ANTIBIOTICS AS GROWTH STIMULANTS FOR DAIRY CATTLE:
A REVIEW

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The feeding of antibiotics to farm animals has brought about a new era in livestock production. The beneficial effects of adding small quantities of various antibiotics to poultry and swine rations have been well established. The merits of feeding antibiotics to ruminants are still of considerable interest to rumen nutritionists, physiologists, and bacteriologists.

Most of the present interest in antibiotics as supplements to animal feeds was initiated in early 1950 and stemmed from the production of vitamin B₁₂ and the feeding of crude fermentation products as sources of this vitamin (52), although Harned et al. (36) reported in 1948 that Duomycin (aureomycin) did improve the growth rate of chicks. These products were commonly named animal protein factor (A.P.F.) concentrates, and one of the products in general use was the fermentation product of Streptomyces aureofaciens.

Stokstad et al. (117) reported in early 1949 that a fermentation product of Streptomyces aureofaciens produced a growth response in chicks which was greater than the growth response obtained from vitamin B₁₂. Early in 1950, Stokstad and Jukes (116) observed that crystalline aureomycin produced similar results. This observation was confirmed by others working with chicks and pigs (16, 26, 43, 51, 90, 97, 126). Luecke et al. (76) also reported that streptomycin improved the growth rate of young pigs. Since these early reports it has been well established that various antibiotics, namely, aureomycin (chlortetracycline), terramycin (oxytetracycline), penicillin, bacitracin, and streptomycin (dihydrostreptomycin), stimulate the growth rate of monogastric farm animals, such as the chick, turkey, and pig.

The effect of antibiotics on ruminants might be expected to be different from that on simple-stomach animals since ruminants depend basically on bacterial synthesis for proper nutrition. The results of antibiotic feeding to ruminants at first appeared to be contradictory. Workers at the Louisiana (99), Kansas (3), and Cornell (73) stations found that aureomycin promoted growth and possibly helped to eliminate seours in young dairy calves. On the other hand, Bell et al. (10) reported adverse effects from the feeding of aureomycin to beef steers, and Colby et al. (24) found that aureomycin depressed feed consumption and reduced the growth of lambs. Colby et al. (23) also found that these adverse effects could not be overcome by the feeding of various members of the vitamin B-complex group in addition to aureomycin. These workers (22) had found earlier that aureomycin lowered the blood level of vitamin B₁₂ in lambs, thus suggesting an interference with rumen vitamin synthesis. Penicillin and strep-

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1 Orders for reprints of this article at 50 cents each will be accepted by the editor until Dec. 1, 1955.
tomycin were also fed, but these did not cause the severe reactions of aureomycin, although no beneficial effects were observed. Bell et al. (11) found that the feeding of 600 mg. daily of crystalline aureomycin to 620-lb. Hereford steers produced a marked anorexia and diarrhea within 48-72 hours. The level was reduced to 200 mg. daily and was fed without serious reactions to all but two steers, which still reacted to the treatment. The digestibility of dry matter was reduced 60% and the digestibility of crude fiber 45% by aureomycin. Aureomycin also increased the blood levels of urea nitrogen significantly. It was proposed by these workers that aureomycin had a depressing effect on the cellulolytic microorganisms in the gastro-intestinal tract.

With these conflicting reports it became apparent that there was a major difference in the reaction among ruminants to antibiotic treatment. In these early studies the major difference was apparently the result of the varying ages of the experimental animals. Bell et al. (10) used about 600-lb. yearling beef steers, and Colby et al. (22) in one trial used fattening lambs and in another trial used lambs ranging in ages from 4 to 12 weeks and in weight from 7.5 to 68.0 lb. In the latter trial an animal protein factor concentrate containing aureomycin was used rather than crystalline aureomycin. In contrast to these studies, Bartley et al. (3), Loosli and Wallace (73), and Rusoff (99), all working with young dairy calves, observed beneficial effects from the feeding of aureomycin. Since the young calf is essentially a monogastric animal and not a ruminant, it was speculated that these conflicting results depended on whether or not the microflora of the rumen was developed at the time of antibiotic administration.

In this review an attempt will be made to adequately consider all antibiotics in respect to all classes of dairy cattle to the extent of published data. Some unpublished data have been included since their inclusion helped to complete the discussion.

The subject of antibiotics as components of dairy cattle rations will be discussed principally according to class of dairy cattle, namely young calves, growing animals, and mature animals, such as lactating cows, steers, and dairy bulls. Throughout this review the trademark names of the antibiotics will be used rather than the chemical name of these products since the trademark name is the one in general use.

**YOUNG CALVES**

The principal interest concerning antibiotics for young dairy calves has been their effect on (a) growth, (b) calf scours, (c) feed consumption and feed efficiency, and (d) metabolism and the possible mode of action of antibiotics. These various points of interest will be discussed separately insofar as possible, but when it seems advantageous they will be combined with each other.

A. Growth.

1. Various antibiotics. The feeding of antibiotics to farm animals has been a continuation of the interest in the role of vitamin B₁₂ in their nutrition since animal protein factor (A.P.F.) concentrates were used as sources of vitamin
B₁₂ rather than the crystalline vitamin. Because of this some early workers fed various A.P.F. concentrates which contained factors other than vitamin B₁₂, and these later were found to be antibiotics. Unfortunately, in a few reports the source of the A.P.F. was not given; therefore, the antibiotic which it might have contained is not known.

a. Aureomycin. Rusoff and Haq (108) in June, 1950, questioned the feeding value of A.P.F. concentrates in the rations of young dairy calves. The concentrate (Merck & Co., No. 3) used by these workers was added to an all-plant calf starter at a rate sufficient to supply 10 mg. of vitamin B₁₂ per ton. No advantages could be found by including this concentrate in the ration of the calves. The antibiotic content of the A.P.F. was not stated. Williams and Knodt (128, 129) reported similar findings, using two A.P.F. concentrates, one supplied by Merck and Co., and the other by Lederle Laboratories. These supplements were added to milk replacement rations containing 60% milk products. The antibiotic content of these products was not indicated.

In November, 1950, Bartley et al. (3) at the Kansas station reported that an A.P.F. concentrate containing aureomycin stimulated the growth rate of dairy calves from birth to 42 days of age. These calves were fed the equivalent of about 15 mg. daily of aureomycin per 100 lb. of body weight. The growth rate of the aureomycin-fed calves was the same as that of Ragsdale standards (95), but the growth of the control calves was considerably less. The control calves gained 18.0 lb. in 42 days and the A.P.F.-fed calves gained 30.8 lb., or 71.1% faster. The incidence of calf scours was much lower in the aureomycin-fed calves, and these calves also showed more thriftiness and an improved over-all condition. These data caused the authors to conclude that aureomycin enhanced the growth of the calves by preventing scours. Certainly it would appear that the disease problem in this study was great and that aureomycin was beneficial under these conditions. Rusoff (99, 100) reported also in November, 1950, that an A.P.F. concentrate containing aureomycin improved the growth rate of calves. However, the Louisiana worker was using dairy calves which were 14 weeks of age, and some of these calves had previously been fed an A.P.F. concentrate containing vitamin B₁₂. This trial was conducted from the time the calves were 14 weeks of age until they were 34 weeks of age. Aureomycin increased the growth rate of the calves over the control calves 60, 36, and 30% after 2, 4, and 6 weeks of the experiment. After 8 weeks of aureomycin feeding, the response had decreased to 8% and after 20 weeks there was no difference between the two groups of calves. This work indicated that aureomycin did not cause anorexia or diarrhea and apparently had no effect on rumen function of ruminating calves. These results were in contrast to the results of Bell et al. (10) and Colby et al. (24), who indicated that the feeding of antibiotics produced adverse effects.

Also in 1950, Loosli and Wallace (73) reported a growth response in young calves both from an A.P.F. concentrate containing aureomycin and from crystalline aureomycin. Both of these supplements were fed in a milk substitute at the rate of 10.0 g. per ton of the crystalline antibiotic. The control calves gained 0.92 lb. and the antibiotic-fed calves 1.11 lb. daily for the first 8 weeks. As was
reported by the Kansas workers (3), a significant reduction in calf scours was observed from the feeding of aureomycin. This work is of special interest since the A.P.F. concentrate and crystalline aureomycin produced similar growth responses. Seemingly, the growth response from the A.P.F. supplement was due to its aureomycin content rather than to the vitamin B₁₂ which it contained. These workers postulated that the reason Rusoff and Haq (108) and Williams and Knodt (128, 129) had not observed a significant growth response from the A.P.F. concentrates used by them was that a small number of calves was involved in their studies and the product was not fed in the milk; therefore, it was not consumed in large enough quantities early in life. The Cornell workers (73) employed 27 pairs of calves in their study. Although this possibly could have been true, the type of A.P.F. concentrate fed could also have been a factor. In both studies no indication of the antibiotic content of the supplements was given.

In the report of Williams and Knodt it will have to be assumed that consumption of the A.P.F. supplement did occur, since it was fed as a part of the milk replacer ration. The growth responses produced by crystalline aureomycin or aureomycin supplements (Aurofac) in young calves were reconfirmed by various workers within 12 months after the first results were published (9, 48, 75, 85, 88, 103, 105). Rusoff et al. (103, 105) fed both the crude aureomycin supplements and crystalline aureomycin and obtained similar results with both products.

Interest has been shown concerning the effect of the calf's age on the growth response produced by antibiotic feeding. The Louisiana workers (105) observed that aureomycin-fed calves began to gain in weight faster than the control calves at about 5 weeks of age. An improvement in over-all condition was noted from the feeding of aureomycin. These workers also observed a breed difference in the response to aureomycin supplementation. Aureomycin produced a 25% increase in growth in Jersey calves but only an 18% increase in Holstein calves. These differences, however, were not statistically significant. Loosli et al. (75) and Loosli (72) reported the results of antibiotic studies involving 40 pairs of Holstein calves fed a milk replacer ration early in life and hay and calf starter in addition. Half of the calves were fed an aureomycin supplement the first 8 weeks of life. For the first 8 weeks the antibiotic-fed calves gained approximately 22% faster, but growth data to 16 weeks of age indicated that no further growth improvement was made by the aureomycin-fed calves. Murley et al. (88) evaluated aureomycin in the rations of calves fed either a whole milk, hay, and concentrate ration or a reconstituted skim milk, hay, and concentrate ration. A greater growth response was obtained when aureomycin was added to the whole milk ration, 31.9% as compared with 17.2%, but part of this difference probably can be explained by the fact that the whole milk-fed calves not given any antibiotic gained at a slower rate than calves fed reconstituted skim milk and no antibiotic.

