



This information is current as of July 16, 2017.

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J Immunol 2016; 196:3499-3506; ;
doi: 10.4049/jimmunol.1502625
<http://www.jimmunol.org/content/196/9/3499>

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The Opportunity To Eradicate Peste des Petits Ruminants

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Peste des petits ruminants (PPR) is a highly infectious disease of sheep and goats that is caused by PPR virus, a member of the genus *Morbillivirus* that includes the viruses that cause rinderpest (RP) in cattle. RP was the first animal disease to be globally eradicated in 2011 and is only the second disease, after smallpox, to have ever been eradicated. PPR is one of the principal constraints to small ruminant production in Africa, Asia, and the Middle East. The epidemiology of PPR and RP as well as the technologies available for their diagnosis and control are similar. The conditions that favored the eradication of RP are also largely present for PPR. In this work, we outline the evolving strategy for eradication in light of current opportunities and challenges, as well as the lessons from other eradication programs in animal and human health. The global PPR situation and technology for its control are summarized. A strategy based on the lessons from previous eradication efforts that integrate epidemiology, social science, and economics as tools to target and motivate vaccination is summarized. Major aspects of the cost and benefit-cost analysis of the indicated program are presented. The overall undiscounted cost of eradication was estimated as \$3.1 billion, and the benefit-cost ratio for the most likely scenario was estimated at 33.8. We close with a discussion of the possible next steps. *The Journal of Immunology*, 2016, 196: 3499–3506.

Peste des petits ruminants (PPR) is a highly infectious disease of sheep and goats that is caused by PPR virus, a member of the genus *Morbillivirus* that includes the viruses that cause rinderpest (RP) in cattle, measles in humans, and distemper in dogs (1). RP was the first animal disease to be globally eradicated in 2011 and is only the second disease, after smallpox, to have ever been eradicated. PPR is one of the principal constraints to small ruminant production in Africa, Asia, and the Middle East. The epidemiology of PPR and RP as well as the technologies available for their diagnosis and control are similar. The conditions that

favored the eradication of RP are also largely present for PPR. It is recognized that as with RP, PPR occurs in many regions of the world that are politically unsettled and possess limited resources. However, these constraints were overcome with RP and the challenges for PPR are similar. As a result, stakeholders in the international animal health community have been advocating for the global eradication of PPR, and this has led to a robust examination of strategic alternatives for eradication.

The World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations discussed the potential for the global eradication of PPR in April of 2015 in Abidjan, Cote d'Ivoire. The meeting provided a platform to discuss strategic options and the role of epidemiology, vaccination, and the capacity of national veterinary services to manage an eradication program. Management of disease eradication programs is an adaptive and dynamic process that builds on existing knowledge, new learning, and new technologies. In this work, we outline an evolving strategy for PPR eradication in light of these discussions, and the current global PPR status and technologies for control are summarized. We highlight lessons learned from previous animal and human disease control programs of relevance to PPR eradication. Based on these lessons, a strategy is proposed that is underpinned by a clear understanding of the immune response of an animal both to vaccination and field infection and that integrates epidemiology, social science, and economics as tools to target interventions. Surveillance and epidemiological assessment are used to focus vaccination on specific populations to achieve defined immunity targets within a specified time period. The program will enhance incentives for livestock owners and service providers to fully participate through appropriate attention to social and economic concerns. Major aspects of the cost and benefit-cost analysis of the indicated program are also presented. We close with a discussion of the possible next steps (2).

Small ruminants and PPR

Small ruminants are important for the livelihoods and food security of rural households in the developing world. Animal

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Abbreviations used in this article: DIVA, differentiating infected from vaccinated animals; GREP, Global RP Eradication Program; OIE, World Organization for Animal Health; PPR, peste des petits ruminants; RP, rinderpest.

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source proteins are the most accessible and practical means of enhancing nutrition for the world's poor. The demand for livestock products is expected to increase by 37% per capita, requiring an increase in overall production of 92% by 2050 (3). The need for milk alone is expected to triple in sub-Saharan Africa (4). Owing to their smaller size, low cost per head, and rapid reproduction, small ruminants are an important means of improving livelihoods for the poor. Small ruminants are suited to a diverse range of environments and often forage and browse from landscapes that otherwise would be of limited food production value. Animal disease is a major constraint to small ruminant meat and milk production, and many pastoral communities consider that PPR ranks highly among the most important diseases of livestock (5). PPR occurs in Africa, the Middle East and Turkey, and Central, South, and East Asia (Fig. 1). During the last 10 y it has spread to new areas, including North Africa, southern Africa, China, and Kazakhstan (1, 6–8).

