Evaluation of the effects of immune system activation versus disease on pig growth

A.P. Schinckel[1], PhD; L.K. Clark, DVM, PhD; A.L. Grant, PhD; G.G. Stevenson, DVM, PhD; J.J. Turek, PhD
[1]Department of Animal Sciences, Purdue University

Management programs for improving the health status of pigs have been developed and are being refined. Examples of these technologies include all-in—all-out (AIAO) production, off-site nurseries, grow-finish units, and medicated early weaning programs. These health management programs produce differences in the duration and intensity of individual and combined diseases and an animal's immune system response to antigens. In most cases, immune system responses are a reflection of the disease status. The effects of initial antigen exposure and disease effects must be separated and evaluated to make further refinements in commercial production health management programs. Two trials have been conducted to evaluate the impact of immune system activation via antigenic challenge on pig growth.

Trial 1: Effect of antigenic challenges on growth and composition

One hundred-forty terminal cross barrows were weaned and transported to an off-site nursery at 10–14 days of age, i.e., segregated early weaned (SEW). Seventy-six of these barrows served as controls and received no antigenic challenge and were part of a lean growth evaluation trial. The remaining 64 barrows received either a moderate or more intense level of antigenic challenge. Antigens, including a lipopolysaccharide and vaccines (either modified live or killed), were given between 12 and 84 days of age, at times corresponding to expected commercial exposure based on antibody titers from 12–84 days of age (**Tables 1a and b**). Pigs were randomly assigned to nursery pens with 8–9 pigs per 4 × 4 ft. pen. The pigs were fed a series of diets designed to maximize lean growth (**Table 2**). Nursery pigs were weighed and feed consumption was recorded at 7 to 10 day intervals. At 52 days of age, the pigs were transported to an open-front building. Within each treatment group, four pigs were randomly assigned to each 6 × 12 ft. pen.

In the open-front unit, pigs were weighed and feed consumption was recorded biweekly. Real-time ultrasonic measurements, including tenth rib backfat depth and loin eye area, were taken from approximately 70 lb body weight at biweekly intervals until the day before slaughter. The pigs were slaughtered when the pen averaged approximately 260 lb. Midline carcass backfat, carcass length, and optical probe measurements were recorded.

Table 1a: The sequence of antigens used for moderate and intense antigenic challenges.

	Antigenic Challenge	
Age	Moderate	More Intense
12	V1	V1
21	V2	V2
28	V1'	V1
35		V2
42		V3
49	V4	V4
63		V3
84	V4	V4

The mean live weights for the three antigen treatments are shown in **Table 3**. The antigen treated pigs were significantly lighter than the control pigs at 28 days of age. The magnitude of the weight differences between the three treatments increased up to 107 days of age and decreased thereafter. After 107 days of age, the antigen treated pigs grew faster ($p<.05$) than the control pigs, at 2.56, 2.52 and 2.24 lb mean average daily gain, for the intense, moderate and control pigs, respectively. The antigen challenged pigs required 5.6 more days to reach 230 lb and 3.6 more days to reach the mean end weight of 264 pounds.

In the nursery, antigen challenged pigs had significantly lower growth rates and feed intakes (**Table 4**). There were no significant differences in feed conversion. The means for the growth rate, feed intake and feed conversion are shown in **Table 5**. The unadjusted means and means adjusted for initial weight of the period have different interpretation. From 53–93 days of age, the antigen challenged pigs grew more slowly and had lower feed intakes ($p<.001$). However, when the data are adjusted for differences in initial weight of each growth phase, the feed intakes and growth rates are almost identical. The majority of the reduced growth and feed intake in the antigen treated pigs is caused by their lighter initial weight. Overall, when differences in initial weight are accounted for, there are no significant treatment effects from 54 days to an average weight of 264 pounds.

