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Possible control and eradication of peste des petits ruminants from India: technical aspects

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Summary

The peste des petits ruminants (PPR) is an acute and highly contagious, notifiable viral disease of sheep and goats that causes substantial morbidity and mortality. There are three cell culture-based live attenuated PPR vaccines available (one from an African isolate and two from Indian isolates). The PPR vaccine produced by the Indian Veterinary Research Institute has been extensively evaluated in the field and found safe and potent in sheep and goats in India. Diagnostic tests, such as the sandwich enzyme-linked immunosorbent assay (s-ELISA), competitive ELISA, single and duplex reverse transcriptase-polymerase chain reactions (RT-PCRs) and RT-PCR-ELISA at the Indian Veterinary Research Institute have also been validated on a large scale. Furthermore, the expertise that remained after the successful eradication of rinderpest in the National Project on Rinderpest Eradication can be utilised effectively for the eradication of PPR without much additional budgetary expense. Thus, the availability of an effective vaccine, accurate diagnostic tests for PPR and an experienced infrastructure prompt us to propose a national project for a peste des petits ruminants eradication programme on the lines of National Project on Rinderpest Eradication. This would greatly enhance the prospects of PPR eradication not only on a national level but also from the Asian continent, alleviate poverty and, in turn, contribute to the national economy.

Keywords

Control, Eradication, Goat, India, Peste des petits ruminants, Rinderpest, Sheep.

Indicazioni dall'India per il controllo e l'eradicazione della peste dei piccoli ruminanti: aspetti tecnici

Riassunto

*La peste dei piccoli ruminanti (PPR) è una malattia notificabile virale acuta e fortemente contagiosa che colpisce caprini e ovini, caratterizzata da morbilità e mortalità elevate. Esistono tre vaccini vivi attenuati basati su colture cellulari (uno da isolato africano e due da isolati indiani). Il vaccino prodotto dall'*Indian Veterinary Research Institute*, ampiamente testato su campo, è risultato sicuro ed efficace per caprini e ovini indiani. Una convalida su larga scala è giunta anche dai test diagnostici come ELISA, ELISA competitiva, RT-PCR singola e duplex e RT-PCR-ELISA condotti presso l'*Indian Veterinary Research Institute*. L'esperienza acquisita nell'ambito del Progetto nazionale per l'eradicazione della peste bovina può essere adottata per debellare la PPR senza gravare ulteriormente sui costi. Pertanto, a fronte della disponibilità di un vaccino efficace, di test diagnostici accurati per la PPR e delle precedenti esperienze si propone un Progetto nazionale per l'eradicazione della peste dei piccoli ruminanti sull'esempio del Progetto nazionale per l'eradicazione della peste bovina. Questa iniziativa aumenterebbe notevolmente le*

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possibilità di debellare la PPR, non soltanto dall'India, ma dal continente asiatico, riducendo la povertà e contribuendo all'economia nazionale.

Parole chiave
Caprini, Controllo, Eradicazione, India, Ovini, Peste bovina, Peste dei piccoli ruminanti.

Introduction

Peste des petits ruminants (PPR) is an acute, highly contagious and transboundary viral disease of sheep and goats with variable rates of morbidity and mortality that can reach up to 100% and 90%, respectively (16). The clinical disease is characterised by pyrexia, oculo-nasal discharge, necrotising and erosive stomatitis, pneumonia and enteritis (7). The causative agent is PPR virus (PPRV), a member of the genus *Morbillivirus* of the family *Paramyxoviridae* (42). PPR was first reported from the Côte-d'Ivoire (West Africa) (9). However, it was misdiagnosed for a long time in other parts of Africa, the Middle East and Asia, including India, for rinderpest and pasteurellosis.

Despite the fact that the first report on PPR in India was in 1989, between 1993 and 1994, many veterinary laboratories in the country were still continuing to report cases of pasteurellosis which were typical PPR cases. No further cases of rinderpest in sheep and goats were reported in India after the official recognition of PPR in the country (40).

Epidemiological knowledge and current status of peste des petits ruminants on the subcontinent

In India, PPR – with its first report from Arasur (Tamil Nadu) (29) – is enzootic throughout the country and is similarly present in neighbouring Nepal, Bangladesh and Pakistan (38). PPR outbreaks can affect an entire flock with 70% to 90% mortality (43). However, these levels may differ in enzootic areas where some older animals may have survived an earlier infection. Outbreaks are relatively more common in goats than in sheep in northern India (38); however, a recent report indicates that outbreaks are more common in sheep than in goats in southern India (22). Pregnant animals may abort (18). Temporally, the number of outbreaks is higher (51.7%) after the winter until early autumn (March to June) than during the other seasons. In India, the overall seroprevalence of PPR in small ruminants is 33% (38), which is comparatively higher in sheep (36.3%) than in goats (31.4%). The disease is prevalent in almost all regions of India (23, 39).

