ORIGINAL RESEARCH

Effects of antigenic challenge on growth and composition of segregated early-weaned pigs

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Summary: *The purpose of this study was to evaluate the impact of antigen exposure on pig growth from 12 days of age to market weight. One hundred forty barrows were weaned at 10–14 days of age and placed in an off-site nursery. Control barrows (n = 76) received no antigenic challenge. Sixty four barrows, 32 per treatment, received either a moderate or an intense level of antigenic challenge. Antigens, including an* Escherichia coli *lipopolysaccharide and vaccines, were administered at 12 to 84 days of age, which corresponds to ages of exposure to infectious agents on commercial farms between 12 and 84 days.*

Antigen-treated pigs weighed significantly less (P < 0.05) than control pigs on all weigh days between 28 days of age and market; however, after 107 days of age, the antigen-treated pigs grew 11% faster than the control pigs. Antigen-challenged pigs required approximately 4 days more than control pigs to attain 120 kg (264 lb).

Although loin eye area, optical probe muscle depth, and carcass lengthwere initially greater for control barrows, due to compensatory lean growth in the antigen-treated pigs after 107 days of age, the treatment differences in lean mass decreased to 1.4 kg at 120 kg (264 lb).

The antigenic challenges used in this trial explained only a small percentage of the differences in performance between minimal-disease segregated early-weaned pigs used in this experiment and contemporary conventionally weaned commercial pigs.

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Pork producers have the economic incentive to produce lean pork as efficiently as possible. Each producer should consider cost-effective management changes to maximize expression of genetic potential of their pigs. Strategies for producing high-health pigs, including segregated early weaning (SEW) and all-in–all-out (AIAO) production, can be used to maximize the profitability of lean pork production.[1–3]

Research in several species indicates that an animal's immune system response to disease organism antigens is a major cause of reduced growth rates. Poultry injected with antigens to common disease organisms express both decreased protein accretion and reduced feed intake.[4] The decreased protein accretion rates observed in chicks are mediated through various cytokines. These antigen-induced cytokines cause a cascade of physiological changes, including decreased levels of growth hormone and insulin-like growth factor-1 (IGF-1).[5] Recent research indicates that medicated early-weaned pigs accrue protein at higher rates[6] and have higher levels of IGF-1 than conventionally reared pigs.[7]

Refining health-management programs requires a greater understanding of the underlying biological mechanisms by which diseases reduce lean growth rate. Different health management programs produce differences in health status, i.e., differences in both the duration and intensity of individual and combined diseases, and variation in the animal's immune system response to antigens. In most cases, immune-system responses are a reflection of disease status. The effects of initial antigen exposure and effects of disease must be separated and evaluated to assure producers that vaccine use will not have the same effect on performance as the disease for which it is used. The objective of this trial was to evaluate the impact of immune system activation, via antigenic challenge (vaccination), on pig growth from 12 days of age to market weight.

Materials and methods

Treatments

One hundred forty terminal-cross barrows were weaned and transported to an off-site nursery at 10–14 days of age. Seventy-six control barrows received no antigenic challenge. Sixty-four barrows received either a moderate or more intense level of antigenic challenge (32 barrows per treatment). Antigens, including

an *Escherichia coli* lipopolysaccharide and vaccines, either modified-live or killed, were given between 12 and 84 days of age, at times corresponding to expected commercial exposure (Table 1). A lipopolysaccharide is a polymer of lipid and saccharide molecules that has been extracted and purified from the cell walls of Gram-negative bacteria. Lipopolysaccharides have been used by researchers to induce acute antigen challenges.[4] Vaccines used in this trial would be expected to produce a milder but more prolonged antigenic challenge.

Housing

Pigs were randomly assigned to pens in the SEW unit at the Purdue University swine research center with eight to nine pigs per pen (1.22m × 1.22m [4.00 × 4.00 ft]). Treatments were randomly assigned to pens with nine control pens and four pens each for the moderate and intense treatments. All pigs were fed the same 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 1.80 × 3.80m (5.91 ft × 12.47 ft) pen with 19 control pens, and eight pens each for the moderate and intense treatments. While in this open-front unit, pigs were weighed at 61 and 68 days of age. The initial start date for open-front unit data was assigned when the pigs in the pen averaged approximately 27.2 kg (60 lb) at either 61 or 68 days of age. From that date, pigs were weighed and feed consumption was recorded biweekly.

