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Pijoan Lecture

Epidemiology of a new PRRS virus isolate and outbreak

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The price of freedom is eternal vigilance. – attributed to Thomas Jefferson

We must all hang together, or most assuredly we shall all hang separately. – Benjamin Franklin

Summary

A new PRRSV strain with an RFLP of 1-18-2 was discovered in the spring of 2007 in the north central region of the USA causing severe outbreaks in finishing and sow herds. By the end of 2007 it had wreaked havoc, with extended episodes of 100% preweaning mortality, 10-20% sow mortality, and 50% death loss in finishers. The virus strain was novel and completely unrelated to the high pathogenicity PRRSV that swept through China one year earlier. Due to cooperation among producers, veterinarians, and scientists at the University of Minnesota, data were collected that revealed extensive epidemiologic details about its clinical signs, spread, pathogenicity, and genetics. We learned that:

- Understanding pig flow and movement was essential to understanding virus movement through these areas.
- Piglet monitoring, molecular diagnostics, and PRRSV sequencing revealed virus movement that otherwise would have gone undetected.
- The virus spread through movement of infected pigs and by aerosol.
- New infections in sow farms continued to increase the number of infected pigs moving into the population and regions, thus compounding the problem.
- Open communication among producers, veterinarians and scientists is critical to an effective, coordinated and rapid response. The value of producer and veterinarian willingness to share detailed information about the outbreak in tracking the spread of this virus cannot be over-emphasized.

The outbreak demonstrated the importance of sustained monitoring and surveillance. Freedom from PRRS will certainly require eternal vigilance as long as elimination of the virus from herds is the goal. Importantly, the field experiences provide fresh evidence that tools for control and prevention of PRRS exist. Physical prevention of virus through high biosecurity and air filtration is an effective means of maintaining herds free of PRRSV. Cost is currently an issue, but this dynamic may change with energy and feed cost fluctuations. Elimination of existing virus in a herd is achievable by mass exposure and herd closure. Reduction of disease in finishing herds by immunological cross-protection due to vaccination or previous virulent virus exposure has been observed. All of this evidence shows that the swine industry is acquiring the abilities and tools to gain the upper hand in the battle with PRRS, to turn the tide, and eventually achieve control and elimination.

Onset of a regional PRRS outbreak

By the spring of 2007 the north central USA swine industry was producing high numbers of PRRS-negative pigs. Depopulation/repopulation, direct virus exposure and herd closure were controlling infection in sow herds. Many systems had also implemented routine monitoring of herds to understand the flows and to confirm that negative pigs were being moved to finishing. The populations in these areas had a high number of negative pigs, probably more than at any time before PRRS became prevalent in the industry. In one example, a large producer was down to 1 positive herd or a total of 6% of their sows. However, by January, 2008, more than 60% of sow herds in this system had turned positive. What happened to upset seemingly effective programs to control PRRS needs to be understood to prevent a future repeat.

The problem began in March, 2007, in the pig belt of northern Iowa and southern Minnesota. A 3,200 sow farm at the end of a herd closure project suffered an exceptionally severe outbreak of PRRS, experiencing 650 abortions, 250 dead sows, and up to 50% mortality in wean-to-finish groups. The PRRSV isolated from sick animals had an unusual RFLP cut pattern not previously observed. Initially referred to as 1-?-2, it was later classified at a 1-18-2. In the next few months, fifteen more farms in the same region broke with PRRS and the same virus, more than 99% similar in ORF5, was isolated. Two sow herds, seven wean-to-finish sites, one nursery, one feeder-to-finish and 4 finishers were affected. Clinical signs varied

from routine diagnostics with coughing, lethargy and 5-6% mortality to high abortion rates and deaths in sow herds and mortality reaching > 50% in a finishing unit at 100 days after placement. Affected finisher sites routinely observed a rise in mortality of 5-15%. The area or regional outbreak appeared to quiet down in the summer, with infrequent but severe outbreaks in which the 1-18-2 virus was present. However, the situation changed dramatically in the fall of 2007.

