Peste des petits ruminants
PPR

PPR is a highly contagious viral disease affecting domestic small ruminants (goats and sheep), dromedaries, and some wild small ruminants. Long overlooked, the disease is now endemic in most countries of Africa, the Middle East, and Asia. It causes considerable losses in herds and endangers the livelihoods and food security of the most impoverished populations. Despite the existence of a highly effective vaccine, PPR continues to spread geographically, putting disease-free countries in the South and North at risk of virus incursion and disease emergence.

To limit the socio-economic impacts, and based on the conviction that animal health is a global public good, OIE and FAO have made the development of a global strategy for the progressive control and eradication of PPR a priority of the GF-TADs (Global Framework for the progressive control of Transboundary Animal Diseases).

CIRAD-SAVOIRS
Direction régionale Languedoc-Roussillon
Service d'Appui à la Valorisation Opérationnelle de l'Information sur la Recherche Scientifique
TA 178/05 - Avenue Agropolis - 34398 Montpellier Cedex 5 - France

Tel.: 33 (0)4 67 61 57 88 - Fax: 33 (0)4 67 61 59 73 - E-mail: espace.idees@cirad.fr
Web: http//savoirspartages.cirad.fr/

ISBN: 978-2-87614-698-3
EAN: 9782876146983
ISSN: 1620-0705
Legal deposit: 1st trimester 2015

Collection "Les savoirs partagés®"

Peste des petits ruminants

PPR

Contributors

Authors:

Georgette CHARBONNIER, Géraldine LAVEISSIERE

in collaboration with:

Renaud LANCELOT, Thierry LEFRANÇOIS, Geneviève LIBEAU, Cécile MINET
UMR CIRAD-INRA CMAEE (Emerging and Exotic Animal Disease Control)

Joseph DOMENECH
OIE (World Organisation for Animal Health)

and with contributions from:

Michel LAUNOIS for the original illustrations and line drawings

and the support of:

Jacques PAGES
CIRAD Partnership Platforms Delegate
Scientific Adviser. French Permanent Representation to IFAD, FAO and WFP

Research, writing and coordination:

Georgette CHARBONNIER

Original graphic design and layout:

Géraldine LAVEISSIERE

Partnership relations:

Michel LAUNOIS

Translation into English:

Grace DELOBEL

Distribution:

Françoise CHIRARA

Published with the financial support of several institutional partners, this educational handbook on peste des petits ruminants is not meant for sale. It is meant to be distributed among diverse audiences with the aim of contributing to the dissemination of scientific knowledge and to supporting teaching projects reaching the greatest number of people possible.

 - ISBN : 978-2-87614-698-3 - ISSN : 1620-0705

Peste des petits ruminants

PPR

Based on an original idea of:

Service d'**A**ppui à la **V**alorisation **O**pérationnelle
de l'**I**nformation sur la **R**echerche **S**cientifique (SAVOIRS)

Peste des petits ruminants (PPR), a disease first described in 1942, often is compared to rinderpest, a disease officially declared eradicated in 2011. As the present handbook reminds us, this comparison is due, among other reasons, to the similarity of the clinical signs of the two diseases.

The first mention of rinderpest appears to date back to 3 000 B.C. The struggle against this terrible bovine disease led to the establishment of the first veterinary school in the world in 1761 in Lyon (France). Unlike rinderpest, which was able to affect all ruminants but was most devastating in cattle and buffalo, PPR, as its name indicates, is above all a disease of small ruminants.

Gargadennec and Lalanne gave this name after observing for the first time in 1940 a highly contagious disease which was similar to rinderpest but only afflicted goats and sheep. A similar observation was made in 1941 by another author, Cathou, in Dahomey, the present-day Benin. In 1955, the disease was described in Senegal, and during the 1960s, it was identified in Nigeria and Ghana.

For a very long time, almost up to the early 1980s, PPR was associated with West African countries. However, since the 1990s our understanding of its geographical distribution has evolved extremely rapidly. Today, the disease extends across Africa, from North Africa to Angola and Tanzania, through the Middle East, Turkey, and Central Asian countries, and up into China.

This distribution zone covers an area holding nearly 1.7 billion goats and sheep. It also includes regions with the highest proportion of poor small farmers in the world. The fight against PPR is consequently also a fight against poverty.

It is with this in mind that the FAO and OIE will, through a coordinated global plan of action, undertake a campaign to eradicate the disease. This goal could be achieved relatively rapidly if there is a political will to do so and the required financial resources are made available. In effect, the technical means which made possible the global eradication of rinderpest also are available for PPR: a highly effective vaccine and specific diagnostic tests. These are reviewed in this excellent handbook, one created by experts in the field, and which I hope will be widely distributed.

Berhe TEKOLA
Director
Animal Production and Health Department
United Nations
Food and Agriculture Organization

The identification in West Africa of peste des petits ruminants as a separate disease from rinderpest was a highly significant event in the history of infectious animal plagues.

Peste des petits ruminants was first described in 1942 in the Ivory Coast by Gargadennec and Lalanne as a disease affecting goats and sheep comparable to rinderpest, but which was not transmitted to bovine animals. This observation allowed them to conclude the existence of a disease similar but distinct from rinderpest which affected small ruminants. They called it the "peste des petits ruminants", today known by its acronym, PPR.

PPR is caused by a morbillivirus which is closely related to the virus responsible for rinderpest. Soon after it was described for the first time, the disease left its original birthplace to spread through Africa and invade Asia; it now covers major portions of both continents. It is thus very widespread, as attested by the handbook offered to us by CIRAD in its collection, "Les savoirs partagés®". PPR is a virulent and devastating disease with extremely negative consequences for the economy, food security, and livelihoods of livestock farmers, particularly in poor rural areas. It is considered to be one of the most important animal diseases in Africa, the Middle East, and Asia.

The eradication of rinderpest, which was officially declared in 2011 by the World Organisation for Animal Health (OIE) and the United Nations Food and Agriculture Organization (FAO), brought to the fore the importance of PPR and the need to fight the disease.

This is why these two organizations have organized an international conference on the control and eradication of PPR on 31 March to 2 April 2015 in Abidjan, Ivory Coast, the same country where the disease was first described, to present and adopt a global PPR control and eradication strategy.

The eradication of PPR will have major positive repercussions by guaranteeing the means of subsistence of millions of rural poor. It also will highlight the fundamental role played by veterinary services in the fight against poverty and the improvement of food security. On 30 May 2013, the General Assembly of the OIE adopted resolution n°30 indicating the procedure OIE member countries (now numbering 180) should follow to obtain official recognition of their PPR disease status. Through this procedure, member countries can be declared disease-free either over their entire territory or in certain areas.

The work presented by CIRAD is meant for a broad audience and will raise awareness about the most important concepts related to this disease.

I hope that this handbook will be widely distributed and I sincerely thank everyone who has participated in the project, in particular the authors and those who have collaborated with them, as well as those who have taken the initiative to publish it.

Bernard VALLAT
Director-General
World Organisation for Animal Health












From Neolithic times until today

Small ruminants, goats and sheep, are the descendents of wild ancestors which lived in the "Fertile Crescent", a Middle Eastern region straddling parts of modern day Turkey, Iraq and Iran. Goats descended from the wild goat (*Capra aegragus*) while sheep descended from the Urial (*Ovis orientalis*). They first began to be domesticated by early farmers-herders around 10 000 BC during the Neolithic period. Over the centuries, these animals remained an integral part of peoples' daily lives and accompanied them on their migrations, eventually spreading across the world to Europe, Africa, and Asia thanks to their extensive capacity to adapt.

Goats and sheep figure prominently in many mythologies and religions.

At present, there are over 200 breeds of goats and nearly 900 breeds of sheep in the world. A minority are reared in the North, where many local breeds have disappeared or are endangered, their place taken by animals bred to produce meat and milk. Countries in the South host a multiplicity of breeds adapted to their diverse living conditions, which include hostile desert and mountain environments, wetlands and temperate climate zones, and confined spaces in urban and peri-urban areas. Although sheep are more demanding than goats, the two species often are combined in mixed herds.

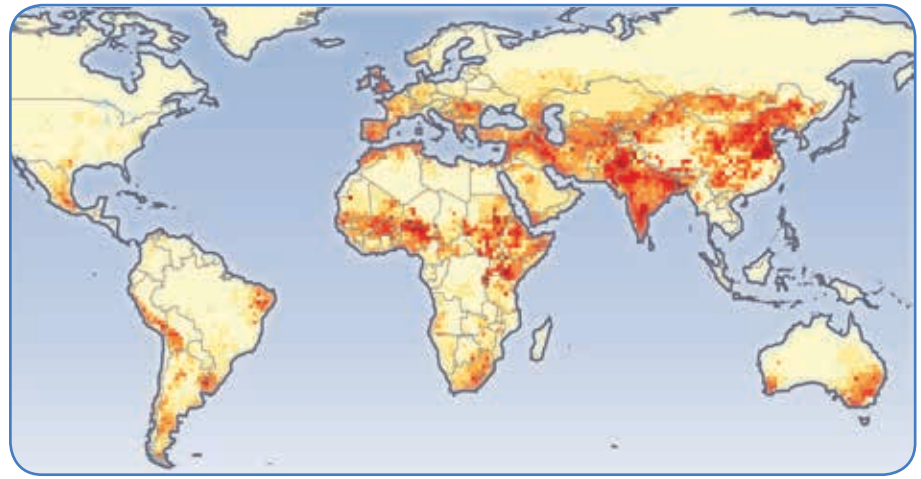
Small ruminants in the South

Goats and sheep do not enjoy the same status as cattle. They are seen as animals of the poor. Goats are even called "the poor man's cow". Compact, sturdy, and easy to handle, small ruminants are an integral part of the lives of the most disadvantaged populations in numerous countries in the South. They often are the sole resource available to farmers in areas unsuitable for other types of farming, and to impoverished rural migrants living on the outskirts of cities. Small ruminants are less demanding and cheaper to buy and maintain than cattle, and can survive on the sparse pastures of arid and semi-arid regions, sometimes supplemented with harvest by-products and food residues (vegetable peels, bran, meal scraps…).

By providing milk and meat for immediate home consumption, they provide families food security and meet their animal protein needs, particularly those of vulnerable individuals such as children, the elderly, and pregnant women. They also produce wool and hides and their manure contributes greatly to organic soil enrichment.

The majority of small ruminants are kept in rural villages and are raised in extensive production systems based on traditional agro-pastoral practices which rely on shepherds and herds moving to find water, pasture land, and salt cure areas. In Sahelian countries, they represent 30 to 40% of ruminant production. The movement of animals through nomadism and transhumance is today a risk factor in the spread of animal diseases.

Global distribution of sheep and goats (head/km^2)



FAO - Gridded livestock of the world (GLW) - 2014

Along with poultry, goats and sheep are the main species kept by low income populations in the world. According to the FAO, in 2013 nearly 83% of the global small ruminant population was located in developing Asian and African countries. These countries hold 94% of the global goat population and nearly 73% of the global sheep population.

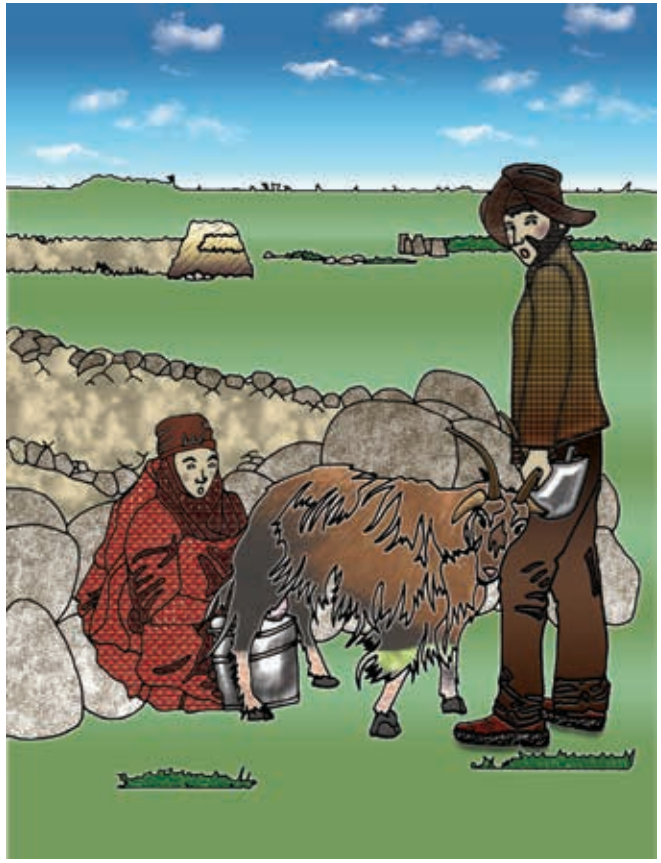
A piggybank for the poorest of the poor

In countries in the South, the key role played by small ruminants in the everyday lives of people living in rural villages and urban and peri-urban areas is now well recognized. These animals are a critical element in the fight against poverty. They contribute effectively to improving the livelihoods and economic self-sufficiency of vulnerable families.

With a low purchase price and production cost, small ruminants are considered to be a kind of live, short-term savings account which can be rapidly converted into cash to cover planned (school fees, religious festivals and family gatherings) and unplanned (health problems, poor harvest, funerals) expenses. Prolific breeders due to a short reproductive cycle of six months to one year, generations are rapidly renewed, increasing the size and value of the herd or flock. The animals thus constitute both a store of wealth and a source of regular income for families. There are no dietary, religious, or ethnic restrictions on their sale. According to the FAO, in 2013 their sale in humid and sub-humid regions represented respectively 30% and 80% of household incomes. In arid and semi-arid regions, these percentages were 17% and 58%. The amount is highest when the small ruminants involved are goats which continue to produce milk even in drought periods.

When climate conditions, conflict or disease lead to the loss of animals, the economic, nutritional, and social consequences for families are often dramatic. To address this vulnerability, numerous development and humanitarian assistance projects distribute small ruminants to refugees and village communities. Sometimes made possible by a micro loan or through a village animal bank, the grant of one or several small ruminants constitutes a first step out of social exclusion and food and nutritional insecurity. However, small ruminant husbandry will only secure the livelihoods of these populations if support measures ensure that the animals are maintained in good health.

According to the FAO, out of a population of 5.5 billion people in the developing world, 2.6 billion live on at least 2 dollars a day, and 1.4 billion extremely poor live on less than 1.25 dollars per day. In this population, about 752 million are rural livestock farmers, 45% of whom live in South Asia and 25% in sub-Saharan Africa.



Small ruminants are both a capital asset and a savings account for poor households.

Reinforce the resilience of vulnerable populations

Small ruminants provide a safety net for the most impoverished:

- *They can adapt to even the harshest environments.*
- *They require little maintenance or space.*
- *They grow and reproduce rapidly.*
- *They can be sold easily and quickly.*
- *They require only a few investments in infrastructure and health monitoring.*
- *They are a source of food and income for households.*

Social and cultural roles

In numerous societies, small ruminants fill social and cultural roles. They frequently are slaughtered and consumed during traditional ceremonies marking important life events (births, marriages, funerals) or religious festivals. They serve as dowries for future brides, and are used as gifts when there is a birth, to strengthen ties, or to honour visitors. They reflect the status and social integration of a family. In pastoral communities where livestock farming takes centre stage, the disappearance of small livestock has repercussions that go beyond economic impoverishment. It can lead to social marginalization and to the migration of livestock farmers towards cities where they encounter peri-urban poverty and crowding.

In countries in the South, small ruminant husbandry often is the work of women, who rarely hold the right to own or use land. They supervise reproduction and production. Across all cultures, women are almost always responsible for milking, making and selling dairy products, and feeding and caring for the animals. This is an activity that provides them a certain financial independence and social status, and which contributes to promoting gender equality. Sheep and goats can be kept close to the home or allowed to wander and can be watched over easily by other members of the family such as children.

When disease hits

Poor livestock farmers in countries in the South often are vulnerable to animal diseases. Regardless of their livestock farming system, lifestyle, or environment (rural, urban, or peri-urban), or whether they live in Asia or Africa, these farmers are hindered from managing health risks due to weak veterinary services, a lack of trained professionals, inadequate training and information on animal health, and difficult access to veterinary services, medicines and vaccines. When a family's diet and income depend on goat and sheep production, disease directly impacts the household's daily life. The loss of animals and their reduced market value due to debilitating side effects (weight loss, delayed growth, drop in fertility) keep households trapped in poverty and destroys or weakens their resilience, meaning their capacity cope with recurrent crisis situations (poor harvests, natural disasters, political instability), which had been sustained by their small ruminant production.

Numerous diseases affect sheep and goats with varying degrees of gravity and different impacts at the global, country, and herd scale. Some are highly contagious and affect numerous countries such as peste des petits ruminants, sheep pox, and goat pox. Their spread is determined by the mobility of animals in extensive livestock systems, particularly in the Sahel, and by the legal and illegal movement of animals to meat consuming countries. Other diseases, such as heartwater, bluetongue and Rift Valley fever, are related to the environmental conditions governing the transmission of pathogens by vectors (ticks or insects). Yet others, such as brucellosis, Rift Valley fever, hydatidosis, are also zoonoses, common to both humans and animals.

Main infectious and parasitic diseases of small ruminants

Infectious diseases			Parasitic diseases	
Viruses	Bacteria		Roundworms	Flat worms
	With a cell wall	Without a cell wall		
Peste des petits ruminants	Heartwater	Contagious caprine pleuropneumonia	Haemonchosis	Hydatidosis ◆
Sheep and goat pox	Corynebacterium			
Bluetongue	Brucellosis			
Rift Valley fever ◆	Anthrax ◆			
Rabies				
Contagious ecthyma				

◆ Zoonoses Vector-borne diseases

"Sheep and goats are essential for the food security and incomes of pastoral communities. The presence of disease directly affects household wealth."

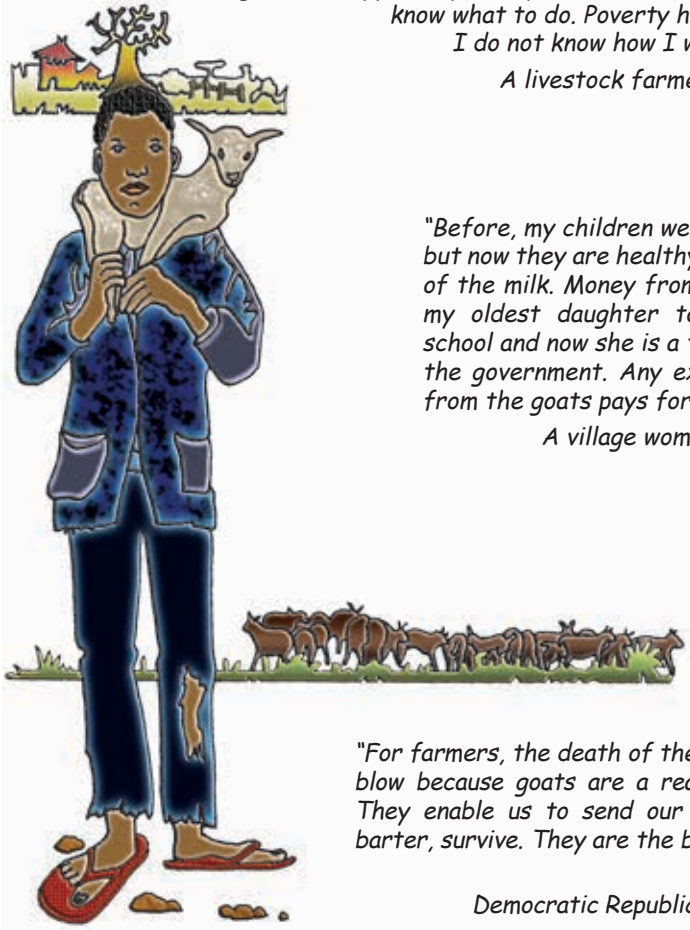
Juan Lubroth - FAO, 2010

"A goat can pay for the education of children. It is not just an animal; it is a means for people to procure food, milk, or money to invest in education."

A veterinarian - Uganda, 2014

"I am a poor livestock farmer. These animals were my only source of income. Almost all were killed by disease. I sold goats to support my family. Now that they are dead, I don't know what to do. Poverty has hit my house and I do not know how I will feed my family."

A livestock farmer - Cameroon, 2012



"Before, my children were under-nourished, but now they are healthy and happy because of the milk. Money from the goats enabled my oldest daughter to go to secondary school and now she is a teacher working for the government. Any extra income we get from the goats pays for schooling."

A village woman - Tanzania, 2009

"For farmers, the death of these animals is a hard blow because goats are a real source of money. They enable us to send our children to school, barter, survive. They are the basis of our society."

A villager
Democratic Republic of the Congo, 2012

"It has been hard to put together dowries ever since this epidemic started decimating our goats. A young man might plan to bring a goat to his in-laws as a preliminary dowry present, but on the day he is to visit, the goat dies."

A village head
Democratic Republic of the Congo, 2013

"Three of the five goats given to one of our daughters died the day after the dowry ceremony. We decided to start accepting cash instead of goats. "

A villager - Democratic Republic of the Congo, 2013

"How I will I pay the school fees for my children next year now that all 7 of my goats have died? Who will help me?"

A widow - Democratic Republic of the Congo, 2012

"The cost of attending a boarding school is 750 Kenyan shillings per month (€6.5). Maasai families must sacrifice two goats to pay for each year of school."

Arte documentary: Chemins d'école, chemins de tous les dangers *(Path to school, path of danger). Kenya, 2013*

Viral and highly contagious

PPR is one of 10 diseases affecting goats and sheep with major health and socio-economic impacts. It is the most devastating viral disease of small ruminants. It also can affect dromedaries and some wild small ruminants. Its mortality and morbidity rates (diarrhoea, pneumonia, weight loss, fertility loss, reduced milk production) are high and can reach from 80 to 100%. The World Organisation for Animal Health (OIE) and the FAO class it among the highly contagious transboundary diseases with serious socio-economic repercussions. However, unlike foot-and-mouth disease in cattle, it is not considered to be a disease of economic interest impacting the balance of world trade. Affecting small livestock, goats and sheep, it is seen as a disease of public concern that impedes the development of livestock farming at a local and national scale and threatens the food security and livelihoods of millions of poor farmers in developing countries in Africa, the Middle East, and Asia. Beyond the consequences for animal health, PPR also is a threat to the food security and health of people in these countries.

"Lomoo [a local name for PPR in Kenya] has impoverished us. I had a herd of 800 goats. In three months, PPR killed 300."

A village head - Kenya, 2008

PPR is listed by the OIE as a compulsorily notifiable disease in the case of outbreaks. An international study published in 2002 by the ILRI (International Livestock Research Institute) estimated that over 750 million goats and sheep were affected by PPR.

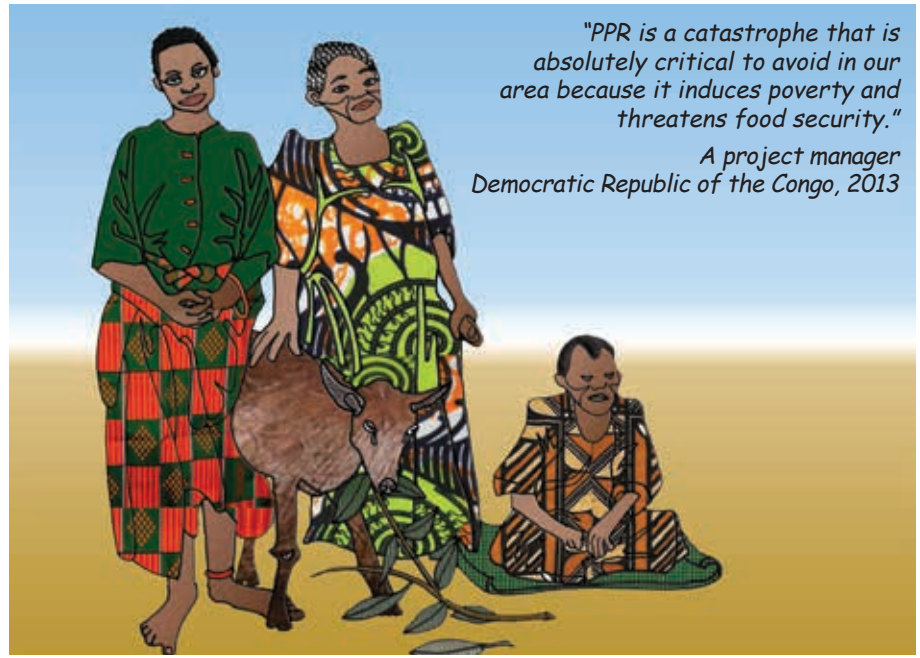
Today, more than one billion small ruminants in over 70 countries are at risk of contracting PPR.

Some background history

PPR was first described in 1942 by two French veterinarians, Gargadennec and Lalanne. In 1940, they were confronted with a devastating epizootic among goats and sheep in the Ivory Coast.

The symptoms were similar to those of other known diseases. They first suspected bluetongue disease, then ulcerative stomatitis, and finally identified the clinical signs as being similar to those of rinderpest, a highly contagious viral disease that was at the time decimating cattle and buffalo herds. As the cattle in contact with these small ruminants did not show any sign of infection, they named the disease, "peste des petits ruminants ".

In 1941, an identical deadly infection in Dwarf goat herds in Benin was described by Cathou under the name, "ovine and caprine species plague ". A few years later, in 1955, the disease was reported in Senegal. Outbreaks in Nigeria and Ghana were reported between 1960 and 1970, sometimes under different names which reflected their clinical expression: pseudo-rinderpest, stomatitis pneumoenteritis complex and *kata* (a local Nigerian name, pidgin English for "catarrhal") in Nigeria. It was during this time that the French name given by those who first discovered the disease, "peste des petits ruminants ", was adopted as its scientific name. The acronym, PPR, is used widely today.



"PPR is a catastrophe that is absolutely critical to avoid in our area because it induces poverty and threatens food security."

A project manager
Democratic Republic of the Congo, 2013

In the shadow of rinderpest

For 30 years, PPR was associated with West Africa. However, in 1972 a disease affecting goats in Sudan that was first diagnosed as rinderpest proved to be PPR, revealing a geographic distribution beyond the area initially assumed. Today, PPR is endemic in most countries in Africa, the Middle East, and Asia. Its presence in North Africa and Turkey puts the disease at the doors of Europe.

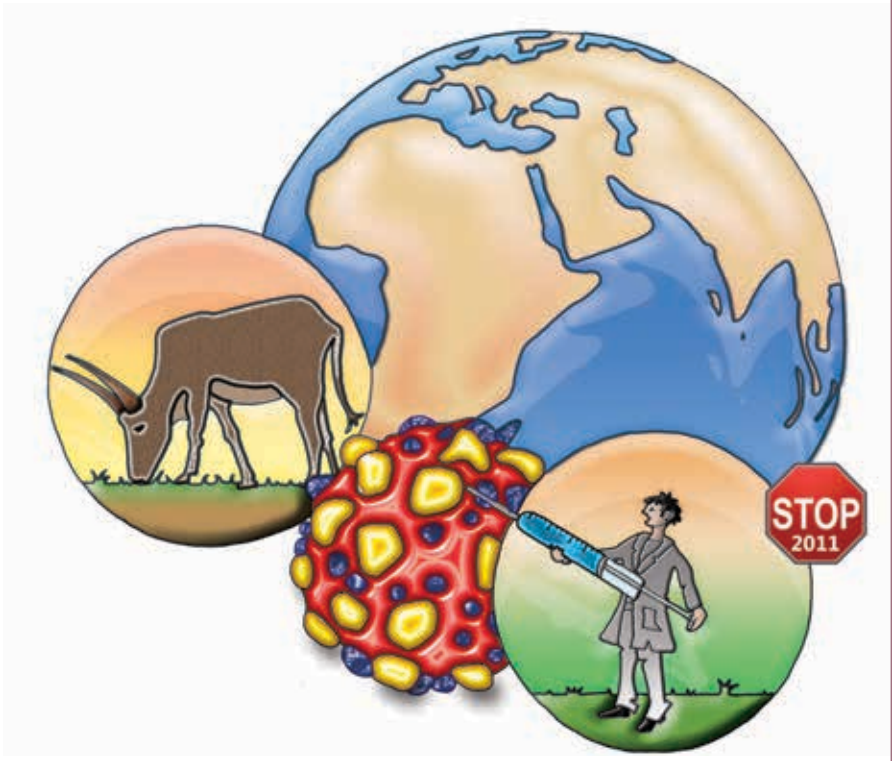
Like all transboundary diseases, the intensified movements and trade of animals, whose populations are growing, benefit the virus. However, these are not the only reasons behind the disease's global reach.

Bovine animals are considered an epidemiological dead end for the PPR virus.

Scientists today know that PPR is not a new disease and that it was present in West Africa since the end of the 19th century, well before it was first described. It was simply impossible to distinguish PPR from other diseases with similar clinical signs.

The high incidence (incidence measures the new number of cases in a population by unit of time) of such diseases, the absence of powerful diagnostic tests, and a low level of interest in small ruminants' health long obscured the presence of PPR and delayed its identification. Today, it is acknowledged that the rinderpest cases among small ruminants in Senegal in 1871 and in Guinea in 1927 likely were actually outbreaks of PPR. The same is true of India, where the first PPR epizootic was officially recognized in 1987, yet a disease affecting goats and sheep resembling rinderpest reported in 1940 and 1942 probably was PPR.

Although a highly effective vaccine has been available for 25 years, PPR continues to spread and expose previously disease-free countries in the South and North to the risk of virus incursion and disease emergence.



Rinderpest, a disease of the past

According to historical documents, the first epizootic of rinderpest in Europe took place sometime between 376 and 386 AD, near the end of the Roman Empire. However, some believe the disease may have been one of the seven plagues of Egypt. Eurasian in origin, rinderpest has decimated hundreds of millions of cattle and buffalo in Europe, Asia, and Africa and has caused severe famines. It remains one of the most deadly transboundary animal diseases of domestic and wild mammals belonging to the Bovidae *family. Thanks to coordinated international collaboration, and after 80 years of struggle, rinderpest was officially declared eradicated in 2011. In human history, this is only the second disease to have disappeared from the planet, the first being human smallpox, and the first animal disease to do so.*

*The global fight against rinderpest led to the creation in 1924 of OIE (*Office international des épizooties*), named today the World Organisation for Animal Health. Rinderpest also was largely responsible for the foundation of the first veterinarian schools in France in the 18th century.*

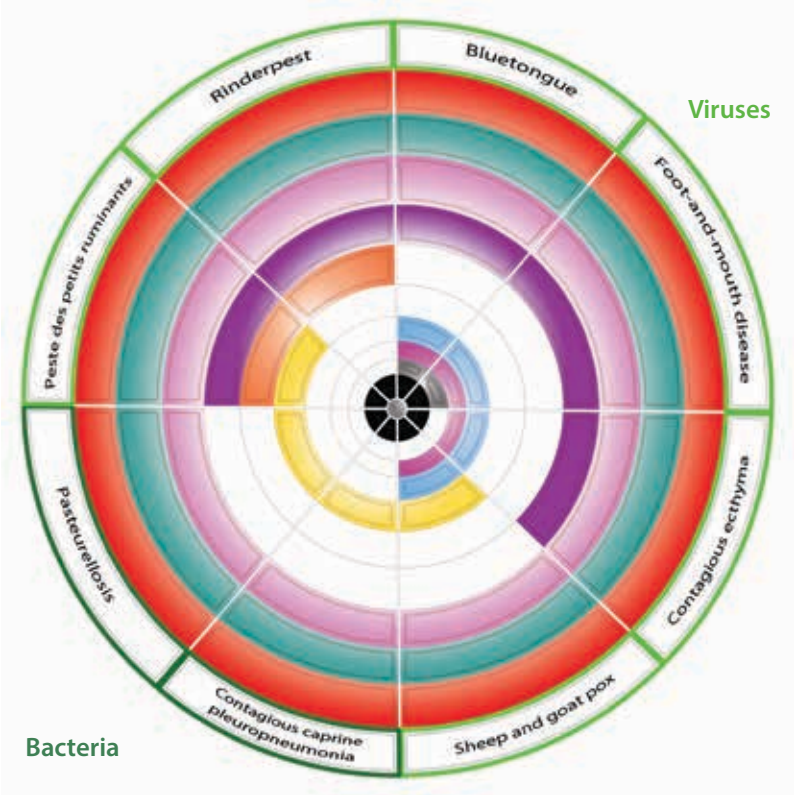
Four forms

PPR also is described as a "stomatitis pneumoenteritis complex", which reflects how the virus affects the mucous membranes of an animal's digestive and respiratory systems. Its clinical signs closely resemble those of rinderpest, a disease which has now been eradicated.

PPR can take 4 forms depending on the susceptibility of the species, breed and animal infected. All 4 forms can be present within the same herd.

Misleading clinical signs

No clinical signs suggesting PPR are specific to the disease. They can all be confused with other diseases.



Differential clinical diagnosis of PPR: Hyperthermia - Discharge - Lacrimation - Lesions on mucous membranes - Diarrhoea - Difficulty breathing - Oedema - Vesicles - Lameness.

Acute form: This is the form observed most frequently. After a 5 to 6 day incubation period, the disease manifests itself with a sudden rise in body temperature, which can reach 40 to 42°C. The animal is listless, refuses to eat, and its hair stands erect. The animal withdraws from the herd and has difficulty moving. The mucous membranes of the mouth and eyes become congested. One or two days after the onset of fever, lacrimation and discharge appear, at first clear and watery, then mucopurulent. The eyelids gum together and the obstructed nostrils render breathing difficult. Occasionally a productive cough characteristic of bronchopneumonia signals the presence of a secondary bacterial infection. Four or five days after the appearance of the first clinical signs, the temperature drops, followed by the onset of occasionally bloody diarrhoea and oral lesions. These become covered by a necrotic, whitish, pulpy tissue (with a mushy consistency) which emits a nauseating odour when the animal opens its mouth. In females, pus and erosive lesions are visible on the vulvo-vaginal mucous membranes. At this stage, pregnant animals abort. Death follows in 70 to 80% of cases, on average 10 days after the onset of the first clinical signs, in animals often in a state of hypothermia. When an animal recovers, convalescence is rapid and generally takes no more than one week.

Peracute form: This is observed most often in young goats over 4 months old which are no longer protected by maternal antibodies. Incubation lasts about 3 days. The disease begins with the same clinical signs: a high fever (40 to 42°C) followed by congestion of mucosa manifested by watery eyes and serous discharge. However, it evolves more rapidly. After 5 or 6 days, 100% of infected animals die even if they have shown no erosive lesions, diarrhoea, or secondary bacterial infection.

Subacute form: Despite the frequent occurrence of microbial complications, this is the least severe form of the disease. It is not fatal. After a 5-day incubation period, the disease causes a fever which remains moderate (39 to 40°C) and lasts only 1 to 2 days. All of the other clinical signs are discrete and may go unnoticed. Small amounts of discharge dry around the nostrils to form crusts that can steer the diagnosis towards another disease, contagious ecthyma.

Sub-clinical form: Asymptomatic or unapparent, it often is observed in sheep in the Sahel. In the absence of clinical signs, it is only revealed through serological investigations.

"An animal [a goat] with this disease rarely survives more than three days."

A village head - Democratic Republic of the Congo, 2013

Establishing the identity

The first clinical descriptions of PPR and the strong resemblance of the clinical signs with those of rinderpest steered scientists towards thinking that the two diseases were closely related and involved a similar viral pathogen. In 1956, Mornet *et al.* concluded that the PPR virus (PPRV) was a variant of the rinderpest virus which had adapted to small ruminants and lost its virulence for cattle. Starting in 1962, cell culture studies began to reveal the similarities and differences between the two viruses.

Using an electronic microscope, in 1967 Bourdin and Laurent-Vautier observed that the structure of PPRV was identical to that of the rinderpest virus and validated its membership in the same family, the *Paramyxoviridae*. The similarity of its biological and physiochemical characteristics with the rinderpest virus was a sign that it was a member of the same genus, *Morbillivirus* (*Morbilli*, short for *morbus*: disease, pest, plague). During the 1970s, serological studies, cross-protection tests and biochemical analyses of the two viruses allowed the differences between them to be identified and showed that although closely related, the PPR virus was distinct from the rinderpest virus. In 1979, its distinguishing features were recognized. Gibbs *et al*. proposed that PPRV become the fourth morbillivirus, joining the rinderpest virus, the measles virus, and the distemper virus, all three responsible for devastating diseases in their respective hosts. Other viruses found in marine mammals have further enriched the *Morbillivirus* genus since the 1990s: the phocine distemper virus and viruses affecting cetaceans (dolphin and porpoise morbilliviruses). Since then, other viruses have joined their ranks, such as that identified recently in domestic cats. Scientists do not rule out the possibility of discovering new morbilliviruses in the future.

The search for PPRV's origins

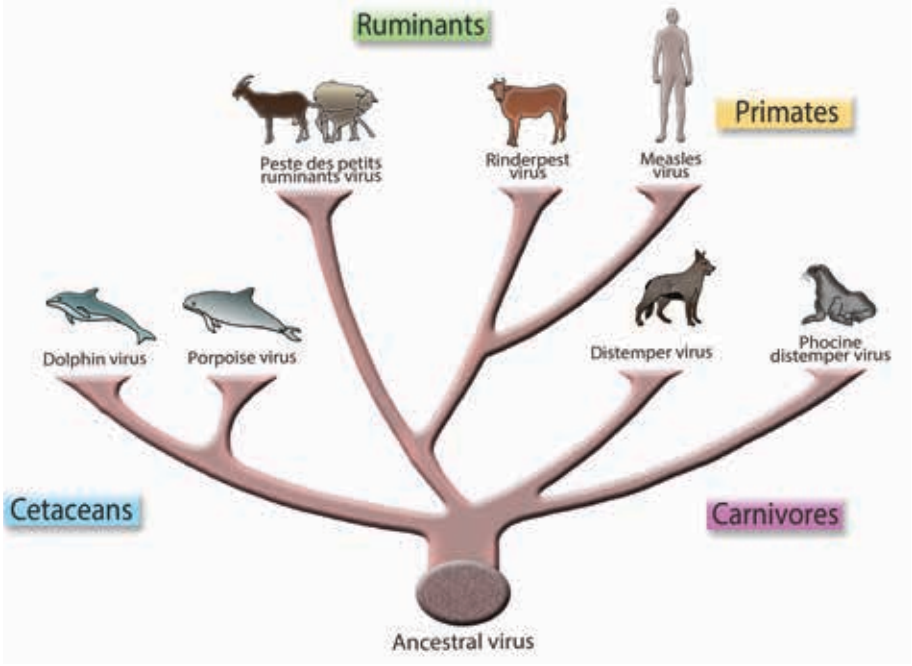
Morbilliviruses form a group of 6 viruses causing devastating diseases in humans and animals. Their respective host ranges are narrow but they can occasionally cross species barriers. Their strong genetic likeness and close antigenic proximity allows scientists to affirm that they all descended from the same archaevirus.

To persist, morbilliviruses need to circulate in large populations which renew themselves. The large herds of ruminants in Asia created an ideal environment for them. They were the historical source of the rinderpest virus.

During the Neolithic period, people settled down and became livestock farmers, living in close contact with their herds. When the human population became sufficiently dense to ensure the maintenance of the virus (between 250 000 and 500 000 receptive individuals), the species barrier was crossed. The rinderpest virus mutated, adapted to humans, and became the measles virus. In 2010, a study by Furuse published in *Virology Journal* indicates that this divergence occurred between the 11th and 12th century AD.

