Acta virologica **64**: 216 – 225, 2020 doi: 10.4149/av_2020_211

Historical analysis of epizootiological situation of rabies on the territory of the Slovak Republic

A. ONDREJKOVÁ[1], Š. ŠVRČEK[1], R. ONDREJKA[1], Z. BENÍŠEK[1†], J. SÜLI[2], V. KOPŘIVA[3], S. ZEMANOVÁ[1], Z. BENKŐ[1], Ľ. KORYTÁR[1*]

[1]Department of Epizootiology and Parasitology, University of Veterinary Medicine and Pharmacy in Košice, Komenského 73, 041 81 Košice, Slovak Republic; [2]Department of Chemistry, Biochemistry and Biophysics, University of Veterinary Medicine and Pharmacy in Košice, Košice, Slovak Republic; [3]State Veterinary and Food Administration of the Slovak Republic, Bratislava, Slovak Republic

Summary. – Currently, Slovakia is a rabies-free country, but the epizootiological situation of rabies was not always favorable. The main reservoir species of rabies virus in the first half of the last century was the domestic dog. Since 1906, hundreds of cases were reported, of which approximately 90% were infected dogs. The disease had a typical urban character. Since 1929, the number of rabid domestic animals decreased due to the implementation of dog vaccination campaigns in particular parts of Slovakia. From the second half of 1950s, red foxes (*Vulpes vulpes*) have become an important reservoir of the RABV. In this time period urban rabies in Slovakia changed into sylvatic form. One effective method of prevention and control of wildlife rabies is an oral rabies vaccination of red foxes. It is carried out in Slovakia since 1993. A detailed development of the rabies epizootiological situation on the territory of the Slovak Republic until the application of oral antirabies immunisation of foxes and the current situation after its performance is the main object of this review.

Keywords: rabies; Lyssavirus; red fox; incidence; oral vaccination

Introduction

Rabies is an acute, progressive infectious disease of the central nervous system (CNS) of homoiothermic animals, including human. *Lyssa*, which means "mad" or "violent", is the ancient Greek name for rabies. The existence of the disease resembling rabies is mentioned in records older than 5,000 years. The first historic evidence describing illness after bites by dogs recorded ancient Egyptians and Mesopotamians in their written texts (Blaisdell, 1994).

Except for Antarctica and a few rabies-free island territories, rabies occurs on all continents (Hanlon and Childs, 2013).

From the global point of view, the rabies poses one of the most important threats for the public health. Nevertheless, the rabies belongs to the neglected zoonotic diseases with a highest incidence among humans and susceptible animal species in Africa and Asia (Fooks *et al*., 2014). Approximately 50,000–60,000 people die from rabies each year (Wunner and Briggs, 2010).

Rabies is caused by a negative stranded RNA virus belonging to the genus *Lyssavirus* in the family *Rhabdoviridae* of the order *Mononegavirales*. All lyssaviruses are neurotropic pathogens (Fooks *et al*., 2017).

According to ICTV (2019), the genus *Lyssavirus* includes 16 recently known and classified viruses. Phylogenetic analyses targeted on lyssaviruses distinguish two genetically and immunopathologically distinct phylogroups (Badrane *et al*., 2001). Phylogroup I includes Rabies lyssavirus (RABV), Australian bat lyssavirus (ABLV), Duvenhage lyssavirus (DUVV), European bat 1 lyssavirus (EBL-1), European bat 2 lyssavirus (EBL-2), Aravan lyssavirus (ARAV), Khujand lyssavirus (KHUV), Bokeloh bat

*Corresponding author. E-mail: korytar.uvm@gmail.com; phone: +421-907 816 472. †Deceased author.

Abbreviations: CNS = central nervous system; ICTV= International Committee on Taxonomy of Viruses; RABV = rabies virus; SVFA = State Veterinary and Food Administration of the Slovak Republic

Table 1. Geographical distribution and reservoirs of classified lyssaviruses (ICTV, 2019)

Genotype	Species	Distribution	Reservoir
1	*Rabies virus*	Worldwide	Carnivora Chiroptera
2	*Lagos bat virus*	Sub-Saharan Africa	Chiroptera
3	*Mokola virus*	Sub-Saharan Africa	unknown
4	*Duvenhage virus*	South Africa	Chiroptera
5	*European bat lyssavirus 1*	Europe	Chiroptera
6	*European bat lyssavirus 2*	Europe	Chiroptera
7	*Australian bat lyssavirus*	Australia	Chiroptera
-	*Aravan virus*	Central Asia	Chiroptera
-	*Khujand virus*	Central Asia	Chiroptera
-	*Irkut virus*	East Siberia	Chiroptera
-	*West Caucasian bat virus*	Caucasus	Chiroptera
-	*Ikoma lyssavirus*	East Africa	African Civet (*Civettictis civetta*)
-	*Shimoni bat virus*	East Africa	Chiroptera
-	*Bokeloh bat lyssavirus*	Europe	Chiroptera
-	*Gannoruwa bat lyssavirus*	East Asia	Chiroptera
-	*Lleida bat lyssavirus*	Europe	Chiroptera

lyssavirus (BBLV), Irkut lyssavirus (IRKV) and Gannoruwa bat lyssavirus (GBLV).

Phylogroup II includes Lagos bat lyssavirus (LBV), Mokola lyssavirus (MOKV) and Shimoni bat lyssavirus (SHIBV).