Peste des petits ruminants status in India

India has 28 states and 7 union territories. The country possesses 61 and 124 million sheep and goats (total: approximately 185 million), respectively (11). Currently, a seroprevalence rate has been recorded for 16 states (38). The economic aspects of any disease comprise both tangible and intangible losses. Tangible losses are direct, whereas, the intangible losses are indirect. In India, PPR alone accounts for direct economic losses of US$3.6 million if overall mortality is rated at 5% (43) but this figure rises to approximately US$13 million if the mortality rates are set at 29% for goats and 17% for sheep (Table I) (43). However, state losses could not be calculated as the morbidity/mortality data is incomplete. The knowledge of the geographic distribution of PPR in India has increased rapidly in recent years, which may be due to the following:

- economic importance
- public and regulatory concerns
- the availability of indigenous diagnostics for the specific diagnosis of PPR (32)
- the availability of vaccines.

The above-mentioned facts, as well as presence of a suitable infrastructure motivated us to propose a national programme for the eradication of PPR from India initially, and across the Asian continent thereafter.

Tools available

Diagnostics

PPR diagnosis is achieved by collation of data on the following:

- clinical symptoms
- post-mortem lesions
- laboratory investigation.

Table I
Economic aspects of peste des petits ruminants in India

Parameter	Goats	Sheep
A. Population (millions)	124	61
B. Adults (%)	60	65
C. Young (%)	40	35
D. Probability of an outbreak (%)	50	30
E. Susceptibility (%)	40	30
F. Adult morbidity (%)	64	48
G. Adult mortality (%)	29	17
H. Lamb/kid morbidity (%)	70	50
I. Lamb/kid mortality (%)	42	26
J. Value/adult	1 700	1 300
K. Value/young animal	800	600
L. Loss due to mortality in adults (in millions) = (A × B × G × J)	36 679	8 763
M. Loss due to mortality in young animals (in millions) = (A × C × H × K)	16 666	3 331
N. Total mortality losses (in millions) (L + M)	53 345	12 094
O. Total mortality losses in small ruminants(USD millions) = (N goats) + N (sheep)	1 308.78	
P. Total value of adults (USD millions) = (A × B × J)	126 480	51 545
Q. Total value of young animals (USD millions) =(A × C × K)	39 680	12 810
R. Total value of goats and sheep (USD millions) = (P+Q)	3 323.2	1 287.1
S. Total value of small ruminants (USD millions) = [R (goat) + R (sheep)]	4 610.3	
T. Percentage losses due to PPR= (N/P × 100)	32.1	18.79
U. Percentage losses due to PPR in small ruminants = (O/S × 100)	28.39	

Estimates are based on realistic values; however, area-specific variations can occur
PPR peste des petits ruminants

Initially, tentative diagnoses were made using agar gel immunodiffusion (AGID), counter-immuno-electrophoresis and indirect enzyme-linked immunosorbent assay (i-ELISA). However, now cDNA hybridisation (32), reverse transcriptase-polymerase chain reaction (RT-PCR) (3), virus neutralisation test (VNT) (5) and monoclonal (MAb)-and polyclonal antibody (PAb)-based ELISAs (4, 17, 33, 34) are being employed. A battery of tests described below can be employed in the event of the implementation of a project to eradicate PPR. AGID and 'pen-side' diagnostic tests, such as the chromatographic strip test, have also been developed but not marketed; while the former has been replaced by more modern tests, the latter has still to become commercially available (44).

Antigen detection

MAb-based sandwich/immunocapture ELISA (s/ic-ELISA) is more commonly employed for laboratory diagnosis of PPR in India for suspected clinical swabs/tissue. This diagnostic kit has been found specific for the detection of PPR virus antigen in clinical specimens (32, 33). The relative diagnostic sensitivity (DSn) and specificity (DSp) of the test are 89% and 93%, respectively. The ic-ELISA performed earlier for PPR antigen detection was based on similar principles.

Antibody detection

Competitive/blocking ELISA (c/b-ELISA) is a simple test for screening PPRV antibody in serum samples. Most of these tests are on a par with the VNT which is a gold standard test for PPRV antibody detection. The performance of the PPR c-ELISA kit used in India is similar to that of a commercial kit (Biological Diagnostic Supplies Limited [BDSL], Ayrshire, Scotland) and VNT (34, 36). The relative DSn and DSp of the c-ELISA vis-à-vis VNT were 92.2% and 98.84%, respectively (34).

