The purpose of the work is to develop universal recommendations for clinicians for the management of patients with tick-borne borreliosis.

Tasks of the study was to compare the distinctive features of epidemiological anamnesis, clinical manifestations, indicators of laboratory and instrumental diagnostics and criteria of dispensary registration of patients with tick-borne borreliosis of erythema and non-erythema form.

We have analyzed about 34 patients from the maps of municipal institutions in Ulyanovsk. Forms of borreliosis were divided evenly into erythemic and non-erythemic forms in 17 patients (50%)

In the first 7 days 9 (26%) patients addressed, on 8–14 days — 5 (15%), on 15–30 days — 4 (12%) and 16 (47%) arrived at a later date. The complaint in 100% was the presence of itching and in 50% of erythema, which was accompanied by subjective sensations (burning sensation or compaction — 17 (50%), increase — 9 (26%) patients. In 3 (8%) patients complications with the defeat of the musculoskeletal system (rheumatoid arthritis) were revealed. Serological diagnosis (ELISA) was performed in 17 (50%) patients. Antibodies were found in 14 (41%), IgM levels ranged from 0.470 to 0.633. Terms of appearance were different (15–43 days). In 3 (9%) people the level was below normal. The remaining half of the patients were not examined for various reasons. Clinical and electrocardiographic manifestations of dysfunction of the circulatory system were noted in non-erythematous form (50%).

Serological diagnosis of tick-borne borreliosis by ELISA, due to the late appearance of antibodies in the early stages of little informative, which necessitates the introduction of modern rapid methods. Patients with non-erythematous form of tick-borne borreliosis require more attention and detailed laboratory and instrumental diagnosis, as there is a risk of complications from vital organs and systems.

4.4

doi: 10.15789/2220-7619-2018-4-4.4

DETECTION OF GENETIC MARKERS OF TICK-BORNE RICKETTSIOSIS WITH THE PCR

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There are seven species of pathogenic rickettsia belong to the spotted fever group were reported to be circulating in Russian: *R. conorii, R. sibirica, R. heilongjiangensis, R. slovaca, R. aeschlimannii, R. helvetica* and *R. raoultii*. But only first three of them were reported to cause the confirmed diseases in our country. The regions that are endemic for *R. sibirica* and *R. heilongjiangensis* are: coast of Primorsky Krai, the Amur River, coast of lake Baikal, the Reserve Krasnoyarsk Stolby, Altai, Khakassia. Crimean peninsula was reported to be endemic by *R. conorii*. All of these regions are the popular places for tourism. Real-time PCR test system "RealBest DNA Rickettsia species" (AO "Vector-Best", Novosibirsk) was developed to detect the DNA markers of the pathogenic rickettsia in clinical specimens. It also can be used for detection of rickettsia in ticks without defining the species. Using the developed test system, more than 7000 tick from 10 regions of Russia were tested. The percentage of rickettsia-infected ticks varied from 7 to 92% in dependence of region and tick's species. After the sequencing of DNA of positive samples in regions of genes *gltA, ompA, ompB* and *sca4* it was determined that there are 11 rickettsia species are circulating with 7 of them that are pathogenic: *R. sibirica, R. heilongjiangensis, R. conorii, R. slovaca, R. aeschlimannii, R. massilae* and *R. mongolotimonae*.

Also using the developed test system the DNA-markers of *R. sibirica* and *R. heilongjiangensis* were determined in the clinical samples (blood samples, urine, swabs of skin eschar, eschar biopsy) derived from patients that were hospitalized in the Far East, Western and Eastern Siberia with the diagnosis "tick-borne rickettsiosis". With the goal of the ability of determination of these two pathogens, the PCR test system "RealBest DNA Rickettsia sibirica/Rickettsia heilongjiangensis" was developed additionally. Using this test system it was found, that the frequency of presence of *R. heilongjiangensis* in tick varies from 0.7 for *I. persulcatus* to 29% for *H. oncinna*. The occurrence of the *R. sibirica* varies from 0.6 for *D. silvarum* up to 17% в *D. nuttalli*. It was proven that both of the developed PCR test systems can be successfully used for determination of circulating pathogenic rickettsia in natural foci, detection of their DNA markers in ticks for the diagnosis of the tick bitten people, as well as for analysis of clinical samples in the laboratory diagnostics tick-borne rickettsiosis.

4.5

doi: 10.15789/2220-7619-2018-4-4.5

DATABASE OF LEPTOSPIRA PROTEIN SPECTRA FOR MASS-SPECTROMETRY IDENTIFICATION

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Leptospirosis is found all over the world both in humans and in many species of agricultural, domestic and wild animals. The disease caused by individual serovars of the pathogen is characterized by a severe clinic and high mortality. *Leptospira* grow very slowly and only on special nutrient media. Together with the difficult pathogen isolation there is also the problem of its identification. According to the modern genosystematics several molecular biology methods were proposed to determine the *Leptospira* species. Mass-spectrometry direct profiling of proteins is easy to set up and widely used to diagnose most bacterial infections, while the available databases of *Leptospira* spectra are absent.

The aim of this study was the development of a protein spectra database for identification of the *Leptospira* species.

Our database contains information about 28 *Leptospira* reference strains of 28 serovars including eight most common species *L. interrogans*, *L. borgpetersenii*, *L. kirschneri*, *L. santarosai*, *L. noguchii*, *L. inadai*, *L. weilii*, *L. biflexa*, as well as the protein spectra of these strains in the format for the software "MALDI Biotyper 3.0". According to the serological classification the presented strains belong to 21 serogroups: *Icterohaemorrhagiae, Grippotyphosa, Canicola, Pomona, Tarassovi, Australis, Sejroe, Autumnalis, Bataviae, Ballum, Pyrogenes, Javanica, Hebdomadis, Louisiana, Panama, Lyme, Sarmin, Djasiman, Mini, Manhao, Sema-*

ranga. The database can be updated and edited. The protein spectra files can be entered into "MALDI Biotyper 3.0" and newer versions database by creating reference spectra and importing them into the Taxonomic Tree.

