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Original article

RABIES IN EUROPE IN 2010–2019

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Summary

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The paper presents the epizootic and epidemiological situation of rabies in European countries during the last decade. The presented results indicate that the oral immunisation of fox anti-rabies (ORV), used in many European countries, significantly reduced the number of rabies cases found in ground mammals, but did not eliminate the virus at all. Currently, the largest reservoir of the virus are Eastern European countries where there are no immunisation activities or their effectiveness is low. Due to the absence of geographical barriers, the virus reappears in countries that have been described as free from rabies. As a rule, it is dragged into these areas along with the movement of companion animals and by people travelling to countries where the prevalence of the virus is common. It should be emphasised that due to the significant elimination of the virus in wild and domestic animals, it found quite quickly found a new reservoir in a specific group of mammals, having the ability to fly, like bats. Currently there is no possibility of carrying out any preventive measures in bats, so all the virus strains found in this group of animals are dangerous to humans, raising possibilities of epidemiological threat. It should be noted that despite the significant elimination of rabies in many European countries, given the almost unlimited possibilities of virus transmission to new areas, it still poses a serious threat to public health. Thus, it is necessary to constantly monitor the occurrence of the virus and possibly take preventive actions in terms of its elimination from the environment.

Key words: epidemiologic situation, epizootic situation, Europe, oral immunisation, rabies

INTRODUCTION

Rabies is a zoonotic infectious disease of the central nervous system caused by neurotropic viruses belonging to the genus *Lyssavirus*, which, along with other genera, belongs to the *Rhabdoviridae* family within the Mononegavirales order. Despite the fact that in February 2019 the International Committee of Virus Taxonomy (ICTV) updated the taxonomy of the Mononegavirales order, there were no changes within the genus *Lyssavirus*. It includes 16 classified species, and two more are pending classification (Amarasinghe *et al.,* 2018; Maes *et al.,* 2019).

Rabies as a disease was already known in ancient times. The first mention of it comes from the Code of Hammurabi dating back to the 18th century BC.

Information on the occurrence and course of this disease is also found in the records of Democritus and Aristotle. Quite often it is defined as the oldest of infectious diseases known to mankind (Smreczak, 2007; Smreczak & Żmudziński, 2019). All warm-blooded animals, including humans, are susceptible to virus infection. The first significant attempts at preventive measures were made in the 18th century, and the breakthrough in this respect was 1885, when the first vaccinations were carried out. They concerned a man bitten by a dog with rabies symptoms (Smreczak, 2007; Ridder, 2018). It is a global disease, which from the beginning of its diagnosis has been associated with biting by dogs. Currently it occurs on all continents except Antarctica. Despite the diverse administrative and veterinary activities in the field of virus prevention and control, it remains one of the most dangerous zoonoses in the world. According to the World Health Organization, it occurs in over 150 countries around the world and kills approximately 59,000 people, where about 40% of cases involve children under 15 years of age. For several years, the highest incidence, and thus also mortality, reaching 95% of all deaths in the world as a result of this disease occurs in Africa and Asia, where dogs remain the main reservoir of the virus. Transmission to humans is most commonly caused by bites or scratches by infected animals (Knobel *et al.,* 2005; Gliński & Kostro, 2013; Ridder, 2018; Satora *et al.,* 2018).

