PROBLEMS CREATED BY THE PRESENCE OF ANTIBIOTICS IN MILK AND MILK PRODUCTS—A REVIEW

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Introduction

The presence of antibiotics in milk and milk products has produced problems of concern to the dairy industry and to public health officials. This paper will attempt to summarize information on that subject. Information has previously been summarized (*33*) on levels of antibiotics in milk and milk products, effects of dairy manufacturing processes on antibiotics and the attitude of the Food and Drug Administration on antibiotic-contaminated milk supplies.

Dairy Industry Problems

The largest single problem of the dairy industry created by the presence of antibiotics in fluid milk is slow or complete absence of acid production by bacterial starter cultures employed in the manufacture of a variety of products. Other problems may be encountered in the ripening of cheese or in the use of dye reduction tests to determine the quality of milk which contains antibiotics.

Serious outbreaks of yeast mastitis have been noted in cows previously treated with penicillin (*19*). The treatment of such infections with heretofore unused antibiotics or drugs may bring about problems for the dairy industry different from those encountered thus far.

Starters

The results of studies on concentrations of different antibiotics needed for the partial or complete inhibition of activity by various pure or mixed starter cultures are tabulated in Tables 1, 2, 3, and 4.

Results obtained by various workers on levels of penicillin needed in milk for the partial or complete inhibition of mixed or pure starter cultures are summarized in Table 1. The following conclusions can be drawn from the data: (*a*) *Streptococcus lactis* and *S. cremoris* appeared to be more resistant to penicillin than *S. thermophilus;* (*b*) of all the pure cultures listed, *S. thermophilus* seemed to be the least resistant to penicillin; (*c*) the lactic streptococci were partially inhibited by the presence of 0.0017 to 0.1 unit of penicillin per ml. of milk and completely inhibited by 0.025 to 1.0 unit of penicillin per ml. of milk; (*d*) *Streptococcus durans* was inhibited completely by the presence of 0.10 unit of penicillin per ml.; (*e*) the lactobacilli appeared to be more resistant to penicillin than the streptococci; (*f*) *Lactobacillus lactis* and *L. helveticus* appeared to be less resistant to penicillin than most strains of *L. casei, L. acidophilus* and *L. bulgaricus;* (*g*) the lactobacilli appeared to be partially inhibited by the presence of 0.03 to 0.6 unit of penicillin per ml. of milk and completely inhibited by 0.05 to 5.0 units of penicillin per ml. of milk; (*h*) there was considerable variation in penicillin resistance between strains of the same species of *Lactobacillus;* (*i*) a micrococcus was completely inhibited by the presence of 0.05 unit of penicillin per ml. of milk; (*j*) *Propionibacterium shermanii* was less resistant to penicillin than the lactobacilli and *Leuconostoc citrovorum* appeared to be approximately equal to the lactobacilli in resistance; and (*k*) resistance of mixed cultures to penicillin ranged between that of the streptococci and the lactobacilli.

Changes in morphology of lactic streptococci may be associated with penicillin inhibition. Involution forms of *S. lactis and S. cremoris* have appeared in the presence of the antibiotic concentrations (*21*). Antibiotic levels which caused nearly complete inhibition of the cultures, produced marked increases in the length of the cells. The cocci emerged as elongated rods, apparently because of difficulty in cell division. Similar morphological changes were also observed when *S. lactis* and *S. cremoris* were grown in milk which contained 0.30 unit of penicillin per ml. (*16*). Streptococci in yogurt appeared swollen and existed in longer chains when 0.1 unit per ml. of penicillin was present (*16*). In recent work, Baughman and Nelson (*3*) found that cells of *S. thermophilus* tended to form long chains in concentrations of penicillin as low as 0.03 unit per ml. The gram-positive staining reaction of *S. lactis* and *S. thermophilus* was reversed by exposure to various low concentrations of penicillin. Several tests for the presence of penicillin in milk have been based on the lack of resistance to the antibiotic on the part of the lactic streptococci and rods (*32, 36, 44, 46*).

