



Knowledge

PCVAD: review of findings about this multifaceted disease

SUMMARY

Faced with devastating death loss and unanswered questions, the U.S. swine industry is economically and scientifically concerned with porcine circovirus-associated diseases (PCVAD). Porcine circovirus-type 2 (PCV2) is the primary pathogenic DNA virus

in this disease syndrome. It is commonly found in most swine populations, yet that doesn't mean that pigs will experience signs of PCVAD.

Concurrent infections with other diseases like porcine reproductive and respiratory syndrome (PRRS), mycoplasmal pneumonia and porcine parvovirus (PPV),

along with environmental factors compound the disease's severity. There are still many unanswered questions about this multifaceted disease, but current research findings and clinical experience offer background and information essential for managing PCVAD.

Disease history

First identified in 1974 in a continuous porcine kidney cell line, porcine circovirus-type 1 (PCV1) was found to be widespread, but not pathogenic, in the pig population.¹ A closely related virus was discovered in 1997 and named PCV2. This type was found in association with a new emerging disease called postweaning multisystemic wasting syndrome (PMWS).

At the end of 2004, eastern Canada experienced a severe form of the disease syndrome now called PCVAD. Operations experienced rapid weight loss and high mortality in finishing age pigs. Besides these signs, there are a variety of other clinical presentations that are consistent with PCV2 infections. The change in the disease's name

was an attempt by the American Association of Swine Veterinarians (AASV) to recognize the variability in clinical signs currently associated with exposure to the virus in pigs.

Within months of Canada's initial struggle with PCVAD, U.S. pork producers also were experiencing the extreme form of the disease in their grow/finish pigs. Pig companies in southeastern United States, specifically North Carolina, were dealing with high death loss associated with PCVAD in 2005 and early 2006. However, the Midwest didn't start seeing it until 2006. Prior to 2005, Tim Loula, DVM, Swine Vet Center, St. Peter, Minn., says that they had no confirmed cases of PCVAD.² But all seven veterinary consultants that work at the

center agreed that they had suspect farms where they thought circovirus was possibly related to problems on those farms. In late spring/early



summer of 2006, more clinical cases of the high-death-loss syndrome were seen. By the beginning of 2007, almost all of their clients experienced PCVAD in at least some of their production sites or flows.

Disease background

Known facts about PCV2 help advance the discussion on PCVAD:

- PCV2 infection is common in most swine populations³
- Most pigs will become infected prior to reaching market weight³
- The vast majority of infections are subclinical, meaning that almost every pig has been exposed to PCV2, but they may not be showing clinical signs of PCVAD³
- There is broad variability in the outcomes of PCV2 infection³
- Co-infection with various disease agents – PRRS, parvovirus, immune stimulants, certain oil-based vaccines or other inflammatory responses in the pig – typically result in higher levels of virus in the blood or viremia and longer duration of that virus in the blood, which can lead to the development of clinical PCVAD³

Most piglets are born from infected immune sows and thus will have maternally derived antibodies to PCV2 during their first seven to eight weeks of life.¹ Piglets have varying amounts of passive protection and when exposed to PCV2, most pigs will become infected between 2 and 12 weeks of age.

Transmission of PCV2 is not well understood, but experimental studies suggested that it is transmitted by direct contact via oral and nasal routes and even indirectly through

Structural characteristics of PCV2¹

- At 17 nanometers in diameter, it is the smallest porcine virus
- Genome contains 1768 nucleotides
- Similarity on nucleotide level between PCV1 and PCV2 is 76 percent
- PCV2 isolates from different geographical regions or from pigs with different disease syndromes show a high similarity of 94 percent or more
- Highly resistant and hardy, which can make inactivation and disinfecting against it difficult

the air.¹ Researchers are still exploring the potential and importance of it possibly being transmitted through semen or transplacentally.