Due to the high epizootic and epidemiological threat in many countries, programmes for reducing the population of endangered animals remaining both as reservoir and virus vector have been carried out for several years. Initially, this concerned the population of free-living and feral dogs. However, it soon became apparent that these programmes were not very effective, and the virus found a new reservoir among wild animals, mainly foxes. Due to the fact that immunisation of dogs with traditional vaccines proved to be much more effective, based on this concept further actions were taken in the form of oral immunisation of free-living foxes to reduce and eliminate the virus in the population of these animals. The concept of oral immunisation of free-living foxes was developed in the 1960s. The first field research on this issue was carried out in Switzerland in 1978, and the next: in 1983 in Germany (Rupprecht *et al.,* 2004). Since then, the number of rabies cases has been significantly reduced in countries where fox vaccination has been undertaken. This can be confirmed by the results of vaccination in Poland. During 18 years of vaccination, the number of cases decreased from 1,119 to 11 cases, of which only one was recorded in free-living foxes and the remaining in bats (Sadkowska-Todys & Łabuńska, 2002; Flis, 2018; 2020). A similar trend has also occurred in other Western European countries. The effect of this is that some European countries have been recognised as free from rabies virus. This confirms that if the virus is eliminated in foxes in the wild, it also does not occur in domestic animals (Rupprecht *et al.,* 2004). However, in some countries with rabies-free status, the virus has re-emerged (Cliquet *et al.,* 2014).

Nevertheless, despite the significant reduction in the number of rabies cases in carnivores, there are currently no effective methods of vaccination of bats, which are a fairly significant source of danger. There is a real possibility of transmission of this pathogen transmitted by rabid bats to other animal species and even humans.

The threat is important because bats are the most common mammals in the world, and in terms of the species described they are second only to rodents, populating almost all continents, constituting about 20% of known mammal species (Calisher *et al.,* 2006).

The aim of the study was to assess the epizootic and epidemiological status of rabies in wild and domestic animals, with particular emphasis on bats, and the occurrence of the virus in humans throughout Europe over the last decade.

MATERIALS AND METHODS

Material

The material for work was data on the occurrence of rabies from the World Health Organization (WHO) Rabies - Bulletin - Europe information system and information from the literature related to the topic of work.

Research

As part of preventive measures, every European country is required to provide data to WHO regarding rabies that have been diagnosed in wild and domestic animals, bats, as well as cases found in humans. In addition, countries that use oral fox immunisation (ORV) as part of anti-rabies prophylaxis carry out monitoring studies on the effectiveness of these activities. The effectiveness assessment is conducted on the basis of trends of changes of cases, animals susceptible to rabies in a given country. Three methods are usually used in these tests. The first is based on immunofluorescence of brain prints and allows determining the presence of the virus in the collected material. The second method is based on the analysis of bone cuts, which allows determining the presence of a marker contained in the vaccine used, and at the same time confirms the vaccine's acceptance by the animal. Serum neutralisation RFFIT (Rapid Fluorescent Focus Inhibition Test) and ELISA (Enzyme-Linked Immunosorbent Assay) tests are used to determine antibodies in the blood serum. In addition, monitoring of cases in domestic animals and bats suspected of occurrence of the virus is carried out in each country.

Analysis

The obtained data were summarised in tabular forms, taking into account the number of rabies cases in wild animals, domestic animals and bats, as well as in humans. Based on the obtained data, a geographical pattern of rabies in the first year covered by the assessment (2010) and in 2019 was made, which allowed depicting regions of the greatest threats, trends of changes and the current epizootic and epidemiological status in individual European countries.

RESULTS

Rabies in wild animals

In 2010, in Europe, including the Russian Federation, 23,000 cases of rabies in wild animals were recorded (Table 1). Among European countries, the most cases (6,059) were recorded in Ukraine followed by 2,803 in Belarus. Quite a high number of cases were also found in Romania and Croatia. In the remaining countries, the occurrence of rabies was much lower, but Poland, Turkey and Moldova deserve to be mentioned. A high number of cases was also found in Italy and Serbia. In the remaining 15 European countries diagnosed with rabies in wild

