

**K** EFFECTS OF AN ACUTE RESPIRATORY DISEASE CHALLENGE  
ON GROWTH, THERMAL RADIATION, AND ACUTE PHASE  
PROTEIN PRODUCTION IN GROWING PIGS<sup>1</sup>

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**Summary**

Forty-seven growing pigs (initially 65 ± 2 lb) were used in a metabolism study to determine the effects of a single respiratory disease challenge on growth performance, infrared thermal radiation, and serum acute phase proteins. Thirty pigs were challenged with *Actinobacillus pleuropneumonia*, and seven pigs were assigned to an ad libitum-fed nonchallenged control group. Ten additional nonchallenged pigs were pair-fed the feed intake of an *A. pleuropneumonia*-challenged counterpart. There were five 4 d collection periods (d 4 to 7, d 8 to 11, d 12 to 15, d 16 to 19, and d 22 to 25), and the *A. pleuropneumonia* challenge occurred on d 8. Serum haptoglobin and amyloid A concentrations increased in the disease-challenged pigs compared to pigs in both nonchallenged treatments. Growth performance was decreased during the immune challenge period but partially recovered by the end of the experiment on d 25. Average surface body temperature also decreased briefly in the disease-challenged pigs compared to pigs in both nonchallenged treatments. These results suggest that a single acute respiratory disease challenge is accompanied by long-term compromises in growth performance, but performance partially recovers as the pigs overcome the immunological challenge.

(Key Words: Growing Pigs, Growth, Acute Phase Proteins, Respiratory Disease.)

**Introduction**

Chronic disease challenges that restrict lean growth potential have been minimized by wide-scale adoption of all-in/all-out, multisite production and segregated early weaning. However, short-duration, acute disease challenges still occur. An acute disease challenge usually results from a pathogen infecting immune-naive groups of pigs. The pathogen spreads rapidly within the group, and within a short period, immunity develops and performance partially recovers. Although lean growth rate has been improved dramatically in high-health production systems, acute disease challenges appear responsible for a large majority of the variation in lean growth rate between groups of pigs and among individuals within a group.

Previous research by our laboratory (KSU 1998 Swine Day, Report of Progress 819) indicated that although short-term decreases in nitrogen (N) balance and growth performance were evident, long-term effects of an enteric disease challenge by *Salmonella typhimurium* were negligible. Because economically important disease challenges in growing swine are primarily enteric or respiratory, we were curious if a similar immune response pattern would occur when *Actinobacillus pleuropneumonia* was used as the respiratory disease agent. Furthermore, we wanted to test infrared thermography (IRT) for detecting differences in surface body

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temperature associated with immunological stress. This new method to assess general health may have potential as a diagnostic tool.

Therefore, our objective was to characterize the effects of an acute respiratory disease challenge on growth performance, surface temperature profile, and hepatic acute phase proteins.

### Procedures

The experimental protocol used in this study was approved by the KSU Institutional Animal Care and Use Committee. Forty-seven nonlittermate high-health barrows (PIC C22 × L326; initially  $65 \pm 2$  lb) were obtained from the university swine herd after serological testing to ensure *A. pleuropneumonia* (*App*) negative status. Pigs were blocked by weight and time and allotted to one of three experimental treatments. Pigs were selected in groups of 12 from the same farrowing group and assigned randomly to either the *App* challenge or control group. Within the control group, pigs were assigned randomly to receive ad libitum feed intake or to be pair-fed the previous day's feed intake of an assigned *App*-challenged pig. Once the pair-fed control pigs were allotted to an *App* challenge pig, they were not reassigned at the start of each period but were fed the feed intake of the same *App*-challenged pig.

Because of a 23% mortality rate in the *App*-challenged pigs, adjustments were made to maintain the control pair-fed pigs on test. If the challenge pig of a pair died, the pair-fed control was reassigned to a new challenge pig. Every effort was made to reassign the control with a challenge pig with weight and prior feed intake pattern similar to those of the deceased challenge pig. The pair feeding was performed to elicit the responses independent of feed intake. Water was supplied at a 3.5:1 ratio with feed on a wt:wt basis, consistent with previously published research (i.e., 2.5 lb water per pound of dry feed). All pigs were fed and watered twice daily at 7:30 a.m. and 7:30 p.m. Orts were collected daily. Because of the expected greater variation in performance of the *App*

group, 30 pigs were assigned to that group, 10 pigs to the control pair-fed group, and 7 to the control ad libitum-fed group. All pigs were fed a common corn-soybean meal diet formulated to 1.15 % total lysine, without synthetic amino acids, added fat, or antibiotics (Table 1). Following a 3 d adjustment period, there were five 4 d collection periods (d 4 to 7, d 8 to 11, d 12 to 15, d 16 to 19, and d 22 to 25), and the *App* challenge occurred on d 8. These periods correlated to prechallenge, challenge, recovery (8 d), and postchallenge. The latter period was selected to be at least 14 d postchallenge. Pigs assigned to the *App* challenge treatment were inoculated intranasally with doses ranging from  $5 \times 10^7$  to  $1 \times 10^8$  cfu *A. pleuropneumonia* in 3 mL culture medium; the control pigs were given 3 mL sterile culture medium intranasally.

