Chapter 9

Active Natural Foci of Tick-Borne Neuroinfection in the North-West Region of Ukraine

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Additional information is available at the end of the chapter

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1. Introduction

The formation natural foci of tick-borne infections is closely connected to three physically–geographical zones in Ukraine: Ukrainian Polissya (mixed forest zone - (woodlands), Forest–Steppe zone, Steppe zone and two extra-zonal natural areas – Carpathian and Crimean mountains.

On the territory of Ukrainian Polissya there are favourable conditions for the formation of natural foci of mainly those types of arboviruses and bacterial infections, which are transmitted by ticks – tick-borne viral encephalitis, Tribec, Uukuniemi, ixodid tick-borne borreliosis, human granulocytic anaplasmosis (HGA), others.

Tick-borne viral encephalitis (TBVE), ixodid tick-borne borreliosis (ITBB) and mixed-infection (TBVE and ITBB) are the most prevalent feral herd transmissible infections in Ukraine. Numerous aspects of these infections require to be better looked into or need more accurate definitions. First of all, this refers to the regional peculiarities of epidemiology and clinical manifestations, diagnostics, treatment and also the efficiency of preventive measures taken. There is an urgent need in studies of special clinical features of late manifestations and chronic course of these neuroinfections, as well as their better timely diagnostics and etio-pathogenetic therapy.

2. Abiotic and biotic peculiarities of Volyn oblast

Volyn oblast is located on far north-west part of Ukraine and occupies the western part of plain territories of two geographic zones of Ukraine – Ukrainian Polissya and Forest-Steppe. On the

south it borders with Lviv oblast, on the east with Rivne oblast, on the north with the Republic of Belarus, on the west (along the Western Bug) with Poland.

Climate of Volyn oblast is mild-continental, with mild winters, short periods of freezing, frequent thaws, mild summers, without significant heat waves, heavy percipitation, long springs and autumns. Average January temperature is +4,5 ºC, for July it is +18,6 ºC. Vegetation period lasts for about 200 days. The sums of the temperatures for the periods with stabile temperatures above +10, make 2495-2580 ºC. Percipitation makes 550-600 mm a year. Relative humidity of the air is in the reverse proportion to its temperature: in the winter it exceeds 80 %, in the summer it reaches 65-70 % [1].

Territory of Volyn oblast is the part of Eastern-European province of broadleaf forests of the European Broadleaf Zone. The landscapes of the zone are of two types: Polissya, with high prevalence of swamps, meadows, oak-pine and narrow-leaf forests and Forest-Steppe type zone, with prevalence of meadow steppes and oak-hornbeam forests in prehistoric times, which are mainly farming lands nowadays.

Due to its zoo-geographic parameters, Volyn oblast is a borreal-forest zoo-geographic type of zone. Its territory hosts 301 vertebral species, among them 183 species of nesting and non-migrating birds, 64 species of mammals. Among small mammals, which are within the range of parasitory system of tick-borne infections, there are *Sorex araneus*, *Castor fiber*, *Apodemus agrarius*, *Arvicolla terrestris* (*amphibious*), *Microtus oeconomus*. To woods species belong *Sciurus vulgaris*, *Microtus subterraneus*, *Meles meles*. In zoocenozes also are distributed *Dryomys nitedula*, *Glis glis*, *Muscardinus avellanarius*, *Myodes Clethrionomys glareolus*, *Sylvaemus sylvaticus*, *Sylvaemus tauricus, Talpa europaea, Erinaceus europaeus* [2]. All territory of the oblast is within the area of *I. ricinus* ticks - main vector of tick-borne pathogenes in Europe.

The findings of the complex studies and surveillance, conducted in the period of 1990-2011, showed the presence of active natural foci of TBVE and ITBB on the considerable part of the territory of the oblast.

Aims of study: to look at the incidence rates of tick-borne infectious diseases and analyse the range of their clinical manifestations in north-west region of Ukraine taking Volyn oblast as a sample territory during the period of 1990-2011.

3. Tikc-borne viral encephalitis

3.1. TBVE Epidemiology

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

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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 [3, 4].

For 2011 enzootic as to TBVE territories, distinguished according to one or combination of such characteristics as natural infection (presence of antigen) of ixodid 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 33 settlements of 9 districts of Volyn oblast [5] (fig.1).