The PPR ELISA kits are being produced in-house at the Indian Veterinary Research Institute (IVRI) in Mukteswar and are being supplied throughout the country (Table II) for sero-epidemiological and clinical surveillance (35). By December 2008, 165 PPR c-ELISA kits for testing 82 500 serum samples in duplicate (1 65 000 samples singly) and 107 PPR s-ELISA kits for testing 10 700 clinical samples in duplicate (21 400 samples singly) had been supplied over the previous three years to various laboratories and disease diagnostic centres countrywide. The transfer of technologies to state laboratories when using these kits has increased the testing capacity in these laboratories rather than concentrating this activity only at the National Morbillivirus Referral Laboratory in Mukteswar. The Mukteswar laboratory tested 7 033 field and experimental samples between 2001 and 2007, in comparison to 10 700 samples tested at state laboratories over the same period. Similarly, 7 839 serum samples were handled between 2001 and 2007 for seroprevalence, whereas state laboratories screened 82 500 samples during the same period. This implies the capability of the state laboratories and availability of trained manpower in the field which will be useful, if the national PPR eradication programme is launched.

Detection of nucleic acid sequences

RT-PCR is the method of choice for detecting the presence of PPRV nucleic acid sequences in clinical samples and various RT-PCR formats have been reported (3, 6). The homologous primer-virus combinations amplify 372 bp fragments in typical PCR but only 235 bp fragments in nested PCRs. Furthermore, a 96-dot/slot format of nucleic acid hybridisation has also been reported (21) and could be applied for screening samples on a large-scale, including putrefied samples. Recently, a one-step single-tube multiplex RT-PCR was developed at the IVRI for the detection and differentiation of PPR and rinderpest viruses using N and M gene-specific primers. This results in the amplification of N (337 bp) gene products for both PPRV and rinderpest virus samples, and only M (191 bp) gene product in PPRV samples enabling differentiation of rinderpest and PPR (3).

Detection of virus in critical samples

The samples collected during the early or late phases of the disease constitute critical samples as the virus load in these samples is much lower and routine tests may not give the best results. In this respect, RT-PCR-ELISA and nucleic acid hybridisation assays have been evaluated at our institute and were found

Table II
Cost factor analysis for competitive ELISA and sandwich ELISA kits for peste des petits ruminants, 2001-2007

Test	Year	Samples tested at NMRL	Samples tested at field	Grand total tested	Cost of analysis (USD millions)		Revenue saved (USD millions)
					BDSL kits	IVRI kits	
PPR competitive ELISA kit[a]	2001-2007	7 839[a]	82 500	90 339	0.0452	0.009	0.036
PPR sandwich ELISA kit[b]	2001-2007	7 033[a]	10 700	17 733	0.266	0.0088	0.258
Sub-total (USD millions)							0.294
RP competitive ELISA kit[a]	2001-2006	4 268	183 000	187 268	0.09364	0.0188	0.075
Grand total (USD millions)							0.369

(a) including experimental laboratory clinical samples
(b) cost analysis per sample by IVRI (kit) (a) and (b) = USD0.10 and USD0.50 (the rates at the time) and that of the BDSL kit =USD0.50 and USD15, respectively

NMRL National Morbillivirus Referral Laboratory, Mukteswar
BDSL Biological Diagnostic Supplies Limited, Ayrshire, Scotland
IVRI Indian Veterinary Research Institute
PPR peste des petits ruminants
ELISA enzyme-linked immunosorbent assay
RP rinderpest

sensitive for the detection of viral nucleic acid in such samples.

Reverse transcriptase-polymerase chain reaction enzyme-linked immunosorbent assay

RT-PCR-ELISA is a sensitive assay for the detection of several viruses. The assay can detect viral RNA in the infected tissue culture fluid with a virus titre as low as 0.01 $TCID_{50}$/100 µl and is 100 and 10 000 times more sensitive than the s-ELISA and RT-PCR, respectively. Furthermore, it is a more appropriate test for the diagnosis of PPR in the early and late phases of infection (6-17 days post infection) of infection from nasal and ocular swabs, and differentiates PPR from rinderpest, when virus-specific probes are employed (26).

Nucleic acid hybridisation

Nucleic acid hybridisation is applied to identify closely related nucleic acid molecules of complex and homogeneous probe populations. RT-PCR is a sensitive method of diagnosing PPRV infection but is cumbersome for routine testing of samples on a large scale. These drawbacks can be overcome with cDNA hybridisation and its variants (21). The cDNA probes prepared using the N gene sequence of the PPRV and rinderpest virus have led to accurate diagnosis. It is also suitable in diagnosing infection from putrefied samples that are often observed in field conditions in temperate countries like India.

