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To the Graduate Council:

I am submitting herewith a thesis written by Bertie Albert D'Souza entitled "Oleandomycin, Terramycin and a Combination of Penicillin, Streptomycin and Sulfaquinoxaline for Growing Finishing Swine." I recommend that it be accepted for nine quarter hours of credit in partial fulfillment of the requirements for the degree of Master of Science, with a major in Animal Husbandry.

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OLEANDOMYCIN, TERRAMYCIN AND A COMBINATION OF PENICILLIN,
STREPTOMYCIN AND SULFAQUINOXALINE FOR
GROWING FINISHING SWINE

A THESIS

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CHAPTER I

INTRODUCTION

To materially increase the production of meats, milk and eggs with less feed requires the use of scientific knowledge. In the last five to ten years, this has been made possible through the use of antibiotics, hormones and other drugs to stimulate a faster growth rate in animals with greater utilization of feed. "The medication of feed stuffs is a recent feeding innovation that has economic implications. These technical changes in feeding practices are improving the efficiency of feed conversion, that is, the pounds of livestock product produced per hundred pounds of feed. They also affect the organization of production on the farm," Scoville (1956). One benefit of economic importance to the livestock farmer that has come out of the development of antibiotics is their use in livestock feeds. Penicillin, Chlortetracycline, Oxytetracycline, and bacitracin have been used in livestock feeds in the past few years. In 1954, 490,000 pounds of these drugs were mixed into livestock feeds which resulted in savings to the farmers through greater efficiency of production according to Welch and Mart-Ibeanes (1957). Antibiotics hold promise for further profitable investigations and exploitation in livestock production.

While antibiotics may help to increase the income of the farmer, they may play a greater role in the nutrition of man throughout the world. A nutritionist has estimated that antibiotic supplements for hogs can save two million tons of feed annually in the U. S. A., McKeen (1952).

Knowledge so far gained on the role of antibiotics in nature seems to point out hope of further useful findings on the influence of environmental bacteria on the growth of farm animals. A drug or combination of drugs that would completely inactivate all bacteria in the intestinal tract to provide a germ free animal for studying the vitamin requirements as reported by Moore et al. (1946), or to compare the growth of such germ-free animals, with those animals whose bodies and environment hold a high concentration of bacteria, are areas that seem to be of practical benefit. Similarly, the effects of continued administration of antibiotics on animals in relation to their vitamin and mineral requirements or the anatomical and physiological consequences that can follow prolonged use of antibiotics still demands study. Obviously, the field of antibiotics is a fascinating area for continued research. The research undertaken with antibiotics in applied feeding trials on farm stock, and the basic, or fundamental work with laboratory animals cannot be considered complete. Additional work is needed to identify new antibiotics and each new antibiotic has to be tested in every possible way to determine its properties and potential in livestock production.

Oleandomycin is a new antibiotic that has recently been placed on the market. It must be evaluated as a growth stimulant for swine and compared to known antibiotics in this respect.

This study was designed to evaluate Oleandomycin, and a combination of antibiotics with a sulfa drug in relation to a control ration and a standard antibiotic used for growing-finishing swine. The work was done at the University of Tennessee Animal Husbandry-Veterinary Science Blount Livestock Farm from December, 1958 to May, 1959.

CHAPTER II

REVIEW OF LITERATURE

Early Work and Discovery of Growth Stimulating Activity of Antibiotics

Early observations of increased growth in animals following the administration of chemotherapeutic agents indicated a relationship of these drugs with changes in growth rate. At that time it was evident that these chemotherapeutic agents, and particularly the sulfa drugs, caused an inhibition in growth by their bacterio-static effect on the intestinal microflora. Black et al. (1941) showed that on a purified basal ration, 0.5 per cent sulfa guanadine greatly reduced the growth rate of young rats. When liver extract was fed with 0.5 per cent sulfa guanadine optimum growth was obtained. Whereas, when p-amino benzoic acid was fed with 0.5 per cent sulfa guanadine from the beginning of the treatment there was a definite growth response. These results indicated a possible synthesis of rat-growth factors by the intestinal bacteria. Luckey et al. (1946) found that the addition of sulfasuxidine to a purified ration for chicks increased the demands for synthetic folic acid by about three times. This situation indicated that bacterio-static agents lead to the prevention of biosynthesis of B vitamins in the alimentary tract by inhibiting the normal growth of the intestinal microflora. Smith and Robinson (1945) reported that streptomycin and streptothricin administered orally to mice caused a rapid pronounced reduction in the number of coliform and non lactose fermenting organisms in the feces. Both drugs caused a distinct change in the intestinal flora. Similarly, Kornberg et al. (1943) produced

agranulocytopenia and anaemia in rats by feeding sulfathiazole, sulfadiazene or sulfanilamide at a 1.0 per cent level using a purified diet. Feeding certain liver fractions counteracted the effects of the continued administration of these sulfa drugs in four to ten days. Similar results were found by Light et al. (1942).

Moore et al. (1946) found that sulfasuxidine and streptomycin singly or in combination gave an increased growth rate in chicks receiving a basal ration supplemented with folic acid, but they failed to sterilize the intestinal tract though there was a marked reduction in the coliform bacteria.

During this period of research it was shown that the addition of animal protein to a plant protein diet of chicks and swine greatly accelerated growth. This finding later led to the isolation from liver of the "animal protein factor," (vitamin B₁₂), Ricks et al. (1948). 'APF' was thought to be responsible for the differences in the growth promoting properties in animal protein over plant proteins. Later on, vitamin B₁₂ was found in the cultures of streptomyces griseus and a streptomyces aureofaciens and crude residues from these fermentation broths were tried as feed supplements. Since these residues showed evidence of higher growth stimulating activity than crystallin vitamin B₁₂, Stokstad and Jukes (1950) demonstrated that chlortetracycline and streptomycin with vitamin B₁₂ can promote further growth in chicks. Thus began the role of antibiotics in animal nutrition.

Antibiotic Effect in Swine Feeding

Braude et al. (1953) made a review of the work on antibiotics since

the first report appeared in 1949-50. The object of the work was to determine the relative effectiveness of different antibiotics, the factors influencing their response, and to understand the mode of action. They found aureomycin and terramycin more effective than penicillin, bacitracin and streptomycin. Terril et al. (1954) found aureomycin to be more effective than bacitracin in stimulating growth rate. Hansen et al. (1955) found the addition of terramycin and penicillin increased gains of pigs significantly, but the withdrawal of the antibiotic when pigs attained 125 pounds of weight had a depressing effect on rate of gains thereafter. Wallace et al. (1953) found feed utilization figures were in favor of those pigs on a high level of antibiotic through the growing-fattening period. Complete withdrawal of the antibiotic caused a decrease in gains, lower feed consumption and poor feed conversion. The inference was that antibiotic supplement should be continued through the entire growing-fattening period for optimum gains. Carpenter (1951) tested five antibiotics, namely, aureomycin, terramycin, streptomycin and chloromycetin and obtained a growth response. All the antibiotics except chloromycetin was effective in controlling diarrhea. Vitamin B₁₂ or streptomycin given either orally or parenterally stimulated growth of weaned pigs, but there was no added advantage when both were given together. Vitamin B₁₂ had no effect on diarrhea, but streptomycin did control diarrhea.

