

## Original researches

## Retrospective study of rabies epidemiology in Ukraine (1950-2019)

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**Abstract.** During many decades, rabies remained endemic on the territory of Ukraine. In certain historical periods, the epizootic process of rabies developed with the alternate inclusion of different species of animals as a source and a reservoir of the virus which are of great interest to many scientists. Therefore, the purpose of our study was to conduct an analysis of rabies epidemiology on the territory of Ukraine from 1950 to 2019 based on collected reliable archival data. Collected archival data have shown that over the past 70 years sources of rabies infection varied from domestic to wild carnivorous and vice versa with three major epizootic peaks. The first and the highest peak in the entire study period was recorded in 1951 (3 724 cases) and was caused by the spread of the rabies virus solely through dogs. The second peak with lower number of cases was recorded in 1979 (1 594 cases) when the dominant role in the spread of rabies virus turned to foxes. Finally, the third peak in 2007 (2 932 cases) was triggered by the combination of animals (foxes, dogs, and cats) as the source of the pathogen. Considering significant peaks and downturns and the varying degrees of involvement of domestic and wild animals in spreading of the pathogen, we have identified five historically important stages in the development of the epizootic process: the stage of «urban» or «dog» rabies (1950–1959), relative stability (1960–1969), «sylvatic» or «fox» rabies (1970–1990), relative safety (1991–1999), and expansion (2000–2019). At the stage of «urban» rabies dogs played a significant role as a source and a reservoir of the virus. In the epizootic aspect, dogs made up 54.3 % of all rabies cases, while cats and wild animals (wolves, raccoon dogs, foxes, raccoons, martens, and lynxes) – 1.58 % and only 0.05 % respectively. Domestic animals (cattle, pigs, horses, goats, etc.) made up the rest 44.07 %, but they were «victims» and did not contribute to the further spread of the virus. Moreover, in 89 % of cases dogs were a source of rabies for humans. The stage of «relative stability» was marked by decline of epizootics throughout Ukraine and decrease in the number of deaths to 140 per year. «Sylvatic» or «fox» rabies stage was characterized by the involvement in the epizootic process of a new species of animals – the red fox (*Vulpes vulpes*). During this stage the proportion of wild animals in the total number of cases was 33.9%, cats – 17.7%, and dogs – 12%. In 46.5% of cases foxes were the main source of rabies for humans, while cats and dogs in 34.2% and 11.8% of cases respectively. The stage of «relative safety» was marked by the repeated prolonged decline of epizootics and the increasing role of dogs and cats in the epizootic process. The last stage of the expansion took place against the background of the increasing population size and proportion of rabies cases among domestic carnivores (up to 44.6%) and foxes (up to 36.5%), which contributed to the widest distribution of the virus, and remains a significant problem nowadays. While in the period of «urban rabies» vaccination of dogs together with the regulation of their population allowed to reduce the number of rabies cases by 26 times in 15 years, nowadays regulation of fox and domestic carnivores populations in combination with oral vaccination of wild and parenteral vaccination of companion animals, unfortunately, do not give visible result. So, it is extremely important not only to increase the quality of preventive measures against rabies, but also to increase their quantity in order to cover all three major sources of rabies – dogs, cats, and foxes.

**Keywords:** urban rabies; sylvatic rabies; stages of rabies in Ukraine; rabies epizootics; reservoirs of rabies; sources of rabies; dog rabies; fox rabies; preventive vaccination.

## Ретроспективний аналіз поширення сказу в Україні (1950-2019)

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**Анотація.** Протягом багатьох десятиріч територія України залишалася ендемічною щодо сказу. У певні історичні періоди епізоотичний процес сказу розвивався із почерговим включенням різних видів тварин у ролі джерела та резервуару для вірусу, що цікавило багатьох вчених. Тому метою нашої роботи було зібрати достовірні архівні дані в хронологічному порядку щодо поширення сказу як серед тварин, так і серед людей та провести ретроспективний аналіз епізоотичної ситуації зі сказу починаючи з 1950 року на території України. Провівши ретельний збір архівних даних ми виявили, що за останні 70 років джерела збудника сказу змінювались від домашніх м'ясоїдних до диких і навпаки з трьома основними піками епізоотій. Перший і найбільший за весь досліджуваний період пік був зафіксований в 1951 році (3 724 випадки) і спричинений поширенням сказу виключно через собак. Другий пік з меншою летальністю зафіксували в 1979 році (1 594 випадки), коли домінуюча роль у поширенні сказу перейшла до лисиць, і, нарешті, третій пік в 2007 році (2 932 випадки) був спровокований поєднанням у ролі джерела збудника лисиць, собак і котів. Враховуючи значні піки і спади та різний ступінь участі домашніх і диких тварин у розповсюдженні збудника сказу, ми встановили п'ять історично важливих етапів розвитку епізоотичного процесу: етап «міського» або «собачого» сказу (1950–1959 рр.), відносної стабільності (1960–1969 рр.), «сильватичного» або «лисячого» сказу (1970–1990 рр.), відносного благополуччя (1991–1999 рр.) та експансії (2000–2019 рр.). На етапі «міського» сказу показовим була участь собак у ролі джерела і резервуару вірусу, у цьому разі, в епізоотичному аспекті, собаки становили 54,3% від усіх хворих тварин, коти – 1,58%, а дикі (вовки, єнотоподібні собаки, єноти, куниці, шакали, рисі) – лише 0,05%. Домашні тварини (ВРХ, ДРХ, свині та коні) становили інші 44,07%, але були лише жертвами нападів і не забезпечували передачу вірусу сказу. В епідемічному значенні собаки в 89% були джерелом сказу для людей. Етап «відносної стабільності» ознаменувався згасанням епізоотії по всій Україні і зниженням летальності до 140 голів за рік. Етап «сильватичного» або «лисячого» сказу визначався залученням в епізоотичний процес нового виду тварин – рудої лисиці. У цьому випадку частка диких упродовж етапу становила 33,9%, котів – 17,7%, а собак – 12%. В епідемічному значенні основними джерелами сказу для людей були в 46,5% – лисиці, в 34,2% – коти, та в 11,8% – собаки. Етап «відносного благополуччя» відзначився повторним спадом епізоотії і зростанням ролі собак та котів у епізоотичному процесі. Останній етап «експансії» мав місце на тлі зростаючої чисельності популяції та захворюваності домашніх м'ясоїдних до 44,6% і лисиць до 36,5%, що сприяло максимальному розповсюдженню вірусу і становить актуальну проблему сьогодення. Таким чином, якщо в період «міського сказу» вакцинація собак разом з регулюванням чисельності цих тварин дозволила знизити випадки сказу в 26 разів протягом 15 років, то в наш час регулювання чисельності лисиць і домашніх м'ясоїдних у поєднанні з пероральною вакцинацією диких та з парентеральною вакцинацією домашніх тварин, на жаль, не дає видимих результатів, тому на сьогодні вкрай необхідно не просто посилити якість антирабійних заходів, а й збільшити їх кількість, щоб охопити всі три основних джерела збудника сказу.

**Ключові слова:** міський сказ; сильватичний сказ; етапи сказу в Україні; епізоотії сказу; резервуари вірусу; джерела сказу; лисячий сказ; собачий сказ; парентеральна вакцинація; пероральна вакцинація.

## Introduction

Rabies is an ancient infectious disease with one of the highest case fatality rates, causing tens of thousands of human fatalities and millions of cattle deaths annually, worldwide (Selimov, 1978; Cárdenas-Canales's et al., 2020).

Rabies is propagated globally by viruses of Family *Rhabdoviridae*, Genus *Lyssavirus* (Wei et al., 2018). All mammals are susceptible to infection, but lyssavirus reservoirs are represented by several species of *Carnivora*, with viral global diversity and distribution *in toto* driven by a wide variety of the *Chiroptera* (Rupprecht et al., 2011).

Carnivores are the main reservoirs of the virus in nature and dogs play a significant role in the transmission of rabies to humans in most developing countries. Whereas, in developed countries mainly wild animals are responsible for the spread of rabies (Gholami et al., 2017).

Wavefront velocities have been quantified in foxes by Anderson et al. (1981) and Gucht & Roux (2008), in skunks by Kuzmina et al. (2013), in raccoons by Biek et al. (2007), and in vampire bats by Benavides et al. (2016), and generally advance between 10 km and 40 km per year. The main route of RABV transmission to naive animals is by direct inoculation (e.g., bites) inflicted by a rabid host as reported by Fisher et al. (2018), and Vos et al. (2009).

This infectious disease is distributed widely on all continents except Antarctica and demonstrates both host species and geographic variation in viral genetics (Maki et al., 2017). Though, as reported by Rupprecht et al. (2018), Antarctica is believed to be free of all lyssaviruses, but no laboratory-based surveillance has taken place to support this supposition (Picot et al., 2017).

Rabies was endemic in eastern Europe throughout the history. In ancient times and the Middle Ages, the disease was probably distributed in steppe and forest-steppe zones where wild canids predominately maintained its circulation. Undoubtedly, rabies was distributed throughout the tundra zone of Europe before the arrival

of Slavonic peoples. The conditions for independent circulation of rabies virus among dogs (*Canis lupus familiaris*) were absent due to the low population density of dogs and scattered settlements. Historically, wolves (*Canis lupus*) played a significant role in rabies distribution which was the distinguishing feature for the Eastern Europe. Fox rabies had been registered, but it did not attract special attention. Probably, it was not widely distributed, at least in the second half of the 19th century. Landscapes had changed as a result of human activities and, consequently, the distribution of wild canids also changed. Rabies had penetrated forest zones following human settlement and anthropogenic activities. The rabies-affected area progressively extended northwards and, apparently, dog rabies took hold in cities and urban areas during the 18th and 19th centuries. As a result, the social and economic significance of rabies increased and became of greater interest to medical and veterinary specialists. Measures for dog and wolf populations reduction were carried out in some areas. However, state programs and laws for rabies prevention and control were absent (King et al., 2004).

