We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



14

Natural Focal Transmissible Infections with Neurological Manifestations in Ukraine

H. Biletska, I. Lozynskiy, O. Drul, O. Semenyshyn,
I. Ben, A. Shulgan and V. Fedoruk
Lviv Research Institute of Epidemiology and Hygiene
Ukraine

1. Introduction

Ukraine is a country in the East of Europe. It lies between latitudes 44° and 53° N, and longitudes 22° and 41° E. It has an area of 603,628 km², making it the largest contiguous country on the European continent. Ukraine borders the Russian Federation to the east and northeast, Belarus to the northwest, Poland, Slovakia and Hungary to the west, Romania and Moldova to the southwest, and the Black Sea and Sea of Azov to the south and southeast, respectively. Ukraine is subdivided into twenty-five oblasts (provinces) and one autonomous republic (AR), Crimea. Additionally, the cities of Kiev, the capital, and Sevastopol, both have a special legal status.

Forming of natural foci of transmissible zoonoses in Ukraine is related with the presence of three physical-geographical areas: mixed forests (Ukrainian Polissya), Forest-Steppe, Steppe and two, placed extrazonal physical-geographical areas (Carpathian and Crimean Mountains).

Largely forested area in the western region is 20% of Polesie - 25,7%, in Ukrainian Carpathians - over 60%. Prevails landscape of broadleaf forests, which grows about 120 trees and shrub species, including pine, oak, fir, beech, ash, hornbeam, linden, maple. Variety of natural-vegetable associations, favourable abiotic terms (temperature and humidity) are pre-conditions of existence of numerous representatives of vertebral and bloodsucking arthopods – potential reservoirs and vectors of various infections pathogenes. On territory of Ukraine existence of natural foci of transmissible infections of different etiology is well-proven long-term researches: viral (TBE, CCHF, WNF, HFPS, Kemerovo, Ukuniemi, Caliphornia serologic group and other), bacterial (tularemia, Lyme-borreliosis), ricketsial (Q-fever, HGA, Ixodo-Rickettsiosis Marseliensis). On the breadth of geographical distribution, weights of clinical manifestatons and remote consequences most actuality for the health protection of country is presented by a tick-borne encephalitis (TBE) and Lyme-borreliosis (LB).

2. Tick-borne encephalite in Ukraine

Tick-borne encephalitis (synonyms - taiga encephalitis, Russian spring–summer encephalitis, central european encephalite - further in the text referred to as TBE) - natural foci disease of viral etiology with primary lesions of central nervous system. Virus affects

the tunics, white and grey substances of a brain and spinal cord, spinal and cranial roots, peripheral nerves.

TBE was first described in 1927 by Austrian scientist H. Schneider under the name of epidemiologic seasonal meningitis of unknown etiology' in suburbs of Vienna, a capital of Austria. In former Soviet Union, in Far East, TBE was first described in 1932. In 1937 L. Zilber with his team of scientists isolated the causative agent of this disease – virus and discovered the transmitting vector – ticks.

From modern times position TBE virus is a polytypical type of high prevalence, which is characterized by a significant geographical and intrapopulative variability due to the range of antigens and biological features. Its area constantly widens over the southern part of forest zone of extra-tropical Eurasia from the Atlantic to the Pacific Ocean [Votjakov V.,1978].

Studies of TBE molecular epidemiology conclude that there are 3 main genotypes of TBE virus in nature, which concur with antigens subtypes. It was shown proven that far-east genotype of TBE virus (genotype 1) prevails in the regions of Russian Far East and in Japan. In Eastern and Western Siberia, in Ural and European part of area on the territory of Russia absolutely prevails Ural-Siberian type (genotype 3). Westward, on the territory of Eastern European countries including Ukraine, in Central, Western and Northern Europe there prevail strains of western genotype (genotype 2).

Thus each genotype has its own areal. However some strains of a far-east genotype can be found with different detection rates in other regions as well, and, for example, make about 10 % of natural virus population in Eastern Siberia.

Within TBE areal there are significant distinctions among complication of the course of the disease, predominance of certain clinical forms, lethality. Thus, there is no form of total infection in terms of far-east TBE, while in terms of western TBE (Belarus) it makes 20,4%, meningeal – 32,2% and 50%, meningoencephalitic – 30,2% and 0%, polioencephalomyelitic – 21,5% and 0%, myeloradiculoneuritic – 10,9% and 2,7%[Votjakov V.,1978, Randolf SE.,2002]. Lethality in terms of western TBE is of a fraction of a percent, while in terms of far-east TBE the percent of lethality is very high: meningoencephalitic form – 13,3%, polioencephalomyelitic form – 62,5%. Apparently western TBE differs from far-east TBE by considerably milder course and favourable outcome. Feverous period is longer (11 days) than in terms of eastern nozogeographic form (8-9 days) and is often characterized by two-wave course. Constant symptoms of western nozogeographic form are radicular pains and distal type of paresis, lesions of nuclei of a brain stem and cervical part of spinal cord are uncommon. The course of an acute period is slighter: without comatosic condition with respiratory disorders and generalized convulsions. About 10 000 clinical cases of TBE are registered yearly. There is noted the increase in TBE morbidity in recent decade. In western European countries, where it has never been found any eastern subtype of TBE virus neither in patients' blood nor in ticks, the TBE mortality rates range from 0% to 3,9%, and paresis – from 3,0% to 23,5% [Kunz Ch.,1992, Gratz N.,2005].

2.1 Stages of TBE studing in Ukraine

TBE is one of the most common arbovirus infections in Ukraine. Human gets infected with TBE from ticks or by consuming raw, mostly goat's milk. In 1950‑1960s a significant part of all TBE cases in European part of a former Soviet Union territory was caused by alimentary infection.

First in Ukraine TBE virus was isolated in 1960 from blood of the patient and ticks *I.ricinus* in Zkarpattia and Volyn oblasts.

Virological surveillance, that has been conducted by scientists of the laboratory of Transmissible Virus Infections (TVI) of Lviv Scientific Research Institute of Epidemiology and Hygiene of Ministry of Health of Ukraine, enabled detection of 38 strains of TBE virus. Most of them (26 strains) were isolated from *I.ricinus* ticks, whose rates of TBE infection in active natural foci are 19,5%, from mouse-like rodents (*Apodemus agrarius, Ap. sylaticus*) – 2 strains, from birds (*Fulica atra*) – 1 strain and from TBE patients – 9 strains (table 1).

Material name	Number of objects studied		Number of isolated arboviruses strains:							
	exam-ples	pools	Total in strains:		TBE	WN	TAH	TRI	BAT	UUK
			no	%						
Clot of blood and cerebro-spinal fluid	198	237	14	11,1	5	7	2	0	0	0
Ticks (Ixodidae)	143000	3119	51	40,5	26	0	0	3	3	19
Mosquitoes (Culicidae)	218000	2906	37	29,4	0	13	4	0	18	2
Small mammals	8700	1745	6	4,7	6	0	0	0	0	0
Wild birds	1750	435	18	14,3	1	3	0	1	5	8
T o t a l s	371648	8441	126	100	38	23	6	4	26	29

Table 1. Results of virological examination of biological objects and identification of isolated arboviruses in Ukraine during 1970-2007 years

Due to their antigen characteristics, strains of TBE virus isolated in Ukraine belong to ricinus serotype (genotype 2) and have almost same biological characteristics as causative agent of Central-European encephalitis of countries of Eastern and Western Europe [Vynograd I., 1996].

We found that the formation of arbovirus natural foci is closely connected to three physically–geographical zones in Ukraine – mixed forest zone (Ukrainian Polissya -1), forest – steppe zone (2), steppe zone (3) and two extra-zonal natural areas – Carpathian (4a) and Crimean mountains (5) (fig.1).