Ikoma lyssavirus (IKOV), Lleida bat lyssavirus (LLBV) and West Caucasian bat lyssavirus (WCBV) are not included into phylogroups now.

Two novel lyssaviruses, Taiwan bat lyssavirus (TBLV) (Hu *et al*., 2018) and Kotalahti bat lyssavirus (KBLV) (Norieki *et al*., 2018) are not classified up to date (ICTV, 2019). Mammalian reservoirs include carnivores (Carnivora) and bats (Chiroptera). The known reservoir organisms and geographical distribution of all classified lyssaviruses are summarised in the Table 1.

The RABV circulating in dogs is responsible for more than 99% of human infections worldwide (Knobel *et al*., 2005). Lyssaviruses are most often transmitted by the bite or by a scratch of an infected animal. In this way, the virus crosses the dermal barrier and reaches the tissue of a susceptible host, where it can begin to spread (Jeffries *et al*., 2013). After reaching the motor neurons, the lyssavirus propagates up to the CNS. Lyssavirus follows neuronal connections in the organism of its host, which protects the virus from the immune system of the infected macroorganism (Johnson *et al*., 2010). In the CNS, the lyssavirus replicates and disseminates to almost all compartments of the system.

In addition to the most common route of infection by a bite, other ways of transmission of lyssaviruses have been described. Crandell (1991) reported RABV infection in Polar Foxes (*Vulpes lagopus*) via consumption of infected carcasses. (Anderson *et al*., 1984) described a contact with mucosa as another possible way of RABV infection. Transmission of lyssaviruses by aerosol was also recorded (Constantine, 1962; Johnson *et al*., 2006). Transmission between dead-end hosts including human occurs under exceptional conditions in cases of organ or corneal transplantations (Maier *et al*., 2010). RABV may be secreted to the breast milk (Dutta, 1998). Transplacental transmission has been reported in animals but has not been documented in humans (Singh *et al*., 2017).

Rabies of humans and animals is preventable by vaccines. Approximately 15 million people receive rabies post-exposure prophylaxis annually (Wilde *et al*., 2013).

In countries, where canine rabies has been eliminated, wild animals like foxes, raccoons and skunks are still important reservoir species. For this reason, these species pose an important target of vaccination campaigns (Dietzschold *et al*., 2004).

Until now, especially for the species at risk of rabies virus infection, prophylactic and pre-exposition vaccinations remain the main and sole approach to prevent the disease (Franka *et al*., 2009).

Inactivated rabies vaccines, which are known for their safety, represent an important tool for rabies control (Hampson *et al*., 2011). In Europe and North America, several live attenuated rabies vaccines such as SAD B19, SAG-1 and SAG-2 (Muller *et al*., 2009; Prager *et al*., 2011) have been successfully applied as pre-exposure prophylaxis by oral immunisation of wildlife. These vaccines are derived from the Street Alabama Dufferin (SAD) field strain isolated from a dog in North America in 1935 (Geue *et al*., 2008).

Epizootiological situation of rabies at the beginning of the 20th century

The first rabies cases on the territory of the Slovak Republic were identified at the end of the 19th century, involving rabies cases of dogs and cats. The urban rabies form occurred in Slovakia prior to the Second World War; as is evident from the high number of people treated after exposure to rabid dogs in the Pasteur Institute of the State Hospital in Košice (Strimpl, 1931; Jiroušková *et al*., 1990) (Table 2). The main reservoir species of the rabies virus in the first half of the last century was the domestic dog. The rabies cases in dogs accounted for almost 90% of those confirmed to be positive. In the former Czechoslovakia, 132 people died from rabies and 25,000 people were post-exposure vaccinated between 1919 and 1937. Most cases of rabies have been reported in domestic carnivores and livestock in villages and small towns. Data on the occurrence of rabies in Slovakia at that time are incomplete, but we can assume that the epidemiological situation in rabies was the same as in Central Europe (Matouch *et al*., 1998).

The disease had a typical urban character; domestic dogs were considered the main reservoir of rabies. At that time, veterinary measures focused on the elimination of suspicious and stray dogs and cats (Matouch *et al*., 2002). According to our data, rabies in wild animals was not a problem, so it received little attention. Bites by rabid animals other than dogs were rare (Jiroušková *et al*., 1990).

The diagnosis of rabies was initially performed only on the basis of clinical signs or necropsy of dead animals. Laboratory diagnostics of rabies began in 1920 at the State Diagnostic and Serotherapeutic Veterinary Institute at Ivanovice na Hané. However, the capacity of this laboratory was only sufficient to test domestic animals and humans (Strimpl, 1931).

Since 1929, the number of rabies cases in domestic animals has been gradually decreasing, 608 cases in 1928 (519 dogs, 47 cats, 32 cattle, 2 goats), 455 cases in 1929 (401 dogs, 24 cats and 30 other domestic animals) and 33 in 1939 (Table 3). The reduction was achieved by large vaccination campaigns of dogs in some parts of Slovakia and Bohemia during 1929–1931 (Ursíny and Stolzová-Sutorisová, 1970).

