PROCEEDINGS OF THE SHEVCHENKO SCIENTIFIC SOCIETY

DOI: 10.25040/ntsh2024.01.18

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Received: 02 Apr, 2024 Accepted: 25 May, 2024 Published: 28 Jun, 2024

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Disclosures: The authors declared no conflict of interest.

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Review & editing: Nataliya Vynograd, Sonię Grychtoł, Wiesława Kołodziej, Ihor Chaklosh, Zoriana Vasylyshyn, Liudmyla Kozak.

require ethical approval.

Funding: The authors received no financial support for their study.



## Original research: Clinical sciences

Proceedings of the Shevchenko Scientific Society. Medical Sciences 2024, 1 (73). https://doi.org/10.25040/ntsh

Access, Peer Rev

www. mspsss.org.ua

For correspondence: Danylo Halytsky Epizootic-Epidemiological Features of Rabies in the Eastern Pekarska Street, Lviv, Ukraine, 79010, European Region at the Current Stage

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Rabies is an especially dangerous anthropozoonosis caused by viruses of the Rabdoviridae family, genus Lyssavirus, known for over 4,000 years. There is no effective antiviral treatment for rabies, although immunobiological drugs have been developed, the timely application of which can prevent a fatal outcome in humans. Protection of the population from rabies includes control of zoonotic reservoirs and sources of the pathogen infection.

The aim of the study was to assess the epizootic-epidemiological situation of rabies in Ukraine and Poland, considering risks caused by the active phase of the Russian-Ukrainian war. A comprehensive epidemiological method was used to analyze state official data regarding indicators of the epizootic process of rabies, the number and nature of human injuries due to animal attacks, and to determine trends during 2021–2023. A comparative-descriptive technique was applied to compare the effectiveness of vaccination against rabies in domestic, pet, and wild animals and to assess the risks of changes in the epizootic situation.

Since the 1940s, a natural focal ecotype of rabies has formed in the Eastern European region, where wild carnivores are reservoirs and pathogen sources. In Ukraine, combined foci are registered with the natural focal ecotype of rabies, involving dogs, cats, and large and small ruminants in the epizootic process. The epizootic rabies situation in Ukraine worsened during the war due to the disruption of animal vaccination, increased feral domestic and farm animals, especially in the combat zone, and the cessation of regulating the normative number of red foxes. The epizootological well-being in Poland could be compromised if the rabies disaster area spreads from the border territories of Ukraine.

There are real risks of worsening the epizootic-epidemiological situation of rabies in Ukraine, posing a threat of transboundary spread to other countries.

Keywords: War, rabies, epizootic-epidemiological situation, Ukraine, Poland, Ethical approval: This study did not preventive and anti-epidemic measures.

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Rabies is a hazardous acute viral disease of animals and humans, characterized by signs of polioencephalomyelitis, paralysis, and absolute mortality. The causative agents of rabies are neurotropic RNA-containing viruses belonging to the family of *Rabdoviridae*, genus *Lyssavirus*. According to the WHO, rabies is among the top five most dangerous zoonotic diseases, causing significant socio-economic damage. Annually, more than 1 million animals and about 70,000 people die from this disease worldwide [1].

A disease with clinical manifestations corresponding to rabies was described in the 23rd century BCE in the Babylonian Code. In the 1st century BCE, Cornelius Celsus named the disease *hydrophobia*, considering it a typical clinical symptom. In 1872, George Fleming suggested leaving the term *hydrophobia* for human diseases and calling the animal disease Rabies [2].

From ancient times until the beginning of the 17th century, local epizootics of rabies among wild animals were observed on the planet. In the 17th to 19th centuries, there was a panzootic among domestic animals and epidemics of hydrophobia among people [3]. Key events in the history of the fight against rabies were the use of a vaccine created by Louis Pasteur for treating a human in 1885 and the establishment by the French researcher P.A. Remlinger of the viral etiology of the disease in 1903 [4]. From the 20th century to the present, a panzootic of rabies among wild animals is observed on the planet; outbreaks among domestic animals are contained by vaccination; and in 167 countries, sporadic and outbreak morbidity among people is registered [5].