- territory with domination of *I. ricinus*
- territory of massive breed of *I. ricinus*
- territory without massive breed of *I.ricinus*
- separate foci of breed of *I.ricinus*

1 - mixed forest zone
2 - forest–steppe zone
3 - steppe zone
4 – Carpathian mountains
5 - Crimean mountains

Fig. 1. Prevalence of *I.ricinus* L. on the territory of Ukraine
(data from the Institute of Zoology, Academy of Science of Ukraine)

Thus on the territory of Ukrainian Polissya, in Carpathian and Crimean mountains there are favourable conditions for the formation of natural foci of mainly those types of arbovirus, which are transmitted by ticks – TBE, Tribech, Ukuniemi. In forest-steppe zone - both arbovirus transmitted by ticks and those by mosquito. In a steppe zone intensively circulate arboviruses associated with blood-sicking mosquitoes: West Nile, Sindbis, Californian serological group (Tahinja, Inko), Batai and others (fig.2).

2.2 TBE Epidemiology in Ukraine

Natural TBE foci in Ukraine are mainly associated with Polissya territories (Volyn, Rivne, Zhytomyr, Kyiv and Chernigiv oblasts), Pre-Carpathian and Trans–Carpathian regions [Vynograd I., 1996]. This predisposes different circulation intensity rates of TBE virus on different territories. Thus, immune layer of farm animals against TBE virus gets considerably thinner from west to east. We found 8,2% of seropositive farm animals in Zakarpattia (Trans-Carpathian), 9,4% - in Western forest-steppe zone territories, 6,3% - in pre-Dnister region (Kyiv, Vinnytsia and Cherkasy oblasts), and 3,5% in left-bank region (Poltava, Kirovograd and Dnipropetrovsk oblasts). The same tendencies are observed also in human population.

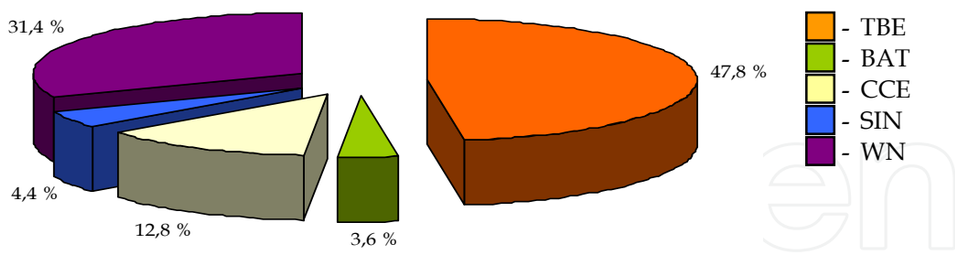


Fig. 2. Nosologic structure of arboviral infections in Ukraine

The percent of immune layer against TBE among healthy people (donors) in Zakarpattia was 6,8 %, in western oblasts 5,2 %, in right-bank- 3,8 % and in Eastern (from Dnipro) oblasts 1,6 – 2,4 %. In TBE natural focuses in the Volynska oblast and to Crimea percent seroprevalense among clinically healthy donors to virus TBE has been- 30,3 – 75,2 %.

2.2.1 Vectors and hosts

Intensive circulation of TBE virus was also detected among mouse-like rodents population. 15,8% of all observed samples of them have antibodies to TBE virus.

Implementation of ELISA method for detection of antigen and antibodies to TBE virus significantly contributed to our knowledge concerning the peculiarities of circulation of the mentioned virus in Ukraine. We detected the main reservoirs and carriers of the virus in nature. These are *I. ricinus* ticks (68,1% of all infected ticks) and *D. reticulatus* (30,6%). Apart from the main carriers, such species as *D. marginatus, H. plumbeum, H. marginatum, Rh. rossicus* also participate in virus circulation.

Among mouse-like rodents the main role is of Cl. glareolis (26,8%), A. agrarius (22,5%), M. arvalis A. sylvaticus and A. flavicollis, M. oeconomus, M. socialis, M. musculus, Sorex araneus.

For 2010 enzootic as to TBE territories, distinguished according to one or combination of such characteristics as natural infection (presence of antigen) of ixodic ticks and small mammals (potential carriers and reservoirs of pathogen) with causative agent, diagnosed cases of the disease with local infection, high degrees of population immunity, were registered in almost all administrative oblasts of Ukraine except some of eastern oblasts (Sumska, Luganska).

2.2.2 TBE morbidity

During the period of 2003-2010 we observed 223 cases of sero conversion in diagnostic titers of people from 14 oblasts of Ukraine: Polissya – Volyn oblast (77 cases), Rivne oblast (8), Zhytomyr (1), Sumy (23); forest-steppe zone – Lviv oblast (19), Khmelnytsk oblast (2), Vinnytsia oblast (1); steppe zone – Dnipropetrovsk (6), Donetsk (9), Zaporizhia (26), Mykolaiv (1), Kherson (13) oblasts; in Zakarpattia (36). We also observed highly intensive circulation of TBE virus in the Crimea.

For present moment local cases of TBE among people are registered yearly in 16 out of 25 oblasts of Ukraine, in cities Kyiv and Sevastopol. However the official data don't reflect the real state of things with the morbidity in Ukraine. The present condition can be explained basically due to the prices of import diagnostic systems which are not affordable for most of medical institutions and lack of Ukrainian diagnostic systems production. Due to this fact, the official data on TBE morbidity in Ukraine show the lowest rates compared to other countries of Eastern Europe and don't show a tendency to increase. During the period of 1955 to 2007 there were only 562 TBE cases registered, while 122 of them were registered in the period of 2000 – 2010 (fig. 3). And correspondingly, the indices of morbidity in Ukraine during the decade varied in the range 0,005 – 0.1/100 000 population, including per oblast from 0 – 1,5 and make only 0,02 (2010).

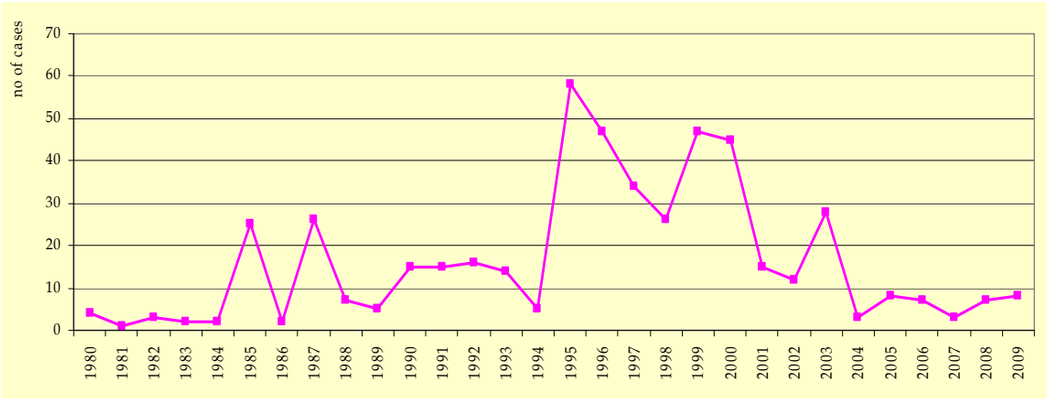


Fig. 3. Cases of TBE in Ukraine (1980-2009)

According to their clinical manifestations we distinguish three main basic forms of acute tick-borne encephalitis: feverous, meningeal and focal. Feverous form is characterized by the milder course and favorable prognosis. Its leading feature is a fever without any signs of meningitis and organs pathology. Meningeal form is characterized by presence of meningeal syndrome, which is accompanied by changes in liquor. The main manifestations of focal forms are symptoms of focal lesions of nervous system, which complicates the course of the disease. Due to its clinical manifestations the focal form of TBE is often separated according to the degree of lesions of different parts of nervous system: meningoencephalitic form, polio-encephalo-myelitic form, myeloradiculoneuritic form etc (table 2).

2.3 TBE in Ukrainian Polissja

The most active natural TBE foci in Ukraine are located on the territory of Volyn oblast (Ratniv, Kivertsi, Kamen–Kashyr raions) and Autonomous Republic of Crimea (Simferopol, Bilogiria, Bakhchisarai, Sudak raions and Great Yalta) [Vynograd I.,1983].

