PRRS CONTROL IN THE REGION

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1.   Introduction

Porcine reproductive and respiratory syndrome (PRRS) is recognised as an economically important swine disease worldwide, and is characterised by either reproductive failure in pregnant sows or respiratory tract distress particularly in suckling pigs [7, 32, 37]. The syndrome was first recognised in the United States of America (USA) in the mid 1980's and was called 'mystery swine disease' or 'blue ear disease'. The causative agent, PRRS virus, was first discovered in the USA in 1987 [1, 4, 36], was subsequently found in Europe [1], and was identified in Asia in the early 1990s [12, 31]. PRRS is the cause of significant economic losses in pig production worldwide, especially in large-scale production systems [2]. In the USA alone, PRRS is estimated to cause about USD 560 million in losses per year to the swine industry [13].

In the People's Republic of China in 2006, a disease that was called 'porcine high fever syndrome (PHFS)' emerged and spread throughout the country causing very severe disease in pigs. The disease was characterised by high fever (40-42°C) in all age groups, abortions in sows and high mortality in suckling piglets, weaners and growers [34]. Several laboratories in China isolated PRRS viruses from pigs suffering from PHFS. The subsequent genetic and pathogenicity analysis of those viruses indicated that the disease was associated with an atypical highly virulent strain of PRRS virus. The disease caused by this new variant strain is now called highly pathogenic PRRS [10, 34, 38, 39].

Highly pathogenic PRRS (HP-PRRS), which thus emerged in China in 2006, has spread to South-East Asian countries since 2007. It has caused severe damage to pig production and has become a burden for pig producers in the region [5]. A clear understanding of the characteristics of the disease, the virus and its epidemiology are needed so that appropriate control measures can be established and applied in order to reduce the economic losses caused by this disease and prevent it spreading to other regions of the world. This aim of this report is to review currently available information on HP-PRRS to serve as the basis for developing practical and effective control measures against this disease.

2.   Characteristics of the HP-PRRS; the virus and the disease

The aetiological agent of PRRS is an RNA virus of the order *Nidovirales*, family *Arteriviridae*, genus Arterivirus [20]. There are two related but antigenically and genetically distinguishable strains: genotype I, with the prototype Lelystad virus representing the viruses predominating in Europe, and genotype II, represented by VR 2332, the prototype strains originally found in North America. There are significant genetic and antigenic differences between these initial isolates. They share less than 70% genetic sequence homology. Genetic and antigenic variability between isolates, even within a country, remains a continuous challenge to the control of the disease. The virus genome varies from 15 kb to 15.5 kb in length and comprises at least eight open reading frames (ORFs) that encode nearly 20 mature proteins [Gao *et al.*, 2004].

Genetic sequence analysis revealed that HP-PRRS virus is a variant strain that belongs to genotype II PRRS virus (North American genotype). Phylogenetic analysis of the ORF5 gene showed that HP-PRRS virus was very close to two PRRS viruses previously detected in China,

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which implies that it might have evolved from these viruses [34]. Further analysis of a non-structural protein (NSP2) found a unique feature of HP-PRRS virus, namely the non-continuous deletion of 30 amino acids (at position 482 and positions 534-562). This deletion is proposed as a genetic hallmark of HP-PRRS virus, although it was shown that the deletion is not responsible for the increased virulence of HP-PRRS virus [38].

The pathogenicity of HP-PRRS virus has been studied by various research groups, but with differing results in terms of the level of pathogenicity among the studies. An animal study was conducted by the United States Department of Agriculture (USDA) National Animal Disease Center (Iowa, USA) on the Vietnamese strain of HP-PRRS virus to determine its degree of virulence [11]. The pigs inoculated with the isolated virus had high fever for 2 weeks and mild to severe respiratory distress, but showed no mortality. They seroconverted within 8 dpi (days post infection), and the virus was reisolated from serum, lungs and spleen in most animals. Another animal experiment was carried out at the National Institute of Animal Health, Tsukuba, Japan, using Vietnamese HP-PRRS virus isolates of 2007 and 2010 [33]. The results showed that both Vietnamese HP-PRRS viruses caused severe disease in the inoculated pigs, with clinical signs of high fever within 1 to 2 dpi and the fever continued until 15 to 16 dpi. On post-mortem examination, the pigs had pneumonia and enlargement in various lymph nodes. Histopathology showed a severe interstitial pneumonia, cell necrosis and germinal centre hyperplasia in lymph nodes, and multifocal lympho-histocytic infiltration in many organs. High mortality was not observed in these experiments. The findings in China showed some differences, especially in terms of mortality [34, 35]. Chinese HP-PRRS virus caused mortality of up to 100% in 5-week-old pigs and up to 57% mortality in 11-week-old pigs within 6–10 days post exposure. Jian *et al.* (2008) reported that an infectious cDNA clone made from a field isolate in China caused 100% mortality in the experimental infection. In the field, variations in the clinical manifestations were observed between herds, with variations in the severity of clinical disease and with mortality ranging from 0% to 100%. These findings and observations suggest that there is an increased virulence of HP-PRRS virus compared to classical PRRS virus, but the level of pathogenicity of HP-PRRS may vary depending on the strain, as shown by Li *et al.* (2010). It seems reasonable to conclude that PHFS is the multifactorial syndrome triggered by HP-PRRS virus as a major factor followed by secondary infections with various agents that result in the different clinical manifestations [11].

