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NATURAL-FOCAL DISEASES IN THE VLADIMIR REGION (RUSSIA)

ABSTRACT. The paper describes a study that monitored the epidemiological situation of a complex of natural-focal diseases in the Vladimir region (Russia), from 1958 to 2012. The morbidity rates of these natural-focal diseases have been differentiated by territory using ArcView 3.1 (GIS software). The activity of natural foci for each zooanthroponosis varied between administrative districts in the region. A schematic map has been compiled; the map reflects the danger of infection caused by natural-focal diseases in the Vladimir region. The paper discusses the role of the anthropogenic factor in natural-ecosystem development: it likely promotes the transit and localization rates of carriers. Correlation and regression analysis of the data showed that climatic factors such as the average temperatures in July and September in the preceding year influence Lyme disease (Lyme borreliosis) patterns. This is likely related to particular stages in the life cycle of *Ixodidae* ticks. Using multiple linear regression analysis, a mathematical model for the prediction of Lyme borreliosis patterns has been created.

KEY WORDS: Vladimir region, epidemiological situation, natural-focal diseases, predicting.

INTRODUCTION

Today the study of patterns in the natural circulation of the infectious agents of natural-focal diseases is becoming increasingly relevant, especially in the context of climate change and anthropogenic territorial changes. Aside from that, natural-focal disease monitoring is gaining relevance due to active migration to certain regions, which leads to populations without an appropriate immune system response in various zones with natural foci. Similarly, the risk of infection has been rising because of the increased popularity of gardening and outdoor activities [Istomin, 2006].

Ranges of many wild animals and, in many cases, blood-sucking arthropods are localized in specific territories, where natural foci are formed. Natural foci boundaries are controlled by endotherm and arthropod (in transmissible infections) ecology. Within these boundaries, infectious agents are transmitted between animals. People only become infected only when they are within a natural focus [Zuyeva, 2005].

Active human impact on natural ecosystems, along with a decline in conservational, epizoological, and epidemiological activity, promotes the transmission of infectious agents of natural-focal diseases and intensifies their epidemiological manifestation. In terms of registered morbidity rates, natural-focal diseases are relatively insignificant in the structure of human infectious diseases. However, the endurance of natural foci and their often unpredictable spurts of activity increase the morbidity rates for these diseases [Kormilenko, 2010].

Determining factors that influence morbidity rates, analyzing territorial distribution, zoning by degree of epidemiological risk, and defining high-risk groups are the most pertinent objectives in research today [Utenkova, 2009].

A lack of necessary funding and absence of specialized entomologists and zoologists in Rospotrebnadzor's (the Russian Federal Service for Surveillance on Consumer Rights Protection) regional branches and of testing systems to gage the presence of infectious agents of natural-focal diseases in a carrier-present areas represent serious and sometimes impossible-to-overcome obstacles for objective research. Bearing in mind the problems listed above, only morbidity rates can objectively indicate the epidemiological situation and allow prediction.

Many authors note the relationship between zooanthroponoses disease patterns and ecological, socio-economical, and climatic factors [Antov, 2005, Aminev, 2013, Kolominov, 2012, Utenkova, 2004], however the data can be quite contradictory.

The ecological and geographical characteristics of a region influence the tick population size, whereas the infection rate is influenced by climatic factors [Suntsova, 2004].

A number of authors note that climate indices such as precipitation rates, humidity, and average monthly temperature in the months that precede the epidemic season influence natural-focal disease morbidity rates. Based on statistically significant data, attempts have been made to create a prognostic model [Aminev, 2013, Kolominov, 2012].

MATERIALS AND METHODS

The studies were conducted in the Vladimir region. The territory's topographic features are determined by its location within the East European Plain which has low elevations and minor terrain irregularity. The southwestern part of the region is occupied by the Meshchera lowlands – a homogenous and flat wetland area that is sometimes interrupted by sandy ridges. There are many forest lakes with turbid water, large wetlands overgrown with alders and aspens and sandy hillocks with tall pines, and juniper bushes and heather. The Oksko-Tsninskiy embankment, composed of limestone, stretches out longitudinally in the eastern part of the region, south of the city of Kovrov. The northwestern elevated part of the region consists of branches of the Klinsko-Dmitrovsky ridge. These branches take the shape of ridges and flat morainic hills. The absolute elevation reaches 240 meters. This is the most elevated area in the Vladimir region. The surface is heavily dissected by deeply embedded riverbeds, ravines, and gulches. The relative elevations reach 40–60 meters. The Nerlinsko-Klyazminskaya lowlands are located in the northern and northeastern part of the region, along the left bank of the Klyazma River. On its western side, they merge with the Balakhninskaya lowland in the Nizhny Novgorod region. This land is 100 meters above mean sea level and has an abundance of wetlands and lakes.