Bartley et al. (9) reported an extensive trial comparing two levels of aureomycin supplementation, 3 and 9 g. of an aureomycin supplement per 100 lb. of body weight daily. This trial was conducted from 1 week of age to 22 weeks of age. At the end of the 22nd week the control calves had gained 356%; the
calves fed 3 g. of aureomycin supplement, 410%; and those fed 9 g. of aureomycin supplement, 400% of their initial body weight. Ragsdale growth standards (95) indicated that the calves should have increased in weight 340%. In contrast to the earlier Kansas study (3), the control calves made satisfactory gains in this experiment; thus, by comparison the supplemented calves showed a response to aureomycin when the level of infection was not high. Murdock et al. (85) reported results which showed that aureomycin feeding produced a growth response up to 6 weeks of age but by the time the calves were 12 weeks of age both the controls and the aureomycin-fed calves had made similar gains. Morrison and Deal (84) approached the question of feeding antibiotics to young dairy calves in a slightly different manner than had been done previously. These workers, believing that the first 2 weeks of a calf’s life were the most critical time, attempted to evaluate antibiotics during this period. An aureomycin supplement was fed in the milk for the first 2 weeks after the calf was removed from the dam at 3 days of age. The supplement was fed at the rate of 1% of the dry matter of the milk. The amount of pure aureomycin fed was not noted. The supplement had no effect on the average daily gain to 12 weeks of age, general health, incidence of scours, or feed consumption. No indication was given as to the level of infection that was present; therefore, unless calf scours or other infections were problems, it is doubtful if any advantages of the antibiotic could be expected during this short period of supplementation.

b. Terramycin. Not until the summer of 1951 were there any indications that other antibiotics might be of value in stimulating the growth rate of calves or reducing the incidence of scours. Cason and Voelker (17) fed two levels of a terramycin supplement, to supply 15 and 30 mg. of terramycin per 100 lb. of body weight daily, for the first 8 weeks of the calf’s life. In this study a growth response was obtained, but it was not great enough to be statistically significant. The terramycin supplement did appear, however, to aid in the control of calf scours. The same workers (120) reported three experiments with antibiotics in November of 1951. In Experiment 1, the feeding of 30 mg. of terramycin per 100 lb. of body weight daily increased the growth rate of calves about 21%, which was significantly greater than the growth of the control calves. No indication was given as to the length of the trial. In Experiment 2, calves fed 100 mg. of terramycin daily gained 28% faster than the control calves. Murdock et al. (85) reported that terramycin improved the growth rate of calves from birth to 6 weeks of age, but when terramycin supplementation was discontinued at this age the antibiotic-fed calves grew at a slower rate during the period 6-12 weeks of age than the control calves, resulting in a slight growth depression for terramycin-fed calves over the entire 12-week feeding period.

The information available on the value of terramycin in the rations of calves is not nearly so voluminous as that concerning aureomycin. Several reports (54, 55, 65, 69, 78, 83, 127) in recent years have added much needed information concerning the feeding value of this antibiotic. Kesler and Knodt (55) fed Holstein calves a milk replacement ration supplemented with 20 mg. of terramycin per 100 lb. of body weight daily. This ration was fed for 8 weeks, at which
time one-half of the control calves were fed terramycin, and terramycin feeding was discontinued on one-half of the terramycin-fed calves. The calves fed terramycin were 22.7% heavier at 8 weeks than the control calves but their gains were about equal to those of a third group fed whole milk. Cessation or initiation of terramycin feeding at 8 weeks of age had very little effect on growth, thus showing that the maximum growth response was obtained by the time calves were 8 weeks old.

In a later report, which apparently included some of the data previously reported (54), the statement was made that terramycin improved the growth rate of the calves up to 8 weeks of age but not to 16 weeks of age. It was also stated in the later report that starting terramycin feeding at 7 weeks of age reduced the growth rate of the calves. In a second trial calves were fed a milk replacement ration containing 2 g. of crystalline terramycin per 100 lb. of milk replacement. Terramycin was fed for only 7 weeks, although the trial was 12 weeks in length. In this study terramycin stimulated the growth rate of calves, as measured by both weight gain and increase in height at withers.

MacKay et al. (78) reported that a terramycin supplement improved the growth rate of Holstein, Ayrshire, Guernsey, and Jersey calves over the growth rate of control calves. Since several breeds were involved and it was difficult to balance both groups in respect to breeds, the increase in growth rate was compared to Ragsdale standards (95). The control calves gained 13.6% and the terramycin calves 20.2% faster than Ragsdale standards. The length of the trial was from birth to 12 weeks of age, and terramycin was fed at the rate of 30 mg. per 100 lb. of body weight daily. The calves consumed from 19 to 82 mg. of terramycin daily. The antibiotic-fed calves appeared to be in better condition than the calves not fed terramycin, and the feces of the terramycin calves were firmer than those of the control calves.

Moody et al. (83) reported that terramycin stimulated the growth rate of female calves more than that of male calves and found no evidence that small calves responded more to terramycin supplementation than did the larger calves. Lassiter et al. (69) found that crystalline terramycin did not improve the growth rate of Holstein and Jersey calves fed a limited amount of milk and an all-plant starter, whereas a terramycin supplement had stimulated the growth rate of calves 12% in a previous trial (65) when a similar system of feeding had been employed. A slight beneficial effect on calf scours was noted from the feeding of crystalline terramycin. Williams and Jenson (127) observed no improvement in the growth of calves when terramycin was included in a milk replacement feed.

c. Penicillin. The third antibiotic to receive consideration was penicillin. Because it has proven to be of considerable value in stimulating the growth rate of chicks and, to some extent, swine, it might be expected to perform similarly in the rations of young dairy calves. The results to date are very much to the contrary. Bloom and Knodt (12) and Knodt and Bloom (58) reported that potassium penicillin when fed at the rate of 10 p.p.m. in a milk replacement feed significantly lowered the gains of Holstein calves. Some deaths were recorded, and penicillin lowered the consumption of starter considerably. The
Pennsylvania workers (60) later reported results of feeding both potassium and procaine penicillin in a milk replacement feeding program. Potassium penicillin was fed at a level of 0.5 g. per 100 lb. of milk replacement feed. Procaine penicillin was fed at the levels of 0.1 g., 0.3 g., 0.9 g., and 2.7 g. per 100 lb. of milk replacer. All levels of procaine penicillin and the one level of potassium penicillin reduced the average daily gains of the calves, as compared with the control calves, from birth to either 8 or 12 weeks of age. All levels of procaine penicillin with the exception of the 0.3 g. level produced improved gains over those of calves receiving the 0.5 g. level of potassium penicillin. In this study there did not appear to be a depression in feed consumption, as was observed in the earlier studies (12, 58). The incidence of scours was high among calves of all groups but was about twice as severe in penicillin-fed calves as in calves not fed penicillin. Penicillin appeared to increase the incidence of scours rather than to reduce it, as had been shown to be true of aureomycin and, possibly, of terramycin. Gardner et al. (32) fed veal calves procaine penicillin at the rate of 15 mg. per pound of milk up to 56 days of age. Under these conditions penicillin had no effect on the growth rate of the calves. Voelker and Jacobson (121) fed procaine penicillin G to calves from 4 to 88 days of age on a whole milk replacement diet. The calves fed penicillin gained only 86% as much as the control calves and consumed slightly less concentrates. The calves were fed penicillin at the rate of 40 mg. daily for the first 60 days and 80 mg. daily from the 61st to the 88th day of life. Hibbs et al. (41) found that procaine penicillin did not improve significantly the growth rate of calves fed a hay to grain ratio of 3:2, although a slight improvement in growth was observed.

In contrast to these studies, Ilogue et al. (44) reported favorable results from the feeding of a mixture of bacitracin and penicillin (4:1), and Kon et al. (62) reported similar results with procaine penicillin. In the Cornell study (44) the mixture of bacitracin and penicillin significantly increased the growth rate of calves for the first 7 weeks (18%) and decreased the days of abnormal feces. However, at 16 weeks of age there was no difference between the calves fed the antibiotic and the control calves as far as weight gain was concerned. It is of interest to note that the bacitracin-penicillin fed calves consumed less starter than the control calves. This is in agreement with the results of Bloom and Knodt (12). Although in the Cornell studies a group of calves fed only penicillin was not included, the reduction in starter consumption by the bacitracin-penicillin calves was probably due to the presence in the mixture. Kon et al. conducted two experiments with procaine penicillin with calves from birth to 12 weeks of age. Penicillin was fed at the level of 80 mg. per calf daily. In Experiment 1 the control calves gained 1.04 lb. daily, whereas the penicillin-fed calves gained 1.25 lb. daily. In the second experiment a slight increase in growth was obtained, but it was not nearly so great as in the first experiment, the control calves gaining 1.30 lb. and the calves fed penicillin 1.40 lb. daily. These growth differences were not statistically significant. Aureomycin was used in a third experiment, and both aureomycin and penicillin caused a marked reduction in the incidence of calf scours. These English workers
also observed a greater growth response from the feeding of antibiotics to calves born during the fall months than with calves born during the spring months. It was believed that this observation could be related to the seasonal incidence of infection, which was believed to be highest during the fall months.

It is difficult to explain the conflicting reports in the literature concerning the feeding of penicillin to young dairy calves. Kon et al. (62) fed 80 mg. of penicillin per calf daily, whereas Knodt and Ross (60) fed from 0.2 to 19 mg. daily, depending upon the age of the calf, the level of penicillin fed, and the amount of milk replacement fed, since the penicillin was included in the milk substitute at various levels. This shows that actually Kon et al. fed penicillin at a higher level than Knodt and Ross. It is difficult to understand how a lower level of penicillin would cause a growth depression and a higher level of the same antibiotic would produce a growth stimulation. Such factors as climate, environmental conditions, feeding programs, level of infection present, and the location of the two experiments must be considered in the interpretation of these data. Voelker and Jacobson (121) fed 40-80 mg. daily and Hibbs et al. (41) fed 0.9 mg. of penicillin per calf daily for the first 7 weeks and 1.0 mg. per pound of feed the remainder of the trial.