Table 1b: Antigen information

Antigen	Source
V1	
Strepbac® w/Imugin®	(*Strep suis* bacteria) Oxford Lab
Parashield'	(*Hemophilus parasuis* bacteria) Grand Lab
Litterguard LT	(*E coli* vaccine) SmithKline Beecham
E coli Lps	sustype 055:B5 50 mg/kg in PBS Sigma Chemical
V1'	
E coli Lps	sustype 055:B5 50 mg/kg in PBS Sigma Chemical
V2	
Toxivac AD	(Atrophic Rhinitis, Past mult AαD toxigenic strains) Nobl Lab
SC-54	(Salmonella) Nobl Lab
V3	
Maxi Vac-Flu	(Influenza) Syntro-Vet
V4	
Respisure'	(*Mycoplasma hyopneumonia*) SmithKline Beecham
PneuPac"	(Actinobacillus, pleuro pneumonia bacteria, Serotypes 1,5,7) Schering Plough

Table 2: Formulated values (as-fed basis) of crude protein (CP), lysine and percent added fat of diets fed during each growth phase*

Diet	Age, day	CP	% Lysine	Feed Additive	% Fat Added
Nursery	12-22	22.1	1.55	Apramycin	2.0
Nursery	23-44	21.8	1.50	Carbadox	3.5
Nursery-Grower	45-72	20.0	1.32	Carbadox	5.0
Transition	73-85	19.0	1.25	Tylosin	5.0
Grower	86-107	18.0	1.00	Tylosin	4.0
Finisher	107-market	17.1	.90	Tylosin	4.0

*The first nursery diet contained 6% spray dried porcine plasma, 24% lactose, and 5% fish meal, the second nursery diet contained 2% spray dried whole blood meal, 5% fish meal and 16% lactose. The nursery grower diet contained 1.0% spray dried whole blood and 1.0% fish meal.

The mean adjusted backfat thickness and loin eye area measurements are shown in **Table 6**. Overall, there are no significant differences between the antigen treatments for backfat thickness. However, the antigen treated pigs did have substantially smaller loin eye areas at 72 lb liveweight. The differences in loin eye area became smaller as the pigs become heavier. At 264 lb liveweight the antigen challenged pigs had only a 0.17 in^2 difference in loin eye area.

There were no significant differences in dressing percent, optical probe percent lean, or backfat depth (**Table 7**). Carcasses of the control pigs tended to have larger loin depths ($p<.10$) and longer carcasses than antigen treated pigs ($p<.04$).

Insulin-like growth factor-1 (IGF-1), a growth factor important in regulating growth, was different at 63 days of age ($P<.05$) for the three treatments. Mean concentrations were 61.2, 103.0, and 62.1 ng/mL for control, moderate, and intense treatments, respectively.

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Table 3: Mean liveweights and days to 230 and 264 pounds liveweight

	Control		Moderate		Intense		
Age	Mean	SE	Mean	SE	Mean	SE	Prob
12.0	8.8	.13	8.8	.20	8.6	.20	.91
19.0	11.6	.17	11.2	.26	11.1	.26	.60
23.0	14.3	.22	13.0	.34	13.4	.34	.09
28.0	16.8	.27	15.0	.41	15.2	.41	.04
33.0	23.1	.38	20.6	.59	20.3	.59	.01
44.0	37.4	.58	34.7	.92	31.7	.92	.001
54.0	51.5	.71	45.2	1.10	43.9	1.10	.001
65.0	64.5	1.3	56.7	2.0	51.9	2.0	.001
79	94.1	1.9	82.0	2.9	78.5	2.9	.001
93	128.0	1.9	112.4	3.0	108.6	3.0	.001
107	162.1	2.5	142.0	3.8	138.7	3.8	.001
121	197.0	2.5	180.4	3.8	176.0	3.8	.001
135	227.3	2.6	209.6	4.0	204.3	4.0	.001
146	253.0	2.6	239.6	4.0	239.2	4.0	.005
Days to 230 lb	136.6	.9	142.0	1.4	142.4	1.4	.001
Days to 264 lb	151.8	.8	155.6	1.3	156.0	1.3	.02

Table 4: Impact of antigenic challenge on rate and efficiency of growth in nursery pigs