The Vladimir region is in a temperate and continental climate zone, which is characterized by a warm summer, moderately cold winter with stable snow cover, and well-defined intermediate seasons. The majority of the region is sufficiently humid. Precipitation is unevenly spread throughout the area, with the lowest precipitations rates in the eastern part.

The flora is quite diverse and consists of about 1200 species. Pines and birches dominate sandy soil and sandy loam, fir trees and aspens dominate clay soil and clay loam, and coniferous trees with underbrush dominate bog soil.

The fauna consists of 62 mammal species, 43 fish species, 212 bird species, 10 amphibian species, 6 reptile species, and approximately 1500 invertebrate species. The most epidemiologically significant species are rodents – bank voles (*Myodes glareolus*), tundra voles (*Microtus oeconomus*), striped field mice (*Apodemus agrarius*), house mice (*Mus musculus*), brown rats (*Rattus norvegicus*); and *Ixodidae* ticks – *I. ricinus* and *I. persulgatus*.

The materials from the authors' own field work on collecting epidemiological data in the Vladimir region, as well as statistical data from 1958 to 2012 were used in this study.

The data on natural-focal disease morbidity rates were taken from the Vladimir Oblast Center for Hygiene and Epidemiology, as well as from Rospotrebnadzor's official reports on infectious and parasitic diseases.

The degree of natural-focal disease infection risk in human population was gaged using a point system. Each natural-focal disease morbidity rate was calculated per 100 000 people. The morbidity rates for each separate zooanthroponoses in a particular district were summed and, based on the total, each district was assigned a rank that corresponded to the degree of risk: 1 (low risk), 2 (moderate risk), or 3 (high risk).

In order to evaluate the influence of hydrometeorological factors on the natural-focal disease morbidity rates, data on the following indices were used: average monthly temperature, number of days with precipitation per month, atmospheric pressure, snow cover size, and oxygen levels in the atmosphere from 1977 to 2012.

Initially, factors (predictors) were determined that were statistically significantly correlated with morbidity rates ($p \leqslant 0{,}05$), using Pearson's correlation coefficient. Elucidating factors like these is worthwhile even when cause-and-effect relations cannot be interpreted. As long as the correlation is statistically significant, a lack of knowledge about its role in shaping the dynamic of the process in question should not lead to a removal of these indicators from a prognostic equation [Caughley, 1979, Korotkov, 1999]. The influence of climate indices for the current and preceding years on morbidity rates was also taken into consideration when calculating the correlation coefficient (i.e. by shifting climate indices one year back relative to the morbidity rate).

Afterwards, by using multiple linear and nonlinear regression analysis the most significant predictors were incrementally determined. A prognostic equation was derived using the R^2 value and distribution of residuals. STATISTICA software was used to conduct correlation and regression analysis.

ArcView 3.1, GIS software, and Microsoft Paint were used to compile and edit the maps.

RESULTS AND DISCUSSION

Vladimir region's natural conditions allow for the circulation of the infectious agents of a number of natural-focal diseases, which is confirmed by the statistical data gathered in this study. The analysis demonstrates that territory is endemic to the following natural-focal infections: hemorrhagic fever with renal syndrome (HFRS), Lyme borreliosis (or Lyme disease), leptospirosis and tularemia. However, Lyme borreliosis has by far the highest morbidity rates among all infections.

The focal activity of different zooanthroponoses in the region varies. Therefore, the highest HFRS morbidity rates (per 100 000 people) from 1978 to 2012 were recorded in the Gorokhovetsky, Kameshkovsky, and Yuryev-Polsky districts; the highest leptospirosis morbidity rates in the same time period were recorded in the Gorokhovetsky and Petushinsky districts; the highest Lyme borreliosis morbidity rates from 2005 to 2012 were recorded in the Kolchuginsky, Petushinsky, and Kovrovsky districts; the highest tularemia morbidity rates from 1958 to 2012 were recorded in the Gus-Khrustalny district.

Experience shows that information on the degree of infection risk not just for a single infection, but for the entire complex of natural-focal diseases, is necessary for planning and human activity in any area.