By the 1930s, both ecological types of rabies existed in the European region: urban (anthropurgic) and sylvatic (natural focal) and a transitional variant between them. In urban foci, dogs (*Canis lupus familiaris* or *Canis familiaris*) were the reservoir of the virus, while in sylvatic foci, primarily foxes (*Vulpes vulpes*) and wolves (*Canis lupus L.*) served as reservoirs. Active reduction of the stray dog population in human settlements, control over the rules of domestic animal keeping, and the introduction of their vaccination led to a significant decrease in the activity of urban rabies foci but resulted in the dominance of natural foci. Since the 1940s, a sylvatic ecotype of rabies has formed in the Eastern European region, with the red fox (*Vulpes vulpes*) being the pathogen reservoir. Pathogen circulation in nature is also supported by other animal species, but they are not considered main hosts [1].

In the Republic of Poland, dogs were the primary reservoir and source of the rabies pathogen after World War II. A significant decrease in animal rabies morbidity began after 1949 when mandatory vaccination of dogs against rabies was introduced, resulting in only 73 cases of canine rabies registered in 1956. The rabies problem remained in the country as the pathogen circulated among wild carnivorous animals. By the late 1970s, the number of diseases among them exceeded the similar indicator in domestic animals. By 1990, 2045 rabies cases were detected in the Republic of Poland, including 1668 among wild animals (1374 in foxes). The highest number of cases was in the voivodeships of Poznan (157), Opole (139), Koszalin (133), Szczecin (130), Bydgoszcz (123), and Slupsk (103). Isolated cases were found in the voivodeships of Lubelskie, Lomzyn, Lódźiskie, and Podkarpackie, but no cases were recorded in the Bielsko-Biała Voivodeship. By 2009, a steady trend of decreasing cases of rabies in carnivorous animals was observed: only eight sick animals, including six foxes. However, since 2010, there has been an increase in rabies epizootic indicators, significantly caused by the migration of rabid animals, confirmed by sequencing of the pathogen isolates. In the period after 2009, most rabies cases were detected in the Lesser Poland and Subcarpathian voivodeships. The main obstacle and limitation in the fight against rabies in the southeastern part of Poland were difficulties with immunizing foxes living in close proximity to or within human settlements. Many rabies cases in the Lesser Poland and Subcarpathian voivodeships were detected in recent years near buildings [6].

According to the Annex to Commission Implementing Regulation (EU) 2018/1882 of December 3, 2018, on the application of certain provisions concerning the prevention and control of diseases to categories of listed diseases and the creation of a list of species and groups of species with a significant risk of disease spread included in this list (OJ EU L 308 of 04/12/2018, p. 21), rabies virus infection in carnivorous animals, turtles, pigs, equines, cervids, and camels was included in categories B+ D+, while in bats, it was included in category E, where: 1) "Category B disease" means a disease from the list that must be controlled in all Member States with the aim of its eradication throughout the EU, as defined in Article 9 Section 1 Letter b of Regulation (EU) 2016/429 of the European Parliament and of the Council of March 9, 2016 on transmissible animal diseases and amending and repealing certain acts in the area of animal health ("Animal Health Law") (OJ L 84 of 31/03/2016, page 1, as amended), hereinafter referred to as "Regulation (EU) 2016/429"; 2) "Category D disease" means a disease from the list for which measures are necessary to prevent its spread through its presence within the EU or movement between Member States, as defined in Article 9 Section 1 Letter e of Regulation (EU) 2016/429 [6].

According to Article 31, as an exception from Article 1 of Regulation (EU) 2016/429, Member States that are not free of Category B disease across their entire territory or in specific zones or compartments must implement a program aimed at the eradication of said disease or demonstrating that they are free from it. Free, implemented in populations of animals affected by this disease, and covering relevant parts of the territory of this state or relevant zones or compartments (referred to as "mandatory disease eradication program"), which remains until the conditions for granting the status of disease-free territory of the Member State, or given zone, are met. Member States submit the draft mandatory eradication program to the European Commission for approval [6].