There was little interest in wildlife from the point of view of veterinary and public services; although high fox mortality was observed occasionally, e.g. 1919–1920, foxes were not investigated in the laboratory and the etiology remained unexplained. We found no information about rabies in wild animals between 1919 and 1939 in historical records, although Ursíny and Stolzová-Sutorisová (1970) claimed that rabies was sporadically recorded in foxes and wolves in eastern parts of Slovakia and western Ukraine. Despite a slight increase in 1935–1937, the overall epide-

Table 2. Number of human patients in the Pasteur Hospital in Košice (Czechoslovakia) from 1928 to 1930 (Jiroušková *et al.*, 1990)

Number of:	1928 (8 months)	1929	1930
Accepted patients	894	976	676
Treated patients	884	970	672
Bited by health dogs	86	155	127
Bited by rabid dogs	334	391	223
Bited by unknown dogs	310	290	186
Contact with infected animal	110	134	51
Patient who drank milk from rabid cows	32	-	81
Patient who dissected cadavers of rabid cows and was teared	12	-	4

Table 3. Laboratory confirmed cases of rabies from 1906 to 1939 (Ursíny and Stolzová-Sutorisová, 1970)

Year	Dogs	Cats	Others	Σ	Year	Dogs	Cats	Others	Σ
1906	387	0	0	387	**1928**	519	47	42	608
1907	337	7	2	346	**1929**	401	24	30	455
1908	887	0	0	887	**1930**	203	10	11	224
1909	519	5	26	550	**1931**	162	9	9	180
1910	568	0	6	574	**1932**	95	1	0	96
	Data not available				**1933**	76	7	5	88
1919	333	26	6	365	**1934**	47	2	3	52
1920	151	9	2	162	**1935**	76	2	5	83
	Data not available				**1936**	89	3	4	96
1924	533	52	49	634	**1937**	78	2	11	91
1925	483	36	29	548	**1938**	41	4	2	47
1926	472	37	27	536	**1939**	32	0	1	33
1927	382	26	47	455	**Summary**	**6871**	**309**	**317**	**7497**

Σ – total number of rabies cases in a particular year.

miological situation in rabies stabilized (Matouch *et al.*, 2002).

No records from the years 1940–1947 were preserved, as the Institute for rabies diagnostics was seriously damaged during the war. After the war, the incidence of rabies increased, most cases were diagnosed in winter, from January to April and the lowest incidence was in July to September, the incidence of rabies was bound to the borderline and nearby regions in Moravia and Slovakia (Matouch *et al.*, 2007).

The epidemiological situation changed after the Second World War, when the immunisation of dogs against rabies started. Immunisation was voluntary since 1927, becoming obligatory in 1953.

Cases of rabies in domestic carnivores (mainly dogs) were gradually replaced with cases in wild carnivores (foxes and wolves). This is confirmed by the incidence of rabies in individual animal species: from 1921 to 1943, confirmed positive cases of rabies in dogs presented 89.3% of the total and in wild animals only 0.04%.

Most cases of rabies have been diagnosed in foxes since the second half of the 1950s. It was in this period that the urban form of rabies changed to sylvatic, which clearly required a change in the strategy to combat this severe zoonosis (Müller *et al.*, 1998). Wild animals have become the reservoir of rabies in Europe, especially foxes, which played a key role in the exposure of domestic animals. At the same time, their share of human exposure increased (Matouch and Vitásek, 2002).

From 1945 to 1960 the epizootiological situation in Slovakia changed, with rabies being diagnosed in dogs only in 9% of the total number of confirmed cases and in 80.1% in wild animals; 93.3% of them were foxes (Ursíny and Stolzová-Sutorisová, 1970) (Table 4). The total number of confirmed cases sharply dropped during this period.

The rabies epizootiological situation worsened from the second half of the 1960s; more than 300 positive cases were confirmed just in 1968. The number of positive cases constantly increased until the end of 1980s. Almost 7,000 rabies cases and 2 cases of bat lyssavirus infection (Švrček *et al.*, 1991; 2001; Ondrejková *et al.*, 2004) were recorded in Slovakia in the last 25 years. The last case of human rabies in Slovakia was identified in 1990 (Švrček *et al.*, 1999).

All measures adopted during the 1970s and 1980s and directed at the reduction of population density of foxes – the main reservoir species of rabies (payment of shooting

Table 4. Rabies cases in domestic and wild animals in the Slovak Republic from 1947 to 1992 (Ursíny and Stolzová-Sutorisová, 1970; Ondrejková *et al.*, 2004)

Year	DA	WA	n	Year	DA	WA	n
1947	16	1	17	**1970**	81	182	263
1948	5	0	5	**1971**	90	157	247
1949	2	0	2	**1972**	121	206	327
1950	0	1	1	**1973**	47	143	190
1951	13	16	29	**1974**	73	133	206
1952	8	1	9	**1975**	69	60	129
1953	8	4	12	**1976**	62	98	160
1954	11	10	21	**1977**	54	121	175
1955	0	1	1	**1978**	39	90	129
1956	1	0	1	**1979**	46	22	68
1957	1	0	1	**1980**	19	34	53
1958	4	5	9	**1981**	8	39	47
1959	2	1	3	**1982**	47	66	113
1960	6	9	15	**1983**	42	114	156
1961	6	14	20	**1984**	51	161	212
1962	10	56	66	**1985**	42	66	108
1963	11	75	86	**1986**	39	122	161
1964	4	104	108	**1987**	41	117	158
1965	3	84	87	**1988**	34	204	238
1966	10	67	77	**1989**	29	182	211
1967	15	145	160	**1990**	40	187	227
1968	77	324	401	**1991**	40	165	205
1969	20	120	140	**1992**	44	258	302
				Summary	**1 391**	**3 965**	**5 356**

DA = rabies cases in domestic animals, WA = rabies cases in wild animals.

premium, gassing of the fox lairs, poisoning of foxes by strychnine baits, sterilization of foxes by baits) – showed to be ineffective (Švrček *et al*., 1995).

