Addressing the Growth Gap

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Introduction

The rate of pig growth and efficiency of feed use both have a substantial impact on the profitability of pig production enterprises. Yet these performance characteristics of pigs raised commercially are well below the potential of the animal and the levels achieved under experimental conditions. For example, Campbell and Taverner (1985) measured growth rates of over 1100 g/day for entire male pigs grown from 45 to 90 kg live weight during experiments, whereas the identical strain and sex of pig grew at less than 800 g/day over the same weight range in commercial piggeries.

There are many published examples of this phenomenon that indicate that pigs housed separately in pens under either ideal experimental environments or in boar test buildings grow from between 20 to 30% faster than similar animals raised in commercial units. In addition, commercially raised animals tend to be fatter than their counterparts given the same amount of feed as pigs raised under experimental conditions. The slower growth rate, reduced efficiency of feed use and fatter carcasses of commercially raised pigs relative to their genetic potential have been estimated, using the AUSPIG decision support software, to decrease the profitability of pig enterprises by as much as 25% (Black *et al.*, 1994).

The reduced performance of pigs raised in commercial environments has been termed the "growth gap". Understanding its causes and ameliorating its impact represents a significant opportunity for the pig industry. This opportunity has been recognised with substantial funding for the "Growth Gap Program" by the Pig Research and Development Corporation and several commercial companies.

Reasons for the growth depression

Factors likely to contribute to the reduced growth rates and increased fatness of commercially housed pigs include social interactions associated with group housing and competition for feeders, characteristics of the building and stocking arrangements that affect air quality and the climatic environment, disease and other substances that initiate an immune response within the animal.

Chapple (1993) reported that simply increasing the size of a group from 1 to 8 pigs could decrease growth rate by up to 10% and increase body fatness. The reduced growth rate is associated primarily with a lowering of feed intake, which may result from the stress of being in a group, but the design and placement of feeders may also affect an animal's willingness to feed while in a group situation. During the 1970's, Carr and Hansen (see Black and Carr, 1993) replicated pens from boar test sheds in the centre of commercial grower units and observed that the growth rate of boars

transferred from the test sheds declined immediately to the lower rates observed for animals grown in the commercial units. This experiment indicated that there was a significant depression in feed intake and growth rate associated with characteristics of the building. Part of the reduced performance may have been associated with higher temperatures generated by the large number of pigs in the shed, but this is unlikely where spray cooling is available. Part of the decline in performance may have been associated with reduced air quality due to high levels of ammonia, respirable dust, immunogenic substances such as β -glucans and non-pathogenic organisms, mycotoxins and/or disease organisms.

There is evidence that all the factors listed above can act as stressors to the animal and that their effects are additive with each contributing progressively to the reduced performance of commercially housed livestock (McFarlane *et al.*, 1989). Stressors stimulate both the endocrine and immune systems of the animal with the release of hormones, such as cortisol and adrenalin, and cytokines, such as the interlukins, respectively. These chemicals control many aspects of metabolism and can depress food intake, reduce protein deposition and increase fat deposition. The interaction between the chemicals released by these systems allows an animal to vary its response to the environment between the limits of mere survival to full growth. In addition, there is evidence that some strains of pigs and individual animals react differently to the same level of apparent stressors.

Research strategy

The Goal of the Growth Gap Program is to improve the growth rate and carcass composition of commercially housed pigs to levels approaching those of pigs grown under ideal conditions. This goal is to be achieved through several research objectives covering different aspects of the factors likely to be contributing to the reduced performance of commercially raised pigs.

Objective 1. Improve the performance of group penned pigs raised under commercial conditions using management and intervention strategies

The primary focus of this objective is to identify and quantify the effects on performance, the endocrine/cytokine profile and the genes activated in animals subjected to hot environments, the psycho-social stress of group housing, feeder design and position, and the non-pathogenic and pathogenic stimulation of the immune system.