d. Other antibiotics. Available data on the value of other antibiotics in the rations of young dairy calves are extremely limited. Hogue et al. (44) fed streptomycin at levels of 10, 20, and 40 mg. per 100 lb. of body weight daily up to 7 weeks of age. The control calves gained 0.78 lb. daily, whereas the streptomycin-fed calves gained 0.92 lb. daily, or about 18% faster. The trial was conducted for 16 weeks, and at the end of this period the average daily gain over the entire period was the same for both groups. The aureomycin-fed calves gained 1.00 lb. daily, or 28% faster, than the control calves. All antibiotics significantly increased daily gain and heart girth and decreased the days of abnormal feces up to 7 weeks of age. Rusoff et al. (111) reported on the effect of soluble streptomycin on the growth of young dairy calves. Streptomycin was fed at levels of 30 and 50 mg. per calf daily to 12 weeks of age. The 50-mg. level improved the growth rate of the calves 15%, but the 30-mg. level failed to have any effect on average daily gain. During the first 8 weeks the 50-mg. streptomycin-fed calves had very loose feces and long, rough haircoats. Results were presented which indicated that streptomycin stimulated the growth of the calves mostly after 8 weeks of age. Owen and Allen (92) fed calves a whey product milk replacement feed from 4 to 88 days of life and supplemented this ration with terramycin, bacitracin, chloromycetin, or arsenic acid. Terramycin stimulated daily gain 33%, bacitracin 24%, and chloromycetin only 10%. All antibiotic-fed calves increased faster in height at the withers, but not in chest and barrel circumference, than the control calves. Rusoff and Davis (104) found that neither tyrothricin nor bacitracin stimulated the growth of calves. Ellsworth et al. (30) observed that aureomycin improved the growth rate of calves 23% and bacitracin improved the growth rate 14% from 3 days to 100 days of age. These calves were fed considerable quantities of either whole milk or reconstituted skim milk. The growth of the control calves was 24% greater than Ragsdale standards.
By 1952 it had been established that various antibiotics, particularly aureomycin, and probably terramycin, did stimulate the growth rate of calves early in life. Since that time, studies which added more information as to the value of antibiotics in the rations of calves under varied feeding conditions were reported by MacKay et al. (77), Lassiter et al. (64), Voelker and Jacobson (121), Murley and Pou (89), and King and O’Dell (57). In the study by Murley and Pou aureomycin did not improve the growth rate of the calves. Considerable interest has been manifested as to the factors which might influence the response obtained from the feeding of antibiotics to calves.

2. Effective antibiotic level. One of the most important questions concerning the feeding of antibiotics to dairy calves is the amount of antibiotic which must be fed to obtain a maximum growth response and to have a significant effect on the incidence of scours. Information of this nature is extremely difficult to interpret because the methods of feeding antibiotics have not been consistent. Only data on the oral administration of antibiotics will be discussed at this point because this method appears to be the only practical means of administration. Also, in most cases only data on the value of various levels of antibiotics obtained in the same experiment have been included in order to avoid the effect of different feeding regimes and other uncontrollable factors.

As previously mentioned, Bartley et al. (9) fed 3 and 9 g. of an aureomycin supplement per 100 lb. of body weight daily. The amount of pure aureomycin fed is not known, but both levels produced similar improvements in growth. In a later study, these workers (2) fed calves 15 and 45 mg. of aureomycin per 100 lb. of body weight daily from birth to 25 weeks of age. The 45-mg. level was more effective in controlling scours and colds and stimulated growth more than the 15-mg. level. The control calves gained 291% of their initial body weight; the 15-mg. fed calves, 314%; and the 45-mg. level calves, 349%. Evidence was presented which indicated that the higher level of antibiotic feeding reduced the difference between sexes in the growth response to the antibiotic. Another interesting observation was that Holstein calves responded to the 45-mg. level as measured by increased growth rate only up to 10 weeks of age, whereas Holstein calves fed the 15-mg. level responded from birth to 25 weeks of age. Jersey calves responded to both levels from birth to 25 weeks of age. When the growth data of Holstein calves fed 45 mg. of aureomycin per 100 lb. of body weight was considered from birth to 25 weeks of age, a significant response from the antibiotic was not observed, although a significant growth response was obtained through the first 10 weeks of the trial. The greatest response from aureomycin feeding was obtained during the first 5 weeks and during the 22-25 week period. No explanation was given for the stimulation in growth during the latter period. In a third study (7), the Kansas workers fed 45 mg. and 90 mg. of crystalline aureomycin daily from birth to 25 weeks of age. Both aureomycin treatments reduced the incidence of infections. The 45-mg. level produced significantly greater gains than the 90-mg. level up to 12 weeks of age. Based on the results of this experiment, these workers proposed that the optimum level of aureomycin feeding should be 45 mg. per 100 lb. of body weight daily for the first 12 weeks and 15 mg.
from 13 to 25 weeks of age. Pritchard et al. (93) found no advantage of feeding 60 mg. per 100 lb. of body weight over 15 mg. of terramycin daily. Both levels stimulated the growth of calves slightly over that of the control calves, but this increase was not statistically significant. These workers, however, made a significant observation on the continuation of feeding antibiotics in a dairy herd: The percentage response from the feeding of antibiotics over the growth of the control calves had reduced over a 3-year period. The lack of growth response was not due to poorer growth of antibiotic-fed calves but to improved growth of control calves with each succeeding year. This can probably be explained by the fact that the level of infection of the housing facilities was reduced over the 3-year period by the continued feeding of antibiotics. This supports the initial work of Bartley et al. (3), in which a 70% growth response was obtained from the feeding of aureomycin. This extremely high percentage growth response from aureomycin feeding was probably due to the high incidence of calf scours, which resulted in below normal growth of the control calves. Hogue et al. (44) reported the results of studies involving the feeding of aureomycin, streptomycin, and a mixture of bacitracin and penicillin (4:1) at levels of 10, 20, and 40 mg. per 100 lb. of body weight daily. No advantage was observed for any particular level of feeding. All levels of each antibiotic improved growth up to 7 weeks of age. These authors concluded there were no advantages of feeding antibiotics to calves past 7 weeks of age.

Mochrie et al. (82) studied the value of various levels of aureomycin in a calf starter upon the growth rate of calves. An aureomycin supplement was fed at levels equivalent to 9, 18, 36, and 54 mg. of aureomycin per pound of starter. Half of the calves were housed in a temperature-controlled barn and the other half in a barn with uncontrolled temperature. The length of the trial was from 2 to 119 days of age of the test animals. Aureomycin at all levels increased daily gain, height at withers, heart girth, and girth of paunch, but these increases in growth were not statistically significant. There was very little difference between the growth rate of the calves fed the various antibiotic levels. Although it was not pronounced, the data indicated that aureomycin stimulated the growth rate of the calves housed in the unheated barn more than that of the calves in the heated barn. Apparently this fact was not related to the level of infection under the two systems of housing because none of the levels of aureomycin had a significant effect on the incidence of scours.

Pennsylvania workers (13, 14, 59, 61) have conducted a series of trials testing various levels of aureomycin in milk replacement feeds. Knodt and Ross (59) fed levels of 0, 2, 4, 6, and 10 g. of aureomycin per 100 lb. of milk replacement. All levels of aureomycin improved the growth rate of the calves at 8 and 12 weeks of age, although the stimulation from the 6-g. level was very slight. It was not stated but is assumed that aureomycin was fed for only the first 8 weeks. The 2-g. level of aureomycin per 100 lb. of milk replacement improved growth more than any other level at 8 weeks of age and was a close second over the 12-week period. Based on these data, it appears that 2 g. of aureomycin per 100 lb. of milk replacer was adequate to produce a maximum growth response.
Bloom and Knodt (13) in a later trial fed 0.5 g., 1.0 g., and 2.0 g. of aureomycin per 100 lb. of milk replacement in both the pure and supplement form. In this study the greatest growth stimulation was obtained during the first 4 weeks of the trial. A growth response was produced by all levels of aureomycin feeding from both the crystalline and the crude form of aureomycin. When the calves were 8 weeks of age, the greatest response was obtained from the feeding of 1.0 g. of aureomycin in the pure form and 0.5 g. and 1.00 g. of aureomycin in the crude form. However, at 12 weeks there was no difference between the levels of aureomycin feeding in the crude form, but the 1.0 g. level produced the greatest growth response when aureomycin was fed in the crystalline form. As can be seen from these data, there appears to be no consistent relationship between the levels of aureomycin fed and the growth response obtained. Knodt et al. (61) reported similar results from the feeding of 2, 6, and 10 g. of aureomycin per 100 lb. of milk replacement supplied by an aureomycin supplement. All levels of aureomycin stimulated the growth rate of the calves over the control calves, but there was no significant difference between the various levels of aureomycin.

The Pennsylvania workers fed aureomycin at various levels of a milk replacement ration. In all other studies with one exception (82) the antibiotic was fed so that each calf received a given amount daily or at a certain level per 100 lb. of body weight daily. Mochrie et al. (82) fed aureomycin at various levels in a calf starter. Since the basis for the feeding of aureomycin has varied, an attempt will be made to correlate the data of the Pennsylvania workers with other available data on the optimum level of antibiotic that should be fed. Since in the Pennsylvania work the amount of antibiotic consumed daily varied with the age of the calf, according to the milk replacement feeding program, the amount of antibiotic fed at various ages will be calculated. Usually, the amount of milk replacement fed was 0.4 lb. for the first 10 days, 1.0 lb. from the 11th to the 28th day, 1.2 lb. from the 29th to the 42nd day, and 1.4 lb. from the 43rd to the 49th day (61). This means that calves fed the antibiotic at the rate of 1.0 g. per 100 lb. of milk replacer received 4 mg. daily for the first 10 days, 10 mg. daily for the 11th-28th day, 12 mg. daily for the 29th-42nd day, and 14 mg. daily for the 43rd-49th day. When Bloom and Knodt (13) fed 0.5 g. of aureomycin per 100 lb. of milk replacement, the calves received only 2 to 7 mg. of aureomycin daily over the 7-week trial. In their study when this amount of aureomycin was supplied by crystalline aureomycin a satisfactory growth response was not obtained, but the same amount from a crude supplement did produce a significant growth response.

In studies by the Pennsylvania workers (13, 59, 61) a satisfactory growth response was obtained when aureomycin was included in the ration at the rate of 2.0 g. of aureomycin per 100 lb. of ration. The calves fed this level consumed from 8 to 28 mg. of aureomycin daily. When this level of antibiotic feeding was converted to an amount of antibiotic per 100 lb. of body weight, estimated values were used since the weights of the calves are not known for any particular age. However, if it is assumed that the Holstein calves weighed 90 lb. at less than 10 days of age and 160 lb. at 7 weeks of age, the calves received about 9 mg. of
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Aureomycin per 100 lb. of body weight daily during the period from birth to 10 days of age and 18 mg. per 100 lb. of body weight daily during the period from the 43rd to the 49th day. These values agree closely with the results of Hogue et al. (44), which showed that the feeding of 10 mg. per 100 lb. of body weight daily stimulated growth as much as 40 mg. per 100 lb. of body weight. Pritchard et al. (93) found that the feeding of 15 and 60 mg. of antibiotic per 100 lb. of body weight daily stimulated growth similarly. Bartley et al. (2), however, found that 15 mg. did not produce the same growth response as that obtained by the feeding of 45 mg. of aureomycin per 100 lb. of body weight. In a later study 45 mg. was as effective as 90 mg. per 100 lb. of body weight as a growth stimulant. Mochrie et al. (82) found that 9 mg. of aureomycin per pound of starter possessed the same growth-promoting properties as 54 mg. Based on these studies, it appears that the minimum effective level of aureomycin, and probably of terramycin, for feeding young dairy calves is approximately 15-20 mg. of antibiotic per 100 lb. of body weight daily. This conclusion does not agree with the observations of Warner (123), who stated that the optimum level of aureomycin feeding was about 30 mg. per calf daily, but it should be remembered that at the time Warner established this level of aureomycin feeding, much of the data used by the present author was not available. It should be pointed out, however, that a slightly higher level than 15-20 mg. per 100 lb. of body weight probably should be used by farmers to combat high level infections that might exist on some farms. Present data indicate that milk replacement feeds should contain about 20 mg. of antibiotic per pound of feed.

