

## NATURAL SCIENCES

## REVIEWS AND LECTURES

**Vilyuisk encephalomyelitis.  
Infectious nature of the disease and pathogenesis  
(Review)**

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**Abstract.** Vilyuisk encephalomyelitis (VEM) is a degenerative disease of the central nervous system, in the acute form it is manifested by meningoencephalitis that tends to develop into a prolonged chronically progressive pan-encephalitis. A rapidly progressive variant of the disease is characterized by fatal consequences within 12 months. Despite 60 years of investigation of Vilyuisk encephalomyelitis by experienced scholars, the cause of the disease has not been yet clarified, however, there are some obvious clinical, pathological and epidemiological evidences that VEM is a contagious infectious disease that presents as latent and chronic infections. In the structure of VEM, a special place is occupied by unique variants of the disease with a two-phase course of the disease. We assume that this group of diseases is caused by serotypes Theiler's murine encephalomyelitis virus (TMEV). If VEM is caused by TMEV, it is likely that these viruses have a special mechanism of transmission to susceptible populations of Homo sapiens. The disease may be caused by the non-structural L\* protein of the virus.

**Key words:** Vilyuisk encephalomyelitis, study history, infections, Human Vilyuisk encephalomyelitis virus (HVEV), TMEV, nonstructural L\* protein.

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**Introduction**

The first mention of the disease resembling Vilyuisk encephalomyelitis (VEM) appeared in R. K. Maak's work "Vilyuisk district of the Yakut region" in 1887 [1], and only in 1926 T. A. Kolpakova, a member of the expedition of the USSR Academy of Sciences that studied the Yakut ASSR, provided a scientific description of the clinical picture of the disease. The findings and results of this expedition were published by T. A. Kolpakova in 1933 [2]. Fundamental research of the disease was initiated in 1951 by P. A. Petrov, the first neurologist who began to study the disease. He managed to give a

detailed description of the clinical picture of the disease [3, 4]. In 1954 S. M. Kirova, the staff member of the Neurology Department of the Leningrad Military Medical Academy, agreed with the opinion expressed by Yakut neurologists P. A. Petrov and A. I. Vladimirtsev, which stated that this disease is a completely new and unknown disease of the human nervous system. In 1956, Professor A. N. Shapoval was the first one who called this disease "Vilyuisk encephalomyelitis" [5].

The disease has been registered only among the indigenous population of Yakutia (the Sakha, Evens, Evenks). This circumstance generated a number of hypotheses that deny the infectious nature of the

disease. Some researchers have suggested that VEM is a clinical feature of the manifestation of multiple sclerosis among the indigenous population of Yakutia, although this data was not issued in the form of a scientific article, it should be mentioned.

We put forward the anthroozoonotic hypothesis of VEM. The article is being prepared for publication. In this paper, we clarify the details of this hypothesis, analyze the historical aspects of the studies that highlighted the infectious nature of the disease, and discuss the role of Theiler virus (Theiler's murine encephalomyelitis virus TMEV) in the development of the disease. The infectious nature of the disease has been stated since the beginning of a broad scientific study of VEM. This point of view was supported by A. N. Shapoval [5] K. M. Chumakov [6], P. A. Petrov [4], A. I. Vladimirtsev [7], L. G.

Goldfarb [8], D. K. Gajdusek [8]. It should be noted that the main provisions of the infectious nature of the disease were scientifically substantiated by a group of researchers headed by L. G. Goldfarb [9].

**Purpose of research.** An attempt to identify the causes of failures in the isolation and identification of the infectious VEM agent.

**Materials and methods.** We reviewed scientific literature on the infectious nature of VEM, as well as personal observations of the patients with VEM made within the last 30-40 years.