Oral immunisation of red foxes against rabies in Slovak Republic

The idea of immunisation of foxes against rabies was expressed by prof. Baer in the early 1960s. One effective method of rabies control of wild animals is the oral vaccination of red foxes against rabies (Wandeler, 2000). The current rabies epizootiological situation not only in Slovakia, but also in other European states, is closely associated with its performance or non-performance. Oral immunisation must be carried out with due regard to the specific conditions of each country. The basic prerequisite for successful oral anti-rabies vaccination in wild animals was a detailed elaboration of the strategy of implementation of individual vaccination campaigns aimed at eliminating rabies in large territorial units (Müller *et al*., 1998).

According to the WHO and OIE recommendations, the oral immunisation of free-living red foxes against rabies is of great importance in the control of fox rabies. It is a pre-emptive, effective, ecologically harmless, financially and technically manageable measure. By 1994, oral anti-rabies vaccination had begun in 17 European countries, with about 15 million vaccine doses distributed annually (Stöhr and Meslin, 1996).

The oral vaccination of red foxes against rabies in Slovakia began in 1992 (Švrček, 1992; Švrček *et al*., 1995; Ďurove *et al*., 1996a) based on the resolution of the State Veterinary Administration of the Slovak Republic in Bratislava, in co-operation with Mevak Inc. Nitra, Associated Laboratory for Rabies Research of University of Veterinary Medicine and Institute of Experimental Veterinary Medicine in Košice, the Hunting Association, the State Veterinary Institutes and other related institutes. The oral vaccination of red foxes against rabies was performed in selected areas of the Slovak Republic in 1992 and 1993 in two phases (spring and autumn). The oral vaccine Kamark (Mevak Inc. Nitra, Slovak Republic) was used (Švrček *et al*., 1993, 1998).

After detailed evaluation of the efficacy of oral vaccination in selected areas, a program of vaccination for the whole republic for 1994-1996 was elaborated. Besides vaccine Kamark, the vaccine Lysvulpen (Bioveta Inc., Ivanovice na Hané, Czech Republic) was also used in the spring campaign in 1994 (Table 5). The effectiveness of its implementation was shown after just the first year, when the number of positive cases of rabies decreased to 50%. In 1997, a nationwide anti-rabies vaccination of red foxes was discontinued, resulting in an increase in

Table 5. Oral rabies vaccination of free-living red foxes in Slovak Republic from 1992 to 1996 (Kopřiva *et al.*, 2009)

Year	Campaign	Vaccination baits			Treated area (km²)
		Sort	Producer	Number	
1992	Spring/Autumn	Kamark	Mevak Inc., SR	30,000	2,000
1993	Spring/Autumn	Kamark	Mevak Inc., SR	100,300	6,687
1994	Spring/Autumn	Kamark Lysvulpen	Mevak Inc., SR Bioveta Inc., ČR	650,000	47,000
1995	Spring/Autumn	Kamark	Mevak Inc., SR	650,000	47,000
1996	Spring/Autumn	Kamark	Mevak Inc., SR	552,800	36,400

Table 6. Occurrence of rabies in domestic and wild animals in Slovakia from 1993 to 1999 (Ďurove *et al.*, 1992b; Kopřiva *et al.*, 2009)

Year	Domestic animals		Wild animals				Total
	total	%	foxes	%	total	%	
1993	80	16.4	393	80.4	409	83.6	**489**
1994	113	20.0	428	75.7	452	80.0	**565**
1995	62	23.3	197	74.0	204	76.7	**266**
1996	73	21.2	256	74.2	272	78.8	**345**
1997	52	20.0	198	76.4	207	80.0	259
1998	67	16.2	336	81.2	347	83.8	**414**
1999	83	16.5	392	77.9	420	83.5	**503**
Summary	**530**	**18.7**	**2200**	**77.4**	**2311**	**81.3**	**2841**

positive cases of rabies until 1999. In 1997–1998, the oral immunisation against rabies was renewed in selected areas of the Slovak Republic, especially in areas of rabies prevalence (Kopřiva *et al*., 2009).

A total of 413 cases were reported in 1998, of which 16% were infected domestic animals and 84% were infected wild animals (Table 6). Numerous outbreaks were spread throughout the territory, with the highest concentration in the southwestern area, near the borders with Austria and Hungary.

The State Veterinary and Food Administration of the Slovak Republic (SVFA) developed a triennial program of oral immunisation against rabies in 1999, specifically for the period of 2000–2002 (Hlinka, 2002). In the spring of 2000, the whole territory of the Slovak Republic was vaccinated by air, only in several districts the vaccination baits were spread manually. The vaccine Lysvulpen (Bioveta Inc., Ivanovice na Hané, Czech Republic) was used; the vaccinated area was 30,000 km^2 (Table 7). In the autumn of 2000 an additional Lyssavac vaccine (Pharmagal Bio Ltd. Nitra, Slovak Republic) was used (Table 7) (Kopřiva *et al*., 2009).