Data reported by various workers on levels of chlortetracycline needed in milk for the partial or

TABLE 1 — THE CONCENTRATION OF PENICILLIN NEEDED IN MILK TO INHIBIT VARIOUS PURE AND MIXED CULTURES AS REPORTED BY DIFFERENT AUTHORS

Pure or Mixed Culture	Level of Antibiotic Needed for Inhibition		Reference
	Partial	Complete	
	(units/ml.)	(units/ml.)	
Streptococcus cremoris	0.05-0.10	0.5	28
Streptococcus cremoris	0.05-0.10		22
Streptococcus cremoris		0.1-1.0	27
Streptococcus cremoris	0.07	0.15	22
Streptococcus cremoris		0.1-0.25	34
Streptococcus durans		0.10	41
Streptococcus lactis		0.1-1.0	27
Streptococcus lactis		0.25-0.50	34
Streptococcus lactis		0.05	41
Streptococcus thermophilus	0.0017-0.17		35
Streptococcus thermophilus		0.025-0.05	34
Streptococcus thermophilus	0.01		17
Streptococcus thermophilus-H		0.05	41
Streptococcus thermophilus-T		0.05	41
Lactobacillus acidophilus	0.3-0.6		51
Lactobacillus bulgaricus	0.3-0.6		51
Lactobacillus bulgaricus-488		0.10	41
Lactobacillus bulgaricus-444		0.10	41
Lactobacillus bulgaricus-R		0.30	41
Lactobacillus bulgaricus-V71		0.20	41
Lactobacillus bulgaricus-V12		0.05	41
Lactobacillus casei	0.3-0.6	2.0	51
Lactobacillus casei		1.0-5.0	34
Lactobacillus casei		0.05	39
Lactobacillus helveticus		0.1-1.0	27
Lactobacillus helveticus	>0.3		2
Lactobacillus helveticus		0.25-0.50	34
Lactobacillus lactis-A		0.05	41
Lactobacillus lactis-B		0.05	41
Lactobacillus lactis-V104		0.05	41
Lactobacillus lactis-431		0.30	41
Lactobacillus lactis-kw		0.30	41
Lactobacillus lactis-V109		0.05	41
Lactobacillus lactis-MYC		0.05	41
Leuconostoc citrovorum	0.4-0.8	1.6->1.6	28
Micrococcus-8406		0.05	41
Propionibacterium shermanii	0.1		17
S. lactis + *S. cremoris*	0.012-0.096		5
S. lactis + *L. citrovorum*		0.1	18
S. lactis + *L. dextranicum*		0.1	18
S. lactis + *L. bulgaricus*		1.00	41
Butter culture	0.017-0.17		35
Buttermilk starter	0.1		30
Cheese starters (2)[a]	0.05-0.16	0.32	45
Cheese starters (6)[a]	0.05-0.10	0.50	28
Cheese starter	>0.10	>0.10	24
Cheese starter	0.20		50
Cheese starter	0.10		14
Cheese starter		0.02-10.0	38
Cheese starter	0.10		42
Cheese starter	0.10-0.20		4

[a]Two and six different cultures tested respectively.

TABLE 2 — THE CONCENTRATION OF CHLORTETRACYCLINE NEEDED IN MILK TO INHIBIT VARIOUS PURE AND MIXED CULTURES AS REPORTED BY DIFFERENT AUTHORS

Pure or Mixed Cultures	Level of Antibiotic Needed for Inhibition		Reference
	Partial	Complete	
	(micrograms /ml.)	(micrograms /ml.)	
Streptococcus durans		0.20	*41*
Streptococcus lactis		0.05	*41*
Streptococcus thermophilus	0.001-0.01		*35*
Streptococcus thermophilus-H		0.3	*41*
Streptococcus thermophilus-T		0.3	*41*
Lactobacillus bulgaricus-488		3.0	*41*
Lactobacillus bulgaricus-444		5.0	*41*
Lactobacillus bulgaricus-R		3.0	*41*
Lactobacillus bulgaricus-V71		2.0	*41*
Lactobacillus bulgaricus-V12		0.3	*41*
Lactobacillus casei		0.05	*41*
Lactobacillus lactis-A		1.0	*41*
Lactobacillus lactis-B		1.0	*41*
Lactobacillus lactis-V104		3.0	*41*
Lactobacillus lactis-431		0.5	*41*
Lactobacillus lactis-kw		1.0	*41*
Lactobacillus lactis-V109		0.3	*41*
Lactobacillus lactis-MYC		1.0	*41*
S. lactis + L. citrovorum		10.0	*18*
S. lactis + L. dextranicum		10.0	*18*
L. lactis + L. bulgaricus		10.0	*41*
Butter culture	0.01-0.1		*35*
Cheese starter	0.2		*24*
Cheese starter		0.5	*30, 31*
Cheese starter		0.25	*6, 7*
Cheese starter		1.0	*26*
Cheese starter	0.25		*42*
Cheese starter	0.02		*37*

complete inhibition of mixed or pure starter cultures are summarized in Table 2. The results appear to indicate the following: (*a*) the streptococci, in general, were less resistant to chlortetracycline than the lactobacilli; (*b*) variations in degree of resistance existed between different strains of the same species of *Lactobacillus;* (*c*) mixed starter cultures were somewhat more resistant to chlortetracycline than the streptococci and somewhat less than some of the lactobacilli.