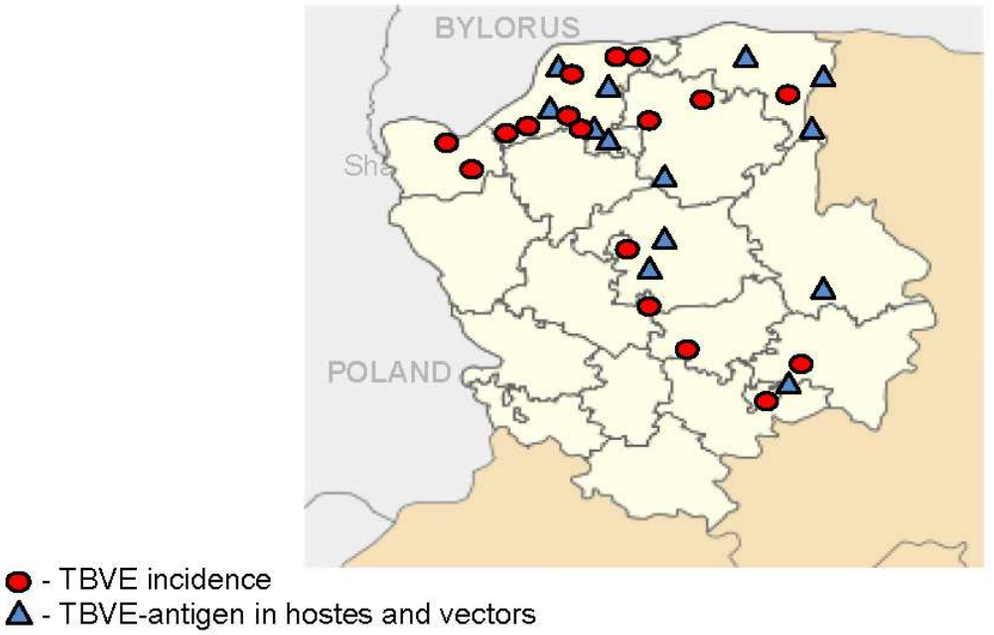

Figure 1. Shematic map of TBVE enzootic territories in Volyn oblast

The main reservoirs of TBVE virus in nature are *Microtus arvalis*, *Myodes glareolus*, and *Apodemus agrarius,* where the part of *M. arvalis* makes more than 50 %.

Among ixodid ticks, the species which are more often infected with TBE virus are *Dermacentor reticulatus* (64,3 %), while among the *Ixodes ricinus* this number is 35,7% [6].

3.2. TBVE incidence rates

Tick-borne viral encephalitis is one of the most prevalent arboviral infections in Ukraine. People get infected with it through the tick bite or by consuming raw, mainly goat milk.

For present moment local cases of TBVE 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 [7].

During the period of 1955 to 2010 there were only 580 TBVE cases registered, while 132 of them were registered in the period of 2000–2011 (fig. 2). And correspondingly, the indices of

morbidity in Ukraine during the decade varied in the range 0,001 – 0,03/100 000 population, including per oblast from 0–1,5 [8].

During the period of 2003-2010 we observed 223 cases of seroconversion in diagnostic titers of people from 14 oblasts of Ukraine. Among them in Volyn oblast - 77 cases [9].

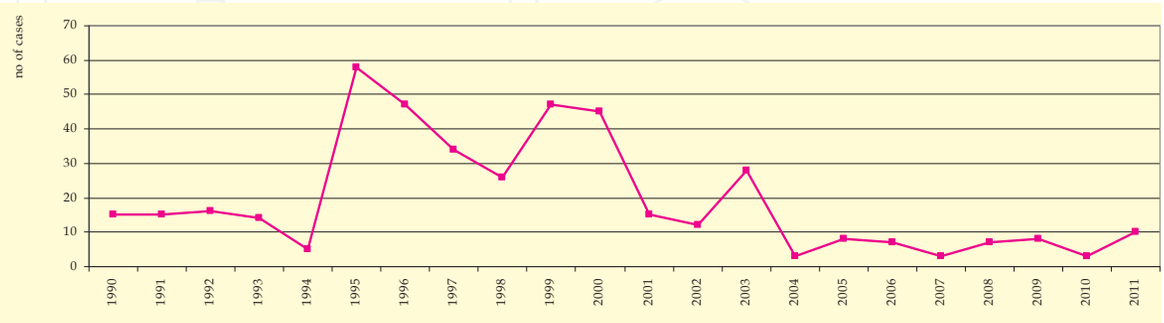

Figure 2. Cases of TBVE in Ukraine (1990-2011)

On the territory of Volyn oblast on the whole, there were 187 cases of TBVE reported. This is almost third of all reported cases for Ukraine (32,5 %).

Within the range of natural foci described, the TBVE morbidity is characterized by a sporadic occurance, its clinical course is similar to western noso-geographic form of the disease. The considerable part of foci forms of TBVE was reported from Ukrainian Polissya (Volyn, Zhytomyr and Kyiv oblasts) [10].

