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ФЕНОМЕН ПРИРОДНОЙ ОЧАГОВОСТИ ЗООНОЗНЫХ ИНФЕКЦИЙ: НОВАЯ ГИПОТЕЗА

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Ключевые слова: природный очаг, зооноз, возбудитель болезни, чума, вид-эдификатор, фаза динамики численности, эффект «бутылочного горлышка», энзоотогенез, инновационные технологии.

Аннотация. В статье рассматривается проблема феномена природной очаговости зоонозных (особо опасных) инфекций. Предлагается гипотеза энзоогенеза очаговой инфекции на основе эффекта «бутылочного горлышка», которая согласуется с накопленными научными фактами.

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Keywords: natural focus, zoonotic disease, pathogen, plague, species-edificator, population dynamics phase, "bottleneck" effect, enzootogenesis, innovative technologies.

Abstract. The article considers the problem of the phenomenon of natural foci zoonotic (especially dangerous) infections. A hypothesis of enzoogenesis of focal infection that based on the effect of the "bottleneck", which is consistent with the accumulated scientific facts.

The problem of epidemics that took thousands of people's lives with sudden disease always excited in mankind. It is known, about 2,400 years ago, Hippocrates first came to the conclusion that the cause of the mass plague may be a special substances getting into the human body called miasma, concentrated in space and soil. Only in the XIX century microbiological breakthrough discoveries made it possible to identify the objective nature of epidemics. It became clear that people may be affected by the deadly disease being on any particular area – population or nature.

The founder of the doctrine of natural foci of human and animal diseases, academician Y.N.Pavlovsky in the 30-ies of the last century, formulated this concept as a certain land of the geographical landscape in conjunction with a set of carriers or donors and vectors of the pathogen of the disease [1]. Under the carriers and donors he meant warm-blooded animals, and vectors - arthropod invertebrates. Other original definition of the essence of natural foci of disease belongs to V.N.Beklemishev [2], who considered foci of infection as the pathogen population together with all range of vertebrates, which supports the population - the hosts and arthropod vectors. Subsequently, to the present time in the literature there were still a lot of similar interpretations of the term "natural focus of infection". However, they are all complement or clarify the above mentioned definition and have no principle originality. It is important to emphasize that all these works have given the original idea of the spatial structure and patterns of current epizootic and epidemic processes, as well as contributed to the development of the theory and practice of natural foci of zoonotic infections. However, nosogeography of such human infectious diseases, as plague, tularemia, leptospirosis, rabies, Crimean-Congo haemorrhagic fever, pasteurellosis and others are still poorly understood and are of important scientific and practical problem.

Over 22 years (1971-1993), the author studied the natural foci of tularemia, plague, leptospirosis in Kazakhstan and Central Asia, working in the Central Asia Research Institute for Plague Control of

Ministry of Health of the USSR and the Kazakh Scientific Research Anti-Plague Institute of Ministry of Health of the Republic of Kazakhstan. Published a number of scientific works on the spatial structure (topology) of tularemia and plague foci as well as leptospirosis [3,4, 5, 7, 8, and others]. In addition, the author was a consultant on the zoological work at Aralomorsk, Ural and Guriev anti-plague stations in conjunction with well-known specialists in plague V.P.Hrustselevski and A.S.Burdelov; executive in charge of the annual "Review and forecast of epizootic state of natural foci of plague in Central Asia and Kazakhstan" and co-author of "Guide to the landscape and epizootic zoning of plague natural foci of Central Asia and Kazakhstan", as well as the executive in charge of republican methodical documents [6, 9, and others].In addition, he is the author of environmentally friendly method of controlling a great gerbil by long-term toxic "points", which with 100% efficiency is used as a measure of prevention in advance of the plague around the shift settlements, livestock and wintering sites [28]. For the years there were received the original scientific results, which should be shared with the scientific community.

To a question about the phenomenon of natural foci of zoonoses

Nowadays, thanks to the efforts of many researchers, the natural focus of zoonosis is structured by core separation (elementary focus) and its surrounding infection removal zone. In the core, there is a continuous flow of epizootic diseases, while infection removal zone is a portion of the temporary stay of the pathogen. The area of the core is always smaller than the area of infection removal, and together they provide a common focus area. Generally, the foci areas are calculated in two ways: living area of the main carrier or the maximum area that epizootic had ever covered.

There were also identified the main types of foci: autochthonous - existing outside of human activities; anthropurgic - resulting from human activities and synanthropic-formed within the settlements. In addition, there are the so-called “combined” or “associated” foci, in the case where multiple infections found in a particular area.

The most studied are recognized natural foci of plague in the former Soviet Union. Over the past 100 years,spatial and biocenotic structure of enzootic areas became known. Over time, natural foci of plague with the appropriate names have turned into official administrative structure, a kind of natural and man-made conglomerate formed as a product of regulatory decisions to streamline the ongoing anti-epidemic preventing measures, taking into account the regional natural and geographical factors.

