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# REDUCED USE OF ANTIBIOTIC GROWTH PROMOTERS IN DIETS FED TO WEANLING PIGS: DIETARY TOOLS, PART 2

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Diets formulated to maximize performance of weanling pigs need to support the development of intestinal tissue, support intestinal colonization with beneficial, mainly lactic acid-producing bacteria, and support development of the intestinal and overall immune system. This objective is not likely to be achieved using one single strategy, but there is strong evidence that diets formulated with cereal grains other than corn, with a low concentration of crude protein and with the use of direct-fed microbials, will improve intestinal health and performance of weanling pigs. Further improvements may be observed if the grain part of the diet is fermented prior to feeding or if the diet is fed in a liquid form, but the need for specialized equipment limit the implementation of this strategy. Dietary supplements such as essential oils and nucleosides or nucleotides may also be useful, but more research is needed to verify the effects of these substances.

Keywords: Alternatives; Antibiotics; Feeding; Growth promoters; Pigs

Managing swine without using antibiotic growth promoters represents a challenge. Disease problems often are elevated and general performance is compromised on farms practicing nonmedicated swine production. That is true in particular during the immediate post weaning period, whereas antibiotics often can be removed from diets fed to growing-finishing pigs without encountering any apparent disease problems (1). The major problems in weanling pigs are occurrences of diarrhea that are most often related to infections with E. coli (2). Because of the difficulties associated with weaning pigs without antibiotics many producers are looking for alternative growth promoters or management strategies. At this point, however, there are no "magic bullets" available, but there are a variety of options that may improve performance of weanling pigs. Many of these options are equally effective in feeding programs using antibiotic growth promoters and programs without such promoters. While a variety of specific management strategies should be implemented to secure adequate post-weaning performance (3), a discussion of these programs is beyond the scope of this article. The current contribution will discuss a few nutritional strategies that may be used to improve weanling pig performance. Additional nutritional strategies are discussed in a separate article in the current proceedings (4). The discussion will mainly focus on strategies that can reduce the

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occurrence or the severity of diarrhea in weanling pigs. From this follows that factors that can improve the development of intestinal tissue, that can change the intestinal microflora to increase concentrations of "favorable" microorganisms, and factors that improve overall intestinal health of weanling pigs are important.

### ALTERNATIVE 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 nonstarch polysaccharides (NSP), and there are differences in the composition of the NSP fraction among the grains. Therefore, each grain has a different effect on the physiology of the gastrointestinal tract and the population of inhabitant microorganisms (5). Recent work in Australia has indicated that pigs fed diets based on cooked white rice and animal proteins are less susceptible to intestinal infections than are pigs fed diets based on other cereal grains (6,7). The reason for these observations may be that diets based on cooked rice and animal proteins contain mainly easily fermentable carbohydrates and very little NSP. Therefore, the majority of the carbohydrates are digested and absorbed in the small intestine and only small quantities of NSP will enter the large intestine, which in turn reduces the nourishment for microbes, including pathogens. This results in less fermentation, lower production of short-chained fatty acids, and a change in the microbial population in the large intestine (8,9). It has been shown that pigs experimentally infected with swine dysentery (6) or *E. coli* (9) had reduced colonization of pathogens in the large intestine if they were fed low-NSP diets based on cooked rice rather than diets containing greater levels of NSP. It appears that dietary concentrations of soluble NSP and resistant starch are highly correlated with the ability of pathogens to colonize in the intestinal tract of pigs (6). It has also been reported that pigs fed a diet based on cooked rice have greater daily feed intake, increased daily gain, lower visceral weights, and improved carcass gain compared with pigs fed diets containing greater levels of NSP (9,10). In agreement with these observations data from Spain showed that weanling pigs fed diets based on cooked rice rather than cooked corn or cooked oats had improved growth performance and a reduced incidence of diarrhea (11-14). The increased feed intake often observed for pigs fed diets containing cooked rice has been explained by an increased glycemix index in rice compared with corn (15). There is, therefore, strong evidence that diets fed to weanling pigs containing cooked rice as the main cereal source may improve pig performance and reduce the incidence of diarrhea. This effect is obtained because such diets contain reduced levels of soluble NSP and resistant starch, which in turn reduce the ability of pathogens to colonize in the intestinal tract of pigs.

This theory is in contrast to data showing that diets based on barley or oats also may reduce diarrhea in pigs (16) and improve growth performance (17). Recently, it was also reported that diets based on naked oats resulted in improved growth performance during the initial seven days post-weaning compared with diets based on corn, sorghum, or oats (Table 1). Diets based on barley and oats contain both soluble and insoluble NSP along with resistant starch. However, these grains may also contain unidentified nutrients that potentially can improve intestinal health of young pigs. Dietary NSP also increase the production of short chain fatty acids in

#### **REDUCED USE OF ANTIBIOTIC GROWTH PROMOTERS**

	Gain source					
Item	Corn	Sorghum	Oats	Naked oats		
Average daily gain, g	$95^x$	$74^x$	81 <sup>x</sup>	$129^{\nu}$		
Average daily feed intake, g Average gain:feed ratio, g/g	$\frac{160^x}{0.60^{xy}}$	$146^{x}$ 0.51 <sup>x</sup>	$145^{x}$ $0.55^{x}$	$195^{\nu}$ $0.66^{\nu}$		

Table 1 Effects of grain source in starter diets fed to weanling pigs from d 0-7 post-weaning<sup>a,b</sup>

<sup>a</sup>Unpublished data from Stein and colleagues.

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

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

the large intestine. This may 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 (18). Dietary NSP may also reduce the production of toxic nitrogenous compounds and support gut development. In addition, barley and oats contain relatively high quantities of beta-glucans that may have prebiotic effects because they stimulate lactic acid production (19,20). Thus, beneficial effects of including barley, oats, and naked oats in diets fed to weanling pigs have been documented in a number of experiments, but the exact mechanisms remain to be elucidated.

