Evaluation of induction of porcine dermatitis and nephropathy syndrome in gnotobiotic pigs with negative results for porcine circovirus type 2

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Objective—To determine whether porcine dermatitis and nephropathy syndrome (PDNS) could be experimentally induced in gnotobiotic swine.

Sample Population—Plasma samples from 27 sows and 20 conventional weaned piglets were obtained, and 30 gnotobiotic pigs were used in experiments.

Procedures—3 experiments were conducted. Groups of 3-day-old gnotobiotic pigs were inoculated with pooled plasma samples obtained from healthy feeder pigs in a herd that was in the initial phases of an outbreak of respiratory disease; gross and histologic lesions of PDNS were detected in the inoculated pigs. In a second experiment, 2- and 3-day-old gnotobiotic pigs were inoculated with porcine reproductive respiratory syndrome virus (PRRSV) and with PRRSV-negative tissue homogenate containing genogroup 1 torque teno virus (g1-TTV); Lesions of PDNS were detected.

Results—Pigs inoculated with pooled plasma or the combination of tissue-culture–origin PRRSV and g1-TTV tissue homogenate developed systemic hemostatic defects, bilaterally symmetric cutaneous hemorrhages, generalized edema, icterus, bilateral symmetric renal cortical hemorrhage, dermal vasculitis with hemorrhage, and interstitial pneumonia consistent with a clinical and pathologic diagnosis of PDNS. The PRRSV RNAs and g1-TTV DNAs were detected in plasma; all pigs seroconverted to PRRSV, and all had negative results for porcine circovirus type 2 when tested by use of PCR assays.

Conclusions and Clinical Relevance—These data suggested that PDNS is a manifestation of disseminated intravascular coagulation in swine. For the experimental conditions reported here, combined infection with g1-TTV and PRRSV was implicated in the genesis of these lesions. (Am J Vet Res 2008;69:1615–1622)
dence of PDNS is sporadic, the case fatality rate is often high. In Europe and the United Kingdom, in particular, the incidence of PDNS may exceed that of PMWS.5 Studies of naturally developing disease have revealed that young swine are more severely affected than are older swine and that the clinical course in individual pigs wanes within 2 or 3 weeks after onset of the cuta-
neous lesions. Swine affected by PDNS are almost in-
v invariably infected with PCV2.11,12 yet experimental infec-
tions of swine with PCV2 have not resulted in a single
instance of PDNS in infected swine.16-20 even when they
have been coinfected with PRRSV.3,12

Gross lesions characteristic of PDNS are distinct-

ive.1,3,10-13 Subcutaneous hemorrhages may be confused with

Erysipelas-associated vasculitis; in Europe, these
hemorrhages may be confused with classical swine fe-
ver or African swine fever. An accurate exclusion di-
agnosis for classical swine fever or African swine fever is critical.10-12 Renal lesions are diagnostic for PDNS. Grossly affected kidneys have a mottled appearance, and the renal cortices are accentuated as pale white to tan discolorations or as multifocal hemorrhages. Histo-
logic lesions of PDNS consist of segmental necrotizing
vasculitis of the dermal and subdermal vasculature and
resultant hemorrhages and a distinctive renal glomer-
ular lesion characterized by thickening of glomerular
basement membranes with protein deposits (that in-
clude IgG, complement,11,12 and other plasma proteins),
modest neutrophilic glomerular cellular infiltrates, and, ultimately, glomerular sclerosis.6,10,11,13,24,25 Proteinuria and edema (nephrotic syndrome) are often characteristic of the clinical syndrome.23 In the experience of 2 of the authors (SK and GA), vascular and glomerular les-
ions do not contain PCV2 nucleocapsid or viral replicase
proteins, nor do they hybridize with DNA probes to PCV2
viral DNAs.11 Despite these negative findings, it is widely
believed that PDNS is an expression of PCV2 infection, and
PDNS is generally grouped within the PCVD com-
plex.14,15 even though the experimental evidence for cause
and effect regarding PCV2 is lacking.

During a diagnostic investigation into the early
phases of a disease outbreak in a closed swine herd with
a high health status in which the pigs were routinely
vaccinated against PRRSV by use of a modified-live viral
vaccine, plasma samples were obtained from 20 clini-
cally normal 14- to 16-week-old pigs to examine exper-
imental transmission of disease into gnotobiotic swine.