Growth performance

Days-to-104 kg (230 lb) were estimated using the age and weight at which each pig was closest to 104 kg (230 lb). Days-to-120 kg (264 lb) was estimated using the end-test age and weight. National Swine Improvement Federation (NSIF) equations were used to estimate the age to 104 and 120 kg (230 and 264 lb).

Body composition measurements

Real-time ultrasonic measurements, including tenth rib backfat depth and loin eye area, were taken by an NSIF-certified technician at biweekly intervals beginning at approximately 27.2 kg (70 lb) bodyweight, and ending the day before slaughter. The pigs were slaughtered at weekly intervals when the weights of the pigs in the pen averaged approximately 120 kg (260 lb). Midline carcass backfat, carcass length, and optical probe measurements were obtained. Prediction equations derived from a large dissection experiment were used to predict carcass fat-free lean mass from real-time ultrasonic measurements.

Table 1

The sequence of antigens used for moderate and intense antigenic challenges

	Antigenic Challenge	
Age (days)	Moderate	More intense
12	V_1	V_1
21	V_2	V_2
28	V_1	V_1
35		V_2
42		V_3
49	V_4	V_4
63		V_3
84	V_4	V_4

V_1: Strepbac® w/Imugin®(*Streptococcis suis* bacterin, Oxford Lab, Worthington, MN); Parashield™ (*Haemophilus parasuis* bacterin, Grand Lab, Larchwood, IA); Litterguard LT (*E. coli* vaccine, Pfizer, West Chester, PA); *E.coli*Lps (serotype 055:B5, 50 mg/kg in PBS, Sigma Chemical)

V_1': *E.coli*Lps (serotype 055:B5, 50 mg/kg in PBS, Sigma Chemical)

V_2: Toxivac AD (*Bordetella bronchiseptica*, *Pasteurella multocida* A ∝ D toxigenic strains, NOBL Lab, Sioux Center, IA); SC-54 (*Salmonella cholerasuis*, NOBL Lab, Sioux Center, IA

V_3: Maxi Vac-Flu (swine influenza virus, Syntro-Vet, Lenexa, KS)

V_4: Respisure™ (*Mycoplasma hyopneumoniae*, Pfizer); PneuPac® (*Actinobacillus pleuropneumoniae* bacterium, Serotypes 1,5,7; Schering Plough, Omaha, NE)