Dot-enzyme-linked immunosorbent assay

A simple dot ELISA using nitrocellulose membrane (NCM) as solid support was developed for the detection of PPR viral antigen from caprine and ovine clinical materials. It is simple, rapid, economical, does not require expertise and a pen-side test (27).

Differential diagnosis of peste des petits ruminants and similar diseases

PPR, bluetongue, contagious pustular dermatitis, capripox infections, foot and mouth disease, contagious caprine pleuropneumonia are the important notifiable viral diseases of ruminants that are classified as 'notifiable' by the World Organisation for Animal Health (Office International des Épizooties: OIE) (13, 44). PPR is prevalent in West Africa, the Middle East, Bangladesh, Pakistan and India (29). Countries with enzootic PPR and related diseases need to have diagnostics that help to perform differential diagnosis. Differentiation of these infections based on host and clinical sign(s) is not definitive which means that laboratory confirmation and differentiation is necessary, particularly in cases where small ruminants act as source of infection. The conventional tests, such as virus isolation and virus neutralisation are slow and laborious. Furthermore, nucleic acid hybridisation, c/s-ELISAs and immuno-histochemical staining are less sensitive than PCR. RT-PCRs are now being used more often to diagnose viral diseases of animals (3, 14, 30).

Vaccines

While specific chemotherapy is not available, palliative treatments using anti-PPR serum, antibiotics (tetracyclines), anti-diarrhoeals (to prevent secondary bacterial infections), vitamin preparations and dextrose (fluid balance) are practised. However, such remedies have limited practical applications when compared to the value of the animals being treated. Prevention includes strict quarantine of exposed animals and restriction of animal movements. However, strict implementation of sanitary measures is difficult in a developing country like India where PPR is enzootic (35).

Therefore, the only effective way to control PPR in the country is mass immunisation of the susceptible population (sheep and goats). Thus, control and eradication of PPR from India as well as Asia requires an effective and adequate vaccine which is available commercially across the country. At one time PPR in India was controlled using heterologous attenuated tissue culture rinderpest (TCRP) vaccine. However, after the launch of the National Project on Rinderpest Eradication (NPRE) in India, the OIE advised that the use of such vaccine could interfere with any rinderpest serological surveillance

programme being contemplated. The government of India accepted this advice.

Until recently, only one homologous PPR vaccine employing an African isolate of PPR virus (NIG 75/1) was available (7). Now two additional cell culture-based live attenuated PPR vaccines are available with the two Indian isolates, namely: Sungri from goats (37) and Arasur from sheep (TN1 vaccine virus) (29, 37). Both the Indian PPR virus vaccine isolates belong to Asian lineage 4 and the use of vaccines made from this lineage will be more appropriate for India and Asia than that from other (African) lineages which would carry a risk of introducin exotic viruses that hitherto have not been encountered on the continent. Although earlier TCRP virus (Plowright strain) was widely used as a vaccine strain, there were no tools to distinguish virus lineages. There are restrictions on the handling of exotic viruses that are not present in India.

The PPR vaccine developed at IVRI employs the PPRV Sungri isolate of goats affected with PPR during 1996 from a village called Sungri (Himachal Pradesh in India) and has been attenuated in Vero cells with up to 59 passages. The vaccine has been subjected to extensive laboratory and field trials and was found safe, potent and economical in sheep and goats. Seroconversion and protection has been observed in 90% of the vaccinates (39). Furthermore, the vaccine is not immuno-suppressive and it is safe, even in pregnant animals (23, 28, 39). With a field dose of 10^3 $TCID_{50}$, protective immunity is conferred for >6 years (V. Balamurugan.V and A. Sen, unpublished data) without boosters which makes this vaccine well suited for a mass immunisation programme. Other features include its availability in different doses with diluents either 1M $MgSO_4$ or 0.85% normal saline solution. The shelf-life is >1 year at 4°C, diluted vaccine is stable even up to 8 h, requires a cold chain and 1 ml is administered subcutaneously in the region of the neck. The vaccine has been used in small ruminants in extensive field trials throughout the country (Table III) with no adverse reactions. The cost of the vaccine is USD0.04 per dose. The vaccine technology has also been transferred to two multinational companies and from five state veterinary biological production units for commercialisation. Similarly, the PPR vaccine of Tamilnadu Veterinary and Animal Sciences University (TANUVAS) is efficacious in sheep and widely used in southern India (37).