Table 1. Prevalence of rabies in wild animals in Europe in the last decade

Country	Years									
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Albania	1	1	2	1	1					
Belarus	2,803	2,173	1,326	1,025	728	486	115			
Bośnia-Hercegovina	30	15	7	1						
Bulgaria	6	4	3	2	2					
Croatia	1,092	504	181	36	1					
Estonia	1	1								
Georgia	20	20	20	20	19	15	13	12	6	1
Greece	40	40	40	33	8					
Hungary	54	45	45	45	23	2	2	1		
Italy	199	1								
Kosovo	1	1	1	1						
Latvia	14									
Lithuania	49	18	6	3	3	3	1	1	1	
Macedonia	8	8	2							
Moldova	225	192	174	145	120	79	46	35	19	
Montenegro	71	14								
Poland	791	668	546	330	176	94	19	6	5	1
Romania	1,372	1,034	790	472	127	26	8	4	4	3
Russian Federation	9,527	8,099	7,065	6,062	5,064	4,113	2,557	1,671	870	148
Serbia	170	73	35	17	12	9	6	2	1	
Slovak Republic	10	10	10	10	5	5				
Slovenia	15	4	4	1						
Spain	1	1	1	1						
Turkey	441	426	377	320	268	173	105	53	11	
Ukraine	6,059	5,338	4,736	3,902	3,252	2,783	2,238	1,763	1,164	331

animals, the number of cases ranged from 1 to 54. In 21 European countries, rabies in wild animals was not found in 2010. In the following years, the number of rabies cases in wild animals decreased every year, and some countries became virus free. In 2019, the number of cases of rabies found in wild animals decreased nearly 50-fold (Fig. 1). During this period, rabies in wild animals was found only in 5 countries, a total of 484 cases (in descending order: Ukraine, Russia, Romania, Georgia and Poland) in which it occurred in 2010. No new cases of rabies were diagnosed in countries where it has not existed before.

Rabies in domestic animals

In 2010, a total of 26,701 cases of rabies in domestic animals were diagnosed in European countries (Table 2). As in wild animals, most cases were found in Russia

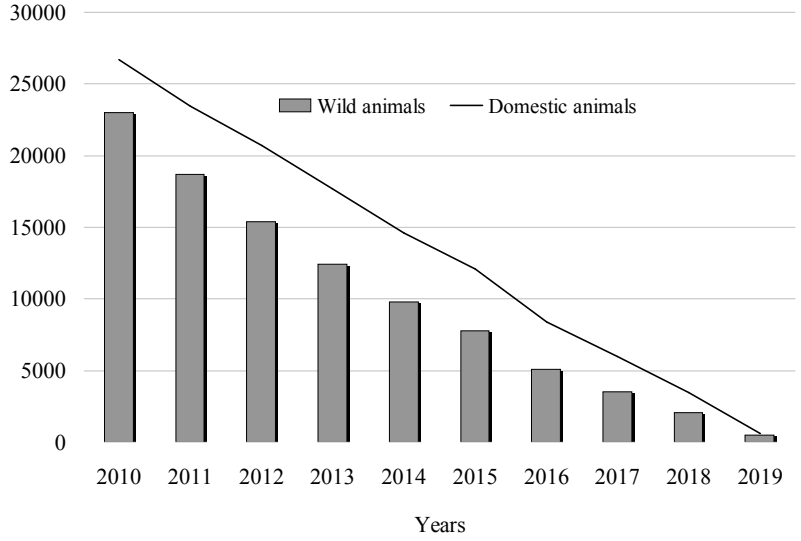

Fig. 1. Prevalence of rabies in wild and domestic animals in Europe during the last decade.

(n=10,497) and Ukraine (n=8,878). A large number of cases were also diagnosed in Turkey, Belarus, Moldova, Romania and Georgia. In addition, Poland and Croatia were countries with increased incidence of rabies among pet animals. In other countries where the virus was present during this period, 1 to 29 cases were diagnosed. In 20 European countries, rabies in pets has not been found. Rabies in domestic animals was found in 3 countries where it did not occur in wild animals (France, Germany, the Netherlands). In addition, it was not found in domestic animals in Estonia and Kosovo, while in wild animals it was diagnosed in these countries. In the ten-year period, the number of countries diagnosed with rabies decreased to 5, and the number of cases found dropped 42 times (Fig. 1). In decreasing order, the countries where rabies was found in pets were: Ukraine, Russia, Georgia and one case in Romania and Spain.

