



## **Porcine Circovirus PCV-2**

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Porcine circovirus type 2 (PCV2) is considered by most to be the etiologic agent of postweaning multisystemic wasting syndrome (PMWS), but it is also found in association with numerous other conditions. These conditions include porcine dermatitis and nephropathy syndrome (PDNS), porcine respiratory disease complex (PRDC), congenital tremors (CT) type AII, reproductive failure and enteritis. Although PCV2 has been determined to be associated with many of these conditions, there is still no scientifically sound proof that it is the causal agent. Much of the role played by PCV2 in today's swine industry is still a mystery. We do know that the incidence of PCV2 associated conditions continue to rise in the U.S. PCV2 associated diseases have increased from 37 cases in 1997 to 1,116 cases in 2002 at the Iowa State University Veterinary Diagnostic Laboratory (ISU-VDL).

PCV1 was detected in swine populations but, to date, has not been associated with any clinical disease. Although PCV1 and PCV2 are antigenically similar, they can be differentiated by molecular tests. Like PCV1, PCV2 is prevalent in virtually every herd. Much research is focused on trying to determine why the prevalence of PCV2-associated disease is relatively low while the prevalence of PCV2 is so high. There may be numerous contributing factors in the development of the various disease conditions.

### **PMWS**

PMWS was first recognized in high health Canadian herds in 1991 and is seen in almost every country now. Although morbidity is usually 100%, mortality can approach 5-50%. This syndrome most often affects pigs 4-12 weeks of age and is diagnosed by meeting all of the following three criteria:

1. Clinical signs and gross lesions - wasting, slowed growth, enlargement of inguinal lymph nodes and frequently dyspnea, noncollapsed and mottled lungs and occasionally jaundice

2. Characteristic histological lesions - lymphocyte depletion in secondary lymphoid tissues, granulomatous inflammation in numerous organs, interstitial pneumonia and often basophilic cytoplasmic inclusion bodies in macrophages
3. Demonstration of PCV2 within lymphoid tissue lesions by IHC, PCR or *in situ* hybridization; virus isolation is also offered by some laboratories.

There has been much uncertainty in the relationship between PCV2 and PMWS but Bolin et al demonstrated that Koch's postulates could be fulfilled by inoculating cesarean-derived, colostrum-deprived (CDCD) pigs with PCV2 and producing clinical signs of PMWS. Similar work has been performed using an infectious genomic clone of PCV2 in specific pathogen free (SPF) pigs to produce the gross and microscopic lymphoid lesions of PMWS. Although PCV2 has been shown to induce PMWS lesions in CDCD and SPF pigs, the presence of additional factors are required.

It has been suggested that immune stimulation may play an integral role in the development of PMWS in PCV2 infected pigs. This may be a result of any type of management or environmental stress, coinfection with another pathogen or administration of vaccines and adjuvants. Coinfection with porcine parvovirus (PPV) has shown to potentiate the replication and tissue distribution of PCV2 and increase the severity of clinical signs and lesions of PMWS. Although several farms have implemented PPV vaccination programs for growing pigs to try to control PMWS, research has shown that vaccination for PPV does not increase or decrease the severity or incidence of PMWS in dually infected pigs. Dual vaccination of PCV2 infected pigs for *Mycoplasma hyopneumoniae* and *Actinobacillus pleuropneumoniae* has experimentally induced a longer viremia, wider tissue distribution of PCV2 and increased severity and incidence of lymphoid depletion as compared to nonvaccinated pigs. Recent work has demonstrated that oil-in-water adjuvants may contribute to PCV2 induced disease more than other types of adjuvants.

There is no proven treatment or prevention for PMS, but administration of corticosteroids appears to be beneficial in an acute outbreak to reduce the severity of the disease and death loss. This observation may suggest that the syndrome is an immune-mediated disease.

### **PDNS**

PDNS was first described in 1993 in the United Kingdom, but presently has a worldwide distribution. Although PCV2 is often found in cases of PDNS, the current diagnostic criteria for PDNS does not include the detection of PCV2, but does include these two criteria:

1. Necrotizing skin lesions (mainly on rear legs and perineal region) and/or swollen and pale kidneys with generalized cortical petechiae.
2. Systemic necrotizing vasculitis and necrotizing and fibrinous glomerulonephritis

Currently, PDNS is considered to be a type III hypersensitivity reaction, although the antigen associated with this immune-complex disease is not definitively known.