In the year 2001, the two oral rabies vaccines mentioned above were used again. The whole territory of the country was vaccinated by air, with the exception of a small area and some suburban districts, where the vaccination baits were spread manually (Kopřiva *et al*., 2009). In the autumn campaign of 2002 and the spring of 2003, a new rabies oral vaccine Lyssagal cps. a.u.v. (Pharmagal Bio Ltd. Nitra, Slovak Republic) was used (Hlinka, 2002).

Due to aggravation of the epizootiological situation in rabies, protocols for oral vaccination against rabies were re-evaluated and the oral vaccine used was changed (SVFA, 2003). The vaccine Lysvulpen (Bioveta Inc. Ivanovice na Hané, Czech Republic) has been used for oral vaccination against rabies on the territory of Slovakia since autumn 2003.

The oral immunisation control is performed according to the instructions for use elaborated by SVFA of the Slovak Republic before each vaccination campaign. Not only the vaccine, but also the baits for oral immunisation of wild animals must fulfil a complex series of recommendations (Wandeler, 1991; Švrček, 1992).

One of the first field control examinations is the control of the acceptance of vaccination baits, because the ingestion of the majority of spread baits by the target animals – red foxes – over a period of 3–5 days indicates

Table 7. Oral anti-rabies vaccination of free-living red foxes and vaccines used in the Slovak Republic from 2000 to 2019 (Kopřiva *et al*., 2009; Kopřiva unpublished data)

Year	Campaign	Vaccination baits			Treated area (km^2)
		Vaccine	Producer	Number	
2000	S/A	Lysvulpen Lyssavac	Bioveta Inc. CR Pharmagal Bio Ltd.	675,180	30,000
2001	S/A	Lysvulpen Lyssavac	Bioveta Inc. CR Pharmagal Bio Ltd.	767,180	30,000
2002	S/A	Lyssavac Lyssagal	Pharmagal Bio Ltd.	798,600	32,422
2003	S/A	Lysvulpen	Bioveta Inc., CR	700,000	33,250
2004	S/A	Lysvulpen	Bioveta Inc., CR	876,000	33,250
2005	S/A	Lysvulpen	Bioveta Inc., CR	844,900	13,800
2006	S/A	Lysvulpen	Bioveta Inc., CR	844,900	12,000
2007	S/A	Lysvulpen	Bioveta Inc., CR	844,900	12,000
2008	S/A	Lysvulpen	Bioveta Inc., CR	844,900	12,000
2009	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2010	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2011	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2012	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2013	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2014	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2015	S/A	Lysvulpen	Bioveta Inc., CR	NA	NA
2016	S/A	Lysvulpen	Bioveta Inc., CR	614,050	12,458
2017	S/A	Lysvulpen	Bioveta Inc., CR	620,300	12,458
2018	S/A	Lysvulpen	Bioveta Inc., CR	632,800	12,708
2019	S/A	Lysvulpen	Bioveta Inc., CR	632,800	12,708

S = summer, A = autumn, NA = data not available.

Table 8. Rabies in domestic and wild animals including foxes in Slovakia from 2000 to 2019 (Kopřiva *et al.*, 2009; SVFA, 2019)

Years	Domestic animals		Wild animals				Total
	total	%	foxes	%	total	%	
2000	71	20.2	267	76.0	280	79.8	**351**
2001	12	13.8	70	80.4	75	86.2	**87**
2002	19	16.8	90	79.6	94	83.2	**113**
2003	42	12.9	247	75.8	284	87.1	**326**
2004	4	6.2	54	84.4	60	93.8	**64**
2005	4	8.0	44	88.0	46	92.0	**50**
2006	0	0	4	100.0	4	100.0	**4**
2007–2012	0	0	0	0	0	0	**0**
2013	2	28.6	4	57.1	5	71.4	**7**
2014	0	0	0	0	0	0	**0**
2015	0	0	5	100.0	5	100.0	**5**
2016–2019	0	0	0	0	0	0	**0**
Summary	**154**	**15.3**	**785**	**77.9**	**853**	**84.7**	**1007**

Table 9. Summary of wild and domestic animals tested for rabies in Slovakia from 2000 to 2019 (Kopřiva *et al.*, 2009; SVFA, 2019)

Year	Wild animals				Domestic animals				Total No. of tested animals	
	Foxes		Others		Dogs & cats		Others			
	+	–	+	–	+	–	+	–	+	–
2019*	0	555	0	29	0	108	0	8	0	700
2018	0	699	0	42	0	151	0	6	0	898
2017	0	1743	0	61	0	163	0	8	0	1975
2016	0	1716	0	51	0	172	0	7	0	1946
2015	5	1 874	0	33	0	217	0	9	5	2 133
2014	0	1 396	0	32	0	226	0	10	0	1 664
2013	4	3 535	1	45	2	213	0	4	7	3 797
2012	0	3 369	0	44	0	242	0	13	0	3 668
2011	0	3 264	0	60	0	279	0	20	0	3 623
2010	0	2 922	0	42	0	323	0	16	0	3 303
2009	0	3 203	0	86	0	391	0	28	0	3 708
2008	0	3 422	0	77	0	484	0	25	0	4 008
2007	0	3 751	0	86	0	445	0	31	0	4 313
2006	1	3 630	0	105	0	485	0	21	1	4 241
2005	44	1 767	2	126	4	654	0	42	50	2 589
2004	54	1 563	6	109	3	660	1	50	64	2 382
2003	295	1 791	13	159	43	676	3	72	354	2 698
2002	94	1 452	3	130	16	713	1	80	114	2 375
2001	72	1 027	4	116	11	674	0	62	87	1 879
2000	292	1 416	13	164	66	793	4	69	375	2 442
Summary	**861**	**44 095**	**42**	**1 597**	**145**	**8 069**	**9**	**581**	**1 057**	**54 342**

