Chapter III

BENEFIT'S

BENEFITS

ANTI BACTERIALS

Mode of Action

The subtherapeutic uses of antibacterial for food animals include not only disease prevention but also weight promotion and feed efficiency. All antibacterial have the ability to suppress or inhibit the growth of certain micro-organisms, but their chemical composition and effectiveness against specific organisms may vary widely. Yet there is no direct correlation between chemical composition and the weight-promotion and feed-efficiency effects, so even though specific, non-antimicrobial effects can be shown for certain antibacterial, there is disagreement over how low levels of antibacterial bring about increased growth and feed efficiency.

At least three modes of actions have been postulated, and each has varying degrees of research support.

1. **A metabolic effect,** where the antibacterial directly affects the rate or pattern of the metabolic processes in the host animal.
2. **A nutrient-sparing effect,** where antibacterial reduce the dietary requirement for certain nutrients by stimulating the growth of desirable organisms that synthesize vitamins or amino acids, by depressing the organisms that compete with the host animal for nutrients, by increasing the availability of nutrients via chelation mechanisms, or by improving the absorptive capacity of the intestinal tract.
3. **A disease-control effect,** through suppression of organisms causing disease that reduce weight gain but result in no obvious symptoms of disease in the host animal,

There is much evidence that metabolic reactions in the host animal are influenced by antibacterial. For example, tetracycline affects water and nitrogen excretion in rat liver homogenates (Brody et al., 1954). But the rate of metabolism may be influenced by systemic and digestive tract infections and absorption of microbially produced toxins from the gastrointestinal tract, so the metabolic effect could be attributed to a disease-control effect. Furthermore, the metabolic effects cannot account for the growth promotion in animals fed diets supplemented with moderate levels of antibacterial in view of the nature of the animal responses, the tissue levels of antibacterial when added to the diet at growth-promotant levels, and the levels necessary to mediate such biochemical processes. And, as to be discussed shortly, a direct metabolic effect should not vary greatly with environmental conditions.

The nutrient-sparing effect has considerable research support, but it could also be classified as a type of disease-control effect. Certain intestinal organisms synthesize vitamins and amino acids that are essential to animals, and other bacteria require and compete with the host animal for these essential nutrients. Diets containing penicillin may increase the number of intestinal coliforms other than E. *coli* (Anderson et al., 1952), and these organisms may synthesize nutrients that are dietary essentials for the host animal. If a diet is deficient in a specific nutrient, it could be partially corrected by microbial synthesis.

Antibacterial may also depress the growth of organisms competing with the host animal for nutrients. The bacteria most affected by chlortetracyclines are the lactobacilli (March and Biely, 1952). The lactobacilli require amino acids in relatively similar proportional amounts as do pigs, and the levels and sources of protein that support maximum growth in pigs are also near optimum for the multiplication of lactobacilli in the intestinal tract (Kellogg et al., 1964). Those antibacterial most effective in reducing the number of these organisms in the intestinal tract are also the most effective as routine growth promotants (Kellogg et al., 1966).

Antibacterial may also improve absorption of nutrients by the host animal (Catron et al., 1953). Structurally, this seems to be related to thickness of the intestinal wall, which is thinner with rations containing antibacterials versus no antibacterial (Coates, 1953; Russoff et al., 1954, Braude et al., 1955). The thinner wall implies a potential for improved absorption and is assumed to result from the inhibition of the organisms that damage or produce toxins that damage the intestinal tissue.

The nutritive and antibacterial response relationships still appear secondary to the disease-control effect. Early in the history of antibacterial supplements to animal feeds, it was noted that the degree of response to antibacterial was inversely related to the general well-being of the experimental animals. Healthy, well-nourished animals do not respond to antibacterial supplements when housed in carefully cleaned and disinfected quarters that have not previously housed other animals (Speer et al., 1950; Catron et al., 1951; Coates et al., 1951; Hill et al, 1952).

Studies involving clean and contaminated environments illustrate that the response to antibacterial is greater in contaminated or previously used environments. For example, pigs housed in an old barn had an increased growth rate of 14.2 percent versus 7.5 percent in the new barn (table 11). The response of chicks to chlortetracycline in a new environment was a 12.6-percent improvement versus 18.2 percent for chicks from the same hatch that were reared in a previously used environment, and 1.6 percent versus 23.9 percent when penicillin was used (table 12). The relative improvements in growth rates from supplementing diets with antibacterial often are inversely related to the growth rate of the controls—i. e., the difference in antibacterial response in clean versus contaminated environments is often the result of the controls in the contaminated environment doing poorly in comparison with controls in the clean environment. Tables 13 and 14 summarize this relationship across a number of experiments.

The growth-depressing effect can also build up over time with the continued use of specific animal facilities. This effect from nonspecific infections in a chick-starting facility is summarized in table 15. Emptying, cleaning, and fumigating the facility improved performance but did not approach the level of performance of the first hatch.

