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THE REASONS FOR PUBLIC HEALTH CONCERNS ABOUT ANTIBIOTICS IN FEEDS

Lyle R. Brown

IN APRIL of 1970, the Food and Drug Administration established a task force of distinguished scientists to study the problems or anticipated problems associated with the continued use of antibiotic supplements in animal feeds. The commission released its findings and its recommendation on January 31, 1972. The Task Force concluded that¹: (1) antibiotics given in subtherapeutic amounts favor the selection of antibiotic resistant bacteria, (2) that animals that receive either subtherapeutic or therapeutic levels of antibiotics may serve as reservoirs of pathogenic bacteria which can produce human infections, (3) that the number of multi-drug-resistant bacterial strains carrying R-factors has increased and that this increase is related to the use of antimicrobial agents, (4) that resistant bacteria have been found on meat and meat products, and (5) that there has been an increase in antibiotic resistant organisms in man.

THE TASK Force identified the important areas of concern with regard to antibiotics in animal feed as follows: (1) the human health hazard, (2) the animal health hazard, and (3) the antibiotic effectiveness. It is the first two of these concerns which will be discussed.

A WIDE variety of feed additives and feed supplements have been used in the past ten or twenty years. These have included a number of antibiotics that are common to both animal and human disease therapy.

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Included in this group are: streptomycin, tetracyclines, dihydrostreptomycin, neomycin, spectinomycin, penicillins, sulfonamides, and chloramphenicol. In addition some drugs such as tylosin and virginiamycin have been used in animal feeds but are not used routinely in human medicine.

WHAT HAS been the effects of the use of these antibiotics in feed? It has been known for some time that the microbial population present in the intestinal tract of animals is converted from one of drug sensitive to one of drug resistance when antibiotics are fed.² This resistance occurs because of the selective growth advantage of any spontaneously resistant mutant bacterial cells that might either be ingested or produced during normal growth of the microbial population in the animals. The resistance of these cells is of two basic types as is shown in table 1. Chromosomal resistance refers to resistance with the characteristics as described in that figure and is of major significance only if the bacteria containing this information is of public or animal health significance. This type of resistance allows the normally susceptible bacterium to grow in the presence of the antibiotic and since many of the other members of the flora are inhibited by the administration of the antibiotics, this organism will predominate as long as the drugs are present. Once the antibiotics are removed, the ability of this organism to continue to colonize the intestinal tract or other habitat in the animal will be dependent upon characteristics other than its drug resistance and its persistence is uncertain. If it is well adapted to its environment, it can remain indefinitely. Otherwise, it may be crowded out by other organisms. It retains its ability to grow in the presence of the antibiotics and thus, if secondary challenges are given, this organism will continue to grow and divide and will pass on

its resistance to its progeny.

THE SECOND type of drug resistance in the microbial population is mediated by R-factors of multiple drug resistance transfer factors. These R-factors are extra chromosomal pieces of genetic information or "episomes" which confer on the cells that contain them, three important properties: (1) resistance to one or more antibiotics, (2) the ability to transfer this multiple drug resistance to other bacteria of the same or different species, (3) the ability to transmit their drug resistance to their progeny. It is the first and second properties listed above that has emphasized public health concern. In theory, once the information to inactivate or inhibit the action of a number of antibiotics is present on a R-factor, the cell which harbors that R-factor can transmit this factor to a number of other bacteria, both pathogenic and non-pathogenic for humans, and produce human and animal infections refractory to antibiotic therapy.

LARGE NUMBERS of R-factor strains are found in the fecal material of both animals and humans. Seventy to ninety percent of the fecal flora in some swine have been shown to carry R-factors³. In our own studies we have found 40 to 60 percent of the strains present in some fecal samples to contain transferable R-factors. There was also a correlation between the R-factors found and the types of antibiotics that were being fed. Others have shown that the inclusion of one antibiotic in the feed will select for multiple drug resistance determinants. Recent studies indicate that the transmission of antibiotic resistance can occur in vivo in the intestinal tract of the animal in question. However, the frequency of this transfer is much disputed.

THERE HAS been increased incidence of salmonella infections in animals and in humans during the past decade⁵. In the United States there are approximately one hundred deaths a year from this disease. In addition, human illness and deaths have been reported due to antibiotic sensitive and antibiotic resistant bacteria of animal origin. Food producing animals may serve as a reservoir for R-factor containing strains, and these bacteria can then be passed on to the consumer through contaminated food supplies. There is data to support this hypothesis since these organisms have been isolated from both meat and meat products.

DUE TO THE inherent nature of the R-factors, clear and unambiguous identification of particular R-factors is difficult. To date there is not any good epidemiological evidence to show that an R-factor down on the farm has been responsible for causing human clinical infection. It is difficult to design studies to answer these questions.

WHAT WOULD good epidemiological evidence show? To show that the R-factors that are selected down on the farm as a result of antibiotic feeding are responsible for a particular disease problem in either animals or man it is necessary to (1) be able to unequivocally identify the R-factor involved which is difficult as indicated above, (2) to show that it was selected in the animal on the farm and was not given to them in the feed, by some source of human contamination, or in the water supply, and (3) that it was transmitted by food contamination or some other mode to the victim. This type of evidence would state categorically that the animal being fed antibiotics was the cause of a health problem. However, this rigorous proof is not required to say that a health hazard exists. The circumstantial evidence that animals can serve as a reservoir, that this reservoir of resistant bacteria

can infect man, and that drug therapy is then difficult is sufficient to classify the phenomenon as a health hazard and for legal action to be required. Individually, these properties and characteristics have been shown to exist.

SOME AUTHORS argue that the continued effectiveness of the growth promotion capability shown with antibiotic feeding is evidence that R-factor strains and other resistant bacteria are not a problem⁷. The reasons for the growth promotion are not known and it is conceivable that the organisms involved in the health considerations are totally unrelated to this growth promotion effect if indeed it does exist. Recent reports on the use of tylosin in swine feeds has indicated that the growth promotion effectiveness of this antibiotic has been completely lost in some herds.

WHAT SPECIFIC organisms are of public health concern? Staphylococcus aureus, normally present on the skin of farm animals causes mastitis in cattle and arthritis in poultry. The drug resistant staphylococci cause serious and frequently fatal infections in man. These organisms have not been shown to carry resistance transfer factors. The second major group of organisms is the gram-negative enteric bacteria. This group includes human and animal pathogens with R-factors. Of major concern in this group are Salmonella, Escherichia, Klebsiella, Shigella, Proteus, and Serratia. R-factors can be transferred between all of these genera.

IN SUMMARY, a wide variety of drug resistant organisms, pathogenic for man and animals, are causing an increasing incidence of disease. In addition, a strong selective environment exists down on the farm to perpetuate and increase this reservoir of unwanted organisms. The public

health concern is to eliminate this reservoir and thus the risks to animals and man from continued antibiotic feeding.