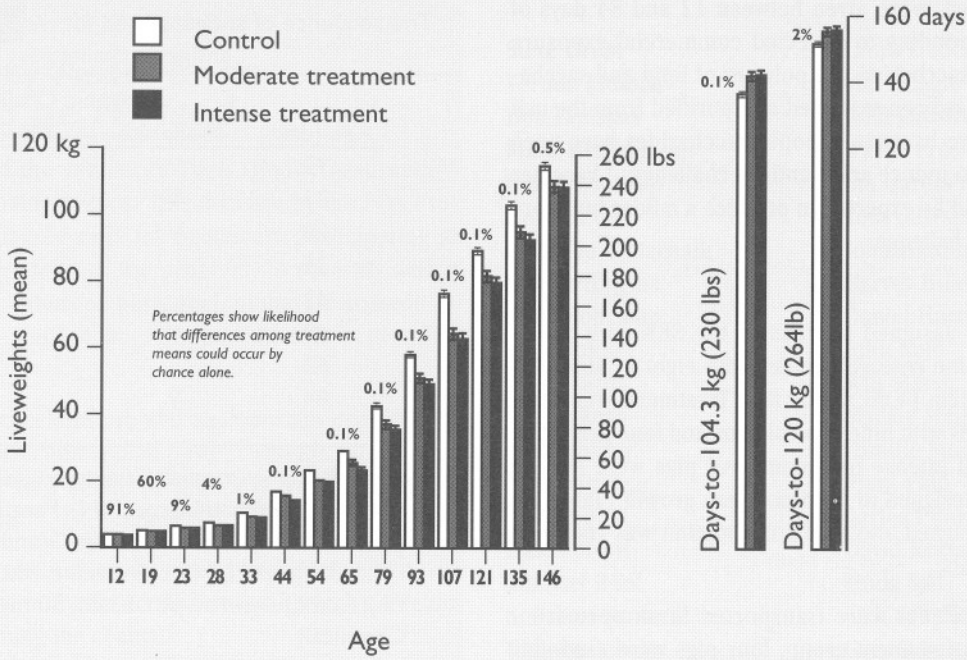
Table 2

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

Diet	Age, days	CP	% Lysine	Feed additive	% Added fat
Nursery I	12–22	22.1	1.55	Apramycine	2.0
Nursery II	23–44	21.8	1.50	Carbadox	3.5
Nursery-grower I	45–72	20.0	1.32	Carbadox	5.0
Transition II	73–86	19.0	1.25	Tylosin	5.0
Grower	87–107	18.0	1.00	Tylosin	4.0
Finisher	108–market	17.1	0.90	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.

Figure 1



Mean liveweights and days-to-104.3 and -120 kg liveweight. Percentages indicate probability that the differences among treatment means could occur by chance alone.

Statistical analysis

The data were statistically analyzed using the Proc GLM function of the Statistical Analysis System (SAS, 1988). The ultrasonic and carcass measurements were adjusted for liveweight. Growing-finishing performance traits were analyzed both with and without adjusting for initial weight.

Health monitoring

The health status of all pigs was observed and recorded daily. Pigs that were observed to be sick during the course of the study were treated intramuscularly with 44,000 IU penicillin and 0.3 mg dexamethasone per kg body weight daily for 3 days. All dead pigs were necropsied to determine cause of death. At 4.5 months of age, ten pigs from each of the three treatment groups were randomly selected and serologically tested for antibodies to *Mycoplasma hyopneumoniae* (ELISA 20 test, Oxford Labs) and *Actinobacillus pleuropneumoniae* (hemolysin neutralization assay, Brad Fenwick, Kansas State University). At the conclusion of the study, a representative group of early-weaned pigs from each treatment group (16 untreated controls, 19 moderate immune-stimulated, 17 intense immune-stimulated), as well as 61 pigs from the farm of origin were examined at slaughter for evidence of heart, lung, and liver lesions. Representative samples of all abnormal lung tissue were examined histologically, and culturally evaluated for bacteria. Frozen sections were examined by direct-fluorescent antibody testing for *M. hyopneumoniae*.

Results

Growth performance

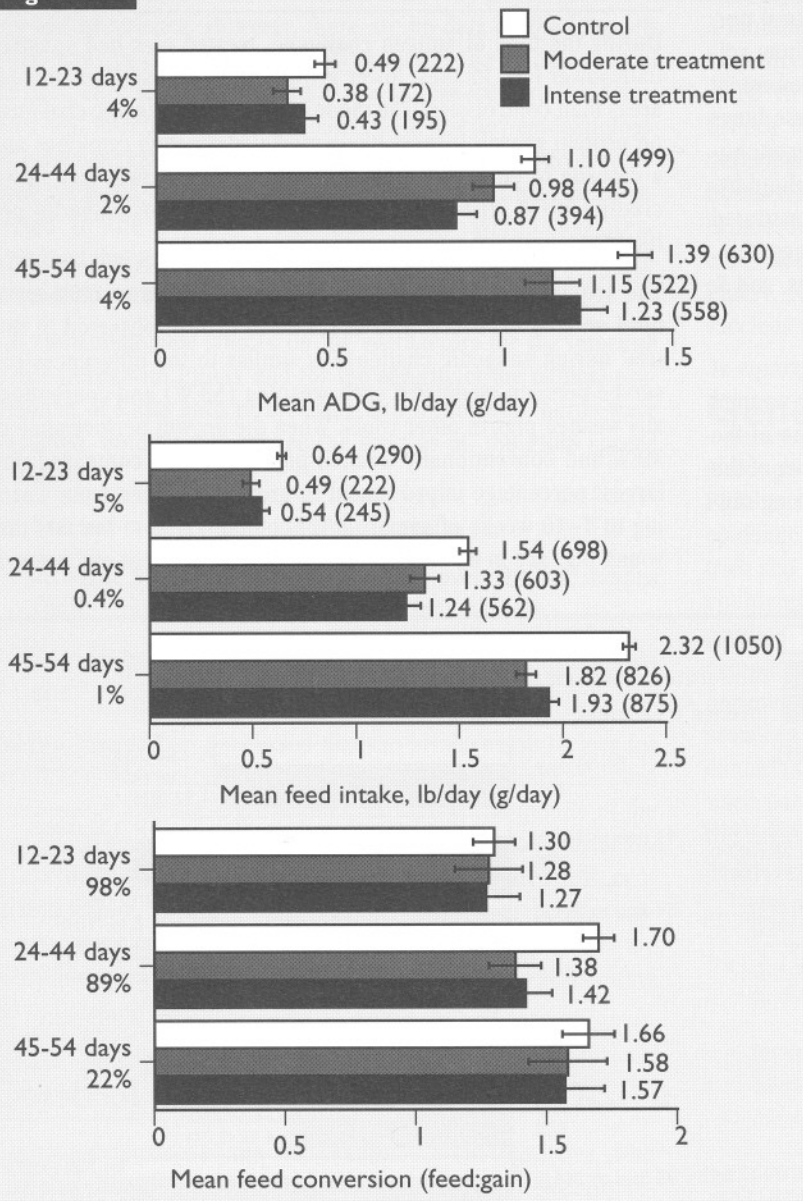
The antigen-treated pigs were significantly lighter ($P \leq 0.05$) than the control pigs at 28 days of age (Figure 1). The magnitude of the weight differences between the three treatments increased to 107 days of age and then decreased. After 107 days of age, the antigen-treated pigs grew faster ($P < 0.05$) than the control pigs:

