GROWTH STIMULATION

A Comparative Evaluation of Several Antibiotics on Chick and Swine Growth

WALTER E. GERARD, DAVID C. READ, and JOSEPH M. PENSACK

Research and Development Department, Commercial Solvents Corp., Terre Haute, Ind.

A series of seven chick feeding experiments was conducted to compare the effectiveness of several antibiotics in stimulating growth under standardized conditions. A swine study was designed to compare, under average farm conditions, the growth and feed conversion values of some of these antibiotics. Bacitracin, erythromycin, *l*-ephenamine penicillin G, and the recently discovered antibiotic *B* stimulated chick growth significantly. Erythromycin, feed supplements containing aureomycin–vitamin B_{12}, and penicillin-bacitracin, stimulated swine growth significantly and lowered the feed costs. A method of evaluating new antibiotics is presented. This method utilizes successive individual chick feeding experiments in which a single antibiotic at several concentrations is compared to a standard antibiotic at a single concentration. On the basis of feed costs in the swine study, all groups fed rations supplemented with antibiotics were more economical to raise than the group fed the control ration. The most economical gain was obtained with the group receiving the lower concentration of the penicillin-bacitracin antibiotic supplement.

THE USE OF ANTIBIOTICS as growth factors in animal nutrition is reported in the literature. In 1946, Moore *et al.* (*8*) noted increased growth when streptomycin was fed to chicks. This report was the first to show the growth stimulating action of an antibiotic. Early in 1950, Stokstad and Jukes (*10*) announced that fermentation products of *Streptomyces aureofaciens* promoted the growth of chicks fed rations adequately supplied with all known nutrients including Vitamin B_{12}. The complete report (*11*) published later concluded that growth responses in chicks on corn-soya type rations were also produced by crystalline aureomycin hydrochloride and to a lesser extent by streptomycin. Numerous experiments by other investigators, such as the one by Whitehill *et al.* (*12*), verified the initial work with chicks.

Matterson and Singsen (*7*) evaluated the chick growth stimulating properties of five antibiotics. In each of five experiments these antibiotics were compared at a concentration of 9 grams per ton of feed. The results at 8 weeks of age indicated that penicillin and bacitracin appeared to act differently from the other antibiotics tested and that bacitracin and penicillin gave the greatest growth responses followed in order by aureomycin, terramycin, and streptomycin. Bentley (*1*) also reported increased growth responses when bacitracin, penicillin, aureomycin, and terramycin were fed to chicks at concentrations of 20 grams of antibiotic per ton of ration. Recent reports, such as the one by Elam *et al.* (*4*), have confirmed the growth responses obtained by feeding antibiotics to chicks.

The early work of Leucke *et al.* (*6*), Jukes *et al.* (*5*), and Carpenter (*3*) indicated that antibiotics stimulated swine growth. A comprehensive review by Braude *et al.* (*2*) citing 111 references evaluated antibiotics in swine nutrition. These reviewers concluded that aureomycin, bacitracin, penicillin, streptomycin, and terramycin produced growth responses in swine. However, these workers found little evidence that combinations of antibiotics were more effective than a single antibiotic.

In this investigation a series of seven chick feeding experiments were conducted to compare the effectiveness of several antibiotics in stimulating growth under standardized conditions. Each study compared the growth stimulating properties of a single antibiotic at several concentrations with a standard antibiotic control at a single concentration.

The swine study was designed to compare, under average farm conditions, the growth and feed conversion values of aureomycin, erythromycin, and a penicillin-bacitracin combination.

Studies on Chicks

Evaluation Procedure Day-old White Rock chicks of both sexes were used in all chick studies. The chicks were placed in electrically heated, thermostatically controlled batteries with raised wire-screen floors. The 20 batteries used in each experiment were located in air-conditioned rooms. All rations tested were fed ad libitum to replicate lots of 20 chicks each for a 30-day test period. At the end of the test period, the chicks were weighed individually, and the resulting data was subjected to statistical treatment by Student's *t* tests according to Snedecor (*9*).