In conclusion, it is evident that the choice of cereal grain in diets fed to weanling pigs does influence not only growth performance, but also intestinal health of the pigs. Results indicate that there are two options for improving performance and health of pigs. One option is to reduce the concentration of dietary NSP, and soluble NSP and resistant starch in particular. This will result in reduced nourishment for microbes in the hind gut, and, therefore, reduced colonization by pathogens. The other option is to great grains containing specific NSP that have prebiotic effects in the hind gut of pigs. Barley, oats, and naked oats seem to contain such NSP, but much work is still needed to understand the mechanisms by which these NSP assert their effects.

#### LOW PROTEIN DIETS

The single most important nutritional factor for reducing scouring in pigs is to reduce the dietary crude protein concentration. Excessive dietary protein intake may increase the quantities of protein entering the large intestine, and, thus, increase microbial fermentation. Undigested feed protein may also accelerate the production of toxic nitrogenous compounds including ammonia which is harmful to intestinal health (21–23). Therefore, low-protein diets reduce scouring (24,25) and improve intestinal health (21) compared with diets containing higher levels of protein. If low-protein diets are supplemented with crystalline amino acids, normal pig performance can be maintained (26–28). A reduction in dietary crude protein from 21.2% to 18.4% with the addition of synthetic amino acids linearly decreased the incidence of diarrhea of weanling pigs, but no differences in pig performance, were observed (29). Likewise, le Bellego and Noblet (30) reduced dietary crude protein level from 22.4% to 16.9% with the addition of synthetic amino acids without reducing pig performance.

#### H. H. STEIN AND D. Y. KIL

By supplementing low protein diets with crystalline sources of lysine, methionine, threonine, and tryptophan it is usually possible to reduce the dietary concentration of crude protein by 3%-4%, while maintaining dietary levels of indispensable amino acids at or above the requirement of the pig. Most conventional diets fed to weanling pigs are formulated to contain 21 to 23% crude protein. By substituting some of the protein containing ingredients for crystalline amino acids such diets may be formulated to contain 18%–19% crude protein, which will reduce problems with scouring (29). However, if no antibiotics are included in the diets, it may be necessary to formulate diets containing less than 18% crude protein during the immediate postweaning 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 (31). Because the time period that amino acid requirements are not full filled 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. Decreased growth rate is generally compensated for after pigs are allowed to consume a diet adequate in crude protein (32). In a recent experiment in our laboratory, we fed pigs diets containing either 20.8 or 15.7% crude protein during the initial two weeks postweaning. During the following three weeks, each group of pigs was fed either a normal (17.5%) or a high crude protein (19.3%) diet. Results of this experiment showed that pigs fed the low crude protein diet during the initial two weeks postweaning had a reduced growth rate during this period. However, if they were allowed to consume a highprotein diet during the following three weeks they compensated and there were no differences over the entire 35-day postweaning period (Table 2).

In conclusion feeding low-protein diets during the immediate postweaning period will reduce diarrhea and improve intestinal health of the pigs. If it is necessary

1.6						
	Treatment					
Item	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><i>v</i></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>	$778^{xy}$	735 <sup><i>v</i></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	$0.65^{x}$	$0.70^{\nu}$	$0.64^{x}$	0.73 <sup>z</sup>	0.007	
Average gain:feed ratio, g/g, day 0-35	$0.66^{x}$	$0.70^{v}$	$0.65^{x}$	$0.70^{\nu}$	0.007	

**Table 2** Effects of feeding low protein diets followed by either normal or high protein diets to weanling  $pigs^{a,b}$ 

<sup>a</sup>Unpublished data from Stein and colleagues.

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

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

to reduce dietary amino acids to levels that are below the pig's requirement for maximal growth, pigs will compensate during the following period if they are allowed access to a diet that is adequate in amino acids.

### NUCLEOTIDES AND NUCLEOSIDES

The need for nucleotides is elevated during periods of rapid growth, during periods of stress, and in immunocompromised animals (33,34). In newly weaned pigs all of these factors are present; therefore; it is expected that they have a high requirement for nucleotides. In addition, weaning is often associated with intestinal atrophy and dietary nucleotides contribute to intestinal development and repair (35). Because nucleotide synthesis is an energy- and glutamine-requiring process (36) and because newly weaned pigs are often deficient in both energy and glutamine it is possible that pigs are unable to synthesize sufficient quantities of nucleotides during the immediate postweaning period. In a typical starter diet fed to weanling pigs, the concentration of 5'CMP is close to the concentration found in the DM of sow's milk during the last half of lactation, but the concentration of 5'AMP, 5'GMP, 5'IMP, and 5'UMP is much lower than in sow's milk (37,38; Table 3). Assuming that the concentrations of nucleotides in sow's milk are representative of the requirement of the pigs, it is easily concluded that a typical starter diet fed to young pigs is deficient in four of the five nucleotides. Newly weaned pigs, therefore, are facing the dilemma of increased nucleotide needs for the development of intestinal functions and structures, immune system development, and control of intestinal pathogens; but at the same time they are being fed a diet that does not provide the necessary quantities of nucleotides for these functions. In addition, they often have a low feed-intake during this period and, thus, a low intake of energy and glutamine, which are needed for the synthesis of new nucleotides. It may, therefore, be beneficial to add additional nucleotides or nucleosides to such diets.