- intense-challenged pigs had a mean ADG of 1.16 kg (2.56 lb),
- moderate-challenged pigs had a mean ADG of 1.14 kg (2.52 lb), and
- control pigs had a mean ADG of 1.02 kg (2.24 lb).

Because the intense-challenged pigs did not differ significantly from the moderate-challenged pigs, they were pooled; the antigen-challenged pigs required 5.6 more days to attain 104 kg (230 lb) and 3.6 more days to attain 120 kg (264 lb) than the control pigs.

In the nursery, antigen-challenged pigs had significantly lower growth rates and feed intakes than control pigs (Figure 2). There were no significant differences in feed conversion. The unadjusted means and means adjusted for initial-weight pigs (Figure 3) at the beginning of the period must be interpreted differently. From 53–93 days of age, the antigen-challenged pigs grew more slowly and had lower feed intakes ($P < 0.001$). However, when the data are adjusted for differences in initial weight, the feed intakes and growth rates are almost identical. The majority of the reduced growth and feed intake in the antigen-treated pigs is associated with their lower initial weight. From 93 days of age to the

Figure 2



Impact of antigenic challenge on rate and efficiency of growth in nursery pigs. Percentages indicate probability that the differences among treatment means could occur by chance alone.

end of the test, the antigen-treated pigs consumed less feed. Also, the intensely treated pigs were more efficient converters of feed to gain. However, adjusting for initial weight reduced the differences among the treatments. Overall, when differences in initial weight were accounted for, there were no significant treatment effects from 54 days to an average weight of 120 kg (264 lb).

Body composition measurements

Overall, there were no significant differences among the antigen treatments for backfat thickness (Figure 4). However, the antigen-treated pigs did have substantially smaller loin eye areas than control pigs at 32.7 kg (72 lb) (2.26 cm^2 [0.35 in^2] smaller, $P < 0.01$). The differences in loin eye area decreased as the pigs become heavier. At 120 kg (264 lb), the difference in loin eye area between control and antigen-challenged pigs was 1.1 cm^2.

There were no significant differences in dressing percent, optical probe percentage lean, or any of the backfat depth measurements (Figure 5). Carcasses of the control pigs tended to have larger loin depths ($P < 0.09$) and significantly longer carcasses than antigen-treated pigs ($P < 0.04$).

Carcass fat-free lean mass was substantially greater (1.95 kg [4.3 lb], 16%) for the control pigs at 79 days of age (Figure 6). The difference increased to 3.33 kg (7.35 lb) at 107 days while the percentage difference (15.5%) remained similar. At 154 days of age, the difference between the antigen-treated and control pigs decreased to 1.41 kg (3.1 lb) and was not statistically significant.

