

# ANTIBIOTIC RESIDUES IN MILK AND MILK PRODUCTS—A REVIEW

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## INTRODUCTION

Antibiotic therapy has been employed by farmers and veterinarians for over a decade in the treatment of infectious diseases of dairy cattle the most common of which, undoubtedly, has been mastitis. In some instances, the drugs have been incorporated into feed as a dietary supplement. Such uses have led to the presence of antibiotic residues in milk and subsequently to industry-wide problems.

This paper will attempt to summarize available information on: (a) the presence of antibiotics in the milk of treated cows, market milk and milk products; (b) effects of some manufacturing processes on antibiotic residues in milk and milk products; (c) measures suggested for reduction of antibiotic residues in milk; and (d) the attitude of the Food and Drug Administration on the presence of antibiotics in milk and milk products. Problems created by the presence of antibiotics in milk and milk products will be discussed in another paper (46).

## ANTIBIOTICS ADMINISTERED BY INTRAMAMMARY INFUSION

### *Kinds Used*

Antibiotics, regardless of kind, are most commonly administered to mastitic animals in a solution or suspension which is infused into the infected quarter or quarters of the udder.

Penicillin, perhaps, was the first of a series of antibiotics employed in mastitis treatment. Its use was suggested in 1946 (35) and regularly since then (33,38, 40, 45). According to a recent survey (70) penicillin was found in market milk more frequently than any other antibiotic.

Other antibiotics suggested for use in the treatment of mastitis are: streptomycin (39, 51, 66) chlortetracycline (aureomycin) (23, 27, 39, 42, 43, 51), oxytetracycline (2, 51), bacitracin (6, 39), neomycin (1), subtilin (39), chloramphenicol (39) and polymyxin (70).

Combinations of antibiotics have also been suggested for the treatment of mastitis. A test of three different mixtures (68) showed that a combination of neomycin and penicillin was most effective of those tested. A mixture of neomycin, bacitracin and penicillin was second in effectiveness while a combination of neomycin and bacitracin was least effective of those tested.

A recent survey (70) indicated that antibiotics other than penicillin were found in market milk but in fewer instances. Those found included: streptomycin, bacitracin, one of the tetracyclines or a combination of these antibiotics.

A study on vehicles used to carry antibiotics for mastitis treatment has shown that penicillin diffusion into milk was greatest when the antibiotic was contained in a base composed of liquid and white petroleum (57). The addition of beeswax to the base decreased the rate of diffusion.

### *Levels Used*

The quantity of antibiotic used for an individual udder infusion varies according to: (a) the kind of antibiotic used; (b) the severity of the infection; (c) the frequency with which the antibiotic is to be administered during the course of treatment; and (d) the judgment of the person administering the antibiotic.

Considerable variation can be noted in the sizes of dosages of antibiotics suggested by various investigators for intramammary infusion in the treatment of mastitis. Suggested levels of penicillin range from less than 10,000 units (3, 4) to 300,000 units (33) with the most frequently reported dosage as 50,000 units (10, 36, 51, 56). Streptomycin dosages reported for use per infected quarter include five to 25 mg. (66), 200 mg. (30, 51) and 100 to 500 mg. (62). Single udder infusions of 200 mg. (5, 8, 9, 51) and 400 mg. (37) of chlortetracycline per quarter have been reported.

Single doses of 200 mg. of chloramphenicol (51, 54) and 200 mg. of oxytetracycline (51) per quarter have been used in mastitis therapy.

Best results were obtained with bacitracin when 100,000 units were infused into the infected quarter three times at 24 hour intervals (6).