Whitehair et al. (1951) reported that aureomycin, streptomycin, penicillin and sulfathalidine were very beneficial in the treatment of digestive disturbances in young pigs. In the event of chronic digestive disturbances in a herd these drugs can be given in feed, but in an acute

situation therapeutic treatment of individuals was the best method. Cunha et al. (1950) found that aureomycin increased the rate of gain, efficiency of feed utilization, appetite, bloom and smoothness of hair coat; the antibiotic also prevented periodic scours which occurred in the control pigs. When aureomycin, streptomycin and penicillin were compared they found penicillin to be least beneficial for growth increase. Streptomycin stimulated growth to a small extent, but not as much as aureomycin which gave by far the best response. Their data indicated differences in response may occur with various antibiotics, rations and species. Cuff et al. (1950) studied the effects of antibiotics in sixty-three "runt" pigs. A runt pig was defined as an unthrifty pig weighing less than twenty pounds at fifty-six days. These pigs were self fed a basal ration containing 18 per cent protein to which varying amounts of vitamin B₁₂, APF, and aureomycin had been added. They found the added APF significantly improved the daily gains while the addition of vitamin B₁₂ did not significantly effect gains. There was no measurable interaction between APF and vitamin B₁₂ or between vitamin B₁₂ and aureomycin. Whereas, pigs receiving aureomycin had significantly higher daily gain, were more uniform in size, more thrifty in appearance and exhibited less scouring than pigs on other treatments. These results indicated that slow growing (runt) pigs respond well to low level antibiotic feeding.

Cunha et al. (1950) using a corn-peanut meal ration showed that APF and vitamin B₁₂ were different in their responses in pigs. Burnside et al. (1949) found APF increased the feeding value of peanut meal and soybean meal in such a way as to equal that of fish meal. With the same corn-peanut

meal ration Cunha found APF and vitamin B₁₂ spared the methionine needs of pigs. His later studies indicated that APF contained vitamin B₁₂ plus some other factor. These findings seem to be in agreement with those of Stokstad et al. (1950) who found that the APF supplement supplied some unidentified factor for the chick in addition to vitamin B₁₂.

Catron et al. (1952) fed a total of 128 pigs with corn-soybean meal ration, supplemented with minerals and vitamins including vitamin B₁₂ from weaning to 200 pounds in dry lot. Aureomycin in varying levels and different protein levels were used to determine whether previously recommended protein levels were too liberal for the present day feeding practices and to note the effect of antibiotics on protein needs of pigs. Protein levels were reduced by 3 per cent when the pigs reached seventy-five pounds and again when the pigs reached 150 pounds. They found, in the absence of antibiotics the rate of gain for the entire feeding period varied significantly among the different protein levels. These results showed in the absence of an antibiotic the 16-13-10 per cent protein levels supplied the needs of protein for pigs from weaning to market. Whereas, in the presence of an antibiotic a level of 14-11-8 per cent protein produced gains equal to the higher levels of protein. Aureomycin added at the rate of 10 mg. per pound of ration appeared to exercise a protein "sparing-like" effect on the lower levels of protein. In effect, pigs receiving an antibiotic in their feed gained an average of 0.12 pounds per day more and consumed twenty-three pounds less feed for every hundred pounds of body gains made than those that did not receive an antibiotic. Braude and Johnson (1953) maintained that the protein sparing effect of antibiotics

cannot be explained on the basis of nitrogen retention. They explained the apparent protein-sparing effect noticed was due to the fact that the requirement of protein and particularly the "protein-carbohydrate" ratio are not the same in fast growing animals as compared to animals growing at a normal rate. Whatever factor is responsible for the fast rate of growth in animals receiving antibiotics may indirectly also alter the optimum protein-carbohydrate ratio which may explain the lower protein requirements for the antibiotic treated animals. Phillips and Bohstedt (1954) found that vitamin B₁₂ had no effect in increasing the rate of gain, feed efficiency, haemoglobin or protein utilization. Aureomycin had no effect on high protein fed pigs after they reached seventy pounds in weight, while the performance of pigs with lower body weight was increased. However, aureomycin alone or in combination with vitamin B₁₂ increased the protein utilization by pigs. Protein levels of 17.0, 13.7 and 11.7 per cent with aureomycin and vitamin B₁₂ added were equal to protein levels of 21, 18.2 and 15 per cent without aureomycin and vitamin B₁₂.

Carpenter (1951) found that feeding an APF supplement containing aureomycin for 49 to 90 days prior to parturition did affect litter size and survival of new born pigs. He found that the post weaning growth rate and feed efficiency was increased in pigs fed a creep diet with aureomycin during the suckling period. Reducing the level of antibiotic supplement at weaning time or three weeks after weaning gave a decrease in rate of gain and efficiency of feed utilization, and a high incidence of diarrhea. Hanson (1951) reported that aureomycin and terramycin added to a creep feed for suckling pigs improved the rate of growth and prevented scours.

Bacitracin and penicillin did not stimulate growth or control scours.

Wahalstrom (1955) found that in two dry-lot trials and one pasture trial no appreciable advantage when combinations of antibiotics were used as compared to aureomycin alone. Bridges and Dyer (1952) fed penicillin and streptomycin singly and in combination in a cottonseed meal ration. Both penicillin and streptomycin increased the rate of gain.

Smith et al. (1956) fed chlortetracycline at levels of 100, 200 and 400 gms. per ton of feed prior to and twenty-six days after vaccination for hog cholera. They found that immunity was not affected by chlortetracycline. Brown and Luther (1950) stated that levels as low as three parts per million of antibiotics increased growth rate of pigs fed balanced vegetable rations containing vitamin B₁₂. These pigs were superior to pigs fed a practical ration containing animal protein. Luecke et al. (1951) found streptomycin and aureomycin at 10 mg. per pound of ration gave a growth response. Procaine penicillin at 1 to 5 mg. per pound of feed was satisfactory, while APF containing aureomycin gave excellent growth when fed at levels of 0.35 per cent in B vitamin fortified corn-soybean ration.

