

SWINE RESEARCH AT GUELPH: EXPLORING ALTERNATIVES TO ANTIBIOTICS

Bob Friendship
Department of Population Medicine
University of Guelph

ABSTRACT

The era of antibiotics in livestock feed for growth promotion and control of enteric disease may be coming to an end. In order to prepare for this possible development, researchers at the University of Guelph have been exploring a wide range of possible alternative approaches. These include genetic selection for disease resistance, genetic modification so that animals produce antimicrobial factors, and other methods of immune stimulation. As well, we are studying ways to modify the diet that encourages beneficial bacteria and discourages pathogens, and additions to the diet of beneficial bacteria or immunoglobulins to provide passive protection.

This paper examines specific work relating to alternative approaches to control of post-weaning *E. coli* diarrhea. Techniques that have been used include probiotics, prebiotics, egg-yolk antibody products, and vaccines. Generally, none of these techniques have been shown to be effective to date demonstrating that this is a complex and difficult problem.

INTRODUCTION

There is growing pressure on the livestock industry to reduce the use of antimicrobial drugs - the practice of using antibiotics at low levels in the feed for growth promotion is particularly under scrutiny. The greatest benefit of antibiotics when used as a means of improving feed efficiency and promoting growth, occurs in the nursery period and therefore, it is not surprising that surveys of drug use on Ontario pig farms have revealed that almost all pigs are fed antibiotics during the immediate post-weaning period (Dunlop et al, 1998).

The post-weaning period is a time at which the pig is particularly vulnerable to disease, especially enteric bacterial infections. A survey of about 500 Ontario pig farms (Dewey et al, 2000) that categorized herds into those with high death loss (>3%) and low death loss (<1%) found that the disease problem with the highest prevalence on the high mortality farms was *E. coli* (94% of herds). Further investigation of Ontario nurseries with Post-Weaning *E. coli* Diarrhea (PWD) found antibiotic use to be quite high in nursery operations with *E. coli* problems (Amezcuca et al, 2001).

Commonly, six or more different antimicrobial drugs are used during the nursery period on farms where PWD is a problem and antibiotic resistance has been shown to be a concern. The K88 *E. coli* strains isolated from these Ontario herds show multiple antibiotic resistance

including some resistance developing to relatively new antibiotics such as apramycin (Amezcuca et al, 2001).

The example of post-weaning *E. coli* diarrhea in Ontario nurseries illustrates the need to develop alternative therapeutic approaches. Over time, resistance will develop so that these drugs will not be effective, but it is possible that before that happens regulations will change so that the use of antibiotics might be greatly restricted. If either scenario comes to pass, how will this disease (or other diseases like this) be handled?

In our survey of herds with PWD, we were unable to identify management or other risk factors which could explain why certain herds have problems. This suggests that this problem can not be easily solved by simple changes to husbandry or feeding practices. Many of the herds instituted control measures that consisted of multiple treatments making it difficult to assess whether one particular measure had any impact. Common control measures used on Ontario farms with PWD include: antibiotics in feed and water and by injection, acidifiers in water and/or feed, high levels (> 2,000 ppm of zinc oxide in feed, prebiotics and/or probiotics in feed, immunoglobulins in feed (spray dried porcine plasma or chicken egg-yolk antibodies), vaccines (oral live bacteria or killed intramuscular bacterins).

RESEARCH SUMMARY

We have attempted to investigate some of these alternatives to antibiotics with respect to controlling post-weaning *E. coli* diarrhea. Our approach has been to try field trials on commercial farms where the disease is a consistent problem, as well, we have developed an experimental model where pigs are challenged with a controlled amount of *E. coli* organisms.

In each case, during a field trial, antibiotics and zinc oxide are removed from the feed and pigs are randomly allocated to a control group without treatment and a treated group. Generally, the level of diarrhea observed in both the treated and control groups have been similar and typically worse than before the antibiotics and zinc were removed.

Table 1: Results of K88 (F4) *E. coli* vaccination with killed autogenous and a live attenuated vaccine in a herd with endemic post-weaning diarrhea

	Treatment		
	Control	Injectable Vaccine	Oral Live Vaccine
Number of pigs	113	130	124
Pigs with diarrhea (%)	10.5	7.7	14.2

One explanation for the lack of success might be that more than *E. coli* alone is present on these farms, possibly viruses and other bacteria contribute to the treatment failure. Therefore,

evaluation of each treatment in a controlled laboratory environment was undertaken. Pigs were assigned to treatment and control groups and then given 5ml of a broth containing a known amount of K88+ *E. coli*. Signs of diarrhea and illness were observed in some of the pigs as early as 6 hours after oral challenge with the *E. coli*. To date, we have not observed an advantage to using intra-muscular vaccines, chicken egg-yolk antibody products, prebiotics (fructose oligosaccharides) or probiotics.

Table 2: The incidence of mortality and diarrhea in weaned pigs receiving either a control diet or a diet containing egg-yolk antibodies (Chernysheva et al, 2002)

	Farm 1 (n=204)		Farm 2 (n = 235)	
	Control	Treatment	Control	Treatment
Number of pigs	101	103	109	126
Mortality	5	5	3	4
Diarrhea	57	61	24	46

Interestingly, one of the most promising studies of growth performance in newly-weaned piglets was an evaluation of a herb extract containing cinnamon, thyme, and oregano (Radford et al, 2002). During the first week following early weaning, growth performance was improved as a result of adding 0.5% and 0.75% of the herbal extract product to the non-medicated diet. This resulted in higher body weights at 21 days post-weaning for those two treatments, as compared to the non-medicated control diet (0% diet).