The most active natural TBVE foci, which manifested itself with group morbidity, was detected in Ratne district of Volyn oblast. It was confirmed by isolation of TBVE virus strains from *I. ricinus* ticks and results of antigen screening in *D. reticulatus*, *I. ricinus* and body organs of *Apodemus agrarius*.

During the period of April-October 1995, there were more than 80 patients hospitalized, with fever, and the air-ways and central nervous system lesions. The largest part of cases was reported during the period of June-September, which is related to the berries-mushrooms season.

The largest part of cases appeared in residential areas that are in the close proximity to the forests and is caused by tick bites.

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 TBVE (32,0 %) were due to a consumption of raw goat and cow's milk and its products. The development of a severe and complicated clinical forms of a disease was more common in terms of the transmitting way of infection ($P<0,05$).

In general TBVE 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 (fig. 3), coordination disorders, insignificant quantity of paralytic forms and cases of a development of a chronic disease.

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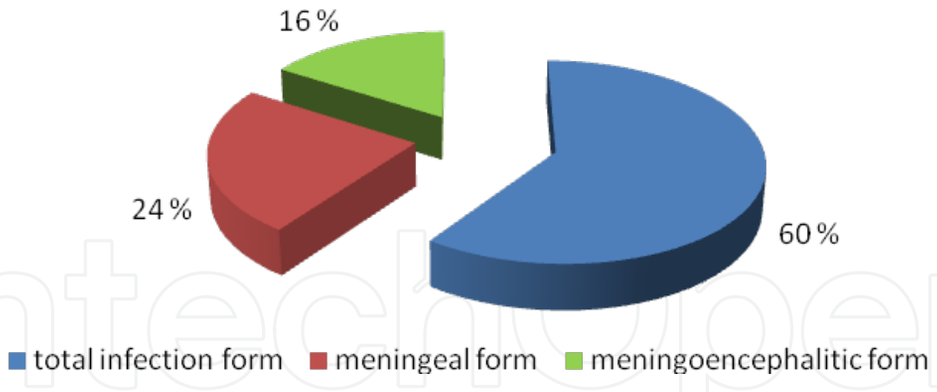

Figure 3. The main clinical forms of TBVE in Volyn oblast

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 TBVE" [12].

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 TBVE 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 ($P>0,05$).

We found that TBVE area includes Ratne and some more districts, which is confirmed by new cases reported, positive results of TBVE antigen screening in *Ixodid* ticks and rodents, and positive immune layer among healthy population in Kivertsi, Kovel, Rozhysche, Lyuboml, and Lutsk districts [13].

4. Ixodid tick-borne borreliosis (Lyme Borreliosis)

4.1. Natural foci of ITBB

In the course of our investigation of *I. ricinus* and *D. reticulatus* ticks collected in Kivertsi, Ratne and Turiysk districts of Polissya in 1998-2011, natural infectioning with *Borrelia burgdorferi s. l.* was identified in 19,8 % of *I. ricinus* and 3,8 % of *D. reticulatus* on the average. The highest prevalence of infected *I. ricinus* – 25,0 % - was identified in Kivertsi, Ratne (19,3 %) and Manevychi (16,7 %) districts, while the lowest rates were reported from Turiysk - 6,7 %. Sixty-two population units in all 16 districts of the oblast were found ITBB enzootic.

4.2. Population immunity

The evidence of the endemic status of ITBB natural foci on the territory of the oblast were collected in terms of serologic screening of 2122 persons among healthy population of five districts of Ukrainian Polissya (Kivertsi, Kovel, Manevychi, Ratne and Rozhysche) and three districts of a Forest-Steppe zone (Volodymyr-Volynskyi, Ivanychi and Lutsk) (table 1).

Seropositive layer of screened persons was within the range of 18,6-45,6 % (the mean value for oblast was 28,6 %), thus exceeding 10 % threshold - the estimated level of active natural foci of Lyme-borreliosis in other districts [14]. More than 20 % of population in 5 out of 12 screened districts of Volyn oblast (Volodymyr-Volynskyi, Gorohiv, Kovel, Lutsk and Ratne were found to have higher titres of Ig G antibodies (1:400-1:1600).