Quoting Botvinkin & Kosenko (2004) a species transformation of the rabies distribution took place after the Second World War. Thus, in 1942 in the delta of Volga river only individual cases of rabies in raccoon dogs (*Nyctereutes procyonoides*) were found, but in the winter of 1945–1946 immense number of rabies cases among wolves (*Canis lupus*) and red foxes (*Vulpes vulpes*) was registered. Moreover, Isakov (1949) emphasized that the raccoon dog was the most affected species. At the same time, wide spread of fox rabies was described in the Crimean Peninsula (Pavlov, 1953). In 1944–1946, rabies epidemic among wolves and martens (*Martes martes*), occurred in Kyiv and Zhytomyr provinces of Soviet Ukraine near the border with Belarus, where fox rabies took place simultaneously (Scherbak & Ryaboshapka, 1978). In 1947, sporadic cases of fox rabies were observed in Moscow and the Tula province (Russian Soviet Republic) as reported by Selimov, (1978). The outbreak of rabies in foxes has been reported in Voronezh province on both banks of the Don in 1945–1946 (Chirkova, 1953). Thus, during

1942–1947, rabies epizootics among foxes and raccoon dogs were simultaneously observed at different points distanced from one another by hundreds of kilometers. In some of these places, for example, in Moscow province and Crimea, fox rabies soon disappeared (Botvinkin, & Kosenko, 2004).

It is considered that the European fox rabies epizootics started from two foci located in East Prussia and in the delta of Volga river (Vedernikov, 1974; Selimov, 1978; Blancou & Aubert, 1991). However, it is not supported by all the facts. Indeed, fox rabies wave moved from west to east and southeast of Ukraine and Belarus (Vedernikov, 1974; Scherbak & Ryaboshapka, 1978). In 1951–1954 a fox rabies outbreak was observed extending from Penza province bordering the Volga to 700 km north of the delta. Perhaps, it is more reasonable to assume that rabies had reached this point from the Don (Voronezh province). In 1949, a fox rabies outbreak was described in the Asian part of the Union of Soviet Socialist Republics (USSR) in Kazakhstan, more than 1 000 km to the east of the Volga delta. Therefore, on the wide territory from East Prussia to the south of Kazakhstan, some independent points of wildlife rabies activity took place during the ten-year period (Kuzmin et al., 2004; Botvinkin & Kosenko, 2004).

According to Kantorovich (1968) the circulation of rabies virus in Eastern Europe was via a single host vector. Thus, in Western Europe the red fox was the main host species, although many other species might act as victims. A feature of Eastern European rabies was the significant role of other canids (wolf, raccoon dog, and corsac fox) which took part in rabies virus distribution. Almost everywhere two or three canid species were affected simultaneously, so virus circulation was evidently maintained by host changes within the canid family. Perhaps the red fox alone provided rabies virus circulation in the steppe zone of Ukraine, where wolf and raccoon dog were almost absent. At the same time, raccoon dog certainly held the second place as a vector and a reservoir of the disease. Attacks by rabid wolves were reported more frequently from the regions with high population density of this predator. The problem of wolf attack remained to the present time in Belarus and many regions of Russia and Ukraine. However, in recent years wolves have not been an independent reservoir of the disease.

In Europe rabies was historically reported in dogs and was progressively eliminated at the turn of the 20th century in most European countries through dog control measures (extermination, movement restriction and muzzling). From the 1940s, the virus adapted to another species – red fox and spread westwards and southwards from the Poland-Russia border to the rest of Europe with a speed of 20–60 km/year as reported by Cliquet et al. (2014).

Since the dissolution of the USSR the rabies situation remained the same. Fox rabies still predominated in Russia, Ukraine and Belarus (King et al., 2004). It was assumed that with an increase of the fox density, the number of contacts between foxes would also increase. Therefore, rabies could spread in the fox population when a certain threshold density was reached, which has led to epizootic emergence (Vitasek, 2012). Consequently, efforts to halt the spread of this viral disease were directed to reduce the red fox population below this threshold. For this purpose, different methods were applied, e.g. hunting, fumigation of fox dens, digging up the cubs, poisoning. However, it was recognized that those methods did not provide good results in the long term (Vitasek, 2012).

Thus, by the middle of 1990s, rabies prevalence among animals has increased again in many Eastern European countries (parts of Eastern Europe). As noted by Grishok (1977), in the 20th century Ukraine was one of the highly rabies endemic Soviet Union republic. However, despite the severe epizootic situation, the country did not carry out primary systematization and analysis of epizootic surveillance data, which were introduced only during the post-war period.

In the early 21st century, the epizootic situation on rabies in Ukraine remained insufficiently controlled with constant

fluctuations in prevalence and significant outbreaks of disease. The analysis of rabies situation demonstrated that unlike some European countries, where rabies was reported only among wild animals, dogs and cats were actively involved in the epizootic process in Ukraine. Therefore, we can observe an enzootic «evolution» to the intensification and consolidation of the «sylvatic» and «urban» rabies (Polupan et al., 2017a; 2017b).

Moreover, Polupan et al. (2019) reported that in 2003, 2005, 2006, 2007, and 2008, over 2 000 rabies cases per year were recorded, 37% of which were found in foxes.

Multiple factors contributed to the spread of rabies among domestic animals. The most important factors appear to be the ecology of foxes, their synanthropy, high density (5–6 foxes/100 km<sup>2</sup>), as well as presence and density of stray dogs, and the contact of foxes with dogs and cats (Maki et al., 2017). Another reason for rabies epizootics was the low percentage of coverage of antirabic immunoprophylaxis in domestic animals (Nychyk et al., 2013). This contributed to a high number of rabies cases in dogs (over 19% of all rabies cases) and in cats (over 25% of all cases) in Ukraine. A particular problem was a large population of stray animals (Polupan et al., 2019).

An increase in the number of rabies cases among domestic carnivores was reflected in the increase of rabies cases occurring in humans. Thus, in the period from 1997 to 2017, in 39.3% of cases cats were the source of rabies, in 29.3% – dogs, while foxes were the source of infection only in 20.7% of cases (Makovska et al., 2018).

Thus, researchers on the one hand, and rabies control services, on the other, should constantly monitor this disease, which is still endemic in animals and humans in Ukraine. To this end, we need to have a thorough understanding of the history of the epizootic process of rabies, to know the causes of epizootics in the past and ways to eliminate them in order to prevent rabies epizootics in the future.

Numerous articles on the epidemiology of rabies in Ukraine have been published, however, there has not been a complete account of the history of the epizootic process of rabies on its territory from the second half of the 20th century to the present. So, the aim of our study was to collect reliable archival data in chronological order regarding the proportion of rabies cases among animals and humans and to conduct an analysis of rabies epidemiology on the territory of Ukraine in the last 70 years.

## Materials and methods

In our work we used materials in archives of the laboratory of neuroinfections of the Institute of Veterinary Medicine of the National Academy of Agrarian Sciences of Ukraine (IVMNAAS) for the period from 1950 to 2018, the L.V. Gromashevsky Institute of Epidemiology and Infectious Diseases of the NAMS of Ukraine and the State Institution Public Health Center of the Ministry of Health of Ukraine for the period from 1945 to 2019 together with the reports from oblast administrations and regional veterinary medicine laboratories of the State Service of Ukraine on Food Safety and Consumers Protection (SSUFSCP) for 2000–2019, as well as information from the WHO Rabies Bulletin Europe.

Since in the postwar period there was no primary systematization and analysis of epizootic surveillance data in Ukraine, and existing data were fragmented and not preserved, we were able to conduct a thorough collection of data on rabies cases in chronological order from 1950.

Data collected after 2014 do not include reports from the Autonomous Republic of Crimea and the occupied territories of Donetsk and Luhansk oblasts of Ukraine.

MS Excel statistical methods were used to process the data. Some curves were constructed in the DataHero program. Choropleths were used to indicate proportion of rabies cases according to the

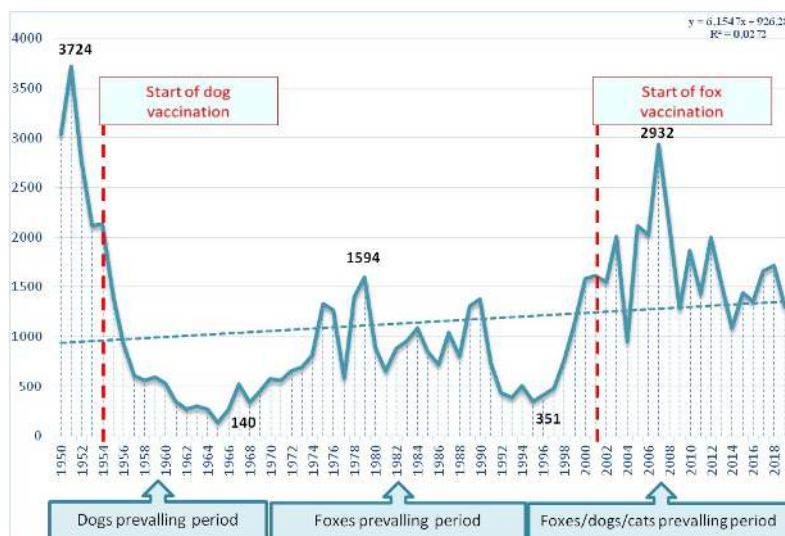


Fig. 1. Dynamics of rabies outbreaks in 1950-2019 in Ukraine

distribution by geographical area, highlighted in different colors or shades according to the mapping data variables. This allowed us to visualize the values assigned to different geographic regions and to display variations or patterns within a specific location.