In studies with pigs it has been demonstrated that dietary nucleotides reduce oxidative stress caused by high concentrations of polyunsaturated fatty acids in the diet (39). A combination of a dietary supplement of glutamine and nucleotides was also shown to improve feed intake, intestinal villus height, and serum IgG

	Nucleotide					
Item	5'AMP <sup>a</sup>	5'CMP <sup>a</sup>	5'GMP <sup>a</sup>	5'IMP <sup>a</sup>	5'UMP <sup>a</sup>	
Total in starter diet <sup><math>b</math></sup> Sows milk <sup><math>c</math></sup>	6 117	58 56	2 185	4 23	1 2334	
Difference	-111	2	-183	-19	-2333	

 Table 3 Calculated nucleotide concentration (ppm) of a starter diet for weanling pigs and of sow milk (DM-basis)

<sup>*a*</sup>Adenosine 5'monophosphate (5'AMP), cytidine 5'monophosphate (5'CMP), guanosine 5'monophosphate (5'GMP), inosine 5'monophosphate (5'IMP), and uridine 5'monophosphate (5'UMP).

<sup>b</sup>Diet formulated to contain the following feed ingredients: corn, 49.32%; whey powder, 20%; soybean meal, 8%; fish meal, 8%; spray dried protein plasma, 7.5%; vitamins, minerals, oil, crystalline amino acids, 7.18%.

<sup>c</sup>Data from Mateo, 2005 (37).

		Treatment					
Item	Control diet	30% nucleoside diet	nucleoside nucleoside		<i>P</i> -value, Linear effect	<i>P</i> -value, Quadratic effect	
Cl. perfringens	4.76	4.26	3.00	0.105	0.01	0.29	
Bifidobacterium spp. L. acidophilus	7.68 8.82	8.35 9.33	8.32 9.21	0.217 0.125	0.05 0.01	0.08 0.02	

**Table 4** Microbial counts  $(\log_{10} \text{ cfu/g})$  in fecal samples from weanling pigs fed diets from d 0 to 14 postweaning supplemented with 30% or 150% of the nucleoside concentration in porcine milk<sup>*a,b*</sup>

<sup>a</sup>Means of six observations per treatment group.

<sup>b</sup>Data from Mateo, 2005 (37).

concentrations in pigs challenged with a lipopolysaccharide injection (40). Dietary supplementation with purified nucleotides to milk replacers of newborn bull calves challenged with lipopolysaccharides resulted in calves that tended to have higher mean IgG levels compared with the unsupplemented control calves (41). Nucleotide supplementation also increased lymphocyte stimulation to phytohaemagglutinin and concanavalin-A challenges in weanling pigs by 50% and 30%, respectively (42). Results of these studies suggest that dietary sources of nucleotides play a role in developing, maintaining, and enhancing the immune system.

Dietary nucleotides enhance intestinal absorption of iron, affect lipoprotein and long chain polyunsaturated fatty acid metabolism, have trophic effects on the intestinal mucosa and liver, and reduce the incidence of diarrhea (43,44). The fecal flora of infants fed a nucleotide-supplemented commercial milk formula had a predominance of bifidobacteria (45), while enterobacteria dominated in the fecal flora of infants fed a commercial formula without nucleotide supplementation (46). These studies suggest that nucleotide supplementation may positively influence the microflora in the gastrointestinal tract which leads to a lowering of gastric pH and hinders the proliferation of pathogenic bacterial species as evidenced by a lower rate of diarrhea (47). Recently, it was shown that dietary nucleosides added to starter diets for weanling pigs in quantities equal to either 30% or 150% of the quantities found in porcine milk increased concentrations of L. acidophilus and Bifidobacterium spp. in fecal extracts from the pigs, whereas the concentration of *Cl. perfringens* was reduced (37; Table 4). Dietary nucleosides may also enhance the growth and maturation of intestinal epithelial cells as evidenced by an increased formation of mucosal protein, DNA, taller villi in the small intestine, and an increased maltase to lactase ratio (36,40,48,49).

It appears from the above that there is a growing body of research indicating beneficial effects of supplementing diets fed to weanling pigs with nucleotides or nucleosides. However, studies that demonstrates these effects under commercial conditions still need to be conducted. In addition, sources of nucleotides that can be economically included in diets fed to weanling pigs have yet to be identified.

# **DIRECT-FED MICROBIALS**

Direct-fed microbials, or probiotics, are live cultures that are added to diets for pigs or other animal species. Presumably, these organisms will 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. There are three main categories of organisms that are commonly referred to as probiotics:

- 1. Bacillus (gram positive spore-forming bacteria)
- 2. Lactic acid producing bacteria (Lactobacillus, Bifidobacterium, Enterococcus)
- 3. Yeast

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 gastrointestinal (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 needs to be stabilized and have the ability to survive in feed

It follows from the above that direct fed microbials are organisms that are able to colonize in the GI tract of an animal and, thus, improve intestinal health by competitive exclusion of pathogens. Most of the commercial products on the market are either lactic acid producing bacteria or yeast. Concentrations of enteric lactic acid producing bacteria usually are reduced during the immediate postweaning period, which enables pathogens, and *E. coli* in particular, to increase in concentration with an increased risk of intestinal diseases as a result (50). It is, therefore, not surprising that there is a substantial interest in providing newly weaned pigs with lactic acid producing bacteria to restore the balance in the intestinal tract. Among the organisms most often used in this group are *Lactobacillus acidophilus*, *Lactobacillus* spp, *Enterococci faecium*, *Bacillus lichiniformis*, *Bacillus subtillis*, *Bifidobacterium bifidum*, *Bifidobacterium thermophilus*, and others (51).

In vivo experiments in which lactic acid producing bacteria were fed to weanling pigs have yielded variable results. Recently, it was reported that in 30 out of 31 trials in which a combination of *Bacillus lichiniformis* and *Bacillus subtilis* had been included in diets fed to weanling pigs a positive growth response had been obtained (52). In several experiments, in which other lactic acid producing bacteria were fed to weanling pigs, positive responses were also reported (53–59). However, there are also reports of experiments in which no effects of these organisms were obtained (60).

