

# Edema disease: A search for a genetic link

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**Summary:** Clinical observations and diagnostic tests indicated that edema disease was a major cause of death in the nursery of a small farrow-to-finish operation in southern Minnesota. One of the three boars on the farm sired a significantly higher percentage of pigs that died in the nursery in February 1992 ( $P < .05$ ). Based on this clinical data, we investigated whether this boar was siring pigs with a genetic predisposition to edema disease. Pigs sired by this boar and pigs from another boar on the farm were weaned and transported to the National Animal Disease Center. Seven pigs from each boar were orogastrically challenged with an edema-disease causing strain of *Escherichia coli* and three pigs from each boar were challenged with a non-pathogenic strain of *E. coli*. Principals sired by either boar developed subclinical edema disease. The principals had reduced weight gain relative to the control pigs. Also, histologic evidence of subclinical edema disease (vascular necrosis) was noted in some of the principals sired by either boar. The boar that sired the pigs did not significantly influence susceptibility to subclinical edema disease in experimentally challenged pigs. The discrepancies between data from the farm and data from experimental challenge suggest that susceptibility to edema disease was not solely inherited from the boar.

In April 1991, a 70-sow farrow-to-finish swine herd in southern Minnesota experienced increased death loss in 25- to 30-lb pigs about 10-12 days after they were moved to the nursery. This herd had three boars, all purchased from the same source, and gilt replacements were selected from within the herd. Heats were skipped, and then females were mated to one of the three boars according to parity, so that new gilts were mated to the youngest boar (Boar A), parity-one females to the next oldest (Boar B) and parity-two-plus females to the oldest boar (Boar C). After weaning at 3-4 weeks of age, pigs were moved to a continuous-flow, partial-slat nursery and fed a starter diet ad libitum.

PigCHAMP® reports indicated that death loss in the nursery increased from 2.6% in the first quarter of 1991 to 15.5% in the last quarter of 1991. Clinical signs were subtle. Often, an affected pig would separate itself from the rest of its penmates and

would seem anxious or afraid. It would then develop convulsions and die, occasionally within 1 hour of the first manifestation of any problem. Stress of any kind (e.g., moving, mixing, injections) seemed to trigger clinical signs and death. Postmortem examination of a typical pig submitted in August 1991 revealed multiple foci of malacia in the medulla, with replacement by phagocytic cells (Table 1). There were peribronchial lymphocytes and interstitial thickening in the lungs, and *Bordetella bronchiseptica* was isolated from the lungs. The lung was fluorescent-antibody negative for the presence of *Mycoplasma hyopneumoniae* and swine influenza. Cultures from the brain were negative for pseudorabies. The cause of death was listed as edema disease.

Death loss continued and three piglets were submitted for postmortem examination in October 1991 (Table 1). One piglet was diagnosed with suppurative pneumonia, one with mulberry heart disease, and one had brain lesions suggestive of edema disease. In a December 1991 postmortem examination of two pigs (Table 1), beta-hemolytic *Escherichia coli* was isolated from the small intestines. The diagnosis was again edema disease.

## Clinical Observations

Immediately after the initial diagnosis of edema disease, we established a medication regime that included sulfamethazine and electrolytes. The herd responded poorly to the medication program. Pigs weaned in December 1991 and February 1992 were moved into the nursery and penned by litter to allow us to investigate the possibility of a genetic association between incidence of edema disease and sire (Table 2).<sup>1</sup> In the December 1991 weaning, no boar sired a significantly disproportionate number of pigs that died ( $P > .05$ ). However, the practitioner and producer observed different clinical signs in the pigs that died. Pigs sired by Boar B had clinical signs suggestive of edema disease (convulsions for a short period of time followed by death). Pigs sired by Boar C exhibited emaciation and labored breathing before death, suggesting pneumonia or perhaps porcine reproductive and respiratory syndrome (PRRS). In the February 1992 weaning, Boar B's offspring had significantly higher postweaning mortality than pigs sired by Boars A and C ( $P < .05$ ). Boar B sired a significantly higher percentage of pigs that died (34.0%), compared to Boars A and C (5.8 and 4.4%, respectively) (Table 2). There was a significant association between postweaning mortality and month of weaning between December 1991

BTB: National Animal Disease Center, United States Department of Agriculture, Agricultural Research Service, Ames, Iowa 50010; RAG: Faribault Veterinary Clinic, Faribault, Minnesota; RBM: Department of Clinical and Population Sciences, College of Veterinary Medicine, University of Minnesota.

