

FOCUS ON

Porcine reproductive and respiratory syndrome (PRRS) virulence jumps and persistent circulation in Southeast Asia

Contributors: Klaas Dietze; Julio Pinto; Sherrilyn Wainwright; Christopher Hamilton; Sergei Khomenko

1. ABSTRACT

Since 2006, the pig sectors of China, Viet Nam, the Philippines and Thailand, have been continuously hit by atypical highly virulent strains of Porcine Reproductive and Respiratory Syndrome (PRRS). In 2010, the disease affected additional countries in Southeast Asia, including Lao People’s Democratic Republic and Cambodia, while causing a higher than expected epidemic wave in Thailand, underlining the regional burden PRRS represents today. Clinical symptoms of PRRS include reproductive failure in breeding stock and respiratory tract illness in young pigs. The significant economic losses to swine producers comprise an overall estimated fatality rate of approximately 20% (up to 100% in single production units) for the newly emerged virulent strains. For East and Southeast Asia, with the highest pig densities worldwide, the persistence of this disease poses a growing socioeconomic concern. Given the structure of the production sector, additional virulent pathogens may soon follow.

2. ABOUT THE VIRUS AND THE DISEASE

Aetiology and pathogenesis

Porcine Reproductive and Respiratory Syndrome (PRRS) is a highly contagious viral disease that was first recognized almost simultaneously in Western Europe and North America in the late 1980s. It is caused by the Porcine Reproductive and Respiratory Syndrome Virus (PRRSV), a small single-stranded, non-segmented RNA virus. The virion is enveloped, spherical and ranges in size from 45 to 80 nm in diameter. PRRSV is differentiated into two genetically distinct genotypes: Type 1, or European genotype, with a predominant spread on the European continent and Type 2, or North American genotype, that is mostly isolated on the American continent (North and South), as well as in Asia. Even for RNA viruses, PRRSV shows a remarkable genetic variability. Genetic differences between Type 1 and Type 2 of approximately 40% for whole genome sequences are documented and the calculated rate of nucleotide substitution is the highest reported so far for an RNA virus. These facts open-up a wide field of research with regard to virus phylogenesis, as well as to the immunology involved.

The PRRS virus compromises the cellular immune response and damages mucosal surfaces. Primary virus rep-

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lication takes place in local macrophages from where the virus rapidly spreads to lymphoid organs and lungs. Other tissues may also be infected, but not as commonly. Infection can occur via the respiratory, oral and venereal routes, as well as intramuscular, intraperitoneal or intravenous inoculation. Viraemia develops in pigs 12-24 hours post-infection, with the highest titres at 7-14 days. Most pigs are viraemic for no longer than 28 days. Congenitally and postnatally infected piglets remain persistently infected, harbouring the virus in their tonsils and/or lymph nodes.

In the environment, PRRSV favours moist and cold conditions, at or below 20° C, with a pH range of 5.5-6.5. The virus is shed by infected pigs in all secretions, including faeces, saliva and semen. Pork and pork products have been shown to be of negligible risk in the transmission of PRRSV.

Virus Classification

Order	Nidovirales
Family	Arteriviridae
Genus	Arterivirus
Species	Porcine Reproductive and Respiratory Syndrome Virus
Genotypes	Type 1: European genotype Divided into subtypes 1 (pan European), 2 and 3 (East European) Type 2: North American genotype

Clinical signs of PRRS vary with the strain of virus, the immune status of the herd and management factors. The incubation period ranges from 3-37 days.

Dermatological signs: There may be a reddish to blue

discolouration and blotching of the skin, most often of the ears (which gives PRRS the name of 'Blue ear disease') and the vulva, and may also include the trunk of the infected pigs. Subcutaneous oedema of the rear limbs and, in neonates, of the eyelids and periorbital area, cranium, and snout, may also be present, especially with the European genotype of PRRSV.