Table 3: Growth performance of newly-weaned piglets receiving herbal extract (n=162)

	Inclusion level of commercial herb product			
	0%	0.25%	0.5%	0.75%
Weaning weight (kg)	5.30	5.37	5.46	5.40
Weight at 21 days (kg)	7.99	8.19	8.84	8.32

Researchers at Guelph have looked at the value of dietary supplementation of different organic acids as an alternative to the use of antibiotics in the diets of early-weaned pigs (Borysenko et al, 2001). Various diets were evaluated: a control diet (containing lincomycin 44 at 1 kg/tonne of feed), a negative control without antibiotic, and a ration with lactic acid, a ration with fumaric acid and a diet with formic acid (containing 0.2% of each acid). There were no differences between treatment groups with regards to visceral organ growth, feed conversion efficiency, white blood cell counts, and diarrhea scores.

CONCLUSIONS

What this demonstrates is that there are no simple solutions to this problem. In the past, if the pig gut was overwhelmed by a particular pathogenic bacteria, we simply used a product that killed the disease-causing micro-organisms and probably much of the other flora as well (much like using “Roundup” to solve a weed problem). The challenge we face in a future that may not include antibiotics is to develop a healthy gut micro-flora that is not reliant on broad spectrum antibiotics to keep the disease causing bacteria in check. We need to figure out what normal or healthy intestinal flora are and what aspects of the diet encourage the growth of these beneficial bacteria and discourage the proliferation and overgrowth of the disease causing bacteria like K88+*E. Coli*. This approach may include the addition of beneficial bacteria in the diet, the use of phages (virus to kill bacteria), methods to simulate gut immunity, and dietary manipulation to encourage certain bacteria and discourage others. Our work will primarily focus on probiotics and prebiotics to accomplish these goals.

The following definitions are offered to explain what is meant by these terms and where our research is focused.

PROBIOTICS

Definition. A term used to refer to preparations of live micro-organisms that are added to feed to improve the health of the host by beneficially influencing the indigenous microbes.

Application in Swine. The most widespread use of probiotics in swine is for the control of bacterial gastro-intestinal disease in young growing pigs, particularly *Salmonellosis* and *Colibacillosis* (*E. Coli*). The bacteria most commonly used as probiotics are *Lactobacilli*, but some work has been done using *Enterococcus faecium* and *Bifidobacterium sp.* It is generally thought that administration of the probiotics about the time of weaning when the piglet gut is immature and the permanent bacterial population has not been fully established is the most appropriate period to attempt to influence the microbial flora of the intestine. Probiotics mainly act in the small intestine.

Research Needs. The concept of probiotics is not new and yet has not been carefully evaluated. There is a need for the selection of strains of bacteria that are efficacious in the control of specific pig disease and there is a need to develop feeding programs that complement the use of probiotics and encourage a healthy gut micro flora.

PREBIOTICS

Definition. A term used to refer to non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improving the health of the host.

Application in Swine. The main focus of work has been to reduce the negative effects of bacterial diseases of the pig’s colon, such as swine dysentery colonic *Spirochetosis*, and *Salmonellosis*, by indirectly encouraging the growth of bacteria considered to be associated

with a healthy gut, primarily *Lactobacilli* and Bifidobacteria. Generally, prebiotics have also led to a change in metabolic activity of the intestinal flora causing an increase in carbohydrate fermentation and a decrease in protein degradation and fermentation. Carbohydrate fermentation generally results in harmless or even beneficial products, whereas protein fermentation results in production of potentially harmful products.

Research Needs. It is unclear whether prebiotics are complementary to the use of probiotics and a great deal of work is needed to determine optimums inclusion, overall efficacy, and which prebiotics work best under various circumstances.

LITERATURE CITED

- Amezcuca, M.D.R. 2001. Post-weaning diarrhea and mortality caused by *Escherichia coli* - Investigation of risk factors and control methods. MSc Thesis, University of Guelph.
- Borysenko, M., Fan, M.Z., Archbold, T., Atkinson, J.L., Dewey, C.E. 2001. Dietary supplementation of different organic acids as an alternative to the use of antibiotics in the diets of early-weaned pigs. Ontario Swine Research Review, p. 15 .
- Chernysheva, L., Friendship, R., Gyles, C. 2002. Does feeding of specific chicken egg antibodies control post-weaning *E. coli* diarrhea? Proc. Amer. Assoc. Swine Vet., Kansas City, pp 315-317.
- Dewey, C.E., Johnston, T., Oldfield, L., Whiting, T. 2000. The impact of disease on nursery pig production. Workshop #7, Amer. Assoc. Swine Practitioners, Indianapolis. , pp 3-11.
- Dunlop, R.H., McEwen, S.A., Meek, A.H., Friendship, R.M., Clarke, R.C., Black, W.D. 1998. Antimicrobial drug use and related management practices among Ontario swine producers. Can.Vet. J. 39: 87-96.
- Radford, M., Jeurond, E., Schumann, B., Clunies, M., and deLange, C. 2002. Supplementation of diets with herb extract enhances growth performance in newly-weaned piglets. Ontario Swine Research Review, pp 37.