Speer et al. (1956) fed pigs individually at different protein levels. The rations were made up of soybean meal fortified with minerals and vitamins, with and without the addition of chlortetracycline hydrochloride. The pigs were put on alfalfa pasture at a weight of 30 to 200 pounds. Statistically significant responses in growth rate, feed intake and feed efficiency were obtained. Luecke et al. (1950) reported that the addition of vitamin B₁₂ to the basal ration resulted in approximately a 10 per cent increase in body weight gain as against the gains of animals fed

the basal meal alone. The inclusion of vitamin B₁₂ and streptomycin to the basal ration gave about a 40 per cent increase in weight gain. Dried animal protein factors gave similar effects to B₁₂ and streptomycin.

Work at the Purdue University by Briggs and Beeson (1951) involved the feeding of healthy pigs with various combinations of aureomycin, streptomycin and vitamin B₁₂ concentrates in an all plant protein ration. Pigs on the basal ration made 1.6 pounds per day, and had a feed requirement of 392 pounds per hundred pounds of body gain. When 15 mg. of streptomycin per pound of ration or 10 mg. of crystallin aureomycin per pound of ration were given, there were increases from 11.0 to 13.0 per cent in average daily gains and 14.0 to 16.0 per cent feed efficiency. When vitamin B₁₂ was added at levels of 12.5 mg. per pound, in addition to the antibiotic, the results were similar to those fed aureomycin. This work also showed that supplementing practical rations for pigs with either of the two antibiotics and/or vitamin B₁₂ resulted in more uniformity in the pigs and prevented bloody dysentery.

Dinussan et al. (1951) found the addition of cobalt-chloride to rations made with locally grown grains increased the rate of gain 0.1 to 0.2 pounds per day. While Kline et al. (1954) found the addition of 2.88 ppm cobalt to a ration with or without antibiotic did not improve the growth performance of pigs. Pigs receiving B₁₂ and cobalt made similar gains as those given only cobalt. The daily feed intake and efficiency were not affected by the addition of B₁₂ or cobalt. The addition of an antibiotic definitely brought about an improvement in gain and this gain disappeared with removal of the antibiotic. Bacterial studies of feces

showed a marked increase in fungi counts in pigs fed antibiotics and a decrease in fungi count in those receiving vitamin B₁₂.

The effect of antibiotics on the carcass characteristics was an issue of considerable experimentation. Price (1954) studied the carcasses of forty-six barrows, fed on various levels of aureomycin, vitamin B₁₂, terramycin and trace minerals. He found the average backfat thickness of the pigs receiving antibiotics was slightly greater than those of the control, but the difference was not significant. The average lean cut weights and average percentage of lean in the lean cuts was similar in all groups. Hansen et al. (1955) found adding vitamin B₁₂ or any of the antibiotics did not affect the percentage of moisture, crude protein or fat in the carcasses. They concluded aureomycin, terramycin and penicillin per se do not directly affect carcass quality. Teh-cheng Huang and McCay (1953) found pigs receiving terramycin had a higher dressing percentage than the controls. In gross analysis, the pigs fed terramycin yielded more total fat and lean meat by weight, but a lower percentage of lean meat and a higher percentage of fat than the controls.

Oldfield and Hale (1953) investigated the activity of antibiotic administered to very young suckling pigs in several different methods. The different groups of suckling pigs were administered penicillin, by intramuscular injections, another received the same dose of penicillin orally by capsule, the next received the same dose of penicillin divided among four oral weekly doses, and the fourth group was control. The results indicated some advantage for antibiotic supplementation for pigs which are suckling and for the parenteral method of administration. Larson and

Carpenter (1952) conducted two experiments to determine the amount of aureomycin excreted in the feces of pigs receiving aureomycin orally and intraperitoneally. The result of the experiment showed that aureomycin administered orally or by injection is excreted in the feces of pigs. The amount excreted varied with the pigs from day to day. The injected aureomycin was found in feces twenty-four hours after administration and apparently reached the maximum value in seventy-two hours. The oral administration reached the maximum in the feces within forty-eight hours. Harrel and Heilman (1949) showed that in man, aureomycin given orally was excreted by the liver through the bile. It is possible, that in the pig, aureomycin enters the intestinal tract of the pig through the bile.

This review will seem incomplete without a brief consideration of the possible mechanism involved in the growth promoting responses obtained from antibiotics. This aspect of antibiotic action continues to baffle all investigations to the present time. Never-the-less, there has been various conjectures and postulates. All experimental evidence now seems to converge on the intestinal bacteria. These postulates have been a positive nitrogen balance, disease-level, antibiotic action is like that of a drug acting on the general nutrition of the organism and antibiotics acting through a possible vitamin sparing action in the organism. The disease level concept originated following the experiments by a large number of investigators, on S. aureofaciens fermentation product. Terril and Krider (1950), Cunha (1949), and Catron (1949) obtained marked effects in the control of diarrhea followed by improvement in growth. This led to the postulation that the antibiotic effect, varied with disease level, a term

introduced by Catron. Germ free environment concept, seems to be opposite to disease level concept. For instance, a high disease level would make the antibiotic growth effect large while in a germ free condition, antibiotic action would tend to be small. This view is partially supported by the report of Coats and co-workers (1951) which showed that the disappearance of antibiotic effect can occur in a germ free clean area. When chicks of the same hatch were divided and one group reared under clean laboratory conditions without penicillin they weighed 190 gms., the other reared in a less clean building and supplemented with penicillin also weighed 190 gms., while the third, unsupplemented control, weighed only 167 gms. All chicks received the same basal ration. When all these chicks were mixed at fourteen days of age both lots depressed in growth unless they received an antibiotic supplement. Experimental findings on the effect of antibiotics for the animals on clean and dirty environment gave rise to the belief that antibiotic effect may be due to suppression of growth suppressing organisms. Bird (1951) advanced the belief that antibiotics altered the internal ecological relationship of the microflora and this formed the basis for the stimulating effect on growth in pigs. Inhibition of some microorganisms will favor the growth of other organisms in the digestive tract. The decrease in the requirements of several vitamins and for proteins could be explained either on the basis of encouragement of nutrient synthesizing forms of microorganisms or the suppression of nutrient utilizing forms of microorganisms. Elam et al. (1953) advanced the idea that antibiotics inhibited toxin producing bacteria. Their experiments showed a close relationship between an antibiotic, arsenical,

combinations of antibiotics, and a combination of antibiotic and arsenical in reduction of the number of clostridia per gram of fecal material.

CHAPTER III

EXPERIMENTAL PROCEDURE

For this experiment, fifty-six weanling Duroc and Hampshire pigs were allotted to fourteen lots on the basis of breed, sex, and weight. Two lots were randomly assigned to each of the following treatments:

1. Control
2. Control plus 10 grams oxytetracycline
3. Control plus 3 grams oleandomycin
4. Control plus 12.5 grams sulfa quinoxaline, 5.0 grams penicillin, and 12.5 grams streptomycin
5. Control plus 6 grams oxytetracycline, 2 grams oleandomycin
6. Control plus 5 grams oxytetracycline, 6.25 grams sulfa quinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin
7. Control plus 2 grams oleandomycin, 6.25 grams sulfa quinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin

The pigs were identified by ear notches according to the United States Department of Agriculture system of ear notching.