Clinical signs

Clinical signs of PCVAD typically start in the grow/finish phase of production. Because of the wide range of clinical signs that may be expressed, one or more of these clinical signs are found in PCVAD cases:

- Coughing
- Difficulty breathing
- Diarrhea
- Poor body condition/rapid weight loss
- General enlargement of lymph nodes
- Skin discoloration
- Death

Diarrhea and coughing may be observed during the first two to three weeks after placing pigs into the finisher.² Diarrhea is often the first symptom noticed and the producer may think his ileitis control is no longer working or the herd is breaking with Salmonella.²

In the next several weeks, pigs will rapidly lose weight and death loss will increase.² Death loss often peaks at five to eight weeks into the finisher phase.² After that, weekly death loss begins to decrease, but there is often an increase in bottom-end or fallback pigs and pigs that need to be culled.²

PCVAD diagnostic criteria

Since PCV2 is common in healthy pigs and the clinical signs of PCVAD may mimic any number of respiratory and enteric pathogens, a set of diagnostic criteria were



developed to define PCVAD as a diagnosis. Typically, PCVAD is diagnosed when there are:

- Typical clinical signs, especially high mortality³
- Characteristic microscopic lesions (lymphoid depletion with granulomatous replacement)³
- Significant quantities of PCV2 in the affected tissues³

Yaeger has expanded those diagnostic requirements to encompass the range of PCV2-associated diseases. In his paper, diagnosis should also be based on supporting evidence of confirmatory microscopic lesions and the presence of significant quantities of PCV2 and how it's distributed in affected tissues.³

Variability in clinical signs and the diversity of different tissues the virus affects complicate diagnostics. And what causes the virus to localize in one tissue in some pigs and not in those of others, is not completely understood. Studies have demonstrated that replication of the virus is enhanced by activation of the immune system and differences in immune activation between organs may contribute to the observed variation in clinical signs.³ Therefore, an evaluation of one tissue will not hold the answer to the impact of PCV2 infection.

PCV2 vs. Agent X

There is debate on whether PCV2, along with other factors that may contribute to its devastation in the field, is the cause of PCVAD or if another unidentified agent, Agent X, is the culprit.

According to several different research teams, PCV2 is the primary pathogenic DNA virus in PCVAD. Reynaud et al., Harms et al., Bolin et al., Ladekjaer-Mikkelsen, Okuda

et al., Pogranichniy et al., and Opriessnig et al., have been able to experimentally reproduce clinical signs, characteristic PCVAD histological lesions and mortality using PCV2 alone.⁴ Harms et al., Bolin et al., Ladekjaer-Mikkelsen et al., Okuda et al., Brunborg et al., Olvera et al., and Green et al., have also found a direct correlation between the quantity of PCV2 found in the blood and tissues and the severity of PCVAD.⁴ Plus, results have been promising for vaccines containing only PCV2 antigen.⁴

On the other hand, scientists that believe another agent may cause or trigger PCVAD question why all herds tested so far in North America are infected with PCV2, but only a fraction of them are suffering PCVAD losses.

Factors affecting PCVAD

Evidence and experiences from the field combined with data from experimental models confirm that PCVAD is multifactorial.⁵ See Figure 1.