Reproductive failure in sows: The disease is first characterized by acute illness with lethargy and reduced appetite and spreads quickly through a herd over 7–10 days. Clinical signs are infertility, agalactia, lowered farrowing rates, a marked increase in late term abortions, and still-born, mummified or weak live born piglets. Respiratory disease may also be present. Sows can transplacentally transmit PRRSV to their unborn piglets.

Respiratory disease in piglets and grower pigs: In piglets that survive the pregnancy and neonatal phases, PRRS manifests as respiratory disease and is often complicated by secondary infections. Concurrent infection with *Pasteurella multocida*, Porcine Circovirus Type 2 (PCV2), *Mycoplasma hyopneumonia*, *Streptococcus suis*, *Salmonella choleraesuis*, *Haemophilus parasuis* and swine influenza virus is common. High death rates can be observed, typically 30–50 percent in young piglets and 4–20 percent in post-weaning pigs.

In post-weaning and grower pigs, clinical signs include dyspnoea, anorexia, lethargy, cutaneous hyperaemia, rough hair coats, and decreased weight gain. Secondary infections are common. Older pigs might show only minor respiratory signs.

Subclinical infection often occurs in finishing pigs, boars, gilts, and sows; in some herds, infection is generally asymptomatic.

Post mortem lesions: Although PRRSV produces a multisystemic infection in pigs, gross lesions are usually only observed in skin, respiratory and lymphoid tissues and vary depending on the viral strain, the individual stress factors and the presence of secondary infections. Interstitial pneumonia and enlarged lymph nodes can occur in all ages of swine. However, lesions are most commonly observed in neonatal and young, weaned piglets. With severe disease, lungs are mottled, tan and red, and fail to collapse; the cranioventral lobes tend to be most affected. Lymph nodes are enlarged, sometimes haemorrhagic, and can range from solid to polycystic.

The body condition of foetuses from late-term abortions ranges from fresh to autolyzed; umbilical haemorrhage has been reported to be a gross lesion of PRRSV infection.

Diagnosis and Treatment

Clinical diagnosis: Disease signs are similar to many other viral or bacterial swine diseases (see list of differential diagnoses below) and the clinical picture can be blurred by co-infection with other pathogens. Therefore, diagnosis of PRRS should be based on clinical signs and post-mortem examination (noted above), in conjunction with laboratory tests. The disease should be suspected with reproductive failure, high levels of neonatal mortality and respiratory problems in pigs of any age.

Differential diagnoses for reproductive disease include classical swine fever (CSF), African swine fever (ASF), leptospirosis, porcine parvovirus, porcine en-

terovirus, haemagglutinating encephalomyelitis virus, *Toxoplasma gondii*, and Aujeszky's disease.

For respiratory and postweaning disease, swine influenza, enzootic pneumonia, proliferative and necrotizing pneumonia, *Haemophilus parasuis* infection, haemagglutinating encephalomyelitis virus, porcine respiratory coronavirus, syncytial pneumonia and myocarditis, porcine circovirus-associated disease, post-weaning multisystemic wasting syndrome and Nipah virus infection should be considered.

Laboratory tests: A wide range of serological tests can be used for the detection of serum antibodies, ideally performed during recent infections. However, these tests only indicate that a pig has been exposed to the virus either naturally or through vaccination, but cannot tell if the pig is still infected. The enzyme-linked immunosorbent assay (ELISA) has the advantage of being able to test a large number of samples within a short period of time and has been developed to distinguish between the American and European types. The European antigenic type can also be detected with the immunoperoxidase monolayer assay (IPMA), using alveolar macrophages and the American type with the indirect immunofluorescence assay (IFA), using MARC-145 cells.

To determine the actual presence of the virus, reverse-transcription polymerase chain reaction (RT-PCR) is recommended. A multiplex PCR assay has been designed to differentiate between North American and European PRRSV isolates. Confirmation of PRRSV also includes immunohistochemistry staining (IHC), fluorescent antibody staining (FA) and in situ hybridization of fixed tissues.