TABLE 3 — THE CONCENTRATION OF STREPTOMYCIN NEEDED IN MILK TO INHIBIT VARIOUS PURE AND MIXED CULTURES AS REPORTED BY DIFFERENT AUTHORS

Pure or Mixed Culture	Level of Antibiotic Needed for Inhibition		Reference
	Partial	Complete	
	(micrograms /ml.)	(micrograms /ml.)	
Streptococcus thermophilus	0.05-0.10		*35*
Streptococcus thermophilus	5.0		*17*
Propionibacterium shermanii	5.0		*17*
S. lactis + L. citrovorum		10.0	*18*
S. lactis + L. dextranicum		10.0	*18*
Butter culture	0.1-0.2		*35*
Cheese starter	0.04		*37*

Table 3 presents a summary of data reported by various workers on concentrations of streptomycin needed in milk for the partial or complete inhibition of mixed or pure starter cultures. The data seem to indicate the following: (*a*) considerable variation in resistance of cultures existed according to the limited available data; and (*b*) mixed starter cultures studied

TABLE 4 — THE CONCENTRATION OF DIFFERENT ANTIBIOTICS NEEDED IN MILK TO INHIBIT VARIOUS PURE AND MIXED CULTURES AS REPORTED BY DIFFERENT AUTHORS

Antibiotic	Pure or Mixed Culture	Level of Antibiotic Needed For Partial Inhibition[a]	Reference
		(micrograms /ml.)	
Bacitracin	*Streptococcus thermophilus*	0.05-0.10	*35*
	Butter culture	0.10-0.20	*35*
Chloramphenicol	*Streptococcus thermophilus*	0.05-0.10	*35*
	Butter culture	0.10-0.20	*35*
	Cheese starter	0.02	*37*
Neomycin	*Streptococcus thermophilus*	0.10-1.0	*35*
	Butter culture	0.10-1.0	*35*
Oxytetracycline	Cheese starter	0.01	*37*
Tetracycline	*Streptococcus thermophilus*	0.001-0.01	*35*
	Butter culture	0.01-0.1	*35*
Tyrothricin	Cheese starter	1000.0	*42*

[a]No data given on concentration of antibiotic needed for complete inhibition.

appeared to be more susceptible to streptomycin than pure cultures.

Limited data on the inhibitory effects of various other antibiotics on pure and mixed starter cultures are summarized in Table 4. From the data presented it is evident that: (*a*) *S. thermophilus* was partially inhibited by the presence in milk of 0.05 to 0.10 ug. per ml. of bacitracin or chloramphenicol, by 0.1 to 1.0 ug. per ml. of neomycin and by 0.001 to 0.01 ug. per ml. of tetracycline; (*b*) butter cultures were partially inhibited by the presence in milk of 0.10 to 0.20 ug. per ml. of bacitracin or chloramphenicol, 0.10 to 1.0 ug. per ml. of neomycin or 0.01 to 0.1 ug. per ml. of tetracycline; and (*c*) cheese starters were partially inhibited by the presence in milk of 0.02 ug. per ml. of chloramphenicol, 0.01 ug. per ml. of oxytetracycline or 1000 ug. per ml. of tyrothricin.

Cheese

Cheese can sometimes be made from milk which contains antibiotics by: (*a*) increasing the size of the inoculum; (*b*) lengthening the period required for acid production; or (*c*) increasing the amount of salt added.

Whitehead and Lane (*50*) made a series of cheddar cheeses from milks with different levels of residual penicillin. When 0.05 unit of penicillin per ml. of milk was present, there was an average delay of 25 minutes in acid production during manufacture but no differences in composition or taste were noted in the ripened cheese. The presence of 0.10 unit of penicillin per ml. of milk resulted in a delay of 34 minutes in acid production and yielded ripened cheeses some of which had a low acidity (pH above 5.0), pasty body, and fermented or yeasty aroma. When 0.15 unit of penicillin per ml. was present, the delay in acid production was at least 35 minutes and in seven out of eight instances it was impossible to reach a normal final acid content in a reasonable length of time. The ripened cheeses all had a high pH value, pasty body and yeasty flavor. The presence of 0.2 unit of penicillin per ml. of milk resulted in slow acid production before and after salting. No cheeses were made and allowed to ripen. When 0.5 unit of penicillin per ml. of milk was present, acid development ceased in the milk soon after the rennet was added.