### *Levels and Persistence in Milk from Treated Cows*

After an antibiotic is infused into the udder for the treatment of mastitis some of it may be absorbed by the tissues of the udder and appear in the blood. Concentrations of 0.08 to 0.10 ug. per ml. were found in the blood serum 12 hours after 400 mg. of chlortetracycline was infused into one quarter of the udder of a cow (37). Further evidence of absorption by tissues is provided by studies which showed that some of the antibiotic infused into the udder was

TABLE 1 — PENICILLIN RESIDUES IN MILK FROM TREATED COWS AS REPORTED BY VARIOUS AUTHORS

TREATMENT Units/Treatment	PENICILLIN RESIDUES IN MILK Time Counted From Last Treatment (Units/ml. milk)		REFERENCE
5,000-25,000-3X <sup>a</sup>	12 hrs.:	1-10	3,4
20,000-1X	12 hrs.:	3.0-4.5	38
	24 hrs.:	0.2-0.4	
25,000-1X	24 hrs.:	14.0	62
25,000-1X	12 hrs.:	2-6	48
25,000	12 hrs.:	4.1	65
25,000-1X	24 hrs.:	+ <sup>c</sup>	33
50,000	12 hrs.:	+	36
	24 hrs.:	±	
	36 hrs.:	-	
50,000-3X	72 hrs.:	>0.05	55
50,000-2X (100% of herd)	48 hrs.:	0.39-pooled milk	10
	72 hrs.:	0.14-pooled milk	
50,000-2X (50% of herd)	48 hrs.:	0.27-pooled milk	10
	72 hrs.:	0.05-pooled milk	
50,000-2X (25% of herd)	48 hrs.:	0.08-pooled milk	10
	72 hrs.:	0.02-pooled milk	
50,000-1X	8 hrs.:	+	50
75,000-1X	12 hrs.	+	44
100,000 <sup>b</sup> -1X	72 hrs.	+	73
100,000	84-144 hrs.:	+	18
3000,000 <sup>b</sup> -1X	72-192 hrs.:	+	33

<sup>a</sup>Indicates number of treatments administered at indicated level.

<sup>b</sup>Procaine penicillin in oil with aluminum monostearate was used.

<sup>c</sup>Plus (+) sign indicates presence of detectable level of penicillin but quantitative values were not given.

subsequently voided in urine by the cow (26).

The portion of infused antibiotic which is not absorbed by udder tissues is voided in milk and the quantity varies as to the individual cow. A comparison of two cows (29) showed that one excreted 2.7 per cent and another 84 per cent of the amount of antibiotic infused into the udder. The average rate of excretion was listed at about 40 per cent. Hargrove, *et al.* (25) found that 26 to 49 per cent of infused penicillin and 39 to 58 per cent of infused streptomycin was excreted in milk obtained from cows after treatment.

Other factors which influence the quantity of antibiotic in milk from treated cows (17) are the following: (a) concentration and kind of antibiotic used; (b) the carrier or vehicle employed in the antibiotic preparation; (c) the amount of milk drawn from the gland; and (d) the time interval between treatment and milking.

The results of various studies on the presence of penicillin in the milk from cows treated for mastitis by means of udder infusion are summarized in Table 1.

Considerable variation existed in treatments given animals by the different investigators, but the following generalizations can be made from a study of the results:

(a) There probably was some variation in the amount of penicillin excreted in the milk by individual cows. This is evidenced by the reported ranges of residual antibiotic in milk (3, 4, 18, 33, 38, 49) and is in agreement with the work cited above (25, 29).

(b) Highest concentrations of penicillin were found in the milk removed from the udder during the first 24 hours after treatment (36, 38).

(c) The use of higher concentrations of penicillin in treatment resulted in the presence of the antibiotic in the milk from treated cows for longer periods of

time. Dumais (18) used 100,000 units of penicillin for treatment and found detectable levels of penicillin in the milk from treated cows 84 to 144 hours later. Jackson and Bryan (33) used 300,000 units for treatment and found penicillin residues in milk from treated cows 72 to 192 hours later. In evaluating their results (33) it must be remembered that they used penicillin in an oil suspension with added aluminum monostearate to prolong the maintenance of therapeutic antibiotic levels in the udder.