(+) = No. of infected animals, (–) = No. of non-infected animals, (*) = in 2019 data available only until June 30th.

their attractiveness (Wandeler, 1991). Laboratory investigations are an integral part of effectiveness and quality verification; this step is primarily conditioned by controlled shooting of young foxes in the vaccination zone (Ondrejková *et al.*, 2000).

The current epizootiological situation in the Slovak Republic

The reduction of rabies incidence in domestic and wild animals is achieved by the epizootiological effectiveness of oral immunisation against rabies over the entire terri-

tory of the country. In 1995 the number of positive rabies cases in wild animals, particularly in red foxes, markedly decreased (Table 6) following the first whole-territory oral vaccination against rabies (Ďurove *et al*., 1996b); the situation was analogous in 2001 (87 positive cases) and 2002 (113 positive cases) (Table 8) (Kopřiva *et al*., 2009; SVFA, 2019). In 2002, two new vaccines (Lyssavac and Lyssagal) were used for oral vaccination against rabies. In 2003, an increased number of rabies cases were diagnosed (326 positive cases). Consequently, the State Veterinary and Food Administration of the Slovak Republic re-evaluated the effectiveness of the vaccines and came to the resolution to use the vaccine Lysvulpen.

In 2004, rabies was confirmed in 64 animals (4 cases in domestic and 60 in wild animals). According to the Slovak National Reference Laboratory for Rabies Zvolen, in 2005 marked reduction in positive cases was recorded. On average, red foxes account for 77.4–77.9% of all positive cases, respectively, of all diagnosed positive cases in 1993–2019. Together with other wild animal species, this value represents more than 84% of all laboratory confirmed rabies cases (in 1993–1999: 81.3%; in 2000–2019: 84.7%). Rabies cases in domestic animals in 1993–1999 represented 18.7%; in 2000–2019 it was 15.3%; in 2006 there were no cases. No case of rabies was diagnosed in domestic or wild animals in Slovakia in 2007 (Table 8) (Kopřiva *et al*., 2009; SVFA, 2019).

Slovakia was a country with no rabies status until 2012. In 2013, 7 cases of rabies were confirmed in the territory of the Slovak Republic near the border with Poland (4 foxes, 1 marten and 2 dogs). In 2014, no cases were confirmed in Slovak Republic, but in 2015 a total of 5 cases of rabies were identified. All rabies-positive animals were foxes found in the state area near the border with Poland (Table 8) (Kopřiva *et al*., 2009; SVFA, 2019).

Currently, Slovakia is a rabies-free country.

The incidence of rabies in the Slovak Republic demonstrates, among other things, the effectiveness of oral rabies immunisation of red foxes – the main reservoir species of rabies. Data from the last 19 years show an improvement in the epizootiological situation in rabies. The decrease in rabies cases in domestic and farm animals corresponds with the situation in the wild ones. During last 19 years, the Slovak National Reference Laboratory for Rabies in Zvolen tested more than 54,000 animals for rabies (Table 9) (Kopřiva *et al*., 2009; SVFA, 2019).

Conclusion

An implementation of surveillance and monitoring programs, pre-exposition vaccination of domestic carnivores and oral vaccination of foxes are among the key activities determining successful prevention of rabies incidence in the Slovak Republic. Preventive actions must be performed effectively in the whole state territory and especially focused on the high-risk areas close to the neighboring countries with confirmed circulation of RABV.

Currently, the epizootiological situation of rabies in Slovakia is good thanks a continual oral anti-rabies vaccination of foxes. The 40th successful vaccination campaign was performed in the autumn 2019.

Acknowledgments. This work was financially supported by the project APVV-0605-12 granted by the Slovak Research and Development Agency.

References

Anderson LJ, Williams LP, Jr, Layde JB, Dixon FR, Winkler WG., Am. J. Public Health 74, 370–372, 1984. https://doi.org/10.2105/AJPH.74.4.370

Badrane H, Bahloul C, Perrin P, Tordo N., J. Virol. 75, 3268–3276, 2001. https://doi.org/10.1128/JVI.75.7.3268-3276.2001

Blaisdell JD., Vet. Hist. 8, 22–28, 1994. https://doi.org/10.1515/jpme.1994.22.1.28

Constantine DG., Public Health Rep. 77, 287–289, 1962. https://doi.org/10.2307/4591470

Crandell RA., Arctic fox rabies. In Baer GM (Ed.): The natural history of rabies. CRC Press, Boca Ranton, pp. 291–306, 1991.