PRRS situation in southern Minnesota and northern Iowa Fall of 2007 and winter of 2008

In September and October, breaks started occurring in negative herds. Detection occurred through monitoring of piglets for viral infection. Historically piglet monitoring was done by observing for clinical signs. Now, more proactive monitoring picks up infection earlier. In this case it helped to understand that things changed very rapidly within the landscape of southern Minnesota and northern Iowa. The PRRS breaks resulted in more positive pigs getting out into finishing areas. The unique RFLP characteristic of the 1-18-2 virus allowed it to be tracked around the country, and facilitated the analysis of routes of infection. Transportation of infected piglets to naïve finishing sites accounted for some cases of spread, and local spread due to imperfect biosecurity or aerosol spread also appeared to be important. Spread between farms with no identifiable connection was most readily explained by aerosol transmission. Scott Dee and colleagues at the University of Minnesota have extensively documented that aerosol transmission can occur and that highly pathogenic viruses that grow to high levels in pigs and shed prolifically also spread more easily. Given that there were many negative populations throughout the countryside in large concentrations of 2,000 to 5,000 animals, it was probable that these outbreaks produced a very large virus cloud. Rapid virus spread through naive populations by direct contact and aerosolization caused many problems on the farrowing side with the classic signs of PRRS, including abortions, stillborns, mummies, and high preweaning mortality; all the reproductive signs of disease that are expected to varying degrees with different PRRSV isolates. In the same way, disease in the nursery and grow-finish units was more severe, with higher mortality, more separation, and poorer pig growth. The conditions for catastrophe were ripe with many negative animals in the population. Once the virus started circulating in the fall which is when a higher percentage of outbreaks tends to occur, it exploded across Minnesota and Iowa in pig-dense areas. There were a very high number of outbreaks and many different viruses circulating through the pig population.

Recognition of a problem. Descriptive characterization of the spread of a new PRRS virus

One of the first cases in the Swine Vet Clinic practice was in a PRRS-negative finishing barn that had been placed into a very pig dense area and within a mile of the index herd. Mortality was greater than 20%. Diagnostics identified a PRRS virus, but sequencing showed no matches in the population except for the index herd. This virus appeared to be more aggressive in the grow-finish phase. Pigs came into the site at 10 weeks of age. PRRS with high mortality occurred at about 8 to 10 weeks into the finisher, and poor growth through the rest of the finishing phase. Infection spread to both sites with the same source of pigs as well as a 3rd and 4th site within 2 miles of the same location. Other cases followed showing similar types of lesions in grow-finish when exposed to the 1-18-2 virus. PRRS in the farrowing house was even more severe with over 300 abortions or 25% of the sows aborting. Many abortions were in late term sows that had more death loss and very high piglet mortality. There were weeks of 100% preweaning mortality, which just had not been seen before in PRRS outbreaks. Otherwise, these herds behaved like a typical PRRS break just at a higher level. Sequencing identified the 1-18-2 virus with very little variation from the original virus that was identified. Clinically the picture in these herds was fairly easy to grasp; it was a more aggressive virus with more rapid spread and more severe disease. Initially it appeared to be coming into herds by aerosol because the herds had either been through eradication for an extended period of time or were negative and had never seen PRRS virus before. It was a new introduction of a new virus, not a rebreak with a pre-existing virus. Looking back, veterinarians and producers in southern Minnesota participated together to try to understand what was going on. They saw that where ever pigs moved, the virus would follow and set up a new pocket of infection that would spread out from that pocket and just continue to move through the population. This confirmed that the virus moved via aerosol and into the naïve populations.

Variation in the outbreak characteristics: reproductive and respiratory disease parameters