In order to evaluate the territory in question, we suggest a method that involves equalizing all cases of zooanthoponosis infections with regard to their danger to public health. In

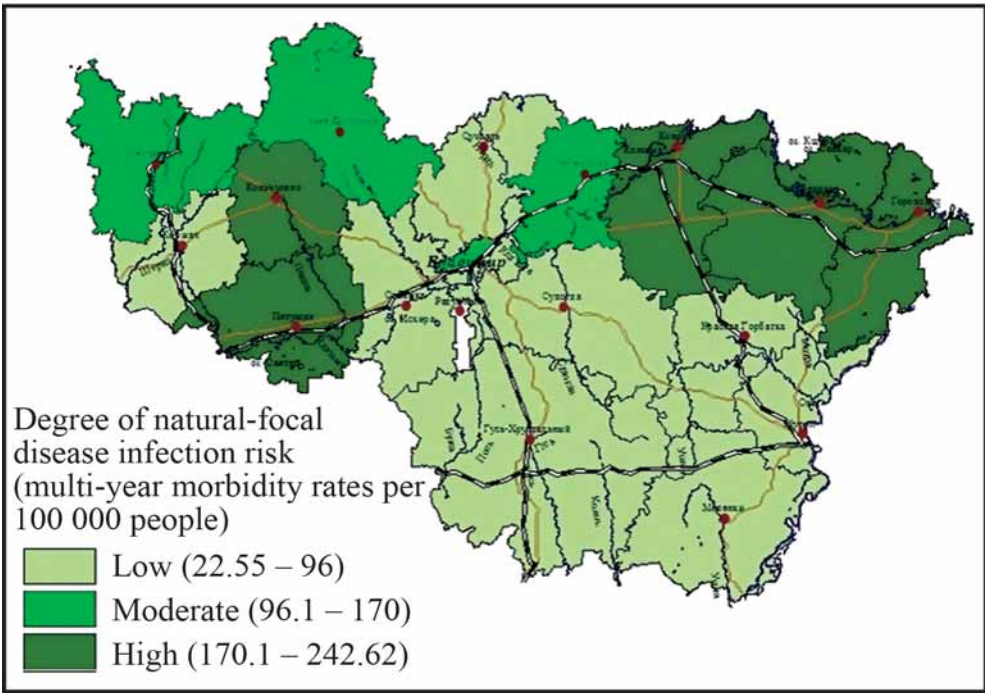

Fig. 1. Natural-focal disease infection risk in the Vladimir region.

other words, in this model, becoming infected with a carrier of tularemia poses the same health risk as becoming infected with a carrier of Lyme borreliosis.

The final map reflecting the natural-focal disease infection risk for the population of the Vladimir region was compiled based on ranking of the multi-year zooanthroponosis morbidity rates. Our analysis demonstrates that the natural-focal disease infection risk varies in different districts in the region (Fig. 1).

Furthermore, an attempt was made to locate factors that influenced the Lyme borreliosis epidemiological process, as cases of this disease were registered most frequently in this territory.

In the Vladimir region, Lyme borreliosis morbidity rates have been monitored since 2005. 1211 cases have been registered from 2005 to 2012, and the morbidity rates have increased by 46 %. The highest morbidity rates have been recorded in the Kovrovsky, Kolchuginsky, and Petushinsky districts. The disease is unevenly distributed throughout the territory: for example, there has only been one case of infection in the Melenkovsky district during the entire monitoring period. However, the epidemiological situation in the north of the region is most serious, even though the southern districts are more heavily populated (Fig. 2).

First, the potential influence of land development on Lyme borreliosis was analyzed by conducting a spatial correlation analysis and comparing the Lyme borreliosis morbidity rates; then, the influence of forest and wetland cover were analyzed. This analysis established that there is no statistically significant correlation between the above indices ($r = -0.19$ $p = 0.47$; $r = -0.26$ $p = 0.33$ respectively) in the Vladimir region.

In our view, this fact deserves attention. A few decades ago, tick-borne infections generally

