Sponsors

University of Minnesota
College of Veterinary Medicine

College of Agricultural, Food and Environmental Sciences

Extension Service

Swine Center

Editors
W. Christopher Scruton
Stephen Claas

Layout
David Brown

Logo Design
Ruth Cronje, and Jan Swanson;
based on the original design by Dr. Robert Dunlop

Cover Design
Shawn Welch

UK PMWS study tour: Lessons for US animal agriculture

Mark J. Engle, DVM
Director, Swine Health Programs, National Pork Board

Introduction

Since the late 1990s, post-weaning multisystemic wasting syndrome (PMWS) has been identified as a significant problem in many parts of the world.[1] Today, porcine circovirus type 2 (PCV2) is considered by many to be the causative agent of PMWS.[2, 3] However, the role of PCV2 in PMWS and porcine dermatitis and nephropathy syndrome (PDNS) remains a controversial issue. PCV2 is a ubiquitous virus that has been present for two to three decades in pig populations around the globe. Although the pathogenesis of PMWS is still unclear, this disease has been credited for major losses to producers. Britain's Meat and Livestock Commission estimated the two syndromes cost its swine industry US$50 million in 2001. This paper reflects the efforts of the National Pork Board (NPB) to better understand PMWS and its potential impact on US pork producers.

Many believe that PMWS is the same syndrome in both Europe and the US based on the presence of similar histologic lesion descriptions and the apparent association with PCV2. However, distinct clinical differences have been reported. PMWS primarily affects nursery pigs in the UK while PMWS is more frequently associated with finishing pigs in the US. UK mortality rates associated with PMWS and porcine dermatitis and nephropathy syndrome has been described in the 20-40% range. Mortality in the US and Canada typically ranges from 3-10%. Other European countries have reported mortality rates similar to the UK.

Concerns with the apparent inconsistencies in clinical expression between Europe and North America caused the National Pork Board Swine Health Committee to direct the NPB staff to assemble a team to travel to the UK and study these syndromes. Individuals participating on the multidisciplinary team included the following:

- Jim Niewold, Chair of the NPB Swine Health Committee and pork producer from Illinois
- Bob Morrison, a veterinary epidemiologist from University of Minnesota
- Perry Harms, a diagnostic pathologist and staff veterinarian for Smithfield Premium Genetics
- Mike Ellis, an animal scientist from University of Illinois
- Eric Bush, a swine veterinary epidemiologist sponsored by USDA/APHIS
- Eric Neumann, a veterinarian with NPB
- Mark Engle, a veterinarian with NPB

The team had two overall objectives:

- Establish the scope of PMWS and PDNS in the UK and determine if these syndromes differed substantially between the UK and the US.
- If substantial differences did exist, develop a strategy to minimize the potential future impact of the diseases on the US pork industry.

From November 11-15, 2002, the team visited farms, worked in diagnostic facilities, and attended meetings in the UK to complete the first objective. The second objective of the trip was partially completed by compiling all of the participants' observations and their identification of risk factors into a final report. Much of the study team's final report is reflected below and, therefore, their contributions to this document are deservedly acknowledged.

In addition, communications with international colleagues are on-going, and US field investigations are in progress.

PMWS: Is the disease a reality?

Prior to the study trip, individual members of the study team differed in their belief as to whether PMWS was an actual disease. Thus, the first question that needed to be answered was: Is PMWS a truly distinct, clinico-pathologic disease? Because PMWS reflects a wide variety of clinical symptoms, we felt it was important to define a "case." Our case definition simply followed the outline described in the scientific literature:

- The presence of wasting or ill-thrift with or without other clinical signs
- Evidence of microscopic lymphoid depletion
- Presence of PCV2 associated with the lesion

(Note: The current case definition for PMWS requires PCV2 to be part of the syndrome.)

In reality, a trip to an affected farm displays an array of clinical specimens that paint a much fuzzier picture. At the level of an individual pig, the case definition above works reasonably well. However, it became apparent that this was much too simplistic a view when trying to identify affected farms since wasting pigs can be found on nearly all farms, microscopic lymphoid depletion occurs in apparently healthy pigs (reported to us by a Scottish diagnostician), and most pig populations (including those in England) have had exposure to PCV2 for decades, according to the scientific literature. A pig diagnosed with PMWS in the UK would more likely have been called something else in the field in the US—such as endocarditis, polyserositis, porcine reproductive and respiratory syndrome (PRRS), porcine respiratory disease complex (PRDC), light birthweight, etc.