All of the pigs were in apparent good health and in a thrifty condition. The pigs were sprayed for lice with a mixture of four pounds DDT in fifty gallons of water at the beginning of the experiment and about midway of the experimental period. The pigs were also treated for worms with piperazine just prior to the experiment and midway of the experimental period.

The basal or control rations were calculated to meet, or exceed the minimum requirements for pigs as recommended by the National Research

Council, Beeson et al. (1953), (Table I). The 16 per cent protein ration was used until the pigs in a lot averaged 110 to 120 pounds body weight and the 14 per cent ration was then fed until the end of the experiment. The rations were fed ad lib from "self feeders." All rations were mixed at the University farm with a mechanical mixer of 1000 pounds capacity. The antibiotics and vitamin premixes were weighed separately and combined before placing them in the mixer.

Each lot of four pigs was placed in concrete pens 5 feet by 20 feet in size and equipped with automatic waterers and "self feeders." About 10 feet of each pen was under roof and about 10 feet of each pen was exposed. The pens were cleaned daily.

All pigs were weighed at the start of the experiment and every fourteen days until the experiment ended. Feed "weigh backs" were taken each time the pigs were weighed. When three pigs in a lot had reached 200 pounds of weight the remaining pig was removed and the lot was concluded.

The data was treated statistically by the method of analysis of variance described by Snedecor (1956).

TABLE I

COMPOSITION OF THE CONTROL RATION

	16 Per cent protein	14 Per cent protein
	Lb.	Lb.
No. 2 yellow corn	731.50	801.50
Soyabean oil meal (44 per cent)	150.00	100.00
Meat and bone meal (50 per cent)	50.00	30.00
Dehydrated alfalfa meal (17 per cent) (100,000 units vitamin A per pound)	50.00	50.00
Dicalcium phosphate	10.00	10.00
Salt	5.00	5.00
Trace minerals premix	2.00	2.00
B vitamin supplement ^a	1.00	1.00
Vitamin B ₁₂ supplement ^b	0.25	0.25
Vitamin D supplement ^c	0.25	0.25
	1000.00	1000.00

^aContained 2 grams Riboflavin, 4 grams Calcium Pantothenate, 9 grams Niacin and 90 grams Choline Chloride per pound.

^bContained 20 milligrams of vitamin B₁₂ per pound.

^cContained 6,803,500 I.U. vitamin D₃ per pound.

CHAPTER IV

RESULTS AND DISCUSSION

The purposes of this experiment were fourfold: 1) To evaluate the effect of a new antibiotic, Oleandomycin. 2) To evaluate the efficiency of a combination of antibiotics. 3) To evaluate the effectiveness of a combination of antibiotics with the inclusion of a sulfa drug, sulfaquinoxaline. 4) To compare the advantages of the above against a control ration and a standard antibiotic, terramycin (oxytetracycline) as growth stimulants for growing-finishing swine.

Under the conditions of this experiment the data for average daily gains did not show any statistical significance between treatments for the entire feeding period or for the period from 46 pounds to 112 pounds of body weight. However, the 10 gram per ton level of oxytetracycline gave a 3.92 per cent increase in average daily gain over the controls, the combination of oleandomycin, streptomycin, penicillin and sulfaquinoxaline gave a 3.27 per cent increase and the combination of streptomycin, penicillin and sulfaquinoxaline gave a 0.65 per cent increase. Oleandomycin gave a decrease of 9.8 per cent in average daily gain as compared to the controls, the combination of oxytetracycline, streptomycin, penicillin and sulfaquinoxaline gave a decrease of 5.88 per cent and the combination of oxytetracycline and oleandomycin gave a decrease of 1.96 per cent. The performance of the individual pigs is given in Table III and the summary is given in Table II.

The feed utilization was generally satisfactory in all groups. There was no statistically significant difference between treatments. The

TABLE II

SUMMARY OF RESULTS OF OLEANDOMYCIN, TERRAMYCIN, AND A COMBINATION
OF PENICILLIN, STREPTOMYCIN AND SULFAQUINOXALINE
FOR GROWING-FINISHING SWINE

Treatment ^a	I	II	III	IV	V	VI	VII
No. of lots per treatment	2	2	2	2	2	2	2
No. of pigs per treatment	8	8	8	8	8	8	8
Average initial weight	47	46	45	46	47	46	47
Average final weight	199.5	201.6	185.6	197.7	196.0	193.3	201.7
Average no. days on experiment	101	99	102	99	100	102	98
Average daily gain, 46 to 112 lb.	1.38	1.34	1.37	1.31	1.24	1.24	1.49
Average daily gain, 46 to 200 lb.	1.53	1.59	1.38	1.54	1.50	1.44	1.58
Per cent change from controls in average daily gain		+3.92	-9.80	+0.65	-1.96	-5.88	+3.27
Average daily feed per pig	4.99	5.04	4.75	5.06	4.98	4.73	4.92
Feed per pound of gain	3.20	3.20	3.46	3.31	3.34	3.27	3.14

^aTreatments are: I, control; II, control plus 10 grams oxytetracycline; III, control plus 3 grams oleandomycin; IV, control plus 12.5 grams sulfaquinoxaline, 5.0 grams penicillin, and 12.5 grams streptomycin; V, control plus 6 grams oxytetracycline, 2 grams oleandomycin; VI, control plus 5 grams oxytetracycline, 6.25 grams sulfaquinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin; and VII, control plus 2 grams oleandomycin, 6.25 grams sulfaquinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin.

TABLE III

PERFORMANCE OF INDIVIDUAL ANIMALS

	Animal no.	Initial weight	Final weight	Weight gain	No. days on treatment	Average daily gain
Treatment I						
Replicate 1	D.M. 32-4	51	192	141	105	1.34
	D.F. 34-4	42	177	135	105	1.29
	H.M. 30-8	38	193	155	105	1.48
	H.F. 32-2	54	202	148	105	1.41
Average		46.25	191.00	144.75	105.00	1.38
Replicate 2	D.M. 26-8	39	208	169	98	1.72
	D.F. 29-2	53	232	179	91	1.97
	H.M. 32-6	43	187	144	98	1.47
	H.F. 28-2	53	205	152	98	1.55
Average		47.00	208.00	161.00	96.25	1.68
Treatment average		46.62	199.50	152.80	100.62	1.53
Treatment II						
Replicate 1	D.M. 26-9	56	230	174	91	1.91
	D.F. 29-1	47	201	154	91	1.69
	H.M. 21-5	41	201	161	105	1.53
	H.F. 30-1	39	190	151	105	1.44
Average		45.75	205.75	160.00	98.00	1.64
Replicate 2	D.M. 32-5	35	192	157	105	1.50
	D.F. 34-1	44	210	166	98	1.69
	H.M. 26-4	53	203	150	91	1.65
	H.F. 24-5	49	185	136	105	1.30
Average		45.25	197.50	127.50	99.75	1.54
Treatment Average		45.50	201.62	143.62	98.87	1.59