Table 1

Diagnosis summary of postmortem findings

Date	# Pigs Posted	Histology	Bacteriology and Virology	Presumptive Diagnosis
August 1992	3	<ul style="list-style-type: none"> <li>multiple foci of malacia in; medulla</li> <li>interstitial thickening in lungs</li> </ul>	<ul style="list-style-type: none"> <li><i>Bordetella bronchiseptica</i> cultured from lungs;</li> <li>negative for <i>Mycoplasma hyopneumoniae</i>, swine influenza, and pseudorabies</li> </ul>	edema disease
October 1991	3	Pig 1: suppurative pneumonia; Pig 2: angiopathy in brain; Pig 3: necrosis of myocardial fibers	<i>Streptococcus suis</i> serotype 7	Pig 1: suppurative pneumonia; Pig 2: edema disease; Pig 3: Mulberry heart disease
December 1991	2	jejunum — severely congested villi; lung — mildly thickened alveolar septa	$\beta$ -hemolytic <i>Escherichia coli</i> from intestines of both pigs	edema disease (both pigs)

Table 2

Comparison of death loss by siring boar

Date of weaning		No. litters weaned (SE)	No. pigs weaned	Total weaned	No. died postweaning	Postweaning mortality (%)
December 1991	Boar A	7	8.9 (1.6)	62	1	1.6
	Boar B	8	10.8 (2.0)	86	11	12.8
	Boar C	5	9.8 (1.6)	49	6	12.2
February 1992	Boar A	5	10.4 (1.7)	52	3*	5.8
	Boar B	5	10.6 (2.3)	53	18*	34.0
	Boar C	2	12.0 (0)	24	1*	4.2

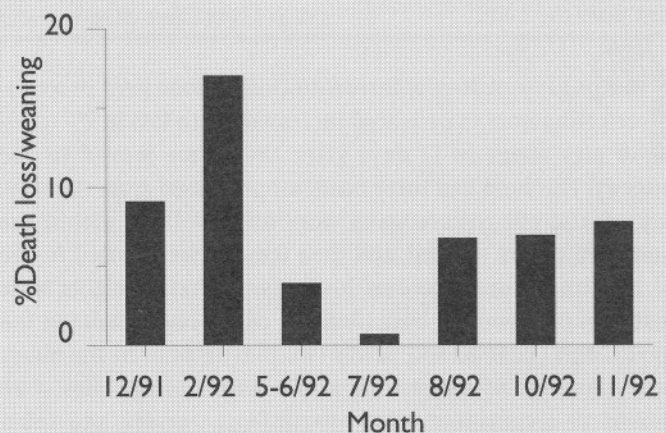
\*Death loss values are as recollected by the practitioner and producer; written records of postweaning death loss for this weaning are unavailable.

and November 1992 ( $P < .05$ , Figure 1). Mortality was higher in February (17.1%) compared to all other months combined (2.9%) ( $P < .01$ , Figure 1).

The practitioner performed necropsies on the three dead pigs from the February weaning and made a presumptive diagnosis of edema disease based on clinical signs, necropsy results, and bacteriology. A pure culture of beta-hemolytic *E. coli* was cultured from the small intestines of two of the pigs, and one of the isolates was sent to investigators at the National Animal Disease Center (NADC). This isolate contained the genes for Shiga-like toxin-IIv (SLT-IIv) and the F107 pilus. It caused histologic lesions characteristic of subclinical edema disease,<sup>3</sup> vascular necrosis in brain and intestines,<sup>2</sup> in weaned pigs inoculated orogastrically as previously described<sup>2</sup> with  $1 \times 10^{10}$  colony-forming units.