**Table 1. Diet Composition**

Ingredient	Percent
Corn	64.04
Soybean meal, 46.5% CP	32.89
Monocalcium phosphate	1.22
Limestone	1.10
Salt	.35
Vitamin premix	.25
Trace mineral premix	.15

<sup>a</sup>Diet was formulated to contain 1.15% lysine, .75% Ca, and .65% P.

All pigs were housed in two similar environmentally controlled rooms based upon health status and were kept in adjustable individual stainless steel metabolism cages (5 ft × 2 ft).

Serum was harvested from blood samples drawn via jugular venipuncture on d 5, 9, 13, 17, and 23 at least 2 h after feeding and analyzed for  $\alpha$ -1 acid glycoprotein (AGP), amyloid A, and serum haptoglobin concentrations.

All pigs were euthanized humanely on d 27 by intravenous sodium pentobarbital administration. After the pigs were

euthanized, they were transported to the KSU veterinary medicine diagnostic laboratory for disposal.

Average surface body temperature was collected on d 7, 8, 9, 12, 16, 20, 22, and 25, to determine the effects of feeding regimen or disease challenge. Infrared thermographs of the left side of each pig's body were taken using a stationary short wavelength (3-5  $\mu\text{m}$ ), 256  $\times$  256 focal plane array, 16°FOV lens thermal imaging camera, at a distance of approximately 6 feet from the left side of each pig. Captured images were collected by a certified technician onto a computer disk for analysis of the pig's average surface body temperature.

All data were analyzed as a randomized incomplete block design using a mixed model procedure with repeated measures. Pigs were blocked by initial weight and time with individual pig as the experimental unit. Periodic samples by pig were used for the repeated measures. Average surface body temperature was adjusted to a common temperature of 21°C. Linear and quadratic polynomial contrasts were used to determine the effects of *App* challenge over time on all response criteria. Within the challenge treatment, the challenge pigs that were actually paired with a control pig (pair-fed) were separated to compare results of disease challenge directly between pigs of similar feed intake levels.

## Results and Discussion

A disease status effect and a linear time effect ( $P < .05$ ) were observed for ADG (Table 2). The disease status effect was a result of decreased ADG from d 8 to 11 of the *App*-challenged pigs ( $P < .01$ ) and the pair-fed control pigs ( $P < .04$ ) versus the ad libitum-fed control pigs. Decreased ADG also was observed from d 12 to 15 for the pair-fed control pigs versus *App*-challenged pigs ( $P < .06$ ) or ad libitum-fed control pigs ( $P < .04$ ). The decreased ADG associated with disease challenge and pair feeding carried through for the d 8 to 25 overall post-challenge period. Average daily gain was lower for both *App* ( $P < .02$ ) and the pair-fed con-

trols ( $P < .03$ ) compared to ad libitum-fed controls.

A tendency for a disease status by time interaction was observed for ADFI ( $P < .06$ ), primarily as a result of decreases in d 8 to 11, d 12 to 15, and d 16 to 19 ADFI for both the *App* pigs and the pair-fed control pigs versus the ad libitum-fed control pigs ( $P < .05$ ). In addition, ADFI remained lower for the pair-fed control pigs versus the ad libitum-fed control pigs from d 22 to 25 ( $P < .05$ ). These decreases in ADFI resulted in lower overall postchallenge ADFI for *App* pigs and pair-fed control pigs versus ad libitum-fed control pigs ( $P < .01$ ). Average daily feed intake tended to be lower for the pair-fed pigs compared only to their pair challenge counterparts on d 16 to 19 ( $P < .09$ ) and was different on d 22 to 25 ( $P < .02$ ). These differences resulted in a tendency for decreased ADFI for the pair-fed controls versus the *App* pigs from d 8 to 25 ( $P < .09$ ). This discrepancy in d 8 to 25 ADFI is a result of the pair-fed controls being fed the net feed intake of their challenged counterpart 24 h later. Feeding the net feed intake 24 h later leads to lower feed intake because of the time lag between periods and feed wastage of the pair-fed pigs. Feed efficiency (G/F) also appeared worse for pair-fed controls compared to *App*-challenged pigs and ad libitum-fed control pigs from d 12 to 15 ( $P < .05$ ). Feed efficiency was not different between pair-fed control pigs and their challenged counterparts during any period ( $P < .54$ ). This indicates that the decrease in feed efficiency was primarily due to severe reductions in feed intake. In general, large differences in growth performance were observed during the d 8 to 11 challenge period and the d 12 to 15 recovery period. Furthermore, the differences associated with an acute respiratory challenge were not completely overcome by d 25, leading to differences in growth for the overall postchallenge period. This indicates that these pigs did not completely recover by the end of the experiment, so the effects of the respiratory challenge on growth performance are more long term.