The growth effects of the antibiotic

under evaluation were compared to the growth obtained from two control feeds. One control consisted of a complete chick feed containing no antibiotic and was designated as the basal ration. This ration (Table I) was of the corn-soya type and contained 3 per cent fish meal and added vitamin B_{12}. The standard antibiotic control contained 2 grams of (*l*-*N*-methyl-1,2-diphenyl-2-hydroxyethylamine salt of penicillin G, Compenamine, Commercial Solvents Corp.) per ton of basal ration. The weight difference between the chicks fed the basal ration and those fed the ration containing 2 grams of *l*-ephenamine penicillin G was taken as 100% growth response. The growth obtained from each concentration of the antibiotic being evaluated was compared with this weight difference, and a percentage growth response was calculated for each sex. These data were recorded on a semilogarithmic plot with concentration of antibiotic represented logarithmically on the abscissa and the per cent growth response arithmetically on the ordinate. The resulting curves graphically illustrate the effect of concentration of antibiotic in the feed on the growth rate of chicks.

This comparative evaluation of antibiotics on chick growth differs from earlier published evaluations in that each antibiotic is individually compared to the standard antibiotic control in a separate experiment. In this manner each new antibiotic can be compared under standardized conditions with the other antibiotics previously evaluated. The savings resulting from this method become considerable as additional antibiotics are studied.

Table I. Composition of Basal Ration for Chicks

	Pounds
Ground yellow corn	1201
Solvent soybean oil meal (50% protein)	480
Standard wheat middlings	100
Menhaden fish meal	60
Dehydrated alfalfa meal	50
Steamed bone meal	50
Ground oats	20
Pulverized limestone	20
Iodized salt	10
Choline chloride, 25%	4
Vitamin A & D supp. (4000 A + 750 D units/gram)	2
Riboflavin supp. (BY-21, Commercial Solvents Corp.) 8 mg./lb.	1
dl-Methionine (feed grade)	1
	Grams
Manganese sulfate (feed grade)	227
Vitamin B_{12} supp. (Proferm-6, Commercial Solvents Corp.) 6 mg./lb.	227
Niacin	16
Calcium pantothenate	5

Erythromycin, and antibiotics *A* and *B*, were evaluated in October to December of 1952. The other four antibiotic evaluations were made in January and February of 1953.

Growth Response In the first experiment crystalline *l*-ephenamine penicillin G was fed to triplicate lots of chicks at concentrations of 1, 2, 5, 10, 23, and 50 grams per ton of feed. These antibiotic concentrations were designed to facilitate plotting the results on the semilogarithmic graphs. It will be noted from the data presented (Table II and Figure 1) that the growth produced by all of the feeds supplemented with penicillin was relatively uniform throughout the concentration range and, furthermore, was significantly greater than the growth obtained from the basal ration.

Bacitracin was tested in the second experiment at concentrations of 1,4,14, and 50 grams per ton of ration. Note that the growth response (Figure 2) produced by the feed supplemented with higher concentrations of bacitracin exceeds that produced by the feed containing 2 grams of penicillin per ton.

The data of the third experiment are presented (Table II and Figure 3) for aureomycin fed at concentrations of 1, 7, and 50 grams per ton of feed. Under the conditions of this experiment the feeds