Protein spectra were obtained at 10–20-fold study of the samples extracted with acetonitrile/formic acid on a mass spectrometer "Microflex LT" (Bruker Daltonics, Germany) using a "Flex Control 3.3" program. The database was tested with eight strains isolated in Siberia and at the Far East in 2012–2016, and 18 *Leptospira* cultures from the collection of Gamaleya State Research Centre for Epidemiology and Microbiology. The results of identification of pathogenic *Leptospira* completely coincided with the data of multilocus sequencing. The created database is intended for specialists of microbiological and scientific laboratories engaged in diagnostics and study of leptospirosis.

4.6

doi: 10.15789/2220-7619-2018-4-4.6

INFORMATION TECHNOLOGY APPLICATION FOR NATURAL FOCI INFECTIONS MONITORING AND PREDICTION

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Amur Region's climate-geographical features, flora and fauna specifics led to the emergence of persistent natural foci of several infections, including tick-borne encephalitis, hemorrhagic fever, tularemia, and listeriosis. Amur Region registers from 100 to 200 cases of natural foci infections every year. The largest share of these infections is tick-borne.

The Amur Region Rospotrebnadzor Service introduced in 2017 the Epidemiological Surveillance System (EpiS), creating one information space for the entire epidemiological service network in the region and ensuring connectivity with the primary healthcare organizations. EpiS enabled rapid collection and exchange of information, supports epidemiological investigations with accurate geo-location based on GLONASS/GPS coordinates and delivers outbreak early warning capabilities. The natural foci locations and Anthrax cases historical data for the past 180 years was converted into an electronic register of the territories and sites and embedded into the EpiS. It is planned to expand this registry for other natural foci infections.

Operational information on morbidity in conjunction with the historical information and other epidemiologically significant factors is displayed in the Emergency Operations Center (EOC) in near real-time on detailed regional maps. The EOC strengthens and supports current situation monitoring as well as in-depth epidemiological investigation and analysis of the situation.

In 2018 the Amur Region Rospotrebnadzor Service also introduced modern methods for predicting morbidity based on the deep neural networks technology. This forecasting method demonstrated its effectiveness for a number of infections, in particular, Influenza-like illness (ILI) and Acute Intestinal infections, due to the integrated consideration of historical data, socio-hygienic characteristics and environmental factors. The prognostic models are built on the entire available data archive and allow identifying stable patterns leading to a change in the morbidity dynamics. The prediction accuracy reached 85–90% for the ILI. The use of such forecasting methods allows strengthening preventive measures to combat infectious morbidity.

4.7

doi: 10.15789/2220-7619-2018-4-4.7

ANALYSIS AND FORECASTING INCIDENCE OF BRUCELLOSIS IN THE REPUBLIC OF DAGESTAN

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From 300 to 500 cases of brucellosis among people are registered in Russian Federation annually. Sixty three percent of these cases occur in the North Caucasus Federal District (NCFD). Assessing the structure of the brucellosis incidences among the population of NCFD during 2005–2017 we found that 2122 reported cases (67%) occurred in the Republic of Dagestan.

The current situation calls for the need to improve methods of epidemiological diagnosis. To assess the epidemiological situation of brucellosis and to forecast the epidemic situation in the Republic of Dagestan for 2018 we analyzed the official statistics of brucellosis cases among people. The forecast for the number of cases was executed using two methods — the classical method of linear approximation and by the method developed by us, using the Wald's graph plot. The proposed method allows to determine the monthly minimum and maximum number of cases of brucellosis in the forthcoming period, therefore predicting the total minimum and maximum levels of morbidity.

According to the result of the statistical analysis, the threshold level of incidence of brucellosis disease (Mediterranean fever) in the Republic of Dagestan between 2005–2017 amounted to 14 cases. The average values of incidence of disease during long-term observations fluctuated between 12 and 20 cases during different seasons of the year, with the most cases occurring in June.

As a result of the conducted analysis, it was established that in the Republic of Dagestan in 2018, the monthly increase in the incidence level amounted to 1.6 new cases of brucellosis, the aggregate minimum prognosis of the incidence level is 10 new cases, while the maximum prognosis is 28 new cases. 123 cases are forecast in the Republic of Dagestan in 2018.

Therefore, according to the latest findings utilizing Wald's graph plot, it has been established that the brucellosis epidemiological situation in the Republic of Dagestan in 2018 is unstable. The exceedance of the threshold level points to the possible decline of the epidemiological situation. The suggested method of brucellosis epidemiological case forecast contributes to the optimization of the epidemiological process management, allows for the timely evaluation of the activity of the epidemic outbreak areas and prompt and swift decision making for the purposes of their localization and liquidation.

4.8

doi: 10.15789/2220-7619-2018-4-4.8

THE DYNAMICS OF TICK VECTORS INFECTION RATE WITH IXODIC TICK BORRELIOSIS CAUSATIVE AGENTS IN KHABAROVSK REGION DURING THE EPIDEMIC SEASON OF 2017–2018

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Ixodic tick borreliosis are among the most prevalent illnesses in the group of tick-borne diseases in Russia.

The objective of the research was to perform a comparative evaluation of infestation rate of engorged Ixodic