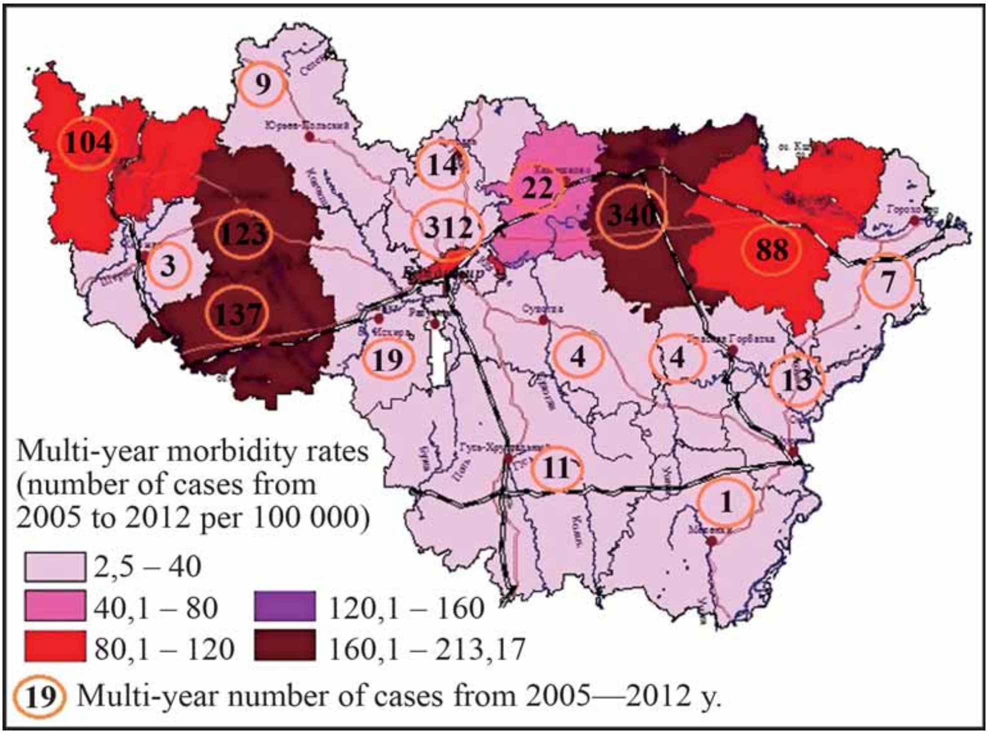

Fig. 2. Lyme borreliosis morbidity rates in the Vladimir region.

affected people living in the taiga or in forested landscapes; they were not very common among the urban population in central oblasts of the Nonchernozem belt. Evidently, that explains why there was no urgent need to organize medical monitoring in such areas. Today the situation has changed dramatically: morbidity rates have been increasing independently of differences in landscape characteristics. This can be explained by the fact that commercial land and land intended for development used to be quite isolated from one another. However, in the last 20–30 years Russia's population has significantly changed its way of life and thus its ecological niche. Human mobility has increased and far more suburban homes, vacation homes, summer cottages, rural recreational zones, and roads have been built. The structure of rural settlements has also changed because of the arrival of urban populations. Forests, especially on their outskirts, are often settled, as well as meadows and former arable land. Abandoned croplands are intensely overgrowing, creating new convenient ecological niches for the circulation of Ixodidae ticks and their hosts. Therefore, the boundaries of more or less isolated (naturally structured) ecosystems are disintegrating, leading to negative transformations. Evidently, it can be asserted that it is not climate change that is to blame for the spread of Lyme disease (by the way, this explanation has recently gained popularity, because it absolves humans of personal responsibility!); rather, anthropogenic activity which disrupts the ecological balance is the real culprit.

Our study also analyzed the potential influence of the following climate indices on Lyme borreliosis: average monthly temperature, the number of days per month with precipitation, humidity, atmospheric pressure, snow cover size, and monthly oxygen levels in the atmosphere from 2004 to 2012 (a total of about 100 different indices).

Correlation analysis of the array of indices revealed a statistically significant correlation between the Lyme disease morbidity rates and the following indices: the average temperature in July of the previous year ($r = 0.77$ $p < 0.05$), the average temperature in September of the previous year ($r = –0.91$ $p < 0.05$), the humidity in January of the previous year ($r = 0,71$ $p < 0.05$), snow depth in March ($r = 0.94$ $p<0.05$), and oxygen levels in the atmosphere in July of the previous year ($r = –0.94$ $p < 0.05$).

Because Lyme borreliosis' epidemiological process begins in late April, only the values that precede the beginning of the epidemiological process can be included in the model. Multicollinearity was ruled out in modeling by removing predictors with pair correlations from the prognostic equation.

Ultimately, the following predictors were used in the prognostic model: the average temperature in July of the preceding year, the average temperature in September of the preceding year, and the humidity in January of the preceding year (these indices do not have pair correlations with each other).

As a result of this incremental multiple nonlinear regression analysis, achieved via STATISTICA software, the most significant epidemiological predictors were determined and a prognostic equation was derived. Its validity was defined by the R^2 value and the distribution of residuals.

The software demonstrated that the most significant values influencing the epidemiological process are the average temperature in July of the previous year and the average temperature in September of the previous year. The software ruled out the humidity in January of the previous year because it did not have a significant effect on the epidemiological process, despite its high correlation with morbidity rates.