Table II. Antibiotic Growth Response Data from Chicks

Antibiotic Supplement	Added, Grams per Ton	Females: No. of living chicks	Females: Average weight, grams	Females: % Growth response	Males: No. of living chicks	Males: Average weight, grams	Males: % Growth response
None	..	31	291	0	24	316	0
Penicillin[a]	1	26	309	38	16	384[b]	108
Penicillin	2	25	338[b]	100	17	379[b]	100
Penicillin	5	28	322[c]	66	15	382[b]	105
Penicillin	10	19	348[b]	121	12	363[d]	74
Penicillin	23	34	323[d]	68	24	368[b]	83
Penicillin	50	19	319[c]	59	19	356[c]	63
None	..	31	290	0	15	283	0
Penicillin	2	22	320[d]	100	34	341[b]	100
Bacitracin	1	30	278	−41	24	312[c]	50
Bacitracin	4	28	296	23	30	328[d]	77
Bacitracin	14	26	303	42	31	338[b]	96
Bacitracin	50	11	305	49	28	364[b]	139
None	..	34	307	0	26	358	0
Penicillin	2	31	348[b]	100	18	435[b]	100
Aureomycin	1	29	328	52	25	392[c]	45
Aureomycin	7	20	307	−2	29	364	8
Aureomycin	50	25	318	27	31	372	18
None	..	24	311	0	42	370	0
Penicillin	1	24	334	47	27	383	31
Penicillin	2	25	360[b]	100	36	411[b]	100
Terramycin	1	36	314	6	21	384	34
Terramycin	7	18	346	71	15	366	−8
Terramycin	50	24	343[c]	65	31	374	10
None	..	27	266[e]	0	28	276[e]	0
Penicillin	2	36	325[b]	100	34	363[b]	100
Erythromycin[f]	1	35	278	20	29	323[b]	54
Erythromycin	7	33	308[b]	72	39	329[b]	62
Erythromycin	50	38	318[b]	88	37	354[b]	90
None	..	27	313	0	29	343	0
Penicillin	2	18	378[b]	100	30	373[c]	100
Antibiotic *A*	1	29	304	−15	30	331	−38
Antibiotic *A*	3	29	315	3	29	333	−33
Antibiotic *A*	7	27	308	−9	29	339	−11
Antibiotic *A*	19	29	322	14	30	331	−39
Antibiotic *A*	50	19	317	6	20	334	−27
None	..	30	299	0	27	331	0
Penicillin	2	40	325[c]	100	37	350	100
Antibiotic *B*	1	21	318	74	34	336	25
Antibiotic *B*	4	33	308	35	23	349	93
Antibiotic *B*	14	28	310	44	27	350	98
Antibiotic *B*	50	26	337[d]	149	28	367[d]	188

[a] *l*-Ephenamine salt of penicillin G (Compenamine).
[b] $P < 0.001$.
[c] $P < 0.05$.
[d] $P < 0.01$.
[e] A different strain of White Rocks was used for this experiment.
[f] Erythromycin (Ilotycin).

containing the various concentrations of aureomycin generally failed to significantly stimulate growth above the basal ration.

In the fourth experiment terramycin was fed to chicks at concentrations of 1, 7, and 50 grams per ton of feed. It will be noted from the data presented (Table II and Figure 4) that the growth produced by all of the feeds supplemented with various concentrations of terramycin was not significantly greater than the growth produced by the basal ration with the exception of the 50 grams per ton concentration, where significance was observed in the female chick growth.

A sample of crystalline erythromycin (Ilotycin, supplied by the Eli Lilly Research Laboratories) was tested in the fifth experiment at concentrations of 1, 7, and 50 grams per ton of feed. Highly significant growth responses (Figure 5) were obtained in five out of the six sex-treatment groups.

Two relatively pure antibiotics recently discovered in our own laboratories were evaluated in experiments six and seven. They are designated as antibiotics *A* and *B*. Antibiotic *A*, now identified as actithiazic acid (1-4-thiazolidone-2-caproic acid) or Mycobacidin, was fed at concentrations of 1, 3, 7, 19, and 50 grams per ton of ration to triplicate lots of chicks. The data (Table II and Figure 6) indicate that antibiotic *A* does not stimulate growth in chicks.

Antibiotic *B*, a narrow spectrum antibiotic, was fed at concentrations of 1, 4, 14, and 50 grams per ton of feed. The growth obtained (Figure 7) from the feed containing 50 grams of antibiotic *B* per ton was highly significant over the growth produced by feeding the basal ration.

A striking conclusion from a review of the seven growth response curves is the significantly large growth response that resulted from feeding a concentration of 2 grams of *l*-ephenamine penicillin G per ton of complete chick feed. In addition, significantly high chick growth responses were obtained by feeding bacitracin, erythromycin, and antibiotic *B* at high concentrations in the feed.