A major area of research has been to investigate the relative effect of group size and environmental factors. In one experiment weaner pigs were housed in either single or group pens in a shed cleaned each day and sprayed frequently to reduce dust concentrations compared weaners housed in a shed that was not cleaned before the pigs were introduced or during the experiment. The experiment confirmed pervious observations that the group penning of pigs reduced feed intake and growth rate compared with pigs penned individually when they were housed in a clean environment. However, the research also showed that there was no difference in the performance of group and individually penned pigs when they were housed in a dirty environment. The performance of pigs in the dirty environment was similar to that of group penned pigs housed in the clean environment. The reduced performance of group penned pigs compared with individually penned animals is thought to be due to the stressors associated with social interaction between pigs. Stress is expressed by changes in the corticotrophic and catacholamine hormones and the pro-inflammatory cytokines. Plasma cortisol concentration measured in the group penned pigs, irrespective of the cleanliness of the environment. The dirty environment also induced continuous phosphorylation of the adrenaline receptors in the lymphocyte white blood cells leading to a suppression of the immune system, reduced number of Natural Killer cells, reduced B-cell function and reduced feed intake.

It has been recognised previously that some strains of pigs cope better with social stress than others where some are relatively placid while others are aggressive when put in adverse situations. It was suggested that this difference in temperament could be quantified by measuring, over a short period of time with a decibel meter, the total noise emitted from a pig when it was restrained with a nose rope. A preliminary study indicated that there was a full range in vocalisation score in a group of pigs (Figure 1) and that quiet pigs consumed 10% more feed than noisy pigs when housed individually in pens.



Figure 1. Vocalisation score in dB for individual pigs restrained for 44 seconds.

The effect of temperament on plasma cortisol concentrations had not been measured. However, a preliminary study identified that immunisation against adrenocorticotrophic hormone (ACTH), which stimulates cortisol release, resulted in the development of antibodies to ACTH and a reduced plasma cortisol concentration following stimulation of the pig with insulin.

An experiment was conducted in a clean environment at the Elizabeth McArthur Institute (EMAI) to evaluate the effects of pig temperament and immunisation against ACTH on feed intake, growth rate, carcass characteristics and muscle pH 60 minutes post-slaughter in pigs penned in either groups of 6 or individually. The results (Tables 1 & 2) indicated that:

- (i) Pigs with low vocalisation, irrespective of whether they are in group or in single pens, eat approximately 10% more feed than those with high vocalization;
- (ii) ACTH immunisation resulted in the production of antibodies and reduced plasma cortisol concentration in pigs subjected to stress, but basal concentrations were not affected by immunization;
- (iii) ACTH immunisation tended to improve the efficiency of feed conversion for pigs in group pens, particularly the high vocalisation pigs;
- (iv) Neither placing pigs in groups of quiet pigs only nor ACTH immunisation raised feed intake of group penned pigs to within 9% of that recorded for individually penned pigs;
- (v) Muscle pH tended to be higher in pigs with low vocalisation.

Although pig temperament, as measured by vocalisation, had a substantial effect on feed intake, the grouping of low vocalisation pigs does not raise their intake to the rates observed for individually penned pigs housed in a clean environment. These results suggest that neither the selection of pigs for low vocalisation nor immunisation against ACTH will raise the performance of group penned pigs to those that are individually penned when housed in a clean environment. Nevertheless, selection of pigs for low vocalisation resulted in an increase in the intake and performance of both group and individually penned pigs. The heritability of vocalisation and association with the performance of pigs reared in a commercial environment is currently being investigated.

The reason for reduced performance of group penned pigs appears to be related to adverse social interactions. However, recent experiments investigating the effects of providing hides and extra feeding spaces has not increased the performance of group penned pigs nor has the provision of extended periods of lighting. Two final experiments are being conducted to investigate possible ways of improving the performance of group penned pigs. The first is investigating the effects of very large group size (>100 pigs/pen) with the hypothesis that smaller stable social groups may form within the large group. The second will be an attempt to create a single pen environment within a group pen by providing individual feeders with pig-length openmesh dividing fences.

Table 1. Mean (\pm SEM) live performance and carcass measurements for grower pigs (57 - 87 kg live weight) housed in either individual (n=16) or group pens (6 pigs per pen; n=8) with either low or high vocalisation animals, and vaccinated with ACTH-adjuvant or adjuvant (adj) alone.