Experiment 1—Plasma samples obtained from 20
conventionally reared pigs (11 barrows and 9 gilts; 14 to 16 weeks old) were screened for PCV2 DNA by use
of PCR assays.26 Of these, 18 had negative results and
2 had positive results for PCV2 DNA. Plasma from the
2 pigs with positive results was discarded, and the 18
remaining PCV2-negative plasma samples were pooled
designated as passage 0). Then, 8.5 mL of pooled plas-
ma was inoculated IP into each of three 3-day-old gnoto-
biotic pigs (day of inoculation was designated as day 0).
Two inoculated pigs were euthanized on day 28 after
inoculation, and the remaining pig was euthanized on
day 35 after inoculation.

Experiment 2—A 10% (wt/vol) liver homogenate in
 Hank’s minimal essential medium was made from
hepatic tissues obtained from one of the pigs in experi-
ment 1 that was euthanized on day 28 after inocula-
tion. The homogenate was clarified by centrifugation,
and the supernatant was divided into aliquots (2.0 mL/aliquot) and designated as in vivo passage 1. This was used as an IP inoculum for 13 gnotobiotic pigs from 2 subsequent litters. Three separately housed gnotobiotic pigs were not inoculated and were used as control pigs. Of the 13 pigs inoculated with passage 1 supernatant, 1 became moribund and was euthanized on day 5 after inoculation, 3 were euthanized on day 7 after inoculation (1 was moribund), 3 were euthanized on day 13 or 14 after inoculation (1 was moribund), 2 were euthanized on day 21 after inoculation, and 4 were euthanized on day 32 after inoculation. One control pig was euthanized on days 7, 14, and 32 after inoculation, respectively.

Experiment 3—A litter of 11 gnotobiotic pigs was assigned to 3 separately housed challenge-exposure groups. Group A (n = 3 pigs) was injected IP with PRRSV that had been recovered from the passage 1 homogenate by use of culture and a single in vitro passage on MARC cells. This PRRSV isolate (ie, PRRSVp1) was a noncytopathogenic North American strain as determined by use of a combination of immunoreactivity with monoclonal antibody specific for North American strains and PRRSV-specific reverse transcriptase–PCR assay. Group B (n = 4 pigs) was injected IP with the fourth in vivo passage of g1-TTV (ie, g1-TTVp4) and with PRRSV recovered from the first-passage homogenate. Control pigs were in a parallel experiment that assessed the effects of g1-TTVp4 alone in gnotobiotic swine.\(^2\)

Group C (n = 4 pigs) was injected with first-passage homogenate used as inoculum in experiment 2. One group B pig had clinical signs of wasting and respiratory distress and was euthanized on day 8 after inoculation; the 10 remaining pigs, despite the fact they had transient anorexia and diarrhea, survived and were euthanized on day 27 (group A) or 28 (groups B and C) after inoculation.

Pathologic examinations for the 3 experiments—Pigs were euthanized as indicated in the aforementioned experiments. Gross lesions were photographed, and tissue samples from the peripheral lymph nodes, spleen, thymus, bone marrow, lungs, liver, kidneys, and ileum were collected into tissue cassettes; fixed for 24 hours in cold 100% ethanol; and then processed by routine histologic methods for embedding in paraffin and sectioning. Five-micron-thick section replicates were stained with H&E, Jones silver, PAS, and PTAH stains; section replicates were also evaluated via immunohistochemical analysis to detect PCV2 nucleocapsid protein\(^1\) and porcine fibrinogen or fibrin by use of a monoclonal antibody against porcine fibrinogen or fibrin,\(^4\) followed by development with a commercially available avidin-biotin complex kit.\(^6\)

Results

Animals—An infectious disease history of the source herd for 2003 through the spring of 2006 was reconstructed by assessment of antibody titers against common pathogens of pigs. All 27 sows tested had antibodies against PCV2 and PPV but were seronegative for PCV2 DNA by use of PCR assays. Serologic testing revealed that the herd was seronegative for TGEV and variably seropositive for EMCVs. A few sows had positive results for PRRSV by use of an ELISA, but these were low titers with a sporadic incidence (0 or 1 sowly) and were attributable to residual vaccination-associated titers in these sows. The herd seroconverted to swine influenza virus in the middle of 2005, although clinically evident respiratory disease in the pigs was not expressed. Serum from all sows, except for 1, had positive results for porcine g1-TTV DNA by use of an nPCR assay.