PERFORMANCE OF INDIVIDUAL ANIMALS (continued)

	Animal no.	Initial weight	Final weight	Weight gain	No. days on treatment	Average daily gain
Treatment III						
Replicate 1	D.M. 34-7	53	200	147	98	1.50
	D.F. 32-1	34	172	138	105	1.31
	H.M. 30-5	47	196	149	105	1.42
	H.F. 29-7	49	192	143	105	1.36
Average		45.70	190.00	144.25	103.25	1.40
Replicate 2	D.M. 30-5	49	186	137	105	1.30
	D.F. 34-3	32	173	141	105	1.34
	H.M. 24-10	58	201	143	91	1.57
	H.F. 29-5	39	165	126	105	1.20
Average Treatment average		44.50 45.10	181.25 185.62	136.75 140.50	101.75 102.50	1.35 1.38
Treatment IV						
Replicate 1	D.M. 31-8	38	201	163	98	1.66
	D.F. 26-4	42	209	167	98	1.70
	H.F. 20-5	56	204	148	98	1.51
	H.M. 28-5	51	202	151	98	1.54
Average		46.75	204.00	157.25	98.00	1.60
Replicate 2	D.M. 25-8	48	201	153	98	1.56
	D.F. 29-4	35	160	125	105	1.19
	H.M. 31-7	52	203	151	91	1.66
	H.F. 20-1	47	202	155	105	1.48
Average Treatment average		45.50 46.12	191.50 197.75	146.00 151.62	99.75 98.87	1.47 1.54

TABLE III

PERFORMANCE OF INDIVIDUAL ANIMALS (continued)

	Animal no.	Initial weight	Final weight	Weight gain	No. days on treatment	Average daily gain
Treatment V						
Replicate 1	D.M. 34-6	48	200	152	91	1.67
	D.F. 31-9	45	200	155	98	1.58
	H.M. 24-9	49	200	151	98	1.54
	H.F. 31-3	47	171	124	98	1.26
Average		47.25	192.75	145.50	96.25	1.51
Replicate 2	D.M. 34-9	47	183	136	98	1.39
	D.F. 31-3	44	201	157	105	1.50
	H.M. 23-10	46	201	155	105	1.48
	H.F. 24-1	49	212	163	105	1.55
Average Treatment average		46.50 46.87	199.25 196.00	152.75 149.12	103.25 99.75	1.48 1.50
Treatment VI						
Replicate 1	D.M. 32-2	40	182	142	105	1.35
	D.F. 26-1	58	200	142	91	1.56
	H.M. 27-6	47	192	145	105	1.38
	H.F. 32-1	38	165	127	105	1.21
Average		45.75	184.75	139.00	101.50	1.38
Replicate 2	D.M. 31-10	59	204	145	98	1.47
	D.F. 25-4	44	195	151	105	1.43
	H.M. 32-7	36	192	156	105	1.49
	H.F. 31-2	46	217	171	105	1.63
Average Treatment average		46.25 46.00	204.00 194.37	155.75 147.37	103.25 102.37	1.51 1.44

TABLE III

PERFORMANCE OF INDIVIDUAL ANIMALS (continued)

	Animal no.	Initial weight	Final weight	Weight gain	No. days on treatment	Average daily gain
Treatment VII						
Replicate 1	D.M. 26-10	50	207	155	98	1.60
	D.F. 30-4	64	204	140	91	1.54
	H.M. 27-7	34	208	174	105	1.65
	H.F. 32-5	43	190	147	105	1.40
Average		47.75	202.25	154.00	99.75	1.55
Replicate 2	D.M. 23-5	46	210	164	98	1.67
	D.F. 31-2	56	207	151	98	1.54
	H.M. 31-4	46	200	154	91	1.69
	H.F. 30-2	40	188	148	98	1.51
Average		47.00	207.25	154.25	96.25	1.60
Treatment average		47.37	204.75	154.12	93.00	1.58

average daily feed intake per pig was generally uniform for all the lots, averaging 4.63 pounds per day. The feed per pound of body weight gain averaged 3.27 pounds.

Luecke and Hoefer (1958) found that levels of 20 grams of penicillin, 50 grams of streptomycin and 50 grams of sulfaquinoxaline per ton of feed improved the average daily gain. However, they did not get any response from levels of 12.5 grams streptomycin, 5 grams penicillin and 12.5 grams sulfaquinoxaline. In this experiment a 3 gram level of oleandomycin was used while they used 10 grams of oleandomycin per ton of feed. Ten grams of oxytetracycline was used per ton of feed in both experiments. Even at the high levels of antibiotics used in their experiment, Luecke et al. found neither terramycin nor oleandomycin to have any effect on the growth of pigs used in that study.

Jordan et al. (1958) thought that the continuous feeding of antibiotics had probably changed the kind of microorganism which normally inhabit the intestinal tract, resulting in a decrease in antibiotic response. Therefore, a combination of antibiotics would result in a greater response by affecting a larger number of bacteria than a single antibiotic would effect. They used arsonicals, sulfaquinoxaline and antibiotic combinations. One such combination of antibiotics was 3.30 grams of penicillin, 8.38 grams streptomycin and 8.38 grams of sulfaquinoxaline per ton of feed. Pigs fed a combination of penicillin, streptomycin and sulfaquinoxaline from 35 to 177 pounds gained 18 per cent faster than control pigs fed no additives. This data is at variance with those of this experiment. Similarly, a combination of aureomycin, bacitracin, penicillin and terramycin in the feed resulted

in an increase of 9.8 per cent in rate of gain, while pigs fed with a combination of bacitracin and penicillin gained 6.8 per cent more than controls. A combination of aureomycin, bacitracin, penicillin and terramycin gave a 2.7 per cent increase in feed efficiency. All other combinations had little or no effect on feed efficiency.

The data in this experiment with streptomycin, sulfaquinoxaline and penicillin combinations showed that there was no perceptible difference between the controls and the treatment groups. However, the average daily gains of pigs in this study compares very favorably with those obtained at Michigan and Purdue, while the daily feed consumption for the pigs in this study was slightly less than those of the other mentioned studies. Data on the feed utilized per pound of gain were 3.27 pounds of feed per pound of gain in this study, in the Michigan study it was 3.3 pounds, and in the Purdue study 3.4 pounds.