Since regulating fox populations in EU countries did not ensure the elimination of the virus from their populations, another strategy for eradicating rabies in foxes was introduced in the late 1980s – widespread oral vaccination, which proved to be highly effective. In the Republic of Poland, a campaign for the oral vaccination of wild foxes against rabies started in 1993, and subsequently, the country actively joined the EU's rabies elimination program.

The Republic of Poland undertook measures to eliminate rabies using 6,007,728 doses of vaccines Lysvulpen; Rabigen SAG2 oral suspension; Rabitec, covering eight regions with a total area of 100,564 sq. km. Similar measures were carried out in Ukraine in the 50-kilometer border buffer zone with the Republic of Poland, covering 38,450 sq. km [7]. The introduction of vaccination in the buffer zone proved to be a highly effective measure in influencing the epizootic process of wild animal rabies in Ukraine [8]. By 2019, the last five detected cases were all in border territories with Belarus, Ukraine, and Moldova. By 2020, the rabies virus circulation among carnivorous mammals had been halted in all EU countries, as well as in Switzerland, Norway, and Iceland [1]. At the current stage, rabies in these countries poses a danger as an imported infection with animals without proper veterinary control [9] or infection in endemic areas by traveling EU citizens [10], as well as through the transplantation of tissues or organs contaminated with the rabies virus [11]. However, high risks of transboundary spread of this dangerous pathogen from other enzootic territories of countries where the circulation of the rabies virus continues should be considered [12].

According to the Law of March 11, 2004, "On the Protection of Animal Health and Control of Infectious Animal Diseases," rabies is one of the infectious diseases of animals subject to mandatory control in Ukraine. Ukraine remains an enzootic territory for rabies, where natural (wildlife) and anthropurgic (dog-mediated rabies) foci are registered, cases of the disease in wild, domestic, and farm animals are detected, and sporadic cases of rabies among humans are registered. The epizootic situation in Ukraine regarding rabies is determined by the diversity of reservoirs and pathogen sources: rabies has been registered among 19 species of wild and 10 species of domestic (dogs and cats) and farm animals (fur animals, horses, pigs, small ruminants (SR), and cattle (C)) and sporadically among humans [13].

In anthropurgic and combined foci, cats, dogs, cattle, small ruminants, pigs, and horses are reservoirs and sources of the rabies pathogen. The natural type of epizootics is caused by the circulation of the pathogen among foxes (*Vulpes vulpes*) – both as a reservoir of the pathogen and raccoon dogs (*Nyctereutes procyonoides*), wolves (*Canis lupus L.*), water voles (*Arvicola spp.*), bats (*Microchiroptera*), European badgers (*Meles meles*), squirrels (*Sciurus vulgaris*), and pine martens (*Martes martes*) [14].

In Ukraine, anthropurgic and combined rabies foci have evolved since the beginning of the active phase of the Russian-Ukrainian war due to the uncontrolled increase in the number of stray and homeless dogs and cats, insufficient vaccination coverage of domestic and farm animals, and violation of animal keeping regulations. Internal movement of people from the eastern region of Ukraine was accompanied by the movement of domestic and farm animals, a significant portion of which were not vaccinated against rabies. According to official sources, as a result, the share of laboratory-confirmed cases of rabies in dogs and cats increased from 53.2% (2021) to 59.4% (2022) and 68.4% (2023) among all positive cases of animal rabies. A similar trend was observed in cattle and small ruminants, with 7.5% of verified rabies cases in 2021, 8.3% in 2022, and 10.1% in 2023 of the total number of sick animals [15]. In 2022, with the government's support, rabies prevention measures for animals were intensified: specialists of the State Consumer Service conducted 2.284 million vaccinations against rabies, including 1.372 million for dogs and 912,000 for cats [16].