PPRV detached itself earlier, around the 1st century AD, from the common ancestral branch that gave birth to the rinderpest and measles viruses. From an evolutionary point of view, PPRV is thus distant from these two viruses, while the rinderpest and measles viruses are closer together.

The phylogenetic tree of the morbilliviruses
based on the partial sequence of the N nucleoprotein gene



Up close

Under an electron microscope, PPRV appears more or less spherical and pleomorphic (changes shape). Its diameter varies between 150 to 700 nanometres, with the majority of particles between 400 and 500 nanometres, slightly larger than the size of the rinderpest virus (approximately 300 nanometres). Like all of the viruses in the *Paramyxoviridae* family, PPRV is an enveloped virus.

In this "whole" virus, the viral envelope is formed by a double layered lipid membrane 5 nanometres thick borrowed from the infected cell when the virion is formed. The outside of the envelope is spiked with two kinds of spicules, each 10 nanometres long, which are inserted into the membrane. These spicules are two glycoproteins, the fusion (F) protein and hemagglutinin (H). The inside surface of the envelope is lined with the matrix (M) protein. The envelope defines a kind of sac that contains two elements which are mandatory for all viral particles: the genome and the capsid.

The PPRV genome is a single-stranded RNA (ribonucleic acid) molecule. It is enveloped by a protein capsid largely constituted by N nucleoprotein sub-units. These form a long, hollow sheath approximately 1 micrometre long and 18 nanometres in diameter that wraps around the RNA molecule like a sleeve. The two are indissolubly bonded by the phosphate and ribose of each RNA nucleotide. The ensemble constitutes a levogyre (left-leaning), flexible N-RNA nucleocapsid with a helical symmetry that folds over itself inside the virion. Under an electron microscope, a herring bone structure can be observed. Each bone-like shape represents a coil of the helix. Electron microscopes made it possible to establish that there are 13 N nucleoproteins per coil. In the PPRV, the nucleocapsid thus forms a kind of spring with 200 coils. Despite its compact structure, it can loosen its form so that the nitrogenous bases of the RNA molecule can be read during the virus multiplication cycle.

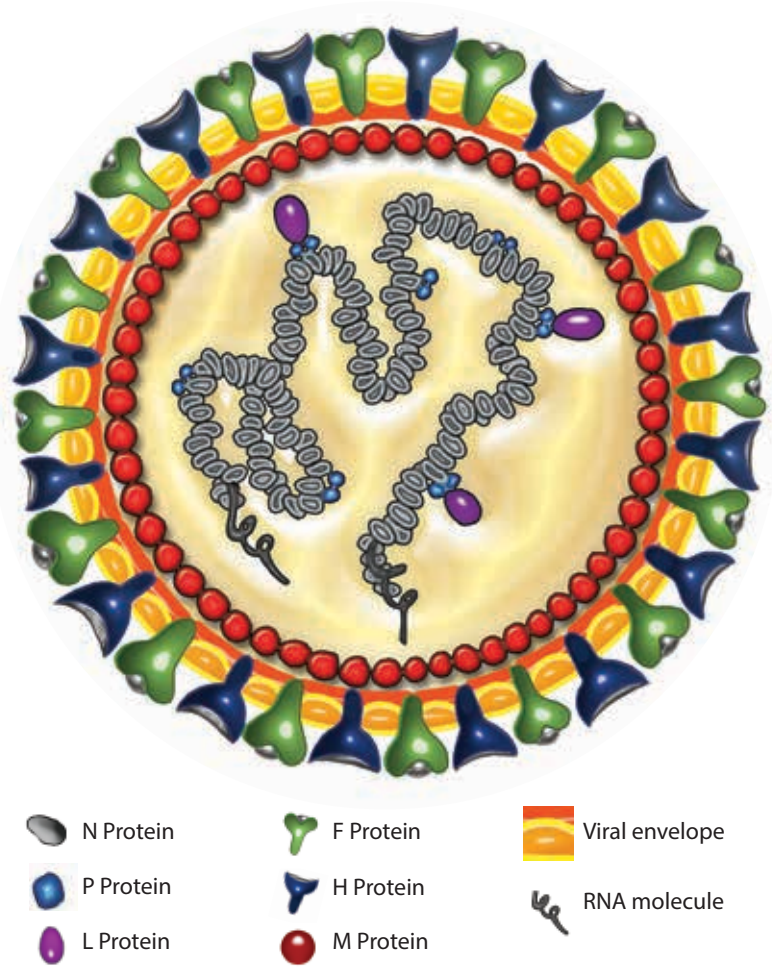
Two other proteins, RNA polymerase L and its cofactor, phosphoprotein P, combine with the N-RNA nucleocapsid to form the ribonucleoprotein complex (RNP). Their presence is critical for the virion to initiate its multiplication cycle inside the infected cell. The "naked" viral RNA is not directly infectious.

PPRV's identity card

Group: V (negative single-stranded RNA virus)
Order: *Mononegavirales*
Family: *Paramyxoviridae*
Sub-family: *Paramyxovirinae*
Genus: *Morbillivirus*
Species: PPR virus

The Paramyxoviridae are a large family of human and animal pathogens with significant public health and economic impacts. New emerging viruses such as the Hendra and Nipah viruses are members.

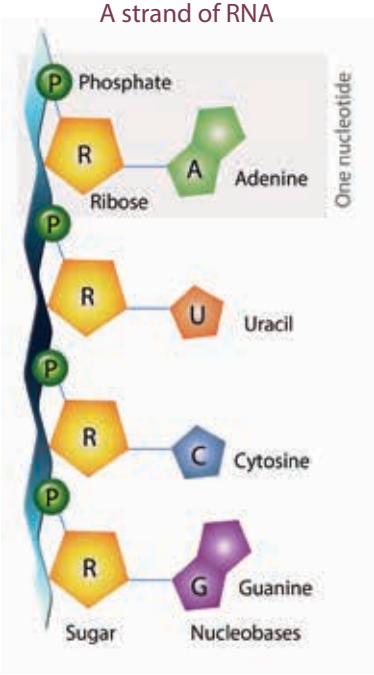
PPRV ultrastructure



Six genes

The complete sequencing of the PPR virus genome was achieved in 2005. Its RNA consists of a chain of 15 948 nucleotides. This is one of the longest genomes of the *Morbillivirus* genus. That of rinderpest has 15 882 nucleotides. It follows the "rule of six", as do all of the viruses in its genus.

A strand of RNA



Rule of six

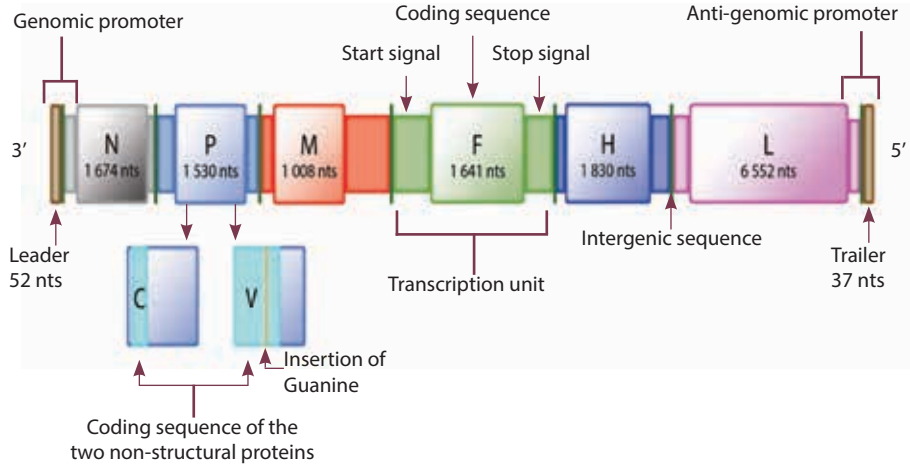
Among the Paramyxoviridae*, each N nucleoprotein is linked and interacts with 6 nucleotides of the viral RNA. Therefore, the total number of nucleotides must be a multiple of 6, otherwise the RNA dependent - RNA polymerase considers the RNA molecule incompatible. When that is the case, it does not initiate the viral multiplication cycle.*

All of the morbilliviruses share the same genome organization. Their RNA is unsegmented. It presents itself as a single molecule made up of a sequence of 6 non-overlapping genetic units (transcription units). Each unit begins with a start signal followed by a coding sequence, and ends with a stop signal. They are separated by intergenic non coding sequences of 3 nucleotides. The RNA is said to be negative-sense because it cannot be translated directly into protein. Each gene must first be transcripted into a messenger RNA by the viral polymerase L, then translated into a viral protein by the enzymatic machinery of the host cell.

The 6 genes, which encode 8 proteins, are lined up in a linear, well-established order on the RNA molecule. From left to right, moving from the 3' to the 5' end, the sequence is as follows: 3'-N-P/C/V-M-F-H-L-5'. Five genes (N, M, F, H, L) are monocistronic. They only encode a single messenger RNA molecule, thus just one viral protein. The sixth, the P gene, is polycistronic and an example of genetic information compaction. It directs the synthesis of 3 proteins, the structural protein P and 2 non-structural or auxiliary proteins C and V, through shifts in the reading frame. The latter proteins are only present in the cytoplasm of the infected cell during the viral cycle.

Two "extracistronic", non-coding regions are situated at the 3' and 5' ends of the RNA molecule and help regulate two stages of viral multiplication: transcription and replication. They are respectively the leader and the trailer. The leader combines with the first non-coding sequences of the N gene to form the genomic promoter used by the polymerase to synthesize the messenger RNAs. The trailer and the last non-coding sequences of the L protein constitute the antigenomic promoter used by the polymerase to synthesize the antigenome (positive RNA), the intermediary of the viral genome replication.

The RNA genome of the PPR virus



The PPRV proteins

The structural proteins

Proteins on the outside of the viral envelope

They prompt the host protective immune response. These antigens are in contact with the antibodies in the outside environment.

Fusion protein or F glycoprotein
546 aa

This is a well conserved protein responsible for the fusion of the viral envelope with the membrane of the host cell. It also intervenes in the membrane fusion of the infected cell with healthy neighbouring cells, producing syncytiums (multinucleated giant cells). It engenders a neutralizing humoral immunity and a cellular immunity.

During the infection cycle, it is synthesized as a precursor protein, F0, which only becomes active once it has cleaved into 2 sub-units, F1 and F2, thanks to a cellular protease. If the F0 does not mature, the viral particles released are not infectious.

Hemagglutinin or H glycoprotein
609 aa

This also is known as an attachment protein. It determines the cell tropism of the virus. It allows the virus to bond to one or more receptor membranes. It has both hemagglutinin and neuraminidase activities (a distinguishing feature of PPRV). It induces the production of the neutralizing antibodies behind the humoral defence response.

Protein on the inside of the viral envelope

Matrix (M) protein
335 aa

This is the smallest and best conserved viral protein. It serves to bind the ribonucleocapsid with the 2 surface glycoproteins, H and F. Its main role is in the formation of new virions. An anomaly in its synthesis hinders the virus from finishing its cycle.

Nucleocapsid proteins

N nucleoprotein
525aa

This is the most abundant protein. It is responsible for the helicoidal structure of the nucleocapsid and protects the RNA. It plays a major role in regulating viral transcription and replication.

It is the main viral antigen but the antibodies produced against it are not neutralizing. It is used in molecular diagnostic tests. Sheltered from immunogenic pressures, it is very conserved, as in the other morbilliviruses, and serves as a reference for the epidemiological monitoring of PPR.

Phosphoprotein or P protein
509 aa

It acts as a co-factor of the L protein and enables it to bind to the nucleocapsid. Together, they form the RNA-dependent RNA polymerase complex responsible for the synthesis of messenger RNA and the replication of the viral RNA of the genome.

It intervenes in the encapsidation of newly synthesized viral RNA by bonding to the N nucleoprotein to form a soluble N-P complex in the cytoplasm and to hinder N from associating with RNA of the infected cell.

Polymerase or L protein
2 183 aa

This is a large protein coded by a gene representing half of the genome, but it is the least abundant. It is very well conserved. In association with the P phosphoprotein, it forms the RNA-dependent RNA polymerase complex which ensures the synthesis of messenger RNA and the replication of the genomic RNA.

The non-structural proteins

These block the innate host immune response to allow the spread of the virus.

C protein
177 aa

This is the smallest protein. It is produced from the same gene as the P protein but through an alternative reading frame. Its transcription begins at a start codon located at position 23 on the P gene.

During the viral cycle, the C protein intervenes to regulate RNA-dependent RNA polymerase during the genome transcription stage.

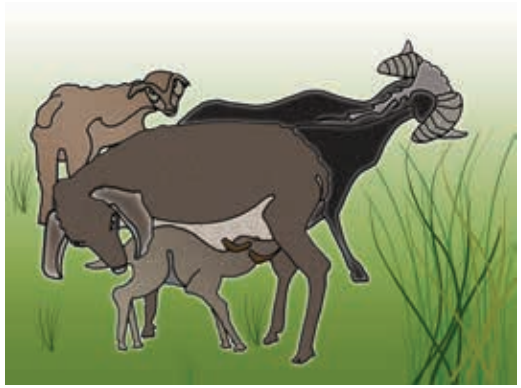
V protein
299 aa

Its synthesis is directed by the P protein gene but the messenger RNA transcripted is different. During transcription, a supplementary base (the G base, or Guanine) inserts itself at a precise point on the P gene thanks to a stutter mechanism of the polymerase known as editing. Upstream of the insertion point, the V protein is identical to P and shares the same start codon. Below the insertion point, the nucleobase sequence is modified and generates a new transcription stop signal (at position 894) before the end of the gene.

During the viral cycle, the V protein intervenes to regulate RNA-dependent RNA polymerase during the genome replication stage.

Four lineages but a single serotype

In PPRV, as in all of the other viruses in its genus, the RNA-dependent RNA polymerase commits random genetic errors during genome replication because it is not equipped with a translation proof-reader. The ensuing mutations cause a certain amount of variability in the succession of nucleic acids and lead to the co-existence of several different but very similar RNA molecules. By comparing the genetic sequences of several PPRV strains, scientists identified 4 distinct lineages but only one serotype. This means that the antigenic sites important for induction of immunity do not vary and that a vaccine made with one lineage will protect an animal against the three others.



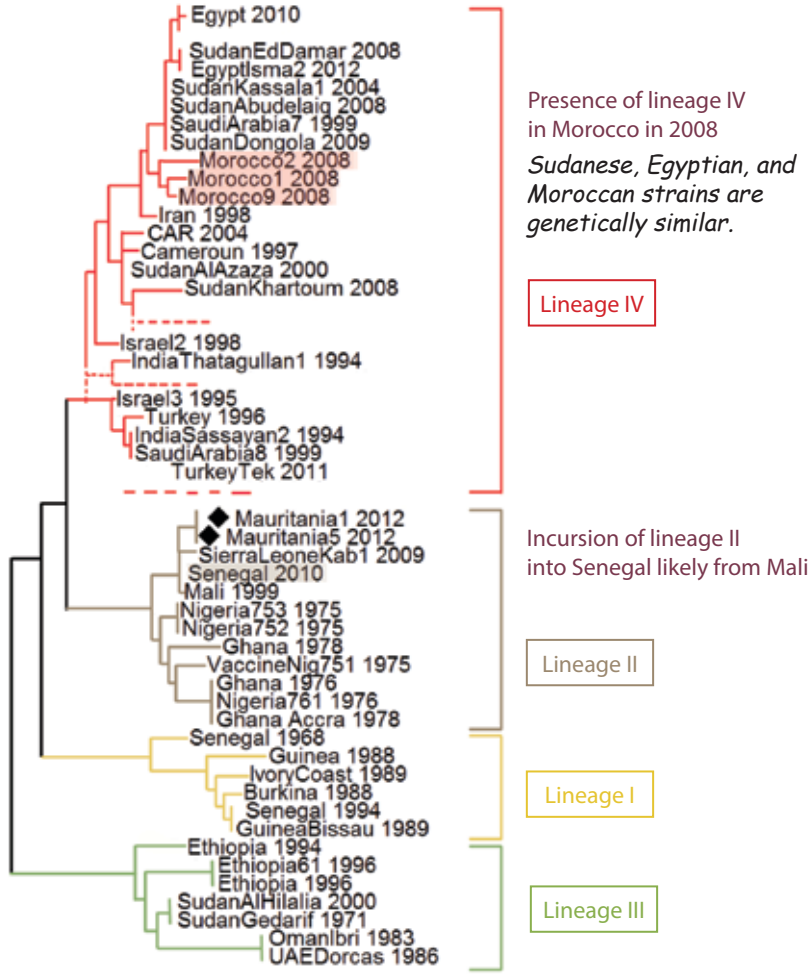
Samples taken directly from the sick animal in the field can enable the serological and virological diagnosis to be established.

The phylogenetic link between these 4 lineages was first established in 1996 by Shaila *et al.*, using the partial sequencing (an operation that determines the order of nucleobases) of the fusion F protein gene (a 322 nucleotide long segment) and then by Kwiatek *et al.* in 2007 based on a 255 nucleotide fragment of the N nucleoprotein gene. These 2 proteins, F and N, are considered to be representative markers that dispense with the need to conduct a complete sequencing of the genome.

However, N, which is less exposed to pressure from the immune system, best reflects the geographic movements of the virus over time. These movements are related to historic trade and transhumance routes. Molecular epidemiological studies therefore prefer to focus on the N protein to establish phylogenetic and phylogeographic trees. Lineages I to IV were numbered according to the apparent progression of the disease from the west towards the east. Lineages I to III originated in Africa. Lineage IV is Asian in origin but is now widespread in Africa.

The identification and comparative analysis of genetic sequences of strains isolated in different countries of Africa, the Middle East and Asia at different periods and in different hosts (goats, sheep and dromedaries) render it possible to better understand and monitor at the global level the distribution and spread of the disease, as well as the circulation dynamics of the 4 lineages of the virus.

Extract of a phylogenetic tree
based on the partial sequence of N nucleoprotein gene



Phylogenetic trees help identify animal movement networks behind the spread of PPRV.

Domestic small ruminants

As the name indicates, PPR is primarily a disease affecting goats and sheep. Within the same environment, goats generally are more susceptible to the virus than sheep. They express the disease in severe, acute, or peracute forms which most frequently result in death. Sheep resist the virus better. They develop a protective immunity and only express the disease in its mild, sub-acute or unapparent forms.

There are exceptions to this, likely due to the susceptibility of particular breeds: susceptibility to the virus depends on the breed. Dwarf African goat breeds in humid and sub-humid areas are more severely affected by PPR than large Sahelian breeds in arid and semi-arid regions. This difference also is because at the same temperature, PPRV is more stable in a humid atmosphere than in a dry one.

Even if morbilliviruses have a relatively narrow host range, PPRV shows that the species barrier can be crossed towards phylogentically similar cells such as bovines, dromedaries and wild small ruminants.

Dromedaries

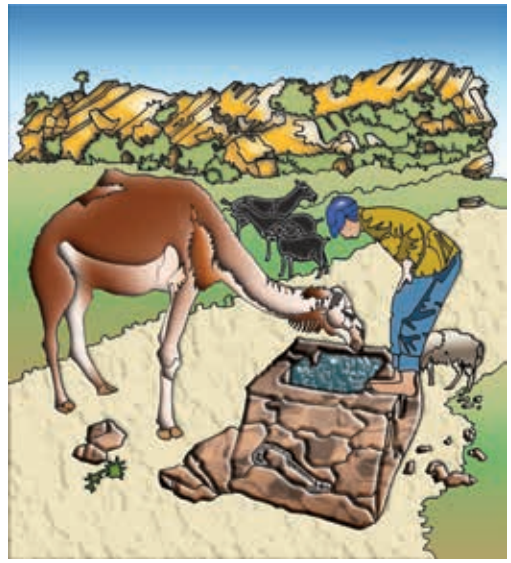
Since 1992, dromedaries have been suspected of being possible PPRV hosts. Serological surveys conducted in different countries - Sudan, Egypt, and Ethiopia - revealed seropositivity in dromedaries but with no clinical signs, and the virus was not isolated.

In 1995, François Roger, a CIRAD veterinarian, strongly suspected PPRV to be the cause of an outbreak in Ethiopia of a highly contagious disease that appeared to be new in the dromedary population. It was characterized by an acute respiratory syndrome with morbidity reaching 90%. Proof was provided in 2004 in Sudan. The virus was detected by laboratory diagnostic tests during an epizootic outbreak of the same disease in its peracute form with bloody diarrhoea, the sudden death of seemingly healthy animals, abortion in females and a mortality rate of over 50% in adults.

Receptivity to a virus is the capacity of a host to harbour a virus and allow it to multiply without showing clinical signs.

Susceptibility to a virus is the capacity of a host to clinically express the action of a virus.

In countries where traditional extensive livestock management systems lead animals to share watering holes and pastures, the risk of virus transmission between sheep, goats and dromedaries is high. Even if the epidemiological role of dromedaries still needs to be clarified, they are suspected of being cross-border carriers of PPRV and of contributing to the geographic spread of the disease.



Dromedaries illustrate PPRV's capacity to jump the species barrier.

Bovines

Cattle and water buffalo (*Bubalus bubalis*) are susceptible to the PPR virus, as proven by the presence of anti-PPR antibodies in their serum, but they do not manifest any clinical signs. It was this absence of clinical signs that allowed the disease to be identified and distinguished from rinderpest. For many years, this was the only differential diagnostic method available to distinguish between the two diseases. A few cases of calves and buffalo expressing signs of the disease (hyperthermia, oral lesions) were noted in the past, but these reactions probably were linked to a diminished immune capacity in animals weakened by an intercurrent infection (one unrelated to PPR).

In the epidemiological cycle of PPR, bovines are seropositive for the virus but do not excrete it, and are considered to be an epidemiological dead end. However, with the success of GREP (Global Rinderpest Eradication Program), the antibody cross-protection provided them by rinderpest vaccination was not maintained and has now disappeared. This raises questions regarding their contamination in PPR endemic areas and their possible role in the circulation and transmission of the disease.

Pigs

The experimental inoculation of pigs with PPRV produced no clinical signs. The animals reacted by producing antibodies but did not transmit the virus to goats. Pigs are considered to be an epidemiological dead end.

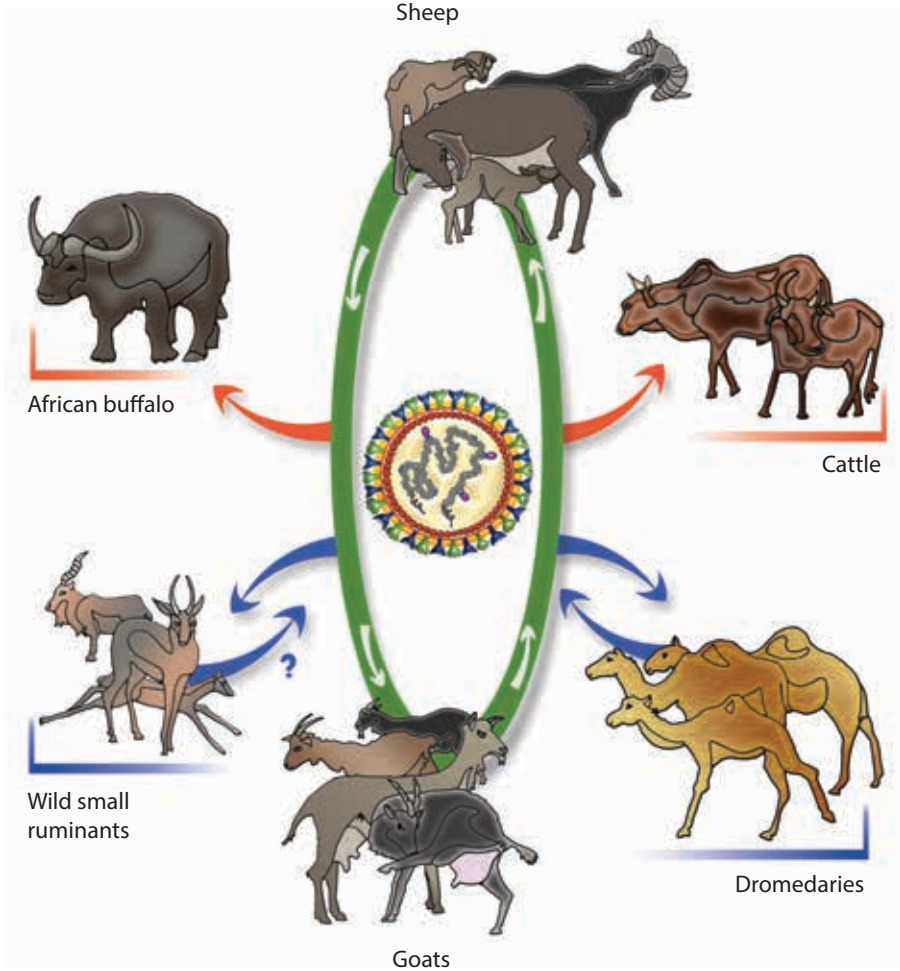
Wildlife

The susceptibility of wild small ruminants to PPRV was first reported in 1976 when white-tailed deer (*Odocoileus virginianus*) were experimentally infected. The clinical presentation of the disease was identical to that of naturally infected domestic small ruminants. In 1987, the disease was described in semi-wild animals in a United Arab Emirate zoo: Dorcas gazelles (*Gazella dorcas*), Nubian ibex (*Capra ibex nubiana*), Gemsboks (*Oryx gazella*), Blackbucks (*Antilopa cervicapra*), Laristan sheep (*Ovis orientalis laristani*). In 2002, it was reported for the first time in Saudi Arabia in a semi-wild herd of 200 gazelles (*G. dorcas* and *G. thomsoni*) in a subacute form with 52% morbidity and 100% case fatality rates. In 2007, PPR cases were reported in Tibet (China) in wild bharal (*Pseudois nayaur*). On the other hand, African buffalo (*Syncerus caffer*) are, like domestic bovines, an epidemiological dead end.

The role of wildlife in the epidemiological cycle of PPR and virus circulation is not yet entirely understood. Wild small ruminants may contribute to the geographic spread of the disease through their migratory movements, which can stretch over long distances, but the hypothesis of the maintenance of the infection in wild populations outside those living close to infected goat and sheep herds has not yet been demonstrated. They could be «spill over» hosts. As with rinderpest, wild animals clearly are more victims than reservoirs of the virus.

In areas of Asia where the disease is endemic, regular epizootics in small ruminant herds lead to high mortality in wild species, of which some are on the list of species in danger of extinction, notably bharals in Tibet, ibex in Pakistan, and wild goats in Kurdistan. In Africa, the spread of the disease in the direction of the large game reserves on the southern end of the continent, where the density of wild and domestic animals is high, could be a threat for the wild herbivore populations that must share their grazing areas with herds of goats and sheep.

The epidemiological cycle of PPR



Undercover transmission

PPR is one of the most highly contagious diseases of small ruminants. Infection usually takes place through direct contact between susceptible and infected animals. In the early stages of infection, during hyperthermia, all bodily secretions and excretions are highly contaminated. Coughing and sneezing project virulent aerosols into the air. The airborne transmission of the disease is rapid in herds of animals living close together. Transmission is horizontal; there is no vertical transmission of PPR through the placenta.

Virus excretion begins during the incubation stage, before the appearance of the first clinical signs, and can last up to over 2 months following recovery, as has been observed in goat faeces. These periods of silent virus presence, without any visible clinical signs, increase the risk of disease spread to other small ruminants, both domestic and wild.

Goats are more susceptible to PPRV than sheep.

Contamination also is possible by the ingestion of infected food or drink. Feeding and drinking troughs and soiled bedding also can be indirect sources of infection, but only for short periods because PPRV, like all of the morbilliviruses, cannot survive long outside the organism of a host animal. Its lipid bilayer envelope inherited from the cell host cannot withstand the heat and strong sun of countries in the South. When it loses its envelope, PPRV loses its infectivity.

The persistence of PPRV in the environment is a parameter that needs to be researched more fully in order to be considered in risk analyses and epidemiological models designed to assess the probability of the introduction of PPR through animal movements towards disease-free countries such as those of the European Union.

A fragile virus

Temperature	PPRV is sensitive to heat. This hinders the use of vaccines in certain countries in the South and has led to the development of thermostable vaccines. PPRV has a half life of 2 minutes at 56°C and 3 hours at 37°C. It can withstand cold better than heat. In refrigerated or frozen tissue, PPRV has a half life of 10 days at 4°C and 24 days at -20°C.
pH	At a normal temperature, the virus is stable between a pH of 5.8 to 9.5. It is rapidly destroyed at acidic pH values below 4 and alkaline pH values above 11. The acidification of meat during maturation helps but does not guarantee the inactivation of the virus. Meat from infected carcasses could present a risk of viral dissemination, but this is more likely in a context of bioterrorism than natural transmission. Although PPR is not a zoonoses, the consumption of animals infected with PPR, like the meat of all sick animals, is advised against.
UV radiation	PPRV is sensitive to ultra-violet rays, and thus to sunlight and desiccation.
Chemical agents	PPRV is destroyed by organic solvents of lipids (ether, chloroform, toluene). It is inactivated by quaternary ammonium-based detergents, glycerol, phenol, formalin and beta propiolactone.

Within a herd

PPRV spreads rapidly within a herd, causing heavy losses for farmers. Surviving animals are protected for life against a new infection and do not constitute a danger for their fellows as soon as they reach the end of the viral excretion period; there are no chronic carriers of the virus. The disease will only reappear in a herd when the virus can maintain itself there again; meaning once a population of susceptible animals has been reconstituted. If one third of a herd is renewed each year, this corresponds to a periodicity of 3 years.

Mixed herds are a risk factor in the transmission of PPR.

In endemic areas, livestock and herd management practices are risk factors for the spread of the disease and epizootic outbreaks.

This is the case when herds are mixed, combining animals with different levels of viral susceptibility such as goats and sheep, or where small ruminants cohabit with dromedaries. It also is the case when mobility through nomadism and transhumance promotes frequent and repeated contact between animals with unknown disease status, when rangelands and watering points are shared, when individuals of varying ages and origins are regrouped for sale, and when animals are introduced or reintroduced into a herd without observing a quarantine period. When migration routes are modified to avoid areas of drought, insecurity or conflict, the risk of spreading the virus also is increased.

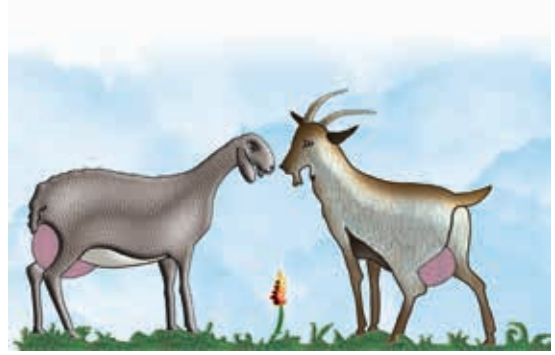
In pastoral societies, local social and cultural practices of trading, loaning, and giving small ruminants susceptible to infection increases the risk of introducing the disease into as yet disease-free areas. Large herds with a high density of animals, often associated with intensive livestock farming, also are environments with a high risk of PPRV.

Age also has an impact on the level of seroprevalence of livestock and on the epizootic risk. Small ruminants which have been kept in a herd for more than 3 years due to their production functions have a higher probability of having been contaminated and immunized than younger animals. This is particularly true for females, which show higher seroprevalence. Used for reproduction and to provide milk for home consumption, females are kept for longer periods than males. The latter often are sold by the age of two to cover the family's financial needs. However, at the individual level, no difference in susceptibility between males and females of the same age has been demonstrated.

Serological monitoring of PPR within a herd enables a better understanding of infection dynamics as a function of local and regional agro-climatic conditions and livestock farming practices, and to identify areas at risk. Studies clarifying the epidemiological situation in a country are critical for implementing PPR control strategies using vaccination.

"I had 9 she-goats and 4 bucks in my family, but now all that is left is one she-goat which I have moved."

A farmer - Democratic Republic of the Congo, 2012



"In response to the threat, farmers move their animals away from infected villages to areas where no outbreaks have yet been signalled, which causes healthy herds to become contaminated."

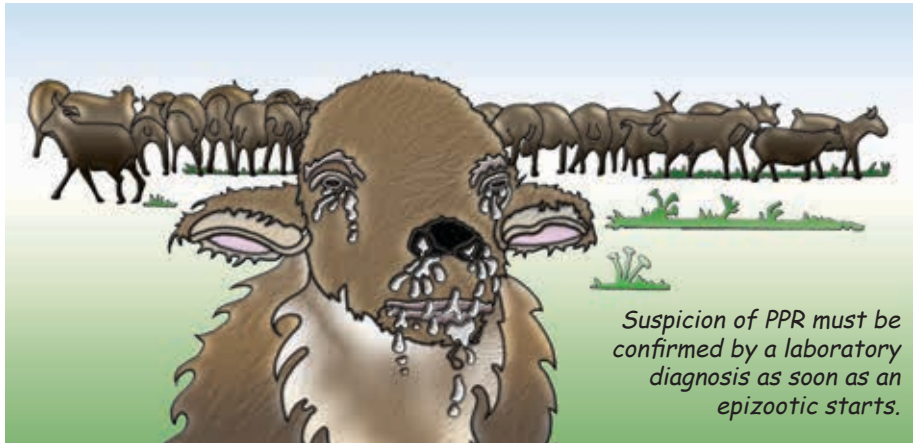
An FAO representative - Democratic Republic of the Congo, 2012

Under the control of the virus

PPRV, like the other morbilliviruses, has an affinity for two kinds of tissue, lymphoid cells and epithelial mucosa. This dual tropism, lymphotropism and epitheliotropism, explain the disease's clinical characteristics.

The virus contaminates "naive" animals through their oral and nasal passages. After entering into the organism, it multiplies first in the oropharynx and local lymphoid tissues. All of the immune cells (lymphocytes, macrophages, reticular cells) can be a target for virus multiplication. The newly formed virions spread throughout the host's organs and tissues with a preference for digestive, pulmonary, and respiratory mucosa and the immune system. The resulting tissue damage, which can be observed post-mortem, is responsible for the clinical manifestations of the disease: discharge, lacrimation, diarrhoea.

Biochemical and enzyme analyses show changes in kidney function (high urea and creatinine) through the multiplication of the virus in its cells and low blood parameter values (erythrocytes and haematocrit) linked to internal intestinal and renal haemorrhaging. In parallel, the PPRV infection induces cell death through apoptosis in immune cells, leading to severe immunosuppression. This weakening of the animal's natural defences through leukopenia (reduction in the number of white blood cells) opens the door to secondary bacterial and viral infections which interfere with the normal progression of the disease and complicate its diagnosis. These opportunistic infections significantly increase the mortality rate associated with PPR. The animals which recover are protected against PPRV for the remainder of their economic life.



Suspicion of PPR must be confirmed by a laboratory diagnosis as soon as an epizootic starts.

***Post mortem* diagnosis**	
Carcass	The animal appears emaciated. The hindquarters are soiled with faeces.
Digestive tract	Tissue necroses are found in the mouth (on the tongue, gums, and palate). Characteristic linear lesions are visible on the pharynx and oesophagus. The intestinal mucous membranes of the colon and rectum are very congested and haemorrhagic with lesions resembling zebra stripes. In females, erosive lesions also are found on genital mucosa.
Respiratory tract	The damage is linked to associated secondary infections. In advanced stages of the acute form of the disease, signs of secondary bronchopneumonia are visible on the trachea, which is very congested and contains a foamy liquid, and on the lungs, which present hard, purple-red apical and cardiac lobes.
Lymphoid organs	The lymph nodes are oedematous. The spleen is congested and bloated. Lesions are frequently found on the Peyer's patches (lymphoid tissue).

Host immune responses

Within the same species and even within the same breed, the response of a host animal to PPRV depends on its immune status and age. An immunosuppressed animal is susceptible to the virus regardless of its age.

In enzootic areas, offspring of seropositive females are immunized up to the age of 3-4 months by the maternal antibodies contained in colostrum. Beyond that point, the maternal protection diminishes but the animal's own immune defences are not yet fully established. Young animals below the age of one year consequently are the most severely affected by the disease.

Adults show cell-mediated and humoral immune responses to 3 viral proteins, N, F, and H, but of these, only the 2 surface proteins, F and H, are involved in the protective immunity. Over the course of the infection, hemagglutinin H is the preferred target of the neutralizing antibodies behind the humoral defence response. The F fusion protein engenders cellular immunity involving the T lymphocytes (lysis of infected cells).

The N nucleoprotein, a major antigen of the virus, is the most immunogenic but the antibodies produced by the infected animal are not neutralizing and provide no protection. However, they are being used as the basis for the development of molecular diagnostic tests. The nucleoprotein nonetheless intervenes in the immune process by inducing cell death in lymphocytes.

The immunogenicity of all PPRV strains is high and independent of their genetic variability. When an animal recovers from a natural infection or is in contact with a virus strain through vaccination, it acquires long term immunity for all of the other strains and can no longer be infected by the disease. From an immunological perspective, this means that variations in the nucleotide sequences of the F and H proteins do not involve the important antigenic sites. From an epidemiological perspective, this consequently means that PPR has a cyclical nature. The virus can only maintain itself in a population if susceptible individuals regularly join the population.

PPRV shows a variable pathogenicity, or virulence, but no relationship has been established between viral lineage and level of virulence. This variability in virulence is likely linked to the susceptibility of the host, which is a function of the host's breed and species. The virus might have varying affinities for the lymphocytes. The most virulent virus strains may be those which have the capacity to multiply rapidly while attenuated strains may have reduced infectivity due to changes in their tissue affinity, resulting in reduced epitheliotropism.

Within the cell

PPRV must inhabit a living cell to reproduce. It directs the cell to produce copies of the PPRV's own genome and structural proteins. The process takes place in 3 stages: entry of the virion into the cell, unfolding of the viral cycle, and exit of the synthesized virions.

Two special features of PPRV and RNA viruses of the same genus

The RNA-dependent RNA polymerase carried by the virus plays two roles: that of the transcriptase to synthesize messenger RNA which are translated into viral proteins, and that of the replicase to reproduce copies of the genome.

The two steps of the viral cycle, transcription and replication, take place without separating from the RNA-Nucleoprotein complex. The viral RNA is never "naked", neither in the virions, nor in the infected cells.

Entry of the virion into the cell

The first step is the attachment of PPRV to the surface of the host cell. The infection starts when the viral H hemagglutinin recognizes a particular cell receptor protein. It is known under the acronym, SLAM (Signalling Lymphocyte Activation Molecule), or CD150. It is expressed on the surface of lymphatic tissue lymphoid cells. This receptor appears to serve as a cellular anchor for all morbilliviruses, and explains their natural tropism for immune cells and the immunosuppression which results when these cells are destroyed en masse.

Once the H-SLAM link has been established, the second external viral protein (F) modifies its conformation and begins the fusion between the viral envelope and the cell membrane. The nucleocapsid is released into the cell cytoplasm where the infection cycle unfolds in two steps: transcription and replication.

Scientists recently discovered that another protein, Nectin-4, serves as an epithelial cell receptor for the measles and distemper morbilliviruses. Also identified in upper respiratory tract epithelial cells of sheep, it could explain the tissue lesions of the nose, mouth cavity, and trachea of infected animals.

Unfolding of the viral cycle

During transcription, the required virus multiplication cycle is initiated, leading to the synthesis of messenger RNA.

