Rabies – Still A Disease to be Feared – but Vaccination is Winning the Battle in Many Areas of the Globe

Rabies is a deadly disease, normally spread to humans from infected animals through a bite, scratch, or even a lick on broken skin. Without prompt treatment the disease is invariably fatal. This is why many countries have made great efforts to eliminate the disease within their borders but, despite this, rabies is still widespread across large areas of the globe. The only continent in the world totally free from rabies is Antarctica – and that's because no mammals live there!

The first written evidence appearing in about 2000BC suggests it to be the oldest known infectious zoonotic disease in the world. While ancient people did not know that it was caused by a virus, they were aware that it could be transmitted from dogs to humans. However, four millennia later it is still causing deaths. It is estimated that, globally, 60,000 people die from rabies every year. In India alone, considered to be the country with the most human cases – although it is not an officially notifiable disease there – it is thought there are 20,000 to 30,000 cases annually.

In China and other Asian countries where autopsies are not carried out due to cultural considerations, diagnosis is often based on clinical symptoms. The number of cases, therefore, is based on 'best guesses' following dog-bite incidences in humans.

Rabies is an acute infection of the central nervous system, caused by lyssaviruses. In humans, the incubation period can vary from under a week to over a year. Early symptoms can include malaise, headaches, fever and sensitive skin, followed by anxiety, confusion and the classic fear of water followed by paralysis, coma, and finally death. Not surprisingly, it is classed as one of the most horrendous diseases humans can contract.

Both domestic and wild animals can carry the rabies virus and they may be able to transmit the disease before it is apparent that they are ill. It is estimated that, each year, 15 to 20 million people are vaccinated against rabies after being bitten by a potentially-rabid animal. Without post exposure prophylaxis (PEP), with life-saving vaccines hundreds of thousands more people would be dying from rabies every year. So it can be seen it is still a large-scale problem even 4000 years later.

There are islands, both large and small, such as Australia, Great Britain and New Zealand, that are free from the rabies virus, but where countries are part of a larger land mass, problems remain as wildlife do not respect political borders!

This has been the case in Europe, for instance. After the Second World War, fox rabies spread through Europe quite rapidly. Detected initially around the Kalingrad region of Russia, between Poland and Lithuania, it quickly spread across the breadth of Europe from western France and down to Greece.

Given the seriousness of the disease, this 'invasion' of fox rabies stimulated research into the best way of vaccinating such a widespread wildlife population. Catching foxes by trapping them for individual vaccination would be difficult, time-consuming and costly. Immunising enough animals by this method would also be unlikely to be very successful in establishing a sufficient level of 'herd immunity'.

As a result, research into oral vaccines for animals against rabies was instigated and in 1978 the first field trial took place in Switzerland. Oral vaccines had the big advantage that wildlife did not have to be handled and baits containing the vaccine could be distributed by a variety of methods – by hand, from vehicles and even by air – giving a large area of coverage in a relatively short period of time.

IDT Biologika, based at Dessau-Rosslau, Germany, has been in the forefront of this research. In fact, the company helped develop a system of bait distribution known as SURVIS in the mid-1990s: a satellite and computer-aided automatic bait airdrop system allowing targeted deployment of baits from aircraft. SURVIS or SURVIS-derived systems have now become the gold standard in nearly every European call for tenders for combating rabies.

The company has just celebrated the production of its 1000th batch of Fuchsoral vaccine, equivalent to 260 million doses in 19 countries around the world – a nearly unparalleled success story, not just for IDT but for rabies control as a whole. The product has made a crucial contribution to the elimination of fox-mediated rabies in Germany and other European countries.

Therefore the company, which has been making biological products for nearly 100 years, can claim great expertise in this field.

More than 95 per cent of people who die of rabies have been bitten by a rabid dog. In Europe today, very few people die of rabies due to developments in vaccine production and strict controls. Central to this was the vaccination of dogs and stringent control of free-roaming dogs. There have been cases where tourists have become infected while abroad, some deaths from bat-transmitted rabies and organ transplants, but these are rare.

Apart from Turkey, since the end of the Second World War dog rabies has not been endemic in any European country.

