

# **FEEDING THE PIGS' IMMUNE SYSTEM AND ALTERNATIVES TO ANTIBIOTICS**

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## **ABSTRACT**

Diet formulation and feeding strategies may be used to boost the pigs' immune system and reduce the negative impact of weaning. Post-weaning diarrhea can be reduced or prevented by feeding diets that have low concentrations of crude protein. Such diets may supply fewer amino acids than recommended and pig growth rate may be reduced, but if pigs are provided a diet with a normal or elevated concentration of protein after the immediate post-weaning period, then the overall post-weaning performance will not be compromised. Diets that are based on barley, oats, or naked oats have been shown to improve pig performance compared with diets based on wheat or corn, and there is evidence that the fiber fraction in barley and oats help improve intestinal health of pigs. However, it has also been shown that diets based on cooked white rice may improve performance and the immune status of the pig.

Diets fed in a liquid or in a fermented liquid form improve pig performance compared with diets fed in a dry form, and the liquid diets help maintain intestinal integrity during the post-weaning period. It is, therefore, recommended that weanling pigs should be fed liquid diets to maximize performance. Many feed additives are available for inclusion in diets fed to pigs. Positive responses on pig performance have been reported in some, but not all, studies in which the inclusion of acidifiers, probiotics, or pre-biotics was studied. However, there are many unknowns regarding the usage of these additives, and the responses to the inclusion of them are not always predictable.

## **INTRODUCTION**

Producing pigs without using antibiotic growth promoters represents a challenge. Disease problems often are elevated and general performance is compromised on farms practicing non-medicated swine production. That is true in particular during the immediate post-weaning period whereas antibiotics can often be removed from diets fed to growing-finishing swine without introducing major disease problems (Wierup, 2001). Because of the difficulties associated with producing pigs without antibiotics, many producers are looking for alternative growth promoters or management strategies, but at this point, no "magic bullets" are available. Producing swine without in-feed antibiotics requires a combination of different strategies. These strategies can be divided into three categories: Management strategies, nutritional strategies, and alternative dietary supplements. Many different approaches have been proposed within each strategy, but the one thing these approaches have in common is that they all aim at improving the pigs' ability to prevent pathogenic bacteria from colonizing in the intestinal system. This can be accomplished via an improved immunological response

to pathogens or via mechanisms that prevent the pathogens from adhering to intestinal tissue, and thus, reduce the damaging effects of the pathogens. In this summary, some of the approaches that are available to improve the pigs' ability to reduce the impact of intestinal pathogens will be discussed. However, this is not a complete list of strategies or supplements that may be used and other strategies or products that are equally or more effective than the ones discussed here, may be available.

## **NUTRITIONAL STRATEGIES**

### **Low-Protein Diets**

The single most important nutritional factor for reducing scouring in pigs fed diets without antibiotic growth promoters is to reduce the dietary crude protein concentration because undigested crude protein entering the large intestine will increase microbial fermentation in the hind gut and provide substrates for pathogens. It is also likely that the increased metabolic demand for deaminating excess amino acids and excreting the extra nitrogen compromises the pigs' immune system. In addition, undigested feed protein may accelerate the production of toxic nitrogenous compounds including ammonia which is harmful to intestinal health (Bolduan et al, 1988; Pluske et al., 2002; Nyachoti et al., 2006). Therefore, formulating low-protein diets supplemented with crystalline amino acids results in less diarrhea and fewer intestinal problems than using diets with greater protein concentrations (Ball and Aherne, 1987; Bolduan et al., 1988; Goranson et al., 1995). For most groups of pigs, it is possible to reduce the dietary concentration of crude protein by 3-4% without compromising the pig's requirement for amino acids (Cinq-Mars et al., 1988; Hansen et al., 1993; Han et al, 1995). In a recent experiment, it was demonstrated that by reducing the dietary crude protein concentration from 21.2 to 18.4, a linear reduction in diarrhea was observed, but growth performance was not affected (Reynoso et al., 2004). The low protein diets that were used in this experiment were fortified with crystalline amino acids, which is likely the reason performance could be maintained. Likewise, le Bellego and Noblet (2002) reduced dietary crude protein concentration from 22.4% to 16.9% with the addition of crystalline amino acids without reducing pig performance.

