Controlling Rabies in Foxes Unprecedented Success in Europe

The European Union (EU) aims to eliminate fox-mediated rabies from its territory by 2020. At first sight, this seems a rather ambitious goal considering that this horrifying disease has tormented humans and animals in Europe since ancient times.

Highly efficacious and safe vaccines for humans are available in Europe and, consequently, human rabies cases are extremely rare, the majority being reported in Russia. However, the potential threat remains, as the disease has not been eliminated from the main reservoir host species, the red fox (Vulpes vulpes). This zoonotic disease has the highest fatality rate among humans of any infectious disease known, so its elimination from such a large geographical area as the EU would be a major accomplishment. This is especially so when considering the red fox is an evasive wildlife species making control difficult to implement.

The latest rabies epidemic among red foxes is believed to have started in the Kaliningrad region of Russia, which borders Poland and Lithuania, in the 1940s. It then spread to most countries of Eastern, Central and Western Europe by the mid-1970s. Initially, control efforts concentrated on reducing the density of the fox population, through intensified hunting, culling cubs, poisoning and gassing of dens, to below a threshold that could sustain transmission. These population reduction efforts were not only highly controversial, they had little impact and, retrospectively, were actually considered to be counterproductive.

With the development of oral vaccination of foxes against rabies – using vaccine-loaded baits distributed in the environment – a completely new approach to wildlife disease management became available. The first field trial took place in Switzerland in 1978, followed by efforts in other European countries, starting with Germany, Italy, France and Belgium.

Rabies Bulletin Europe

By coincidence, shortly before the first field trial, a European database and rabies reporting system was established by the World Health Organization (WHO), in 1977. Called the WHO Rabies Bulletin Europe (RBE), it aimed to meet the demand for adequate and reliable rabies surveillance data across borders. The use of this single reporting system has encouraged collaborative control efforts in neighbouring countries through the evaluation of shared epidemiological data – even across political boundaries! Cross-border cooperation is essential for sustained rabies control, especially for a disease with a wildlife reservoir species that does not respect borders or political boundaries.

Of course, during the initial years of RBE when the Cold War was nearing its height, the political climate in Europe sometimes hindered uncensored data- sharing. However, despite this situation, RBE did not only collect and analyse data across political divides, it also enabled certain countries to improve their rabies surveillance data collection system. Initially, RBE appeared in printed form on a quarterly basis but nowadays is available electronically (www.who-rabies-bulletin.org). This European rabies database is maintained by the WHO Collaborative Centre for Rabies Surveillance and Research. Initially, it was compiled at the Federal Research Institute for Virus Disease of Animals in Tübingen, Germany, but now it is based at the Friedrich-Loeffler-Institute in Insel Riems – Greifswald, Germany.

This availability of detailed European rabies data – spanning four decades of oral rabies vaccination (ORV) campaigns – gives a unique opportunity to analyse progress in the elimination of fox-mediated rabies in Europe.

Rabies Incidence

During the past four decades, 31 European countries implemented ORV programmes within their territories. The total area ever covered, at least once, with vaccine baits between 1978 and 2018 encompassed 2.73 million km² (Fig 1). This peaked in 2007 when baits were concurrently distributed over approximately 1 million km². As a result of the implementation of ORV, the number of rabies cases reported annually in Europe to the RBE steadily declined from 15,355 in 1978 to 4027 in 2018, with intermediate peaks in 1984 and 1989. However, to appraise the true impact of ORV on the rabies incidence, it is necessary to differentiate geographical and time-based use of this disease management tool.