TABLE 1 - Properties of Antibiotic Resistant Bacteria.

Type of Resistance	
<u>Chromosomal</u>	<u>R-factor</u>
1. Growth in presence of antibiotics.	Growth in presence of antibiotics.
2. Transmitted to progeny.	Transmitted to progeny.
3. Non-infectious: not transmitted to other bacteria.	Infectious: transmitted inter and intra species and genus.
4. Does not promote bacterial conjugation.	Promotes conjugal transfer of genetic information.

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THE ROLE OF ANTIBIOTICS IN SWINE FEEDS

Thomas H. Jukes

LATE IN 1948, we found that crude residues from the production of chlortetracycline contained vitamin B₁₂ and a second, unknown substance that promoted the growth of chickens and pigs. Cunha et al (1949) noted that chlortetracycline fermentation residues produced a marked increase in growth of pigs simultaneously with the arrest of diarrhea. In some pigs, the growth rate was doubled. Similar findings were reported frequently in 1949 and 1950, when antibiotic feeds were used in treating pigs with bloody diarrhea. This second substance was, of course, chlortetracycline itself (Jukes et al 1950).

FROM THE first, it was evident that the finding of antibiotics produced resistant microorganisms in the digestive tract; indeed, this process takes place almost by definition, because the surviving organisms have to be tolerant of antibiotics. Some typical experiments showed a temporary drop in numbers of intestinal bacteria for the first day or two, followed by a return to levels higher than before.

WHAT WE were not prepared for was the fact that the changed and resistant flora were in some way beneficial, either from the presence of certain new bacterial strains, or the absence of certain former strains or species. Indeed, it took us some time to adjust to such a concept, accustomed as everyone was to the idea of resistant pathogens.

PRIOR TO the commercial introduction of chlortetracycline in animal

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feeds, we went through a period in 1949 and 1950 of extensive testing in the state and federal agricultural experiment stations and elsewhere, in the U.S.A. and in a number of other countries. Many experiments with domestic and laboratory animals were carried out. A number of bacteriologists addressed themselves to the matter of resistant organisms in the intestinal tracts of animals fed antibiotics. This work was carried out without knowledge of the resistance transfer factor; instead, the net end result of antibiotic feeding was measured. The results varied greatly. Sieburth and co-workers found variations associated with different basal diets, different bacteriological procedures, the age of the experimental animals, and the types and levels of antibiotics used (1954). Extreme variations in the cecal and fecal microflora were found even from day to day.

SOME EXAMPLES of the variations obtained from penicillin and tetracyclines include increases, decreases and no change in E. coli, lactobacilli, aerobes, anaerobes and total enterococci (Jukes, 1955).

THE EFFECT of antibiotics on farm animals will vary according to the extent of biological insult imposed on the host by various levels of bacterial invasion. This is the "disease-level" concept. Not unrelated to this is the "risk-benefit" evaluation. The risks we are prepared to take in producing food will be proportional to our needs for it. A man who is well-fed will be quite finicky about risks. Does this mean that the point has been reached at which antibiotics should be withdrawn from animal feeds in the U.S.A.? Do we have so many pigs that we can ignore the need for feeding them by the most economical means? I do not think so.

ANTIBIOTICS IN the feed often improve the performance of farm

animals that are exposed to conditions that are loosely termed "stress". These conditions include excessively hot and cold ambient temperatures; crowding; shipping; and vaccination. Among the manifestations or results are runtiness and a number of diarrhea-like conditions in pigs.

HERE WE are admittedly in an area that is outside the boundaries of rigid scientific definition. Nevertheless, this area is currently the most important practical use of antibiotics, for it has repeatedly been shown in controlled experiments under farm conditions, that the most important economic yields from the feeding of antibiotics to domestic animals is in preventing the deleterious effects of so-called stressful conditions.

SEVERAL INVESTIGATORS reported that the growth response to antibiotics diminished because of improved growth by the controls.

HAYS (1969) has summarized information from his own laboratory and that of Braude which shows a reciprocal relationship between the rate of gain of controls and the response to antibiotic feeding. In both instances, the difference between controls and supplemented pigs steadily decreased as greater growth occurred in the control groups. The findings summarized in Table 1 were from experiments conducted subsequently to 1960.

SUCH RESULTS are incompatible with an increase in resistant pathogens. Instead, they seem to indicate that a deleterious infection disappeared from the environment.

MY IMPRESSION is that the response to low level supplementation lessened after the first year or two. The responses to higher levels are difficult to compare with respect to different years because so much inherent variation depends on the types of microorganisms that are encountered in various locations. Variability from year to year is

well illustrated in results with pigs reported by Teague (1962).

THE RECENT trend in antibiotics for pig feeding is to use mixtures of antibiotics with other drugs such as sulfonamides. Some recent findings are as follows:

PEO (1967) reported experiments in which various antibiotics, with or without other chemotherapeutic drugs, were fed to young pigs starting at two weeks of age. The experimental periods lasted for 4 to 7 weeks. The supplemented pigs gained an average of 30% more on 8% less feed than did the unsupplemented controls.

CHANEY AND Waddill (1966) followed the growth of pigs, with and without various antibacterial drug supplements, for about 7 weeks. The growth responses ranged from 2 to 10 percent. Nickelson, et al (1965), found that feeding an antibiotic-sulfonamide mixture to young pigs significantly increased their rate of growth and reduced the incidence of the lesions of atrophic rhinitis at the time of slaughter. Ruiz, et al (1968), found that female pigs that received antibiotics gave birth to 1.3 more pigs per litter than did the controls. Other investigators who have recently reported on the continued efficacy of antibiotics in the feeding of pigs include Welch, et al (1965), and Jensen, et al (1965).

HAYS (1969) reviewed a number of recent reports on the efficacy of antibiotic feeding for cattle and, especially, pigs. He concluded that "antibiotics have now been used routinely and successfully in livestock production for more than 15 years", and pointed out that the use would become increasingly important as the demand for protein increased with the expanding world population. This demand was recently emphasized by the Director General of the FAO (1970), who states that in the Indicative World Plan "for the immediate future, the emphasis is on filling the gap

in meat supplies through a rapid expansion of pig and poultry production". He says that "an average growth of pig and poultry production of between 5 and 10 percent over the entire period of the plan would, however, have to be attained. This formidable goal would have to be achieved largely by industrial methods. . ."

IT IS DIFFICULT to see how such a goal could be reached if the use of antibiotics in feeds were markedly curtailed. Such a curtailment would undoubtedly reduce the production of pigs and poultry at the time when an increase is needed.

Antibiotic Residues in Food Products Derived from Domestic Animals

MUCH OF the recent scientific discussion of antibiotics in feeds has arisen from the discovery of the episomal transfer of resistance.

