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Review

Terrestrial rabies control in the European Union: Historical achievements and challenges ahead

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ABSTRACT

Due to the implementation of oral rabies vaccination (ORV) programmes, the European Union (EU) is becoming progressively free of red fox (*Vulpes vulpes*)-mediated rabies. Over the past three decades, the incidence of rabies had decreased substantially and vast areas of Western and Central Europe have been freed from rabies using this method of controlling an infectious disease in wildlife. Since rabies control is a top priority in the EU, the disease is expected to be eliminated from the animal source in the near future. While responsible authorities may consider the mission of eliminating fox rabies from the EU almost accomplished, there are still issues to be dealt with and challenges to be met that have not yet been in the focus of attention, but could jeopardise the ultimate goal. Among them are increasing illegal movements of animals, maintaining funding support for vaccination campaigns, devising alternative vaccine strategies in neighbouring Eastern European countries and the expanding distribution range of several potential rabies reservoir species in Europe.

Introduction

Rabies has been known for millennia and is the oldest recorded zoonotic disease (Dunlop and Williams, 1996). The causative agents are different lyssavirus species of the Rhabdoviridae family in the order Mononegavirales (Dietzgen et al., 2012). Whilst the majority of lyssavirus species are associated with the order Chiroptera (bats), the assumed historical reservoir of all lyssaviruses, the prototypic rabies virus (RABV), resides primarily in carnivores globally and in bats in the Americas (World Health Organization (WHO), 2013). Rabies is present worldwide, but the greatest burden of the disease is in developing countries, where dog-mediated rabies causes approximately 74,000 human deaths annually, in particular in Asia and Africa (World Health Organization (WHO), 2013; Fooks et al., 2014).

Control of canine rabies at the animal source would lead to almost complete prevention of human rabies cases and major economic benefits, in particular for developing countries, which are often least capable of dealing with the disease (Shwiff et al., 2013). In contrast to the developing world, wildlife-mediated rabies is the major problem in the northern hemisphere. Various carnivores serve as reservoirs for the virus, harbouring several distinct RABV variants, for example those adapted to raccoons (*Procyon lotor*, North America), striped skunks (*Mephitis mephitis*, North America), coyotes (*Canis latrans*, North America), grey foxes (*Urocyon cinereoargenteu*, North America), red foxes (*Vulpes vulpes*, Eurasia and North America), raccoon dogs (*Nyctereutes procyonoides*, Eurasia), arctic foxes (*Alopex lagopus*, Arctic) and mongooses (Herpestidae family, Caribbean and Southern Africa). In addition to these terrestrial reservoirs, several species of insectivorous, haematophagous and frugivorous bats are also reservoirs for lyssaviruses (Banyard et al., 2011, 2013).

Canine rabies has been controlled successfully in Europe and the Americas, where mass vaccination of dogs has led to virtual disappearance of the infection in animals and humans (Rupprecht et al., 2008; Müller et al., 2012; Vigilato et al., 2013). Promising developments have also been seen in several other regions, e.g. on the island of Bohol (The Philippines), Kwazulu Natal (Republic of South Africa) and Tanzania, where concerted actions have eliminated rabies from dog populations (Lapiz et al., 2012; Nel et al., 2012). Terrestrial wildlife rabies has also been eliminated in Europe.

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Whilst other review papers have dealt in detail with historical, technical and financial aspects of rabies control in Europe (Wandeler, 1991; Cliquet and Aubert, 2004; Müller et al., 2012), in the present paper we reflect on the efforts to control the disease in Europe and provide an opinion on current and future challenges.

The last epizootic

Historically, dogs and Eurasian wolves (*Canis lupus lupus*) were considered to be the two main vector species in Europe. Wolf rabies seemed to dominate in rural areas and dog rabies in cities and larger villages. In the last part of the 18th century, there was a peak in wolf attacks and rabies cases (Moriceau, 2008). Subsequently, rabies cases in wolves decreased rapidly, related to the steady decrease of the wolf population, which was destroyed by all possible means. It remains unknown if wolves in these early times were merely a vector species or actually also a reservoir for the virus.

In the 19th century, canine rabies was dominant in Europe, excluding Scandinavia. By applying veterinary sanitary measures, such as killing dogs suspected of infection, muzzling and quarantine, canine rabies was controlled and even eliminated in some countries, e.g. the United Kingdom became rabies-free in 1902 (Fooks et al., 2004). However, in most other European countries, dog rabies was not controlled until the middle of the 20th century, when parenteral mass vaccination of dogs and cats became available (Müller et al., 2012).