**Chronology of research.** The study of the nature of Vilyuisk encephalomyelitis (VEM) can be divided into three periods: the Early (Soviet period), the Modern period, which can be divided into the following stages: the 1st stage of research – the period of intensive scientific study of VEM (1992 -

**Table 1. Chronology of VEM research**

The early period of research VEM	
1854 (1887)	Maak R.K. firstly described some disabled aboriginal affected by “bokhoror”, disease resembling VEM.
1926 (1933)	Kolpakova T. A. first described the clinical picture of the disease, but regarded it as a complication of the flu.
1951	Petrov P. A. began to work as the first neurologist in the focus of VEM and drew the attention of the health authorities of Yakutia to this disease. He first discovered and clinically described VEM.
1954	The staff of the neurology Department of the Leningrad military medical Academy Kirov S. M. came to the conclusion that VEM is a completely new, unknown disease of the human nervous system.
1956	Professor Shapoval A. N. for the first time called the disease “Vilyuisk encephalomyelitis”.
1954 – 1957	Under the leadership of Shapoval A. N. and Chumakov K. M. conducted research to determine the viral etiology of the disease.
1960	Sarmanova E. S. reported the isolation of 11 viral isolates from clinical specimens isolate, V-1 designated as “Vilyui virus”, and then it was renamed to “Human virus Vilyuisk encephalomyelitis” (VHEV)
1965 – 1996	Goldfarb L. G. for the first time isolated SCA1 from the group of patients with VEM, continued the study of Platonov F. A.
1968	Vladimirtsev A. I. organized the encephalitis Department, which will become the center of scientific research of VEM, in addition, he developed a system of dispensary observation of patients and risk groups.

Continuation of table 1

Modern period Stage I (period of intensive study of the causes of VEM)	
1992	President of the Republic of Sakha(Yakutia) M. E. Nikolayev approved the programme of research: "Biology of Vilyuisk encephalomyelitis»
1996	the First international scientific conference on VEM, in Yakutsk
2000	Vladimirtsev V. A. unified clinical manifestations of VEM
2000	Second international scientific conference on VEM, in Yakutsk
2004 – 2007	Grant of the Ministry of Health. ISTC project № 2539 R: "study of Vilyuisk encephalomyelitis: isolation of etiological agent, development of rational methods of treatment and prevention."
2006	Third international scientific conference on VEM, in Yakutsk
2008 – 2010	The Order of MH RS(I) "The Study of the etiology and pathogenesis of Vilyuisk encephalomyelitis" on 2008 – 2010
2011	IV international scientific conference on the VEM, in the city of Yakutsk
2014	Goldfarb L. G., Vladimirtsev V. A., Renwick N., Platonov F. A. published the monograph "Vilyuisk encephalomyelitis»
2016	V international scientific and practical conference " problems of Vilyuisk encephalomyelitis and other neurodegenerative diseases: modern issues of etiology and pathogenesis»
Stage II (the period of curtailment of research VEM)	
2018	Reorganization of the Health Research Institute Into the Research Center of the NEFU Medical Institute, termination of funding for VEM research. Since 2010, there have been no reliably confirmed cases of VEM. The anthrozoootic hypothesis of VEM is formulated.

2016); the 2nd stage of research, dating from 2018, is characterized by decrease of scientific interest to VEM (see table. 1). Fading interest can be explained by the fact that classical clinical manifestations of the disease has not been observed since about 2010.

### Possible causes of VEM

The search for the causes of the disease was carried out in two ways: the search for antibodies to infectious agents in the blood serum and experi-

mental inoculation of experimental animals with biomaterial of patients.

Thus, antibodies against a variety of infectious agents were detected in the serum of patients with VEM (see table. 2) causing encephalomyelitis of different etiology. But it should be noted that antibodies against malaria were found in low titers in 100% of the sera studied [10], for other infections the percentage of positive results was not high, and in some cases the percentage of positive results did not differ from the control (see table. 2). It is not