Virus isolation (VI) is difficult, but can be attempted from serum, ascitic fluid, and tissues (lung, tonsils, lymph nodes and spleen). PRRSV is best cultured on porcine alveolar macrophages and MARC-145 cells.

Treatment: There is no specific treatment for PRRS. Treatment can be symptomatic and aim to prevent secondary bacterial infections.

Prevention: Strategies to prevent PRRSV introduction to production units have to build on two main pillars. The most important, and not a disease specific prevention method, is the application of basic biosecurity measures. Reducing the opportunities for virus introduction through animal segregation, increased hygiene for visitors, application of animal quarantine for pigs entering a herd and appropriate cleaning and disinfection at critical production stages will effectively contribute to the prevention of disease introduction.

Additionally, both attenuated live and inactivated vaccines are commercially available, but it is important to match the genotype of the vaccine with that circulating in the pig population. While vaccination of pigs does not prevent PRRSV infection, it may reduce clinical disease and transmission of the wild-type virus. It is important to note that the modified-live vaccine virus can persist in pigs and be disseminated through semen and oral fluids; it should therefore not be used in naïve herds, pregnant sows or breeding gilts and boars.

Distinguishing infected from vaccinated animals is currently not possible. Furthermore, there is a potential risk that vaccinal virus can revert to a more virulent form and cause disease.

3. PRRS AND THE PIG SECTOR: GLOBAL CONTEXT AND REGIONAL PECULIARITIES

Developments in pig production

Terrestrial animal meat consumption worldwide is topped by pork. Due to changes in consumption patterns based on increasing incomes in developing and in-transition countries with fast growing economies, the global demand for pork has been constantly rising over the past decades. Together with poultry, the pig sector is the fastest growing livestock subsector, with numbers that will reach the one billion mark before 2015, representing a two-fold increase compared with the 1970s. Pig production has reached global distribution, excluding only a few regions with cultural and religious reservations towards pork consumption.

Pig production worldwide is dominated by an increasing dichotomy of production systems. This is reflected by the mainly subsistence driven, traditional small-scale production on the one side and highly specialized, vertically integrated industrialized farms on the other. The latter follows a distribution pattern similar to the intensive poultry sector – concentrating close to centres of urbanization and/or input sources. At the intermediate stage, diverse types of commercial and semi-commercial production systems can be found, usually combining some aspects of industrialized pig production with local husbandry traditions and a reduced dependence on external inputs.

Since the end of the Second World War, swine production in Europe and North America has undergone an enormous process of intensification with relatively stable stock numbers since the late 1970s and a 90% reduction of the number of pig farms. This process is ongoing and, with the increase of internationally operating companies in the pig sector, has also begun in other regions of the world.

China and Southeast Asia, with a strong cultural background in pig husbandry and with some of the highest animal densities, have developed similarly over the past decade. China alone hosts almost 50% of the world's pig population and the process of intensification has picked up enormous speed to supply growing urban centres with an increased demand for pork and other livestock commodities.

Yet on a global scale, and definitely in Southeast Asia and China, a large proportion of animals are still kept in traditional small-scale and backyard settings. In high pig density areas in Asia, this leads to the close proximity of production systems of different sizes and biosecurity levels – important factors which determine the scope and effect diseases might have on pig populations.

The linkages and interactions between production systems in a given setting can be very distinctive and must be understood when addressing disease control and prevention measures. Strategies should avoid one-size-fits-all recommendations, leaving enough flexibility to identify epidemiologically significant risk factors at sub-national levels.