Magruder et al. (1958) working with baby pigs to evaluate the growth promoting effect of oleandomycin, obtained average daily gains of 0.82 to 0.87 pounds with levels of 10, 25 and 50 grams per ton compared to the gains of 0.73 and 0.70 pounds made by the controls. This was a small growth difference (0.09-0.17) in spite of the larger levels of the antibiotics fed than in this study (3 grams). In two additional experiments with doses of 2.5, 5.0 or 10 grams per ton of oleandomycin or oxytetracycline at 50 grams per ton they produced growth increments of 4 to 8 per cent, while a combination of oleandomycin and terramycin at these levels produced growth increments up to 20 per cent. In experiments with growing-finishing swine, their controls averaged 1.32 to 1.66 pounds per day and with the

addition of oleandomycin at 2 to 10 grams per ton they obtained growth responses of just 1 to 6 per cent. The combinations of oleandomycin and terramycin resulted in increases from 4 to 6 per cent. These investigators found the feed efficiency responses to be more variable and of lower magnitude than growth effect. These findings do not agree with those in this study. The literature shows work on feeding trials to evaluate this new antibiotic, oleandomycin on swine, was done by Magruder and associates (1958), and Luecke and Hoefer (1958), while Reynolds et al. (1958) fed oleandomycin to lambs and steers. Luecke and Hoefer at Michigan found oleandomycin had no significant growth effect on pigs as was found in this study.

With respect to the effectiveness of a combination of antibiotics the results obtained are not perceptible. Similarly, the addition of sulfaquinoxaline to a combination of antibiotics has not been encouraging. The combinations of sulfaquinoxaline with oleandomycin, penicillin and streptomycin gave an increase of 3.27 per cent faster growth over controls whereas other combinations of antibiotics, namely, sulfaquinoxaline, penicillin and streptomycin, oxytetracycline and oleandomycin; and oxytetracycline, sulfaquinoxaline and streptomycin failed to provoke an improved growth response. From the studies of Luecke and Hoefer, it would seem the levels of penicillin, streptomycin and sulfaquinoxaline used in this study were too low since they were able to obtain growth responses with this combination of feed additives only with high levels. The response with oxytetracycline, which is an antibiotic commonly used in swine rations, was also very small in this study, resulting in an increase of 3.2 per cent

over the controls. Lastly, the growth rate of pigs fed the control rations seemed to be quite satisfactory as compared to the other treatment groups.

From the data of the results obtained in this study the following are evident: 1) Pigs on the control ration seemed to do as well as the antibiotic treatment groups. 2) Terramycin, generally an effective antibiotic for swine, showed little response. 3) The efficiency of feed utilization was quite satisfactory for all treatments. 4) The growth stimulating effects of combinations of antibiotics and sulfaquinoxaline were not evident.

A review of the literature on antibiotic supplementation in nutrition over the years shows that some research workers have noticed a decreasing difference in the rate of growth in pigs now fed antibiotics and those used as controls. There is a trend of thought that continuous widespread feeding of antibiotics in swine rations has probably modified the kind of microorganisms that normally inhabit the digestive tract or have caused still further internal ecological alterations and that the intestinal microflora have adapted themselves to the changed ecological alterations. As a result of the increase in the modified microorganisms, or the new adaptations of the microflora to the changed ecology brought about by widespread antibiotic feeding, the responses now to antibiotics are not what they were before. In other words, an antibiotic response is less, or is increasingly diminished in a place where antibiotics were in use for a period of time. The converse will also then be true, namely, the response can be high in an area where antibiotics are used for the first time. This situation can be explained in two ways. In one case the continuous feeding of antibiotics to swine

in quarters where pigs are fed and housed can cleanse the premises of all contaminating organisms (as antibiotic effect on microorganism can be as effective in vitro as in vivo) in such a way that there is less and less ingestion of contamination both in controls and antibiotic treated animals. The consequence of this condition is that pigs not fed antibiotics (controls) will manifest a high degree of growth rate, better finish, freedom from skin and other internal and external ailments and would grow as fast as antibiotic treated ones. Obviously, the differences in the rates of growth, finish and uniformity in the two lots will appear less and less palpable. The real position in this test is that both the controls and "antibiotic-fed" groups are growing faster.

The other explanation for less antibiotic response in growth of animals following their long use in an area may be that the modified microflora of the intestinal tract have acquired the ability to tolerate antibiotics. This is not a new concept as situations like this do occur in nature. Field entomologists and workers have observed a high degree of tolerance in mosquitoes and flies to D.D.T. in an area where D.D.T. had been used for some time where previously D.D.T. was lethal. Antibiotic resistance strains of streptococci and staphylococci have been identified. If this was not so, most of the organisms responsible for lowered growth rate, should have been eliminated with the widespread use of antibiotics since 1949. But nature has the subtle ability to overcome biological perils to protect the different forms of life and their continuation.

Again, the degree of response to an antibiotic seems to have a direct relation to the extent of contamination. Bowland (1955) showed that

contamination of quarters in which pigs are fed increases the response to aureomycin. He showed pigs fed aureomycin in quarters previously used by pigs gained at the rate of 1.29 pounds daily as against 0.96 pounds gained by pigs kept in the same premises and fed the same ration without aureomycin. While there was only a 3 per cent increase in weights in pigs fed aureomycin over those not fed the antibiotic when the pigs were quartered in a clean premise not used by pigs previously. The early work of Coates et al. (1951) with chicks to study the mode of action of antibiotics is another work that supports this view. Speers et al. (1950) have reported a short experiment where healthy pigs did not respond to inclusions of aureomycin in the ration.

In general, antibiotics impart their maximum influence under certain stress conditions. Such stress conditions are poor sanitation, poor rations and other similar situations which tend to reduce the vitality of the animals, Bowland (1955) and Carpenter (1951). These conditions are more common on average farms than in experiment stations such as the one in which this study was made. The largest response to antibiotic feeding has been observed on average farms, Braude et al. (1953). In this experiment practically all visible or apparent stress conditions were removed as such and thus the responses obtained to antibiotics fed were perhaps less.

Again, the responses to antibiotic feeding is most perceptible under high disease-level conditions, Carpenter (1951), Carpenter and Larson (1952), and Catron et al. (1950). As this experiment was conducted under very good sanitary conditions, the degree of disease level was far less than what it is under average farm conditions. Perhaps this can also be a reason for

the low antibiotic response in this study. Jones (1959) observed that aureomycin or hygromycin B had no significant effect on rate of gain in his experiments conducted on pigs in the same farms. Differences in average daily gains or feed conversion between treatments or replications within treatments were not significant in the study. Research in the use of antibiotics in animal nutrition has shown that the degree of antibiotic response in swine feeding is influenced by the type of rations fed. When pigs are put on a ration that is well balanced and nutritious they will respond less to antibiotics. Even with good rations the responses seem to vary, depending on the kinds of feed used, Heidebrecht et al. (1951) and Burnside et al. (1949). These factors may have played a part in the good growth rate in the control lots of pigs and satisfactory feed utilization by the pigs in all treatments and in the lack of response from the antibiotics.