Regardless, the evidence put forth by our colleagues in the UK along with our own observations convinced our team that the wasting syndrome being described as PMWS is a real disease. Many affected producers described having very definite, pre-infection, acute, endemic, and convalescent phases (rarely a "back to normal" phase). Few production records were made available to us, but those that were demonstrated levels of mortality that most producers would be unwilling to live with if they had the means to control it. It did not appear that the wasting pigs were simply a result of known diseases combined with poor management. There seemed to be some other element present, which became apparent around the fall of 1999, that made the affected farms different than simply a poorly managed farm.

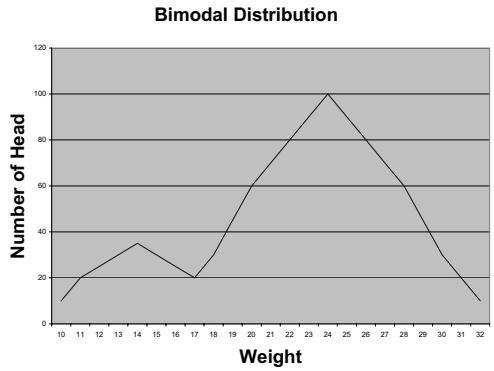
We spent some amount of time attempting to understand the wasting phenomenon that is the hallmark of PMWS. The idea was put forward to try to understand the shape of the weight distribution of pigs that might be found in an affected nursery. A hypothesis was generated based on the histograms in **Figures 1** and **2**.

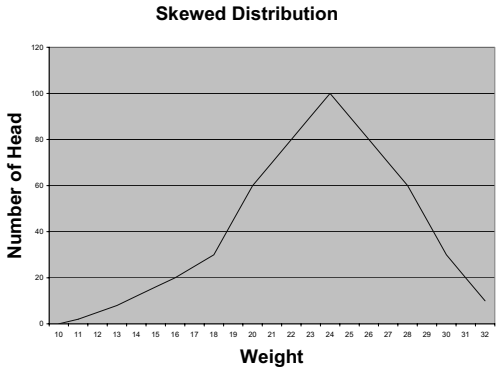
If the weight distribution in an affected population appeared like the bimodal distribution in **Figure 1**, we speculated that the wasting could be investigated through a case-control, risk factor analysis, anticipating the ability to identify one or two important criteria that put the affected pigs at risk. If an affected population appeared more like the skewed population in **Figure 2**, we suspected the cause of wasting may be more multifactorial, such that exposure to more risk factors would make a pig waste more severely, and vice-versa. Determining causation, and subsequently developing control measures, would be infinitely more difficult in this situation.

The rate at which affected pigs lost weight was unclear. Some producers were convinced that a healthy, robust pig could become ill and lose weight to the point that the spine and ribs were protruding in the course of two to three days. The issue was felt to be important because, if wasting was the identifying clinical sign for PMWS that triggered the cascade of treatment and control measures, we did not know if these measures were being initiated early, middle, or late in the stage of the disease. This timing significantly confounds diagnosis of the primary etiology, diagnosis of secondary infections, identification of temporally related risk factors, and evaluation of treatment and control strategies. At the affected farms we visited with significant concurrent infections, the wasting pattern seemed to be more similar to the skewed distribution. The one affected farm we visited that was negative to several notable pathogens, including *M. hyopneumoniae* and Lelystad Virus (LV), the wasting pattern was probably better represented by the bimodal distribution.

Anecdotal history

The consensus of the producers, practitioners, and animal health officials was that the disease did not seem to be present prior to 1999. It was reported to us that PMWS in England was first observed on a farm in the East Anglia region in the summer of 1999. We discovered, after our visit, that this farm was an outdoor production system which became positive for *M. hyopneumoniae* at the same time PMWS emerged. The introduction of *M. hyopneumoniae* provided evidence that this farm had suffered a biosecurity breech. During 2000, PMWS appeared in succession in Thames Valley, South West of England,





Lincolnshire, South Humberside, and Yorkshire. It was claimed that the initial spread of the disease between regions could be linked to pig movements. The subsequent spread of the problem within a region was considered to be linked to transfer between outdoor sow operations by wildlife and also transport. The restricted animal movements as a result of classical swine fever (CSF) and foot-and-mouth disease (FMD) outbreaks were credited with causing an increased prevalence and severity of PMWS in all the pig-dense regions of England. Interestingly, changes in production practices, such as the banning of gestation stalls and bedded systems for sows and grow-finish pigs, became fully effective in 1999. In addition, it was also reported to us that the fall season and feeding of new crops seemed to bring about new outbreaks and increase the severity of existing infections.