It is usually possible to reduce the dietary concentration of crude protein in diets fed to weanling pigs to approximately 18% by including crystalline amino acids in the diets without under-supplying any indispensable amino acids. However, sometimes it may be necessary to formulate diets containing less than 18% crude protein during the immediate post-weaning period to avoid scouring and intestinal malfunctions. In such diets, it may not be possible to include the indispensable amino acids at recommended concentrations. Therefore, growth performance will be compromised. However, if the pigs suffer from diarrhea, they will also have reduced performance (Goranson, 1997). Because the period of time that amino acid concentrations are sub-optimal is usually relatively short (i.e., 2-4 weeks), it is of little or no practical consequence that growth performance is slightly reduced during this period. Recent data indicate that pigs fed diets containing approximately 20% less amino acids than recommended (NRC, 1998) will have a reduced daily gain of 40 – 60 g per day (Table 1). If such diets are fed during the initial two weeks post weaning, then a total of 560 - 840 g of

gain is sacrificed. However, if the protein concentration in the diet is returned to normal levels from day 15 post-weaning, then the pigs on the low-protein diets will compensate and by day 35 post-weaning, there is no difference in the body weight of pigs regardless of the protein concentration they received during the initial 2 weeks post weaning (Stein and Kil, 2006; Table 1). These observations are consistent with data demonstrating that pigs will compensate for protein restriction during one period of growth by utilizing proteins more efficiently when dietary protein levels are restored to normal values (Kyriazakis et al., 1991; Reynolds and O'Doherty, 2006).

It is, therefore, concluded that the incidence of diarrhea during the post-weaning period may be reduced by feeding low-protein diets without compromising overall nursery pig performance.

**Table 1. Effects of feeding low protein diets followed by either normal or high protein diets to weanling pigs <sup>a,b</sup>**

Item	Treatment:	High/low	High/high	Low/low	Low/high	SEM
Crude protein/lysine, day 0 - 14		20.8/1.35	20.8/1.35	15.7/1.15	15.7/1.15	-
Crude protein/lysine, day 14 - 35		17.5/1.15	19.3/1.34	17.5/1.15	19.3/1.34	-
Average daily gain, g, day 0 - 14		171 <sup>xy</sup>	180 <sup>x</sup>	148 <sup>xy</sup>	129 <sup>y</sup>	16
Average daily gain, g, day 14 - 35		516	529	499	535	13
Average daily gain, g, day 0 - 35		377	389	359	373	11
Average daily feed intake, g, day 0 - 14		249	257	228	237	18
Average daily feed intake, g, day 14 - 35		790 <sup>x</sup>	756 <sup>xy</sup>	778 <sup>xy</sup>	735 <sup>y</sup>	17
Average daily feed intake, g, day 0 - 35		574	556	558	535	15
Average gain:feed ratio, g/g, day 0 - 14		0.68	0.70	0.65	0.55	0.029
Average gain:feed ratio, g/g, day 14 - 35		0.65 <sup>x</sup>	0.70 <sup>y</sup>	0.64 <sup>x</sup>	0.73 <sup>z</sup>	0.007
Average gain:feed ratio, g/g, day 0 - 35		0.66 <sup>x</sup>	0.70 <sup>y</sup>	0.65 <sup>x</sup>	0.70 <sup>y</sup>	0.007

<sup>a</sup> Data from Stein and Kil, 2006.

<sup>b</sup> Values are means of six pens per treatment with 5 pigs per pen.

<sup>xyz</sup> Values lacking a common superscript letter are different ( $P < 0.05$ ).

### Selected Cereal Grains

In most parts of the world, the major cereal grains used in diets fed to weanling pigs are corn, wheat, sorghum, or barley. These grains contain varying quantities of starch and non starch polysaccharides, which results in differences in the effects these grains have on intestinal physiology and on the concentration of the microorganisms in the intestinal tract (Bach Knudsen, 2001). Work in Australia has indicated that pigs fed diets based on cooked white rice and animal proteins are less susceptible to infections than are pigs fed diets based on other cereal grains with higher fiber contents (Pluske et al., 1996; 1998). Therefore, weanling pigs fed such diets have fewer incidences of diarrhea than pigs fed diets based on corn starch (Pluske et al., 2003), which often results in improved pig performance (Vicente et al., 2004, Mateos et al., 2006). The majority of the carbohydrates in diets based on cooked rice are digested in the small intestine with a subsequent absorption of monosaccharides. Therefore, only small quantities of non-starch polysaccharides will enter the large intestine, which in turn prevents pathogenic bacteria from getting nourishment in the GI-tract. Therefore, a change in

the microbial population is observed, fewer pathogens are able to colonize in the intestinal tract, and fewer short chain fatty acids are produced (Siba et al., 1996; McDonald et al., 1999).

