Alternative strategies to antibiotic growth promoters in diets for swine

By Hans H Stein, PhD

Associate Professor

South Dakota State University

Brookings SD

Ensminger Interantional Conference

Seoul National University,

Korea

1. Introduction

Managing swine 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 for growing-finishing swine without introducing major disease problems (Stein, 2002). Because of the difficulties associated with producing pigs without antibiotics, many producers are looking for alternative growth promoters or management. At this point, however, there are no "magic bullets" 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. In this summary, the major approaches within each strategy will be discussed. Focus will be on feeding pigs during the immediate post-weaning period.

2. Management strategies to improve pig performance

The management strategies that have proven to work the best to overcome the problems associated with swine production without in-feed antibiotics are the ones that build on the pig's basic environmental, nutritional, and immunological requirements. While management programs that are constructed around these principles have proven not to be completely effective in preventing or eliminating the problems on all farms, they have worked well on many farms and present a minimum requirement for the further work in the area.

2.1 Environmental comfort

The importance of a warm and draft-free environment within the animal's thermoneutral zone cannot be over-emphasized. Controlling the heating and ventilation systems, therefore, is absolutely critical to make sure that the temperature, the humidity, and air movement are within optimal limits. Air concentrations of ammonia, hydrogen sulfite, and other noxious gasses should also be controlled.

2.2. Minimize comingling

Comingling pigs in the nursery or in the growing-finishing building from different farms should absolutely be avoided because the pigs come in with different pathogens and different levels of immune protection. This is also true if pigs are sourced from sow farms that are thought to have an equivalent health status. Comingling of pigs from the same farm should also be avoided if possible, however for practical reasons, some mixing is usually necessary right after weaning. Movement of pigs from one pen to another should be kept at an absolute minimum and movement between rooms or buildings should never be tolerated. Using a wean to finish system rather than a traditional 3-site production system represents an opportunity to reduce the number of times pigs are moved and mixed.

2.3 Later weaning

One of the reasons in-feed antibiotics are usually needed in diets fed to newly weaned pigs is that the pigs are usually weaned at an age of two to three weeks. At this age, the pig's active immune system is not yet developed and the pig largely depends on a liquid milk-based diet provided by the sow. Weaning at this age creates

a lot of constraints for the pig. If weaning is postponed until the pig is 3 to 5 weeks old, the immune system will be better developed enabling the pig to better prevent pathogens from causing diseases in the pig. In addition, if pigs are weaned at 4 to 5 weeks, they will be consuming quit a bit of creep feed prior to weaning making the dietary transition to an all-dry and largely vegetable diet less stressful. Therefore, the need for a dietary antibiotic is reduced, and pigs are more likely to be successfully weaned without using an in-feed antibiotic.

The downside to later weaning is that more farrowing crates are needed on a given farm because sows stay in the crates for a longer period of time. In contrast, fewer pig spaces in the nursery are needed and less of the expensive starter diets are needed during the immediate post-weaning period. If sows are weaned 4-5 rather than 2-3 weeks after parturition, they will farrow more live born pigs in the next litter and they will have shorter weaning to breeding intervals, fewer non-productive sow days, and higher farrowing rates. Therefore, the overall profitability in the sow herd is unlikely to be compromised, however, research is needed to verify this hypothesis.

3. Nutritional Strategies

3.1 Low-protein diets

The single most important nutritional factor for reducing scouring in pigs fed diets without antibiotics is to reduce the dietary crude protein concentration. In general, formulating low-protein diets supplemented with synthetic amino acids results in fewer intestinal problems than using diets with a higher protein content. (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. However, for nursery pigs, it may be necessary to formulate diets

containing less than 18% CP 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 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. Unpublished research from our laboratory indicate that pigs fed diets containing approximately 20% less amino acids than recommended (NRC, 1998) will result in a reduction in daily gain of approximately 60 g per day. If such diets are fed during the initial two weeks post weaning, then a total of 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 42 post-weaning, there is no difference in the body weight of the pigs regardless of the protein concentration they received during the initial 2 weeks post weaning. However, the pigs on the low protein diets have lower incidences of diarrhea right after weaning. If antibiotics are not included in the diets, this may be an effective way of reducing problems with scours during the post weaning period.

3.2 Selected cereal grains

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; 1997). It has also been demonstrated that weanling pigs fed diets based on cooked rice and animal

protein have fewer incidences of diarrhea than have pigs fed diets based on corn starch (Pluske et al., 2003). The reason for these observations are presumed to be that such diets contain only rapidly fermentable fiber sources which in turn prevents pathogenic bacteria from getting nourishment in the GI-tract. However, this theory is in contrast to the fact that diets based on barley or oats have also been reported to reduce diarrhea in pigs. Such diets contain both fermentable and non-fermentable fibers, but barley and oats may also contain unidentified nutrients that improve overall digestion of pigs. Therefore, 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). Unpublished results from South Dakota State University indicate that this is also the case if diets are based on naked oats rather than corn, milo or wheat.
The reason for these results has yet to be elucidated and more work needs to be conducted in this area. However, at this point the recommendation is that for nursery pigs and growing-finishing pigs encountering problems related to intestinal disorders, barley- or oat-based diets should be fed.