Table III
Field testing /supply of peste des petits ruminants vaccine doses (×1 000s) in different states of India, 2000-2006

Serial No.	States	Field testing 2000-2003	Field supply 2002-2006
1	Andhra Pradesh	153.65	338.20
2	Chhattishgarh	–	657.26
3	Haryana	–	12.65
4	Himachal Pradesh	80.75	329.72
5	Jammu and Kashmir	30.00	165.66
6	Jharkhand	–	47.95
7	Karnataka	42.53	103.50
8	Madhya Pradesh	0.56	72.75
9	Maharashtra	0.20	85.70
10	Orissa	41.25	122.00
11	Punjab	0.30	0.050
12	Rajasthan	19.50	65.94
13	Uttar Pradesh/Uttarakhand	40.95	5 024.91
14	Uttarakhand	–	6 066.85
15	West Bengal	45.20	101.59
	Total	454.90	7 734.74

Veterinary infrastructure

The disease control infrastructure in the country has offices both at central and regional levels. The Centre for Animal Disease Research and Diagnostic (CADRAD) facility is the central disease referral facility that coordinates the regional disease diagnostic laboratories (RDDLs). There is a need for a disease registry, both at state and national levels, to ensure effective reporting and coordination of outbreak occurrence and monitoring. The setting up of a network and database is valuable in the development of a coordinated approach to the effective implementation of any control programme. Hence it is proposed that effective data collection points are designated and a network is set up along the same lines as that devised for the Advanced Research Projects Agency Network (ARPANET). This would help to provide a rapid appraisal of the vaccination status, serological and epidemiological data access, target population identification, movement of animals and tracking and locating prospective animal target foci.

Laboratory infrastructures

The laboratory infrastructures developed during the NPRE are now being used for a national foot and mouth disease control programme. Upgrading and expanding this infrastructure is envisaged during the next five-year plan (XII plan) for which an adequate budget will be provided. Sixteen state ELISA laboratories were functional under the NPRE with the assistance of the Federal Government together with State Veterinary Colleges of Agricultural and Veterinary Universities. The trained staff of these laboratories can be employed for an eradication project against PPR.

Facilities for mass vaccine production, storage warehouses, field dispensaries and the transportation of vaccine (cool packs/gel bags) used for the NPRE would be available for PPR vaccine manufacture and distribution. In the same way, the Central Vaccine Quality Control Laboratory established at the IVRI under the aegis of the NPRE for the quality control of rinderpest vaccine could be utilised for independent PPR vaccine quality controls.

Mobile laboratories

A number of mobile laboratory vans were provided to state laboratories under the NPRE to conduct serological monitoring and surveillance. These units can be put back into service for similar activities in the PPR eradication project without much added investment.

Trained (expertise) manpower

Expert scientific and technical staff to handle vaccines at various stages from the production warehouse to delivery in the field is crucial for any immunisation programme to succeed. Adequate trained scientists (veterinarians), technical and para-veterinary staff are available throughout the country for the production of vaccines and diagnostic kits, vaccination work and diagnostic services. These specialists were trained to use rinderpest c-ELISA kits and TCRP vaccine (31), which was widely used in the NPRE. In addition, the principle of the PPR c-ELISA kit is similar to that of the rinderpest c-ELISA and >88 technical/scientific personnel and students from various state ELISA laboratories and veterinary colleges have been trained in the application of these kits. Many such students are engaged in various disease diagnostic laboratories of state animal husbandry departments and/or veterinary colleges and universities. This ensemble of trained staff can perform the serological surveillance work in the event of a PPR eradication project being launched.

Moreover, the Department of Animal Husbandry, Dairying and Fisheries (DAHD&F) of the Government of India has also recognised the Rinderpest Laboratory at the IVRI in Mukteswar as the National Morbillivirus Referral Laboratory which functions as a central referral laboratory and provides referral services as and when required. This laboratory has contributed continuously in the field of rinderpest and PPR vaccines and diagnostics. Current research focuses on the development of recombinant protein-based diagnostics to avoid the risk of handling live viruses which would be required during the post-eradication phase of PPR.