PMWS diagnosis

Our group concurred that, based on our clinical and gross observations, we would describe most of these cases as PRDC in the US. Infections that we believed to be PRRS, *M. hyopneumoniae, H. parasuis,* and *S. suis* appeared to be frequently present.

The diagnostic approach to pigs submitted with a field diagnosis of PMWS appeared to be somewhat limited. A positive diagnosis would be based on the presence of classical findings of wasting, lymphoid depletion, and the presence of PCV2 (in their hands, microscopically visible inclusion bodies). Enlarged lymph nodes were a frequent finding as were concurrent infections with *H. parasuis.* Financial constraints and a diversion of laboratory resources toward FMD and BSE have prevented much of the "diagnostic due diligence" we have come to expect from our US laboratories. While virus isolation (VI), antigen staining (IHC), polymerase chain reaction (PCR), and genomic sequencing have become routine and economically justifiable in US laboratories, the same tests do not appear to be receiving widespread use in England.

There was no attempt to detect a novel virus through virus isolation or low-specificity/high-sensitivity virus family-specific PCRs on clinical specimens. It seemed that veterinarians, producers, and diagnosticians have assumed that PCV2 does in fact cause PMWS so other agents or a novel co-infection were not pursued. The lack of investigation in PMWS cases for a potential novel pathogen should not be considered unique to the UK. In the US, samples submitted to the diagnostic labs are worked up extensively using a preexisting battery of tests for known pathogens. However, due to case load and financial constraints, VI or family specific PCRs are not routinely employed at US diagnostic labs either. PMWS is diagnosed in the US based on the case definition described earlier, where the association of PCV2 with the lesion results in a positive diagnosis and a conclusion to the case.

PMWS risk factors identified in the UK

There are many risk factors, in addition to infectious agents, that must be considered when evaluating a disease one believes may have multifactorial causation. A great deal of our thoughts and discussions focused on what these other risk factors may be. The team reached a consensus on a number of factors that were distinctly different between English and American pork production which may be useful in future investigation efforts regarding PMWS. These risk factors include the following:

Novel primary pathogen or coinfection

Although our team was divided on the issue, much discussion among our team centered around the possibility of the emergence of a novel primary pathogen or a novel co-infection to the UK swine population.

H. parasuis and Salmonella spp.

In addition to PRRS, several other specific infectious agents bear mentioning. *Haemophilus parasuis* and *Salmonella* spp. were evident in several pigs on the post-mortem examinations we conducted. Our hosts agreed that these two agents seemed to be frequently found on PMWS farms. Porcine proliferative enteropathy, porcine epidemic diarrhea virus, and swine influenza virus were also suggested as possibly having a role.

Feeding and nutrition

Feeding practices and nutrition were substantially different than in the US. Of particular interest was the extensive use of small grains (wheat and barley to the near total exclusion of corn), peas, rapeseed meal, by-products (brewers' waste, biscuit meal, and wheat mids), and the very limited use of animal proteins (fishmeal, blood products, plasma protein). The predominance of single-site production and continuous flow grow-out facilities frequently limited the number of diet phases fed and their ability to smoothly transition from one phase to the next. Some comments were made about the possibility of wheat gluten enteropathy and soy hypersensitivity playing a role in the clinical picture. It must be noted that these are the same kinds of ingredients and feeding technology that were predominant prior to the appearance of PMWS. Regardless, nutrient concentrations for protein and amino acids were typically higher than in the US.

Facilities

There is a predominance of single-site, continuous flow facilities with solid flooring and the use of bedding in the UK. A decade of poor profitability has prevented much reinvestment into the swine industry. Very few "typical US" style buildings were noticed. Many buildings tended to be masonry construction, provided little separation between the pigs and excreta, and were suboptimally ventilated. Of course, all of these observations are relative to

what we consider to be "optimal" in the US. They were successfully raising pigs in these same systems prior to the appearance of PMWS in 1999.

Mycotoxins

The potential role of mycotoxins is contentious among the industry leaders. The theory being bantered about is a result of the introduction of a new small grain fungicide during the growing season of 1999. This "strobilurin" fungicide effectively prevents the growth of its targeted fungus, but at the same time appears to have created a niche for some competing fungi and presumably their toxins. Minimal, if any, research has been done to investigate the role of small grain mycotoxins. We were unable to discern if this fungicide was being used elsewhere in the world. However, Scottish farmers appeared to be using the same fungicide and had not experienced cases of PMWS until just recently.