As we moved through the winter of 2008 the 1-18-2 virus appeared in some herds that had previously been exposed to a PRRS virus. One herd in particular was in the process of going through a PRRS eradication in which they had done a direct virus exposure to the whole herd and were still in the lock-down phase so all animals had

previous exposure to PRRS. PRRS-positive clinical signs were identified, even though the farm was expected to be negative based on testing piglets on a monthly basis. Sequencing was done to determine if it was a new virus and established that it was a 1-18-2. The clinical signs were not as severe in these herds and looked to be more typical of a very mild PRRS break. It is difficult to understand why the difference between some of the negative and naïve herds that have broken with the 1-18-2 versus the herds that have had exposure other than there is some cross-protection from the previous strains. In another case, a herd had used direct virus exposure, gone through a herd closure, and had 5 monthly negative tests in a row. Then a positive pool sequence showed up in December. They had a few abortions (1-2% per week) but no other real clinical signs in the herd except that preweaning mortality may have gone up 2%. Sequence identification was a 1-18-2. The herd was still closed, so all animals had immunity at the time. The virus never really materialized and the disease never moved out to become more severe in the herd. The virus was observed to move downstream in the nursery and finishing units. Those pigs continue to shed for a period of time but problems were never observed in the resident sow herd. These experiences demonstrate that the 1-18-2 virus can show different faces depending on the immunologic status of the pigs, with the most severe forms being in the negative and naïve herds. As we move into positive herds or herds with differing levels of cross-protection due to previous exposure to a PRRS virus, the severity of disease associated with infection with 1-18-2 is reduced.

Variation in outbreak characteristics: Pathological and virological characteristics

Affected pigs appeared to have typical signs and symptoms of PRRS, including fever, pneumonia, dyspnea, and anorexia. Lung lesions were typical, both grossly and microscopically, except more severe. Lung involvement was extensive. Encephalitis and myocarditis, which have been reported previously in unusual cases of PRRS, were not observed. The findings were consistent with a PRRSV that grows aggressively but maintains a typical lung and lymphoid tissue distribution. Controlled studies of viral pathogenesis would help to clarify this issue.

The PRRSV associated with disease spread. Genomic analysis

Sequencing of ORF5 showed that the 1-18-2 PRRSV appeared to represent a new family of viruses (Figure 1). The sequence was more than 7% different from all other known viruses, of which there are more than 7,000 in the public domain. The entire genomic sequence was obtained to gain further insights into the genetic basis for its increased virulence. Overall, the distinctive genotype observed in ORF5 was present in other open reading frames, so that the entire genome of 1-18-2 was uniformly different and distinct from other known PRRS viruses. Previously, deletions in nonstructural protein 2 (nsp2) were associated with the increased virulence of MN184 isolates. The 1-18-2 isolate showed the same pattern of deletions (Figure 2). Thus far, genetic analysis does not explain the origin of 1-18-2 or its virulence. The virus is distinct from the high pathogenicity PRRS virus that has devastated the Chinese swine industry. That virus is in a different genetic cluster and shows extensive genetic variation across its entire genome from 1-18-2.

Status of 1-18-2 PRRS in July, 2008

Affected herds seem to be reacting much like any other after a PRRS virus outbreak once herd immunity stabilizes. They return to good production. Even though outbreaks are severe in negative herds, going through the abortion phase, high stillborns, high mummies, high preweaning mortality, sow death loss and sows that are having difficulty in the finishing, they then return to more normal production. As the herds get through one farrowings cycle and move out to 20 weeks post infection, many of them are going back to normal production. Herds that have performed direct virus exposure and herd closure are starting to generate negative pigs. It appears that we can handle the virus much as we have other viruses. The jury is still out since most of the outbreaks occurred in November and December of 2007. It is just getting to the point in time of 200 days of herd closure and knowing if we will handle 1-18-2 as we have handled other viruses in the past. So far the tests that have been done look promising.

Protecting the finishing populations going forward

The swine industry has proven that there are several methods that reproducibly eradicate PRRSV from sow farms, with herd closure being most economical and effective. Air filtration has been shown by Drs. Dee, Reicks and Feder to be an effective method of preventing spread, but it is still expensive and not widely used. One of the challenges has been to protect the grow-finish population by other means going forward so we do not create the opportunity for more virus spread within areas like we saw this last fall. Can we make these populations less susceptible to the virus and less likely to shed large amounts of virus in an area? Can we use attenuated live virus vaccines to reduce the potential of shedding in these negative populations. Research done by Scott Dee and colleagues at the University of Minnesota has shown that vaccination helps to reduce shedding. Finishers that were vaccinated in 1-18-2 problem areas performed better than the negative pigs that had been placed previously. We have to learn

Figure 1: Dendrogram showing genetic relationships of recent virulent PRRSV isolates from southern Minnesota and northern Iowa. The 1-18-2 strains are circled. The Chinese high pathogenicity PRRSV is boxed.