Color variables were used to indicate the variable data, which was displayed in each of the regions represented on the map in the form of transitions from one shade to another within the same color.

The construction of choropleths was performed in QGIS software 3.4.6. Shape-files were used to construct the cartograms of borders of Ukrainian oblasts from <https://www.diva-gis.org/gdata>.

## Results

During 1950–2019 more than 80 000 rabies cases in animals were registered in Ukraine with three peaks of the disease outbreak. The first peak was in 1951, the second – in 1979, and the third – in 2007 (Fig. 1).

The Figure 1 shows the fluctuation of the epizootic process, which is expressed by sharp increases and decreases in the number of rabies cases among all animal species. Each peak represents the number of cases in different animal species. The interval between the maximum peaks (1951, 1979, and 2007) was 28 years, between medium (1975–1979, 1984–1990, 2000–2007, 2012–2018) – 5–9 years, between the minimum (1967–1970, 1974–1976, 1978–1982, 1987–1989, 2003–2005, 2010–2012, 2015–2017) – 3–4 years.

Subsequently, we determined that in the last 70 years the sources of rabies have changed three times. Each significant peak was registered when the highest number of cases occurred in the population of the most numerous animal species in a given historical period. Thus, in 1950–1969 dogs were the main source of the rabies virus, in 1970–1994 – foxes, and in 1995–present – the main source of the virus was represented by all 3 species of animals: foxes, cats and dogs (Fig. 2).

As can be seen from the chart, number of rabies cases among dogs was quite variable. In the early 1950s it reached its maximum, however, in the late 1960s the number of cases has significantly decreased, while in the 1990s it started to increase again.

In the 1950s rabies outbreaks among foxes and cats were practically not registered. However, in the early 1970s the role of foxes increased sharply and continued to be maintained with small fluctuations. Number of rabies cases in cats also increased at the same time as in foxes and continued to increase steadily annually.

So, throughout the study period, the frequency of rabies occurrence in each animal species was different. Analyzing the archival data, we have determined the proportion of rabies cases among each animal species and the absolute number of deaths among humans at specific intervals. Obtained results are presented in Table 1.

The results presented in Table 1 show that from 1950 to 2019 the role of wild animals (foxes, raccoon dogs, badgers, raccoons, martens, wolves, jackals, lynxes, ferrets, rats, roe deer, bats) and

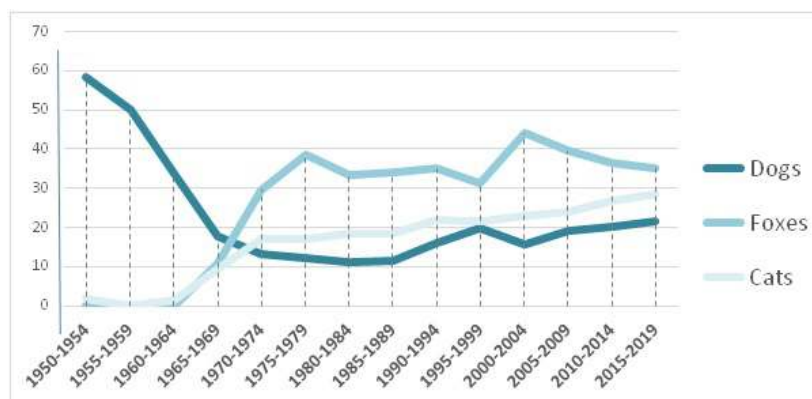


Fig. 2. Frequency of rabies outbreaks in prevailing sources of virus in every 5-year periods

**Table 1.** Proportion of different species of animals in the total number of rabies cases in Ukraine for every 5-year period in %

Years	Total number of cases in animals (absolute number)	Wild animals, %	Domestic carnivores, %			Farm animals, %	Humans (absolute number)
			Total	Total including			
				Dogs	Cats		
1950–1954	13 724	0.05	60.03	58.45	1.58	39.92	980
1955–1959	4 088	–	50.16	50.16	–	49.84	356
1960–1964	1 708	0.12	35.13	33.72	1.41	64.75	111
1965–1969	1 663	10.65	27.45	17.91	9.54	61.90	73
1970–1974	3 292	29.71	30.34	13.36	16.98	39.95	91
1975–1979	6 169	38.50	29.40	12.20	17.20	32.10	63
1980–1984	4 469	33.50	29.30	11.00	18.30	37.20	24
1985–1989	4 712	34.00	29.90	11.50	18.40	36.10	17
1990–1994	3 429	35.00	38.00	16.00	22.00	27.00	12
1995–1999	3 140	28.89 (25.8*)	38.5	18.38	20.13	32.61 (30.73**)	4
2000–2004	7 699	41.67 (37.17*)	38.15	15.96	22.18	20.18 (18.13**)	12
2005–2009	10 560	43.67 (39.02*)	42.93	19.04	23.88	12.97 (11.70**)	15
2010–2014	7 844	41.73 (36.66*)	46.42	19.93	26.49	11.86 (10.19**)	16
2015–2019	7 111	37.87 (33.03*)	51.46	22.18	29.28	10.67 (8.94**)	14

Note: \* – foxes (since 1995); \*\* – cattle

**Table 2.** Main stages of development of epizootic process of rabies in Ukraine (1950–2019)

Stage	Stages (phases)		Name of stage	Number of cases		Species of animals				
	Years			Peak	Decline	Domestic carnivores		Wild carnivores		Farm animals
	Begin	End				Dogs	Cats	Foxes	Other	
I	1950	1959	Urban or dog rabies	1951 (3 724)	–	2 092	86	–	–	1 546
II	1960	1969	Relative stability	–	1965 (140)	37	5	1	1	96
III	1970	1990	Sylvatic or fox rabies	1979 (1 594)	–	154	227	599	89	525
IV	1991	1999	Relative safety	–	1995 (351)	66	68	61	13	143
V	2000	2019	Expansion	2007 (2 932)	–	495	669	1 193	155	417
				–	2014 (1 086)	217	281	421	48	117

cats in spreading of the virus increased by 757 times (from 0.05 to 37.87%) and 18.5 times (from 1.58% to 29.28%) respectively, while the role of dogs and farm animals decreased in 2.6 and 3.7 times respectively. We can see that in the early 1950s, domestic carnivores made up about 60% of all cases and were the only carriers of rabies, whereas remaining 40% of cases were registered among farm animals that were victims, and there were no cases among wild animals at all. At the end of the study (in the 2000s), the proportion of rabies cases among wild carnivores was about 40%, while among domestic carnivores it was about 50%. Hence, nowadays about 90% of carnivores are involved in the spread of rabies virus.

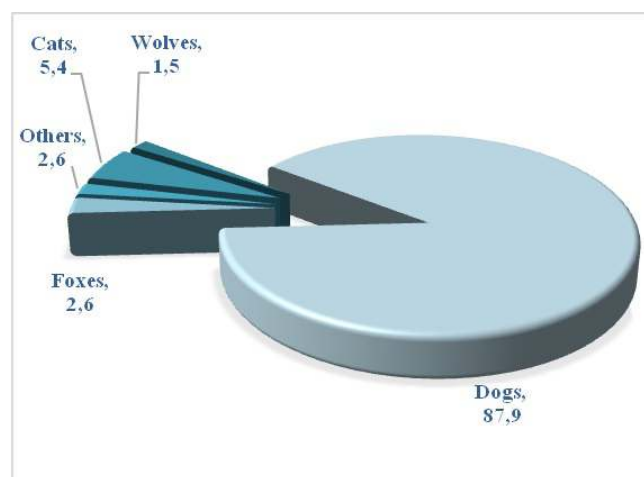
Considering changes in the sources of the virus in different periods and changes in the proportion of all species of animals in the total number of cases, as well as the role of different species of animals in the epizootic process, our further analysis was aimed at determining the main stages of the development of the epizootic process.

Thus, we have established 5 stages, each of which is associated with specific historical efforts of rabies elimination and differs by the number of cases, main peaks and declines of rabies epizootics (Table 2).

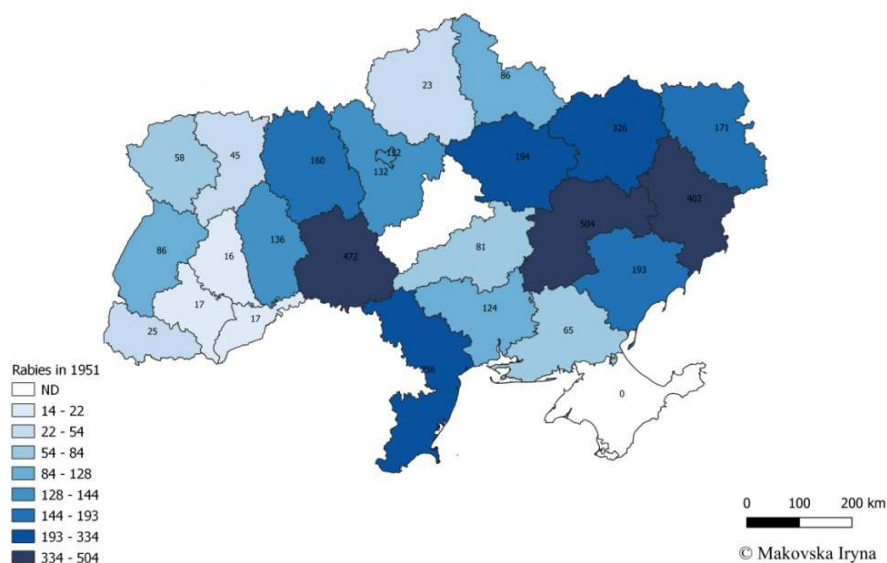
According to our results presented in Table 2, we can see that each stage was characterized by the most important peaks and downturns, which were associated with the dominance of a certain carnivorous species and the degree of effectiveness of control measures. The features of each stage are described below.