Yeast cultures are also available for inclusion in diets fed to weanling pigs. These products may be either in the form of live yeast or dried yeast. Positive performance responses to the inclusion of yeast in diets fed to weanling pigs have been reported (61-63). It has also been reported that dietary yeast may reduce the concentration of total coliforms in the intestinal tract of pigs (64). However, no effects of including yeast to diets fed to weanlig pigs were reported from other experiments (63,65,66).

Based on the currently available data it may be concluded that there are at least some direct fed microbials that have successfully been shown to improve performance of weanling pigs. However, results reported so far have been somewhat inconsistent, but that does not necessarily mean that direct fed microbials cannot improve pig performance. Future work needs to focus on organisms that can consistently improve performance and/or intestinal health of weanling pigs.

# **ESSENTIAL OILS**

Antimicrobial properties of various extracts of herbs and spice preparations have been reported for many centuries. These compounds have been used extensively to treat a variety of human diseases by Native Americans, by Middle East cultures, and in Chinese medicine. Among the diseases treated are intestinal problems. The essential oil of the plant is often the biologically active component of herbs and spices (67), but this is not always the case (68). An essential oil is defined as a volatile oil usually having the characteristic odor or flavor of the plant from which it is obtained. Therefore, essential oils may improve performance of animals not only by reducing intestinal microbial activity but also by increasing palatability of diets. These oils are generally accepted for use as additives by Food and Drug Administrations (69). The antimicrobial 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 (68,70). The inhibitory properties of 50 essential oils against 25 different bacteria have been reported (68). Oils that contain phenolic structures have stronger antimicrobial properties than oils without phenolic structures (71). The mode of action of essential oils has not been established, but the activity may be related to changes in lipid solubility at the surface of the bacteria (69). It also has been demonstrated that the hydrophobic constituents of essential oils allow them to disintegrate the outer membrane of E. coli and S. typhimurium, and thus inactivate these pathogens (72).

Of the essential oils that are used in weanling pig diets garlic, oregano, thymol, and carvacrol have received the most interest. Antimicrobial activity of garlic against both gram-positive and gram-negative bacteria has been reported (73). In diets fed to newly weaned pigs, feed efficiency and rate of gain was not different for pigs fed diets supplemented with 0.05% garlic compared with pigs fed diets supplemented with Carbadox (74). In addition to the antimicrobial activity, garlic also reduces the production of free radicals, lipid peroxides, and blood lipid concentration (75).

The addition of oregano extracts to broiler diets has been shown to reduce the severity of coccidioses (76). In an experiment with growth-retarded growingfinishing pigs it was shown that dietary oregano may improve performance and immune system activation (77). Oregano has also been shown to have strong in-vitro antimicrobial properties against a number of pathogens often found in the intestinal tract of pigs (78). However, although oregano is marketed for inclusion in diets fed to weanling pigs, it has not been possible to find any reports in the peer-reviewed literature that document that performance of weanling pigs is improved by the dietary inclusion of oregano. Thymus and carvacrol are two of the compounds present in oregano and both have been shown to have strong antimicrobial properties in several in vitro studies (72,78,79). However, there are no reports available that demonstrate improved growth performance, if thymus or carvacrol is fed to weanling pigs.

It has also been reported that combinations of more than one type of oils will elicit a stronger antimicrobial response than if only one type is used (70,80). Namkung and colleagues (81) fed a combination of oregano, thyme, and cinnamon to weanling pigs at a dietary concentration of 0.75%. Pigs fed this diet had a lower daily gain and daily feed intake than control pigs fed the same diet without the essential oil. The authors explained these effects by a strong smell of the diet containing the essential oils.

In conclusion, there is strong evidence that many essential oils have significant in vitro antimicrobial activities against a variety of pathogens normally present in the intestinal tract of pigs. These compounds may, therefore, hold promise as feed supplements that can be used to control enteric diseases in weanling pigs. 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 peerreviewed 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.

### FERMENTED LIQUID FEEDING

Liquid feeding generally results in fewer intestinal problems than dry feeding. Improved growth rate and feed intake of weanling pigs fed diets in a liquid rather than in a dry form has been reported from several experiments (82–84). In ten experiments conducted in Denmark, daily weight gain was improved by 12.3% on average for pigs fed liquid diets compared with pigs fed dry feed (85). Studies in the US have shown even greater improvements in performance for pigs fed liquid diets rather than dry feed (86–88). It also has been reported that pigs fed a liquid diet during the initial 14 days postweaning will reach marked weight 3.7 days sooner than their littermates that were fed the same diet in a dry form (88). The reason for the improved performance of liquid-fed pigs may be that gastric pH is reduced in pigs fed liquid or fermented liquid diets because the number of lactic acid bacteria and the acidity of the diet is increased (89,90). Therefore, pathogenic bacteria growth is inhibited or reduced (91). The increased feed intake during the postweaning period for pigs fed liquid diets prevents the atrophy of intestinal villi that often is observed in pigs provided a dry diet (92–94). 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. Increased contents of short chained fatty acids and reduced microbial activity in the intestines of pigs fed liquid or fermented liquid diets may also contribute to improved performance (95).

Fermentation of the liquid feed prior to feeding has been reported to reduce the concentration of pathogens in the diet and in the intestinal tract of the pigs (96,97). 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 (97,98). Thus, fermented liquid feeding could have characteristics similar to probiotics and organic acidifiers.