PRRS dynamics in Southeast Asia

In the summer of 2006, a new variant of PRRSV was reported from China and was first classified as high fever disease (HFD). It was later identified as an atypical form

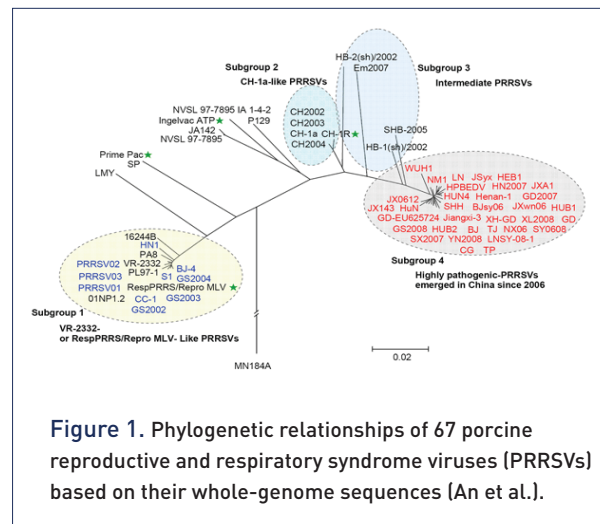


Figure 1. Phylogenetic relationships of 67 porcine reproductive and respiratory syndrome viruses (PRRSVs) based on their whole-genome sequences (An et al.).

of PRRS that, according to the China Animal Disease Control Center (CADC), affected almost 2 120 000 pigs and caused 400 000 deaths. Clinically, the atypical PRRS differs greatly from the 'traditional' PRRS and is characterized by high fever (40–42°C), petechiae, erythematous blanching rash and by high mortality rates of up to 100% for single production units in swine of all ages, including grown and fattening pigs. On a molecular basis, the common characteristic of all highly virulent (HV) PRRSV isolates from China is the shared 30 amino acid deletion that has been proposed as a genetic marker of the HV-PRRSV. Phylogenetic analysis of PRRSV isolates from China have classified them into subgroup 4, all of them sharing a >99% homology of their genomic sequence (see Figure 1).

One possible explanation of the 2006/07 PRRS epidemic in China and later in Viet Nam is that the ancestor PRRSV of North American origin (Type 2) evolved into a highly virulent strain under the selection pressure in China, driven by changes in pig husbandry practices, the epidemiological linkage of a large number of animals under very diverse production settings and environmental factors (temperature and relative humidity in summer). Secondary bacterial infection may contribute to the clinical appearance of this highly virulent PRRS.

The disease then re-emerged in its epidemic form in 2007 and has persisted ever since with differing impacts on the pig population. From 1 January 2007 to 22 August 2007, statistics released by the Chinese Government reported 826 outbreaks of PRRS in 26 provinces, autonomous regions and municipalities, including 257 000 diseased pigs, 68 000 dead pigs and 175 000 pigs destroyed (culled). Among these 26 provinces, those along the Yangtze River in the south of China were the most affected (Hebei, Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong, Henna, Hubei, Hunan, Guangdong, Guangxi, Hainan, Chongqing, Ningxia, Xinjiang, Tianjin, Liaoning, Gansu).

In retrospect, evidence can be found that PRRSV has been circulating in China since 1996 and in the Mekong delta of Viet Nam since 2000, yet at this earlier stage no severe clinical symptoms were associated with it.

During 2007, virulent strains of PRRSV emerged also in Viet Nam and the Philippines. The spread pattern in Viet Nam (2007 – 2010) suggests the occurrence of new strains in the northern part of the country earlier in

March 2007. This coincides with the Tet-Holiday, one of the major 'harvest times' in pig production and increased people and product movement in the country. A second wave of infection, apparently with the same virus strain, occurred in June 2007 in the south of the country (see Figure 3). The 2010 surveillance data from northern Viet Nam revealed a 'new' 2010 PRRSV variant, whilst in the southern part of the country a mix of new and older variants was detected.

In the Philippines the disease has been spreading mainly in areas with higher pig densities and increased commercial pig production. The number of detected cases has been rising each year, peaking in 2009 (2010 results are not yet available). During surveillance, it became clear that most positive cases also tested positive for other pig pathogens such as CSF virus, PCV2 and Swine Influenza Virus (SIV).

Thailand reported highly virulent PRRS for the first time in 2008 but, even including 2009 data, case numbers were low (25 cases in 2008 and 33 in 2009). In 2010, the disease caused an epidemic wave of major concern on small-scale commercial farms with 145 outbreaks as of October 2010 (latest available information). Co-infections with other swine diseases were also reported,

but seemed to be less dominant than those reported from the Philippines.