The RNA-dependent RNA polymerase recognizes the leader, binds to the 3' end of the virus genome at the level of the genomic promoter, and initiates transcription of the coding sequence of the first gene, the N nucleoprotein. When it reaches the termination signal, it releases the synthesized messenger RNA. It then reinitiates the transcription of the next gene, located 3 nucleotides (CUU for PPRV) away from the intergenic region, and continues like this in a sequential manner up to the L gene. However, at each intergenic sequence, its reinitiation frequency drops, leading to a decreasing gradient (called the transcription gradient) in the amount of messenger RNA produced. In other words, the intergenic sequences are "attenuated". There is a greater abundance of messenger RNA of the first gene, N, than of the last gene, L. This mechanism is a form of regulation aiming to produce the right proportion of each protein for the future virions. Each messenger RNA is translated into a protein by the ribosomes of the infected cell. Once produced, the viral proteins migrate towards cellular organelles (endoplasmic reticulum and Golgi apparatus), then H and F steer themselves towards the plasma membrane.

When sufficient viral N and P proteins have accumulated, transcription gradually gives way to replication, which is the complete copy of the virus genome. As PPRV is a negative-stranded RNA virus, it must produce an intermediary molecule, the antigenome (a positive RNA strand).

RNA polymerase, which plays the replicase role, identifies the trailer and binds to the 5′ end of the virus genome at the level of the antigenomic promoter. Ignoring attenuating intergenic signals, it makes a complete complementary copy of negative RNA without stopping. The positive RNA produced is encapsidated at the same time that it is synthesized. The nucleocapsid N-antigenome then serves as a matrix for the synthesis of new negative RNA that also will encapsidate themselves. The latter then can serve as a matrix for the synthesis of new positive RNA, be used for the synthesis of messenger RNA, or associate with neo-structural proteins to form new virions. A regulatory mechanism maintains a ratio of one antigenome for every 10 genomes.

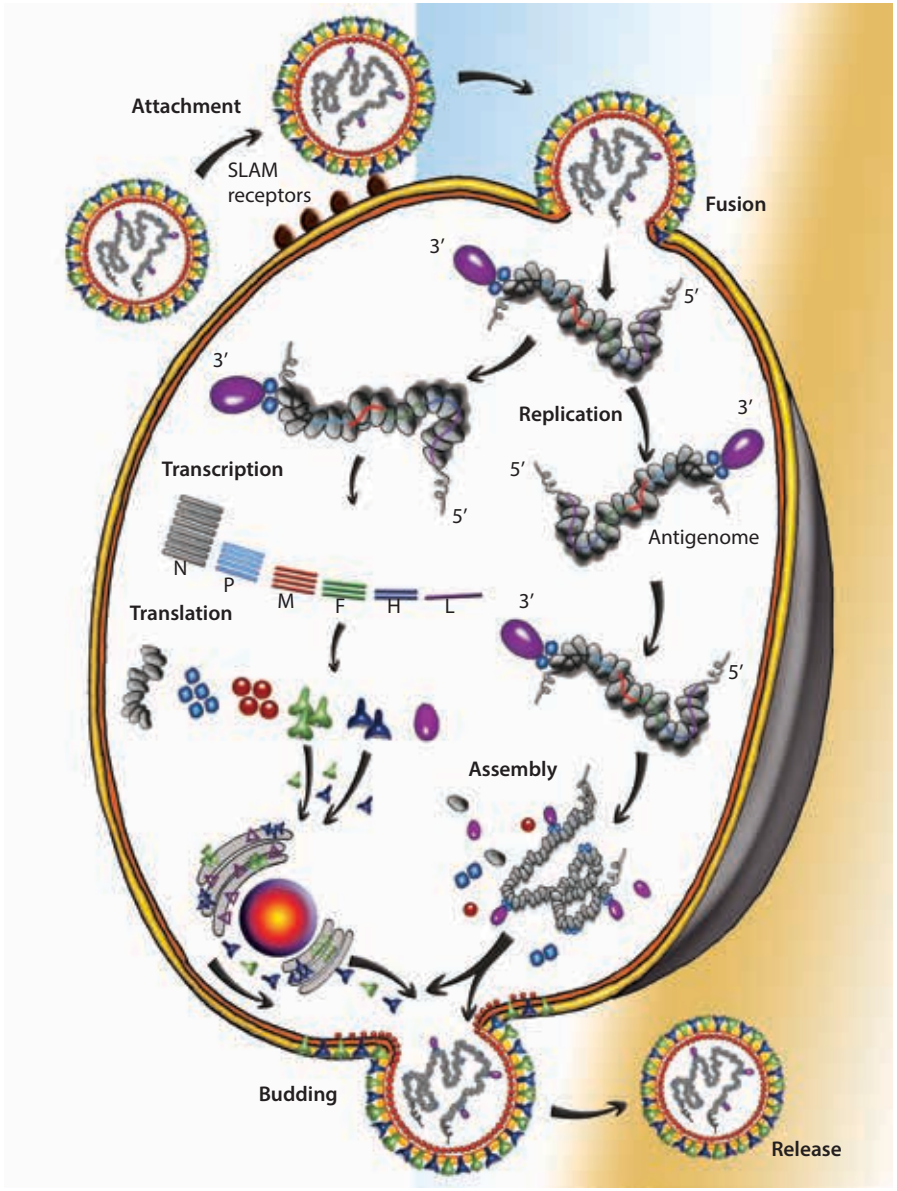
It is then the turn of the matrix (M) protein to intervene as the band leader in the assembly of new virions. Thanks to its affinity for the N nucleoprotein, it establishes links between the neo-nucleocapsids and the H and F proteins, future spicules of the viral envelope inserted on the cell membrane.

Release of new virions

The whole virions are formed and released by budding through the cell membrane. They are only completely released once the H glycoprotein has intervened. Its neuraminidase enzyme activity breaks the bond between the viral spicules and the sialic acid of the cell membrane. PPRV is the only morbillivirus equipped with this capacity.

After their release, the virions spread and contaminate other cells. They also can pursue a cell-to-cell infection process. The expression of the two viral H and F proteins on the surface of the infected cell allows these proteins to interact and fuse with healthy neighbouring cells without passing through the extracellular environment. They form syncytiums (multinucleate giant cells) which allows their progression without interference from neutralizing antibodies.

The multiplication cycle of PPRV



A cyclical and seasonal disease

PPR evolves in two epidemiological forms, one epizootic, the other enzootic. When PPR hits previously disease-free areas where animals have had no prior exposure to the virus, the disease is epizootic. Its clinical expression is most often acute with mortality and morbidity rates which are a function of the susceptibility of the species and breed, but which can reach 90 to 100%. In numerous countries in Africa, the Middle East, and Asia, it is present in an enzootic form with a low mortality rate (20% or less) and variable but high seroprevalence rates which can exceed 50%. In these areas, the virus circulates quietly, its clinical expression unapparent, but it remains ready to clinically manifest itself as soon as the population of susceptible small ruminants is sufficiently large, or when animals are in poor health, environmental conditions are favourable, or social, cultural, or economic practices increase the risk of virus transmission. The disease then expresses itself in epizootic outbreaks that appear with a cyclical and/or seasonal frequency.

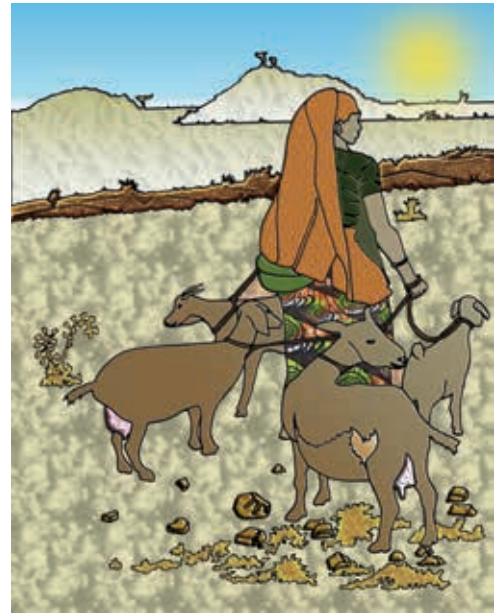
The cyclical character of PPR is determined by the strong immunogenicity of PPRV and the length of the economic life of goats and sheep. The conjunction of these two factors favours the expression of the disease. The high herd replacement rate of 30% per year, compared for example to only 10% in cattle, creates an immunologically naive population of small ruminants at the level of village communities which is sufficiently large for the virus to be maintained and for epizootic outbreaks to occur.

"A goat is like a savings account. It is a source of income. It feeds the people, both in the countryside and in the cities."

An FAO representative - Democratic Republic of the Congo, 2012

The seasonal character of PPR is determined by climate factors which favour the survival of the virus in the outside environment and/or weaken the resistance of animals, and by the movements and regroupings of small ruminants due to agricultural, livestock, and trade practices.

With the arrival of the cool or rainy seasons, the temperature and humidity are favourable to the virus and increase its survival time. Animals which have just survived a long period of drought are often thin and weak. Their weakened immune defences render them susceptible to pathogens and benefit the virus. Epizootic peaks are frequent and numerous. In Sahelian Africa, this context of physiological stress is aggravated by the arrival of the harmattan, a dry, dusty wind which favours respiratory infections.



"In my village, out of over 400 goats, only about twenty old bucks still survive."

Village head - Democratic Republic of the Congo, 2013

The seasonal migrations of herds in search of available forage and water begin just when climate conditions are increasing the risk of contamination. These migrations are an important factor in the spread of the virus towards disease-free regions. In certain West African countries such as Mauritania, transhumance routes stretch over hundreds of kilometres, with movement from the north towards agro-pastoral areas in the south. These areas hold high concentrations of animals and lie near the borders of Mali and Senegal where frequent cross-border movement takes place. A study published in February 2014 in the journal, *Emerging Infectious Diseases*, confirms this and shows the existence of a gradient of increasing seroprevalence from the north to the south of Mauritania related to herd movements.

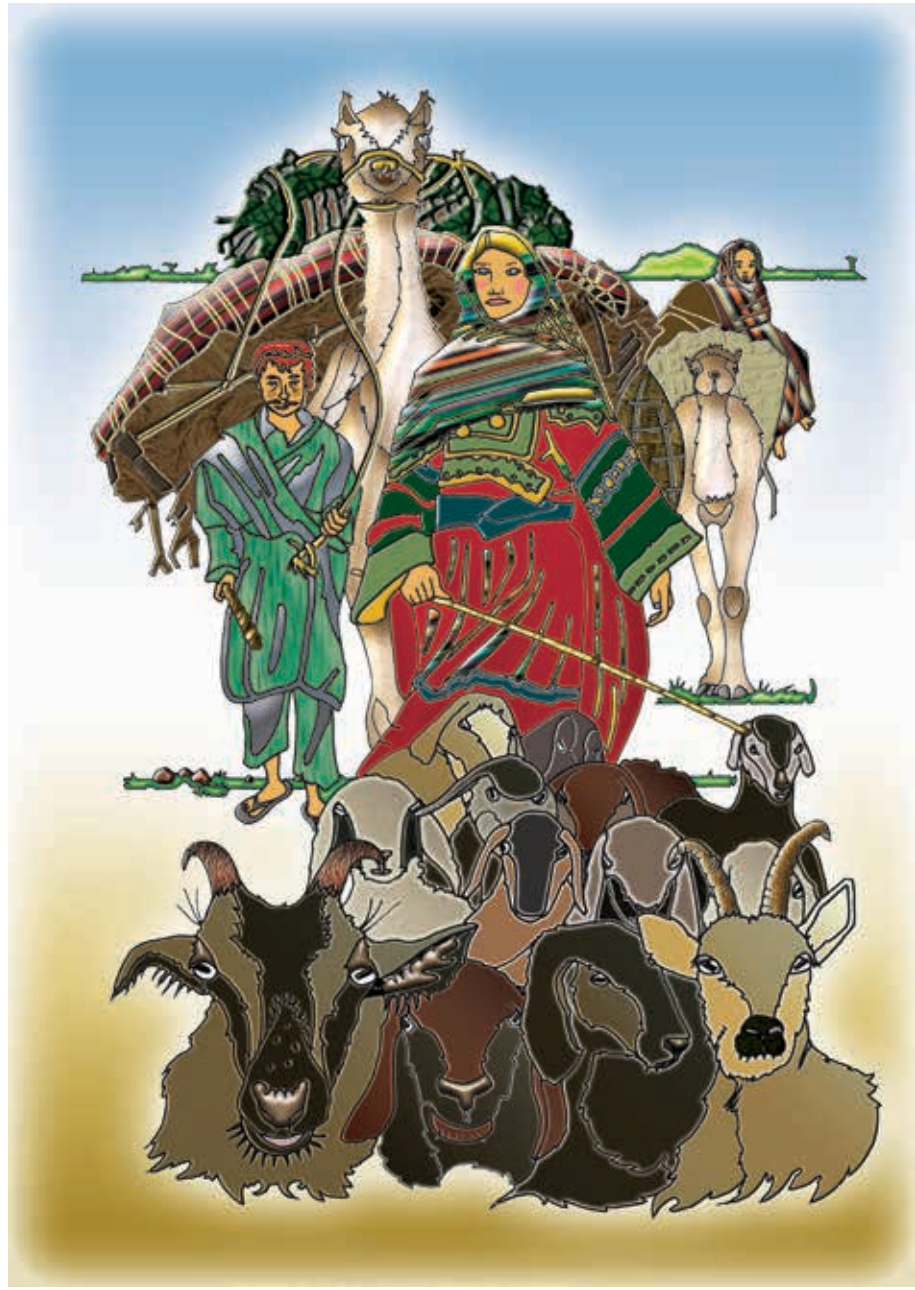
The same holds true in Asia where, in a country with very different ecological zones such as Nepal, the return of small ruminant herds from mountain pastures before the start of the cold season contributes to increased epizootic outbreaks in sedentary herds in the plains. In other countries of Africa and Asia, recurrent droughts oblige nomad populations to open new transhumance routes, helping to increase the risk of encounters between healthy and sick animals.

Each year, traditional and religious festivals are occasions for intense trading activity involving goats and sheep. The animals are brought from pastoral areas to livestock markets and slaughterhouses in towns to meet the high demand for meat. This gathering together and mixing of small ruminants from many different points of origin facilitate virus transmission.

When animals are sold or traded, geographically scattered inside a country but also sent towards bordering countries, they are likely to spread the disease when they are still in the incubation stage, well before the appearance of clinical signs, or when the disease is expressed in the sub-clinical form. The same holds true when the export and import of animals take place without sanitary controls. The emergence of PPR on the island of Grande Comore at the end of 2012 is an example of virus introduction into this Indian Ocean area via the importation of infected goats from Tanzania. Epidemiological monitoring in different countries confirms that there are more epizootic outbreaks of PPR during these festival periods, with a greater concentration near trade routes.

"People here live simply and have few resources. There is a lot of poverty. Animals are the main source of income for everyone. If a PPR epidemic were to break out, up to 90% of sheep and goats could die."

A veterinarian - Yemen, 2013



Risk factors

Virus
- Persistence in the environment (temperature, humidity).

Animal
- Species
- Breed.
- Age.
- Health status (weakened by illness, ill-nourished).
- Immune status (immunosuppressed).

Herd
- Large herds.
- Mixed herds of susceptible animals (goats, sheep).
- Introduction of animals of unknown origins without a health guarantee or quarantine period.
- Return from markets of unsold animals.
- Mixing of local sedentary herds with transhumant herds.
- Animals of different ages forced to live closely together.
- Accommodating animals in transit.

Environment
- Variability of climate factors according to the season (temperature, humidity, wind).
- Agro-ecological zones (mountains, plains).
- Agro-pastoral zones with a high density of small ruminants.
- Agro-pastoral border zones.

Livestock rearing practices
- Pastoralism (seasonal transhumance, nomadism).
- Changes in usual routes (conflict, insecurity, drought).
- Cross-border pastoralism routes.
- Sharing pastures and watering points leading to a mixing and regrouping of vulnerable (young) and high risk (sick adult) animals.

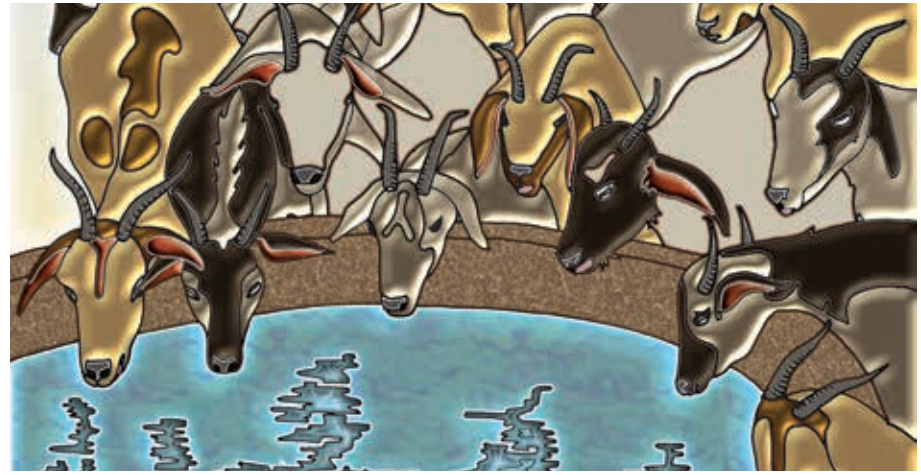
Markets and trade
- Gathering animals and live animal markets.
- Legal and illegal cross-border movements of animals.
- Imports and exports without health inspections.
- Increasing commercial trade between livestock rearing areas towards meat consuming areas to meet growing demand for animal protein.
- Trade routes.

Risk factors

Social, economic, and cultural practices

Human behaviour
- Religious festivals giving rise to intense trade movements and the setting up of slaughter centres.
- Trading, loaning and giving animals.
- Theft of animals.
- Risky livestock farmer behaviour by moving animals in PPR areas to disease-free areas.
- Migration of rural populations in infected areas towards disease-free urban areas.
- Fleeing areas of socio-political or climate insecurity.

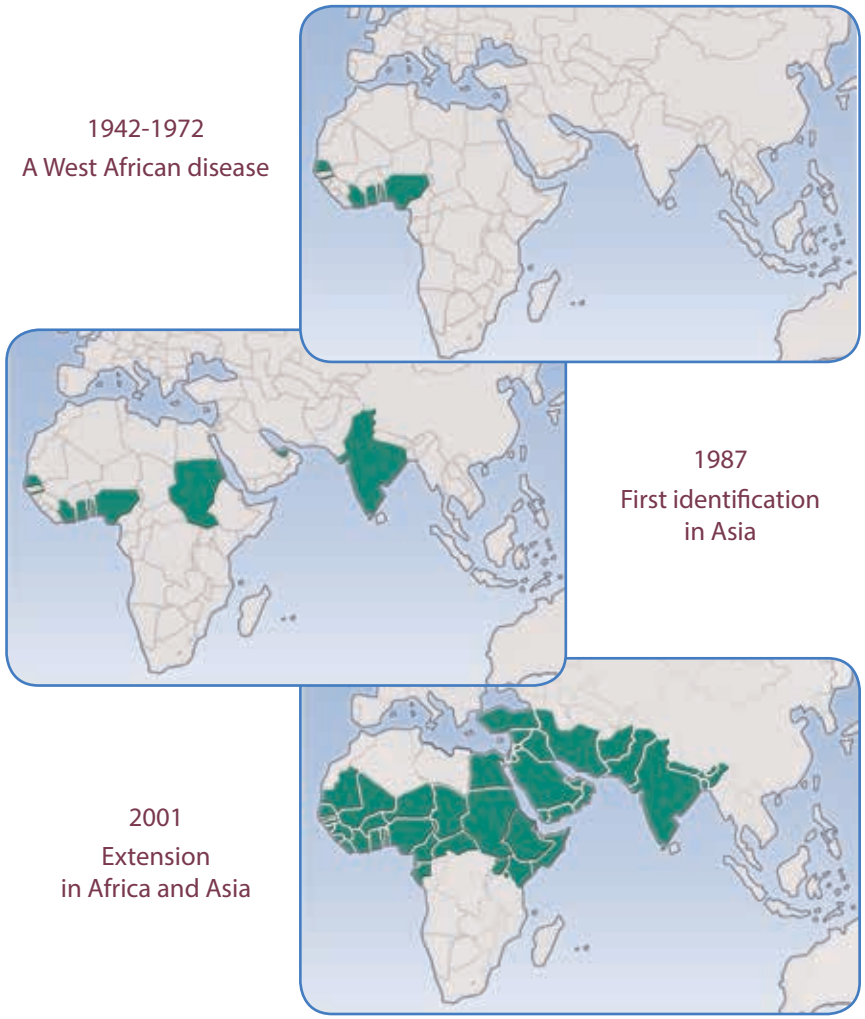
Health surveillance
- Insufficient knowledge about the disease in disease-free areas and of some people keeping animals.
- Insufficient health monitoring.
- Difficult access to veterinary services, medicines, and vaccines.
- Insufficient training and information.
- Lack of trained health officers and veterinarians.
- Absence of vaccination.



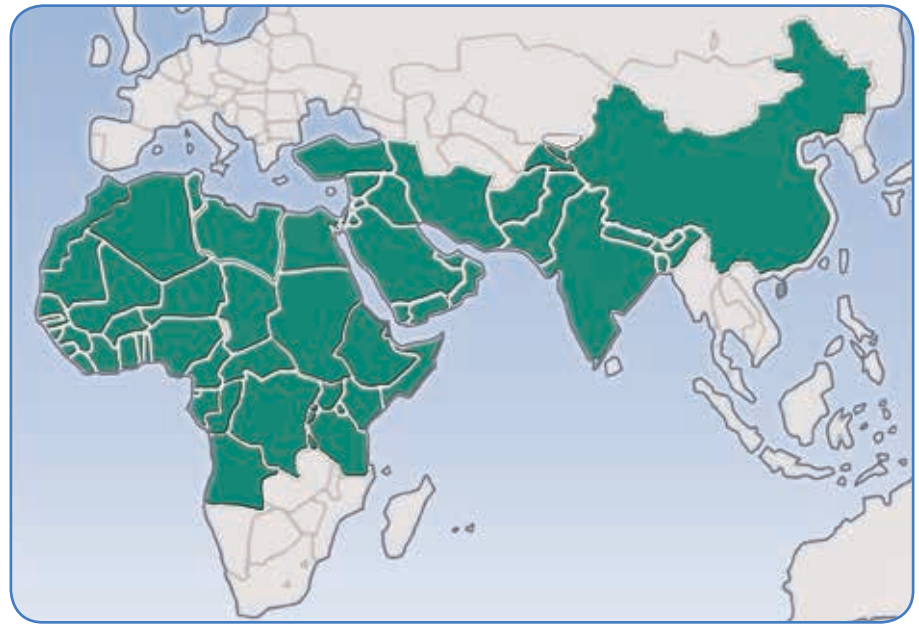
Watering points are sources of contamination.

A spreading transboundary disease

The history of PPR began 75 years ago when it was identified in the Ivory Coast. Up until the 1970s, it was only reported in coastal West African countries: Benin, Senegal, Togo, Nigeria, and Ghana. In the beginning of the 1970s, it appeared in Sudan. Between 1980 and the early 1990s, it spilled over from the African continent onto the Arabian Peninsula (Oman 1983, Saudi Arabia 1988, Kuwait and the United Arab Emirates 1991) and the Middle East (Lebanon 1986, Jordan 1989, Israel 1993, Iran and Iraq 1994). It reached South Asia in 1987 when it was diagnosed in India. It has become a panzootic.



It is pursuing its geographic spread in an easterly direction, giving the impression that it is colonizing territories that were freed of rinderpest following the global eradication program coordinated by the FAO and OIE. It covers South Asia (Bangladesh 1993, Pakistan 1994, Afghanistan 1995, Nepal 1995, Maldives 2009, Bhutan 2010), extends through Central Asia (Kazakhstan and Tajikistan 2004) to East Asia, appearing first in western China (Tibet 2007) before spreading throughout China at the end of 2013 when there was a massive and rapid spread of the disease. Positive test results obtained on serum sampled from small ruminants in 2006 in Vietnam indicates that PPRV is also likely present in Southeast Asia.



2014 : A transboundary disease with increasing incidence

In Africa, at the end of the 1990s PPR was reported in all of the countries in the sub-Saharan region, from the Atlantic Ocean to the Red Sea, where it has now become endemic. Over the past ten years, it has gradually spread towards East Africa (Ethiopia 2007) and headed south over the Equator to cover a belt of countries between Gabon and Somalia, including the Democratic Republic of the Congo, Uganda, Kenya, and Tanzania. Positive serological results have been obtained in Rwanda and Burundi. In 2012, PPR was identified for the first time in Angola and on the Comoros islands in the Indian Ocean, raising the risk of virus incursion into neighbouring Mozambique, Malawi, and Madagascar and movement towards the large game reserves of southern Africa where domestic and wild small ruminants co-exist.

Morocco was infected for the first time in 2008. After Egypt, which has been infected since at least 1989, it was the second North African country to declare the disease to the OIE. In 2007, serological traces of the infection were observed in Tunisia, and the country declared clinical outbreaks of PPR in 2011, at the same time as Algeria. This disease presence in countries along the southern rim of the Mediterranean has extended to Turkey since 1999. PPR remained localized in the Asian part of the country until 2004, when outbreaks in Thrace near the border to Bulgaria and Greece alerted international health organizations to the risk of its introduction into Europe.

The global epidemiological PPR situation is constantly evolving and its transboundary spread recently seems to have accelerated in both Asia and Africa. In most countries where the disease it endemic, it re-emerges in a cyclical and seasonal pattern, but it also emerges in new areas and in new countries, indicating highly active viral circulation. Monitoring its progression is based on declarations of epizootic outbreaks to the OIE by the health authorities of the countries concerned. These notifications can by complemented by serological (detection of antibodies) and virological (detection of the virus) field surveys in enzootic and epizootic zones to identify the viral lineage involved, monitor the movements of the virus, understand spread factors and/or assess the impact of vaccination campaigns.

The FAO estimates that in 2014, over 70 countries were affected by PPR. Over the 8-year period between 2005 and 2013, outbreaks of the disease were reported in 37 countries in Africa and 21 countries in Asia and the Middle East. Its continued spread is threatening the livelihoods and food security of over one billion extremely poor smallholders and pastoralists, and is the source of great concern for the international community.

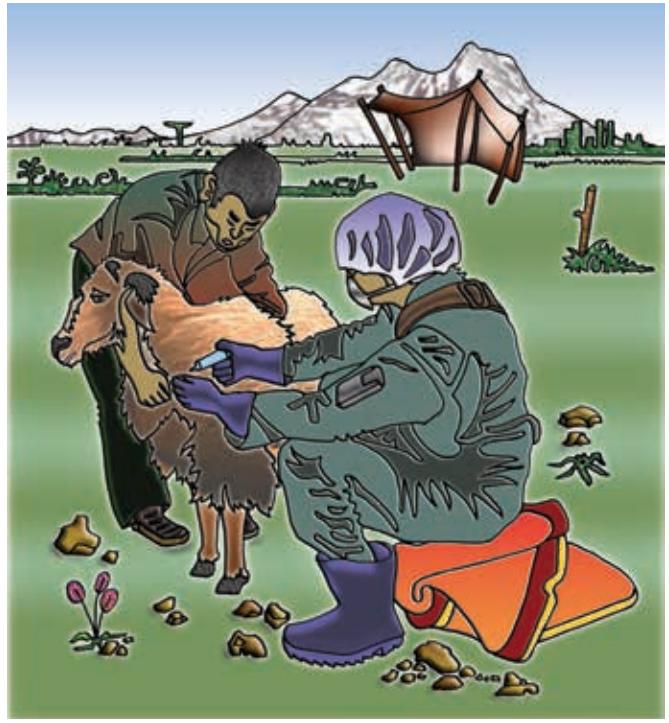
Reasons for its spread

Scientists know today that in the past, PPR was present in numerous countries where rinderpest raged, but it was overlooked or misdiagnosed in the absence of reliable tests that could distinguish between the two diseases. After the last rinderpest outbreak was stamped out in the early 2000s, international animal health organizations turned their attention to PPR, which had been hitherto neglected.

When the circulation of the rinderpest virus was arrested and the vaccination campaigns against this disease ceased, small ruminants were left completely exposed to PPR. It had been fairly common for veterinary services to vaccinate small ruminants with the rinderpest vaccine, which conferred excellent cross-immunity against PPR. During the control phase of the rinderpest eradication program, the use of this vaccine, even for small ruminants, was banned, yet a homologous PPR vaccine was not yet in circulation to fill the gap.

Furthermore, some argue that the end of rinderpest vaccinations in cattle increased their receptivity to the PPR virus and that cattle could play a role in PPR transmission, something which has never been demonstrated.

The setting up of PPR surveillance and control programs, raising awareness of local populations, the provision of sensitive and specific immunosorbent and molecular diagnostic techniques, and the compulsory notification of disease emergence to the OIE since 2004 have confirmed the extensive geographic cover of the disease. Moreover, although a highly effective attenuated vaccine has been available since 1989, the absence of large scale vaccination campaigns has led to the emergence of the disease in areas and countries that previously had been disease-free, and facilitated the passage of the virus to other species such as dromedaries.



To fight animal diseases is to contribute to the fight against poverty and to ensure the food and nutrition security of the poorest people of the world.

Over the past few years, the key factors behind the speed of the geographic spread of the disease are related to the growing world population of small ruminants, human migration, and the mobility of animals due to livestock practices and trade.

The movement of animals over long distances and beyond national frontiers dictated by traditional pastoral and transhumance livestock practices facilitates encounters between healthy and infected animals and contributes to the spread of the virus. The same is true of the uncontrolled migration of people accompanied by their small livestock. Their flight from socio-political insecurity (massive displacement of refugees to escape armed conflict), economic insecurity (rural exodus to escape poverty), and climate insecurity (recurrent drought, catastrophic flooding) increases the risk of PPR spreading to disease-free regions and countries.

However, the primary factor behind the spread of PPR is the intensification of animal movements to meet an increasing demand for animal protein. The demographic and economic development of mega-cities and consequent increase in demand for meat induce the ever increasing trade of live animals, which are moved from rural production areas to urban consumption zones. Trade flows are particularly important during religious holiday periods in Islamic countries. Small ruminants often cross borders, sometimes illegally, without undergoing any health controls.

"My husband is chronically ill but now that I have the goats I can sell one to pay for hospital fees and transport to the hospital and I have seen an improvement in my husband's health. I get 4,500 Malawian kwachas (51 US$) for one goat. I can buy food and my children never go to bed hungry like before".

A village woman - Malawi, 2009

Depending on the epidemiological status of the country of origin, which most often is endemic, the risk of the South-South spread of PPR through the introduction of infected animals must be considered from both a health and economic perspective even if small ruminants do not have an impact on international markets in the same way as cattle.

The development of an effective PPR surveillance and control strategy thus must now rely on linking epidemiological field knowledge regarding animal mobility (trade and migration routes) at the local, national, regional, and international level with molecular data on the spatial distribution of PPRV lineages.

What is the risk for Europe?

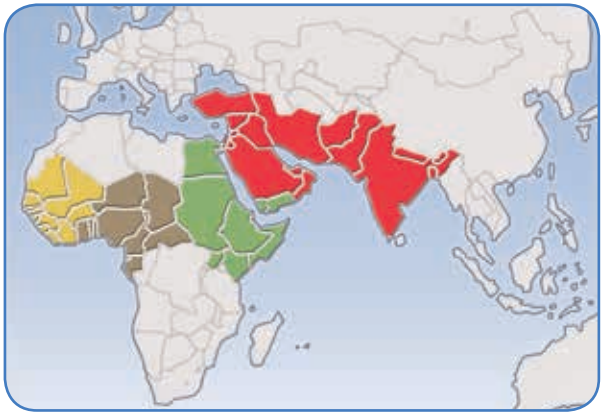
The presence of PPR in countries on the southern shores of the Mediterranean, North Africa, Turkey, and the Middle East, led the European Food Safety Authority (EFSA) to assess the risk of the virus crossing the borders towards goat and sheep stocks in European Union countries. In a January 2015 study entitled, *Scientific opinion on the peste des petits ruminants*, it notes that the most frequent and efficient route for the introduction of PPR into a country is the entry of infected live animals. As the importation of live small ruminants from endemic countries in the South was banned by European health legislation, the risk of PPRV introduction is linked to the illegal movements, for example, via private vehicles. Indirect virus introduction pathways, either through contaminated meat products or fomites, such as livestock transport vehicles which have not been disinfected, theoretically are possible but viral transmission to a disease-free animal is highly unlikely.

The risk of PPR introduction in France was estimated to be minimal to none (level 1 and 2 on a scale of 9). If, however, the virus enters French territory or that of a European country, the application of regulations in force should enable rapid control (slaughter and/or vaccination before culling) and renders unlikely the risk of endemisation and serious economic consequences for the sectors concerned. Nonetheless, the most effective prevention measures to reduce the risk of PPR spread at the global level rely on reinforced cooperation between European Union countries and endemic countries in the South.

Lineages on the move

The development of phylogenetic analyses and molecular diagnostic methods using sequencing, alongside the existence of gene banks, have rendered it possible to determine the lineage of the strain causing an epizootic PPR outbreak and to deduce its geographic origin in order to better understand epidemiological situations. The case of the 2008 Moroccan epizootic illustrates this point well. After genetic typing identified the virus strain responsible as lineage IV, the initial hypothesis that PPR had been introduced from West African countries (where viral lineages I and II circulate) was dismissed.

Early phylogeny studies conducted at the end of the 1990s on samples collected over a 30-year period established that the strains found in West Africa were lineages I and II. Lineage I was present in the Ivory Coast (where PPR was first identified), Senegal (where the first viral strain was isolated), Guinea, Guinea-Bissau and Burkina Faso. Lineage II was present in Ghana, Nigeria (the source of the PPRV vaccine strain), Benin, and Mali. Lineage III virus strains were identified along the shores of the Red Sea in East Africa (Ethiopia, Sudan) and in part of the Arabian Peninsula (Oman, United Arab Emirates). Lineage IV, first isolated in India at the end of the 1980s, was distinguished by its broad geographic cover and its confinement to Asia. This initial distribution of virus lineages reflected separate genetic evolution due to limited exchanges between these geographic regions.

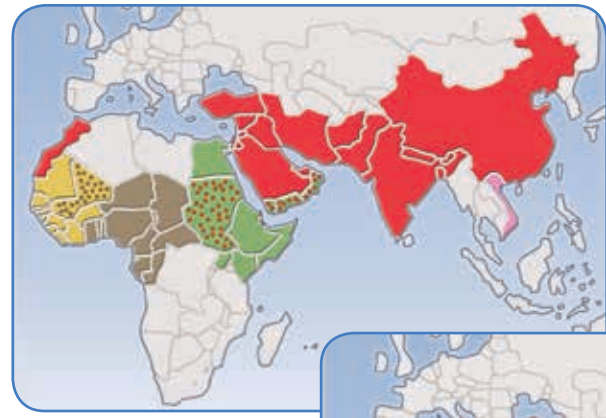


Known distribution of the 4 PPRV lineages in 2001

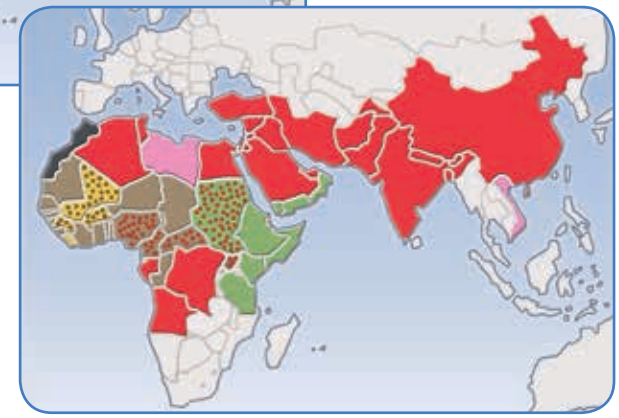
However, since the late 1990s, the geographic spread of the disease, with the emergence of PPR outbreaks in countries which had been disease-free, and re-emergence in countries and zones known to be enzootic, has radically changed the situation.

Epidemiological surveillance has revealed that lineage IV is continuing to spread in Asia in an easterly direction, but is also extending west and invading Africa, where it is becoming the dominant lineage. In 2000, it was discovered in Sudan, in East Africa, where it cohabitated with the native lineage III and passed into a new host, the dromedary. It then spread to Egypt and across North Africa, finally reaching Morocco in 2008. Today (2015), lineage IV is present across North Africa with the exception of Morocco, which succeeded in eradicating the disease through mass vaccination campaigns. It also is circulating in the northeast of Africa (Sudan and Eritrea) and in Central Africa (Cameroon, Central African Republic, Uganda) where it coexists with lineage II. The most recently infected African countries, Angola and Comoros, are an indicator of its spread from the north to the south of Africa.

A similar phenomenon occurred in West Africa with lineage II, today alone present in Senegal, having taken the place of lineage I.



Known distribution of the 4 PPRV lineages in 2008



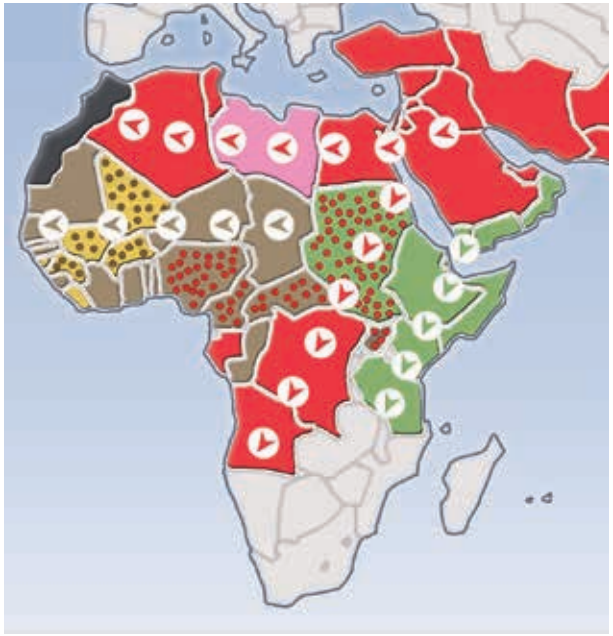
Known distribution of the 4 PPRV lineages in September 2014

Lineage I
Lineage II
Recent spread
Lineage III
Lineage IV
Recent spread
Seropositivity
Absence of PPR since 2009

These upheavals in the distribution of lineages must be interpreted cautiously as epidemiological data collected in the field remains very incomplete due to inadequate surveillance. While the link between animal mobility and the spread of the virus is now certain, it cannot alone explain the dominance of lineage IV in West and Central African countries which have no tradition of small ruminant exchanges with countries east of the Red Sea.

One answer may be found in the capacity of PPRV to adapt its pathogenicity to selective changes in its environment, notably to the different susceptibility of its different hosts. Thanks to its capacity to mutate, which is characteristic of RNA viruses, PPRV releases a multitude of viral particles into the tissues of infected animals. These particles are genetically close but subtly different from the initial strain, forming virus sub-populations with different replicative potential known as viral quasispecies. When one of these sub-populations acquires a favourable genetic ability, it assumes the upper hand through a greater power of dispersion and becomes the dominant player. The most invasive strains are today classed in lineages II and IV, but this could change tomorrow. In effect, nothing can link invasive power, which is likely connected to virulence, to membership in any particular lineage identified by phylogenetic criteria.

Virus routes



Assumed spread of PPRV lineages:

- East-West in North and West Africa
- North-South in East and Southern Africa

Lineage II

Lineage III

Lineage IV

In contrast, these mutations are probably related to a crossing of the species barrier. This jump is facilitated by the crowding together and abundance of various genetically similar host species: ovines, caprines, bovines, dromedaries, wild ruminants... We should thus learn from past lessons revealed by advances in genetic study methods (rinderpest and measles viruses share a common ancestor) and avoid the emergence of new viruses by eradicating PPRV as rapidly as possible.