The performance of pigs fed fermented liquid feed was summarized from several experiments (85). On average, fermented liquid feeding resulted in an increase in growth rate of 13.4% compared with nonfermented liquid feeding and by 22.3% compared with dry feed. However, in a few experiments there were no improvements in pig performance when fermented liquid feed was provided rather than dry feed (99,100). The reason for these differences may be that fermentation, if not carefully controlled, can result in increases in coliform bacteria that may be detrimental to the intestinal microflora. Fermentation may also result in feed that has a pH lower than 4.0, which will reduce feed intake of the pigs. Reduced feed to gain ratios has also been reported for pigs fed fermented feed compared with pigs fed dry feed (85). This is probably due to fermentation of sugars and free amino acids present in the diets. Recently, it has been demonstrated that fermentation of only the carbohydrate source in the diet (i.e., the cereal grain) improves average daily gain and the gain to feed ratio (94). It also has been reported that the loss of lysine during fermentation may be prevented if small concentrations of lactobacillus are included in the fermentation (101), but the effects on other amino acids has not been reported. Therefore, there seems to be several options for avoiding the reduction in the gain to feed ratio.

Based on the available research, it is evident that feeding liquid or fermented liquid feed to pigs during the postweaning period has a positive effect on pig performance and intestinal health. This is, therefore, an option that deserves consideration when feeding programs for weanling pigs are designed. The availability of soluble coproducts from the fermentation industry may offer new ingredients that could be included in a program based on liquid or fermented liquid feeding.

#### CONCLUSIONS

A variety of strategies are needed to successfully wean pigs without the use of antibiotic growth promoters. Among the dietary tools that may be considered are reducing dietary crude protein concentration, use of cereal grains other than corn, and possibly the use of direct fed microbials. While there is never a guarantee for success, these strategies have shown to be effective in reducing intestinal problems and improving pig performance in a majority of the experiments that are reported in the literature. Use of fermented liquid feed is another option that has shown promising results, but this technique requires specialized equipment and a commitment to hygiene and may, therefore, not be applicable for all producers. Supplementing diets with essential oils has the potential to reduce concentrations of pathogens in the intestinal tract of weanling pigs, but, at this point, there is a lack of documentation for the effectiveness of essential oils in diets fed to pigs kept under commercial conditions. Dietary nucleosides or nucleotides may also be useful, but more research is needed to verify if performance can be improved using such supplementations.

#### REFERENCES

- 1. Wierup M. The experience of reducing antibiotics used in animal production in the Nordic countries. Intl J Antimicrob Agents 2001; 18:287–290.
- Laine T, Yliaho M, Myllys V, Pohjanvirta T, Fossi M, Anttila M. The effect of antimicrobial growth promoter withdrawal on the health of weaned pigs in Finland. Prev Vet Med 2004; 66:163–174.
- Stein HH. Experience of feeding pigs without antibiotics: A European perspective. Anim Biotech 2002; 13:85–95.
- 4. Pettigrew JE. Dietary Tools: Part 1. Anim Biotech 2006; 17:In Press.

- Bach Knudsen KE. Development of antibiotic resistance and options to replace antimicrobials in animal diets. Animal Nutrition and Metabolism Group Symposium on 'Quality inputs for quality foods.' Proc Nutr Soc 2001; 60:291–299.
- Pluske JR, Siba OM, Pethick DW, Durmic Z, Mullan BP, Hampson DJ. The incidence of swine dysentery in pigs can be reduced by feeding diets that limit the amount of fermentable substrate entering the large intestine. J Nutr 1996; 126:2920–2933.
- Pluske JR, Durmic Z, Pethick DW, Mullan BP, Hampson DJ. Confirmation of the role of rapidly fermentable carbohydrates in the expression of swine dysentery in pigs after experimental infection. J Nutr 1998; 128:1737–1744.
- Siba PM, Pethick DW, Hampson DJ. Pigs experimentally infected with Serpulina hyodysenteriae can be protected from developing swine dysentery by feeding them a highly digestible diet. Epidemiol Infect 1996; 116:207–216.
- McDonald DE, Pethick DW, Pluske JR, Hampson DJ. Adverse effects of soluble nonstarch polysaccharide (guar gum) on piglet growth and experimental colibacillosis immediately after weaning. Res Vet Sci 1999; 67:245–250.
- Pluske JR, Hampson DJ. Rice-based diets in pigs: For protection against bacterial infections. Rural Industries Research and Development Corporation Publication 2005; 5:143.
- Mateos GG, Alcantarilla A, Latorre MA, Lazaro R, Gomez E, Laso N. Influence of type of cereal and level of fiber on performance of early-weaned piglets. J Anim Sci 2001; 79(Suppl.1):106.
- 12. Lopez E, Latorre MA, Valencia DG, Lazaro R, Mateos GG. Inclusion of oat hulls in diets for piglets based on native or cooked cereals. J Anim Sci 2003; 81(Suppl.1):47.
- Vincente B, Valencia DG, Lazaro R, Latorre MA, Mateos GG. Use of rice in substitution of corn in diets for young pigs. J Anim Sci 2004; 82(Suppl.1):456.
- Mateos GG, Martin F, Latorre MA, Vicente B, Lazaro R. Inclusion of oat hulls in diets for young pigs based on cooked maize or cooked rice. Anim Sci 2006; 82:57–63.
- Vicente B, Valencia DG, Gonzales JM, Menoyo D, Lazaro R, Mateos GG. Glycemic index of young pigs fed rice or corn either raw or cooked. J Anim Sci 2006; 84(Suppl.1):45.
- Paulicks BR, Roth FX, Kirchgessner M. Effects of potassium diformate(Formi<sup>®</sup> LHS) in combination with different grains and energy densities in the feed on growth performance of weaned pigs. J Anim Physiol Anim Nutr 2000; 84:102–111.
- Medel P, Salado S, de Blas JC, Mateos GG. Processed cereals in diets for early-weaned piglets. Anim Feed Sci Technol 1999; 82:145–156.
- Montagne L, Pluske JR, Hampson DJ. A review of interactions between dietary fibre and the intestinal mucosa, and their consequences on digestive health in young nonruminant animals. Anim Feed Sci Technol 2003; 108:95–117.
- Bach Knudsen KE, Canibe N. Breakdown of plant carbohydrates in the digestive tract of pigs fed on wheat- or oat-based rolls. J Sci Food Agric 2000; 80:1253–1261.
- O'Connell JM, Callan JJ, O'Doherty JV. The interaction between cereal type and lactose level on piglet performance and diet digestibility post weaning. Anim Sci 2005; 81:265–269.
- Bolduan G, Jung H, Schnabel E, Schneider R. Recent advances in the nutrition of weaner piglets. Pig News Info 1988; 9:381–385.
- Pluske JR, Pethick DW, Hopwood DE, Hampson DJ. Nutritional influences on some major enteric bacterial disease of pigs. Nutr Res Rev 2002; 15:333–371.
- Nyachoti CM, Omogbenigun FO, Rademacher M, Blank G. Performance responses and indicators of gastrointestinal health in early-weaned pigs fed low-protein amino acidsupplemented diets. J Anim Sci 2006; 84:125–134.
- Ball RO, Aherne FX. Influence of dietary nutrient density, level of feed intake and weaning age on young pigs. II. Apparent nutrient digestibility and incidence and severity of diarrhea. Can J Anim Sci 1987; 67:1105–1115.

