигенам, в сыворотках жителей Архангельской области – антитела к вирусу клещевого энцефалита, *Borrelia burgdorferi sensu lato, C. бurnetiid и E. chaffeensis/ E. muris* а в сыворотках жителей Псковской области - антитела к вирусу клещевого энцефалита, *Borrelia burgdorferi sensu lato* и *E. chaffeensis/ E. muris.* У мужчин IgG – антитела к клещевым инфекциям определялись чаще (55,2%), чем у женщин (44,8%.). IgG –антитела к клещевым инфекциям были определены практически равномерно у жителей всех возрастов от детского (до 18лет) до пожилого (старше 60 лет). Обсуждение: представленные результаты первого комплексного обследования жителей европейского Севера России на наличие в их сыворотках крови IgG -антител к клещевым инфекциям, свидетельствует о широком распространении этих инфекций и, вероятно, о существенной гиподиагностике инфекций, вызываемых *C. 7urnetiid, Anaplasma phagocytophilum,* and *Ehrlichia chaffeensis /E.muris.*

Ключевые слова: серопревалентность; антитела; клещевой энцефалит; болезнь Лайма; гранулоцитарный анаплазмоз человека; моноцитарный эрлихиоз человека; Ку-лихорадка; Европейский Север России.

Introduction

TBDs are among important drivers of habitat quality, public and herd health, as well as the epidemiological safety of the local population [4]. Recent social changes and stronger anthropogenic impacts on abiotic components of landscapes may contribute to the evolution of those infections [24, 28]. In this regard, any advance in understanding of TBDs real distribution within a territory is of great importance for prevention of these diseases.

TBD incidence rate is an important factor that defines prophylaxis volume and methods within an administrative unit. However, it does not always reflect to a full degree the real spread of TBD, since that depends much on the awareness of the local population, their health seeking behavior, availability and quality of medical care, qualification of medical personnel, availability of laboratory diagnostics, etc. There is a high risk of underdiagnosis since most of the human TBDs appear as subclinical forms [4]. Many patients are asymptomatic or experience mild symptoms and, as a rule, do not seek medical help, thus reducing the reported incidence rate. However, the absence of pronounced symptoms does not exclude the probability of chronic TBD course, resulting in disability or even fatal outcome [24, 28, 7, 49]. Knowledge of TBDs actual distribution is necessary to improve its effective prevention in the area. The detection of IgG antibodies to TBD pathogens in blood sera of humans is a method for indicating the real level of infection in the local population.

Among all TBDs it is TBE that poses the most socially important problem in the Russian Federation, being diagnosed in 46 subdivisions. At least 1508 cases of TBE were reported in 2018, including 153 in children under 14. TBE incidence rate was 1.3 per 100 thousand inhabitants; in 98% of cases the disease developed after tick bites. Twenty two cases of TBE were fatal; i.e. the infection case fatality rate was 0.7% [7].

In 1996-2017, in Komi, in the European North of Russia, the TBE case fatality rate was 2.3% [28].

The incidence of both TBE and LD remains rather high in NWFDRF [28, 2, 11, 9, 51]. For example, from 2006-2017 in Komi, the average TBE incidence rate ran to 1.4, while that of LD was 0.8 [28].

HGA, HME and Q fever are practically not recorded in the European north of Russia, although in some cases they are responsible for irreversible damage to the internal organs and disability of patients [4].

The choice of territories under study of human sera derives from the northward spread of ixodid ticks in the European north of Russia [9]. Such *expansion* in *the tick's* geographic range contributes to favorable conditions for TBDs distribution.

The objective of our work was to study the seroprevalence of IgG antibodies against TBEV, *Borrelia burgdorferi sensu lato, Coxiella 9urnetiid, Anaplasma phagocytophilum,* and *Ehrlichia chaffeensis/E.muris* in the healthy population of NWFDRF: in the AO, LO, PO, Komi and Karelia. The purpose was to study the variation in seroprevalence of these indicators in different territories and whether there are age and gender differences.