However, there is a reasonable question. If this is a natural focus of plague, it should be always possible to detect the causative agent? But in practice this does not happen. For example, it is believed that focal plague area in Eurasia covering tens of millions of hectares. It is hard to imagine that plague epizootic areas may reach even half of the focal areas. Moreover, for many years a significant epizootic areas remain to be virtually sterile when the results of a wide serological screening can not even detect traces of *Yersinia pestis*. There take place a long inter epizootic period. This means that conception of natural foci of plague or other infections is very relative.

So, it is proposed to consider the problem of enzootic of a territory from the point of view of the "bottleneck" effect. The concept of this effect in population genetics shows a sharp decline in genetic diversity and gene pool of the animal population, which occurs between the two cycles of population dynamics (critical fall and rise). Population abundance curve in the narrowest part is similar to the neck of the bottle and got a figurative name. It is important to note that the originally because of its multiplicity, each population has the maximum and own genetic diversity. But with a catastrophic decline in its population, for example, due to the influence of environmental and anthropogenic factors,the gene pool becomes poor. In the case of increasing of the population, conditions for inbreeding and random variation of allele frequencies in the genotype of the species arise. The most important factor in reducing of genetic variability of a population is genetic drift. Last can be seen in fixing of an allele in genes in animal populations that are in depressed phase. Therefore, in small populations, and there is a decrease of genetic diversity, or gene pool [10].

The main types of the dynamics of the number of animals are postulated by S.A.Severtsov:

- Stable type: corresponds to ungulates and carnivores, with the period of oscillation, or rise and fall of the population - 10-12 years. The life expectancy of these animals is the highest;
- Labile type: corresponds to hares, large rodents (marmots, ground squirrels), small predatory. Period of oscillation varies from 5 to 10 years. Life span animals less than 10 years;

- Ephemeral type: characterized by severe numerical instabilities, with deep depressions and mass outbreaks among the population of small rodents. The frequency of the population dynamics is 4-5 years. Life span no more than 4 years [11].

To date, it is published many works that reflect the patterns of dynamics of the number of animals, related to the influence of epizootic, common to all mammalian species in the natural foci of tularemia, plague, pasteurellosis, leptospirosis, viral infections. Mass disease in populations are recorded periodically, as a rule, among the common species – edificators of forest, steppe, desert and mountain ecosystems.

The edificatory species are the most numerous species of animals, which play a leading role in the structure and functioning of ecosystems (edificator – from Latin language - builder). They influence the range of flora and fauna biogeocoenose, being major consumers of biomass [12]. The main Kazakhstan edificators from *Mammalia* provided in the table.

Table - Types of mammalian edificators of plain and mountain landscapes of Kazakhstan

Systematic status	Zoonotic diseases	Geographical region
Rodents		
Small ground squirrel *(Spermophilus pygmaeus)*	Plague	Steppes of Volga and Ural interfluve and Transurals
Grey marmot *(Marmota baibacina)*	Plague	Terskey Alatau
Great gerbil (*Rhombomys opimus*)	Plague	Caspian desert, Aral Sea region, Kyzylkum, Moyynkum, Southern Balkhash
Midday gerbil (*Meriones meridianus*)	Plague	Volga-Ural sands
Tamarix gerbil (*M.tamariscinus*)	Plague	Volga-Ural sands
Red-chickweed gerbil (*M. libycus*)	Plague	Betpak Dala, Ili valley
Water vole (*Arvicola terrestris*)	Tularemia	Forest-steppe and steppe of north and east of Kazakhstan
Carnivorous		
Fox (*Vulpes vulpes*)	Rabies	All Kazakhstan
Hoofs		
Saiga antelope (*Saiga tatarica*)	Pasteurellosis, FMD	Semi-deserts and steppes of the west and central Kazakhstan
Lagomorphs		
Tolai hare (*Lepus tolai*)	Tularemia	Valleys of desert rivers Ili, Chu and Syrdarya

High number of edificatory species observed in the phase of abundance peak has negative impact on the ecology and biology of the populations. D. Chitty, based on the theory of stress or generalized adaptation syndrome (proposed by H.Selye) the first time in 1960 stated genetic damage in vole populations occurring in the phase of their high number [16]. Then there were published several papers on the effects of stress on the incidence of chromosomal damage on the example of the house mouse (*Mus musculus*), water, ordinary (*M. arvalis*) voles and other species [13-15 et al.]. T.S.Shishkina et al., also referring to H.Selye noted that the high number of great gerbils decreases their immunity due to stress from overcrowding and as a result, the virulence of circulating in the population plague pathogens increased. The authors suggest therefore taking into account the virulence characteristics of the strains of this microbe as well as the immune status of animals [17].