3.3. Restricted feeding

Restricted feeding results in fewer intestinal problems and fewer incidences of diarrhea than does ad libitum feeding (Goranson et al., 1995). Feeding as often as 4 - 6 times per day may be required during the initial two weeks post-weaning if an in-feed antibiotic is not included. 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.

3.4 Liquid feeding/fermented liquid feeding

Liquid feeding generally results in fewer intestinal upsets than does dry feeding. The reason for this observation is probably that the gastric pH is reduced in pigs fed liquid or fermented liquid diets. Therefore, pathogenic bacteria growth is inhibited or reduced (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; 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 to pigs fed dry feed (Jensen and Mikkelsen, 1998). 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 (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., 1999; Scholten et al., 1999). However, fermentation of the entire diet may reduce the gain to feed ratio (Jensen and Mikkelsen, 1998). This is probably due to fermentation of sugars and free amino acids present in the complete diets that may result in unbalanced diets being fed to the pigs. 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 (Scholten et al., 2002).
The dietary inclusion of solubles from the 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 although a scientific evaluation of these products is still non-existing.

4. Alternative dietary supplements

4.1 Acidifiers

The inclusion of organic acids in diets for 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 (Bolduan et al., 1988), Citric acid (Falkowski and Aherne, 1984; Henry et al., 1992), and Propionic acid (Bolduan et al., 1988) have been reported. Usually, between 1 and 2% of the products are included in diets for 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 en several experiments (i.e., Broz and Schulze, 1987; Blank et al., 1999), but not in other experiments (Bolduan et al., 1988; Gabert et al., 1995).

The addition of inorganic acids to diets for 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 (Øverland et al., 2000; Canibe et al., 2001), calcium formate (Kirchgessner and Roth, 1990; Pallauf and Huter, 1993), and sodium formate (Kirchgessner and Roth, 1987).

In conclusion, 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 of the other products may work as well.

4.2 Probiotics

Probiotics are live cultures 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 frowth 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

As follows from the above, the idea behind using probiotics is that they can enhance the health of the intestinal tract of the pig by competitive exclusion if they are able to survive and colonize in the GI-tract of the animal. However, the research conducted using probiotics have shown variable results. Kornegay and Risley (1996) fed two different *Bacillus* products to growing pigs. They showed an increase in the number of *Bacillus* spores in the feces from the pigs indicating that these probiotic are able to survive and colonize in the GI-tract of the pigs. However, fecal counts of coliforms were not consistently reduced indicating a poor ability of these substances to inhibit the growth of pathogenic bacteria in the GI-tract. These results mirror practical experiences with probiotics in that inconsistent responses is often observed.

4.3 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 and trans-galactooligosaccharides) are believed to improve pig performance by stimulating the proliferation of Bifidobacteria in the large intestine. Bifidobacteria suppress the growth of pathogenic bacteria (i.e., *E. coli*) by stimulating the production of acetate, which decreases the pH and may reduce 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. At this point, results with these products obtained in practical diets for pigs are inconclusive, and in general, specific fractions of dietary fibers are not included in diets for neither nursery pigs nor growing finishing pigs. However, as already pointed out, the inclusion of barley and oats in diets for nursery pigs has been shown to improve pig performance and decrease scouring indicating that these cereal grains may contain certain fibers that are beneficial to the animals. Also other intact fiber sources (i.e. soy hulls, alfalfa meal, sugar beet pulp) are sometimes included in nursery diets, although the

experimental evidence of a possible positive influence of these products is non-existing.

4.4 Extracts from herbs and spices

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). These extracts are generally accepted for use as additives by Food and Drug Administrations (Dabbah *et al*, 1970).
The inhibitory properties of 50 essential oils against 25 different bacteria have been reported (Deans and Richie, 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 Richie, 1987; Piccaglia et al., 1993). 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 (Dabbah et al., 1970).

Of the various herb and spice preparations, garlic has received a condsiderable amount of interest. Antimicrobial activity of garlic against *Bacillus subtilis, Salmonella typhimurium, Staphylococcus aureus, Streptococcus faecalis* and *Listeria monocytogenes has been reported*. In diets fed to newly weaned pigs, feed efficiency and rate of gain was not different for pigs fed diets supplemented with 0.5% garlic compared to pigs fed diets supplemented with Carbadox . It has also been reported that combinations of more than one type of oils will illicit a stronger antimicrobial response than if only one type is used (Shelef *et al*, 1980; Piccaglia *et al*, 1993).

