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Immune Protection in Animals: The Examples of Rinderpest and Foot-and-Mouth Disease

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Summary

Fading immune protection in farmed animals may present a problem, particularly in free-ranging animals in nomadic and transhumant pastoral systems, where animals are not readily available for large-scale blanket vaccination programmes. Two veterinary examples of fading immune protection are discussed: rinderpest and foot-and-mouth disease (FMD). Both are devastating viral diseases of cattle that have a huge impact on the farming economy. Both diseases can be controlled by vaccination, although the post-vaccination immunity afforded by the rinderpest vaccine is markedly different from that induced by FMD vaccines. These differences may in part explain the respective advancement of international eradication campaigns: while global eradication of rinderpest is imminent, FMD viruses are still actively circulating in many parts of the world.

Keywords: food-and-mouth disease; immune protection; rinderpest; vaccination

Rinderpest

Rinderpest Virus and Clinical Disease

Rinderpest is a viral disease of cattle that has a long history. The virus, a member of the *Morbillivirus* genus, mainly infects cattle (*Bos taurus* and *Bos indicus*). Morbidity is high, while the mortality rate is high with virulent strains, but variable with mild strains. A summary of the disease and the causative agent has been provided by the World Animal Health Organization (OIE) (http://www.oie.int/eng/maladies/fiches/a_A040.htm).

Clinical disease is easy to diagnose since infected animals classically present with the 'four Ds': discharge, diarrhoea and dehydration, leading to death. All domestic ruminant species can be infected including water buffalo and small ruminants. Wild ruminants, such as the African buffalo (*Syncerus caffer*) and all types of antelopes, as well as African warthogs (*Phacochoerus* spp.) are also susceptible to the virus, but do not act as a reservoir (Rossiter *et al*., 2006). In contrast, wildlife species are only infected sporadically and this most likely involves spread from cattle (Kock *et al*., 2006). The virus is thought to have emerged in central-east Asia and to have spread to Africa, where devastating outbreaks have been reported. Rinderpest was first identified in 1887 in eastern Africa and outbreaks spread through the entire sub-Saharan continent, arriving in western Africa in 1892 and in South Africa in 1896. The virus travelled to South America (Brazil) in 1921 and to Australia in 1923, although it never became established in these countries. North America has remained free of rinderpest.

Rinderpest Vaccines

Rinderpest viruses are of a single serotype (although three phylogenetic lineages have been described) and the attenuated strain used in vaccines confers life-long protection in cattle (Taylor *et al*., 2006). Some of the first-generation rinderpest vaccine strains were attenuated in goats. Egg- and rabbit-attenuated strains followed, which were replaced by tissue culture vaccines in the 1960s, when virus was grown on calf kidney cell cultures (Plowright and Ferris, 1962). In the mid-1980s, a heat-tolerant rinderpest virus strain was developed on Vero cells (Mariner *et al*., 1990). The thermostability of the vaccine strain (needed to

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reduce cold chain requirements) and the means of reconstitution of the vaccine and application to cattle in the field in warmer and remote areas proved essential for advancement of the eradication campaigns in Africa. Pilot studies in east and west Africa were conducted before the more widespread use of this product.

Herd Immunity and Rinderpest Control

The total control of rinderpest was proved to be possible when a high percentage of the total population of cattle were made permanently and solidly immune to infection through vaccination. This concept was further refined when modelling studies indicated that intermediate levels of rinderpest vaccination (60–80% of the susceptible population) could in fact prolong epidemics and account for persistence, whereas lower or higher coverage would result in shorter epidemics and drive infection to extinction at local or population levels (Fig. 1; Mariner *et al*., 2005). Post-infectious immunity (in surviving animals) as well as post-vaccination immunity proved to be life-long. Waning immunity at the level of individual animals is not therefore an issue with rinderpest vaccines. However, in the final stage of rinderpest eradication, it was essential to ascertain that the virus would not persist in parts of the Somali ecosystem, despite the problems associated with suboptimal vaccine coverage (Kock *et al*., 2006). Waning population immunity can occur through recruitment of naïve animals to the population after their maternal immunity has waned (maternally-derived antibody [MDA] disappears at around 10–11 months of age in cattle) and through gaps in coverage in previous vaccination campaigns. Moreover, calves with high titres of MDA do not respond to vaccination. Large scale vaccination campaigns have been implemented in cattle in various parts of the world and the target of maintaining strong herd immunity has been monitored serologically, using virus neutralisation assays (before 1985) and enzyme linked immunosorbent assays (ELISA; after 1985).

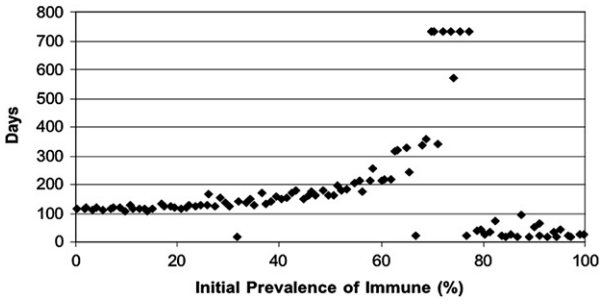

Fig. 1. Persistence of rinderpest in a given population as a function of the initial prevalence of protective immunity: the duration of an epizooty is longest when pre-outbreak immunity is between 60% and 80% (Mariner *et al*., 2005).

Rinderpest Eradication Campaigns

Large scale institutionalized vaccination campaigns aimed at eradicating rinderpest were implemented in southern India in the 1970 and 1980s, but these campaigns failed. The Indian government then proposed the establishment of a National Programme for Rinderpest Eradication, which proved successful by 1995. However, animals in Pakistan were still infected at that time and India maintained vaccination along its border until 2001, when Pakistan also achieved eradication. Similarly, multiple vaccination campaigns have proven necessary in Africa.

In 1962, 17 African countries reported active rinderpest infection and an international campaign called Joint Programme 15 (JP15) was started in 22 countries. This programme covered the entire intertropical region, over a period of 10 years and extended from west to east Africa, ending in the Horn of Africa. The first vaccine used was the goat-adapted vaccine, until this was replaced by Plowright's tissue culture-adapted virus vaccine. In 1976, the expected date of eradication, only two countries reported the disease.

However, the virus remained present in certain specific ecological niches such as in the Niger River delta in Mali and in some parts of southern Sudan and western Ethiopia. The achievements of JP15 were tragically undone when a new panzootic started in the Niger River (Sudd) and spread eastwards along the Sahel at the beginning of the 1980s and a second focal outbreak erupted in southern Sudan that spread rapidly westwards. One third of the cattle of the Fulani populations died; in Nigeria alone two million cattle fell sick and half a million perished. The epizootic spread south through Uganda by cattle looted by the victorious Tanzanian troops and ravaged the wildlife population of Tanzania.

With renewed vigour, the European Commission (EC) and other partners participated in the implementation of the Pan-African Rinderpest Campaign (PARC), which began in 1987 in 34 African countries and was coordinated by the Inter-African Bureau for Animal Resources of the African Union (AU-IBAR). In the mid-1990s, only limited foci of infection persisted in war-torn Sudan and Somalia. The Somali focus spilled over into Kenya and Tanzania, causing havoc in wildlife, but not in cattle. The virus was recovered from a gum erosion in one animal and proved to be an old African strain, virulent for wildlife, but non-fatal for cattle. At the end of the PARC project, rinderpest had not been totally eliminated and a new programme implemented by the AU-IBAR and mostly supported by the EC, the Pan-African Control of Epizootics (PACE), was put in place to continue the fight against the disease.