In contrast with the above results it also has been reported that the inclusion of barley and oats in diets fed to weanling pigs may reduce the incidence of diarrhea (Medel et al., 1999; Paulicks et al., 2000). Barley and oats contain both fermentable and non-fermentable fibers and they will, therefore, stimulate fermentation in the hind gut in contrast to diets based on cooked white rice. However, barley and oats may also contain unidentified nutrients that improve overall digestion of pigs and performance of newly weaned pigs fed diets based on barley or oats is elevated compared to pigs fed diets based on corn or wheat (Medel et al., 1999). Data from our laboratory indicate that this is also the case if diets are based on naked oats rather than corn, milo, or wheat (Stein and Kil, 2006; Table 2). The reason for these observations may be that the increased production of short chain fatty acids that results from the fermentation of the fibers in barley and oats may stimulate the expression of certain cytokines in the intestinal tract of the pigs (Pie et al., 2007). This in turn would improve the immune status of these pigs, which may explain the positive performance results from pigs fed diets based on barley or oats. Barley and oats also contain relatively high quantities of beta-glucans that may have prebiotic effects because they stimulate lactic acid production (Bach Knudsen and Canibe, 2000; O’Connell et al., 2005). The improved production of short chain fatty acids may also stimulate water and electrolytes absorption, improve gut morphology, and reduce colonic pH to levels that are unfavorable for pathogens, which in turn may reduce the incidence of diarrhea (Montagne et al., 2003).

These results indicate that two options for improving performance, health, and the immune status of weanling pigs are available. One option is to reduce the concentration of dietary fiber to reduce the nourishment for microbes in the hind gut, and therefore, reduce colonization by pathogens in the intestinal tract of the pigs. The other option is to use cereal grains containing specific fibers that have prebiotic effects in the hind gut of pigs. Barley, oats, and naked oats seem to contain such fibers and the inclusion of these grains in diets fed to weanling pigs may, therefore, improve performance and intestinal health of the pigs.

**Table 2. Effects of grain source in starter diets fed to weanling pigs from day 0 – 7 post-weaning<sup>a,b</sup>**

Item	Grain source:	Corn	Sorghum	oats	Naked oats
Average daily gain, g		95 <sup>x</sup>	74 <sup>x</sup>	81 <sup>x</sup>	129 <sup>y</sup>
Average daily feed intake, g		160 <sup>x</sup>	146 <sup>x</sup>	145 <sup>x</sup>	195 <sup>y</sup>
Average gain:feed ratio, g/g		0.60 <sup>xy</sup>	0.51 <sup>x</sup>	0.55 <sup>x</sup>	0.66 <sup>y</sup>

<sup>a</sup> Data from Stein and Kil, 2006.

<sup>b</sup> Values are means of six pens per treatment with 5 pigs per pen.

<sup>xy</sup> Values lacking a common superscript letter are different ( $P < 0.05$ ).

## **Restricted Feeding**

Feeding weanling pigs a restricted amount of feed will reduce intestinal problems and incidences of diarrhea compared with pigs that are allowed to consume their diets on an ad libitum basis (Goranson et al., 1995). The reasons for this observation have not been elucidated, but it is possible that reduced feed intake results in less undigested feed entering the large intestine, and, therefore, less fermentable substrate for the pathogens in the intestines. Restricted feeding also results in a reduced pH in the intestinal tract, which may prevent pathogens from colonizing in the upper gut. Feeding as often as 4 to 6 times per day may be required during the initial two weeks post-weaning to prevent pigs from developing diarrhea. Usually, this can be accomplished by feeding the pigs on a floor-mat during this period. For older pigs, restricted feeding is usually not practical because most feeding systems are based on ad libitum intake of feed.

