PREVENTION OF ANTIBIOTICS IN MILK—PRESENT STATUS

D. C. GROVE


Much has already been written about the presence of antibiotics in milk—how they may get there, the public health implications of their presence, and possible ways of keeping them out of this important food. A review of some background information on this problem is in order at this time.

Antibiotics may get into milk in two ways. First, through deliberate addition to the milk as a preservative at the farm or at the milk processing plant and, secondly, by their inadvertent addition through use of antibiotic infusions in the treatment of mastitis. While we know that occasionally some unscrupulous persons may deliberately use antibiotics as milk preservatives, it is our belief that this practice is not widespread and does not constitute the main source of contamination of milk with these drugs.

Because antibiotics are effective against organisms commonly causing mastitis in dairy animals, a great number and variety of antibiotic preparations have been introduced on the market for the treatment of this disease. If these preparations are used, and the milk taken from the treated animal is not discarded for a 72-hr. period after the last treatment, then the milk may well contain antibiotics. Unfortunately, many farmers will send their milk to the processing plant within 24 or 48 hr. after treating the animal with these drugs and this, in our opinion, is the main source of contamination. A recent survey in the State of Pennsylvania revealed that 77% of the dairy farmers were not discarding milk from treated animals for a 72-hr. period.

Perhaps many farmers believe that any small amount of penicillin in their milk will be diluted sufficiently by antibiotic-free milk when it is mixed at the processing plant so that it will not be detected. The Sarcina lutea microbiological assay method for penicillin used in our laboratories is capable of detecting 0.003 unit per milliliter. Thus, 50,000 units of penicillin in 4,000 gal. of milk (approximately 0.003 unit per milliliter) can be detected.

The Food and Drug Administration has conducted three market surveys to determine the frequency with which antibiotics may be found in milk or dairy products. The first survey was made in January, 1954. A variety of dairy products were tested, including fluid milk, powdered milk, evaporated milk, ice cream, butter, and cheese. Only the fluid milk samples contained penicillin. Ninety-four samples of milk were tested for antibiotic activity. Twenty-eight of these were raw milk, 53 were pasteurized, and 13 were not identified. Three samples of the pasteurized milk contained penicillin (0.084, 0.015, and 0.001 unit per milliliter, respectively), as confirmed by the penicillinase identity test. One sample of the raw milk showed activity on bacitracin test plates; however, it was not possible to prove that the activity was due to bacitracin, since there is no identity test for small quantities of this drug. None of the unidentified samples showed antibiotic activity.

A second, more extensive, survey was conducted about a year later, in December, 1954, and January, 1955 (3). In this study, 474 samples of milk were tested not only for penicillin but also for streptomycin, bacitracin, oxytetracycline, chlortetraacyline, and tetracycline. In all samples but one, penicillin was the only antibiotic found. In this study, there were 22 samples of raw milk and none of these showed antibiotic activity. However, this may have been due to the small number tested. Of the 474 samples tested 55, or 11.6%, were positive for penicillin.

The presence of penicillin in milk, of course, constitutes an adulteration under the Federal Food, Drug, and Cosmetic Act. However, it was considered desirable to try to find out the possible public health significance of these small quantities of penicillin in milk. In an attempt to do this, the results of the second survey were sent to a number of nationally recognized experts in the fields of antibiotic therapy, pediatrics, and allergy, along with the following questions which they were requested to answer:

1. In your opinion are these amounts of antibiotics in milk dangerous for the consumer to ingest on the basis of his daily consumption?
2. Specifically, do you think these amounts may:
   (a) Sensitize the nonsensitive individual?
   (b) Cause a reaction in the exquisitely sensitive individual?
   (c) Cause emergence of resistant microorganisms?
   (d) Change the normal intestinal flora?
   (e) Change the normal oral flora?

Of the 31 replies received, the majority answered “no” or “probably no” to all questions except the one concerning the possibility of a reaction in the extremely sensitive or allergic
individual. The great majority were of the opinion that the ingestion of the amounts of penicillin found in milk could conceivably cause a reaction in the exquisitely sensitive individual.

It was believed that the first two surveys were not broad enough in their scope to get an accurate picture of the true incidence of antibiotic residues in the nation's milk supply. Therefore, a third and considerably more extensive survey was conducted and completed in February, 1956 (4). In this survey, 1,640 samples of pasteurized and 66 samples of market (raw) milk were tested for a total of 1,706. All states and the District of Columbia were included in the survey. Of the 1,706 samples tested 101, or 5.9%, contained residues of penicillin. The amounts of penicillin found ranged from 0.003 to 0.550 unit per milliliter, with an average of 0.032 unit.

As in the previous surveys, each sample was also tested quantitatively for streptomycin, bacitracin, and the tetracyclines. Of the total number of samples tested 17, or about 1%, appeared to contain one of the tetracyclines, bacitracin, or a combination of these antibiotics. Only one sample contained streptomycin. The overall percentage of positive samples of penicillin or other antibiotics was 6.9%, compared to 11.8% found in the second survey.

