Introduction

Since 1987 when the first epidemics of Porcine Reproductive and Respiratory Syndrome (PRRS) were recognized in the United States it has spread to most countries in the world where pigs are raised. In doing so, it has cost the industry an enormous amount of money and frustrated farmers as they try to exclude the disease from their herds or control its sometimes-devastating effects on production. At this time, only Sweden and Australia are presumed negative. In the early days, PRRS was known by a variety of names usually describing the associated clinical signs. In the USA it was initially called “mystery swine disease” reflecting the frustration researchers experienced as they attempted to identify the cause. In Mexico it was called “blue ear disease” and in other countries “porcine epidemic abortion and respiratory syndrome” and “swine infertility and abortion syndrome”. In 1991 researchers at the Central Veterinary Research Institute in Lelystad, The Netherlands, were able to reproduce the reproductive signs of the disease with a virus. The strain isolated in Lelystad (LV), while similar to the US strain (VR-2332), is sufficiently different genetically and antigenically to be a distinct strain. Outbreaks in Europe are usually caused by strains like the LV and outbreaks in the Americas (and countries purchasing breeding stock from there) are usually caused by variant strains more similar to VR-2332. Subsequently, we have come to realize that many different strains of the virus exist with differing virulence, tissue tropism, and ability to replicate. PRRS is a member of the family of viruses called Arterividae and, in common with other members of this group (lactate dehydrogenase-elevating virus, equine arteritis virus, and simian haemorrhagic fever virus), they cause a variety of clinical signs ranging in severity from subclinical to fatal. In addition, they persist in the host, replicate in white blood cells (macrophages) and mutate readily. These attributes contribute to many of the difficulties we have in trying to cope with PRRS.

The range of clinical signs is best illustrated by the difference in signs seen in Europe and Mexico where blue discoloration of the skin (especially the ears) was common, compared to North America where those signs were rarely seen. With North American strains, some isolates induced encephalitis and myocarditis whereas others don’t and some are more or
less virulent compared to LV. In addition, US isolates vary in their effect on reproduction. These variations arise from the large repertoire of genomic strains. PRRS, like other single strand RNA viruses, is very small (15,000 base pairs) and relies on multiple strains to carry information to assure adaptability in a changing environment. PRRS viruses mutate through base substitution and deletion, as well as reassortment of nucleotide sequences within a single viral genome or through combination with other field strains of PRRS viruses (Kapur et al., 1996). Compounding the problem has been the use of modified-live vaccines that are able to replicate, spread through populations, and mutate to a more fit status.

**Epidemiology**

PRRS was first identified as a clinical entity in the US in 1987 but there is serological evidence that it was in Canada in 1979, USA and Korea in 1985, and in Japan and Germany in 1988. We don’t know where the virus came from but some have proposed that it came from a wildlife reservoir, possibly feral pigs. Interestingly, although the LV and VR-2332 strains are different they are similar enough to suggest that they had a common ancestor but evolved differently as they adapted to their own niches. If we accept that they had a common ancestor then we are left with the possibility that source viruses still exist and contribute to the magnitude of the current strain variation. A large variation in viral genomic possibilities contributes to the development of new future strains and complicates control efforts.

Although PRRS is endemic in most countries there are still herds in all countries that remain negative. The prevalence of positive herds is very difficult to estimate because the modified-live vaccines produce serum antibodies that are indistinguishable from those produced by the “wild” virus and because those vaccine viruses can infect naïve pigs. In addition, no statistically valid random sampling of the populations of interest have been undertaken. Our best estimate of prevalence is that, of those farms not using modified-live vaccine, 59% are positive to PRRS.

**Infection**

The PRRS virus is highly infectious with 10 or fewer particles capable of establishing an infection when exposed by the intranasal route. Other routes (oral, vaginal, or eye) require higher doses, usually of the order of $10^4$ to $10^5$ particles. Breeding females can be infected with both undiluted (Yeager et al., 1993) and extended semen carrying the virus (Gradil et al., 1996).

**Shedding**

Post-infection, pigs will shed the virus for extended periods in saliva (42 days), semen (43-92 days) and mammary secretions. The results on fecal shedding are mixed: Wills et al.; (1997) reported finding no infectious virus in feces up to 42 days post-infection. In contrast, Yoon et al.; (1993) reported extensive fecal shedding over 35 days while Rossow et al.; (1994) found only intermittent shedding. Regardless of the origin, infected pigs shed virus in copious amounts and quickly contaminate their surroundings.

