History of Porcine Circoviral Disease (PCVD) and Current Western Canadian Situation

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▪ Terminology

Porcine Circoviral Disease (PCVD) and Porcine Circovirus Associated Disease (PCVAD) are synonymous names for a disease syndrome caused by porcine circovirus type 2 (PCV2) and originally described as Postweaning Multisystemic Wasting Syndrome (PWMS). The North American industry is reluctant to use "PWMS" for several reasons including the potential negative connotations of the word "wasting" has on consumer purchasing habits, and because PCV2-affected pigs do not always demonstrate weight loss. While the acronyms PCVD and PMWS have been widely used over the last decade, the American Association of Swine Veterinarians has recently endorsed PCVAD. For the purpose of this paper, I will use PCVD, consistent with the European Research Consortium (www.pcvd.org), which has advanced our understanding of PCV2 biology more than any other research body worldwide.

▪ Historical Perspective of PCVD

Postweaning multisystemic wasting syndrome (PWMS) was first described by Harding (1996) and Clark (1996) at the Western Canadian Association of Swine Practitioners (WCASP) conference in 1996, and later at the American Association of Swine Veterinarians (AASV) meeting in Quebec City in 1997. These conference presentations described a novel, devastating disease affecting nursery and grower pigs in a select number of biosecure high health western Canadian herds characterized by wasting, respiratory disease, enteritis, enlarged lymph nodes and jaundice. These affected herds were primarily located in Alberta and Saskatchewan, and included the widely publicized Saskatchewan 600-sow, farrow-to-finish herd that experienced a

16-20 month epizootic (Harding et al., 1998). The fact that this 600-sow herd was a closed, high health status herd, confirmed negative for PRRS virus and virtually all other respiratory and enteric pathogens, strongly suggested the epizootic was not caused by known pathogens. Moreover the frequent liver involvement in early PMWS cases was paramount to our recognition in 1995 of a novel syndrome, and more specifically that the syndrome was not PRRS. In late 1996, towards the end of the epizootic, Dr. Ted Clark made the link between PCV2 and PMWS following correspondence with a colleague, Dr. Barbara Daft. The first experimental reproduction of PMWS clinical signs and lesions was completed using PCV2 and porcine parvovirus (PPV) coinfection in gnotobiotic pigs (Ellis et al. 1999). Krakowka et al. (2001) experimentally reproduced disease in immunostimulated gnotobiotes using PCV2 alone leading to the hypothesis that PCV2 causes PMWS but immunostimulation is a key event in the pathogenesis of the disease.

▪ The 1991 Canadian Index Farm

The first known and documented outbreak of PMWS in the world occurred in western Canada in 1991 on a 40-sow farrow to (25 kg) feeder pig operation located in a remote region of northeastern Saskatchewan. The herd had been depopulated and was restocked with high health breeding stock in January 1990. One year later, the herd experienced nursery mortality of 12-15% associated with sudden death, ill thrift and icterus (jaundice). Clinical signs consisted of jaundice (caused by diffuse liver necrosis), diarrhea (caused by a focal necrotizing enteritis), and pneumonia (caused by granulomatous interstitial pneumonia and Pneumocystosis). Evidence of immunosuppression (lymphoid depletion) was observed microscopically. Multiple diagnostic submissions had failed to identify known pathogens. Serum antibody levels were consistently 1/3 to 1/4 of normal values. While the etiology was never confirmed, liver toxins were suspected and the problem went away within 12 months. Years later and subsequent to the original reporting of PMWS by Harding and Clark in 1996, a retrospective examination of stored paraffin embedded tissues was undertaken and PCVD (PMWS) was diagnosed.

▪ The Pathogenesis of PCV2: a Current Understanding

While the pathogenesis of PCVD has been extensively debated, PCV2 infection is clearly a necessity (Allan & Ellis, 2000; Krakowka et al., 2001) and is the only virus consistently recovered from PWMS cases. Several key factors of the pathogenesis are now known including:

- the accumulation of PCV2 in dendritic cells, a specific class of immune cells involved in pathogen surveillance (Vincent et al., 2003) in subclinically infected but otherwise healthy pigs;
- the pivotal roles of immune stimulation and viral upregulation in clinical disease expression (Krakowka et al., 2001);
- the presence of high PCV2 levels in clinically ill and significantly lower levels in healthy pigs (Ladekjaer-Mikkelsen et al., 2002; Brunborg et al., 2004);
- PCV2 infection in early life being a risk factor for the development of clinical disease (Rose et al., 2003; Lopez-Soria et al., 2005); and
- the hallmark histological lesions of granulomatous inflammation and lymphoid depletion (Krakowka et al., 2000; Segales & Domingo, 2002) in clinically sick animals.