	Control		Moderate		Intense		
	Mean	SE	Mean	SE	Mean	SE	Prob
Period 1 - 12-23 days of age							
ADG, lb/day	.49	.03	.38	.04	.43	.04	.04
Feed Intake lb/day	.64	.02	.49	.04	.54	.04	.05
Feed Conversion	1.30	.08	1.28	.13	1.27	.13	.98
Period 2 - 23-44 days of age							
ADG, lb/day	1.10	.04	.98	.06	.87	.06	.02
Feed Intake lb/day	1.54	.04	1.33	.07	1.24	.07	.004
Feed Conversion	1.70	.06	1.38	.10	1.42	.10	.89
Period 3 - 44-54 days of age							
ADG, lb/day	1.39	.05	1.15	.08	1.23	.08	.04
Feed Intake lb/day	2.32	.03	1.82	.05	1.93	.05	.01
Feed Conversion	1.66	.10	1.58	.15	1.57	.15	.22

Table 5: Least square means for growth rate, feed intake, and feed conversion in finishing

	Unadjusted Means							Means adjusted for initial weight						
	Control		Moderate		Intense			Control		Moderate		Intense		
	Mean	SE	Mean	SE	Mean	SE	Prob	Mean	SE	Mean	SE	Mean	SE	Prob
54-93 days of age														
Avg. daily gain, lb/d	1.96	.03	1.78	.04	1.72	.04	.001	1.88	.03	1.86	.04	1.82	.04	.30
Feed intake, lb/d	4.80	.07	4.18	.11	4.10	.11	.001	4.50	.08	4.49	.09	4.49	.09	.99
Feed Conversion	2.45	.04	2.36	.06	2.38	.06	.18	3.40	.04	2.41	.06	2.46	.06	.59
93 days of age - 264 lb														
Avg. daily gain, lb/d	2.35	.04	2.28	.06	2.34	.06	.35	2.32	.04	2.34	.06	2.40	.06	.23
Feed intake, lb/d	8.02	.06	7.73	.10	7.81	.10	.002	7.86	.06	7.89	.09	7.83	.09	.61
Feed Conversion	3.43	.04	3.43	.06	3.27	.06	.08	3.42	.04	3.44	.06	3.30	.06	.18
54 days of age - 264 lb														
Avg. daily gain, lb/d	2.18	.04	2.10	.06	2.11	.06	.24	2.12	.04	2.10	.06	2.19	.06	.47
Feed intake, lb/d	6.73	.04	6.44	.07	6.31	.06	.002	6.57	.04	6.61	.06	6.54	.06	.67
Feed Conversion	3.11	.04	3.09	.06	3.00	.05	.39	3.18	.04	3.05	.06	2.98	.06	.23

Table 6: Least squares means for real-ultrasonic measurements.

	10th Rib Backfat, in							Loin Eye Area, in^2						
	Control		Moderate		Intense			Control		Moderate		Intense		
Weight	Mean	SE	Mean	SE	Mean	SE	Prob	Mean	SE	Mean	SE	Mean	SE	Prob
72	.32	.01	.32	.02	.33	.02	.90	2.22	.03	1.90	.05	1.84	.05	.004
88	.40	.01	.42	.02	.40	.02	.50	2.60	.03	2.53	.05	2.43	.05	.05
120	.54	.01	.55	.02	.54	.02	.92	3.26	.04	3.25	.06	3.11	.06	.21
153	.69	.02	.70	.03	.70	.03	.98	3.77	.04	3.60	.06	3.50	.07	.10
189	.85	.02	.86	.03	.83	.03	.82	4.56	.06	4.36	.10	4.26	.10	.14
248	1.19	.03	1.17	.04	1.15	.04	.85	5.59	.07	5.40	.09	5.36	.09	.17

*Adjusted for liveweight.

