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RINDERPEST ERADICATION: GLOBAL SUCCESS, RISK OF RE-EMERGENCE AND ELICITATION FOR ERADICATION OF OTHER MORBILLIVIRUSES

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Abstract: **Global vaccination campaign led to the eradication of rinderpest worldwide, which was certified by the Federation of Agricultural Organization (FAO) and World the Assembly of the World Organisation for Animal Health (OIE). Since 2011, there has been no case of rinderpest anywhere in the world, but it remains a concern for the re-emergence of the disease. The reasons for the escalated fear about the potential for rinderpest re-emergence include re-introduction is conceivable, through niche replacement or another morbillivirus pathogen spillover. There are five distinct morbilliviruses recognized in the genus including the human measles virus (MV), rinderpest virus (RPV), canine distemper virus (CDV), peste-des petits ruminants virus (PPRV) which affect goats and sheep, phocine distemper virus (PDV). This article provides an overview of the spectacular success in achieving the eradication of RPV and reviews the various methods adopted in the eradication campaign which could be used to eradicate other viruses of the same genus.**

Keywords: **Rinderpest, Eradication, Morbillivirus, PPR.**

I. INTRODUCTION

Rinderpest virus (RPV) belongs to the genus *Morbillivirus* of the family *Paramyxoviridae*, and is closely associated with the measles virus MV. Other distinct Morbilliviruses have been recognized in the same genus including, canine distemper virus (CDV) phocine distemper virus (PDV)and peste des petits ruminants virus (PPRV) [1]. Rinderpest spread exclusively from animal to animal therefore it is not zoonotic [2]. Transmission occurs through direct contact with an infected individual via body secretions [3]. The virus is shed in the nasal discharge days before the clinical signs appear. The infected body fluids can also contaminate food and water supplies and create a possible infection route [4].Rinderpest was the second viral disease in history that was declared eradicated globally in 2011; the first was smallpox in 1980.Theinitiative to eradicate rinderpest was due to the impact of the disease on human welfare and international livestock trade [5]. Elimination of rinderpest in Europe was achieved progressively from the 18th century. The methods adopted for the eradication include isolation and slaughter of infected animals, quarantine and vaccination [2]. It took another 73 years before the disease was completely eradicated from other parts of the world. Rinderpest was officially declared eradicated in 2011 by Federation of Agricultural organization (FAO) and World Organization for Animal Health (OIE) [1].

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The disease of such historical impact should always be given the attention it deserves particularly in terms of surveillance. In 1988, there was a limited outbreak at the borders of Georgia, despite concerted efforts towards eradication [5]. The outbreak was due to the vaccine used, not wild virus infection, it was, however, detected through border surveillance and was controlled effectively. Many of the rinderpest prototype viruses or vaccines are still available in laboratories and research institutes [6], proper surveillance for both the laboratories and the research institutes should be intensified for the possible accidental or intentional re-introduction of the virus to cattle populations [6].

The virus of rinderpest has historical, economic and political consequences, and was the second infectious disease to be eradicated on earth through international collaborations [5]. Many argue that the unique rinderpest characteristic makes its eradication feasible, and therefore, strategies followed can be used in eradicating many infectious diseases [5]. Despite that there wasa series of challenges encountered during the campaign for rinderpest eradication; however, the International community demonstrated collaborative efforts for ensuring the cattle plague was completely eradicated. This was achieved through one of the successful programs initiated by the FAO called the Global Rinderpest Eradication Program (GREP). The practices employed by the GREP could be potentially applied to eradicate other infectious diseases [3].

In order to maintain the rinderpest-free status globally, this review paper focuses on how to strengthen surveillance to ensure that it doesn't resurface. The paper also highlights how the strategies used could be replicated in the eradication of other related infectious viral diseases.

II. RISK OF RINDERPEST RE-EMERGENCE

Rinderpest was eradicated in 2011, but it remains a source of concern for the re-emergence. There are various reasons for the escalated fear about the potential for smallpox re-emergence; for instance, re-introduction is conceivable, through the intentional or accidental release of laboratory stocks, niche replacement or other morbillivirus pathogens spillover [6]. Any deliberate or accidental release of rinderpest virus in the naïve cattle population will cause a serious devastating impact on the global economy [7].

The risk from vaccines and rinderpest virus in the repositories.

