Peste des petits ruminants

P.-C. LEFÈVRE and A. DIALLO *

Summary: The peste des petits ruminants (PPR) is proving to be a disease which has an increasingly significant economic impact on a number of countries in Africa and the Middle East, and possibly also on the Indian sub-continent. The antigenic relationships which exist between the PPR and rinderpest viruses pose problems for diagnosis which complicate rinderpest control and eradication programmes.

Progress has recently been made in regard to diagnosis (specific nucleic probes and monoclonal antibodies), as well as control (homologous vaccine).

International legislation remains to be established and epidemiological surveys should be conducted in order to determine the exact geographical distribution of the disease.

KEYWORDS: Goats - Morbillivirus - Peste des petits ruminants - Rinderpest - Sheep.

INTRODUCTION

Since its first description in Côte d'Ivoire by Gargadennec and Lalane in 1942, the peste des petits ruminants (PPR) has received growing attention because of its geographical distribution, being widespread in Africa and the Middle East, and also because of its economic impact, which is still underestimated due to confusion with other diseases to which PPR predisposes animals.

Moreover, because of its close relationship to rinderpest, PPR has to be taken into account in rinderpest control programmes.

In the light of the importance of PPR, this comprehensive paper was based on information provided by many countries. Reports on the status of PPR were submitted by Côte d'Ivoire, Egypt, Jordan, Mali, Oman, Senegal and the Sudan. The United Kingdom and the USA have reported on research conducted in these countries.

Finally, numerous countries in Europe, Africa and Asia (including Botswana, Congo, Ethiopia, Kuwait, Lesotho, Madagascar, South Africa, Sri Lanka and Zambia) have reported that PPR does not occur.

The references cited at the end of this paper are purposely incomplete because further references can be obtained from recent reviews (14, 22).

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GEOGRAPHICAL DISTRIBUTION AND ECONOMIC IMPORTANCE

So far, PPR has been reported only on the African continent, in the Arabian Peninsula and certain countries of the Middle East (Fig. 1).

Table I shows the list of infected countries arranged according to the intensity of the disease (from the FAO/WHO/OIE Animal Health Yearbooks for 1985, 1986, 1987 and 1988).

<table>
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<td>Distribution of peste des petits ruminants</td>
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**Africa**

- Disease not recorded: Algeria, Angola, Botswana, Burundi, Central African Republic, Congo, Djibouti, Ethiopia, Guinea, Equatorial Guinea, Libya, Madagascar, Malawi, Morocco, Mozambique, Namibia, Rwanda, Sierra Leone, Somalia, South Africa, Swaziland, Tunisia, Uganda, Zaire, Zambia, Zimbabwe
- Suspected but not confirmed: Liberia
- Exceptional cases or low incidence: Burkina Faso, Egypt (1987), Mali, Niger
- Endemic or high frequency: Benin, Cameroon, Gambia, Ghana, Côte d'Ivoire, Mauritania, Nigeria, Senegal, Sudan, Togo
- No information available: Chad, Gabon, Guinea Bissau, Kenya, Tanzania

**Arabian Peninsula**

- Disease not recorded: Kuwait
- Exceptional cases or low incidence: Bahrain, United Arab Emirates, Yemen (Arab Republic)
- Endemic or high frequency: Oman (1983)
- No information available: Saudi Arabia, Yemen (People's Democratic Republic)

**Middle East and Asia**

Lebanon reported PPR on a single occasion in 1986 and Jordan reported the disease for the first time in 1989.

In Asia, Nepal reported the disease up to 1987, but not in 1988. PPR virus might have been identified in India in 1989.

In 1989 the disease was also reported in Egypt, but incidence is very low.

Similarly, in India, an outbreak of a disease resembling PPR occurred in the Villupuram district of Tamil Nadu State, and the results of tests with a nucleic probe indicate that PPR virus was involved (23).
FIG. 1

Geographical distribution of the peste des petits ruminants
1985-1988
In fact, the disease is probably more widespread than it was thought to be a few years ago, and it is still spreading from the West African countries, which may be considered as the cradle of PPR. The disease might pass unnoticed, or it might be confused with other infections favoured by PPR.