Wessner (*49*) reported that acid production by a mixed culture (*Streptococcus lactis*, *S. cremoris* and *S. diacetilactis*) during the manufacture of cheese was retarded 0, 2, 3.5, 9, 15, 19.5, 31.5 and 38 minutes by the presence in the milk of 0.01, 0.02, 0.03, 0.05, 0.08, 0.10, 0.15, and 0.20 unit of penicillin per ml., respectively. Cheeses were examined when they were three months old and the following observations were made: (*a*) cheeses made from milk which contained 0.02 unit of penicillin per ml. were discolored, cracked, strongly putrified and had a pH value of six; (*b*) a reduction in penicillin content to 0.12 unit per ml. of milk yielded cheeses similar to those just described; (*c*) milk with 0.08 unit of penicillin per ml. yielded cheese similar in appearance and odor to that described in (*a*) above but with a pH value of 5.8; (*d*) cheeses made from milk with 0.04 unit of penicillin per ml. showed signs of a butyric acid fermentation, had a pH value of 5.6 and some were cracked and slightly putrid; (*e*) a butyric acid fermentation and a pH value of 5.4 were noted in cheeses made from milk which contained 0.02 unit per ml. of penicillin; and (*f*) cheese that appeared normal and had a pH value of 5.3 was made from milk with 0.005 unit of penicillin per ml.

Hunter (*22*) reported that cheddar cheeses made from milk which contained from 0.07 to 0.10 unit per ml. of penicillin were slightly sweet, weak and lumpy or curdy at 14 days. After three months, the cheeses had a weak, pasty body and flavors varied from "slightly off" to rancid and fermented.

Kästli (*27*) noted that coliform organisms were able to grow in curd from milk which contained penicillin and their growth resulted in the spoilage of a batch of cheese while in the press.

The presence of chlortetracycline in milk (more than 0.25 ug. per ml.) resulted in retarded acid development, slow flavor development and a weak and pasty body in cheddar cheese according to Bradfield, *et al.* (*8*). They also found it impossible to make cottage cheese from such milk.

Quality Tests

The length of time needed for the reduction of the dye in the methylene blue test for milk quality was increased when concentrations of 0.1 to 0.5 unit of penicillin per ml. of milk was present as shown by results of Hunter (*20*). The reduction time was also prolonged in storage milks which contained antibiotics.

Johns and Desmaris (*25*) found that concentrations of 0.05 and 0.5 unit of penicillin per ml. of milk caused an appreciable delay in the reduction time of methylene blue when added to such milk. The retarding influence was found greatest when the dye reduction time was longest and hence the resazurin test (3 hour completion time) was less affected than the methylene blue test.

The reliability of the phosphatase test was not impaired by the presence of antibiotics in milk (*12*).

Remedial Measures

Several remedial measures to overcome dairy plant problems produced by residual antibiotics have been proposed. The addition of penicillinase, an enzyme which inactivates penicillin, to milk prior to inoculation with starter cultures has been suggested (*2, 9, 11, 13, 23, 28, 29, 45*). Recommended rates for addition of penicillinase to milk are: (*a*) 0.02 mg. per 100 ml. of milk containing a total of five to ten units of penicillin (*28, 29*); or (*b*) 0.36 part penicillinase for one part of penicillin in milk (*11*).

The use of a heavy inoculum of starter has been suggested by Claybaugh and Nelson (*13*) as another method for use to attempt to nullify effects of antibiotics in milk from which fermented products are to be made.

The third method suggested to overcome the antibiotic problem is the development and use of starter cultures which are resistant to antibiotics. Katznelson and Hood (*28*) reported the development of a penicillin resistant starter which was able to coagulate milk in the presence of three units per ml. of penicillin and which retained its resistance through 20 passages in the absence of penicillin. Success in developing penicillin resistant starters was also reported by Trembath (*45*). Auclair (*2*) found it possible to slightly increase the resistance to penicillin of *Lactobacillus helveticus.*

Shahani and Harper (*40, 41*) found that oxytetracycline-resistant cultures of *Streptococcus lactis* coagulated milk in 12 to 14 hours while sensitive cultures did so in six to eight hours. The addition of glucose-1-phosphate; fructose-1, 6-diphosphate; coenzyme 1 or lactase to the milk resulted in an appreciable acceleration of acid production by the resistant strains. No appreciable increase in acid production was noted when phosphorylase, aldolase or adenosine triphosphate (ATP) was added to the milk. It was believed that resistant strains failed to form sugar-phosphate esters during the early stages of incubation and hence failed to produce substantial quantities of lactic acid. Acid production appeared to be directly related to the phosphorylation system of the organisms.