From 79–107 days of age, the control pigs had significantly ($P \leq 0.05$) higher lean growth rates than the antigen-treated pigs. From 107–154 days of age, the antigen-treated pigs had significantly higher lean growth rates than the control pigs. This higher lean growth rate from 107–154 days of age is primarily a reflection of the increased liveweight growth of the antigen-treated pigs during this age interval. The slightly lower real-time backfat depths at the end of the test for the antigen-treated pigs also accounted for part of the increased estimate of lean mass and growth. There was no clinical evidence of pneumonia throughout the trial. All 30 pigs from the three treatment groups that were serologically tested at 4.5 months of age were seronegative for *M. hyopneumoniae* and *A. pleuropneumoniae*.

A total of seven pigs (six control, one intensely immune-stimulated) died and were necropsied prior to the end of the study. Pulmonary adhesions were noted in the pig subjected to intense immune stimulation; however, no bacteria were isolated. The cause of death in two control pigs was attributed to gastric ulcer and inguinal hernia, respectively. *Streptococcus suis* was isolated from the lungs of three pigs with lesions of alveolitis. The sixth control pig had epicarditis from which no causative organism was isolated.

We observed no gross lesions in the lungs of 51 of the 52 SEW pigs examined at slaughter. In one pig, however, the cranioventral portion of the right cranial lung lobe, comprising approximately 1% of the lung volume, was dark red and firm (pneumonic). Histopathologic examination of this lung lesion revealed a granulomatous inflammatory reaction associated with bi-refringent plant material that was interpreted as foreign-body pneumonia associated with inhalation of feed dust. Bacteria were not isolated from this lesion by aerobic bacterial culture and the direct fluorescent antibody test for *M. hyopneumoniae* was negative.

Of 61 farm-of-origin pigs that were examined at slaughter, 23 (38%) had firm red pneumonic lesions in the cranioventral portions of the lungs that comprised 1%–19% of the total lung volume (average of 8.0%). The pneumonia observed was consistent with that caused by *M. hyopneumoniae*. Eighteen of these lungs were examined histologically and a lymphocytic bronchointerstitial pneumonia with marked peribronchiolar lymphoid hyperplasia was observed. *M. hyopneumoniae* was demonstrated by direct-fluorescent antibody testing in 14 of the 18 lungs. *Pasteurella multocida* was isolated from three of these lungs, and *S. suis* type 3 was isolated from one lung.