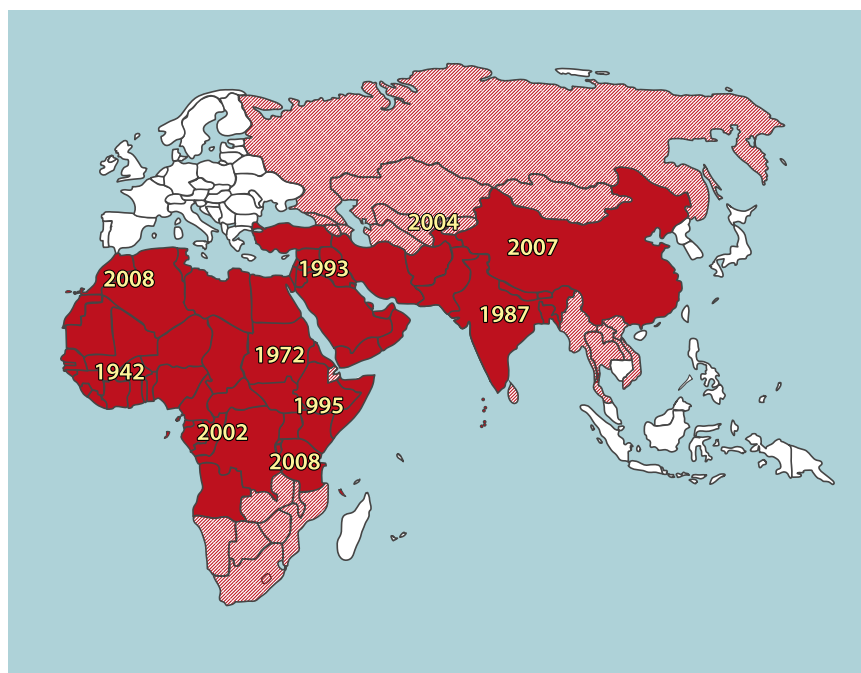
Small ruminants affected by PPR show signs of fever, ocular and nasal discharges, oral mucosal erosions, bronchopneumonia, and diarrhea (9). Morbidity and case fatality rates can vary widely, being very high, up to 100% in naive populations, but they can be lower depending on the virus strain, host species, breed (1), and nutritional status.

The role of hosts other than domestic small ruminants has drawn considerable scrutiny. Numerous studies have documented seroconversions in cattle and buffaloes, but neither clinical disease nor transmission to other susceptible animals has been found. Both cattle and buffaloes are considered dead-end hosts and should not therefore play a role in the persistence of the virus (10), and in fact they may serve as valuable but benign sentinel species in the absence of the availability of differentiating infected from vaccinated animals (DIVA) technology for PPR (11). Pigs undergo subclinical infection by experimental inoculation or contact with infected goats, but they are unable to transmit the virus and therefore are not important in the spread of the disease. It is unclear whether camels contribute to the dissemination of PPR virus,

but their role, if any, would be minor. The number of possible outbreaks recorded is low and there is no evidence of persistence in camel populations to date. PPR infection and disease have been confirmed in a number of wild artiodactyl species (12). Available evidence indicates that PPR does not persist in wildlife populations and that exposure to infected sheep and goats precedes outbreaks in wildlife (as demonstrated with RP) (13). Reports of clinical disease in wildlife are limited to mixed populations of small ruminant livestock and wildlife kept under ranch-like conditions in the Middle East and caprine species in Asia. No clinical disease has been recorded in wildlife in Africa. Wildlife populations have not been noted to sustain infection or act as a source of infection for domestic animals (14). It is of course scientifically impossible to prove an absolute negative. Due diligence requires that monitoring alternate hosts continue. However, given the high volume of surveillance data, research, and literature on the subject, the failure to find evidence that hosts other than domestic sheep and goats contribute to the maintenance of PPR in nature should give confidence.