№	Districts	Total of observed patients	Found positive:			
			n	%	incl. in titres 1:400-1:1600	
					n	%
1	Volodymyr-Volynskyi	114	52	45,6	49	43,0
2	Gorokhiv	99	30	30,3	30	30,3
3	Ivanychi	20	5	25,0	0	0
4	Kamin-Kashyrs	59	11	18,6	10	16,9
5	Kivertsi	452	124	27,4	80	16,9
6	Kovel	206	80	38,8	37	18,0
7	Liubeshiv	111	31	27,9	31	27,9
8	Lutsk	194	64	33,0	57	29,4
9	Manevychi	347	80	23,0	64	18,4
10	Ratne	418	108	25,8	96	23,0
11	Rozhysche	49	12	24,5	11	22,4
12	Staro-Vyzhva	53	14	26,4	6	11,3
	Total	2122	609	28,6	471	22,2

Table 1. Seroprevalence of ITBB in human probands from different areas of Volyn oblast

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The same districts had on the average 1,6 times higher level of the specific antibodies among the group of high professional risk (forestry workers), which was anticipated. This can be expained by the permanent being in natural foci, they contact with infected ticks more often (table 2). The antibodies were detected in 129 out of 281 (45,9 %) of the screened persons.

№	Districts	Total of observed patients	Found positive:	
			n	%
1	Kivertsi	46	29	63,0
2	Kovel skyi	74	25	33,8
3	Manevychi	21	9	42,8
4	Ratne	39	24	61,5
5	Rozhyshche	65	26	40,0
6	Staro-Vyzhva	36	16	44,4
	Total	281	129	45,9

Table 2. Seroprevalence of ITBB in human risk groups from different areas of Volyn oblast

4.3. Epidemiology

Upon observation of 1117 patients from 15 administrative districts of Volyn oblast, who were suspected of having ITBB or diagnosis which don' t exclude it (primarily with the preliminary diagnosis of TBVE), the antibodies to *B. burgdorferi s. l.* in diagnostic titres (1:100-1:1600) were detected in 267 (23,9 %) (table 3).

№	Districts	Number of patients*	Antibodies found:		Range of morbidity**
			n	%	
1	Volodymyr-Volynskyi	34	5	14,7	3,9
2	Gorokhiv	20	3	15,0	1,9
3	Ivanychi	76	11	14,5	3,7
4	Kamin-Kashyrsk	18	2	11,1	2,7
5	Kivertsi	150	21	19,0	3,6
6	Kovel	127	28	22,0	3,5
7	Lokachi	19	3	21,4	4,4
8	Lutsk yi (incl. Lutsk city)	262	92	35,1	5,3
9	Liubeshiv	18	3	16,7	8,3
10	Liuboml	14	3	21,4	7,5
11	Manevychi	31	5	16,1	2,3
12	Ratne	225	72	32,0	12,6
13	Rozhysche	62	7	11,3	4,3
14	Staro-Vyzhva	14	2	14,3	3,2
15	Shatsk	47	7	14,9	5,9
Total		1117	267	23,9	2,1

* - number of patients observed with the fever and a tick bite

** - range of morbidity (mean for 2000-2011 year, per 100 000 population)

Table 3. Results of serologic revealtion of ITBB patients in Volyn oblast

According to the data of clinically-epidemiological survey of 267 laboratory-confirmed cases, we determined the main clinical manifestations and epidemiologic peculiarities of ITBB.

Almost 80 % (77,9 %) of the patients experienced the tick bite or "unknown insect's bite", which preceded the development of the disease. The incubative period in the course of tick borrelioses lasted 10 days on the average-from 3 to 45 days.

Seasonal character of tick borrelioses - spring-summer, which responds to the period of seasonal activity of *I. ricinus* ticks. First cases are reported in April, peak of prevalence (45,0 %) is observed in June, July and August, the latest new cases come out in November. Thus the season of the highest risk of infectioning lasts for 6-8 months - from April to November. If we compare encephalitis and tick-brome borreliosis, we can see that the cases of ITBB (up to 14-15 %), are reported in winter and early spring, but this is related to the clinical manifestations of 2-3 stages of the disease (fig. 4).