According to Carrol and Krider (1956) "pigs that weighed 50 pounds increased their weights to 75 pounds at a feed cost of only 347 pounds of feed for each 100 pounds of gains made, while pigs that weighed 125 pounds increased their weights to 150 pounds on 392 pounds of feed per 100 pounds of gain." The feed consumed for 100 pounds of gain in body weight under all the treatment groups averaged only 320 pounds in this study. In the same token the growth stimulating effects of combinations of antibiotics used in this experiment cannot but be what they were; namely, the effects of these mixed antibiotics and sulfaquinoxaline have been masked by the intrinsic effects of growth resulting from good management, low disease level and balanced rations fortified with vitamins and minerals.

From the results of the treatment with oleandomycin, one inference to be drawn is that its antibiotic growth stimulating effect does not surpass that of a standard antibiotic, terramycin, usually used in swine rations.

CHAPTER V

SUMMARY

In this experiment fifty-six weanling Duroc and Hampshire pigs were allotted to fourteen lots on the basis of weight, sex and breed. Two lots of four pigs each were randomly assigned to each of the following treatments:

1. Control
2. Control plus 10 grams oxytetracycline (terramycin)
3. Control plus 3 grams oleandomycin
4. Control plus 12.5 grams sulfaquinoxaline, 5 grams penicillin, and 12.5 grams streptomycin
5. Control plus 6 grams oxytetracycline, 2 grams oleandomycin
6. Control plus 5 grams oxytetracycline, 6.25 grams sulfaquinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin
7. Control plus 2 grams oleandomycin, 6.25 grams sulfaquinoxaline, 2.5 grams penicillin, and 6.25 grams streptomycin

Under the conditions of this study there was no significant difference between the different treatments in the average daily gains of pigs. However, the combination of oleandomycin, sulfaquinoxaline, penicillin and streptomycin gave a 3.27 per cent faster rate of gain over controls and terramycin gave a 3.9 per cent increase in rate of gain over controls. The feed conversion was generally satisfactory for all treatments. There was no significant difference between the different treatments in the pounds of feed required per pound of gain. Oleandomycin did not show any perceptible growth stimulating activity over control, oxytetracycline or the combination

of antibiotic treatments. The combination of antibiotics with the addition of sulfaquinoxaline did not give a response over oxytetracycline or over the controls in this study.

The pigs on control rations performed as well as the treated animals.

BIBLIOGRAPHY

BIBLIOGRAPHY

- Bird, H. R. 1951. Antibiotic growth stimulants. *Science* 114:3.
- Black, S., J. M. McKibbin, and C. A. Elvehjem. 1941. The use of sulphaguanidine in nutrition experiments. *Proc. Soc. Exper. Biology and Med.* 47:308.
- Bowland, J. P. 1955. Effect of environment on growth and carcass quality of swine fed antibiotic supplement and/or vigofac. *Jour. An. Sci.* 14:1243.
- Braude, R., H. D. Wallace and T. J. Cunha. 1953. Value of antibiotic in the nutrition of swine - a review. *Antibiotic and other supplements. Antibiotic and Chemiotherapy.* 3:271.
- Braude, R., and Conner Johnson. 1953. Effect of aureomycin on nutrition and water metabolism in growing pigs. *Jour. Nutrition.* 49:505.
- Bridges, J. H., I. A. Dyer, and W. C. Burkhardt. 1952. Effect of penicillin and streptomycin on growth rate and bacterial count in feces of pigs. *Jour. An. Sci.* 11:474.
- Briggs, J. E., and W. M. Beeson. 1951. Further studies on the supplementary value of aureomycin, streptomycin and vitamin B₁₂ in a plant protein ration for growing-fattening pigs. *Jour. An. Sci.* 10:820.
- Brown, J. H., and H. G. Luther. 1950. Effect of antibiotics and other growth stimulating substances in the ration of growing and fattening pigs. *Jour. An. Sci.* 9:650.
- Burnside, J. E., T. J. Cunha, A. M. Pearson, R. S. Glasscock, and A. C. Shealy. 1949. Effect of APF supplementation of pigs fed different protein supplements. *Arch. Biochem.* 23:328.
- Carpenter, L. 1951. Effect of antibiotics and vitamin B₁₂ on growth of swine. *Arch. Biochem. and Biophysics.* 32:187.
- Catron, D. V., A. H. Jenson, P. G. Homeyer, H. M. Maddock, and G. C. Ashton. 1952. Re-evaluation of protein requirements of growing fattening swine as influenced by feeding an antibiotic. *Jour. An. Sci.* 11:221.
- Catron, D. V. 1949. Recent developments in swine nutrition. *Vet. Med.* 44:215.
- Carpenter, L. E., and N. L. Larson. 1952. Swine dysentery treatment with four nitro-4 hydroxy phenyl arsonic acid and antibiotic. *Jour. An. Sci.* 11:282.
- Carrol, W. E., and J. L. Krider. 1956. *Swine production.* pp. 241. Second Edition McGraw-Hill Book Company, Inc., N. Y.

- Catron, D. V., A. B. Hoerlein, P. G. Bennett, P. W. Cuff, and P. C. Homeyer. 1950. Effect of vitamin B₁₂, APF, and antibiotic in enteritis in swine. *Jour. An. Sci.* 9:651.
- Coats, M. E., C. D. Dickinson, G. F. Harrison, S. K. Kon, S. H. Cummins, and W. F. J. Cuthbertson. 1951. Mode of action of antibiotics in stimulating growth of chicks. *Nature.* 168:132.
- Cuff, P. S., H. M. Maddock, V. C. Speer, and D. V. Catron. 1950. Rations for slow growing (runt) pigs. *Jour. An. Sci.* 9:653.
- Cunha, T. J., G. B. Meadows, H. W. Edwards, R. F. Sewell, S. B. Shawer, and A. M. Pearson. 1950. Effect of aureomycin and other antibiotics in pigs. *Jour. An. Sci.* 9:662.
- Cunha, T. J., J. E. Burnside, H. M. Edwards, C. B. Meadows, R. H. Benson, A. M. Pearson, and R. S. Glasscock. 1950. Effect of animal protein factor on lowering protein needs of the pig. *Arch. Biochem.* 25:455.
- Cunha, T. J., J. E. Burnside, D. M. Buschman, R. S. Glasscock, A. M. Pearson, and A. L. Shealy. 1949. Effect of vitamin B₁₂ animal protein factor and soil for pig growth. *Arch. Biochem.* 23:324.
- Dinussion, W. E., E. W. Klosterman, E. L. Lasley, G. C. Holm, and M. L. Buchanan. 1951. Cobalt, B₁₂ (APF) and meat scraps for growing fattening swine. *North Dakota Agr. Exp. Bimonthly Bul.* 13:146.
- Elam, J. F., R. C. Jacobs, W. L. Tidwell, L. L. Green, and J. R. Couch. 1953. Possible mechanism involved in the growth-promoting response obtained from antibiotics. *J. Nutr.* 49:307.
- Hansen, L. E., E. F. Ferrin, A. A. Andrews, and W. J. Aunan. 1955. Growth and carcass characteristics of pig fed antibiotic for part or all of the growing fattening period. *Jour. An. Sci.* 14:30.
- Heidebrecht, A. A., O. B. Ross, C. K. Whitehair, and R. W. McVicar. 1951. The value of adding aureomycin to a good ration for growing pigs. *Oklahoma Misc. Pub. No. M.P.* 22:79.
- Jones, A. 1959. The effect of hygromycin B as a growth stimulant and as an anthelmintic for swine. M.S. Thesis, University of Tennessee.
- Jordan, C. E., J. H. Conrad, and W. M. Beeson. 1958. The effect of feed addition on growing finishing swine. *Purdue Swine Day.* Aug. 22.
- Jukes, T. H. 1957. Antibiotics in nutrition - foreword by Welch, H., and Marki-Ibanez. Antibiotic monographs. Medical Encyclopedia. Inc. N. Y.
- Kline, E. A., J. Kastelic, G. C. Ashton, P. S. Homeyer, L. Quinn, and D. V. Catron. 1954. The effect on the growth performance of young pigs by adding Cobalt Vitamin B₁₂ and antibiotic to semi-purified rations. *J. Nutr.* 53:543.