PPR shares many of the characteristics of RP that made it an eradicable disease. PPR is an acute infection measured in days, and for practical purposes the virus does not survive outside the host. Infection results in death or lifelong immunity. The virus must continually find new susceptible hosts capable of onward transmission to survive in nature. Understanding the immune response of animals to both field infection and vaccination was fundamental to the final successful eradication of RP and is equally important if success with PPR is to be achieved. Critically, these viruses induce a neutralizing Ab response that lasts for the life of the animal and is protective against all strains of the virus. For PPR, effective and inexpensive vaccines are available that produce a similar lifelong protective immunity as does wild virus infection, and they protect against all known serotypes (15). Thermostable vaccines have been developed to overcome difficult field conditions that will be encountered in many PPR-infected countries. Note that young animals should acquire neutralizing Abs when receiving colostrum from

FIGURE 1. PPR-infected and at-risk countries in Africa, Asia, and Europe. Countries considered infected are colored in red, and countries at high risk of infection are indicated with red stripes. Countries in white are considered free and at low risk.



an immune mother and these can persist for up to 6 mo. This has to be taken into account when designing serosurveillance for accreditation of disease freedom. Of course it is important to recognize that these maternally derived Abs can interfere with the response to vaccination, and therefore such young animals would require a repeat vaccination to ensure that lifelong protection occurs. Cell-mediated immune responses do occur following infection with PPR virus and these differ between virulent field virus and vaccine-induced responses. Significantly, there appears to be a reduction in the number of Th cells ~4 d after infection with wild-type virus that does not occur following PPR vaccination. This may account for the immunosuppression noted in general with morbilliviruses. It is also apparent that a cell-mediated immune response is important for protection along with the presence of neutralizing Ab (16), but all current vaccines do appear to generate such responses. If a recombinant vaccine were to be considered for use, it would be important to demonstrate that similar immune responses are generated (17, 18).

Virus transmission occurs mainly by direct contact; the PPR virus does not survive for long outside the host; the infectious period is short; and animals do not become carriers, either dying or recovering with subsequent lifelong immunity. Diagnostic tests with high sensitivity and specificity are also available commercially. However, in contrast to cattle, sheep and goat populations in countries at risk can be very large and the life cycle is much shorter. This means that vaccination to eliminate infection needs to be delivered in intensive and efficient bursts to reach and maintain high herd immunity levels. An additional challenge is that sheep and goats have a lower value per head compared with cattle, so sheep and goat keepers may be less likely to invest in disease control given its higher relative cost. These factors described above all argue against the process of mass vaccination of populations. It would be virtually impossible to ensure that an effective immune response is reached in global populations at a national level to ensure the elimination of the virus. To eliminate the virus, it would be far more effective to identify the pockets of endemicity responsible for virus persistence and create high levels of vaccination immunity in these defined populations, as was done in the final stages of RP eradication.

The impact of PPR on small ruminant productivity includes mortality, loss of milk, meat, fibers, and hides, weight loss, impaired growth, and abortion. As PPR is an epidemic disease, its impacts are clustered at the household and community levels. When it occurs, PPR results in shortages of milk and meat to feed the family, as well as lack of animals for sale to provide cash to purchase cereals and other foodstuffs, basic household necessities, as well as essential health and educational needs. Fewer animals are available for social purposes such as loans and gifts, marriages, and funerals, and thus important social events may be postponed for months or years. Livelihood impacts that affect the well-being of communities are hard to quantify, but they are among the most important cited by communities (19).

We have estimated the annual mortality rate due to PPR in infected countries and, from this, assessed the value of these losses (2). The small ruminant population from the 65 countries reported as being infected at the end of 2014 was 1.44 billion animals. We calculated the value of a typical sheep or goat using average carcass weight and price per

kilogram of sheep and goat meat by country from the FAOSTAT database (20). The annual PPR mortality rate in infected countries was determined to be 2.6%, ranging from 1.4 (denoted as the low mortality scenario) to 4.7% (denoted as the high mortality scenario); we consider this to be a conservative estimate. The calculation was based on a review of PPR outbreaks described in the literature (18 references) to obtain a median within-flock mortality rate of 13.2% and interquartile range of 4.9–26.3%. We extrapolated to the population level by estimating the proportion of flocks affected each year under different lengths of epidemic cycle. From these data, we estimate that annually there are 37.4 million PPR-associated small ruminant deaths (ranging from 20.2 million to a maximum of 67.7 million in low and high mortality scenarios, respectively). The value of this mortality is \$1.475 billion, ranging from \$794 million to \$2.7 billion in low and high mortality scenarios, respectively.