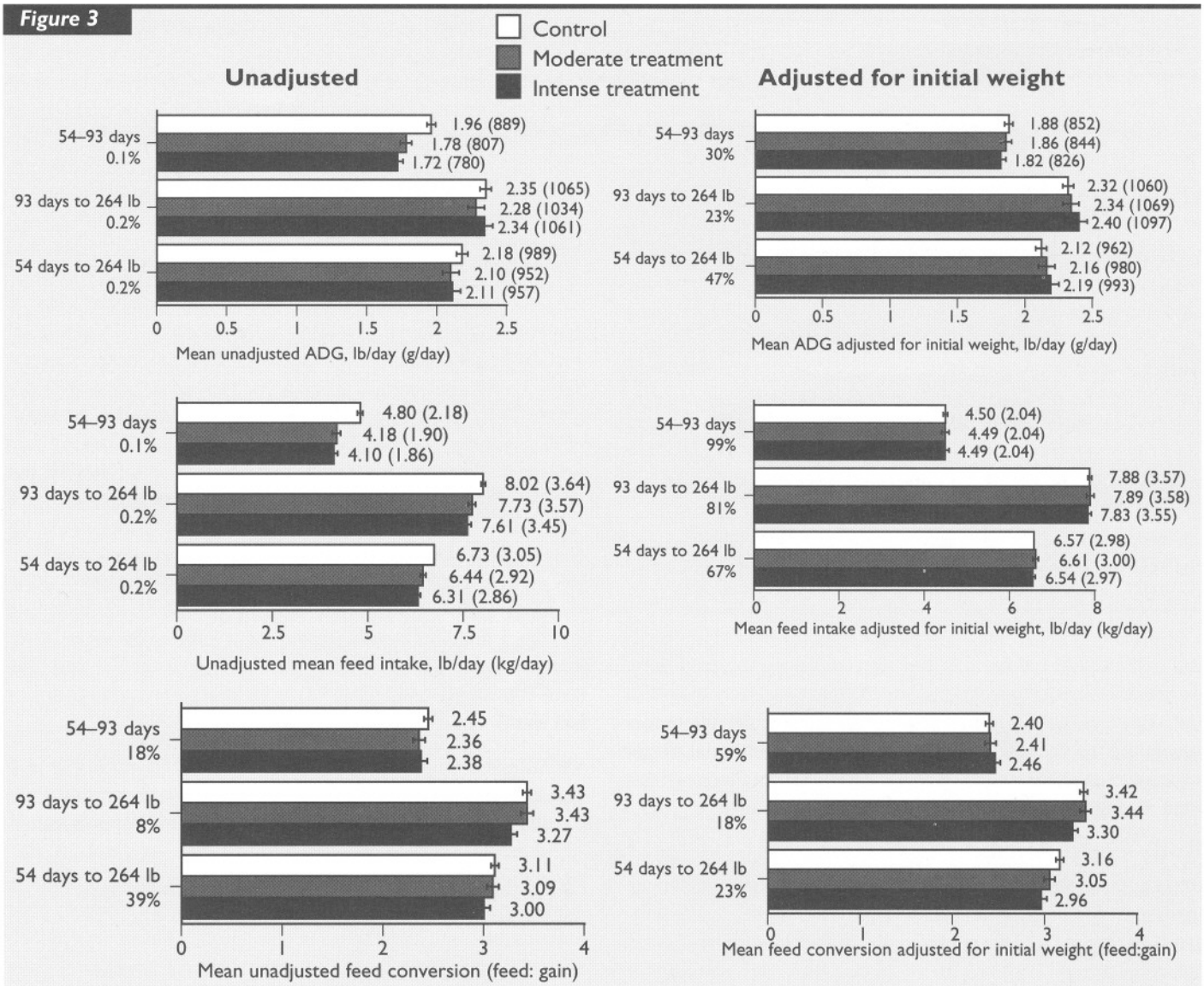
Fibrous pericarditis was observed in some pigs of all groups at slaughter examination; nine of 52 (17.3%) of the early-weaned pigs and five of 61 (8.1%) of the on-farm controls. None of the early-weaned pigs had gross liver lesions at slaughter; two of the 61 farm-of-origin pigs examined had moderate liver scarring suggestive of ascarid larval migrans.

Discussion

During the time of antigen challenge, treated pigs had substantially lower feed intakes, lower growth rates, and smaller loin eye areas than control pigs. The mode of action of antigenic challenge on protein growth is most likely mediated through cytokines and a cascade of endocrine-paracine responses.[4] Growth factors including IGF-1, IGF-1 binding proteins, and prostaglandin are likely involved.[5,7–9]