A disease status by time interaction was observed for serum haptoglobin and amyloid

A concentrations ( $P < .01$ ; Table 3). Serum haptoglobin levels were elevated for the *App*-challenged pigs versus the ad libitum-fed control pigs and the pair challenge controls on d 9, d 13, and d 17 ( $P < .01$ ), and were highest on d 13. Serum amyloid A concentrations exhibited a pattern similar to that of serum haptoglobin levels but changed more rapidly. Serum amyloid A levels of the *App*-challenged pigs were elevated above those of both nonchallenged control treatments on d 9 ( $P < .001$ ) and d 13 ( $P < .004$ ), with the peak on d 9. Alpha-1 acid glycoprotein levels did not exhibit a similar pattern and did not differ among any treatments during any time period. The lack of an acute phase response in the control pigs indicates that our biosecurity measures were adequate, and the control pigs did not have an active immune response. The differential responses of the acute phase proteins suggest two things. First, acute phase proteins may be more disease specific than originally thought. Previous research by our laboratory using *S. typhimurium* as the disease agent resulted in elevated levels of both haptoglobin and AGP, but serum amyloid A was not measured. Secondly, consistent with earlier published research, the kinetics of individual acute phase proteins is not similar, but each appears to have its own reaction time course during the host immune response.

A disease status by time interaction was observed for average surface body temperature ( $P < .02$ ; Table 4). The interaction resulted from *App*-challenged pigs having decreased body temperature on the day of the challenge compared to that for both control treatments ( $P < .005$ ). The interaction was a further result of decreased body temperature of the pair-fed control pigs when compared to the *App*-challenged pigs 12 d after challenge ( $P < .04$ ). These differences in body temperature likely were due to decreased metabolic heat production from reductions in previous ADFI. However, the lack of consistent changes in surface body temperature suggests that the pig is an efficient regulator of internal body heat production, and that

when heat production is altered, heat loss also is moderated to maintain temperature.

A major portion of the differences in growth performance between *App*-challenged pigs and ad libitum-fed control pigs was due to feed intake differences. The differences between the pair-fed controls and ad libitum-fed controls indicate the differences in performance from feed intake. Differences in growth for the *App*-challenged pigs compared to the pair-fed controls were not as apparent and indicate that an *App* challenge reduces growth performance mainly through reductions in ADFI. We hypothesize that the reductions in ADFI are associated directly with the decreased oxygen exchange capacity of the *App*-challenged pigs' lungs, and that the decreased oxygen exchange capacity decreases the internal capacity to utilize available metabolic fuels. Thus, the pig adjusts its feed intake to meet its capacity for aerobic cellular energy utilization.

The results of this experiment are consistent with previous studies indicating that growth performance is affected negatively by immune activation. It also indicates that the intranasal dose of  $5 \times 10^7$  to  $1 \times 10^8$  cfu of *A. pleuropneumonia* is sufficient to produce an acute immune response.

Previously, we evaluated the effects of an acute *S. typhimurium* challenge on pig performance and found few or no long-term effects. This experiment suggests that an acute respiratory challenge of *A. pleuropneumonia* is longer acting, and that pig growth performance does not recover as quickly, leading to greater economic losses. These responses are more in line with long-term effects observed in the commercial swine industry. In contrast to commercial conditions, though, the lack of additional environmental stresses, such as social interaction with penmates, reinfection from other pigs, and competition for feed and water, likely contributed to a more vigorous recovery of survivors in this experiment.

The results of this experiment indicate that a single acute disease outbreak is accompanied by long-term compromises in growth

performance from both decreased feed intake and increased nutrient partitioning to the immune system.