(d) The duration of penicillin in the udder was influenced by its carrier. Several investigators (33, 74) found that procaine penicillin in oil with added aluminum monostearate served to extend the period during which penicillin was detected in the milk of treated cows. Experiments of Foley, *et al.* (20) further substantiate the importance of the vehicle in determining the length of time that penicillin remains in the udder. They found that when penicillin was incorporated into a mixture of mineral oil, water, lanolin, propylene glycol derivatives and a non-ionic wetting agent it lasted longest in the udder and 0.4 to 4 units were present per ml. of milk after 72 hours. When the vehicle consisted of mineral oil, water and lanolin, 1.5 to 20 units per ml. of milk were detected after 36 hours and when the vehicle was water, none was detected at that time. Hughes, *et al.* (31) reported that procaine penicillin, when infused into the udder, persisted for about 12 hours longer than did calcium penicillin.

(e) The work of Broggler, *et al.* (10) indicated that if a moderate dose of penicillin (50,000 units) was administered, a significant amount (0.14 units/ml) was detectable in milk from the treated animal 72 hours later.

Results of several investigations on residual streptomycin in the milk from udders of cows treated for mastitis by means of streptomycin infusion are summarized in Table 2. Streptomycin residues have been

TABLE 2 — STREPTOMYCIN RESIDUES IN MILK FROM TREATED UDDERS OF COWS AS REPORTED BY VARIOUS AUTHORS

TREATMENT <sup>a</sup> Mg./Treatment	STREPTOMYCIN RESIDUE IN MILK		REFERENCE
	Time Counted From Last Treatment (ug./ml. of milk)		
50-250	2 hrs.:	35.4	65
	12 hrs.:	9.7	
100-500	24 hrs.:	>20	61
200	8-72 hrs.:	+ <sup>b</sup>	50
250	8 hrs.:	+	30

<sup>a</sup>A single dose was administered for the complete treatment.

<sup>b</sup>Plus (+) sign indicates presence of detectable level of streptomycin but quantitative values were not given.

TABLE 3 — CHLORTETRACYCLINE RESIDUES IN MILK FROM TREATED UDDERS OF COWS AS REPORTED BY VARIOUS AUTHORS

TREATMENT <sup>a</sup> Mg./Treatment	CHLORTETRACYCLINE RESIDUES IN MILK		REFERENCE
	Time Counted From Last Treatment (ug./ml. of milk)		
100-200	48 hrs.:	0.64-5.1	47
200	12 hrs.:	3.5-25.0	8, 9
200	12 hrs.:	20	5
	72 hrs.:	0.66	
200	8-96 hrs.:	+ <sup>b</sup>	50
400	12 hrs.:	50-400	37
	48 hrs.:	1-10	

<sup>a</sup>A single dose was administered for the complete treatment.

<sup>b</sup>Plus (+) sign indicates presence of detectable level of chlortetracycline but quantitative values were not given.

reported as present in milk for as long as 72 hours after treatment (51). Other workers (62, 66) have reported that significant levels of streptomycin were found in milk 12 and 24 hours after the animal was treated.

Table 3 summarizes the results of various studies on residues of chlortetracycline in milk from cows treated by intramammary infusion of the antibiotic. From this table it can be seen that: (a) chlortetracycline persisted in the milk of treated cows for 96 hours (51); (b) higher levels of antibiotic were present in milk at 12 and 48 hours after treatment when a higher initial dose was used (5, 8, 9, 48); and (c) variation existed between cows in the amount of antibiotic excreted as evidenced by the ranges of antibiotic in the milk reported by three of the five authors (8, 9, 37, 48).

Barnes (2) studied the use of oxytetracycline in the treatment of bovine mastitis. When normal quarters received one infusion of 400 mg. of oxytetracycline, the antibiotic persisted in the udder for an average of 37.3 hours after treatment. The use of three treatments of 400 mg. of oxytetracycline administered at 24 hour intervals resulted in the presence of detectable amounts of the antibiotic in the udder for an average of 45.3 hours. The persistence of the drug in the udder was increased to 54 hours when three infusions of 800 mg. of oxytetracycline each were administered at 24 hour intervals. Barnes (2) further reported that: (a) variations in concentrations of residual oxytetracycline occurred in milk from different quarters of the same cow as well as from different cows; and (b) there was no consistent accumulation of the drug in the udder as shown by the concentration of residual antibiotic attained in the

milk or by the time needed for the udder to clear itself of the antibiotic after treatment.