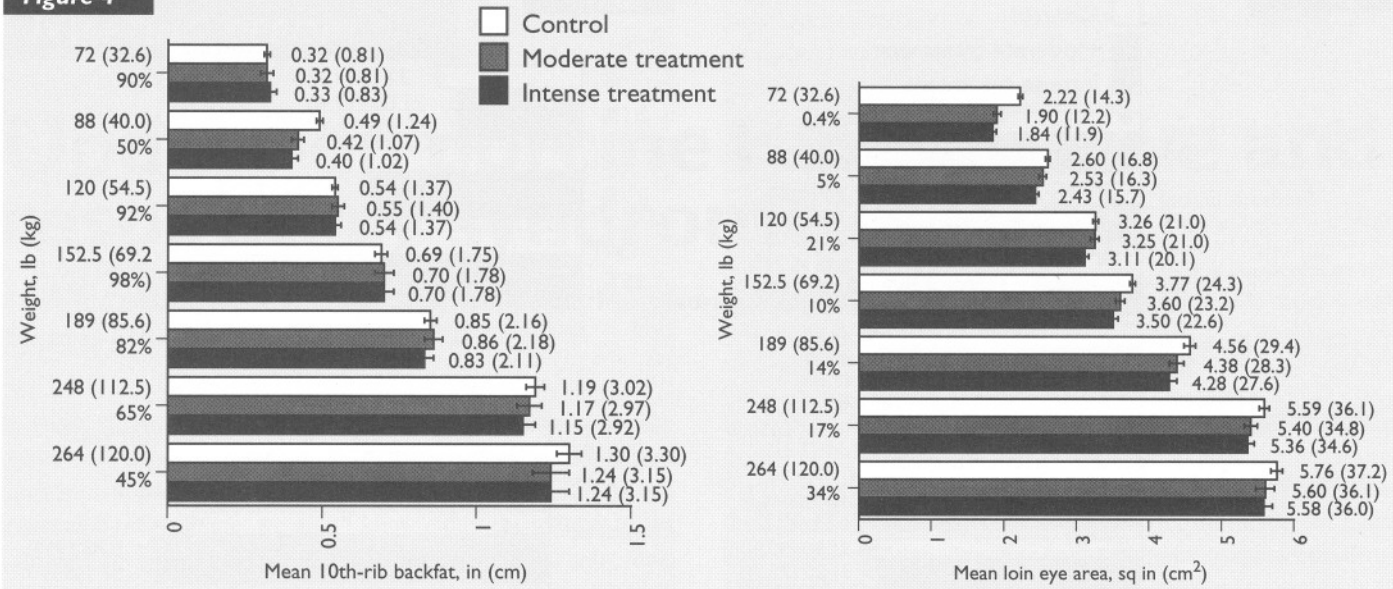
The sequence of antigens was designed to recreate commercial herd antigen exposure. The decrease in growth observed in this trial during antigenic challenge is similar to the differences observed between medicated early weaning (MEW) and conventionally weaned pigs in other trials. When the growth performance of MEW and conventionally weaned pigs have been compared, the largest percentage improvement in growth has been from weaning to 7–10 weeks of age.[6,10–12] This is likely due to the fact that young pigs are in an energy-dependent growth phase and are pri-

Figure 3



Least-squares means for growth rate, feed intake, and feed conversion in the finishing phase. Percentages indicate probability that the differences among treatment means could occur by chance alone.

Figure 4



Least-squares means for real-time ultrasonic measurements, adjusted for live weight. Percentages indicate probability that the differences among treatment means could occur by chance alone.

marily gaining lean (i.e., protein and water), and are sensitive to changes in energy or protein intake.

Although designed to reflect commercial herd antigen exposure, the antigenic challenges in this trial did not reduce grow-finish performance levels to those observed in commercial production. Pigs raised in the source commercial herd via conventional weaning followed by AIAO management averaged 179 days-to-104-kg (230 lb) with 2.67 cm (1.05 in) backfat at 112 kg (245 lb), when measured by the same optical probe at the same pork processing plant. Other researchers have found 35-day differences in days-to-109-kg (240 lb) between MEW and conventionally weaned pigs.[13] The antigen challenges provided in this trial account for only 13% (5.6 of 43) of the difference between the control and commercial pigs for days-to-104-kg (230 lb). Most of the 43-day difference (87%, 37.4 days) between the control versus commercial environments must be attributed to increased immune system activation via actual disease, direct disease effects, management, and overall environmental conditions.

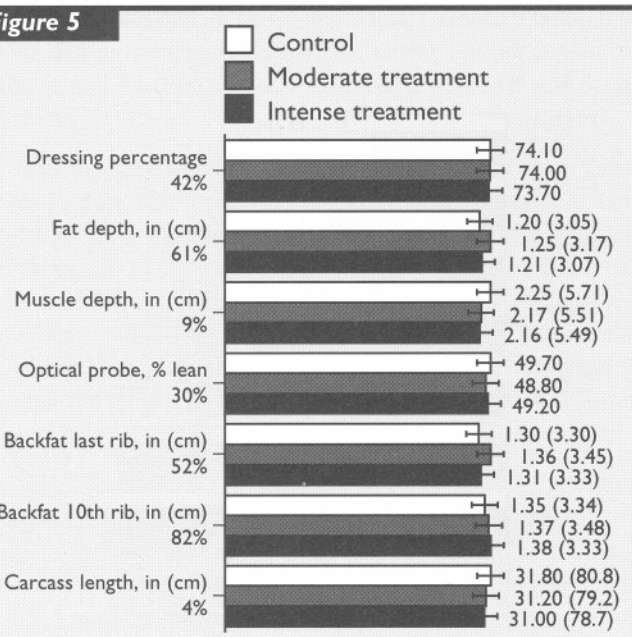
After 107 days of age, approximately 3 weeks after the last antigen challenge, pigs that had been antigen challenged had higher live and lean-growth rates than control pigs. This compensatory growth has been observed in pigs[14,15] and turkeys[16] that have been fed diets limited in protein followed by diets adequate in protein.[14,16] In this experiment, the pigs were given almost ideal conditions to express compensatory growth in terms of nutrition, pen space, minimal disease status, and thermal neutral temperatures. Had the environment been less favorable, it is likely that the ability of the pigs to express their potential for compensatory lean growth would have been limited. In that case, the differences in liveweight and lean mass observed at 107 days of age would probably have been maintained throughout the duration of the trial.