**Table 2. The results of the search for pathogens of infectious diseases among patients with VEM**

Type of pathogen	Name	in %	Method	Source
1	2	3	4	5
Virus	Virus VEM (V-1)	Neutralized by the serum and 47.0% of patients in the VEM	Isolated by inoculation of CSF in patients with VEM in mice	[13]
Virus	Vilyuisk Human Encephalomyelitis Virus (VHEV)	Unknown	The strain transferred from the Institute of Poliomyelitis (Moscow) Selected from old Sarmanova 's materials	[14]
Virus	Theiler virus	Unknown		[15]
The Simplest (Protista)	Acanthamoeba castellanii	Positive in one patient	Allocated by infection of laboratory animals with brain tissue of a woman with VEM	[16]
Virus	Herpes viruses	+	Greene Chip, Agilent Technologies, VEM patients	[17]
Virus	Flaviviruses	+	Greene Chip, Agilent Technologies, VEM patients	[17]
Virus	Parechoviruses	+	Greene Chip, Agilent Technologies, VEM patients	[17]
Virus	Alpha viruses	+	Greene Chip, Agilent Technologies, VEM patients	[17]
Bacteria	Borrelia (Borrelia spp.)	3.3% (2)	The sero-screening test VEM patients	[10]
The Simplest (Protista)	Causative agent of babesiosis (Babesia spp.)	1,6%(1)	The sero-screening test VEM patients	[10]
The Simplest (Protista)	Acanthamoeba castellanii	1,6%(1)	The sero-screening test VEM patients	[10]
The Simplest (Protista)	Токсоплазма	1,6%(1)	The sero-screening test VEM patients	[10]
The Simplest (Protista)	Malaria parasites	Weakly positive 100,0% (61)	The sero-screening test VEM patients	[10]
Virus	Alphaviral equine encephalomyelitis	18,0% (11)	The sero-screening test VEM patients	[10]
Virus	San Louis encephalitis virus (Flavivirus)	9,8% (6)	The sero-screening test VEM patients	[10]
Virus	California encephalitis virus	16,4% (10)	The sero-screening test VEM patients	[10]
Virus	Herpes simplex 6	33,3% (12)	The sero-screening test VEM patients	[10]
Virus	Bourne	6,6% (4)	The sero-screening test VEM patients	[10]

1	2	3	4	5
Virus	Herpes SV-40	33,3% (6) control 11,1% (2)	PCR amplification of specific sites of herpesviruses, cerebrospinal fluid and blood serum of patients with VEM	[18]
Helminths	Toxocara canis	70,0% (7), control 13,0% (1)	Immunoblotting of blood serum of patients with VEM and healthy	[19]
Virus	Varicella Zoster	50,0% (5), control 50,0% (4)	CSF ELISA	[19]
Virus	Herpes simplex 1	40,0 (4), control 38,0% (3)	CSF ELISA	[19]
Virus	Herpes simplex 2	40,0% (4), control 63,0% (5)	CSF ELISA	[19]
Bacteria	Borrelia	53.8% (21), control 22.0% (9)	Sum of pathological levels of IgG / IgM Borrelia, blood serum	[20]
Bacteria	Borrelia	10.3% (4), control 0,0%	Positive immunoblot IgG / IgM Borrelia, blood serum	[20]
Bacteria	Eubacteria	82,0% (9), control 27,0% (2)	Positive eubacterial PCR, CSF	[20]
Bacteria	Borrelia	27,0% (3), control 14,0% (1)	Pathological levels Of IgG Borrelia (> 3 U / ml), CSF	[20]

clear how to explain it. In Yakutia the last case of malaria was diagnosed in 1964 [11], and the last malaria was eliminated in the Vilyui group of districts. Currently, 33 species and 4 genera of blood-sucking mosquitoes are distributed on the territory of Yakutia. One of them is a subspecies of *Anopheles messeae* Fall., as well as a large genus of *Aedes*, which are carriers of vector-borne diseases [12].