- Goransson L, Lange S, Lonroth I. Post-weaning diarrhoea: Focus on diet. Pigs News and Information 1995; 16:89N–91N.
- Cinq-Mars D, Goulet G, Brisson GJ. Response of piglets to suboptimal protein diets supplemented with lysine, methionine, threonine and tryptophan. Can J Anim Sci 1988; 68:311–313.
- Hansen JA, Knabe DA, Burgoon KG. Amino acid supplementation of low-protein sorghum-soybean meal diets for 5- to 20-kilogram swine. J Anim Sci 1993; 71:452–458.
- Han IK, Heo KN, Shin IS, Lee H. Protein sparing effect and amino acid digestibility of supplemental lysine and methionine in weanling pigs. Asian-Aust J Anim Sci 1995; 8:393–402.
- Reynoso E, Cervantes M, Figueroa JL, Cuca JM. Productive response of pigs to lowprotein diets added synthetic amino acids and yeast culture. Cuban J Agri Sci 2004; 38:269–275.
- le Bellego L, Noblet J. Performance and utilization of dietary energy and amino acids in piglets fed low protein diets. Livest Prod Sci 2002; 76:45–58.
- Goransson L. Alternatives to antibiotics—the influence of new feeding strategies for pigs on biology and performance. In Recent Advances in Animal Nutrition; Garnsworthy PC, Wiseman J, Eds; Nothingham University Press, Nottingham, UK, 1997:45–56.
- Kyriazakis I, Stamataris C, Emmans G, Whittemore CT. The effects of food protein content on the performance of pigs previously given foods with low or moderate protein contents. Anim Prod 1991; 52:165–173.
- Kulkarni AD, Rudolph FB, van Buren CT. The role of dietary sources of nucleotides in immune function: A review. J Nutr 1994; 124:1442–1446.
- 34. Carver JD, Walker WA. The role of nucleotides in human nutrition. Nutr Biochem 1995; 6:58–72.
- Uauy R, Stringel G, Thomas R, Quan R. Effect of dietary nucleosides of growth and maturation of the developing gut in rat. J Pediatr Gastroenterology Nutr 1990; 10:497–503.
- Rodwell VW. Metabolism of purine and pyrimidine nucleotides. In Harpers Biochemistry (25th ed.); Murray RK, Granner DK, Mayes PA, Rodwell VW, Eds; Appleton and Lange, Stamford, CT, 2000:386–401.
- Mateo CD. Aspects of Nucleotide Nutrition in Pigs. PhD. Dissertation. South Dakota State University, Brookings, SD, 2005.
- Mateo CD, Peters DN, Stein HH. Nucleotides in sow colostrum and milk at different stages of lactation. J Anim Sci 2004; 82:1339–1342.
- Salobir J, Rezar V, Pajk T, Levart A. Effect of nucleotide supplementation on lymphocyte DNA damage induced by dietary oxidative stress in pigs. Anim Sci 2005; 81: 135–140.
- Yu IT, Wu JF, Yang PC, Liu CY, Lee DN, Yen HT. Roles of glutamine and nucleotides in combination in growth, immune response, and FMD antibody titres of weaned pigs. Anim Sci 2002; 75:379–385.
- Oliver CE, Bauer ML, Schroeder JW, Keller WL, Park CS. Dietary nucleotides enhance calf immune function. FASEB J 2002; 16:5.
- Zomborsky-Kovacs M, Tuboly S, Biro H, Bardos L, Soos P, Toth A, Tornyos G. The effect of β-carotene and nucleotide base supplementation on haematological, biochemical and certain immunological parameters in weaned pigs. J Anim Feed Sci 1998; 7: 245–251.
- 43. Cosgrove M. Perinatal and infant nutrition. Nucleotides. Nutr 1998; 14:748-751.
- 44. Schlimme E, Martin D, Meisel H. Nucleosides and nucleotides: Natural bioactive substances in milk and colostrum. Br J Nutr 2000; 84:59–68.