The activity of TBE natural foci in Volyn oblast was manifested by group infection of people in 1995. In the period of April-October central raion hospital of Ratniv raion hospitalized more than 80 people with fever and lesions of respiratory and central nervous system. Forty six of them were serologically diagnosed with TBE. The layer of seropositive as to TBE virus among healthy people ranged in different villages from 14,8% to 50% with the mean value of 33,3%. The presence of a natural TBE foci in Ratniv raion was also confirmed by isolating of a TBE virus strain from ticks I.ricinus and numerous cases of indication of TBE antigen in

I. ricinus and *D. reticulatus* ticks and in internals of *Apodemus agrarius*. Areal of TBE virus apart from the most active Ratniv and less active Lutsk raions includes also Kivertsi, Kovel, Rozhyshen and Liubomyl raions of Volyn oblast, which is indicated by yearly reporting of TBE cases and detections of a virus antigen in ixodic ticks and mouse-like rodents.

Years, Country	Quantity of patients	Total infection form, %	Meningeal form, %	Meningoence-phalitic form , %	Polioencephalo-myelitic form, %
1996, Germany	300		50,0	38,0	12,0
1998, Horvatia	92		9,8	85,9	4,3
1995, France	21	4,8	28,6	62,0	4,8
1987, Russia, Ural region	190	34,6	50,6	10,6	4,2
1984, Poland	215		58,1	28,4	6,9
1992, Austria	117		61,0	24,0	15
1994, Slovenia	1044		63,0	30,1	6,9
1975, Chechia	633	0,7	6,3	84,0	9,0
2002, Lytva	133		43,6	43,6	3,8
2002, Ukraine, Polissja	80	60,0	24,0	16,0	
1996, Ukraine, Forest-steppe	56	35,7	41,0	21,4	1,9
1989, Ukraine, AR Crimea	52	67,0	15,4	17,3	

Table 2. Clinical forms of TBE in countries of Europe and in Ukraine

The disease was registered in spring-autumn period, starting in May and ending in November, with the peak in July-August. The main means of infection was transmitting (68,0%). The cases of alimentary infection with TBE (32,0%) were due to a consumption of raw cow's milk and its products. The development of a serious and complicated clinical forms of a disease was more common in terms of the transmitting way of infection ($P<0,05$).

In general TBE in Volyn is characterized by one-wave feverous period, with predomination of feverous (60%) and meningeal (24%) forms of a disease with only 16% of focal form, coordination disorders, insignificant quantity of paralytic forms and cases of a development of a chronic disease.

Clinical manifestations are similar to the western type of this infection, but there predominated one-wave character of thermal curve, while two-wave type of fever and changes in hemogram were observed in half frequency. The temperature curve of part of the patients had three waves.

In terms of neurological complaints there predominated the vertigo, walk unsteadiness, bones and lips tremor. Sensitivity disorders in forms of paresthesia were common as well. From the side of vegetative nervous system during the acute period the leading symptoms were the following: bradycardia, growth of blood pressure, clearly manifested hyperhidrosis, stable diffuse dermographism. In the acute period of the disease some

patients developed thyroid enlargement, asymmetry of skin temperature. Highly notable were various 'pseudonevrasthenic' complaints which followed the course of the disease: memory decrease, irritability, obsessive fears and thoughts, emotional lability. The before-mentioned clinical form was called by author as 'attenuate TBE' [Morochkovski R., 2002].
Almost half of patients – (48,2%) – the initial stage of the disease was characterized by some prodromal indications, manifestation of which wasn't pathognomonic for the given disease. As a result of a transmissible form of infection ($P<0,05$), there were more complicated manifestations of it, when in terms of clearly manifested intoxication and general-cerebral syndrome, changes from the side of a nervous system there developed a disfunction of a vegetative nervous system which prevailed in different parts of it ($P<0,05$), there were observed pathologic indications in cardio-vascular system ($P<0,05$), liver enlargement ($P<0,001$). All disorders of a vegetative nervous system were of central genesis as a rule, and developed mainly as a result of more considerable lesions of a central nervous system. As a common indication there was observed a skin hyperhidrosis, especially of a local character, which developed in all patients with poliomyelitic –like form of a disease.
It has to be mentioned that the rates of TBE forms with the lesions of a central nervous system which followed the tick bites and those which followed the alimentary way of infection didn't differ significantly ($P>0,05$).

2.4 TBE in forest-steppe zone

In a forest-steppe zone of Ukraine, within the described natural foci, the TBE morbidity is of a sporadic character and the course of the disease is varied.
In Pre-Carpathian zone, forest-steppe and steppe zones TBE is characterized by a two-wave course of a feverous period accompanied by a meningoencephalitic syndrome and insignificant quantity of focal lesions of a central nervous system.
In terms of study of immunity structure of healthy population there was observed the decrease in immune layer against TBE virus from west to east. There was noted the same tendency – the specific gravity of TBE cases was falling from 9,2% in Zakarpattia (Transcarpathian) to 7,0% in western oblasts, 4,2% in pre-Dnister forest-steppe regions, and few cases (1,7%) in the left-bank Ukraine. This serves the evidence of a connection between TBE morbidity in a forest-steppe zone of Ukraine with natural foci of a virus of a right-bank part of a forest-steppe zone.
The TBE incidence rates among pediatric populations are considerably lower than those of adults: among age groups of 0 to 20 years old – 12,5% of total number of cases. The incidence rates of elderly population (60 years old and more) made 3,5%, and 83,9% of all cases are people of the most productive age (20-60 years old), who populate the forest-steppe zone of Ukraine (fig. 4). TBE virus caused 24,8% of cases of arbovirus etiology.
Most of observed TBE cases were characterized by central nervous system lesions, without any focal symptoms in their course. A syndrome of a general fever with the
body temperature of 39-40°C which remained steady for 4-6 day was common for all cases as well. The patients had severe headaches with a frontal-temporal localization, nausea, hypersensitivity to bright light, dryness and tickling in a throat. Meningeal syndrome was observed in 1/3 of all cases. Lesions of brain tunics were indicated by a vertigo, nausea, vomiting, rigidness of occiput muscles, positive syndromes of Curnig, Brudzinski, pain in Kerrer's points. Feverous period lasted for 9-17 days. Full recovery, without residual effects, was observed on 21-35 day of a disease.

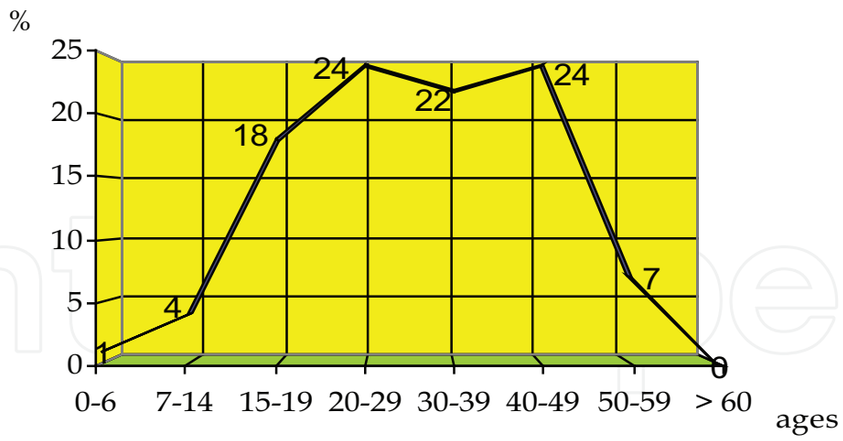


Fig. 4. Age morbidity structure of TBE

Focal form was observed in 21,4% of cases. It was characterized by a long-lasting hyperthermia with clearly manifested syndrome of total infection. Part of patients had a two-wave course of fever with the more complicated course of a second wave- it was characterized by encephalitic lesions. They were manifested by loss of consciousness, sometimes with psychomotor agitation. Among the indications of focal lesions there were observed hyperkinesis and hemiparesis. The disease lasted for 35-60 days. Three patients were released from hospital with signs of ataxia, slight signs of shoulder girdle muscles paresis. Three patients had muscle atrophy as residual effect.

It has to be mentioned that focal forms of TBE were detected by us only in western oblasts of Ukraine (Lviv, Ivano-Frankivsk and Zakarpattia oblasts). Lesions of peripheral nervous system were observed in one patient and were manifested by an exacerbation of a chronic polioradiculoneuritis which the patient had.

In 35,7% of TBE cases the course of a disease was complicated by lesions of respiratory system in terms of a syndrome of total infection. A feverous period had a one-wave course and lasted for 3-9 days. Nine patients were clinically diagnosed with pneumonia or bronchitis [Lozynski I., 1996].