In 2000 a group of researchers (Retroviral Research Laboratory of the Pacific Biomedical Research Center, the University of Hawaii at Manoa, Laboratory of Central Nervous System Studies of National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA and the Research Institute of Health of the Sakha (Yakutia) Republic, Russia) made the following conclusion based on the data of serological studies: "... it is possible to exclude from the list of candidates viruses transmitted by arthropods (including alphaviruses, flaviviruses and bunyaviruses), retroviruses." The authors ex-

cluded from the list of likely candidates infectious agents transmitted by ticks (*Lyme* bacteria, protozoa Babesiosis), *Treponema pallidum*, *Leptospira*, *Toxoplasma Gondii*, and parasitic worms (*Taenia solium*, *Echinococcus granulosus*, *Srongiloides stercoralis*, *Toxocara canis*, *Trichinella spiralis*). It was noted that: "Among the few interesting cases, it can be noted that serum antibodies to the Born disease and *Plasmodium* antigens were detected in VEM patients" [10].

It should be noted that numerous attempts to isolate the infectious agent by inoculation of experimental animals with biological material of patients with VE, ranging from Guinea pigs and ending with primates were not successful (see table. 3).

#### What is the relationship between malarial *Plasmodium* and VEM?

According to the data of R. Yanagihara et al. (2000) from 61 patients with VEM, all patients had a weak reaction to antibodies of one of the four

**Table 3. Experiments on vaccination of biological material of patients with VEM experimental animals [21]**

Type	Number of animals	Inoculum
<i>Mustela putorius furo</i>	8	10% brain suspension
<i>Cavia cobaya</i>	10	10% brain suspension
<i>Monodelphis domestica</i>	12	Cerebrospinal fluid
<i>Saimiri sciouius</i>	10	10% brain suspension
<i>Cebus</i>	2	Cerebrospinal fluid
Rabbit	15	10% brain suspension

strains of malarial *Plasmodium* [10]. We suggest that malarial *Plasmodium* may be the cause of virus virulence factors in the human body. One of the main candidates for the etiological factor of VEM, in our opinion, is Theiler virus. The virus, identified by S. E. Sarmanova [13] and called Vilyuisk Human Encephalomyelitis Virus (VHEV) [14], is defined as a contaminant [22]. Russian virologist Prof. G. G. Karganova isolated a new virus from the same material preserved by E. S. Sarmanova [15]. According to the RNA sequences, this virus differs from VHEV (G.G. Karganova's personal communication). It should be noted that the recently discovered Sikhote-Alin virus (SAV) viruses and Syr Darya valley fever virus were identified as Theiler viruses [23].

It is believed that Theiler's murine encephalomyelitis virus (TMEV) is not virulent to man, but it is possible that the virus is the cause of development of symptoms of Vilyuisk encephalomyelitis. It should be indicated that viruses have a system of protection from the interferon. In the course of evolution viruses have acquired species-specific defense strategies of the funds of the host defense. For example, TMEV produces unstructured L\* protein. This protein is encoded by a portion of RNA that is outside the reading and thus does not contain various genomic regulators. According to F. Sorgeoos et al. L\* protein is species-specific and inhibits RNase L providing innate host immunity [24]. It was found that the L\* protein HMEV does not

inhibit human RNase L [22]. This gene encodes the enzyme ribonuclease L, whose activity is induced by interferon. The activated enzyme lyses all RNA in a cell (both cellular and viral).

The relationship of the malaria plasmodium and VEM is probably due to the swamp, where the malaria mosquitoes bred. According to our anthropozoonotic hypothesis VEM (article in press), the disappearance of *Arvicola Terrestris* (water rat, qutero in Yakut) on the territory of Yakutia coincides with a decrease and cessation of the VEM incidence of the population. And this rodent is a reliably established TMEV reservoir. The same reservoirs for malaria mosquitoes breed are the habitat of *Arvicola Terrestris*, of course, will be contaminated with its feces contained TMEV viruses.

