

Porcine reproductive and respiratory syndrome virus

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Abstract

Porcine reproductive and respiratory disease (PRRS) is an economically important disease around the globe; it has been estimated to cost the swine industry in USA approximately US\$ 560 million annually. It is well established that PRRS is caused by an enveloped, single-stranded positive-sense RNA virus known as porcine reproductive and respiratory syndrome virus (PRRSV). The inability to successfully control PRRS across farms via traditional methods (e.g. vaccine and animal flow) has led to a growing interest in area-based eradication. Important to such an initiative is information on PRRSV transmission within and between herds and intervention strategies to prevent its spread. This paper will review the current literature on selected areas of PRRS known to be important to the topic of pathogen elimination, including etiology, clinical manifestations, direct and indirect routes of transmission, as well as discuss measures for disease control, prevention and eradication.

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1. Introduction

Porcine reproductive and respiratory syndrome (PRRS) is an economically important disease of swine, estimated to cost the swine industry in USA approximately US\$ 560 million per year [1]. Clinical outbreaks of PRRS were first reported in the late 1980's in USA; however, the etiology of the disease remained unknown [2,3]. Clinical signs included severe reproductive failure, post-weaning pneumonia, growth reduction, decreased performance, and increased mortality [2,3]. Similar clinical outbreaks were reported in Germany in 1990 and were widespread throughout Europe by 1991 [4]. In 1991, the etiologic agent, porcine reproductive and respiratory syndrome virus (PRRSV) was identified by investigators in The Netherlands and USA [5,6].

Today, PRRSV is endemic in the global swine population; however, several countries, including Sweden, Switzerland, New Zealand, and Australia claim to be free of the disease [7–10].

2. Etiology

The PRRSV is an enveloped, single-stranded positive-sense RNA virus, approximately 50–65 nm in diameter that is classified in the order Nidovirales, family Arteriviridae, genus *Arterivirus* along with equine arteritis virus, lactate dehydrogenase-elevating virus of mice, and simian hemorrhagic fever virus [6,11]. Properties of these viruses include the ability to induce prolonged viremia, persistent infections, and replication in macrophages [12]. Being an enveloped virus, PRRSV survivability outside of the host is affected by temperature, pH and exposure to detergents. It is known that PRRSV can survive for extended intervals (>4 months) at temperatures ranging from –70 to –20 °C [6]; however, viability decreases with increasing

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temperature. Specifically, recovery of PRRSV has been reported for up to 20 min at 56 °C, 24 h at 37 °C, and 6 days at 21 °C [6]. The PRRSV remains stable at pH ranging from 6.5 to 7.5; however, infectivity is reduced at pH <6.0 or >7.65 [13]. Detergents are effective at reducing infectivity of the virus and lipid solvents such as chloroform and ether are particularly efficient at disrupting the viral envelope and inactivating replication [6].

Regarding genetic diversity, there are two major prototypes of PRRSV, the European isolate (Lelystad virus, LV) and the North American isolate (VR-2332). In addition to differences between isolates, it has been determined that there is ample genetic variation within both isolate types, as confirmed by analysis of the nucleotide and amino acid sequences of the open reading frame (ORF) regions of LV and VR-2332. Amino acid sequences for VR-2332 as compared to LV are 76% (ORF 2), 72% (ORF 3), 80% (ORFs 4 and 5), 91% (ORF 6) and 74% (ORF 7), and sequence analysis indicates that viruses are evolving by random mutation and intragenic recombination [14–17].

3. Clinical manifestations

As described earlier, outbreaks of PRRS involve episodes of reproductive failure (third-trimester abortions, premature parturition, and elevated levels of fetal losses, i.e. mummies and stillbirths and neonatal death) as well as reduced growth performance and elevated mortality, secondary to respiratory disease [2,3]. However, the intensity of the disease appears to vary among isolates and variation in the pathogenicity of PRRSV virulence has been observed in experimentally-infected animals. Studies found that pigs experimentally infected with nine different isolates of PRRSV (from USA) had major differences in clinical disease, rectal temperatures, and gross and histological lung lesions [18,19]. In these studies, animals infected with mildly virulent isolates or the LV had transient pyrexia, dyspnea and tachypnea, whereas infection with highly virulent isolates induced labored breathing, pyrexia, lethargy, and anorexia. Furthermore, studies have reported that the impact on reproductive performance may be also isolate-dependent [20]. Finally, the degree of clinical PRRS may be related to elevated viral concentration in blood and tissues, secondary to the ability of highly virulent isolates to replicate more efficiently in the host [21]. A recent study concluded that the infection of susceptible pigs with highly virulent isolates of PRRSV resulted in longer periods of viremia, increased severity of clinical signs and mortality, and significantly higher viral loads in blood

and tissues than those that were mildly virulent or cell-culture adapted [21].