2.5 TBE natural foci in the Crimea

The discovery of TBE natural foci in the Crimea is of a great importance because the territory is intensively exploited as a recreational zone. The discovery of TBE natural foci was preceded by the detection of antibodies against the virus in farm animals (sheep, cattle) and birds which inhabit forest landscapes. The rates of seropositive animal units were 18,1% and 19,8% respectively. The first patient with laboratory proved diagnosis of TBE was hospitalized in 1980 [Evstaf'ev I., 2001]. The following studies enabled isolation of TBE virus from ticks and rodents, it also led to the detection of number of serologically proved TBE cases.

The main carrier of TBE in the Crimea is *I. ricinus*, more than 95% of all isolated TBE strains were isolated from this species. According to the data obtained in studies of the Crimean Sanitary Station, the rates of ticks infection with TBE virus are low (the level of infection with virus is 0,5%). There was also detected the participation in pathogene circulation of *Hyalomma plumbeum, D. reticulatus Fab., D. marginatus Sulz* by isolating TBE viruses from

them. The peculiarity of Crimean TBE natural foci is virus-carrying of *H.plumbeum* ticks (13,7%), which keep the intensity of virus circulation in nature. The main feeders of preimaginal stages of ixodic ticks and reservoirs of virus in nature are background small mammals: *S. uralensis*, *S. flavicollis*, *M. obscurs*, and *Crocidura suaveolens* [Omelchenko O., 1989].

The highest rates of *I. ricinus* ticks population were registered in Simferopol-Zui forests, with totals of morbidity for three years of surveillance (2,00-2,35 per 100 000 population) four times higher than in regions of periphery of the Crimean mountains, where there is the most numerous population of *H. plumbeum* ticks.

The study of antigene structure of strains, isolated from ticks which inhabit different foci of the Crimean peninsular, showed a significant polymorphism of a TBE virus population. Initially it was detected that there circulate both strains of a western variant ('Absetar'), which are common for European countries, and of an eastern variant ('Sofia'). The deeper study showed, that five strains isolated from *I. ricinus* had antigene differences from a reference strain 'Sofia' in one out of three domains of glycoprotein E. This epitope of Crimean strains was significantly different from that of a virus detected in the Far East of Russia (1 genotype).

Etiological diagnostic of yearly seasonal neuroinfections in the Crimea proved their connection with natural TBE foci. In 1985-1987 there were hospitalized 173 persons due to the tick bites and development of feverous diseases; 50 patients were laboratory diagnosed with TBE. The study of immune status showed a considerable level (12,0%-18,0%) of population immunity of almost all regions of a mountain-forest zone of the peninsular, which also indicates a potential epidemic hazard of this territory in respect of TBE. In Simferopol and Bilogiria regions, where there were detected the highest morbidity rates, 55,1%-75,2% of healthy population had antihemagglutinin to TBE virus.

Since 1985 premountain-mountain forest part of the Crimea has been defined as natural foci of TBE. After the outbreak of the disease there started the intensification of TBE studies in the Crimea. Since 1985 the number of registered TBE cases ranged from 2-3 to 33 cases yearly. Real state of things with morbidity is considerably higher, due to the fact that a lot of TBE cases are not diagnosed and not detected, which is connected to non-specific course of TBE and prevalence of feverous and not distinct forms.

Simferopol, Bilogiria, Bakhchisarai, Alushta, Kirov and Krasnogvardeisk regions as well as forest-park zones of Yalta, Alushta and Simferopol are defined as endemic TBE regions. According to the official statistic data for the recent ten years, the morbidity rates in the AR of the Crimea are from 0,05 to 1,5 per 100 000 population. In recent years we annually register from 2 500 to 4 500 reports from people, who suffered from tick bites.

3. Lyme-borreliosis in Ukraine

Among the infections which take stably high positions in the structure of infectious pathology of population and cause more considerable medically-social and economical damages in comparison to other zoonoic diseases, equally with a tick-borne encephalitis Lyme-borreliosis (LB) is of the highest topicality in Eurasian continent. LB is transmissible natural-focal zoonosis, caused by spirochaete of genus *Borrelia*. LB is characterized by the propensity to a chronic course, polysystemic lesions of skin, nervous and cardio-vascular system, liver, spleen, eyes and locomotor system. The disease has several stages of its

development, apart from infection stage and primary manifestations. Immunity is unsterile, causative agent has a long-term persistence in an organism, with possible super- and reinfections. The first description of LB was given in 1977 in the US, and in 1982 they deciphered its etiology. The use of modern molecular-biological techniques enabled detecting of more than 10 (up to 15) genotypes of LB causative agent [Strube et al., 2010], which were consolidated in *Borrelia burgdorferi* sensu lato complex. Apart from known 'classical' pathogenic representatives - *Borrelia* (*B.*) *burgdorferi sensu stricto* (s. s.), *B. afzelii* и *B. garinii* [Baranton et al.,1992; Canica et al.,1993], the recent studies proved the role of *B. bavariensis* (a close relative of *B. afzelii*) *B. bissettii*, *B. lusitaniae*, *B. valaisiana*, *B. spielmanii* in infectious pathology. Genetical variety of causative agents determined the change of LB definition from «a monoinfection» to «a group of nosoologically independent infectious diseases» of human [Gratz, 2005]. There is some basement for assumption that genotype and antigenic differences of *Borrelia* determine peculiarities of pathogenesis and clinical manifestations of the disease in different regions. Intensive study of LB in the late twentieth century has established the pandemic spread of the disease. Lyme-borreliosis occurs on all continents except Antarctica. In the USA they annually report of 12 000 to 40 000 cases of LB [MMWR, 2007], incidence rates in Russia – up to 70 [Naumov, 2005], in Europe are – 70-130 in per 100 000 population [Gratz, 2005].

3.1 Stages of LB studing in Ukraine

First cases of LB in Ukraine were diagnosed later than in other, including neighbouring, countries – in 1989-1993 [Nebogatkin&Semenova,1994].. Since 1995 there have started studies on LB in Lviv Scientific Research Institute of Epidemiology and Hygiene, Ministry of Health of Ukraine. The official registration of a new nosologic form of LB has been held since 2000. In the course of implementation of clinical and laboratory diagnostics of LB the topicality of this disease came into light. Among the most important characteristics of current LB in Ukraine the following has to be mentioned: a) constant broadening of a nosoarea; b) rapid increase in population morbidity rates; c) prevalence of urban population among cases in total (70%-80%); d) increase in number of patients who were bitten by ticks under different social and behavioral conditions; e) prevalence of human infections in antropurgical foci; f) increase in number of infected ticks in nature; g) formation of urban foci; h) circulation of five pathogenic *Borrelia* genotypes; i) pathomorphism of the disease with the prevalence of neurological and rheumatological (arthritis) forms; j) existence of territorial and population-combined foci of LB-TBE and LB-HGA and cases of mixed infections.

3.2 LB natural foci

3.2.1 The vectors

LB areal in Ukraine coincides with the areal of European forest tick *I. ricinus,* which is the main vector of *B. burgdorferi* sensu lato in European countries. By method of dark-field microscopy we detected that on the average from 6,45% of *I. ricinus* in Carpathian mountains to 10,8% in Polissya with maximum of 25,0% in some biotopes are carriers of *Borrelia*. Out of *I. ricinus* ticks collected in western part of Lviv oblast we isolated 4 genotypes of *Borrelia*: *B. b. sensu stricto*, *B. afzelii, B. garinii* и *B. valaisiana* (atypic), in the southern part – *B. b. sensu stricto, B. afzelii, B. garinii* и *A14S*. Thus for present days in Ukraine we discovered 5 genotypes of *B. b.* sensu lato out of 7 genotypes existing and

discovered in Europe. Currently in Ukraine natural infection with *Borrelia* has been proved also for *I. trianguliceps* [Akimov&Nebogatkin, 1997], and more than once, for *D. reticulatus* [Biletska et al., 2007], and in recent years - for *D. marginatus* in regions where these species prevail (Donetsk and Kharkiv oblasts) (fig. 5).