The latest countries to report this new variant of PRRS were Cambodia and Lao People's Democratic Republic, both reporting their first cases in 2010 in smaller commercial units. Myanmar had not found positive cases, but with the epidemic wave in neighbouring Thailand in 2010, surveillance was increased. The spread of PRRS in the region over time and space is summarized in the maps of Figure 2.

4. PORK VALUE CHAINS AND RISKS OF PRRS

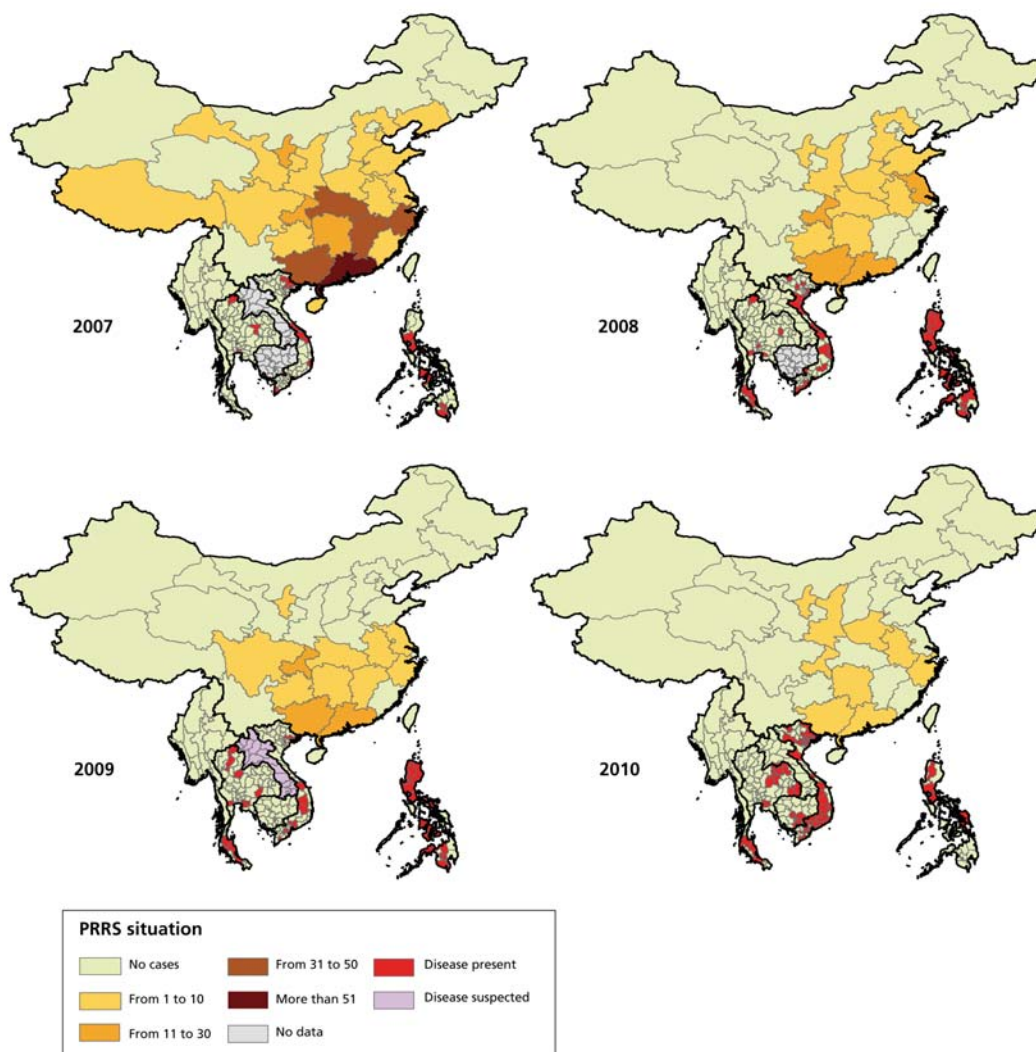
Viet Nam

In Viet Nam, one of the countries affected by the highly virulent PRRS strain, pork is one of the most important agricultural products, contributing 58% to the total agricultural GDP.