MANY MEMBERS of the public, however, will ask questions about antibiotic residues in their food. It is therefore appropriate to discuss antibiotic residues in food produced from domestic animals; first, what quantities of such residues are present, and second, what are their pharmacological as well as their bacteriological effects?

SOME ANTIBIOTICS are found in the tissues of animals when they are fed in the diet. In most of the results, the highest levels (as one would expect) are in the kidney; these are followed by blood, liver, muscle and fat (Table 2). The levels in pig, chickens and turkey muscle were reported to be about one-thousandth of the level in the diet. Penicillin was not detectable in pig or chicken tissues following feeding, and lincomycin, tylosin, erythromycin, and bacitracin were not detected in chicken muscle. Chlortetracycline levels in the tissues fell quite rapidly following withdrawal from the diet and were destroyed by cooking. The longest persistence was in the kidney. In certain quarters,

however, virtually complete disappearance of antibiotics from meat is not acceptable. In a hearing on a bill to legalize organic foods that I attended recently, the representative of the Rodale Press was asked the following question: "If a young calf were given a single injection of penicillin to save its life, would this prevent it from being classified as organic beef a year or two later?" The Rodale representative refused to say no. The objection to using antibiotics in this case is therefore predominantly ritualistic. It has been pointed out by the Swann report, and recently by the FDA that "there are no known instances in which harmful effects in man have resulted from antibiotic residues in food other than milk" (from penicillin mastitis treatments) and that "no cases of sensitivity or anaphylactic reactions in human beings from eating meat containing antibiotic residues have been documented."

THE ANTIBIOTICS most commonly used in feeds for disease control are chlortetracycline, oxytetracycline, tylosin and penicillin. Long-term toxicological studies at levels up to 5 percent of the diet have been reported for the first three of these. They are essentially non-toxic. The studies turned out to be of geriatric rather than toxicological interest, because survival was often better in the treated groups than in the controls, as in the case of chlortetracycline. The tetracyclines have been used in human medicine at high levels for many years with a minimum of side effects or allergic responses, and the widespread use of antibiotics in animal feed for 20 years has been accompanied by the continued usefulness of these same antibiotics in clinical medicine.

THE SUBCOMMITTEE on Economic Value of the Task Force on Antibiotic Feeding (1972) has assessed the benefits derived from using low levels of

antibiotics in feeds for improving growth rate and feed efficiency. I have briefly summarized these extensive findings with pigs in Table 3. The improvement is outstanding with young pigs, and reduces the time needed to bring them to 40 lbs. weight, thus greatly lowering the production cost. Much less growth effect is found with older pigs, but they reach market weight earlier.

MUCH OF the current discussion of antibiotic feeding has been triggered by reports of salmonellosis in England. I regard the British situation as differing from ours because of the dirty methods of meat handling and the lack of refrigeration over there. I was born there, and I know what the butchershops smell like. Dr. John Walton has described in Nature and elsewhere (1971) the unsanitary procedures in England that lead to fecal organisms from animals reaching the consumer, via the abattoir and the market.

I CONCLUDE that the responsibility for the spread of resistance in human clinical medicine rests primarily with those who are using antibiotics in clinical practice, not with the feed industry. All the evidence in the U.S.A. points to hospitals and other human clinical contacts as being responsible for the spread of resistance, no matter whether episomal or chromosomal. The continued efficacy of antibiotics in animal feeds shows clearly that there is no significant resistance problem at the level of the farm. This efficacy has been abundantly documented in the relevant scientific literature and by numerous unpublished reports. The recent evidence was gathered and summarized by the committee on economics of the Antibiotic Task Force. There has been some comment that the Task Force committee translated the results into dollars. Dollars in this case express the increase in growth

caused by elimination of pathogenic microorganisms. The continued efficacy of antibiotic feeding to pigs is striking, definite and illogical. A recommendation of the FDA Task Force states that "The feeding of antibacterial agents would logically seem to give rise to a human health hazard" (1972). Claude Bernard said, in 1865, "If an idea presents itself to us, we must not reject it simply because it does not agree with the logical deductions of a reigning theory". The use of so-called logic, or inductive reasoning, as a substitute for the experimental approach was also condemned by Louis Pasteur and Albert Einstein.

IN SUMMARY, the use of antibiotic feeds for pigs is of benefit to the consumer. There is no evidence that as practiced in Canada and the U.S.A., it leads to the accumulation of significant residues in meat. Nor is there evidence for the spread of transferable resistance from farms into microorganisms that cause public health problems to the human population.

THE FACT that antibiotic feeding of farm animals continues to be effective shows that this practice in the vast majority of cases is not causing pathogenic resistance among the animals that are exposed to it.

TABLE 1 - Relationship between Growth Rate of Control Pigs and Pigs Fed a Combination of Penicillin and Streptomycin*

Daily Gain in Weight of Controls (lbs.)	No. of Comparisons	Improvement over Controls by Pigs Fed Antibiotics	
		Gain in Weight (%)	Feed Efficiency(%)**
0.2 to 0.4	2	22.0	8.2
0.4 to 0.6	3	27.0	4.5
0.6 to 0.8	4	20.4	5.6
0.8 to 1.0	7	16.1	11.1
1.0 to 1.2	9	12.3	6.4
1.2 to 1.4	9	9.4	1.9
1.4 to 1.6	20	5.6	4.7
1.6	7	3.8	1.8
Total	61		
Average Improvement		10.7	5.1

*Data summarized from agricultural experiment station reports since 1960.

**Pounds of feed per pound of gain.

TABLE 2 - Tissue Levels of Antibiotics Following Feeding.

Antibiotic Level (ppm)	Time Fed (days)	Species	Days of withdrawal	Tissues and Residue Level (ppm)			
				K	L	M	F
CTC, 100	98	Swine	0	.51	.46	.08	0
CTC, 100	98	"	5	.07	.04	0	0
Penic, 50	98	"	0	0	0	0	0
CTC, 200	21	Chickens	0	2.2	.62	.26	.12
CTC, 200		"	4	.26	.03	0	0
CTC, 2000	5	"	0	12.	1.6	.63	.17
CTC, 2000		"	3	.20	.02	0-.02	0
Linco, 400	10	"	0	.37	.24	0	0
Linco, 400		"	2	0	0	0	0
Tylo., 50		"	0	0	0	0	0
Tylo., 1000		"	3	0	Tr.	0	0
Eryth., 400	8	"	0	0	0	0	0
Baci., 1000	108	"	0	0	0	0	0
OTC, 220		"	0	5.6	1.2	.3	
Penic, 200	42	"	0	0	0	0	0

Chicken data summarized from review by Shor (1971).

Swine data from Messersmith et al (1967).

K = kidney, L = liver, M = muscle, F = fat.

TABLE 3 - Effect of Antibiotics on Rate of Gain and Production Cost in Pigs.