- Konberg, A., F. S. Daft, W. H. Sabrell. 1943. Production and treatment of granulocytopenia and anemia on rats fed sulfonamides in purified diet. *Science* 98:20.
- Larson, N. L., and L. E. Carpenter. 1952. The fecal excretion of aureomycin by pigs. *Arch. Biochem. and Biophysics*. 36:239.
- Light, R. F., L. J. Cracas, and C. T. Oleot and C. N. Fry. 1942. Inhibition of symbiotic synthesis of B. complex factors by sulfonamides. *Jour. Nutr.* 24:427.
- Luckey, T. D., P. R. Moore, C. A. Elvehjem, and E. B. Hart. 1946. The activity of synthetic folic acid in purified ration for the chick. *Science*. 103:682.
- Luecke, R. W., F. Thorpe, H. W. Newland, and H. N. McMillon. 1951 Growth promoting effects of various antibiotics of pigs. *J. An. Sci.* 10:538.
- Luecke, R. W., W. W. McMillon, and F. Thorpe. 1950. The effect of vitamin B₁₂ animal protein factor and streptomycin in the growth of young pigs. *Arch. Biochem.* 26:326.
- Luecke, R. W., and J. A. Hoefer. 1958. Antibiotic and antibiotic-sulfa drug combinations. The annual Michigan swine day. Aug. 14.
- Magruder, W. D., W. C. Sherman, W. M. Reynolds, and H. C. Luther. 1958. A new antibiotic, Oleandomycin in swine ration. *Jour. An. Sci.* 17:1177.
- McKeen. 1952. Antibiotic feed supplement can increase world food supply. *Chem. and Eng. No.* 30:324.
- Moore, P. R., A. Evanson, T. D. McCoy, C. A. Elvehjam, and E. B. Hart. 1946. Use of sulfasuxidine, streptothricin and streptomycin in nutritional studies in the chick. *Jour. Biol. Chem.* 165:437.
- Nutrient requirements of swine. Pub. 295. Natl. Research Council 1953.
- Oldfield, J. E., and O. M. Hale. 1953. A comparison of methods of administration of penicillin to suckling pigs. *Jour. An. Sci.* 11:772.
- Phillips, P. H., and C. Bohstedt. 1954. The influence of crystalline aureomycine and vitamin B₁₂ on the protein utilization of growing fattening swine. *Jour. An. Sci.* 13:184.
- Price, E. A. 1954. Effect of ration containing antibiotics and trace mineral salts on the chemical composition and physical characteristics of pork carcasses. *Jour. An. sci.* 13:338.
- Ricks, E. L., Bink, W. G., F. R. Koniuszy, T. R. Wood, and K. Folkers. 1948. Crystalline vitamin B₁₂ science. 107:396.

- Scorville, O. J. 1956. Medicated feed as an economic factor in livestock industry. Symposium on medicated feeds. Medican Encyclopedia, Inc., N. Y.
- Smith, D. G., H. J. Robinson. 1945. The influence of streptomycin and streptothricin on the intestinal flora of mice. Jour. Bacteriology. 50:613.
- Snedecor, G. W. 1957. Statistical methods. Fifth Edition. Ames, Iowa. Iowa State College Press.
- Stokstad, E. L., and T. H. Jukes. 1950. Further observations on the "animal protein factor." Proc. Soc. Exper. Biol. and Medicine. 73:523.
- Smith, R. H., Ferguson, and V. L. Sanger. 1956. Effect of high levels of aureomycin in the ration of development of immunity following vaccination against hog cholera. Am. Vet. Med. Assoc. Jour. 129:162.
- Speer, V. C., C. E. Combs, G. C. Ashton, and D. V. Catron. 1956. Protein levels with and without an antibiotic for growing finishing swine. Jour. An. Sci. 15:1152.
- Speer, V. C., R. L. Vohs, D. C. Catron, H. M. Maddock, and C. C. Culbertson. 1950. Effect of aureomycin and animal protein factor on health pigs. Arch. of Biochem. 29:454.
- Terril, S. W., D. E. Becker, C. R. Adams, and R. J. Meade. 1954. The response of growing fattening pigs to bacitracin, aureomycin and other supplements. Jour. An. Sci. 11:84.
- Terril, S. W., and J. L. Krider. 1950. A comparison of solvent soybean oil meals and the effect of adding aureomycin dried whey product with whey fermentation solubles and APF, in dry lot rations of weanling pigs. Jour. An. Sci. 9:670.
- Teh-Cheng Hwang and Clive M. McCay. 1953. The effect of terramycin on the growth and body composition of pigs. Jour. Nutr. 50:129.
- Wahelstrom, R. E. 1955. Antibiotics in growing fattening pig rations. South Dakota Agr. Exp. Sta. Bul. 446:1.
- Wallace, H. D., L. T. Albert, W. A. Ney, C. E. Combs, and T. J. Cunha. 1953. Effect of reducing and discontinuing aureomycin supplemental during growing fattening period of pigs fed corn-peanut meal, corn-soybean meal, and corn-cottonseed meal. Jour. An. Sci. 12:316.
- Whitshair, C. K., A. A. Heidelbrecht, and O. B. Ross. 1951. Antibiotic for digestive disturbances. Veterinary Med. 46:81.