**Table 2. Effect of *Actinobacillus pleuropneumonia* Challenge and Feeding Regimen on Growth Performance in 65- to 120-lb Pigs<sup>a</sup>**

Item <sup>b</sup>	Nonchallenged		<i>A. pleuropneumonia</i>		Probability (P <)			
	Ad Libitum	Pair Fed	Ad Libitum <sup>c</sup>	Ad Libitum				
	Trt 1	Trt 2	Trt 3	Trt 4	1 vs. 2	2 vs. 3	2 vs. 4	1 vs. 4
Pigs per treatment	7	10	10	30				
D 4 to 7								
ADG, lb	1.96 ± .37	1.67 ± .37	2.04 ± .35	1.84 ± .21	.56	.25	.68	.75
ADFI, lb	3.39 ± .35	3.26 ± .30	3.40 ± .34	3.52 ± .19	.76	.75	.40	.71
G/F	.59 ± .29	.48 ± .29	.60 ± .28	.51 ± .15	.78	.76	.93	.80
D 8 to 11								
ADG, lb	2.38 ± .38	1.42 ± .32	.95 ± .37	1.19 ± .23	.04	.34	.50	.003
ADFI, lb	3.82 ± .35	2.85 ± .30	2.83 ± .34	2.69 ± .20	.02	.99	.64	.003
G/F	.63 ± .29	.42 ± .24	.12 ± .36	.24 ± .17	.56	.54	.52	.22
D 12 to 15								
ADG, lb	2.20 ± .38	1.23 ± .32	1.66 ± .37	1.89 ± .23	.04	.35	.06	.44
ADFI, lb	4.22 ± .35	2.48 ± .30	2.74 ± .34	3.01 ± .21	.001	.57	.11	.001
G/F	.54 ± .29	-.22 ± .24	.001 ± .36	.38 ± .17	.04	.65	.04	.61
D 16 to 19								
ADG, lb	2.93 ± .38	2.43 ± .32	2.50 ± .35	2.68 ± .23	.28	.86	.49	.54
ADFI, lb	4.51 ± .35	3.23 ± .30	3.69 ± .34	3.78 ± .21	.003	.31	.09	.05
G/F	.66 ± .29	.75 ± .24	.64 ± .34	.69 ± .17	.80	.82	.83	.93
D 22 to 25								
ADG, lb	2.64 ± .38	2.54 ± .32	1.94 ± .35	2.13 ± .23	.82	.21	.26	.21
ADFI, lb	5.05 ± .35	4.21 ± .30	4.75 ± .34	4.97 ± .21	.05	.24	.02	.83
G/F	.53 ± .29	.62 ± .24	.42 ± .34	.43 ± .17	.81	.67	.49	.74
D 8 to 25								
ADG, lb	2.55 ± .25	1.92 ± .22	1.78 ± .22	1.92 ± .23	.03	.71	.89	.02
ADFI, lb	4.40 ± .24	3.18 ± .21	3.50 ± .21	3.57 ± .15	.01	.27	.09	.01
G/F	.60 ± .18	.40 ± .16	.31 ± .22	.43 ± .13	.34	.76	.86	.36

<sup>a</sup>Forty seven pigs were used in a randomized incomplete block design with individual pig as the experimental unit. Effects were analyzed using a mixed model with repeated measure.

<sup>b</sup>A challenge effect and a linear time effect were observed for ADG (P<.05). A challenge effect and both linear and quadratic time effects were observed for ADFI (P<.05). This resulted in a tendency for a challenge by time interaction for ADFI (P<.06).

<sup>c</sup>Treatment 3 is a subset of challenged pigs from treatment 4 that were paired with a pair-fed pig in treatment 2.

**Table 3. Effect of *Actinobacillus pleuropneumonia* Challenge and Feeding Regimen on Serum Acute Phase Proteins in 65- to 120-lb Pigs<sup>a</sup>**