In any case, it is certain that serological surveys should be conducted systematically in countries adjoining those countries known to be infected.

The economic importance of PPR has not been examined in detail and is difficult to estimate.

A survey conducted in Nigeria put the annual losses at 1.5 million US dollars (12).

There are considerable regional differences in epidemiological patterns, which influence methods of assessing economic impact. In the Guinean zones of Africa where PPR occurs in the epizootic form, it may have dramatic consequences for animal owners because a morbidity rate of 80%-90%, accompanied by a mortality rate between 50% and 80%, is not uncommon. In endemic regions where PPR is seldom fatal but usually occurs as a subclinical or even inapparent infection, it opens the door to many other infections and its impact on animal production is certainly considerable.

Table II, derived from reports submitted by the countries cited, gives some idea of the number of outbreaks observed, but it is probable that many more are never reported.

**Virology**

**Structure**

PPR virus (PPRV) belongs to the genus *Morbillivirus* of the family *Paramyxoviridae*, as do the measles, canine distemper and rinderpest viruses, with which there is a close antigenic relationship (10). It is a very polymorphic virus, although usually spherical. Its size varies between 150 and 700 nm, with most particles measuring 500 nm (2).

The PPRV is composed of a helicoidal nucleocapsid surrounded by a lipoproteic envelope. Owing to the presence of this envelope, the virus is easily destroyed by means of lipid solvents and is very delicate, particularly outside the host.

The nucleocapsid is formed by a genome surrounded by three viral proteins, the most important of which is the nucleoprotein (N protein) (4). The viral genome is a simple, negative RNA fragment and therefore it cannot be translated directly into proteins and has to be transcribed into messenger RNA. This stage is accomplished by an RNA-dependent polymerase complex, formed by two other nucleocapsid proteins: a polymerase-associated protein (P) (a phosphorylated protein) and a large polymerase protein (L).

*N Protein*

This is the major viral protein and possibly plays an important role in inducing antiviral immunity. Currently, the great interest in this protein is the use of its cDNA as a potential specific diagnostic probe.
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<tbody>
<tr>
<td>Côte d'Ivoire</td>
<td>9</td>
<td>6</td>
<td>12</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Egypt</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Jordan</td>
<td>75</td>
<td>125</td>
<td>134</td>
<td>51</td>
<td>14</td>
</tr>
<tr>
<td>Mali</td>
<td>23</td>
<td>20</td>
<td>55</td>
<td>23</td>
<td>16%</td>
</tr>
<tr>
<td>Fatality rate</td>
<td>30%</td>
<td>41%</td>
<td>41%</td>
<td>16%</td>
<td>27%</td>
</tr>
<tr>
<td>Oman (since 1983)</td>
<td>13</td>
<td>50</td>
<td>103</td>
<td>131</td>
<td>61 (to July)</td>
</tr>
<tr>
<td>Outbreaks</td>
<td>732</td>
<td>674</td>
<td>27,414</td>
<td>8,654</td>
<td>1,931</td>
</tr>
<tr>
<td>Animals</td>
<td>262</td>
<td>234</td>
<td>&gt; 1,485</td>
<td>&gt; 452</td>
<td>&gt; 195</td>
</tr>
<tr>
<td>Deaths</td>
<td>262</td>
<td>234</td>
<td>&gt; 1,485</td>
<td>&gt; 452</td>
<td>&gt; 195</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>12.3%</td>
<td>5.4%</td>
<td>3.1%</td>
<td>0.9-5.2-17%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Sudan</td>
<td>190,500</td>
<td>190,700</td>
<td>1,650</td>
<td>14,670</td>
<td>?</td>
</tr>
<tr>
<td>Sheep affected</td>
<td>&gt; 195</td>
<td>&gt; 1,485</td>
<td>&gt; 452</td>
<td>&gt; 195</td>
<td>&gt; 195</td>
</tr>
<tr>
<td>Goats affected</td>
<td>190,500</td>
<td>190,700</td>
<td>1,650</td>
<td>14,670</td>
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The lipoprotein envelope is coated with spicules measuring about 10 nm (2) and is composed of two glycoproteins:

**Haemagglutinin (H protein)**

Despite its name, this protein has no haemagglutinating activity and is thus called because it is the equivalent of the haemagglutinin of the measles virus. It enables the virus to become attached to the membrane of the target cell.