Dietzschold ML, Faber M, Mattis JA, Pak KY, Schnell MJ, Dietzschold B., Vaccine 23, 518–524, 2004. https://doi.org/10.1016/j.vaccine.2004.06.031

Ďurove A, Ondrejka R, Švrček Š, Süliová J, Beníšek Z, Závadová J., Evaluation of effectiveness of oral rabies vaccination of red foxes in Slovakia (in Slovak). Inf. Symp. Košice (Slovak Republic), Proceedings, p. 7, 1996a.

Ďurove A, Švrček Š, Sokol J, Süliová J, Ondrejka R, Beníšek Z, Závadová J, Janusová K, Lovás B, Borsuková O, Kubinec J., Wien. Tierärztl. Mschr. 83, 158–163, 1996b.

Dutta JK, J. Indian Med. Assoc. 96, 359, 1998.

Fooks AR, Banyard AC, Horton DL, Johnson N, McElhinney LM, Jackson AC., Lancet 348, 1389–1399, 2014. https://doi.org/10.1016/S0140-6736(13)62707-5

Fooks AR, Cliquet F, Finke S, Freuling C, Hemachudha T, Mani RS, Müller T, Nadin-Davis S, Picard-Meyer E, Wilde H, Ashley C. Banyard AC., Nat. Rev. Dis. Primers 3, 17091, 2017. https://doi.org/10.1038/nrdp.2017.91

Franka R, Wu XF, Jackson FR, Velasco-Villa A, Palmer DP, Henderson H, Hayat W, Green DB, Blanton JD, Greenberg L, Rupprecht CE., Vaccine 27, 7149–7155, 2009. https://doi.org/10.1016/j.vaccine.2009.09.034

Geue L, Schares S, Schnick C, Kliemt J, Beckert A, Freuling C, Conraths FJ, Hoffmann B, Zanoni R, Marston D, Mcelhinney L, Johnson N, Fooks AR, Tordo N, Muller T., Vaccine 26, 3227–3235, 2008. https://doi.org/10.1016/j.vaccine.2008.04.007

Hampson K, Cleaveland S, Briggs D., PLoS Negl. Trop. Dis. 5, e982, 2011. https://doi.org/10.1371/journal.pntd.0000982

Hanlon C, Childs J., Epidemiology. In Jackson AC (Ed.): Rabies: Scientific Basis of the Disease and its Management. 3rd ed. Academic Press, Waltham MA, pp. 61–122, 2013. https://doi.org/10.1016/B978-0-12-396547-9.00003-1

Hlinka D., Slov. Vet. Čas. 6, 17–18, 2002. https://doi.org/10.7748/ns.17.4.18.s37

Hu SC, Hsu CL, Lee MS, Tu YC, Chang JC, Wu CH, Lee SH, Ting LJ, Tsai KR, Cheng MC, Tu WJ, Hsu WC., Emerg. Infect. Dis. 24, 782–785, 2018. https://doi.org/10.3201/eid2404.171696

ICTV (2019): Virus taxonomy. Classification and Nomenclature of Viruses. Online (10th) Report of the International Committee on Taxonomy of Viruses. https://talk.ictvonline.org/ictv-reports/ictv_online_report/ Accessed Dec. 2019.

Jeffries CL, Banyard AC, Healy DM, Horton DL, Johnson N, Fooks AR., Rabies Virus Neurovirulence. In Singh SK, Růžek D (Eds): Neuroviral Infections. CRC Press, Boca Raton, pp. 373–394, 2013.

Jiroušková M, Bačová J, Molnár A., Folia Fac. Med. Univ. Šafarikianae Cassoviensis 47, 361–368, 1990.

Johnson N, Cunningham AF, Fooks RA., Vaccine 28, 3896–3901, 2010. https://doi.org/10.1016/j.vaccine.2010.03.039

Johnson N, Phillpotts R, Fooks AR., J. Med. Microbiol. 55, 785–790, 2006. https://doi.org/10.1099/jmm.0.46370-0

Knobel DL, Cleaveland S, Coleman PG, Fevre EM, Meltzer MI, Miranda ME, Shaw A, Zinsstag J, Meslin FX., Bull. World Health Organ. 83, 360–368, 2005.

Kopřiva V, Pliešovský J, Matejčík R., Wien. Tierärztl. Mschr. 96, 1–7, 2009.

Maier T, Schwarting A, Mauer D, Ross RS, Martens A, Kliem V, Wahl J, Panning M, Baumgarte S, Müller T, Pfefferle S, Ebel H, Schmidt J, Tenner-Racz K, Racz P, Schmid M, Strüber M, Wolters B, Gotthardt D, Bitz F, Frisch L, Pfeiffer N, Fickenscher H, Sauer P, Rupprecht CE, Roggendorf M, Haverich A, Galle P, Hoyer J, Drosten C., Clin. Infect. Dis. 50, 1112–19, 2010. https://doi.org/10.1086/651267

Matouch O, Jaroš J, Vitásek J., Vzteklina v ČR a její tlumení orální vakcinací lišek. Aktuální otázky zoonóz. Sborník referátů, Brno, 49–52, 2002.

Matouch O, Jaroš J, Vrzal V., Vet. Med. (Praha) 43, 245–248, 1998.

Matouch O, Vitásek J., Rabies Bull. Eur. 26, 5–8, 2002.