Rabies in bats

In 2010, rabies virus was diagnosed in 360 bats in 16 European countries (Table 3). The majority of cases occurred in Germany, the Netherlands, Poland and France. It is quite interesting and worrying that the virus in bats was found in 10 countries where it was not diagnosed in wild animals and in 7 countries where the virus was not found in domestic animals. In 2019, 29 cases of the virus were found in bats from 6 European countries. Most diagnoses were from Poland, Germany and the Netherlands. Three cases were found in the United Kingdom and one in each Spain and Ukraine. Most cases of the virus in bats (58.6%) were found in countries where the virus was not present in wild animals. The exception was Poland, where one case was found in a free-living fox and 10 – in bats. A slightly different situation occurred when rabies prevalence was compared in bats and pets: 44.8% of cases of virus in bats were found

Table 2. Incidence of rabies in domestic animals in Europe in the last decade

Country	Years									
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Albania	3	3	3							
Belarus	1,486	1,225	817	612	452	344	136			
Bośnia-Hercegovina	13	10	2	2	1					
Bulgaria	4									
Croatia	139	75	23	2						
France	4	4	3	3	2	2				
Georgia	483	483	483	483	369	254	154	102	68	26
Germany	2	1	1	1						
Greece	8	8	8	6	2					
Hungary	7	6	6	6	4	2	2	2		
Italy	11									
Latvia	5	3	2							
Lithuania	7	5	3	1						
Macedonia	1	1	1							
Moldova	742	650	606	451	364	267	131	101	59	
Montenegro	15	3	1							
Poland	174	152	118	80	38	22	4	1		
Romania	576	445	347	208	67	26	16	6	4	1
Russian Federation	10,497	9,135	8,172	7,279	6,134	5,235	3,420	2,532	1,542	239
Serbia	16	9	1							
Slovak Republic	2	2	2	2						
Slovenia	1									
Spain	29	27	27	22	15	11	5	3	1	1
The Netherlands	1	1	1							
Turkey	3,597	3,445	3,194	2,755	2,257	1,633	1,138	771	328	
Ukraine	8,878	7,737	6,910	5,749	4,884	4,269	3,372	2,494	1,449	368

in countries where rabies was also diagnosed in domestic animals.

Diagnosed cases of the virus in humans

During the period covered by the assessment, the number of cases of the virus in humans dropped dramatically (Table 4). In 2010, 74 such cases were found, most in Russia (n=45), Georgia (n=9) and Turkey (n=5). Three cases were recorded in Belarus, two in Ukraine and the United Kingdom. In the remaining 8 countries, the virus was found sporadically. In 2019, 1 case of human rabies was confirmed in Norway.

Geographical distribution of the virus during the last decade

Geographical patterns of the occurrence of rabies virus in wild animals indicate its gradual elimination from many European countries (Fig. 2). While in 2010 the virus

Table 3. The occurrence of rabies in bats in Europe in the last decade

Country	Years									
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Belarus	1	1	1							
Belgium	2	2	2	2	2	2	2	1		
Czech Republic	1	1	1	1	1	1				
Finland	2	2	2	2	2	2	2	1		
France	43	37	31	26	25	22	17	11	7	
Germany	123	118	107	93	84	77	64	41	26	9
Hungary	5	4	2	1	1	1				
Luxembourg	1	1	1	1						
Moldova		1	1	1	1					
Norway	1	1	1	1	1	1				
Poland	61	55	51	48	40	33	29	23	15	10
Spain	17	16	14	12	11	9	5	4	4	1
Switzerland		1	1	1	1	1	1	1		
The Nether-lands	70	60	53	37	33	30	25	16	7	5
Ukraine	15	14	13	13	10	8	8	5	3	1
United Kingdom	18	18	18	18	18	17	16	14	13	3