Clinical PMWS appears to be triggered by a number of infectious and non-infectious factors. Virtually all commercially raised pigs are subclinically infected with low levels of PCV2 (Larochelle et al., 2003; Harding, 2000) yet most remain healthy and do not develop clinical disease because triggering factors are absent. The exact mechanism(s) of the triggering factors is not known, but simultaneous infections with other pathogens including PRRS virus, *Mycoplasma hyopneumoniae*, swine influenza virus (SIV), and parvovirus, or the absence of good production practices exacerbate clinical disease.

▪ Strain Variation and PCVD

The occurrence in 2004 of a new PCV2 strain (PCV2-321) of potentially enhanced virulence in eastern Canada has been widely reported. While the occurrence of PCV2-321 coincides with the epizootic PCVD outbreaks in Ontario and Quebec, the enhanced virulence of this novel PCV2-321 strain has not yet been proven experimentally or by field studies. While the “321-story” provided a convenient explanation for the eastern Canadian outbreak, concurrent infections with new strains of PRRSv and SIV, which were also circulating in the eastern pig population, cannot be ruled out as potential contributors. Moreover, case-control studies evaluating the virulence of PCV2 strains in France and the Netherlands failed to identify any single mutation or variant strain that was correlated with clinical disease or increased virulence (Boisseon et al., 2004; Grierson et al., 2004). That being said, the PCV2 strains isolated today from clinical herds in Canada are usually genetically different from those of the late 1990s. However, the more important questions are: 1) whether strain variation is biologically significant, and 2) whether Canada prematurely announced to its trading partners the presence of a potentially more virulent PCV2-321 without the irrefutable evidence confirming

its enhanced virulence. Truly, well designed case-control and experimental studies are needed in Canada to test the virulence of these new PCV2 isolates. Several research groups in North America are investigating this issue.

The Western Canadian Situation

Following the herd outbreaks in the mid-1990s, western Canada entered a period of quiescence during which time PCVD was rarely diagnosed, but caused devastating disease throughout Europe and many other non-European countries. Following the re-emergence of PCVD in eastern Canada in 2005, sporadic but sometimes devastating cases were reported in the west. To characterize the severity and extent of PCVD in western Canada, a brief descriptive survey of WCASP practicing veterinarians was undertaken in May 2006. Veterinary practices in all 4 western provinces participated in the survey. PCVD was reported to be a clinical entity (sufficient to require ongoing attention of the farm management and veterinarians) in 14% of herds; primarily in finisher and farrow-to-finish herds. PCVD was noted in pigs between 5 and 17 weeks of age, and most commonly between 8 and 14 weeks of age. The most common clinical signs of PCVD included (in order of frequency): wasting, pallor, diarrhea, and laboured breathing (dyspnea).

Informal discussions with a select number of western Canadian veterinarians between May and September 2006 have indicated that the prevalence and severity of PCVD has stabilized or potentially worsened in western Canada, except in herds where PCV2 vaccination has been initiated.

PCVD Control & PCV2 Vaccines

At the time of writing, there are two vaccines licensed in Canada on a temporary emergency basis, and two others awaiting registration. Public domain research documenting the efficacy of these experimental vaccines is limited, but the preliminary experimental and field research data provided by the pharmaceutical companies pertaining to their respective products is promising. Moreover, a number of independent US and Canadian veterinarians reported, at the Allen D. Leman Swine Conference in September 2006, very encouraging mortality figures from vaccinated and non-vaccinated grow-finish groups. Thus, the North American industry appears to be in a very fortunate and unique position. After ten years of development, effective PCV2 vaccines are now available when needed most.

The PCV2 vaccines are targeted for usage in the breeding herd to enhance the passive (colostral) immunity of piglets, or in the feeding herd to initiate active immunity post-weaning. The use of autogenous vaccines has been suggested, however it is unlikely that autogenous PCV2 vaccines would be effective, and more importantly may not be safe, because PCV2 is difficult to grow in tissue culture, and is very resistant to inactivation. But regardless of whether a PCV2 vaccine is used, control measures should also be targeted at controlling infective and non-infective co-factors, and implementing good production practices. Concurrent disease, inappropriate (non-PV2) vaccination protocols and poor management are well-documented risk factors for the exacerbation of clinical disease.

