

Research article

ANALYZING RISKS OF INCIDENCE OF TICK-BORNE ENCEPHALITIS IN AREAS WITH DIFFERENT CLIMATIC AND GEOGRAPHICAL CONDITIONS

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Ticks are natural reservoirs and vectors of a virus that is an infectious agent of tick-borne encephalitis, a communicable disease with great medical and social significance. Tick-borne encephalitis (TBE) is widely spread in Arkhangelsk region (AR) located in the Arctic zone in Russia where substantial climatic changes are taking place at the moment.

Our research involved examining spatial and temporal distribution of numbers of people bitten by ticks, a number of people bitten by ticks per 100 thousand, a number of TBE cases and TBE incidence in districts and settlements in AR. We calculated relative risks of TBE incidence among people bitten by ticks in AR from 1980 to 2019.

We analyzed dynamics of indicators showing numbers of people bitten by ticks per 100 thousand and TBE incidence among people living in Arkhangelsk region. The analysis revealed that a number of bitten people grew slowly in 1980–1990, then there was an exponential growth in 1990–2010, and then the trend stabilized in 2010–2019. Dynamics of TBE incidence was completely in line with changes in number of bitten people up to 2014 but there was a substantial drop in TBE incidence after that.

Spatial distribution of numbers of bitten people and TBE incidence revealed that average number of bitten people amounted to 25.1 per 100 thousand in the northern districts in 1980–2019 and was statistically significantly lower than in the central and southern districts ($p < 0.001$). Average long-term incidence was the highest (7.9 per 100 thousand) in the southern districts in comparison with the central (3.0 per 100 thousand; $p < 0.001$) and northern ones (0.7 per 100 thousand; $p < 0.001$). Maximum relative risks of TBE incidence was detected in the southern districts in 1990–1999 (38.8) in comparison with the northern ones.

We made an assumption about probable reasons for declining TBE incidence in Arkhangelsk region detected over the last years given the growing numbers of bitten people.

Key words: ticks, tick-borne encephalitis, relative risk, Arkhangelsk region.

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Ticks are an important medical issue. These blood-sucking arthropods are not only vectors of various infectious agents, for example, viruses of tick-borne encephalitis, tick borreliosis, human monocytic ehrlichiosis and granulocytic anaplasmosis, but also reservoirs of several pathogens [1, 2]¹. Each tick bite should be considered potentially dangerous for a bitten person's health; it should be seen as potential contagion with mixed infections². Meanwhile, a number of tick attacks constantly grows in the Russian Federation (RF). In 2018 it increased by 12.6 % against average rates detected in 2013–2017 and reached 502,794 cases [3]. Tick-borne encephalitis (TBE) is the most socially significant issue in the RF among all tick-borne infections. In 2018 1,508 cases of the disease were registered in the RF and 153 out of them were among children younger than 14. TBE was detected in 46 RF regions and the incidence rate amounted to 1.3 per 100,000 population; the disease developed after a tick bite in 98 % of cases. 22 TBE cases had a lethal outcome; lethality amounted to 0.7 [3].

Previously we established that TBE incidence rates in the Arkhangelsk region (AR) and the RF in general had opposite trends. There was a considerable growth in the indicator in the AR which, in our opinion, was to a great extent due to expansion of territories where TBE cases were detected; on the contrary, in the RF there was an apparent descending trend starting from 90ties last century¹.

Our research aim was to reveal the latest trends regarding changes in habitats of *I. Persulcatus* and dynamics of TBE incidence and also to describe relative risks of TBE incidence among people bitten by ticks in the AR.

Materials and methods. We took data from the federal statistical forms No. 1 and 2

“Data on infectious and parasitic diseases” and also used the results of operative seasonal monitoring over TBE provided by Rospotrebnadzor Regional Office in the Arkhangelsk region.

We analyzed data on a number of people living in different districts in the region who were bitten by ticks in 1980–2020. Each case was confirmed by an official document stating a date and a place of a bite (Report form No. 058/u entitled “An emergency notification about infectious disease, parasitic disease, food poisoning, an unusual reaction to vaccination, or post-vaccination complications). When analyzing these data, we calculated a number of people bitten by ticks during one year per 100 thousand people living on a given administrative territory. We also calculated TBE incidence (a number of TBE cases during one year per 100 thousand people) in the AR in 1980–2020. TBE was diagnosed based on clinical and epidemiologic data and, as a rule, was confirmed by serological diagnostic techniques (from 84.1 % cases in 2008 to 100 % cases in 2020).