**I. Stage of urban or dog rabies (1950-1959)**

The first stage of «urban» rabies was characterized by a high number of rabies episodes in animals and humans, which was strongly pronounced in 1950–1954, when rabies was prevalent mostly in dog population. These were the highest rates for the whole research period with a peak of 3 724 cases and 1 326 endemic units in 1951.



**Fig. 3.** The source of rabies in humans in Ukraine in 1945–1955, %



**Fig. 4.** The geographical distribution of rabies in 1951.

(ND – no data. Dark blue indicates the areas with the highest number of cases and light blue indicates the lowest).

At the same time, in 5 years the overall number of cases in animals was 13 726 and in humans – 980. Among animals the proportion of rabies cases was the highest in dogs – 58.4% and in farm animals – 39.9%, while wild animals had the lowest rates – 0.05% (Tab.1.).

According to archival data from the Center for Public Health of the Ministry of Health of Ukraine in the period from 1945 to 1955 the main source of rabies for humans were dogs (87.9%) (Fig. 3).

Figure 3 clearly shows that at this stage dogs posed the greatest threat for humans, while cats and wild animals constituted minimal risk of infection.

The geographical distribution of rabies cases during the highest peak of epizootics of urban rabies is presented in Fig. 4.

This map shows that during the peak of the urban or dog rabies epizootics the whole territory of Ukraine was endemic. The most affected areas were Eastern regions (most notably Donetsk

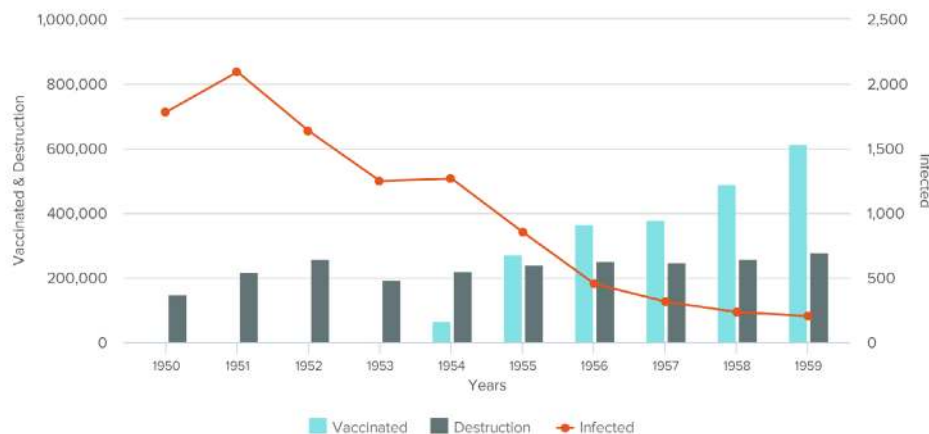
and Dnipropetrovsk oblasts) and Vinnytsia in the central part. In addition, high number of cases was observed in Kharkiv, Poltava and Odesa oblasts. Only the territory of the Crimean Peninsula was free of rabies.

Given the extremely challenging epidemic situation for rabies, the government has begun implementing various eradication measures to eliminate the disease.

1) Preventive vaccination of dogs.

Putting into practice preventive vaccination of dogs was a new additional measure that could ensure the elimination of rabies. In Ukraine, a large-scale campaign for parenteral vaccination of dogs began in 1954, which yielded positive results. Thus, 64 824 dogs were vaccinated in 1954, and by 1959 this number had increase to 612 556 vaccinated dogs per year, i.e. by 9.5 times more, and continued to increase with each year.

2) Catching and shooting stray and feral dogs.



**Fig. 5.** Effect of vaccination and destruction of dogs on the canine rabies outbreaks

During the post-war years, the organization of stray animal trapping units was handed over to the municipal departments of city and district executive committees. Later, by 1959, the Ministry of Agriculture of Ukraine organized sanitary and veterinary stations to control rabies in all regional centers where quarantine measures for rabid animals and animals suspected of being diseased were carried out as well as veterinary and sanitary advocacy.

Much attention was paid to trapping stray animals, especially in hunting grounds. In general, shooting of dogs was carried out steadily in the amount of 250 000 animals a year. Comparison of the effectiveness of dog destruction and combination of destruction with vaccination is presented in Fig. 5.

This chart shows that since 1950 dog eradication measures (shooting) have not significantly reduced the number of rabies cases, whereas with the increase of vaccinated animals (since 1954) in combination with shooting, the number of rabid dogs started to decline every year – from 1 267 cases in 1954 to 203 cases in 1959.

### 3) Extermination of wild carnivorous animals.

Primarily, it was decided to kill wolves, because one wolf could consume about 1 ton of meat a year and was an absolute enemy of wild ungulates (deer, moose, etc.), domestic animals and humans. For this purpose, various methods of extermination were used, such as shooting, baits with poisonous or hypnotic substances, and trapping young animals. A decent financial reward was paid for each wolf. Thus, it was possible to reduce the population of wolves in nature.

### 4) Introduction of requirements for dog owners.

Rules and regulations relating to the keeping of animals were introduced in order to oblige owners to timely vaccinate, put on muzzles on dogs and pay fines in the event of a breach of these rules.

## II Stage of relative stability (1960-1969)

A period of mass spread of rabies was followed by decline of epizootic, which was called the Stage of relative stability. This period was characterized by a sharp decrease in the number of rabies cases among dogs and only sporadic cases among wild animals.

During this time, the lowest number of rabies cases was recorded. Thus, comparing with the peak of 1951 with 3 724 rabies cases, in 1965 the decline in number of rabies cases was observed with only 140 sick animals throughout Ukraine.

Thus, in 15 years the number of rabies cases in animals has been reduced by more than 26 times. At this stage, over 10 years the total number of cases was 3 417 and average annual number of cases was about 340. Herewith, the highest frequency was observed in farm animals.

Despite the significant decline in occurrence, rabies control measures, especially vaccination campaigns, continued to be implemented even more intense (Table 3).

According to the Table 3, number of vaccinated dogs in the late 1950's was about six hundred thousand, while in the late 1960's this number increased to two million animals.

## III. Stage of sylvatic or fox rabies (1970-1990)

The third Stage of sylvatic rabies was characterized by a change in source of infection in both animals and humans. According to our estimates, it began in 1970 when wild animals, mostly foxes, were actively introduced to the epizootic process. Their numbers increased with every single year, which led to a new epizootics of fox rabies with a peak of 1 594 cases in 1979.

The prevalence was strongly pronounced during 1975–1979. Thus, in 5 years 6 169 and 63 cases were registered in animals and humans, respectively. Among animals the highest rates of rabies cases were observed in wild – 38.5% and in farm animals – 32.1%, while in dogs it was the lowest 12.2% (Table 1).

An increase in the proportion of wild animals (mainly foxes) by 6.3 times, cats – by 3.1 times and a decrease in the proportion of dogs by 2 times and farm animals by 1.8 times compared to 1960s, were noted.

The main source of infection for humans at this stage were foxes – 46.5% (Fig. 6).

As can be seen from Fig. 6, the role of dogs and wolves has decreased during the period of fox rabies while the role of foxes and

**Table 3.** Preventive vaccination and destruction of dogs in the Ukrainian Soviet Socialist Republic (USSR)

Years	Vaccinated dogs	Destructed dogs	Rabies cases		Number of endemic units
			Among dogs	Total (among all animals including dogs)	
1950	333	147 500	1 781	3 033	1 215
1951	594	217 900	2 092	3 725	1 326
1952	269	259 600	1 634	2 720	1 047
1953	1 928	191 600	1 247	2 115	814
1954	64 824	221 700	1 267	2 131	766
1955	271 565	240 200	852	1 407	547
1956	366 338	251 400	453	931	404
1957	380 505	249 300	314	600	319
1958	490 049	260 100	233	560	319
1959	612 566	280 800	203	590	276
1960	658 817	251 600	163	527	282
1961	599 122	201 100	123	344	139
1962	829 500	196 400	111	272	156
1963	995 400	217 000	93	297	177
1964	1 278 718	205 600	86	268	140
1965	1 086 348	147 000	37	140	88
1966	1 210 400	109 200	27	215	96
1967	1 566 800	130 100	94	517	293
1968	1 667 300	105 000	72	336	223
1969	1 717 700	113 600	76	455	240
1970	1 972 609	119 600	72	576	396

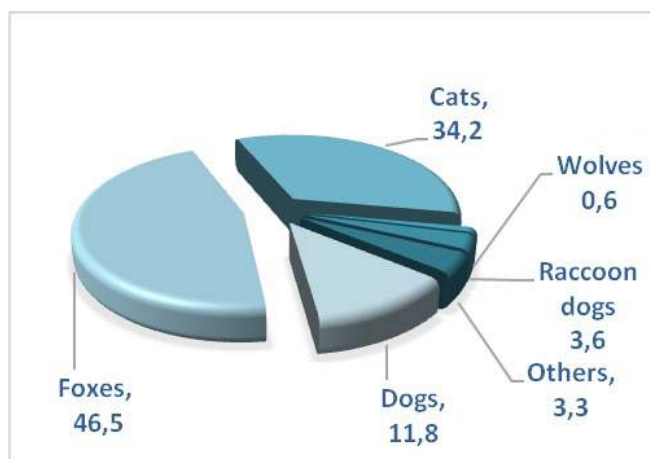


Fig. 6. The source of rabies in humans in Ukraine in 1966–1975, %

cats has increased. In addition, there was a risk of infection from raccoon dogs.

The geographical distribution of rabies cases during the highest peak of the fox rabies epizootic in 1979 is presented in Fig. 7.