The SEW procedures used to rear pigs in this study prevented infection of the pigs with *M. hyopneumoniae, A. pleuropneumoniae, P. multocida*, and *Ascaris suis*, whereas littermate pigs that were weaned 7–9 days later and reared AIAO on the farm of origin were infected with these organisms and developed signs and lesions of disease. These findings suggest that there was transmission of these organisms from the dams to their offspring prior to weaning in the farm-of-origin group, but not in the SEW groups of pigs. In contrast, the pigs in the SEW groups had a higher prevalence of fibrous pericarditis than the pigs in the farm-of-origin group. The authors hypothesize that these lesions were the result of *H. parasuis* infection, since this organism was known to be present on the farm of origin and is known to escape elimination by SEW techniques that do not include antibiotics. These results corroborate previous work that suggested that SEW procedures allow pigs to be reared free of many diseases present in a conventional AIAO operations without the use of the excessive medication or vaccination procedures used in medicated early weaning programs.[3]

Implications

- Immune system activation via *E. coli* lipopolysaccaride and multiple vaccines from 12–84 days of age reduces liveweight growth, feed intake, and muscle growth during the time of antigen challenges.
- The use of an *E. coli* lipopolysaccaride and vaccines to recreate similar initial antigenic challenges as occur in commercial conditions resulted in small reductions in growth when compared with reductions attributed to commercial conditions.

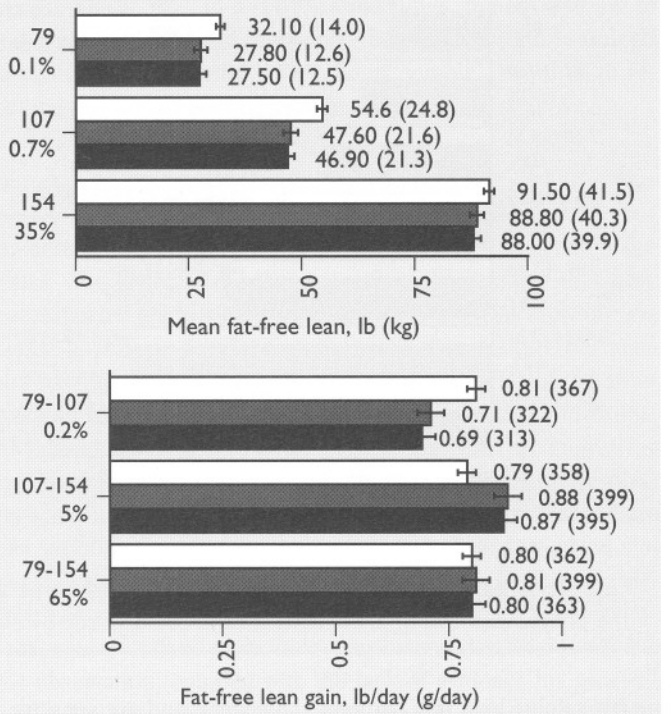
Figure 5



Least-squares means for the carcass measurements, adjusted for liveweight. Percentages indicate probability that the differences among treatment means could occur by chance alone.

- High-health pigs under ideal conditions have the potential to grow substantially faster, and attain market weight 40–60 days earlier than conventionally weaned pigs.
- Pigs exposed to antigens that caused decreased growth rate in the nursery appeared to express compensatory gain when health status, environment, and nutrition were not limiting.

Figure 6



Least-squares means for fat-free lean mass and fat-free lean growth rate. Fat-free lean estimated from ultrasonic backfat thickness, loin eye area, and liveweight. Percentages indicate probability that the differences among treatment means could occur by chance alone.

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