**Virus survival**

If conditions are right (about 4°C, pH 7.5) the virus can survive from days to weeks. However, it is very susceptible to adverse conditions, especially drying, and will die off within hours as conditions change from optimum. On the usual pig-associated fomites (plastic, steel, wood, straw, clothing, slurry etc.) at normal environmental temperatures (25-27°C) PRRS virus survives less that a day but it can survive in water for up to 11 days. Thus, normal clean-up procedures with disinfection and drying will kill the virus. The PRRS virus is susceptible to all the commonly used disinfectants including chlorhexidine, formaldehyde, chlorine, iodophors, sodium hydroxide, quaternary ammonium compounds, and the phenolics.

**Carriers**

Persistence is a marked characteristic of PRRS viral infections as some pigs harbor the virus for at least 157 days and possibly longer. In contrast, it is difficult to infect other pigs unless they are in very close contact, that is, the disease is not highly contagious. The low infectivity of the virus has ensured the survival of the virus in a herd. Viral survival depends on a proportion of the population being persistent with occasional shedding while the rest is susceptible. Dee proposed that these subpopulations are important for the long-term survival of the infection in herds (Dee et al., 1993).

**Hosts**

Mallard ducks are susceptible to PRRS virus and can excrete it in their feces for up to 39 days post experimental infection (Zimmerman et al., 1997). In addition, they can also spread it among themselves
and are capable of infecting pigs. Although mallards may not be significant vectors in the field, it does indicate that birds can carry the virus and infect pigs. But again, the significance of this in field outbreaks is still unknown. Rodents are not susceptible to PRRS virus (Hooper et al., 1994). Dr. Scott Dee (pers com) has shown that mosquitoes can carry PRRS virus between viremic and susceptible pigs.

**Transmission**

Researchers find it difficult to transmit the disease between pigs, which is surprising given the widespread distribution of the disease. Experimentally, Torremorrell et al. (1997) were only able to infect 2 of 8 pen-mates of acutely infected pigs and Wills et al., (1997) found it much easier to infect pen-mates than pigs separated by 1 meter and less. There is some evidence from *lactate dehydrogenase-elevating virus (LDV)* in mice that pigs may be infected via inoculation of skin lesions contracted when pigs are mixed and fighting breaks out. This has yet to be proven for swine.

The most commonly accepted way for disease to be transmitted between herds is by the use of contaminated semen or by the introduction of infected (carrier) animals. Transmission by aerosol is possible but it probably does not play as significant a role as it does in the transmission of other diseases such as foot and mouth disease. Le Potier et al., (1997) estimated the sources of infection for herds in France and these are likely to serve as our best estimate for other countries too:

- 56% infected pigs
- 20% infected semen
- 21% indirect spread (trucks, boots, clothing etc)
- 3% unidentified

Within herds, once infected, the virus tends to circulate forever and is very hard to eliminate. We don’t know why the virus is so persistent but it is probably associated with carrier pigs (discussed above), the birth of susceptible neonates and introducing naïve pigs (gilts and boars). Unfortunately, maternal antibodies do not provide adequate protection and any protection they do provide is short lived. Consequently, when pigs are mixed at weaning up to 100% become infected. Also, there is a relationship between sow herd stability and seroprevalence in the nursery and finishing phase. As more cases of viral replication occur within sows in a sow farm, the more shedding pigs there are at weaning. The more weaned pigs that are shedding, the earlier and faster the conversion of the nursery group. Earlier and faster conversions are more associated with nursery mortality. When viral replication in individual sows is a rare event in a sow herd, weaned pigs convert later and slower. Eventually, nursery pigs do not convert at all and slowly do so in the finishing phase. Le Potier et al., (1997) reported that, for one farm, in-herd bred replacement gilts did not seroconvert until post mating.

**Signs of disease**

Many factors influence the effect PRRS virus has when it enters a herd. Around the world, clinical signs vary depending on how the herd is managed, the strain of the virus, and the immune status of the herd.

When the PRRS virus infects a totally naïve herd, 5-75% of pigs show acute illness with lethargy and anorexia. Within a week the disease will spread throughout all stages of production and pigs will be off feed for 1-5 days. If pigs are well segregated (by production stage) owners report a “wave” of “off-feed” pigs moving through the farm as the virus spreads.

**Clinical signs in sows**

When the PRRS virus infects a totally naïve herd about 1-3% of sows will abort at all stages of gestation up to 100 days. Some sows may die. If a more virulent form of the virus is involved, as recently documented in the USA, abortions may rise to 50% and 10% of sows may die (Halbur and Bush, 1997). In addition, any disease that is circulating sub-clinically can increase dramatically and the farm can be doubly burdened with outbreaks of respiratory disease or parasites such as mange. Sows in late gestation are at a higher risk of abortion than others. At 7-10 days after initial infection, sows in late gestation (100 days plus) will start to farrow prematurely. This occurs because the virus crosses the placenta and affects piglets in-utero. This phase is characterized by an increase in late term abortions as well as the births of small, weak, stillborn, and mummified pigs. Many affected sows experience difficulty conceiving and have delayed returns to estrus and low conception rates.