Clinical findings—All 3 pigs in experiment 1 remained clinically normal throughout the course of the experiment. In contrast, all inoculated pigs of experiment 2 that received the first-passage homogenate derived from pigs in experiment 1 developed clinical signs of disease. One day after IP inoculation with the first-passage homogenate, all 13 pigs in experiment 2 became mildly anorectic, sluggish, and lethargic. These signs persisted for the subsequent 4 or 5 days. Mild dyspnea was detected on day 3 after inoculation and continued through days 7 to 10 after inoculation. Diarrhea (loose feces) developed after day 3 and persisted for 7 to 10 days, although the severity varied among inoculated pigs in that some still had diarrhea when euthanized on day 32 after inoculation but others did not. Of the 13 inoculated pigs in experiment 2, 3 became recumbent and unresponsive (days 5, 7, and 13 after inoculation, respectively) and were euthanized. Uninoculated control pigs remained clinically normal throughout the experiment. During experiment 3, 1 pig of group B developed severe diarrhea and dyspnea on day 6 after inoculation and was euthanized on day 8. The remaining pigs in this litter remained clinically normal, except for pigs of groups B and C that had transient diarrhea, and survived the viral challenge exposure until euthanized on day 27 or 28 after inoculation.

SeroLogic and virologic testing—Plasma and serum samples obtained from all inoculated pigs at ≥7 days after inoculation, regardless of the specific experiment, contained g1-TTV DNAs as determined from results of an nPCR assay. None of the serum samples from the pigs contained PCV2 viral DNAs when examined by use of PCR assay. Tissue section replicates from all inoculated and control pigs were tested immunohistochemically for PCV2 viral nucleocapsid, and all had negative results. Two of 3 pigs in experiment 1 had g1-TTV DNAs and antibodies against PRRSV. All pigs in experiment 2 seroconverted to PRRSV antigens by day 21 after inoculation, and sera obtained immediately before pigs were euthanized contained PRRSV RNAs as determined by use of the reverse transcriptase–PCR assay. Sera obtained immediately before euthanasia from all pigs of experiment 3, except for the pig euthanized on day 8 after inoculation, had antibodies against PRRSV. The pig euthanized on day 8 had positive results for PRRSV RNA. Sera obtained immediately before pigs were euthanized were tested for other viral pathogens of swine, including TGEV, PPV, and EMCV; results for all of those pathogens were negative (data not shown).

Results of pathologic examinations for experiment 1—Gross findings in both pigs euthanized on day 28 after inoculation were mild generalized lymphadenopathy associated with prominent development of
lymphoid follicles, moderate thymic atrophy, and pale to tan livers. Histologically, lymphol follicular hyperplasia and thymic atrophy were confirmed, and modest lymphocytic-histiocytic inflammatory cell infiltrates into hepatic sinusoids (mild multifocal nonsuppurative hepatitis) were evident. Basement membranes of renal glomeruli were thickened with an eosinophilic acellular material that stained with the Jones silver, PAS, and PTAH stains. These glomerular deposits had positive results when tissue sections were stained for porcine fibrinogen or fibrin (Figure 1). Minimal lymphadenopathy and lymphocytic hepatitis were evident in the third pig, which was euthanized on day 35 after inoculation.

**Results of pathologic examinations for experiment 2**—Gross and histologic findings for experiment 2 were grouped on the basis of day on which the pigs were euthanized.

**Day 5 to 7 after inoculation**

A systemic circulatory disturbance was evident and was manifested as mild subcutaneous edema, mild icterus, and thin poorly clotted blood. Mild generalized lymphadenopathy was detected in these pigs, and the lungs were tan and distended but notatelectatic. The livers were mottled and yellow to tan, and the renal cortex of 1 pig had multifocal petechial hemorrhages. Histologically, renal glomeruli were distended with protein deposits that had positive results when stained for PTAH; glomeruli also had positive results when stained with the Jones silver and PAS stains. Glomerular deposits had positive results for fibrinogen or fibrin. Glomerular-associated hemorrhages were evident. Lymphoid tissues had lymphofollicular hyperplasia; thymi had T-cell depletion (thymic atrophy). Hepatocytes had cellular swelling and degeneration and diffuse lymphocytic and histiocytic inflammatory infiltrates that were most prominent in the hepatic sinusoids. The alveolar walls and capillary vasculature of the lungs contained mononuclear inflammatory cells, scattered neutrophils, and protein deposits, which were consistent with a morphologic diagnosis of acute diffuse (mild) interstitial pneumonia. A few subtle but distinct disruptions of the endothelial lining of larger pulmonary vessels were identified and were associated with poorly formed intravascular microthrombi.