Table 11. –Effect of Chlortetracycline on Weight Gains of Pigs in Different Environments

Environment and chlortetracycline fed	Daily gain: Average (9)	Daily gain: Improvement (%)	Feed efficiency[b]: Average	Feed efficiency[b]: Improvement (%)
New barn:				
Control	604	–	4.15	–
Chlortetracycline (9 g/ton)	649	7 5	3 9 2	5 5
Old barn:				
Control	604	–	4.21	–
Chlortetracycline (9 g/ton)	690	142	3 7 8	102

[a] J P Bowland 1956 Influence of environment on response of swine to antibiotic and/or Vigofac supplements *Univ Alberta Press Bull* 41 (2) 12 Alberta Canada
[b] Units of feed per unit of gain
SOURCE Hays 1978 table 7

Table 12. –Response of Chicks to Chlortetracycline (CTC) and Penicillin in New and Previously Used Environment

Environment	Treatment	4-week weight (g)	Improvement (%)
Bird et al.[a]			
New house	Control	254	–
	CTC, 10 ppm	286	12.6
Previously used house	Control	176	–
	CTC, 10 ppm	208	182
Coates et al.[b]			
Greenford Lab[c]	Control	184	–
	Penicillin	187	1.6
Reading Lab[c]	Control	155	–
	Penicillin	192	23.9

[a] H R Bird R J Lillie and J R Sizemore 1952 Environment and stimulation of chick growth by antibiotics *Poultry Sci* 31907
[b] M E Coates C D Dickinson G F Harrison S K Kon S H Cummins and W F J Cuthbertson 1951 Mode of action of antibiotics in stimulating growth of chicks *Nature* 168332
[c] Reading Lab had been previously used to house chicks but the Greenford Lab had not
SOURCE Hays 1978 table 8

Effectiveness

What is the quantitative gain in livestock production with the use of antibacterial in feed? Have they continued to be effective?

Table 13. –Relationship Between Growth Rate of Control Animals and Animals Fed Antibiotics (Pigs)

	Daily gain in weight (g)		Response to antibiotic
No. of tests	Control animals	Antibiotic-fed animals	Improvement (%)
4 . .	94	245	161
1	136	227	67
12	182	336	85
13	227	340	50
1 6	272	449	65
3 1	318	481	51
1 2	363	499	38
1 8	409	563	38
16	454	572	26
36 .	499	572	15
32	545	627	15
3 9	590	636	8
4 8	636	713	12
20	681	735	8
22	726	790	9
1	772	881	14

[a]Adapted from R Braude H D Wallace and T J Cunha 1953 The value of antibiotics in the nutrition of swine a review *Antibiotics and* Chemotherapy 3271
SOURCE Hays 1978 table 13

Table 14.–Relationship Between Growth Rate of Control Pigs and Pigs Fed a Combination of Penicillin and Streptomycin

		Improvement over controls by pigs fed antibiotics	
Daily gain in weight of controls (g)	No of comparisons	Gain in weight (0/0)	Feed efficiency (%)
91 to 182	2	220	8 2
181 to 272	3	270	4 5
272 to 363	4	204	5 6
363 to 454.	7	161	11 1
454 to 545	9	123	6 4
545 to 636	9	9 4	1 9
636 to 726.	20	5 6	4 7
726	7	3 8	1 8
Total	61		
Average Improvement. %		107	5 1

[a]Data summarized from agricultural experiment station reports 1960 to 1967 V W Hays Biological bass for the use of antibiotics m livestock production *The Use of Drugs in Animal Feeds* Proc Symp Publ 1679 p 11 (Washington DC National Academy of Sciences 1969)
SOURCE Hays 1978 fable 14

How effective are specific antibacterial compared to others? These questions are difficult to answer with any degree of precision, but the general conclusions can be made that antibacterial continue to be effective for increasing production and that some antibacterials are clearly more effective in specific food animals than in others.

There are a number of confounding factors that make an evaluation of the quantitative effect difficult. First, antibacterial now are so widely used that most of the experimental data comes from the early years of use—i.e.,

Table 15.–Effect of a "Nonspecific Infection" on Chick Growth[a]

Hatch no.	Average gain, O to 7days (g)	Relative gain (%)
1	44.2	100.0
2	42.7	96.6
3	41,5	93,9
4 .	40,1	90.7
5 . .	428	96.8
6 .	41 8	94.6
7 .	409	925
8 . .	402	91 0
9	395	89.4
1 0	352	797
Depopulation and fumigation		
11 .,	37.7	853
1 2	26,2	593
Depopulation and fumigation		
1 3	382	86.4
1 4	345	781
15 .,	283	640

[a]H M Scott 1962 The effect of a non-specific infection on chick growth Proc III Nutr Conf p 23 University of Illinois Urbana
SOURCE Hays 1978 fable 1 f

from the 1950's and early 1960's. For experiments conducted later, especially those in which field trials were used, it is often difficult to tell whether the animals used were previously fed feeds containing antibacterial. And as discussed earlier, the housing conditions of the animals also contribute to the effect of antibacterial usage; previously used facilities usually result in greater response.