In conclusion, the area of feeding herbs and spices to pigs as alternatives to antibiotics holds some promise, - however, there is a need for more research in this area.

4.5 Nucleosides

The need for nucleotides is elevated during periods of rapid growth, during periods of stress, and in immuno-compromised animals. In newly weaned pigs, all of these factors are present – therefore, it is expected that they have a high requirement for nucleotides during this period. Because nucleotide synthesis is an energy- and glutamine-requiring process and because newly weaned pigs are often deficient in both energy and glutamine, it is possible that pigs are not able to synthesize sufficient quantities of nucleotides during the immediate post-weaning period. If this is correct, dietary nucleotides have to be supplied. In a typical starter diet for 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 (Mateo and Stein, 1994). Assuming that the concentration of nucleotides in sow's milk are representing of the requirement of the pigs, it is easily concluded that a starter diet for young pigs is deficient in four of the five nucleotides. It may, therefore, be beneficial to add additional nucleotides to such diets. In a recent experiment in our laboratory, we added nucleosides to a deficient starter diet (Mateo et al., 2004). We used nucleosides rather than nucleotides because dietary nucleotides need to be digested to nucleotides before absorption. Blood samples and fecal samples were collected from weanling pigs on the day of weaning, on day 7 post-weaning and on day 14 post weaning. Blood samples were analyzed for IgG concentrations, while the microbial

flora was quantified in the samples. Results of the experiment showed that fecal counts of *Cl. perfringens* was reduced in samples collected from pigs fed a nucleoside supplemented diet as compared to the non-supplemented control diet. On day 14 post-weaning, the fecal counts of *L. acidophilus* and *Bifidobacterium spp.* also were higher in pigs fed the nucleoside containing diet. These results indicate that nucleoside supplementation during the immediate post-weaning period may positively influence the gastrointestinal microflora by decreasing *Cl. perfringens* and increasing *L. acidophilus* and *Bifidobacterium spp.* This observation was subsequently confirmed in an in-vitro experiment that showed that nucleotides have antibacterial properties against *Cl. perfringens* and *e.coli*. The implication of this finding is that pigs fed diets supplemented with nucleosides may have improved intestinal health, less scoring, and improved performance. Although no improvement in serum IgG was observed in the above experiment, the improved intestinal health may also lead to an improvement in the immune system of animals fed diets supplemented with nucleotides. A reduced concentration of enterobacteria and an increased number of probiotic bacteria (i.e. *L. acidophilus* and *Bifidobacterium spp.)* may also result in improved intestinal morphology and improved nutrient uptake. This hypothesis is being tested in a current research project at South Dakota State University.

4.6 Minerals

Because of the high buffering capacity of limestone and inorganic phosphate sources, decreasing or omitting the dietary inclusion of these ingredients can reduce scouring. Exogenous phytase is added to improve the digestibility of phytate-bound phosphorus and the requirement for calcium can be met by using calcium salts rather than limestone.

Copper sulfate is added to all nursery diets at levels between 150 and 175 ppm. Zinc oxide is often added to starter diets at levels of 2000 – 4000 ppm. However, this routine cannot be legally practiced in all countries in the world, while it is a common routine in other countries (Goransson, 1997). High concentrations of zinc oxide in starter diets for pigs have been shown to control post-weaning diarrhea with the same efficiency as do AGP without causing any toxicity symptoms (Goransson, 1997). In addition, in several experiments, zinc oxide fed at pharmacological levels (i.e. 2000 – 4000 ppm) was shown to have a growth promoting effect of the same magnitude as what is usually expected from AGP (e.g. Hahn and Baker, 1993; Smith et al., 1997; Hill et al., 2000).

5. Conclusions

A variety of strategies are needed to successfully wean pigs without the use of antibiotic growth promoters. Management schedules that have been shown to reduce the risk of developing diarrhea in pigs need to be used. These schedules include later weaning and the use of wean to finish buildings. Diet composition also needs to be considered. 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. The usage of pharmacological levels of zinc oxide in nursery diets is widespread in many countries, - but it is not always in accordance with national law. Several feed additives may also be effective in reducing diarrhea in post-weanling pigs. Among these are probiotics, acidifiers, oligosaccharides and certain essential oils. Dietary nucleotides may also be helpful in increasing the immune status of the pig. However, more research is warranted to better understand

the digestive processes of the pig and, thus, overcome the problems associated with omitting antibiotics from swine diets. Future research will likely focus on measures that can improve the immune status of weaned pigs and at the same time enhance performance.

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