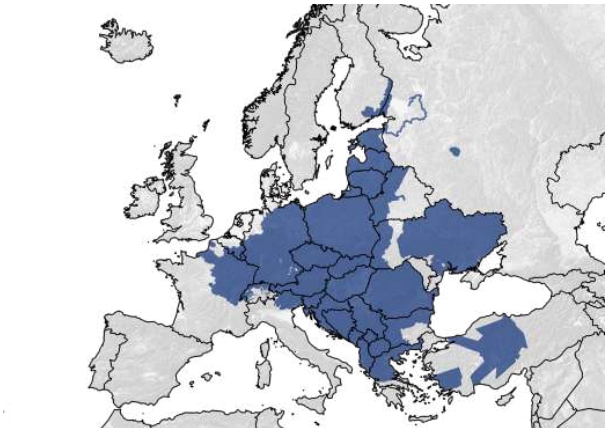

Figure 1: Map of Europe and the areas covered by ORV. All maps were kindly created by Patrick Wysocki, IfE, FLI.

Data from the RBE database has been stratified into four geographical regions:

1. The west – and central European countries that started with ORV campaigns early (1978-1993).
2. Countries that started relatively late with sustained optimised ORV programmes (Baltic countries).
3. Countries that started with coherent cross-border ORV programmes within the last 10 years.
4. Countries in far-Eastern Europe with no comprehensive ORV programme (Belarus, Russia, Ukraine and Moldovia).

Of the European countries that have implemented ORV programmes, Turkey is excluded from this analysis. Turkey is the only country in Europe with dog-mediated rabies. Sustained rabies transmission in foxes occurred in the Aegean region of Turkey following a spill-over from dogs in

the late 1990s. ORV campaigns targeted at red foxes were undertaken during the periods 2008–2010 and 2014–2016. Although these campaigns clearly demonstrated the feasibility of fox rabies control by ORV in Turkey, the impact on the rabies incidence is hampered by persistent dog-mediated rabies.

Trial-and-error Phase – Geographical Area 1 (West and Central Europe)

In west and central Europe, the red fox was the main reservoir for rabies. In the early 1970s, innovative research in the US had shown that red foxes could be immunised by the oral route against rabies using attenuated rabies viruses. West and central European countries were the first to test the principal concept of ORV under field conditions. They developed the basis for future successful implementation of large-scale ORV with Switzerland, Germany and France spearheading those developments.

During the initial years between 1978 and 1989, a trial-and-error approach was used. No detailed protocol was available on the geographical and time-based distribution of oral rabies vaccine baits for the countries pioneering this novel method of controlling rabies. In addition, vaccines as well as baits were still under development and subject to improvement, especially regarding potency, safety and stability. Consequently, progress was sometimes protracted during the first decade as setbacks had to be experienced and lessons learned. Notwithstanding, it soon became evident that ORV was a breakthrough in fox rabies control.

In 1989, the EU decided to include rabies in its co-financing policy for disease eradication, turning ORV field trials into true rabies eradication programmes. This has been a strong stimulus for fox rabies control in Member States ever since. In 2002, the European Commission issued a report evaluating ORV efforts within the EU, thus providing a standard operating protocol for ORV campaigns and subsequent monitoring. Significant progress was only reported after this optimised ORV-strategy occurred, having gained sustained financial support from the EU for Member States and neighbouring countries (Fig. 3). In the final phase, residual foci of infection or re-infections contributed to outbreaks in Hungary and Poland, respectively. However, with improved distribution of baits, these outbreaks were successfully controlled. In 2018, only one rabies case was reported in the EU, in Poland at the border with Belarus.

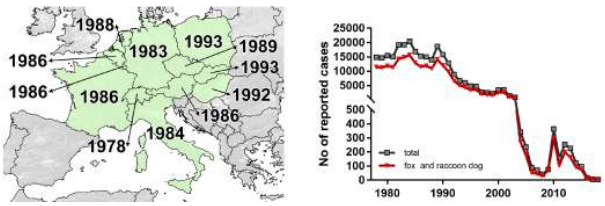

Figure 2: Map of geographical area 1 (left) with starting year of ORV indicated. Right: Number of reported rabies cases in this area from 1977 – 2018. The peak in 2010 and the following years is exclusively related to outbreaks in Poland and Hungary

Optimised ORV – Geographical Area 2 (Baltic Countries)

The epidemiology of rabies in the Baltic countries is also driven by the raccoon dog (Nyctereutes procyonoides), since this is the second most reported species, next to the red fox, as the main reservoir for the disease. The racoon dog is an invasive species, originally introduced in the 1920s as hunting game to the European part of the former Soviet Union. It readily adapted to the local environment. As a result, there was a dramatic increase of the incidence of rabies after the turn of the millennium.