Second, controlled experimental conditions often produce results less than those found in field conditions. Aside from cleaner housing in controlled experiments, often less animals are housed per facility, and runt animals usually are not included.

Third, the degree of increased production also may depend on the animal's lifecycle and the conditions of feeding. Responses may vary depending on whether it is calves or heifers/steers being fed, whether they are on high-roughage (hay) or high-energy (grain) diets, whether it is the first few weeks of life versus the whole lifespan of the animal in which feeds are supplemented with antibacterial, etc. Animals are often fed antibacterial-supplemented feed throughout their lifespan, and the effects may be attributable mostly to certain periods of that time.

Cattle. Antibacterial approved for growth promotion and feed efficiency are the tetracyclines and bacitracins. Cattle show a greater response to tetracycline on high-roughage, low-energy rations than on high-grain, high-energy diets. However, increased use of high-grain rations for the finishing of cattle increases the incidence of liver abscesses, and antibacterial are used continuously for prevention. The tetracycline are the most widely used, but tylosin and bacitracin are also approved for such use. Although related to high-grain diets, the etiology of these abscesses isunknown.

The responseto antibacterials varies with the type offeed, feedlot conditions, stress factors, and disease level of the cattle, so results are not consistent. A summary of a large number of experiments shows that tetracyclines at a level of 70 to 80 mgm daily per animal have on the average increased weight gain 6 percent and improved feed efficiency (feed per pound gained) 4 percent (Beeson, 1978). The incidence of liver abscesses from high-grain, high-energy diets is not known, but 30 percent or more of the livers could be expected to be abscessed without the use of antibacterial, andsuchabscesses also cause reductions in weight gain. Davis (1978) estimates that the use of antibacterial reduces the incidenceof liver abscesses from over 50 percent to approximately 18 percent.

Inits reporton the economic impacts ofa ban on antibacterials, USDA (1978) used the following criteria for weight gain: (1) 700-lb yearling cattle are fed for 156dayswithanti-bacterial-supplemented feed, (2) with a marketing weightof 1,050 to 1,062 lbs with antibacterials, and (3) a marketing weight of 1,038 lbs without antibacterials. This would result in a reduced marketing weightof 12 to 24 lbs per animal, or a differenceof 1.2 to 2.3 percent.

Sheep. Antibiotics are not generally used on a subtherapeutic basis but rather for treating specific diseases. Only the tetracyclines have been found to be beneficial for weightgain and feed efficiency, and they are primarily used in lambs. The major response occurs initially in the feeding period (Beeson, 1978).

Pigs. Table 16 provides rough comparisons of different antibacterial at different times in the feeding life of pigs. In the experiments summarized in the table: (1) "starter" pigs initially weighed 11 to 27 lbs, with finished weights of 30 to 110 lbs; (2) "grower-developer" pigs initially weighed 34 to 45 lbs, with finished weights of 90 to 114 lbs; and (3) "growing-finishing" pigs initially weighed 32 to 59 lbs, with finished weights of 134 to 207 lbs. Responses were generally greater in young pigs. Excluding combinations that included penicillin or tetracycline, responses equal to tetracycline or penicillin were obtained with tylosin, virginiamycin, mecadox, tylan-sulfa, bacitracin, and lincomycin. Bacitracin had a smaller feed-efficiency effect, but the others were comparable to penicillin or tetracycline.

Table 17 summarizes the effect of tetracycline over three decades for swine at similar stages in the production cycle as covered in table 16. Effectiveness has been maintained for starter pigs and diminished but still positive for more mature swine.

Poultry. Table 18 summarizes the response to different antibacterial by chickens to 4 weeks and 8 weeks from hatch. The greatest response takes place early in the growth cycle. After 8 weeks from hatch, there is only a small difference between birds fed and not fed antibacterial-supplemented feeds. Several antibacterial produce similar results as tetracycline and penicillin—namely, virginiamycin, streptomycin, erythromycin, and lincomycin.

Table 19 averages the effectiveness of tetracycline, penicillin, bacitracin, and the arsenicals for chicks up to 4 weeks of age for specific years. Effectiveness in the early phase of the growth cycle has been maintained.

Table 20 summarizes the effectiveness of selected antibacterial on egg production and matchability. Of the six antibacterial listed, tetracycline has the greatest effect, followed by bambermycin and penicillin.

The results for turkeys are generally similar to those for chickens (table 21).