To compare a number of bitten people and TBE incidence in different years, the whole observation period was divided into equal time periods, 10 years each (a decade): the 1st one, from 1980 to 1989 ; the 2nd, from 1990 to 1999; the 3rd, from 2000 to 2009; the 4th, from 2010 to 2019. Official statistical data on population in the AR were taken from Rosstat official web-site³.

We applied one-way analysis of variance with the Bonferroni correction to reveal differences in a number of bitten people and TBE incidence between the districts located in the southern, central, and northern zones. We calculated relative risks (*RR*) and 95 % confidence intervals (95 % *CI*) to compare

¹ Tokarevich N.K., Stoyanova N.A., Gracheva L.I., Trifonova G.F., Tronin A.A., Shumilina G.M., Glushkova L.I., Galimov R.R. [et al.]. Infektsii, peredayushchiesya iksodovymi kleshchami, v Severo-Zapadnom federal'nom okruge Rossii. Analiticheskii obzor [Tick-borne infections in the Northwestern Federal District in Russia. Analytical review]. St. Petersburg, Feniks, 2008, 120 p. (in Russian).

² Korenberg E.I., Pomelova V.G., Osin N.S. Prirodno-ochagovye infektsii, peredayushchiesya iksodovymi kleshchami [Tick-borne natural foci infections]. In: A.L. Gintsburg, V.N. Zlobin eds. Moscow, OOO Kommentarii Publ., 2013, 464 p. (in Russian).

³ The Federal State Statistics Service: official web-site. Available at: <http://www.gks.ru/> (June 12, 2021) (in Russian).

TBE incidence rates in different zones as per decades. Critical level of statistical significance (p) was taken as equal to 0.05. All the data were statistically analyzed with SPSS 28 software package.

Geographical background. The AR is located in the north of the European part in the RF in a zone that borders the Arctic. The region includes 19 districts and 6 cities and its total area amounts to 330.1 thousand square kilometers (without the Nenets Autonomous Area and polar islands). We divided the whole region territory into three conditional zones, northern, central, and southern, to provide better visualization of changes in territorial distribution of people bitten by ticks and registered TBE cases (Figure 1). There were substantial differences between these three zones regarding ecological and epidemiological situation associated with this infection. Overall area covered with forests didn't change significantly over the analyzed period in the AR and amounted to 23 million hectares in 2019⁴.

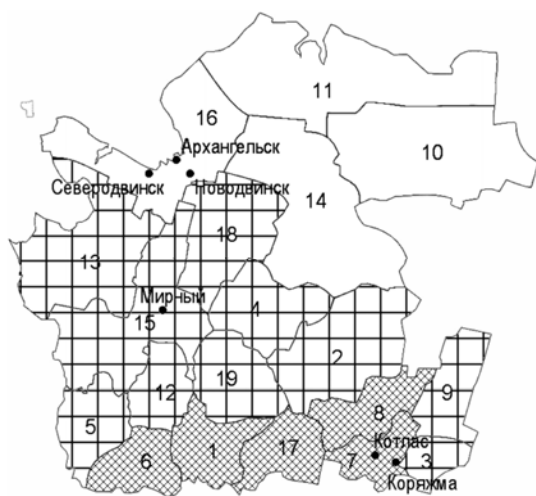


Figure 1. Districts in the Arkhangelsk region:
 1 – Velskiy, 2 – Verkhnetoemskiy, 3 – Vilegodskiy,
 4 – Vinogradovskiy, 5 – Kargopolskiy, 6 – Konoshskiy,
 7 – Kotlasskiy, 8 – Krasnoborskiy, 9 – Lenskiy,
 10 – Leshukonskiy, 11 – Mezenskiy, 12 – Nyandomskiy,
 13 – Onezhskiy, 14 – Pinezhskiy, 15 – Plesetskiy,
 16 – Primorskiy, 17 – Ust'yanskiy,
 18 – Kholmogorskiy, 19 – Shenkurskiy

Ixodes persulcatus prevails in the AR (more than 99 %) and this species is a major source of TBE virus spread among people [4].