Matouch O, Vitásek J, Semerad Z, Malena M., Rev. Sci. Tech. 26, 577–584, 2007. https://doi.org/10.20506/rst.26.3.1762

Muller T, Batza HJ, Beckert A, Bunzenthal C, Cox JH, Freuling CM, Fooks AR, Frost J, Geue L, Hoeflechner A, Marston D, Neubert A, Neubert L, Revilla-Fernandez S, Vanek E, Vos A, Wodak E, Zimmer K, Mettenleiter TC., Arch. Virol. 154, 1081–1091, 2009. https://doi.org/10.1007/s00705-009-0408-7

Müller T, Schlüter H., J. Etlik Vet. Microbiol. 9, 35–39, 1998.

Nokireki T, Tammiranta N, Kokkonen UM, Kantala T, Gadd T., Transbound. Emerg. Dis. 65, 593–596, 2018. https://doi.org/10.1111/tbed.12833

Ondrejková A, Franka R, Ondrejka R, Švrček Š, Süli J, Beníšek Z, Zubrický P, Bajová V, Bugarský A, Bourhy H., Bull. Vet. Inst. Pulawy 48, 11–13, 2004.

Ondrejková A, Ondrejka R, Švrček Š, Süli J, Beníšek Z, Franka R., Slov. Vet. Čas. 25, 358–360, 2000.

Prager KC, Woodroffe R, Cameron A, Haydon DT, Biol. Conserv. 144, 1940–1948, 2011. https://doi.org/10.1016/j.biocon.2011.03.025

Singh R, Singh KP, Cherian S, Saminathan M, Kapoor S, Manjunatha Reddy GB, Panda S, Dhama K., Vet. Q. 37, 212–251, 2017. https://doi.org/10.1080/01652176.2017.1343516

Stőhr K, Meslin FX., Vet. Rec. 139, 32–35, 1996. https://doi.org/10.1136/vr.139.2.32

Strimpl V., Věstník veřejného zdravotnictví a tělesné výchovy 13, 279–288, 1931.

SVFA (2019): State Veterinary and Food Administration of the Slovak Republic, Besnota. https://www.svps.sk/zvierata/choroby_besnota.asp. Accessed Dec. 2019.

Švrček Š., Oral vaccination of foxes against rabies. Methodical instructions (in Slovak). ŠVS SR, Bratislava, 12 pp, 1992.

Švrček Š, Beníšek Z, Vrtiak OJ, Závadová J, Ďurove A, Húska M, Süliová J, Ondrejka R, Paulík Š, Fejfar V, Láni D., The current epizootiological situation and immunoprophylaxis of rabies (in Slovak). I. Symposium about the diseases of carnivores. Košice (Slovak Republic). Proceedings 27–30, 1991.

Švrček Š, Ďurove A, Ondrejka R, Sokol J, Süliová J, Závadová J, Lovás B, Beníšek Z, Vrtiak OJ, Selimov MA, Žuffa T, Feketeová M, Dušeková J, Kubinec J, Žurek A, Borsuková O, Maďar M, Švehlíková J., Bull. Vet. Inst. Pulawy 42, 96–97, 1998.

Švrček Š, Ondrejka R, Ondrejková A, Süli J, Závadová J, Beníšek Z, Maďar M, Franka R., Scientific bulletin of Uzhgorod National University, Series: Biology 9, 138–141, 2001.

Švrček Š, Sokol J, Lovás B, Ďurove A, Borsuková O, Süliová J, Ondrejka R, Kubinec J, Beníšek Z, Žurek A., Epizootiological situation and control of rabies in the Slovak Republic. WHO Rabies Conference, Budapest (Hungary). Proceedings 19, 1995.

Švrček Š, Sokol J, Ondrejková A, Lovás B, Závadová J, Ondrejka R, Süliová J, Beníšek Z, Maďar M, Jánek F., Analysis of epizootiological situation of rabies in Slovakia and other European countries (in Slovak). Conference „Animal Health and Diseases – Current Problems of Epizootiology and Infectology". Košice, Slovak Republic. Proceedings 24–27, 1999.

Švrček Š, Vrtiak OJ, Ďurove A, Ondrejka R, Závadová J, Süliová J, Beníšek Z, Húska M, Žuffa T, Feketeová M, Dušeková E, Šnirc J, Žurek A, Láni D, Blecha J, Mandelík M, Dušek J, Salaj J, Hojsík J, Lovás B, Gašpar P., Oral antirabies vaccine; verification of its effectiveness and harmlessness, preliminary results of the field application (in Slovak). Final Report of UVM and MEVAK a.s. Nitra, 88, 1993.

Ursíny J, Stolzová-Sutorisová M., Rabies (in Slovak). Príroda, Bratislava, pp. 113, 1970.

Wandeler AI., Oral immunization of wildlife. In Baer GM (Ed.): The Natural History of Rabies. CRC Press, Boca Raton, 485–503, 1991.

Wandeler AI., Schweiz. Arch. Tierheilk 142, 455–462, 2000.

Wilde H, Hemachudha T, Wacharapluesadee S, Lumlertdacha B, Tepsumethanon V., Rabies in Asia: The classical zoonosis. In One health: the human-animal-environment interfaces in emerging infectious diseases. Springer, Berlin, pp. 185–203, 2013. https://doi.org/10.1007/978-3-642-36889-9

Wunner WH, Briggs DJ., PloS Negl. Trop. Dis. 4 (3), e591, 2010. https://doi.org/10.1371/journal.pntd.0000591