Effect on Production

The effects of tetracycline, penicillin, sulfa, and nitrofurans on production of meat

Table 16.–Response of Pigs to Antibiotics

	Average daily gain (% Improvement)			*Feed/gain (% Improvement)*		
Antibiotic	*Starter*	*Grower-developer*	*Growing-finishing*	*Starter*	*Grower-developer*	*Growing-finishing*
Tetracycline,	10.84	1093	6,58	625	388	255
Penicillin	945	—	—	868	—	—
Penicillin-streptomycin	1485	—	3.87	7.42	—	1,74
Tetracycline-penicillin-sulfamethazine	2250	1746	—	8.48	—	639
Bacitracin	9,72	510	2.50	326	250	267
Tylosin	1481	10,94	464	603	420	1,47
Virginiamycin	1100	10.69	573	502	660	325
Bambermycin	000	2.45	1 89	– 099	1 17	1 17
Tylan-sulfa	1765	512	—	676	215	—
Mecadox	18.56	1513		864	6.91	—
Lincomycin	11 11	—	—	757	—	
Nitrofuran	8,00	—	1 42	233	—	O 58

SOURCE V W Hays Effectiveness of Feed Additive Usage of Antibacterial Agents in Swine and Poultry prepared for the Office of Technology Assessment U S Congress 1978 (typescript) fables 5 26 and 27

Table 17.–Continued Effectiveness of Tetracycline in Swine

	Average daily gain (% Improvement)			*Feed/gain (0/o improvement)*		
Time period	*Starter*	*Grower-developer*	*Grow/rig-finishing*	*Starter*	*Grower-developer*	*Growing-finishing*
1950-56	870	17.36	940	545	6.27	455
1957-66, .,	11 69	6.02	588	793	1 95	1 14
1967-77	1063	597	455	2.99	242	092

SOURCE V W Hays Effectiveness of Feed Additive Usage of Antibacterial Agents in Swine and Poultry prepared for the Off Ice of Technology Assessment U S Congress 1978 (typescript) tables 5 26 and 27

Table 18. –Response of Chickens to Antibiotics

	Weight gain (% Improvement)		*Feed/gain (% improvement)*	
Antibiotic	*4 weeks*	*8 weeks*	*4 weeks*	*8 weeks*
Tetracycline	733	369	509	231
Penicillin	811	293	4.46	276
Bacitracin	630	0.95	324	220
Arsenicals	494	3.44	701	315
Bambermycin	377	235	1 80	1,94
Lincomycin	9.25	448	828	3.30
Nitrofuran	– 328	1 98	– 261	1.47
Oleandomycin	501	448	225	1.78
Streptomycin	726	—	1 89	
Virginiamycin	1598		9.06	—
Erythromycin	720	—	5.05	—
Tylosin	2.82	—	1 00	—

SOURCE V W Hays Effectiveness of Feed Additive Usage of Antibacterial Agents in Swine and Poultry prepared for the Off Ice of Technology Assessment U S Congress t978 (typescript) tables 35 and 36

Table 19.–Improvement in Chick Performance: All Years Versus Since 1970 (To Approximately 4 Weeks of Age)

	Weight gain (% Improvement)		*Feed/gain (% Improvement)*	
Antibiotic	*All/years*	*Since 1970*	*All years*	*Since 1970*
Tetracycline	7.33	6.79	5.09	538
Penicillin . ,	811	1220	446	714
Bacitracin	631	7.34	324	2.75
Arsenical	4.94	471	701	4.81

SOURCE V W Hays Effectiveness of Feed Additive Usage of Antibacterial Agents in Swine and Poultry prepared for the Office of Technology Assessment U S Congress 1978 (typescript) table 37

Table 20.–Effect of Selected Antibiotics on Egg Production, Feed Per Dozen Eggs, and Matchability (in % Improvement)

Antibiotic	*Egg production*	*Feed/dozen eggs*	*Hatchability*
Tetracycline	11.91	891	147
Penicillin	5.52	504	397
Bacitracin . .	0.95	228	697
Arsenical . .	2.34	1 29	581
Bambermycin	879	11.73	249
Erythromycin	1.36	1.36	035

SOURCE V W Hays Effectiveness of Feed Additive Usage of Antibacterial Agents In Swine and Poultry prepared for the Off Ice of Technology Assessment U S Congress 1978 [typescript) fables 39

Table 21 .–Response of Turkeys to Antibiotics

Antibiotic	Weight gain (% improvement) 4 weeks	8 weeks	To market weight	Feed/gain (% improvement) 4 weeks	8 weeks	To market weight
Tetracycline .	1489	13.21	—	8.37	5.88	—
Penicillin	1531	10.24	5.73	7.87	5.62	2,64
Bacitracin	9.82	4,97	7.23	4,71	2.73	1.59
Streptomycin	814	453	—	469	192	—