Table 7: Least square means for the carcass measurements*

	Control		Moderate		Intense		
Variable	Mean	SE	Mean	SE	Mean	SE	Pr
Dressing percentage	74.1	0.35	74.0	0.44	73.7	0.44	.42
Fat depth, in	1.20	0.04	1.25	0.05	1.21	0.05	.61
Muscle depth, in	2.25	0.073	2.17	0.04	2.16	0.04	.09
Optical probe, % lean	49.7	0.38	48.8	0.46	49.2	0.46	.30
MidlineCarcass Measurements							
Backfat last rib, in.	1.30	0.04	1.36	0.06	1.31	0.06	.52
Backfat 10th rib, in.	1.35	0.04	1.37	0.06	1.38	0.06	.82
Carcass length, in.	31.8	0.13	31.2	0.22	31.0	0.22	.04

*Adjusted for liveweight.

Table 8: Effect of antigen exposure and commercial health status on liveweight growth, thymus weight, and IGF-1 levels

		Treatment		
Variable	Age	SEW	SEW + Antigens	Commercial Herd
Liveweight, lb	24	16.6	17.7	13.2
	95	132.7	127.5	93.5
Thymus weight, g	24	19.9	17.9	9.3
	95	205.8	203.2	71.4
IGF-1 ng/mL	24	92.9	96.5	20.1
	95	121.7	114.4	50.5
pg TNFα/mg DNA	95	10.5	37.1	61.6

5 pigs per treatment per age.

Trial 2: Evaluation of antigen Exposure versus disease exposure

The second trial utilized three treatments: (1) conventional commercial health status pigs managed via continuous flow; (2) SEW; and (3) SEW with the moderate level of antigen exposure to produce similar immune system activation as the commercial herd environment. Large thymus glands have been previously observed in medicated early weaned pigs.[1] Immune system activation did not reduce growth rates, cause thymus atrophy, or lower IGF-1 levels to the extent of commercial environment exposure to disease (Table 8). The increase in IGF-1 levels at 95 days of age is in agreement with the 30% higher IGF-1 levels in medicated early weaned pigs at 49 days of age.[2]

Discussion

The sequence of antigens was designed to simulate commercial herd antigen exposure. During the time of antigen challenge, treated pigs in trial one had substantially lower feed intakes, lower growth rates, and smaller loin eye areas than control pigs.

Table 9: Average daily gain, days to 230, average daily feed intake, and feed conversion of finishing pigs in AIAO versus conventional continuous use management system*

Item	ADG	Days to 230	Average Daily Feed Intake	F/G
AIAO	1.73 ±.01***	172 ± 0.8***	5.26 ±.05***	3.03 ±.02
Continuous	1.54 ±.01	183 ± 1.1	4.89 ±.05	3.18 ±.03
Barrows	1.66 ±.01**	176 ± 1.0**	5.26 ±.04***	3.18 ±.02
Gilts	1.82 ±.01	180 ± 1.0	4.89 ±.04	3.03 ±.03

*Summary of 6 replications, total of 132 pens. (Cline et al., 1992)
**P<.05, *** P<.01

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When the growth performance of SEW and conventional weaned pigs have been compared, the largest percentage improvement in growth has been from weaning to 7-10 weeks of age. This is likely due to the fact that young pigs are in an energy dependent growth phase, primarily gaining lean (i.e., protein and water) and thus are sensitive to changes in energy or protein intake.[3]

Although designed to reflect commercial herd antigen exposure, the antigenic challenges to SEW pigs in the two trials did not reduce performance level to those observed in commercial production. Barrows raised in the source commercial herd via conventional weaning followed by all-in—all-out management, averaged 179 days to 230 lb with 1.05 in backfat at 245 lb liveweight. The antigen challenges provided in the first trial only accounted for 13% (5.6/43) of the difference between the control and commercial pigs for days to 230 pounds. Eighty-seven percent, 37.4 days of the control versus commercial environment differences must be accounted for by the combined effects of increased immune system activation via actual disease, direct disease effects via cell damage, and release of other response mediators, management, and overall environmental conditions.

All-in—all-out management and mycoplasmal pneumonia vaccination research also indicate that severity and/or duration of disease causes depressed growth and feed intake. In a Purdue study, AIAO pigs grew faster and more efficiently than the controls[4] (P<.01). Average daily gain and days to 230 for the AIAO was 0.19 lb more and 11 days less, respectively, than the control group (Table 9). Ninety-four percent of the control pigs had lung lesions indicating the presence of pneumonia, with an average of 15.1% of the lung infected. Fifty-two percent of the AIAO pigs had evidence of lesions with an average of 4.1% of the lung infected.