Results. Territorial and spatial distribution of people bitten by ticks in the region.

Overall, 122,470 people living in the AR were bitten by ticks over the analyzed period. A number of tick bites grew constantly. Thus, it amounted to 2,840 in 1980–1989; 15,030, in 1990–1999; 38,820 in 2000–2009; and 64,780 in 2010–2019. Average numbers of bitten people – bitten people¹⁰ grew by 22.8 times over a period from 2010 to 2019 against 1980–1989. Overall, there were no statistically significant differences in numbers of bitten people in the southern and central zones (540.9 and 356.5 per 100 thousand people) during 40 years of observation ($p = 0.159$). An average number of bitten people in the districts located in the northern zone amounted to 25.1 per 100 thousand people in 1980–2019 and was statistically significantly lower than in the southern and central zone ($p < 0.001$).

In 1980–1989 bitten people, as a rule, lived in the southern zone in the AR. People living in the Velskiy and Kotlasskiy districts in the southern zone and the Krasnoborskiy and Nyandomskiy districts in the central zones were the most frequently bitten by ticks. There were only sporadic tick bites registered in other administrative districts in the central zone and there were no tick bites registered in that time period in the northern zone. Numbers of people bitten by ticks in the AR taken in dynamics and their spatial distribution are given in Table 1 and Figure 2.

There was an apparent growth in a number of bitten people in most districts in the AR over the analyzed period. In the 4th decade in the observation period people were bitten by these blood-sucking arthropods in almost all districts in the region including the northern zone. Very few cases when people applied for medical aid due to tick bites were registered

⁴ O sostoyanii i ispol'zovanii zemel' v Rossiiskoi Federatsii v 2019 godu: gosudarstvennyi (natsional'nyi) doklad [On the situation and use of lands in the Russian Federation in 2019: The State (National) report]. *The Federal Service for State Registration, Cadastre and Cartography*. Moscow, 2020. Available at: <https://rosreestr.gov.ru/upload/Doc/16-upr/%D0%94%D0%BE%D0%BA%D0%BB%D0%B0%D0%B4%20%20%D0%B4%D0%BB%D1%8F%20%D0%B4%D0%B8%D1%81%D0%BA%D0%B0%2011.12.pdf> (June 12, 2021) (in Russian).

Table 1

Distribution of people in the AR bitten by ticks as per decades and administrative districts in 1980–2019 (bitten people¹⁰)

Districts	Zones	Decades			
		1 st (1980–1989)	2 nd (1990–1999)	3 rd (2000–2009)	4 th (2010–2019)
Velskiy	southern	46	244	653	942
Verkhnetoemskiy	southern	16	7	159	234
Vilegodskiy	southern	2	6	60	168
Vinogradovskiy	central	3	40	162	285
Kargopolskiy	central	22	59	135	304
Konoshskiy	southern	17	76	304	417
Kotlasskiy	southern	41	327	296	296
Krasnoborskiy	central	45	163	264	338
Lenskiy	central	2	6	64	125
Leshukonskiy	northern	0	0	1	3
Mezenskiy	northern	0	0	0	1
Nyandomskiy	central	16	38	218	414
Onezhskiy	central	3	12	99	242
Pinezhskiy	northern	0	0	6	25
Plesetskiy	central	4	20	139	274
Primorskiy	northern	0	0	3	13
Ust'yanskiy	southern	7	14	263	488
Kholmogorskiy	central	1	10	78	171
Shenkurskiy	central	5	11	174	316
Arkhangelsk	northern	0	11	83	271
Kotlas	southern	41	276	464	539
Novodvinsk	northern	0	0	12	32
Severodvinsk	northern	0	8	58	204
Mirmiy	central	1	8	10	51
Koryazhma	southern	12	125	280	331
Arkhangelsk region		284	1,503	3,982	6,478