**Day 13 or 14 after inoculation**

Gross and histologic lesions with more severity were detected in pigs euthanized on day 13 or 14 after inoculation. Bilaterally symmetric subcutaneous hemorrhages were evident in the ventral portion of the abdomen and hindquarters of 1 pig euthanized on day 13 after inoculation (Figure 2); the subcutaneous hemorrhages in the hindquarters were associated with ulcers on the tail. Bilaterally symmetric hemorrhages were evident in the inguinal region of a second pig; anasarca, icterus, anemia, and hemostatic defects were also detected in that pig. Livers were mottled, and the lungs were distended and nonatelectatic. Accentuation of renal glomeruli (white cortical foci) and hemorrhages in the renal cortex were evident in 2 pigs (Figures 3 and 4); accentuation of glomeruli without hemorrhages was evident in a third pig.

Histologic examination revealed that the skin lesions consisted of lymphocytic and histiocytic inflammatory vasculitis and perivasculitis, subepidermal edema, and microhemorrhages. Livers contained multiple foci of inflammatory cells similar to those seen in pigs euthanized on day 7. The lungs were dramatically altered. Alveolar walls were markedly distended with a mixed inflammatory cell infiltrate consisting of lymphocytes, plasma cells, macrophages, and a few neutrophils, which closely resembled photomicrographs of PRRSV-induced pneumonia in gnotobiotic pigs.\textsuperscript{24} In addition, alveolar spaces frequently contained brightly stained refractive eosinophilic protein hyaline-like deposits, which contained a mixture of mononuclear inflammatory cells and other cellular debris that had positive re...
sults when stained for fibrin or fibrinogen (Figure 5). Hemorrhages in the renal cortex were confirmed, and renal glomeruli had prominent membranous thickening (Figure 6). This thickening was attributable to accumulations of proteins, including fibrinogen or fibrin deposits in or on the glomerular basement membranes.

Multifocal nonsuppurative interstitial nephritis accompanied the glomerular lesions. Similar to results for pigs euthanized on days 5 to 7, reactive follicular lymphoid hyperplasia was evident in lymphoid tissues.

**Day 21 after inoculation**

Two pigs euthanized on day 21 after inoculation were clinically normal, except for residual diarrhea. Gross and histologic lesions were evident in the kidneys and lungs but were less severe, compared with changes seen in pigs euthanized on day 13 or 14. Grossly, there were no subcutaneous hemorrhages, although mild subcutaneous edema was detected in 1 pig; both pigs had thin, watery, and poorly clotted blood. Peripheral lymph nodes were large, thymi were atrophic, and livers were considered normal, but the lungs were firm and distended. In these pigs, histologic changes reflected gradual resolution of acute lesions in the kidneys, lungs, and liver that were evident in pigs euthanized on days 5 to 7 and day 13 or 14. In the liver, numerous foci of infiltrating lymphocytes, plasma cells, and histiocytes were detected, with the histiocytes beginning to organize into granulomatous foci around areas of hepatocyte loss and sinusoidal expansion. In the kidneys, foci of interstitial fibrosis and accumulations of mononuclear inflammatory cells were detected in association with segmental tubular dilatation. Renal glomeruli contained protein material and stained strongly for fibrinogen or fibrin, as determined by use of immunohistochemical analysis; concurrent segmental fibrosis was also evident. The lungs were affected with interstitial pneumonia, which appeared to be resolving. Other than the severe thymic atrophy, both pigs had mild lymphofollicular and histiocytic proliferation, with the histiocytic proliferation evident in the lymphatic sinusoids.

**Day 32 after inoculation**

By day 32 after inoculation, gross lesions detected were minimal and consisted of moderate generalized lymphadenopathy (4/4 pigs), mild thymic atrophy (2/4 pigs), and a pale or tan liver (3/4 pigs); kidneys were grossly normal. Histologically, mild interstitial pneumonia was evident in 3 of 4 pigs. In the liver, modest multifocal accumulations of lymphocytes, monocytes, and plasma cells were detected. Renal lesions in all 4 pigs had a multifocal distribution but varied in intensity among the 4 pigs. In all 4 pigs (Figure 7); staining for fibrinogen or fibrin yielded equivocal results. The number of affected glomeruli was low and varied from a high of approximately 10% affected glomeruli to a low of 1%. Accompanying this glomerular lesion were multifocal areas of interstitial fibrosis, renal tubular dilatation, and lymphoplasmacytic cellular infiltrates.