The activation of the epizootic process in natural foci during this period was due to non-compliance with regimes and volumes of oral immunization of wild carnivorous animals by ground distribution of baits with vaccine, cessation of fox population control through culling, as in 2022, a temporary ban on hunting was imposed considering the Law of Ukraine of February 24, 2022, No. 2102-IX "On Approving the Decree of the President of Ukraine 'On the Introduction of Martial Law in Ukraine,'" but was later partially resumed. The share of foxes positive for rabies out of the total number of animals of this species examined was 2.7% in 2021 and 2.9% and 12.9% in 2022 and 2023, respectively [17].

According to the Western Interregional Management of Forest and Hunting Economy, in 2024, the fox population in the hunting grounds of Lviv Region exceeds the established norm by three times and amounts to 3,227. This creates a threat of rabies spread among wild and domestic animals and humans [18].

Laboratory studies on rabies have confirmed that other wild animals are involved in the epizootic process: the golden jackal (*Canis aureus*), wolf (*Canis lupus L.*), raccoon dog (*Nyctereutes procyonoides*), wild boar (*Sus scrofa*), pine marten (*Martes martes*), European badger (*Meles meles*), beaver (*Castor*), muskrat (*Ondatra zibethicus*)/weasel (*Mustela nivalis*), voles (*Arvicola spp.*), hamster (*Mesocricetus auratus*), and mice (*Mus spp.*). Over three years, there were sporadic cases of rabies detected among the above species of wild animals, and the share of positive laboratory cases was 39.3% (2021), 32.4% (2022), and 22.4% (2023). Migration of wild animals and rodents – potential sources of the rabies virus to human habitats, change in distribution areas, and increased population density indicators have been observed.

The first year of the active phase of the war significantly complicated the organization of epizootological surveillance for rabies. For instance, if in 2021, 1,369 suspected cases of rabies in animals were detected and examined in the laboratory in the country, of which 728 (53.2%) were laboratory-verified, then in 2022, this indicator decreased to 1,013 cases (544 positive – 55.5%). However, in 2023, the number of laboratory-confirmed cases of animal rabies increased to 1,254 (57.6%) upon examining 2,143 animals. In 2023, there was a 2.3-fold increase in animal rabies cases compared to 2022. Rabies was detected in 421 cats, 317 dogs, 225 red foxes, and 82 cattle. During the war, the capabilities to implement the main directions of national rabies control programs significantly decreased: oral vaccination of carnivorous animals, depopulation of red foxes, vaccination of domestic and farm animals, epizootological monitoring of natural foci, control of stray dogs and cats, etc. In areas of military operations, vaccination of carnivorous animals is not carried out considering the security situation, as well as in de-occupied territories with significant amounts of mines contamination. The possibilities of vaccination have been significantly complicated due to the ban on the use of airspace for distributing bait with vaccines. However, despite the objective difficulties, oral vaccination in 2023 was carried out over an area of 118,710.816 km<sup>2</sup> of Ukraine, and in addition, 4.9 million domestic animals were vaccinated against rabies. In Lviv Region, vaccination was conducted over an area of 1,828 km<sup>2</sup>, where 45.7 thousand vaccine doses were distributed by ground method [15].

During this period, there was a worsening of the epizootic situation regarding animal rabies in the western Ukrainian regions bordering Poland. For instance, in Lviv Region bordering Poland, 21 cases of animal rabies were laboratory-confirmed in 2021 (12 foxes, 6 stray dogs, 3 cats), in the following two years – 40 (18 foxes, 3 martens, 10 stray dogs, 9 cats) and 93 (36 foxes, 2 martens, 1 badger, 24 stray dogs, 30 cats) cases respectively. In Volyn Region, these figures over three years were 26 (2021), 36 (2022), and 49 (2023), and in Zakarpattia Region – 4 (2021), 11 (2022), and 16 (2023), respectively [15].