Several other factors such as animal age and bacterial co-infection can influence virus replication and clinical signs. Studies comparing the effects of age determined that younger animals (4–8 weeks of age) infected with PRRSV had a longer viremia, as well as higher excretion rates and replication rates in macrophages when compared to older (16–24 weeks) pigs [22,23]. Additionally, certain bacterial agents, e.g. *Bordetella bronchiseptica* and *Mycoplasma hyopneumoniae* appeared to enhance the duration and severity of PRRSV-induced pneumonia and lung lesions [24,25]. Furthermore, PRRSV infection increased the susceptibility of pigs to *Streptococcus suis* type 2 infection and enhanced the severity of *Salmonella choleraesuis* infection [26,27].

4. Transmission

4.1. Direct routes

Direct routes of PRRSV transmission within and between pig populations include infected pigs and contaminated semen. The PRRSV has been recovered from a variety of porcine secretions and excretions including blood, semen, saliva, feces, aerosols, milk and colostrum [28–32]. Vertical transmission during mid- to late-gestation has also been reported [33,34]. Horizontal transmission has been reported following direct contact between infected animals and naïve animals [35], as well as transmission via semen of infected boars [36]. Specifically, infectious PRRSV and PRRSV RNA have been detected in the semen of experimentally infected boars up to 43 and 92 days, respectively post-infection [29,37]. Fecal shedding remains a highly debated issue; several studies report the presence of PRRSV in feces from 28 to 35 days following experimental infection, whereas others report no detection of virus in fecal samples [28,32].

4.2. Persistence

Persistent infection is a characteristic of the Arterivirus group [12]. The PRRSV persistence results as a “smoldering” infection at which virus is present at low levels within the animal, eventually decreasing with time [38,39]. The mechanism in which the virus uses to evade the immune system remains unknown. The duration of PRRSV persistence has been documented in a number of studies, but results are highly variable. Using polymerase chain reaction, (PCR) testing, PRRSV RNA has been detected in breeding gilts

(6–7 months of age) out to 120 days post-infection [40] with shedding to naïve sentinels reported up to 86 days [35]. In regards to PRRSV persistence at the population level over time, PRRSV was detectable in 100% of 60 experimentally inoculated pigs 3 weeks of age up to 63 days post-infection and in 90% of the same pigs on 105 days post-infection [41]. The in utero infection of fetuses at 85–90 days of gestation resulted in congenitally infected offspring with detectable PRRSV RNA in sera at 210 days post-farrowing [42]. Sentinel pigs co-mingled with these infected pigs (98 days post-farrowing) developed anti-PRRSV antibodies 14 days later [42]. Finally, prolonged persistence of PRRSV in individual animals, ranging from 154 to 157 days post-infection has been reported [43,44].

4.3. Indirect routes

4.3.1. Fomites

Several routes of indirect transmission by fomites have been identified in recent years. Specifically, boots and coveralls have been identified as potential sources of PRRSV to naïve pigs [45]. The risk of transmission via these routes can be reduced through the use of protocols (i.e. changing boots, coveralls, washing hands, showering and incorporating 12 h intervals between pig contact periods [45]). Needles have also been recognized as an indirect means of PRRSV transmission between pigs, demonstrating the need for proper needle management [46]. Finally, mechanical transmission of PRRSV through a series of coordinated sequence of events involving fomites (boots, coolers and containers, shipping parcels, vehicles) and behavior patterns of farm personnel has also been demonstrated in cold and warm weather [47,48]. However, studies have demonstrated that certain intervention strategies, such as the use of disposable footwear, boot baths, the wearing of gloves and double-bagging products designated for entry into farms substantially reduced the level of PRRSV contamination on the surface of objects and mechanical spread of the virus [49].