2. Materials and methods

The blood serum of healthy donors was sampled in 5 administrative divisions of NWFD RF: Komi, Karelia, AO, LO, PO. The territory of NWFD RF involves numerous islands, however, all samples were collected in mainland territory only.

Figure 1 shows a map of NWFD RF with the designation of its administrative units.

Figure 1. Administrative divisions of the Northwestern Federal District: 1- Arkhangelsk Oblast (AO), 2- Vologda Oblast, 3- Kaliningrad Oblast, 4 – Republic of Karelia (Karelia), 5 – Komi Republic (Komi), 6 – Leningrad Oblast (LO), 7- Murmansk Oblast, 8 – Nenets Autonomous District, 9- Novgorod Oblast, 10- Pskov

Oblast (PO), 11 – St. Petersburg city. Five surveyed divisions (1, 4, 5, 6, 10) are marked out in dark. https://creativecommons.org/licenses/by-sa/3.0/deed.en.

Blood was sampled in 2018-2019 after informed voluntary consent of donors and based on their personal data (Table 1). The inclusion criteria were as follows: good health at study entry; no professional risk of TBD acquisition; no history of vaccination against TBD and/or other infections caused by flaviviruses; no manifest forms of TBD; no diseases or conditions that affect the results of serological studies; residence in the territory under study and no trips out of it for several years at least.

Blood was sampled from the cubital vein into vacuum tubes, followed by centrifugation (10 min, 3000 rpm), freezing and storage of sera at -70°C. Subsequent transportation of the material was carried out in compliance with the “cold chain”. All sera samples were analyzed by ELISA with commercial test systems for detection of:

- IgG antibodies to TBEV – “VectoVKE-IgG” (CJSC “Vector-Best”, Novosibirsk),
- IgG antibodies to *Borrelia burgdorferi sensu lato* – “LimeBest” (CJSC “Vector-Best”, Novosibirsk),
- IgG antibodies to *Coxiella 10urnetiid*, “Anti-Q” (Pasteur Institute, St. Petersburg),
- IgG antibodies to *Anaplasma phagocytophilum* – “GACh-ELISA-IgG” (LLC “Omnix”, St. Petersburg),
- IgG antibodies to *Ehrlichia chaffeensis/E. muris* – “MECH-IFA-IgG” (LLC “Omnix”, St. Petersburg).

All sera samples were tested according to the manufacturer’s manuals. The test results were classified as positive, negative, or borderline according to the instructions enclosed in the diagnostic systems. Considering the probability of false positive results due to the common antigenic sites of some antigens, any borderline results were regarded as negative. In addition, for a more objective assessment of the results on TBEV, all sera containing IgG antibodies to TBEV according to VectoVKE-IgG system (Vector-Best CJSC, Novosibirsk, Russia) were simultaneously studied using the test system Enzygnost® Anti-TBE/FSME Virus (IgG,) (Siemens Healthcare, GmbH, Marburg, Germany), both with specificity 99.5% according to the manufacturer's manual.

The distribution of our sera donors'by gender, age and territory of residence is shown in Table. 1.

3. Results

In this study 1244 sera samples were tested for TBD pathogens. The parallel studies of 152 sera samples analysed for IgG antibodies to TBEV by VectoVKE-IgG were confirmed by Enzygnost® Anti-TBE Virus (IgG). The results of detection of IgG antibodies to the TBD pathogens *Borrelia burgdorferi sensu lato, Coxiella 11urnetiid, Anaplasma phagocytophilum,* and *Ehrlichia chaffeensis/E.muris* are shown in Table 2.

From the 1244 studied sera samples IgG antibodies to TBD pathogens were detected in 270 (21.7%), where 26 (2.1%) samples contained antibodies to more than one pathogen. The overall seroprevalence was highest in LO (30.4%), then followed by Komi (22.6%), Karelia (20.2%), PO (19.4%) and AO (14.6%). IgG antibodies to all five TBD pathogens (TBEV, *Borrelia burgdorferi sensu lato, C. 11urnetiid, Anaplasma phagocytophilum* and *E. chaffeensis/E. muris*) were found in sera samples from Komi, Karelia and LO. In AO we revealed antibodies to four (TBEV, *Borrelia burgdorferi sensu lato, C. 11urnetiid and E. chaffeensis / E. muris*), while in PO only to three of them (TBEV, *Borrelia burgdorferi sensu lato* and *E. chaffeensis / E. muris*).