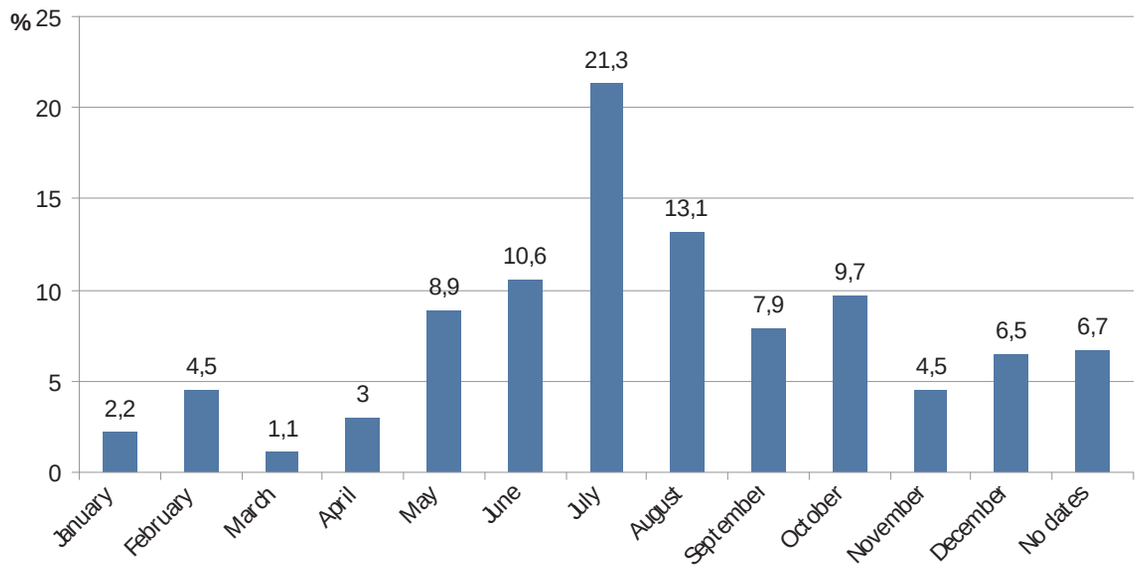

Figure 4. Seasonal distribution of ITBB cases in Volyn oblast, 2000-2011 (n= 267)

Within the structure of patients with the laboratory confirmed diagnosis of ITBB there prevailed the residents of big and small towns of the region - 58,1 % (154), rural population's part made 41,9 % (111). The zones of major infectioning were forest zones and forest-park zones attached to them. Seventy cases of infectioning occurred within the rural/countryside areas (26,2 %). There was a new phenomena in the science of epidemiology observed - a considerable urbanization of natural foci: 13,1 % of patients were infected on the territory of recreation zones (parks, natural relax zones, gardens, etc) of oblast's center - Lutsk city as well as districts' centers. In fact, we have ample evidence to claim that there are not natural foci, but anthropurgic and transient foci of ITBB and other TBI on the territory of Volyn oblast.

Within the gender structure of patients male made 40,2 %, female - 59,8 %.

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All age groups were found vulnerable to ITBB - from the age of 1,2 to 80 years old people. Children below 10 and senior citizens (above 60) get sick less often - 9,0 % and 9,8 % (5 persons) respectively (fig. 5). Age risk group is the one of adult working age, 31-60 years old (52,7 % of cases, 141 persons).

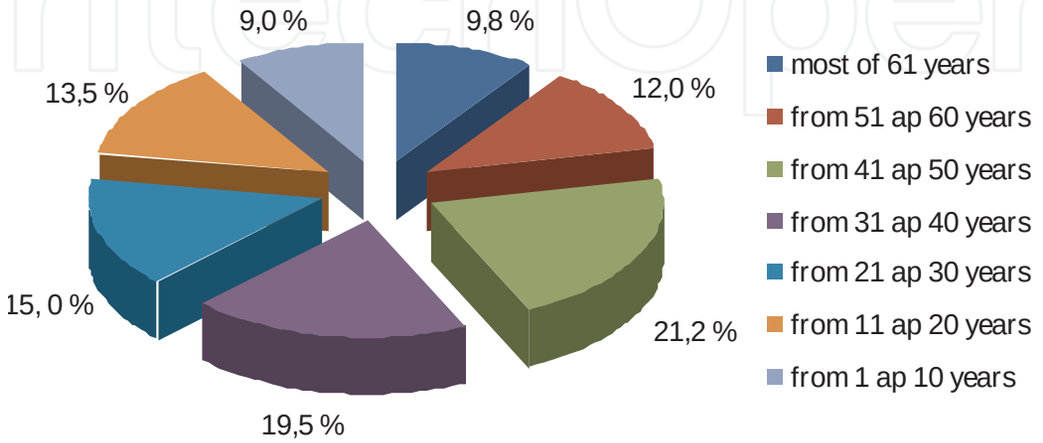

Figure 5. ITBB cases by age in Volyn oblast, 2000-2011 (n= 267)

Concerning the socially-professional structure of the disease, the highest risk of infectioning (62,2 %) was detected among office and labour workers, pensioners and unemployed.

4.4. Clinical manifestations

The spectrum of the main clinical manifestations was analysed according to the reported cases and was found typical for ITBB (table 4).

Clinical manifestations	Detection rates:		
	Volyn oblast		Ukraine
	n	%	%
ME	156	58,4	64,9
Syndrome of total infectioning	182	68,2	43,3
Nervous system lesions	86	37,0	21,4
Locomotor system lesions	56	21,0	24,1
Heart lesions	23	8,6	8,3

Table 4. Frequency and spectrum of ITBB clinical manifestations

The initial clinical manifestation of the disease was erythema migrans (58,4 %) and a syndrome of total infectioning (68,2 %).