Table 4. Reported cases of rabies in people in Europe in the last decade

Country	Years									
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Belarus	3	3	1							
France	1	1	1	1	1	1	1	1		
Georgia	9	9	9	9	6	2	2	2	2	
Italy	1	1								
Norway	1	1	1	1	1	1	1	1	1	1
Portugal	1	1								
Romania	1	1	1							
Russian Federation	45	39	29	25	18	16	10	5	2	
Spain	1	1	1	1	1					
Switzerland	1	1	1							
The Nether-lands	1	1	1	1						
Turkey	5	5	5							
Ukraine	2									
United Kingdom	2	2	2	1	1	1	1	1	1	

dominated in the countries of Eastern and partly Central and Southern Europe, during the ten-year period it was eradicated from most countries of Central and Southern Europe. Russia and Ukraine still remain the main reservoir of this group of animals.

A similar situation occurred with rabies in domestic animals (Fig. 3). In 2010, the countries of Eastern and

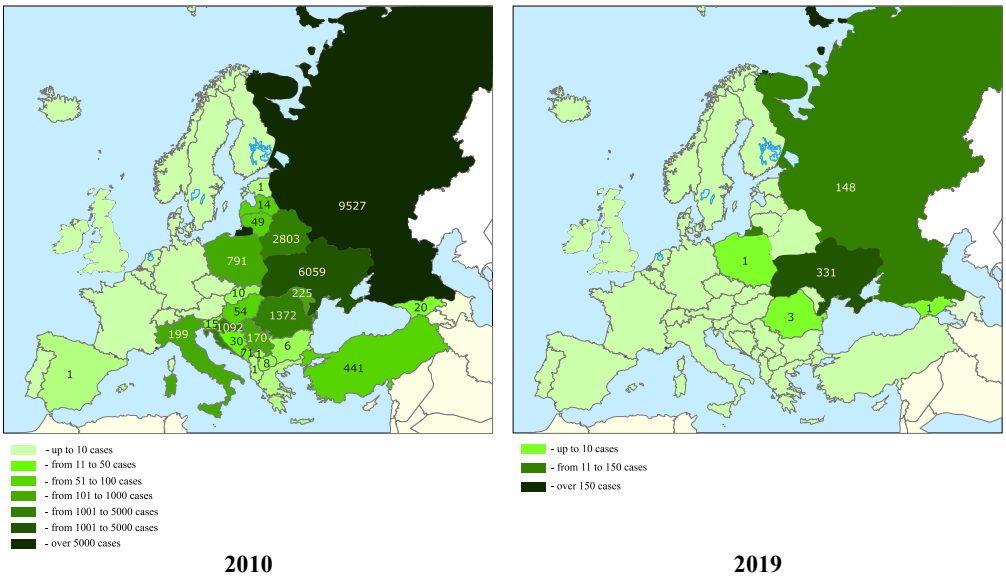

Fig. 2. Geographic pattern of occurrence of rabies in wild animals in Europe during the last decade.