SOURCE V W Hays, Effectiveness of Feed Additive Usage of Ant! bacterial Agents in Swine and Poultry, prepared for the Office of Technology Assessment U S Congress 1978 (typescript). tables 41, 42, and 43

have been estimated recently by USDA (1978) and Headley (1978). These estimates were designed primarily to estimate the effects on the income of livestock producers and on consumer prices. Both estimates were generated from the same model. However, the expected effects differ in magnitude and time trend because of the application of different assumtions (e.g., demand elasticities) to the basic model. The USDA analysis projected impacts for 5 years, and Headley's projected impacts for 10 years from the time of banning. In the USDA analysis, the initial decrease in production was expected to increase net producer revenues because of higher prices. Both production and prices of most affected species were projected to recover to approximately their baseline levels by the fifth year. Headley's analysis concluded that the banning of selected or all four antibacterial would increase aggregate farm income and increase consumer expenditures from $5.7o to $19 per capita.

In both analyses, the effects were assumed to be additive, and no consideration was given to the availability of alternative antibacterial. Both analyses mention that the estimated effects would be less if these were considered. Alternatively, the hypothesis that small producers may be forced out of business was not considered. Production decreases would be greater for the short term if this factor had been included. The long-term effects, however, might not have been affected.

The economic consequences for producers and consumers and the long-term effects postulated are obviously matters over which much disagreement exists. However, the estimates of immediate consequences of selected or complete banning of these four antibacterial can serve as first-order, rough approximations of the kinds of production increases attributable to these antibacterial. As noted above, the availability of replacement antibacterial (see tables 16, 18, 19, 20, and 21) is not considered.

USDA's analysis estimated the effects of the four antibacterial separately for beef, pork, chickens, and turkeys. It also examined the effects on egg production, dairy calves, and lambs. Headley's analysis estimated the effects on beef, pork, chickens, and turkeys from a ban on (a) tetracycline and penicillin, (b) nitrofuran and sulfa, and (c) all four antibacterial. Since both analyses assumed these effects to be additive, they were comparable. Lambs, dairy calves, and egg production are not addressed here.

The percent changes in production are comparable and both use 1976 data, but the analyses differed slightly in the measure of production. Both used ready-to-cook weights for chickens (broilers) and turkeys, but Headley used carcass weights for beef and pork, while USDA used live weights at times of slaughter. USDA's estimates are therefore adjusted to reflect carcass weights. Headley's translation from percentage to pounds differs slightly from that obtained in USDA's analysis, so the former is adjusted to coincide with the latter.

Table 22 summarizes 1976 production figures for beef, pork, broiler chickens, and tur-

Table 22.–Production of Meat Animals, 1976

Animal products	Millions of pounds
Beef[a] .	25,969
Pork[a] .	12,425
Broiler chickens[b] . . .	8,970
Turkeys[b] . .	1,960

[a]Carcass weight
[b]Ready-to-cook weight
SOURCE Extracted from USDA, 1978 and Headley, 1978

keys. Table 23 compares USDA's with Headley's estimates on the effect of banning selected antibacterial expressed in percentage decreases. The analyses are comparable for each meat product, although the effect of specific antibacterial may differ, such as for nitrofurans on chickens and turkeys,

Using USDA's separate analyses for each food animal and each antibacterial, table 24 summarizes the range of impacts for each antibacterial. Among the individual antibacterial, the greatest impact relative to total production would be through banning tetracycline; pork and chicken would be the most affected,

As mentioned earlier, USDA's and Headley's analyses differed in the estimated impact of banning these antibacterial. Though banning of the four antibacterial is estimated to decrease production by the percentages and pounds summarized in tables 23 and 24, the effect on the total market over a number of years would not be equivalent to these estimates. For both USDA's and Headley's analyses, table 25 summarizes the percent change in the quantity of meat produced or consumed, table 26 summarizes the percent change in farm prices, and table 27 summarizes changes in retail prices. Headley's analysis was for a lo-year period following a ban, while USDA's analysis extended only 5 years beyond the initial year of the hypothetical ban. The primary difference between the two analyses is that Headley consistently estimates a larger impact than USDA on decreased production, increased farm prices, and increased retail prices. Headley's estimates drop slightly after the first 2 years, but remain at a fairly constant level over the following years, while the USDA analysis has a high initial impact that diminishes over the 5-year period. Both analyses predict the minimal impact to be on beef and the maximum impact on poultry.