#### ANTIBIOTICS ADMINISTERED BY OTHER METHODS AND THEIR OCCURRENCE IN MILK

Antibiotics for the treatment of mastitis are most commonly administered to dairy cows by means of intramammary infusion. These drugs, however, can be and often are used for the treatment of infectious diseases other than mastitis and then may be administered by injection. Antibiotics may also be administered to dairy cattle orally either for treatment of disease or as a feed supplement.

##### *Injected*

Two cows were injected subcutaneously with an initial dose of 5,000 units of penicillin per pound of body weight and with three later doses of 2,500 units per pound of body weight given at six hour intervals (73). The antibiotic level in the blood 15 minutes after the initial injection was eight units per ml. which decreased to 0.5 units per ml. in five hours. After each later injection, the antibiotic level per ml. rose to two, two and one units at the seventh, 14th and 19th hours respectively. The level of penicillin in milk after 15 minutes was less than 0.05 unit per ml. but after five hours had risen to 0.84 unit per ml. After the second injection, there was 0.78 unit per ml. and this value rose slightly after each subsequent injection. The milk, 30 hours after the final injection, contained 0.06 unit of penicillin per ml. Results obtained by Sadek (53) indicated that when penicillin was administered to a cow either subcutaneously or intramuscularly at the rate of 5,000 units per pound of body weight, the penicillin appeared in the milk at a level of at least 0.032 unit per ml. for 24 hours with twice a day milking. These data differ somewhat from an earlier report (27) in which it was claimed that the udder is not a major systemic outlet for penicillin in the blood.

Barnes (2) reported that oxytetracycline could not be demonstrated in milk from cows which had received intramuscular or intravenous injections of one gram doses.

##### *Fed*

Chlortetracycline was fed to cows at the rate of 390 mg. per cow per day in work reported by Martin, *et al.* (61). No detectable amount of chlortetracycline was found in the milk from any of the cows fed the antibiotic and no significant difference was noticed in numbers of bacteria present in their milk.

Different groups of dairy cows were fed 0.1, 0.5 or 1.0 mg. of chlortetracycline per pound of body weight per day by Henderson, *et al.* (28). They found the antibiotic present in detectable amounts in the blood

and milk of the cows which received either the 0.5 or one mg. level of chlortetracycline.

#### LEVEL OF RESIDUAL ANTIBIOTICS IN MARKET MILK AND MILK PRODUCTS

The quantity of antibiotic present in milk drawn from treated udders of cows has previously been discussed in this paper. When the milk from antibiotic treated animals (intramammary, orally, injected) is added to the milk of untreated animals, the antibiotic in the former is diluted by the latter and hence the quantity of antibiotic in "market milk" is different from that in the milk from treated animals. The quantity of antibiotic in a given volume of market milk will depend on: (a) the number of treated and untreated cows whose milk makes up the total; (b) the amount of milk produced by both treated and untreated cows; (c) the quantity of antibiotic used in treatment; (d) the vehicle carrying the antibiotic; and (e) the time elapsed between treatment and addition of milk from the treated animal to the market milk supply (15, 17).

##### *Market Milk*

A series of recent surveys in the United States, Canada and Great Britain have been conducted to determine the quantity of antibiotics in market milk supplies.

Perhaps one of the first reported surveys of antibiotics in market milk was conducted in New York State in 1951 (41). A total of 1,794 samples of fresh, blended and pasteurized whole milk were obtained from dairy plants or route wagons in 36 counties. Six per cent of the samples tested contained antibiotics and they were present in the range of 0.05-0.1 unit per ml. of milk. Penicillin was found most frequently and most antibiotics appeared in the milk during the spring of the year.

During the years, 1954, 1955 and 1956 three U. S. surveys of fluid milk supplies were made by the Food and Drug Administration to determine the degree of antibiotic contamination.

The first survey (70, 72) was made on both raw and pasteurized milk obtained from seven of the 16 Food and Drug Administration districts and showed that 3.2 per cent of 94 samples contained penicillin and 1.07 per cent contained bacitracin.