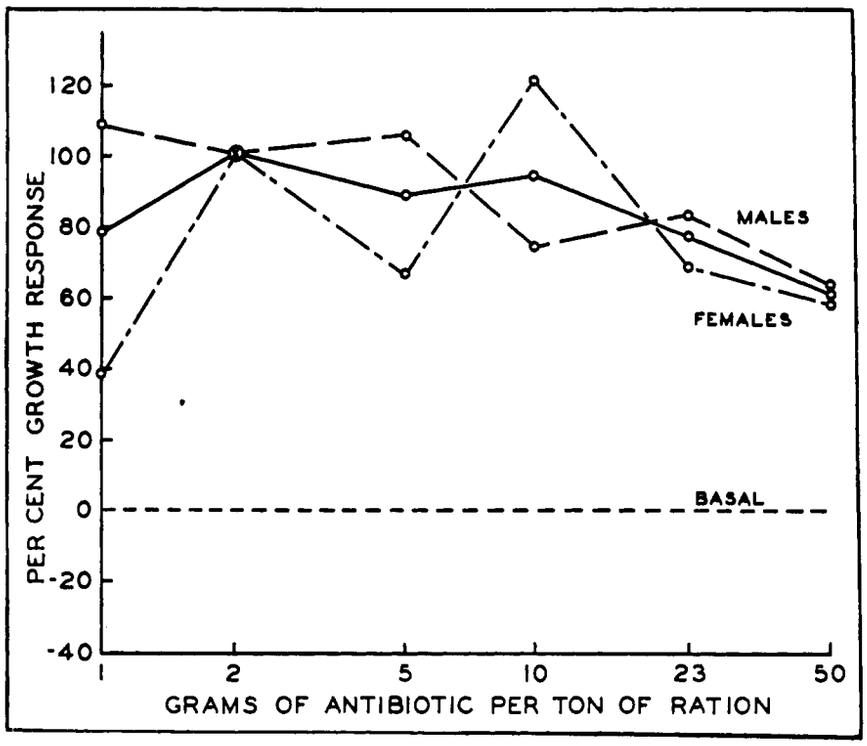

Figure 1. Penicillin growth response curves

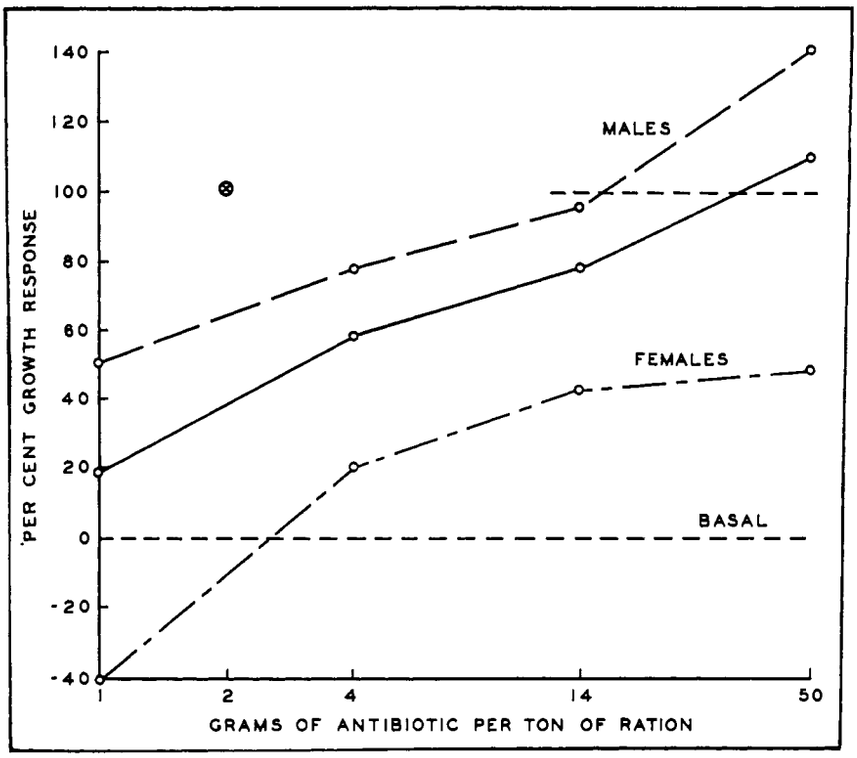

Figure 2. Bacitracin growth response curves

Studies on Swine

Evaluation Procedure In the following investigation two commercial antibiotic feed supplements and one crystalline antibiotic were studied for their growth stimulating, feed conversion, and feed cost values for swine. These materials were crystalline erythromycin, an aureomycin–vitamin B_{12} feed supplement (Aurofac, Lederle Laboratories Div., American Cyanamid Co.) and a penicillin-bacitracin antibiotic feed supplement (Penbac, Commercial Solvents Corp.). The aureomycin–B_{12} feed supplement contained 1.8 grams of aureomycin and 1.8 mg of vitamin B_{12} per pound of supplement. The penicillin-bacitracin combination antibiotic feed supplement contained 1 gram of *l*-ephenamine penicillin G and 5 grams of bacitracin per pound of supplement.

Sixty-five weaned purebred Hampshire pigs of approximately 45-pounds average weight were allotted into five groups on the basis of weight, sex, litter, and general condition. The pigs had previously been weaned from sows which had been fed balanced rations in dry lot. Each lot