At the end of, or shortly after, World War II, fox rabies outbreaks and the subsequent establishment of fox rabies were registered in several regions in Eurasia (Kuzmin et al., 2004; Wandeler, 2004). It is assumed that the European fox rabies epidemic emerged in an area around Kaliningrad (Seroka, 1979). In the following years, the epidemic wave spread further west and south, eventually reaching the western and central parts of France by the mid-1970s. Initial efforts to reduce the fox population density below the threshold which could maintain infection included increased hunting, culling of cubs, poisoning, trapping and den gassing. These measures were controversial and had minimal effect on the spread and incidence of rabies. In particular, disruption of the fox population structure resulted in increased migration, enhancing contacts and thus increasing spread of the disease (Aubert, 1992).

It was only with the advent of oral rabies vaccines, which had been pioneered in North America (Baer et al., 1971), that control of the disease in wildlife became a viable option. Since oral delivery of inactivated vaccines is a relatively ineffective method of inducing an immune response, all available oral rabies vaccines are based on replication-competent infectious viruses. In addition to the use of efficacious and safe vaccines, baits and baiting strategies had to be developed. Switzerland was the first European country to commence field trials of oral rabies vaccination, using chicken heads as baits for foxes (Steck et al., 1982a, 1982b). The Swiss initiative was soon followed by other European countries, including France, Belgium and Germany. As well as the development of machine-made baits and large scale aerial distribution, which appeared as milestones in the European effort to control and eventually eliminate fox rabies, baiting strategies evolved and were constantly adapted and improved (Müller et al., 2012).

Recording bait uptake and seroconversion has been an integral part of all campaigns to monitor and evaluate the performance of ORV. However, the relevant indicator for evaluating the success of ORV programmes has been the incidence of rabies; reported rabies cases in Europe decreased from a peak in 1984 (24,315 cases) to 5242 cases in 2013.[1] After several setbacks caused by a multitude of reasons (Rupprecht et al., 2008), due to implementation of ORV programmes in 24 countries, large parts of Western and Central Europe became rabies free, including Finland, the Netherlands, Italy, Switzerland, Lichtenstein, France, Belgium, Luxembourg, the Czech Republic, Germany and Austria (Freuling et al., 2013a).

Challenges to wildlife rabies control in the 21st century

Multispecies reservoir problem?

Initial efforts to control rabies in red foxes in Europe seemed to be jeopardised by the emergence of a novel invasive species, the raccoon dog, which was originally introduced as hunting game to the European part of the former Soviet Union in the 1920s and readily adapted to the local environment. Since then, the raccoon dog has colonised large parts of Eastern and Central Europe, and an end of the spread is not in sight (Nowak, 1984; Kauhala and Kowalczyk, 2011) (Fig. 1). Although not yet proven, there is evidence that this invasive species could act as another reservoir, since it plays a significant role in the epidemiology of rabies and is the second most frequently reported species to be infected in Eastern and Central Europe (Freuling et al., 2013b). Fortunately, the available oral rabies vaccine baits developed for foxes are also highly efficacious in raccoon dogs, and the distribution system and strategies for foxes can be applied to raccoon dogs too (Müller et al., 2012).

Another potential challenge is in the North Polar regions of Eurasia. There is circumpolar transmission of the arctic variant of RABV by arctic foxes, whereas the region currently is considered to be free of red fox-mediated rabies. Increasing evidence suggests that increasing temperatures allow red foxes and racoon dogs to migrate further north into tundra regions of the North Polar region, possibly spreading red fox-mediated rabies over vast, as yet unaffected areas, e.g. in Russia's far north and into Scandinavia, bypassing the established vaccination belt at the Finnish–Russian border. Also, the likelihood of interaction with arctic foxes may increase, with possible spill-over infection of the arctic RABV variant from arctic foxes into red foxes (Freuling et al., 2013b). In Europe, the arctic RABV variant has been identified on Svalbard Island (Johnson et al., 2007). On the other hand, due to climate change, the risk may become smaller, since animal numbers in the Arctic are declining and reduced ice masses may make it impossible for rabid arctic foxes to move across the Arctic.

Co-financing policy of the European Union

As the area to be covered by ORV becomes larger, the costs of control for countries in the infected zone increase. Only concerted actions across borders will lead to successful control of rabies. Coordination of ORV campaigns has been organised through bi- or multi-lateral meetings. In view of the importance of rabies as a zoonotic disease and the feasibility of its control, at the beginning of the 1990s the European Union (EU) declared rabies elimination a high priority and started co-financing control efforts, even in countries outside the EU (Demetriou and Moynagh, 2011; Müller et al., 2012). This was a tremendous catalyst for the large scale application of ORV in Central and Eastern Europe. The co-financing policy of the EU provided financial security for member states and enabled those member states with weaker economies to allocate money for implementation of sustained ORV programmes, as well as prevention of re-infection from endemic neighbouring regions or non-EU countries.

It has become clear that a long-term financial commitment is necessary to guarantee elimination of rabies in the wildlife reservoir, since the final phase of elimination is disproportionately the

[1] See: www.who-rabies-bulletin.org (accessed 9 October 2014).