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The number of samples from each territory was not sufficient to conclude on statistically significant differences in frequency of antibodies to the pathogens in this study.

However, from Table 2 the seroprevalence of IgG antibodies to TBEV and *Borrelia burgdorferi sensu lato* was 2.1 and 3.4 times higher in LO than in AO, respectively, while in Komi, Karelia and PO the percent of antibody-positive samples for these pathogens essentially did not differ, except for a slightly higher prevalence of *Borrelia* in PO and LO. In other territories the seroprevalence of IgG antibodies to TBEV did not vary significantly.

The highest seroprevalence to *A. Phagocytophilum* was recorded in LO, to *E. chaffeensis/E. muris* the highest prevalence was detected in AO, and for *C. 12urnetiid* IgG antibody seroprevalence in Karelia, Komi and LO was nearly the same.

IgG antibodies to all studied TBD pathogens were detected more often in men (55.2%) than in women (44.8%). The difference is especially demonstrated for IgG antibodies to TBEV where seroconversion was 15.7% in men, while only 9.9% in women.

In our study IgG antibodies to TBD did not depend considerably on the donor's age, being nearly the same for juniors (<18 years) and seniors (> 60 years). However, IgG antibodies to *B. burgdorferi sensu lato* and *A.phagocytophilum* were detected in juniors somewhat more often than in seniors. IgG antibodies to *Coxiella 12urnetiid* were highest in seniors (> 50 years), while IgG antibodies to *Borrelia* and *Anaplasma*, on the contrary, were highest in the youngest group (<18 years) (see Table 3).

4. Discussion

Ixodid ticks are among the most important vectors of human TBDs, including TBE, LD, HGA and HME [4, 31]. The epidemiological profiles of those TBDs are

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nearly similar. Therefore, in the majority of cases IgG antibodies against TBEV, B. *burgdorferi sensu lato, A. phagocytophilum*, and *E. chaffeensis/ E. muris* are indicative of frequent exposure to infected ticks within the studied territories. Seroprevalence is indicative of both the activity in TBD natural foci and the risk of infection in the local population [4]. On the contrary, the probability of catching Q fever directly from ixodid ticks is insignificant [25]; therefore, the IgG antibodies against *C. 13urnetiid* are more indicative of Q fever anthropogenic foci activity. The role of ixodid ticks in the *C. 13urnetiid* distribution is largely due to the infection of wild, agricultural and domestic animals. In addition, these blood-sucking arthropods infected with *C. 13urnetiid* feed on migratory birds that transfer the infection to virgin territories [17, 50].

Here we present our first comprehensive serosurvey of humans in five administrative units of the NWFDRF for the presence of IgG antibodies against TBEV, *B. burgdorferi sensu lato, A. phagocytophilum* and *E. chaffeensis/ E. muris* and *C. 13urnetiid*. The results indicate that the proportion of TBD-infected populations in different territories varies.

Our results on the seroprevalence of IgG antibody to TBEV in AO (6.8%) and in Komi (12.6%) are close to those reported earlier (7.9% and 13.7%, respectively) [9, 53]. The index varies much depending on the territory under study. E.g., in the south of AO, it reached 20.9% [9]. Seroprevalence being the result of a permanent dynamic process depends both on the activity of TBD natural foci and the frequency of humans' exposure. An illustrative example is the increased seroprevalence of IgG antibodies to TBEV in the population of Komi between 2001 and 2013 from 3.5% to 13.7%, probably due to climatic changes [51], that favor both northward expanding of tick geographic ranges and exposure of local inhabitants to infected tick bites [53]. An increase in TBEV seroprevalence is typical not only for the North of Russia; a similar trend has been observed in some regions of the Czech Republic [36].