The second survey (72) was more extensive than the first since milks were obtained from all 16 of the Food and Drug districts. A total of 474 samples were examined and 11.6 per cent were found to contain penicillin in amounts ranging from 0.003 to 0.08 unit per ml. of milk. One sample was found to contain tetracycline.

A total of 1,706 samples of raw and pasteurized

market milk from each of the 48 states and the District of Columbia were checked for antibiotic residues in the third survey (70, 71). Penicillin, in concentrations of 0.003 to 0.55 unit per ml. of milk was found in 5.9 per cent of the samples. Seventeen other samples contained bacitracin, one of the tetracyclines or a combination of two of these drugs.

Shahani, *et al.* (60) conducted a smaller survey and found that critical concentrations of antibiotics were present in 1.3 per cent of 151 raw milk samples obtained from individual dairy herds.

A survey (50) was conducted in 1954 to determine the incidence of starter inhibitors in individual herd milks delivered to 30 dairy plants in Dane, Dodge, Columbia and Manitowoc Counties, Wisconsin. It was found that 4.3 per cent of all the milks tested contained substances which significantly reduced the activities of starter cultures. When the samples were divided on the basis of type of milk plant to which they were delivered, it was found that: (a) 5.5 per cent of the milk delivered to cheese factories contained substances which inhibited starters; (b) 3.9 per cent of the milk delivered to fluid milk plants contained inhibitory substances; and (c) 1.3 per cent of the milks delivered to condenseries contained inhibitory substances. These substances were believed to be primarily antibiotics.

The presence of antibiotics in milk has also been reported outside the United States. A Canadian survey (34) showed that starter cultures were inhibited by 7.3 per cent of 344 herd milks sampled in the summer of 1952.

Surveys were carried out in Great Britain (64) during the summer of 1951 and the winter of 1953. Results obtained in 1951 showed that 1.4 per cent of samples from herd milk in one test and 2.8 per cent in another test contained from less than 0.25 unit to 15.0 units of penicillin per ml. of milk. Work in 1953 showed that 3.2 per cent of the samples obtained from herd milk contained between 0.1 and 1.17 units of penicillin per ml. of milk.

Results from surveys conducted in Great Britain during 1954 and 1955 (7) showed: (a) there was no seasonal trend in the quantity of penicillin in milk; (b) of 143 raw milk samples taken from cheese vats, weigh tanks and transport tankers, 2.5 per cent contained 0.4 or more units of penicillin per ml. of milk and 15 per cent contained 0.01 or more units of penicillin per ml. of milk; and (c) of 575 samples taken from herd milk, 5.35 per cent contained 0.01 or more units of penicillin per ml.

#### Other Dairy Products

Information is limited on antibiotic residues in dairy products other than milk. No antibiotic resi-

dues were found in cheese, butter, dried milk and evaporated milk by the Food and Drug Administration in a survey made in 1954 (70, 72). Work reported by Hansen, *et al.* (23) showed that antibiotics were present in a dried milk made from a milk mixture which contained one per cent milk from cows whose udders were recently treated with antibiotics.

Samples of whey and dried skim milk were analyzed for the presence of residual penicillin by Hagen and Ellickson (22). They found from 0.05 to 0.10 unit of penicillin per ml. in those samples of whey which contained the antibiotic. Penicillin-positive samples of dried skim milk contained between 0.5 and 2.5 units of penicillin per gram.

#### EFFECTS OF SOME MANUFACTURING PROCESSES ON RESIDUAL ANTIBIOTICS IN MILK

After raw milk leaves the farm and arrives at the dairy plant, it is subjected to various manufacturing processes before it reaches the consumer. Most common of these processes are: (a) various heat treatments as found in pasteurization, evaporation and drying; (b) freezing; and (c) concentrating effects of drying, evaporation and separation. Since various components of milk are affected by some or all of these treatments, it is possible that antibiotics, if present, may also be affected.