This observation seemed to jeopardise control efforts. Fortunately, however, the ORV approach used for foxes also worked for this species. This was revealed in outbreaks of rabies in southern Finland in 1988 that were exclusively driven by this species. They were brought under control using ORV within just two years. The much more rapid decline in reported rabies cases, compared with western and central Europe, is obvious (see Figure 4). This was because the Baltic countries that started sustained ORV programmes in the early 2000s (2004–2007) benefited from experience and optimised ORV protocols, including the use of machine-made baits and implementation of aerial distribution of baits. Within 10 years, rabies incidence fell to zero. Re-infection from neighbouring endemic areas in Russia and Belarus caused only single rabies cases in recent years with no sustained onwards transmission.

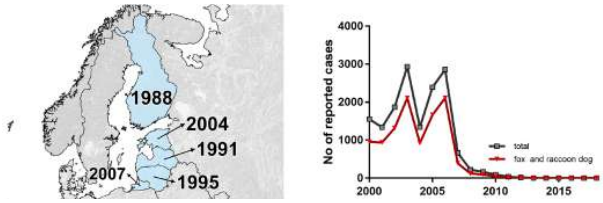

Figure 3: Map of geographical area 2 (left) with starting year of ORV indicated. Right: Number of reported rabies cases in this area from 2000–2018.

Coherent ORV – Geographical Area 3 (Balkan Countries)

As in western and central Europe, on the Balkan peninsula fox-mediated rabies had been predominant with cyclical fluctuations that peaked in 2008. Slovenia and Croatia were the first countries to implement ORV in this region – in 1989 and 1991, respectively. Thanks to financial support from the EU, sustained ORV programmes were launched in the remaining rabies endemic Balkan countries between 2009 and 2011. Emergency-response campaigns conducted in Northern Greece in 2013 eliminated fox rabies, after incursion from neighbouring Northern Macedonia, within a short period of time.

What makes the performance of ORV in this region truly remarkable is that, in contrast to the other two ORV regions, here a coherent cross-border vaccination strategy was implemented. The entire endemic region was almost continuously targeted right from the beginning. Also, computer-supported, automatic aerial distribution and geographic information systems (GIS)-based assessment of bait distribution, developed in the meantime, became standard. Within nine years, rabies cases in the Balkan decreased from 1647 cases in 2009 to only five in 2018 (Figure 4).

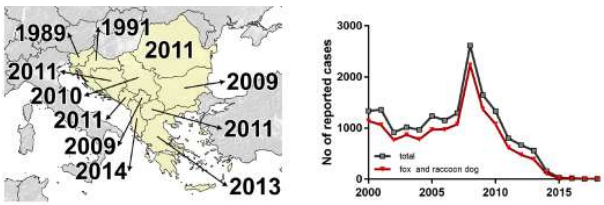

Figure 4: Map of geographical area 3 (left) with starting year of ORV indicated. Right: Number of reported rabies cases in this area from 2000–2018.

Impaired Use of ORV

Currently, Eastern Europe and adjacent parts of Asia still remains an endemic area for fox-mediated rabies. The pattern of rabies appears different compared with other European counties, for example:

1. The size of the infected area is enormous, and
2. A very low human population density may bias rabies surveillance towards domestic animals.

Although Belarus, Russia and the Ukraine implemented ORV field trials in parts of their territories, for various reasons they did not have any impact on the rabies incidence; these countries are still far from implementing comprehensive ORV programmes (Fig. 5).