**Fusion protein (F)** has the ability to fuse:

- either the viral membrane to that of the target cell, enabling the nucleocapsid to be liberated into the cytoplasm;
- or the membrane of an infected cell to that of an adjoining cell, this being the basis of syncytium formation and of the spread of the virus without previous extracellular release.

F protein is synthesised in an inactive form (F0). It acquires its biological properties only after cleavage by a cellular protease which gives rise to two subunits (F1 and F2) linked by a disulphide bond. This process provides F1 with a very hydrophobic end which plays a vital part in fusion activity.

H and F proteins enable the virus to become attached to the target cell and to release its nucleocapsid into the cytoplasm. The neutralising antibodies produced by the infected host are directed against these proteins. Therefore, the genes of these two proteins might be of use in producing a PPR vaccine, with the help of genetic engineering.

In addition to the H and F proteins, there is a third viral envelope protein which coats its inner surface: the membrane protein (M). This provides the link between both external glycoproteins and the nucleocapsid and plays an important part in virus formation.

N, P, L, H, F and M proteins are structural proteins because, together with the genome and the envelope, they constitute the viral particle. There is a seventh viral protein (C protein) which differs from the others in being non-structural; it is found only in cells infected by the virus. Its exact function is not yet known.

**Biological properties**

While the symptoms characteristic of PPR result from infection of epithelial cells of various mucous membranes, the virus is primarily lymphotropic, like the other morbilliviruses. This property gives rise to numerous bacterial and parasitic complications which aggravate the clinical picture and prognosis of the disease.

Various cell culture systems have been used by different authors to propagate the virus (cited in 14):

- embryonic kidney cells from small ruminants;
- ovine embryonic dermal cells (personal observation);
- simian kidney cells;
- continuous cell lines: MDBK, MS, BHK21, BSC, Vero.
As in all paramyxoviruses, the cytopathic effect (CPE) of PPRV results in syncytium formation. This commences as a rounding of some cells, which become refringent. Then some cells gradually fuse to form polycarons. When stained with hematoxylin-eosin, the infected cells are seen to contain eosinophil intracytoplasmic (and sometimes intranuclear) inclusions (13).

The size of the giant multi-nucleated cells varies according to the type of cell used for virus propagation. The syncytia formed by Vero cells are few and small, in contrast to those which are obtained with primary explants of ruminant cells, and generalisation is accompanied by rounding of refringent cells, which gradually become detached from the cell layer.

**Virus replication**

Little is known about the different stages of multiplication of PPR virus, but they are probably similar to those of the measles virus, which has been studied in greater detail.

Viral infection begins with the liberation of the nucleocapsid into the cytoplasm of the cell due to the fusion of cellular and viral membranes. Then viral RNA polymerase starts to transcribe the genome into messenger RNA (mRNA) in the order of arrangement of the genes, an order which is known for measles virus as follows: N - P/C - M - F - H - L (from the 3' extremity of the genomic RNA to its 5' extremity) (20). Results of gel electrophoresis of the mRNAs induced by PPR virus are identical with those obtained for other morbilliviruses (1). They are translated into different proteins by enzymes of the target cell. Each messenger gives rise to one protein; the second one, however, is translated into two reading frames resulting in structural P protein and non-structural C protein. Once the concentration of the viral proteins reaches a sufficient amount, polymerase turns to the synthesis of new genomes, each of which is surrounded by N, P and L proteins to form nucleocapsids. These migrate to a region of the membrane where M, F and H proteins are already present. At this site a bud forms and expands until it detaches from the target cell as a mature virus. According to Laurent (13), the budding process starts 12 h after infection of sheep cells by PPRV and continues until the seventh day. Its importance drops with the increase of syncytia.

**Different types of PPR virus**

The intrinsic pathogenicity of the rinderpest virus is known to vary considerably (25).

Some strains show slight variations in the electrophoretic migration profile of their proteins, unrelated to the variation mentioned above (4).