## **Functional Proteins**

Protein is added to diets for pigs to provide amino acids that can be used for tissue protein synthesis. However, it is recognized that certain proteins may have functions other than strictly providing amino acids and several proteins are believed to improve the immune status of weanling pigs. For example, it has been shown that the dietary inclusion of spray dried plasma may improve the immune status of weanling pigs (Touchette et al., 2002; Bosi et al., 2004), which reduces the pigs' susceptibility to E.coli infections (Bosi et al., 2001; van Dijk et al., 2002, Owusu-Asiedu et al., 2003). The immunoglobulins that are present in spray dried plasma are the functional units that provide the improved immunity (Pierce et al., 2005). Spray dried plasma also has been shown to down-regulate the inflammatory process in healthy pigs (Touchette et al., 2002; Bosi et al., 2004), which in turn may contribute to increased feed intake and direction of nutrients towards gain of body weight. It is, therefore, not surprising that reviews of a large number of studies in which spray dried plasma was included in diets fed to weanling pigs has shown that plasma increases average daily growth rate by approximately 25% (Coffey and Cromwell, 2001; van Dijk et al., 2001). Spray dried plasma is, therefore, commonly included in diets fed to weanling pigs.

If it is correct that it is the immunoglobulins in spray dried plasma that provide the improvement in pig immunity then it would be expected that other sources of immunoglobulins also can improve the immune status of pigs. The most abundant source of immunoglobulins is immunoglobulins from dairy cows that are present in the whey protein fraction of cows' milk. It has been demonstrated that the inclusion of whey proteins in diets fed to weanling pigs may improve performance (Nessmith et al., 1997; Grinstead et al., 2000). However, in a recent analysis of data from 11 experiments in which whey proteins had been used, it was shown that the average improvement in growth rate obtained by the addition of whey proteins to diets fed to weanling pigs is only 4% (Pettigrew, 2006).

Egg proteins also contain immunoglobulins and the inclusion of dried whole eggs to diets fed to weanling pigs may also improve pig performance (Schmidt et al., 2003; Hong et al., 2004). If hens are immunized against certain pathogens, they will produce antibodies against these pathogens and the antibodies will be present in the eggs from these hens. It is therefore

possible to increase the concentrations of antibodies in eggs against certain pathogens and if these eggs are fed to weanling pigs, the pigs will gain an improvement in their immune status. It has been demonstrated that if eggs containing high concentrations of antibodies against *E.coli* are fed to weanling pigs, these pigs will experience fewer cases of *E.coli* associated diarrhea (Yokoyama et al., 1997; Marquardt et al., 1999). There are, however, relatively large costs involved in the production of these eggs, and this practice is, therefore, not widely used in the industry.

Because of the positive effects of adding immunoglobulin containing proteins to diets fed to weanling pigs, it is a common practice to use at least one of the above proteins in starter diets, which improves the pigs' immune status. The greatest improvements in immune status and average daily gain are obtained when spray dried plasma is used, but other proteins may also provide benefits.

### **Liquid Feeding/Fermented Liquid Feeding**

Liquid feeding generally results in fewer intestinal upsets than dry feeding because liquid diets reduce gastric pH, which results in reduced or inhibited growth of pathogens in the intestinal tract (Geary et al., 1996; van Winsen et al., 2000). Liquid feeding also prevents the atrophy of intestinal villi that often is observed during the post-weaning period in pigs provided a dry diet (Deprez et al., 1987; Gu et al., 2002; Scholten et al., 2002). With a healthier and more intact villi-structure in the small intestine, it is likely that pigs are less susceptible to *E.coli* infections, which in turn can explain why liquid feeding has a positive influence on overall pig health and pig performance.

In ten experiments, daily gain was improved by 12.3% on average in pigs fed liquid diets compared with pigs fed dry feed (Jensen and Mikkelsen, 1998). However, other experiments have reported a greater improvement in pig performance for pigs fed liquid diets rather than dry diets (Zijlstra et al., 1996; Kim et al., 2001). Increased concentrations of short-chain fatty acids, reduced microbial activity, and improved immune status in pigs fed liquid or fermented liquid diets rather than a dry diet may also contribute to improved performance (Scholten et al., 1999).