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Here we studied the seroprevalence of IgG antibodies to TBEV in the healthy population of the Northwestern Russia, while researchers in Europe focus mostly on occupationally-risk groups. However, in many European countries the reported TBEV-seroprevalence in high risk occupationally exposed groups is much less (e.g., only 2.3% in France [44]), than that of healthy donors in NWFDRF, where the seroprevalence is 12.2%. Serosurveillance of 1213 healthy donors in Western Norway showed little to no TBEV prevalence among local residents [32]. Similar results were obtained from a survey of healthy donors in other areas (Vestfold and Telemark counties) in Norway. Only 0.4% of them had antibodies to TBEV [39, 37].

Our findings on seroprevalence of IgG antibodies to *B. burgdorferi sl.* In NWFDRF (3.5%) do not differ much from those reported in other European countries. E.g., in Belgium *B. burgdorferi sl* seroprevalence in a healthy population of blood donors was 2.6-2.9% [21].

HGA must be classified as an emerging infection in NWFDRF. HGA was first diagnosed in 1990 in Wisconsin (USA) in a patient with a tick bite history and severe febrile illness [18]. However, under-diagnosis of HGA is typical for many countries, including USA [41]. The incidence of human HGA cases in Europe is lower (estimated under 300) than reported from the USA, where a steady increase has been reported since 2001, with more than 15,000 accumulated cases until 2015 [16]. HGA cases have now been reported from Austria, Croatia, France, Italy, Latvia, the Netherlands, Norway, Poland, Slovenia, Spain, and Sweden [38, 40]. There is an incongruence between human seroprevalence and observed clinical cases that might arise from incomplete diagnosis, or a high rate of asymptomatic infections [42]. In Russia, as well as in other European countries, HGA is rarely registered. In many territories of Russia, where ticks infected with *A. phagocytophilum* were found, HGA is not diagnosed [8]. A similar situation is observed in NWFDRF, where *A. phagocytophilum* was also found in ticks [26], and HGA is not diagnosed in humans either. It is possible that HGA patients are given a different diagnosis, for example,

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"Flu" or "fever of unknown etiology." The discrepancy between the relatively high seroprevalence rates for *A. phagocytophilum* (4.3% in LO), and the lack of diagnosis of this infection in humans in NWFDRF, revealed by us, is probably due to the wide spread of asymptomatic forms of this disease and the imperfection of its diagnosis [42]. Despite the obviously ubiquitous presence of *A. phagocytophilum* in ticks and various wild and domestic animals in the European North of Russia [26], the reported HGA clinical cases are very rare, and territories with *A. phagocytophilum*-infected ticks are much more numerous than those with a few registered HGA cases [42]. However, in S.P.Botkin hospital in St. Petersburg antibodies to HGA were detected in 16 of 934 tick-bitten febrile patients, while no other antibodies to TBD pathogens (TBEV or *B. burgdorferi sensu lato*) were found. In two of these 16 patients an increase in IgG antibodies to *A. phagocytophilum* was recorded which, along with the clinical picture and pre-existing tick bites, made it possible to diagnose HGA [12]. In Europe rather high HGA seroprevalence rate was detected in TBE-suspected patients: 30.96% in Belgium [20], 25% in Slovakia [35], 16.28% in donors in Norway [32], 11.4-28% in Sweden [41, 47], and 3.5-9.4% in Poland [19, 54]. According to our findings the average level of HGA seroprevalence in the healthy population of NWFDRF was 1.6% (though 4.3% in LO) that is less than in most of the European countries mentioned above. This comparatively low seroprevalence, on the one hand, may stem from lower *A. phagocytophilum* prevalence in the territories under study; on the other hand, it may be due to different methods of antibodies detection and differences in the surveyed contingents. To detect IgG antibodies to *A. phagocytophilum* in Europe the IFA assay was mostly applied to survey "occupational risk" groups, while here we used ELISA and applied it in healthy donors without "occupational risk". However, in our opinion, even the relatively low figures for *A. phagocytophilum* seroprevalence in LO, Komi and Karelia substantiate the need to examine tick-bitten febrile patients for the presence of antibodies to *A. phagocytophilum*.