The flow of live animals

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. Most piglets

Figure 2. The spread of highly virulent PRRS in Southeast Asia (2007 - mid-2010)



are produced in this area (Thai Binh, Hung Yen Hai Duong, Ha Nam); lower quality animals are traded and transported to the mountainous areas, while some of the high quality animals find their way to the south of Viet Nam (see Figure 3).

Thai Binh is a major collection point with a total of five collection centres. Collectors transport pigs to other Red River Delta provinces, southern Viet Nam, Lao People's Democratic Republic, or China. If insufficient quantities of animals are available in the Thai Binh province, collectors buy animals elsewhere and ship them to Thai Binh. Live piglets, fatteners and finishing pigs are mainly exported live to China, whereas frozen carcasses are exported to Hong Kong, SAR.

Fatteners and finishing pigs are also transported to the southern part of Viet Nam (refer to left map of Figure 3). Pig movements between participants in these value chains also match and explain the rapid spread of PRRSV, taking into consideration that 40% of pork is supplied by smallholders that keep between one and ten pigs. There is a high-risk of PRRSV transmission through the daily flow of pigs into Hanoi and Hai Phong to service both local populations and regional exports into southern and north-eastern Viet Nam and for exports to Hong Kong, SAR, and other (currently limited) international markets. The pork marketing chain is complex and presents opportunities for PRRSV spread through re-grouping, splitting of animal groups and poor biosecurity practices (e.g. lack of cleaning and disinfection of livestock transport vehicles and equipment used for pigs and people). In Lang Son (and other northern mountainous provinces), 100% of the young fattening stock is brought in from outside the area without any control.

The flow of ready to slaughter animals and pork

A minority of farmers slaughter animals on farm, but the majority of live pigs are picked-up on farm by collectors and then sold on to urban retailers. These middlemen are notified by slaughterhouses about which farms have pigs available for slaughter. Biosecurity levels of partici-

pants in the different value chains (Figure 4) explain how pig diseases, including PRRS, CSF and FMD can spread in Viet Nam between provinces. It is possible to distinguish between three different value chains for pork, depending mainly on different preferences of consumer groups:

1. In the marketing of pork destined for rural consumers, fattened animals are picked up from farms by collectors, slaughtered and sold on to retailers who sell pork at local markets.
2. To feed into the markets of cities and smaller urban centres, animals are picked up from farms by local or regional collectors linked to the marketing chain. Local collectors might slaughter and sell the meat to either urban retailers or assemblers, or sell animals to small slaughterhouses from where the meat goes on to urban consumers. Farmers also sell their animals directly or through local agents to local slaughterhouses. From there the meat is distributed to internal organ collectors, meat processors, restaurants and urban retailers. The majority of rural and urban consumers prefer to buy pork at 'wet markets' due to the general perception that the hygiene of wet markets is better and prices are lower than in supermarkets. Consumers also prefer 'fresh' (warm) meat to so-called 'machine killed' and chilled meat because it is regarded as being fresher and easier to keep. Only around 4% of pork is purchased at supermarkets. Quality standards are generally non-existent in Viet Nam and therefore consumers are not concerned if veterinary stamps of quality assurance are missing.
3. The third group of 'consumers' is the licensed food industry, including the export oriented companies. Producers sell animals, either directly or via assemblers, to these food companies. The assemblers or export middlemen travel around the country to collect pigs that meet specific quality criteria in order to sell them on to export companies.

Most pigs for the Hanoi market are slaughtered in unregulated slaughterhouses in Ha Tay. The two slaughterhouses in the area meeting modern standards have higher fees for slaughter due to increased running costs, making it hard to compete on the market for ready-to-slaughter hogs. Pigs for the official export market must be slaughtered in licensed and inspected premises and there is a seasonal fluctuation in demand for pork in rural areas (winter is higher than summer).