Diseases such as PPR occur as focal epidemics and the impact is highly clustered. The average global impacts do not reflect the severity of impact on individual households and communities that can be devastated by PPR outbreaks. Epidemics are associated with mortality rates of up to 100% in individual herds/flocks and result in hunger, destitution, and social collapse (19).

Suitable vaccines and diagnostics are available

Central to our proposed approach is the requirement to identify infected populations, circumscribe these through surveillance on the ground, and then eliminate the virus from these populations through limited but highly effective focused vaccination. To achieve this, it is critical that reliable diagnostic tests capable of confirming PPR diagnoses in the field and laboratory are available as well as highly effective vaccines. The currently available diagnostic tests and vaccines are thought to be capable of meeting the critical requirements of eradication through this epidemiological evidence-based approach.

Currently, a PPR diagnostic test capacity is available to confirm clinical diagnosis of PPR, measure the serological response to PPR infection and vaccination, confirm the absence of infection both in individuals and in populations, differentiate PPR from other similar diseases of small ruminants, and finally to genetically characterize the PPR virus as an aid for describing the flows of virus through populations.

Diagnostic tests that are currently available are discussed below.

Pen-side test. A rapid immunochromatographic strip test has been developed and shows extremely high sensitivity and specificity. The standard devices are hermetically sealed and offer a long shelf life, ideal for initial investigations of field events (21). This test can confirm or refute the presence of virus in a location in real time, thus enabling effective surveillance to underpin targeted vaccination.

Immunocapture ELISA. The mAb-based immunocapture ELISA has been shown to be PPR Ag specific. This assay allows local laboratories to make a rapid primary diagnosis of PPR outbreaks with limited resources, and no tissue culture or PCR capability is required (22). This test is a valuable adjunct to the pen-side test described above, in providing reassurance that the specificity of the field assay is as claimed, and in the absence of pen-side assay availability it is an essential tool.

Gene detection. The PCR is the most sensitive assay for confirming PPR diagnosis. Originally, the reverse transcriptase

PCR was used but has now been superseded by the real-time PCR, which offers significant advantages in sensitivity and in limiting laboratory cross-contamination. There are now a number of alternative approaches to using this technology (e.g., loop-mediated isothermal amplification) (23–25).

Virus sequencing. Nucleotide sequencing of the PCR product offers the opportunity to differentiate specific PPR lineages and more effectively trace the source of outbreaks and enhance our understanding of the epidemiology of PPR virus. Such technology is available in PPR OIE reference laboratories (26). The use of this assay becomes vital in understanding virus circulation, the distribution of different virus clades, and the differing roles these might play in the epidemiology of the disease in the field.

Competitive ELISA for seromonitoring and serosurveillance. An mAb-based competitive ELISA is available to detect PPR-specific Abs in blood for monitoring the response of national herds (which may be multispecies) to PPR vaccination. This can be implemented as a standard assay for global use. Implementation should include a system of internal controls and performance monitoring to ensure standardization of results and international confidence in the data generated (27).

In an eradication program, the ability to determine the immune status of a subpopulation is a crucial step in underpinning decision-making as to whether to vaccinate a subpopulation or adopt alternative epidemiologically based approaches, such as movement restrictions. As the program progresses, these assays will become critical in demonstrating freedom from circulating virus. Clearly, it will become important at that stage to determine whether detected Abs are generated by vaccine or wild-type virus. It is at this point that the availability of a DIVA vaccine would confer a significant advantage.

Although the existing pen-side test for PPR can be used to confirm PPR, it would be useful to have an assay that could confirm a number of differential diagnoses, which could be considered to be components of a clinical pneumoenteritis syndrome and other similar priority small ruminant diseases. For example, enabling field services and laboratories to rapidly distinguish and confirm a diagnosis of PPR, contagious caprine pleuropneumonia, sheep and goat pox, pasteurellosis, bluetongue, and foot-and-mouth disease would be useful. This could be achieved through a battery of independent tests; however, a multiplexed assay testing samples simultaneously on a uniform technical platform against an array of pathogens would be more cost effective and practical to implement. This technology is now within practical reach and would greatly facilitate the global eradication effort but is not a prerequisite for commencing global eradication.