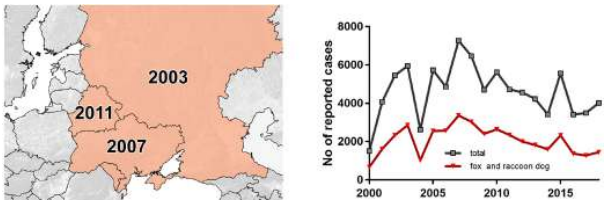

Figure 5: Map of geographical area 2 (left) with starting year of ORV indicated. Right: Number of reported rabies cases in this area from 2000–2018.

Conclusion

Within the past 40 years, the implementation of ORV has reduced the rabies incidence in Europe by 74 per cent. While this may not seem effective considering the financial efforts, 99 per cent of all reported rabies cases (4027) in Europe in 2018 (excluding Turkey) originated from the far Eastern European countries with no sustained ORV programme (geographical area 4). In contrast, in all other European countries (excluding Turkey), only 10 cases were reported in 2018.

Getting rid of the last remaining one per cent of rabies cases costs disproportionately more time and effort than the first 99 per cent. However, it seems that the challenging target of extinguishing fox rabies from the EU is feasible by the year 2020. Since 2000, indeed, after successful rabies elimination ORV programmes have been discontinued in several countries. However, due to the rabies situation in the far Eastern European countries, the establishment of a vaccination belt is required to prevent the re-emergence of rabies in neighbouring countries. This has been implemented in Finland since the 1990s. The EU has been supporting the establishment of such a 'cordon sanitaire' by co-financing ORV in Member States and neighbouring non-EU countries. As this vaccination belt covers large areas in several countries, long-term sustainability is required.

In Eastern Europe, vast endemic areas still have to be covered by ORV. The fact that these countries would have to bear all costs related to ORV themselves probably hampers the implementation of large-scale ORV programmes over their entire territories in the near future. Therefore, support for the development and design of alternative, more cost-efficient and new vaccination and surveillance strategies, should be considered. In this context, natural barriers like rivers need to be taken into account.

However, although largely effective, these barriers to immunity, artificial or natural, are not entirely impermeable so vigilance remains of utmost importance. In case of a breach, a rapid response through emergency ORV campaigns can quickly restore the rabies-free status. Hence, collecting and sharing rabies surveillance data through the RBE remains essential for safeguarding the unprecedented success in rabies control achieved in Europe.

Challenges Ahead

One of the major challenges will be upholding the rabies-free status within the EU. The threat of becoming re-infected through invading rabies-infected wildlife from the far eastern European countries and possible preventive measures ("vaccination belt") have already been discussed. However, another possible way of re-introduction is a sustained spill-over from imported pets originating from rabies-endemic countries. Until now, these cases have not been able to spread to susceptible wildlife, predominantly thanks to immediate control measures employed. However, the risk cannot be ignored.

As for other diseases, such as foot-and-mouth disease (FMD), some countries have established a vaccine bank for an emergency vaccination campaign in case of an outbreak. Unfortunately, the establishment and maintenance of such a vaccine bank is relatively expensive. Hence, the establishment of an EU vaccine bank for oral rabies vaccine baits could be more cost-effective than for maintaining them in the individual Member States.

Recently, other potential rabies reservoir species have become more abundant and their population range has expanded considerably in Europe. These include the raccoon (Procyon lotor), golden jackal (Canis aureus), small Indian mongoose (Herpestes auropunctatus) and Egyptian mongoose (H. ichneumon). All these species cannot be reached by a single oral rabies vaccine bait type due to, for example, different food preferences, animal size and vaccine dose needed. Furthermore, for some of these species no product is available; not licensed and/or under development.

Vaccine, delivered by oral bait, has been a highly successful method of controlling rabies in wildlife.

The red fox is the major host species for rabies in Europe, a zoonotic disease with the highest fatality rate among humans.

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Raccoon dogs, next to the red fox, as the main reservoir of rabies in Eastern Europe.

Aerial distribution of vaccine-loaded baits has enabled vaccination to take place in habitats, not otherwise easily accessible.

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