Fermentation of the liquid feed prior to feeding has been reported to further decrease the risk of developing intestinal problems in pigs (Geary et al., 1996; Scholten et al., 1999; Brooks et al., 2003). Other benefits of fermented liquid feeding include improved protein digestion due to lower stomach pH and probiotic effects resulting from the supply of lactic acid bacteria via the fermented feed (Brooks et al., 2003). Thus, fermented liquid feeding could have characteristics similar to probiotics and organic acidifiers. On average, fermented liquid feeding resulted in an increase in growth rate of 13.4% compared with non-fermented liquid feeding and by 22.3% compared with dry feed (Jensen and Mikkelsen, 1998).

Fermentation of the entire diet may reduce the gain to feed ratio (Jensen and Mikkelsen, 1998) because of fermentation of sugars and free amino acids in the diet. However, it has been demonstrated that fermentation of only the carbohydrate source in the diet (i.e., the cereal grains) improves average daily gain and the gain to feed ratio (Scholten et al., 2002),

and it is, therefore, recommended that only the cereal grains are fermented. Alternatively, the fermentation of free amino acids during fermentation may be prevented if small concentrations of lactobacillus are included in the fermentation (Niven et al., 2006). Therefore, there seems to be several options for creating fermentation conditions that are not detrimental to pig performance.

It is concluded that liquid and fermented liquid feeding of weanling pigs improves intestinal health, immunity, and pig performance. Producers who have the ability to feed such diets, may, therefore, want to consider this option. The dietary inclusion of solubles from the industrial fermentation industry such as from beer breweries, ethanol plants, or enzyme fermentation plants are also believed to have a positive effect on intestinal and overall health of the pig but a scientific evaluation of these products still needs to be conducted.

## **DIETARY SUPPLEMENTS**

### **Acidifiers**

The inclusion of organic acids in diets fed to weanling and growing pigs has been reported in numerous papers. Of all alternative dietary supplements, the products belonging to the group of organic acids are probably the best researched. Positive responses to the inclusion of Fumaric acid (Falkowski and Aherne, 1984; Giesting and Easter, 1985; Giesting et al., 1991; Radecki et al, 1988), formic acid, citric acid and Propionic acid have been reported (Falkowski and Aherne, 1984; Henry et al., 1985). Usually, between 1 and 2% of the products are included in diets fed to weanling or growing pigs. Despite many years of research, the mode of action of acidifiers has not yet been elucidated. Improved nutrient digestibility has been reported in several experiments (i.e., Broz and Schulze, 1987; Blank et al., 1999), but not in other experiments (Gabert et al., 1995).

The addition of inorganic acids to diets fed to weanling pigs has also been researched. Positive responses to the inclusion of phosphoric and hydrochloric acid (Mahan et al., 1996) were reported, whereas the addition of sulfuric acid had a negative effect on pig performance. As was the case for organic acids, the mode of action of inorganic acids has not been elucidated.

Another group of diet acidifiers include salts of acids. These products have also been researched extensively. Positive responses were reported from experiments in which weanling pig diets were supplemented with Potassium diformate (Overland et al., 2000; Canibe et al., 2001), calcium formate (Kirchgessner and Roth, 1990; Pallauf and Huter, 1993), and sodium formate (Kirchgessner and Roth, 1987).

Therefore, there is strong evidence that pig performance may be enhanced if starter diets are supplemented with an acidifier. Of the various acidifiers on the market, fumaric acid and potassium formate have shown the most promising results, but many other acids may work equally well. Many commercial acidifiers contain combinations of organic and inorganic acids and are often included in diets at relatively low inclusion levels. Because the combination

of acids included in these products are often proprietary, the effects of these products cannot always be verified.

## **Probiotics**

Probiotics are live cultures of bacillus, lactic acid producing bacteria, or yeast that are added to diets for piglets. For a culture to have a positive effect on pig performance, the following needs to be verified:

- The culture needs to be able to establish itself in the GI-tract of the animal
- The culture needs to have a high growth rate
- The culture needs to excrete metabolites that have a suppressing effect on pathogens
- It should be possible to grow the culture under commercial conditions
- The culture need to be stabilized and have the ability to survive in feed

Probiotics are supposed to colonize in the intestinal tract of the animal and increase in concentrations to dominate the intestinal microflora, which in turn will prevent intestinal pathogens from colonizing. They may also suppress pathogens by competitive exclusion.