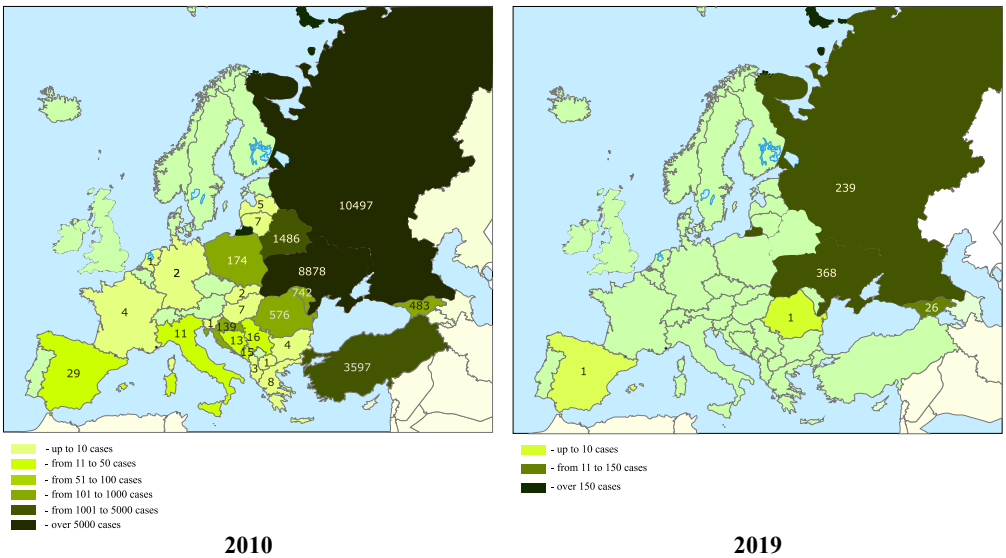

Fig. 3. Geographic pattern of occurrence of rabies in domestic animals in Europe during the last decade.

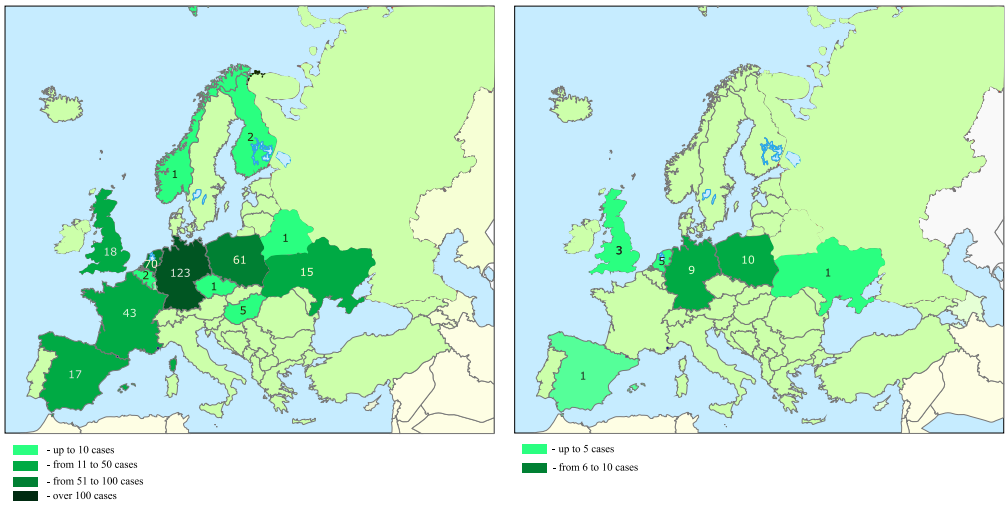

Fig. 4. Geographical pattern of the occurrence of rabies in bats in Europe during the last decade.

Southern Europe remained the main regions constituting the virus reservoir. However, in this group of animals, the virus was also found in the countries of Central and Western Europe (Poland, Germany, France and Spain). Over the past decade, the virus has been successfully eliminated from almost all Western and Central European countries, and Russia and Ukraine remain the main areas of its occurrence.

In 2010, rabies in bats was diagnosed in 14 European countries (Fig. 4). Most cases were found in the countries of Central and Western Europe. It was also found in countries where the virus was not diagnosed in both wild and domestic animals during this period. A significant number of cases were found in the Netherlands or Great Britain and in a few Scandinavian countries. During the ten-year evaluation period, the number of cases and countries where the virus was diagnosed in bats significantly decreased. In 2019, Poland, Germany and the Netherlands remained the main reservoir for bats. Despite the reduction in the number of diagnosed cases of rabies in bats, in the situation of eliminating the virus in Central European countries in wild and domestic animals, bats can constitute a new reservoir and vectors of virus spread.