The final multiple nonlinear regression equation is shown below:

$$y = –577.938 – 0.84(x1^2) + 58.538(x2) – 0.037(x2^3);\ R^2 = 0.99\ p < 0.001$$

y – Lyme borreliosis morbidity rate in the population; x1 – average temperature in September of the previous year; x2 – average temperature in July of the previous year.

According to the equation, the epidemiological process of Lyme borreliosis depends on the average temperature in July of the previous year and the average temperature in September of the previous year; the dependence on July's temperatures is stronger.

The R^2 value allows us to infer that this model describes the epidemiological process with a probability of 99 %.

The data in Table 1 allows us to compare the observed morbidity rate values and the predicted values, as well as the residuals.

Table 1. Predicted Values and Residuals of Multiple Nonlinear Regression

Year	Observed Morbidity Rates	Predicted Morbidity Rates	Residuals
2005	150	157.4	–7.4
2006	127	129.0	–2
2007	96	91.9	4.1
2008	179	176.8	2.2
2009	194	194.4	–0.4
2010	94	93.5	0.5
2011	198	200.9	–2.9
2012	219	212.9	6.1

To ensure the accuracy of the derived equation, the distribution of recursive residuals was analyzed: the plot in Fig. 3 demonstrates that all the values lie close to the line and are normally distributed.

Therefore, the conclusion we have reached is statistically accurate [Trukhacheva, 2013].

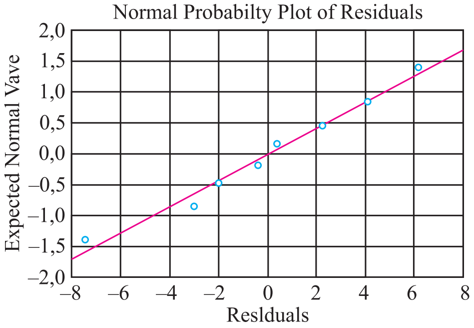

Fig. 3. Normal Probability Plot of Residuals in Multiple Nonlinear Regression.

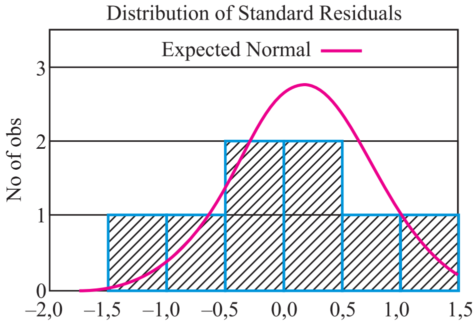

Fig. 4. Distribution of Standard Residuals.

The histogram of standard residuals that shows the distribution of residuals close to the normal (Fig. 4) also supports the validity of the model.

The derived model indicates that the epidemiological process of Lyme borreliosis depends on the average temperature in July of the previous year and the average temperature in September of the previous year. This can most likely be explained by the life cycle of *Ixodidae* ticks. The positive correlation between Lyme borreliosis and the average temperature in July can be explained by the abundance of hosts in this period, which contributes to the ticks' development and thus the spread of the infectious agent of Lyme borreliosis. The negative correlation between Lyme borreliosis and the average temperature in September can be interpreted in the following way: high temperatures in September cause recently molted females to search for hosts; which then (after the first frost) leads to their death and the death of their eggs (if the females found a host and had a sufficient food supply). Lower temperatures in September cause recently molted female ticks to enter diapause and successfully endure low temperatures in the winter.

Conclusions

1. The Vladimir region is endemic to the following natural-focal infections: HFRS, Lyme borreliosis, leptospirosis, and tularemia. The natural foci of these infections are confined to different territories. The compiled map reflects the risk of infection caused by various natural-focal diseases in the Vladimir region.

2. The Lyme borreliosis morbidity rate in the Vladimir region is not related to the extent of forest or wetland cover in any of the territories. These parameters were traditionally thought to define the spread of *Ixodidae* ticks. We have demonstrated that anthropogenic factors lead to the destruction of natural ecosystems and the delocalization of infectious agents and thus the disease itself.

3. The identified climate indices (the average temperature in July of the previous year and the average temperature in September of the previous years) are likely to have to affect the ticks' life cycle, which in turn impacts the epidemiological situation in the region.

4. The derived mathematical model can be used to predict the epidemiological situation and to take the appropriate steps to fight Lyme borreliosis. The model demonstrates that higher Lyme borreliosis morbidity rates are associated with a year preceded by hot July and cold September. ■

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