Antimicrobials

We were told the use of growth promoting antibiotics was scaled back during the 1990s. However, our discussions with practitioners led us to believe that, in actuality, total usage and the spectrum of available antimicrobials has probably not changed much. Some producers reported beneficial effects by supplementing swine diets with combinations of herbs and essential oils.

Crowding

As stated earlier, there was widespread agreement that animal movement restrictions put in place during the CSF and FMD outbreaks contributed to the severity of the PMWS problem. During this period nursery and growing pig facilities became perpetually overcrowded. This stress exacerbated the already identified PMWS problems.

Parity

It was reported to us that pigs born to older parity sows are at higher risk for experiencing PMWS. This theory was reported to us anecdotally by several sources during the week. The two small datasets we were able to see did not support this conclusion. The significant confounder in the argument is that the parity distribution on many farms is skewed toward the older parities because of past animal movement restrictions due to CSF and FMD. Thus, more pigs are being born to older parity sows.

Stress

Madec's 20 principles and variations are being attempted with mixed results. Madec's principles are essentially a lesson in good husbandry. Minimizing cross-fostering, good sanitation, age segregation, all-in/all-out, etc. are the hallmarks of his program. Some individuals we spoke with were passionate about their success in using them. Others used bits and pieces of the 20 principles and felt there was some benefit. Still others said that they were not helpful at all in controlling the disease. If there was any consensus, it was that "stress" made any PMWS affected farm worse. The top five stressors related to us were: weather/environment, mixing of pigs, lack of age segregation, poor hygiene, and concurrent disease.

Sire line, gender, previous litter status

A university farm with PMWS was able to share some risk factor information from their herd because they had individually identified and tracked offspring. They reported that genetic line, parity, litter size, and the appearance of PDNS lesions did not predispose pigs to PMWS. However, sire line, gender, and having PMWS pigs in the previous litter did appear to put pigs at risk of experiencing PMWS. Although the integrity of this dataset was excellent, it was very limited in size.

Water supply

The difference in water supply to swine buildings in England as compared to the US is noteworthy. Livestock farmers are not permitted to connect livestock water supply to any centralized water system. Pigs were generally supplied from an elevated float-controlled open tank providing gravity flow to the pens. We speculated about the possibility of contamination in these "open" water supplies.

Gilt isolation and acclimatization

Gilt isolation and acclimatization appeared to receive much less attention than what is typical in the US. As we saw primarily growing pigs, we were not able to get first-hand knowledge about gilt management. When asked, a number of farm managers indicated that their source herd received replacement gilts every three weeks. Veterinarians readily admitted the challenges they have in getting more producers convinced of the value of gilt isolation and acclimatization. These discussions resulted from our reaction to seeing some of the PMWS case farms and remarking how similar they looked to the downstream flow of an unstable, PRRSV-infected breeding farm. Do the same gilt isolation and acclimatization programs we use to control PRRS hold true for PMWS?

Disease-resistance selection

There was much speculation that we have unwittingly selected away from some important disease-resistance components as we have intensively selected for other traits. This debate was lively; however, no research to answer the question has been attempted.

PDNS-similar lesions

A diagnostician we worked with offered two hypothesis for PDNS that bear further study. One is a related lesion in mice created by a DON toxin mediated IgA nephropathy. The other is a similar dermatitis seen in humans called Henoch-Schoenlein Purpura (HSP). Interestingly, it has

distribution on the body similar to that of PDNS and follows a well documented seasonal pattern that appears to mimic the seasonal incidence of PDNS.

Weaning age

Weaning age in England is on average several days to several weeks longer than in the US. The significance of wean age in PMWS is unclear; however, we know this is critically important for numerous other diseases and should be included in this list.

The relative importance of any of these potential risk factors is still unknown. However, this list provides a good framework for our study of the disease in the US and may also be of value to our European colleagues.

Recent international information

PMWS was one of three diseases targeted at a recent emerging disease conference in Rome, Italy. Interestingly, while epidemics of this syndrome are occurring in previously naïve countries and further investigation continues in endemic countries, the theory that PCV2 is the sole causative agent is being continually challenged.

