The Rationale For Medicated Feeds

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The development of effective coccidiostats and the discovery that specific antibiotics and arsenicals increased growth rates of animals led to the extensive adoption and use of medicated feeds for prophylactic disease control and growth promotion in young animals. In general, experience with medicated feeds during the past 12 years has shown that the drugs fed have increased efficiency of production and they have made possible the large concentration of animals, especially poultry, which characterizes modern production methods. Experience has shown also that these drugs are not a satisfactory substitute for good management and sanitation practices—but they are a most helpful adjunct to such practices. Some feed additives are toxic to the animals when fed at excessive levels. Safe levels of these drugs have been well defined, and proper feed formulation assures their use in a satisfactory manner.

THE USE of feeds as a vehicle for medication of farm animals is an old practice. However, under production practices prior to World War II such medication appeared to be limited primarily to attempts to control internal parasites, especially worms in chickens, and to control outbreaks of diarrhea in pigs. Flocks and herds were usually small, by today's standards, and generally were provided with extensive areas of pasture or range in season.

A growing poultry industry as well as livestock production was stimulated by the war and a need for greater food supplies. As the poultry industry grew and birds were confined to more limited areas, particularly in broiler production, coccidiosis increased and became one of the most important diseases with which the producer had to contend (*20*). Extensive research during the 1940's led to the development in the late 40's of effective coccidiostats for medication of feed, and during the past 12 years several new coccidiostats have been developed to aid the continuing battle against the troublesome coccidia.

It was observed in 1942 that feeding sulfanilamide in low concentrations stimulated growth (*18*). Similarly, an apparent growth response from the feeding of sulfasuxidine was reported in 1944 (*4*), and in 1946 increased growth was observed in chicks fed streptomycin (*21*). These growth effects tended to pass unnoticed because the foci of the experiments had other objectives.

In 1946 it was reported that 3-nitro-4 hydroxyphenylarsonic acid had a marked effect on growth of chickens and turkeys when given in the drinking water (*23*). This finding was extended to application in the feed in 1949 (*22*) and confirmed by others the same year (*3*).

The isolation of vitamin B_{12} in 1948 and its production by fermentation procedures led to studies of antibiotic fermentation residues as sources of B_{12} (*28*). These and subsequent studies soon demonstrated that antibiotics per se had a favorable effect on growth of pigs as well as chicks and turkeys (*28*). The impact of these studies and those with 3-nitro-4 hydroxyphenylarsonic acid resulted in a new concept in animal production, viz., that antibacterial substances could serve a useful and widespread role in animal nutrition and prophylactic disease control.

Development of effective coccidiostats for feed use and the new concept of the usefulness of antibacterial agents in production ushered in the modern era of non-nutritive feed additives in 1949–50. Literally hundreds of experiments with many kinds of livestock and birds have been reported during the past 12 years, not only with the drugs studied initially but with many new ones developed since 1950.

The number of compounds and their uses are too numerous to present here, but some data taken from the literature on swine have been selected because of the writer's specific interest in this area. In 1949–50, active research on animal protein factor (APF) supplements and antibiotics was under way at many experiment stations in the Corn Belt. However, the first published reports on the effects of specific antibiotics came from a joint study by American Cyanamid and the Florida Experiment Station (*17*), from the Michigan Experiment Station (*19*), and from the Hormel Institute (*5*).

The data of Jukes *et al.* (*17*) showed clearly that chlortetracycline controlled diarrhea and improved the growth of pigs fed a corn–peanut meal ration and that their APF supplement also supplied the antibiotic effectively. Luecke *et al.* (*19*) demonstrated that streptomycin markedly increased gains of pigs fed a corn–soybean meal diet as did the APF supplement (which contained chlortetracycline), but neither improved efficiency of feed conversion. Carpenter fed a mixed diet to pigs from a herd in which a chronic and severe disease situation prevailed (*5*). In this instance, the APF supplement which supplied vitamin B_{12} but little or no antibiotic activity increased gains and feed conversion efficiency somewhat but was not as effective as chlortetracycline or the supplement which contained this antibiotic.

The author's first experience with antibiotics came in 1950 (*30*). The pigs used weighed about 37 pounds initially and appeared to be in excellent thrift. Half of them were allotted to four pens and were fed shelled corn and either of two protein-vitamin-mineral supplements, with or without an antibiotic supplement, on a free-choice basis. Half of the pigs were allotted to four pens and fed ground shelled corn and either of two supplements in complete mixed rations. The P-V-M supplements differed in that one contained 25% distiller's dried solubles, whereas in the other, soybean meal was substituted for distiller's solubles.

