A. Mechanics of action of antibiotics

An antibiotic is a chemical compound secreted by a living organism which is detrimental to the life of another living organism. These antibiotic compounds may function as follows:

1. Disturbing normal chain of events through which CHONS and other metabolites are absorbed from the environment.

2. Surface activity (Tyrothricin) causing disruption of structural integrity of the cell.

The antibiotic substances commonly employed in livestock feeding experiments exhibit antibiotic action by means of the first method shown.

At the present time, the antibiotics most successfully used in the field of livestock production are: aureomycin, terramycin, and penicillin (poultry). Aureomycin and terramycin are both broad spectrum antibiotics being effective in vitro against many gram + and gram - types of organisms. Penicillin, a narrow band antibiotic, is quite an effective agent against gram + types of organisms. It is in addition very low in its toxicity as compared to the more toxic wide band antibiotics.

Effectiveness in vivo of antibiotics

The bacterial population in the rumen and other portions of the digestive tract are known to have an important function in the digestion of cellulose consumed in large quantities by ruminants and in the synthesis of certain vitamins, notable the B complex group. Therefore, it is imperative that note be taken of the effect antibiotics have on the digestive flora.

Studies of the effect of penicillin on the intestinal microflora in swine (1) showed that there was considerable variation in the number of bacteria present within treatments. Pigs fed penicillin (2.2 mg. per pound of feed) showed a significant increase in coliform organisms. The addition of penicillin to the basal ration resulted in a highly significant correlation between coliform bacteria and rates of gain. No significant correlation existed between rates of gain and either Shigella, Proteus, or Staphylococcus count. It is possible that penicillin retarded the growth of some organisms which normally are antagonistic toward coliform bacteria, or that penicillin might simply retard some organism which normally competes with coliform bacteria for some nutrients (1).

Streptomycin (2.50 mg. per pound of feed) had but little effect on this group. (coliform) However, combinations of penicillin and streptomycin had a stimulating effect on the number of coliform bacteria. The inclusion
of penicillin, streptomycin or a combination of the two had no significant effect on the Staphylococcus genus.

When penicillin and streptomycin were fed singly, the average Proteus counts were 68 and 72 million per gram compared to 37 million for pigs fed the basal ration. However, when combinations fed, there was a highly significant increase in the number of Proteus bacteria. 204 million per gram.

Voelker (2) subjected calves to different treatments. (1) 30 mg. terramycin per 100 lbs. body weight; (2) 100 mg. terramycin per 100 lbs. of body weight; Aurofac 2.5 per cent of the grain ration. He found that there were no significant differences in bacteria population due to antibiotic feeding (as a result of bacteriological studies with colon material.)

The administration to chicks of aureomycin, bacitracin, and terramycin at the rate of 10 grams per ton of feed, and penicillin at the rate of 4 grams per ton of feed showed the following results (4). The administration of penicillin, inactivated penicillin, and combination of penicillin and aureomycin, and bacitracin and penicillin, produced a very significant decrease in total number of fecal clostridia.

In work done on chicks by Romoser, Sharp, and Cowles (5), Aerobacter aerogenes was isolated from chick ceca and found to be resistant to penicillin and aureomycin. Slight but consistent growth responses were obtained when viable organisms were added to the rations with or without the antibiotic.

Kesler (3) found that the addition of terramycin approximately 20 mg. per 100 lb. body weight to young calves showed no consistent differences in thiamin levels in the rumen. The data indicates a higher level of riboflavin. However, the addition of terramycin to the diet of calves 8 - 10 weeks old fed 10, 20, 40 mg. terramycin/100 body weight for three consecutive days showed no elevation in riboflavin. Terramycin then had no adverse effect on rumen synthesis. However, cellulose digestion was lower in the antibiotic supplement calves. This effect seemed to be more pronounced when terramycin was administered by capsule and thereby went directly into the rumen rather than being included in the feed.

The relationship between antibiotics and the level of nutrition has been investigated. Antibiotics (aureomycin and penicillin) were shown to have a greater stimulating action with rations which are well balanced in amino acids than with rations deficient in some amino acid. Antibiotics do not lower the dietary level of protein required by the chick. In order to take full advantage of the growth stimulating properties of antibiotics, it is necessary to provide a diet of high energy and optimum protein content as well as one balanced in amino acids (6).