<u>Category</u>	<u>Measurement</u>	<u>Controls</u>	<u>Antibiotics</u>	<u>%Difference</u>
(a)	Average daily gain (lbs)	0.673	0.869	+ 12.9
	Production cost	\$10.71	9.01	- 15.9
(b)	Average daily gain (lbs)	1.54	1.63	+ 5.8
	Production cost	\$22.10	21.80	- 1.4

(a) 29 experiments; growth from 15 to 40 lbs., Canada to Florida, 1960 - 1968.

(b) 21 experiments; growth from 40 to 210 lbs., South Dakota to Florida, 1960 - 1971.

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IF NOT ANTIBIOTICS, WHAT ALTERNATIVES IN SWINE PRODUCTION?

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THE PRIMARY means by which antibiotics in rations improve performance of pigs is through suppressing bacteria that have an adverse effect on performance. These bacteria most frequently inhabit the digestive tract, or are primary or secondary invaders of the respiratory tract. In the former, the presence of the antibiotic in the digestive tract appears to have special merit and presumably is effective directly at the site of bacterial production and action.

ANTIBIOTICS USED in rations to lessen the adverse effects of respiratory invaders presumably act through circulating levels of antibiotic in the blood. Among such uses are preparations fed to decrease the severity of effects of atrophic rhinitis and virus pig pneumonia.

INASMUCH AS antibiotic effects are mainly advantageous through suppressing problems caused by primary or secondary bacterial invaders, it follows that successful alternative programs must also be effective in controlling or preventing problems of this kind. Herd management procedures that eliminate atrophic rhinitis, virus pig pneumonia, and transmissible gastro-enteritis are well established in the Specific Pathogen Free approach. In the absence of these diseases, there is not the problem of secondary bacterial invaders for which use of antibiotics is generally recommended. Herds established and maintained free of these major diseases have generally shown favorable production levels (Underdahl, 1966).

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THERE HAS not been complete satisfaction with nor acceptance of the SPF program by the swine industry; it is, nevertheless, sound in theory and of proven practical value when implemented in strict accordance with its essential conditions. These conditions are: (1) obtaining non-infected or non-carrier animals; (2) repopulation with these animals in facilities that have been thoroughly cleaned, disinfected, and allowed to remain uninhabited for four to six weeks; (3) prevention of introduction of diseases through purchased animals or by permitting herd animals to come in contact with infected animals or premises; (4) exclusion of persons, equipment and vectors that have been in contact with infected animals.

OPERATION OF purebred herds by these procedures involve several major changes that are not readily acceptable to a large segment of the purebred industry at present. These stringent requirements impose the following conditions: (1) it is necessary to have a complete break in herd operation or to establish the non-diseased herd at a different location; (2) it is difficult, though not impossible, to retain for continuing production the existing outstanding animals in the herd; (3) it is necessary to change existing patterns of competition in livestock shows; (4) it is possible to introduce animals only from those sources that are approved as free of major diseases; and (5) it is necessary to restrict access to the herd to those individuals who follow a prescribed protective routine before entering the production areas. These are burdensome and disturbing requirements for long-established producers who have operated successfully in the existing purebred industry system.

ANOTHER REAL or presumed practical deficiency of the SPF system is the lack of ready availability of herds of outstanding production and

carcass merit. If this is indeed an existing deficiency, it can be eliminated and many of the other essentials of SPF herd management made easier by adoption of SPF or SPF-like systems by a major proportion of swine producers. Widespread adoption can eliminate some of the most serious diseases for which antibiotics are now used to reduce severity of production losses. Reliance upon such programs may become a necessity if concentrated production programs are to continue in the absence of disease-repressing additives.

FOR HERDS operated in a SPF-like program, likelihood of introduction of major bacterial diseases that respond to antibiotic treatment is greatly reduced. Even in such herds, sporadic bacterial scouring of severe consequence may occur. In such instances, *Escherichia coli*, a normal and abundant bacterial inhabitant of the digestive tract, usually are present in greatly increased numbers and are indicated as a major cause of the scouring (Sandine, et al, 1972). So prevalent is E. coli-induced scouring that production oriented publications frequently provide information on techniques for prevention and control of such scouring. One such publication, entitled "Points to Prevent *E. coli* Scours" (National Hog Farmer, July, 1972) lists three major points: (1) Reduce the number of E. Coli bacteria in the pig's environment; (2) Avoid lowering the natural resistance of baby pigs; and (3) Increase the pig's immunity to colibacillosis.

THE BEST prevention and control would be to reduce E. coli in the pig to levels that do not cause scouring, or to change E. coli numbers in proportion to other enteric bacteria that have a counter-action effect. Effective antibiotics in essence do this. Another approach is by biological control through use of competing or protective bacteria.

The Animal Science and Microbiology Departments, with financial assistance from the Graduate Research Council and a private company (Microlife Technics, Inc., Sarasota, Florida) have been engaged in pilot studies of this approach.

THE BACTERIA used are frozen concentrated cultures of *Lactobacillus acidophilus*. These are administered through the drinking water to provide the bacteria in a concentration of not less than 10^8 per ml. Changes in numbers and proportions of *E. coli* and *L. acidophilus* with increasing time on experiment are shown in tables 1 and 2; incidence of scouring for treated and control pigs is shown in table 3.

TABLE 1 - Number and Proportion of Coliforms and Lactobacilli per Gram of Feces in Control Pigs.

Week of Experiment	Number of Samples ¹	Number of Coliforms x10 ⁸	Number of Lactobacilli x10 ⁸	L/C Ratio
0	22	32.13	44.52	1.39
1	35	11.25	15.44	1.37
2	21	8.90	16.63	1.86
3	18	8.60	13.86	1.61
4	15	7.06	8.96	1.27
5	29	7.26	24.31	3.35
6	29	6.76	15.80	2.34
7	33	10.88	5.10	0.47

¹Taken at random in 12 pens of approximately 125 pigs.

TABLE 2 - Number and Proportion of Coliforms and Lactobacilli per Gram of Feces in Pigs Receiving *L. acidophilus* in Drinking Water.

Days on Experiment	Number of Samples ¹	Number of Coliforms (x10 ⁸)	Number of Lactobacilli (x10 ⁸)	L/C Ratio
0-5	66	10.58	12.08	1.14
6-12	34	8.29	17.17	2.07
13-19	41	3.84	16.81	4.38
20-26	39	2.52	13.15	5.22
27-33	30	1.04	20.12	19.35
34-40	34	0.83	18.68	22.51
41-47	32	1.55	25.26	16.30
48-54	29	0.97	21.52	22.19

¹Taken at random in 12 pens of approximately 125 pigs.

TABLE 3 - Incidence of Scouring in Pens of Control and Lactobacillus-fed Pigs.

Group	Number of Pens	Total Incidence ¹	% Requiring Treatment	% Incidence > Slight Scouring
Control	29	35	34	55
Treated	21	13	9	9

¹Incidence is counted as any scouring in a pen; reoccurrence after a week of non-scouring was counted as a separate incidence.