- Tanaka R, Mutai M. Improved medium for selective isolation and enumeration of Bifidobacterium. Appl Env Microbiol 1980; 40:866–869.
- 46. Uauy R. Nonimmune system responses to dietary nucleotides. J Nutr 1994; 124:157–159.
- 47. Yu VY. The role of dietary nucleotides in neonatal and infant nutrition. Sing Med J 1998; 39:145–150.
- Carver JD. Dietary nucleotides: Cellular immune, intestinal and hepatic system effects. J Nutr 1994; 124:144–148.
- Sanderson IR, Youping HE. Nucleotide uptake and metabolism by intestinal epithelial cells. J Nutr 1994; 124:131–137.
- 50. Doyle ME. Alternatives to Antibiotic use for Growth Promotion in Animal Husbandry. FRI Briefings; Food Research Institute, University of Wisconsin, Madison, WI, 2001.
- Johnson E, Conway P. Probiotics for pigs. In Probiotics, the Scientific Basis; Fuller R, Ed; Chapman and Hall, London, UK, 1992.
- 52. Kremer B. DFM products provide consistent outcomes. Feedstuffs 2006; April 24:14–15.
- Muralidhara KS, Sheggeby GG, Elliker PR, England DC, Sandine WE. Effect of feeding lactobacilli on the coliform and lactobacillus flora of intestinal tissue and feces from piglets. J Food Protec 1977; 40:288–295.
- 54. Lessard M, Brisson GJ. Effect of a lactobacillus fermentation product on growth, immune response and fecal enzyme activity in weaned pigs. Can J Anim Sci 1987; 67:509–516.
- 55. Abe F, Ishibashi N, Shimamura S. Effect of administration of bifidobacteria and lactic acid bacteria to newborn calves and piglets. J Dairy Sci 1995; 78:2838–2846.
- 56. Apgar GA, Kornegay ET, Lindemann MD, Wood CM. The effect of feeding various levels of Bifidobacterium globosum A on the performance, gastrointestinal measurements, and immunity measurements of growing-finishing pigs. J Anim Sci 1993; 71:2173–2179.
- Tortuero F, Rioperez J, Fernandez E, Rodriguez ML. Response of piglets to oral administration of lactic acid bacteria. J Food Protec 1995; 58:1369–1374.
- Zani JL, Dacruz FW, Dossantos AF, Gilturnes C. Effect of probiotic CenBiot on the control of diarrhea and feed efficiency in pigs. J Appl Microbiol 1998; 84:68–71.
- Kyriakis SC, Tsiloyiannis VK, Vlemmas J, Sarris K, Tsinas AC, Alexopoulos C, Jansegers L. The effect of probiotic LSP 122 on the control of post-weaning diarrhea syndrome of piglets. Res Vet Sci 1999; 67:223–228.
- 60. Jost M, Bracher JA. The effect of Sanobiotic R S, a multiactive probiotic growth promoter, in rearing piglets. Appl Env Microbiol 1999; 66:4200–4204.
- Maloney CA, Nemecheck CS, Hancock JD, Park JS, Cao H, Hines RH. Effect of a yeast product in pelleted diets for weanling pigs. J Anim Sci 1998; 76(Suppl. 2):47.
- Mathew AG, Chattin SE, Robbins CM, Golden DA. Effects of a direct-fed yeast culture on enteric microbial populations, fermentation acids, and performance of weanling pigs. J Anim Sci 1998; 76:2138–2145.
- van Heughten E, Funderburke DW, Dorton KL. Growth performance, nutrient digestibility, and fecal microflora in weanling pigs fed live yeast. J Anim Sci 2003; 81: 1004–1012.
- 64. White LA, Newman MC, Cromwell GL, Lindemann MD. Brewers dried yeast as a source of mannan oligosaccharides for weanling pigs. J Anim Sci 2002; 80:2619–2628.
- 65. Kornegay ET, Rhein-Welker D, Lindemann MD, Wood CM. Performance and nutrient digestibility in weanling pigs as influenced by yeast culture additions to starter diets containing dried whey or one of two fiber sources. J Anim Sci 1995; 73:1381–1389.
- Jost M, Bracher JA. Yeast products as feed additives in weanling piglets. Agrarforshung 2000; 7:56–61.

- 67. Zaika LL, Kissinger JC, Wasserman AE. Inhibition of lactic acid bacteria by herbs. J Food Sci 1983; 48:1455–1459.
- 68. Deans SG, Ritchie G. Antibacterial properties of plant essential oils. Int J Food Sci 1987; 5:165–180.
- 69. Dabbah RV, Edwards M, Moats WA. Antimicrobial action of some citrus fruit oils on selected food-borne bacteria. Appl Microbiol 1970; 19:27–31.
- Piccaglia R, Marotti M, Giovanelli E, Deans SG, Eaglesham E. Antibacterial and antioxidant properties of medditarian aromatic plants. Indust Crops and Prod 1993; 2:47–50.
- Dorman HJD, Deans SG. Antimicrobial agents from plants: Antibacterial activity of plant oils. J Appl Microbiol 2000; 88:308–316.
- Lambert RJW, Skandamis PN, Coote PJ, Nychas GJE. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. J Appl Microbiol 2001; 91:453–462.
- 73. Ross ZM, O'Gara EA, Hill DJ, Sleightholme HV, Maslin DJ. Antimicrobial properties of garlic oil against human enteric bacteria: Evaluation of methodologies and comparisons with garlic oil and garlic powder. Appl Env Microbiol 2001; 67:475–480.
- Jost M. Einsatz von Knoblauchpulver im Ferkelaufzuctfutter. Agrarforshung 1996; 3:479–481.
- 75. Close WH. Producing pigs without antimicrobial growth promoters. Adv Pork Prod 2000; 11:47–56.
- Giannenas I, Florou-Paneri P, Papazahariadou M, Christaki E, Botsoglou NA, Spais AB. Effect of dietary supplementation with oregano essential oil on performance of broilers after experimental infection with *Eimeria tenella*. Arch Anim Nutr 2003; 57:99–106.
- Walter BM, Bilkei G. Immunostimulatory effect of dietary oregano etheric oils on lymphocytes from growth-retarded low-weight growing-finishing pigs and productivity. Tijdschr Diergeneeskd 2004; 129:178–181.
- Burt SA, Reinders RD. Antibacterial activity of selected plant essential oils against Escherichia coli O157:H7. Letters Appl Microbiol 2003; 36:162–167.
- Cossentino S, Tuberoso CIG, Pisano B, Satta M, Mascia V, Arzedi E, Palmas F. In-vitro antimicrobial activity and chemical composition of Sardinian Thymus essential oils. Letters Appl Microbiol 1999; 29:130–135.
- 80. Shelef LA, Naglik OA, Bogen DW. Sensitivity of some common food-borne bacteria to the spices sage, rosemary, and allspice. J Food Sci 1980; 45:1042–1044.
- Namkung H, Li M, Gong J, Yu H, Corttrill M, de Lange CFM. Impact of feeding blends of organic acids and herbal extracts on growth performance, gut microbiota and digestive function in newly weaned pigs. Can J Anim Sci 2004; 84:697–704.
- 82. Braude R, Newport MJ. A note on a comparison of two systems for rearing pigs weaned at 2 days of age, involving either a liquid or a pelleted diet. Anim Prod 1977; 24:271–274.
- Lecce JG, Armstrong WD, Crawford PC, Ducharme GA. Nutrition and management of early weaned piglets: Liquid vs dry feeding. J Anim Sci 1979; 48:1007–1014.
- Partridge GG, Fisher J, Gregory H, Prior SG. Automated wet feeding of weaner pigs versus conventional dry diet feeding: Effects on growth rate and food consumption. Anim Prod 1992; 54:484.
- Jensen BB, Mikkelsen LL. Feeding liquid diets to pigs. In Recent Advances in Animal Nutrition; Garnsworthy PC, Wiseman J, Eds; Nottingham University Press, Loughborough, UK, 1998.
- Zijlstra RT, Wang KY, Easter RA, Odle J. Effect of feeding a milk replacer to early weaned pigs on growth, body composition, and small intestinal morphology compared with suckled littermates. J Anim Sci 1996; 74:2948–2959.