The same analysis carried out with PPR shows only two variants:

- African strains having the same migration profile;

- Middle Eastern strains which resemble each other but differ from the African strains in the slightly greater molecular weight of N protein. This difference could not be linked to any difference in pathogenicity.

PPR has not so far been recorded among sheep in the Middle East, although they seem to be infected with the virus (26). Sheep are known to be very resistant to
PPRV, and in Africa the disease is sometimes confined to goats. In contrast to rinderpest virus, no variation in intrinsic pathogenicity has been demonstrated for PPRV.

**Differentiation between PPRV and rinderpest virus (RPV)**

Both viruses are highly pathogenic for small ruminants and it is impossible to distinguish the two diseases clinically. Moreover, strains of PPR virus nonpathogenic for cattle have been considered as variants of RPV (18). For a long time, a distinction between these viruses was based on experimental inoculation of both cattle and small ruminants and on the cross virus-neutralisation test. Biochemical studies have revealed differences between the viruses in the molecular weights of their constituent proteins, detected by electrophoresis on polyacrylamide gel (4). However, within the same virus there can be slight variation in the electrophoretic migration profile from strain to strain, a variation linked to the molecular weight (MW) of the N nucleoprotein in the following way:

- MW of the N of typical RPV (e.g. Kuwait strain) > MW of the N of the reedbuck strain of RPV > MW of the N of RBT1 strain of RPV > MW of the N of PPR virus (Middle Eastern strains) > MW of the N of PPR virus (African strains).

Use of a DNA copy of the N protein gene as a diagnostic probe reveals that there is no intermediate situation (6) because:

- all RPV strains (including reedbuck and RBT1 strains) are recognised solely by the RPV probe;
- all African and Middle Eastern strains of PPRV react solely with the PPR probe.

Monoclonal antibodies against N protein of RPV or PPRV provide a more sensitive analysis of the relationships between the two viruses. Some antibodies are specific for either virus, while others recognise common antigenic sites (15, 16).

**SYMPTOMATOLOGY**

There are three main forms of PPR: hyperacute, acute and subclinical (or inapparent).

**Hyperacute form:** This occurs frequently in goats. The first symptom, after an incubation period of about two days, is pronounced hyperthermia (41-42°C), followed rapidly by general illness (prostration, apathy, harsh coat and anorexia), with nasal discharge and lacrimation. There may be constipation during the first days, giving way to profuse diarrhoea.

The evolution is rapid, lasting for 5-6 days after the onset of hyperthermia, and death occurs without time for any other striking symptom to appear.

**Acute form:** This is more characteristic of the disease and resembles rinderpest in small ruminants. The incubation period is 3-4 days and the initial stages are identical with those of the hyperacute form. The following symptoms appear:
— seromucous nasal discharge, becoming mucopurulent and blocking the nose;
— a congestive area appears along the dental margin of the gums, developing into erosive and then ulcerative lesions of the gums, tongue, buccal cavity, palate and even the larynx. The tongue becomes coated with a whitish, malodorous deposit;
— pulmonary involvement usually occurs, with a dry cough which rapidly becomes loose.

In the absence of complications, illness may last 8 to 10 days, terminating in either death or in recovery with long-lasting immunity.

The commonest complications are:
— pneumonia, or bronchopneumonia, with bacterial superinfection, particularly by *Pasteurella haemolytica* or *Pasteurella multocida* type A;
— reactivation of a latent parasitosis, such as coccidiosis, piroplasmosis or trypanosomiasis;
— abortion.

Subclinical or inapparent forms seem to be particularly prevalent in certain regions because of the innate resistance of local breeds. In such cases, the disease lasts for 10 to 15 days with inconstant symptoms. At a late stage, papules or pustules, similar to those of contagious ecthyma, may appear.

Inapparent forms are particularly severe because they encourage respiratory disease which cannot be identified as PPR. They are usually detected only by serological surveys (19, 22).

**IMMUNITY**

After recovery, the animals have a solid immunity to reinfection. The exact duration of this protection has not been established, but the animal will probably be protected for several years, perhaps even for its entire economic life. This immunity is provided by neutralising antibodies, although precipitating antibodies (8), or antibodies capable of inhibiting the haemagglutination of measles virus, have also been demonstrated.