Soon after the experiment started pigs

in each of the control lots (no antibiotic) developed a diarrhea which persisted for several weeks. The pigs fed the antibiotic supplement remained thrifty throughout the experiment. Thus the use of the antibiotic doubled the rate of gain and decreased the feed required per unit of gain approximately 25%. Others have reported similar striking results from the feeding of antibiotics to unthrifty or to runt pigs. But, in this test the pigs appeared to be in excellent health at the start of the experiment.

Subsequent studies by the author and associates at the University of Minnesota also showed significant effects on growth rate of weanling pigs due to the feeding of chlortetracycline, oxytetracycline, or procaine penicillin, but very little effect on efficiency of feed conversion (*13*).

From the start, concern had been expressed that the continuous use of specific antibiotics in feeds would eventually result in an increase of drug-resistant strains of pathogenic microorganisms. This concern is understandable in view of the fact that drug-resistant organisms have developed in human medicine. In many experiment station herds after the first 2 or 3 years of antibiotic use it did appear that the antibiotics had indeed lost their effectiveness, and the Minnesota Station herd was not an exception. After 5 years of experiments in dry lot, a review of the Minnesota data showed that the antibiotics used had not lost their effectiveness (*14*). Rather, the response in any given season or year was a direct reflection of the previous history and thrift of the pigs fed. Teague has recently reviewed the results obtained in the Ohio Station herd, after 9 years' experience with chlortetracycline (*29*). His data show variable responses in gain similar to those found in the Minnesota data and indicate that this antibiotic has not lost its effectiveness.

In many recent experiments at many stations no growth response has been obtained from the feeding of antibiotics. In some studies, more recently developed antibiotics have been more effective than some of the older ones, and in other studies the reverse has been the case. Unfortunately, from an economic standpoint, it often is not possible to determine in advance whether or not a given group of pigs will benefit from the inclusion of an antibiotic in the ration. Hence an antibiotic or combination of antibacterial agents is routinely added to the rations fed, at least until the pigs reach a weight of 100 pounds.

Carpenter fed 3-nitro-4 hydroxyphenylarsonic acid to growing pigs from a herd chronically affected with swine dysentery (*6*). The drug produced a remarkable improvement in growth rate and efficiency of feed conversion. No symptoms of toxicity in the pigs were observed when the level fed was 0.005%. Higher levels were toxic to the animals. Assays of the liver and kidneys of treated pigs showed that arsenic was retained in these tissues but the residue was quickly excreted when the arsenical was removed from the diet. Illinois workers also have reported a brief study which showed that this arsenical effectively increased live weight gains and feed efficiency of unthrifty pigs (*2*). In a later study, Carpenter and Larson demonstrated that 3-nitro-4 hydroxyphenylarsonic acid and 4-nitrophenylarsonic acid as well as the antibiotics, chlortetracycline, oxytetracycline, bacitracin, and penicillin were effective in controlling swine dysentery (*7*). However, the best control was obtained by combining an arsenical and one of the antibiotics. The combination of an arsenical and an antibiotic is used extensively on problem farms today.

In a preliminary Minnesota study, the addition of 0.005 or 0.01% sodium arsanilate to a mixed ration for pigs increased live weight gains about 11% (*1*). In subsequent studies with arsanilic acid fed to weanling pigs, gains have been increased in some experiments but not in others (*11, 14, 15*). In two trials with sucklings pigs arsanilic acid was as effective as chlortetracycline or procaine pencillin when added to the pig starter (*12*). All significantly increased 8-week weights, and efficiency of feed conversion was also increased. Recent studies at Indiana have shown that arsanilic acid at 90 grams per ton as well as various antibiotics and combinations of antibiotics, all fed at a level of 10 or 20 grams per ton, produced essentially equal and significantly faster gains by weanling pigs than those made by unsupplemented animals (*8–10, 16*).

From the start, the author was concerned about the matter of tissue residues and several assays were made (*11, 14, 15*). These showed that arsenic is retained in the tissues, particularly the liver and kidneys. The level retained in muscle, fat, or skin is very low and has not exceeded 0.5 μg. per gram in any of the assays. Furthermore, when arsanilic acid is withdrawn from the ration, tissue residues are promptly excreted. It was noted that tissues from pigs not fed arsanilic acid contained low levels of arsenic. This suggests that the normal environment (feed and water) of the pig contains low levels of arsenic.

In view of the low levels of arsenic found in tissues of swine fed arsanilic acid or 3-nitro-4 hydroxyphenylarsonic acid, in comparison with natural accumulation in crustaceans, it appears that concern about tissue arsenic residues is unnecessary. The recent report by Overby and Frost that about 97% of the arsenic retained in livers of pigs fed arsanilic acid is unavailable to the rat supports this view (*25*).