4.3.2. Transport vehicles

Transport vehicles have recently been investigated as a potential route of mechanical PRRSV transmission. Using a 1:150 scale model, naïve pigs were susceptible to acquiring PRRSV through contact with the interior of a transport model contaminated with PRRSV; however, drying the transport vehicle reduced infection [50]. Recently, a means to enhance drying time through the application of high velocity warm air (thermo-assisted drying and decontamination system) was demonstrated

to be an effective method of eliminating PRRSV from the interior of a contaminated transport [51]. In combination with drying, disinfectants are also widely used to sanitize transport vehicles post-usage; however, differences in disinfectant efficacy following application to PRRSV-contaminated transport vehicles has been observed [52]. Based on these studies, it appears that peroxygens, quaternary ammonium chlorides and glutaraldehyde-quaternary ammonium chloride combinations are highly effective products.

4.3.3. Insects

Insects (mosquitoes (*Aedes vexans*) and houseflies (*Musca domestica*)) are commonly observed in swine facilities during the summer months and have been shown to mechanically transmit PRRSV from infected to naïve pigs under experimental conditions [53,54]. The site of the virus in the insect is the intestinal tract [55]. Insects are not biological vectors of PRRSV [56,57]; therefore, the duration of retention of PRRSV within the intestinal tract of insects is dependent upon virus load post-ingestion and environmental temperature [57]. Transport of PRRSV by insects throughout an agricultural area has been reported for up to 2.4 km following contact with an infected pig population [58]. Finally, control of on-farm insect populations has been demonstrated using a combination of screening of the air inlets of swine facilities along with the use of targeted insecticides and habitat management [59].

4.3.4. Avian and non-porcine mammalian species

Previous studies have investigated the role of various mammals (rodents, raccoons, dogs, cats, opossums, skunks) and birds (house sparrows and starlings) in the transmission of PRRSV [60]; none were capable of serving as mechanical or biological vectors [60]. However, migratory waterfowl have been proposed as vectors of PRRSV spread between farms, due to their migratory nature and their tendency to nest on or near to swine farm lagoons. Since PRRSV can survive in water for up to 11 days [61] and in swine lagoon effluent for up to 7 days [62], this appeared to be a plausible hypothesis; however, contrasting results regarding the ability of Mallard ducks to replicate and shed PRRSV to pigs via the fecal–oral route have been reported [63,64]. Therefore, this question remains unanswered at this time.

4.3.5. Aerosols

Currently, aerosol transmission of PRRSV between farms remains highly controversial. Early data collected during outbreaks in England proposed that the virus can be spread through aerosols up to 3 km [65], and recent

data from a large scale epidemiological study also suggested aerosols as a potential route of indirect transmission throughout swine producing regions [66]. Aerosols have often been blamed for “local spread,” of PRRSV, a term used to describe transmission of the virus throughout a region via undetermined routes [67]. However, results from experiments evaluating aerosol transmission of PRRSV have been inconsistent, with experimental and field trials reporting different findings. Studies conducted under laboratory conditions have shown that aerosol transmission may occur over short distances; one trial demonstrated that experimentally infected pigs were able to transmit virus to close and indirect contact groups separated by 46 and 102 cm in separate trials [68]. Several other studies showed that experimentally infected pigs were able to infect sentinel pigs via aerosols over distances of 1 m [69–71]. Recently, it has also been demonstrated that viable virus could be transported up to 150 m using a negative pressure straight tube model, resulting in the infection of naïve sentinel pigs [72].

Despite these data, aerosol transmission of PRRSV has been difficult to prove under controlled field conditions. Field trials attempting to transmit PRRSV through aerosols to naïve sentinel pigs were not successful, despite the use of large populations of experimentally infected pigs and commercial conditions [73–75]. However, these studies all used the same variant of PRRSV, an isolate of low virulence referred to as MN-30100 that had been recovered from a persistently infected sow within an endemically infected farm [35]. This observation led to the question of whether aerosol shedding and transmission of PRRSV may be isolate-dependent. This hypothesis was supported from previously published data involving the use of a mildly virulent reference isolate (VR-2332) and a highly virulent isolate (MN-1b). Results indicated that differences existed in seroconversion rates, recovery of virus from infected animals and transmission of PRRSV to naïve pigs, [69]. To test the hypothesis, Cho and others conducted a series of experiments to assess whether PRRSV isolate pathogenicity significantly influenced virus concentration in aerosols, the frequency of shedding, and transmissibility of PRRSV in aerosols [76,77]. Two isolates were evaluated: MN-184 (a highly virulent isolate) and MN-30100, an isolate of low virulence. There were significant differences in the frequency of shedding and transmission in aerosols from pigs experimentally infected with MN-184 when compared to aerosols recovered from pigs infected with MN-30100 [76,77]. However, differences in the concentration of PRRSV in