A broad analysis of the foregoing data on the mode of action seems to be best summed up by Norris (7). According to Norris (7) "The possibility exists that antibiotics restrict the growth of bacteria which destroy essential nutrients or compete with the animal for them, and at the same time promote the development of bacteria which are able to synthesize essential nutrients. Antibiotics may also stimulate these bacteria to produce increased quantities of essential nutrients but evidence of this is lacking." Of course, there is al-
ways the problem of the development of resistant strains of organisms to the antibiotics which have been used, especially if administered in insufficient amounts.

**Antibiotics to ruminants - Calves**

The effect of age on the response of ruminants to antibiotic feeding has been investigated by Perry, Beeson, Hornback, and Mohler (9). Twenty Four mg. aureomycin/ 100 lb. live weight was administered daily by capsule to calves running with dams, creep feeding and pasture available. They found scouring seldom occurred in the group receiving antibiotics. Aureomycin fed calves averaged 14.5 pounds more per calf at 80 days than controls. Aureomycin completely cured all scouring when administered to calves in control lab.

An experiment with calves - birth to 12 weeks old fed 30 mg. terramycin hydrochloride per 100 lb. body weight was conducted by MacKay, Riddell, and Fitzsimmons (10). They noted that calves of all breeds receiving terramycin made greater average daily gains than the control animals. There was no significant difference in feed utilization. They noted that the supplemented calves showed more bloom and increased appetite.

Kesler (3) found that calves fed terramycin showed a greater intake of calf starter at an earlier age and postulates that this has been a contributing factor to increased gains.

Calves started at ages of 6 - 9 weeks were fed an average of 37.5 to 60 mg. terramycin per head per day (10). The calves fed terramycin showed an initial increase over the control calves in growth but at the end of 8 weeks there was little difference noted in rate of gain.

In the experiment by Voelker (2) calves fed 100 mg. terramycin/100 lb. gained 20% more than controls. However, the calves receiving terramycin consumed more feed, and so did not have greater feed efficiency as a result. Voelker (2) reports that no harmful effects were observed in feeding 200 mg. daily of pure aureomycin plus 2.5% aurofac in the grain ration.

**Antibiotics to ruminants - Cattle**

The foregoing data has indicated some definite advantage to supplementing young calves which are not consuming large quantities of roughage with antibiotics. However, its application to older ruminants which are consuming larger quantities of roughage has been a matter of some question with many workers. The following survey of the literature shows some of the more recent findings in this matter.

Perry, Beeson, Hornback, and Mohler (9) fed 540 lb. steers and heifers aureomycin in the supplement. 63.5 mg. per head the first 14 weeks, 127 mg. per head next 6 weeks, and 190.5 mg./head last 6 weeks. The results showed that the calves fed antibiotics gained 1.64 lb./day, controls gaining 1.52 lb./day.

The effect of antibiotic supplement on 713 lb. yearling steers was also investigated (9). Two lots were on a fattening ration and two lots were on a growing ration. Each animal in the antibiotic lot was given 75 mg. aureo-
mycin in the supplement. The steers fed the growing ration (roughages) and receiving aureomycin grew significantly faster than controls. They showed an 18% increase in efficiency of gain. However, of considerable interest is the fact that in the fattening lots, aureomycin did not affect the growth and fattening rate of steers. Both lots fed antibiotics showed a depressed appetite during first week, but regained it rapidly. This seems to be characteristic of ruminants supplemented with antibiotics.

A fourth trial in which increasing levels of aureomycin were administered showed that the gradual addition of aureomycin did not give growth stimulation observed when a level of 75 mg. per steer/day was started.

No benefit was obtained where aureomycin either in crystalline form or as a crude concentrate containing residual Vitamin B<sub>12</sub> was added to a basal fattening diet fed to yearling heifers (8). A rather low level was fed, 2 mg. aureomycin/lb. air dried feed, which could possibly be associated with such small response. The equality of gains of lot receiving Vitamin B<sub>12</sub> suggests that the aureomycin destroyed or reduced B<sub>12</sub> synthesizing organisms.