Table 23. –Estimated Percentage Change in Livestock Production From Banning Selected Antibiotics (First Year)

Animal product	*Projection*	*Penicillin*	*Tetracycline*	*Nitrofuran*	*Sulfa*	*Cumulative effect*
Beef	USDA	NA[b]	– O 4 to – 0.8	NA	NA	– O 4 to – O 8
	Headley	- l o	—	NA	—	– 1.0
Pork	USDA	NA	– 34 to – 15.6	NA	– 1 5to – 22	– 49 to - 178
	Headley	– 4.0	—	– 2,5	—	- 6 5
Broiler chicken	USDA	– 21 to – 3.8	– 64 to – 11.5	+ 02 to – 5.7	NA	– 8.3 to – 210
	Headley	– 2 2	—	– 120	—	– 14.2
Turkey	USDA	– 1 4 to – 28	– 2.8 to – 46	– 1 9 to – 8.7	NA	– 61 to – 161
	Headley	– 3.2	—	– 120	—	— 152

[a]Penicillin tetracycline and sulfa considered banned at subtherapeutic levels and nitrofurans considered banned at all levels
[b]Not applicable
SOURCE USDA 1978 Headley 1978

Table 24.–Estimated Decrease in Livestock Production From Banning Selected Antibiotics (First Year) (millions of pounds)

Animal product	*Total production (1976)*	*Penicillin*	*Tetracycline*	*Nitrofuran*	*Sulfa*
Beef[b]	25,969	NA	104 to 208	NA	NA
Pork[b]	12,425	NA	422 to 1,938	NA	186 to 273
Broiler chicken[c]	8.970	188 to 341	574 to 1,032	18to511	NA
Turkey[c].	1,960	27 to 55	55 to 90	37 to 171	NA

[a]Penicillin tetracycline and sulfa considered banned at subtherapeutic levels and nitrofurans considered banned at all levels
[b]Carcass weight
[c]Ready to cook weight
SOURCE Table 22 and USDA percent estimates table 23

Table 25. –Percent Change in Quantity of Meat[a] From a Ban on the Use of Selected Antibiotics

Year[c]	Beef USDA	Beef Headley	Pork USDA	Pork Headley	Broiler-chicken USDA	Broiler-chicken Headley	Turkey USDA	Turkey Headley
1.	–0,19to – 0,28	– 0.9	-4.86 to – 17,90	– 5.8	– 8.24 to – 22.70	– 15.4	– 5.98to – 1470	– 21,8
2..	– 0,04 to + 0,04	–1 1	– 3.86 to – 14.17	– 55	– 3.61 to – 9.10	– 8.9	– 4.23 to – 10.45	– 19.3
3.,	+ 0,10 to + 0,25	– 0.7	– 2.68 to – 9.86	– 5.8	– 2,27 to – 5.75	– 9.7	– 3.54 to – 8.74	– 17.7
4	+ 0.14 to + 0,24	– 0,4	– 1.40 to – 5.15	– 6.2	– 2.15 to – 5.46	– 9.1	-2.71 to – 6,66	-15,9
5	+ 0.30 to + 0,56	– 0.4	–0.84to – 3.02	–6.0	– 2.16 to – 5.50	– 7.7	– 2.62 to – 6.44	–16.7

[a]USDA's figures based on quantity of meat produced Headley's figures based on annual civilian Consumption Only first 5 years Of Headley's analysis included
[b]Penicillin tetracycline and sulfa considered banned at subtherapeutic levels and nitrofurans considered banned at all levels
[c]Year of banning equals year °
SOURCE USDA 1978 table 17 Headley, 1978 table 10

Table 26.–Percent Change in Farm Prices From a Ban on the Subtherapeutic Uses of Selected Antibiotics

Year[b]	Fed beef (liveweight price) USDA	Fed beef (liveweight price) Headley	Hogs (liveweight price) USDA	Hogs (liveweight price) Headley	Broiler-chickens (wholesale price) USDA	Broiler-chickens (wholesale price) Headley	Turkeys (liveweight price) USDA	Turkeys (liveweight price) Headley
1.	+ 4,30 to + 15,34	+ 4,7	+ 5,02 to + 16.13	+ 18.5	+ 12.99 to + 35.65	+ 51.8	+ 11.61 to + 25.64	+ 37,6
2,	+ 3,30 to + 11.27	+37	+ 3.83 to + 1297	+ 12.2	+ 6.94 to + 20.00	+ 28.4	+ 6.70to + 16.42	+ 28,4
3	+ 2.00to + 5.03	+ 4.0	+ 2.34 to + 800	+ 12.4	+ 3.09 to + 8.98	+ 38.4	+ 3,42 to + 8.88	+ 38.4
4	+ 1.00 to + 2,00	+ 2,8	+ 1,59 to + 524	+ 14.0	+ 2.67 to + 7.46	+31.3	+ 3,51 to + 8,79	+ 31.3
5..	Oto + 0.96	+ 2.3	+ 1 14 to + 353	+ 15.5	+ 2.25to + 6.04	+ 35.0	+ 3,54 to + 8,88	+ 35.0

[a]Penicillin tetracycline, and sulfa considered banned al subtherapeutic levels and nitrofurans considered banned at all levels
[b]Year of banning equals Year 0
SOURCE USDA, 1978 table 16, Headley 1978 table 11