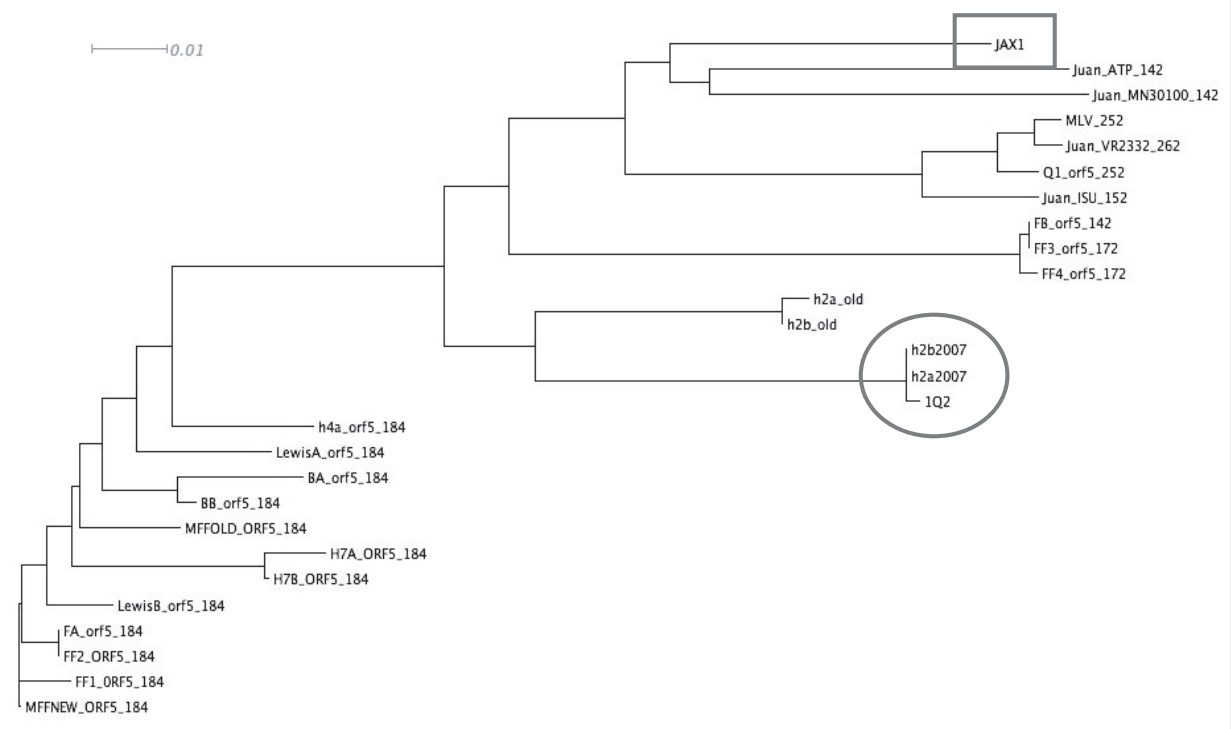

Figure 2: Nsp2 nucleotide sequence deletion pattern in 1-18-2 (equals 1Q2) is the same as MN184-type viruses. It matches the consensus deletion pattern observed in 12 MN184-type viruses displayed above the 1-18-2 sequence.