These data indicate favorable results from daily intake of live L. acidophilus, and suggest that this approach may offer a means of establishing and maintaining desired enteric bacterial conditions.

Tables 4 and 5 show growth data.

TABLE 4 - Growth Performance of Suckling Pigs Fed Lactobacillus Through Drinking Water.

	No. Pigs	Days on Experiment	Initial Weight lb	Weaning Weight lb	Average Daily Gain lb
Control	67	15.2	10.5	18.0	0.49
Treated	26	16.0	9.8	16.7	0.37
Control	13	26.5	10.7	23.4	0.49
Treated	49	26.2	11.2	26.9	0.61

TABLE 5 - Growth Performance of Weaned Pigs Fed Lactobacillus Through Drinking Water.

	No. Pigs	Days on Experiment	Initial Weight lb	Final Weight lb	Average Daily Gain lb
Control	31	29.1	19.6	35.1	0.53
Treated	28	29.9	31.2	59.8	0.95
Control	21	42.9	15.8	45.5	0.69
Treated	32	43.7	18.4	53.8	0.80
Control	18	62.8	21.0	82.8	1.01
Treated	25	52.0	22.0	78.5	1.03

THE DATA above lack precision in that the primary emphasis in these experiments was on bacterial changes. All pigs were otherwise routinely managed, including the inclusion of the antibiotic preparation ASP-250 in the ration. Growth from 21 days age to weaning would be expected to be influenced by differences in milk production of the dam. This may account for much of the differences in the two preweaning groups. It is of interest, however, that the 49 treated pigs that were on experiment 26 days had the highest average daily gains of any of the preweaning groups.

IN THE postweaning groups, the treated pigs were from groups that had received L. acidophilus in the preweaning period. They would, therefore, be expected to have already established the changes in enteric microflora resulting from daily intake of L. acidophilus. This could provide a reasonable explanation for the favorable growth performance seen in groups 1 and 2.

BECAUSE OF the manner in which the data were developed, the growth results should be taken only as indications. As such, they are encouraging in that they are consistent with expectations based on the reduction of E. coli that occurred, and on the lowered incidence of scouring observed.

THEORETICALLY IT should be possible to reduce E. coli to low levels in the entire herd through this procedure. If such is achieved, the low level of E. coli present at farrowing should result in an absence of the troublesome scouring problems so prevalent in many herds; it should also be possible to maintain this favorable status throughout the entire production cycle. Experiments are now in progress at Oregon State University to determine the actual results in a program designed to

accomplish these objectives.

IT IS possible that other bacteria may be found that have even more beneficial effect. If this approach does regularly result in effective prevention of scouring, its use combined with management programs that accomplish the essential features of the SPF program would eliminate the most prevalent disease problems for which effective preventative programs are not currently available in the absence of antibacterial feed additives.

OTHER MANAGEMENT programs can be used to minimize the occurrence of scouring. Still effective, though laborious to implement, are sanitation measures and farrowing schedules that provide a complete break in use of facilities. Thorough cleaning and disinfection is accomplished during the vacancy, followed by at least a few days of non-use. Mr. Paul Van Marcke (1972), General Manager of N. V. Hens'-Voeders, a large Belgian swine production concern, recently described their program as "an all in - all out system" in which a group of pregnant sows and their subsequent litters are moved as a group into cleaned, disinfected facilities at each stage of the production cycle. During vacancy of the facilities, the floors are scrubbed, disinfected, heat-seared with a "flame-thrower", and then painted with a low grade plastic paint or a thin cement coating. Antibiotics as feed additives have not been permitted in Belgium for many years.

THE EFFECT of copper, especially copper sulfate, as a feed additive has been studied by many researchers. In general, levels of 125 to 250 ppm have resulted in favorable growth responses; the 250 ppm level resulted in toxicity in some experiments, but generally gave more favorable responses than 125 ppm when toxicity levels were not encountered.

Dietary protein source and level appear to be related to copper effect; in general, pigs fed diets supplemented with animal proteins responded more favorably to copper supplementation than when plant proteins were used as supplements.

THE EFFECT of copper as a feed additive is in many ways similar to the effect of antibiotics: (1) it reduces unfavorable enteric bacteria; (2) it increases growth rate and feed efficiency; (3) its effect is more favorable prior to 125 lbs. than afterwards; (4) it increases gains more than feed efficiency; (5) and its effect on carcass merit is inconsistent and usually not large.

SEVERAL MAJOR problems exist concerning use of copper as a feed additive for swine: (1) occurrence of toxicity symptoms; (2) elevated tissue stores of copper, especially in the liver; (3) copper content of manure can result in levels toxic to sheep when manure is disposed of heavily onto pasture; (4) and it is not approved by the FDA for use in swine rations. It thus appears that, at present, copper as a feed additive is not an alternative to antibiotics for swine.

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MORTALITY IN BABY PIGS: SOME FACTORS TO CONSIDER

H. C. Stanton and H. J. Mersmann

THE HIGH mortality of baby pigs remains a serious problem to the swine producer even though husbandry practices have been steadily improving. This problem is common throughout the world as indicated by mortality figures representing herds from the United States and from Europe. Surveys still indicate that 20-30% of the total number of piglets born are lost by weaning (1,3,5,6). Approximately 5-7% of these losses are stillbirths while the remainder of the deaths occur between birth and weaning, particularly during the first seven days of life. Some of these deaths may be directly attributed to birth defects and specific disease but still many neonates die from factors which are impossible to clearly identify (3). We will attempt to identify problem areas in the following discussion.

STILLBIRTHS SEEM to be associated predominantly with: 1. persistent intrauterine hypoxia, presumably occurring during prolonged farrowing, 2. interruption of the maternal-fetal connection through umbilical cord rupture, cord constriction and placental and/or fetal abnormality and 3. prolonged gestation. These three general problems accounted for about 81% of the stillbirths in one survey (5).