HME, despite its clinical resemblance to HGA, is characterized by more severe course and a higher mortality rate [24]. HME is widespread in the southeastern, southern, central, and mid-Atlantic parts of the United States. In 2015, *E. chaffeensis* infection was reported in 35 states, with most numerous cases in Missouri, Arkansas, New York, and Virginia. In the European Union, *E. chaffeensis* is not subject to registration [38], however, HME cases have been reported in Serbia [15], Czech Republic, Denmark, Sweden, and other countries [29], but those findings are fragmentary. In the Russian regions diagnosis of HME cases are rare compared to detection of *E. chaffeensis/E. muris* in ticks [28]. However, our earlier serological studies revealed the HME occurrence in the North-West of Russia: e.g., in the healthy population of St. Petersburgs outskirts the seroprevalence of IgG antibodies to *E. chaffeensis/ E. muris* was 4.4% [52].

In this study the seroprevalence of IgG antibodies to *E. chaffeensis / E. muris* in average was 1.5%. It was revealed in all territories under study and varied from 0.7% (in Karelia) to 4.9% (AO). Those findings are consistent with an earlier communication on detection of IgG antibodies to *E. chaffeensis / E. muris* in the sera of 23.3% of febrile patients hospitalized in Arkhangelsk city after tick bites [52].

Q fever is diagnosed in humans and animals, and its natural or household foci are identified practically all over the world, with the possible exception for New Zealand [14]. Not all countries have mandatory registration of Q fever incidence, however, the infection is usually diagnosed where appropriate research is carried out [34]. In Europe, Q fever is regularly notified in many countries, e.g., in Bulgaria, France and Germany [27]. The largest known Q fever outbreak reported to date involved approximately 4,000 human cases (25 fatal) and occurred during 2007–2010 in the Netherlands [25, 22, 45]. In the NWFDRF, a large outbreak of Q fever was recorded at the end of 20^{th} century [1].

In our study, IgG antibodies to *C. 17urnetiid* were detected in all studied territories, with the exception for PO, while in Karelia, Komi and LO it was rather high (> 3%).

However, Q fever is not diagnosed in NWFDRF in recent years, and only one Q fever case was diagnosed in LO in 2017-2019.

Among the reasons for Q fever under-diagnosis is the difficulty of its clinical recognition due to pronounced polymorphism of the disease manifestations and the absence of pathognomonic symptoms. Significant under-diagnosis of Q fever causes irrational treatment, resulting in chronicity. Chronic Q fever is a very frequent outcome of the disease. For example, in the south of France 5-8% of all endocarditis cases are caused by *C. 17urnetiid* [49]. Such development of the disease in humans is often fatal [43].

Comparison of IgG antibody seroprevalence in LO (3.3%) with the same long-term indicator in the city of St. Petersburg (0.4%) [5] lends indirect support to the view that ixodid ticks play a relatively small role in *C. 17urnetiid* infection in humans. The overwhelming majority of St. Petersburg residents annually spend their recreation time in LO and tick-bitten by ixodid ticks [11]. However, the IgG antibody seroprevalence in the city residents is much lower than in the LO population, because a larger part of the LO population tend to temporary be in contact with animals at livestock enterprises or private farms compared to city residents.

In our study, IgG antibodies to TBDs were detected in humans of various ages, from children (<18 years) to the elderly (> 60 years). Similar findings are available for Russia as a whole [6]. The age dependence of seroprevalence was insignificant.

The most significant gender differences in seroprevalence rates were related to TBE.

In men, the seroprevalence of IgG antibodies to TBEV exceeded that in women, probably to a certain extent due to their exposure to ticks during traditional out-of-doors occupations (fishing, hunting, hiking, etc.).

Analysis of modern literature on infections transmitted by ixodid ticks suggests that any disease resulting from tick bites should be considered as a potential mixed infection. Coinfection of two or more pathogens during the disease development complicates the diagnosis of mixed infections [3]. It was found that in northwestern Russia, mixed infection without pronounced clinical manifestations occurs 7.6 times more often than with the development of the clinical picture of diseases [13, 10]. In our study, antibodies to two or more pathogens were detected in 2.1% of sera samples, and as a rule, those were IgG antibodies to TBEV and *Borrelia burgdorferi sensu lato*. Our findings do not allow us to determine whether people were infected with those two pathogens simultaneously or from different tick bites. Although, considering the pathogens ability to persist in a human body, it can be assumed that individuals with coinfections may have a greater risk of chronicity.