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**Figure 3**—Photograph of the kidney of a gnotobiotic pig 14 days after inoculation with first-passage tissue homogenate. Both kidneys contained bilaterally symmetric renal cortical hemorrhages. Scale on the bottom is in centimeters.

**Figure 4**—Photograph of the cross section of a kidney from the pig of Figure 3. Notice that the hemorrhages are largely restricted to the renal cortex. Scale on the bottom is in centimeters.

**Figure 5**—Photomicrograph of a section of lung from a gnotobiotic pig inoculated 21 days previously with first-passage tissue homogenate that contained g1-TTV and PRRSV. The alveolar spaces contain protein debris, viable and dead or dying mononuclear inflammatory cells, and acellular debris. H&E stain; bar = 0.32 µm.
after inoculation; as a group, they had the same constellation of gross and histologic lesions that were evident in group C pigs of experiment 3 and the pigs euthanized on day 32 in experiment 2. Similar to results for experiment 2, pigs in experiment 3 inoculated with PRRSV alone or g1-TTVp4 and PRRSV in combination had lymphofollicular, zonal T-cell, and reticuloendothelial proliferation. The lungs were moderately to severely affected with interstitial pneumonia, similar to the results for pigs of group A (inoculated with PRRSV alone). The renal glomeruli in the kidneys of all pigs of groups B and C were moderately to severely affected with membranous glomerulonephropathy; the 3 pigs of group B that survived until they were euthanized on day 32 had multifocal moderate to severe renal glomerular sclerosis (fibrosis).

**Discussion**

To our knowledge, this is the first report in which the experimental induction of PDNS-like cutaneous and renal lesions in swine has been described. In another report, investigators described necrotizing vascular lesions in the kidneys of specific-pathogen–free swine experimentally infected with PRRSV. In the experiments reported here, all PDNS-affected gnotobiotic pigs had negative results for PCV2, as assessed by combinations of negative results for serologic testing and PCR assay and a lack of PCV2 nucleocapsid protein in any tissues. Rather, these experiments strongly associated induction of PDNS-like lesions with g1-TTV and PRRSV coinfection. It appears that g1-TTV is critical for expression of PDNS lesions on the basis that it was detected in the passage 0 and first-passage inocula and was intentionally included with PRRSV in the inoculum for experiment 3. In retrospect, the source of PRRSV was likely 1 or more of the plasma samples (passage 0) collected from healthy feeder pigs. Further investigations into the cause of the illness in the source herd revealed that soon after plasma samples were obtained, the herd became seropositive for PRRSV, even though an aggressive vaccination program against PRRSV was in place at this facility. The source of PRRSV that infected this herd has not been identified.

Gross and histologic lesions identified as diagnostic for PDNS have been attributable to combinations of primary segmental vasculitis23 and associated microthrombosis or immune complex phenomena.10,11,22 In a field setting in Canada,1 the vasculitis detected in PRRSV-infected swine was widespread and associated with vascular lesions in most organ systems; the TTV status of these pigs is not known. In the series of experiments reported here, vascular disease was sufficiently severe that it resulted in vasculitis and hemorrhages restricted to the skin and renal cortices. It is difficult to ascribe the glomerular lesions in affected gnotobiotic pigs as attributable to an immune complex inflammatory insult per se because these lesions were detected as early as day 7 after inoculation and were of maximal intensity by day 13 or 14 after inoculation, which are time points well before a substantial immune response would be expected. In addition, pigs did not seroconvert to PRRSV antigens until day 21 after inoculation, which suggested that if immune complexes were
involved, there must have been glomerular deposition of proteins before antibodies against PRRSV were produced in sufficient quantity to participate in the genesis of glomerular lesions. Finally, there was a paucity of infiltration of neutrophils into glomeruli; neutrophils represent a cell type that is classically associated with acute immune complex phenomena. Thus, the lesions of PDNS in gnotobiotic swine were mild when compared with results for field cases of PDNS. Although the reason or reasons for this are unknown, it is likely that the microbe-free status combined with the general lack of immunologic activation associated with gnotobiotic conditions could account for the difference in severity of PDNS lesions.