This figure demonstrates that eastern oblasts, especially Donetsk, Kharkiv and Poltava, had the highest number of rabies cases during the peak of the sylvatic rabies, while in the west the increased number of cases was observed only on the territory of Khmelnytskyi oblast. The lowest number of cases was recorded in the western oblasts on the border with Poland. In addition, high prevalence was reported in Zaporizhzhia, Kharkiv, Chernihiv, Zhytomyr and Odesa oblasts.

#### IV. Stage of relative safety (1991-1999)

The next stage began after fading of the fox rabies epizootics. At this stage, reduction of number of cases to only 351 animals and 0 humans in 1995 was noted. Thus, in 16 years (1979–1995) it was possible to reduce the number of animal cases by 4.5 times from 1 594 to 351.

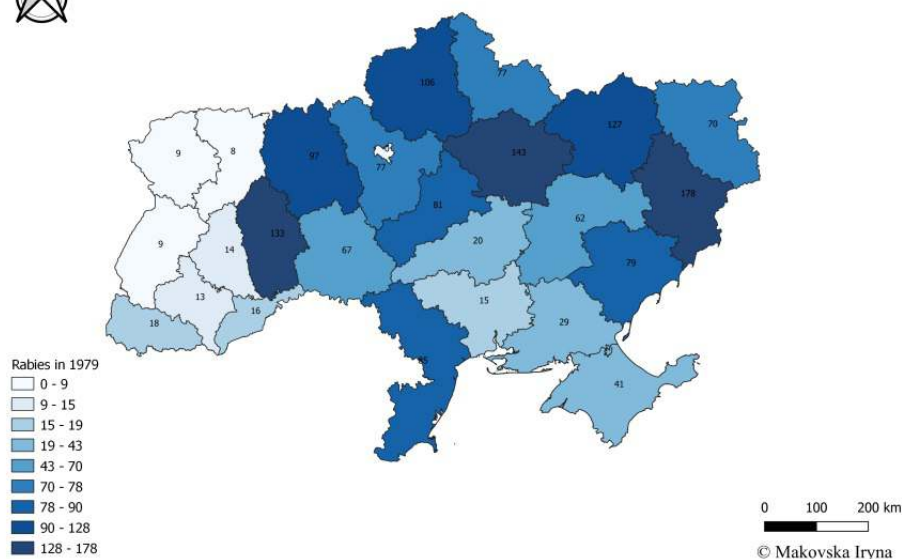


Fig. 7. The geographical distribution of rabies in 1979. (Dark blue indicates the areas with the highest number of cases and light blue indicates the lowest)

Due to the success of rabies control and low number of animal and human cases, we have called this period – Stage of relative safety. However, it lasted for only 9 years.

Given the tense epizootic situation due to the high number of cases among foxes at the previous stage, the focus of rabies control measures was shifted to reduction of fox population, which continued in the 1990s and was carried out by hunters (Fig. 8).

However, as we can see from Fig. 8, the percentage of foxes harvested at the stage of relative safety was negligible.

An important fact at this stage was the prevalence of domestic carnivores as a source of rabies over foxes. A detailed description of the percentage of each species of animals within a 5-year interval is presented in Table 2.

#### V. Stage of expansion (2000-2019)

The most important stage with a peak of rabies occurrence of 2 932 cases in 2007 was a Stage of expansion, characterized by a particular involvement in the epizootic process of domestic carnivores (Fig. 9).

It should be noted that, in contrast to the «urban» rabies where dogs prevailed, at this stage foxes, which accounted for 88.5% of wildlife rabies cases, were the sources and reservoirs of rabies in 36.5% of overall cases. In addition to foxes, domestic carnivores (cats – 25.5% and dogs – 19.1%) were complementary sources of the spread of the virus. Farm animals, which accounted for 13.9% of all outbreaks, were preys (victims).

Figure 9 shows that by 2007 rabies occurrence in wild and domestic animals almost coincided, and after 2007, number of cases among domestic animals increased which has intensified in 2016, where number of rabies cases in cats have exceeded those in foxes and dogs.

This situation has been significantly influenced by parenteral vaccination campaigns for domestic carnivores against rabies. Comparative numbers of vaccinated dogs and cats are presented in Table 4.

As can be seen from this table, over the past 5 years, plans for the vaccination of domestic carnivores have been implemented by 90–100%, apart from 2016, when the percentage of implementation was critical 32–35%. In addition, it should be noted that according



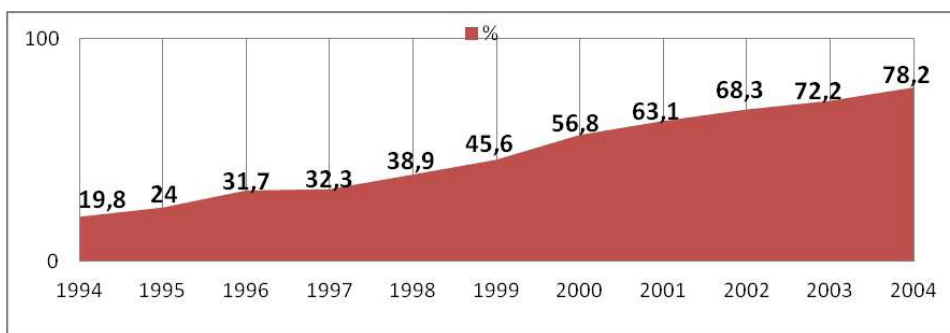


Fig. 8. The number of foxes harvested in 1994–2004, %

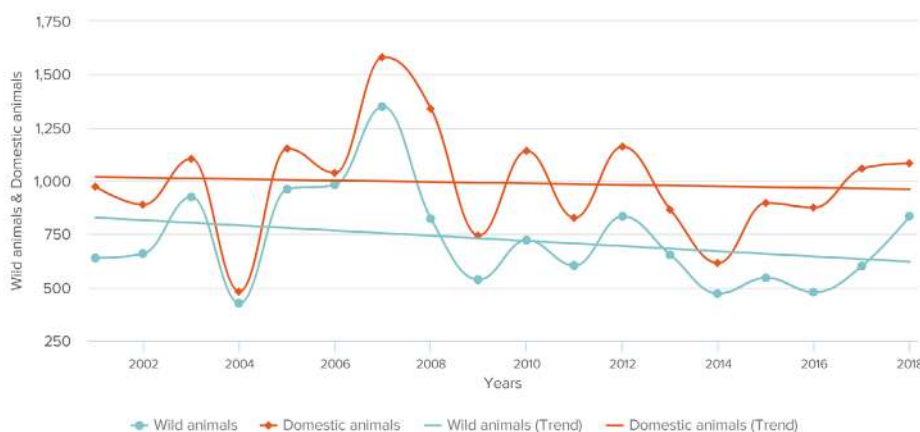


Fig. 9. Dynamics of rabies outbreak in wild and domestic animals in 2000–2019 (orange indicates the number of cases in domestic and blue – in wild animals)

Table 4. Implementation of the plan for the preventive vaccination of dogs and cats in Ukraine in 2015–2019

Years	Animal species					
	Dogs			Cats		
	Planned, million animals	Vaccinated, million animals	%	Planned, million animals	Vaccinated, million animals	%
2015	3.7	3.4	91.9	1.6	1.5	93.7
2016	3.7	1.2	32.4	1.7	0.6	35.3
2017	3.5	3.4	97.1	1.7	1.7	100
2018	3.6	3.3	91.7	2.1	2	95.2
2019	3.4	3.4	100	2.1	2.2	104.7

to the plan, the number of cats to be vaccinated was half that of dogs.

Moreover, at this stage, since 2001, the government has launched campaigns for the oral vaccination of wild carnivores. However, they were carried out selectively on the territory of the highly endemic regions and were funded by the state budget and on the territory of the buffer zone, namely the western regions (Lviv, Volyn and Zakarpattia oblasts) bordering the European Union with the financial assistance of the European Union countries.

In the epidemiological aspect during the specified period the main source of rabies in humans were cats – 38.6% (Fig. 10).

As can be seen from Fig. 10, the role of foxes has decreased during this stage while the role of cats and dogs has increased. In addition, there was a risk of infection from bats.

The geographical distribution of rabies cases during the highest peak of epizootic is presented in Fig. 11.

This figure shows that rabies was widely spread on the territories of the eastern and the southeastern regions, especially

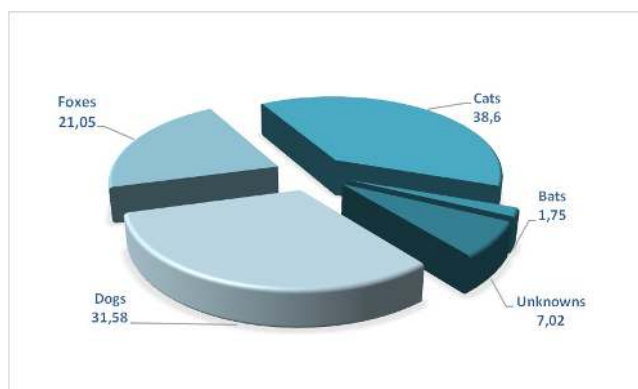
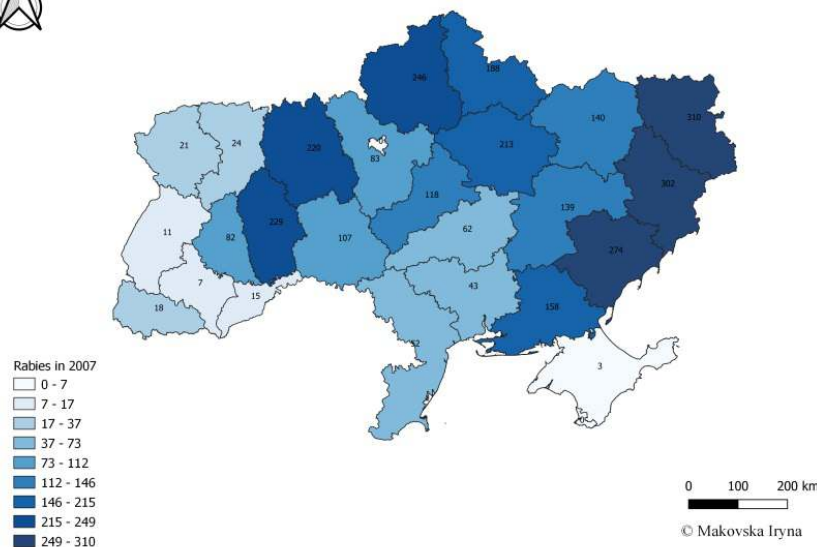


Fig. 10. The source of rabies for humans in Ukraine in 2000–2019, %



**Fig. 11.** The geographical distribution of rabies in 2007.  
(Dark blue indicates the areas with the highest number of cases and light blue indicates the lowest)

in Zaporizhzhia, Donetsk and Luhansk oblasts. In addition, high prevalence was observed in the northern - Chernihiv, in the central - Zhytomyr, and in the western - Khmelnytskyi oblasts. Only territories of Lviv, Ivano-Frankivsk, Chernivtsi oblasts and Autonomous Republic of Crimea were moderately affected.