**EPIDEMIOLOGY**

The epidemiology is still imperfectly understood, but it is possible to draw general conclusions from the information available for rinderpest.

**Species affected**

Small ruminants are the species most involved, but to various degrees: goats are clearly more susceptible than sheep and the disease often occurs in goats without affecting sheep living in close proximity.
When cattle are inoculated with PPRV, they develop transient hyperthermia followed by seroconversion which provides firm protection against subsequent exposure to rinderpest virus.

Recently, outbreaks of PPR among wild animals have been reported from a zoo (9), namely:
- Laristan sheep (Ovis orientalis laristani);
- Dorcas gazelles (Gazella dorcas);
- Nubian ibex (Capra ibex nubiana);
- gemsbok (Oryx gazella).

Experimentally, the white-tailed deer (Odocoileus virginianus) has proved to be susceptible (11).

Although the role of wild animals in the epidemiology of PPR has not been clearly established, it does not seem to be very important.

Transmission

The virus is excreted in tears, nasal discharge, expectorant and all other secretions.

Transmission takes place directly between a sick and a susceptible animal; indirect transmission is unlikely in view of the low resistance of the virus in the environment. The same applies to transmission of the virus over distances by animate or inanimate vectors.

Because animals with PPR either die or acquire a firm immunity, there are no latent virus carriers. The only sources of the virus, therefore, are sheep and goats in the incubation period, or those affected by the disease.

Susceptibility factors

In addition to species (goats being more susceptible than sheep), breed plays an important role in the susceptibility of goats. Guinean breeds (West African dwarf goats: Lagoon, Kirdi and Djallonké breeds) are considerably more susceptible than the major Sahelian breeds.

Age is also important, with animals aged 3 to 18 months being more severely affected than adults or unweaned young.

Climatic factors are not negligible and outbreaks are most frequent during the rainy season or the cold dry season.

Epidemiological patterns

Two patterns seem to dominate in Africa:

- epizootic outbreaks, apparently cyclic, interrupted by silent periods of 4 to 6 years. This pattern is seen most often in humid zones and along African coasts exposed to oceanic influences (Mauritania, Senegal, Nigeria);
- the enzootic type with rare outbreaks of clinical disease affecting a high proportion of animals. Endemic regions are essentially those of the Sahel (Mali, Niger, Chad).
According to ecological zones, these variations may be explained by the greater resistance (at the same temperature) of Paramyxoviridae in regions of low relative humidity, which means that PPRV will survive longer in dry regions and might thereby engender genetic resistance to infection.

**DIAGNOSIS**

Clinical diagnosis of the hyperacute and acute forms is not particularly difficult, especially in a favourable epidemiological context, but laboratory diagnosis is required to distinguish PPR from rinderpest. Subclinical and inapparent forms are practically impossible to diagnose but should be suspected in outbreaks of pulmonary or intestinal disease.

Samples are taken as follows:

- live animals: swabs of tears or nasal discharge, blood treated with anticoagulant (because the virus is associated with leukocytes) and possible biopsy specimens from prescapular lymph nodes;
- at slaughter or post-mortem examination: portions of spleen, lymph nodes, lungs and other organs bearing lesions, taken within 2 h of death.

To isolate the virus, it is vital to have samples from the early stages of the disease; otherwise, bacterial superinfection may hide the virus. Samples should be kept cold and sent to the laboratory as soon as possible.

The gel immunodiffusion test can be performed rapidly under the same conditions as those practised for rinderpest, to give a result within 24-48 h. With practice, the use of hyperimmune sera against PPR and rinderpest makes it possible to distinguish the two diseases by a spur formation in the precipitation lines.

Counter immuno-electrophoresis has been applied successfully to the homogenate of lymph nodes (17).

The most sensitive cells for virus isolation are primary explants of foetal ovine kidney.

A specific nucleic probe using a fragment of the cDNA of the N protein gene has been developed, but it is still in the experimental stage, particularly in regard to the problem of enzyme labelling.