**Clinical signs in boars**

In addition to the signs of acute illness (lethargy and anorexia), boars can experience a lack of libido and decreased semen quality (Prieto et al., 1994) including decreased motility and abnormal chromosomes. Also, more sperm with bent tails are noted.
The same problems have been observed when naïve boars were vaccinated with modified live vaccine (MLV).

**Clinical signs in piglets pre-weaning**

Piglets that are born weak can experience mortalities of exceeding 60% with death usually occurring in the first week of life. You should expect 100% mortality for piglets born prematurely. Affected suckling piglets often have a characteristic swollen conjunctiva and eyelids; some veterinarians consider these signs to be pathognomonic when present in baby piglets. Other signs include watery diarrhea, apathy, thumping, emaciation from lack of food intake and splay leg. In addition, all the signs associated with secondary infections may accompany the signs mentioned above.

**Clinical signs in wean-to-finish pigs**

Clinical signs observed in suckling pigs can continue until they die or are slaughtered. These signs include lethargy, anorexia, thumping and other signs associated with secondary infections. Such multiple infections lead to the characteristic signs of “ill-thrift” and associated reductions in average daily gain and feed conversion, which increases pen variation and the prominence of poor doing pigs with rough hair coats. Consequently, mortalities often exceed 15%.

**After the epidemic**

Without successful control, herds may show clinical disease in the sow herd and subsequent nursery and finishing phases. The virus seems to be maintained in herds by virus excretion from piglets infected in-uterus that remain infected for life, or simply infected pigs that cross-infect their pen-mates. Clinical signs are especially prominent as piglets become susceptible when maternal immunity wanes at about four weeks post weaning. Naïve replacement gilts and boars introduced into endemic herds experience the same problems as detailed above.

**PRRS Associated Respiratory Disease (Porcine Respiratory Disease Complex or PRDC)**

The offspring of endemic sow herds often have recurring problems in every group of weaned pigs or finishing pigs. The problems are associated with expression of disease by opportunistic or ubiquitous organisms that are normally present, but usually offer little challenge. The effect of PRRS viral replication on cellular immunity contributes to the expression and severity of pathogens like *Hemophilus parasuis*, *Streptococcus suis*, and *Mycoplasma hyopneumoniae*. PRDC represents the largest financial loss associated with PRRSv infections.

**Diagnosis**

Because PRRS can have so many effects it is not surprising that the diagnosis is difficult and involves many components: production records, clinical history, signs, serology, pathology and virus isolation are all used in arriving at a diagnosis. While a diagnosis based solely on clinical signs can be perilous it is also dangerous to declare a herd PRRS negative based on the absence of signs. Many infected herds show mild, or no, ill effects; this may be due to strain expression, good management, or other unidentified factors.

**Production records:**

Performance can vary greatly but an examination of the records will usually reveal signs consistent with the description above: decreased farrowing rate, increase in non-productive days, increase in abortions and premature farrowings, fewer pigs born alive and increased neonatal mortality. Parity analysis of endemic infected herds usually reveals that the lower parity sows are the most affected. This is especially true in systems that enter replacement females unexposed to resident PRRSv strains. Charting the number of abortions over time often indicate periods of acute PRRSv expression quite well. Many producers recognize a benchmark level of abortions per week (e.g., 6 abortions per week in a 2400 sow farm) that signal establishment of acute expression.

**Serology:**

Appropriate tests include Enzyme Linked Immunosorbent Assay (ELISA), immuno-flourescent antibody (IFA), serum virus neutralization (SVN) and immunoperoxidase monolayer assay (IPMA). ELISA is commonly used because it is inexpensive, automated, and sufficiently accurate. Unfortunately, none of the serologic tests can distinguish between the “wild” and modified-live virus vaccines. Therefore, vaccination can be problematic to test-interpretations in some herds. As with most diseases, both acute and convalescent serum samples should be submitted to help diagnose a recent outbreak. The need for paired sera is especially true when the sera of aborted sows is involved.
Virus Isolation and Detection:

Virus can be isolated from serum 4-6 weeks post infection in young pigs but as little as 1-2 weeks post infection in sows and boars. Pigs infected before birth may carry virus in their serum for up to 15 weeks. Samples for virus isolation should be refrigerated immediately. The best samples are obtained from young fevered pigs. Techniques used to identify PRRS virus include ImmunoHistoChemistry (IHC), ImmunoFluorescent Assays (IFA), and Polymerase Chain Reaction (PCR). PCR is very accurate and is commonly used especially when tissues have started to autolyse. PCR is more sensitive than virus isolation especially when pigs are recovering from infection. Viral isolations are biased compared to PCR because “cell adapted” modified-live vaccine strains grow well on cell culture lines. Herds that are vaccinated with modified-live vaccine often have PCR and live viral isolations of doubtful significance.