The geographic spread of PPR resulting from very active virus circulation, its adaptation to new geographic areas and to new hosts, and games of dominance, extinction and coexistence between lineages, are challenging research and reference laboratories. They have begun epidemiological studies to better understand the link between the genetic plasticity of PPRV, channels of disease spread, and movements of animals. The results will be extremely useful for the establishment of a PPR control strategy.

GenBank: a genetic sequence bank

Genbank is a collaborative database of nucleic acid sequencing maintained by the NCBI (National Center for Biotechnology Information, USA). The development of molecular biology technologies in the 1990s, notably complete and partial genome sequencing, enabled a bank of gene sequences of PPRV strains to be constituted within GenBank that were based on collections held by research and reference laboratories. The bank holds sequence data of F, H, and N protein gene fragments, which allowed the strains to be grouped into 4 viral lineages, and the full sequence of the genomes of a few strains.

Up until 2013, only 639 PPRV nucleic acid sequences were available in the GenBank, of which only 11 complete genomes belonged to virus lineages I, II, and IV. Among them was the vaccine strain of lineage II, Nigeria 75/1 (accession n°: X74443). In 2014, GenBank obtained several new complete sequences, that of a lineage II strain isolated in 2013 by CIRAD in Senegal (accession n°: KM212177), and for the first time that of several strains of lineage III coming from countries in East Africa (Uganda 2012: KJ867543; Ethiopia 1994: KJ867540) and the Middle East (United Arab Emirates 1986: KJ867545; Oman 1983: KJ867544). This genetic bank is indispensable in tracing the viral lineages involved in PPR epizootics.

A history that remains incomplete

The evolutionary history of PPRV is a recent phenomenon that has unfolded rapidly. A molecular biology study published in the journal, *Emerging Infectious Diseases*, in December 2014 found that the most recent ancestor shared by the 4 PPRV lineages dated back to the beginning of the 20th century, a few dozen years before PPRV was identified and recognized as being distinct from the rinderpest virus. Lineage III, today present in East Africa and the southern part of the Arabian Peninsula, diverged first, followed by lineage I. Lineages II and IV separated more recently.

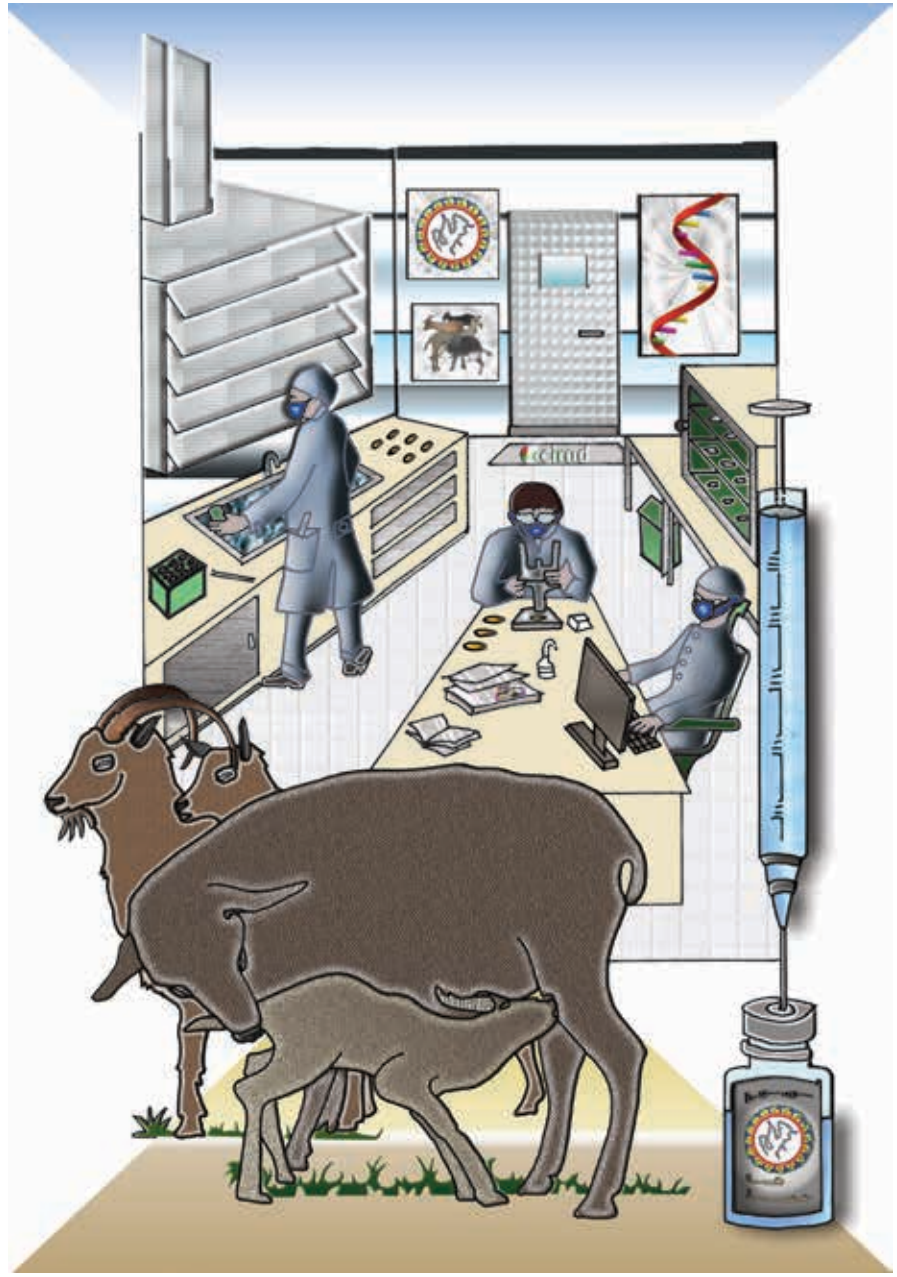
Phylogeographic analyses confirm that lineages I and III are linked to Africa. Lineage I likely originated in Senegal, lineage II in Nigeria, lineage III in Sudan, and Asian lineage IV probably in India. These results are consistent with epidemiological knowledge of the disease and suggest that PPR was introduced into West and East Africa as commercial trade and transhumance movements intensified.

The demographic analysis of PPRV confirms the genetic stability of viral lineages up to the mid-1990s, followed in the 2000s by increased genetic diversity reflected in the occurrence of numerous epizootic outbreaks in endemic countries, the incursion of the virus into previously disease-free countries, and the rapid adaptation of certain lineages through mutation. The use up to the 1990s of a heterologous attenuated rinderpest vaccine to fight PPR in small ruminants may have slowed the genetic evolution of the virus, limiting its genetic variability and potential to spread.

Several facets of PPRV's history remain unknown, notably the moment that it adapted to small ruminant populations. However, ongoing research into its genome is opening new avenues that could facilitate understanding of the factors behind the disease's emergence and spread.

"The disease is at the gates of Europe. Our strategy is systematic vaccination. An effective, universal, inexpensive vaccine exists."

Bernard Vallat - OIE Director-General, 2014



In the field

Clinical diagnosis

Suspicion of PPR is based on a combination of several clinical signs that should alert livestock farmers, notably fever associated with nasal discharge and lacrimation, which appear suddenly in several small ruminants in a herd. However, these three elements are not enough to establish a diagnosis because they are not specific to PPR. They also are expressed in other pathologies of small ruminants present in PPR endemic areas such as contagious ecthyma and contagious caprine pleuropneumonia.

A rigorous differential comparison of symptoms and the careful inspection of all animals in a herd are thus critical to assemble all of the clinical and lesional clues which are not all always visible on a single individual. Depending on the breed, species, age and immune status of animals, the disease can take different clinical forms within the same herd. This poses additional difficulties for untrained farmers trying to identify the disease, especially if PPR is accompanied by confusing secondary infections such as respiratory pasteurellosis.

The occurrence at the herd level of outside events considered to be risk factors must be taken into account and can reinforce the suspicion of PPR. This global analysis of the epidemiological situation is very important in disease-free areas where the risk of disease emergence is high.

Post-mortem diagnosis

Post-mortem examination of animals with the macroscopic observation of characteristic tissue lesions on digestive, respiratory, and lymphoid organs will confirm the provisional clinical diagnosis. It will only be definitive following the laboratory examination of samples drawn from living animals (blood samples, swabs of nasal and ocular secretions, scraping of gingival mucosa) and dead animals (tissue fragments from lungs, intestines, lymph nodes and spleen) to discover the direct or indirect presence of the virus.

"My neighbours and I have all lost our goats. I took a loan from an NGO to get medicines. Three fifths of the animals in the area are dead despite peoples' efforts to protect them."

A villager - Democratic Republic of the Congo, 2008

Laboratory diagnosis

Simple, rapid and reliable laboratory methods have been developed over the past 30 years and are routinely used today to confirm the field diagnosis. They rely on different enzyme-linked immunosorbent assay (ELISA) tests to detect antibodies and antigens in biological samples, and on Polymerase Chain Reaction (PCR) molecular biology techniques to detect the virus genome.

Serological diagnosis

Competitive ELISA is the leading serological diagnostic test. The method is known for its simplicity, specificity, and capacity to test a large number of samples in a short period of time (results in 2 hours) because it can be automated. It is well suited for emergency situations and provides reliable results even when sterile conditions have not been strictly respected. It operates by detecting traces of the virus in an animal's serum through the presence of PPR antibodies; it does so by putting viral N and H antigen proteins into competition with monoclonal anti-N and anti-H antibodies.

The method is used in serological surveys to assess the prevalence of PPR antibodies in herds while taking into account the individual characteristics of the animals (age, breed, species, sex). It allows the early detection of virus circulation in a geographic area in the absence of all clinical signs, and even before virus isolation. In the absence of any vaccination campaign, the seropositivity of an animal is an indicator of its contact with the pathogen and its natural immunity.

With this indirect diagnosis of PPR based on antibody detection, it is possible to assess and update the epidemiological situation of PPR in a region or a country, follow its spread dynamics in space and over time to identify at-risk zones, and characterize the factors explaining its variability. These are all highly useful indicators for the implementation of a vaccination-based PPR control strategy.

Different competition ELISA tests are available and are sold as kits, and their performance is regularly improved through technical innovations. CIRAD developed a competition ELISA (ID Screen® PPR Competition) in collaboration with a private partner (ID.vet, Montpellier) based on the N nucleoprotein, the most transcripted because its gene is first on the RNA molecule.

The anti-N antibodies produced by the infected animal consequently are the most abundant antibodies in the serum and therefore are the focus of serological analyses even though they do not provide any protection. This test was validated by the OIE as an alternative to the viral seroneutralization test, or VNT, which is more stringent (requires cell cultures, manipulation of the live virus, and sterile serums), and time consuming (results in 2 weeks). VNT nevertheless remains the method prescribed by the OIE, and is used in reference laboratories to confirm results and for the international trade of animals. The competition ELISA developed by The Pirbright Institute targets the anti-H antibodies.

Virological diagnosis

Proof of the presence of PPRV in samples is provided by direct diagnostic methods. They are based on the identification of antigen proteins, the identification of viral genetic material, or the isolation of the virus itself.

The detection of antigen proteins in tissue samples and secretions of infected animals uses variations of the ELISA technology: sandwich ELISA and immunocapture ELISA. A sandwich ELISA diagnostic kit (ID Screen® PPR Antigen Capture) based on anti-nucleoprotein monoclonal antibodies developed by CIRAD is now marketed by the company, ID.vet (Montpellier, France).

Through an industrial partnership, CIRAD also has developed a prototype rapid diagnostic test (pen-side test) using immunochromatography (Lateral Flow Device) for the detection of viral antigens. Currently in the process of being validated, it will offer countries in the South a diagnostic tool which is easy to use in the field and provides an immediate reading (several minutes) of results. Other similar tests have been developed by other laboratories (for example, The Pirbright Institute). For the time being, these tests have not yet been widely used in the field.

The detection of viral genetic material relies on molecular biology techniques. One used routinely in numerous laboratories is the standard RT-PCR technique (Reverse transcription - Polymerase Chain Reaction). It is specific, rapid, and very sensitive, but requires specialized equipment and very careful implementation to obtain reliable results. After viral RNA is extracted, the technique involves two steps. In the first step, reverse transcription converts the viral RNA into complementary DNA (cDNA). In the second step, polymerase DNA is used for the exponential amplification of a nucleotide sequence framed by specific primers located on the gene of either the N protein, which is the most abundantly transcripted, or the F protein.

This gene amplification reaction permits the sequencing and genotyping of the virus by identifying its lineage. It allows phylogenetic and phylogeographic studies to be conducted which are indispensible for the epidemiological monitoring of PPR and an understanding of the movements of the virus.

Standard RT-PCR cannot be automated. Real-time RT-PCR, also known as quantitative RT-PCR (QRT-PCR), is today used in high capacity (in terms of numbers of samples) reference laboratories for surveillance and screening. Its results allow the rapid identification of the virus strain involved in an outbreak, but it cannot be used in epidemiological studies. A variation is the RT-LAMP (Loop mediated isothermal amplification technique), which is based on a polymerase chain reaction at a constant temperature. It was adapted by the FAO and International Atomic Energy Agency (IAEA, Vienna, Austria) into a molecular diagnostic field kit for rapid screening (under one hour). While the confirmation of results by a reference laboratory remains necessary, this mechanism, which was tested in Cameroon in 2012, is an example of a technological innovation helping veterinarians in countries in the South which can speed up the implementation of control measures aiming to curtail the spread of the disease.

"Previously, I had to collect samples and then return to my laboratory or wait for samples to be sent to me from the field. It sometimes took weeks, or even an entire month, to be able to test the samples and confirm an outbreak."

A veterinarian - National Veterinary Laboratory (LANAVET), Cameroon

Virus isolation through cell cultures is indispensable for the precise molecular characterization of a virus strain. Specimens taken from animals must be of good quality in order for the viral particles to remain alive and infectious. Only qualified laboratories are able to use this technique, which is long (1 to 2 weeks) and cumbersome. Virus isolation is done after the virus is injected into primary sheep kidney or lung cells or into Vero cells (green monkey kidney cells). In the past few years, the use of transgenic cells expressing on their surface the SLAM receptor protein, CD 150 of PPRV, has considerably reduced the time required for virus multiplication. The virus strains obtained are referenced in a strain bank that is very useful for epidemiological studies.

Old but still valid

After unfruitful attempts in the 1960s to develop a live attenuated PPR vaccine, the decision was made to use the existing rinderpest vaccine. The close antigenic and immunogenic properties of these two morbilliviruses were expected to give small ruminants vaccinated against rinderpest a broad immunity against the PPR virus. This heterologous vaccine also had the advantage of being inexpensive due to the large scale production of the rinderpest vaccine for cattle.

It was used up to 1989, when CIRAD (Diallo *et al*.) and The Pirbright Institute released a homologous attenuated virus vaccine obtained through the successive passage in cell cultures (Vero cells or green monkey kidney cells) of a PPRV lineage II strain, 75/1, isolated in Nigeria in 1975. Its genetic sequence, referenced as X74443, is available in the GenBank. Without risk for pregnant females, it provides immunity for at least three years, which covers the usual economic life of a goat or sheep. Protection becomes effective 14 days after a single injection. At the time, its adoption presented the advantage of not interfering in the epidemiological cycle and serological surveillance of rinderpest while providing small ruminants cross protection against this disease.

In 1998, the OIE approved its adoption in PPR vaccination campaigns. In parallel, the continued use of the heterologous vaccine was prohibited to avoid introducing a bias into epidemiological studies of rinderpest. Although other vaccines used in India were developed from lineage IV PPRV strains (Sungri 96, Arasur 87 and Coimbatore 97), it is today the most widely used vaccine worldwide, recommended by the OIE for the vaccination of small ruminants.

In 25 years, it has proved its safety, effectiveness independent of the viral lineage involved, and low large-scale production costs. The mass vaccination campaign undertaken in 2008 to contain the PPR epizootic in Morocco is an illustration: 25 million doses of vaccine were produced in several weeks by the Moroccan laboratory, Biopharma based on the parent strain, Nigeria 75/1, which was provided by CIRAD, and over 20 million sheep were successfully vaccinated.

A preventive vaccine is administered before the emergence of the disease. The animal reacts by producing antibodies that neutralize the virus.

A curative or therapeutic vaccine is administered when the disease has occurred. It acts to restrain the virus from multiplying.

As for all morbilliviruses, the weak point of the vaccine is sensitivity to heat. In countries in the South, it is not always easy to maintain the cold chain during vaccination campaigns. Experiments to achieve thermal stability by associating a cryoprotectant containing trehalose or tris-trehalose have succeeded in prolonging its half life of several hours to 21 hours at 37°C after reconstitution, and up to 14 days at 45°C in a freeze-dried state.

Its other drawback in the framework of a PPR control program is that it does not allow a vaccinated animal to be serologically distinguished from an animal that was naturally infected by the virus. Over the last dozen years, advances in the field of molecular genetics have opened new research avenues for its improvement. One is looking into the development of recombinant vaccines. Another, one promising for the fight against viral diseases, is directed at developing therapeutic antivirals

New generation vaccines

The attenuated vaccine expresses the same antigens as the wild virus. It is therefore impossible from a serological point of view to recognize if the antibodies are the result of vaccination or infection. To remove this constraint, for the past twenty years several international scientific research teams, including that of CIRAD, have been trying to obtain DIVA vaccines (Differentiation of Infected and Vaccinated Animals).

There is no question that such vaccines would benefit areas in the South where the disease is endemic. They allow both the circulation of the virus and the effectiveness of vaccination campaigns to be monitored. Under the framework of the PPR eradication program, the use of an attenuated DIVA vaccine represents a saving of time and money in epidemiological surveillance by also allowing targeted vaccination.

The same holds true for countries which are currently disease-free, such as those in the European Union, where the risk of the introduction of seropositive animals cannot be dismissed given the intensity of global trade and the rapid geographic spread of PPR over the past few years. To be able to identify the disease status, vaccinated or infected, of a small ruminant renders it possible to avoid the precautionary mass culling of animals, which is no longer acceptable to civil society. From an economic and social perspective, it also is a means for countries to prove the absence of infection, a way of ensuring the uninterrupted cross-border circulation of goats and sheep, and a tool to guarantee disease-free countries the maintenance of their PPR-free status once it has been accorded by the OIE.

These DIVA vaccines can be recombinant vector vaccines able to express foreign genes. The viruses of the *Capripoxvirus* genus, large DNA viruses of the *Poxviridae* family, are known as to be excellent vaccine vectors. Thanks to molecular genetics tools, they are used as "Trojan horses" to carry antigens into the vaccinated animal and induce an immune response. Their genetic plasticity renders them able to express different antigens without affecting their replication. A recombinant capripox/PPR vaccine was obtained by inserting into the genome of an attenuated capripox strain the F or H genes of the external membrane glycoproteins of PPRV, which are those which induce a host immune response. The operating principle of these DIVA vaccines is simple. With appropriate diagnostic tests based, for example, on the N nucleoprotein of PPRV, it is possible to distinguish a vaccinated animal, which would be seronegative with the N-PPR test, from an infected animal, which would be seropositive using the same test.

The other advantage of this bivalent capripoxvirus-PPR vaccine is to provide in a single vaccination, and thus at less cost, good immune protection against these two important diseases of goats and sheep, sheep and goat pox and PPR, which are endemic in the same geographic areas. This recombinant vaccine is furthermore heat resistant. Trivalent recombinant vaccines have been developed associating three diseases: capripox, PPR, and Rift Valley fever.

Other DIVA vaccines are marked recombinant vaccines obtained by the deletion (loss), substitution, or insertion of genes or gene fragments in the virus genome thanks to negative RNA virus manipulation and reverse genetic technologies. These allow an infectious clone of the vaccine virus carrying a mark distinguishing it from the parent strain to be obtained in vitro. Research undertaken over the past few years is seeking to obtain a PPR DIVA vaccine based on the genetic recombination of the current Nigeria 75/1 vaccine strain, which does not allow infected animals to be distinguished from vaccinated ones.

Until recently, no infectious clone of the PPR vaccine virus could be generated, although positive results were obtained with other morbilliviruses like the rinderpest, measles, and distemper viruses. However, this step was successfully completed in 2012 and a patent (FR 1257980) filed by CIRAD now protects a marked PPR vaccine strain obtained by the addition and substitution of an epitope (immunogenic sequence of nucleotides) on the N nucleoprotein. Today, research continues into the development of a vaccine virus PPRV 75/1 with a double marker and the refinement of suitable diagnostic tests. This future DIVA vaccine will be very useful during vaccination programs under the framework of a PPR eradication program.

Towards new antivirals

As for all viral disease, there is no specific therapeutic treatment against PPRV. Medical treatments based on antibiotics limit the effects of secondary respiratory infections but do not target the virus. They provide relief to the animal but their results are unpredictable and their cost high from the perspective of animal production. For the same essentially economic reasons, there is no veterinary antiviral curative treatment to fight against the disease in an infected animal. The only treatments used are preventive vaccinations.

However, when this antiviral therapeutic strategy is part of an approach to eradicate the disease and fight poverty, the economic investment involved becomes more acceptable. This is the rationale underlying CIRAD's research on biological antivirals. As a PPR reference laboratory, its approach is to develop a curative PPR vaccine by using a molecular genetic technique, RNA interference.

Discovered in the 1990s, this natural biological mechanism allows living animal and plant organisms to inhibit and consequently control the level of expression of their genes. It sets in play short RNA fragments, the interfering RNA or siARNs (small interfering RNA), which are capable of stopping the reading and translation of the genetic code into proteins. By bonding to the messenger RNA, they lead to its degradation and the inhibition of the corresponding protein. This mechanism also applies to the expression of viral genes.

In 2005, researchers at CIRAD identified and patented (FR 0513029) three synthetic siARNs able to inhibit over 80% of the in vitro replication of the PPR virus. Different in vivo delivery systems of these siARNs are being evaluated to assess their effectiveness and safety in a non-infectious "mouse" model based on bio-imagery. Research currently is focusing on assessing the risk of the emergence of resistant mutant PPRV strains which escape the inhibition of these siARNs. This step is indispensable for the development of reliable and effective therapeutic vaccines. They represent major progress in the fight against animal and human viral diseases for which there is only a preventive vaccine.

The economic impact remains under-estimated

Since 2004, the FAO and OIE have recognized PPR as one of the five most damaging transboundary diseases in Africa, Asia, and the Middle East for small ruminant production and poverty alleviation efforts. The health effects of the disease are now well known. However, few quantified studies have examined PPR's economic and social consequences. Assessments undertaken in several countries during epizootics reported considerable losses with an order of magnitude of several tens to several hundreds of millions of US dollars.

In 2010, the FAO estimated that a PPR epizootic which raged through two regions of Tanzania caused losses amounting to US$ 67.9 million. In just one year, more than half of the herds contracted the disease and households lost 72% of their livestock. Their loss in terms of animal deaths and reduced income was calculated to be US$ 490 per household. In Turkana district, Kenya, production losses rose to US$ 2.4 million between 2006 and 2008. In Pakistan, the annual negative impact of PPR was estimated at US$ 342 million.

In 2012, a GALVmed (Global Alliance for Livestock Veterinary Medicines) study estimated the annual losses caused by PPR in South Asia to be US$ 3 billion, half of which were production losses. This handful of examples demonstrates that the cost and socio-economic impact of PPR epizootics are particularly high for farmers and village communities, but also for national and regional economies.

"Small ruminants represent a high percentage of economic growth potential for the future. By targeting investments on small ruminants, the poorest farmers, in particular women, are reached."

Bernard Vallat – OIE Director-General, 2012

The incidence of PPR results in:

- *direct financial losses linked to animal mortality, which can reach up to 100%, and a drop in their production potential (weight loss, lower reproductive capacity, reduced milk production).*
- *indirect financial losses linked to the lower value of surviving animals, reduced genetic heritage, restrictions on movements and sales, and veterinary expenditures made to fight the disease.*

The presence of the disease in countries around the Mediterranean, and its rapid geographic extension over the past few years in both Africa and Asia, where a large 2013 epizootic in China endangered over 216 million heads of goats and sheep, demonstrate the urgent need to develop and launch national, regional and global programs to control this hitherto neglected disease.

"Before, I could sell my goats, but that is no longer possible. A healthy goat use to sell for 3000 Kenyan schillings (US$ 50), but the price has fallen to 300 Kenyan schillings (US$ 5) in some regions."

A villager - Kenya, 2008.

Components of the control of PPR

Disease-related factors

Positive elements

- A single serotype.
- Virus transmission through direct contact.
- The virus is infective for only a short period outside a host.
- No prolonged carrier state after infection.
- No currently known animal reservoir outside domestic small ruminants.
- Existence of sensitive and specific diagnostic tools.
- Existence of a safe and effective vaccine that can be used against all of the viral lineages, confers life-long immunity with a single dose, and is inexpensive to produce.

Innovations soon to be available:

- A bivalent thermostable vaccine (PPR and sheep/goat pox).
- Rapid tests that can be used in the field.
- A new generation vaccine inducing the production of antibodies that differ from the antibodies produced through natural infection.

Constraints

- The rapid turnover of small ruminant populations, which maintains a population of susceptible animals.
- Local and cross-border mobility of animals (intensity of trade, transhumance).
- Differences in susceptibility and receptivity depending on breed and species.

Questions

- Clarify the role of dromedaries, wildlife, and bovine animals in the PPR epidemiological cycle.
- Understand virus population dynamics and the determinants of virulence.
- Develop a dynamic map of trade and transhumance routes for each country.
- Identify control measures adapted to the epidemiological situation (enzootic country, disease-free country at high risk, disease-free country), different livestock systems and herd management practices, and the socio-economic context.
- Determine the appropriate vaccination strategy (when to vaccinate? how often? vaccinate which animals? vaccinate dromedaries?).

Cross-cutting factors

- An effective organization of national veterinary services with technical and financial support to strengthen their surveillance, diagnostic, and disease control capacities.
- Strong coordination within well-structured, regional and sub-regional epidemiological surveillance networks.
- Strengthening laboratory production and quality control capacities to produce a sufficient quantity of high quality vaccines meeting international and OIE standards and the creation of regional vaccine banks in Africa and Asia.
- Training, sharing information and experience among actors and the local management of control programs based on partnerships between livestock farmers, community animal health workers, veterinarians, laboratory personnel and research and development experts.
- The existence of regularly updated roadmaps specific to each sub-region in Africa (5), the Middle East (1) and Asia (3) to provide a global strategic framework for the progressive control of PPR.
- Political support, financial commitments, public-private partnerships and strong coordination between international, regional, and national institutions and bodies.

"My goats are not sick and I do not know anything about this disease but I was told that I should get my animals vaccinated so they do not get sick. So I came.

We are a family of 7. We do not own land and we do not cultivate anything ourselves. We only have Allah. Sometimes we sell a young goat so we can buy what we need."

An old woman - Yemen, 2013

Progressive control through vaccination

Despite a lack of data on the socio-economic impact of PPR epizootics, cost of control measures to be set up, and expected benefits, it is certain that the loss of small ruminant livestock fuels poverty and impedes rural development in the countries in the South where the disease is present. This situation should be sufficiently convincing to obtain the political and financial support of governments and international donors for a global PPR eradication mechanism. The control of the PPR epizootic in Morocco in 2008 through a national, multi-annual, mass vaccination campaign of goats and sheep effectively demonstrated that its eradication is possible.

"Animal health is a priority for the modernization of livestock farming. Every year, we lose thousands and thousands of small ruminants because the animals have not been vaccinated against the peste des petits ruminants."

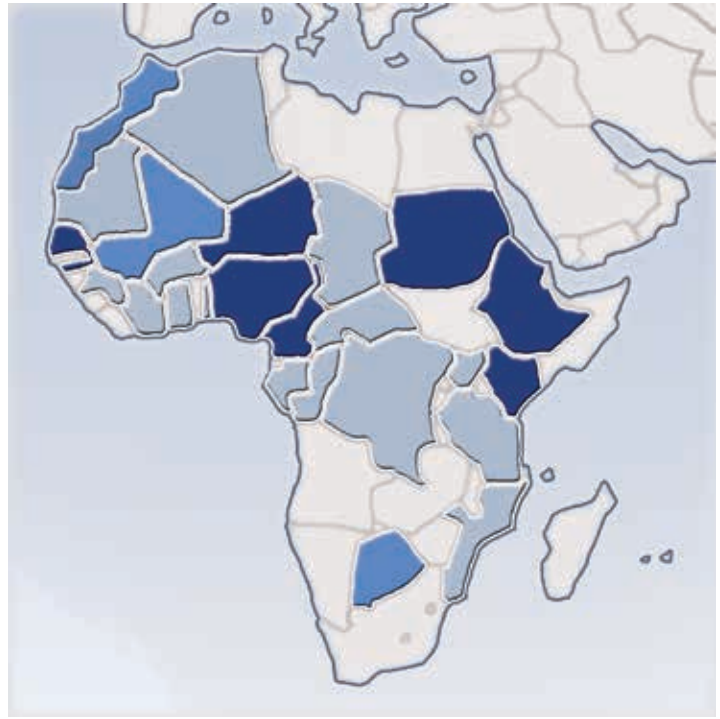
Minister of Livestock and Production Animals - Senegal, 2014

Vaccination campaigns are regularly conducted at the local and national level of various countries infected by PPR, but these initiatives are not coordinated and remain limited in scope. To harmonize efforts and increase their effectiveness, the FAO and OIE have worked to develop a specific strategy for the control of PPR through vaccination. It is designed to be coordinated at the regional and global level, and is based on the production of high quality vaccines by accredited laboratories with facilitated access for all countries thanks to the establishment of vaccine banks, and on national mass vaccination campaigns combined with measures to assess the results of these campaigns. If this strategy is implemented, the expected result is the global eradication of the disease within the next 15 years, but in certain countries and regions, eradication could be achieved even more rapidly, in about 5 years. The challenge now is to convince financial partners to support this initiative.

Vaccine banks

These are based on a concept developed by OIE to set up virtual rolling stocks of vaccines. When there is an emergency, this system enables a sufficient quantity of vaccines meeting international quality standards to be supplied to infected countries. The vaccine banks also set the stage for countries to gradually assume ownership of control programs and implement them effectively.

Diagnostics and vaccine production in Africa



Diagnostic tests and vaccine production at the national level.
Cameroon, Ethiopia, Kenya, Niger, Nigeria, Senegal, Sudan

National production of live attenuated vaccines.
Botswana, Mali, Morocco

Diagnostic tests available in animal health laboratories.
Algeria, Benin, Burkina Faso, Congo, Ivory Coast, Gabon, Ghana, Guinea, Mauritania, Mozambique, Uganda, Tanzania, Chad, Central African Republic, Democratic Republic of the Congo

Some constraints on vaccination: Free expression in Burkina Faso

The shortage of veterinarians and vaccinators

"What works well is when even goats and sheep are vaccinated, the animals stay healthy. What does not work well is when the veterinarian gives injections on just one day in the village."

"Many animals never were vaccinated because the veterinarian only gave vaccinations in the village on a single day."

"It is hard to get treatment from the veterinarian because if not many animals are sick, he often does not come out to us. When that happens, we have to bring our animal in to get care."

"The veterinarians told themselves that the Peulh herders have more sheep and goats than we do, so they went out to the Peulh."

The organisation of vaccination operations

"We farmers do not like it when the vaccinations are given in a pen with all the animals grouped together; it is true that it makes the job easier for the vaccinator, but it doesn't work for me."

"Going door-to-door makes it possible to vaccinate more small ruminants; it is not possible to group small ruminants together to vaccinate them the way you can with cattle."

The choice of the vaccination period

"The vaccination period for sheep and goats is not good because it falls when it is hot."

"Shots against diarrhoea should be given to sheep and goats in October-November because that is when there are cases of diarrhoea."

"Injections should be given to sheep and goats in the months of August-September before the disease breaks out."

The packaging of vaccines

"Packaging the vaccine in a 100-dose vial is not adapted to the size of our livestock farms... once a vial is opened...it gets thrown away when there are less than 100 animals."

The choice of communication channels and the importance of relations of confidence

"The one who tells the farmers should be their president, he knows the farmers in the village, so the information is sure to get passed on."

"The town crier provided the information about the vaccination."

"The farmers' president gave me the information about vaccinating sheep and goats."

"I got the information about vaccinating sheep and goats in the market from farmers from another village who had already vaccinated their animals."

"What works is the announcement of information at ceremonies, telephone calls, door-to-door vaccination campaigns."

2030: a world without PPR?

It took over 50 years to eradicate rinderpest through 5 consecutive international programs. The first program began in 1962; the last, GREP (Global Rinderpest Eradication Program), ended in 2011. Such a long period of time was required due to the obstacles encountered during this first attempt to eradicate an animal disease. However, the dynamic created by its success, the lessons learned and the infrastructure set up are an incentive and a springboard for the international health organizations, FAO and OIE, to develop and implement a coordinated global strategy for the progressive control and eradication of PPR and to make this one of the priorities of the GF-TADs (Global Framework for the progressive control of Transboundary Animal Diseases).

This global strategy will be officially presented in March 2015 by the FAO and OIE.

It will be implemented at the global level in three 5-year stages, but the time frame in each region and country will vary according to its epidemiological situation and capacity to implement prevention and control measures.

The strategy is based on a succession of four steps. An initial assessment of the epidemiological situation is followed by disease control, essentially through vaccination, and then the actual eradication of the disease through intensified control measures. The last step aims to ensure that the virus has ceased to circulate, notably through post-eradication epidemiological surveillance.

This allows countries to engage in an official procedure set up by the OIE in March 2014 to recognize their disease status in relation to PPR. Obtaining the disease-free status will encourage countries affected by PPR to implement preventive sanitary and medical measures to fight this disease. In 2015, 48 member countries historically free of PPR, including the countries of Europe, figured on the OIE list of PPR-free countries.

"Actions against animal disease are not based on a concept of agricultural or commercial goods, but on global public goods. In effect, they serve the interests of all people and all generations by reducing poverty, contributing to public health and food security."

Bernard Vallat - OIE Director-General, 2011

• Scientific opinion on peste des petits ruminants. EFSA Panel on Animal Health and Welfare. - *EFSA Journal*, 2015, 13(1), 94 p.

• Evolutionary genetics underlying the spread of peste des petits ruminants. Libeau G., Diallo A., Parida S. - *Animal Frontiers*, 2014, 4(1), p. 14-20.

• Peste des petits ruminants virus infection of small ruminants: a comprehensive review. Kumar N., *et al.* - *Viruses*, 2014, 6(6), p. 2287-2327.

• Molecular evolution of peste des petits ruminants virus. Muniraju M. *et al*. - *Emerging Infectious Diseases*, 2014, 20(12), p. 2023-2033.

• Peste des petits ruminants virus, Mauritania. El Arbi A.S. *et al*. - *Emerging Infectious Diseases*, 2014, 20(2), p. 334-336.

• Role of wild small ruminants in the epidemiology of peste des petits ruminants. Munir M. - *Transboundary and Emerging Diseases*, 2014, 61(5), p. 411-424.

• Peste des petits ruminants. Wallingford : CAB International, 2013, 20 p. Animal Health and Production Compendium.

• Peste des petits ruminants virus. Munir M. – *In* : Mononegaviruses of veterinary importance. Vol. 1: Pathobiology and Molecular Diagnosis. Wallingford : CAB International, 2013, p. 65-96.

• FAO, OIE, IAEA. Workshop on PPR prevention and control, Dar-es-Salaam (Tanzania), 10-12 June 2013.
- PPR situation worldwide. Domenech J. - p.19-21.
- Understanding virus lineage evolutions, gaps and challenges, research priorities. Diallo A. - p. 22-23.
- Laboratory diagnostic and molecular epidemiology of peste des petits ruminants. Libeau G. - p. 38.

• Supporting livelihoods and building resilience through peste des petits ruminants (PPR) and small ruminants diseases control. Rome : FAO, 2013, 16 p. FAO Animal Production and Health Position Paper.

• Peste des petits ruminants, the next eradicated animal disease? Albina E. *et al.* - *Veterinary Microbiology*, 2013, 165(1-2), p. 38-44.

• Update on PPR epidemiology, diagnosis and its control. Couacy-Hymann E. - *Revue Africaine de Santé et de Productions Animales*, 2013, 11(5), p. 59-65.

• Peste des petits ruminants infection among cattle and wildlife in Northern Tanzania. Lembo T. *et al*. – *Emerging Infectious Diseases*, 2013, 19(12), p. 2037-2040.

• Analysis of small ruminants' pastoral management practices as risk factors of peste des petits ruminants (PPR) spread in Turkana District, Kenya. Kihu S.M. *et al.* - *Research Opinions in Animal and Veterinary Sciences*, 2013, 3(9), p. 303-314.

• Un transfert de technologie réussi pour le contrôle de la peste des petits ruminants. Bonnet P., Lancelot R., Libeau G., Saint Martin G. - Montpellier : CIRAD, 2013, 2 p.

• RNA interference against animal viruses: How Morbillivirus generate extended diversity to escape small interfering RNA control. Holz C.L., *et al*. - Journal of Virology, 2012, 86 (2), p. 786-795.

• Des moyens de lutte efficace contre la PPR. Vaccin adapté et mobilisation nationale. Libeau G., Bonnet P. - Montpellier : CIRAD, février 2012, 2 p.

• Spécificités de la santé animale en régions chaudes : le cas des maladies infectieuses majeures en Afrique. Lancelot R., Zundel E., Ducrot C. – *INRA Productions Animales*, 2011, 24(1), p. 65-76.

• Asian lineage of peste des petits ruminants virus, Africa. Kwiatek O. *et al*. - *Emerging Infectious Diseases*, 2011, 17(7), p. 1223-1231.

• Global distribution of peste des petits ruminants virus and prospects for improved diagnosis and control. Banyard A.C. *et al*. - *Journal of General Virology*, 2010, 91(12), p. 2885-2897.

• Origin of measles virus: divergence from rinderpest virus between the 11th and 12th centuries. Furuse Y., Suzuki A., Oshitani H. - *Virology Journal*, 2010, 7(1), p.52.

• An outbreak of peste des petits ruminants (PPR) in camels in the Sudan. Khalafalla A.I. *et al.* - *Acta Tropica*, 2010, 116(2), p. 161-165.

• Infections à *Morbillivirus* chez les ruminants : la peste bovine en voie d'éradication et la peste des petits ruminants en extension vers le Nord. Minet C. *et al*. - *Virologie*, 2009, 13(2), p. 103-113.

• Analyse quantitative du risque d'introduction de la peste des petits ruminants en France. Miller M. *et al.* - *Epidémiologie et Santé Animale*, 2009, 56, p. 217-226.

• Le point sur l'épizootie de peste des petits ruminants au Maroc en 2008. Dufour L., Dufour B., Libeau G., Diallo A. - *Epidémiologie et Santé Animale*, 2009, 56, p. 243-248.

• La peste des petits ruminants : une maladie longtemps ignorée. Diallo A. - *Bulletin de l'Académie Vétérinaire de France*, 2008, 161(3), p. 273-277.

• The threat of peste des petits ruminants : progress in vaccine development for disease control. Diallo A. *et al*. - *Vaccine*, 2007, 25(30), p. 5591-5597.

• Evaluation of the virulence of some strains of peste des petits ruminants virus (PPRV) in experimentally infected west african dwarf goats. Couacy-Hymann E. *et al.* - *Veterinary Journal*, 2007, 173(1), p. 178-183.

• Control of peste des petits ruminants and poverty alleviation? Diallo A. - *Journal of Veterinary Medecine*, Series B, 2006, 53(special issue), p. 11-13.