3. HP-PRRS in the region

3.1. HP-PRRS in China

The emergence of HP-PRRS was detected in China in June 2006 for the first time. It affected over two million pigs, of which 400,000 in 16 provinces had died by the end of 2006 according to the China Animal Disease Control Center (CADC). Provinces along the Yangtze River in the south of China have been the most affected [17]. The disease continued in 2007, and it is reported to have infected 310,000 pigs, of which more than 81,000 in 26 provinces had died by the end of 2007 [25].

While the disease was initially reported in both the commercial and backyard sectors, it now seems to be concentrated in the latter, where control is a greater challenge, especially in remote areas. A compulsory PRRS vaccination policy has been implemented in high-risk areas and in high-value herds (breeding pigs and large-scale commercial farms), using a newly developed vaccine matching the circulating strain. As of 22 August 2007, the authorities had administered 314 million doses of inactivated vaccine to immunise more than 100 million pigs, one fifth of the nation's total [Martin *et al.*, 2007]. Currently, several kinds of live attenuated vaccine, including those made from HP-PRRS virus, are widely used. The disease situation is endemic and is said to be under control.

3.2. HP-PRRS in South-East Asia

3.2.1. Vietnam

In March 2007, HP-PRRS was found in Hai Duong province in the northern part of Vietnam. Clinical and pathological findings in the affected pigs were similar to those observed in the 2006 HP-PRRS outbreaks in China [Youjun *et al.*, 2008]. By August 2007, 44 outbreaks in two epidemics had been reported, the first one in the northern provinces between March and May, and the second one in the southern provinces

during June and July. A total of 44,000 pigs were affected, of which over 4,000 died [18].

HP-PRRS has become endemic in Vietnam and has been regularly reported since its emergence in March 2007. Data from the Department of Animal Health of Vietnam on HP-PRRS for a three-year period (2007–2009) indicate that HP-PRRS was reported in 57 out of 64 provinces in Vietnam. In 2010, Vietnam was hit by another severe epidemic of HP-PRRS, with 541 outbreaks in total [22]. Since then, HP-PRRS outbreaks have been reported almost every month. However, there seems to be a seasonal pattern in the occurrence of HP-PRRS in Vietnam: winter to spring in the north, and summer to autumn in the south.

3.2.2. Laos

In June 2010, HP-PRRS outbreaks confirmed by the laboratory were reported at the capital city of Vientiane [15]. By the end of August 2010, 31 pig farms in 7 districts (housing a total of 13,977 pigs) had reported the disease. The disease was characterised by high fever (40–42°C), abortion, and high mortality in pigs of all age groups. A field investigation was carried out on 8 farms, including backyard farms and large-scale operations. The mortality rate varied according to the type of pigs: 28% in sows, 48% in finishing pigs, 91% in piglets and 6% in boars. A total of 3,546 pigs died of the disease. The average mortality rate was 25%.

3.2.3. Thailand

The first case of HP-PRRS in Thailand was detected in Phitsanulok province in early 2010. There was increased mortality in pigs, with reproductive failure and respiratory distress in all age groups [28]. The production system that has been affected is mainly the backyard sector with low farm biosecurity. In total, 660 out of about 2,970 pigs from 90 small pigholders in the province were affected.

A public awareness campaign has been launched to provide information, education and communication to all target audiences in order to educate farmers about HP-PRRS and encourage them to enhance their biosecurity level by applying basic principles.

3.2.4. Myanmar

In Myanmar, HP-PRRS was detected for the first time in February 2011, when 210 out of 559 pigs died at a farm in Naypyidaw district, Mandalay province [29]. HP-PRRS subsequently spread to the other districts (Aungmyetharsan, Chanayetharsan, Mahaaungmye, Chanmyatharsi, Pyigyitagun, Amarapura and Madaya) in the Mandalay region, killing more than 1,000 pigs. The disease initially occurred among small farms in urban areas, before spreading to suburban areas.