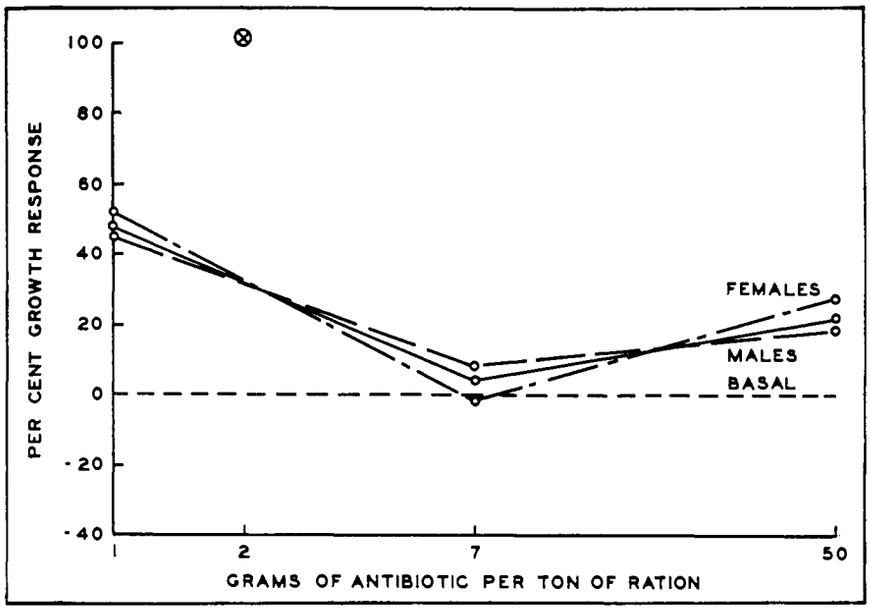

Figure 3. Aureomycin growth response curves

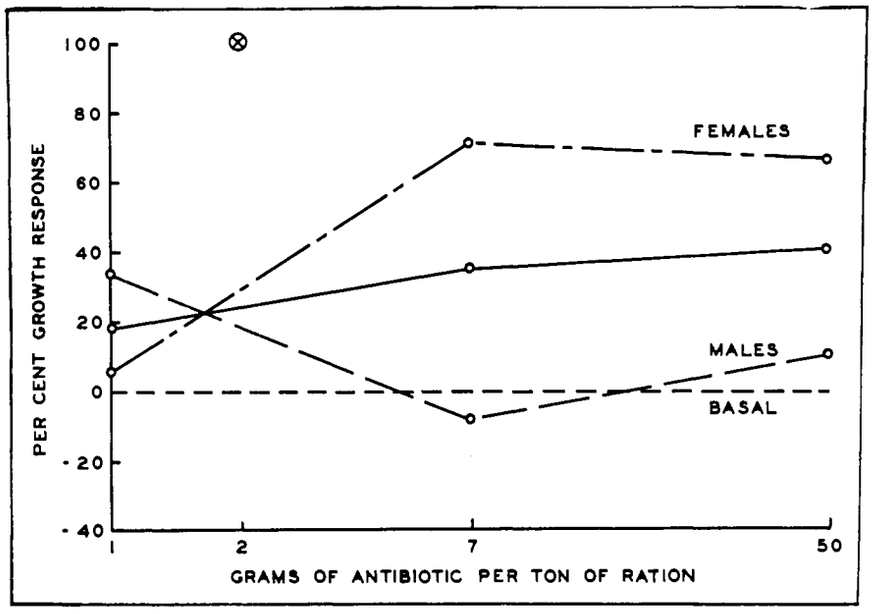

Figure 4. Terramycin growth response curves

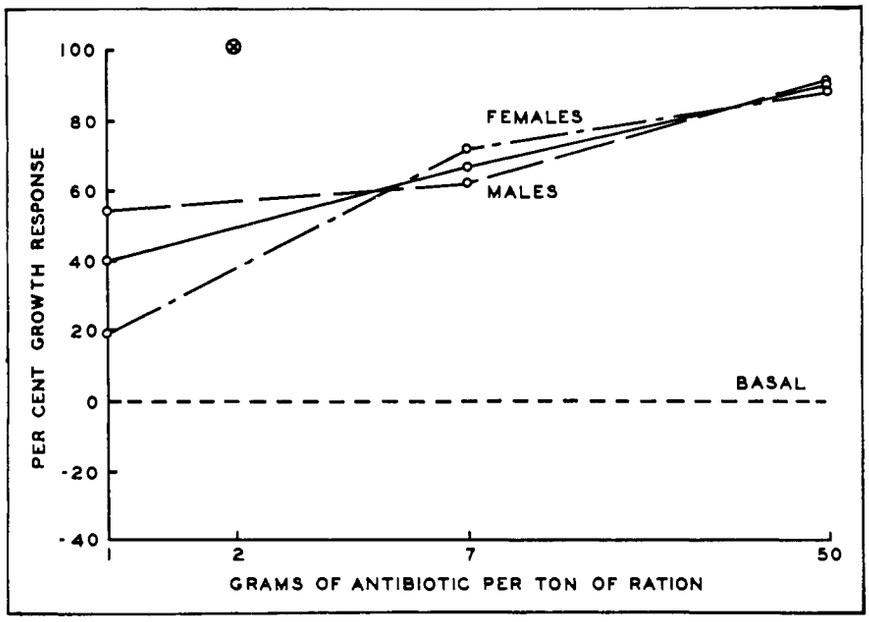

Figure 5. Erythromycin growth response curves

of pigs was placed in a one-half acre Ladino clover pasture which contained adequate housing. A fresh supply of water was maintained. The pigs were self-fed shelled corn and a pelleted protein-vitamin-mineral supplement (Table III). The antibiotics were added to this basal supplement at the following concentrations: erythromycin at 45 grams, aureomycin–vitamin-B_{12} supplement at 25 pounds, and the penicillin-bacitracin supplement at 5 and 10 pounds per ton.

Table III. Composition of Basal Supplement for Swine

	Pounds
Solvent soybean oil meal (44% protein)	1608
Steamed bone meal	140
Pulverized limestone	100
Menhaden fish meal	60
Iodized salt	40
Fish solubles	20
Vitamin A & D supp. (4000 A + 750 D units/gram)	9
Trace mineral mixture	8
Vitamin B_{12} supp. (Proferm-6) 6 mg./lb.	8
Choline chloride, 25%	4
Riboflavin supp. (BY-21) 8 mg./lb.	3
	Grams
Niacin	64
Calcium pantothenate	16

In order to compare the growth responses, all pigs were weighed individually at 101 days on test. At that time the first lot, the penicillin-bacitracin supplemented pigs, had attained an average weight of 200 pounds. To obtain comparable data with respect to feed efficiencies and feed costs the remaining lots were reweighed when the average lot weights were approximately 200 pounds. The growth data (Table IV) were treated statistically by analysis of variance as outlined by Snedecor (*9*).