Cambodia

The Cambodian pig sector is dominated by small-scale farming systems and lacks a developed commercial marketing chain of relevant scale. Pig numbers have been decreasing over the past three years due to overall production and health constraints. Since the domestic demand for pork cannot be covered by the Cambodian pig producers, it is estimated that approximately 1 000 head of pigs or pig carcasses are imported to the country. High prices for pork in Cambodian consumption centres like Phnom Penh and Siem Reap make imports of this commodity attractive even though, with the occurrence of significant pig diseases in neighbouring countries, imports of live animals are officially banned and pork imports are subject to import regulations.

Figure 3. Movement of pigs and piglets and PRRS spread in May-August 2007 in Viet Nam (FAO, 2008)

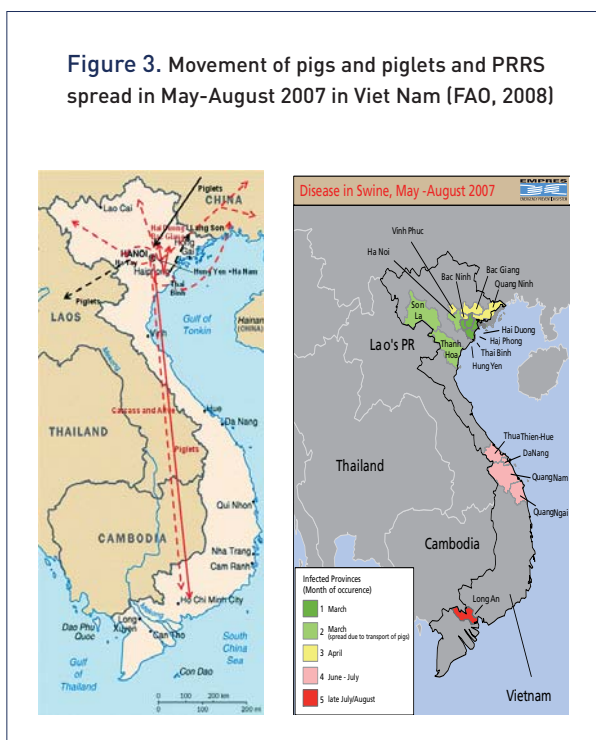
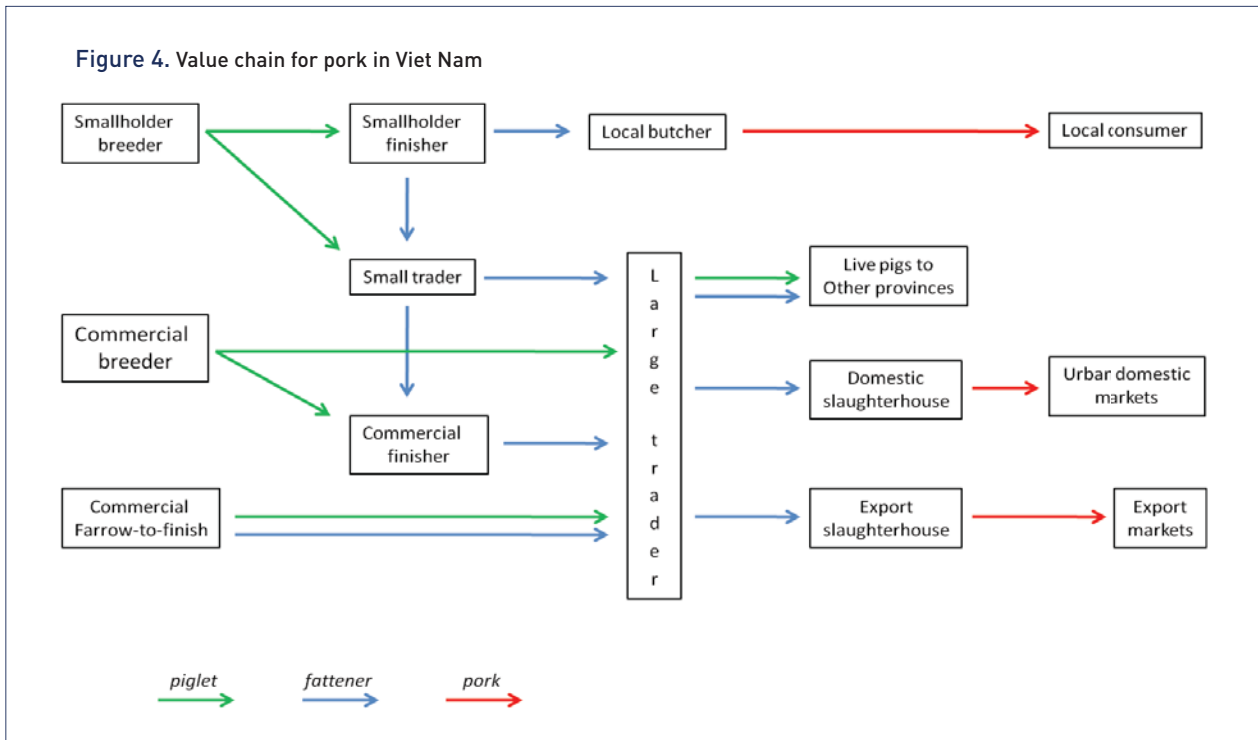