Fig. 5. Vector of *B. burgdorferi* sensu lato in Ukraine

According to Akimov, 5 more species can participate in *Borrelia* circulation - *I. crenulatus, I. kaiseri, I. redikorzevi, I. hexagonus, H. punctata.* .More frequent cases of *Borrelia* exposure in *D. reticulatus* and their infection rates in places of their prevalence (mixed forest zone), serve the evidence of their being secondary carriers of LB. The mean index of infection of *D. reticulatus* in Europe and in Russia is between 1,72% and 3,6% [Rudakova, 2005, Nijhof, 2007], while in Ukraine – 5,4% (8,0%-15,4%-2010). We got some evidences of existence on the territory of Volyn, Lviv and Sumy oblasts polivectorial (bivalent) natural LB foci, where Borrelia carriers are ticks of two background types - *I. ricinus* and *D. reticulatus,* which makes the risk of infection of population with LB considerably higher.

3.2.2 The hosts

It is known that in different natural LB foci borrelia can be kept during the long term and transmitted to ticks by 2-3 basic and up to 10-15 additional types of mammals and also birds, which get their feed from the earth [Gorelova et al., 2001; Peteny et al., 1996; Miyamoto et al., 1997; Humair et al., 1998; Humair, Gem, 1998; Pichon et al., 2000]. For 2002 terriofauna of Ukraine had 132 species, among them 53 species and 29 genders of micromammals [Zagorodniuk, 2002]. Reservoir role of certain species of these mammals which inhabit natural LB foci remains unstudied, except western region. Occurring everywhere in different landscape subzones of western part of Ukraine 5 species of small rodents of *Muridae* family are wide spread: 3 species of *Murinae* family (mice): *Apodemus agrarius*. (index of abundance – 20,22%), *Apodemus flavicollis* (6,61%) and *Apodemus sylvaticus* (7,81%), 2 species of *Microtinae* family (voles): *Clethrionomys glareolus* (26,52%) and *Microtus arvalis* Pal. (22,58%) and 1 species of *Insectivora* family - *Sorex araneus* (5,19 %). On the average 10,04% (5,77% - 13,14%) of these animals had antibodies against Borrelia detected, which corresponds to the showings from LB foci of high activity. Among vertebral of countries of Central and Western Europe the main role in circulation and reservation of LB causative agents belongs to (*A. flavicollis*) and (*Cl. glareolus*) [Stefancikova, 2004]. In different regions of Ukraine the indices of infection with borrelia of *Cl. glareolus* (14,1-14,3%), *A. silvaticus* (12,7%) and *A. flavicollis* (8,0%) were almost the same as findings of studies in other European countries (12,5% and 17,4% respectively), which serves the evidence of first-priority part of these species in borrelia reservation on the territory of western region of

Ukraine. Four more species of *Rodentia* were found seropositive: *A. agrarius, M. arvalis* и *Mus musculus* and *S. araneus* (table 3).

Landscape zones	No. exa-mi-ned	No. of serum-positive small mammals	Examined small mammals species:						
			A. agrarius Pal.	*A.flavicollis* Mart.	*M.arvalis*	*M. glareolus* Sch.	*Mus musculus* Linn.	*S.araneus* Sch.	*A.silvaticus* Linn.
Ukrainian Polissya	703	66 (9,4%)	19 (11,8%)	4 (3,8%)	10 (8,9%)	18 (14,1%)	11 (15,3%)	1 (2,3%)	3 (4,4%)
Forest-steppe	459	59 (12,9%)	12 (9,8%)	2 (8,0%)	38 (21,6%)	5 (7,9%)	2 (33,3%)	0	0
Carpathian region	365	32 (8,8%)	10 (7,0%)	0	10 (12,9%)	3 (14,3%)	0	0	9 (12,7%)
Total	1988	157 (7,9%)	41 (7,5%)	6 (3,2%)	58 (11,3%)	26 (10,8%)	13 (10,1%)	1 (1,8%)	12 (7,7)

Table 3. Prevalence of antibodies to *Borrelia burgdorferi s.l.* in small mammals

3.2.3 Epidemiology

Currently in Ukraine due to its morbidity rates LB has the first place among all tick-borne natural foci infections. In the period of 2000-2010 there were officially registered 4597 cases, the index of morbidity increased by 23,2 times: from 0,12 in 2000 up to 2,79 per 100 000 population in 2010 respectively (fig. 6).

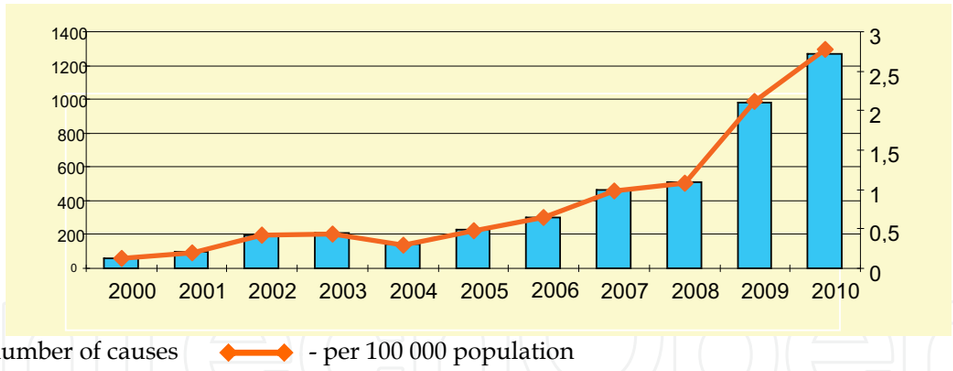
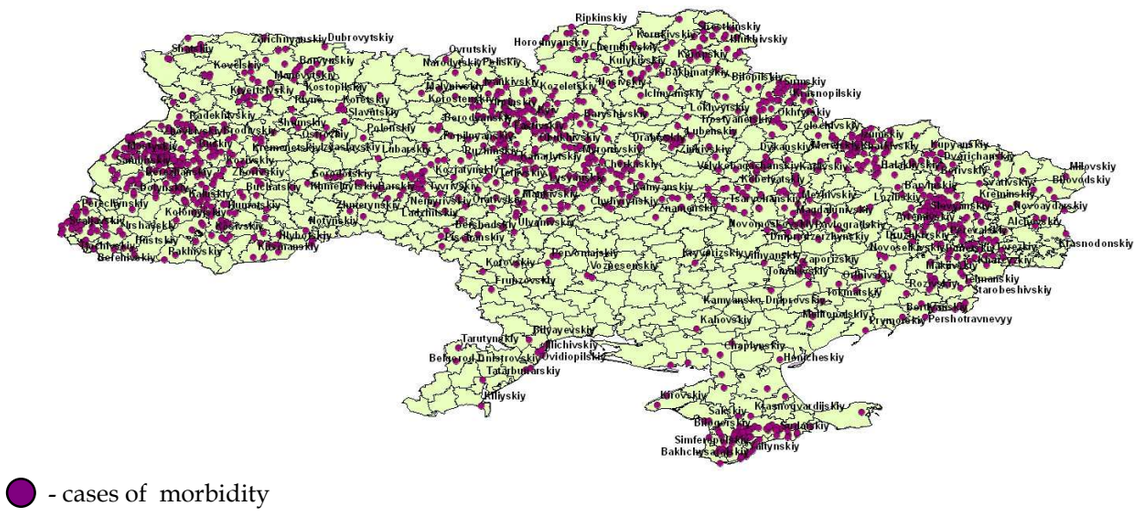


Fig. 6. Lyme-Borrelioses morbidity in Ukraine (2000-2010)

In some administrative regions of Lviv and Donetsk oblast and in Kyiv, where there have been formed special centers for LB surveillance, this index reaches 11,2–19,4 per 100 000 population, thus coming to proximity with these indices in other (neighbouring) European countries. Cases of LB have been registered in all regions of Ukraine: in 25 administrative oblasts and in Autonomous Republic of Crimea (fig. 7).