3.2.5. Other countries

In Cambodia, HP-PRRS emerged in three provinces (Battambang, Kampong Cham, and Kampot) in August 2010. The disease quickly spread to five other provinces: Kampong Chhnang, Prey Veng, Svay Rieng, Takeo and Kandal [26]. The current status is not known.

In the Philippines, the first outbreak of HP-PRRS was detected in Tabuk province in August 2010. It was initially suspected to be a mixed infection of classical swine fever and porcine reproductive and respiratory syndromes, but was subsequently confirmed as HP-PRRS [27]. The outbreak killed 300 pigs. In the Philippines the disease has mainly been spreading in areas with higher pig densities and increased commercial pig production.

On 26 June 2013, India reported its first outbreak of PRRS. The outbreak occurred in a farm in Aizawal district of Mizoram state; out of the 305 pigs in the farm, there were 57 cases and 10 animals died (OIE Report). It has not yet been confirmed whether or not the outbreak is due to HP-PRRS virus.

4. **The factors influencing HP-PRRS spread**

In South-East Asia and China, a large proportion (up to 70%) of animals are still kept in traditional small-scale and backyard settings [8], and this leads to the close proximity of production systems of different sizes and biosecurity levels — important factors that can determine the scope for disease spread and the effect that diseases might have on pig populations. Since more than 70% of pig producers are smallholders, a major problem that prevails is the low level of knowledge and understanding among livestock producers regarding the benefits of disease control. Although commercial pig raisers are aware of the benefits of disease control, they are not as knowledgeable about the requirements for a cooperative national disease monitoring programme [3]. Medium- and small-scale pig farmers generally have the traditional farrow-to-finish systems, often with very close mixing of age groups. Replacement stock often comes from a variety of sources and of unknown health status with no adequate quarantine before entry. Hygiene application is usually very poor or does not exist with respect to the contact between farm workers and pigs outside their farms, or between outsiders and pigs housed within the farms. In small-scale hog-raising, disease control is normally done through vaccination. The use of high levels of combinations of antibiotics and anti-bacterial agents without adequate supervision or veterinary advice is very common [8].

Pork is one of the most important agricultural products in the region and pork consumption is highest in terms of total meat produced in some countries (Cambodia, China, Philippines and Vietnam). The increasing consumption of pork leads to an increase in commercial pig production. Statistical data reveal that HP-PRRS has been spreading mainly in areas with higher pig densities. In Vietnam, the Red River Delta forms the main area for intensive pig production in the northern part of the country and constitutes a prime location for pig diseases, including for the emergence of highly virulent PRRS. From here, there is a trade in live pigs, including piglets, fatteners and finishers to the south of Vietnam. Pig movements in these value chains also match and likely explain the rapid spread of PRRSV. The movement of pigs infected with HP-PRRS, even dead pigs, could also be responsible for the disease spreading between neighbouring countries [16].

Transboundary spread of HP-PRRSV from southern China to South-East Asia clearly suggests that biosecurity failures have occurred, including failure to control animal movements and trading among neighbouring countries at borders. Virus spread within a country also confirms the failure of biosecurity control, primarily via uncontrolled human movements within highly contaminated areas, especially at loading zones and slaughterhouses [R. Thanawongnuwech, personal observation]. Sharing such contaminated areas with other vehicles may increase the spread of the pathogen within the community.

5. **Summary of pattern of spread and countries' response**

Since its emergence in areas of high pig density in China in 2006, HP-PRRSV has made its way around South East Asia. It seems evident that the disease is following the intensification path of pig production. It became established first in countries with a larger share of commercial production units and high animal densities (Vietnam, Thailand) and later affected countries with a less developed commercial sector (Cambodia and Laos) due to the absence of disease surveillance at community level, weakness of the Veterinary Services in dealing with outbreaks in a timely manner, lack of biosecurity in value chains and the absence of regulations and incentives to control pig diseases.

Without blaming countries or production systems per se for facilitating the spread of this virus, the overall tendency of PRRS to affect commercial holdings and eventually spill over to small-scale and subsistence-driven producers is reflected well in this sub-region. The role of small-scale holdings for virus persistence in areas with a high density of pigs (in lower density areas PRRS infection usually dies out) will require special attention. The current picture in southern Vietnam suggests that the virus is continuing to circulate, yet it will be less likely to spill back to larger commercial units if biosecurity measures are in place.

With the emergence of a highly virulent pig disease, the national veterinary authorities are confronted with the task of developing new approach to control the disease. In response to the first introduction of the disease, countries have tended to pursue stamping-out policies in order to eliminate the pathogen. In Vietnam, where outbreaks have continued to occur, possibly as a result of reintroductions, culling has been shown to be a less effective measure and the country has shifted towards vaccination of susceptible animals.