Group size	Single				Group				
Vocalisation	Low		H	High		Low		High	
Vaccination	ACTH	adj	ACTH	adj	ACTH	adj	ACTH	adj	
i) Live performan	ice								
Intake (g/d)	2995	2959	2787	2869	2557	2630	2451	2376	
	(96.8)	(103.7)	(41.9)	(80.7)	(20.1)	(15.6)	(2.5)	(86.3)	
Gain (g/d)	1223	1196	1178	1137	1060	1057	1124	990	
	(68.9)	(59.2)	(35.8)	(38.1)	(28.4)	(43.1)	(62.8)	(37.4)	
Feed:gain	2.5	2.5	2.4	2.5	2.4	2.5	2.2	2.4	
	(0.12)	(0.14)	(0.04)	(0.14)	(0.07)	(0.23)	(0.01)	(0.02)	
ii) Carcass measurements									
Dressed weight (kg)	69.4	69.0	70.5	66.5	68.0	66.8	64.7	65.6	
	(2.19)	(1.80)	(2.62)	(2.19)	(1.65)	(1.65)	(2.56)	(3.52)	
Ultrasound P2	15.8	15.3	15.5	14.5	13.2	13.2	13.2	12.5	
(mm)	(1.11)	(1.25)	(1.50)	(0.87)	(0.72)	(0.71)	(0.52)	(0.70)	
pH60*	6.42	6.50	6.15	6.28	6.41	6.43	6.43	6.37	
	(0.165)	(0.141)	(0.104)	(0.048)	(0.08)	(0.05)	(0.06)	(0.08)	

* pH measured in the *L. dorsi* muscle at 60 minutes post-slaughter

Table 2. Mean (\pm SEM) plasma cortisol concentration^a in growing pigs at week 0 (28 kg), 5 (after first ACTH boost, 57 kg) and week 9 (after second ACTH boost, 87 kg) for animals chosen for low and high vocalisation, and with either ACTH-adjuvant vaccination or adjuvant alone.

Vocalisation	Ι	LOW	High		
Vaccination	ACTH	Adjuvant	ACTH	Adjuvant	
Week 0	20.6	19.0	22.7	18.4	
	(4.12)	(2.26)	(2.91)	(2.04)	
Week 5	8.2	18.9	11.2	13.9	
	(1.33)	(5.34)	(1.71)	(2.42)	
Week 9	9.6	10.2	10.5	10.2	
	(0.96)	(1.66)	(0.96)	(1.37)	
Week 9/15 min ^b	11.3	24.8	11.8	16.9	
	(0.90)	(5.61)	(1.32)	(1.71)	

^a Each pig on weeks 0, 5 and 9 was restrained with a nose snare and bled by venipuncture within 1 minute.

^b On week 9, each pig was restrained with a nose snare 15 minutes after the first blood sample and bled by venipuncture within 1 minute.

Objective 2. Develop selection criteria for breeding pigs that are less susceptible to the stressors of a commercial environment

1. Immune response criteria

Over 1000 blood samples were collected at 24 weeks of age from pigs used in the PrimeGro experiment at Bunge Meat Industries (BMI), Corowa. These samples were analysed for several immune response characteristics, including total white blood cell, neutrophil, lymphocyte, monocyte, basophil and eosinophil number; neutrophil:lymphocyte ratio; neutrophil function; natural killer cell function; lymphocyte proliferation; immunoglobulin G concentration; CD2, CD3, CD4, CD8 percentage and CD4:CD8 ratio.

The experiment showed that the heritability for several traits was above 0.2. One trait had high genetic correlations with P2 and feed:gain (r = -0.44, -0.66, respectively). Despite there being a significant genetic-environment interaction for many of the traits, it was regarded as being extremely unlikely that high correlation between the promising trait and feed:gain was a chance event. The results supported the conclusion that it is highly likely that pigs can be selected for an increase in innate immunity.

2. Differential display determination of gene activation state

The aim of the differential display component of the program is to identify genes in which the activation state is either increased or decreased by stressors associated with commercial pig production. Once the most appropriate genes have been identified, a rapid method for measuring their activation state in blood lymphocytes could be used to i) quantify the stress status of any group of pigs and ii) select pigs that are less susceptible to stress and that will perform better under normal commercial pig raising conditions.

The activation state of lymphocyte genes from pigs subjected to a wide range of stressors has been investigated. Over 70 potential genes as indicators of stress have been identified from experiments involving L45 cell culture systems, L45 cell incorporation into nude mice and various stress treatments to pigs. In order to confirm that the activation state of these candidate genes is altered by stress, an experiment was conducted where pigs with an extremely high-health-status were subjected to different stressors, both individually and concurrently. The treatments included intra-tracheal inoculation with *Actinobacillus pleuropneumoniae* (App), serovar 1 isolate HS54, and exposure to both low and high ambient temperatures. Vocalisation measurement was performed on the pigs following nose roping. The experiment achieved the aim of mild clinical and subclinical forms of the App disease.