Thus, currently the epizootic process gains characteristic features of urban rabies stage due to the threatening increase in dog and cat population and number of cases among them, which stimulates the exacerbation of both epizootic and epidemic situations.

### Discussion

This paper presents the results of archival data analysis that showed a permanent fluctuation of the epizootic process of rabies within 70 years. The significant peaks of epizootics are explained by the inclusion of different species of animals into the epizootic process at certain stages. Whereas the significant downturns are explained by the effectiveness of rabies control measures and, at the same time, the extinction of the population due to the disease, especially in the period of epizootics in foxes. According to Mogilevsky (1997), it is known that 70% of fox population die out during the rabies epizootic.

Thus, the first peak in 1951 was triggered by the high number of cases in dog population, and the first downturn in 1965 was the result of mass vaccination campaigns (since 1954) and shooting (since 1950) of dogs.

The second peak was recorded in 1979 as a result of the high number of rabies cases in fox population, and the second downturn in 1995 was the result of the regulation of both fox and dog populations, the continuation of parenteral vaccination campaigns against dog rabies and the extinction of fox populations during epizootics.

The last peak in 2007 was due to the high number of rabies cases among foxes, dogs and cats. The third recorded downturn in 2014 can be explained by the lack of data on the spread of rabies on the occupied territories of Ukraine, namely the Autonomous Republic of Crimea and parts of Donetsk and Luhansk oblasts as a result of hostilities, which affected the lack of data on the rabies diagnosis.

Regrettably, equal intervals of 28 years between major

peaks have not found scientific justification, so it is most likely a coincidence. On the other hand, patterns of the average intervals of 3-4 years between peaks and downturns were highlighted in the works of other national and foreign authors Grishok (1977), Mogilevsky (1997), Botvinkin & Kosenko, (2004), Fooks (2005).

Moreover, it should be noted that during the period of urban rabies, there was a steady decline without increase in number of cases. When foxes joined the epizootic process, constant increases and decreases began to be recorded. According to Selimov (1978) the number of foxes in population changes by 2-4 times every 3-4 years and by 8-10 times every 9-12 years and depends mainly on fluctuations in the number of murines. From these statements we get the following pattern - if we do not regulate the number of foxes cyclically, then every 3-5 years there will be a slightly rise in epizootic curve, and after 9-12 years - significant recrudescence. Thus, the epizootic process will be a constant subject to the «fox» pattern.

The reason for the change in the main source of rabies on the territory of Ukraine in the 1950s was the post-war devastation in the country, followed by the post-war expansion, the settlement of new territories and the extermination of wild animals (wolves, bears, lynxes and eagles). This situation has contributed to the growth of both domestic and stray dog population, as well as to non-compliance with the rules of keeping pets. A major cause was poor vaccination coverage of domestic carnivores.

In this regard, the 4th Session of the WHO Expert Committee on Rabies (1959) considered that preventive vaccination was one of the most important measures to control rabies, and strongly recommended to conduct vaccination campaign covering all dogs in countries where rabies was previously registered (WHO, 2018).

Thus, mass vaccination of dogs began in the early 1950s. The first large-scale field trials were conducted in Kharkiv and Dnipropetrovsk. Vaccination campaigns gradually increased to include every region. For example, in Kharkiv, dog vaccination began in 1955. So far, despite trapping of stray dogs up to 10 000-14 000 annually, the number of rabies cases has not declined significantly. In 1954, 128 rabid dogs were registered. When 22 397 animals were vaccinated in 1956, the number of rabies cases in dogs was reduced to 6 cases (Selimov, 1978).

Results of the study of the effect of vaccination and destruction of dogs on the number of rabid dogs throughout Ukraine, presented in Fig. 3, show that the destruction of dogs itself did not provide significant results, whereas together with parenteral vaccination campaigns against rabies in dogs, it was an effective measure and helped to reduce rabies cases in dogs from 1 367 cases in 1954 to 203 cases in 1959.

In addition to carnivores, in the 1950s farm animals (especially cattle) made up a significant percentage of rabies cases. However, their role in the epizootic process was extrinsic, and fluctuations in number of rabies cases depended mainly on their population size (also on husbandry and grazing). For example, during the peak of rabies epizootic in 1951, there were 1 546 rabies cases among farm animals, while livestock population, according to the State Statistics Committee of Ukraine, was 38.2 million. During the peak in 2007 there were 417 rabies cases among farm animals, however, the livestock population was only 20.6 million.

Moreover, we cannot consider farm animals as active participants of the epizootic process, since in their natural habitat they do not provide a mechanism for the virus transmission. These facts are discussed in the works of Mogilevsky (1997), Hikufe et al. (2019).

In the 1960–1970s a source of rabies infection changed from dogs to foxes, which could be explained by the fact that the fox, due to ecological features, was able to occupy a dominant position among wild carnivorous animals in Ukraine. This was aided by the destruction of natural enemies in the fox habitat.

Elimination of natural enemies contributed to the constant growth of fox population. Thus, according to Scherbak & Ryaboshapka (1978) in 1925–1940 the estimated number of foxes on the territory of Ukraine was 40 000–80 000 annually, reaching up to 135 000 in some years, while in 1950–1960 it increased from 153 000 to 350 000–370 000 foxes. Hence, the leading role of foxes in the epizootic process was confirmed by a steady growth of their population on average by 3–4 times, and on some territories by 5–6 times.

According to Mogilevsky (1997) it is known that in the absence of regulation of fox populations cyclically, there is the rise in rabies epizootic every 3–5 years, and during the year there are 2 seasonal rises. The first rise in rabies epizootic coincides with the mating season (early spring), whereas the second rise is related to the settlement of young animals (autumn and winter). In summer, when foxes are busy with their brood, and in winter, before the onset of estrus, when foxes move alone, their mobility is limited and the number of rabies cases is minimal.

In addition, it was found that when the population density is up to 2 individuals, the infection proceeds without clinical manifestation. If the population density exceeds 2 individuals per 1000 hectares, the epizootic process acquires the characteristic features of an epizootics.

Moreover, Scherbak & Ryaboshapka (1978) reported that the number of rabies cases among foxes in Ukraine has been increasing every year since 1965. The estimated value of the incidence of fox rabies in 1965 was 4.6, while in 1979 – 529.6, demonstrating an increase by 115 times. The highest absolute number of fox rabies cases in the USSR within 15 years (1965–1979) was registered in the Polissya region – 1 422 or 46.7% of all detected cases. The incidence of fox rabies per 1000 ha of hunting grounds on the territory of the Polissya was up to 0.14, forest-steppe – 0.065, steppe – 0.032, and in the Carpathian area – 0.044. The highest values per unit area were recorded for the group of Polissya and forest-steppe oblasts (Zhytomyr, Kyiv, Chernihiv, Sumy, Khmelnytskyi, and Cherkasy).

As mentioned by Grishok (1977), within 5 years (1975–1979) in the USSR 1 053 rabies cases were registered in foxes, 22 in wolves, 26 in raccoon dogs, 28 in badgers, 93 in martens, and 11 in ground squirrels.

This tendency was traced in the archival data of the Republican Sanitary and Epidemic Station (SES), according to which in the period of 1971–1980 in 62 (45.6%) out of 136 human rabies cases foxes were the source of infection, unlike to only 23 cases (1.9%) out of 1 195 in 1951–1960. This confirms the increasing role of foxes in the epizootic and epidemiological significance compared to the previous stages.

It should be noted that almost 100% of red fox population in Eastern Europe is a reservoir of rabies virus, while in the United Kingdom (island territory) red fox is not a reservoir species, meaning that rabies virus does not persist in their body, as evidenced by Fooks (2005).

Therefore, the main reasons that contributed to the increase in the number of cases and distribution of rabies among foxes at the stage of «fox» rabies were: firstly, the shift in the ecological balance in nature caused by the destruction of fox's natural enemies (wolves, jackals, bears, eagles, etc.) by humans; secondly, the synanthropization of foxes, meaning the active adaptation of this species to changes in natural habitat of humans such as urbanization, change of landscapes (replacement of mature forests by young growth, drying out of swamps); thirdly, the intensification of agriculture (increase arable land, land reclamation), which led to an increase in the number of murines that formed the basis of the fox nourishment; fourthly, the high sensitivity of foxes to rabies, as demonstrated also by Pastoret & Brochier (1999), Ivanov & Nedosiekov (2009) and also increased excitability and aggression that promoted carrying forward of the epizootics for 30–50 km per year; fifthly, the frequency and seasonality of fox epizootics.