GENERAL WEAKNESS at birth is perhaps the most common factor identified in the sequelae of events leading to the early death of

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live-born piglets (5,6). Although weakness is quite common in small neonates, it is by no means restricted to this group and may occur in large animals as well. Weakness, unless extreme, is seldom a primary cause of death; but we can readily see how a weak piglet will be a prime target for starvation, disease, sow-induced injuries and chilling. Perhaps "relative weakness" should be considered as a central point in a mosaic representing the interaction of factors associated with the death of live-born piglets (Figure 1). We have attempted, in this simple diagram to identify certain physiological defects of the baby pig which may contribute to his weakness and/or demise. Each of these will be briefly considered:

1. Impaired or Defective Energy Metabolism: The newborn piglet has very little neutral body fat (< 1%) which he can mobilize for energy (13). Furthermore, his liver does not burn mobilized fatty acids very efficiently and, therefore, he must rely predominantly on blood sugar and tissue glycogen stores for energy (12). However, he even has problems fully using carbohydrate since at birth much of his blood sugar is fructose which he cannot use as fuel (3). The piglet has large stores of glycogen in his liver and muscles that are rapidly depleted to provide glucose needed for energy immediately after birth (10). However, the process of glucose tissue utilization may be deficient (3) and aerobic metabolism of glucose in the liver is probably not optimal in the very young pig since the number of mitochondria (organelles responsible for the aerobic conversion of glucose to energy) is low for the first 48 hours of life (11). Finally, the newborn piglet has a low capacity for synthesizing new carbohydrate (gluconeogenesis) (10) and must depend upon his tissue

stores and diet for this form of energy. Considering his metabolic defects, it is not surprising that this neonate is very susceptible to starvation and may develop severe hypoglycemia eventually leading to death ("baby pig disease") (3, 13). Furthermore, any intrauterine event which reduces the piglets' energy reserves may be expected to result in a stillbirth or under less severe circumstances, a weak neonate. Nutritional problems after birth could obviously lead to the death of a weak pig.

2. Thermoregulation: The baby pig is very susceptible to chilling since his thermoneutral temperature (that temperature where he does not increase his metabolism to conserve body heat) is 34-35° C (93-95° F) (2,13). Hence a neonate which is chilled will be using large portions of his energy stores to maintain his body temperature, a luxury which he cannot afford, as we saw in the previous section. The chilled pig may become lethargic and not nurse which compounds the weakness and its consequences and makes him even more susceptible to disease or sow-induced injuries.

3. Immature Immunity: The newborn piglet obtains antibodies from colostrum and has no inherent immunity (8). Furthermore, blood protein levels are low at birth, the neonate's blood volume is low and he may develop subcutaneous edema (3,14). The output of the heart is dependent upon blood volume and it is conceivable that the cardiovascular reserve is lower in newborn than in the older piglets which have attained adequate blood protein levels and blood volume. When the baby piglet does not nurse properly, he will not get adequate immunological and other plasma proteins which he will use for subsequent protection from disease and for establishing plasma

volume (7).

4. Poor Nutrition: The baby piglet has many nutritional requirements which must be met through nursing or, in some cases, augmented by exogenous administration (iron). The newborn piglet must not only be capable of competing for a teat with his littermates but is also very dependent upon the nutritional quality of the milk. Weak piglets would be particularly vulnerable with a sow whose milk is not qualitatively adequate (3).

CERTAIN PRACTICES may significantly reduce newborn piglet mortality:

1. England and Chapman (4) have demonstrated that small, weak piglets survive and prosper if they are given a warm environment, adequate nutrition and protection from the dam. Adequate attention to all piglets at the time of farrowing and for the first few days after farrowing should significantly reduce losses. Particular emphasis should be placed on keeping the animals warm, being sure that they nurse soon after birth for colostrum and energy and that they can compete with their littermates during nursing. The economics in favor of these practices are obvious.

BAUMAN et al. (1) calculated that a sow consumed 1000 lbs. of feed during gestation, or if we base it on a litter of 8 pigs, 125 lbs. of feed per pig. Each piglet lost at birth means the loss of 125 lbs. of feed. This loss increases as the piglet approaches weaning and animals which die near weaning may represent an investment of 210 lbs. of feed. The cost of labor and capital investment brings this loss even higher and makes a compelling argument for reducing piglet deaths through intensive husbandry.

2. Automatic artificial rearing may significantly improve survivability since nutrition and environment can be controlled and the hazard of sow-induced injuries is eliminated. This will not alleviate the problem of stillbirths and losses that occur during the time the piglets are kept with the sow to obtain colostrum. Lecce (7) found that 83% of disadvantaged piglets (< 1 kg in body) judged likely to die survived when artificially reared 36 hours after birth. The piglets which died (17%) were found to have consumed little or no colostrum while they were with the sow.

3. Research is underway to find ways to improve the vigor of the piglet by improving the maternal influence in utero. It is possible that this may be achieved with nutrition and/or drugs. These treatments may complement but cannot replace good husbandry practices.

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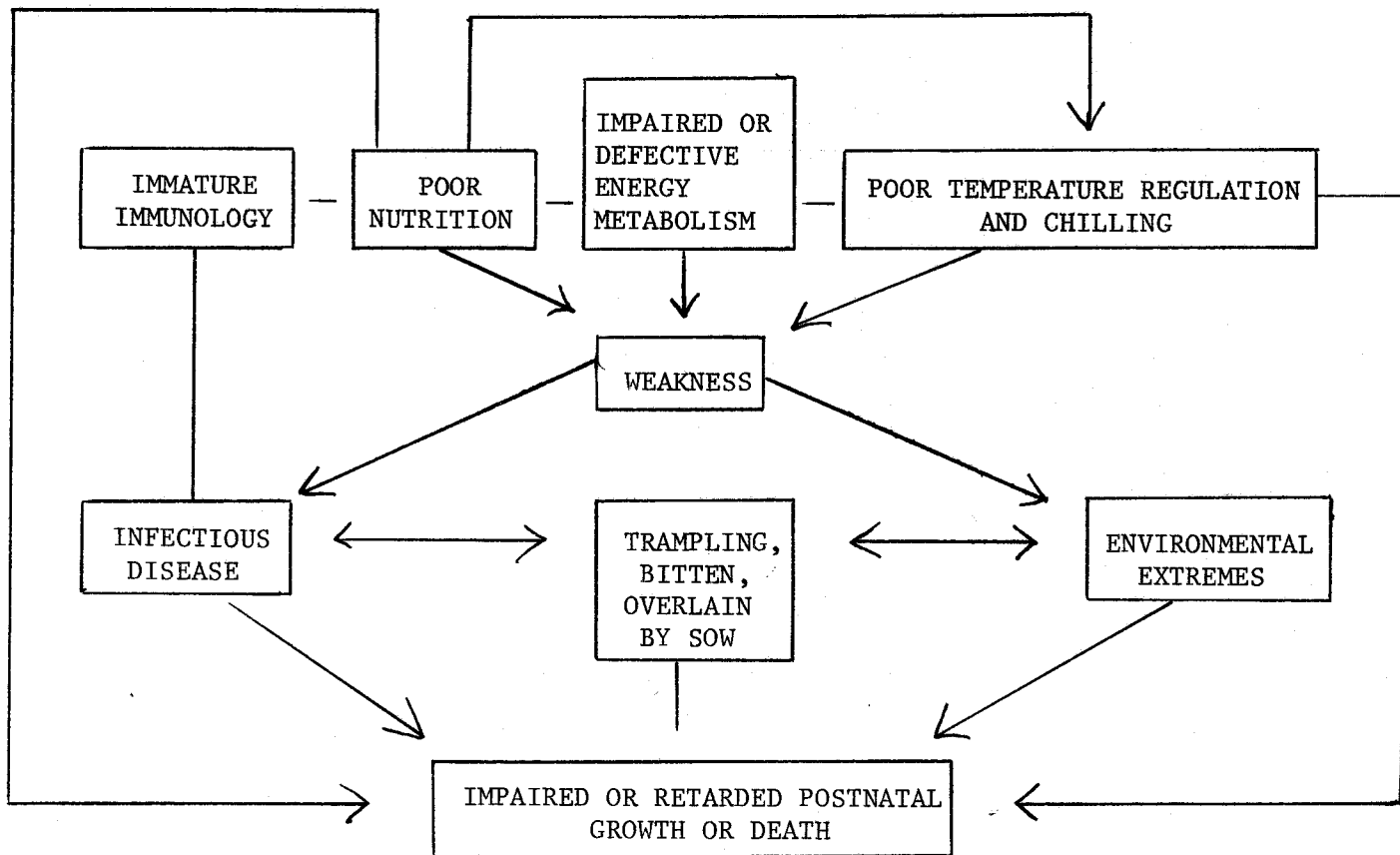