### The etiology of VEM

L. G. Goldfarb et al. [9] found out that VEM originated in the left-bank areas of the Vilyui river near lake Mastakh in a mixed Yakut-Evenk population and then spread to the right bank of the river and populated areas of Central Yakutia. The authors suggested that the disease originated in a population whose ancestors moved to Vilyui at the beginning of our era, according to the views of the famous Yakut historian and ethnographer G. V. Ksenofontov. Using haplogroups and haplotypes of STR-loci of Y-chromosome and mtDNA it is possible to determine the genetic history of the popula-

tion of Mastakh Yakuts and VEM patients. This is important in determining the cause of the disease.

Above we mentioned that all the attempts to infect experimental animals with biological material of patients were not successful. What is the cause of failure? We see three reasons for this:

1. Perhaps, patients' materials gained for inoculation of experimental animals did not contain the virus, due to the fact that the replication of the virus occurs only in the acute period of the disease, when feverish. The body is likely to eliminate the virus rapidly, but the further development of the disease is supported by unknown infectious virus molecules, probably incorporated into the genome of infected cells of the patient, or as in the case of the experimental model of TMEV infection, the virus persistence is preserved in very low titers [25];

2. Another mechanism infection. In the case of VEM, we are dealing with a completely new, previously unknown mechanism of transmission of an infectious agent, and the infectious agent is a previously unknown molecule or agent of protein nature;

3. Only genetically predisposed people (including experimental animals) can be susceptible to the virus, or it is transmitted only from person to person.

A completely new, previously unknown mechanism of transmission of infectious agent in VEM is based on a number of scientific facts:

\* Infection of experimental animals with biological material of patients with acute, subacute and chronic stage of VEM was not successful. See. table. 1.;

\* Patient A., 35 years old with dz: Encephalomyelitis with suspected VEM in the acute stage in the first weeks of the disease, a lumbar puncture was made and the resulting CSF was sent to a laboratory in Bethesda (USA). The patient A. recovered and was discharged from the hospital. In the laboratory of CSF a hamster was inoculated and it fell ill and died of paralysis. A thorough search for an infectious agent, including viruses, was not successful. Subsequently, patient A. died of VEM, but the pathomorphological study of the brain was not performed;

\* Development of VEM (subacute and chronic phases and/or stages) has a two-phase character. The

relative well-being (stage of intermission) is continued by the second most difficult phase. Inoculation of experimental animals with biomaterials of patients received from the second phase did not cause the development of the disease. Thus, it can be assumed that further progression of the disease could occur without replication of the virus. But, nevertheless, we cannot exclude that many experiments failed due to the very low titer of the virus in the biological materials of patients.

### Pathogenesis

According to the conclusion of A.P. Avtsyn and A.A. Zhavoronkov [26] pathomorphological changes in VEM are characterized by the presence of a distinct inflammatory component and "corresponds to the definition of the disease as a non-purulent focal encephalomyelitis with serous meningitis". Inflammatory changes had been observed since the initial description of the disease. Inflammation of the soft meninges of the brain lead to spikes that causes obliteration of subarachnoid spaces [27], obstruction of outflow of CSF and the development of hydrocephalus [28]. Autoimmune processes are involved in the pathogenesis of VEM [29, 30, 31], but they can be attributed to secondary ones according to pathomorphological, laboratory and clinical data with a high degree of confidence.

In VEM intrathecal production of oligoclonal IgG was detected, which is consistently present for more than 30 years after the onset of the disease [32, 33]. Diagnostic test showed sensitivity - 93%, specificity - 80%. This test has been implemented as one of the main tests of differential diagnosis of VEM with non-inflammatory degenerative neurological diseases.

Patients with VEM have severe and persistent inhibition of interferon system, phagocytic dysfunction and deficiency of T-cell immunity [34, 35]. According to the authors, all these defects increase susceptibility to bacterial and viral infection. But, nevertheless, inhibitors of interferon Genesis were discovered in blood serum, and the reason for the decline in the level of T-cells in peripheral blood is not clear. Most likely, it is secondary. The secondary nature of the oppression of interferonogenesis

is confirmed by these genetic studies. Thus, among patients with VEM of acute and subacute forms, on the contrary, alleles of the gene predominate, contributing to a high level of interferon production [36].