When testing sera by the ELISA methods one cannot completely exclude the possibility of false-positive results. To minimize this risk in our study we interpreted the borderline results as negative, and similar results from two different test systems in parallel was required to conclude that a sample was positive.

However, for our purpose, the absolute figures are less important than the variation in seroprevalence of those indicators in different territories, and in persons of different ages and gender.

5. Conclusions

A sizable portion (on average 21.7%) of NWFDRF population is infected with TBD pathogens. The percent of infected population varies significantly depending on the territory. The presence of IgG antibodies to TBD pathogens in the sera of humans in the absence of reported incidence is indicative of underdiagnosis of those

TBDs. The discrepancy between our findings on seroprevalence and the reported TBDs prevalence is largely due to the absence of pathognomonic symptoms in these diseases, its mild, asymptomatic clinical course in some cases, and insufficient laboratory diagnostics. Significant underdiagnosis of TBDs as a consequence of irrational treatment results in chronic course and lethality, therapeutic misconception, erroneous ideas about the real distribution of TBDs and the lack of proper alertness of medical staff to those diseases.

Men are infected with TBDs more often than women. However, people, starting from children (<18 years old) to the elderly (>60 years old) were found to be infected with TBD pathogens almost evenly irrespective of age. Infection with two or more TBD pathogens was detected in 2.1% of the surveyed humans.

The detection of IgG antibodies to TBD pathogens in the northern territories, where TBDs never had been diagnosed, confirms indirectly the northward expansion of tick habitats [9, 53, 47]. Similar expansion of ixodid tick habitats has also been observed in other countries of the Northern Europe [48, 33, 46]. Of particular concern is the health of the indigenous population of the North, who historically had never been exposed to ticks and more vulnerable to tick-borne infections [30].

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FIGURES

Fig.1. Administrative divisions of the Northwestern Federal District: 1- Arkhangelsk Oblast, 2- Vologda Oblast, 3- Kaliningrad Oblast, 4 – Republic of Karelia, 5 – Komi Republic, 6 – Leningrad Oblast, 7- Murmansk Oblast, 8 – Nenets Autonomous District, 9- Novgorod Oblast, 10- Pskov Oblast, 11 – St. Petersburg city. The surveyed divisions (1, 4, 5, 6, 10) are highlighted in red. Foreign territories are highlighted in grey.

Рисунок 1. Административно-территориальные образования Северо-Западного федерального округа: 1- Архангельская область, 2- Вологодская область, 3- Калининградская область, 4- Республика Карелия, 5- Республика Коми, 6- Ленинградская область, 7- Мурманская область, 8- Ненецкий автономный округ, 9- Новгородская область, 10- Псковская область, 11- город Санкт-Петербург. Обследуемые образования (1, 4, 5, 6, 10) отмечены красным цветом, прочие территории выделены серым цветом.