Table 27.–Percent Change in Retail Price[a] From a Ban on the Subtherapeutic Uses of Selected Antibiotics

Year[c]	Beef USDA	Beef Headley	Pork USDA	Pork Headley	Poultry (chickens & turkey USDA	Poultry (chickens & turkey Headley
1.	+ 2.7 to + 10.4	+ 3 6	+ 4 5 to + 14.7	+ 168	+ 10.3 to + 276	+ 13,3
2,	+ 2.2 to + 7.7	+ 2.8	+ 3,5 to + 11,8	+ 11 6	+ 57 to + 15,9	+ 8,7
3	+ 1.4 to + 3.4	+ 3.2	+ 2 1 to + 7.3	+ 11 8	+ 26 to + 7.4	+ 10.3
4..	+ 0.7 to + 14	+ 2 2	+ 1.4 to + 4.8	+ 125	+ 24 to + 6.5	+ 10,0
5	0 to + 0.7	+ 1.8	+ 1 0 to + 3.2	+ 135	+ 2.2 to + 5.6	+ 9,7

[a]USDA based on consumer price index Headley based on retail price index
[b]Penicillin tetracycline and sulfa considered banned at subtherapeutic levels and nitrofurans considered banned at all levels
[c]Year of banning equals year 0
SOURCE USDA f978 table 21 Headley 1978 table 12

DIETHYLSTILBESTROL (DES)

Mode of Action

DES is a synthetic estrogen that differs in structure and metabolism from naturally occurring estrogen, but there is no evidence that natural or other synthetic estrogens differ substantially in their harmful or toxic effects (DES Report, 1978). DES has a potency 10 times that of the standard estradiol, and it is this relative potency that has made it the preferred drug for growth promotion and feed efficiency.

DES increases cellulose digestion by bovine rumen micro-organisms in vitro and in *vivo.* Stilbestrol has been shown to increase the coefficients of digestibility of cellulose in sheep from 41.9 to 48.7 percent and the crude protein digestibility from 37.5 to 44.7 percent [Brooks et al., 1954). However, the following evidence supports the hypothesis that the systematic growth-promotion and feed-efficiency effects of DES are the result of endogenous androgen (male hormone) production:

- DES accelerates protein anabolic processes in cattle and results in an increase in nitrogen retention (Clegg and Cole, 1954).

- Introduction of exogenous estrogen triggers endogenous androgen secretion as a compensatory mechanism (Gassner et al., 1951; Whitehair et al., 1953).
- Melengestrol acetate (MGA), a synthetic progesteronal steroid also used for growth promotion and feed efficiency, produces biological effects closely related to the effect of naturally occurring progesterone. The effect of naturally occurring progesterone is cyclic and permits ovulation in the nonpregnant heifer. In the pregnant heifer endogenous progesterone maintains the corpus luteum, which prevents ovulation. MGA inhibits estrus and ovulation and allows the development of mature follicles in the ovary. These persistent, mature follicles produce increased amounts of estrogen, which in turn stimulate weight gain and improve feed efficiency. The interruption of estrus is temporary, normal estrus usually returning after MGA is discontinued. MGA will not stimulate weight gain in nonovulating, spayed, or pregnant heifers, in steers, or in bulls (Beeson, 1978).
- Testosterone also can be used to promote growth and increase feed efficieny. This can be accomplished by adding testosterone to the feed or by not castrating bull calves.

Effectiveness

Dose responses from different levels of DES are not linear. Excessive levels will depress performance and lead to undesirable side effects. Steers (castrated males) and heifers (immature females) respond differently, and response varies with the type of feed (e.g., pasture vs. grain) and whether DES is given orally or under the skin. Approved oral doses of DES are 5 to 20 mg per head per day for cattle. [1] The approved implant levels for cattle are 30 or 36 mg.[2]

The effects of DES are limited to increased weight gain and feed efficiency. The effect on milk production has been inconsistent and it is not used for that purpose. Feedlots account for most use. DES increases weight gain from 15 to 19 percent and feed efficiency from 7 to 12 percent in steers, and 10 percent for weight gain and 7 percent for feed efficiency in heifers (Beeson, 1978).

In addition to DES, several other drugs are used for fattening cattle. As previously discussed, these include melengesterol acetate (MGA), monensin, zeranol, and estradiol benzoate plus testosterone or progesterone. MGA is a progesteronal steroid that is effective only in heifers. Studies covering a lo-year period (1968-77) show that it produces more weight gain and feed efficiency than either oral DES or estrogen implants. Table 28 summarizes these results. Monensin improves feed efficiency by 10 percent but has no effect on weight gain in cattle. Implants of zeranol, an estrogen-like compound, have from 30 to 50 percent of the growth-promotion and feed-efficiency effects of DES. Implants of estradiol-progesterone for steers and estradiol-testosterone for heifers have similar quantitative effects as DES. Beeson (1978) concludes that the data generally show that the quantitative effects are similar and recently reconfirmed previous research showing that estradiol-progesterone implants are equal to DES implants for improving weight gain and feed efficiency in steers (Beeson et al., 1977). Finally, the use of uncastrated young bulls will partially substitute for DES and other similar growth stimulants, improving both weight gain and feed efficiency about 10 percent (Beeson, 1978). But bulls are difficult to carry over as yearlings to be fed-out, and there is a consumer prejudice against bull meat.