• Rinderpest and peste des petits ruminants. Virus plagues of large and small ruminants. Barett T., Pastoret P.P., Taylor W.P. - Londres : Academic Press/Elsevier, 2005, 341 p.

• Detection of antibodies of rinderpest and peste des petits rumiants viruses (*Paramyxoviridae*, *Morbillivirus*) during a new epizootic disease in Ethiopian camels (*Camelus dromedarius*). Roger F. *et al.* - *Revue de Médecine Vétérinaire*, 2001, 152(3), p. 265-268.

• La peste des petits ruminants. Lefèvre P.C., Diallo A. - *Revue Scientifique et Techniques de l'OIE*, 1990, 9(4), p. 935-950.

• Classification of peste des petits ruminants virus as the fourth member of the genus *Morbillivirus*. Gibbs E.P.J. *et al.* – *Intervirology*, 1979, 11(5), p. 268-274.

• La peste des petits ruminants au Sénégal. Données nouvelles. Bourdin P., Doutre M.P. - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1976, 29(3), p. 199-204.

• Note sur la structure du virus de la peste des petits ruminants. Bourdin P., Laurent Vautier A. - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1967, 20(3), p. 383-386.

• La peste des petits ruminants en Afrique occidentale française. Ses rapports avec la peste bovine. Mornet P. *et al.* - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1956, 2(4), p. 313-342.

The United Nations Food and Agriculture Organization (FAO) strives to achieve a world free of hunger and malnutrition where food security and agriculture contribute to improving everyone's standard of living, in particular that of the poorest, in an economically, socially, and environmentally sustainable manner.

The three overarching objectives of FAO Member States are first to eradicate hunger, food insecurity, and malnutrition, progressively building a world in which everyone has regular access to sufficient, healthy, and nutritious food. This enables everyone to satisfy their food needs and preferences and lead active, healthy lives. The second objective is to eliminate poverty and promote social and economic growth for everyone by improving food production, encouraging rural development, and building sustainable livelihoods. The third objective is to ensure that natural resources, including land, water, air, climate and genetic resources, are managed and used in a sustainable manner for the good of present and future generations.

The FAO develops, collects, and shares crucial information regarding food, agriculture, and natural resources, which are all global public goods. The FAO plays a connector role by identifying and collaborating with different partners with established technical expertise, and by facilitating dialogue between those who hold knowledge and those who need it. By turning knowledge into action, the FAO links the field to national, regional and global initiatives within a mutually reinforcing network.

FAO: Via delle terme di Caracalla - 00100 Rome - Italie
Tel.: (+39) 06 57051 - Fax: (+39) 06 570 53152 - Web: www.fao.org

The World Organisation for Animal Health (OIE) is an intergovernmental organisation created in 1924 under the name, Office International des Epizooties, and has today 180 member countries. OIE manages the global animal health surveillance and early-warning system and plays a key role in the fields of veterinary science information and research. The peste des petits ruminants is on the list of 116 diseases of land and marine animals monitored by OIE, and is one of the priority diseases for which a global control and eradication strategy has been developed. OIE acts with the ongoing support of 296 reference laboratories and collaborating centres and 13 regional and sub-regional offices around the world.

OIE fulfils its mandate through the following activities: ensuring transparency in the global situation of animal diseases (including zoonoses); gathering and disseminating veterinary scientific information, notably disease prevention and control methods; ensuring sanitary safety of the world trade in animals and animal products (as the international reference organization for animal health under the framework of the World Trade Organisation SPS agreement, OIE develops standards for international trade in animals and animal products); defining and supporting the good governance of veterinary services; and promoting animal welfare.

OIE also works to reinforce policies promoting animal production, food security and poverty reduction, implement strategies to prevent and manage animal-human interface risks, and analyze the impact of climate and environmental change on the emergence and occurrence of animal diseases. Reinforced support for the improvement of the global quality of diagnostic and research laboratories, veterinary education, and veterinary statutory bodies bolsters OIE's actions in favour of good governance and the global reduction of biological risks.

OIE: 12, rue de Prony - 75017 Paris - France
Tel.: 33 (0)1 44 15 18 88 - Fax: 33 (0)1 42 67 09 87 - Web: www.oie.int

A public-sector financial institution, the French Development Agency (AFD) has worked for over 70 years to fight poverty and support sustainable economic growth in developing countries and French Overseas Provinces. AFD executes policies defined by the French government.

Active on four continents through a network of 71 agencies and representative offices, of which nine are in French Overseas Provinces and one in Brussels, AFD finances and supports projects working to improve people's living conditions, promote economic growth, and protect the planet.

In 2013, AFD dedicated €7.8 billion to finance projects in developing countries and in French Overseas Provinces. These funds will contribute, in particular, to educating children, improving maternal health, promoting equality between women and men, supporting farmers and small enterprises, and reinforcing access to water, energy and transportation. The newly financed projects also will contribute to fighting climate change, notably allowing a saving of 3.3 million tons of CO2 equivalent per year.

As a development bank, AFD is ready to support governments in their investment needs for the implementation of a global PPR control strategy in their countries.

AFD: 5, rue Roland Barthes - 75012 Paris - France
Tel.: 33 (0)1 53 44 33 99 - Fax: 33 (0)1 44 87 99 39 - Web: www.afd.fr

A public industrial and commercial enterprise, CIRAD is a French research centre under the joint authority of the Ministry of National Education, Higher Education, and Research and the Ministry of Foreign Affairs and International Development. A targeted research organisation, CIRAD bases its multidisciplinary scientific programs on development needs, from field to laboratory and from a local to a global scale. The challenge: to contribute to sustainable development in rural areas and agricultural sectors in developing countries with a particular focus on the world's poorest.

The joint research unit, CIRAD-INRA CMAEE (Emerging and Exotic Animal Disease Control), conducts integrated research aiming to improve surveillance, anticipation of emergence and spread risks, and prevention and control of animal and zoonotic diseases of economic and health importance for countries in the South, of which some are threatening countries in the North.

An OIE reference laboratory and FAO PPR reference centre, the unit is pursuing research on assessing epidemiological situations, studying the diversity of viral strains, characterizing these strains and the plasticity of their genome, developing new diagnostic and treatment tools and vaccines, and developing integrated control strategies. PPR is recognized by governments and international organisations as the leading infectious disease of small ruminants. Its progressive control and eradication will require an iterative definition of control methods and strategies based on interdisciplinary research outputs to which the unit is contributing.

CIRAD – Direction Générale: 42, rue Scheffer – 75116 Paris – France
Tel.: 33 (0)1 53 70 20 00 – Fax: 33 (0)1 47 55 15 30 – Web: www.cirad.fr

UMR CIRAD-INRA CMAEE - Campus international de Baillarguet
TA A-15 / A - 34398 Montpellier Cedex 5 - France
Tel.: 33 (0)4 67 59 39 04 – Web: http://umr-cmaee.cirad.fr/

Web: http://savoirs partages.cirad.fr/

Printed by:
SOULIÉ Imprimeur Frontignan
Legal deposit: 1st trimester 2015

Contributors

Authors:

Georgette CHARBONNIER, Géraldine LAVEISSIERE

in collaboration with:

Renaud LANCELOT, Thierry LEFRANÇOIS, Geneviève LIBEAU, Cécile MINET
UMR CIRAD-INRA CMAEE (Emerging and Exotic Animal Disease Control)

Joseph DOMENECH
OIE (World Organisation for Animal Health)

and with contributions from:

Michel LAUNOIS for the original illustrations and line drawings

and the support of:

Jacques PAGES
CIRAD Partnership Platforms Delegate
Scientific Adviser. French Permanent Representation to IFAD, FAO and WFP

Research, writing and coordination:

Georgette CHARBONNIER

Original graphic design and layout:

Géraldine LAVEISSIERE

Partnership relations:

Michel LAUNOIS

Translation into English:

Grace DELOBEL

Distribution:

Françoise CHIRARA

Published with the financial support of several institutional partners, this educational handbook on peste des petits ruminants is not meant for sale. It is meant to be distributed among diverse audiences with the aim of contributing to the dissemination of scientific knowledge and to supporting teaching projects reaching the greatest number of people possible.

© CIRAD 2015 - ISBN : 978-2-87614-698-3 - ISSN : 1620-0705

Peste
des petits ruminants

PPR

Based on an original idea of:

Service d'**A**ppui à la **V**alorisation **O**pérationnelle
de l'**I**nformation sur la **R**echerche **S**cientifique (SAVOIRS)

Cirad-Savoirs

Foreword

Peste des petits ruminants (PPR), a disease first described in 1942, often is compared to rinderpest, a disease officially declared eradicated in 2011. As the present handbook reminds us, this comparison is due, among other reasons, to the similarity of the clinical signs of the two diseases.

The first mention of rinderpest appears to date back to 3 000 B.C. The struggle against this terrible bovine disease led to the establishment of the first veterinary school in the world in 1761 in Lyon (France). Unlike rinderpest, which was able to affect all ruminants but was most devastating in cattle and buffalo, PPR, as its name indicates, is above all a disease of small ruminants.

Gargadennec and Lalanne gave this name after observing for the first time in 1940 a highly contagious disease which was similar to rinderpest but only afflicted goats and sheep. A similar observation was made in 1941 by another author, Cathou, in Dahomey, the present-day Benin. In 1955, the disease was described in Senegal, and during the 1960s, it was identified in Nigeria and Ghana.

For a very long time, almost up to the early 1980s, PPR was associated with West African countries. However, since the 1990s our understanding of its geographical distribution has evolved extremely rapidly. Today, the disease extends across Africa, from North Africa to Angola and Tanzania, through the Middle East, Turkey, and Central Asian countries, and up into China.

This distribution zone covers an area holding nearly 1.7 billion goats and sheep. It also includes regions with the highest proportion of poor small farmers in the world. The fight against PPR is consequently also a fight against poverty.

It is with this in mind that the FAO and OIE will, through a coordinated global plan of action, undertake a campaign to eradicate the disease. This goal could be achieved relatively rapidly if there is a political will to do so and the required financial resources are made available. In effect, the technical means which made possible the global eradication of rinderpest also are available for PPR: a highly effective vaccine and specific diagnostic tests. These are reviewed in this excellent handbook, one created by experts in the field, and which I hope will be widely distributed.

Berhe TEKOLA
Director
Animal Production and Health Department
United Nations
Food and Agriculture Organization

The identification in West Africa of peste des petits ruminants as a separate disease from rinderpest was a highly significant event in the history of infectious animal plagues.

Peste des petits ruminants was first described in 1942 in the Ivory Coast by Gargadennec and Lalanne as a disease affecting goats and sheep comparable to rinderpest, but which was not transmitted to bovine animals. This observation allowed them to conclude the existence of a disease similar but distinct from rinderpest which affected small ruminants. They called it the "peste des petits ruminants", today known by its acronym, PPR.

PPR is caused by a morbillivirus which is closely related to the virus responsible for rinderpest. Soon after it was described for the first time, the disease left its original birthplace to spread through Africa and invade Asia; it now covers major portions of both continents. It is thus very widespread, as attested by the handbook offered to us by CIRAD in its collection, "Les savoirs partagés®". PPR is a virulent and devastating disease with extremely negative consequences for the economy, food security, and livelihoods of livestock farmers, particularly in poor rural areas. It is considered to be one of the most important animal diseases in Africa, the Middle East, and Asia.

The eradication of rinderpest, which was officially declared in 2011 by the World Organisation for Animal Health (OIE) and the United Nations Food and Agriculture Organization (FAO), brought to the fore the importance of PPR and the need to fight the disease.

This is why these two organizations have organized an international conference on the control and eradication of PPR on 31 March to 2 April 2015 in Abidjan, Ivory Coast, the same country where the disease was first described, to present and adopt a global PPR control and eradication strategy.

The eradication of PPR will have major positive repercussions by guaranteeing the means of subsistence of millions of rural poor. It also will highlight the fundamental role played by veterinary services in the fight against poverty and the improvement of food security. On 30 May 2013, the General Assembly of the OIE adopted resolution n°30 indicating the procedure OIE member countries (now numbering 180) should follow to obtain official recognition of their PPR disease status. Through this procedure, member countries can be declared disease-free either over their entire territory or in certain areas.

The work presented by CIRAD is meant for a broad audience and will raise awareness about the most important concepts related to this disease.

I hope that this handbook will be widely distributed and I sincerely thank everyone who has participated in the project, in particular the authors and those who have collaborated with them, as well as those who have taken the initiative to publish it.

Bernard VALLAT
Director-General
World Organisation for Animal Health












From Neolithic times until today

Small ruminants, goats and sheep, are the descendents of wild ancestors which lived in the "Fertile Crescent", a Middle Eastern region straddling parts of modern day Turkey, Iraq and Iran. Goats descended from the wild goat (*Capra aegragus*) while sheep descended from the Urial (*Ovis orientalis*). They first began to be domesticated by early farmers-herders around 10 000 BC during the Neolithic period. Over the centuries, these animals remained an integral part of peoples' daily lives and accompanied them on their migrations, eventually spreading across the world to Europe, Africa, and Asia thanks to their extensive capacity to adapt.

Goats and sheep figure prominently in many mythologies and religions.

At present, there are over 200 breeds of goats and nearly 900 breeds of sheep in the world. A minority are reared in the North, where many local breeds have disappeared or are endangered, their place taken by animals bred to produce meat and milk. Countries in the South host a multiplicity of breeds adapted to their diverse living conditions, which include hostile desert and mountain environments, wetlands and temperate climate zones, and confined spaces in urban and peri-urban areas. Although sheep are more demanding than goats, the two species often are combined in mixed herds.

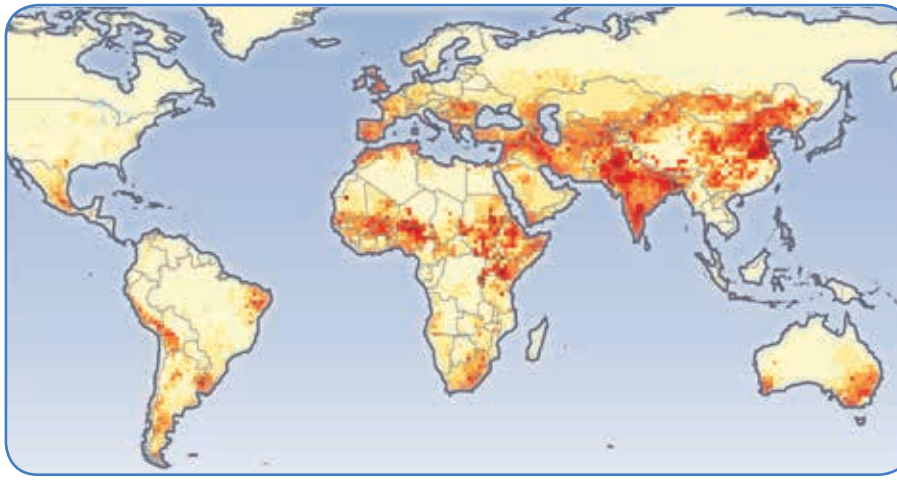
Small ruminants in the South

Goats and sheep do not enjoy the same status as cattle. They are seen as animals of the poor. Goats are even called "the poor man's cow". Compact, sturdy, and easy to handle, small ruminants are an integral part of the lives of the most disadvantaged populations in numerous countries in the South. They often are the sole resource available to farmers in areas unsuitable for other types of farming, and to impoverished rural migrants living on the outskirts of cities. Small ruminants are less demanding and cheaper to buy and maintain than cattle, and can survive on the sparse pastures of arid and semi-arid regions, sometimes supplemented with harvest by-products and food residues (vegetable peels, bran, meal scraps…).

By providing milk and meat for immediate home consumption, they provide families food security and meet their animal protein needs, particularly those of vulnerable individuals such as children, the elderly, and pregnant women. They also produce wool and hides and their manure contributes greatly to organic soil enrichment.

The majority of small ruminants are kept in rural villages and are raised in extensive production systems based on traditional agro-pastoral practices which rely on shepherds and herds moving to find water, pasture land, and salt cure areas. In Sahelian countries, they represent 30 to 40% of ruminant production. The movement of animals through nomadism and transhumance is today a risk factor in the spread of animal diseases.

Global distribution of sheep and goats (head/km^2)



FAO - Gridded livestock of the world (GLW) - 2014

< 1
1- 5
5 - 10
10 - 20
20 - 50
50 - 100
100 - 250
> 250

Along with poultry, goats and sheep are the main species kept by low income populations in the world. According to the FAO, in 2013 nearly 83% of the global small ruminant population was located in developing Asian and African countries. These countries hold 94% of the global goat population and nearly 73% of the global sheep population.

A piggybank for the poorest of the poor

In countries in the South, the key role played by small ruminants in the everyday lives of people living in rural villages and urban and peri-urban areas is now well recognized. These animals are a critical element in the fight against poverty. They contribute effectively to improving the livelihoods and economic self-sufficiency of vulnerable families.

With a low purchase price and production cost, small ruminants are considered to be a kind of live, short-term savings account which can be rapidly converted into cash to cover planned (school fees, religious festivals and family gatherings) and unplanned (health problems, poor harvest, funerals) expenses. Prolific breeders due to a short reproductive cycle of six months to one year, generations are rapidly renewed, increasing the size and value of the herd or flock. The animals thus constitute both a store of wealth and a source of regular income for families. There are no dietary, religious, or ethnic restrictions on their sale. According to the FAO, in 2013 their sale in humid and sub-humid regions represented respectively 30% and 80% of household incomes. In arid and semi-arid regions, these percentages were 17% and 58%. The amount is highest when the small ruminants involved are goats which continue to produce milk even in drought periods.

When climate conditions, conflict or disease lead to the loss of animals, the economic, nutritional, and social consequences for families are often dramatic. To address this vulnerability, numerous development and humanitarian assistance projects distribute small ruminants to refugees and village communities. Sometimes made possible by a micro loan or through a village animal bank, the grant of one or several small ruminants constitutes a first step out of social exclusion and food and nutritional insecurity. However, small ruminant husbandry will only secure the livelihoods of these populations if support measures ensure that the animals are maintained in good health.

According to the FAO, out of a population of 5.5 billion people in the developing world, 2.6 billion live on at least 2 dollars a day, and 1.4 billion extremely poor live on less than 1.25 dollars per day. In this population, about 752 million are rural livestock farmers, 45% of whom live in South Asia and 25% in sub-Saharan Africa.

Small ruminants are both a capital asset and a savings account for poor households.

Reinforce the resilience of vulnerable populations

Small ruminants provide a safety net for the most impoverished:

- *They can adapt to even the harshest environments.*
- *They require little maintenance or space.*
- *They grow and reproduce rapidly.*
- *They can be sold easily and quickly.*
- *They require only a few investments in infrastructure and health monitoring.*
- *They are a source of food and income for households.*

Social and cultural roles

In numerous societies, small ruminants fill social and cultural roles. They frequently are slaughtered and consumed during traditional ceremonies marking important life events (births, marriages, funerals) or religious festivals. They serve as dowries for future brides, and are used as gifts when there is a birth, to strengthen ties, or to honour visitors. They reflect the status and social integration of a family. In pastoral communities where livestock farming takes centre stage, the disappearance of small livestock has repercussions that go beyond economic impoverishment. It can lead to social marginalization and to the migration of livestock farmers towards cities where they encounter peri-urban poverty and crowding.

In countries in the South, small ruminant husbandry often is the work of women, who rarely hold the right to own or use land. They supervise reproduction and production. Across all cultures, women are almost always responsible for milking, making and selling dairy products, and feeding and caring for the animals. This is an activity that provides them a certain financial independence and social status, and which contributes to promoting gender equality. Sheep and goats can be kept close to the home or allowed to wander and can be watched over easily by other members of the family such as children.

When disease hits

Poor livestock farmers in countries in the South often are vulnerable to animal diseases. Regardless of their livestock farming system, lifestyle, or environment (rural, urban, or peri-urban), or whether they live in Asia or Africa, these farmers are hindered from managing health risks due to weak veterinary services, a lack of trained professionals, inadequate training and information on animal health, and difficult access to veterinary services, medicines and vaccines. When a family's diet and income depend on goat and sheep production, disease directly impacts the household's daily life. The loss of animals and their reduced market value due to debilitating side effects (weight loss, delayed growth, drop in fertility) keep households trapped in poverty and destroys or weakens their resilience, meaning their capacity cope with recurrent crisis situations (poor harvests, natural disasters, political instability), which had been sustained by their small ruminant production.

Numerous diseases affect sheep and goats with varying degrees of gravity and different impacts at the global, country, and herd scale. Some are highly contagious and affect numerous countries such as peste des petits ruminants, sheep pox, and goat pox. Their spread is determined by the mobility of animals in extensive livestock systems, particularly in the Sahel, and by the legal and illegal movement of animals to meat consuming countries. Other diseases, such as heartwater, bluetongue and Rift Valley fever, are related to the environmental conditions governing the transmission of pathogens by vectors (ticks or insects). Yet others, such as brucellosis, Rift Valley fever, hydatidosis, are also zoonoses, common to both humans and animals.

Main infectious and parasitic diseases of small ruminants

Infectious diseases			Parasitic diseases	
Viruses	Bacteria		Roundworms	Flat worms
	With a cell wall	Without a cell wall		
Peste des petits ruminants	Heartwater	Contagious caprine pleuropneumonia	Haemonchosis	Hydatidosis ◆
Sheep and goat pox	Corynebacterium			
Bluetongue	Brucellosis			
Rift Valley fever ◆	Anthrax ◆			
Rabies				
Contagious ecthyma				

◆Zoonoses Vector-borne diseases

"Sheep and goats are essential for the food security and incomes of pastoral communities. The presence of disease directly affects household wealth."

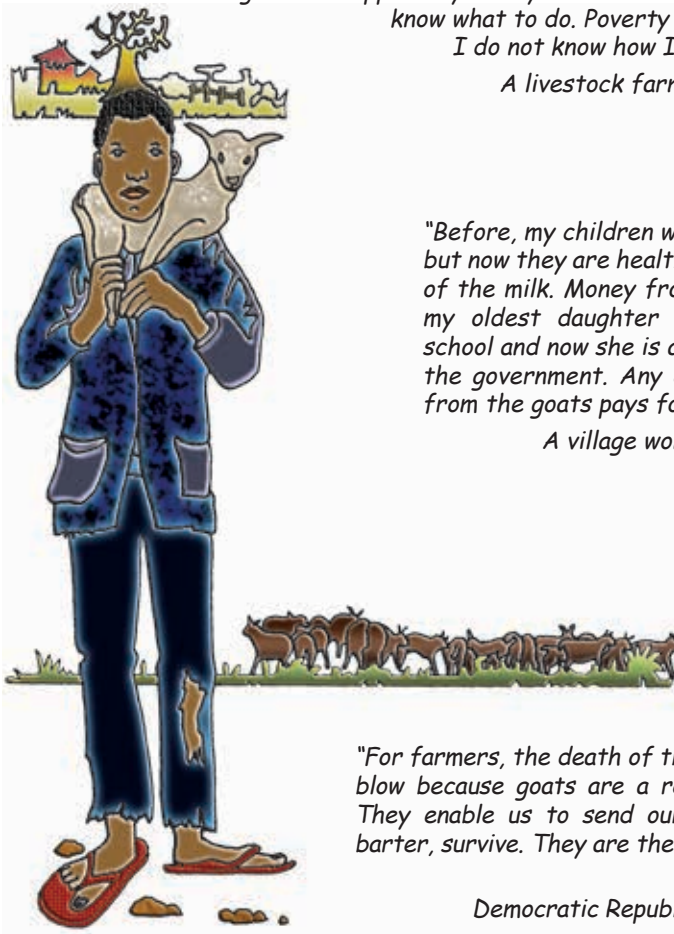
Juan Lubroth - FAO, 2010

"A goat can pay for the education of children. It is not just an animal; it is a means for people to procure food, milk, or money to invest in education."

A veterinarian - Uganda, 2014

"I am a poor livestock farmer. These animals were my only source of income. Almost all were killed by disease. I sold goats to support my family. Now that they are dead, I don't know what to do. Poverty has hit my house and I do not know how I will feed my family."

A livestock farmer - Cameroon, 2012



"Before, my children were under-nourished, but now they are healthy and happy because of the milk. Money from the goats enabled my oldest daughter to go to secondary school and now she is a teacher working for the government. Any extra income we get from the goats pays for schooling."

A village woman - Tanzania, 2009

"For farmers, the death of these animals is a hard blow because goats are a real source of money. They enable us to send our children to school, barter, survive. They are the basis of our society."

A villager
Democratic Republic of the Congo, 2012

"It has been hard to put together dowries ever since this epidemic started decimating our goats. A young man might plan to bring a goat to his in-laws as a preliminary dowry present, but on the day he is to visit, the goat dies."

A village head
Democratic Republic of the Congo, 2013

"Three of the five goats given to one of our daughters died the day after the dowry ceremony. We decided to start accepting cash instead of goats. "

A villager - Democratic Republic of the Congo, 2013

"How I will I pay the school fees for my children next year now that all 7 of my goats have died? Who will help me?"

A widow - Democratic Republic of the Congo, 2012

"The cost of attending a boarding school is 750 Kenyan shillings per month (€6.5). Maasai families must sacrifice two goats to pay for each year of school."

Arte documentary: Chemins d'école, chemins de tous les dangers *(Path to school, path of danger). Kenya, 2013*

Viral and highly contagious

PPR is one of 10 diseases affecting goats and sheep with major health and socio-economic impacts. It is the most devastating viral disease of small ruminants. It also can affect dromedaries and some wild small ruminants. Its mortality and morbidity rates (diarrhoea, pneumonia, weight loss, fertility loss, reduced milk production) are high and can reach from 80 to 100%. The World Organisation for Animal Health (OIE) and the FAO class it among the highly contagious transboundary diseases with serious socio-economic repercussions. However, unlike foot-and-mouth disease in cattle, it is not considered to be a disease of economic interest impacting the balance of world trade. Affecting small livestock, goats and sheep, it is seen as a disease of public concern that impedes the development of livestock farming at a local and national scale and threatens the food security and livelihoods of millions of poor farmers in developing countries in Africa, the Middle East, and Asia. Beyond the consequences for animal health, PPR also is a threat to the food security and health of people in these countries.

"Lomoo [a local name for PPR in Kenya] has impoverished us. I had a herd of 800 goats. In three months, PPR killed 300."

A village head - Kenya, 2008

PPR is listed by the OIE as a compulsorily notifiable disease in the case of outbreaks. An international study published in 2002 by the ILRI (International Livestock Research Institute) estimated that over 750 million goats and sheep were affected by PPR.

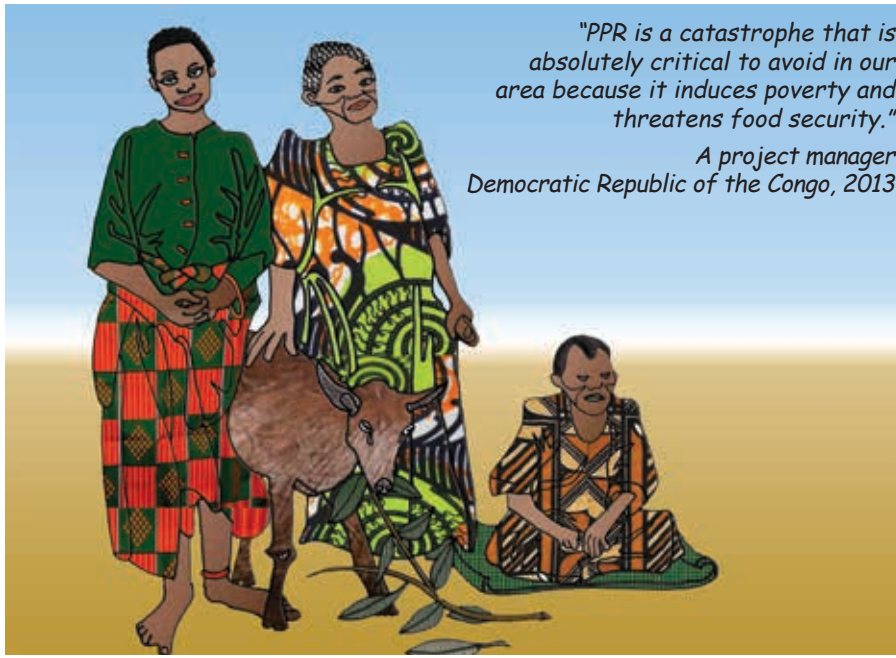
Today, more than one billion small ruminants in over 70 countries are at risk of contracting PPR.

Some background history

PPR was first described in 1942 by two French veterinarians, Gargadennec and Lalanne. In 1940, they were confronted with a devastating epizootic among goats and sheep in the Ivory Coast.

The symptoms were similar to those of other known diseases. They first suspected bluetongue disease, then ulcerative stomatitis, and finally identified the clinical signs as being similar to those of rinderpest, a highly contagious viral disease that was at the time decimating cattle and buffalo herds. As the cattle in contact with these small ruminants did not show any sign of infection, they named the disease, "peste des petits ruminants ".

In 1941, an identical deadly infection in Dwarf goat herds in Benin was described by Cathou under the name, "ovine and caprine species plague ". A few years later, in 1955, the disease was reported in Senegal. Outbreaks in Nigeria and Ghana were reported between 1960 and 1970, sometimes under different names which reflected their clinical expression: pseudo-rinderpest, stomatitis pneumoenteritis complex and *kata* (a local Nigerian name, pidgin English for "catarrhal") in Nigeria. It was during this time that the French name given by those who first discovered the disease, "peste des petits ruminants ", was adopted as its scientific name. The acronym, PPR, is used widely today.



In the shadow of rinderpest

For 30 years, PPR was associated with West Africa. However, in 1972 a disease affecting goats in Sudan that was first diagnosed as rinderpest proved to be PPR, revealing a geographic distribution beyond the area initially assumed. Today, PPR is endemic in most countries in Africa, the Middle East, and Asia. Its presence in North Africa and Turkey puts the disease at the doors of Europe.

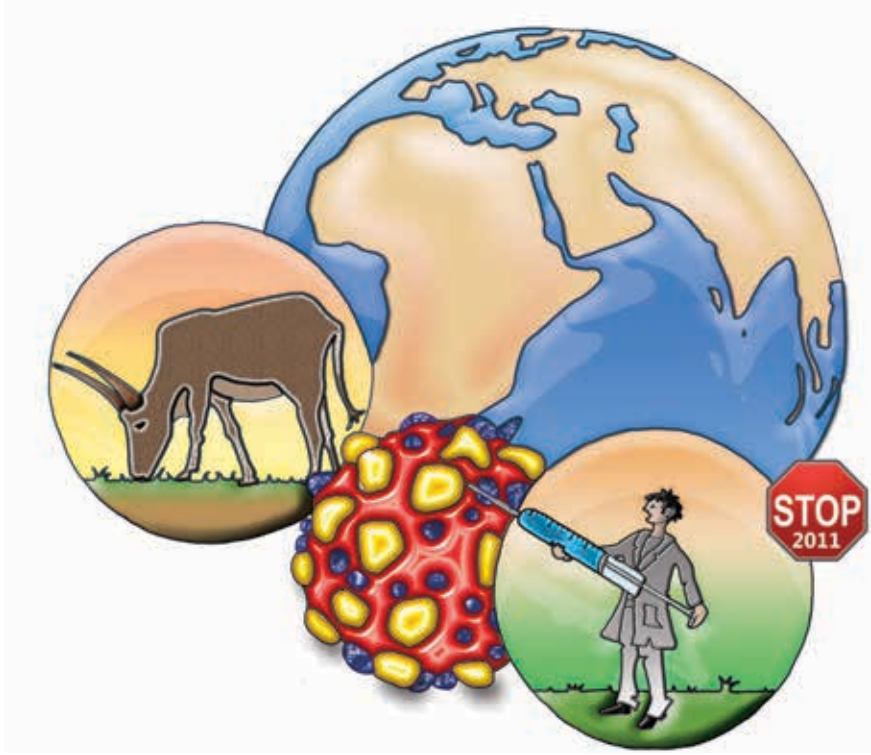
Like all transboundary diseases, the intensified movements and trade of animals, whose populations are growing, benefit the virus. However, these are not the only reasons behind the disease's global reach.

Bovine animals are considered an epidemiological dead end for the PPR virus.

Scientists today know that PPR is not a new disease and that it was present in West Africa since the end of the 19th century, well before it was first described. It was simply impossible to distinguish PPR from other diseases with similar clinical signs.

The high incidence (incidence measures the new number of cases in a population by unit of time) of such diseases, the absence of powerful diagnostic tests, and a low level of interest in small ruminants' health long obscured the presence of PPR and delayed its identification. Today, it is acknowledged that the rinderpest cases among small ruminants in Senegal in 1871 and in Guinea in 1927 likely were actually outbreaks of PPR. The same is true of India, where the first PPR epizootic was officially recognized in 1987, yet a disease affecting goats and sheep resembling rinderpest reported in 1940 and 1942 probably was PPR.

Although a highly effective vaccine has been available for 25 years, PPR continues to spread and expose previously disease-free countries in the South and North to the risk of virus incursion and disease emergence.



Rinderpest, a disease of the past

According to historical documents, the first epizootic of rinderpest in Europe took place sometime between 376 and 386 AD, near the end of the Roman Empire. However, some believe the disease may have been one of the seven plagues of Egypt. Eurasian in origin, rinderpest has decimated hundreds of millions of cattle and buffalo in Europe, Asia, and Africa and has caused severe famines. It remains one of the most deadly transboundary animal diseases of domestic and wild mammals belonging to the Bovidae *family. Thanks to coordinated international collaboration, and after 80 years of struggle, rinderpest was officially declared eradicated in 2011. In human history, this is only the second disease to have disappeared from the planet, the first being human smallpox, and the first animal disease to do so.*

*The global fight against rinderpest led to the creation in 1924 of OIE (*Office international des épizooties*), named today the World Organisation for Animal Health. Rinderpest also was largely responsible for the foundation of the first veterinarian schools in France in the 18th century.*

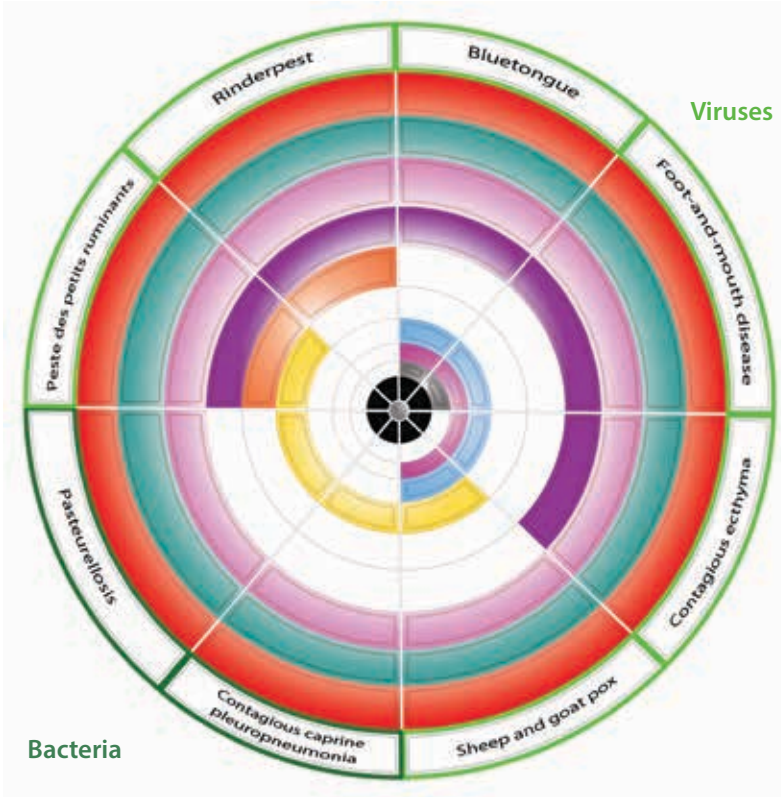
Four forms

PPR also is described as a "stomatitis pneumoenteritis complex", which reflects how the virus affects the mucous membranes of an animal's digestive and respiratory systems. Its clinical signs closely resemble those of rinderpest, a disease which has now been eradicated.

PPR can take 4 forms depending on the susceptibility of the species, breed and animal infected. All 4 forms can be present within the same herd.

Misleading clinical signs

No clinical signs suggesting PPR are specific to the disease. They can all be confused with other diseases.



Differential clinical diagnosis of PPR: Hyperthermia - Discharge - Lacrimation - Lesions on mucous membranes - Diarrhoea - Difficulty breathing - Oedema - Vesicles - Lameness.

Acute form: This is the form observed most frequently. After a 5 to 6 day incubation period, the disease manifests itself with a sudden rise in body temperature, which can reach 40 to 42°C. The animal is listless, refuses to eat, and its hair stands erect. The animal withdraws from the herd and has difficulty moving. The mucous membranes of the mouth and eyes become congested. One or two days after the onset of fever, lacrimation and discharge appear, at first clear and watery, then mucopurulent. The eyelids gum together and the obstructed nostrils render breathing difficult. Occasionally a productive cough characteristic of bronchopneumonia signals the presence of a secondary bacterial infection. Four or five days after the appearance of the first clinical signs, the temperature drops, followed by the onset of occasionally bloody diarrhoea and oral lesions. These become covered by a necrotic, whitish, pulpy tissue (with a mushy consistency) which emits a nauseating odour when the animal opens its mouth. In females, pus and erosive lesions are visible on the vulvo-vaginal mucous membranes. At this stage, pregnant animals abort. Death follows in 70 to 80% of cases, on average 10 days after the onset of the first clinical signs, in animals often in a state of hypothermia. When an animal recovers, convalescence is rapid and generally takes no more than one week.

Peracute form: This is observed most often in young goats over 4 months old which are no longer protected by maternal antibodies. Incubation lasts about 3 days. The disease begins with the same clinical signs: a high fever (40 to 42°C) followed by congestion of mucosa manifested by watery eyes and serous discharge. However, it evolves more rapidly. After 5 or 6 days, 100% of infected animals die even if they have shown no erosive lesions, diarrhoea, or secondary bacterial infection.

Subacute form: Despite the frequent occurrence of microbial complications, this is the least severe form of the disease. It is not fatal. After a 5-day incubation period, the disease causes a fever which remains moderate (39 to 40°C) and lasts only 1 to 2 days. All of the other clinical signs are discrete and may go unnoticed. Small amounts of discharge dry around the nostrils to form crusts that can steer the diagnosis towards another disease, contagious ecthyma.

Sub-clinical form: Asymptomatic or unapparent, it often is observed in sheep in the Sahel. In the absence of clinical signs, it is only revealed through serological investigations.

"An animal [a goat] with this disease rarely survives more than three days."

A village head - Democratic Republic of the Congo, 2013

Establishing the identity

The first clinical descriptions of PPR and the strong resemblance of the clinical signs with those of rinderpest steered scientists towards thinking that the two diseases were closely related and involved a similar viral pathogen. In 1956, Mornet *et al.* concluded that the PPR virus (PPRV) was a variant of the rinderpest virus which had adapted to small ruminants and lost its virulence for cattle. Starting in 1962, cell culture studies began to reveal the similarities and differences between the two viruses.