Pigs derived from a commercial herd with an apparent absence of clinical and pathological evidence for pleuropneumonia and mycoplasmosis were individually penned in 4 rooms at the EMAI controlled environment pig facility. Indwelling aural intravenous catheters were inserted in all pigs on day 0 then App $(1 \times 10^5 \text{ cfu})$ was endotracheally administered to pigs in rooms 2 and 4 on day 1. Room 3 and 4 pigs experienced temperatures below 22°C prior to App challenge then a 30°C heat stress for 24 hrs on day 6. App and heat stress were not applied to room 1 pigs (Shams). Blood samples and feed intake data were collected daily and each pig was monitored for

clinical responses to App. All App challenged pigs showed different clinical signs of pneumonia within 1 day; half of these animals recovered to clinical normality by day 2. By day 4 no clinical signs of disease were evident in pigs that received the App. Post mortem examination revealed lesions of necrotic pneumonia (ranging from 1-15% of affected lung) present in 7/9 App (only) pigs, while all 10 sham pigs were free of necrotic lesions. Challenge with App resulted in a significant (P<0.05) feed intake depression (Figure 2) then returning to near pre-challenge levels at 7 days post-challenge. The App challenged pigs were 5.8 kg lighter (49.5 ± 7.7 , App vs 55.3 ± 5.9 kg, sham) at day 7 post challenge, indicative of a mean weight gain difference between the groups of 6.8 kg over the 12 days of study. Plasma cortisol concentrations (Figure 3) were significantly (P<0.05) elevated at day 1 (post-challenge) in pigs that received App, with respect to sham animals, which corresponded to the period of clinically obvious disease symptoms. At days 5-7 post-challenge, the animals that received App demonstrated a significant (P<0.05) reduction in blood cortisol, compared to the sham group.



Figure 2. Feed intake of 20 pigs (mean liveweight 41 kg) after either *A. pleuropneumoniae* (App) or nil (sham) challenge.



Figure 3. Plasma cortisol concentrations for 20 pigs (mean liveweight 41 kg) after either *A. pleuropneumoniae* (App) or nil (sham) challenge.

Seven of the 70 candidate genes identified have shown promise as indicators of stress. Figure 4 displays the raw gel expression data of gene candidate 4P3110 (~250bp) in 4 animals form each room over the course of the experiment.



Figure 4. Gel expression for gene 4P3110 in 4 animals from each treatment. The lanes are from left to right; lane 1 = standards, lane 2 = day 1, lane 3 = day 2, lane 4 = day3, lane 5 = day 6, lane 6 = day 7, lane 7 = day 8 for an individual pig, lane 8 = blank, lanes 9-14 represent the expression profile of another pig over the same time course, lane 15 is an assay control.

The gels show that there was no activation of the gene in the unstressed, sham operated pigs (Figure 4a). However, the gene was activated on the gel displayed for 2 of the 4 pigs on the day following inoculation with App (Figure 4b). The genes in these two animals remained activated for 2-3 days. The application of 30°C heat for 24 hours on day 6 resulted in a clear activation of the gene on day 6 for 3 of the 4 pigs displayed

(Figure 4c), whereas inoculation with App on day 1 and application of heat on day 6 resulted in a sustained activation of the gene for one pig and a bimodal activation for the other pigs (Figure 4d).

A rapid test kit for assessing gene activation, known as GenieX, which involves observation of a colour change, has been developed for one specific gene (β -adrenergic receptor kinase) and recently converted to identify the expression of gene 4P3110. The activation state of gene 4P3110 using the GenieX assay of the blood samples taken from the current gene marker experiment being conducted at BMI is being investigated to determine the effect of sire groups and any relationship with performance criteria.

A summary of the results so far (Table 3, Gene Expression) indicate significant correlations between gene expression and performance/production traits (feed intake, weight gain, clinical scores, lung lesions, vocalisation) for the 7 most promising genes.