A heart pathology was observed in 8,6 % of patients. Ischemic disease, myocarditis and pericarditis etc were diagnosed in regard to the cardio-vascular lesions.

On the other hand, in more than 20 % of the patients the course of the disease was characterised by the manifestations of locomotor system, the lesions of joints (arthritis, arthralgia) and periarticular tissues (bursitis, synovitis, plexitis).

Neurologic lesions, which are considered to be as prevalent lesions in the course of ITBB as erythema migrans in Europe [4], were observed in 37,0 % of patients, which is 16 % more than in Ukraine on the whole. Thus, according to the accumulative data, in regard to the clinical manifestations in the country on the whole, locomotor system lesions take the second place, after erythema migrans, and make 24,1 %. While in Volyn oblast the second most prevalent manifestation is neuroborreliosis. Taking into consideration the known fact, that there is an ethiologic mutual dependence between some genotypes of a causative agent and nozologic types of ITBB [15, 16], it can be assumed that the considerable prevalence of the patients with nervous system lesions can be caused by the prevalence of *B. garinii* within the spectrum of *B. burgdorferi s. l.*, which is believed to be the cause of neuroborreliosis.

On the acute stage of the disease, among the main manifestations of neuroborreliosis there were lesions of both peripheric nervous system (migrating pains, mono- and polyneuritis of scull nerves, polyradiculoneuritis, lack of skin sensitivity of a local character, paresthesia, relapsing neuritis of a facial nerve), which appeared mostly on the acute stage of the disease, and of central nervous system - manifested by meningitis, encephalitis, meningoencyphalitis, arachnoiditis, rigidity of neck muscles, nausea, headache, which manifested on the second stage of ITBB development. It has to be noted that in Ukraine, the major part of complicated lesions of the central nervous system in the course of ITBB is mainly observed in three oblasts – Volyn, Kherson and Zaporizzya.

On the second stage of Lyme Borreliosis the lesions of a cerebral cortex were manifested by different encephalopathia (9,5 %), such as speech problems, coordination, sleep, sight, memory, short-term black-outs. In a part of the patients (3,43 %) we were observing the signs of astheno-neurotic syndrome, such as often headaches, fatiguability, migrains, nervousness etc, some patients (1,47 %) had torpid paresis of facial muscles, in some rare case (0,49 %) the epileptic syndrome developed.

Cerebrospinal fluid has lymphocitaric pleocitosis, number of cells - dozens and hundreds in 1 mkl; lymphocitis make 70-100 % of total amount of cells, quite often, especially in the course of meningoradiculitis, there is an increase in protein amount - sometimes more than 1-2 mmol/l.

4.5. Neurologic manifestations with or without a erythema migrans

The peculiar feature of neuroborreliosis in Volyn oblast is the lack of the migratory erythema at the initial stage of the disease in 81,4 % of patients, which approximately equals the number

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for Ukraine - 80,9 %, and also the manifestations of total infectioning syndrome - hyperthermia, fatigness, dizzyness in 21,4% (for Ukraine on the whole - 24,1 %).

Overall, the analysis of the clinical course of non-erythemic forms of ITBB and comparing it to erythemic forms, shows that the course of the former was more complicated with the involvement of infectioning of other organs and systems, than that of the latter (fig. 6.)