Thus DES can be replaced by several already-approved drugs to promote weight gain and feed efficiency in cattle.

Effect on Production

Headley's 1978 estimates on the effect on meat production of a ban on selected antibacterials also included estimates of a DES ban. A downward shift in supply of 3.75 percent was predicted for the first year. As for antibacterial, the long-term effect was predicted as a rise in total producer income, and a rise in consumer prices of $7.75 per capita.

[1] 21 CFR 558.225.
[2] 21 CFR 522,690.

Table 28.–No Drug Versus MGA Versus DES Versus Estrogen Implant (1968 -77)[a]

Item	(47 experiments)		(36 experiments)		(12 experiments)			(experiments)		
	No drug	MGA	Oral DES	MGA	No drug	DES[b]	MGA	No drug	Estrogen implant	MGA
Daily gain lb	2.24	2.47	2.38	2.53	2.25	2,35	251	2,40	2.49	2.63
Improvement %	–	10.3	–	6.3	–	4.4	11,6	—	3.8	9.6
Feed/lb gain lb	9.95	9.30	8.85	8.44	8.78	8.59	823	755	7,34	7.14
Improvement %	–	6.5	–	4.9	–	2,2	6.3	—	28	5.4

[a]Summarizing experiments conducted by universities teed manufacturers and Commercial feedlots
[b]Percent improvement not equal to that cited in text because these were comparison experiments and were not necessarily testing the maximum response from DES
SOURCE W M Beeson Use of Drugs and Chemicals as Feed Additives 10 Increase the Productivity of Cattle and Sheep prepared for the Off Ice of Technology Assessment U S Congress 1978 (typescript) table 5

However, Headley estimated that 90 percent of fed cattle received DES or MGA. A spokesman for the National Cattlemen's Association estimates that DES and similar growth stimulants such as zeranol are used in about 80 percent of fed cattle (*CNI* Weekly Report, Oct. 5, 1978) Therefore, if Headley's figures are adjusted by eight-ninth's and ap plied to a total 1976 production of 25,969 million lbs carcass weight of beef (see table 22), DES is estimated to increase beef production by 3.33 percent, or 865 million lbs. This estimate is still high, because DES does not account for all growth-stimulant use.

As in the case of banning selected antibacterial, Headley estimated the effects of a ban on DES over a 10-year period from the time of banning. The combined response of antibacterial and DES approaches an additive effect in beef cattle meat production, but the effect on costs is not additive. When analyzed apart from a ban on the subtherapeutic use of antibacterial, the per capita consumer cost of a DES ban was estimated to be $7.75. If penicillin, tetracycline, sulfa, nitrofurans, and DES were simultaneously banned, per capita consumer costs were estimated at $21.90. If only the antibacterial were banned, per capita costs would be $19. Thus when added to an antibacterial ban, DES was estimated to add only $2.90 to per capita consumer costs, in contrast to $7.75 if only DES were banned.

Table 29 summarizes Headley's estimates of a DES ban on the percent changes in available beef supplies, farm prices, and retail prices. After 5 years, supply is slightly increased over supply before the ban, with decreases in farm prices and consumer prices. After 10 years, supplies are slightly decreased and farm prices and consumer prices increased, but none of these changes is as large as that expected in the 2 years immediately following the ban on DES.

Table 29,–Percent Change on the Supply, Farm Prices, and Retail Prices of Beef From a DES Ban

Year[a]	supply	(Farm prices, liveweight) Fed cattle	Nonfed cattle	Retail prices
1	– 3 7	+ 11.9	+ 15,2	+ 9.1
2	– 3 2	+ 8.6	+ 12.5	+ 6,7
3	– 1 5	+ 5.7	+ 7 7	+ 4.7
4	– 0.5	+ 2.1	+ 2.6	+ 1.9
5	+ 0.5	- 2 5	– 3.6	– 1,7
6	+ 0 2	– 1,4	– 2.8	– 0.8
7	– 0.9	+ 4.0	+ 4.3	+ 3.3
8	– 1,7	+ 8.1	+ 102	+ 6.5
9	– 1 9	+ 10,4	+ 13,7	+ 8.4
10	– 1,2	+ 6 9	+ 9.5	+ 5.8

[a]Year of banning equals year 0
SOURCE Headley 1978' tables 1 2 and 3