Number of enzootic as to LB territories is considerably increasing with every year and for 2010 makes 1809 populated areas in 477 administrative regions. According to the mean value of many years standing index of morbidity in different administrative territories of Ukraine amounts of 0,05 (AR Crimea) to 10,3 cases (Kiev) per 100 000 population. The development of the disease in most cases (85,7%) is connected to sticking of ixodic ticks,

while in 5,6%-10% of cases it may be connected to bites of bloodsucking mosquito (*Culicidae*). Yearly dynamic of LB morbidity is characterized by notable seasonal prevalence, connected to period of activity of carriers (*I.ricinus).* The vast majority of new LB cases (81,7%-85,6%) is registered in May-September. First cases are reported in April (2,9%), last – in November (4,9%) with peak in May-June (70,8%). In the period of April-October there are 95% of tick attacks registered and almost 90,0% of new LB cases. As distinct from tick-borne encephalitis, 3,8% of LB cases for the first time clinically manifested in low-season period (December-February). In polivectorial (binary) LB foci epidemic season may be prolonged (up to 8-9 months) due to early (in March) appearance of *D.reticulatus* in nature (fig. 8).



- cases of morbidity

Fig. 7. Map of Lyme-borrelioses morbidity in Ukraine

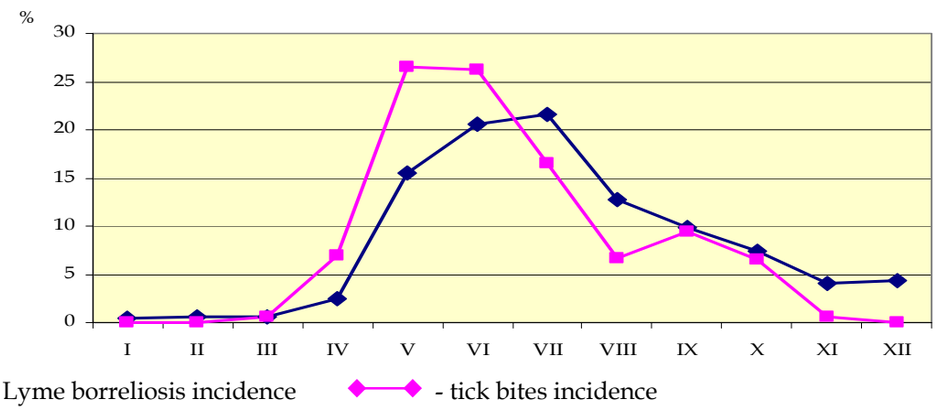


Fig. 8. Dynamics of Lyme borreliosis incidence and tick bites incidence

Part of rural population among LB cases makes only 15,2%, while the main part of cases (84,8%) is urban population of Ukraine. The leading role of LB epidemiology is of antropurgical foci. Their number is increasing rapidly and currently in Ukraine 44,6% of cases of human infection occur within towns and small towns, 11,0%- on the territory of villages and only 34% - in terms of visits to forests with recreational purposes, gathering mushrooms,

berries and the like. There were also noted the cases of tick attacks in residential areas, in out-of-town recreational institutions, in parks and gardens, on the territories of cemeteries.
The rates of contact between population and *B.burgdorferi* are quite high: more than a third (34,3%) of healthy people and from 34,7% to 49,3% of persons, whose jobs are connected with forests, contain antiborrelia antibodies IgG, and from 9,1% to 15,2% of them are within the diagnostics titers. The highest rates of infection (up to 70%) the population with borrelia were detected in Ukrainian Polissya and forest-steppe zone. The results of epidemiological studies of 1104 LB cases, obtained in different random periods (from 2000 to 2010) differ insignificantly. Lyme-borreliosis affects all age groups (from 1,9 to 87), however the age groups of 30-49 (>30,0%) and 50-59 and older (>40,0%) are considered to be high-risk groups. The incidence rates of female population were higher than these of male (>60%). According to socially-professional distribution the groups of the highest risk (>70%) go as follows: employees and workers- 40,6%, retired and unemployed – 34,6%. Persons from the professional risk group (forestry workers, livestock breeders, tree and shrub planting workers) make the least numerous group (1,2% – 1,8%), thus there is no connection between LB and professional activity detected.

3.3 Clinical manifestation

According to the analysis of medical records of 1104 LB cases the main clinical manifestations of the disease are referred to as stages of early local (1) and disseminated infection (2) and only 1,7% - as a stage of a late chronic infection (3) (according to the conventional classification). The spectrum of clinical manifestations of LB in Ukraine includes most of symptoms described in literature. It is known that in Europe LB is mainly manifested by dermal and neurological manifestations [Stanek&Strle, 2009]. Among prevailing forms of LB in Ukraine there are erythematic forms as well (64,9%). Neuroborreliosis has the third position (21,4%) preceded by ME and locomotor apparatus pathologies [Biletska et al., 2001,2008] (fig. 9).

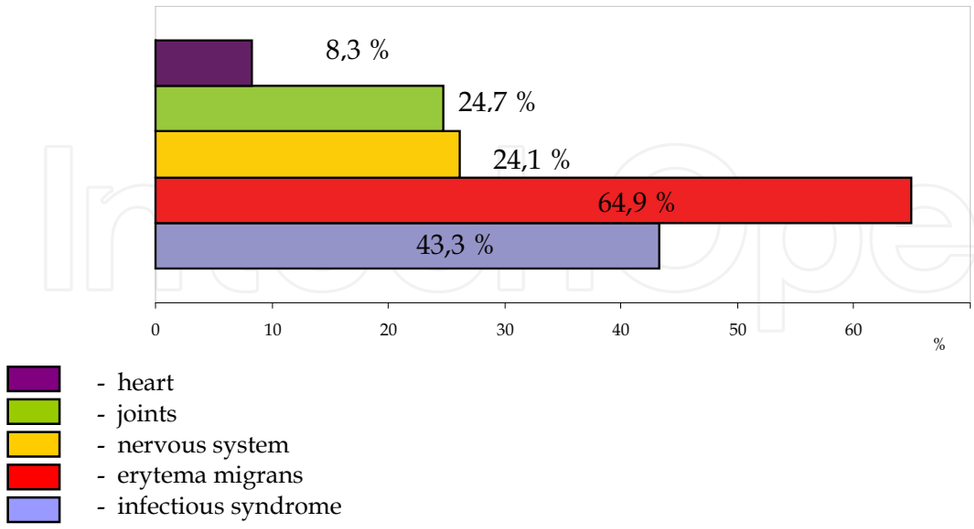


Fig. 9. The main clinical symptoms of LB at the patients

Quite often (60,6%) the erythematic form is accompanied with a fever (up to 38-39°C), asthenia, indisposition, headache, arthralgia, myalgia. On the initial stage of the disease

43,3% of patients were observed with general-infection syndrome. Secondary elements of erythema developed in 4,1% of cases, which is considerably rare in comparison with the USA, where the half of reported cases is accompanied with the before mentioned lesions. The explanation of the great extent of clinical manifestations spectrum was obtained through indication of monoclonal antibodies (IFA) against 4 borrelia types in blood serum of LB patients: *Borrelia afzelii, B. garinii*, and against two strains of *Borrelia burgdorgeri sensu stricto* isolated in the USA and Czech Republic.

It was found out that the causative factors of 75,5% of LB cases were all three pathogenic for a human types of borrelia of *B.burgdorferi s.l.* complex: in 42,6% of cases there were detected antibodies against *B.garinii,* which cause neuroborreliosis, in 19,8% *B.burgdorferi sensu stricto,* which is connected to locomotor apparatus pathology, and in 27,3% *B.afzelii,* which causes dermal lesions. Every fourth case could be hypothetically caused by other (opportunistically) pathogenic type of borrelia.

3.3.1 Features (spectrum) of neurological lesions

In terms of clinically-epidemiological analysis of laboratory- confirmed cases of LB (1104) neurological symptoms were observed in 236 (21,37%) of patients, among them 55,09% of female and 44,91% of male respectively. The age ranged from 1,5 to 68. It has to be mentioned that the most numerous groups were those of teenagers and young adults from the age group of 11-20 years old (23,31%), and also people of active working age from 31 to 40 years old (16,52%) and from 21 to 30 years old (15,15%).