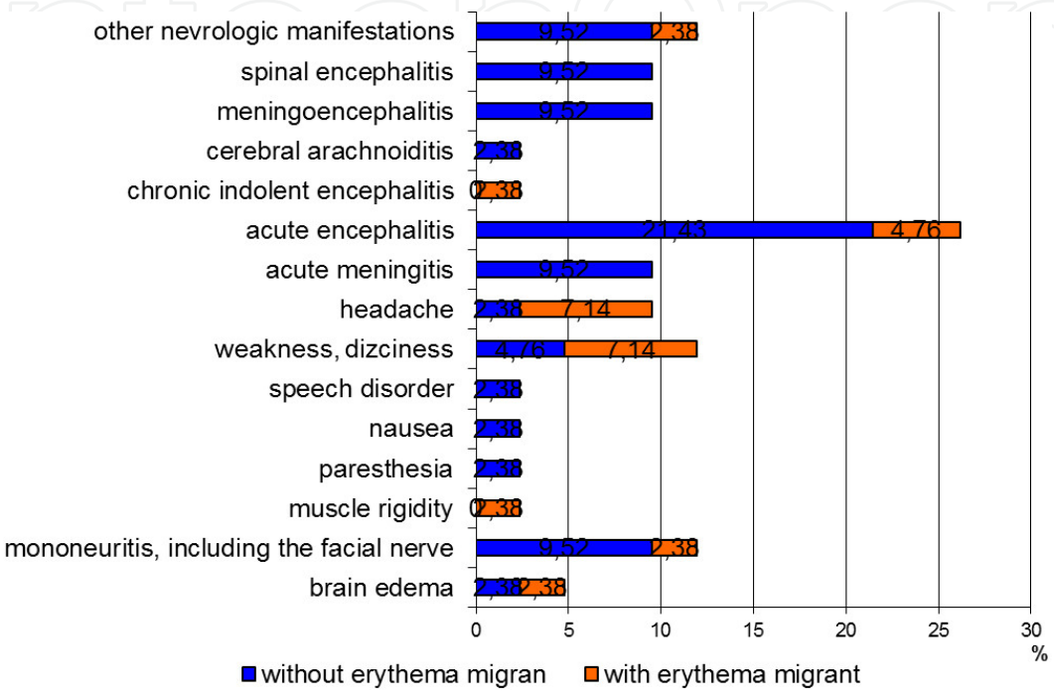

Figure 6. Spectrum of neurological manifestation in patient of erythemic and non-erythemic forms.

There were observed certain differences such as the syndrome of total infectioning with higher and continuous fever, which needs to be confirmed by a larger studies. The symptoms as the headache and dizcyness were observed 1,5 times more often, syndrome asthenovegetative-1,3 times more often.

As for the gender structure, male prevailed and made 53,5 %, while the part of female was 46,5 %. The age of patients was fluctuating of 1,2 up to 80 years, but neurology pathology was observed in children under 10 (18,6 %), teenagers (16,3 %) more often, while the largest group (40,7 %) was made of the persons of working age: 31-40 (25,6 %) and 41-50 (15,1 %) years old.

Up to 50 % of the patients with the borreliosis lesions of the nervous system were sick in the period June-October after the incubatory period, that lasted from few days to few weeks.

Taking into consideration the neuroborreliosis manifestations (neurologic lesions) observed in one third of the patients, we conducted a target serologic examination for ITBB of the patients of out-hospital departments of Volyn oblast. In the course of the examination of 107 patients with the neurologic lesions (hemyparesis, paresthesia, myalgia), the antibodies to Borrelias were detected in 20 (28,9 %), among them 10 cases (27,9 %) - had it in higher titres.

In some patients (6,86 %), the course of the disease and the character of neurologic manifestations (acute outset, temperature reaction, rigidity of neck muscles, fading of reflexes, inflammation of CLS, etc), Lyme Borreliosis was very similar to TBVE, especially in its encephalopoliomyelitic manifestations, which lead to the preliminary diagnosis of TBVE, which was not confirmed by the further serologic tests. Similar indicators of the disease are observed in some regions of Russia [17], but are manifested very rarely in patients from other countries.

4.6. Mixed infections of TBVE-ITBB

The presence of causative agents of different diseases (TBVE, ITBB, HGA) in parazyte systems, common vectors (*I. ricinus* and *D. reticulatus* ticks) and host-reservoirs (*Myodes glareolus* and *Sorex araneus* etc) with certain residing areas of each, predetermine similarities in epidemiologic structure of these infections. It is proved that one ixodid tick can contain 5-7 pathogenes at the same time [18]. The main social factors, predetermining the main features of TBVE, ITTB and HGA are also similar. Given all these facts, it may cause regular simultaneous infectioning of people with several causative agents.