In May 1992, a new water medication program was initiated in the nursery with citric acid and electrolytes continuously present in the water. Antibiotic therapy was intermittent. Gentocin was administered for 2-3 days, stopped for 1 week and then re-initiated for 2-3 days. This treatment was associated with a significant decrease in mortality in the nursery ( $P < .05$ , Figure 1). We decided to discontinue antibiotic therapy for the August 1992 weaning, due to the cost of the antibiotics and be-

Figure 1



The percentage death loss in the nursery at each weaning from December, 1991 to November, 1992.

cause no offspring sired by Boar B were present (he had been replaced by Boar D in April 1992). After cessation of antibiotic therapy, an increase in death loss was noted in the August, October, and November 1992 weanings (Figure 1). A presumptive diagnosis of edema disease, based on clinical signs and postmortems of selected pigs, was made on a majority of the pigs that

died during this time. In December 1992, 6 lb of zinc oxide was added to each ton of starter feed. The producer reported that there were no death losses due to edema disease since the addition of zinc oxide to the feed.

## Experimental Observations

Twenty 3-week-old pigs weaned in July 1992 were transported from the herd to the NADC for studies to determine whether pigs sired by Boar B were genetically predisposed to edema disease and to compare their susceptibility to that of pigs sired by another boar. These 20 pigs were from 10 litters (two pigs per litter), five litters sired by Boar A and five by Boar B. Few offspring from Boar C were available at this time; therefore, his offspring were not included in this experiment.

One day after arrival at the NADC, 14 of these pigs (7 sired by boar A and 7 sired by Boar B) were inoculated intragastrically with  $1 \times 10^{10}$  colony-forming units of S1191,<sup>4</sup> an edema-disease causing F107<sup>+</sup> strain of *E. coli*,<sup>9</sup> as previously described.<sup>2</sup> Six of the pigs (three from Boar A and three from Boar B) served as controls and were similarly inoculated with strain 123, a nonpathogenic strain of *E. coli*.

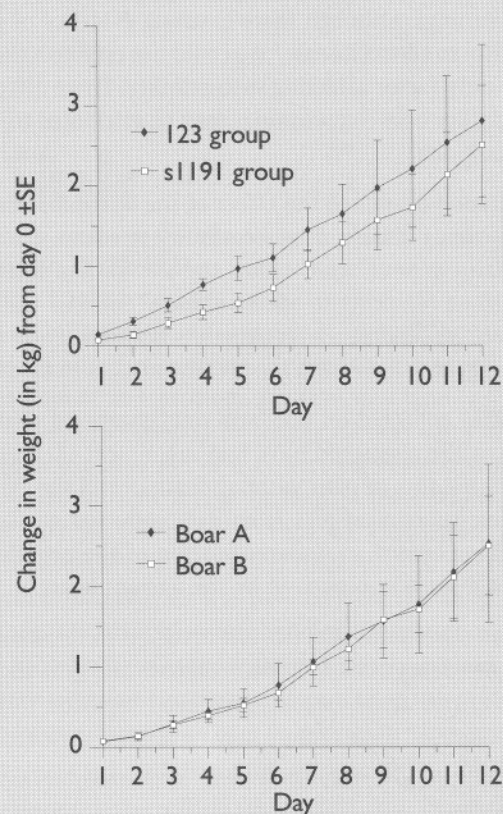
None of the pigs developed signs commonly associated with edema disease, such as ataxia, convulsions or death. Evidence of subclinical edema disease was noted in the principals but not in the controls. The weight gain of the principals was reduced relative to the controls (Figure 2). There was no significant difference in rate of gain among principals sired by either Boar A or Boar B (Figure 1). Fourteen days post-challenge, all pigs were necropsied and samples of brain, small intestine, and colon were examined for histologic evidence of vascular lesions characteristic of subclinical edema disease.<sup>2</sup> Such lesions were present in eight of 14 of the principals and in none of the controls (zero of six). There was no significant difference in the number of pigs with lesions sired by Boar A (five of seven) compared to those of Boar B (three of seven).