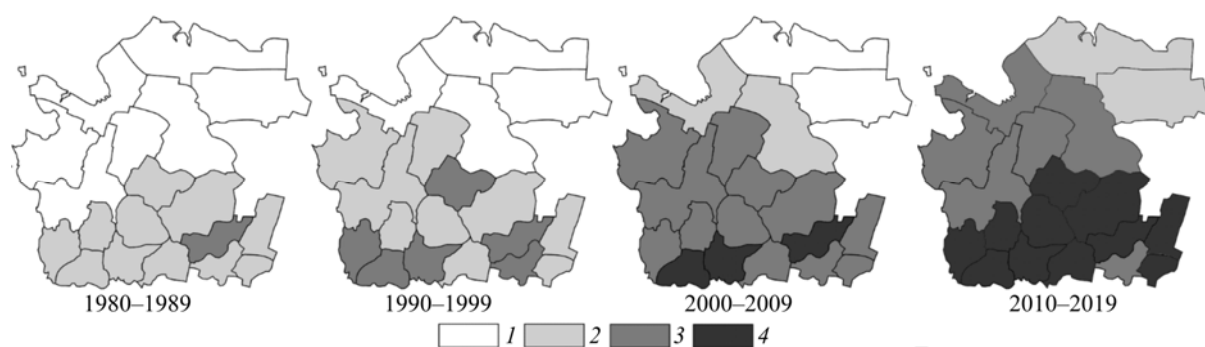


Figure 2. Territorial distribution of people in the AR bitten by ticks in 1980–2019 per 100,000 population: 1) < 10; 2) 10–100; 3) 100–1,000; 4) > 1,000

only in the Leshukonskiy and Mezenskiy districts. A number of bitten people grew more significantly in all other districts in the northern zone. For example, in the Pinezhskiy district there were no registered tick bites prior to 1999; in 2000–2009 a number of bitten people¹⁰ amounted to 6; and it was already

equal to 25 in 2010–2019. Relatively high numbers of bitten people¹⁰ in Arkhangelsk and Severodvinsk, cities located in the northern zone, were probably to a great extent due to intense migration of people who lived in these cities to other districts in the AR and even beyond the region. However, a considerable

growth in a number of bitten people¹⁰ was registered in the Primorskiy district where these two cities were located.

Incidence of tick-borne encephalitis. 1,582 TBE cases were registered in the AR over the analyzed 40-year period. This infection was diagnosed only in 14 people during the whole 1st decade. A significant rise in incidence was detected starting from 1990 and to 2013. Maximum incidence rates were detected in 2009 and 2013 and amounted to 9.9 and 8.7 disease cases per 100,000 population accordingly. Then there was a significant decrease in a number of patients and the rate was 24 or 2.2 per 100,000 population in 2020. On the contrary, a number of people bitten by ticks grew over that period (Figure 3).

Spatial characteristics of TBE incidence rates revealed that average annual long-term incidence was the highest in the southern zone (7.9 per 100,000 population) against the cen-

tral (3.0 per 100,000 population; $p < 0.001$) and northern zone (0.7 per 100,000 population; $p < 0.001$).

Average number of people with TBE grew by almost 50 times in 2000–2009 against 1980–1989 (Table 2).

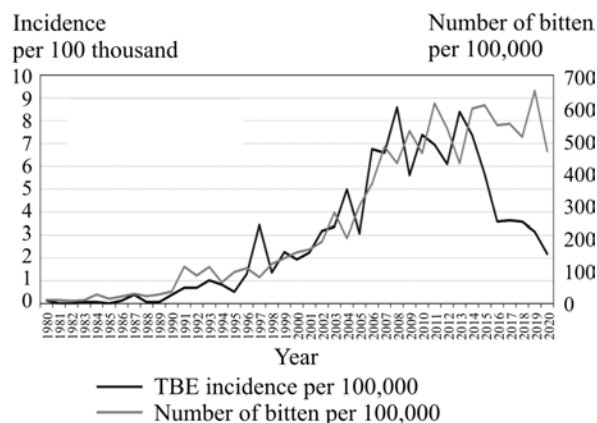


Figure 3. Dynamics of TBE incidence rates and numbers of bitten people in the Arkhangelsk region, (number of bitten people¹⁰)

Table 2

Distribution of patients with TBE as per administrative districts and decades (average number)