Many of the commercial probiotic products on the market are lactic acid producing bacteria that are used to circumvent the drop in the enteric lactic acid producing bacteria that is often observed during the immediate post-weaning period (Doyle, 2001). Recently, it was reported that in 30 out of 31 trials in which a combination of *Bacillus licheniformis* and *Bacillus subtilis* had been included in diets fed to weanling pigs, a positive growth response had been obtained (Kremer, 2006). In experiments where other lactic acid producing bacteria were fed to weanling pigs, positive responses were also reported (Apgar et al., 1993; Zani et al., 1998; Kyriakis et al., 1999).

Yeast cultures may be added to pig diets as live yeast or dried yeast and there is no evidence that one form is better than the other. Positive performance responses to the inclusion of yeast in diets fed to weanling pigs have been reported (Matthew et al., 1998; van Heughten et al., 2003). The positive responses of yeast in diets fed to swine may be a result of the ability of yeast to suppress the concentration of coliform bacteria in the intestinal tract of weanling pigs (White et al., 2002).

## **Non-Digestible Oligosaccharides/Prebiotics**

Certain dietary fibers have been shown to improve intestinal secretions and growth of the digestive mucosa (Mateos et al., 2000), and a number of different fiber fractions have been tested for their ability to enhance pig growth and suppress pathogenic bacteria colonization. The mode of action of the dietary fibers is believed to depend on the specific fraction in question. Readily fermentable non-digestible oligosaccharides (i.e., fructo-oligosaccharides, galacto-oligosaccharides, and trans-galactooligosaccharides) are believed to improve pig performance by stimulating the proliferation of Bifidobacteria in the large intestine, which in turn reduces colonic pH and increases the concentration of lactic acid (Houdijk et al., 2002). It is also believed that galacto-oligosaccharides stimulate beneficial bacterial growth in the large intestine and improves intestinal health (Smiricky-Tjardes et al., 2003). Bifidobacteria also



suppress the growth of pathogenic bacteria (i.e., *E. coli*) by stimulating the production of acetate, which further decreases the pH and reduces the incidence of diarrhea (Mosenthin et al., 1999). Because of the ability of these oligosaccharides to improve the growth of the probiotic bacteria in the GI-tract, they are often called nutra-ceuticals or pre-biotics.

Other fiber fractions (i.e., mannan-oligosaccharides) are believed to improve pig health and performance by binding to specific lectin ligands on the surface of epithelial cells, thus preventing pathogenic bacteria from binding to these ligands resulting in a “flushing” effect on pathogenic bacteria (LeMieux et al., 2003; Rozeboom et al., 2005). Mannan oligosaccharides may also enhance the immune system by directly evoking an antibody response (Davis et al., 2004). Results from several experiments in which mannan-oligosaccharides were used showed an increase in pig performance (LeMieux et al., 2003; Rozeboom et al., 2005).

### **Essential Oils**

Antimicrobial properties of various extracts of herbs and spice preparations have been reported for many centuries. The essential oil of the plant is often the biologically active component of herbs and spices (Zaika et al., 1983) although this is not always the case (Deans and Ritchie, 1987). The activity of plant extracts is related to the composition of the oils and may be influenced by factors such as the genotype of the plant and the growing conditions (Deans and Ritchie, 1987; Piccaglia et al., 1993). The antimicrobial effects of essential oils may be related to changes in lipid solubility at the surface of the bacteria (Dabbah et al., 1970), but disintegration of the outer membrane of certain pathogens has also been demonstrated.

Garlic, oregano, thymol, and carvacrol are among the essential oils that are most commonly used in diets fed to swine. All of these compounds have strong anti-microbial properties *in vitro*, but there are no reports in the peer-reviewed literature that demonstrate that they also have a positive effect on pig performance. In contrast, reduced pig performance has been reported from the inclusion of a combination of oregano, thyme, and cinnamon in diets fed to weanling pigs (Namkung et al., 2004) and no effects on pig performance were reported from studies using other combinations of essential oils (Manzanilla et al., 2004; 2006; Insley et al., 2005).

There are already a number of commercial products containing proprietary blends of essential oils on the market. These products are claimed to improve pig performance, reduce scouring, and sometimes also improve the immunity of the animals. However, at this point, there is a lack of carefully controlled *in vivo* studies reported in the peer-reviewed literature that can support the argument that essential oils have beneficial effects on pig performance or health if included in diets fed to weanling pigs.