However, once control was achieved over rabies in dogs, attention needed to be focused on wildlife – in Europe particularly, foxes and later raccoon dogs were found to be the principal carriers. One of the problems was that in many countries enormous numbers of wild animals were found to be living in urban areas, posing a direct risk to humans and domestic animals, including dogs, cats and farm animals.

Foxes are one of the main reservoir species for rabies in Europe.

There is a tripartite agreement between the WHO (World Health Organization), OIE (World Organisation for Animal Health) and FAO (Food and Agriculture Organization of the United Nations) to eliminate dog-mediated human rabies deaths by 2030. While this is focusing only on dog-related rabies that would mean reducing the number of human cases by more than 95 per cent – a tremendous goal!

I feel that the EU has done a great job with the so-called first-generation oral rabies vaccines. They are still the most widely used in Europe because they are highly efficacious. But, of course, there are certain safety considerations.

IDT Biologika, aware of this risk, therefore set about developing a new, third- generation oral rabies virus vaccine with a greatly enhanced safety profile.

Although they have been very effective in the control of wildlife rabies, it is time to replace first-generation oral rabies virus vaccines with a safer but equally efficient strain which is now available.

The third-generation strain does not pose residual oral pathogenicity for wild rodents as observed with first-generation vaccine strains.

Advances in genetic engineering techniques have enabled the development of the third-generation oral rabies virus vaccines.

IDT has just introduced a new live oral rabies vaccine – Rabitec – after ten years' development work and this is seen as a breakthrough because the high degree of attenuation by genetic modifications at multiple sites has greatly increased the levels of safety offered. The use of genetic engineering has decreased the virulence of the parental vaccine strain while maintaining its potency so it still produces a strong immune response.

The vaccine strain has the highest level of attenuation currently available on the market for such types of vaccines. In contrast to vaccines that are injected directly into the animal's body, this oral vaccine is released into the oral cavity when the animal picks up a blister pack. After chewing the bait and perforating the blister pack, the vaccine is released into the target animal's mouth, where it enters the body through the mucous membranes and tonsils.

Any virus that is swallowed is killed while passing through the stomach, so there is no danger of live virus excretion or contamination of the environment by shedding in the faeces, for instance.

In the case of Europe, now largely free from fox-mediated rabies, obtaining a vaccination belt with the aerial distribution of the vaccine is seen as an important way of safeguarding its borders. To prevent reinfection, the use of vaccines that cannot revert to virulence should be preferred.

Rabitec, a new safe, oral rabies vaccine is presented in a blister pack to immunise foxes and racoon dogs.

The baits can be distributed quickly and easily by air using the SURVIS system and a specially designed dispenser tube.

In addition, worldwide, there are important opportunities to protect endangered species of wildlife, such as the Ethiopian wolf. This is the most endangered canid species in the world, with only a couple of hundred animals in isolated populations in Ethiopia. These could become infected, resulting in entire pockets of populations being wiped out.

Another example is the African wild dog – also endangered in certain regions. Oral vaccination makes great sense as capturing animals for direct injection would be highly problematic and probably dangerous.

Different species of wildlife present problems in various parts of the world. In Europe it has been raccoon dogs and foxes; in the United States, coyotes, grey fox, raccoons and striped skunks are involved; while in the Caribbean islands, Africa and Asia, it can be different mongoose species.

Depending upon the target animals for certain wildlife species, or for dogs, official approval has to be obtained in certain countries. Licensing procedures in Europe are strict and linked to certain species but approval in Europe counts heavily in other parts of the world, many of which have serious problems with rabies.

IDT Biologika works with many governmental and non-governmental organisations and international bodies offering help and advice gathered from more than 25 years of expertise in this very specialised sphere.

Verena Ziethlow

Dr. med vet Verena Ziethlow qualified as a vet at the Free University Berlin, Germany and wrote her doctoral thesis in Bern, Switzerland, where her studies involved specific vaccine strains. She then spent time as a scientific assistant at that university before taking up a post in a general veterinary practice in Germany. Following a number of commercial appointments involving training, education and communication, she joined IDT Biologika, where she is now International Product Manager Specialities. Over the past two years, she has worked closely with the team that developed IDT's new rabies vaccine.

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