Using an electronic microscope, in 1967 Bourdin and Laurent-Vautier observed that the structure of PPRV was identical to that of the rinderpest virus and validated its membership in the same family, the *Paramyxoviridae*. The similarity of its biological and physiochemical characteristics with the rinderpest virus was a sign that it was a member of the same genus, *Morbillivirus* (*Morbilli*, short for *morbus*: disease, pest, plague). During the 1970s, serological studies, cross-protection tests and biochemical analyses of the two viruses allowed the differences between them to be identified and showed that although closely related, the PPR virus was distinct from the rinderpest virus. In 1979, its distinguishing features were recognized. Gibbs *et al*. proposed that PPRV become the fourth morbillivirus, joining the rinderpest virus, the measles virus, and the distemper virus, all three responsible for devastating diseases in their respective hosts. Other viruses found in marine mammals have further enriched the *Morbillivirus* genus since the 1990s: the phocine distemper virus and viruses affecting cetaceans (dolphin and porpoise morbilliviruses). Since then, other viruses have joined their ranks, such as that identified recently in domestic cats. Scientists do not rule out the possibility of discovering new morbilliviruses in the future.

The search for PPRV's origins

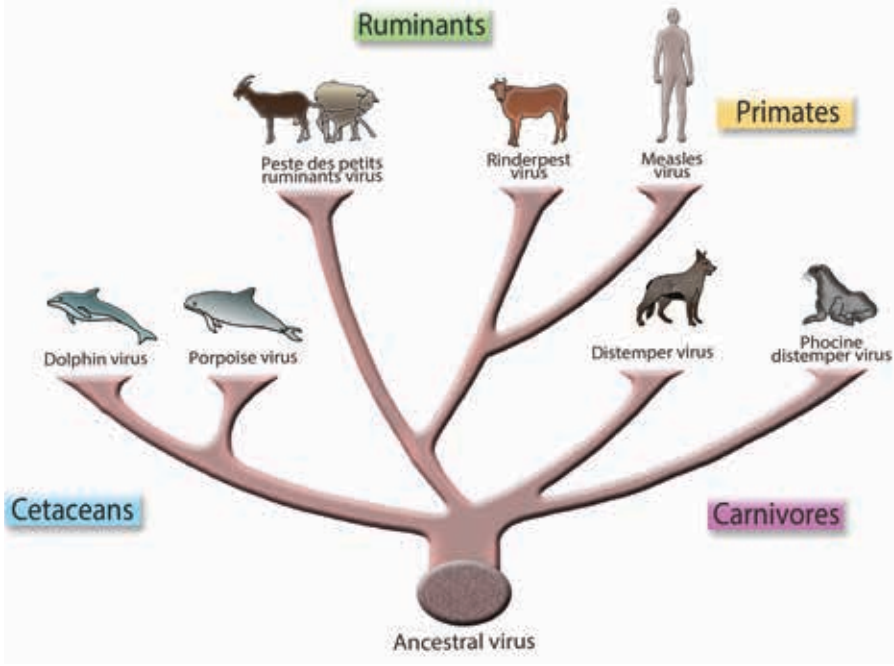
Morbilliviruses form a group of 6 viruses causing devastating diseases in humans and animals. Their respective host ranges are narrow but they can occasionally cross species barriers. Their strong genetic likeness and close antigenic proximity allows scientists to affirm that they all descended from the same archaevirus.

To persist, morbilliviruses need to circulate in large populations which renew themselves. The large herds of ruminants in Asia created an ideal environment for them. They were the historical source of the rinderpest virus.

During the Neolithic period, people settled down and became livestock farmers, living in close contact with their herds. When the human population became sufficiently dense to ensure the maintenance of the virus (between 250 000 and 500 000 receptive individuals), the species barrier was crossed. The rinderpest virus mutated, adapted to humans, and became the measles virus. In 2010, a study by Furuse published in *Virology Journal* indicates that this divergence occurred between the 11th and 12th century AD.

PPRV detached itself earlier, around the 1st century AD, from the common ancestral branch that gave birth to the rinderpest and measles viruses. From an evolutionary point of view, PPRV is thus distant from these two viruses, while the rinderpest and measles viruses are closer together.

The phylogenetic tree of the morbilliviruses
based on the partial sequence of the N nucleoprotein gene



Up close

Under an electron microscope, PPRV appears more or less spherical and pleomorphic (changes shape). Its diameter varies between 150 to 700 nanometres, with the majority of particles between 400 and 500 nanometres, slightly larger than the size of the rinderpest virus (approximately 300 nanometres). Like all of the viruses in the *Paramyxoviridae* family, PPRV is an enveloped virus.

In this "whole" virus, the viral envelope is formed by a double layered lipid membrane 5 nanometres thick borrowed from the infected cell when the virion is formed. The outside of the envelope is spiked with two kinds of spicules, each 10 nanometres long, which are inserted into the membrane. These spicules are two glycoproteins, the fusion (F) protein and hemagglutinin (H). The inside surface of the envelope is lined with the matrix (M) protein. The envelope defines a kind of sac that contains two elements which are mandatory for all viral particles: the genome and the capsid.

The PPRV genome is a single-stranded RNA (ribonucleic acid) molecule. It is enveloped by a protein capsid largely constituted by N nucleoprotein sub-units. These form a long, hollow sheath approximately 1 micrometre long and 18 nanometres in diameter that wraps around the RNA molecule like a sleeve. The two are indissolubly bonded by the phosphate and ribose of each RNA nucleotide. The ensemble constitutes a levogyre (left-leaning), flexible N-RNA nucleocapsid with a helical symmetry that folds over itself inside the virion. Under an electron microscope, a herring bone structure can be observed. Each bone-like shape represents a coil of the helix. Electron microscopes made it possible to establish that there are 13 N nucleoproteins per coil. In the PPRV, the nucleocapsid thus forms a kind of spring with 200 coils. Despite its compact structure, it can loosen its form so that the nitrogenous bases of the RNA molecule can be read during the virus multiplication cycle.

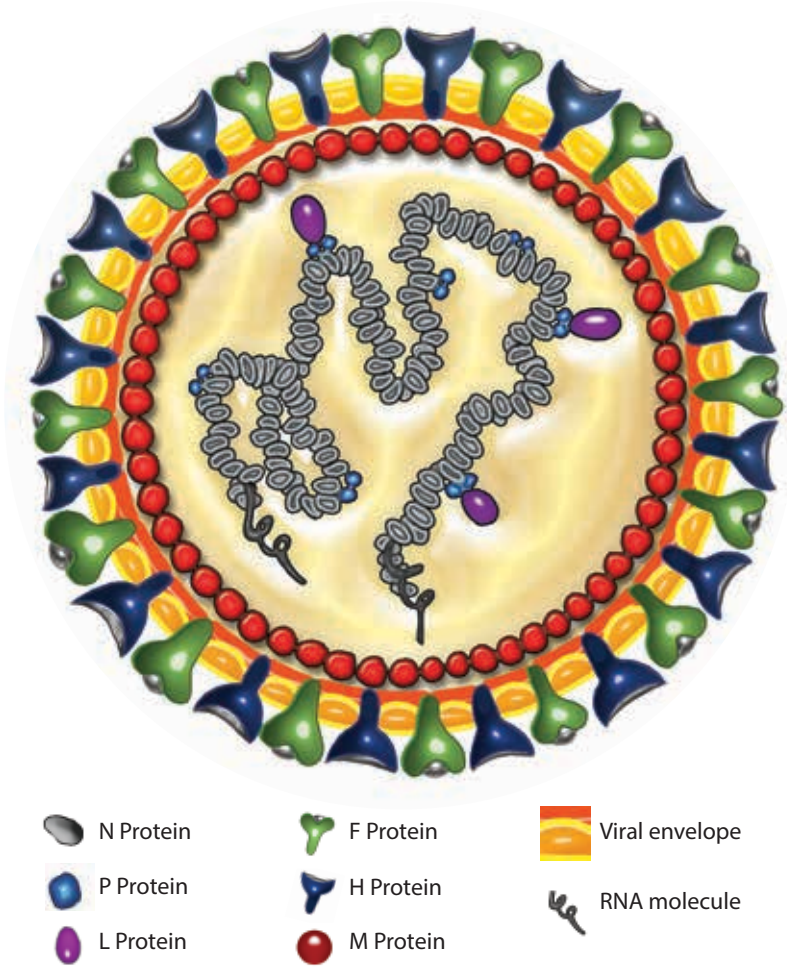
Two other proteins, RNA polymerase L and its cofactor, phosphoprotein P, combine with the N-RNA nucleocapsid to form the ribonucleoprotein complex (RNP). Their presence is critical for the virion to initiate its multiplication cycle inside the infected cell. The "naked" viral RNA is not directly infectious.

PPRV's identity card

Group: V (negative single-stranded RNA virus)
Order: *Mononegavirales*
Family: *Paramyxoviridae*
Sub-family: *Paramyxovirinae*
Genus: *Morbillivirus*
Species: PPR virus

The Paramyxoviridae are a large family of human and animal pathogens with significant public health and economic impacts. New emerging viruses such as the Hendra and Nipah viruses are members.

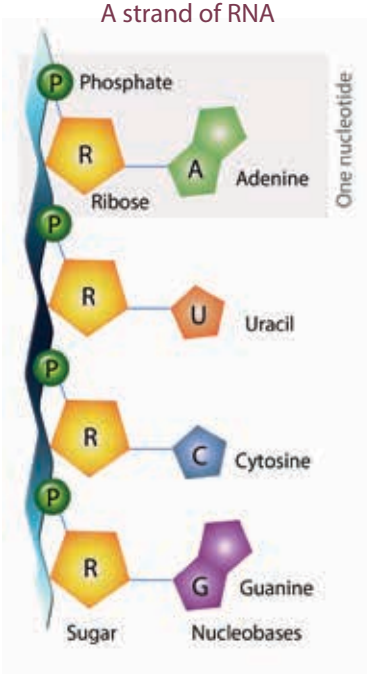
PPRV ultrastructure



Six genes

The complete sequencing of the PPR virus genome was achieved in 2005. Its RNA consists of a chain of 15 948 nucleotides. This is one of the longest genomes of the *Morbillivirus* genus. That of rinderpest has 15 882 nucleotides. It follows the "rule of six", as do all of the viruses in its genus.

A strand of RNA



Rule of six

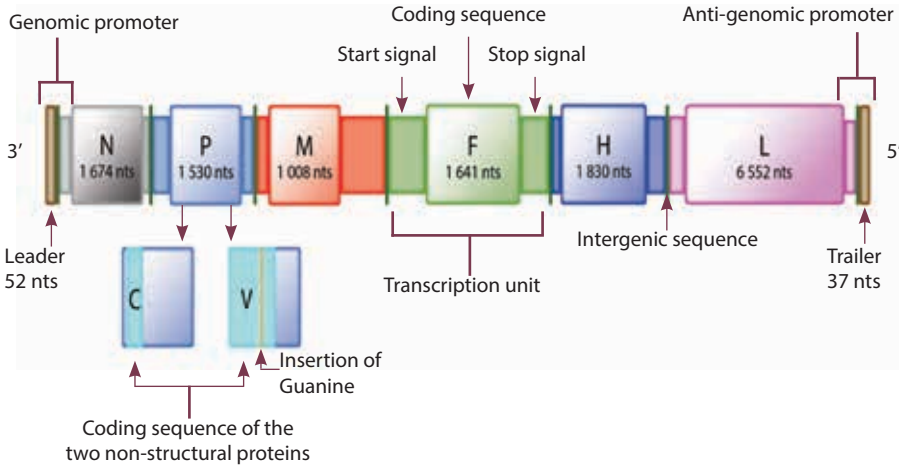
Among the Paramyxoviridae*, each N nucleoprotein is linked and interacts with 6 nucleotides of the viral RNA. Therefore, the total number of nucleotides must be a multiple of 6, otherwise the RNA dependent - RNA polymerase considers the RNA molecule incompatible. When that is the case, it does not initiate the viral multiplication cycle.*

All of the morbilliviruses share the same genome organization. Their RNA is unsegmented. It presents itself as a single molecule made up of a sequence of 6 non-overlapping genetic units (transcription units). Each unit begins with a start signal followed by a coding sequence, and ends with a stop signal. They are separated by intergenic non coding sequences of 3 nucleotides. The RNA is said to be negative-sense because it cannot be translated directly into protein. Each gene must first be transcripted into a messenger RNA by the viral polymerase L, then translated into a viral protein by the enzymatic machinery of the host cell.

The 6 genes, which encode 8 proteins, are lined up in a linear, well-established order on the RNA molecule. From left to right, moving from the 3' to the 5' end, the sequence is as follows: 3'-N-P/C/V-M-F-H-L-5'. Five genes (N, M, F, H, L) are monocistronic. They only encode a single messenger RNA molecule, thus just one viral protein. The sixth, the P gene, is polycistronic and an example of genetic information compaction. It directs the synthesis of 3 proteins, the structural protein P and 2 non-structural or auxiliary proteins C and V, through shifts in the reading frame. The latter proteins are only present in the cytoplasm of the infected cell during the viral cycle.

Two "extracistronic", non-coding regions are situated at the 3' and 5' ends of the RNA molecule and help regulate two stages of viral multiplication: transcription and replication. They are respectively the leader and the trailer. The leader combines with the first non-coding sequences of the N gene to form the genomic promoter used by the polymerase to synthesize the messenger RNAs. The trailer and the last non-coding sequences of the L protein constitute the antigenomic promoter used by the polymerase to synthesize the antigenome (positive RNA), the intermediary of the viral genome replication.

The RNA genome of the PPR virus



The PPRV proteins

The structural proteins

Proteins on the outside of the viral envelope

They prompt the host protective immune response. These antigens are in contact with the antibodies in the outside environment.

Fusion protein or F glycoprotein
546 aa

This is a well conserved protein responsible for the fusion of the viral envelope with the membrane of the host cell. It also intervenes in the membrane fusion of the infected cell with healthy neighbouring cells, producing syncytiums (multinucleated giant cells). It engenders a neutralizing humoral immunity and a cellular immunity.

During the infection cycle, it is synthesized as a precursor protein, F0, which only becomes active once it has cleaved into 2 sub-units, F1 and F2, thanks to a cellular protease. If the F0 does not mature, the viral particles released are not infectious.

Hemagglutinin or H glycoprotein
609 aa

This also is known as an attachment protein. It determines the cell tropism of the virus. It allows the virus to bond to one or more receptor membranes. It has both hemagglutinin and neuraminidase activities (a distinguishing feature of PPRV). It induces the production of the neutralizing antibodies behind the humoral defence response.

Protein on the inside of the viral envelope

Matrix (M) protein
335 aa

This is the smallest and best conserved viral protein. It serves to bind the ribonucleocapsid with the 2 surface glycoproteins, H and F. Its main role is in the formation of new virions. An anomaly in its synthesis hinders the virus from finishing its cycle.

Nucleocapsid proteins

N nucleoprotein
525aa

This is the most abundant protein. It is responsible for the helicoidal structure of the nucleocapsid and protects the RNA. It plays a major role in regulating viral transcription and replication.

It is the main viral antigen but the antibodies produced against it are not neutralizing. It is used in molecular diagnostic tests. Sheltered from immunogenic pressures, it is very conserved, as in the other morbilliviruses, and serves as a reference for the epidemiological monitoring of PPR.

Phosphoprotein or P protein
509 aa

It acts as a co-factor of the L protein and enables it to bind to the nucleocapsid. Together, they form the RNA-dependent RNA polymerase complex responsible for the synthesis of messenger RNA and the replication of the viral RNA of the genome.

It intervenes in the encapsidation of newly synthesized viral RNA by bonding to the N nucleoprotein to form a soluble N-P complex in the cytoplasm and to hinder N from associating with RNA of the infected cell.

Polymerase or L protein
2 183 aa

This is a large protein coded by a gene representing half of the genome, but it is the least abundant. It is very well conserved. In association with the P phosphoprotein, it forms the RNA-dependent RNA polymerase complex which ensures the synthesis of messenger RNA and the replication of the genomic RNA.

The non-structural proteins

These block the innate host immune response to allow the spread of the virus.

C protein
177 aa

This is the smallest protein. It is produced from the same gene as the P protein but through an alternative reading frame. Its transcription begins at a start codon located at position 23 on the P gene.

During the viral cycle, the C protein intervenes to regulate RNA-dependent RNA polymerase during the genome transcription stage.

V protein
299 aa

Its synthesis is directed by the P protein gene but the messenger RNA transcripted is different. During transcription, a supplementary base (the G base, or Guanine) inserts itself at a precise point on the P gene thanks to a stutter mechanism of the polymerase known as editing. Upstream of the insertion point, the V protein is identical to P and shares the same start codon. Below the insertion point, the nucleobase sequence is modified and generates a new transcription stop signal (at position 894) before the end of the gene.

During the viral cycle, the V protein intervenes to regulate RNA-dependent RNA polymerase during the genome replication stage.

Four lineages but a single serotype

In PPRV, as in all of the other viruses in its genus, the RNA-dependent RNA polymerase commits random genetic errors during genome replication because it is not equipped with a translation proof-reader. The ensuing mutations cause a certain amount of variability in the succession of nucleic acids and lead to the co-existence of several different but very similar RNA molecules. By comparing the genetic sequences of several PPRV strains, scientists identified 4 distinct lineages but only one serotype. This means that the antigenic sites important for induction of immunity do not vary and that a vaccine made with one lineage will protect an animal against the three others.

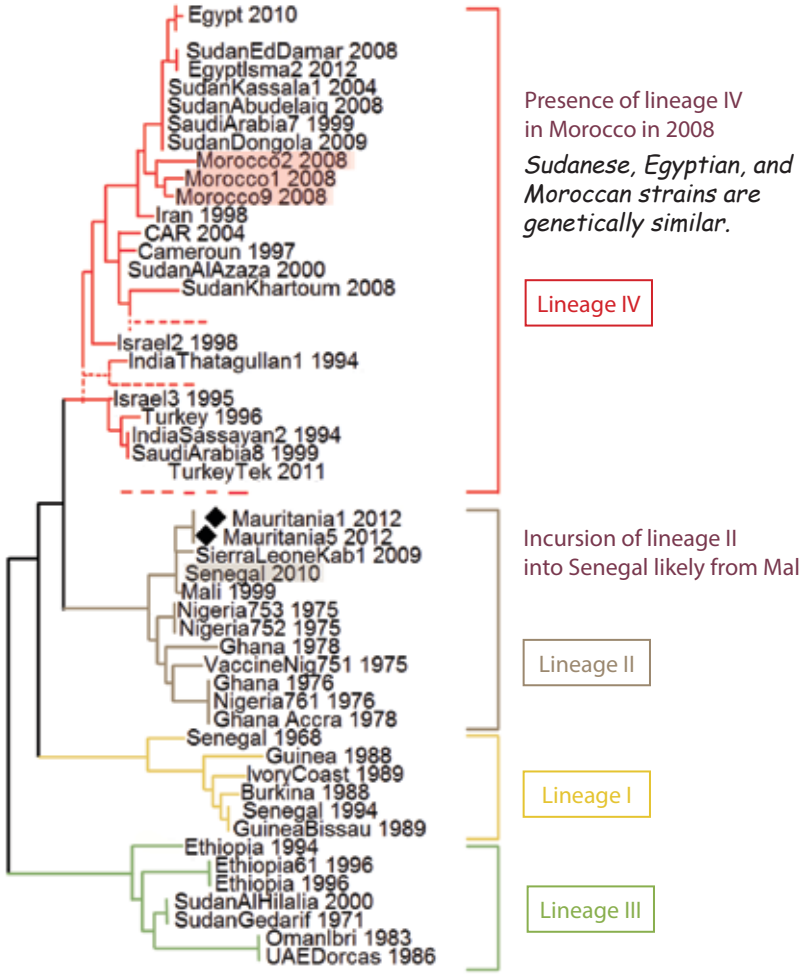
Samples taken directly from the sick animal in the field can enable the serological and virological diagnosis to be established.

The phylogenetic link between these 4 lineages was first established in 1996 by Shaila *et al.*, using the partial sequencing (an operation that determines the order of nucleobases) of the fusion F protein gene (a 322 nucleotide long segment) and then by Kwiatek *et al.* in 2007 based on a 255 nucleotide fragment of the N nucleoprotein gene. These 2 proteins, F and N, are considered to be representative markers that dispense with the need to conduct a complete sequencing of the genome.

However, N, which is less exposed to pressure from the immune system, best reflects the geographic movements of the virus over time. These movements are related to historic trade and transhumance routes. Molecular epidemiological studies therefore prefer to focus on the N protein to establish phylogenetic and phylogeographic trees. Lineages I to IV were numbered according to the apparent progression of the disease from the west towards the east. Lineages I to III originated in Africa. Lineage IV is Asian in origin but is now widespread in Africa.

The identification and comparative analysis of genetic sequences of strains isolated in different countries of Africa, the Middle East and Asia at different periods and in different hosts (goats, sheep and dromedaries) render it possible to better understand and monitor at the global level the distribution and spread of the disease, as well as the circulation dynamics of the 4 lineages of the virus.

Extract of a phylogenetic tree
based on the partial sequence of N nucleoprotein gene



Phylogenetic trees help identify animal movement networks behind the spread of PPRV.

Domestic small ruminants

As the name indicates, PPR is primarily a disease affecting goats and sheep. Within the same environment, goats generally are more susceptible to the virus than sheep. They express the disease in severe, acute, or peracute forms which most frequently result in death. Sheep resist the virus better. They develop a protective immunity and only express the disease in its mild, sub-acute or unapparent forms.

There are exceptions to this, likely due to the susceptibility of particular breeds: susceptibility to the virus depends on the breed. Dwarf African goat breeds in humid and sub-humid areas are more severely affected by PPR than large Sahelian breeds in arid and semi-arid regions. This difference also is because at the same temperature, PPRV is more stable in a humid atmosphere than in a dry one.

Even if morbilliviruses have a relatively narrow host range, PPRV shows that the species barrier can be crossed towards phylogentically similar cells such as bovines, dromedaries and wild small ruminants.

Dromedaries

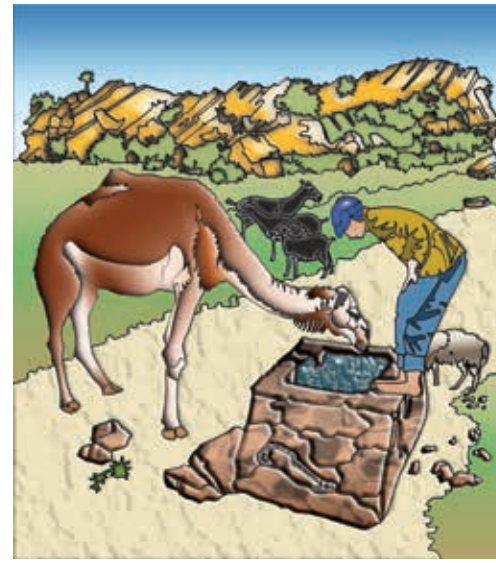
Since 1992, dromedaries have been suspected of being possible PPRV hosts. Serological surveys conducted in different countries - Sudan, Egypt, and Ethiopia - revealed seropositivity in dromedaries but with no clinical signs, and the virus was not isolated.

In 1995, François Roger, a CIRAD veterinarian, strongly suspected PPRV to be the cause of an outbreak in Ethiopia of a highly contagious disease that appeared to be new in the dromedary population. It was characterized by an acute respiratory syndrome with morbidity reaching 90%. Proof was provided in 2004 in Sudan. The virus was detected by laboratory diagnostic tests during an epizootic outbreak of the same disease in its peracute form with bloody diarrhoea, the sudden death of seemingly healthy animals, abortion in females and a mortality rate of over 50% in adults.

Receptivity to a virus is the capacity of a host to harbour a virus and allow it to multiply without showing clinical signs.

Susceptibility to a virus is the capacity of a host to clinically express the action of a virus.

In countries where traditional extensive livestock management systems lead animals to share watering holes and pastures, the risk of virus transmission between sheep, goats and dromedaries is high. Even if the epidemiological role of dromedaries still needs to be clarified, they are suspected of being cross-border carriers of PPRV and of contributing to the geographic spread of the disease.



Dromedaries illustrate PPRV's capacity to jump the species barrier.

Bovines

Cattle and water buffalo (*Bubalus bubalis*) are susceptible to the PPR virus, as proven by the presence of anti-PPR antibodies in their serum, but they do not manifest any clinical signs. It was this absence of clinical signs that allowed the disease to be identified and distinguished from rinderpest. For many years, this was the only differential diagnostic method available to distinguish between the two diseases. A few cases of calves and buffalo expressing signs of the disease (hyperthermia, oral lesions) were noted in the past, but these reactions probably were linked to a diminished immune capacity in animals weakened by an intercurrent infection (one unrelated to PPR).

In the epidemiological cycle of PPR, bovines are seropositive for the virus but do not excrete it, and are considered to be an epidemiological dead end. However, with the success of GREP (Global Rinderpest Eradication Program), the antibody cross-protection provided them by rinderpest vaccination was not maintained and has now disappeared. This raises questions regarding their contamination in PPR endemic areas and their possible role in the circulation and transmission of the disease.

Pigs

The experimental inoculation of pigs with PPRV produced no clinical signs. The animals reacted by producing antibodies but did not transmit the virus to goats. Pigs are considered to be an epidemiological dead end.

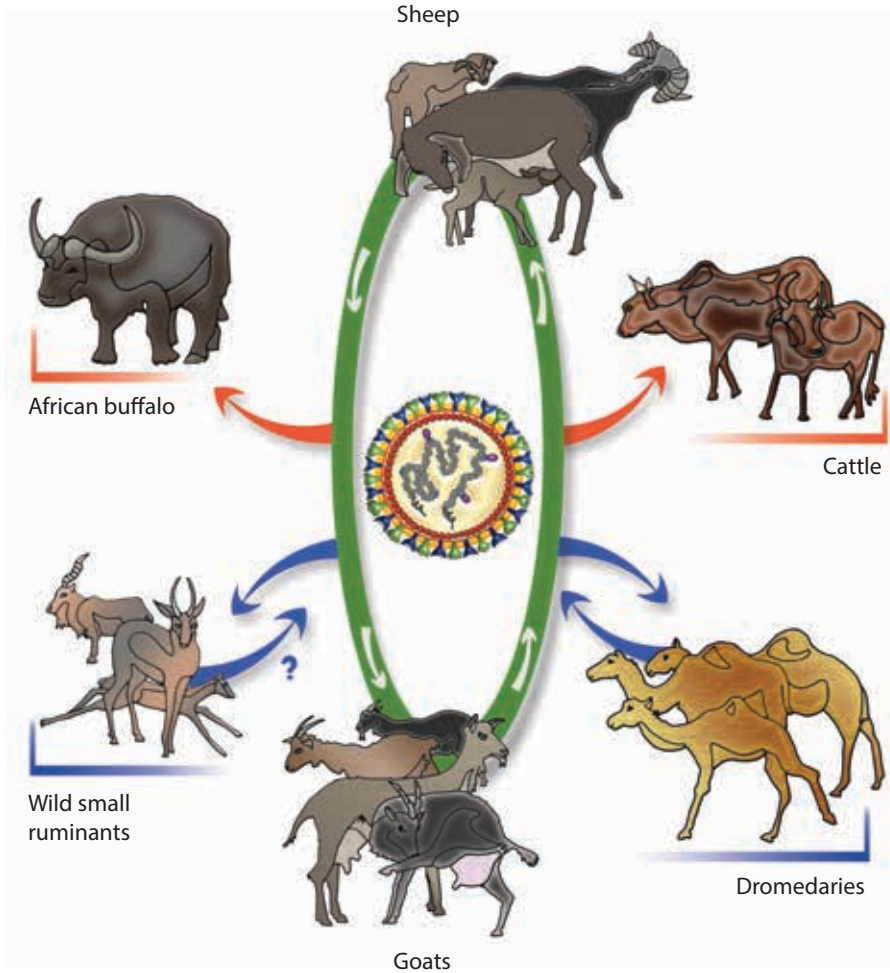
Wildlife

The susceptibility of wild small ruminants to PPRV was first reported in 1976 when white-tailed deer (*Odocoileus virginianus*) were experimentally infected. The clinical presentation of the disease was identical to that of naturally infected domestic small ruminants. In 1987, the disease was described in semi-wild animals in a United Arab Emirate zoo: Dorcas gazelles (*Gazella dorcas*), Nubian ibex (*Capra ibex nubiana*), Gemsboks (*Oryx gazella*), Blackbucks (*Antilopa cervicapra*), Laristan sheep (*Ovis orientalis laristani*). In 2002, it was reported for the first time in Saudi Arabia in a semi-wild herd of 200 gazelles (*G. dorcas* and *G. thomsoni*) in a subacute form with 52% morbidity and 100% case fatality rates. In 2007, PPR cases were reported in Tibet (China) in wild bharal (*Pseudois nayaur*). On the other hand, African buffalo (*Syncerus caffer*) are, like domestic bovines, an epidemiological dead end.

The role of wildlife in the epidemiological cycle of PPR and virus circulation is not yet entirely understood. Wild small ruminants may contribute to the geographic spread of the disease through their migratory movements, which can stretch over long distances, but the hypothesis of the maintenance of the infection in wild populations outside those living close to infected goat and sheep herds has not yet been demonstrated. They could be «spill over» hosts. As with rinderpest, wild animals clearly are more victims than reservoirs of the virus.

In areas of Asia where the disease is endemic, regular epizootics in small ruminant herds lead to high mortality in wild species, of which some are on the list of species in danger of extinction, notably bharals in Tibet, ibex in Pakistan, and wild goats in Kurdistan. In Africa, the spread of the disease in the direction of the large game reserves on the southern end of the continent, where the density of wild and domestic animals is high, could be a threat for the wild herbivore populations that must share their grazing areas with herds of goats and sheep.

The epidemiological cycle of PPR



Undercover transmission

PPR is one of the most highly contagious diseases of small ruminants. Infection usually takes place through direct contact between susceptible and infected animals. In the early stages of infection, during hyperthermia, all bodily secretions and excretions are highly contaminated. Coughing and sneezing project virulent aerosols into the air. The airborne transmission of the disease is rapid in herds of animals living close together. Transmission is horizontal; there is no vertical transmission of PPR through the placenta.

Virus excretion begins during the incubation stage, before the appearance of the first clinical signs, and can last up to over 2 months following recovery, as has been observed in goat faeces. These periods of silent virus presence, without any visible clinical signs, increase the risk of disease spread to other small ruminants, both domestic and wild.

Goats are more susceptible to PPRV than sheep.

Contamination also is possible by the ingestion of infected food or drink. Feeding and drinking troughs and soiled bedding also can be indirect sources of infection, but only for short periods because PPRV, like all of the morbilliviruses, cannot survive long outside the organism of a host animal. Its lipid bilayer envelope inherited from the cell host cannot withstand the heat and strong sun of countries in the South. When it loses its envelope, PPRV loses its infectivity.

The persistence of PPRV in the environment is a parameter that needs to be researched more fully in order to be considered in risk analyses and epidemiological models designed to assess the probability of the introduction of PPR through animal movements towards disease-free countries such as those of the European Union.

A fragile virus

Temperature

PPRV is sensitive to heat. This hinders the use of vaccines in certain countries in the South and has led to the development of thermostable vaccines. PPRV has a half life of 2 minutes at 56°C and 3 hours at 37°C.

It can withstand cold better than heat. In refrigerated or frozen tissue, PPRV has a half life of 10 days at 4°C and 24 days at -20°C.

pH

At a normal temperature, the virus is stable between a pH of 5.8 to 9.5. It is rapidly destroyed at acidic pH values below 4 and alkaline pH values above 11.

The acidification of meat during maturation helps but does not guarantee the inactivation of the virus. Meat from infected carcasses could present a risk of viral dissemination, but this is more likely in a context of bioterrorism than natural transmission. Although PPR is not a zoonoses, the consumption of animals infected with PPR, like the meat of all sick animals, is advised against.

UV radiation

PPRV is sensitive to ultra-violet rays, and thus to sunlight and desiccation.

Chemical agents

PPRV is destroyed by organic solvents of lipids (ether, chloroform, toluene). It is inactivated by quaternary ammonium-based detergents, glycerol, phenol, formalin and beta propiolactone.

Within a herd

PPRV spreads rapidly within a herd, causing heavy losses for farmers. Surviving animals are protected for life against a new infection and do not constitute a danger for their fellows as soon as they reach the end of the viral excretion period; there are no chronic carriers of the virus. The disease will only reappear in a herd when the virus can maintain itself there again; meaning once a population of susceptible animals has been reconstituted. If one third of a herd is renewed each year, this corresponds to a periodicity of 3 years.

Mixed herds are a risk factor in the transmission of PPR.

In endemic areas, livestock and herd management practices are risk factors for the spread of the disease and epizootic outbreaks.

This is the case when herds are mixed, combining animals with different levels of viral susceptibility such as goats and sheep, or where small ruminants cohabit with dromedaries. It also is the case when mobility through nomadism and transhumance promotes frequent and repeated contact between animals with unknown disease status, when rangelands and watering points are shared, when individuals of varying ages and origins are regrouped for sale, and when animals are introduced or reintroduced into a herd without observing a quarantine period. When migration routes are modified to avoid areas of drought, insecurity or conflict, the risk of spreading the virus also is increased.

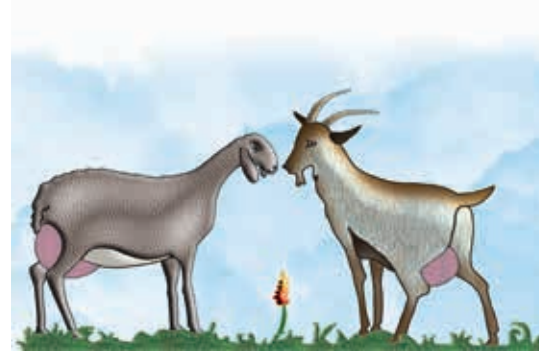
In pastoral societies, local social and cultural practices of trading, loaning, and giving small ruminants susceptible to infection increases the risk of introducing the disease into as yet disease-free areas. Large herds with a high density of animals, often associated with intensive livestock farming, also are environments with a high risk of PPRV.

Age also has an impact on the level of seroprevalence of livestock and on the epizootic risk. Small ruminants which have been kept in a herd for more than 3 years due to their production functions have a higher probability of having been contaminated and immunized than younger animals. This is particularly true for females, which show higher seroprevalence. Used for reproduction and to provide milk for home consumption, females are kept for longer periods than males. The latter often are sold by the age of two to cover the family's financial needs. However, at the individual level, no difference in susceptibility between males and females of the same age has been demonstrated.

Serological monitoring of PPR within a herd enables a better understanding of infection dynamics as a function of local and regional agro-climatic conditions and livestock farming practices, and to identify areas at risk. Studies clarifying the epidemiological situation in a country are critical for implementing PPR control strategies using vaccination.

"I had 9 she-goats and 4 bucks in my family, but now all that is left is one she-goat which I have moved."

A farmer - Democratic Republic of the Congo, 2012



"In response to the threat, farmers move their animals away from infected villages to areas where no outbreaks have yet been signalled, which causes healthy herds to become contaminated."

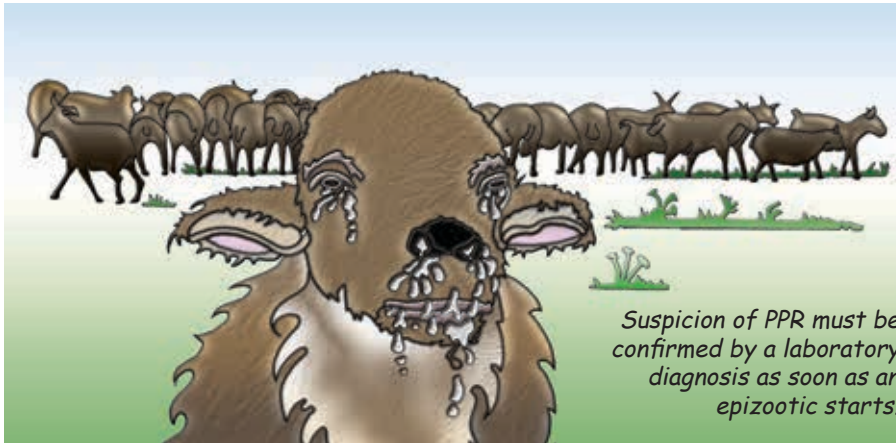
An FAO representative - Democratic Republic of the Congo, 2012

Under the control of the virus

PPRV, like the other morbilliviruses, has an affinity for two kinds of tissue, lymphoid cells and epithelial mucosa. This dual tropism, lymphotropism and epitheliotropism, explain the disease's clinical characteristics.

The virus contaminates "naive" animals through their oral and nasal passages. After entering into the organism, it multiplies first in the oropharynx and local lymphoid tissues. All of the immune cells (lymphocytes, macrophages, reticular cells) can be a target for virus multiplication. The newly formed virions spread throughout the host's organs and tissues with a preference for digestive, pulmonary, and respiratory mucosa and the immune system. The resulting tissue damage, which can be observed post-mortem, is responsible for the clinical manifestations of the disease: discharge, lacrimation, diarrhoea.

Biochemical and enzyme analyses show changes in kidney function (high urea and creatinine) through the multiplication of the virus in its cells and low blood parameter values (erythrocytes and haematocrit) linked to internal intestinal and renal haemorrhaging. In parallel, the PPRV infection induces cell death through apoptosis in immune cells, leading to severe immunosuppression. This weakening of the animal's natural defences through leukopenia (reduction in the number of white blood cells) opens the door to secondary bacterial and viral infections which interfere with the normal progression of the disease and complicate its diagnosis. These opportunistic infections significantly increase the mortality rate associated with PPR. The animals which recover are protected against PPRV for the remainder of their economic life.



Suspicion of PPR must be confirmed by a laboratory diagnosis as soon as an epizootic starts.

Post mortem diagnosis	
Carcass	The animal appears emaciated. The hindquarters are soiled with faeces.
Digestive tract	Tissue necroses are found in the mouth (on the tongue, gums, and palate). Characteristic linear lesions are visible on the pharynx and oesophagus. The intestinal mucous membranes of the colon and rectum are very congested and haemorrhagic with lesions resembling zebra stripes. In females, erosive lesions also are found on genital mucosa.
Respiratory tract	The damage is linked to associated secondary infections. In advanced stages of the acute form of the disease, signs of secondary bronchopneumonia are visible on the trachea, which is very congested and contains a foamy liquid, and on the lungs, which present hard, purple-red apical and cardiac lobes.
Lymphoid organs	The lymph nodes are oedematous. The spleen is congested and bloated. Lesions are frequently found on the Peyer's patches (lymphoid tissue).

Host immune responses

Within the same species and even within the same breed, the response of a host animal to PPRV depends on its immune status and age. An immunosuppressed animal is susceptible to the virus regardless of its age.

In enzootic areas, offspring of seropositive females are immunized up to the age of 3-4 months by the maternal antibodies contained in colostrum. Beyond that point, the maternal protection diminishes but the animal's own immune defences are not yet fully established. Young animals below the age of one year consequently are the most severely affected by the disease.

Adults show cell-mediated and humoral immune responses to 3 viral proteins, N, F, and H, but of these, only the 2 surface proteins, F and H, are involved in the protective immunity. Over the course of the infection, hemagglutinin H is the preferred target of the neutralizing antibodies behind the humoral defence response. The F fusion protein engenders cellular immunity involving the T lymphocytes (lysis of infected cells).

The N nucleoprotein, a major antigen of the virus, is the most immunogenic but the antibodies produced by the infected animal are not neutralizing and provide no protection. However, they are being used as the basis for the development of molecular diagnostic tests. The nucleoprotein nonetheless intervenes in the immune process by inducing cell death in lymphocytes.

The immunogenicity of all PPRV strains is high and independent of their genetic variability. When an animal recovers from a natural infection or is in contact with a virus strain through vaccination, it acquires long term immunity for all of the other strains and can no longer be infected by the disease. From an immunological perspective, this means that variations in the nucleotide sequences of the F and H proteins do not involve the important antigenic sites. From an epidemiological perspective, this consequently means that PPR has a cyclical nature. The virus can only maintain itself in a population if susceptible individuals regularly join the population.