		nsp2 3bp 2049-2051	nsp2 333bp 2117-2449	nsp2 3bp 2598-2600	nsp2 36bp 2605-2640	nsp2 57bp 2663-2719	nsp2 3bp 2737-2739	nsp2 75bp 2769-2843	nsp2 17bp 2793-2809	nsp2 10bp 2816-2825	nsp2 1bp 3530	nsp2 1bp 3581	nsp2 2bp 3589-3590	nsp7 3bp 7234-7236
MFFA	EF532819		YES	YES		YES							YES	
FF1	EF532806		YES	YES		YES							YES	
FSA	EF532804		YES	YES		YES							YES	
FF2	EF532807		YES	YES		YES							YES	
WB	EF532818		YES	YES		YES							YES	
H7A	EF532814		YES	YES	YES	YES							YES	
H7B	EF532815		YES	YES	YES	YES							YES	
MFFB	EF535999		YES	YES		YES					YES	YES		
BB	EF532803		YES	YES		YES							YES	
BA	EF532802		YES	YES		YES							YES	
WA	EF532817		YES	YES		YES							YES	
H4A	EF532812		YES	YES		YES		YES					YES	
1Q2	1-18-2		YES	YES		YES							YES	
H2A	EF532810		YES	YES		YES							YES	
H2B	EF532811		YES	YES		YES							YES	
FF4	EF532809	YES									YES	YES		YES
FSB	EF532805	YES									YES	YES		YES
FF3	EF532808	YES									YES	YES		YES
JXA1	EF112445			YES*		YES	YES		YES	YES	YES	YES		
EF536003	VR2332										YES	YES		
QB	EF536001										YES	YES		

and understand more about vaccine cross-protection to be able to control the virus better as we move forward into the future.

Direct virus exposure done in isolation can be a very successful way of generating negative pigs even in a herd that continues to be positive and can be a reliable method for many farms. Direct virus exposure with herd closure has been very effective in eradicating PRRS virus from herds. Mass exposure gives a point in time in which all animals within a herd are exposed before it is locked down and closed to any new introductions for a minimum of 200 days. This can be done without losing production by having an adequate number of gilts in an additional facility and exposed to the herd virus at the same time as the sow herd so that they can continue to maintain normal flow without having to impact production. This method has been used by many additional herds as well as ten herds that participated in the National Pork Board study. With these technologies we have been able to eradicate the virus from herds repeatedly as long as there is minimal cross-fostering no cross-contamination of piglets in farrowing rooms. After 200 days, negative pigs are reproducibly going out and negative naïve animals introduced into the herd stay negative over an extended period of time. The problem is introduction of an outside virus into the system.

The 1-18-2 virus was not the only culprit that appeared in this time frame. There were many other viruses circulating as well. The 1-18-2 had a characteristic pattern of clinical and genetic signs that made it easier to identify. Because we could identify this different pattern it allowed us to do the following:

- Epidemiology to understand what was going on in the outbreaks.
- Determine how the virus was spreading in the population and region.
- Understand why we were seeing movement that otherwise would have gone undetected.
- See why the virus was popping up in unexpected locations. Once it was traced back it was easy to see that there was area spread and local spread. In some cases of local spread, finishing barns became infected then sow farms became infected, whereas in other cases the virus moved from sow barn to downstream nurseries and finishers.

Understanding pig flow and movement was essential to understanding virus movement through these areas. It revealed one of the weaknesses in area PRRS virus eradication and will be a piece that has to be solved before area eradication can move forward predictably.

Many factors were key to the rapid identification and comprehension of a new PRRSV strain and its rapid spread through a swine-dense region. Piglet monitoring, molecular diagnostics, PRRSV sequencing, dedicated and sustained data collection. Above all, communication by veterinarians and producers who appreciated the overwhelming importance of acting together so that they would not hang separately, which has been the fate of swine producers all too frequently in earlier PRRS outbreaks. Open communication was critical to an effective, coordinated and rapid response. The outbreak also demonstrated the importance of sustained monitoring and surveillance. Freedom from PRRS will certainly require eternal vigilance as long as elimination of the virus from herds is the goal. Importantly, the field experiences provide fresh evidence that tools for control and prevention of PRRS exist. Physical prevention of virus through high biosecurity and air filtration is an effective means of maintaining herds free of PRRSV. Cost is currently an issue, but this dynamic may change with energy and feed cost fluctuations. Elimination of existing virus in a herd is achievable by mass exposure and herd closure. Reduction of disease in finishing herds by immunological cross-protection due to vaccination or previous virulent virus exposure has been observed. All of this evidence shows that the swine industry is acquiring the abilities and tools to gain the upper hand in the battle with PRRS, to turn the tide, and eventually achieve control and elimination.

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