The previous discussion applies only to aureomycin and terramycin. Data available at the present time on other antibiotics are not sufficient to draw valid conclusions as to proper levels of supplementation. It is very difficult to establish a satisfactory value for the amount of antibiotic that should be included in calf starters. This is true because the consumption of starter by the calf early in life is small and variable. The work of Mochrie et al. (82) indicated that 9 mg. of aureomycin per pound of starter produced a maximum growth response, but apparently in this study calf scour was not a problem. It is possible that an added growth response would have been obtained from the feeding of aureomycin if the antibiotic had been included in the milk as well as in the calf starter. At the present time it seems that these antibiotics should be included in calf starters at levels of 10 to 20 mg. per pound of starter.

3. Method of administration. Several research workers have been interested in the effect that the method of administration of an antibiotic might have on the growth response produced. Rusoff et al. (106) studied this problem by supplementing the rations of one group of calves with aureomycin in the milk and the calf starter and giving a second group of calves weekly intramuscular injections of 400 mg. of aureomycin. In this study orally administered aureomycin increased the average daily gain of the calves 24%, whereas the injected aureomycin improved the growth rate only 15% over that of the control calves. The injected calves showed an improvement in condition over the control calves at 9-10 weeks of age, but the orally fed calves did not show this improvement in
condition until 12-16 weeks of age. It was also found that the injection of aureomycin caused a significant increase in the fat content of the 12th rib and that oral administration caused some increase in fat percentage, but to a lesser extent. In a later study with aureomycin the same workers (107) found that injections increased the growth rate of calves 30% and oral feeding 20%. Although these results were contrary to their earlier report, it should be pointed out that the difference between the growth rates of the aureomycin groups was not statistically significant in this study. Richardson et al. (98) found that daily or weekly oral feeding of aureomycin was about equally effective in stimulating the growth rate of calves over that of the controls, but this was not true of weekly subcutaneous implantations or weekly intramuscular injections of aureomycin. Bartley et al. (8) observed that aureomycin given as one weekly intramuscular injection (125 mg.) was not so effective in improving the growth rate of the calves as daily oral administration (45 mg. daily). Based on these reports, it appears that oral administration of antibiotics is as effective, if not more so, than other methods of administration.

Bloom and Knodt (14) and Bartley et al. (8) studied various methods of oral feeding of aureomycin. Bloom and Knodt attempted to determine whether the antibiotic should be placed in a milk replacement and the calf starter, the milk replacement only, the calf starter only, or various combinations of these two. The results of this study indicate that it is not necessary to include the antibiotic in the milk replacement feed if the calf starter contains adequate amounts of the antibiotic and if the starter is consumed in adequate amounts. It should be mentioned that the calves in this experiment consumed about 2 lb. of starter daily from birth to 8 weeks of age, which would be considered very good consumption of feed by calves of this age group. It is possible that this amount of starter may not be consumed by calves under farm conditions and, therefore, if a milk replacement is fed it would probably be advantageous to include an antibiotic in this feed.

Bartley et al. (8) were interested in the same problem. In a study with calves from birth to 8 weeks of age these workers found that the control calves gained 176% of the starting weight; calves fed 1% of an aureomycin supplement (Aurofac 2A) in a calf starter, 185%; calves fed 45 mg. of aureomycin daily by capsule, 191%; calves fed 45 mg. of aureomycin daily in the milk, 207%; and those given weekly injections of 125 mg. of aureomycin, 183%. These results show that when aureomycin is fed only in a calf starter some growth stimulation will be produced but not so much as when the antibiotic is placed in the milk. These data show the necessity of insuring adequate consumption of aureomycin by calves early in life. It appears that when the antibiotic is fed only in a calf starter, maximum effect may not always be obtained, owing apparently to the low consumption of starter early in the life of the calf. These workers explained the lack of maximum growth response from aureomycin administered by capsule by the fact that the capsule probably went into the rumen upon administration, whereas milk enters the abomasum.

Gaunya et al. (33) observed that aureomycin did not improve the growth
rate of calves or influence the incidence of calf scours when included in a calf starter at the rates of only 4.5 and 9 mg. of aureomycin per pound of starter. Apparently the calves did not consume adequate amounts of starter to insure the consumption of the minimum amount of aureomycin required to produce a growth response or to reduce the incidence of calf scours. Certainly, more research is needed to determine more effective means of achieving maximum beneficial effects from the feeding of an antibiotic to calves when it is to be fed in a calf starter.

4. Influence of type of ration. Some consideration has been given to the effects of various types of rations on the growth response produced by an antibiotic. Rusoff et al. (101) in one study found that the type of plant protein in a calf starter, i.e., soybean oil meal, hydraulic cottonseed oil meal, or degossypolized cottonseed oil meal, did not affect the amount of growth response produced by aureomycin. In a later experiment by these workers (102), which appears to be a continuation of the earlier study, it was found that aureomycin stimulated the growth rate of calves to a greater extent when added to a starter containing soybean oil meal than when added to a starter containing either one of the cottonseed oil meals. Lassiter et al. (65) found that an aureomycin supplement improved the growth rate of calves 14% over that of the control calves when added to a calf starter containing corn distillers dried solubles (plant protein) but only 9% when added to a starter containing nonfat dry milk solids (animal protein). The growth rate of calves fed the animal protein ration without an antibiotic was about 10% greater than that of calves fed the plant protein ration without an antibiotic; this may account partly for the greater growth response from aureomycin when added to the plant protein ration. These results are in agreement with those of Sanford (113) and Heuser and Norris (38), working with chicks.

Hibbs and Conrad (39) and Hibbs et al. (42) observed that aureomycin improved the growth of calves raised on a high roughage system but found that variations in the hay to grain ratios (4:1, 3:2, and 2:3) had no effect upon the response from the antibiotic. Elliott and Ellsworth (29) found that the greatest response from aureomycin feeding of lambs was obtained on a high-roughage, low-grain ration and the poorest response on a low-roughage, high-grain ration. Clawson et al. (21) observed that when calves were fed aureomycin to 10 weeks of age the types of hay fed, alfalfa or prairie, had no effect on the growth response produced. However, from birth to 16 weeks of age, calves fed alfalfa hay responded more to aureomycin supplementation than did calves fed prairie hay. Actually, the data which were shown indicated that aureomycin caused a growth depression in calves fed prairie hay between the 10th and 16th weeks of the experiment. This was true also of calves fed aureomycin for the first 10 weeks, with alfalfa hay feeding starting at 8 weeks of age. In all of these comparisons aureomycin was fed only for the first 10 weeks.

Gardner et al. (32) and Swanson and Hinton (118) studied the effect that heavy milk feeding might have on the growth response produced by aureomycin. Gardner et al. found that aureomycin supplementation of a whole milk–veal calf
ration improved the growth rate of milk-fed veal calves. The exact amount of improvement was not stated. Swanson and Hinton fed calves a commercial milk replacer containing 60% milk products at very high levels until the calves were 30 days old and then reduced the milk replacement feeding until they were removed from milk feeding at 51 days of age. Under these conditions aureomycin improved the growth of the calves 24.1% for the first 50 days and 17.5% over a 16-week experimental period. As shown by these two studies, apparently aureomycin will improve the growth rate of calves even when large quantities of milk are fed. McGilliard et al. (79) found that calves fed aureomycin for 35 days followed by end inoculations on the 36th and 41st days gained as fast during a second 35-day period as a control group of calves and faster than calves fed aureomycin to 35 days and then discontinued without end inoculations. The growth of all groups of calves was approximately the same at the end of 16 weeks. Although data were reported on only three calves per group, these data indicate that aureomycin possibly caused some disturbance in normal rumen function.

5. Combination of antibiotics vs. single antibiotics. Some interest has been shown in the feasibility of feeding a combination of antibiotics rather than the single antibiotic. Edgerly (28) found that aureomycin and terramycin improved the growth rate of calves about the same, 17%, but an equal mixture of aureomycin, terramycin, bacitracin, and procaine penicillin improved the average daily gain of the calves over their controls about 27%. It was also observed that aureomycin- and terramycin-fed calves did not grow as fast as control calves 2-3 weeks after the removal of the antibiotic from the ration at 12 weeks of age, but with calves fed the mixture of antibiotics this reduction in the growth curve was not noted when the antibiotics were removed from the ration. Lassiter et al. (67) found that the feeding of a combination of aureomycin and terramycin supplements did not produce a greater growth response or afford other advantages than those produced by the single antibiotics.

6. Crystalline vs. crude antibiotics. Some workers have questioned the relative feeding value of crystalline antibiotics and the crude supplements. Loosli and Wallace (73) found that crystalline aureomycin produced a growth response similar to that secured from an A.P.F. supplement containing aureomycin. Rusoff et al. (103, 105) observed similar results with aureomycin. Bloom and Knodt (13) fed three levels of both crystalline aureomycin and aureomycin supplements. In every respect equivalent amounts of both forms of aureomycin were fed. Although the growth differences between levels or between methods of supplying aureomycin were not statistically significant, the calves fed the crude aureomycin supplement gained faster than the crystalline aureomycin-fed calves at two of the three levels of aureomycin feeding. Bartley et al. (7) fed groups of calves no aureomycin, 45 mg. daily of crystalline aureomycin, 45 mg. daily of aureomycin from Aurofac, and 90 mg. daily of crystalline aureomycin. Growth data from birth to 12 weeks of age of the calves receiving 45 mg. of aureomycin from Aurofac showed that they gained significantly faster than calves fed an equivalent amount of crystalline aureomycin, but from 13 to 25 weeks of age
those fed 45 mg. of crystalline aureomycin gained significantly faster than all other groups. Calves fed 90 mg. of crystalline aureomycin daily at no time gained faster than did calves fed 45 mg. of aureomycin. These workers postulated the presence of a factor(s) in Aurofac which was not in crystalline aureomycin and which benefited the calves until rumen synthesis provided the factor(s).