Proposed strategy

Financial estimate

Sufficient financial support from the Government of India is essential for the launching of any disease control programme. Field supplies of indigenous rinderpest and PPR diagnostic kits already created a saving to the tune of USD0.369 million USD between 2001 and 2007 (Table II). This was mainly due to import substitution of the ic-ELISA (rinderpest and PPR) kit from the United Kingdom. This saving could be used as seed money to initiate the control programme. A provisional estimate for the eradication of PPR eradication is USD199.36 million, which includes the cost of vaccines, diagnostics, manpower, equipment, infrastructures and contingent expenses. Manpower from state veterinary departments, colleges and research institutes would be employed with reasonable incentives. Infrastructures and equipment created during the NPRE could be restored to working order after minor repairs/ renovation. Effective networking and disease monitoring will help in devising the exact status of disease incidence. The expertise of the Project Directorate on Animal Disease monitoring and Surveillance (ADMAS) in Bangalore, the CADRAD facility and their regional centres in India, in addition to the IVRI, will help to gather the baseline epidemiological data that would serve as a prerequisite for the vaccination programme. Initially, there should be an all-out effort to vaccinate the maximal target population in order to confer sterilising immunity. This would be followed by 100% vaccination coverage for two years and a round of serological surveillance. After three years, two rounds of serological surveillance would be required to declare the country free from PPR disease. Following these activities, two cycles of screening for PPR infection would be performed using s-ELISA to declare the country free from PPR infection. The tentative expenditure for the eradication of PPR from India is listed in Table IV. A separate break-up of expenses would be prepared if the programme is launched across the continent. Should that be the case, financial resources from international donor organisations would crucial. In such an event, assistance would be sought from organisations such as the United Nations Food and Agriculture Organization (FAO), United Nations Development Programme (UNDP), European Union and the World Bank. The PPR eradication programme would also involve countries in South-East Asia (South Asian Association for Regional Cooperation: SAARC) to ensure joint efforts in the effective implementation of the eradication program in South-East Asia.

Social, political, regulatory support and professional commitment

Acceptance by the public and regulatory support are essential factors for the success of any disease control and eradication programme. The public will readily accept the vaccination programme. Government support is essential for providing adequate financial assistance, other logistics and appropriate legislature in terms of the willingness to attain the goals set. Politicians often act as mass leaders and help to mobilise the public and create public awareness. They also act as a pivot between regulatory bodies and the public in initiating such programmes. Professional commitment on the part of veterinarians and ancillary personnel involved in a mass immunisation programme would be crucial to the success of the disease control and eradication programme as acknowledged during the rinderpest eradication programme.

Enabling research needed

Peste des petits ruminants in other species and maintenance of infection

PPR has been thought to be a disease of only domestic (sheep and goats) and wild small ruminants (Dorcas gazelles [*Gazella dorcas*], Laristan sheep [*Ovis gmelini laristanica*], gemsbok [*Oryx gazella*] and the Nubian ibex [*Capra ibex nubiana*]) (8). However, PPRV antibody detection in:

- cattle in Mali (1.7%) (41), Cameroon (4.5%) (19), Turkey (15.5%) (20) and Ethiopia (9%) (1)
- camels in Ethiopia (10%) (1)

is of great concern. Similarly, PPRV antigen has also been detected during an outbreak of respiratory disease in camels (24) and buffalo

(12). It is, however, unknown whether these animals serve as carriers and whether they have the potential to spread PPR virus. Efforts need to address this issue as such animals may prove to be a stumbling block in a control and eradication programme. The involvement of reservoir hosts in PPR is as yet unknown but it has been established for rinderpest in wildebeest (*Connochaetes taurinus*) and Dorcas gazelle. The effective identification and monitoring of potential wildlife reservoirs in regard to PPR must be initiated.

Table IV
Estimated cost of eradication of peste des petits ruminants in India (USD millions)

Elements of eradication	Goats[a]		Sheep[a]		Estimated total cost (USD millions)
	Year I (70% of population)	Year II (rest: 30% and 40% increase in population	Year I (70% of population)	Year II (rest: 30% & 40% increase in population	
A. Vaccination @ US$0.04dose (USD millions)	3.472	3.472	1.708	1.708	10.36
B. Diagnosis including serological monitoring					
(i) competitive ELISA @ US$0.30 sample (USD millions)[e]					
a) Seroconversion after vaccination	17.36		8.54		25.9
b) First round of serologicalmonitoring for disease free status[c]	17.36		8.54		25.9[b]
c) First round of serological monitoring for disease free status[c]	17.36		8.54		25.9[b]
(ii) Antigen detection by sandwich ELISA @ US$0.40/sample (USD millions)[e]					
a) First round of antigen detection for infection-free status[d]	34.72		17.08		51.8[b]
b) First round of antigen detection for infection-free status[d]	34.72		17.08		51.8[b
C. Cost of manpower (incentive)					
(i) Scientific/veterinary	–		–		25
(ii) Technical/para-veterinary staff	–		–		10
(iii) Supporting	–		–		5
D. Infrastructure[f]	–		–		10
E. Equipment[g]	–		–		10
F. Contingent expenses[h]	–		–		25
Total estimated cost of eradication USD millions)	128.464		63.196		193.36