Results The analysis of growth data indicated a significant difference ($P<0.05$) between the pigs which received antibiotic in their feed and the pigs which received the control ration. The statistical analysis further indicated that the penicillin-bacitracin combination was fully as effective as the single antibiotic treatments.

The feeds supplemented with aureomycin-B_{12}, erythromycin, and penicillin-bacitracin at the concentrations used in this experiment effected a saving of 9 to 12 days (Table V) in producing marketweight hogs. It was noted that the groups receiving the erythromycin consumed less protein supplement and more corn than the other groups. Possibly this antibiotic exerts a greater protein sparing action than the other antibiotics

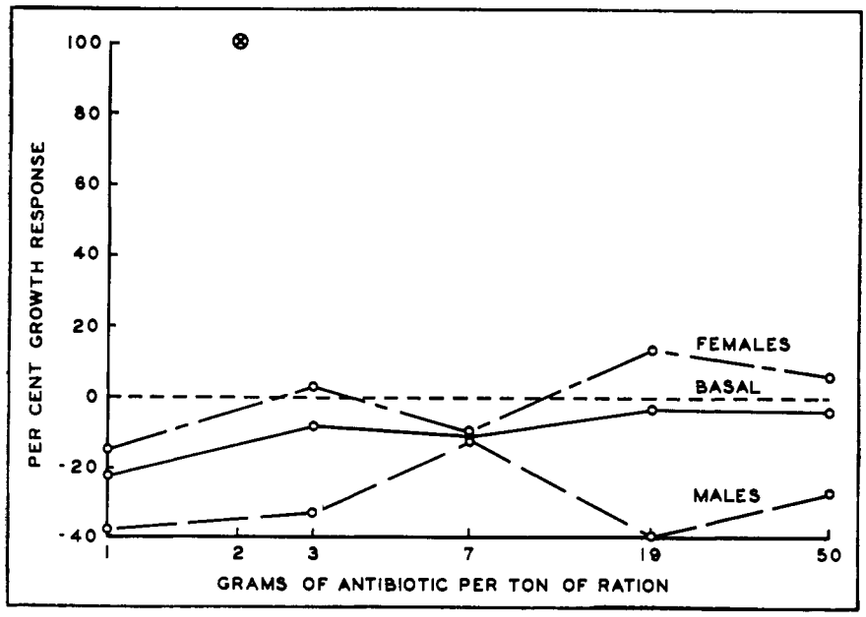

Figure 6. Antibiotic A growth response curves

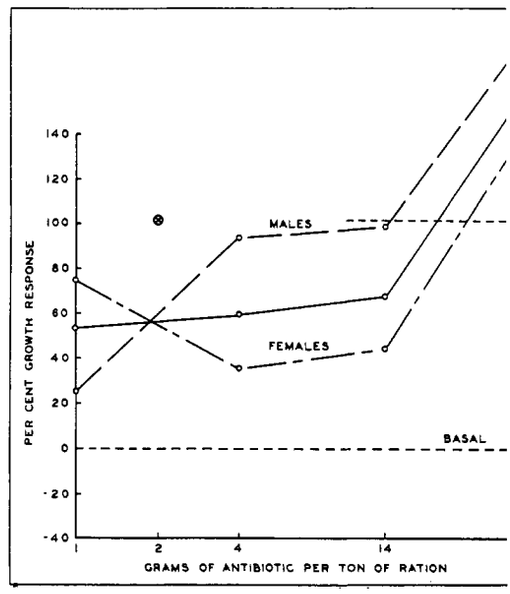

Figure 7. Antibiotic B growth response curves

tested. On the basis of feed costs, all groups fed rations supplemented with antibiotics were more economical to raise than the group fed the ration containing no antibiotic. The most economical gain was obtained with the group receiving the lower concentration of the penicillin-bacitracin combination antibiotic supplement.

Summary

The effectiveness of several antibiotics in stimulating the growth of chicks raised on wire-screen floors and of swine raised under average farm conditions was tested.