7. Skeletal growth. Throughout this discussion very little has been mentioned about the effect of antibiotics on growth other than gain in body weight. Early workers in this field were concerned as to whether the increase in body weight was due to increased fatness and condition or whether skeletal growth was affected. In general, antibiotics seemingly stimulate skeletal growth as well as body weight. Voelker and Cason (120) reported that aureomycin-fed calves showed more structural body growth than did control calves. Since this report, several workers (42, 44, 46, 47, 54, 61, 64, 65, 67, 106, 107) have confirmed the observation of the Arkansas workers. Murley and Pou (89) observed that aureomycin did not increase skeletal growth, but in this trial neither did it increase body weight gains. Rusoff et al. (106) conducted carcass studies of antibiotic-fed calves which showed larger muscles and skeletal size of calves fed aureomycin.

B. Calf scours. Bartley et al. (3) reported that the feeding of an A.P.F. concentrate containing aureomycin to young dairy calves lowered the incidence of scours. These workers therefore proposed that aureomycin enhanced the growth of calves by preventing scours. Loosli and Wallace (73) reported similar results, observing that control calves scoured an average total of 6.9 days per calf from birth to 8 weeks of age and calves fed aureomycin scoured only an average of 2.5 days. Several workers (1, 6, 7, 13, 44, 49, 59, 62, 68, 103) have confirmed these early reports. Morrison and Deal (84), MacKay et al. (77), Voelker and Jacobson (121), Murley and Pou (89), Mochrie et al. (82), Knödöt et al. (61), Swanson and Hinton (118), and Warner (123) reported that aureomycin either had no effect on the incidence of scours or that scours and other types of infections were not a problem under the conditions existing in their studies. In the study by Warner the experiment was conducted in a portion of the housing facilities that had never been occupied by dairy calves, and the level of infection was extremely low. Bortree et al. (15) conducted some field trials on the use of aureomycin for the prevention and treatment of scours. In one trial, 58 cases of scours were treated with 51 animals responding immediately, five gradually, and two dying. In another trial, 67 calves were given a 500-mg. oblet of aureomycin at birth. Forty of these calves remained healthy and 27 developed scours of varying severity. Twenty-one of these calves responded to a single treatment of 500 mg. of aureomycin, six required further treatment, and one calf died. These data are the results of field observations, but evidence is presented which at least indicates that antibiotics, in this case aureomycin, are effective in the prevention and treatment of scours.

Voelker and Cason (120), MacKay et al. (78), and Lassiter et al. (69) observed that terramycin probably helped to reduce the incidence of scours, although apparently none of these studies was conducted under conditions where scours was a major problem.
Very little information is available concerning the use of other antibiotics in the control of scours. Hogue et al. (44) observed that calves fed either aureomycin, streptomycin, or a mixture of bacitracin and penicillin had fewer days of abnormal feces than calves which received no antibiotic for the first 7 weeks of life. Kon et al. (62) reported that procaine penicillin reduced the incidence of scours. On the other hand, Knodt and Ross (60) found that procaine or potassium penicillin increased the incidence. In an earlier study Knodt and Bloom (58) found that penicillin-fed calves had a higher incidence of respiratory ills than did control calves and two penicillin-fed calves died during the experiment, whereas there were no deaths among calves not fed penicillin. Gardner et al. (32) and Voelker and Jacobson (121) failed to observe that penicillin had any effect on the incidence of scours.

Unfortunately, sufficient data are not available concerning the effect of antibiotics on scours when it was a major problem. Several investigators have obtained indications that various antibiotics aid in the control of scours, but very few experiments have been conducted under conditions when disease problems were encountered. Apparently, the first experiment reported by Bartley et al. (3) was conducted under such conditions. In this study it was clearly demonstrated that aureomycin did reduce the incidence of scours.

C. Feed consumption and feed efficiency. There is good agreement among investigators as to the effect of antibiotics on the consumption of feed by dairy calves and how well this feed is utilized. Research work in general indicates that all of the antibiotics studied, with the possible exception of penicillin, increase the consumption of hay, starter, or both, and improve the efficiency of feed utilization over that for calves not fed antibiotics.

Rusoff et al. (105) reported that aureomycin-fed calves consumed more starter than did calves not fed aureomycin. Loosli et al. (75) and Loosli (72) found that aureomycin-fed calves consumed 30-40% more starter and required less TDN per pound of gain than calves which were not fed aureomycin. These workers found that aureomycin had no significant effect on hay consumption. Murley et al. (88) observed an increase in feed efficiency from the feeding of aureomycin to young calves. Several workers (6, 9, 13, 30, 39, 49, 59, 65, 67, 82, 118) have confirmed the early reports that aureomycin does stimulate the consumption of grain or starter. Morrison and Deal (84), MacKay et al. (77), Murley and Pou (89), Bartley et al. (7) and Knodt et al. (61), however, observed that aureomycin had very little effect on starter or grain consumption. Several investigators (7, 59, 61, 75, 82, 84, 107) found that aureomycin had very little effect upon consumption of hay by young dairy calves, but Murley et al. (87) observed that aureomycin-fed calves consumed 21% more hay than did control calves. All calves were fed a basal ration of either whole reconstituted skim milk, hay, and grain. Jacobson et al. (46) confirmed this observation with calves which were 16 weeks of age at the start of the experiment and remained on trial for 12 weeks.

The effect of terramycin on feed consumption and feed utilization by calves has been similar to that reported for aureomycin. Kesler and Knodt (55) observed that the addition of terramycin to a milk replacement ration improved
the appetite of the calves. Kesler (54) later reported that terramycin appeared to stimulate the appetite of the calves for starter but not for hay. In fact, terramycin-fed calves failed to consume as much hay as did the control calves. MacKay et al. (78) reported greater starter consumption for calves fed terramycin than for the controls. Pritchard et al. (93) and Lassiter et al. (69) failed to find that the feeding of terramycin to calves had any effect on the consumption of hay or grain and the utilization of feed. It should be mentioned that very little improvement in growth was observed by Pritchard et al. and that terramycin reduced slightly the growth rate of calves as compared with that of their controls in the study reported by the latter workers.

Disagreement exists concerning the effect of penicillin on dairy calf feed consumption. Bloom and Knodt (12) and Knodt and Bloom (58) reported that the inclusion of 10 p.p.m. of potassium penicillin in a milk replacement feed reduced feed consumption. The control calves consumed, on the average, 211.3 lb. of starter for the first 10 weeks of the trial, whereas calves fed penicillin during this same period consumed only 102.2 lb. of starter. During the next 2 weeks very little difference in starter consumption was observed. Penicillin did not appear to have any effect on hay consumption. In a later study Knodt and Ross (60) again observed a reduction in the growth rate of penicillin-fed calves as compared with calves not fed penicillin, but the growth depression appeared to be due to a higher incidence of scours among penicillin-fed calves rather than to a reduction in feed consumption, although the control calves were slightly more efficient in feed utilization than the penicillin-fed calves. Voelker and Jacobson (121) observed that procaine penicillin G when fed to calves caused a slight reduction in the consumption of starter. On the other hand, Kon et al. (62), Gardner et al. (32), and Hibbs et al. (41) found that penicillin had very little effect on the consumption of feed or feed utilization by calves.

Data concerning the effect of the other antibiotics on feed consumption are extremely limited. Ellsworth et al. (30) found that a bacitracin supplement when fed to calves had no effect on starter or hay consumption but did increase the efficiency of feed utilization. Hogue et al. (44) found that both streptomycin and a mixture of bacitracin and penicillin (4:1) increased feed efficiency of the supplemented calves over the control calves. In this study the calves given bacitracin and penicillin consumed slightly less starter than did those fed aureomycin, streptomycin, or no antibiotic.

On the basis of these data, aureomycin, terramycin, and possibly bacitracin and streptomycin seemingly increase the consumption of feed and/or improve the efficiency of feed utilization in young dairy calves. There appears to be very little difference in the effect of aureomycin and terramycin, although it must be remembered that considerably more research is needed to substantiate the stimulatory effects of terramycin on feed consumption.

In this discussion the term "efficiency of feed utilization" signifies the units of feed required to produce a unit of gain in body weight. This usage should not be confused with an improvement in the utilization of feed as might be determined by metabolism studies. Since antibiotics in general improve the rate
of gain of calves, an improvement in feed efficiency might be expected unless a corresponding increase in feed consumption occurred. Apparently this does not occur, at least not in all cases; therefore, an increase in feed efficiency usually results. These conditions pose the question as to whether the improvement in feed efficiency from the feeding of antibiotics is due to an increased growth rate by an antibiotic-fed calf or an actual improvement in the utilization of a unit of feed. Unfortunately, data are not available concerning young dairy calves as to whether an increase in growth would be obtained if the control calves and antibiotic-fed calves were fed equal amounts of feed throughout the aureomycin feeding period. Eating habits of young calves make this type of data extremely difficult to obtain.

D. Metabolic processes and the possible modes of action of antibiotics. Several workers have studied the effects of antibiotics on various metabolic processes in the young calf in an effort to determine why antibiotics improve the growth rate. Investigators working with chicks have established that antibiotics in the ration probably cause some change in the intestinal flora of the chick that is responsible for the improvement in the growth rate.

Loosli et al. (75) observed that aureomycin when fed to calves under 16 weeks of age had very little effect on the total bacteria count of the rumen or the types of bacteria present. Rusoff et al. (105) failed to find any evidence from the examination of rumen smears that aureomycin had any effect on the microscopic flora of the rumen. Voelker and Cason (120) made bacteriological studies of colon material and found no consistent differences in bacterial population between terramycin-fed calves and those not fed terramycin. Ellsworth et al. (30) observed that neither aureomycin nor bacitracin had any significant effect on the total number of bacteria of either the coliform or streptococci groups in the feces of calves. Bartley et al. (9) and Rusoff et al. (101, 102) reported results similar to the data discussed previously, indicating that aureomycin has no consistent effect on the intestinal microflora of the young calf.

Several investigators have been interested in the effect of antibiotics on the establishment and function of rumen microorganisms in the young calf. Kesler and Knodt (55) found that rumen inoculum taken from calves not fed terramycin digested cellulose in the artificial rumen at the rate of 67.4%, whereas the inoculum from terramycin-fed calves had a cellulose digestive power of only 24.2%. These samples were taken from calves 12 and 16 weeks of age. In another trial it was observed that calves not fed terramycin had a cellulose digestive power of 49.5%, but after they were fed terramycin the cellulose digestion in the artificial rumen dropped to 12.3%. When terramycin supplementation was discontinued, cellulose digestion returned to normal in 6 days. It was further found that neither the thiamin nor the riboflavin level in the rumen of calves at 6, 12, or 16 weeks of age was affected by terramycin feeding. Hibbs and Conrad (39) observed that aureomycin had no effect on the average total steam volatile fatty acids or acetic acid content in rumen juice of calves 12 weeks old. Rumen propionic acid was slightly lower and butyric acid slightly higher in aureomycin-fed calves than in control calves. In a later study, Hibbs et al. (42)
conducted metabolism studies with 13-week-old calves which had been fed aureomycin since birth. These studies indicated that aureomycin had no effect on dry matter, cellulose, or protein digestion. Aureomycin-fed calves did have a slightly higher retention of nitrogen. In those studies and in a subsequent experiment (25) aureomycin had no significant effect on the riboflavin and thiamin content of rumen juice and urine of calves. After aureomycin feeding was discontinued, a slight reduction in growth occurred. During this period a change in "hay group" bacteria of the rumen was noted, which was possibly the reason for the reduction in growth during this period.