Item <sup>b</sup>	Nonchallenged		<i>A. pleuropneumonia</i>		Probability (P <)			
	Ad Libitum	Pair Fed	Ad Libitum <sup>c</sup>	Ad Libitum				
	Trt 1	Trt 2	Trt 3	Trt 4	1 vs. 2	2 vs. 3	2 vs. 4	1 vs. 4
Pigs per treatment	7	10	10	30				
D 5								
Haptoglobin, mg Hgb/dL	49.9 ± 9.0	48.9 ± 7.7	53.8 ± 7.6	48.8 ± 5.1	.93	.66	.99	.91
AGP, μg/mL	720 ± 99	570 ± 89	597 ± 87	610 ± 70	.15	.77	.60	.21
Serum amyloid A, μg/mL	13.0 ± 8.2	8.6 ± 6.5	5.6 ± 5.1	5.4 ± 4.2	.67	.62	.66	.39
D 9								
Haptoglobin, mg Hgb/dL	49.4 ± 9.0	50.3 ± 7.7	92.8 ± 7.6	85.3 ± 5.1	.93	.001	.001	.001
AGP, μg/mL	689 ± 99	608 ± 89	628 ± 87	615 ± 71	.44	.83	.93	.41
Serum amyloid A, μg/mL	7.0 ± 8.2	5.1 ± 6.5	35.6 ± 5.1	47.9 ± 4.1	.85	.001	.001	.001
D 13								
Haptoglobin, mg Hgb/dL	42.1 ± 9.0	47.0 ± 7.7	98.4 ± 7.6	102.1 ± 5.5	.66	.001	.001	.001
AGP, μg/mL	676 ± 99	605 ± 89	622 ± 87	563 ± 73	.49	.85	.60	.21
Serum amyloid A, μg/mL	8.1 ± 8.2	8.8 ± 6.5	30.1 ± 5.3	34.0 ± 4.4	.94	.006	.001	.004
D 17								
Haptoglobin, mg Hgb/dL	37.9 ± 9.0	33.3 ± 7.7	59.2 ± 7.9	63.8 ± 5.8	.68	.02	.001	.01
AGP, μg/mL	673 ± 99	483 ± 89	584 ± 89	550 ± 75	.07	.30	.43	.18
Serum amyloid A, μg/mL	1.8 ± 7.8	2.3 ± 6.8	12.0 ± 5.7	10.7 ± 4.7	.97	.26	.28	.30
D 23								
Haptoglobin, mg Hgb/dL	27.5 ± 9.0	32.1 ± 7.7	38.0 ± 7.6	39.8 ± 5.6	.68	.59	.37	.21
AGP, μg/mL	586 ± 99	392 ± 89	554 ± 87	488 ± 73	.06	.08	.23	.28
Serum amyloid A, μg/mL	1.5 ± 7.8	6.0 ± 6.5	7.2 ± 5.7	4.7 ± 4.5	.64	.94	.86	.71

<sup>a</sup>Forty seven pigs were used in a randomized incomplete block design with individual pig as the experimental unit. Effects were analyzed using a mixed model with repeated measure.

<sup>b</sup>A challenge effect and a linear time effect were observed for ADG (P<.01). A challenge by time interaction, and linear and quadratic time effects were observed for serum haptoglobin and serum amyloid A (P<.01).

<sup>c</sup>Treatment 3 is a subset of challenged pigs from treatment 4 that were paired with a pair-fed pig in treatment 2.

**Table 4. Effect of *Actinobacillus pleuropneumonia* Challenge and Feeding Regimen on Surface Body Temperature (°C) in 65- to 120-lb Pigs<sup>a</sup>**

Item <sup>b</sup>	Nonchallenged		<i>A. pleuropneumonia</i>		Probability (P <)			
	Ad Libitum	Pair Fed	Ad Libitum <sup>c</sup>	Ad Libitum				
	Trt 1	Trt 2	Trt 3	Trt 4	1 vs. 2	2 vs. 3	2 vs. 4	1 vs. 4
Pigs per treatment	5	7	7	17				
Day								
-1	34.1 ± .4	34.4 ± .4	33.9 ± .4	33.9 ± .3	.50	.52	.14	.62
0	34.5 ± .4	34.2 ± .3	33.3 ± .3	33.3 ± .3	.58	.04	.005	.002
1	34.4 ± .4	34.4 ± .3	34.2 ± .3	34.0 ± .3	.97	.47	.18	.25
4	34.5 ± .4	33.5 ± .4	34.3 ± .4	34.2 ± .3	.04	.23	.07	.40
8	34.3 ± .4	33.2 ± .3	33.6 ± .3	33.7 ± .3	.01	.38	.17	.10
12	35.0 ± .4	33.9 ± .3	34.5 ± .3	34.6 ± .3	.01	.25	.04	.26
14	34.3 ± .4	33.9 ± .3	33.7 ± .3	33.7 ± .3	.38	.67	.48	.11
18	34.0 ± .4	34.1 ± .4	34.2 ± .4	34.2 ± .3	.90	.62	.69	.61

<sup>a</sup>Forty seven pigs were used in a randomized incomplete block design with individual pig as the experimental unit. Effects were analyzed using a mixed model with repeated measure.

<sup>b</sup>A challenge by day effect was observed for average surface body temperature (P<.02).

<sup>c</sup>Treatment 3 is a subset of challenged pigs from treatment 4 that were paired with a pair-fed pig in treatment 2.