PPRV shows a variable pathogenicity, or virulence, but no relationship has been established between viral lineage and level of virulence. This variability in virulence is likely linked to the susceptibility of the host, which is a function of the host's breed and species. The virus might have varying affinities for the lymphocytes. The most virulent virus strains may be those which have the capacity to multiply rapidly while attenuated strains may have reduced infectivity due to changes in their tissue affinity, resulting in reduced epitheliotropism.

Within the cell

PPRV must inhabit a living cell to reproduce. It directs the cell to produce copies of the PPRV's own genome and structural proteins. The process takes place in 3 stages: entry of the virion into the cell, unfolding of the viral cycle, and exit of the synthesized virions.

Two special features of PPRV and RNA viruses of the same genus

The RNA-dependent RNA polymerase carried by the virus plays two roles: that of the transcriptase to synthesize messenger RNA which are translated into viral proteins, and that of the replicase to reproduce copies of the genome.

The two steps of the viral cycle, transcription and replication, take place without separating from the RNA-Nucleoprotein complex. The viral RNA is never "naked", neither in the virions, nor in the infected cells.

Entry of the virion into the cell

The first step is the attachment of PPRV to the surface of the host cell. The infection starts when the viral H hemagglutinin recognizes a particular cell receptor protein. It is known under the acronym, SLAM (Signalling Lymphocyte Activation Molecule), or CD150. It is expressed on the surface of lymphatic tissue lymphoid cells. This receptor appears to serve as a cellular anchor for all morbilliviruses, and explains their natural tropism for immune cells and the immunosuppression which results when these cells are destroyed en masse.

Once the H-SLAM link has been established, the second external viral protein (F) modifies its conformation and begins the fusion between the viral envelope and the cell membrane. The nucleocapsid is released into the cell cytoplasm where the infection cycle unfolds in two steps: transcription and replication.

Scientists recently discovered that another protein, Nectin-4, serves as an epithelial cell receptor for the measles and distemper morbilliviruses. Also identified in upper respiratory tract epithelial cells of sheep, it could explain the tissue lesions of the nose, mouth cavity, and trachea of infected animals.

Unfolding of the viral cycle

During transcription, the required virus multiplication cycle is initiated, leading to the synthesis of messenger RNA.

The RNA-dependent RNA polymerase recognizes the leader, binds to the 3' end of the virus genome at the level of the genomic promoter, and initiates transcription of the coding sequence of the first gene, the N nucleoprotein. When it reaches the termination signal, it releases the synthesized messenger RNA. It then reinitiates the transcription of the next gene, located 3 nucleotides (CUU for PPRV) away from the intergenic region, and continues like this in a sequential manner up to the L gene. However, at each intergenic sequence, its reinitiation frequency drops, leading to a decreasing gradient (called the transcription gradient) in the amount of messenger RNA produced. In other words, the intergenic sequences are "attenuated". There is a greater abundance of messenger RNA of the first gene, N, than of the last gene, L. This mechanism is a form of regulation aiming to produce the right proportion of each protein for the future virions. Each messenger RNA is translated into a protein by the ribosomes of the infected cell. Once produced, the viral proteins migrate towards cellular organelles (endoplasmic reticulum and Golgi apparatus), then H and F steer themselves towards the plasma membrane.

When sufficient viral N and P proteins have accumulated, transcription gradually gives way to replication, which is the complete copy of the virus genome. As PPRV is a negative-stranded RNA virus, it must produce an intermediary molecule, the antigenome (a positive RNA strand).

RNA polymerase, which plays the replicase role, identifies the trailer and binds to the 5' end of the virus genome at the level of the antigenomic promoter. Ignoring attenuating intergenic signals, it makes a complete complementary copy of negative RNA without stopping. The positive RNA produced is encapsidated at the same time that it is synthesized. The nucleocapsid N-antigenome then serves as a matrix for the synthesis of new negative RNA that also will encapsidate themselves. The latter then can serve as a matrix for the synthesis of new positive RNA, be used for the synthesis of messenger RNA, or associate with neo-structural proteins to form new virions. A regulatory mechanism maintains a ratio of one antigenome for every 10 genomes.

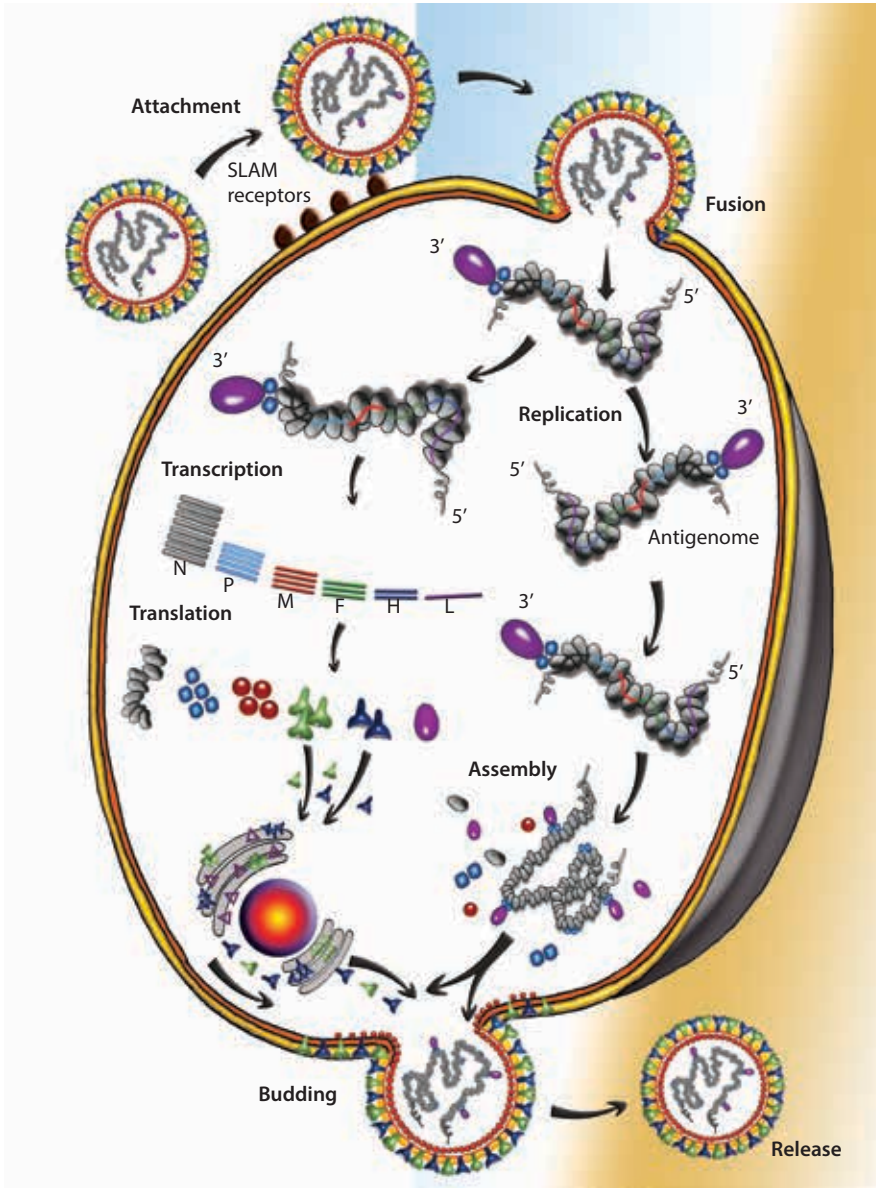
It is then the turn of the matrix (M) protein to intervene as the band leader in the assembly of new virions. Thanks to its affinity for the N nucleoprotein, it establishes links between the neo-nucleocapsids and the H and F proteins, future spicules of the viral envelope inserted on the cell membrane.

Release of new virions

The whole virions are formed and released by budding through the cell membrane. They are only completely released once the H glycoprotein has intervened. Its neuraminidase enzyme activity breaks the bond between the viral spicules and the sialic acid of the cell membrane. PPRV is the only morbillivirus equipped with this capacity.

After their release, the virions spread and contaminate other cells. They also can pursue a cell-to-cell infection process. The expression of the two viral H and F proteins on the surface of the infected cell allows these proteins to interact and fuse with healthy neighbouring cells without passing through the extracellular environment. They form syncytiums (multinucleate giant cells) which allows their progression without interference from neutralizing antibodies.

The multiplication cycle of PPRV



A cyclical and seasonal disease

PPR evolves in two epidemiological forms, one epizootic, the other enzootic. When PPR hits previously disease-free areas where animals have had no prior exposure to the virus, the disease is epizootic. Its clinical expression is most often acute with mortality and morbidity rates which are a function of the susceptibility of the species and breed, but which can reach 90 to 100%. In numerous countries in Africa, the Middle East, and Asia, it is present in an enzootic form with a low mortality rate (20% or less) and variable but high seroprevalence rates which can exceed 50%. In these areas, the virus circulates quietly, its clinical expression unapparent, but it remains ready to clinically manifest itself as soon as the population of susceptible small ruminants is sufficiently large, or when animals are in poor health, environmental conditions are favourable, or social, cultural, or economic practices increase the risk of virus transmission. The disease then expresses itself in epizootic outbreaks that appear with a cyclical and/or seasonal frequency.

The cyclical character of PPR is determined by the strong immunogenicity of PPRV and the length of the economic life of goats and sheep. The conjunction of these two factors favours the expression of the disease. The high herd replacement rate of 30% per year, compared for example to only 10% in cattle, creates an immunologically naive population of small ruminants at the level of village communities which is sufficiently large for the virus to be maintained and for epizootic outbreaks to occur.

"A goat is like a savings account. It is a source of income. It feeds the people, both in the countryside and in the cities."

An FAO representative - Democratic Republic of the Congo, 2012

The seasonal character of PPR is determined by climate factors which favour the survival of the virus in the outside environment and/or weaken the resistance of animals, and by the movements and regroupings of small ruminants due to agricultural, livestock, and trade practices.

With the arrival of the cool or rainy seasons, the temperature and humidity are favourable to the virus and increase its survival time. Animals which have just survived a long period of drought are often thin and weak. Their weakened immune defences render them susceptible to pathogens and benefit the virus. Epizootic peaks are frequent and numerous. In Sahelian Africa, this context of physiological stress is aggravated by the arrival of the harmattan, a dry, dusty wind which favours respiratory infections.

"In my village, out of over 400 goats, only about twenty old bucks still survive."

Village head - Democratic Republic of the Congo, 2013

The seasonal migrations of herds in search of available forage and water begin just when climate conditions are increasing the risk of contamination. These migrations are an important factor in the spread of the virus towards disease-free regions. In certain West African countries such as Mauritania, transhumance routes stretch over hundreds of kilometres, with movement from the north towards agro-pastoral areas in the south. These areas hold high concentrations of animals and lie near the borders of Mali and Senegal where frequent cross-border movement takes place. A study published in February 2014 in the journal, *Emerging Infectious Diseases,* confirms this and shows the existence of a gradient of increasing seroprevalence from the north to the south of Mauritania related to herd movements.

The same holds true in Asia where, in a country with very different ecological zones such as Nepal, the return of small ruminant herds from mountain pastures before the start of the cold season contributes to increased epizootic outbreaks in sedentary herds in the plains. In other countries of Africa and Asia, recurrent droughts oblige nomad populations to open new transhumance routes, helping to increase the risk of encounters between healthy and sick animals.

Each year, traditional and religious festivals are occasions for intense trading activity involving goats and sheep. The animals are brought from pastoral areas to livestock markets and slaughterhouses in towns to meet the high demand for meat. This gathering together and mixing of small ruminants from many different points of origin facilitate virus transmission.

When animals are sold or traded, geographically scattered inside a country but also sent towards bordering countries, they are likely to spread the disease when they are still in the incubation stage, well before the appearance of clinical signs, or when the disease is expressed in the sub-clinical form. The same holds true when the export and import of animals take place without sanitary controls. The emergence of PPR on the island of Grande Comore at the end of 2012 is an example of virus introduction into this Indian Ocean area via the importation of infected goats from Tanzania. Epidemiological monitoring in different countries confirms that there are more epizootic outbreaks of PPR during these festival periods, with a greater concentration near trade routes.

"People here live simply and have few resources. There is a lot of poverty. Animals are the main source of income for everyone. If a PPR epidemic were to break out, up to 90% of sheep and goats could die."

A veterinarian - Yemen, 2013

Risk factors	
Virus	• Persistence in the environment (temperature, humidity).
Animal	• Species • Breed. • Age. • Health status (weakened by illness, ill-nourished). • Immune status (immunosuppressed).
Herd	• Large herds. • Mixed herds of susceptible animals (goats, sheep). • Introduction of animals of unknown origins without a health guarantee or quarantine period. • Return from markets of unsold animals. • Mixing of local sedentary herds with transhumant herds. • Animals of different ages forced to live closely together. • Accommodating animals in transit.
Environment	• Variability of climate factors according to the season (temperature, humidity, wind). • Agro-ecological zones (mountains, plains). • Agro-pastoral zones with a high density of small ruminants. • Agro-pastoral border zones.
Livestock rearing practices	• Pastoralism (seasonal transhumance, nomadism). • Changes in usual routes (conflict, insecurity, drought). • Cross-border pastoralism routes. • Sharing pastures and watering points leading to a mixing and regrouping of vulnerable (young) and high risk (sick adult) animals.
Markets and trade	• Gathering animals and live animal markets. • Legal and illegal cross-border movements of animals. • Imports and exports without health inspections. • Increasing commercial trade between livestock rearing areas towards meat consuming areas to meet growing demand for animal protein. • Trade routes.

Risk factors

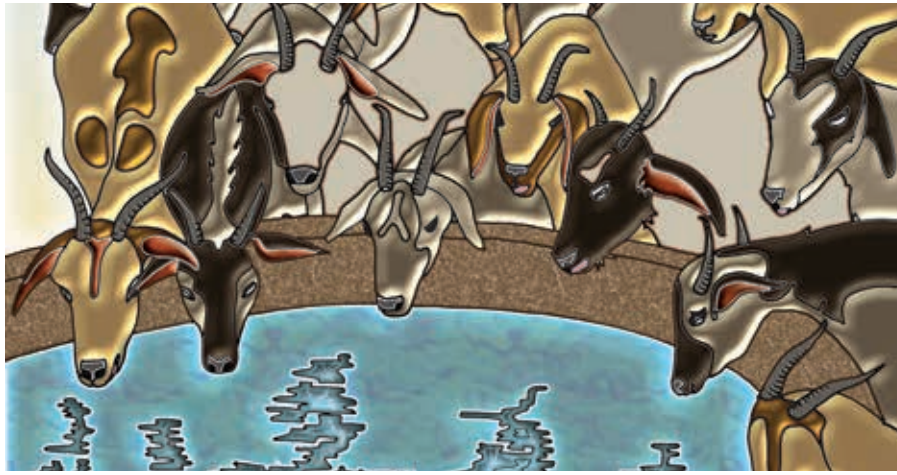
Social, economic, and cultural practices

Human behaviour

- Religious festivals giving rise to intense trade movements and the setting up of slaughter centres.
- Trading, loaning and giving animals.
- Theft of animals.
- Risky livestock farmer behaviour by moving animals in PPR areas to disease-free areas.
- Migration of rural populations in infected areas towards disease-free urban areas.
- Fleeing areas of socio-political or climate insecurity.

Health surveillance

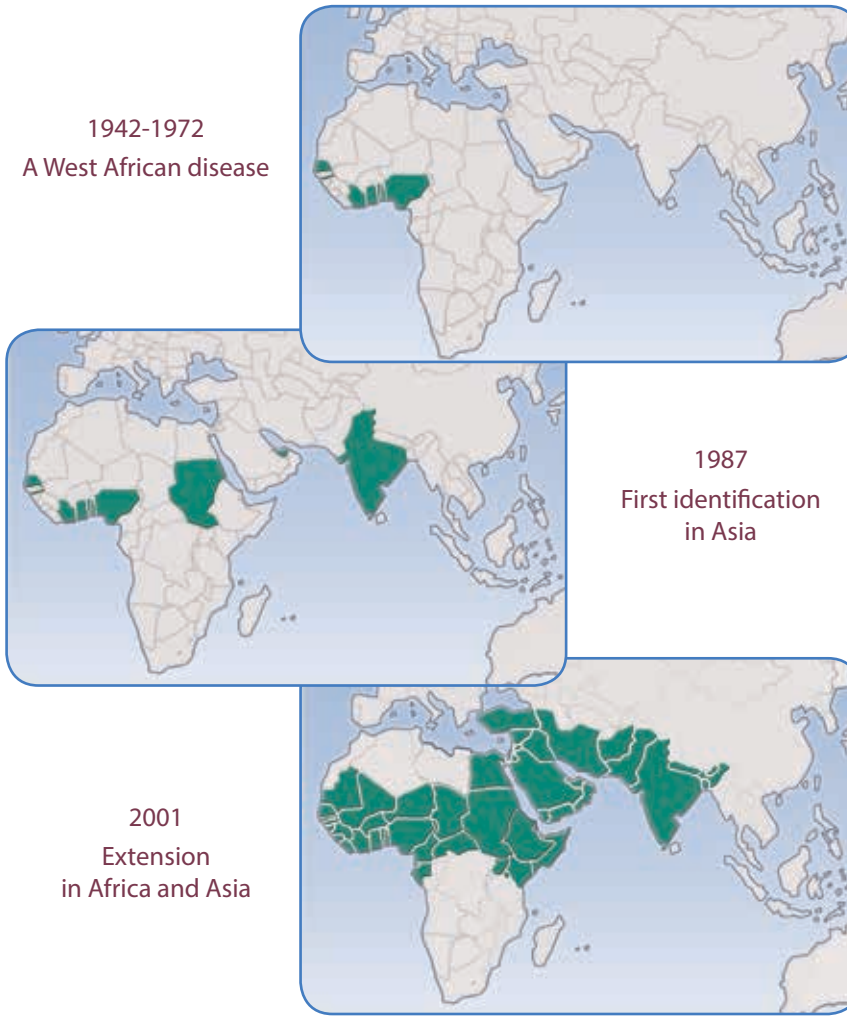
- Insufficient knowledge about the disease in disease-free areas and of some people keeping animals.
- Insufficient health monitoring.
- Difficult access to veterinary services, medicines, and vaccines.
- Insufficient training and information.
- Lack of trained health officers and veterinarians.
- Absence of vaccination.



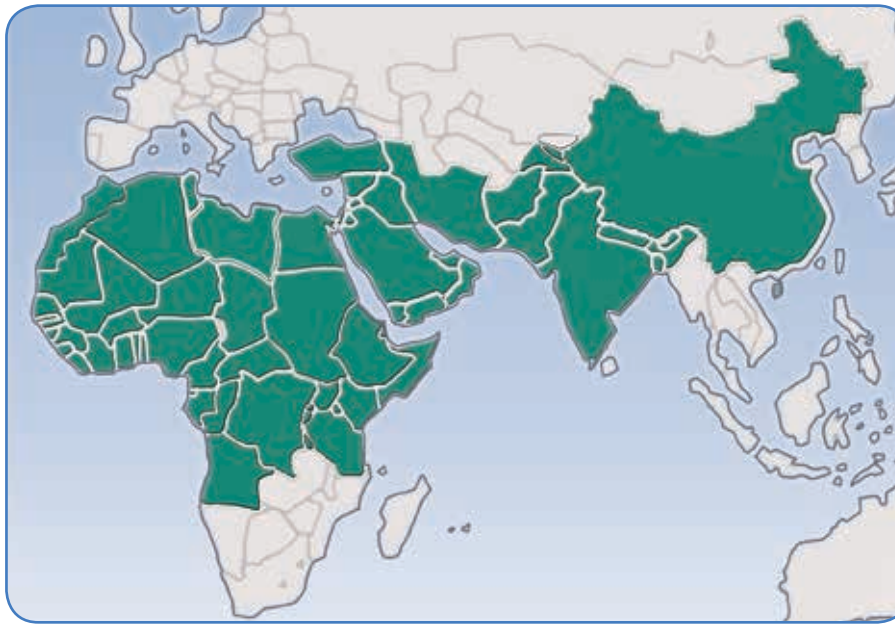
Watering points are sources of contamination.

A spreading transboundary disease

The history of PPR began 75 years ago when it was identified in the Ivory Coast. Up until the 1970s, it was only reported in coastal West African countries: Benin, Senegal, Togo, Nigeria, and Ghana. In the beginning of the 1970s, it appeared in Sudan. Between 1980 and the early 1990s, it spilled over from the African continent onto the Arabian Peninsula (Oman 1983, Saudi Arabia 1988, Kuwait and the United Arab Emirates 1991) and the Middle East (Lebanon 1986, Jordan 1989, Israel 1993, Iran and Iraq 1994). It reached South Asia in 1987 when it was diagnosed in India. It has become a panzootic.



It is pursuing its geographic spread in an easterly direction, giving the impression that it is colonizing territories that were freed of rinderpest following the global eradication program coordinated by the FAO and OIE. It covers South Asia (Bangladesh 1993, Pakistan 1994, Afghanistan 1995, Nepal 1995, Maldives 2009, Bhutan 2010), extends through Central Asia (Kazakhstan and Tajikistan 2004) to East Asia, appearing first in western China (Tibet 2007) before spreading throughout China at the end of 2013 when there was a massive and rapid spread of the disease. Positive test results obtained on serum sampled from small ruminants in 2006 in Vietnam indicates that PPRV is also likely present in Southeast Asia.



2014 : A transboundary disease with increasing incidence

In Africa, at the end of the 1990s PPR was reported in all of the countries in the sub-Saharan region, from the Atlantic Ocean to the Red Sea, where it has now become endemic. Over the past ten years, it has gradually spread towards East Africa (Ethiopia 2007) and headed south over the Equator to cover a belt of countries between Gabon and Somalia, including the Democratic Republic of the Congo, Uganda, Kenya, and Tanzania. Positive serological results have been obtained in Rwanda and Burundi. In 2012, PPR was identified for the first time in Angola and on the Comoros islands in the Indian Ocean, raising the risk of virus incursion into neighbouring Mozambique, Malawi, and Madagascar and movement towards the large game reserves of southern Africa where domestic and wild small ruminants co-exist.

Morocco was infected for the first time in 2008. After Egypt, which has been infected since at least 1989, it was the second North African country to declare the disease to the OIE. In 2007, serological traces of the infection were observed in Tunisia, and the country declared clinical outbreaks of PPR in 2011, at the same time as Algeria. This disease presence in countries along the southern rim of the Mediterranean has extended to Turkey since 1999. PPR remained localized in the Asian part of the country until 2004, when outbreaks in Thrace near the border to Bulgaria and Greece alerted international health organizations to the risk of its introduction into Europe.

The global epidemiological PPR situation is constantly evolving and its transboundary spread recently seems to have accelerated in both Asia and Africa. In most countries where the disease it endemic, it re-emerges in a cyclical and seasonal pattern, but it also emerges in new areas and in new countries, indicating highly active viral circulation. Monitoring its progression is based on declarations of epizootic outbreaks to the OIE by the health authorities of the countries concerned. These notifications can by complemented by serological (detection of antibodies) and virological (detection of the virus) field surveys in enzootic and epizootic zones to identify the viral lineage involved, monitor the movements of the virus, understand spread factors and/or assess the impact of vaccination campaigns.

The FAO estimates that in 2014, over 70 countries were affected by PPR. Over the 8-year period between 2005 and 2013, outbreaks of the disease were reported in 37 countries in Africa and 21 countries in Asia and the Middle East. Its continued spread is threatening the livelihoods and food security of over one billion extremely poor smallholders and pastoralists, and is the source of great concern for the international community.

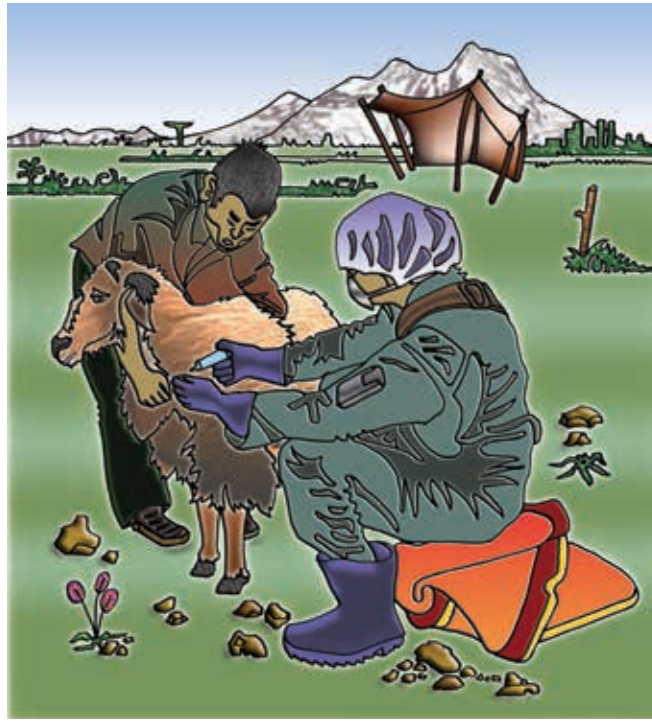
Reasons for its spread

Scientists know today that in the past, PPR was present in numerous countries where rinderpest raged, but it was overlooked or misdiagnosed in the absence of reliable tests that could distinguish between the two diseases. After the last rinderpest outbreak was stamped out in the early 2000s, international animal health organizations turned their attention to PPR, which had been hitherto neglected.

When the circulation of the rinderpest virus was arrested and the vaccination campaigns against this disease ceased, small ruminants were left completely exposed to PPR. It had been fairly common for veterinary services to vaccinate small ruminants with the rinderpest vaccine, which conferred excellent cross-immunity against PPR. During the control phase of the rinderpest eradication program, the use of this vaccine, even for small ruminants, was banned, yet a homologous PPR vaccine was not yet in circulation to fill the gap.

Furthermore, some argue that the end of rinderpest vaccinations in cattle increased their receptivity to the PPR virus and that cattle could play a role in PPR transmission, something which has never been demonstrated.

The setting up of PPR surveillance and control programs, raising awareness of local populations, the provision of sensitive and specific immunosorbent and molecular diagnostic techniques, and the compulsory notification of disease emergence to the OIE since 2004 have confirmed the extensive geographic cover of the disease. Moreover, although a highly effective attenuated vaccine has been available since 1989, the absence of large scale vaccination campaigns has led to the emergence of the disease in areas and countries that previously had been disease-free, and facilitated the passage of the virus to other species such as dromedaries.



To fight animal diseases is to contribute to the fight against poverty and to ensure the food and nutrition security of the poorest people of the world.

Over the past few years, the key factors behind the speed of the geographic spread of the disease are related to the growing world population of small ruminants, human migration, and the mobility of animals due to livestock practices and trade.

The movement of animals over long distances and beyond national frontiers dictated by traditional pastoral and transhumance livestock practices facilitates encounters between healthy and infected animals and contributes to the spread of the virus. The same is true of the uncontrolled migration of people accompanied by their small livestock. Their flight from socio-political insecurity (massive displacement of refugees to escape armed conflict), economic insecurity (rural exodus to escape poverty), and climate insecurity (recurrent drought, catastrophic flooding) increases the risk of PPR spreading to disease-free regions and countries.

However, the primary factor behind the spread of PPR is the intensification of animal movements to meet an increasing demand for animal protein. The demographic and economic development of mega-cities and consequent increase in demand for meat induce the ever increasing trade of live animals, which are moved from rural production areas to urban consumption zones. Trade flows are particularly important during religious holiday periods in Islamic countries. Small ruminants often cross borders, sometimes illegally, without undergoing any health controls.

"My husband is chronically ill but now that I have the goats I can sell one to pay for hospital fees and transport to the hospital and I have seen an improvement in my husband's health. I get 4,500 Malawian kwachas (51 US$) for one goat. I can buy food and my children never go to bed hungry like before".

A village woman - Malawi, 2009

Depending on the epidemiological status of the country of origin, which most often is endemic, the risk of the South-South spread of PPR through the introduction of infected animals must be considered from both a health and economic perspective even if small ruminants do not have an impact on international markets in the same way as cattle.

The development of an effective PPR surveillance and control strategy thus must now rely on linking epidemiological field knowledge regarding animal mobility (trade and migration routes) at the local, national, regional, and international level with molecular data on the spatial distribution of PPRV lineages.

What is the risk for Europe?

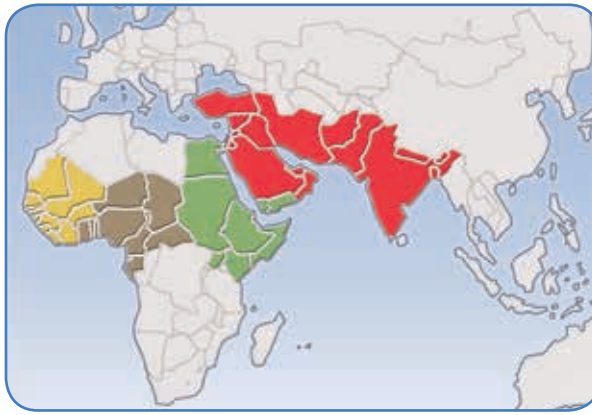
The presence of PPR in countries on the southern shores of the Mediterranean, North Africa, Turkey, and the Middle East, led the European Food Safety Authority (EFSA) to assess the risk of the virus crossing the borders towards goat and sheep stocks in European Union countries. In a January 2015 study entitled, *Scientific opinion on the peste des petits ruminants*, it notes that the most frequent and efficient route for the introduction of PPR into a country is the entry of infected live animals. As the importation of live small ruminants from endemic countries in the South was banned by European health legislation, the risk of PPRV introduction is linked to the illegal movements, for example, via private vehicles. Indirect virus introduction pathways, either through contaminated meat products or fomites, such as livestock transport vehicles which have not been disinfected, theoretically are possible but viral transmission to a disease-free animal is highly unlikely.

The risk of PPR introduction in France was estimated to be minimal to none (level 1 and 2 on a scale of 9). If, however, the virus enters French territory or that of a European country, the application of regulations in force should enable rapid control (slaughter and/or vaccination before culling) and renders unlikely the risk of endemisation and serious economic consequences for the sectors concerned. Nonetheless, the most effective prevention measures to reduce the risk of PPR spread at the global level rely on reinforced cooperation between European Union countries and endemic countries in the South.

Lineages on the move

The development of phylogenetic analyses and molecular diagnostic methods using sequencing, alongside the existence of gene banks, have rendered it possible to determine the lineage of the strain causing an epizootic PPR outbreak and to deduce its geographic origin in order to better understand epidemiological situations. The case of the 2008 Moroccan epizootic illustrates this point well. After genetic typing identified the virus strain responsible as lineage IV, the initial hypothesis that PPR had been introduced from West African countries (where viral lineages I and II circulate) was dismissed.

Early phylogeny studies conducted at the end of the 1990s on samples collected over a 30-year period established that the strains found in West Africa were lineages I and II. Lineage I was present in the Ivory Coast (where PPR was first identified), Senegal (where the first viral strain was isolated), Guinea, Guinea-Bissau and Burkina Faso. Lineage II was present in Ghana, Nigeria (the source of the PPRV vaccine strain), Benin, and Mali. Lineage III virus strains were identified along the shores of the Red Sea in East Africa (Ethiopia, Sudan) and in part of the Arabian Peninsula (Oman, United Arab Emirates). Lineage IV, first isolated in India at the end of the 1980s, was distinguished by its broad geographic cover and its confinement to Asia. This initial distribution of virus lineages reflected separate genetic evolution due to limited exchanges between these geographic regions.

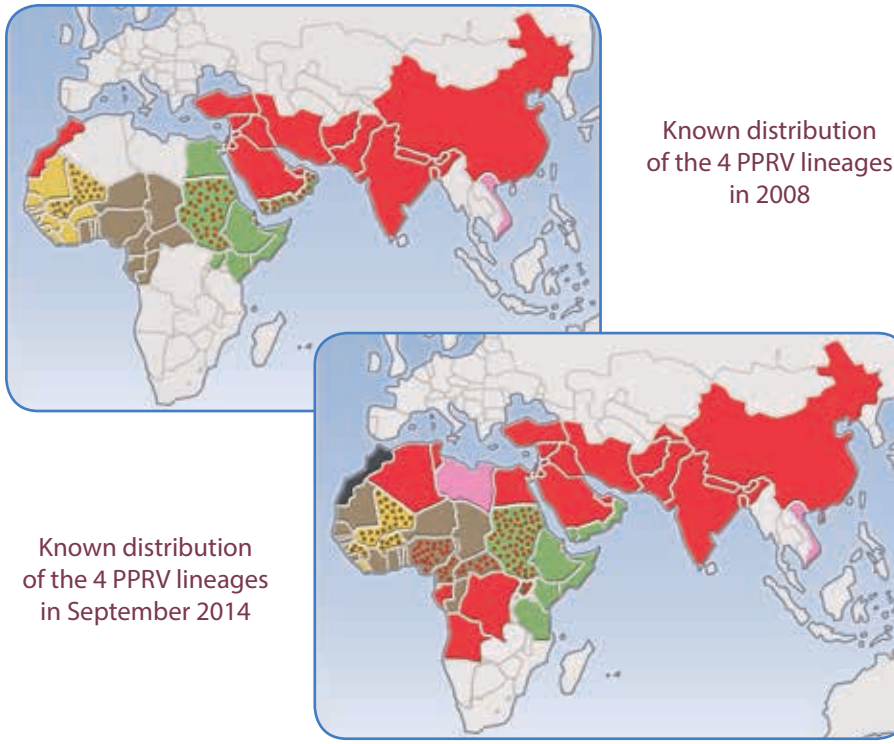


Known distribution of the 4 PPRV lineages in 2001

However, since the late 1990s, the geographic spread of the disease, with the emergence of PPR outbreaks in countries which had been disease-free, and re-emergence in countries and zones known to be enzootic, has radically changed the situation.

Epidemiological surveillance has revealed that lineage IV is continuing to spread in Asia in an easterly direction, but is also extending west and invading Africa, where it is becoming the dominant lineage. In 2000, it was discovered in Sudan, in East Africa, where it cohabitated with the native lineage III and passed into a new host, the dromedary. It then spread to Egypt and across North Africa, finally reaching Morocco in 2008. Today (2015), lineage IV is present across North Africa with the exception of Morocco, which succeeded in eradicating the disease through mass vaccination campaigns. It also is circulating in the northeast of Africa (Sudan and Eritrea) and in Central Africa (Cameroon, Central African Republic, Uganda) where it coexists with lineage II. The most recently infected African countries, Angola and Comoros, are an indicator of its spread from the north to the south of Africa.

A similar phenomenon occurred in West Africa with lineage II, today alone present in Senegal, having taken the place of lineage I.



These upheavals in the distribution of lineages must be interpreted cautiously as epidemiological data collected in the field remains very incomplete due to inadequate surveillance. While the link between animal mobility and the spread of the virus is now certain, it cannot alone explain the dominance of lineage IV in West and Central African countries which have no tradition of small ruminant exchanges with countries east of the Red Sea.

One answer may be found in the capacity of PPRV to adapt its pathogenicity to selective changes in its environment, notably to the different susceptibility of its different hosts. Thanks to its capacity to mutate, which is characteristic of RNA viruses, PPRV releases a multitude of viral particles into the tissues of infected animals. These particles are genetically close but subtly different from the initial strain, forming virus sub-populations with different replicative potential known as viral quasispecies. When one of these sub-populations acquires a favourable genetic ability, it assumes the upper hand through a greater power of dispersion and becomes the dominant player. The most invasive strains are today classed in lineages II and IV, but this could change tomorrow. In effect, nothing can link invasive power, which is likely connected to virulence, to membership in any particular lineage identified by phylogenetic criteria.

Virus routes

Assumed spread of PPRV lineages:

- East-West in North and West Africa
- North-South in East and Southern Africa

Lineage II

Lineage III

Lineage IV

In contrast, these mutations are probably related to a crossing of the species barrier. This jump is facilitated by the crowding together and abundance of various genetically similar host species: ovines, caprines, bovines, dromedaries, wild ruminants... We should thus learn from past lessons revealed by advances in genetic study methods (rinderpest and measles viruses share a common ancestor) and avoid the emergence of new viruses by eradicating PPRV as rapidly as possible.

The geographic spread of PPR resulting from very active virus circulation, its adaptation to new geographic areas and to new hosts, and games of dominance, extinction and coexistence between lineages, are challenging research and reference laboratories. They have begun epidemiological studies to better understand the link between the genetic plasticity of PPRV, channels of disease spread, and movements of animals. The results will be extremely useful for the establishment of a PPR control strategy.

GenBank: a genetic sequence bank

Genbank is a collaborative database of nucleic acid sequencing maintained by the NCBI (National Center for Biotechnology Information, USA). The development of molecular biology technologies in the 1990s, notably complete and partial genome sequencing, enabled a bank of gene sequences of PPRV strains to be constituted within GenBank that were based on collections held by research and reference laboratories. The bank holds sequence data of F, H, and N protein gene fragments, which allowed the strains to be grouped into 4 viral lineages, and the full sequence of the genomes of a few strains.

Up until 2013, only 639 PPRV nucleic acid sequences were available in the GenBank, of which only 11 complete genomes belonged to virus lineages I, II, and IV. Among them was the vaccine strain of lineage II, Nigeria 75/1 (accession n°: X74443). In 2014, GenBank obtained several new complete sequences, that of a lineage II strain isolated in 2013 by CIRAD in Senegal (accession n°: KM212177), and for the first time that of several strains of lineage III coming from countries in East Africa (Uganda 2012: KJ867543; Ethiopia 1994: KJ867540) and the Middle East (United Arab Emirates 1986: KJ867545; Oman 1983: KJ867544). This genetic bank is indispensable in tracing the viral lineages involved in PPR epizootics.

A history that remains incomplete

The evolutionary history of PPRV is a recent phenomenon that has unfolded rapidly. A molecular biology study published in the journal, *Emerging Infectious Diseases*, in December 2014 found that the most recent ancestor shared by the 4 PPRV lineages dated back to the beginning of the 20th century, a few dozen years before PPRV was identified and recognized as being distinct from the rinderpest virus. Lineage III, today present in East Africa and the southern part of the Arabian Peninsula, diverged first, followed by lineage I. Lineages II and IV separated more recently.

Phylogeographic analyses confirm that lineages I and III are linked to Africa. Lineage I likely originated in Senegal, lineage II in Nigeria, lineage III in Sudan, and Asian lineage IV probably in India. These results are consistent with epidemiological knowledge of the disease and suggest that PPR was introduced into West and East Africa as commercial trade and transhumance movements intensified.

The demographic analysis of PPRV confirms the genetic stability of viral lineages up to the mid-1990s, followed in the 2000s by increased genetic diversity reflected in the occurrence of numerous epizootic outbreaks in endemic countries, the incursion of the virus into previously disease-free countries, and the rapid adaptation of certain lineages through mutation. The use up to the 1990s of a heterologous attenuated rinderpest vaccine to fight PPR in small ruminants may have slowed the genetic evolution of the virus, limiting its genetic variability and potential to spread.

Several facets of PPRV's history remain unknown, notably the moment that it adapted to small ruminant populations. However, ongoing research into its genome is opening new avenues that could facilitate understanding of the factors behind the disease's emergence and spread.

"The disease is at the gates of Europe. Our strategy is systematic vaccination. An effective, universal, inexpensive vaccine exists."