The stage of «relative safety» (1990–1999) built a foundation for the beginning of «rabies expansion» stage. Thus, with the collapse of the USSR in 1991, mass planned deratization on the fields, which was carried out mainly at the expense of collective farms and state farms (state funds), ceased. Some fields were simply withdrawn from agricultural use. These factors led to a gradual and significant increase in the number of murines on the fields. If there is enough food (like murines for foxes), the population growth in one pair of foxes can be 300–500%, i.e. 6–10 puppies. In the absence of natural enemies, as noted above, mortality rate in the population does not exceed 20%. Therefore, it is quite natural that there is such a «spike» of the rabies occurrence among foxes.

Low annual number of rabies cases in 1995 (351 animal cases and the absence of human cases) seemed to show positive trends. The number of diseased animals decreased by 4.5 times in 1995 (from 1 594 to 351) compared to 1979. However, with the collapse of the USSR the deratization of the fields did not stop immediately. For several years in a row, it was carried out according to the scheme developed over the years. In the early 1990s, fox fur was still valued by hunters, while nowadays this species of animals is of little interest. In some regions of Ukraine, compensation for hunted fox puppies and adult foxes has been maintained.

However, the gradual cessation of these components of countering foxes as the main reservoir species of rabies virus among wild animals led to a «peak» situation with outbreaks in 2007 (the highest number of rabies cases in animals and humans – 2 932 and 7, respectively).

So, in 2000–2019 the «urban» rabies was not prevalent. Rabies cases among foxes accounted for about 88.5% of all rabies cases among wild animals and 36.5% of total number of rabies cases. However, the proportion of rabid cats and dogs in this period was 25.5% and 19.1% of the total number of rabies cases, respectively. This was due to the poor coverage of preventive vaccination of these animals. This situation is sharply discussed in the work by Kornienko et al. (2019). Indeed, vaccination plans approved at the state level were 2 or more times understated (the actual number of cats and dogs was much higher), as indicated even by foreign experts (Mahadevan et al., 2016; Hunt et al., 2018).

There was a significant number of dogs and cats in rural areas

where breeding of these animals was «arbitrary», as there was no legislation that restricted or regulated such activities. This is a significant problem that was proven by Hampson et al. (2015) when studying the global spread of rabies among domestic carnivores.

In addition, campaigns for oral vaccination of wild carnivores that started from 2001 did not provide significant results, as the territories were treated with different vaccines, frequency and duration (Freuling et al., 2013).

As can be seen from Fig. 1, in the 1970s, and 1990s it was possible to keep epizootics at low rate. Nevertheless, in the 21st century the number of rabies cases was twice as high and, even with the oral vaccination of foxes, the incidence could not be reduced. Thereby, Ukraine remains endemic, which, according to Cliquet et al., (2010) is a concern of developed European countries.

Farm animals, which accounted for 13.9% of all rabies cases in 2000–2019, were of particular note. Once again, it concerned mainly private farms in the countryside and suburbs where livestock grazed and could be attacked by wild animals (mainly foxes), as well as cats and dogs. Because large farms (500–1000 animals each) followed biosecurity measures, cattle were mostly protected against such attacks.

Concerns were raised by increasing numbers of raccoon dogs, and, in individual cases, jackals (entering the territory of southern Ukraine via Romania), in the structure of wild carnivorous, which are also reservoir species of rabies.

In terms of plasticity and ability to adapt to changing natural conditions, these species even exceed the red fox. Thus, without overcoming the problems of red foxes, we can face more difficult tasks of rabies control among raccoon dogs and jackals. The threat posed by the presented species is also described in the works of foreign authors (Recuenca et al., 2012; Dürr & Ward, 2015).

Geographically, from Figures 4, 7 and 10, we can see that rabies was registered on the territories of all geographical areas of Ukraine. However, within 70 years the most endemic area was on the border with Russia, which gives a reason to form a new hypothesis. Due to the movement of animals, a «new serving» of sick animals is constantly coming from the other side. Meanwhile the territories of Western Ukraine bordering Poland, Hungary and Romania, since the 1950s, demonstrate the smallest number of rabies cases. Similar statements regarding the border situation are found in the work of Robardet et al. (2019).

Overall, our results show that in the 20th century in Ukraine only one species of animals (dogs or foxes) prevailed in spreading of rabies, being the main source of infection, and accounted for about 50%, while productive animals were «victims» of attacks. In the 21st century, all three species (dogs, cats, and foxes) are sources of the rabies virus, accounting for about 90%, and only 10% are their victims (farm animals). In such a situation, it is important that all control measures are directed to each individual source of rabies in order to prevent future epizootics and to stop the spread of the disease.

## Conclusions

1. It was found that during 1950–2019 three significant peaks of rabies outbreaks at an equal interval of 28 years were recorded in Ukraine. The first peak occurred in 1951 (3 724 cases), the second – in 1979 (1 594 cases), and the third – in 2007 (2 932 cases).

2. It was found that the source of rabies virus changed three times: for the first time (1950–1969), when dogs were predominant, for the second (1970–1994) – foxes; for the third (1995–till present) – foxes, cats and dogs at the same time.

3. Considering the significant peaks and downturns and varying degrees of involvement of domestic and wild carnivorous in the rabies spread, the main stages of the epizootic process of rabies have been established: the stage of urban or dog rabies (1950–1959), relative stability (1960–1969), sylvatic or fox rabies (1970–1990), relative safety (1991–1999), and expansion (2000–2019).

4. The highest number of deaths from rabies with dogs as the main source of infection was registered during the first stage. In the second stage, the decline of epizootic curve up to 140 cases in 1965 was noted. The third stage was characterized by the spread of the disease through a new species – the red fox, which led to a «fox» epizootic. One could see that during the fourth stage the relevance of the fox in the epizootic process decreased, while domestic carnivores played a significant role in the spread of the virus. The peculiarity of the fifth stage was the increase in the number of cases of rabies equally among foxes, dogs, and cats with predominance in the epizootic process of domestic carnivorous (44.6%) over wild (36.5%), which caused an exacerbation of epizootic and epidemic situation.

5. In order to reduce the spread of rabies, every effort should be made by all responsible entities to eliminate rabies and, first of all, to regulate the number of wild and stray carnivores, and then to carry out mass vaccination.

Our further research will be aimed at creating of rabies cases database for the whole territory of Ukraine, conducting of GIS analysis and developing of mathematical model of rabies distribution in order to monitor the dynamics of the epizootic process, predict and prevent rabies epizootics.

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## References

- Anderson, R. M., Jackson, H. C., May, R. M., & Smith, A. M. (1981). Population dynamics of fox rabies in Europe. *Nature*, 289(5800), 765–771.
- Benavides, J. A., Valderrama, W., & Streicker, D. G. (2016). Spatial expansions and travelling waves of rabies in vampire bats. *Proceedings of the Royal Society B: Biological Sciences*, 283(1832), 20160328.
- Biek, R., Henderson, J. C., Waller, L. A., Rupprecht, C. E., & Real, L. A. (2007). A high-resolution genetic signature of demographic and spatial expansion in epizootic rabies virus. *Proceedings of the National Academy of Sciences*, 104(19), 7993–7998.
- Blancou, J., & Aubert, M. (1991). Fox rabies. In Baer, G. (ed.) *The natural history of rabies*. 2nd edn. In CRC Press, Boca Ration, Ann Arbor, Boston.
- Botvinkin, A. & Kosenko, M. (2004). Rabies in the European parts of Russia, Belarus and Ukraine. In King, A. A., Fooks, A. R., Aubert, M., & Wandeler, A. I. (Eds.), *Historical perspective of rabies in Europe and the Mediterranean Basin*. Paris, OIE World Organization for Animal Health, 47–63.
- Cárdenas-Canales, E. M., Gigante, C. M., Greenberg, L., Velasco-Villa, A., Ellison, J. A., Satheshkumar, P. S., Medina-Magües, L. G., Griesser, R., Falendysz, E., Amezcua, I., Osorio, J. E., & Rocke, T. E. (2020). Clinical presentation and serologic response during a rabies epizootic in Captive Common Vampire Bats (*Desmodus rotundus*). *Tropical Medicine and Infectious Disease*, 5(1), 34.
- Chirkova, A. F. (1953). Materials on dynamic of fox abundance in Voronezh Province in connection with prognoses of its harvests. In *Questions of Fur Animals Biology*. Ministry of Agriculture Publisher, Moscow, 8, 20–31 (in Russian).
- Cliquet, F., Freuling, C., Smreczak, M., Van der Poel, W., Horton, D., Fooks, A., Robardet, E., Picard-Meyer, E., & Müller, T. (2010). Development of harmonised schemes for monitoring and reporting of rabies in animals in the European Union. *EFSA Supporting Publications*, 7(7), 60.