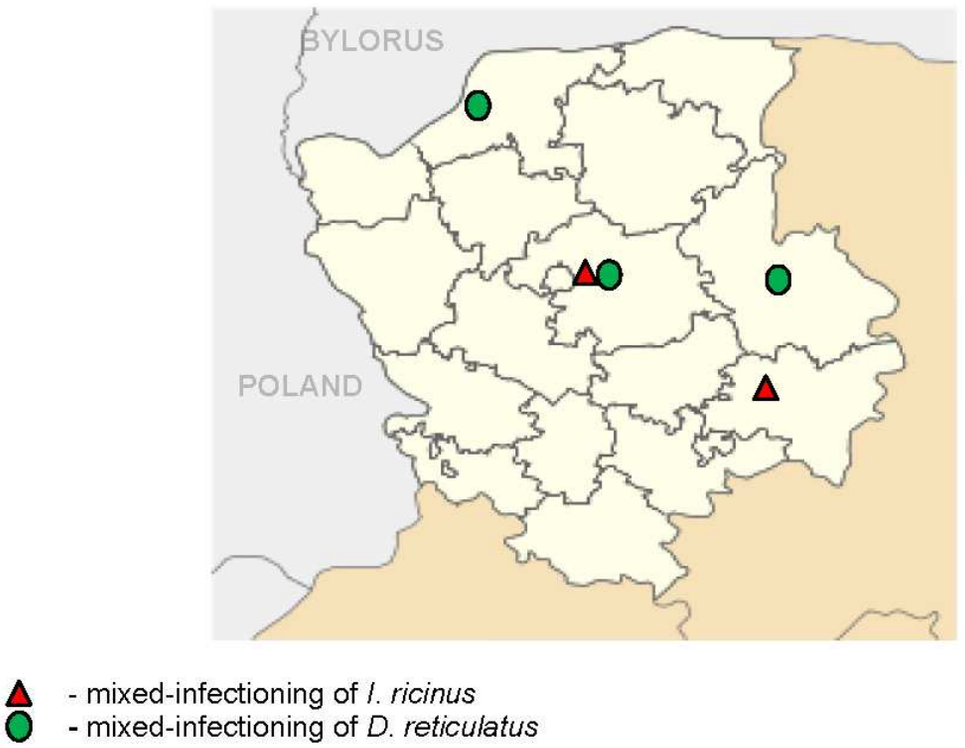

Figure 7. Connected natural foci of ITBB and TBVE in Volyn oblast

Retrospective analysis showed that the considerable part of cases with the preliminary diagnosis of TBVE, was, in fact, the cases of neuroborreliosis, including mixed infections of TBVE and neuroborreliosis.

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In Volyn oblast, we got the evidence of the existance of territory-connected natural foci of ITBB and TBVE for 6 districts (fig. 7). The existance of population-connected foci of these two zoonoses is proven by cases of mixed-infectioning of *I. ricinus* ticks with TBE virus and *Borrelia burgdorferi s. l.*, which we detected in Kovel and Kivertzi districts, and *D. reticulatus* ticks - in Manevychi, Ratne and Kovel districts.

On the territory of oblast out of 267 cases of ITBB 29 (10,9 %) appeared to be TBVE mixed infection: the majority of them were found in Ratne (18) and Lutsk (8) rayons, few of them in Kivertzi (2), Kovel (1), Lyubeshiv (1) and Shatsk (1) districts [19].

5. Conclusions

1. North-West region of Ukraine is one of the regions with high prevalence of TBVE and ITBB.

2. There are an active natural foci of TBVE and ITBB in Ratne district of Volyn oblast. High epidemic potential is confirmed by isolation of TBE virus strains, detection of the antigen of a causative agent in vectors and reservoirs, as well as by a population morbidity.

3. We found the evidence to confirm the previously made hypothesis as for the existance of polivector (binar) TBVE and ITBB foci in Ukraine, where the circulation of the causative agent is done by two dominating species of *ixodids - Ixodes ricinus* and *D. reticulatus*, which makes the risk of a population infectioning higher. The range of vertebral-reservoirs of causative agents of Lyme Borreliosis and TBVE, includes not only those known in Europe, but also other species of small mammals.

4. The TBVE incidence manifests itself by regular sporadic cases of the disease and outbreaks. In terms of clinical manifestations, there dominate forms with total-infectioning with the non-malignant course of the disease (60 %). Meningeal forms make 24 %, meningo-encephalitic -16 %.

5. ITBB is an endemic disease for Volyn oblast, caused by the presence of *I. ricinus* and *D. reticulatus* ticks there. High prevalence rates are reported in Kivertsi, Lutsk, Manevychi, Ratne, Rozhysche districts, were 16,7 % up to 25 % of ticks are infected with the ITBB causative agent, the rates of population contact with ticks is within 30-40 %, risk group makes 40-60 %, mean indicator of the incidence (based on many years of surveillance) is 0,39-4,33 per 100 000 population.

6. The range of clinical manifestations of ITBB includes most of symptoms, which are described in scientific literature: starting from the erythema migrans, and syndrome of total infectioning to nervous system lesions, as well as lesions of locomotor and cardiovascular system. The distinctive feature of the manifestations of the acute form of the disease is high prevalence of non-erythemic forms (41,6 %) as well as high percentage of cases with nervous system involvement (37,0 %).

7. There were numerous combined natural tick-borne mixed infections foci detected: TBVE, ITBB, HGA. First time in Ukraine, there were cases of all possible combinations of mixed infections of these nosologic forms found.

8. The findings of our study serve as a theoretic base for the surveillance over the extremely dangerous natural foci infections in the country, implementation of anti-epidemic and preventive measures into the practice of a health care system, search for the new approach to diagnostic, prevention and treatment of these infectious diseases.

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