### **Minerals**

Several minerals are included in the regulation of the pig's immune system. The role of selenium in protecting biological membranes from oxidative degeneration was established many years ago (Lessard et al., 1991; Oldfield, 2003). A number of functional selenoproteins

are synthesized in the body and the glutathione peroxidase enzymes (GSHPx) have been shown to be part of the body's antioxidant defense system (Reilly, 1998). Dietary selenium is, therefore, necessary to obtain maximal immunity in pigs, but to avoid toxicity due to over supplementation the inclusion of selenium in diets fed to livestock is regulated by FDA and cannot exceed 0.3 ppm. However, recent research indicates that organic sources of selenium are better utilized by pigs than inorganic sources (Mahan and Parrett, 1996; Mahan et al., 1999). As a consequence, to obtain maximum improvements in the immune system, it may be advisable to use organic selenium, rather than inorganic sources of selenium.

Copper sulfate is usually added to nursery diets at concentrations between 150 and 250 ppm, although the nutritional requirement for copper is much lower. Likewise, zinc oxide is often added to starter diets at levels of 2,000 – 4,000 ppm, which is much higher than the nutritional requirement for zinc. However, the inclusion of these minerals at high concentrations in diets fed to nursery pigs has been shown to reduce scouring and to control post-weaning diarrhea without causing any toxicity symptoms (Poulsen, 1995; Goransson, 1997). These effects may be caused by the ability of zinc and copper to reduce concentrations of coliform bacteria in the intestinal tract of weanling pigs (Namkung et al., 2006). Both minerals have also been shown to have growth promoting effects of the same magnitude as what is usually expected from antibiotic growth promoters (Hahn and Baker, 1993; Smith et al., 1997; Hill et al., 2000).

The role of chromium as the glucose tolerance factor, and thus, the importance of chromium in insulin activity has been demonstrated (Steele et al., 1977; Houseknecht and Kahn, 1997). It also has been shown that supplemental chromium may improve the immune response in stressed feeder calves (Chang and Mowat, 1992; Kegley and Spears, 1995), and it has been demonstrated that chromium may modify carcass composition in finishing pigs (Kornegay et al., 1997; Mooney and Cromwell, 1997). Because of the crucial role of chromium in glucose and insulin metabolism and because of the demonstrated roles of chromium in improving the immune system in calves, it is likely that chromium may also contribute to an improvement of immunity in pigs, but at this point, this has not been experimentally verified (van Heughten and Spears, 1997).

Because of the high buffering capacity of limestone and inorganic phosphate sources, decreasing or omitting the dietary inclusion of these ingredients in diets fed to weanling pigs can reduce scouring. Exogenous phytase can be added to improve the digestibility of phytate-bound phosphorus and the requirement for calcium can be met by using calcium salts rather than limestone. Therefore, pigs can be fed diets without any calcium phosphates or limestone during the initial 2 to 3 weeks post weaning. Such diets have much lower buffering capacity than diets containing calcium phosphates and limestone, which will help the pig get through this period without developing diarrhea. However, after the initial post-weaning period, diets with normal levels of Ca and P need to be provided.

## CONCLUSIONS

A variety of strategies are needed to successfully wean pigs. The most effective way to reduce diarrhea in pigs is to reduce the crude protein content of the diets and to change the use of ingredients towards more barley and oats and less wheat and corn. Liquid or fermented liquid feeding may also be used to improve the intestinal health and the immune status of the pigs. Feed additives such as probiotics, acidifiers, and oligosaccharides also be used and all of these additives have well-documented effects on weanling pig performance.

Future developments likely will focus on identifying other means to improve the immune status of weanling pigs. The positive responses and dramatic improvements in growth rates obtained with functional proteins demonstrate that it is possible to influence the immune status of pigs in ways that enable pigs to resist pathogens and become less susceptible to diseases. As the pigs' genome becomes mapped and knowledge about the genomics involved in enhancing the immune system of pigs becomes available, more opportunities for feeding the pigs' immune system may become available. The genomics of beneficial enteric microbes as well as pathogens also will be elucidated, which may further improve the chance of creating diets that will improve the pigs' immune system.

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