Radisson et al. (94) in artificial rumen studies found that rumen samples taken from aureomycin-fed calves had a lower digestion of filter paper cellulose with or without starch or grain, and/or when grass juice was added than rumen samples taken from calves not fed aureomycin. When alfalfa hay replaced filter paper only a slight, if any, inhibition was noted. These workers postulated the presence of a factor in alfalfa hay not in filter paper which prevented the depressing effect of aureomycin on cellulose digestion.

Rusoff et al. (107) reported that aureomycin had no effect on rumen environment (pH or Eh), fiber digestion in the artificial rumen, rumen flora, or B-vitamin levels of rumen fluid. These workers found that the injected aureomycin was excreted mainly in the urine and the oral-administered aureomycin in the feces. Some aureomycin was found in the bile of injected calves, which was thought to explain why aureomycin was found in the feces of injected calves. These workers stated that this probably signified that the rumen had been bypassed; also, since a growth response was produced by the injection of aureomycin, they postulated that the rumen was not the site where aureomycin stimulated growth. It was also stated that the small amount of aureomycin in the intestine of injected calves indicated that probably the intestinal flora was not involved in the growth stimulation. Another interesting observation was that aureomycin-fed calves showed heavier weights and were larger in size of carcass and bone than control calves.

Mann et al. (80) studied the effect of feeding aureomycin to calves on the establishment of normal rumen microflora and microflora. They found that aureomycin-fed calves had a less acid rumen content and produced a rumen pH (less than 6) needed for rumen bacterial and protozoan activity at a much earlier age than calves not fed aureomycin. Aureomycin had very little effect on the final formation of a typical rumen viable streptococcal population. These workers believed that when aureomycin was given orally it did not act directly on the rumen microorganisms. Bartley et al. (6) found that aureomycin had no influence on the strength and number of rumen movements or rumen tone in young calves.

Murley et al. (86) found that aureomycin had no effect on the reducing sugars and nitrogen content of the urine of calves or on the fecal excretions of dry matter, reducing sugars, nitrogen, ether extract, and ash. Murley et al. (87) also observed that when calves were fed a restricted diet, aureomycin produced a slight improvement in the utilization of carbohydrates, nitrogen, ash, and ether
extract, but these differences were not significant. Lassiter et al. (68) studied
the effect of aureomycin on the digestion of feed nutrients by young dairy calves,
checking digestibility at 5, 8, and 11 weeks of age. Although uniform feed
intakes were extremely difficult to obtain at the 5- and 8-week-old trials, it was
contended that these trials were needed since it has been shown that the greatest
stimulation in growth by aureomycin occurs by the time calves are 8 weeks old.
These studies showed that aureomycin had no effect on the digestion of any feed
nutrient over the 12-week trial or for any single digestion period.

Numerous investigators have studied the influence of antibiotics on various
blood constituents. Murley et al. (86) observed that blood sugar levels rose
slightly more rapidly and exhibited a greater increase in aureomycin-fed calves
than in the control calves. These differences were, however, not significant.
Hibbs et al. (39, 40) observed that 8- to 12-week-old calves fed aureomycin main-
tained a blood sugar level of about 9 mg. per 100 ml. higher than that found for
the control calves. Voelker et al. (122) studied 1,500 blood samples from animals
fed aureomycin (200-240 mg. daily) and found that aureomycin had no effect on
blood glucose levels. The age of the animals used in this study was not stated,
but it is believed that the dairy animals involved were growing heifers and not
young calves such as those used by the Ohio workers (39, 40).

Various workers (31, 50, 82, 92, 112, 114, 115, 121) have studied the effect
of antibiotics on such blood constituents as blood erythrocyte count, hemoglobin
percentage, packed cell volume, red blood cell counts, corpuscular volume, cor-
puscular hemoglobin, corpuscular hemoglobin concentration, plasma "Allen" fat
levels, plasma calcium and inorganic phosphorus levels, and the blood levels of
various vitamins but have found none of these blood constituents to be affected
significantly by the feeding of aureomycin to calves. Lassiter et al. (68) found
that aureomycin did not affect blood levels of urea nitrogen but did cause a
significant depression in blood nonprotein nitrogen levels during the first 7 weeks
of the calf's life. It was also during this period that the greatest stimulation
in growth occurred from the feeding of aureomycin. Since aureomycin did not
produce an increase in the digestibility of protein, these data were interpreted to
indicate a greater utilization of absorbed nitrogen by calves fed aureomycin.
Unfortunately, nitrogen balance values were not obtained in these studies.

Rusoff et al. (112) observed that aureomycin had no effect on the weight of
the pituitary, thyroid, or thymus glands or the liver when recorded as a per-
centage of body weight. However, it was found that aureomycin caused a de-
crease in the thickness of the duodenal and jejunal sections of the intestine and
an increase in the thickness of the ileum section of the intestine as compared with
those of the control animals. Hester et al. (37) studied the distribution of orally
administered and injected aureomycin in the bodies of dairy calves that had
shown a growth response from aureomycin supplementation. In the injected
calves the highest concentration was in the urine, with measurable amounts in
the liver and kidneys. None was found in the spleen, thymus, pituitary glands,
or muscles of any calves. When aureomycin was injected, none was found in the
rumen. In the small intestine the concentration increased from the upper to the
lower portions and decreased in concentration in the large intestine between the lower small intestine and the anal end of the large intestine. Voelker et al. (119) concluded from in vitro studies that the growth-promoting action of aureomycin and terramycin was not due to a lowering of the surface tension of the intestinal tract contents since these antibiotics do not lower the surface tension of water, whereas penicillin and various surface-active agents do, yet these latter products did not increase the growth rate of calves.

Little discussion has been devoted to the possible modes of action by which antibiotics stimulate the growth rate of young dairy calves. Two general types of action have been suggested. Bartley et al. (3) proposed that aureomycin improved growth by reducing the incidence of scours. Growth responses have been reported (13, 32, 59, 61, 67, 77, 123), however, from the feeding of antibiotics to calves when the incidence of scours was not a problem. However, such reports do not rule out the possibility of subclinical infections which would probably never result in scours, yet if they were reduced by feeding an antibiotic an increase in growth of the calves would probably result. Considerably more research, possibly under farm conditions, is needed on the effect of antibiotics on the control of scours when the level of infection is high.

Loosli (72) and Jacobson et al. (47) have proposed that antibiotic-fed calves grow faster because of increased appetite. The question arises as to whether such calves eat more because of the action of the antibiotic or because of their larger size.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Consumption of feed (daily)</th>
<th>Length of trial</th>
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<tbody>
<tr>
<td></td>
<td>Control calves</td>
<td>Antibiotic calves</td>
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<tr>
<td>Aureomycin</td>
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<tr>
<td>Loosli et al. (75)</td>
<td>0.59</td>
<td>0.66</td>
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<tr>
<td>Bartley et al. (6)</td>
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<td>0.37</td>
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<tr>
<td>Ibid.</td>
<td>0.91</td>
<td>0.93</td>
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<tr>
<td>Lassiter et al. (67)</td>
<td>1.29</td>
<td>1.34</td>
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<tr>
<td>Bloom and Knodt (13)</td>
<td>1.33</td>
<td>1.31</td>
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<tr>
<td>Hibbs et al. (42)</td>
<td>1.11</td>
<td>1.21</td>
</tr>
<tr>
<td>Mochrie et al. (82)</td>
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<td>0.36</td>
</tr>
<tr>
<td>Ibid.</td>
<td>2.09</td>
<td>2.15</td>
</tr>
<tr>
<td>Murley et al. (87)</td>
<td>1.09*</td>
<td>1.08*</td>
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<tr>
<td>Swanson and Hinton (118)</td>
<td>2.02</td>
<td>2.07</td>
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<td>Terramycin</td>
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<tr>
<td>Lassiter et al. (67)</td>
<td>1.29</td>
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* TDN/lb of body weight.

The data presented in Table 1 are a further attempt to answer this question. The feed consumption (hay and grain) data for supplemented and calves not fed antibiotics from several experiments have been recalculated in terms of daily feed consumption per pound of body weight. In fairness to the original authors it should be stated that these figures have been calculated from the data presented and were not included in the original reports. In a few cases an average starting weight of the calves was assumed to be the average for the breed.
of calves involved in the study. The daily feed consumption per pound of body weight was calculated by dividing the total amount of feed consumed over the experimental period by the end body weight of the calves and by the number of days in the trial. It was impossible to calculate the consumption of feed per pound of body weight at various stages of growth since the weight of the calves and the consumption of feed were quoted only in terms of average daily gain and total feed consumption over the entire experimental period. In the experiment by Bartley et al. (6) this information was already stated in terms of feed consumption per 100 lb. of body weight on a weekly basis.

When the feed consumption data from these experiments are calculated in this manner some very interesting results are revealed. In every experiment, with the exception of the studies by Bartley et al. (6) and Hibbs et al. (42), there was very little difference in the consumption of feed by antibiotic-fed calves and by control calves when the weight of the calves was considered. In the study by Bartley et al. aureomycin-fed calves consumed more hay and grain per pound of body weight during the first 7 weeks of age but not from birth to 12 weeks of age. Mochrie et al. (82) presented data on calves from birth to 5 weeks of age as well as from birth to 16 weeks of age, but in this study aureomycin improved the growth of the calves only about 5% over the 16-week trial. These data certainly do not answer completely the original question but do show that much of the increased feed consumption by antibiotic-fed calves may be due to the larger size of such calves. If antibiotics affected the appetites of calves directly, one might expect calves fed antibiotics to consume more feed per pound of body weight.

Generally, very few data at present indicate that the microflora of the intestinal tract has any great connection with the growth response produced by antibiotics in dairy animals. This does not mean, however, that antibiotics do not cause changes in the flora of the digestive tract of the calf, because it is doubtful if bacteriological methods have been perfected well enough that the microflora of the digestive tract can be characterized accurately to determine all the changes that could occur as a result of antibiotic feeding.