I have reviewed for you some of the background information on this subject. Now, the question is—what should be done about these small residues of antibiotics in milk? The obvious answer is, of course, to prevent these drugs from getting into the milk. I should now like to discuss with you what the Food and Drug Administration has done about this problem.

After the third survey, an invitation was extended to a group of nationally known physicians to form a medical advisory panel to consider the public health problems involved. A meeting was held in Washington, D.C., on September 10, 1956. Invitations to this meeting were also extended to the Associated Veterinary Laboratories, the Animal Health Institute, and the U.S. Department of Agriculture. Also present were representatives from the U.S. Public Health Service, the Food Protection Committee of the National Research Council, Milk Industry Foundation, American Medical Association, American Veterinary Medical Association, and the California Creamery Operators Association.

After an all-day session, during which the problems involved were discussed thoroughly, it was the consensus of the panel that antibiotics other than penicillin when present in milk at the rate and in the amounts found during the survey do not pose, at this time, a public health problem. It was agreed that penicillin is a highly antigenic substance and that even in the very small concentrations found in milk may cause reactions in a highly sensitive individual. At the time of the meeting no one present could cite any authentic cases of reactions due to antibodies following the drinking of milk.

Several instances were discussed where reactions were believed to be due to penicillin in milk, but in each case the milk had not been tested to verify the presence of the antibiotic. Since this time, Zimmerman (6) reported two definite dermatitis reactions due to penicillin in milk. Vickers et al. (2) reported two cases of acute dermatitis caused by penicillin in milk. Undoubtedly, there have been many other cases of dermatitis of unknown etiology that may have been caused by penicillin in milk. As more physicians become aware of this possible unsuspected source of penicillin, the number of reports in the literature will increase.

A large number of cases of severe anaphylactic shock reactions following injection, and occasionally after oral administration, of penicillin have been reported in a survey by Welch et al. (5). About 9% of these reactions resulted in death. So far, none of these severe reactions has been attributable to penicillin in milk, but the possibility remains. A case reported by Coleman and Siegel (1) will give you some idea of the extremely small amounts of penicillin that may cause a reaction in a sensitive individual. In this case, a physician had injected a previous patient with a penicillin preparation, had washed and sterilized the syringe used, and then used it to inject a hormone preparation containing no penicillin. The patient receiving the hormone injection had an anaphylactic shock reaction. By skin tests and passive transfer studies the authors were able to establish that the reaction was due to minute residues of penicillin that had remained in the syringe, even after washing and boiling. They were also able to demonstrate by intracutaneous injections of this patient's serum in a normal subject that the passively sensitized sites would respond to a penicillin dilution of 0.0005 unit/ml., or one part in two billion. Thus, the presence of penicillin in milk, even in small amounts, does present a potential danger to persons sensitive to this drug.

After our meeting with the Medical Advisory Panel, the Food and Drug Administration initiated, with the help of others, the following three-phase program in an attempt to eliminate penicillin from milk:

1. Education of the dairy farmer. The Extension Service of the Department of Agriculture has begun an intensive educational program directed to the farmer, to emphasize the importance of the prevention of mastitis through good sanitary and managerial practices. This may reduce the incidence of mastitis through a corresponding decrease in the use of drugs for treatment. The reasons why the dairy farmer should discard milk from treated animals for a 72-hr. period after the last treatment have also been explained in these educa-
tional talks. The National Milk Producers Federation, which we understand has a membership of some 500,000 dairy farmers, is also actively engaged in this program.

2. **Warning statement.** Prior to July 29, 1957, the statement warning the dairy farmer to discard milk for 72 hr. after the last treatment was not required to appear on the immediate label of each container of mastitis preparations. This statement usually appeared on the circular which accompanied the drug, which contained directions for use. The warning statement is now required on the label of each container. We believe this will make it more likely to be read and understood by the user.

3. **Limitation of quantity of penicillin permitted in mastitis preparations for intramammary use.** Since August 12, 1957, the maximum quantity of penicillin that may be contained in each dose of an antibiotic intended for intramammary infusion has been 100,000 units. Prior to that time, some preparations contained up to 1,500,000 units. It is our belief that 100,000 units of penicillin per dose is adequate to treat penicillin-sensitive organisms causing mastitis. Furthermore, when the smaller dose is used, the drug disappears more quickly from the milk.

We hope that the program now in effect, augmented by other educational programs conducted for the dairy farmers by the various city and state health departments, milk processing plants, practicing veterinarians, and agricultural schools will eliminate penicillin from our milk supply. We intend to conduct a limited survey this summer and a large-scale survey this fall to check the effectiveness of this program. If penicillin continues to appear in milk, more drastic steps will have to be considered, including the prohibition of its use in mastitis preparations. We sincerely hope that the cooperative effort of all interested parties will bring about the desired solution before such drastic considerations become necessary.

**REFERENCES**