DISCUSSION

Oral immunisation of wild animals, introduced in Europe for the first time in 1978 and continued in subsequent years, proved to be an effective tool in controlling and eradicating rabies and contributed to a significant decrease in the number of cases found in both wild and domestic animals. This is confirmed by monitoring data from European countries where the system of oral immunisation of wild animals – ORV, has been implemented (Brochier & Pastoret, 1993; Rupprech *et al.,* 2004; Leonova *et al.,* 2009; Un *et al.,* 2012; Robardet *et al.,* 2013; 2016; Cliquet *et al.,* 2014; Lupulovic *et al.,* 2015; Korou *et al.,* 2016; Henning *et al.,* 2017; Flis *et al.,* 2018; Flis, 2020).

Despite the high costs of preventive measures that are shaped by the purchase of the vaccine and its distribution in the field, the effectiveness of this type of action is high (Flis *et al.,* 2018; Sartore *et al.,* 2018). This is confirmed by the results of monitoring studies showing high rates of seroconversion in foxes often exceeding the level of 50%, and the level of tetracycline biomarker indicating vaccine reaching up to 90%. In Greece, seropositivity in foxes was 60%, while the biomarker level was 70% (Korou *et al.,* 2016). In Italy, in the years 2009–2016 the percentage of foxes found to have a biomarker ranged from 70.97 to 95.51% (Sartore *et al.,* 2018). In Croatia, in 2011–2012, seropositivity ranged from 11.24 to 35.64%, the vaccination rate was from 24.86 to 84.62% (Bedeković *et al.,* 2018). In Poland, where rabies was a serious problem, vaccinations have been carried out since 1993 in the western part of the country, and since 2002 throughout its territory. This contributed to the almost complete elimination of the virus in domestic animals, and in the wild occurs sporadically, mainly in bats (Flis *et al.,* 2018; Flis, 2020). At the same time, in the years 2011–2015, the seropositivity rate ranged from 54.10–79.49%, and the level of vaccine intake ranged from 86.04 to 89.09% (Flis *et al.,* 2018). In the Baltic countries (Lithuania, Latvia, Estonia), vaccinations have been carried out only since their accession to the European Union as part of the implementation of pan-European rabies eradication programmes. The highest level of seropositivity (73%) was found in the autumn of 2010 in Latvia, and the lowest – 30% also in the autumn in Estonia. In turn, the average level of vaccine intake in these countries was 80% (Robardet *et al.,* 2016). In Bulgaria, vaccination was carried out only after the country's accession to the European Union. Despite the increase in rabies in 2007, the first immunisations were carried out in 2009, when 59 cases of rabies were found in that country. These activities quickly led to the eradication of the virus, however, along with this, the number of samples under monitoring has decreased. This situation is so unfavorable that after the re-emergence of rabies in the Republic of Macedonia and Greece (Kirandjiski *et al.,* 2012; Tsioadras *et al.,* 2013; Korou *et al.,* 2016) there is a fairly high risk of cross-border virus transmission (Robardet *et al.,* 2013).

The high effectiveness of immunisation has contributed to the partial or complete elimination of rabies, but it still remains an important endemic disease that affects many European countries. At the same time, the emergence of new cases in countries that have been declared virus-free confirms the need for continuous monitoring and surveillance. Although many Western European countries have declared rabies-free status, rabies, being a cross-border disease, has no geographical barriers and reappears in these countries (Cliquet *et al.,* 2014; Stahl *et al.,* 2014; Giannakopoulos *et al.,* 2016). This can be confirmed by the appearance of rabies in 2 wild foxes from north-eastern Italy in October 2008, 10 years after the country has obtained rabies-free status (De Benedictis *et al.,* 2008; Sartore *et al.,* 2018). In Greece, rabies reappeared in wild and domestic animals 25 years after the country also acquired a rabies-free status (Tsiodras *et al.,* 2013; Korou *et al.,* 2016). Similar situations have also occurred in other countries, and the reasons for this are cases of rabies being transported both by importing animals as well as by people bitten during their stay especially in African and some Asian countries (Gaut-

ret *et al.,* 2011; Carrara *et al.,* 2013). For example, in France, in 1995– 2016, rabies was diagnosed in 7 people, but all of them were infected outside of mainland France (Parize *et al.,* 2018).