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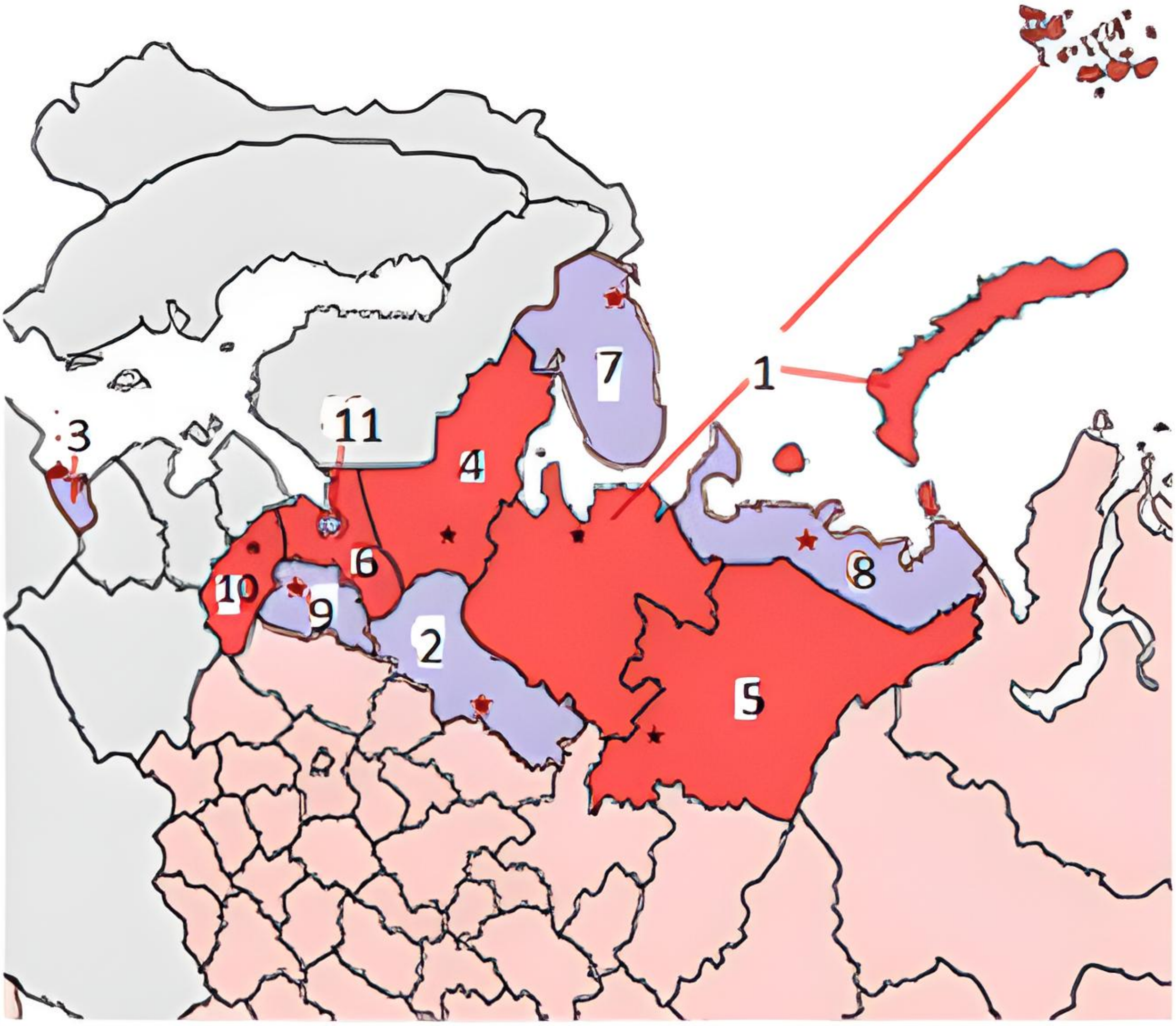

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TABLES

Table 1. Distribution of donors by gender, by age, and by territory of residence

Таблица 1. Распределение доноров по полу, возрасту и территории проживания.

Territory of residence Территория проживания	Number of donors Число доноров	Gender Пол		Age (years) Возраст (лет)					
		Male М	Female Ж	<18	18-29	30-39	40-49	50-59	> 60
Komi Коми	659	246	413	3	62	108	126	150	210
Karelia Карелия	292	148	144	0	35	109	95	45	8
AO	103	24	79	5	12	16	23	19	28
PO	98	42	56	0	21	23	35	17	2
LO	92	36	56	50	18	24	0	0	0
Total Всего	1244	496	748	58	148	280	279	231	248

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Table 2. IgG antibodies to TBD pathogens in sera of NWFDRF residents.

Таблица 2. Антитела IgG к возбудителям КЗ в сыворотке крови жителей СЗФО РФ.