However, the presence of increased susceptibility to bacterial and viral infection cannot be excluded in patients with VEM [37]. There is no need to go far for examples. Thus, only certain susceptible strains of experimental mice are susceptible to TMEV mouse virus [25].

The VEM patients lack antibodies against HMEV virus [9], but according to E.S. Sarmanova serum of 47% patients neutralize the virus [13]. It

should be noted that the TMEV genome is approximately 8100 nucleotides in size, which encodes 12 proteins, including the non-structural protein L\* [38]. When conducting electron microscopy of the brain preparations of VEM patients with acute and subacute forms of the disease, filamentous formations were detected. Similar structures were found after vaccination of a patient's biomaterial with an acute form of the disease in the cytoplasm of infected cells in the form of beams with a diameter of 20-30 nm, consisting of separate filaments, and in the intercellular space - formless filamentous structures. During infection of transplantable cell cultures and experimental mice with the biomate-

**Table 4. Comparative characteristics of TMEV infection and VEM**

Characteristics	TMEV Infection[25]	VEM
Spatial gradient	Two-phase	Two-phase
	Early acute disease with encephalomyelitis	Early acute disease with encephalomyelitis
	Late chronic demyelinating disease	Chronic stage, with the defeat of white matter throughout the Central nervous system; death of neurons, the defeat of gray matter
Topography	Early acute disease	Coincides
	Lesions of gray matter	Coincides
	Chronic demyelinating disease	Secondary demyelination
	Lesions of the white matter of the spinal cord	-
Morphological feature Inflammatory infiltrates		
Inflammatory infiltrates	Early and chronic phase	Present (early active and chronic inactive lesions)
Perivascular inflammation	Present (General)	Present (General)
Inflammation of gray matter	(Only at an early stage)	Present (General)
Violation of the blood-brain barrier	Present (early onset)	Present (early onset)
Demyelination	Is present (chronic phase; the tendency to the spinal cord)	Present (chronic phase, throughout the CNS)
Oligodendroglial damage	Present	Present
Remyelination	Present	Present (usually abortive)



rial of both patients, the latter did not get sick, and cytopathogenic action was not observed in cell cultures [15]. It should be noted that in experimental models of TMEV infection in laboratory mice in the brain by electron microscopy, an accumulation of neurofilament structures inside the neurons was detected [39]. In experiments with TMEV, the unstructured proteins of the L\* virus are responsible for biphasic and chronic encephalomyelitis [25, 40, 41]. It has been established that the L\* protein causes apoptosis of infected mammalian cells [42], is a vector for transporting alien sequences to the central nervous system [43].

### Features of clinical manifestations

VEM is divided into: acute, subacute and chronic stages of the disease. The clinical picture of the disease specific for VEM is characterized by a biphasic course: acute onset, a short intermission period and a second chronic phase. This feature is characteristic of VEM compared with other viral encephalomyelitis. Usually, the acute phase of the disease, which ended in "recovery", is again aggravated and goes into the chronic phase, and often with the transition to panencephalitis. This picture completely coincides with experimentally induced Theiler viruses (TMEV) encephalomyelitis [25]. Probably, these forms of VEM are caused by TMEV-like viruses that are different from human Saffold viruses by the presence of unstructured protein L\*. In the experiments, it is these unstructured proteins that are responsible for biphasic and chronic encephalomyelitis, as we noted above. When comparing the clinical picture of VEM and experimentally caused TMEV encephalomyelitis, it is impossible to say that the clinical manifestations of both diseases are completely coincidental, but there are also common signs. Perivascular infiltrations almost coincide. In both cases, T-lymphocytes predominate over rare B-lymphocytes. The most interesting thing is that the two-phase diseases coincide. Both experimental encephalomyelitis TMEV and VEM have a current like meningoencephalitis with inflammation and necrosis (see Table 4). Comparison of the clinical picture of Bornovirus infection and VEM allows to conclude that the pathology caused by Bornovirus

resembles the acute form of VEM described by P.A. Petrov [3].