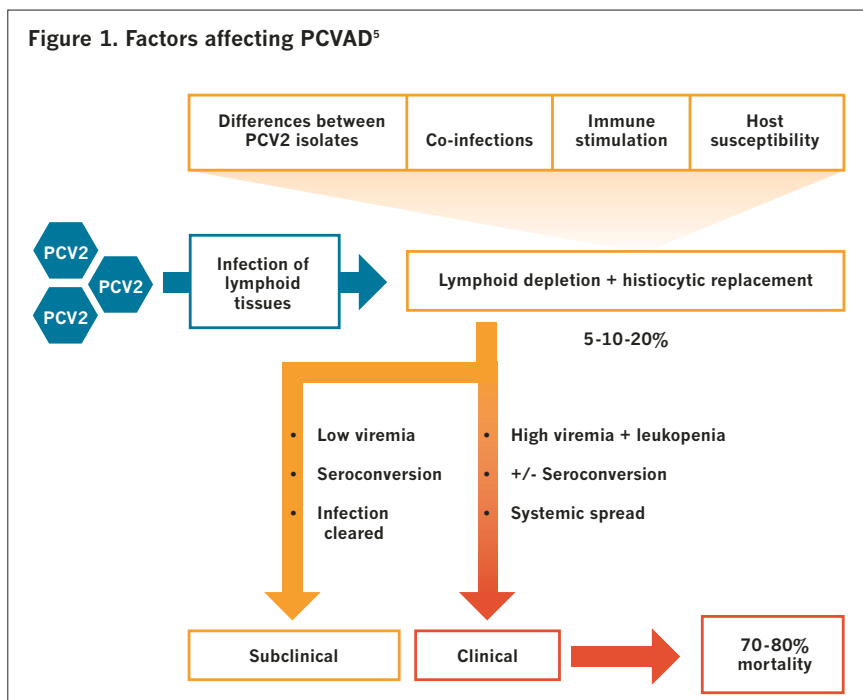
Differences between PCV2 isolates

Opriessnig and Halbur's research and review of findings suggest that minimal genomic differences in PCV2 isolates lead to huge virulence differences. These differences may have important implications for understanding the differences in clinical manifestations of PCV2 infections.⁵ Virulence markers have not been identified and researchers say that it is unlikely that differences in virulence of PCV2 viruses will fully explain the remarkably wide variation in clinical manifestation of the disease from farm to farm.

Co-infections

Other infections compound the problem to make PCVAD even more exasperating to producers. Co-infection with the following are possible:

- PRRS virus (detected in 52 percent of cases where U.S. pigs had PCV2-associated disease⁵)
- Mycoplasmal pneumonia (detected in 36 percent of cases where U.S. pigs had PCV2-associated disease⁵)



- SIV (detected in 5.4 percent of cases where U.S. pigs had PCV2-associated disease ⁵)
- *Haemophilus parasuis*
- *Streptococcus suis*
- Enteric diseases such as ileitis and Salmonella

Infection with PCV2 alone was found in only 2 percent of the cases where U.S. pigs had PCV2-associated disease.⁵

Co-infection with other diseases has been shown to trigger progression of PCV2 to PCVAD. These secondary diseases enhance the amount of PCV2-associated lesions and increase the incidence of PCVAD.

Immune stimulation

Vaccine timing, age of the pig and the relationship to PCV2 infection are important factors that can increase viral load and, consequently, the clinical occurrence of PCVAD. Opriessnig and Halbur exposed pigs to PCV2 at different times relative to vaccination. When the pigs were vaccinated and exposed to PCV2 at the same time, the clinical signs were more severe. When the pigs were vaccinated two to four weeks before PCV2 exposure, the clinical signs were minimal. Because no or minimal PCV2-associated lesions were observed when pigs were vaccinated two to four weeks prior to expected PCV2 exposure,⁵ vaccination two to four weeks before exposure may be recommended.

Adjuvants used in vaccines may exacerbate PCVAD. Hoogland et al. found that oil-in-water adjuvanted vaccines are more likely to enhance PCV2-associated lesions than aqueous-carbopol or aluminum hydroxide adjuvanted vaccines.⁶ Although, all adjuvants increased the severity of lymphoid depletion during the early stage of infection. Oil-in-water adjuvants increased:

- Severity of lymphoid depletion
- Amount of PCV2 in tissue/serum
- Length of viremia in latter stages of infection

Practitioners need to weigh the risk of not using vaccines and thereby potentially allowing co-infections to enhance PCV2-associated diseases, vs. the risk of using certain adjuvanted vaccines on PCV2-infected pigs and thereby potentially increasing the severity of PCV2-associated diseases.⁵ The potentially negative effects of adjuvanted vaccines can be decreased to some degree by changing when the pigs are vaccinated with those products.⁵ This research shows that timing of vaccination when few pigs are viremic with PCV2 is critical to minimizing the clinical impact of the infection.

Host susceptibility

Different breeds or genetic lines within those breeds may have vastly different resistance to PCVAD. Even though all breeds may be susceptible to PCVAD, purebred Landrace pigs in one study were more susceptible to PCV2-associated diseases.⁵ This experiment also found that Pietrain and Large White breeds may have increased resistance to the disease. Further investigation is needed before conclusions about how breeds affect PCVAD can be made.

Managing PCVAD

Because mortality numbers are high during a PCVAD outbreak, Loula says it makes sense to strengthen management measures, including using feedgrade antibiotic medication against secondary diseases or co-infection.²

He recommends creating high-health pigs by increasing respiratory and enteric feedgrade medications during one or more of the following three periods:

- The weaning ration – to control *Haemophilus parasuis*, *Actinobacillus suis* and other respiratory and enteric pathogens, including ileitis
- The last nursery ration – to prepare pigs for the stress of transport to the finisher – a period where more PCVAD is experienced
- The first finisher ration – helps ensure high-health pigs during the last growing phase

According to Loula, high-health pigs are better able to ward off infections and disease outbreaks. They do not experience such devastating percentages of death loss when compared to low-health pigs. See Table 1.