Districts	Zones	Decades			
		1 st (1980–1989)	2 nd (1990–1999)	3 rd (2000–2009)	4 th (2010–2019)
Velskiy	southern	0.10	2.40	20.50	13,50
Verkhnetoemskiy	southern	0.00	0.00	1.90	3,40
Vilegodskiy	southern	0.00	0.40	0.00	0,20
Vinogradovskiy	central	0.00	0.00	0.00	1,30
Kargopolskiy	central	0.20	0.10	2.89	2,10
Konoshskiy	southern	0.10	1.10	7.11	5,50
Kotlasskiy	southern	0.30	4.50	4.80	2,00
Krasnoborskiy	central	0.40	1.40	3.10	2,50
Lenskiy	central	0.00	0.00	0.70	0,60
Leshukonskiy	northern	0.00	0.00	0.00	0,00
Mezenskiy	northern	0.00	0.00	0.00	0,00
Nyandomskiy	central	0.00	0.30	1.80	4,10
Onezhskiy	central	0.00	0.30	0.70	0,50
Pinezhskiy	northern	0.00	0.00	0.10	0,10
Plesetskiy	central	0.00	0.00	1.00	0,90
Primorskiy	northern	0.00	0.00	0.20	0,10
Ust'yanskiy	southern	0.00	0.00	2.40	3,30
Kholmogorskiy	central	0.00	0.20	0.30	0,30
Shenkurskiy	central	0.00	0.00	4.80	6,50
Arkhangelsk	northern	0.10	1.00	3.80	6,60
Kotlas	southern	0.00	4.10	7.50	4,40
Novodvinsk	northern	0.00	0.00	0.50	0,30
Severodvinsk	northern	0.20	0.30	1.40	4,30
Mimiy	central	0.00	0.00	0.00	0,10
Koryazhma	southern	0.00	4.60	5.20	3,80
Arkhangelsk region		1.40	20.70	69.70	66.40

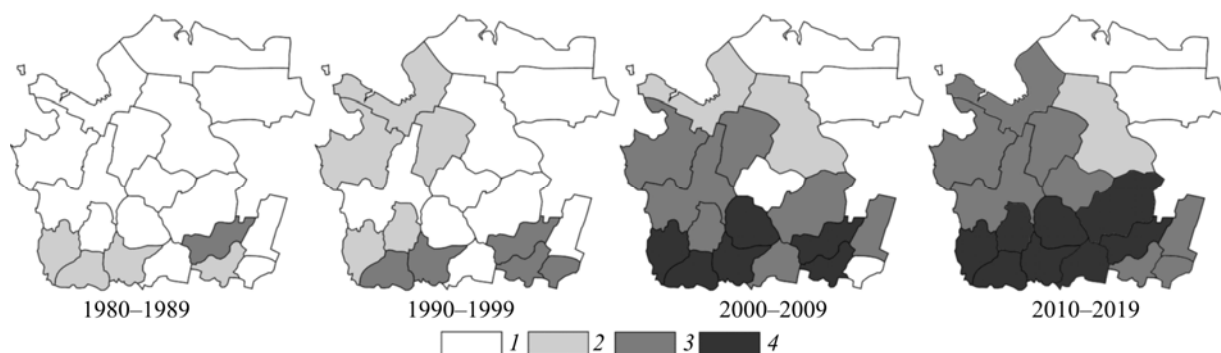


Figure 4. TBE incidence rates in AO, cases/100,000 population: 1) 0.0–0.09; 2) 0.1–0.9; 3) 1.0–4.9; 4) > 5.0

Table 3

Relative risk of TBE incidence as per three zones in the Arkhangelsk region

Decades	Indicator	Zones		
		Northern	Southern	Central
1980–1989	RR	Reference zone	2.1	2.2
	95 % CI		0.1–34.0	0.1–35.9
1990–1999	RR	Reference zone	38.8	4.6
	95 % CI		5.2–292.0	0.42–51.4
2000–2009	RR	Reference zone	18.5	6.1
	95 % CI		7.9–43.1	2.4–15.6
2010–2019	RR	Reference zone	6.9	4.6
	95 % CI		3.5–13.6	2.2–9.7

And if over the 1st decade TBE was registered only in 7 administrative districts in the AR (the Velskiy, Kargopolskiy, Konoshskiy, and Kotlasskiy districts located in the southern zone, the Krasnoborskiy district in the central zone and Arkhangelsk and Severodvinsk in the northern zone), then in the 4th one the infection was registered in the whole region, excluding districts located in the northern zone, the Leshukonskiy and Mezenskiy (Figure 4).