Vaccination will be a core component of the eradication strategy. Existing PPR vaccines are among the most effective vaccines available for any disease. Currently, three excellent live attenuated vaccines have been fully tested and widely used in the field. They are recognized by the OIE and are available for use in the PPR eradication program (28). The strains in use are Nigeria 75/1 from Africa (29) and Sungri 96 and Arasul 87 from India. The Nigeria 75/1 strain has been in use for >2 decades and has performed remarkably well wherever it has been used. The three vaccine strains are known to provide lifelong immunity and to protect against all strains of PPR, and they have

never been known to result in an adverse reaction, although the usual monitoring of the use of modified live virus vaccines is appropriate. Current vaccines, however, do require a cold chain. A thermostable PPR vaccine has now been developed and will soon be more widely available to reduce this constraint.

It is envisaged that the eradication program will facilitate the validation and deployment of thermostable vaccine production techniques for existing strains. The development of new vaccine candidates that allow differentiation of vaccinated animals for those infected by wild virus (DIVA) is to be encouraged. However, DIVA vaccine candidates would need to be evaluated in comparison with conventional vaccines for the full range of vaccine attributes (e.g., efficacy, impact on virus shedding and transmission, duration of immunity, range of protection, safety, minimum dose, ease of production, cost) in addition to diagnostic advantages. Candidate vaccines for DIVA technologies include capripox (30, 31) and adenovirus-vectored vaccines (18, 32). Prior exposure to capripox reduced the immune responses to the PPR Ags in vaccinates and, in the one study where challenge was carried out, incomplete protection against clinical disease. The implications for shedding and transmission were not assessed. The adenovirus-vectored vaccine generated solid protection against challenge for up to 3 mo after inoculation, and 10^8 PFU was determined to be the minimum dose. Prior immunity to the strain of adenovirus used was not thought to be prevalent in small ruminants. These results are promising, but for comparison, the minimum immunizing dose for vaccines based on the Nigerian 75/1 strain is on the order of a single median tissue culture infectious dose, and the duration of immunity has been shown to be at least 3 y.

The greatest advantage for a DIVA vaccine may well be in the latter part of a campaign when it becomes crucial to differentiate evidence of circulating wild-type virus from vaccine-induced immunity. As was the case with RP, currently available non-DIVA vaccines are among the finest vaccines ever developed and fully enable eradication.

Lessons from disease control

An important lesson from both human and animal eradication programs is that countries usually achieve the elimination of virus as a result of an intensive action lasting 1–2 y (33–35). Often there is a period of preparation and practice as knowledge and systems are built, but elimination is finally achieved in a concerted intervention of short duration. Thereafter follows a period of surveillance to validate disease absence and guard against reintroduction. In human health programs, safeguarding free areas is especially challenging due to the rapid, long-distance mobility of human populations. Livestock mobility comes primarily in two forms: pastoral movements in search of water and food, and, second, trade. Pastoral movement is often across borders, and trade movements range from just local to right across the globe. Thus, in animal health, safeguarding free areas can often be achieved by monitoring and managing pastoral movements and trade flows.

RP eradication was based on a dynamic strategy that evolved over time in light of new knowledge on RP and information from other control programs in animal and human health. The program incorporated research and learning and was fortunate to have a relatively small and flexible structure that allowed

open debate and an adaptive approach to management. The principal lessons were as follows:

- Use of eradication strategies with fixed deadlines created a sense of urgency that helped to maintain momentum.
- Decision-making was more effective when guided by epidemiological principles with appropriate attention and respect for social and political realities.
- The control strategy setting needed to be based on continuous monitoring of progress in the control program and incorporate the ability to change track to address new issues such as detection of mild viruses in eastern Africa.
- Interventions were more effective when focused on specific populations and periods of time and had specific epidemiological goals.
- Interventions led to rapid eradication when they targeted critical points in virus transmission using information from surveillance and epidemiological assessments.
- Strategies and interventions were only fully implemented when they were based on realistic economic and social incentives of the different stakeholders (farmers as well as international organizations).
- Quality assurance and monitoring resulted in better vaccines, vaccination, and diagnostics, and they were required for the success of the program.
- Leadership and coordination were more effective when open and inclusive. Stakeholder organizations need to be empowered and motivated to meet the shared goal of eradication.

Although the end is arguably in sight for the eradication of poliomyelitis, political instability and failure of governance systems have considerably delayed eradication (36). In the early 1990s, RP eradication was also delayed by the same issues in several regions of eastern Africa. The RP eradication program addressed this by turning to community-based animal health programs where local herders were trained to deliver primary animal health care, including RP vaccination

with thermostable vaccine. Often nongovernmental organizations provided training and backstopped programs. These local intermediaries were able to work safely and effectively where outsiders could not. In the end, it can be argued it was the herders of South Sudan, Karamoja in Uganda, and the Afar region of Ethiopia who eradicated RP from their own communities.