Territory of residence	Number of samples	IgG- antibody-positive samples (number of positive /seroprevalence, %) IgG-положительные образцы (количество положительных/серопревалентность, %)						
		Antibody-positive to any TBD pathogens	Tick-borne encephalitis virus	*Borrelia burgdorferi sensu lato*	*C. burnetii*	*Anaplasma phagocytophilum*	*E. chaffeensis/ E. muris*	Ат против двух и более вохбудителей КЗ
Komi	659	149 / 22.6	83/ 12.6	21/ 3.2	23/ 3.5	15 / 2.3	7 / 1.1**	15/ 2.3
Karelia	292	59/ 20.2	38/ 13.0	9/ 3.1	9/ 3.1	1/ 0.3	2/ 0.7	5/ 1.7
AO	103	15/ 14.6	7/ 6.8	2/ 1.9*	1/ 1.0	0	5/ 4.9**	1/ 1.0
PO	98	19/ 19.4	11/ 11.2	5/ 5.1	0	0	3/ 3.1	2/ 2.0
LO	92	28/ 30.4	13/ 14.1	6/ 6.5*	3/ 3.3	4/ 4.3	2/ 2.2	3/ 3.3
Total	1244	270/ 21.7	152/ 12.2	43/ 3.5	36/ 2.9	20/ 1.6	19/ 1.5	26/ 2.1

When comparing the seroprevalence rates of IgG antibodies against TBD pathogens significant differences were found:

*in relation to *Borrelia burgdorferi sensu lato* in AO and LO: the corresponding value of Fisher's criterion is 1.651 (while for p = 0.01 the critical value is 1.450),.

**in relation to *E. chaffeensis / E. muris* in Komi and AO: the corresponding Fisher's criterion is 2.244 (while the critical value for p = 0.01 is 1.450).

При сравнении показателей серопревалентности антител IgG к возбудителям КЗ выявлены достоверные различия:

* в отношении Borrelia burgdorferi sensu lato в АО и ЛО: соответствующее значение критерия Фишера равно 1,651 (при p = 0,01 критическое значение равно 1,450).

** в отношении E. chaffeensis/E. muris в Коми и АО: соответствующий критерий Фишера равен 2,244 (при этом критическое значение для p = 0,01 равно 1,450).

Table 3. Age distribution of donors with IgG antibodies to TBD pathogens.

Таблица 3. Возрастное распределение доноров с антителами IgG к возбудителям КЗ.

TBD pathogen	Age distribution of IgG antibody-positive donors (years). Возрастное распределение IgG-положительных доноров (лет). IgG antibody-positive/ all donors; percent of antibody-positive (%) IgG-положительные/все доноры; процент положительных антител (%)						
	<18 n=58	18-29 n=148	30-39 n=280	40-49 n = 279	50-59 n= 231	> 60n- 248	Total n=1244
TBEV	6 /10.3%	1/9 12.8%	39/ 13.9%	39/ 14.0%	24/10.4%	25/10.1%	152/ 12.2%
B. burgdorferi sensu lato	4 /6.9%	3/2.0%	11/ 3.9%	8/ 2.9%	8/3.5%	9/ 3.6%	43/3.5 %
A.phagocytophilum	3/ 5.2%	2/ 1.4%	1/ 0.4%	4/ 1.4%	4/1.7%	6 /2.4 %	20/ 1.6%
E. chaffeensis/ E. muris	2/ 3.4%	5/ 3.4%	1/ 0.4%	4/1.4%	3/1.3%	4/1.6 %	19/1.5 %
C. burnetii	1/ 1.7%	4/ 2.7%	5/ 1.8%	6/ 2.2%	9/ 3.9%	11/4.4%	36/ 2.9%

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Ключевые слова: серопревалентность; антитела; клещевой энцефалит; болезнь Лайма; гранулоцитарный анаплазмоз человека; моноцитарный эрлихиоз человека; Ку-лихорадка; Европейский Север России

Keywords: seroprevalence; antibodies; tick-borne encephalitis; Lyme disease; human granulocytic anaplasmosis; human monocytic ehrlichiosis; Q fever; European North of Russia

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Порядковый номер ссылки	Авторы, название публикации и источника, где она опубликована, выходные данные	ФИО, название публикации и источника на английском	Полный интернет-адрес (URL) цитируемой статьи и/или
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