Since the beginning of the war, there has been an increase in the number of rabies-unfavorable points in the Western Ukrainian region. Thus, in 2023, there were 90 cases in Lviv Region, 47 in Volyn Region, and 16 in Zakarpattia Region. In Lviv Region, unfavorable aspects were predominantly associated with rabies in foxes and other carnivorous animals, in Volyn Region – with rabies in cats, and in Zakarpattia Region – with sick dogs. In 2023, permissions were obtained to resume the regulation of the population of animals – potential sources of the rabies virus in the territories of fifteen administrative regions, including three bordering Poland [17].

Cases of animal attacks on people have caused significant concern both in Ukraine and in the Republic of Poland, including considering the risk of rabies in humans. While no cases of rabies in humans were registered in Poland, in Ukraine, one fatal case was observed in 2023 and two cases in 2022 [19].

In Ukraine, over 51,000 people of various ages sought medical treatment for injuries resulting from animal attacks. Among them, injuries caused by non-stray dogs (over 17,000), stray dogs (11,000), non-stray cats (7,000), stray cats (2,800), wild animals (600), and other unknown animals predominated [19]. In Lviv Region, 1,459 animal bites on humans were registered in 2022 and 1,522 bites in 2023 [17]. In Volyn Region, 1.5-1.7 thousand human bites are registered annually, up to 40% of which are inflicted by unknown animals [20].

The problem of animal bites and scratches is also relevant in the Republic of Poland, where there has been a trend of increasing numbers in the last three years. According to official statistics, 5,275 cases were registered in 2021 (intensity rate (IR) of 13.82 per 100,000 population), 8,151 cases in 2022 (IR of 21.35), and 9,976 cases in 2023 (IR of 26.46). Most cases were registered in the third quarter of 2021 and 2022 [21].

An analysis of the number of animal bites and scratches in the Podkarpackie and Lublin voivodeships bordering Ukraine was conducted. In Podkarpackie Voivodeship, 474 cases of animal-inflicted injuries on humans were detected in 2021, with an IR of 22.4 per 100,000 population. In 2022, these figures increased to 678 cases, IR 32.6. It should be noted that during 2021 and 2022, the Lublin Voivodeship had fewer instances of animal-inflicted injuries on humans: 246 and 390 cases, respectively, with lower intensity rates of 11.8 and 19.2. The proportion of hospitalized individuals among the injured was less in Podkarpackie Voivodeship (0.15-0.42%), while Lublin Voivodeship's indicators were 1.54-3.25% [21].

Therefore, the analysis of the epizootic and epidemic situation with rabies in the Republic of Poland indicates a stable well-being regarding this particularly dangerous disease. Adequately organized epizootological and epidemiological surveillance in the country, timely and proper execution of comprehensive plans by all agencies involved in the national rabies control program allow for predicting stable epizootic and epidemic well-being concerning rabies in the Republic of Poland. Significantly, this will be determined by properly organizing the entire complex of measures in border voivodeships adjacent to countries where the rabies situation is unstable or unfavorable.

In Ukraine, where the war has been ongoing for the third year, the situation with rabies is unfavorable. Intensive migration processes of people and animals from the combat zone have increased the risks of epizootic complications among domestic, farm, and wild animals. The absence of proper regulation of the red fox population through oral immunization of wild carnivorous animals and due to the imposition of hunting bans in most of the state, disruption in the organization of parenteral immunization of dogs, cats, and farm animals, an increase in the number of feral animals, violation of animal keeping regulations, lack of monitoring of the number and species composition of other objective reasons do not allow for the organization of effective anti-epizootic measures against rabies in animals. An increase in the number and density of the settlement of wild carnivorous animals contributes to the intensification of the epizootic process, spreading rabies to populated areas, which poses a threat of infecting people with this pathogen and potentially worsening the epidemic state of the territory, increasing the risks of cross-border spread of rabies. The expansion of the settlement areas of animals – potential sources of the rabies virus, formation of new stationary unfavorable points, requires continuous real-time assessment of the territory's condition and the risks to the population and animals [22], immediate introduction of quarantine and other measures to control the rabies situation. Continuous training of staff from all services and departments involved in the fight against rabies is crucial.

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