Arsanilic acid is toxic to pigs if fed at excessive levels. Illinois workers produced toxic symptoms in young pigs after 39 days of feeding four times the recommended level (*24*). Eight times the recommended level resulted in acute toxicosis. In Minnesota, studies with pigs weighing from 10 to 200 pounds, and which extended over a period of 6 years, there was not a single case of toxicity. Levels fed varied from one-third to approximately 2.5 times the recommended level of 90 grams per ton of feed.

In addition to the newer antibiotics, such as tylosin and oleandomycin and the anthelmintic Hygromycin B, a new group of compounds, the nitrofurans, has been added to the producers' arsenal of defense against parasites and infectious diseases. Among the nitrofurans, furazolidone has shown considerable promise for use in rations of young pigs. Data on these studies are presented in the proceedings of two symposia (*26, 27*).

Most of the studies of swine fed antibacterial agents have been made with young growing pigs. However, several studies have been made with antibiotics, arsenicals, and furazolidone added to the rations of breeding females. Harmful effects due to these drugs have not been reported in a single instance. In all cases, the drugs have been beneficial or have had no effect on reproductive performance or on the vitality of the young produced.

Experience gained up to the present time shows clearly that these drugs are not a satisfactory substitute for good management and sanitation practices. But, they are a most helpful adjunct to such practices.

Regulations concerning the proper and safe use of these drugs are necessary and desirable to ensure a wholesome food supply for our growing population. These regulations are desirable also for the protection of the livestock producer, the feed manufacturer, and the drug manufacturer. However, to provide adequate supplies of food for our rapidly expanding population (230 million anticipated by 1975), it seems important that regulations be written to accomplish these objectives without unnecessary discouragement of needed research and development.

Over-all, it appears to the writer that the first 12 years of the era of non-nutritive feed additives have been remarkably successful in terms of increased efficiency in production of safe, wholesome food products. To obtain a true picture of the tremendous contribution of industry to livestock production in the U. S. it is only necessary to visit some of the less well developed countries of the world. The contrast is impressive. Americans should be very proud of the agricultural chemical industries and their contributions to agriculture, not the least of which is their contribution to animal production, some of which was discussed above.

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Received for review October 11, 1962. Accepted April 4, 1963. Division of Agricultural and Food Chemistry, 142nd Meeting, ACS, Atlantic City, N. J., September 1962. Paper No. 1130, Miscellaneous Journal Series, Minnesota Agricultural Experiment Station, St. Paul, Minn.

FEED ADDITIVES

Are Animal Feed Additives Hazardous to Human Health?

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Recommended levels of Amprolium, zoalene, Arzene, and arsanilic acid were fed to broiler chickens for several weeks. Liver, kidney, fat, and muscle tissue of individual birds were analyzed for specific residues at regular time intervals. Contrary to the steadily increasing drug intake during the experiments, residues in the tissue remained on a constant low level—a safe indication that the drugs did not accumulate. There was no linear increase but only a slight response in the residue levels when multiple (1 to 10) drug levels were used in the feed.

Much of the confusion and uneasiness about the need for and the value of feed additives in animal nutrition today is caused by lack of understanding by the layman. Moreover, some of the information has been distorted. Efficiency in animal production has been raised to an almost unbelievable level as compared with that of 20 or 30 years ago. This leaves the layman suspicious, at least in Europe where people have not experienced as many other technical advances as have people in the United States. The layman believes that food produced with less than half the amount of feed that was needed 20 years ago will probably have only half of the nutrient value. He believes that the increasing profit in animal production is brought about by obscure and even dangerous feed additives and that the consumer pays for this by jeopardizing his health. The first approach to the supposed hazard to man of feed additives must therefore be a consideration of what actually happens in animal production today.

Economizing on Maintenance Feed

The steadily increasing feed efficiency in animal production has little to do with the use of feed additives. Most of it can be explained by our changing attitude toward animal production. Twenty years ago we were content with hens that produced an egg only every third day or 120 eggs per year. Because of better breeding and, to a certain extent, better feeding and management techniques, most hens now lay an egg every 36 hours or 250 eggs per year. This better, or much faster, performance influences feed conversion since energy cannot be lost. Just as heat energy can be transformed into mechanical energy or into electrical power, feed energy must show up in one form or another unless it is wasted in feces or urine. On the average, only 30 to 40% of the feed's net energy will show up in eggs, milk, meat, butter, or body