A good technique for diagnosing PRRS in sick piglets is to collect serum from 10 affected piglets before and after they suckle, then confirm viremia with PCR. In addition, PCR on the sera of fevered aborting sows often indicates viremic status.

Prevention and control

The best advice to any PRRS-free producer trying to avoid PRRS is to not bring PRRS infected pigs into the herd! As discussed above, infected pigs are the primary cause of most initial PRRS outbreaks.

Most modern herds bring female replacements into sow herds to replenish the breeding stock. If live negative animals are introduced into a negative herd, they should be isolated for at least 40 days and blood tested at arrival and 14 days post arrival. If the supply herd is negative and maintains that status, it is acceptable to enter the PRRS negative replacements into PRRS positive sow herds after they have been exposed to, and recovered from, an intentional infection of the sow-farm strain. This is known as acclimation. Acclimation serves to infect replacements in isolation at least 90 days before the replacements are introduced into the positive sow herd. The extended isolation allows time for recovery and development of immunity. PRRS infections result in a rather slow onset of immunity when compared to other diseases of the pig. If the supply herd is positive, but maintains the same infectious PRRS virus strain as the receiving herd, it is acceptable to enter previously infected PRRS positive replacements.

It has been shown that PRRS negative replacement animals can be taken into PRRS seropositive sow farms where few sows are replicating the virus. Before entering the negative animals, a two to four month supply of acclimated replacements are added to the herd and then the herd is closed to all new additions for as long as possible. After the closure period managers should increase the culling rate of old animals and it is thought to be safer to introduce the negative replacements.

The most difficult situation is when the strain dominant on the supplier farm is not the same as the strain expressed on the receiving-sow farm. When producers experience multi-strain infections across their production pyramids it indicates failure to close their pyramids to the foreign strains of genetic suppliers. Rejecting PRRS positive genetic replacement animals may slow genetic improvement as new genetic material is entered only in the form of semen from a negative boar stud. Each herd manager should have a veterinarian discuss the herd’s status and arrive at the optimum procedures for introducing new genes.

Control:

To be successful, any PRRS sow herd control strategy must decrease replication of the virus within a population of sows and boars. Doing this will prevent infection of the neonates. Unfortunately, some herds seem to contain sub-populations of naïve animals at the same time infectious animals are present. The virus replicates when the animals come into contact and the infection is maintained within the herd (Dee et al., 1993). To eliminate these sub-populations:

1. Identify infectious and naïve animals.
2. Implement replacement acclimation to reduce the population at risk. Eliminate naïve replacements.
3. If need be, stabilize the breeding herd. In acute breaks it may be necessary to physically spread the virus and either stop replacement entry for 3 to 4 months or infect a four month supply of replacement animals. The outcome of stabilizing assures that sow-to-pig infections are minimized.
4. Stabilize nursery and finishing herds after the sow herds are stabilized. Continuous flow facilities or sites may need to be depopulated and repopulated.

Addressing these in turn:

Determine how the virus is spreading

Bleed a cross-section of the herd (20 pigs in each strata; e.g., gestation, farrowing, nursery, finisher) and test (SN, IFA, ELISA or a combination). Continuous
vaccination programs may not affect interpretation as multiple vaccinations do not result in increased serologic values after initial exposure. To assist in assessing the herd it is very helpful to find PRRS isolates through PCR and determine the nucleotide sequence of the strain in a less conserved portion of the viral genome known as open reading frame 5. Sequences provide a reference during a future break to determine if the infection was from the entry of an outside strain or the same strain that took the opportunity to express as the result of population dynamics that placed many naïve animals in contact with persisting infectious animals.

**Ensure all replacements are protected**

Introducing naïve replacement gilts into an active infected herd will perpetuate the disease. To control the disease it is best to introduce gilts that have been exposed to PRRS virus in an isolation/quarantine facility. In isolation, gilts and boars can be exposed to PRRS virus from the sow herd. The virus can be transferred by feeding macerated infected pig lungs. The injection of infected serum has been more effective. When it is not possible to effectively transfer the infection, PRRS vaccines are a questionable alternative. Pigs from the main herd are only infective if they are fevered and sick with PRRS or can be induced to do so. Infective animals introduced into isolation facilities can help ensure strain specific exposure. Exposure can be difficult. Replacement gilts should be bled and tested to assess the effectiveness of each acclimation group.