Bell, Whitehair, and Gallup (11) investigated the effect of .6 mg. of aureomycin/day on the digestibility of the ration of steers. (only 4 animals). Aureomycin produced within 2 - 3 days anorexia and diarrhea. "Aureomycin appeared to decrease the digestibility of dry matter and crude fiber as much as from 15 to 50%. The most pronounced effect was on digestibility of crude fiber which would suggest that aureomycin produced an effect on the cellulytic microorganisms in the G.I. tract. It seems noteworthy here to consider the rather large dosage of antibiotic as compared to the experiment by Neumann at Illinois (8).

In summarizing, the following conclusions seem in order:

The effects of feeding aureomycin and terramycin to young calves have resulted in the following:

1. Lower incidence and severity of scour
2. Increased gain in weight.

The application of antibiotic feeding to older ruminants has shown much variation in effect. This seems to be due in part to extremes in dosage. However, some workers have shown that cattle can tolerate aureomycin and terramycin to certain dosage levels with no ill effects. Antibiotics seem to function best in a growing rather than a fattening ration.

Part II

The Use of Antibiotics on Preservation of Beef Carcasses & Cuts

Weiser, Goldberg, Cahill, Kunkle, and Deatherage (12) infused rounds and whole carcasses from freshly killed cattle with aureomycin solution of physiological saline, in which was suspended .75 g. aureomycin per 30 pounds saline, were forced through the arterial system under pressure immediately after slaugh-
Ten percent of the weight of the round was added. Controls were set up with untreated and beef treated with physiological saline alone.

Carcasses were split, one side remaining at room temperature for 48 hours. The other being chilled out immediately.

No flavor differences were noted from aureomycin infused carcasses or rounds. Infused beef was somewhat more moist. However, decreased volume of infusate and increased antibiotic concentration showed satisfactory results and reduced moisture.

Color improvement was shown on infused sides kept at room temperature.

As would be expected, increased tenderness was noted in cattle held at room temperature 48 hours.

Aureomycin was shown to be less stable in beef tissues than in saline at 3° and 25°C. At 4 days, no aureomycin was detectable in the beef.

Very few organisms were present in infused meat even in sides where refrigeration was delayed. All the infused rounds were sound whereas 7 out of 10 control rounds exhibited some off odor.

There was indication that deep spoilage may arise from organisms present in the lymph nodes.

There was no known adverse effect by individuals consuming the beef.

**Bibliography**


(4) Elam. "Possible mechanism involved in growth promoting response obtained from antibiotics". *Journal of Nutrition* 49:307

(5) Romoser, G. L., Sharb, M. S., Combs, E. F. "Studies and mechanisms of antibiotics in promoting chick growth". *Abstract of papers presented at 41st annual meeting of Poultry Science Assoc. - Univ. of Connecticut


(7) Norris, L. C. "What is known about the function of antibiotics" *Proceedings 1952 Cornell Nutrition Conference for Feed Mfg. New York State College of Agriculture* Nov. 6-7, 1952 pp 82-71


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MR. ADAMS: Thank you, Bob. I am sure we will get around to that during the discussion.

For the next part of our program you will notice we were to have had Shelby T. Grey, Chief, Chicago District, Food and Drug Administration, Department of Health, Education and Welfare. He is out of town and we have his very able assistant with us, Mr. James I. Herring, Assistant Chief of the Chicago District of the Food and Drug Administration. He is delivering a paper prepared by Ralph F. Kneeland, who is Assistant to the Commissioner of the Food and Drug Administration in Washington, D. C. (Applause)

MR. HERRING: Thank you, Mr. Chairman and Members of the Conference.

As Mr. Adams has pointed out, I am just a substitute here today to deliver a prepared paper for you.

I should like to state on behalf of the Food and Drug Administration that we do, indeed, appreciate the opportunity of appearing before you on your program to discuss with you very briefly some very important points with respect to the enforcement of the Federal Food, Drug and Cosmetic Act as it relates to animal feeding problems. It is always a pleasure to appear before groups of this type, and we do especially appreciate the opportunity of appearing before you today on this very important subject.

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