Research evaluating isolation-management procedures also indicate that the level of disease exposure and clinical signs of disease affect growth. Research was conducted in which pigs weaned at four weeks of age were assigned to one of three treatments; treatments included isolation at four weeks of age, isolation at eight weeks of age, and continuous flow managed grow-finishing barn.[5] Although mycoplasma titer levels were similar for the two 8 week treatments (isolation or disease exposure), the pigs exposed to more substantial disease exposure had substantially increased coughing (8 vs. 0 pigs of 16 per treatment), lung lesions (16 vs. 0), percent lung involvement (10.4 vs. 0%) and slower growth (62.6 vs. 67.0 kg at 18 weeks of age).

A trial conducted with a mycoplasmal pneumonia vaccine (Respisure, SmithKline Beecham) also indicated that the duration and/or severity of disease affected pig growth.6 One hundred-fifty pigs were randomly allocated to one of three treatments. Treatment one pigs were injected with a *Mycoplasma hyopneumoniae* vaccine at 7 and 21 days of age; treatment two pigs were vaccinated at 6 and 8 weeks of age, and treatment three pigs served as non-vaccinated controls. At two months of age, all pigs were moved into pens within a continuous-flow, growing-finishing facility. Twenty-one control pigs, 13 treatment 1 pigs, and 5 treatment 2 pigs were observed coughing between 2.5 and 5.5 months of age. Pigs in both vaccinated groups gained 7.7% more than the control pigs. (P<.05) during the finishing phase. Days to 230 lb for pigs in both vaccinated groups was nine days less than control pigs. Pigs in both vaccinated groups consumed more feed (+7.9%) than the control pigs during the finishing phase.

Many investigators have used the amount of respiratory disease at slaughter as the measure to relate to pig performance. Using radiographic studies, it was found that cumulative lifetime pneumonia was significantly correlated to live weight at 180 days of age (r2=.42) so that every 1% increase in average lifetime pneumonia reduced 180 day weights by 3.22 pounds. From farm to farm with 21 to 23 day weaning, many herds may have similar antibody levels but have different levels of disease. Stocking density, cubic feet of air space per pig, production system (continuous flow; all in/all-out) and disease interactions (PRV, PRRS) likely all play a role in increasing the duration and severity of respiratory disease.[8] PRRS in a group of 90 SEW boars has little effect on growth. The boars sneezed and reduced feed consumption for 2 to 3 days and continued to grow rapidly. The boars averaged 142 days to 230 pound live weight.

Enteric diseases can also substantially reduce pig growth. Intestinal tissue damage can reduce absorption of nutrients for a prolonged period of time. SEW pigs are not enteric disease free pathogenic. *E. coli* have been found in 28 and 56 day old SEW pigs without clinical signs of the disease. Injection of *E. coli* LPS has not been shown to be a good model of actual disease as its effect can be almost entirely inhibited by oral aspirin or injections of indomethacin.[9] Serial injections of *E. coli* LPS can cause desensitization. Certainly, serial injection of *E. coli* LPS does not reproduce the reduced growth as do the actual chronic disease symptoms. In these trials and others, injection of antigens did not reduce growth, increase the variability in growth rate, or cause the morbidity of actual disease. Also, IGF-1 levels could not be reduced by antigen exposure as in pigs with actual disease. Based on these results and the results of others, it is likely that stress-immune system responses, occurring when the animal is in a prepathological or pathological state, reduce lean growth (protein accretion) and not the initial antigen exposure and recognition.[10]

Summary

The study of disease, immune system activation, environmental, and stress effects on swine growth is in its infancy. We hypothesize that immune system activation is among several correlated responses of the pig to disease that result in reduced growth performance. Thus, additional research in this area is needed if the swine industry is to realize the genetic potential of high lean growth genotypes to result in the most economical production of lean pork.

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