6. Control and prevention of PRRS

The keys to controlling PRRS are as follows:

a) Design and strictly apply biosecurity measures to prevent the entry or re-entry of PRRSV;

b) Stop circulation of the virus among, or the spread of infection to, sows in breeding herds.

The measures currently used to control PRRS include management (e.g. whole-herd depopulation/repopulation and herd closure), biosecurity, test and removal, and vaccination.

Vaccines are available, but their effectiveness is mixed. This could be due in part to the different viral strains that exist, the viral load that infects the animal following vaccination and procedures or conditions at the time of vaccination that affect immune response. Thus, it is not clear how long immunity actually lasts.

Although vaccination of pigs does not prevent PRRSV infection, it may be helpful in herds experiencing problems with PRRS or herds at high risk of PRRSV infection [OIE, 2010]. Vaccination is generally used for the purpose of reducing clinical losses. Compared to other PRRS control strategies, a vaccination strategy involves lower costs for pig producers and is feasible for all types of pig producers (i.e. small, medium and large). Two types of PRRS vaccines are commercially available, a live vaccine and a killed virus vaccine. The live vaccine is well recognised for its protective efficacy against PRRS viruses that are genetically homologous to the vaccine virus. There are concerns, however, regarding its immunogenicity, cross-protective efficacy and safety. PRRS killed vaccine, on the other hand, is well known for its safety, but it only confers limited protection.

A current major obstacle for the development of an ideal PRRS vaccine is the lack of complete knowledge about several aspects of PRRSV, including:

a) the virus strategies to suppress and evade innate and adaptive host immune responses;

b) the virus epitope(s) responsible for such immune suppression and evasion;

c) virus epitope(s) that are common to both NA and EU PRRSV and can confer broad protection; and

d) the role of PRRSV non-structural proteins and structural proteins in virus replication, virulence, immunity and protection.

Efforts are needed to elucidate all these gaps in our knowledge. Addressing these questions will be essential to advance our understanding of PRRSV immunology and to provide valuable information for vaccine development.

Prevention of introduction into a herd

Biosecurity protocols to reduce the risk of PRRSV entry into farms and between herds include the quarantine and testing of incoming breeding stock, use of semen from PRRSV-naive artificial insemination centres, proper sanitation of transport vehicles using validated disinfectants and drying periods, implementation of strategies for personnel/fomite entry into and between farms, proper management of needles and methods of insect control. In addition, recent evidence suggests that the application of filtration systems to air inlets may significantly reduce the risk of PRRSV entry via bio-aerosols into farms located in swine-dense regions.

Prevention of introduction into a country

The main way in which PRRSV has been introduced into previously free countries is undoubtedly via pig movements. The importation of semen has also played a part in some cases. Whilst there is a theoretical risk posed by fresh meat, there has been no documented case of PRRSV introduction via this route. Since the movement of such products is a regular occurrence, even to those countries which remain free, this risk is considered small, provided the hazard of exposure to the pig population of the importing country is reduced. This can be achieved by banning swill feeding and/or ensuring that pig meat is not included therein. The risk posed by vaccinal virus should not

be forgotten, since there is documented evidence of circulation and reversion to a more virulent form. Protocols are in place to reduce the risk posed by live pigs and semen. For live pigs, these include sourcing from farms certified free of infection, use of quarantine periods and serological and virological monitoring, both pre- and post-import. For semen, RT-PCR has proved a useful tool in demonstrating absence of virus in semen batches, but care should be taken to ensure that any extender is compatible with such tests. The borders of a country obviously form the first line of any defence. Illegal pig movements should always be prevented. Where wild pigs may be present, steps should be taken to ensure domestic pig populations are protected from contact. Ports and airports may also provide a potential avenue for introduction, via galley waste and, in the case of ports, the illegal sale of pigs or pig meat transported on board.

7.   Conclusion

Since 2006 when HP-PRRS was detected for the first time in China, the disease has spread to at least six countries in South-East Asia by 2012. It has become endemic in some of those countries, and continues giving severe problems in pig production. The prevention and control of HP-PRRS is currently the highest priority issue for pig producers and animal health authorities in the region. The scientific knowledge on HP-PRRS has been increasing in recent years especially in virology, pathology, and molecular epidemiology. But it is still not enough to establish effective measures and the strategy for prevention and control of the disease. The more research is needed to understand the virus and the disease especially in virus pathogenesis, persistence, transmission, and vaccine development. It is important to monitor the disease status and the virus evolution in each country and the region, and to share those information among all the stakeholders. It would be necessary to develop regional strategy for the control of HP-PRRS. The coordinated implementation of such strategy in all countries in the region would be required for the successful control of HP-PRRS.

In that context, it is also proposed to the OIE to develop new standards on conditions for trade of pigs and pig products as well as for quality of vaccines.

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