Although PRRSV is typically believed to replicate in cells of monocyte and histiocyte lineages, including macrophages, a number of investigators have found PRRSV antigen or antigens and RNAs in other cell types, such as cardiomyocytes and vascular endothelia. Porcine reproductive and respiratory syndrome virus is notorious for causing persistent and intermittent viremia and appears able to coexist in subpopulations of infected swine despite protective amounts of antibodies against PRRSV. Similarly, PCV2 proteins and DNAs are prominent in cells of monocyte lineage (macrophages, histiocytes, dendritic cells, and Kupffer cells) but may also be evident as a panoptopic infection of epithelia (hepatocytes, renal tubules, and respiratory tract epithelium) and endothelia. Although vascular disease may be attributable to PRRSV, such manifestations are uncommon in PCV2-infected swine.

The search for the presumed infectious cause of PDNS has led investigators to consider the major viral pathogens of swine and certain bacterial pathogens of swine as agents that cause PDNS. Some investigators have reported that glomeruli of PDNS-affected pigs contain IgG and complement, which are findings strongly supportive of an immune complex event. The specificity or specificities of the IgG deposits are not known, but they were clearly not associated with deposition of PCV2 antigen-antibody complexes in these sites. Other investigators have suggested that the bulk of the protein that accumulates in glomeruli originates from acute-phase plasma proteins and protein components of the coagulation cascade. In either case, subsequent acute inflammatory responses further damage the structural components of glomeruli such that scarring and fibrosis are expected to develop during convalescence. The case for the involvement of PRRSV is strong because others have described vascular disease associated with PRRSV and PRRSV is known to infect vascular endothelia. However, in all published studies of experimentally induced PRRSV infections, PDNS has not been described as a consequence of PRRSV challenge exposure. Furthermore, PDNS is known to develop in PRRSV-free herds and also is found in countries free of PRRSV infection. All inoculated pigs of experiments 2 and 3 had negative results when tested for viremia against g1-TTVp1 and g1-TTVp4 and became viremic for g1-TTV DNAs in serum by day 7 to 14 after inoculation, as determined by use of an nPCR assay. The TTVs belong to the Anellovirus genus within the family Circoviridae and have been identified in humans, primates, swine, cattle, and cats. They share a structure similar to other Circoviridae as encapsulated, single-stranded, circularized DNA virions. In humans, infection with multiple TTV genotypes is common. Despite attempts to associate TTV infection with clinical disease in humans, the high incidence of subclinical TTV infection in control populations has not supported positive associations with disease. The TTVs are generally considered to be orphan viruses and a part of the normal viral flora of many host species. Porcine TTVs are presumed to be similar to their human counterparts.

Rather than directly implicating a single infectious agent as the cause of PDNS, analysis of our data suggests that the primary underlying pathogenic mechanism for development of PDNS is a rapid-onset systemic coagulation defect or DIC. The provisional diagnosis of DIC is based on the support of hemorrhage from small vessels in the dermis and renal cortices, prolonged bleeding from jugular venipuncture sites, failure of blood coagulation during necropsy, and severe thrombocytopenia (<10,000 platelets/dL; data not shown) detected in several nonclotted blood samples. It is probable that the exudation of fibrin into alveolar spaces as a component of PRRSV-associated pneumonia, microvascular endothelial damage, and microthrombosis all contributed to impaired hemostasis in the pigs reported here. In fact, the term nephropathy (rather than nephritis) speaks directly to the confusion regarding the nature of PDNS-specific renal glomerular lesions. In our series of experiments, renal glomeruli stained strongly with the Jones silver stain for basement membranes and for fibrinogen or fibrin in pigs euthanized on day 7 after inoculation (and variably in pigs euthanized on day 13 or later), which indicated that deposition of plasma proteins preceded IgG deposits. These findings, combined with obvious coagulation defects identified in the pigs, implied that DIC contributed directly to the morbidity in pigs (euthanized on days 5, 8, 13, or 14) and was undoubtedly responsible for the clinical signs of lethargy, anorexia, and diarrhea evident in all pigs inoculated with both viruses.

Perhaps now is the time to reconsider the concept of the genesis of PDNS being caused by PCV2, PRRSV, and other infectious agents. Rather, analysis of our data suggested that PDNS is a manifestation of DIC and that PDNS, regardless of the association or associations with other infectious diseases of swine, is a sudden-onset systemic coagulopathy expressed clinically as microthrombosis of dermal and renal vasculature. If this is the case, then any number or combination of endotheliotropic etiologic agents and bacterial toxemias may activate the coagulation cascade and could potentially initiate DIC and subsequently PDNS in swine.

References