A method of evaluating new antibiotics has been presented that utilizes successive individual chick feeding experiments under standardized conditions.

Bacitracin, erythromycin, *l*-ephenamine penicillin G, and the recently discovered antibiotic *B* were found to stimulate chick growth significantly.

Erythromycin, feed supplements containing aureomycin-vitamin B_{12}, and penicillin-bacitracin, at the concentrations under study, stimulated swine growth significantly and lowered the feed cost per hundredweight gain. The most economical gain was obtained with the lower concentration of the penicillin-bacitracin antibiotic feed supplement.

Literature Cited

(1) Bentley, O. G., in "*Proceedings Ohio Animal Nutrition Conference*," pp. 44–9, Columbus, Ohio, 1951.
(2) Braude, R., Wallace, H. D., and Cunha, T. J., *Antibiotics & Chemotherapy*, **3**, 271–91 (1953).
(3) Carpenter, L. E., *Arch. Biochem.*, **27**, 469–71 (1950).
(4) Elam, J. F., Jacobs, R. L., Tidwell, W. L., Gee, L. L., and Couch, J. R., *J. Nutrition*, **49**, 307–17 (1953).
(5) Jukes, T. H., Stokstad, E. L. R., Taylor, P. R., Cunha, T. J., Edwards, H. M., and Meadow, G. B., *Arch. Biochem.*, **26**, 324–5 (1950).
(6) Leucke, R. W., McMillen, W. N., and Thorp, F., Jr., *Ibid.*, **26**, 326–7 (1950).
(7) Matterson, L. D., and Singsen, E. P., *Agr. Exp. Sta. Storrs (Conn.), Bull.*, **275**, 1–18 (1951).
(8) Moore, P. R., Evenson, A., Luckey, T. D., McCoy, E., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, **165**, 437–41 (1946).
(9) Snedecor, G. W., "Statistical Methods," 4th ed., Ames, Iowa, Iowa State College Press, 1950.
(10) Stokstad, E. L. R., and Jukes, T. H., *Abstracts, 117th Meeting, Am. Chem. Soc.* (Philadelphia) p. 12A (1950).
(11) Stokstad, E. L. R., and Jukes, T. H., *Proc. Soc. Exp. Biol. Med.*, **73**, 523–9 (1950).
(12) Whitehill, A. R., Oleson, J. J., and Hutchings, B. L., *Ibid.*, **74**, 11–13 (1950).

Received for review on April 17, 1953. Accepted August 21, 1953. A revision of a paper presented before the Division of Agricultural and Food Chemistry, at the 123rd Meeting of the AMERICAN CHEMICAL SOCIETY, *Los Angeles.*

Table IV. Antibiotic Growth Response by Swine

(101 days on test)

Antibiotic per Ton of Protein Supplement	Initial Average Weights, Lb.	Average Weights at 101 Days, Lb.	Average Daily Gains, Lbs.
None	44.7	178	1.32
Aureomycin–vitamin B_{12} supp., 25 lb.	45.0	194	1.47[a]
Crystalline erythromycin, 45 grams	45.4	196	1.49[a]
Penicillin-bacitracin supp., 5 lb.	44.8	195	1.49[a]
Penicillin-bacitracin supp., 10 lb.	44.8	200	1.53[a]

[a] $P < 0.05$.

Table V. Summary of Feed Efficiency and Cost Data for Swine-Fed Antibiotic Supplements

(200 pounds average weight)

Antibiotic per Ton of Protein Supplement	No. of Days on Test	Feed per Cwt. Gain, Lb.			Feed Cost per Cwt. Gain, Dollars		
		Supp.	Corn	Total	Supp.	Corn	Total
None	113	64	309	373	4.19	8.28	12.47
Aureomycin–vitamin B_{12} supp., 25 lb.	104	57	306	363	3.89	8.21	12.10
Crystalline erythromycin, 45 grams	104	39	334	373	2.76	8.95	11.71
Penicillin-bacitracin supp., 5 lb.	104	50	303	353	3.34	8.12	11.46
Penicillin-bacitracin supp., 10 lb.	101	60	297	357	4.12	7.97	12.09