Central nervous system (204 patients)		Peripheral nervous system (46 patients)	
manifestations	%	manifestations	%
acute encephalitis	17,6	mononeuritis	21,7
meningoencephalitis	9,3	paresthesias (numbness of fingers, feeling cold in extremities)	76,1
meningitis	31,8	hand tremor	2,2
arachnoiditis	0,5	polyneuritis and polyradiculoneuritis	8,69
meningeal symptoms (rigidity neck muscles)	2,9	-	-
convulsions	2,9	-	-
the consequences of the defeat of the cortex cerebral mozka (speech impairment, coordination, sleep, vision, memory, transient loss of consciousness)	9,8	-	-
asthenic-neurotic syndrome (frequent headaches, severe fatigue, headache, nervousness, etc.)	3,4	-	-
epileptic syndrome	0,5	-	-
sluggish paresis of facial muscles	1,47	-	-

Table 4. Neurologic manifestations of Lyme borrelioses patients

Among the manifestations of neuroborreliosis there were observed both lesions of peripheral nervous system (19,49%), which appeared mostly in the acute stage of the disease and those of central nervous system (86,44%), which appeared in acute stage of the disease and in the 2nd stage (dissemination) of LB as well. The lesions of peripheral nervous system in the acute stage were manifested mostly by perceptibility disorders (76,09%) (paresthesia) such as "gooseflesh", "numbness" of fingers, freezing limbs etc, and also by facial, sciatic, lumbar mononeuritis (21,74%), polyneuritis and polyradiculoneuritis (8,69%), and quite rarely by hands tremor (2,17%) (table 4).

The important clinical peculiarity of acute borreliosis in Ukraine are early (occurring in 2-3 week of the disease) transient lesions of central nervous system. The high rates of acute serous encephalitis (17,65%), meningitis (31,86%), meningoencephalitis (9,31%), arachnoiditis (0,49%), were detected mainly in 135 patients from Kherson (41 case), Volyn (53 cases) and Zaporizhia (41) oblasts. Meningitis as an independent form of LB is more often observed in children, while in adults it is combined with spinal and cranial nerves lesions etc. The dominant symptom which prevailed in most cases was a headache of different intensity (14,21%). More often it is a moderate headache, but it can be also frank. Apart from a headache, there are also observed nausea, vomiting (2,45%), edema of a brain (0,98%), convulsions (2,94%), painfulness which accompanies any movements of eye balls (0,49%). In 24,15% of cases the syndrome of general infection was manifested by hyperthermia, asthenia and vertigo. In terms of neurological observation almost all patients have the lack of neck mobility (2,94%). Other meningeal symptoms are observed less often. Cerebrospinal fluid develops lymphocytic pleocytosis, the number of cells–dozens and hundreds in 1 microliter; lymphocytes make 70%-100% of total quantity of cells; quite often, especially in cases of meningoradiculitis, there is an increase in proteins values – sometimes it is above 1-2 millimole/l; the level of glucose can be within norm. In some cases (6,86%) the course of the disease and neurological symptoms (acute initial stage, thermal reaction, rigidity of occiput muscles, extinction of reflexes, inflammation of CSZ etc), LB was very similar to TBE, especially its encephalic-poliomyelitical manifectations, which predetermined preliminary diagnosis TBE, however it wasn't later confirmed in serological tests [Zinchuk, 2007]. Similar indications of LB are observed also in some regions of Russia, however they are rarely observed in patients from any other countries. On the 2 stage of LB the lesions of cerebral cortex were manifested by various encephalic pathologies (9,80%) such as dysphasia, hypotaxia, sleep disturbance, visual and memory impairment, absence. Some patients (3,43%) had some manifestations of asthenically-neurotical syndrome such as frequent headaches, sudden fatigability, migraines, nervousness etc, some patients (1,47%) were observed to have low-intensity paresis of facial muscles, rare cases (0,49%) developed epileptic syndrome. Sixty percent of patients with borreliosic lesions of nervous system developed radicular painfulness followed by peripheral paresis, which are usually manifested in 1,5 months from the beginning of the disease. The indications of progressive vestibular pathology and psychoorganic syndrome were observed relatively rarely. There was observed the development of chronic processes of the disease with slow intensification of symptomatology in 1,27% of patients. The important feature of neuro-borreliosis in Ukraine is absence of migratory erythema in 80,93% of cases, which considerably complicates the diagnostic of the disease. Among patients with lesions of nervous system only 51,27% of cases reported the fact of a tick bite in anamnesis, the rest 48,73% didn't remember anything like that or denied it absolutely. Due to this it can be assumed that there

were clings of infected nymphs which are often not noticed. Most patients with borreliosic lesions of nervous system (30%-50%) get sick in the period of June and October after incubative period which lasts from several days to several weeks.

4. Mixed infections

Analysing the current epidemiologic situation with LB one more new peculiarity of great importance has to be mentioned. It must have existed before but for us it has become clear only in recent decades. Here we mean the existence and prevalence in Ukraine of territorial and populational combined foci of transmissible tick-borne infections of viral and bacterial nature – TBE and tick-borne borreliosis. It was first shown in our studies that on the most of the territory of Ukraine TBE and LB are actually epidemiologic 'twins' and differ only in etiological factor. Among main epidemiological characteristics there are the following- the same carrier (*I.ricinus*), which makes the areals of two infection practically concurrent, and reservoirs (*A. flavicollis, Cl. glareolus, A. agrarius, M. arvalis, M. musculus, S. araneus*). The retrospective analysis has shown that most of diseases which were diagnosed previously as TBE (30,78%) and most likely are still being diagnosed as so, are in fact tick-borne borreliosis. In terms of a purposeful serological testing of 227 patients of neurological departments from 7 oblasts with the preliminary diagnosis of TBE and prevailing symptoms of encephalitis, meningitis-encephalitis, viral encephalitis etc, we detected the mixed infection of TBE – LB in 21 (9,3%) patients. Overall in the structure of LB morbidity the cases of mixed with TBE infections made from 5,8% to 7,1% and were detected in 9 oblasts. Analysis of clinical manifestations of mixed infections in 30 patients proved the suppositions as to TBE combined with LB has less complications in its course [Aleksejev, 1996]. Combination of LB with TBE was characterized by acute onset of disease (77,9%) with the development of febrile (52,3%), meningeal (32,8%), focal (5,9%) and asymptomatic forms or with only mild symptoms (9,0%). In the structure of clinical manifestations of LB individual cases there is a predominance of one sign of infection, or a combination thereof, or one of the infections are in latent form. Mutual burdening course of mixed infection TBE-LB was not detected. However, the prevalence of natural foci of LB and TBE with a high incidence of LD in the territory of Ukraine, a large proportion of patients with the transition of the disease in chronic forms of the absence of complete data on the peculiarities of clinical manifestations of disease in the combined infection of Borrelia and TBE virus, the complexity of the objective differential diagnosis and lack of efficacy, require further research in this area.

5. Conclusion

Presented materials so far do not qualify for adequate mapping of the current situation in neuroinfections, ecologically related with ticks in Ukraine. But now the data for individual regions showed that the level of incidence and prevalence, tick-borne infection is obviously a leading position among natural focal zoonoses in Ukraine. Undoubtedly, in the near future with the improvement of laboratory diagnosis number of reported cases of TBE and LB will be increase. Will be expand the spectrum of identified infectious diseases also. So, recently obtained evidence of the existence in Ukraine of natural foci of human granulocytic anaplasmosis (HGA), and identified numerous human cases of mixed infection of LB-HGA, TBE-LB-HGA. It identifies the need to continue clinical and epidemiological studies of tick

infections on the territory of Ukraine using standardized criteria for diagnosis (including differential) and the involvement of specialists in various fields.

6. References

Akimov I. & Nebogatkin I. (1997). Some results of the study of ticks in foci of borreliosis in Ukraine. *Bulletin of Zoology*, Nº 4, pp. 91-95.

Aleksejev A., Dubinina E.&Vashukova M. (1996). Borrelia as apparent antagonists of tick-borne encephalitis: parasitological and clinical aspects. *Med. Parasitology and Parasitic Diseases,* Vol . 3, Nº 3, pp. 3-11.

Baranton G., Postic D., Saint Gisons L., Boerlin P., Piffaretti J., Assous M.&Grimont P.(1992). Delineation of Borrelia burgdorferi sensu stricto, Borrelia garinii spp. Nov., and group VS461 associated with Lyme borreliosis. *Int. J. Syst. Bacteriol*., Vol. 42, Nº 3, pp. 378-383.