#### Heat Treatments

The effect of various heat treatments on the activity of penicillin in milk is summarized in Table 4. The work of these authors indicates that penicillin in milk was quite stable to heat and that pasteurization temperatures and times commonly applied to milk and milk products were inadequate for the destruction of the antibiotic if it was present. Some discrepancies exist among the various results obtained at boiling temperatures or above. The data indicate, however, that a portion of the penicillin activity in milk survived boiling for 60 minutes and autoclaving at 15 p.s.i. steam pressure for 15 to 30 minutes.

Antibiotics other than penicillin which may be in milk are also quite heat resistant. It was reported (39, 42, 43) that chlortetracycline was not inactivated by heat treatments of 145° F. for 30 minutes, 190° F. for 60 minutes or 250° F. for 15 minutes. Pasteurization of milk which contained antibiotics did not inactivate any of the following: chlortetracycline, chloramphenicol, streptomycin and oxytetracycline (51).

Shahani (59) reported a reduction of 9.3, 14.2, 18.4, 22.5 and 25.4 per cent in the potency of chlortetracycline in milks which were pasteurized at 143° F. for 10, 20, 30, 40 and 50 minutes, respectively. The loss in potency was 13.5, 20.1, 27.1, 32.5 and 38.2 per cent when milks were pasteurized at 160° F. for the same time periods. More recently he (58) found

TABLE 4 — THE EFFECT OF VARIOUS HEAT TREATMENTS ON THE ACTIVITY OF PENICILLIN IN MILK AS REPORTED BY VARIOUS AUTHORS

Heating Temperature	Time of Exposure	RESULTS OBTAINED	REFERENCE
(°F.)	(min.)		
140	30	5-30% inactivation <sup>a</sup>	21
143	30	Not destroyed	44
145	30	Not destroyed	39
154.4	10	No effect	64
160	1705	Complete inactivation	60
185	10	No effect	64
190	60	Not destroyed	44
190	420	Complete inactivation	60
190.4	30	No effect	64
200	230	Complete inactivation	60
212	15	No effect	68
212	30	50% inactivation	68
212	60	50% inactivation	32
212	60	75% inactivation	68
239	10	Complete inactivation	64
240	15	Not destroyed	44
250	15	Not destroyed	44
250	15	73% inactivation	39
250	25	Complete inactivation	60
250	30	Slight inactivation	54

<sup>a</sup>Penicillin contained in aqueous solution instead of milk.

that pasteurization at 143° F. for 30 minutes resulted in a 30 per cent loss of oxytetracycline activity when 0.84 to 1.0 ug. of the antibiotic was present per ml. of milk. An increase in pasteurization temperature to 160° F. resulted in a 40 per cent loss in activity after 30 minutes of heating. Oxytetracycline in milk was found to be completely inactivated by heating to 160° F. for 190 minutes, 175° F. for 92 minutes and 185° F. for 60 minutes.

#### Freezing

Information about the effects of freezing on residual antibiotics in milk and milk products appears to be lacking in the literature.

#### Concentrating

The separation of milk into cream and skim milk did not result in a concentration of either penicillin or streptomycin in one of the two fractions (23). It

was found (52), however, that chlortetracycline was concentrated in the skim milk fraction of milk from treated cows. During the first four to five milkings after treatment, the antibiotic was most concentrated in the filtrate which remained after the casein and albumin were removed from the skim milk. Later milkings showed the opposite to be true.

Hansen, *et al.* (23) reported antibiotic activity in dried skim milk powder made from a mixture which contained one per cent skim milk from quarters of treated cows. Hagen and Ellickson (22) found penicillin in some samples of commercial dried skim milk. A Food and Drug Administration survey conducted in 1954 (70) showed that no antibiotic activity could be demonstrated in test samples of dried and evaporated milk.