For serological diagnosis, a microplate serum neutralisation test has been described (21); it is capable of distinguishing between PPR and rinderpest antibodies.

A competitive ELISA with monoclonal antibodies has been developed (Obi, personal communication) and another is being standardised (Libeau, unpublished findings).
PROPHYLAXIS

Legislation

PPR is in the OIE List A and carries the reference number A 050 in the FAO/WHO/OIE Animal Health Yearbook.

Texts for regulatory measures are being examined prior to their publication in the International Animal Health Code.

While PPR is a notifiable disease in some countries, one regrets that this is not always the case in Africa.

In infected countries, systematic slaughter of sick and infected animals is the only procedure to follow when an outbreak occurs.

Vaccination

Because of the antigenic relationships between the PPR and rinderpest viruses, the use of rinderpest vaccine prepared from the Plowright strain propagated in cell culture has been recommended for many years (3).

The duration of immunity after vaccination with a dose of $10^{2.5} \text{TCID}_{50}$ is at least 12 months (24).

At present, a number of African countries practise vaccination, as shown by the following examples taken from reports for 1989:

Côte d'Ivoire: 395,000 sheep and goats vaccinated in 1987, 780,000 in 1988 and 1.5 million in 1989 as part of a major programme for development of goat-keeping;

Egypt: Only ring vaccination around confirmed outbreaks, due to the very low incidence of the disease;

Mali: 270,065 animals were vaccinated between 1985 and 1989;

Oman: a vaccination scheme has been in operation since 1982, with 139,000 animals vaccinated in 1986, 75,700 in 1987 and 505,000 in 1988;

Sudan: 970,000 vaccinations performed during 1988-89.

A thermostable rinderpest vaccine prepared from Vero cell cultures is currently under study in the USA and Niger. A vaccine dose of at least $10^{3.2} \text{TCID}_{50}$ has given good protection against challenge infection.

Recently, a homologous vaccine (a strain of PPR virus attenuated and cloned after 63 passages in Vero cells) has been developed with financial support from the European Communities (7) and is undergoing trials in Côte d'Ivoire and Mauritania. The minimum vaccine dose is $10^{2.5} \text{TCID}_{50}$ and some 10,000 goats have been vaccinated in each country. The trial includes clinical and serological surveillance of the animals.

The value of this vaccine lies in the fact that serological surveys, particularly for rinderpest, would be made easier. At present, it is impossible to determine if seropositive small ruminants have been vaccinated or infected with rinderpest virus, creating problems for rinderpest eradication.
FUTURE TRENDS

The following lines of research on PPR are in progress and should be continued in future years:

1. Improvement of diagnostic techniques:
   - preparation of a non-radioactive probe by using synthetic oligonucleotides derived from the N protein gene sequence, which would be easy to use in the field;
   - development of a specific ELISA.

2. Preparation of a recombinant vaccine by inserting F and H genes in a thermostable viral vector (poxvirus).

3. More thorough study of epidemiology and the use of monoclonal antibodies to characterise strains of PPRV isolated in different parts of the world.

During the discussions on PPR during the 58th General Session of the International Committee of the OIE, the following three points were raised:

1. The geographic distribution of PPR is not known precisely and is the cause for some concern, notably in India, where an outbreak has been described in the State of Madras, and in the Middle East, although PPR has been diagnosed only in Jordan.

   In Africa, the representative of Chad assures that his country is free from PPR and that strict surveillance is maintained at the borders to prevent the introduction of the disease.

2. Regarding the virus, chronic carriers do not exist and the virus is no longer excreted by infected animals once seroconversion has occurred. Owing to their sensitivity, sheep kidney foetal cells are recommended for the isolation of the virus, although other cell systems may be used (e.g. Vero cells); in such cases, however, there is a risk of persistent infections without cytopathogenic effect.

3. The homologous PPR vaccine currently in widespread experimental use in Mauritania and Côte d’Ivoire will soon be made available to vaccine-producing laboratories.

To facilitate future sero-epidemiological surveys by eliminating cross reactions, the use of both rinderpest vaccine against PPR in small ruminants and attenuated goat virus vaccine against rinderpest in bovines should be avoided.

* * *

REFERENCES