- Odle J, Harrel RJ. Nutritional approaches for improving neonatal piglet performance: Is there a place for liquid diets in commercial production? Review. Asian-Aust J Anim Sci 1998; 11:774–780.
- Kim JH, Heo KN, Odle J, Han IK, Harrell RJ. Liquid diets accelerate the growth of early-weaned pigs and the effects are maintained to market weight. J Anim Sci 2001; 79:427–434.
- Geary TM, Brooks PH, Morgan DT, Campbell A, Russell PJ. Performance of weaner pigs fed *ad libitum* with liquid feed at different dry matter concentrations. J Sci Food Agric 1996; 72:17–24.
- van Winsen RL, Urlings BAP, Lipman LJA, Snijders JMA, Keuzenkamp D, Verheijden JHM, van Knapen F. Effect of fermented feed on microbial population of the gastrointestinal tract of pigs. Applied Env Microbiol 2001; 67:3071–3076.
- van Winsen RL, Lipman LJA, Biesterveld S, Urlings BAP, Snijders JMA, van Knapen F. Mechanism of salmonella reduction in fermented pig feed. J Sci Food Agric 2000; 81:342–346.
- Deprez P, Deroose P, van den Hende C, Muylle E, Oyaert W. Liquid versus dry feeding in weaned piglets: The influence on small intestine morphology. J Vet Med 1987; 34: 254–259.
- Yang JS, Lee JH, Ko TG, Kim TB, Chae BJ, Kim YY, Han IK. Effects of wet feeding of process diets on performance, morphological changes in the small intestine and nutrient digestibility in weaned pigs. Asian-Aust J Anim Sci 2001; 14:1308–1315.
- Scholten RHJ, van der Peet-Schwering CMC, den Hartog LA, Balk M, Schrama JW, Verstegen MWA. Fermented wheat in liquid diets: Effects on gastrointestinal characteristics in weanling piglets. J Anim Sci 2002; 80:1179–1186.
- Scholten RHJ, van der Peet-Schwering CMC, Verstegen MWA, den Hartog LA, Schrama JW, Vesseur PC. Fermented co-products and fermented compound diets for pigs: A review. Anim Feed Sci Technol 1999; 82:1–19.
- 96. Brooks PH, Moran CA, Beal JD, Demeckova V, Campbell A. Liquid feeding for the young piglet. In The Weaner pig: Nutrition and Management; Varley MA, Wiseman J, Eds; CAB International, Wallingford, UK, 2001.
- Brooks PH, Beal JD, Niven S, Demeckova V. Liquid feeding of pigs. II. Potential for improving pig health and food safety. In Animal Science Papers and Reports. Presented at the Conference: Effect of Genetic and Non-genetic Factors on Carcass and Meat Quality of Pigs. Siedlee, Poland, 2003:April 24–25.
- Mikkelsen LL, Jensen BB. Effect of fermented liquid feed (FLF) on growth performance and microbial activity in the gastrointestinal tract of weaned piglets. In VIIth Intl. Symp. Digest. Phys. in Pigs; European Association for Animal Production, Saint Malo, France, 1997:639–642.
- 99. Lawlor PG, Lynch PB, Gardiner GE, Caffrey PJ, O'Doherty JV. Effect of liquid feeding weaned pigs on growth performance to harvest. J Anim Sci 2002; 80:1725–1735.
- Pedersen C, Ross S, Jonsson H, Lindberg JE. Performance, feeding behavior and microbial diversity in weaned piglets fed liquid diets based on water or wet wheat distillers grain. Arch Anim Nutr 2005; 59:165–179.
- 101. Niven SJ, Beal JD, Brooks PH. The effect of controlled fermentation on the fate of synthetic lysine in liquid diets for pigs. Anim Feed Sci Technol 2006; 129:304–315.