At necropsy, brush border membranes were collected from the ileal epithelial cells of these 20 pigs and incubated with F107-expressing *E. coli* as previously described.<sup>56</sup> The *E. coli* adhered to brush border membranes from all 20 pigs, which suggests that all pigs had intestinal receptors for F107-expressing *E. coli*. This indicates that F107-expressing *E. coli* would adhere to and colonize the small intestine, and that all 20 offspring from both Boar A and B would be susceptible to edema disease.<sup>57</sup>

## Discussion

Edema disease results from generalized vascular damage by SLT-IIv, which is produced by edema disease-causing *E. coli*. The F107 pilus has been identified in a number of edema disease-causing *E. coli* strains and helps the bacteria adhere to and colonize the intestine.<sup>8,9</sup> Genetic susceptibility to edema disease is

Figure 1



Top: daily weight gain ( $\pm$  SE) in 3-week-old pigs inoculated with edema-disease producing strain S1191 ( $n = 14$ ) or control strain 123 ( $n = 6$ ). Bottom: daily weight gain ( $\pm$  SE) in 3-week-old pigs inoculated with edema disease-producing strain S1191 that were sired by either Boar A ( $n = 7$ ) or Boar B ( $n = 7$ ).

due to the ability of F107-expressing *E. coli* to adhere to and colonize intestinal brush border cells,<sup>57</sup> and not due to differences in toxin susceptibility.<sup>10</sup> Genetic resistance is due to the inability of F107-expressing *E. coli* to adhere to and colonize intestinal brush border cells. Susceptibility or resistance to intestinal colonization is inherited in a simple Mendelian manner, with susceptibility being dominant to resistance.<sup>7</sup>

Data collected on the farm in early 1992 suggested that Boar B, in particular, was siring pigs with a genetic predisposition to edema disease. However, this genetic predisposition was not manifested in the May/June 1992 weaning or the July 1992 weaning (the last to contain pigs sired by Boar B), as edema disease was not a major problem for any of the pigs. There was an increase in mortality due to edema disease in the August, October, and November 1992 weanings. Because there were no offspring sired by Boar B present in the herd during these weanings, boars other than Boar B must have sired susceptible pigs. Additionally, the experimental observations in July 1992 at the NADC suggested that Boar B's offspring were no more susceptible to experimentally induced edema disease than were pigs sired by Boar A.

While Boar B's offspring appeared to have a predisposition to edema disease in early 1992, this predisposition was not noted in later weanings. Although there is strong evidence of genetic susceptibility to edema disease,<sup>7</sup> we could not establish that Boar B was the only factor affecting susceptibility. These differences in susceptibility between weanings may be attributed to a number of conditions:

- Our studies examined the effect of the boar on susceptibility to edema disease. As susceptibility to edema disease is a dominant genetic trait, either the sow or the boar could predispose offspring to edema disease.<sup>7</sup> Some of the differences in sire influence on genetic susceptibility at various weanings may have been genetically influenced by the sows.
- The data collected on the farm only measured death loss. Some of the pigs could have had subclinical edema disease (a reduced rate of gain without death),<sup>11</sup> and the exclusion of these subclinical pigs from data collected on the farm may have caused an underestimation of the prevalence of edema disease in pigs sired by the various boars.
- Factors other than genetics are involved in the manifestations of edema disease. Ration composition, growth rate of the pig, and other factors have been reported to have a role.<sup>12</sup> Some of these factors may have been involved in the observed differences in susceptibility between various groups of weaned pigs on the farm.

## Implications

- Pigs weaned in February 1992 and sired by Boar B had more postweaning mortality than those sired by Boars A and C. Edema disease was a common cause of postweaning mortality in this herd. However, we were unable to prove what factor(s) predisposed offspring sired by Boar B to edema disease in February 1992 with the tests that are currently available.
- Sire alone does not control susceptibility to edema disease.
- There are some factors, perhaps genetic, that predisposed Boar B's offspring to edema disease, but we were unable to determine the causative factors in this herd.

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