(a) the total population of goats and sheep in India was 124 and 61 million, respectively, according to the 2003 census
(b) 40% increase annually (40% rise in total population of sheep and goats)
(c) after 4th and 5th years of vaccination
(d) after 6th and 7th years of vaccination
(e) according to the revised rates of the kits
(f) minor repairs and renovation of laboratory premises
(g) repair of old equipments and purchase of new equipment (ELISA readers, freezers, refrigerators and ice boxes)
(h) consumables, including needles/syringes, iceboxes, repair of vehicles of National Project on Rinderpest Eradication and fuel charges

ELISA enzyme-linked immunosorbent assay

Novel vaccines and diagnostics

A state of preparedness in terms of technical, administrative and financial aspects is most important during the post-eradication phase of any disease to address emergency, if such a situation should arise. Preparedness for the post-PPR-eradication phase includes tests for rapid and specific detection of PPRV, active pathogen surveillance and strategic vaccine reserves. Tests, such as the RT-PCR-ELISA (26) and the one-step multiplex RT-PCR (2) for the detection and differentiation of PPRV from rinderpest in critical clinical samples conducted at the containment facility of the High-Security Animal Disease Laboratory (HSADL) in Bhopal for homologous animal challenge experiments, are available. Similarly, as for rinderpest eradication, efforts have already been initiated at the IVRI and substantial progress has been made in developing rapid and more sensitive diagnostic tests.

Synthetic peptide-based antigen/antibody detection assays for PPR include the following:

- multiplex antigenic peptide (MAP) (15)
- synthetic peptide (14, 16).

These assays have the potential for use in serological surveillance and monitoring during the post-PPR-eradication phase. The development of recombinant PPRV 'H' protein-based assays for diagnosis (2) and new generation vaccines utilising PPRV '*H*' or '*F*' genes are also being attempted so that such non-infectious diagnosis and vaccine, respectively, can be used in the event of re-emergence of disease. Preliminary trials of these assays or products have been encouraging, thus leading to the possible future deployment of these products in the diagnosis and control of PPR during the post-eradication phase.

Elimination strategies

Strengths and weaknesses

PPR has become the priority disease for eradication from India. The extensive use of IVRI PPR vaccine countrywide further illustrates that a single PPR vaccine will be effective until some major antigenic variants are reported which is unlikely, especially if we retrospectively inspect the existence of rinderpest virus in the country for over a century without much genetic variation. Thus, the PPR vaccine that is currently available would suffice to control and eradicate PPR. Furthermore, the principle of a PPR diagnostic kit would be similar to that used for rinderpest eradication and can be produced on demand at the IVRI in Mukteswar.

Self-sufficiency

India now has a valuable experience in animal viral disease control and eradication programmes after the successful eradication of rinderpest. The Imperial Bacteriological Laboratory (IBL) (which later became the IVRI) contributed significantly to the development of rinderpest and PPR vaccines and diagnostics and the transfer of technologies. An great number of staff have been trained in this specific area. The vaccine production and quality control technology for PPR has also been transferred to five state veterinary biological production units, namely: West Bengal, Haryana, Maharashtra, Andhra Pradesh and Karnataka and two multinational companies, namely: Messrs (M/s) Intervet India Pvt Ltd, Pune and M/s Indian Immunologicals Limited in Hyderabad. Furthermore, scientific staff of the veterinary biological production units of these states and multinational companies have also received training in PPR vaccine production and quality control. Multinationals have a suitable infrastructure and will be able to produce PPR vaccine in bulk, not only to meet national demand but also for export to other countries in Asia. The transfer of technologies for PPR diagnostic kits is in progress to veterinary biological production units. However, the decision of government to launch a PPR eradication programme in India will automatically accelerate this process as a number of veterinary biological production units have the expertise and infrastructure to produce these kits on demand.

2.6.3 Public and private partnerships

Public-private partnerships have proved to be effective in implementing many very large-scale disease control programmes, such as the polio control and eradication programme in

India. A number of non-governmental organisations (NGOs) are involved in animal husbandry activities in many states. Similarly, several cooperatives are also involved in sheep/goat breeding in certain states, such as Maharashtra, Andhra Pradesh and Karnataka. Participation of NGOs and cooperatives would also be important in a PPR eradication campaign. Large quantities of vaccine would be required to launch the campaign and therefore liaison with private vaccine manufacturers would be warranted. Private companies such as M/s Intervet, M/s Bharat Biotech, M/s Indian Immunologicals and M/s Brilliant Industries will readily accept the PPR vaccine production technology in the event of such an eradication programme being launched.