A common debate in public health policy concerns the trade-offs between the so-called vertical programs that target interventions to a specific disease and the horizontal programs that favor the building of more general health systems capable of addressing multiple targets. Animal health programs have traditionally taken the position that the distinction between vertical and horizontal programs is artificial and unhelpful. Disease-specific and health systems objectives can in fact complement and reinforce each other. In RP eradication, the measurable goal of eradication drove considerable innovation and enhancement of animal health systems (37). Many think that the eradication of PPR offers considerable additional value, as it will require and lead to the strengthening of small ruminant health and animal health services in general. However, as was successfully done with RP, it is crucial not to lose sight of the primary program goal—the eradication of the disease.

A guiding strategy for PPR eradication

Our proposed strategy for the eradication of PPR is a 12-y program consisting of preparatory, eradication, and accreditation phases (Table I). A fourth posteradication phase assures proper closure of the program and capture of the lessons learnt. Within the 12-y program, it is recognized that countries will move at different rates but that the actual elimination of virus will occur in a final 1- to 2-y push. The remainder of the 12-y period is dedicated to preparation for that push and the verification of virus elimination upon completion of the targeted vaccination activity.

The heart of the technical strategy is an integrated program in which surveillance informs where and what populations to

Table I. The timelines, phases, and principal activities of global PPR eradication

Preparation (3 y)	Eradication (5 y)	Accreditation (4 y)	Posteradication (3 y)
Develop and Launch Eradication Systems	Eliminate Infection from All Countries	Verify the Elimination of Infection from All Countries and Declare Global Eradication	Capture Lessons and Mitigate the Risk of the Recurrence of PPR
<ul style="list-style-type: none">• Establish independent and inclusive coordination.• Conduct epidemiological assessments, identify critical control points, and develop national plans.• Launch surveillance and targeted vaccination programs.• Initiate capacity building and epidemiological, social, and technical research.• Establish baselines as well as monitoring and evaluation systems.	<ul style="list-style-type: none">• Implement targeted, intensive vaccination of populations responsible for endemic maintenance of PPR.• Conduct comprehensive surveillance using a variety of methods, including participatory surveillance.• Adaptively manage programs based on results of learning activities.• Progressively move countries to cease vaccination and embark on accreditation.	<ul style="list-style-type: none">• Eliminate any remaining foci of infection.• Assure global cessation of vaccination.• Conduct surveillance and targeted assessments to verify disease absence.• Complete formal accreditation in all countries.• Conduct global risk assessment for occult foci.• Maintain global emergency vaccine banks and production capacity but cease routine production.• Declare global freedom.	<ul style="list-style-type: none">• Document lessons learnt for future programs.• Prepare risk assessment and contingency plan for risk of recurrence of PPR.• Sequestration and/or destruction of PPR viruses.• Integrate posteradication PPR surveillance in national surveillance programs.

The table presents the major activities in each phase of the eradication program. Phases probably will not run concurrently in all countries. The pace of implementation will be adapted to local institutional and epidemiological contexts within the overall time frame of 12 y.

vaccinate, a vaccination scheme we term “smart vaccination.” Central to this approach are a number of underpinning immunological concepts. First, it is recognized that an animal effectively vaccinated will be immune for life from infection by all known PPR viruses. Second, young animals under the age of 6 mo may not respond correctly to vaccination owing to the presence of maternally derived Abs and thus will require revaccination once assuredly susceptible to vaccine take. Third, vaccination seldom reaches all animals and not all animals given vaccination will respond due to problems in application of vaccines in the field, including maintaining the viability of the vaccine (hence the need for postvaccination seromonitoring). Fourth, this virus does not persist for long outside of the host and even in infected animals requires close contact between infected and susceptible animals to spread. Finally, the cost of vaccination in most of the settings where PPR occurs is significant when compared with the value of the animal and the resources available to the owner. Thus, a targeted vaccination strategy, linked with other disease control approaches, makes absolute sense.

This epidemiologically focused vaccination will be delivered through systems that seek to optimize the involvement of public-, private-, and community-based service providers through a good understanding of the incentives for participation. It was estimated that on average, infected countries would need to complete three rounds of vaccination in subsets of populations that represented 50% of the national population. This amounts to a total of ~2 billion vaccinations during the life of the core program.