The fact that the virus is significantly prevalent in Eastern European countries is not without significance. Vaccination of pets is practiced in both Russia and Ukraine. In addition, oral immunisation is carried out in some areas of these countries, but their range and effectiveness are insufficient. In turn, in Russia, the largest number of rabies in foxes and raccoon dogs is found in the western regions, right at the border with Ukraine and Belarus, in and around Moscow (Shulpin *et al.,* 2018). Spatio-temporal analyses of rabies in areas directly bordering Poland have shown that both parenteral vaccination of domestic animals and oral immunisation of foxes (ORV) have proved to be ineffective in ensuring a lasting and long-term reduction of rabies epidemics (Polupan *et al.,* 2019).

As rabies is eliminated in terrestrial carnivores in many European countries, the virus quickly found a new reservoir – bats. Depending on the geographical location in Europe, rabies is caused by different virus strains (Kuzmin *et al.,* 2005; Ceballos *et al.,* 2013; Moldal *et al.,* 2017; McElhinney *et al.,* 2018; Nokireki *et al.,* 2018; Picard-Meyer *et al.,* 2019; Smreczak & Żmudziński 2019; Smreczak *et al.,* 2020). In Europe, rabies in bats is mainly caused by the European bat lyssavirus 1 (EBLV-1) strain, which is found particularly in the late moth bat (*Eptesicus serotinus*) and the desert moth (*Eptesicus isabellinus*). There is also European bat lyssvirus 2 (EBLV-2), found in the redhead (*Myotis daubentoni*) mainly in the British Isles, and in 2015 also confirmed in a bat in Norway. In 2010, Bokeloh bat lyssavirus (BBLV) was also diagnosed in Germany in a Natterer's bat (*Myotis nattererii*). In later years, further cases were registered in Germany, France and Poland (Moldal *et al.,* 2017; McElhinney *et al.,* 2018; Picard-Meyer *et al.,* 2019; Smreczak & Żmudziński, 2019; Smreczak *et al.,* 2020). In addition to these, individual cases of rabies were found to be caused by Lleida bat lyssavirus (LLBV), in Spain, at Schreibers' slouch (*Miniopterus schreibersii*) (Ceballos *et al.,* 2013). In the Caucasus, rabies was diagnosed with West Caucasian bat lyssavirus (WCBV) (Kuzmin *et al.,* 2005). Recently, in Finland, Kotalahti bat lyssavirus (KBLV) was found at Brandt's bat (*Myotis brandtii*) (Nokireki *et al.,* 2018).

Despite the lack of data on rabies in bats in Russia, the first diagnosed case after biting a 20-year-old girl resulting in her death took place in the Far East in 2007 (Leonova *et al.,* 2009). Quite important in this regard is the fact that the clinical picture of rabies acquired from a bat differs from its picture when acquired from a dog, and thus its diagnosis is more difficult and may overlook the occurrence of the virus (Begeman *et al.,* 2018).

CONCLUSION

The presented data indicate that as a result of oral immunisation of free living foxes against rabies (ORV) its occurrence in many European countries has been significantly reduced or eliminated. Still worrying data come from Eastern European countries where preventive actions are not carried out or their effectiveness is low. These countries are currently the primary reservoir for the virus. Due to the lack of geographical barriers for the virus, it appears again in countries recognised as

free from rabies. The virus is also brought to European countries by imports of companion animals and by travellers, especially in African and Asian countries. At the same time, the immunisation activities successfully eliminated it in terrestrial mammals, but the virus found a new reservoir in a specific group of mammals with the ability to fly, i.e. bats. Rabies in this group of animals is caused by various virus strains, all dangerous to humans, and currently there is no preventive action in this regard. In addition, the clinical picture of rabies in humans, where the virus vector was a bat, differs quite significantly from that caused by other animals. Thus, rabies, despite the significant reduction in the number of cases found in animals and humans, still poses a serious epizootic threat to public health.

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