Infrequently introducing many very young (breeder weaners) piglets can be a very practical approach. Breeder weaners will enter as susceptible if they are from a negative multiplier herd. If not, they will lose maternal immunity close to the same time and group susceptibility will be great. This is advantageous as acclimation success is as dependent on replacement susceptibility as exposure method. The young age of the pigs allows a long and isolated recovery period before entry into a commercial herd. The same approach is possible using older nursery pigs, feeder breeders, instead of weaned pigs. Entry of replacements into the commercial herd is limited to about a three month frequency as replacements use is limited by age and can be too young (less than 26 weeks) and too old (more than 38 weeks) depending on genetics and producer. Nursery pigs can be mixed to “stage” to a wider variation of age. Space available for specific acclimation can limit the ability of a system to use feeder breeders or weaner breeders.

Strain multiplicity between commercial farms must be minimal to apply the group acclimation to multiple commercial replacements sent across a pyramid.

**Stabilize the breeding herd**

To assist in stabilizing the herd, breeding animals are sometimes vaccinated with modified-live vaccines. It is questionable if vaccination is effective, as wild strains may differ greatly from commercial vaccine strains. The immunity developed to PRRS is often quite strain specific. Remember that vaccination in late gestation may infect the fetus. Non-pregnant breeding females are vaccinated 3-4 weeks prior to breeding. Infection with wild virus or vaccine precludes effective infection with the same strains.

**Managing the weaned pig**

To control PRRS in the nursery, you have to stop introducing infected piglets. Two strategies exist to control chronic PRRS in weaner pigs:

1. Partial depopulation: All nursery pigs are removed from the site and the nurseries are repopulated from the usual pig flow. This technique is usually effective but sometimes the depopulation needs to be repeated to maintain acceptable levels of production.

2. Vaccination: Vaccine virus may or may not infer protective immunity against a particular field strain. The benefit derived from the vaccination of nursery pigs is variable. The severity of nursery disease is dependent on the number of viremic pigs at weaning. Sow herd control is the first priority to accomplish control of PRDC in nurseries or finishers. Before vaccinating nursery pigs, bleed the piglets to determine when they are being exposed to the virus and how maternal antibodies decay. It is difficult to determine the best time to vaccinate piglets as it takes 6 weeks for immunity to develop. Therefore, it is impossible to identify susceptible pigs, immunize them, and have immune expression in the nursery.

To suppress new infections of piglets in the farrowing house, it is very important to limit cross-fostering to the first 24 hours. Euthanize all poor-doers during acute sow farm episodes and maintain strict all-in/all-out flow in the farrowing house and nursery. These techniques reduce the magnitude and rate of clinical expression, but do not eradicate the virus.
Vaccinations

Generally, modified-live vaccines are more efficacious than killed vaccines. However, modified-live vaccines are able to replicate, spread through populations, and mutate to a more fit status and consequently compound the problem.

Boehringer Ingelheim Vetmedica, Inc sells Resp PRRS/Repro® (called INGELVAC® PRRS-MLV in Europe). In 1994 it was approved for use in 3-18 week old pigs. In 1996 approval was given for administration to non-pregnant gilts and sows. Later, INGELVAC® ATP was added to the line. ATP offers a more recent strain than the original RespPRRS.

Schering-Plough's product (Prime Pac®PRRS) was recently withdrawn from the market for patent infringement.

Intervet sells PRRomiSE PRRS vaccine. PRRomiSe is a killed virus product and an effective alternative to other PRRS vaccines. It was sold by Bayer since 1997.

In deciding whether or not to use a modified-live vaccine you should know:

1. They can cross the placenta and cause congenital infection.
2. They can be transmitted just like the “wild” virus.
3. They can persist for weeks or months
4. They can be shed in boars’ semen and infected breeding females
5. They don’t always work
6. Induced immunity is slow to develop

Vaccination guidelines

• Vaccinate replacement gilts after exposure to the sow farm virus. It is more important that immunity to the sow farm strain is developed. It is hoped that vaccine covers for individual failures to transfer sow farm infection. The benefit may or may not be realized. Vaccinate at least 2 months before sow farm entry and administer 2 doses about a month apart.
• Some producers vaccinate weaners in the nursery.
• Don’t vaccinate pregnant females or boars unless directed to do so by your veterinarian

References