The program will make major investments in surveillance and epidemiological assessment, social science, inclusive coordination, and targeted vaccination.

Surveillance and epidemiological assessment. Vigorous surveillance systems will be essential for implementation of a PPR eradication program that, as we advise, should use targeted vaccination based on an understanding of the immune status in subpopulations and in a highly focused manner to rapidly eliminate foci of infection. In the 1980s and 1990s, in sub-Saharan Africa, under the Pan-African RP Campaign and subsequently the Pan-African Control of Epizootics, surveillance capacity was developed and strengthened, and this was continued and broadened beyond Africa through activities related to the predicted highly pathogenic avian influenza pandemic in the first decade of the new millennium. However, surveillance remains without doubt the most neglected function of official veterinary services. Of the capacity developed during the Global RP Eradication Program (GREP), little remains apart from the knowledge of how to operate in remote and often marginalized areas, which are critically important in the persistence of virus transmission chains (37). Although elements of this knowledge persist and can be built on for PPR eradication, significant investments will need to be made in this area to underpin the eradication strategy. Improved routine disease reporting, often referred to as passive disease reporting, needs to be complemented by a range of active or targeted surveillance activities in the form of serosurveys and disease searching, including the use of participatory techniques (37).

At the outset, the eradication program will build national risk maps as tools for understanding virus ecology based on epidemiological assessments at the population level. The contact structure of small ruminant populations is determined by the

dynamics of human communities and their interactions. Often, developing countries are ethnically diverse and these cultural dimensions delineate animal populations and shape production and trading systems. Epidemiological assessments must therefore include and integrate participatory approaches, serology, confirmatory diagnosis, isolation and genetic analysis of representative strains, and estimations of transmission rate parameters such as the basic reproductive number.

Social science. Application of social science skills came rather late to the RP eradication effort, but there is now much more awareness that planning for eradication requires a sound knowledge of how the disease and its control relate to people's livelihoods and social conditions. Information is gradually accruing about the impact of disease and eradication activities on communities and social attitudes and this has been applied to a cost-benefit analysis and strategy setting. Marketing of small ruminants is the most important activity for many rural livestock owners who see them as a tradable commodity rather than stored wealth as is the case for cattle. As small ruminant movements are important determinants in PPR transmission, understanding migration pathways and the structure and drivers of the evolution of market chains require investment and field intelligence to build such knowledge into the eradication effort. In RP eradication, once interventions incorporated an informed approach to the socioeconomic and cultural incentives for participation by livestock owners and service providers, the national programs progressed rapidly to completion.

Inclusive coordination. Eradication of PPR will be a momentous undertaking that transcends individual organizations and that needs to be informed by a broad spectrum of scientific disciplines, both technical and social, and by a sound knowledge of business practice and an appreciation of the different political settings in countries and regions where the disease occurs. It is clearly understood that this disease occurs in some of the most geopolitically challenging areas of the globe and that other programs, such as the polio eradication program, have struggled to complete eradication in areas such as the tribal areas of northern Pakistan using mostly conventional approaches. Although these areas present a number of challenges, the same challenges were overcome as part of RP eradication using innovative approaches that trained and empowered local actors from all sides of the conflict to conduct control programs. This was accomplished during periods of severe conflict in Afghanistan, Iraq, Somalia, and South Sudan when the international presence in conflict zones was much less than it is today (37). In many cases, nonliterate community members were trained to manage and conduct vaccination programs. In very sensitive situations, professional intermediaries who could bridge the gap between the local political, cultural, and religious authorities and external institutions built the programs. Although sociopolitical challenges continue to evolve, control programs designed in the context of local realities succeed.

None of the expertise, whether technical, managerial, or political, is to be found in a single organization or group of people, nor should any one organization seek to exert ownership of the global effort (38). Leadership and coordination is, however, required to ensure that momentum is sustained. This would best be provided by a coordination mechanism that is independent of any individual organizational hierarchy. Such an autonomous coordinating mechanism, where per-

sonnel are recruited and overseen by a multipartite oversight body representative of the range of stakeholders participating in the program, would support an inclusive ethos that ensured fair representation of all interested parties. The Global Fund for HIV, Tuberculosis and Malaria could provide a useful model in this regard.