Two definite modes of action have been postulated, and apparently there is very little relationship between these two. Rusoff et al. (107) have presented evidence which indicates that in some manner aureomycin might stimulate the pituitary gland to produce more growth hormone, resulting in greater bone metabolism and over-all growth. These workers rule out the rumen of the calf as being the site of action since growth responses from injected aureomycin were observed. A small amount of aureomycin was found in the intestinal tract and feces of injected animals, but this suggested that the bile was probably the means of excretion into the intestinal tract, thus by-passing the rumen. It should be pointed out that Kraus et al. (63) found aureomycin in the saliva of humans after oral administration; this would provide a pathway of excretion that would not by-pass the rumen. In a later study these Louisiana workers (37) could not detect any aureomycin in the rumen of injected calves. This finding certainly makes it appear that the rumen is probably not the site of action of antibiotics.
Another supporting reason for this statement is that several workers have shown that the maximum growth response obtained from the feeding of antibiotics occurs before the calf is 8 weeks of age. It is generally accepted (56) that the rumen does not begin functioning until the calf is about 3 weeks old and is not fully developed until some time later. Knodt and Bloom (13) found that the greatest growth stimulation from aureomycin feeding occurred during the first 4 weeks of the calf’s life.

Rusoff et al. (107) also attempted to rule out the intestinal tract as the site of action of antibiotics by the fact that only very small amounts of aureomycin were found in the intestinal tract and feces of calves injected with aureomycin. These calves were injected with 400 mg. of aureomycin weekly. It should be remembered that this amount of aureomycin, about 57 mg. daily, was about two and one-half times the amount of aureomycin that is believed to be the effective oral level. It is possible, therefore, that enough aureomycin was excreted into the digestive tract by way of the bile ducts to cause a stimulation in growth. In a later study (37) the Louisiana workers did not find any measurable amounts of aureomycin in the pituitary gland. One might expect to find aureomycin in this gland if that is the means by which this antibiotic improves the growth of calves.

Hibbs et al. (42) suggested that the mode of action of antibiotics is one of an alteration in energy metabolism, possibly involving the microflora of the rumen. These workers found that aureomycin-fed calves had significantly higher blood sugar levels than control calves during the 8- to 12-week-old period. By chromatographic separation it was found that 12-week-old aureomycin-fed calves had a lower percentage of propionic acid and a higher percentage of butyric acid in the rumen juice than did control calves. It was believed there was a relationship between these rumen short-chain fatty acid values and blood sugar levels. Therefore, it was suggested that a possible mode of action of antibiotics was through energy metabolism. It was further stated that aureomycin possibly has an energy-sparing effect manifested through its effect on the microflora of the rumen and lower digestive tract. These were very interesting findings, but two things should be remembered in light of these data. Voelker et al. (122) analyzed 1,500 blood samples of dairy animals fed aureomycin and found no effect on blood sugar levels. It is possible that these values were obtained with older animals than the 8- to 12-week-old calves used by Hibbs et al. (42). The other point is the relationship between the time the maximum antibiotic stimulus occurs and the time Hibbs et al. observed this alteration of energy metabolism. It is not known, of course, when the stimulation in growth from the feeding of aureomycin occurred in this experiment, but most workers agree that the greatest stimulation from aureomycin feeding results during the first 7-8 weeks of the calf’s life. Hibbs et al. did not observe this energy relationship until the calves were 8-12 weeks old. These blood and rumen values were checked before the calves were 8 weeks old, but no differences between the aureomycin-fed calves and the control calves existed. Therefore, the time of maximum growth improvement and the time when this energy relationship existed are not the same. It is
possible that the effect of aureomycin on blood sugar and rumen fatty acid levels is a secondary one rather than the primary reason why aureomycin improves the growth rate of calves.

The only other clearly demonstrated effect of aureomycin on metabolic processes in the calf was the depressing effect of aureomycin feeding on blood non-protein nitrogen levels in calves under 7 weeks of age, as reported by Lassiter et al. (68). It was believed that these findings indicated a greater utilization of absorbed nitrogen by aureomycin-fed calves, but these data are too preliminary to draw any conclusions as to the mode of action of antibiotics in the calf. As can be deduced from the foregoing discussion, considerably more information is needed on the effect of antibiotics on the metabolism of the calf before it will be possible to state with any degree of certainty their true mode of action.

GROWING DAIRY ANIMALS

A problem foremost in the minds of dairymen is the question of feeding antibiotics to growing heifers and the long-time effects of feeding antibiotics to dairy animals. Rusoff (100) fed Jersey male calves, ranging from 14 to 34 weeks in age, 90-180 mg. of aureomycin daily. A 60% increase in growth occurred for the first 2 weeks after the initiation of aureomycin feeding, followed by increases in growth of 36% after 4 weeks, 30% after 6 weeks, and 8% after 8 weeks. Over the entire 20-week feeding period there was no difference in the growth rate of the control calves and those fed aureomycin. Aureomycin apparently had very little effect on rumination, and no anorexia or diarrhea was observed in the aureomycin-fed calves. Voelker and Cason (120) fed 4.8-month-old heifer calves on pasture aureomycin for 8 weeks. During the first 6 weeks of this study the aureomycin-fed calves gained 17% more than the control calves. In another trial heifers were fed 200 mg. daily of crystalline aureomycin plus 2.5% of an aureomycin supplement in the grain ration without any harmful effects. Jacobson et al. (47) reported the feeding of aureomycin to calves up to 200 days of age. This experiment was started when calves were 16 weeks old, but half of them had received aureomycin from birth. The group of calves that received aureomycin from birth to 200 days of age were the largest calves at the end of the 28-week trial. Those that received aureomycin from 16 weeks to 200 days of age were the next heaviest animals, followed by the calves that were fed aureomycin from birth to 16 weeks of age; the smallest calves were those that were not fed aureomycin. These workers concluded that previous feeding of aureomycin had some effect on the gain of animals over 16 weeks of age but not so much as the actual feeding of aureomycin from 16 weeks of age to 200 days of age.

Fincham and Voelker (31) divided 40 pairs of heifers into two groups and fed one group 80 mg. of aureomycin daily from birth to 200 days of age and 240 mg. daily to about 2½ years of age. They found that most of the growth stimulation from the feeding of aureomycin occurred before the heifers were 6 months old, but the growth advantage obtained was maintained afterwards. At 18 months of age the control heifers weighed 755 lb. and the supplemented heifers, 794 lb. The aureomycin-fed heifers were bred 19 days earlier than the
control heifers but required 1.6 services per conception as compared with 1.4 for the controls. In a later report Jacobson et al. (49) fed one heifer of each of 17 pairs 240 mg. of aureomycin daily for a minimum of 15 months prior to parturition and during the first lactation. The average body weight for the control heifers 10 days after calving was 939 lb. and for the aureomycin-fed heifers it was 995 lb. Aureomycin feeding had no effect on milk and butterfat production during the first lactation. The average birth weight of calves born to the control animals was 66 lb. and that of calves born to the aureomycin-fed heifers was 76 lb. There was no difference in the average age of the animals in each group at first calving. The calves from each group of heifers were divided into two comparable groups, one receiving aureomycin to 16 weeks of age. The weight gain of the aureomycin-fed calves was 26% greater than that of the unsupplemented calves and apparently was not affected appreciably by the dams' rations.

Bartley et al. (5) reported on the feeding of aureomycin to dairy calves from birth to 13 months of age. Their data concern the period after the calves were 6.6-7.0 months old, although this was a continuation of a previous study. During the next 6 months the control calves gained 233 lb., a 79% increase over the starting weight, while the aureomycin-fed animals gained 237 lb., or a 68% increase over the 6.6 month starting weight. The aureomycin-supplemented calves weighed 57 lb. more when 6.6-7.0 months old than the control calves. These data show that the growth advantage of feeding aureomycin to calves early in life was maintained but there was no further stimulation in growth. It was not known, however, whether it is necessary to feed aureomycin to maintain this early advantage. These data also do not answer the question whether growth stimulation would have been obtained at this older age if aureomycin had not been previously fed. These workers (6) reported that calves fed aureomycin from birth to 7 weeks of age increased in weight 199% of their starting weight to 12 weeks of age as compared with 190% for calves not fed aureomycin and 228% for calves fed aureomycin continuously from birth to 12 weeks of age. At 7 weeks of age aureomycin-fed calves and control calves had increased in weight 155% and 138%, respectively, of their starting weights. Huffman (45) fed one heifer of a set of anastomose twins aureomycin from 42 days of age to about 19 months of age. The end of this period the twin fed aureomycin had gained 781 lb. and the control twin 743 lb. The calves consumed about the same amount of TDN during the 18-month feeding period.

Bartley et al. (9) fed daily doses of 200-800 mg. of aureomycin per 100 lb. of body weight to calves 12-16 weeks old without any detrimental effects. One calf 16 weeks old that had not previously received aureomycin was fed 2,500 mg. of this antibiotic daily for 4 weeks without any harmful effects.

**MATURE DAIRY ANIMALS**

The reluctance of research workers to feed antibiotics to mature dairy animals is based primarily on the adverse effects of aureomycin on rumen function, as reported by Bell et al. (10) in beef animals and Colby et al. (24) in sheep. Wasserman et al. (124) conducted in vitro studies on the effect of various anti-
biotics on cellulose digestion in the artificial rumen by rumen microorganisms. These workers found that low concentrations of penicillin (5.0 and 7.5 units per milliliter) stimulated cellulose digestion but that 15 units per milliliter caused an inhibition of the digestion of cellulose. All levels of neomycin (6.25, 12.5, and 25.0 units per milliliter) increased cellulose digestion, but these effects were inversely proportional to the concentrations of neomycin. Streptomycin had no influence on digestion at 12.5 γ per milliliter but decreased digestion at 25.0 or 50.0 γ as well as did chloromycetin at levels of 25.0 and 50.0 units per milliliter.

Lodge et al. (71) fed dairy animals 240 mg. of aureomycin daily from an early age to maturity and found that cellulose digestion in the artificial rumen was decreased from 83% for animals not fed aureomycin to 72% for those fed aureomycin. When 80 mg. of aureomycin was fed to 4-month-old calves daily, the digestion of cellulose was reduced to 58%, compared to 78% for the control animals. The addition of 1.6 γ of aureomycin per milliliter to the fermentation mixture when inocula from cows not fed aureomycin were used severely inhibited cellulose digestion. This same addition had little effect on the digestion of cellulose by the inocula from aureomycin-fed cows. Jurtshuk et al. (53) found that the presence of both aureomycin and terramycin (100 γ/100 ml.) reduced the ability of rumen bacteria in the "resting state" to utilize the carbohydrates xylose, arabinose, glucose, maltose, and cellobiose in vitro.