Successful rinderpest eradication was declared in 2011, which was the second infectious disease eradicated globally next to the victorious eradication of smallpox in 1980. However, there remains the risk of rinderpest re-emergence, because a number of laboratories across the world are retaining the viable strain of rinderpest virus, in field strain, laboratory-attenuated strain or diagnostic samples [6]. As long as the viable rinderpest virus is retained, concern and uncertainty for possible re-emergence of the disease remain [7**].** The purpose of the survey was to assess the possibility of one host becoming infected and infectious outside the laboratory anywhere in the world within a specific period. However, the outbreak from vaccines could not be devastating as the outbreak in the 1980s. This is in agreement with [8], where the last natural outbreak of smallpox occurred in 1977; a year later infection re-emerged from a laboratory in Birmingham. Similarly, in 1988, there was a limited and less severe outbreak of rinderpest at the border of Georgia attributed to vaccines used. Currently, there are still viable rinderpest viruses and vaccines stock in laboratories and research institutes as shown in table 1.

Table. 1 Model input parameters, the number of laboratories holding virus and the number of repositories holding vaccines.

Laboratories/vaccine repositories Vaccines	Laboratory-attenuated strains (Excluding vaccines)	Field strains		Diagnostic samples
Low-biosafety (BSL-2)	25	6	5	–
High-biosafety (BSL-3, 4)	24	10	5	–
Total	49	16	10	25

This information resulted from a questionnaire survey by [6]. Laboratories for which information was incomplete (i.e. laboratories that reported holding the virus in the past but did not say whether they still do) were assumed to hold virus, and laboratories of unknown biosafety level were assumed to be of BSL-2.

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Even though the risk of re-introduction by the rinderpest virus in the stock is extremely low, there is a need to reduce the number of laboratories holding the virus or to be upgraded to high-biosafety laboratories. In addition, preparedness for sudden re-emergence should be put in place for any accidental or intentional re-introduction of the rinderpest virus.

Risk of re-introduction through niche replacement.

Each organism occupies a particular niche. Rinderpest eradication may allow a vacant niche to be replaced by the original virus or other morbilliviruses if re-introduce [9]. [10] Have contended that there is no basis for the replacement of eradicated diseases. However, despite the rejection of niche replacement, [10], acknowledged the natural concern about vacated smallpox niche when the monkeypox virus emerged in Africa. Certainly, there is an increased number of cattle and buffaloes who have not been exposed to either rinderpest virus or vaccines and are susceptible to morbillivirus. With the concept of niche replacement and animal movement across neighboring countries, rinderpest may likely be re-introduced. Recent work by [11], shows evidence of cross-neutralization between PPRV and the RPV, which clearly shows that the rinderpest niche may have been replaced by other morbillivirus.

Risk of re-introduction from other morbilliviruses.

Rinderpest is caused by a morbillivirus, a genus that infect cloven-hoofed animals. Other related members of this group include measles virus (MV), PPRV, canine distemper (CDV), phocine distemper virus (PDV), feline morbillivirus (FmoPV) and cetacean morbillivirus (CeMV) [12].Basically, PPRV affects goat and sheep, recently, infection in cattle by PPRV was detected in Africa [10], evidence of cross-species infection [12]. Work by [13] confirmed cross-neutralizing antibodies between PPRV and RPV in Tanzania. Therefore, the probability of PPRV mutating into RPV is possible. Goats vaccinated with RPV vaccine show resistance against PPRV. However, transmission from cattle to cattle is not yet established. The genetic alteration capable of causing infection will be a major concern. If this happens, rinderpest–like virus will emerge.

Competitive release as an unintended consequence of rinderpest eradication.

Pathogens vary from one another, but there are some changes in pathogens that occur after eradication or control. After the eradication of RPV, prevalence of PPRV increased in Africa and Asia with the new viral lineage [14]. There is possibility that the present endemic nature of PPR is because of competitive released, as define by [9], competitive release ‘is the ecological phenomenon wherein one species increases in abundance or range because of the decline or removal of a competing species.

In the consideration for pathogen eradication, attention centred on the host species, the severity of the pathogen on the host and the corresponding economic consequences [9]. This view should be extended to cover the ecology of pathogen, in order to know the hazard that may occur after eradication. Incidence of PPR has increase with new different lineage since after the eradication of rinderpest as shown in figure 1. PPR was the disease of goat and sheep, the recent increase of camel involvement in PPR infection with the new lineage of the virus raises concern. Mutation of the virus in camel may serve as the risk factor for transboundary transmission within the African and Asia due to the nature of camel movement.