Figure 4. Value chain for pork in Viet Nam



The country reported its first cases of PRRS in August 2010 and the most likely sources for these outbreaks were infected pigs imported illegally from Viet Nam. Figure 5 below describes the animal movement, in particular pig movement, between the borders of Cambodia and Viet Nam and the pig density.

Summarizing the spread pattern and country reactions

With its emergence in 2006 in areas of high pig density in China, the virus has made its way around Southeast Asia and, at least for the greater Mekong region, 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 (Viet Nam, Thailand) and later affected countries with a less developed commercial sector (Cambodia and Lao People's Democratic Republic) due to the absence of disease surveillance at community level, weakness of the veterinary services in dealing with outbreaks on time, 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 high pig density areas (in the lower density areas PRRS infection usually dies out) will require special attention. The picture of southern Viet Nam suggests the virus continues 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 confronted a new challenge. Diagnostic capacities had to be increased and approaches for disease control designed. During the first introduction, countries tended to pursue stamping out policies in order to eliminate the pathogen. With con-

tinuous outbreaks, as seen in Viet Nam, that might also have been the result of re-introduction, culling has been shown to be a less effective measure and the country has shifted towards vaccination of susceptible animals.

5. THE GLOBAL CONTEXT – DRIVERS AND RISKS

The almost simultaneous emergence on separate continents of two genetically highly diverse genotypes has been a source of ongoing speculation. The current knowledge on PRRSV epidemiology in wild boar and low pig density farming landscapes leaves the industrialization of swine production as a driver of virus evolution and shift in virulence. This process involves massive changes in pig husbandry practices, moving pigs indoors, increases in herd sizes sharing airspace, the breakdown of the traditional farrow-to-finish system into highly specialized multi-site production systems, and increased use of artificial insemination. These factors have led to a pig production chain that provides a conducive host contact network structure that permits sustained circulation of infectious viruses such as PRRSV, including the highly virulent strains.

Geographic corridors linking different livestock sub-populations increasingly pose epidemiological challenges. They explain how highly virulent PRRS, as well as other diseases including foot-and-mouth disease and CSF, spread in East Asia. These dynamics are sustained by farming landscapes with coinciding smallholder farming and intensive production resulting in the increased vulnerability of Eastern Asia to livestock disease epidemics.

Impact on the pig sector

With the growing importance of pig production in many regions of the world, the emergence of a highly virulent strain of a virus that has already reached pig populations around the globe is to be considered a serious animal health threat with a major socioeconomic impact, affecting the livelihoods of millions of pig farmers.

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