TRAIT	B4	4P3	28a	29a	36b	41b	42
Group housing	POS#	NEG#	ID	ID	ID	ID	ID
Feed intake	POS*	NEG*	ID	NO	NEG#	POS*	ID
Weight gain	POS*	NEG*	ID	NO	NEG#	POS#	ID
Carcase weight	POS*	NEG*	ID	NO	NEG#	NO	ID
Lung score	POS*	NEG*	ID	NO	ID	NO	ID
Clinical score	POS#	NEG#	ID	NO	ID	NO	ID
Vocalisation	NO	POS#	ID	NO	ID	NO	ID
Skin temperature	NO	NO	NO	POS*	ID	POS#	ID
Respiration rate	NO	NO	NO	POS*	ID	POS#	ID
Cortisol	NO	NO	NO	NO	ID	NO	ID

Table 3. Gene Expression

POSitive, NEGative or NO apparent Correlation (Pearson) between TRAIT and GENE EXPRESSION # p<0.1- (ie approaching significance), * p<0.05- (ie statistically significant), ID - insufficient data currently available.

Table 3 is a composite of porcine immune cell gene expression profiles in a range of experiments in response to stress stimuli that include pigs: i) exposed to 30° C heat stress, ii) subjected to *Actinobacillus pleuropneumoniae* (App) and *Mycoplama hypopneumoniae* (Mhp), iii) subjected to heat stress plus App (and/or Mhp), iv) a commercial model of poor air quality and housing (single/group) conditions. Please note: Applying more sophisticated statistical analysis to the data is likely to reveal greater information for gene expression applications.

Objective 3. Develop endocrine-based intervention strategies to improve the performance of commercially raised pigs

Several endocrine intervention strategies that have the potential to restore protein deposition rates and increase the growth rate of commercially reared pigs are being investigated. These strategies are focused primarily on manipulating the growth hormone axis of the pig. They include immunisation against somatostatin, stimulation of growth hormone release from the pituitary gland in response to growth hormone releasing hormone (GHRH) by use of the endocrine imprinting concept or directly through growth hormone releasing hormone (GHRP-6), and assessing the effect of early postnatal handling of the piglets.

Somatostatin immunisation has given variable responses and it has proved difficult to obtain consistent antibody production to the somatostatin molecule. Administration of GHRH over the first 3 days of life has produced significant improvements in growth hormone release and increased growth rate of pigs to slaughter. In addition, positive handling of piglets by removing them from the sow for 15 minutes, twice per day for the first 3-4 days of life has been shown on some occasions to increase performance to weaning. However, the results are too inconsistent to be of practical value. Current research is investigating the combined effects of GHRH, GHRP and somatostatin immunisation under commercial conditions.

Objective 4. Develop cytokine based intervention strategies to improve the performance of commercially raised pigs

This research is aimed at identifying the changes in cytokine concentrations associated with different stressors and then manipulating cytokine action to improve the performance of commercially raised pigs. A significant part of the first few years have been spent developing assays for individual pig cytokines, cytokine receptors and acute phase proteins. Following the development of the assays, intervention strategies have been assessed as ways of alleviating the effect the stresses of a commercial environment have on the performance of pigs. The intervention strategies have involved administration of recombinant cytokines and inflammatory cytokine receptor antagonists as well as plasmid delivery of the agents. Several treatments have resulted in significant reduction in the clinical signs of pigs challenged with App. The cytokines and receptor antagonists appear to have both prophylactic and therapeutic The compounds are being evaluated in pigs raised under commercial actions. conditions and also in pigs challenged with the enteric diseases, E. coli and swine The results are extremely promising and compounds and their dvsenterv. administration systems are being held confidential until the Intellectual Property position is secured.

Conclusions

The growth gap between the genetic potential of an animal and the growth rate observed in commercial piggeries appears to be caused by multiple stressors. Social interactions between group-housed animals are a major cause of reduced feed intake and performance. However, pathogenic and non-pathogenic challenges of dirty environments also reduce pig performance. There are differences between animals in their ability to cope with stress. Quieter animals that respond less to an adverse physical challenge eat more and grow faster than non-coping aggressive pigs. Strong heritability and genetic correlation with production characteristics has been found for several immune response measures. In addition, the activation state of several genes has been shown to be closely related to performance of pigs subjected to a range of stressors. The results obtained from the Growth Gap Program suggest that it should be possible to select pigs that perform better in commercial environments. However, it has not yet been possible to find a way of lifting the performance of group housed pigs to the level seen when pigs are housed individually.

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