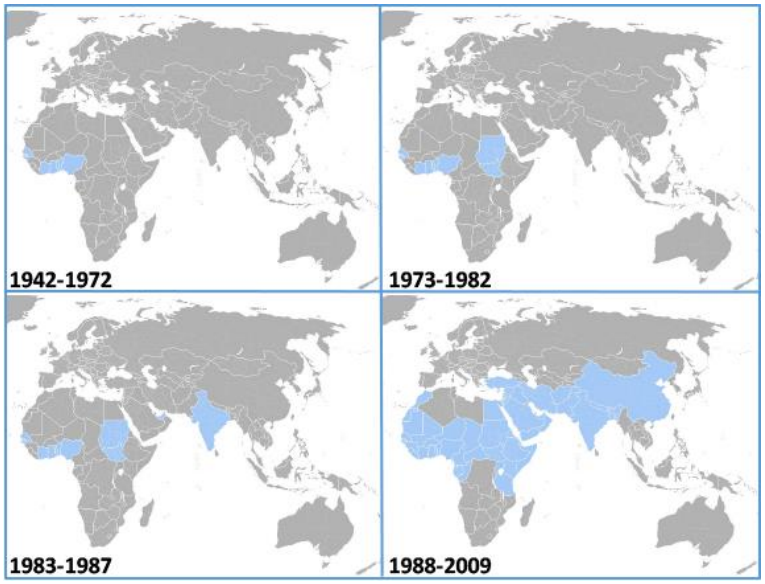

Fig. 1 Map of global prevalence from 1942-2009 of PPR taken from [15]

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Further measures should be taken when eradicating pathogens considering the history of cross-species infection. As suggested by [16], further research on the epidemiology and transmission pathway of the various lineage of the PPR should be carried out to facilitate the eradication of the virus. Eradication of the virus in only the natural host will render the process unsuccessful, because of the infection in an unintended host. There will be possible reintroduction from the unintended host.

Rinderpest eradication: lesson for other infectious disease eradication.

The official announcement and declaration of rinderpest eradication was made by the FAO and OIE in May 2011 [2], marking the end of cattle plague on earth. The devastation by rinderpest caused an estimated economic loss of more than US$ 1 billion and loss of over 200 million cattle [7]. Rinderpest is caused by Morbillivirus, the same genus that causes measles in humans and PPR in small ruminants. The virus of PPR and rinderpest share some biological similarities [12]. However, the variation in the different lineage(citation) of PPR will make eradication process complicated.

Rinderpest eradication: lesson for PPR eradication

The FAO and OIE target 2030 for global eradication of PPR [11]; these two organizations coordinated the successful eradication of RPV. Attenuated vaccines have been effective in prevention of PPR in endemic countries with annual booster. Strategies adopted for RPV eradication will be effective for PPR eradication campaign.

Feasibility of PPR eradication.

PPR is the disease of small ruminants for example goats and sheep. Just like rinderpest, the disease has an impact on animal and human welfare, especially for small-scale farmers in developing countries. A recent study by [11] indicates cross neutralizing antibodies between PPRV and RPV in Africa. However, unlike RPV, PPRV have four different lineages (citation)with different distribution, which will make eradication difficult.

Rinderpest eradication: lesson for measles eradication.

RPV and MV belong to the genus morbillivirus of the family paramixoviridae. Viruses of this genus are highly pathogenic and spread through inhalation of infected particles. The disease caused by these viruses are characterized by high morbidity and mortality in an unexposed host. As shown in Figure 2, measles and rinderpest have a closer phylogenetic relationship than other members of the genus with distinct definitive host. Infection by morbilliviruses results in respiratory and immune system diseases. Measles infection in humans is associated with mild nervous system involvement.

The initial campaign for global measles eradication started in the 1980s [12]. The prevalence of the disease was low in many parts of the world. Therefore, the idea was dropped. Few years later, the Americas eliminated MV through coordinated effort of Pan-American Health Organization (PAHO). In 2001, the World Health Organization (WHO) and other related agencies reduced MV mortality rate through adoption of PAHO strategies of mass vaccination. The adopted strategy reduced the global prevalence of MV in many parts of the world.