Targeted vaccination. We have available highly effective, safe, and affordable vaccines for use in PPR eradication. However, basic knowledge of disease behavior and immune responses in populations and experience in other disease eradication programs, especially RP during the GREP, has taught us that there should be far more to disease control and eradication than institutionalized, pulsed vaccination. It was demonstrated very clearly during GREP that inefficient vaccination in the face of endemic disease frequently did not induce immunity that reached the virus elimination threshold, aiding long-term virus persistence in some extensive populations (39) and resulting in the disease being difficult to detect. It is clear that to be optimally effective in achieving elimination of the PPR virus from an infected population, smart vaccination has to be applied within a systematic and adaptively managed program. Vaccination will be focused on discrete populations of small ruminants where the virus is present, where the immunological status of the animals has been determined, and it will have defined goals in terms of the level of herd immunity to be achieved in a specific time frame. That focus will be achieved through implementation of an efficient surveillance system that includes active field assessments and diagnostic (immunological and virus) studies to disclose current areas of infection, indicate populations at high risk, and understand the social, economic, and epidemiological factors that have contributed to sustained transmission. Vaccination when used must be at high intensity aiming at 100% coverage, in as small a population as is appropriate in light of the epidemiological objective and for the shortest time possible to achieve the objective of virus elimination.

Historically, vaccination was frequently used in uninfected populations where risk of introduction was considered to exist, that is, defensive vaccination, and it was often considered that mass vaccination was the most effective defense, by producing a degree of herd immunity, which would prevent incursion of the virus. However, experience in the regions where PPR is extant has indicated that these approaches rarely sustain levels of herd immunity consistent with the exclusion of infection. Experience has shown that combining surveillance with emergency preparedness is a far more efficient and cost-effective approach (37).

Costs of eradication and benefit-cost analysis

We conducted a benefit-cost analysis to examine the economic benefit of a program to eradicate PPR that took into account direct impacts of PPR, the avoided costs of control, and effects of PPR on the national economy as shown in the following equation (2): net benefit = program cost – (averted cost of mortality + downstream impact + avoided cost of control). The estimated discounted cost of a 12-y program involving 65 infected and 20 at-risk countries is \$3.1 billion. The estimated undiscounted costs are \$2.3 billion. The strategy invests more in epidemiology, surveillance, and diagnostics (\$1.409 billion) then in vaccination (\$1.010 billion).

Taking the value of annual PPR mortality as described above, we assumed that the eradication program would start to reduce

this loss in year 3 by 10%, increasing to 100% by year 10. To estimate the magnitude of impacts on the broader economy due to the value of reduced PPR mortality, both within the small ruminant sector and on other productive sectors of the economy, we used a social accounting matrix from Kenya (J. Kiringai, J. Thurlow, and B. Wanjala, unpublished observations). We estimated the current annual cost of PPR control in infected countries was \$119 million, assuming that 15% of the small ruminant population is vaccinated annually at a cost of \$0.55 (based on cost of RP vaccination during the Pan-African Rinderpest Campaign) (40).

Benefit-cost analysis showed that under the median mortality scenario (as defined earlier), the net benefit of PPR eradication is \$74.2 billion, the benefit-cost ratio is 34:1, and the internal rate of return is 199% when impacts on the broader economy are included. Even in the low mortality scenario, the results are still very favorable. Bearing in mind that we have not attempted to estimate losses due to morbidity, these estimates are likely to be very conservative. Even if program cost increased by 50%, the rates of return are highly favorable.

Conclusions

Following international discussion, the strategy and budget described in this work have largely been agreed upon. Dialogue continues on mechanisms for coordination and fund management. It has been agreed that a contingency, not part of the core budget, will be added for additional targeted vaccination resources for use in the event that a subset of countries are unsuccessful in their first focused vaccination push. Contingency funds would be released based on reassessment of the national strategy. This change will lead to a small reduction in the benefit-cost ratio, but the program still remains an attractive investment.

PPR eradication is immunologically sound and technically feasible, and the likely economic return on investment is highly favorable. The international animal health community has already eradicated one disease with a similar geographic distribution, immunology, and epidemiology in Africa, Asia, and the Middle East. The technical tools available for PPR eradication are remarkably similarly to those used in RP eradication. Additionally, the animal health community is experienced in delivering effective interventions in situations of political instability and chronic conflict. Most importantly, a vision on the way forward is a reality, thus placing PPR eradication within reach.

Disclosures

The authors have no financial conflicts of interest.

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