TABLE 1: Comparison of death loss in grow/finish phase between high- and low-health farms

	High-health farms	High-health farms affected with PCVAD	Low-health farms (may be affected with PRRS, mycoplasma, SIV and ileitis)	Low-health farms affected with PCVAD in addition to other diseases
Percent death loss in grow/finish phase	2%	4%	6-7%	20-30%

He has found that Denagard® (tiamulin) 10⁷ plus chlortetracycline (CTC) has been helpful in treating certain enteric and respiratory disease pathogens.



Denagard 10 and CTC are feed-grade antibiotics approved for concurrent use to provide enteric and respiratory disease coverage, respectively.

In addition to the points above, producers also should conduct a comprehensive review of their entire health program, including vaccination, water medication and feedgrade medication protocols to look for opportunities to enhance their program. They also should improve hygiene and move toward all-in, all-out management by site, if possible. Loula suggests intensifying the vaccination program against a variety of different pathogens and vaccinating at a younger age when pigs are less likely to be infected or viremic with PCV2.

Controlling PRRS is important, as well. Loula suggests eradication, enhancing sow immunity or gilt shutdown protocols. Another option would be to vaccinate the sow herd and grow/finish pigs.

Isolating or removing pigs identified with PCVAD to minimize PCV2 load in the barn also may be considered to help

manage the disease. Desrosiers discusses how depopulation/repopulation could constitute an alternative, but says that caution should be exercised when considering such a costly decision.⁴

Other management improvements suggested by Menard⁸ include:

- Maximizing colostrum intake
- Minimizing cross fostering
- Increasing weaning age
- Using all-in, all-out management
 - By room, by building, by site
 - Batch farrowing to move pig flow to all-in, all-out
 - Best is one age group at a location
- Improving hygiene and sanitation
 - Increase clean, dry-down time, if possible
- Using PCV2 vaccines

Even though PCV2 is commonly found in pigs, PCVAD can be minimized though various methods cited previously. PCV2 infection is similar to a secondary viral invader, so minimizing inflammatory responses through better disease management is beneficial. In addition, minimize immune stimulation by selecting vaccines with minimal adverse events. If possible, try to control and eliminate the diseases you can and manage the viral load in your pigs through vaccination.

Autogenous tissue-extract vaccines

Due to shortage of PCV2 vaccine, some veterinarians have stimulated the pig's immune system by exposing the pig to a formalin-treated tissue extract derived from infected pigs. The American Association of Swine Veterinarians (AASV) and USDA's Center for Veterinary Biologics (CVB) recommend that when using this method the following be met:

- Bacterin must be prepared by the veterinarian within the context of a valid veterinarian-client-patient relationship
- Veterinarian must submit a PCV2 inactivation protocol to CVB
- Veterinarian must document that the PCV2 (contained in the bacterin) has been deactivated

Caution: Do not feed undiluted. Do not use in feeds for animals other than swine. Not for use in swine weighing over 250 lbs.

Contraindication: Swine being treated with Denagard (tiamulin) should not have access to feeds containing polyether ionophores (e.g., lasalocid, monensin, narasin, salinomycin and semduramycin) as adverse reactions may occur. See product label for directions for use and additional information.

1. Nauwynck H, Lefebvre D, Misinzo G, Meerts P, Mateusen B, Sanchez R, Delputte P. Pathogenesis of porcine circovirus 2 infections. *American Association of Swine Veterinarians*. 2007.
 2. Loula T. 2007. Personal communication.
 3. Yaeger M. Diagnosis of PCV2-associated disease – a diagnostic pathologist's perspective. *American Association of Swine Veterinarians*. 2007.

4. Desrosiers R. Overview of PCVAD – The Disease in Eastern Canada & US vs. Europe. *Advances in Pork Production*. 2007;18:35-48.
 5. Opriessnig T, Halbur PG. Current Status of PCVAD: Diagnostic and Research Update. *American Association of Swine Veterinarians*. 2006.

6. Hoogland M, Opriessnig T, Halbur PG. Effects of adjuvants on porcine circovirus type 2-associated lesions. *Journal of Swine Health and Production*. 2006;14(3):133-139.
 7. See product label for directions for use and other information.
 8. Menard J. PMWS interventions preventive measures: Canadian approach. Allen D. Leman Swine Conference. 2006.