- Cliquet, F., Picard-Meyer, E., & Robardet, E. (2014). Rabies in Europe: what are the risks? *Expert Review of Anti-Infective Therapy*, 12(8), 905–908.
- Dürr, S., & Ward, M. P. (2015). Development of a novel rabies simulation model for application in a non-endemic environment. *PLOS Neglected Tropical Diseases*, 9(6), e0003876.
- Fisher, C. R., Streicker, D. G., & Schnell, M. J. (2018). The spread and evolution of rabies virus: conquering new frontiers. *Nature Reviews Microbiology*, 16(4), 241–255.
- Fooks, A. R. (2005). Rabies remains a «neglected disease». *Eurosurveillance*, 10(11), 1–2.
- Freuling, C. M., Hampson, K., Selhorst, T., Schröder, R., Meslin, F. X., Mettenleiter, T. C., & Müller, T. (2013). The elimination of fox rabies from Europe: determinants of success and lessons for the future. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 368(1623), 20120142.
- Gholami, A., Massoudi, S., Kharazian, M. M., Ghazi, M. M., Marashi, M., Bashar, R., Fayaz, A., Fazeli, M., Farahatj, F., Howaizi, N., & Shirzadi, M. R. (2017). The role of the gray wolf in rabies transmission in Iran and preliminary assessment of an oral rabies vaccine in this animal. *Journal of Medical Microbiology and Infectious Diseases*, 5(3), 56–61.
- Grishok, L. (1977). Epizootiology of rabies in Ukrainian SSR. *Veterinary*, 5, 53–56 (in Ukrainian).
- Gucht, S. V., & Roux, I. L. (2008). Rabies control in Belgium: from eradication in foxes to import of a contaminated dog. *Vlaams Diergeenkskundig Tijdschrift*, 77, 376–384.
- Hampson, K., Coudeville, L., Lembo, T., Sambo, M., Kieffer, A., Attlan, M., Barrat, J., Blanton, J. D., Briggs, D. J., Cleaveland, S., Costa, P., Freuling, C. M., Hiby, E., Knopf, L., Leanes, F., Meslin, F.-X., Metlin, A., Miranda, M. E., Müller, T., & Dushoff, J. (2015). Estimating the global burden of endemic canine rabies. *PLOS Neglected Tropical Diseases*, 9(4), e0003709.
- Hikufe, E. H., Freuling, C. M., Athingo, R., Shilongo, A., Ndevaetela, E. E., Helao, M., Shiindi, M., Hassel, R., Bishi, A., Khaiseb, S., Kabajani, J., van der Westhuizen, J., Torres, G., Britton, A., Letshwenyo, M., Schwabenbauer, K., Mettenleiter, T. C., Denzin, N., Amler, S., & Maseke, A. (2019). Ecology and epidemiology of rabies in humans, domestic animals and wildlife in Namibia, 2011–2017. *PLoS Neglected Tropical Diseases*, 13(4), e0007355.
- Hunt, N., Carroll, A., & Wilson, T. P. (2018). Spatiotemporal analysis and predictive modeling of rabies in Tennessee. *Journal of Geographic Information System*, 10(01), 89–110.
- Isakov, U. A. (1949). About rabies among wild animals inhabited in the Delta of Volga. In *Research on Regional, Experimental and Descriptive Parazitology*, 6, 82–86 (in Russian).
- Ivanov, M. I., & Nedosekov, V. V. (2009). Study of «field» rabies virus isolates circulating in Ukraine. *Veterynarna biotekhnolohiia*, 14, 113–119 (in Ukrainian).
- Kantorovich, R. A. (1968). Some aspects of the world distribution and ecology of rabies. In *Medical Geography*, Moscow, 273–320 (in Russian).
- King, A. A., Fooks, A. R., Aubert, M., & Wandeler, A. I. (2004). Historical perspective of rabies in Europe and the Mediterranean Basin. Paris, OIE World Organization for Animal Health.
- Kornienko, L. E., Moroz, O. A., Mezhenyky, A. O., Skorokhod, S. V., Datsenko, R. A., Karpulenko, M. S., Polupan, I. M., Dzyuba, Y. M., Nedosekov, V. V., Makovskaya, I. F., Hibaliuk, Y. O., Sonko, M. P., Tsarenko, T. M., & Pishchanskyi, O. V. (2019). Epizootological and epidemiological aspects for rabies in Ukraine for the period from 1999 to 2018. *Veterinary Science, Technologies of Animal Husbandry and Nature Management*, (3), 90–109.
- Kuzmina, N. A., Lemey, P., Kuzmin, I. V., Mayes, B. C., Ellison, J. A., Orciari, L. A., Hightower, D., Taylor, S. T., & Rupprecht, C. E. (2013). The phylogeography and spatiotemporal spread of South-Central Skunk rabies virus. *PLoS ONE*, 8(12), e82348.
- Kuzmin, I. V., Botvinkin, A. D., McElhinney, L. M., Smith, J. S., Orciari, L. A., Hughes, G. J., Fooks, A., & Rupprecht, C. E. (2004). Molecular epidemiology of terrestrial rabies in the former Soviet Union. *Journal of Wildlife Diseases*, 40(4), 617–631.
- Mahadevan, A., Suja, M. S., Mani, R. S., & Shankar, S. K. (2016). Perspectives in diagnosis and treatment of rabies viral encephalitis: insights from pathogenesis. *Neurotherapeutics*, 13(3), 477–492.
- Maki, J., Guiot, A.-L., Aubert, M., Brochier, B., Cliquet, F., Hanlon, C. A., King, R., Oertli, E. H., Rupprecht, C. E., Schumacher, C., Slate, D., Jakobson, B., Wohlens, A., & Lankau, E. W. (2017). Oral vaccination of wildlife using a vaccinia–rabies-glycoprotein recombinant virus vaccine (RABORAL V-RG®): a global review. *Veterinary Research*, 48(1), 57.
- Makovska, I. F., Nedosekov, V. V., Polupan, I. M., & Latmanizova, T. S. (2018). Distribution trend rabies in cats in Ukraine. *Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies*, 20(92), 18–23.
- Mogilevsky, B. Yu. (1997). Practical rabbiology. Kherson, Dnipro (in Ukrainian).
- Nychyk, S., Zhukorskiy, O., Polupan, I., Ivanov, M., & Nikitova, A. (2013). Improvement Control System of Rabies in Ukraine. *Online Journal of Public Health Informatics*, 5(1).
- Pastoret, P. P., & Brochier, B. (1999). Epidemiology and control of fox rabies in Europe. *Vaccine*, 17(13–14), 1750–1754.
- Pavlov, M. P. (1953). Mass diseases of foxes in Crimean. *Zoonosis Infections*. Kiyv, 135–146 (in Ukrainian).
- Picot, V., Rasuli, A., Abella-Rider, A., Saadatian-Elahi, M., Aikimbayev, A., Barkia, A., Benmaiz, S., Bouslama, Z., De Balogh, K., Dehove, A., Davlyatov, F., Farahatj, F., Gongal, G., Gholami, A., Imnadze, P., Issad, M., Khoufi, S., Nedosekov, V., Rafila, A., & Nel, L. (2017). The middle east and eastern Europe rabies expert bureau (MEEREB) third meeting: Lyon-France (7–8 April, 2015). *Journal of Infection and Public Health*, 10(6), 695–701.
- Polupan, I., Golik, M., & Nedosekov, V. (2017a). Antropurgisation of rabies in Ukraine. *Ukrainian Journal of Veterinary Sciences*, 265, 182–188 (in Ukrainian).
- Polupan, I., Bezymennyi, M., Zh, D., & Nychyk, S. (2017b). Spatial and temporal patterns of enzootic rabies on the territory of Chernihiv oblast of Ukraine. *Journal for Veterinary Medicine, Biotechnology and Biosafety*, 3(2), 31–36.
- Polupan, I., Bezymennyi, M., Gibaliuk, Y., Drozhzhe, Z., Rudoi, O., Ukhovskiy, V., Nedosekov, V., & De Nardi, M. (2019). An analysis of rabies incidence and its geographic spread in the buffer area among orally vaccinated wildlife in Ukraine from 2012 to 2016. *Frontiers in Veterinary Science*, 6, 1–13.
- Recuenco, S., Blanton, J. D., & Rupprecht, C. E. (2012). A spatial model to forecast raccoon rabies emergence. *Vector-Borne and Zoonotic Diseases*, 12(2), 126–137.
- Robardet, E., Bosnjak, D., Englund, L., Demetriou, P., Rosado, P., & Cliquet, F. (2019). Zero endemic cases of wildlife rabies (Classical Rabies Virus, RABV) in the European Union by 2020: An achievable goal. *Tropical Medicine and Infectious Disease*, 4(4), 124.
- Rupprecht, C. E., Bannazadeh Baghi, H., Del Rio Vilas, V. J., Gibson, A., D., Lohr, F., Meslin, F. X., Seetahal, J.F.R., Shervell, K., & Gamble, L. (2018). Historical, current and expected future occurrence of rabies in enzootic regions. *Revue Scientifique et Technique de l'OIE*, 37(2), 729–739.
- Rupprecht, C. E., Turmelle, A., & Kuzmin, I. V. (2011). A perspective on lyssavirus emergence and perpetuation. *Current Opinion in Virology*, 1(6), 662–670.

- Scherbak, Yu., & Ryaboshapka, A. (1978). Ecological and epidemiological problems of wildlife rabies. *Journal of Epidemiology and Immunobiology*, 12, 14–21 (in Russian).
- Selimov, M. A. (1978). Rabies. *Medicine*, Moscow (in Russian).
- Tomah, O., & Lebedeva, N. I. (2015). Red fox (*vulpes vulpes*) number dynamics and its predetermining factors in Zaporizhzhya region. *Biological Conservation*, 17, 52–57 (in Ukrainian).
- Vedernikov, V. (1974). Animal rabies. *Kolos*, Moscow (in Russian).
- Vitasek, J. (2012). A review of rabies elimination in Europe. *Veterinární Medicina*, 49(5), 171–185.
- Vos, A., Freuling, C., Eskiizmirli, S., Ün, H., Aylan, O., Johnson, N., Gürbüz, S., Müller, W., Akkoca, N., Müller, T., Fooks, A. R., & Askaroglu, H. (2009). Rabies in foxes, Aegean region, Turkey. *Emerging Infectious Diseases*, 15(10), 1620–1622.
- Wei, Y., Liu, X., Li, D., Chen, S., Xu, J., Chen, K., & Yang, Z. (2018). Canine rabies control and human exposure 1951–2015, Guangzhou, China. *Bulletin of the World Health Organization*, 97(1), 51–58.
- WHO. (2018). WHO Expert Consultation on rabies. World Health Organization. Technical Report Series, 931, 1–88, back cover.