Bernard Vallat - OIE Director-General, 2014

In the field

Clinical diagnosis

Suspicion of PPR is based on a combination of several clinical signs that should alert livestock farmers, notably fever associated with nasal discharge and lacrimation, which appear suddenly in several small ruminants in a herd. However, these three elements are not enough to establish a diagnosis because they are not specific to PPR. They also are expressed in other pathologies of small ruminants present in PPR endemic areas such as contagious ecthyma and contagious caprine pleuropneumonia.

A rigorous differential comparison of symptoms and the careful inspection of all animals in a herd are thus critical to assemble all of the clinical and lesional clues which are not all always visible on a single individual. Depending on the breed, species, age and immune status of animals, the disease can take different clinical forms within the same herd. This poses additional difficulties for untrained farmers trying to identify the disease, especially if PPR is accompanied by confusing secondary infections such as respiratory pasteurellosis.

The occurrence at the herd level of outside events considered to be risk factors must be taken into account and can reinforce the suspicion of PPR. This global analysis of the epidemiological situation is very important in disease-free areas where the risk of disease emergence is high.

Post-mortem diagnosis

Post-mortem examination of animals with the macroscopic observation of characteristic tissue lesions on digestive, respiratory, and lymphoid organs will confirm the provisional clinical diagnosis. It will only be definitive following the laboratory examination of samples drawn from living animals (blood samples, swabs of nasal and ocular secretions, scraping of gingival mucosa) and dead animals (tissue fragments from lungs, intestines, lymph nodes and spleen) to discover the direct or indirect presence of the virus.

"My neighbours and I have all lost our goats. I took a loan from an NGO to get medicines. Three fifths of the animals in the area are dead despite peoples' efforts to protect them."

A villager - Democratic Republic of the Congo, 2008

Laboratory diagnosis

Simple, rapid and reliable laboratory methods have been developed over the past 30 years and are routinely used today to confirm the field diagnosis. They rely on different enzyme-linked immunosorbent assay (ELISA) tests to detect antibodies and antigens in biological samples, and on Polymerase Chain Reaction (PCR) molecular biology techniques to detect the virus genome.

Serological diagnosis

Competitive ELISA is the leading serological diagnostic test. The method is known for its simplicity, specificity, and capacity to test a large number of samples in a short period of time (results in 2 hours) because it can be automated. It is well suited for emergency situations and provides reliable results even when sterile conditions have not been strictly respected. It operates by detecting traces of the virus in an animal's serum through the presence of PPR antibodies; it does so by putting viral N and H antigen proteins into competition with monoclonal anti-N and anti-H antibodies.

The method is used in serological surveys to assess the prevalence of PPR antibodies in herds while taking into account the individual characteristics of the animals (age, breed, species, sex). It allows the early detection of virus circulation in a geographic area in the absence of all clinical signs, and even before virus isolation. In the absence of any vaccination campaign, the seropositivity of an animal is an indicator of its contact with the pathogen and its natural immunity.

With this indirect diagnosis of PPR based on antibody detection, it is possible to assess and update the epidemiological situation of PPR in a region or a country, follow its spread dynamics in space and over time to identify at-risk zones, and characterize the factors explaining its variability. These are all highly useful indicators for the implementation of a vaccination-based PPR control strategy.

Different competition ELISA tests are available and are sold as kits, and their performance is regularly improved through technical innovations. CIRAD developed a competition ELISA (ID Screen® PPR Competition) in collaboration with a private partner (ID.vet, Montpellier) based on the N nucleoprotein, the most transcripted because its gene is first on the RNA molecule.

The anti-N antibodies produced by the infected animal consequently are the most abundant antibodies in the serum and therefore are the focus of serological analyses even though they do not provide any protection. This test was validated by the OIE as an alternative to the viral seroneutralization test, or VNT, which is more stringent (requires cell cultures, manipulation of the live virus, and sterile serums), and time consuming (results in 2 weeks). VNT nevertheless remains the method prescribed by the OIE, and is used in reference laboratories to confirm results and for the international trade of animals. The competition ELISA developed by The Pirbright Institute targets the anti-H antibodies.

Virological diagnosis

Proof of the presence of PPRV in samples is provided by direct diagnostic methods. They are based on the identification of antigen proteins, the identification of viral genetic material, or the isolation of the virus itself.

The detection of antigen proteins in tissue samples and secretions of infected animals uses variations of the ELISA technology: sandwich ELISA and immunocapture ELISA. A sandwich ELISA diagnostic kit (ID Screen® PPR Antigen Capture) based on anti-nucleoprotein monoclonal antibodies developed by CIRAD is now marketed by the company, ID.vet (Montpellier, France).

Through an industrial partnership, CIRAD also has developed a prototype rapid diagnostic test (pen-side test) using immunochromatography (Lateral Flow Device) for the detection of viral antigens. Currently in the process of being validated, it will offer countries in the South a diagnostic tool which is easy to use in the field and provides an immediate reading (several minutes) of results. Other similar tests have been developed by other laboratories (for example, The Pirbright Institute). For the time being, these tests have not yet been widely used in the field.

The detection of viral genetic material relies on molecular biology techniques. One used routinely in numerous laboratories is the standard RT-PCR technique (Reverse transcription - Polymerase Chain Reaction). It is specific, rapid, and very sensitive, but requires specialized equipment and very careful implementation to obtain reliable results. After viral RNA is extracted, the technique involves two steps. In the first step, reverse transcription converts the viral RNA into complementary DNA (cDNA). In the second step, polymerase DNA is used for the exponential amplification of a nucleotide sequence framed by specific primers located on the gene of either the N protein, which is the most abundantly transcripted, or the F protein.

This gene amplification reaction permits the sequencing and genotyping of the virus by identifying its lineage. It allows phylogenetic and phylogeographic studies to be conducted which are indispensible for the epidemiological monitoring of PPR and an understanding of the movements of the virus.

Standard RT-PCR cannot be automated. Real-time RT-PCR, also known as quantitative RT-PCR (QRT-PCR), is today used in high capacity (in terms of numbers of samples) reference laboratories for surveillance and screening. Its results allow the rapid identification of the virus strain involved in an outbreak, but it cannot be used in epidemiological studies. A variation is the RT-LAMP (Loop mediated isothermal amplification technique), which is based on a polymerase chain reaction at a constant temperature. It was adapted by the FAO and International Atomic Energy Agency (IAEA, Vienna, Austria) into a molecular diagnostic field kit for rapid screening (under one hour). While the confirmation of results by a reference laboratory remains necessary, this mechanism, which was tested in Cameroon in 2012, is an example of a technological innovation helping veterinarians in countries in the South which can speed up the implementation of control measures aiming to curtail the spread of the disease.

"Previously, I had to collect samples and then return to my laboratory or wait for samples to be sent to me from the field. It sometimes took weeks, or even an entire month, to be able to test the samples and confirm an outbreak."

A veterinarian - National Veterinary Laboratory (LANAVET), Cameroon

Virus isolation through cell cultures is indispensable for the precise molecular characterization of a virus strain. Specimens taken from animals must be of good quality in order for the viral particles to remain alive and infectious. Only qualified laboratories are able to use this technique, which is long (1 to 2 weeks) and cumbersome. Virus isolation is done after the virus is injected into primary sheep kidney or lung cells or into Vero cells (green monkey kidney cells). In the past few years, the use of transgenic cells expressing on their surface the SLAM receptor protein, CD 150 of PPRV, has considerably reduced the time required for virus multiplication. The virus strains obtained are referenced in a strain bank that is very useful for epidemiological studies.

Old but still valid

After unfruitful attempts in the 1960s to develop a live attenuated PPR vaccine, the decision was made to use the existing rinderpest vaccine. The close antigenic and immunogenic properties of these two morbilliviruses were expected to give small ruminants vaccinated against rinderpest a broad immunity against the PPR virus. This heterologous vaccine also had the advantage of being inexpensive due to the large scale production of the rinderpest vaccine for cattle.

It was used up to 1989, when CIRAD (Diallo *et al.*) and The Pirbright Institute released a homologous attenuated virus vaccine obtained through the successive passage in cell cultures (Vero cells or green monkey kidney cells) of a PPRV lineage II strain, 75/1, isolated in Nigeria in 1975. Its genetic sequence, referenced as X74443, is available in the GenBank. Without risk for pregnant females, it provides immunity for at least three years, which covers the usual economic life of a goat or sheep. Protection becomes effective 14 days after a single injection. At the time, its adoption presented the advantage of not interfering in the epidemiological cycle and serological surveillance of rinderpest while providing small ruminants cross protection against this disease.

In 1998, the OIE approved its adoption in PPR vaccination campaigns. In parallel, the continued use of the heterologous vaccine was prohibited to avoid introducing a bias into epidemiological studies of rinderpest. Although other vaccines used in India were developed from lineage IV PPRV strains (Sungri 96, Arasur 87 and Coimbatore 97), it is today the most widely used vaccine worldwide, recommended by the OIE for the vaccination of small ruminants.

In 25 years, it has proved its safety, effectiveness independent of the viral lineage involved, and low large-scale production costs. The mass vaccination campaign undertaken in 2008 to contain the PPR epizootic in Morocco is an illustration: 25 million doses of vaccine were produced in several weeks by the Moroccan laboratory, Biopharma based on the parent strain, Nigeria 75/1, which was provided by CIRAD, and over 20 million sheep were successfully vaccinated.

A preventive vaccine is administered before the emergence of the disease. The animal reacts by producing antibodies that neutralize the virus.

A curative or therapeutic vaccine is administered when the disease has occurred. It acts to restrain the virus from multiplying.

As for all morbilliviruses, the weak point of the vaccine is sensitivity to heat. In countries in the South, it is not always easy to maintain the cold chain during vaccination campaigns. Experiments to achieve thermal stability by associating a cryoprotectant containing trehalose or tris-trehalose have succeeded in prolonging its half life of several hours to 21 hours at 37°C after reconstitution, and up to 14 days at 45°C in a freeze-dried state.

Its other drawback in the framework of a PPR control program is that it does not allow a vaccinated animal to be serologically distinguished from an animal that was naturally infected by the virus. Over the last dozen years, advances in the field of molecular genetics have opened new research avenues for its improvement. One is looking into the development of recombinant vaccines. Another, one promising for the fight against viral diseases, is directed at developing therapeutic antivirals

New generation vaccines

The attenuated vaccine expresses the same antigens as the wild virus. It is therefore impossible from a serological point of view to recognize if the antibodies are the result of vaccination or infection. To remove this constraint, for the past twenty years several international scientific research teams, including that of CIRAD, have been trying to obtain DIVA vaccines (Differentiation of Infected and Vaccinated Animals).

There is no question that such vaccines would benefit areas in the South where the disease is endemic. They allow both the circulation of the virus and the effectiveness of vaccination campaigns to be monitored. Under the framework of the PPR eradication program, the use of an attenuated DIVA vaccine represents a saving of time and money in epidemiological surveillance by also allowing targeted vaccination.

The same holds true for countries which are currently disease-free, such as those in the European Union, where the risk of the introduction of seropositive animals cannot be dismissed given the intensity of global trade and the rapid geographic spread of PPR over the past few years. To be able to identify the disease status, vaccinated or infected, of a small ruminant renders it possible to avoid the precautionary mass culling of animals, which is no longer acceptable to civil society. From an economic and social perspective, it also is a means for countries to prove the absence of infection, a way of ensuring the uninterrupted cross-border circulation of goats and sheep, and a tool to guarantee disease-free countries the maintenance of their PPR-free status once it has been accorded by the OIE.

These DIVA vaccines can be recombinant vector vaccines able to express foreign genes. The viruses of the *Capripoxvirus* genus, large DNA viruses of the *Poxviridae* family, are known as to be excellent vaccine vectors. Thanks to molecular genetics tools, they are used as "Trojan horses" to carry antigens into the vaccinated animal and induce an immune response. Their genetic plasticity renders them able to express different antigens without affecting their replication. A recombinant capripox/PPR vaccine was obtained by inserting into the genome of an attenuated capripox strain the F or H genes of the external membrane glycoproteins of PPRV, which are those which induce a host immune response. The operating principle of these DIVA vaccines is simple. With appropriate diagnostic tests based, for example, on the N nucleoprotein of PPRV, it is possible to distinguish a vaccinated animal, which would be seronegative with the N-PPR test, from an infected animal, which would be seropositive using the same test.

The other advantage of this bivalent capripoxvirus-PPR vaccine is to provide in a single vaccination, and thus at less cost, good immune protection against these two important diseases of goats and sheep, sheep and goat pox and PPR, which are endemic in the same geographic areas. This recombinant vaccine is furthermore heat resistant. Trivalent recombinant vaccines have been developed associating three diseases: capripox, PPR, and Rift Valley fever.

Other DIVA vaccines are marked recombinant vaccines obtained by the deletion (loss), substitution, or insertion of genes or gene fragments in the virus genome thanks to negative RNA virus manipulation and reverse genetic technologies. These allow an infectious clone of the vaccine virus carrying a mark distinguishing it from the parent strain to be obtained in vitro. Research undertaken over the past few years is seeking to obtain a PPR DIVA vaccine based on the genetic recombination of the current Nigeria 75/1 vaccine strain, which does not allow infected animals to be distinguished from vaccinated ones.

Until recently, no infectious clone of the PPR vaccine virus could be generated, although positive results were obtained with other morbilliviruses like the rinderpest, measles, and distemper viruses. However, this step was successfully completed in 2012 and a patent (FR 1257980) filed by CIRAD now protects a marked PPR vaccine strain obtained by the addition and substitution of an epitope (immunogenic sequence of nucleotides) on the N nucleoprotein. Today, research continues into the development of a vaccine virus PPRV 75/1 with a double marker and the refinement of suitable diagnostic tests. This future DIVA vaccine will be very useful during vaccination programs under the framework of a PPR eradication program.

Towards new antivirals

As for all viral disease, there is no specific therapeutic treatment against PPRV. Medical treatments based on antibiotics limit the effects of secondary respiratory infections but do not target the virus. They provide relief to the animal but their results are unpredictable and their cost high from the perspective of animal production. For the same essentially economic reasons, there is no veterinary antiviral curative treatment to fight against the disease in an infected animal. The only treatments used are preventive vaccinations.

However, when this antiviral therapeutic strategy is part of an approach to eradicate the disease and fight poverty, the economic investment involved becomes more acceptable. This is the rationale underlying CIRAD's research on biological antivirals. As a PPR reference laboratory, its approach is to develop a curative PPR vaccine by using a molecular genetic technique, RNA interference.

Discovered in the 1990s, this natural biological mechanism allows living animal and plant organisms to inhibit and consequently control the level of expression of their genes. It sets in play short RNA fragments, the interfering RNA or siARNs (small interfering RNA), which are capable of stopping the reading and translation of the genetic code into proteins. By bonding to the messenger RNA, they lead to its degradation and the inhibition of the corresponding protein. This mechanism also applies to the expression of viral genes.

In 2005, researchers at CIRAD identified and patented (FR 0513029) three synthetic siARNs able to inhibit over 80% of the in vitro replication of the PPR virus. Different in vivo delivery systems of these siARNs are being evaluated to assess their effectiveness and safety in a non-infectious "mouse" model based on bio-imagery. Research currently is focusing on assessing the risk of the emergence of resistant mutant PPRV strains which escape the inhibition of these siARNs. This step is indispensable for the development of reliable and effective therapeutic vaccines. They represent major progress in the fight against animal and human viral diseases for which there is only a preventive vaccine.

The economic impact remains under-estimated

Since 2004, the FAO and OIE have recognized PPR as one of the five most damaging transboundary diseases in Africa, Asia, and the Middle East for small ruminant production and poverty alleviation efforts. The health effects of the disease are now well known. However, few quantified studies have examined PPR's economic and social consequences. Assessments undertaken in several countries during epizootics reported considerable losses with an order of magnitude of several tens to several hundreds of millions of US dollars.

In 2010, the FAO estimated that a PPR epizootic which raged through two regions of Tanzania caused losses amounting to US$ 67.9 million. In just one year, more than half of the herds contracted the disease and households lost 72% of their livestock. Their loss in terms of animal deaths and reduced income was calculated to be US$ 490 per household. In Turkana district, Kenya, production losses rose to US$ 2.4 million between 2006 and 2008. In Pakistan, the annual negative impact of PPR was estimated at US$ 342 million.

In 2012, a GALVmed (Global Alliance for Livestock Veterinary Medicines) study estimated the annual losses caused by PPR in South Asia to be US$ 3 billion, half of which were production losses. This handful of examples demonstrates that the cost and socio-economic impact of PPR epizootics are particularly high for farmers and village communities, but also for national and regional economies.

"Small ruminants represent a high percentage of economic growth potential for the future. By targeting investments on small ruminants, the poorest farmers, in particular women, are reached."

Bernard Vallat – OIE Director-General, 2012

The incidence of PPR results in:

- *direct financial losses linked to animal mortality, which can reach up to 100%, and a drop in their production potential (weight loss, lower reproductive capacity, reduced milk production).*
- *indirect financial losses linked to the lower value of surviving animals, reduced genetic heritage, restrictions on movements and sales, and veterinary expenditures made to fight the disease.*

The presence of the disease in countries around the Mediterranean, and its rapid geographic extension over the past few years in both Africa and Asia, where a large 2013 epizootic in China endangered over 216 million heads of goats and sheep, demonstrate the urgent need to develop and launch national, regional and global programs to control this hitherto neglected disease.

"Before, I could sell my goats, but that is no longer possible. A healthy goat use to sell for 3000 Kenyan schillings (US$ 50), but the price has fallen to 300 Kenyan schillings (US$ 5) in some regions."

A villager - Kenya, 2008.

Components of the control of PPR

	Disease-related factors
Positive elements	• A single serotype. • Virus transmission through direct contact. • The virus is infective for only a short period outside a host. • No prolonged carrier state after infection. • No currently known animal reservoir outside domestic small ruminants. • Existence of sensitive and specific diagnostic tools. • Existence of a safe and effective vaccine that can be used against all of the viral lineages, confers life-long immunity with a single dose, and is inexpensive to produce. Innovations soon to be available: • A bivalent thermostable vaccine (PPR and sheep/goat pox). • Rapid tests that can be used in the field. • A new generation vaccine inducing the production of antibodies that differ from the antibodies produced through natural infection.
Constraints	• The rapid turnover of small ruminant populations, which maintains a population of susceptible animals. • Local and cross-border mobility of animals (intensity of trade, transhumance). • Differences in susceptibility and receptivity depending on breed and species.
Questions	• Clarify the role of dromedaries, wildlife, and bovine animals in the PPR epidemiological cycle. • Understand virus population dynamics and the determinants of virulence. • Develop a dynamic map of trade and transhumance routes for each country. • Identify control measures adapted to the epidemiological situation (enzootic country, disease-free country at high risk, disease-free country), different livestock systems and herd management practices, and the socio-economic context. • Determine the appropriate vaccination strategy (when to vaccinate? how often? vaccinate which animals? vaccinate dromedaries?).

Cross-cutting factors

- An effective organization of national veterinary services with technical and financial support to strengthen their surveillance, diagnostic, and disease control capacities.
- Strong coordination within well-structured, regional and sub-regional epidemiological surveillance networks.
- Strengthening laboratory production and quality control capacities to produce a sufficient quantity of high quality vaccines meeting international and OIE standards and the creation of regional vaccine banks in Africa and Asia.
- Training, sharing information and experience among actors and the local management of control programs based on partnerships between livestock farmers, community animal health workers, veterinarians, laboratory personnel and research and development experts.
- The existence of regularly updated roadmaps specific to each sub-region in Africa (5), the Middle East (1) and Asia (3) to provide a global strategic framework for the progressive control of PPR.
- Political support, financial commitments, public-private partnerships and strong coordination between international, regional, and national institutions and bodies.

"My goats are not sick and I do not know anything about this disease but I was told that I should get my animals vaccinated so they do not get sick. So I came.

We are a family of 7. We do not own land and we do not cultivate anything ourselves. We only have Allah. Sometimes we sell a young goat so we can buy what we need."

An old woman - Yemen, 2013

Progressive control through vaccination

Despite a lack of data on the socio-economic impact of PPR epizootics, cost of control measures to be set up, and expected benefits, it is certain that the loss of small ruminant livestock fuels poverty and impedes rural development in the countries in the South where the disease is present. This situation should be sufficiently convincing to obtain the political and financial support of governments and international donors for a global PPR eradication mechanism. The control of the PPR epizootic in Morocco in 2008 through a national, multi-annual, mass vaccination campaign of goats and sheep effectively demonstrated that its eradication is possible.

"Animal health is a priority for the modernization of livestock farming. Every year, we lose thousands and thousands of small ruminants because the animals have not been vaccinated against the peste des petits ruminants."

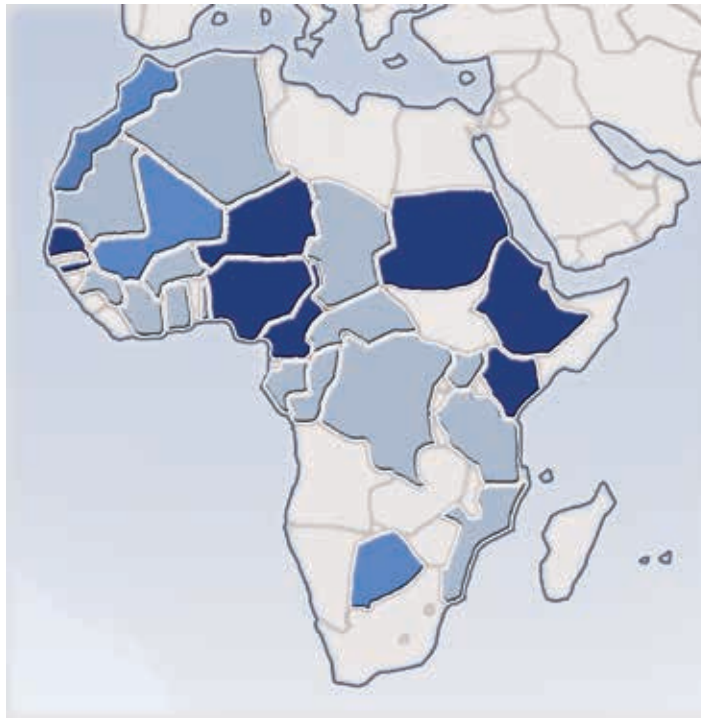
Minister of Livestock and Production Animals - Senegal, 2014

Vaccination campaigns are regularly conducted at the local and national level of various countries infected by PPR, but these initiatives are not coordinated and remain limited in scope. To harmonize efforts and increase their effectiveness, the FAO and OIE have worked to develop a specific strategy for the control of PPR through vaccination. It is designed to be coordinated at the regional and global level, and is based on the production of high quality vaccines by accredited laboratories with facilitated access for all countries thanks to the establishment of vaccine banks, and on national mass vaccination campaigns combined with measures to assess the results of these campaigns. If this strategy is implemented, the expected result is the global eradication of the disease within the next 15 years, but in certain countries and regions, eradication could be achieved even more rapidly, in about 5 years. The challenge now is to convince financial partners to support this initiative.

Vaccine banks

These are based on a concept developed by OIE to set up virtual rolling stocks of vaccines. When there is an emergency, this system enables a sufficient quantity of vaccines meeting international quality standards to be supplied to infected countries. The vaccine banks also set the stage for countries to gradually assume ownership of control programs and implement them effectively.

Diagnostics and vaccine production in Africa



Diagnostic tests and vaccine production at the national level.
Cameroon, Ethiopia, Kenya, Niger, Nigeria, Senegal, Sudan

National production of live attenuated vaccines.
Botswana, Mali, Morocco

Diagnostic tests available in animal health laboratories.
Algeria, Benin, Burkina Faso, Congo, Ivory Coast, Gabon, Ghana, Guinea, Mauritania, Mozambique, Uganda, Tanzania, Chad, Central African Republic, Democratic Republic of the Congo

Some constraints on vaccination: Free expression in Burkina Faso

The shortage of veterinarians and vaccinators

"What works well is when even goats and sheep are vaccinated, the animals stay healthy. What does not work well is when the veterinarian gives injections on just one day in the village."

"Many animals never were vaccinated because the veterinarian only gave vaccinations in the village on a single day."

"It is hard to get treatment from the veterinarian because if not many animals are sick, he often does not come out to us. When that happens, we have to bring our animal in to get care."

"The veterinarians told themselves that the Peulh herders have more sheep and goats than we do, so they went out to the Peulh."

The organisation of vaccination operations

"We farmers do not like it when the vaccinations are given in a pen with all the animals grouped together; it is true that it makes the job easier for the vaccinator, but it doesn't work for me."

"Going door-to-door makes it possible to vaccinate more small ruminants; it is not possible to group small ruminants together to vaccinate them the way you can with cattle."

The choice of the vaccination period

"The vaccination period for sheep and goats is not good because it falls when it is hot."

"Shots against diarrhoea should be given to sheep and goats in October-November because that is when there are cases of diarrhoea."

"Injections should be given to sheep and goats in the months of August-September before the disease breaks out."

The packaging of vaccines

"Packaging the vaccine in a 100-dose vial is not adapted to the size of our livestock farms... once a vial is opened…it gets thrown away when there are less than 100 animals."

The choice of communication channels and the importance of relations of confidence

"The one who tells the farmers should be their president, he knows the farmers in the village, so the information is sure to get passed on."

"The town crier provided the information about the vaccination."

"The farmers' president gave me the information about vaccinating sheep and goats."

"I got the information about vaccinating sheep and goats in the market from farmers from another village who had already vaccinated their animals."

"What works is the announcement of information at ceremonies, telephone calls, door-to-door vaccination campaigns."

2030: a world without PPR?

It took over 50 years to eradicate rinderpest through 5 consecutive international programs. The first program began in 1962; the last, GREP (Global Rinderpest Eradication Program), ended in 2011. Such a long period of time was required due to the obstacles encountered during this first attempt to eradicate an animal disease. However, the dynamic created by its success, the lessons learned and the infrastructure set up are an incentive and a springboard for the international health organizations, FAO and OIE, to develop and implement a coordinated global strategy for the progressive control and eradication of PPR and to make this one of the priorities of the GF-TADs (Global Framework for the progressive control of Transboundary Animal Diseases).

This global strategy will be officially presented in March 2015 by the FAO and OIE.

It will be implemented at the global level in three 5-year stages, but the time frame in each region and country will vary according to its epidemiological situation and capacity to implement prevention and control measures.

The strategy is based on a succession of four steps. An initial assessment of the epidemiological situation is followed by disease control, essentially through vaccination, and then the actual eradication of the disease through intensified control measures. The last step aims to ensure that the virus has ceased to circulate, notably through post-eradication epidemiological surveillance.

This allows countries to engage in an official procedure set up by the OIE in March 2014 to recognize their disease status in relation to PPR. Obtaining the disease-free status will encourage countries affected by PPR to implement preventive sanitary and medical measures to fight this disease. In 2015, 48 member countries historically free of PPR, including the countries of Europe, figured on the OIE list of PPR-free countries.

"Actions against animal disease are not based on a concept of agricultural or commercial goods, but on global public goods. In effect, they serve the interests of all people and all generations by reducing poverty, contributing to public health and food security."

Bernard Vallat - OIE Director-General, 2011

• Scientific opinion on peste des petits ruminants. EFSA Panel on Animal Health and Welfare. - *EFSA Journal*, 2015, 13(1), 94 p.

• Evolutionary genetics underlying the spread of peste des petits ruminants. Libeau G., Diallo A., Parida S. - *Animal Frontiers*, 2014, 4(1), p. 14-20.

• Peste des petits ruminants virus infection of small ruminants: a comprehensive review. Kumar N., *et al.* - *Viruses*, 2014, 6(6), p. 2287-2327.

• Molecular evolution of peste des petits ruminants virus. Muniraju M. *et al*. - *Emerging Infectious Diseases*, 2014, 20(12), p. 2023-2033.

• Peste des petits ruminants virus, Mauritania. El Arbi A.S. *et al*. - *Emerging Infectious Diseases*, 2014, 20(2), p. 334-336.

• Role of wild small ruminants in the epidemiology of peste des petits ruminants. Munir M. - *Transboundary and Emerging Diseases*, 2014, 61(5), p. 411-424.

• Peste des petits ruminants. Wallingford : CAB International, 2013, 20 p. Animal Health and Production Compendium.

• Peste des petits ruminants virus. Munir M. – *In* : Mononegaviruses of veterinary importance. Vol. 1: Pathobiology and Molecular Diagnosis. Wallingford : CAB International, 2013, p. 65-96.

• FAO, OIE, IAEA. Workshop on PPR prevention and control, Dar-es-Salaam (Tanzania), 10-12 June 2013.
- PPR situation worldwide. Domenech J. - p.19-21.
- Understanding virus lineage evolutions, gaps and challenges, research priorities. Diallo A. - p. 22-23.
- Laboratory diagnostic and molecular epidemiology of peste des petits ruminants. Libeau G. - p. 38.

• Supporting livelihoods and building resilience through peste des petits ruminants (PPR) and small ruminants diseases control. Rome : FAO, 2013, 16 p. FAO Animal Production and Health Position Paper.

• Peste des petits ruminants, the next eradicated animal disease? Albina E. *et al.* - *Veterinary Microbiology*, 2013, 165(1-2), p. 38-44.

• Update on PPR epidemiology, diagnosis and its control. Couacy-Hymann E. - *Revue Africaine de Santé et de Productions Animales*, 2013, 11(5), p. 59-65.

• Peste des petits ruminants infection among cattle and wildlife in Northern Tanzania. Lembo T. *et al*. – *Emerging Infectious Diseases*, 2013, 19(12), p. 2037-2040.

• Analysis of small ruminants' pastoral management practices as risk factors of peste des petits ruminants (PPR) spread in Turkana District, Kenya. Kihu S.M. *et al.* - *Research Opinions in Animal and Veterinary Sciences*, 2013, 3(9), p. 303-314.

• Un transfert de technologie réussi pour le contrôle de la peste des petits ruminants. Bonnet P., Lancelot R., Libeau G., Saint Martin G. - Montpellier : CIRAD, 2013, 2 p.

• RNA interference against animal viruses: How Morbillivirus generate extended diversity to escape small interfering RNA control. Holz C.L., *et al*. - Journal of Virology, 2012, 86 (2), p. 786-795.

• Des moyens de lutte efficace contre la PPR. Vaccin adapté et mobilisation nationale. Libeau G., Bonnet P. - Montpellier : CIRAD, février 2012, 2 p.

• Spécificités de la santé animale en régions chaudes : le cas des maladies infectieuses majeures en Afrique. Lancelot R., Zundel E., Ducrot C. – *INRA Productions Animales*, 2011, 24(1), p. 65-76.

• Asian lineage of peste des petits ruminants virus, Africa. Kwiatek O. *et al.* - *Emerging Infectious Diseases*, 2011, 17(7), p. 1223-1231.

• Global distribution of peste des petits ruminants virus and prospects for improved diagnosis and control. Banyard A.C. *et al.* - *Journal of General Virology*, 2010, 91(12), p. 2885-2897.

• Origin of measles virus: divergence from rinderpest virus between the 11th and 12th centuries. Furuse Y., Suzuki A., Oshitani H. - *Virology Journal*, 2010, 7(1), p.52.

• An outbreak of peste des petits ruminants (PPR) in camels in the Sudan. Khalafalla A.I. *et al.* - *Acta Tropica*, 2010, 116(2), p. 161-165.

• Infections à *Morbillivirus* chez les ruminants : la peste bovine en voie d'éradication et la peste des petits ruminants en extension vers le Nord. Minet C. *et al*. - *Virologie*, 2009, 13(2), p. 103-113.

• Analyse quantitative du risque d'introduction de la peste des petits ruminants en France. Miller M. *et al.* - *Epidémiologie et Santé Animale*, 2009, 56, p. 217-226.

• Le point sur l'épizootie de peste des petits ruminants au Maroc en 2008. Dufour L., Dufour B., Libeau G., Diallo A. - *Epidémiologie et Santé Animale*, 2009, 56, p. 243-248.

• La peste des petits ruminants : une maladie longtemps ignorée. Diallo A. - *Bulletin de l'Académie Vétérinaire de France*, 2008, 161(3), p. 273-277.

• The threat of peste des petits ruminants : progress in vaccine development for disease control. Diallo A. *et al*. - *Vaccine*, 2007, 25(30), p. 5591-5597.

• Evaluation of the virulence of some strains of peste des petits ruminants virus (PPRV) in experimentally infected west african dwarf goats. Couacy-Hymann E. *et al.* - *Veterinary Journal*, 2007, 173(1), p. 178-183.

• Control of peste des petits ruminants and poverty alleviation? Diallo A. - *Journal of Veterinary Medecine*, Series B, 2006, 53(special issue), p. 11-13.

• Rinderpest and peste des petits ruminants. Virus plagues of large and small ruminants. Barett T., Pastoret P.P., Taylor W.P. - Londres : Academic Press/Elsevier, 2005, 341 p.

• Detection of antibodies of rinderpest and peste des petits rumiants viruses (*Paramyxoviridae*, *Morbillivirus*) during a new epizootic disease in Ethiopian camels (*Camelus dromedarius*). Roger F. *et al.* - *Revue de Médecine Vétérinaire*, 2001, 152(3), p. 265-268.

• La peste des petits ruminants. Lefèvre P.C., Diallo A. - *Revue Scientifique et Techniques de l'OIE*, 1990, 9(4), p. 935-950.

• Classification of peste des petits ruminants virus as the fourth member of the genus *Morbillivirus*. Gibbs E.P.J. *et al.* – *Intervirology*, 1979, 11(5), p. 268-274.

• La peste des petits ruminants au Sénégal. Données nouvelles. Bourdin P., Doutre M.P. - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1976, 29(3), p. 199-204.

• Note sur la structure du virus de la peste des petits ruminants. Bourdin P., Laurent Vautier A. - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1967, 20(3), p. 383-386.

• La peste des petits ruminants en Afrique occidentale française. Ses rapports avec la peste bovine. Mornet P. *et al.* - *Revue d'Elevage et de Médecine Vétérinaire des Pays Tropicaux*, 1956, 2(4), p. 313-342.

The United Nations Food and Agriculture Organization (FAO) strives to achieve a world free of hunger and malnutrition where food security and agriculture contribute to improving everyone's standard of living, in particular that of the poorest, in an economically, socially, and environmentally sustainable manner.

The three overarching objectives of FAO Member States are first to eradicate hunger, food insecurity, and malnutrition, progressively building a world in which everyone has regular access to sufficient, healthy, and nutritious food. This enables everyone to satisfy their food needs and preferences and lead active, healthy lives. The second objective is to eliminate poverty and promote social and economic growth for everyone by improving food production, encouraging rural development, and building sustainable livelihoods. The third objective is to ensure that natural resources, including land, water, air, climate and genetic resources, are managed and used in a sustainable manner for the good of present and future generations.

The FAO develops, collects, and shares crucial information regarding food, agriculture, and natural resources, which are all global public goods. The FAO plays a connector role by identifying and collaborating with different partners with established technical expertise, and by facilitating dialogue between those who hold knowledge and those who need it. By turning knowledge into action, the FAO links the field to national, regional and global initiatives within a mutually reinforcing network.

FAO: Via delle terme di Caracalla - 00100 Rome - Italie
Tel.: (+39) 06 57051 - Fax: (+39) 06 570 53152 - Web: www.fao.org

The World Organisation for Animal Health (OIE) is an intergovernmental organisation created in 1924 under the name, Office International des Epizooties, and has today 180 member countries. OIE manages the global animal health surveillance and early-warning system and plays a key role in the fields of veterinary science information and research. The peste des petits ruminants is on the list of 116 diseases of land and marine animals monitored by OIE, and is one of the priority diseases for which a global control and eradication strategy has been developed. OIE acts with the ongoing support of 296 reference laboratories and collaborating centres and 13 regional and sub-regional offices around the world.

OIE fulfils its mandate through the following activities: ensuring transparency in the global situation of animal diseases (including zoonoses); gathering and disseminating veterinary scientific information, notably disease prevention and control methods; ensuring sanitary safety of the world trade in animals and animal products (as the international reference organization for animal health under the framework of the World Trade Organisation SPS agreement, OIE develops standards for international trade in animals and animal products); defining and supporting the good governance of veterinary services; and promoting animal welfare.

OIE also works to reinforce policies promoting animal production, food security and poverty reduction, implement strategies to prevent and manage animal-human interface risks, and analyze the impact of climate and environmental change on the emergence and occurrence of animal diseases. Reinforced support for the improvement of the global quality of diagnostic and research laboratories, veterinary education, and veterinary statutory bodies bolsters OIE's actions in favour of good governance and the global reduction of biological risks.

OIE: 12, rue de Prony - 75017 Paris - France
Tel.: 33 (0)1 44 15 18 88 - Fax: 33 (0)1 42 67 09 87 - Web: www.oie.int

A public-sector financial institution, the French Development Agency (AFD) has worked for over 70 years to fight poverty and support sustainable economic growth in developing countries and French Overseas Provinces. AFD executes policies defined by the French government.

Active on four continents through a network of 71 agencies and representative offices, of which nine are in French Overseas Provinces and one in Brussels, AFD finances and supports projects working to improve people's living conditions, promote economic growth, and protect the planet.

In 2013, AFD dedicated €7.8 billion to finance projects in developing countries and in French Overseas Provinces. These funds will contribute, in particular, to educating children, improving maternal health, promoting equality between women and men, supporting farmers and small enterprises, and reinforcing access to water, energy and transportation. The newly financed projects also will contribute to fighting climate change, notably allowing a saving of 3.3 million tons of CO2 equivalent per year.

As a development bank, AFD is ready to support governments in their investment needs for the implementation of a global PPR control strategy in their countries.

AFD: 5, rue Roland Barthes - 75012 Paris - France
Tel.: 33 (0)1 53 44 33 99 - Fax: 33 (0)1 44 87 99 39 - Web: www.afd.fr

A public industrial and commercial enterprise, CIRAD is a French research centre under the joint authority of the Ministry of National Education, Higher Education, and Research and the Ministry of Foreign Affairs and International Development. A targeted research organisation, CIRAD bases its multidisciplinary scientific programs on development needs, from field to laboratory and from a local to a global scale. The challenge: to contribute to sustainable development in rural areas and agricultural sectors in developing countries with a particular focus on the world's poorest.

The joint research unit, CIRAD-INRA CMAEE (Emerging and Exotic Animal Disease Control), conducts integrated research aiming to improve surveillance, anticipation of emergence and spread risks, and prevention and control of animal and zoonotic diseases of economic and health importance for countries in the South, of which some are threatening countries in the North.

An OIE reference laboratory and FAO PPR reference centre, the unit is pursuing research on assessing epidemiological situations, studying the diversity of viral strains, characterizing these strains and the plasticity of their genome, developing new diagnostic and treatment tools and vaccines, and developing integrated control strategies. PPR is recognized by governments and international organisations as the leading infectious disease of small ruminants. Its progressive control and eradication will require an iterative definition of control methods and strategies based on interdisciplinary research outputs to which the unit is contributing.

CIRAD – Direction Générale: 42, rue Scheffer – 75116 Paris – France
Tel.: 33 (0)1 53 70 20 00 – Fax: 33 (0)1 47 55 15 30 – Web: www.cirad.fr

UMR CIRAD-INRA CMAEE - Campus international de Baillarguet
TA A-15 / A - 34398 Montpellier Cedex 5 - France
Tel.: 33 (0)4 67 59 39 04 – Web: http://umr-cmaee.cirad.fr/

Web: http://savoirs partages.cirad.fr/

Printed by:
SOULIÉ Imprimeur Frontignan
Legal deposit: 1st trimester 2015