■ References

Allan GM, Ellis JA. Porcine circoviruses: a review. J Vet Diagn Invest. 2000;12:3-14.

Boisseson C de, Beven V, Bigarre L, Thiery R, Rose N, Eveno E, Madec F, Jestin A. Molecular characterization of porcine circovirus type 2 isolates from post-weaning multisystemic wasting syndrome-affected and non-affected pigs. J Gen Virol. 2004;85(2): 293-304

Brunborg IM, Moldal T, Jonassen CM. Quantification of porcine circovirus type 2 from serum/plasma and tissue samples of healthy pigs and pigs with postweaning multisystemic wasting syndrome using TaqMan-based real-time PCR. J Virol Meth. 2004;122:171-178.

Clark T. Pathology of post-weaning multisystemic wasting syndrome of pigs. Proceedings, Annual Meetings of the Western Canadian Association of Swine Practitioners. Saskatoon SK, October 1996:pp 22-25.

Ellis JA, Krakowka S, Lairmore MD, Haines DM, Bratanich A, Clark E, Allan G, Konoby C, Hassard L, Meehan B, Martin K, Harding J, Kennedy S, McNeilly F. Reproduction of lesions of postweaning multisystemic wasting syndrome (PMWS) in gnotobiotic piglets. J Vet Diagn Invest. 1999;11:3-14.

Grierson SS, King DP, Wellenberg GJ, Banks M. Genome sequence analysis of 10 Dutch porcine circovirus type 2 (PCV-2) isolates from a PMWS case-control study. Res Vet Sci. 2004;77(3): 265-268.

Harding, J.C., Sept 2000. Understanding the epidemiology of porcine circovirus. Saskatchewan Agriculture Development Fund, Project 97000099, 14 pgs.

Harding JCS, Clark EG, Strokappe JH, Willson PI, Ellis JA. Post-weaning multisystemic wasting syndrome: epidemiology and clinical presentation. Swine Health and Prod. 1998;6:249-254.

Harding, J., 1996. Post-weaning multisystemic wasting syndrome: preliminary epidemiology and clinical findings. Proceedings, Annual Meetings of the Western Canadian Association of Swine Practitioners. Saskatoon SK, October 1996:21

Krakowka S, Ellis JA, Meehan B. Ringler S, Rings MD, Allan G. Activation of the immune system is the pivotal event in the production of wasting disease in pigs infected with porcine circovirus-2 (PCV-2). Vet Pathol. 2001;38:31-42.

Krakowka S, Ellis JA, Meehan B, Kennedy S, McNeilly F, Allan G, Viral wasting syndrome of swine: experimental reproduction of postweaning multisystemic wasting syndrome in gnotobiotic swine by coinfection with porcine circovirus 2 and porcine parvovirus. Vet. Pathol. 2000;37:254-263.

Ladekjær-Mikkelsen AS, Nielsen J, Stadejek T, Storgaard T, Krakowka S, Ellis J, McNeilly F, Allan G, Bøtner A: Reproduction of postweaning multisystemic wasting syndrome (PMWS) in immunostimulated and non-immunostimulated 3-week-old piglets experimentally infected with porcine circovirus type 2 (PCV2). Vet Microbiol. 2002:89:97-114.

Larochelle R, Magar R, D'Allaire S. Comparative serologic and virologic study of commercial herds with and without postweaning multisystemic wasting syndrome. Can J Vet Res. 2003;67:114-120.

Lopez-Soria S, Segales J, Rose N, Vinas MJ, Blanchard P, Madec F, Jestin A, Casal J, Domingo M. An exploratory study on risk factors for postweaning multisystemic wasting syndrome (PMWS) in Spain. Preventive Vet Med. 2005;69(1/2):97-107.

Rose N, Larour G, Le Diguerher G, Eveno E, Jolly JP, Blanchard P, Oger A, Le Dimna M, Jestin A, Madec F. Risk factors for porcine multisystemic wasting syndrome (PMWS) in 149 French farrow-to-finish herds. Prev Vet Med.2003;61:209-225.

Segales J, Domingo M. Postweaning multisystemic wasting syndrome (PMWS): a review. Vet Quart. 2002;24:109-124.

Vincent IE, Carrasco CP, Herrmann B, Meehan BM, Allan GM, Summerfield A, McCullough KC. Dendritic cells harbor infectious porcine circovirus type 2 in the absence of apparent cell modulation or replication of the virus. J Virology. 2003;77(24):13288-13300.