We didn't find any differences in TBE incidence rates between the zones in the AR in the 1st decade. In the 2nd decade relative risk of TBE incidence reached its maximum in the southern zone and amounted to 38.8 against the northern zone; TBE incidence in the central zone didn't have any statistically significant differences from that detected in the northern one (Table 3).

Relative risks were high in the 3rd decade in the districts located in the southern and central zones (18.5 and 6.1 accordingly) in comparison with the northern zone. Relative risks of TBE incidence went down in the 4th decade both in the districts located in the southern zone (RR = 6.9) and in the central one (RR = 4.6) and this indicated that TBE occurred in the districts located in the northern zone.

Discussion. Contemporary prevailing tick species, including *Ixodes persulcatus* Sch. 1930, probably occurred as far back as at the end of Pliocene or the beginning of Holocene [5]. Such long evolution helped ticks adapt to a lot of territories with variable natural and climatic conditions and to parasitize on practically all orders of land mammals as well as on many species of birds and reptiles. They usually feed on mammals or birds that are the most widely spread in a given ecosystem⁵.

Over the last decades there have been considerable changes in biotic components in zones located in the northern European part of Russia; for example, forest zones were detected to move farther to the north. Changes in flora have considerable influence on fauna and the latter reacts quite dynamically to any changes in climatic conditions. Wild mammals migrate onto northern territories. Rodents and insect-eaters are a source of food for tick larvae and nymphs thus infecting them with TBE virus. Large mammals bitten by these blood-sucking arthropods exert substantial impacts

⁵ Balashov Yu.S. Parazitizm kleshchei i nasekomykh na nazemnykh pozvonochnykh [Tick parasitism on land vertebrates]. St. Petersburg, Nauka, 2009, 357 p. (in Russian).

on contamination in population of vectors increasing a number of congested female ticks who carry the virus and efficiency of transovarial transmission of the pathogen. 12 new bird species were registered in taiga zones in the western part of the Russian plain in the last quarter of the 20th century; they hadn't been ever detected on those territories before [6]. Migrating birds bitten by ticks can carry TBE virus onto new territories [7, 8].

A considerable growth in a number of people bitten by ticks was registered over the analyzed period in Arkhangelsk region; this was true not only for the southern zone where there were only sporadic cases of tick bites detected in 80ties last century but also in the northern zone where previously people didn't get bitten by these blood sucking arthropods at all. This substantial growth in a number of bitten people can to a certain extent be due to people applying for medical aid more often since they are now much better aware of dangerous consequences tick bites might have.

But at the same time data on registered cases of tick bites and TBE cases on new territories in the AR where this infection was not ever registered in the past indicate that ticks infected with TBE virus have spread farther onto northern territories. Previously, the northern border of tick habitat was located further to the south in the western part of the AR, approximately at the 62nd parallel; as for the eastern part of the region, it reached the northern latitude at which Shangala and Kizem settlements were located [9]. In our opinion, during a 40-year period of observations over ticks their northward migration amounted to not less than 200 kilometers from southern districts in the AR. In 2019 two more districts, namely

Pinezhskiy and Primorskiy, were added to the list of areas that were endemic as per TBE⁶. Similar processes occur on neighboring territories, for example in the Komi Republic [10] and Karelia [11]. Ticks migrated mostly due to a substantial rise in both average annual temperatures and a sum of "effective" temperatures that created natural conditions favorable for *Ixodes persulcatus* and made for longer periods of their activity [12]. Socioeconomic factors may as well contribute into growing numbers of people bitten by ticks [10].

Tick migration onto new territories and, consequently, TBE occurrence in areas that were previously free from this infection are described in many countries where *I. ricinus* prevails [13–16]. The present work has a significant distinction from many others cited in it since it has been accomplished in the region where *I. persulcatus* prevails completely. This tick species differs greatly from *I. ricinus* as per its biological properties; for example, it is much more resistant to cold, therefore, its habitat can be located farther to the north. Moreover, *I. persulcatus* contamination with TBE virus is usually significantly higher than *I. ricinus* contamination [17]⁷.