Biletska H., Lozinskiy I., Burkalo T., Semenyshyn O., Rogochij E., Markovich V., Sakal' M.&Orel T. (2003). Clinical and epidemiological aspects of mixed infection "tick-borne encephalitis-ixodid tick-borne borrelioses. *Scientific Bulletin of Uzhgorod University. Medical series*, Issue 21, pp. 66-69.

Biletska H., Lozinskiy I.& Semenyshyn O. (2002). Differential diagnosis of mixed-borne infections in Ukraine. *Proceedings of: VI Congress of* infectiologists of Ukraine, September, Odessa, 2002.

Biletska H., Podavalenko A., Semenyshyn O.& Lozinskiy I. (2007). Ecology-epidemiological aspects of spreading the Lyme disease in Ukraine. *Problems of modern medical science and training*, Nº 4, pp. 12-14.

Biletska H., Vynograd I., Semenyshyn O., Lozinskiy I., Drul O., Kozlovsky, M, Rogochy E.G.& Sholomey M. (2001). Neurological manifestations of Lyme disease in Ukraine, *Proceedings of: Proc. scientific-practical. Conf. Plenary Session of the Association and infectious disease Ukraine "Neuroinfections. Other infectious diseases"*, Kharkiv, April, 2001.

Canica M.M., Nato F., Merle L., Mazie J. C., Baranton G.& D. Postic. (1993) Monoclonal antibodies for identification of Borrelia afzelii spp. Nov. associated with late cutaneous manifestations of Lyme borreliosis. *Scand. J. Infect. Dis*., Vol. 25, pp. 441-448.

CDC. Lyme disease - United States, 2003–2005 (2007) *MMWR* 56 (23), pp. 573–576.Retrieved from: http://www.cdc.gov/mmwr/preview/mmwrhtml.

Evstaf'ev I. (2001). Results of a 20-year study of tick-borne encephalitis in Crimea. *Journal of Medical Epidemiology and Immunology*, Nº 2, pp. 111-114.

Gratz N. (2005). Vector-borne infectious diseases in Europe, *WHO Regional Office for Europe.* Retrieved from: http://www.euro.who.int/pubrequest.

Kunz Ch. (1992) Die Fruhsommer - Meningoenzephalitis (FSME) in Europa Allgemeinarzt. Vol. 14, Nº 7, pp.691-696.

Lozynskiy I (1996). Arboviruses of Forest-steppen Zone and and their importance to the regional infectious diseases. *Dissertation for the degree of the candidate of medical sciences*, 155 pp.

Morochkovski R. (2003) Clinical characteristics of tick-borne encephalitis in Volyn' and optimization of treatment. *Thesis for the degree of the candidate of medical sciences,* 20 pp.

Nebogatkin I.& Semenova N. (1994) Epidemiology and epizootology of Lyme disease in Ukraine. *Ukrainian Scientific-Medical Youth Journal*. Nº 1, pp. 61–63.

Naumov, RL & Vasil'ieva I. (2005). Affected populations and the incidence of Borrelia Lyme disease. *Medical Parasitology and Parasitic Diseases*, Nº 2, pp. 40-42.

Nijhof A. M., Bodaan C., Postigo M., Nieuwenhuijs H, Opsteegh M, Franssen L, Jebbink. F. & Jongejan F. (2007). Ticks and associated pathogens collected from domestic animals in the Netherlands. *Vector Borne Zoonotic. Dis.*, № 4, pp. 585–595.

Omel'chenko A.A. (1989) Ecology and biological properties of arboviruses selected in south of USSR and their significance in the etiology of seasonal fevers. *Dissertation for the degree of the candidate of medical sciences,* 190 pp.

Randolph S.E.. (2002). The changing incidence of tickborne encephalitis in Europe. *Eurosurveillance Weekly*: June, 2002, Vol. 6, Issue 23

Rudakova S. A., Matusheko E. V., Iakimenko V. V., Tokrevitch N.& Andrejchuk Yu. (2005) A study of possible transovarial and transphase transmission of borreliae by the tick Dermacentor reticulatus (Ixodidae). *Parazitologiia* , Vol. 39, Nº 5, pp. 427–432.

Semenyshyn O. (2009). Ecological and epidemiological characteristics of ixodal tick-borne borrelioses in the western Ukrainian region. *Thesis for the degree of the candidate of medical sciences,* 23 pp.

Stanek, G. & Strle F. (2009). Lyme Disease—European Perspective. *Infectious Disease Clinics of North America,* Vol. 22, Issue 2, pp. 327-339.

Stefancikova A., Bhide M., Pet'ko B., Stanko M., Mosansky L., Fricova J., Derdakova M. & Travnicek M (2004). Anti-Borrelia antibodies in rodents: important hosts in ecology of Lyme disease. *Ann. Agric. Environ Med*., Nº 11, pp. 209–213.

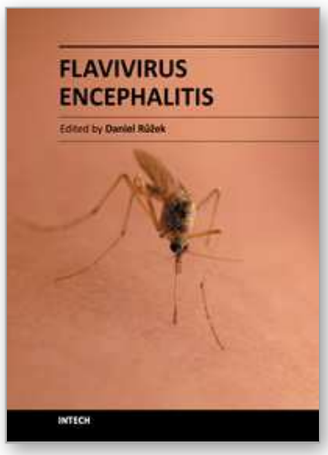
Strube C., Montenegro V.M., Epe Ch., Eckelt E.& Schnieder Th. (2010). Establishment of a minor groove binder-probe based quantitative real time PCR to detect Borrelia burgdorferi sensu lato and differentiation of Borrelia spielmanii by ospA-specific conventional PCR. *Parasites & Vectors*, Nº 3, pp. 69-76.

Zinchuk A. (2007). Lyme borreliozis detection among patients with neurological disorders. *Practical medicine*, Nº 1, pp. 68-72.

Votjakov V., Protas I.&Shdanov V.(1978). *Western Tick-borne Encephalitis*. Medicine, Minsk (Belarus).

Vynograd I.A. (1983). Arboviruses in the Ukrainian SSR and their medical and biological significance. *Dissertation for the degree of the doctor of medical sciences*, 505 pp.

Vynograd I., Biletska H. & Lozynski I. (1996) Tick-borne encephalitis and other arboviruses infections in Ukraine. *Infectious Diseases*, Nº 4, pp. 9-13.



Flavivirus Encephalitis

Edited by Dr. Daniel Ruzek

ISBN 978-953-307-669-0
Hard cover, 478 pages
Publisher InTech
Published online 30, September, 2011
Published in print edition September, 2011

Encephalitis is an inflammation of the brain tissue associated with clinical evidence of brain dysfunction. The disease is of high public health importance worldwide due to its high morbidity and mortality. Flaviviruses, such as tick-borne encephalitis virus, Japanese encephalitis virus, Murray Valley encephalitis virus, or St. Louis encephalitis virus, represent important causative agents of encephalitis in humans in various parts of the world. The book Flavivirus Encephalitis provides the most recent information about selected aspects associated with encephalitic flaviviruses. The book contains chapters that cover a wide spectrum of subjects including flavivirus biology, virus-host interactions, role of vectors in disease epidemiology, neurological dengue, and West Nile encephalitis. Special attention is paid to tick-borne encephalitis and Japanese encephalitis viruses. The book uniquely combines up-to-date reviews with cutting-edge original research data, and provides a condensed source of information for clinicians, virologists, pathologists, immunologists, as well as for students of medicine or life sciences.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

H. Biletska, I. Lozynskiy, O. Drul, O. Semenyshyn, I. Ben, A. Shulgan and V. Fedoruk (2011). Natural Focal Transmissible Infections with Neurological Manifestations in Ukraine, Flavivirus Encephalitis, Dr. Daniel Ruzek (Ed.), ISBN: 978-953-307-669-0, InTech, Available from: http://www.intechopen.com/books/flavivirus-encephalitis/natural-focal-transmissible-infections-with-neurological-manifestations-in-ukraine

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike-3.0 License, which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited and derivative works building on this content are distributed under the same license.

IntechOpen

IntechOpen