Rationalisation of vaccine/diagnostics costs

Universally accessible PPR vaccine and diagnostics of homogenous quality available at a reasonable price will determine the success of a PPR eradication campaign. Large-scale production of PPR vaccine by public-private partnerships and procurement and supply of vaccine by a central regulatory agency should be the hallmark. Since the majority of sheep and goat farmers are unqualified landless and marginal farmers, they would be unable to contribute large sums of money to vaccination costs. Therefore, subsidisation of PPR vaccine to farmers as part of the eradication campaign would further ensure increased compliance of a mass vaccination programme. As vaccine production technology has been transferred to multinational corporations and state governments, this would help bulwark vaccine reserves. The availability of an extensive veterinary infrastructure and efficient deployment of resources would help to achieve total vaccination coverage, thus leading to the eradication of this disease.

Harmonisation of vaccine quality and certification

The existence of only one lineage of PPRV in India and the Asian region makes the issue of PPR control and eradication programme easier than that for rinderpest. However, it would be highly desirable to use a particular candidate vaccine virus to protect both sheep and goats with similar efficiency. The IVRI and TANUVAS vaccines are well suited for use in a PPR eradication programme. In order to ensure homogeneity of the vaccine, quality control of the laboratory facilities at the IVRI used for the rinderpest eradication project could be used to certify the quality of these PPR vaccines.

Reasons for proposing an eradication programme against the peste des petits ruminants

Bluetongue, classical swine fever (hog cholera), foot and mouth disease, PPR, sheep pox and goat pox are enzootic in India. Foot and mouth disease control programmes are already in place in 54 districts of the country with an outlay of USD40 million during the 10th five-year plan and these will receive much greater thrust in the 11th five-year plan in terms of financial allocations, vaccination and serological monitoring. Suitable vaccines and diagnostic tests for mass testing are yet to be made available for bluetongue and classical swine fever. Sheep pox and goat pox vaccines available have proved to be safe and immunogenic in field conditions. Diagnostic tests for the serological surveillance of goat pox are also available. PPR is the only disease among the aforementioned for which diagnostics and vaccines are being used throughout the country. The eradication of rinderpest from India amply demonstrates the capability of the country to launch another such programme, especially for PPRV. Other factors which favour the eradication of PPR include restricted geographic distribution of the disease, transmission by droplet, requiring relative close contact, a short incubation period, no latency and, of course, the economic incentive. Thus, the launching of an eradication campaign against PPR appears technically feasible, economically viable and a practically attainable.

Adoption of disease freedom pathway

With all the above tools, India should adopt a three-stage eradication pathway of the OIE (25, 29). The stages include mass vaccination and serological surveillance for a period of two years and cessation of vaccination and then

declaration of the country as being provisionally free from PPR. Then, after a period of three years of the initial declaration, an application needs to be lodged at the OIE to officially declare the country free from PPR disease. Two years after this, the country could apply to the OIE to be officially declared as 'free from PPR infection'. During this two-year period, two successive annual rounds of serological surveys are considered necessary. Consequently, approximately a total of 8 to 10 years is required to officially declare a country free from PPR.

Perspectives

Refurbishing existing physical infrastructures that were created during the rinderpest eradication project and the transfer of production and quality control technologies on PPR vaccine to state veterinary biological production units, multinational companies and the private sector would help to mount a disease control programme. Recombinant protein-based PPR vaccines are to be evaluated for their efficacy to handle a post-PPR-eradication emergency. It is necessary to develop multivalent gene vaccines comprising cytokines to mount rapid immune response in the post-eradication phase. The PPR vaccine needs to be used and evaluated as a first line of defence in the event of an outbreak, as suggested for foot and mouth disease (10). A combination of vaccination and culling of infected animals is known to be more effective in the early containment of foot and mouth disease; the same approach needs to be explored for PPR so that vaccine can be applied in the early phases of an outbreak.

Conclusions

For the effective control and elimination of PPR, the support of diagnostics and timely vaccination of the susceptible population are imperative once the epidemiology of the disease is fully understood. This was witnessed in the NPRE when vaccines and diagnostics of a similar nature were used. Thus, the availability of PPR vaccine, diagnostic techniques, the support of the public and regulatory backing would contribute favourably to the successful eradication of PPR from India, thereby alleviating poverty in the country initially and the continent of Asia thereafter.

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