Although there has been a certain decrease in TBE incidence in the AR, tick-borne infections are still a vital medical issue in the region. First, a significant share of TBE virus (35 %) in ticks caught in the Komi Republic, a neighboring region to the AR, belongs to the Far East genotype which has high lethality [18]. Secondly, *I. persulcatus* that prevail in the AR are contaminated not only with TBE virus but also with other pathogens with no specific prevention means against them available at the moment⁸. Third, a considerable

⁶ O perechne endemicnykh territorii po kleshchevomu virusnomu entsefalitu v 2019 godu: Pis'mo Rospotrebnadzora ot 31.01.2020 № 02/1305-2020-32 [On the list of territories that are endemic as per tick-borne encephalitis in 2019: The Letter by Rospotrebnadzor dated January 31, 2020 No. 02/1305-2020-32]. The Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing. Available at: <https://www.rospotrebnadzor.ru/upload/iblock/365/o-perechne-endemichnykh-terr.-po-kve-v-2019-g.-31.01.2020.pdf> (June 15, 2021) (in Russian).

⁷ Balashov Yu.S. Iksodovye kleshchi – parazity i perenoschiki infektsii [Ticks as parasites and infection vectors]. St. Petersburg, Nauka, 1998, 287 p. (in Russian).

⁸ Ob itogakh sezona aktivnosti kleshchei v 2021 godu [On the results of the tick activity season in 2021]. The Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing. Available at: http://29.rospotrebnadzor.ru/c/journal/view_article_content?groupId=10156&articleId=902166&version=1.0 (June 13, 2021) (in Russian).

share of local natives who have never been bitten by ticks before can be more susceptible to tick-borne infections than people living in southern districts in the AR [19].

Analysis of changes in a number of bitten people¹⁰ taken in dynamics revealed a slow rise in 1980–1990 followed by an exponential growth in 1990–2010. The same drastic increase was detected in the Komi Republic, the neighboring region. In 2010–2020 the trend stabilized in the Komi Republic and there were only slight changes in a number of bitten people over time. The character of such distribution is probably determined by air temperature, a basic abiotic factor that influences *I. persulcatus* ecology [10].

An apparent decrease in TBE incidence in the AR registered over the last years against growing number of people bitten by ticks is to a large extent due to greater volumes of specific prevention aimed at fighting against the infection.

Thus, a number of vaccinated people in the AR grew by 3.6 times from 6,699 in 2005 to 23,933 in 2015; in 2015 almost 30 % of bitten people were provided with emergency seroprevention with immunoglobulin [4]. Growing natural immunization among population may be another reason for this decrease in TBE incidence. From 1980 to 2020 more than 127 thousand people were bitten by ticks and it amounted to 12 % of the total population in the region. Seroprevalence regarding TBE virus exceeds 20 % among people living in southern districts in the AR [4].

Detected migration of ticks and growing TBE incidence in northern districts in the AR can be typical for other regions with similar natural and climatic conditions. However, we should bear in mind that when we try to detect factors influencing TBE incidence, attention should be paid to decreasing numbers of TBE cases in Russia as a whole. In our opinion, it is quite possible to assume that incidence rates are influenced by biocenotic regularities that

haven't been studied profoundly yet; these regularities determine cyclic changes in intensity of epizootic processes in natural foci.

Conclusion. Therefore, we analyzed a number of bitten people and TBE incidence taken in dynamics over a long period. The analysis revealed that there was ongoing expansion of *I. persulcatus* into northern districts in the AR and this caused TBE incidence on those territories that were previously free from this infection. From 1980 to 2014 a number of people bitten by ticks grew constantly; there was a synchronous growth in TBE incidence. Over the last years TBE incidence declined substantially and a number of bitten people also stabilized. Ticks spread onto northern territories gives grounds for examining them to detect contamination not only with TBE virus but also with other “tick” pathogens; it is also necessary to examine seroprevalence among population living in these districts regarding “tick” infectious agents in order to make preventive activities more efficient.

Our research indicates there is growing risk of TBE contagion in the northern districts in the AR due to ticks migrating northward. Besides, people living on northern territories that haven't been endemic so far haven't encountered tick-borne infections yet; they are not obliged to get vaccinated against TBE and hence they are exposed to elevated risks in case they are bitten by ticks. The accomplished analysis substantiates the necessity to make managerial decisions on organizing epidemiologic and epizootological monitoring on territories that have previously been free from ticks; it is also essential to provide specific and non-specific prevention against TBE and other tick-borne infections for people living there.

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