#### SUGGESTED REMEDIAL MEASURES

Perhaps the single best way to eliminate the problem of the presence of antibiotics in milk is simply to keep the antibiotics out of the milk supplies. This means that milk from treated animals should not be included in the milk supply until it is free from antibiotic residues. The period of time required for elimination of the antibiotic from the milk varies as to: (a) kind and concentration of antibiotic used; (b) stage of lactation of the cow; (c) quantity of milk produced; and (d) severity of the infection. Various recommendations have been made on the period of time which should elapse between the treatment of a mastitic quarter with an antibiotic and the inclusion of milk from that quarter in the general milk supply. A two day waiting period has been suggested if chloramphenicol is used (15, 51) and a three day waiting period if penicillin (11, 56), streptomycin (50) or oxytetracycline (51) is used for treatment. A four day waiting period has been suggested if penicillin (38) or chlortetracycline (51) is used. Krienke (42, 43) reported that chlortetracycline in concentrations inhibitory to lactic starter cultures was present in milk from some cows, six days after treatment.

A program to acquaint farmers with problems caused by antibiotics in milk has been suggested (12). This program is, perhaps, even more necessary today and should be a joint effort by: (a) county and state extension personnel; (b) dairy plants; (c) veterinarians; (d) pharmaceutical companies; (e) agricultural magazines; and (f) radio and TV stations which carry farm programs.

Restricted sales of antibiotics for mastitis treatment might, perhaps, reduce antibiotic contamination of milk in some instances but it is more than likely that the overall picture would be little affected. It makes little difference who administers the antibiotic, farm-



er or veterinarian, if the milk from treated quarters is not withheld from the market for a sufficient period of time.

The addition of a dye to preparations used for treatment of mastitis has been suggested (70). This dye would be secreted in the milk for several days after treatment and serve to insure that milk from treated animals is not included in the general supply. The use of a combination of fat-soluble fluorescein and uranine has recently been suggested for such purposes (24). Such dyes could be detected visually in the milk for 48 hours after treatment and with ultraviolet light for 96 hours.

The Food and Drug Administration, in the summer of 1957, took two steps in an attempt to reduce quantities of penicillin residues in market milk (16). They required that: (a) packages of penicillin preparations to be used for mastitis treatment be labeled with a warning to the producer not to use the milk from an animal just treated; and (b) quantities of penicillin per individual package of preparation for mastitis treatment be limited to 100,000 units. Previously warning statements appeared only on the brochure packed with the penicillin preparation and no limitations existed on the quantity of antibiotic in the preparation.

#### ATTITUDE OF FOOD AND DRUG ADMINISTRATION

It has been suggested by Welch (67) that milk from antibiotic treated quarters of mastitic dairy cows is doubly adulterated, first by the infectious material present and secondly by the antibiotic.

The view of the Food and Drug Administration in regard to the presence of antibiotics in foods has been summarized in a policy statement issued November 30, 1955 and reported by Durbin (19) as follows:

"Direct or indirect addition of antibiotic drugs to foods for human consumption: (a) The Food and Drug Administration has received inquiries concerning the use of antibiotic drugs as food preservatives. Careful consideration has been given to this question and the conclusion has been reached that such use constitutes a public health hazard. Consumption of food so treated may cause sensitization of the consumer to such antibiotics and may result in the emergence of strains of pathogenic micro-organisms resistant to these drugs. (b) The presence of antibiotic drugs in foods intended for human consumption, or the direct or indirect addition of such drugs to such foods, may be deemed an adulteration within the meaning of section 402 of the Federal Food, Drug and Cosmetic Act. (c) This statement of policy will not bar the establishment of safe tolerances for antibiotic drugs in or on raw agricultural commodities under the provisions of section 408 of the Act, where suitable evidence of usefulness of the antibiotic drugs and of safety of residues is available."

#### SUMMARY

Antibiotics have been used in dairy cattle management for more than a decade. They are adminis-

tered to cattle by: (a) infusion into the udder for treatment of mastitis; (b) injection (intramuscular, intravenous or subcutaneous) for treatment of numerous diseases; and (c) orally for treatment of diseases or as a dietary supplement. Such uses have led to the contamination of milk and milk products with antibiotics. The Food and Drug Administration considers antibiotic-contaminated milk as adulterated. Such adulteration can be minimized by exclusion of contaminated milk from the general milk supply. The Food and Drug Administration has attempted to reduce adulteration by limiting the quantity of penicillin in each package of preparation to be used for mastitis therapy and by the requirement that a warning against the use of milk from recently treated animals be placed on the package.

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