aerosols from animals infected with the two isolates were not significant [76,77]. These results have renewed an interest in air filtration as a biosecurity method for reducing the risk of aerosol transmission of PRRSV between farms. Recent research has demonstrated that filtration systems using HEPA filter or HEPA-like (95% DOP at 0.3 μm) filters are superior to alternative methods of air filtration or treatment, such as UVC irradiation, low-cost filters, i.e., fiberglass and electrostatic residential furnace filters, or bag filters [78–80].

5. Control and eradication

A substantial effort toward successfully controlling and eradicating PRRS has been placed on reducing negative production and economic effects of the disease in swine production systems. Emphasis is positioned on the control of PRRSV circulation in the breeding herd in attempts to prevent vertical and horizontal transmission, particularly before weaning [81]. Infected piglets that enter the nursery continue to propagate the virus throughout the population by infecting older pigs in the nursery. In order to control and eventually eliminate PRRSV, critical issues that allow for maintained circulation of PRRSV within herds must be identified and addressed. Such factors include co-existence of genetically diverse isolates, the existence of naïve breeding herd subpopulations, and improper management of gilt replacement pools [82–84]. Attempts to induce protective immunity in pig populations can be initiated through the use of vaccines, and both modified-live and killed (commercial and autogenous) are available. Serum inoculation, i.e., the administration of virus-positive serum via the intramuscular route into naïve animals to expose an at-risk population, is another means of exposure that is currently being practiced [85].

The introduction of properly developed replacement gilts is also an important component of PRRS control at the farm level. This involves exposing incoming naïve animals to the farm-specific PRRSV isolate before entering a positive breeding herd in order to reduce seronegative subpopulations [86]. Means of exposure include vaccination, serum inoculation, contact with infected animals such as nursery piglets with clinical symptoms, and feedback of serum or tissue from infected animals from the herd [85,86]. A minimum of 90 days following exposure is required for animals to recover clinically and establish immunity, thus reducing the likelihood of shedding once introduced into the breeding herd [40].

Several methods of eradication have been shown effective in eliminating PRRSV from positive herds,

including whole herd depopulation/repopulation, test and removal and herd closure. Whole herd depopulation/repopulation has been used for the elimination of multiple swine pathogens including PRRSV. Key elements in maintaining this strategy include purchasing PRRSV-negative animals and consistent diagnostic testing of each incoming group of animals. However, despite its success, several disadvantages exist including inability to preserve genetic material and an increase in production down-time, thus resulting in high implementation costs. Test and removal methods have also resulted in the successful elimination of PRRSV from positive populations [87]. The emphasis of this process is placed on the testing of the entire breeding herd population in order to detect carriers and remove them from the herd. Potential carrier animals are detected through the testing of sera from all animals by ELISA and PCR. Although highly successful in eliminating PRRSV from endemically infected populations, several disadvantages are present, such as the high cost of diagnostic procedures and the potential removal of previously exposed animals that no longer have the virus. Herd closure has also been shown to be a highly efficacious method for elimination of PRRSV. The basis of herd closure is the cessation of replacement gilt introduction for an extended period (4–8 months), resulting in the reduction in viral shedding and elimination of carrier animals [40,88,89]. Although herd closure allows for the preservation of genetics and retains minimal diagnostic costs, it can be costly and can result in the production of an improper parity distribution within the breeding herd. However, these effects can be minimized through the use of off-site breeding projects for replacement gilts.

6. Conclusion

The ability of the veterinary profession to control PRRS has improved as new information is developed and shared throughout the industry. However, further work is required, particularly in the areas of immunology, prevention of area spread and improved diagnostics. Finally, producers and practitioners must work together to develop and apply regional control and eradication programs for PRRS in order to enhance the long-term goal of elimination of the virus from the North American pig population.

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