Haq et al. (34, 35) and Rusoff and Haq (109) fed lactating cows aureomycin and observed no significant effect on milk and fat production, milk composition, bacterial count of milk, appetites of the cows, or rumination. In one study (34) similar results were observed for tyrothricin. No measurable amounts of the antibiotic were found in the milk. Rusoff et al. (110) fed mature dairy bulls 300 mg. of aureomycin daily for 10 weeks without having a significant effect on the number of ejaculations, volume of semen per ejaculate, percent initial motility, motile sperm per ejaculate, or breeding efficiency as measured by the percentage of 60-90 day nonreturns. Warner (123) and Loosli and Warner (74) found that the feeding of 700 mg. daily of aureomycin to cows had no effect on feed consumption, but the feeding of 1,000 mg. daily caused feed refusals. No aureomycin was found in the milk of the cows fed 700 mg. of aureomycin daily for 10 days. No effect on cheese starter activity was observed when 500 mg. of aureomycin was fed daily to cows for 6 weeks. The feeding of 100 mg. of aureomycin daily to milking cows produced neither harmful nor beneficial effects on milk production and feed consumption.

Bartley et al. (4) observed that the feeding of 32 mg. of aureomycin per 100 lb. of body weight daily to lactating dairy cows had no effect on the general health and well-being of the animals, milk or fat yield, consumption of feed, body weight changes, pulse rate, body temperatures, or rumination. The amount of aureomycin fed ranged from 300 to 500 mg. daily per cow. In a later report (87) Kansas workers found that the feeding of this amount of aureomycin to cows had no significant effect on the total plate counts of milk or the amount of acid developed in the milk inoculated with starter. No aureomycin was detected in the milk, and the feeding of aureomycin did not appear to have any effect on the quality
of Cheddar cheese made from the milk. Huffman (45) fed as much as 4 g. of bacitracin daily from a bacitracin supplement to lactating cows and as much as 3 g. of aureomycin from Aurofæc without affecting the production of milk or the appetites of the cows. Streptomycin also was fed at levels of 1, 2, and 10 g. daily without any adverse effects. Similar results were found with the feeding of neomycin.

Lassiter et al. (66) fed yearling dairy steers 500 mg. daily of crystalline aureomycin alone and in combination with a surfactant, Ethomid C/15, to study the effect of aureomycin and surfactants on the digestion of feed nutrients. It was found that crystalline aureomycin decreased dry matter digestibility from 64.0% on the basal ration to 60.5%. This reduction was not statistically significant. Crude fiber digestibility was reduced from 35.5 to 22.7%, and this reduction was significant. When aureomycin and Ethomid C/15 were fed in combination, the depressing effect of aureomycin on dry matter and crude fiber digestion appeared to be lessened. In this study aureomycin had no significant effect on the appetites, consistency of feces, over-all condition of the steers, or digestion of dry matter, crude protein, ether extract, and nitrogen-free extract.

Chance et al. (18, 19, 20) reported a series of studies on the effects of aureomycin on rumen digestion and synthesis. Two fistulated dairy steers were fed 0.5 g. daily of crystalline aureomycin for 15 days, followed by a similar feeding period when 1.0 g. of aureomycin was fed daily. The aureomycin feeding periods were preceded by a 15-day period when no aureomycin was fed. Aureomycin had no effect on the appetites of the steers or body weight changes and did not cause digestive disturbances. The rate of the removal of dry matter, crude fiber, crude protein, and nitrogen-free extract from the rumen was highest when 0.5 g. of aureomycin was fed (19). The feeding of 1.0 g. of aureomycin daily caused an accumulation of dry matter, crude protein, and nitrogen-free extract at the 0-hour of feeding, which was the end of one 24-hour period or the beginning of the next 24-hour period. Both levels of aureomycin caused an accumulation of ether extract at the 0-hour of collection.

In a second study (18) the effect of aureomycin on the concentration and synthesis of amino acids and B-vitamins in the rumen was studied. The 0.5 g. level of aureomycin feeding produced a lower concentration of amino acids at the 6-hour collection period, which was probably due to the increased rate of removal of protein from the rumen during this period. The evidence of any amino acid synthesis was lacking. The amount of riboflavin in the rumen was reduced when 0.5 g. of aureomycin was fed daily. Both levels of aureomycin appeared to lower the synthesis of nicotinic acid.

In a third study (20) the effect of aureomycin on rumen microorganisms with special reference to the streptococci and coliform groups was studied. It was observed that when aureomycin was included in the ration a higher pH existed in the rumen than when the steers were not fed aureomycin. When 0.5 g. of aureomycin was fed daily, an increase in total rumenal bacteria count resulted but not when 1.0 g. of aureomycin was fed daily. Both levels of aureomycin caused a reduction of rumen streptococci, but at the 0.5 g. level of aureomycin
feeding an increase in coliform bacteria occurred in one steer but not in the other. It was noted that at this level of aureomycin feeding the largest amount of nutrients was removed from the rumen. Aureomycin caused an increase in the total bacteria count of fecal material but had no effect on the number of streptococci or coliform groups in the feces. This was believed to be due to the ability of these organisms to adapt themselves quickly to aureomycin, but their metabolism could have been altered. The results of these studies indicated a correlation between the increase in coliform population of the rumen when 0.5 g. of aureomycin was fed and the increased removal of dry matter, crude fiber, crude protein, and nitrogen-free extract from the rumen.

In all of these studies relating to mature dairy cattle it is interesting to note that aureomycin apparently had no pronounced effect on the appetites or the well-being of the animals, whereas the initial data reported with mature ruminants indicated very adverse effects from the feeding of low amounts of aureomycin (200 mg. per day).

**DISCUSSION**

Considerable discussion has been devoted to the effects of antibiotics on the growth, metabolism, health, and well-being of dairy cattle. Consideration has been given to the relative nutritional merits of the various antibiotics in the light of present-day knowledge. The feeding of antibiotics to dairy cattle appears to be justified only in the rations of young dairy calves, or those under 16 weeks of age. The feeding of antibiotics to older animals does not appear to afford any economic advantage and may possibly have some harmful effects.

When antibiotics are included in the rations of young dairy calves the following changes are likely to occur in the normal life span of the calf: (a) increased growth rate as measured by both body weight gains and skeletal growth, (b) lower incidence of scours, (c) increased feed consumption, particularly of concentrates, at an earlier age, (d) improvement in feed efficiency as measured by the pounds of feed required to produce a pound of gain in body weight, and (e) improvement in the condition and the well-being of the young calf. The amount of growth response produced by an antibiotic depends upon many factors, but generally the increase in growth rate has ranged from 10 to 30%. A few studies have been reported in which an antibiotic did not improve growth. The only antibiotics that have been studied enough to merit their inclusion in calf feeds are aureomycin and possibly terramycin. Bacitracin and streptomycin appear to have some growth-promoting properties, but insufficient data are available concerning them. Considerably more information is available on the feeding value of aureomycin than of terramycin; consequently, when feeding recommendations are made this difference must be borne in mind. There is seemingly very little difference in the nutritional merits of these two antibiotics; however, as more information becomes available, this statement may need to be qualified.

In this review very little discussion has been given to the economic aspects
of feeding antibiotics to young dairy calves. The question arises whether the added growth advantage can be justified from an economic standpoint. It is the author's opinion that the answer is in the negative when one speaks of added growth alone. Most dairy animals are raised for the sole purpose of herd replacements. The only exception would be calves sold for veal. For herd replacements, available data indicate that any growth advantage produced by antibiotics is small and is of even less importance when the calf grows to maturity. If animals are to be marketed at an early age, less than 6 months, antibiotics would probably then have some economic value strictly from the standpoint of improving body weight gains.

In this discussion considerably more space has been devoted to the effect of antibiotics on the growth rate of calves than to the effect of antibiotics on calfhood diseases, particularly scours. Since most of the reports have stressed the influence of antibiotics on growth more than on scours, this distinction seemed to be justified. Present reports, however, clearly indicate that the true reason for including an antibiotic in a calf feed is not only to improve growth but to reduce the incidence of calf scours. Reports by Ragsdale et al. (96), Wing (130), Weaver et al. (125), Ormiston (91), Davis (27) and Lassiter and Seath (70) all show that mortality among young dairy calves ranges from 15 to 30% and that calf scours is one of the leading causes of death. This high mortality rate means a tremendous economic loss to dairymen in this country, as well as elsewhere. Since antibiotics apparently reduce the incidence of calf scours, losses can be reduced by their inclusion in calf feeds, thus making an important economic contribution. Based upon foregoing discussions, the effect that antibiotics have on the incidence of scours is the most valid reason for including these products in calf feeds.

Although this field of nutrition has been given considerable attention by research workers, many questions on the feeding of antibiotics to dairy cattle remain unanswered. Information regarding the effect of antibiotics on scours under farm conditions is needed to verify or disprove data collected under experiment station conditions. The long-time experiments in progress need to be continued to study the effects of antibiotics being fed early in the life of the calf or continuously on the later productive life of the cow. Certainly the manner by which antibiotics stimulate growth and reduce scours needs to be clarified.

SUMMARY

An attempt has been made to review the available information on the feeding of antibiotics to dairy cattle as completely and in a manner as unbiased as possible. Many reports used in this review are conflicting; nevertheless, the following conclusions seem to be valid.

1. The antibiotics, aureomycin and terramycin, are the only ones which have been studied sufficiently to warrant valid conclusions. Considerably more research needs to be conducted with terramycin before conclusions concerning its use can be accepted with the same degree of confidence as recommendations for aureomycin.
2. Seemingly no beneficial effects are derived from the feeding of antibiotics to mature dairy cattle.

3. Antibiotics probably improve the growth rate and efficiency of feed utilization of growing dairy animals (over 4 months of age), but unless these animals are to be marketed soon, little economic advantage will result from the feeding of antibiotics.

4. Aureomycin and terramycin stimulate the growth rate of calves from 10 to 30% during the first 16 weeks of age. Most of this growth improvement results before the calves are 8 weeks old. In addition to an improvement in growth, antibiotics appear to reduce the incidence of calf scours, increase feed consumption and feed efficiency, and improve the over-all condition and well-being of the animal.

5. The inclusion of aureomycin or terramycin in the rations of dairy calves seems to be best justified by the beneficial effects of these antibiotics in reducing calf scours and thus calf mortality. Any growth advantage afforded by these antibiotics during the early life of the calf becomes insignificant in a mature animal.

6. Present data indicate that aureomycin should be fed at levels ranging from 15-20 mg. per 100 lb. of body weight daily. There appear to be very few advantages of feeding antibiotics after the calves are 12-16 weeks of age.

7. Two fundamental explanations have been presented regarding the possible mode of action of antibiotics in calves. One of these postulates a stimulation of the pituitary gland and increased production of growth hormone. The other postulation states that antibiotics possibly increase the growth of calves through an alteration in energy metabolism probably involving the microflora of the rumen.

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ANTIBIOTICS FOR DAIRY CATTLE: A REVIEW