### **PRDC**

PCV2 associated pneumonia is the most common presentation of PCV2 associated disease in cases submitted to ISU-VDL. PCV2 is most often associated with lung lesions in pigs coinfecting with PRRSV, SIV or *Mycoplasma hyopneumoniae*; however, there have been uncomplicated PCV2 pneumonia cases reported in western Canada. PCV2 is determined to be associated with PRDC when PCV2 antigen is associated with characteristic lung lesions. These lesions include necrotizing and ulcerative bronchiolitis, granulomatous inflammation in the alveolar septa and mixed inflammation and fibroplasias in the lamina propria and peribronchiolar areas. It is often difficult to differentiate between cases of PMWS and PCV2 associated pneumonia.

PRRSV infection increases PCV2 replication in experimentally dually inoculated pigs and synergism between these two viruses is also commonly observed in the field. Like PPV, PRRSV and PCV2 all replicate in macrophages and can produce immune cell dysfunction. This may be an important factor in the enhanced replication of PCV2 following PPV or PRRSV infection. Although *Mycoplasma hyopneumoniae* infects different target cells, PCV2 and *Mycoplasma hyopneumoniae* coinfecting pigs show more severe clinical respiratory disease and lung lesions, poorer growth performance, longer PCV2 viremia and greater amounts of PCV2 antigen in serum, lymphoid and lung tissues than pigs infected with only one pathogen. The peribronchial lymphoid hyperplasia induced by *Mycoplasma hyopneumoniae* seems to provide an important site for PCV2 replication in a lung.

### **Congenital tremors type AII**

Currently, the association between PCV2 and CT type AII is controversial. A study conducted at Purdue demonstrated by PCR, IHC and *in situ* hybridization that PCV2 was present in CNS and liver tissues from both CT pigs and clinically normal pigs; however, there were more PCV2 infected cells in the CNS of CT pigs than normal pigs. Another study conducted in Europe, however, did not demonstrate an association between PCV2 and CT type AII.

### **Reproductive failure**

Although less common than some other PCV2 associated conditions, PCV2 has been associated with reproductive failure, particularly late-term abortions and increased numbers of mummified fetuses, stillborns and weak pigs. The phenomenon of "stairstep" mummies has been described in which all the fetuses appear to have died during different stages of gestation. The fetuses may have some cardiac hypertrophy and hepatic congestion, but there are not many specific gross lesions observed. There are some characteristic fetal histological lesions, which include severe myocarditis, cardiomyocyte

loss, fibrosis and intranuclear inclusion bodies in cardiomyocytes, as well as passive hepatic congestion. PCV2 can be detected by IHC in the myocardial lesions.

Although it is not always certain how PCV2 is transmitted, it has been proven to be shed in semen of infected boars. It is shed sporadically in semen for at least 47 days post-inoculation.

PCV2 obviously plays a diverse role in the swine industry and the incidence of PCV2 associated disease is on the rise throughout the world. There have been no successful prevention and control programs for PCV2 infection. It is known that PCV2 is present on clinically normal farms as well as farms with reported PCV2 associated disease, but the seroprofile of both types of farms is the same. Currently, control of PCV2 associated disease, particularly PMWS and PCV2 associated pneumonia, is based on implementing management practices that minimize stress, eliminating or minimizing the effect of coinfections and eliminating potential triggering factors that induce immune stimulation.

Many European practitioners have attempted serotherapy with varying results, but this technique carries many inherent risks. There has been some promising research concerning the development of a vaccine for PCV2 using a chimeric infectious DNA clone of PCV2 and PCV1. In this study, the nonpathogenic PCV1 genome backbone induced a specific antibody response to the pathogenic PCV2 capsid antigen that was used to make the clone. Much more work must be performed with this clone to determine its potential usefulness as a commercial vaccine.

Until more of the pathogenesis of PCV2 infection is revealed, it will be difficult to control or eliminate this pathogen from swine herds. Efforts must be focused on managing the disease conditions as effectively as possible. PCV2 is currently a significant research topic around the world and, hopefully, these research efforts will help to unravel much of the mystery surrounding this somewhat elusive pathogen.