It should be emphasized that in the phase of depression of animal species population, there takes place inbreeding in early sibs, then in I and II sibs, that leads to genetic erosion. Due to the laws of genetics, the absolute genetic diversity is possible in the most numerous populations of random mating. The result is an increase in homozygosity, there is a change of gene frequencies and a tendency to consolidate a single locus allele. Thus, inbreeding leads to precipitation of a number of alleles from loci of chromosomes. For example, alleles of the organism responsible for immunity to various infections, and possibly to some environmental factors. Thus, damage in mammalian chromosomes may beoccurred at the peak of population size, but with a decrease in abundance, there is a loss of a number of alleles.

Depressive states of animal population does not preclude the maintenance of single individuals who have a relatively high genetic diversity, which survive in the epizootic. The population increases in numbers again. In the recession phase under the influence of any factor, the gene pool deficiency repeats. Thereby creating the conditions for the re-occurrence of the epizootic.

Finally, the most important. Where do the pathogens affecting animal populations come from? In the inactive (avirulent) stage all of them present everywhere in the soil, water, air, and in the organism of the animals as the part of so-called "banal" microflora and "persistent". The weakness of immunity of animal due to the genetic erosion, in our opinion, provokes a rapid increase in the virulence of the bacterias and viruses, and cause mortality in a population of animals. The spectrum of the determinants of virulence, pathogenicity of various microbes and viruses generated in the species edificators is the result of status of their genetic diversity.

Thus, the main components of enzootogenesis of focal infections are: common species – edificator, phase of its population dynamics and the effect of the "bottleneck" that causes deficiency of genetic diversity. All other are classical concepts: the natural focus of infection, Hostal, Vector, valence of foci become secondary. As well as the dynamics of the epizootic in the space (territory) and in time (chronology), which is characterized by volatility and fragmentation. Nature foci of zoonosis therefore is unstable, with changeable configuration, phenomenon; the trigger epizootics in populations of mammals is previously mentioned genetic syndrome.

The proposed hypothesis earlier was presented on the example of the saiga antelope, which in recent decades has experienced double-effect of the "bottleneck", accompanied by massive pasteurellosis epizootic [18].

To confirm or refute this hypothesis, revealing the cause of enzootic, it is necessary to conduct studies on population genetics of rodents, ungulates and carnivores. This is primarily a molecular genetic DNA analysis techniques using the polymerase chain reaction (PCR), test system for studying the genetic differences of populations using multi loci DNA markers, ISSR test systems to find key genes that control the resistance of species to one or another infectious diseases [19,20]. In other words, the findings of genes responsible for the sensitivity, to plague, pasteurellosis, rabies, etc. pathogens. And on the final stage to carry out diverse experiments to infect animals of different genetic status with pathogens in the laboratory. To study in the enzootic areas the air samples (through bacterial and viral filters), water (open sources) and soil (in the biotops, the burrows of animals) for the detection and study of microbes and viruses, according to morphological, cultural, biochemical, genetic and other characteristics of identical pathogens especially dangerous infections.

About necessity of reorganization of anti-epidemic service

Sanitary and anti-plague system will always be in a great request as long as there is a threat of epidemics of especially dangerous infections. However, it is necessary to be upgraded with the introduction of innovative technologies.

In light of the above hypothesis of enzootogenesis it should be immediately organized a centralized service of the state monitoring of the number of the main objects of the animal world, especially rodents. All account information should be available, stored and practiced in a single coordinating office.

Anti-Plague Service should be fully computerized with a single program with extensive use of GIS technology and remote sensing of enzootic areas, provided with satellite images of very high resolution - Worldview-3 (30 cm / pixel) and the possibility of automatic decryption of dynamics of gerbils, gophers, marmots areas [21 -23]. Required the greater use of short, medium and long-term forecasting of the number of the most important species - edificators - rodents, carnivores, ungulates, lagomorphs. Regularly conduct selective trapping (traditionally for bacteriological and serological studies as well as to determine the level of genetic diversity with the help of DNA analysis). It should mostly be used non-lethal methods of sampling material (wool and waste products) in the format of an international "Convention on Biological Diversity" [24-27].

The full range of selected works in the long term can give an objective opportunity to decrypt the enzootic and rehabilitation phenomenon not only of the plague, but also other dangerous infections.

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ЗООНОЗДЫҚ ИНФЕКЦИЯЛАРДЫҢ ТАБИҒИ ОШАҚТЫҒЫЛЫҚ ФЕНОМЕНІ: ЖАҢА ГИПОТЕЗАСЫ

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Түйін сөздер: табиғи ошақ, зооноз, аурудың қоздырғышы, оба, эдификатор-түрі, сан динамикасының сатысы, «бөтелке құсығының» әсері, энзоотогенез, инновациялық технологиялар.

Аннотация. Мақалада зооноздық (ерекше қауіпті) жұқпалы аурулардың табиғи ошақтығы феноменінің мәселелері қарастырылған. «Бөтелке құсығының» әсері негізінде ошақтық жұқпалы аурулардың энзоотогенез гипотезасы ұсынылады. Бұл гипотезаның қорландырылған ғылыми деректермен сәйкесі мол.

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