Figure 1. SOME GENERAL FACTORS INFLUENCING POSTNATAL PIGLET VIABILITY, SURVIVAL OR GROWTH

PRINCIPLES OF PROTEIN SUPPLEMENTATION

P. R. Cheeke

THE BEST ration for pigs is one which meets their nutritional needs at the lowest cost. There are hundreds of different rations that will give satisfactory performance, but they vary widely in price. The "best" ration today may be a very poor one this time next year, simply because of the constant changes in prices of feed ingredients. For this reason, it is advisable to periodically assess the feed ingredient situation, and modify rations to take advantage of favorable price changes.

THE FORMULATION of rations requires certain information, such as a knowledge of nutrient requirements, composition of feeds, etc. Most feed companies employ nutritionists who have the necessary training to use this information. It is advisable for swine producers to work closely with their feed company, rather than attempting to design rations themselves. The objective of this presentation will be to describe some of the characteristics of proteins and protein supplements, so that a producer may more readily converse with feed manufacturers.

ALTHOUGH PRACTICALLY everyone is familiar with the term "protein", most people would have difficulty in precisely defining what a protein is. To aid in understanding some basic principles of protein

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nutrition, it is convenient to raise some pertinent questions, and then provide answers to them.

WHAT IS a protein?

Proteins are made up of smaller units called amino acids. A protein consists of many thousands of amino acids joined together. The characteristics of different proteins are determined by the amino acid composition.

HOW MANY different amino acids are there?

Proteins contain a total of twenty different amino acids. Fortunately, it is not necessary that all of these be present in the diet.

For swine, there are ten amino acids that must be present in adequate quantities in the feed. These are referred to as essential amino acids. Of these ten, there are three that are likely to be deficient. These are called methionine, lysine and tryptophan.

WHY DO pigs need protein in their diet?

Much of the new tissue formed by growing animals is protein. For example, muscle tissue (meat) is high in protein. In order for the pig to manufacture its body proteins, it needs adequate amounts of the amino acids provided in its feed. If sufficient amounts of the essential amino acids are not present, normal growth cannot occur.

WHY ARE protein supplements needed?

Swine rations are based on grains; feed grains usually lack sufficient total protein to meet the protein requirements of pigs. It is important, however, to note that besides lacking adequate total protein, grains are also deficient in some of the essential amino acids. For example,

wheat and barley are deficient in lysine and methionine, while corn is deficient in these two and also lacks adequate tryptophan.

HOW DOES a nutritionist decide what protein supplement to use? Two major considerations are the cost per unit of protein, and the amino acid deficiency to be overcome. Corn, for example, contains about half the lysine content of wheat. If we have corn and wheat of the same protein content, the corn will require more lysine supplementation, and a different type of supplement will probably be used. The other major consideration is price per unit of protein. For example, if soybean meal costs \$120 per ton, and cottonseed meal costs \$107 per ton, which one is the better buy? The cost per ton doesn't mean anything - what is important is the cost per pound of protein. Soybean meal contains 46% protein, while cottonseed meal contains 41% protein. This calculates out to 13¢ per pound of protein, for each supplement. Even though the cost of the protein is the same, a nutritionist would likely pick soybean meal, because of its more desirable amino acid balance. Thus, even though soybean meal costs \$13 more per ton, nutritionally it is a better buy for swine.

WHY DO young pigs require more protein supplementation than older animals?

In general, the dietary protein requirement decreases with age. There are two major reasons for this. Young pigs have a more rapid growth rate, and the proportion of the gain that is protein is higher than is the case with older animals. Also, young pigs are not able to digest plant proteins as efficiently as older animals can. For this reason, creep and starter rations should contain highly digestible

protein supplements, such as skim milk powder, and dried whey.

WHAT IS the significance of high lysine corn to swine producers?

Corn is very low in lysine, one of the essential amino acids.

Recently, a strain of corn has been developed that contains about twice the normal lysine content. This means that less supplementary lysine is required, so that the cost of protein supplementation is reduced.

IT IS significant to note that the lysine content of "high-lysine" corn is less than the lysine content of feed wheat. It can be anticipated that strains of other cereal grains will be developed, with improved amino acid balances. The significance of this is that the cost of protein supplementation of these high-quality grains should be reduced.

HOW SHOULD home-grown feed grains be used?

It is very desirable to obtain a crude protein analysis of your grains. When the protein content is known, a protein supplement can be designed. The choice of the supplement will depend upon the cost per pound of protein, rather than on the cost of the supplement itself. Close cooperation with your feed supplier in designing a ration is recommended. Large operations may find it profitable to employ the services of a nutrition consultant.

INFLUENCE OF SIRE, SEX, AND STAGE OF GROWTH ON
RESPONSE OF MARKET HOGS TO TWO LEVELS OF PROTEIN

S. M. Boyd, D. C. England, W. H. Kennick and N. A. Hartmann

GENETIC DIFFERENCES in feed utilization have been well established for rations as a whole and are evidenced by effective selection for improvement in feed efficiency. It is reasonable to expect differences to also occur in protein utilization due to the genotype of the animal. These differences may be influenced by sex, weight, and heredity for lean-fat ratio, and other factors controlled by the genetic makeup of the animal. The producer must control and utilize as many of these variables as possible to most effectively produce lean-type animals demanded by the packer. With this in mind, possibly the best way to approach the problem is through a genetic evaluation of the breeding stock being used.

PROGENY OF three purebred Yorkshire boars were used in this study. The widest difference in genetic background existed between sires one and three. The greatest difference, therefore, would be expected to occur between progeny of these two sires. The three sires were bred to a random sampling of Yorkshire, Berkshire, and crossbred sows all from the OSU herd. As the offspring of a particular sire approached 60 pounds, they were randomly divided,

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within sex, into two groups of eight animals each. Each group, consisting of four males and four females, received one of the two experimental rations which varied in protein content (Table 1).