### Is Vilyui encephalomyelitis a threat to human biological safety?

Currently, no one can answer this question in the affirmative or vice versa. To this question, a Creutzfeld-Jakob center employee responded: "Who knows, AIDS has also begun as a regional problem" [44]. In the recently published monograph "New biological threats", Joan Callahan included VEM in the list of encephalitis as a dangerous disease [45].

These fears are confirmed by alarming facts. Thus, in 2002, an article published in the journal *Nature*, in connection with encephalomyelitis disease of laboratory assistant A. europoid nationality, it was noted that VEM "... left its ethnic cell" [44]. Unfortunately, in recent years there have been four deaths of polyethnic patients from encephalomyelitis of unclear origin. The diagnosis was not confirmed by pathological research due to the fact that not a single pathologist had agreed to conduct autopsies due to suspicions of the deceased prion nature of the disease. Currently, it is authentically possible to make a diagnosis of VEM only by pathological studies of autopsy material of the brain of patients. It should be noted that one woman from those deceased patients was examined on possible VEM some years ago and had contact in her youth with VEM patients.

Swine and bird flu are viruses that have been spread in pigs and birds, but not in humans, until a mutation has occurred. In 2009, the first influenza pandemic, designated as porcine, occurred. WHO, in its Guidelines on Managing the Risk of Pandemic Influenza, warns: "Experience with the emergence of such a variety of different influenza strains that transmit from animals to humans illustrates the highly unpredictable nature of influenza viruses such that assumptions about where the next influenza virus with pandemic potential will emerge, or what its characteristics will be, cannot easily be made" [46]. It should be noted that the pandemics of AIDS, Ebola and Zika originated in human populations as a result of the transfer of the virus from zoonotic reservoirs. Thus, it was established that

Human immunodeficiency virus 1 (HIV-1) originated in Central Africa as a result of the transition from chimpanzees to humans during the cutting of carcasses of hunting trophies infected by the Simian immunodeficiency virus (SIV) subspecies of chimpanzees *Pan troglodytes troglodytes* [47]. The cause of the ebolavirus epidemic Zaire (ZEBOV - Zaire ebolavirus) in West Africa 2014-2015 there was a rural-type epidemic spreading to urban agglomerations, and the reservoir of the virus was the flying foxes (Chiroptera, Megachiroptera) eaten by the local population [48]. The Zika virus was identified in 1947 and infects primates and is transmitted through blood-sucking mosquitoes of the genus *Aedes*, until the 2007 epidemic, sporadic cases of human disease were noted. Having emerged in Oceania, the epidemic quickly spread to Southeast Asia, Africa and Latin America. After the epidemic, a sharp increase in the incidence of Guillain-Barre syndrome in Oceania and microcephaly in Brazil, although a causal relationship has not been established [49].

If we draw an analogy with the situation of Vilyuisk encephalomyelitis, the development of the

VEM epidemic [9] resembles the pattern of spread of the above-mentioned infections, which from sporadic morbidity increased to a pandemic. Thus, for hundreds of years or perhaps for thousands of years among the indigenous population of the region there had been a custom of consumption of *Arvicola terrestris*, regarded as a delicacy, and considered to be a proven source of TMEV [50]. For hundreds of years the disease had been observed near the lake Mastakh of the Vilyuisk Ulu of Yakutia. However, in the early 70th, it began to spread to densely populated areas of Central Yakutia [9]. Probably it happened because pathogen had gained the ability to be transmitted from person to person. It is necessary to note that the virus mutates and may circulate in nature. The facts do not exclude the possibility of a highly contagious virus resulting in high mortality. In this context, we share the concern of researchers such as P. A. Petrov, A. Vladimirtsev, L. Goldfarb regarding the threats posed by VE mutation and spread. Thus, the causes and etiopathogenesis of VEM has not been not determined yet, and fundamental medicine must be aimed at solving the problem due to its global importance.

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