French researchers characterized PCV2 in PMWS-affected and -non-affected herds and concluded that PCV2 could not be used to determine PMWS-positive or -negative farms. They confirmed a high prevalence of PCV2 on both PMWS-affected and -non-affected farms. The genomic sequences of the PCV2 isolates were similar and they could not identify any virulence factors in strains from PMWS-positive herds.[4]

Denmark is currently experiencing a PMWS epidemic. The first two cases of PMWS were diagnosed in 2000.[5] Since then, PMWS has been rapidly spreading through the country. As of February 2003, PMWS has been diagnosed in more than 100 herds all over Denmark.[6]

> The disease seems to spread from west to east; this could suggest transmission of wind-spread disease, since the predominate wind is from south-west in this part of Denmark. The rapid spread of the disease, within an area could indicate a wind-spread of an unknown infectious agent. The retrospective Danish investigations indicate that the rapid increase in diagnosed herds last year, is a real increase in number of affected herds and not just due to increased attention on the disease. PCV2 is widespread in Danish pig farms and this means we have to look for another agent or to special disease releasing factors.[7]

The Netherlands estimated that in 2001, the pig production losses due to PMWS/PDNS were approximately 20 million Euro. The disease has progressively spread through the Dutch pig population since 1997 and, as of 2002, includes over 50% of the herds.[8]

Scotland is also experiencing a PMWS epidemic. The disease is continuing to spread quite actively through herds in Scotland. Herds have broken despite "treble-tight biosecurity." "It is strongly suspected that PMWS can be introduced via semen since all other factors seemed to be secured." Diagnosticians in Scotland still hold the view that it is a new syndrome and the primary causative agent, most likely viral, has yet to be identified.[9]

Conclusion

The National Pork Board UK Study Team is considered to be an ideal model for future international disease investigation and collaboration. Experiences with PRRS, PMWS, and other diseases have clearly demonstrated the need for surveillance to detect, assess, and respond to emerging diseases of swine. Today, a void exists within countries and internationally in how the swine industry should respond to emerging diseases. The Office International des Epizooties (OIE) establishes international standards for managing known diseases; however, unknown, emerging diseases are not addressed. The need for nations to protect their industries from emerging diseases or syndromes identified with symptomatically defined case criteria is apparent and will be the driving factor for collaboration. While there is a risk that overly broad application of a system like this could be used inappropriately by countries wishing to limit their trade obligations, proper use of the same system could improve the future health of all countries' livestock industries. Early detection, assessment, and response to emerging diseases on a global scale would minimize their impact on production and allow rapid implementation of prevention strategies. International communication pathways and coordinated efforts for international disease surveillance will be necessary to create a successful model for exchange of information regarding research, diagnostic technology, and disease surveillance.

References

1. Segales J, Domingo M. Postweaning multi-systemic wasting syndrome (PMWS) of pigs. A review. *Vet Q.* 2002; 24: 109-124.
2. Allan GM, Kennedy S, McNeilly F, et al. Experimental reproduction of severe wasting disease by co-infection of pigs with porcine circovirus and porcine parvovirus. *J Comp Pathol.* 1999; 121: 1-11.
3. Bolin SR, Stoffregen WC, Nayar GP, Hamel AL. Postweaning multi-systemic wasting syndrome induced after experimental inoculation of cesarean-derived colostrum-deprived piglets with type 2 circovirus. *J Vet Diagn Invest.* 2001; 13: 185-194.
4. De Boisseson C, Beven V, Bigarre L, Thiery R, Rose N, Eveno E, Madec F, Jestin A, Characterization and Comparison of Porcine Circovirus Sequences from Post-weaning Multisystemic Wasting Syndrome Affected and Non-affected Herds. *Proceedings 4th International Symposium on Emerging and Re-emerging Pig Diseases.* 2003; 186.

5. Hassing AG, Botner A, Ladekjaer-Mikkelsen AS, Baekbo P, Jorsal SE, Bille-Hansen V. *Proceedings ssDNA Viruses of Plants, Birds, Pigs and Primates.* 2001; 93.
6. Hassing AG, Botner A, Ladekjaer-Mikkelsen AS, Kristensen CS, Jorsal SE, Bille-Hansen V, Baekbo P. Characterisation of the First Cases of PMWS in Denmark. *Proceedings 4th International Symposium on Emerging and Re-emerging Pig Diseases.* 2003; 211-212.
7. Rathkjen PH, Conradsen P, Nielsen E, Riising HJ. Spread of PMWS within an Area of Denmark – An Epidemiological Report from Practice. *Proceedings 4th International Symposium on Emerging and Re-emerging Pig Diseases. 2003;* 175-176.
8. De Jong MF, Elbers A, Wellenberg GJ. Factors Associated with PMWS and PDNS: A Case Control Study. *Proceedings 4th International Symposium on Emerging and Re-emerging Pig Diseases.* 2003; 215.
9. Dr. Jill Thomson; SAC Veterinary Science Division (Edinburgh). Personal communication, 2003.