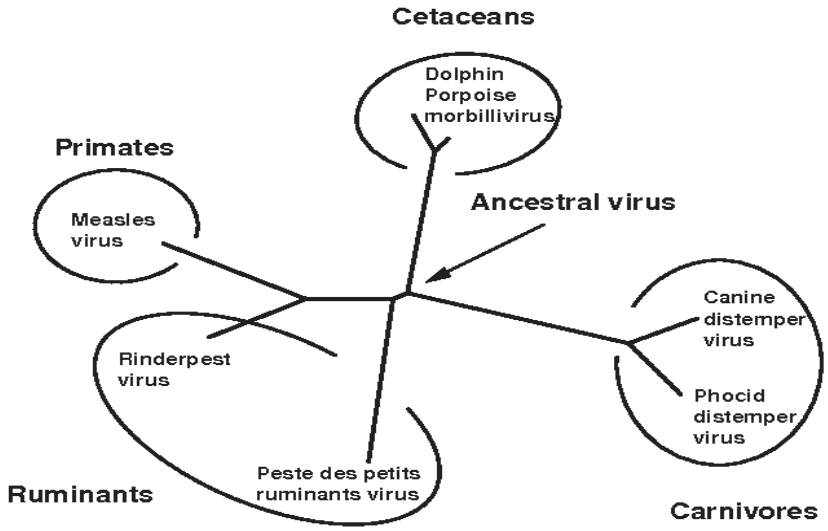

Fig. 2 Ancestral relationship between the viruses from genus morbillivirus [17]

Feasibility of measles eradication

Recent studies show MV infect only human. Reduction in the prevalence of MV was achieved with mass vaccination and surveillance. The biological similarities between the RPV and MV make the eradication of measles attainable. Although, rinderpest eradication was achieved through the concerted efforts of mass vaccination, quarantine and slaughter of infected cattle. However, not all strategies used for rinderpest eradication will be applicable for MV eradication due to host variation.

The first lesson to be derived from rinderpest eradication is the nature of the disease. Both RPV and MV share some biological similarities. MV have a distinct clinical feature (be specific, why mention this in your paragraph), especially in immuno-compromised patient. This serves as an important aspect that distinguishes it from other viral infections. It is encouraging that the WHO established the global MV surveillance and diagnostic laboratories. These centers will help in identifying seropositive patients during the eradication campaign.

Lessons from the vaccine used during rinderpest eradication.

Most importantly, Walter Plowright developed live-attenuated RPV vaccine in the 1960s, which was later improved to be a thermostable vaccine in the 1990s, thereby facilitating its movement to remote areas with no cold chain maintenance facilities during the eradication campaign. MV is live attenuated and effective. However, cold chain is required for movement to areas of low basic amenities. During rinderpest eradication campaign, there was general acceptance of the program by both animal health workers and farmers. On the other hand, there was rejection of vaccinations in many communities in across the world, due to either religion belief or mistrust [18] which could render the MV eradication difficult.

The rinderpest eradication was achieved based on the nature of the host. After concerted mass vaccination for some years, the vaccination was unanimously stopped to enable surveillance on the few areas of infection. Hypothetically, these strategies will not be applicable to humans**.**

III. CONCLUSION

This paper has discussed the fear associated with the current rinderpest eradication status. Importantly, it has highlighted what next should be done to prevent re-emergence, after successful eradication. The major concern after the eradication is the niche replacement and accidental re-introduction of the virus from laboratories remain the major concerned. Some laboratories retain rinderpest virus, some of these laboratories are low-level biosafety laboratories, and the laboratories need to be upgraded to high-level biosafety laboratories. Moreover, preparedness for the viral re-introduction has to be put in place.

The recent detection of rinderpest like disease by [13], in Africa will be a possible replacement of the niche vacated by rinderpest or mutation of another morbillivirus. The vacated niche will serve as opportunity for pathogen to emerged or re-introduced, but this will depend on many factors that will favor the pathogenicity of the new pathogen. Niche replacement should be considered as eradication consequences when targeting eradication of other infectious diseases.

Important lesson for eradication of other infectious diseases will be learned through strategies adopted during rinderpest eradication campaign. This includes the development of thermostable vaccine for used in the remote settlement. Eradication of diseases such as PPR and MV is achievable.

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