Table 1. Experimental ration.

Ingredient	% of Ration 1	% of Ration 2
Wheat	75	66
Alfalfa meal	4	5
Soybean oil meal	10	16
Meat meal	5	8
Molasses	4.5	4.5
Salt	0.5	0.5
Zinc sulphate	12 ozs./ton	12 ozs./ton
Vitamin D	120,000 IU/ton	120,000 IU/ton
Vitamin A	1,200,000 IU/ton	1,200,000 IU/ton
Dicalcium phosphate	1.0	none
ASP-250	0.1	0.1

Both rations were formulated in accordance with U.S.N.R.C. recommendations with the exception of the protein level. Ration one was designed to provide 15% protein and ration two to provide 20% crude protein. Both rations were approximately equal in other nutrients, including energy level. The rations were fed ad libitum from 60 to 225 pounds live weight. This test period was divided into three parts: 60 to 115 pounds; 115 to 170 pounds; and 170 to 225 pounds. Average daily gains and feed efficiencies for each period

were calculated and live backfat probes at 170 and 225 pounds were recorded. Barrows were slaughtered at 225 pounds and carcass data were recorded.

ANALYSIS OF data show that animals on the high protein ration gained faster than animals on the normal protein ration only during the period from 60 to 115 pounds. Backfat thickness was also slightly less on the high-protein-fed animals, but not enough to be statistically significant. Tables 2 and 3 show the effect of protein level on average daily gain and backfat depth.

Table 2. Effect of protein level on average daily gain during three weight ranges.

Ration	60-115 lbs.	115-170 lbs.	170-225 lbs.
Normal Protein	1.49	1.90	1.96
High Protein	1.60	1.89	1.96

Table 3. Effect of protein level on live backfat probe measurement (inches).

Ration	170 lbs.	225 lbs.
Normal Protein	0.72	1.02
High Protein	0.67	1.01

TABLES 4 and 5 show sire effect on average daily gain and backfat depth, respectively. Sire two was the best sire as indicated by average daily gain and feed efficiency of his progeny; this difference was present from 60 to 115 lbs, and from 115 to 170 lbs, but not from

170 to 225 lbs. Differences in backfat thickness were small and not significant.

Table 4. Average daily gain by sire progeny groups during three growth periods.

Sire	60-115 lbs.	115-170 lbs.	170-225 lbs.
No. 1	1.53	1.84	1.94
No. 2	1.66	1.97	1.97
No. 3	1.42	1.87	1.96

Table 5. Sire effect on live backfat thickness of progeny at two weights (inches).

Sire	170 lbs.	225 lbs.
No. 1	0.68	0.99
No. 2	0.71	1.04
No. 3	0.67	1.03

THE EFFECT of sex caused greater mean differences in average daily gain and backfat thickness than did either sires or rations. Males gained significantly faster than females during all three periods of growth and showed significantly greater backfat depth at both weights. Tables 6 and 7 show these results.

Table 6. Average daily gain of barrows and gilts during three weight periods.

Sex	60-115 lbs.	115-170 lbs.	170-225 lbs.
Barrows	1.61	1.99	2.05
Females	1.49	1.80	1.87

Table 7. Sex effect on live backfat thickness (inches) at two weights.

Sex	170 lbs.	225 lbs.
Barrows	0.77	1.11
Females	0.63	0.93

NO INTERACTIONS between sex, sire, and ration in any combinations were observed. This means that (1) the progeny of each sire, compared to the progeny of the other sires, responded similarly on both protein levels; (2) the male and female progeny of a given sire were similar in their comparative merit to the male and female progeny of the other sires; and (3) that males and females of a given sire, compared to those of the other sires, responded similarly to the two protein levels.

THE EFFECTS of sires and rations on carcass traits are shown in Tables 8 and 9, respectively. The differences in carcass data between the rations all slightly favor the higher protein ration, but are not statistically significant.

Table 8. Effect of protein level on carcass data at 225 pounds live weight.

Ration	C.L. ^a	C.B.F. ^b	L.E.A. ^c	L.Wt. ^d	H.Wt. ^e
Normal Protein	30.2	1.55	3.64	24.8	31.3
High Protein	30.4	1.49	3.78	25.1	31.8

^aCarcass length in inches.

^bCarcass backfat in inches.

^cLoin eye area in square inches.

^dLoin weight in pounds.

^eHam weight in pounds.

Table 9. Carcass data means of sire progeny groups of barrows at 225 pounds liveweight.

Sire	C.L. ¹	C.B.F. ¹	L.E.A. ¹	L.Wt. ¹	H.Wt. ¹
No. 1	30.5	1.52	3.53	24.7	31.9
No. 2	30.2	1.56	3.72	24.7	30.6
No. 3	30.4	1.49	3.94	25.2	32.2

¹Abbreviations and units are same as in Table 8.

RATION COSTS averaged \$76.06 per ton for the normal protein ration to \$83.36 per ton for the high protein ration. Analysis of the results show that even though the high protein ration resulted in somewhat improved growth rate, feed efficiency and carcass leanness, there was not enough of an increase in any of the traits to pay for the extra protein costs. The results of the cost analysis are summarized in Tables 10, 11, and 12.

Table 10. Cost per pound of gain on the normal protein ration.

	60-115 lbs.	115-170 lbs.	170-225 lbs.
ADG (lbs.)	1.49	1.90	1.96
Feed used/lb of gain (lbs.)	3.28	3.52	4.00
Feed cost/lb of gain (\$)	.1246	.1338	.1520

Table 11. Cost per pound of gain on the high protein ration.

	60-115 lbs.	115-170 lbs.	170-225 lbs.
ADG (lbs.)	1.60	1.89	1.96
Feed used/lb of gain (lbs.)	3.01	3.45	3.76
Feed cost/lb of gain (\$)	.1264	.1449	.1579

Table 12. Cost per pound of selected carcass yields.

	Normal Protein	High Protein
Ham + loin wt. (lbs.)	56.11	56.89
Feed used/lb of ham + loin (lbs.) ¹	10.30	9.91
Feed cost/lb of ham + loin (\$)	.3914	.4162
Cold carcass weight (lbs.)	167.7	167.6
Feed used/lb of carcass wt (lbs.) ¹	3.45	3.37
Feed cost/lb of carcass wt. (\$)	.1311	.1415

¹

Based on feed consumption from 60 to 225 lbs.

Summary

The results show that higher protein levels increase average daily gain during early growth stages of market hogs. Some improvement in feed efficiency occurred, along with slight improvement in carcass merit, but these were too small to be economically feasible. The added expense of the extra protein in the final feeding periods more than offset any further improvement in average daily gains, feed efficiency or carcass data. Barrows gained more rapidly than gilts at all stages of growth but gilts were leaner at both 170 and 225 pounds. There were no significant interactions of sire, sex, and protein level.

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