It was further reported (*41*) that four cultures of *Lactobacillus lactis* became resistant to 10 p.p.m. of tetracycline after passage through milks which contained increasing concentrations of this antibiotic. Starter cultures which were carried in milk media with a high surface to depth ratio tended to develop a natural tolerance to higher concentrations of various antibiotics (*41*).

Removal of penicillin from milk by washing the fat fraction proved impractical (9) and addition of cystein (*28*) failed to inactivate penicillin present in raw milk.

PUBLIC HEALTH PROBLEMS

The public health problems which may be associated with the presence of antibiotic residues in milk and milk products are as follows: (*a*) exposure of the consumer to antibiotic resistant udder pathogens which may be present in unpasteurized milk products; (*b*) development or aggravation of antibiotic hypersensitivity in consumers; (*c*) alteration of the intestinal flora of consumers and thereby bring about a reduction in vitamin synthesis; and (*d*) alteration of the intestinal flora of consumers to permit the growth and establishment of antibiotic resistant strains of pathogenic microorganisms.

Cheese made from milk obtained from cows previously treated for mastitis by means of penicillin and streptomycin has been incriminated as the source of antibiotic resistant micorococci and streptococci which caused infections in consumers (*1*).

The number of coliform bacteria in the intestinal tract of persons was markedly reduced by the ingestion of 500 ml. of milk which contained either 0.1 mg. per ml. of streptomycin or 0.25 ug. per ml. of chlortetracycline, acording to Stoltz and Hankinson (*43*). The authors have postulated that the antibiotic induced reduction of intestinal organisms would result in the reduction of vitamin synthesis in the intestinal tract.

Broad spectrum antibiotics (the tetracyclines), neomycin, streptomycin (orally), bacitracin and polymyxin are poor sensitizers and hence their presence in milk is of minor concern to hypersensitive or potentially hypersensitive consumers (*48*). The presence of pencillin in milk, however, is of major concern in regard to the hypersensitivity of the consumer (*10, 48*). It was further reported (*48*) that in a survey of 30 authorities in the fields of antibiotic therapy, allergy and pediatrics, the majority felt that concentrations of penicillin found in market milk might cause hypersensitive reactions in "exquisitely sensitive" persons. These same authorities also expressed the views that concentrations of antibiotics found in fluid milk were unlikely to modify the oral or intestinal flora, cause the emergence of resistant strains of pathogenic bacteria or provoke sensitization in an insensitive consumer. Recently allergic dermatitis was noted in patients who had consumed milk which was contaminated with penicillin (*15, 47*).

SUMMARY

The presence of antibiotics in milk has created problems of importance to the dairy industry and to public health officials. Problems of the dairy industry include failures: (*a*) in the curdling of milk and in natural cheese ripening during its manufacture; (*b*) in acid and flavor production during the manufacture of buttermilk and similar products; (*c*) of starter culture growth when propagated in reconstituted skim

milk; and (*d*) of some quality control tests to give valid results. Suggested remedial measures for these problems include: (*a*) development of antibiotic-resistant starter cultures; and (*b*) addition of penicillinase to neutralize penicillin in milk.

Public health hazards associated with consumption of antibiotic-contaminated milk and milk products include: (*a*) allergic responses; (*b*) changes in intestinal function; and (*c*) development of antibiotic-resistant pathogenic bacteria.

REFERENCES

1. Anonymous. Antibiotic-resistant Organisms in Cheese. J. Am. Med. Assoc. **159**: 1788. 1955.

2. Auclair, J. Action inhibitric de la penicilline sur les lactobacilles utilises dans la Fabrication du Gruyere. Lait **31**: 121-133. 1952.

3. Baughman, R. W. and Nelson, F. E. Effect of Penicillin upon the Morpology and Gram-staining Characteristics of *Streptococcus lactis* and *Streptococcus thermophilus*. J. Dairy Sci. **41**: 706. 1958.

4. Baumgarntner, H. Die Penicillinbehandlung des Euters. Schweiz. Arch. Tierheilk. **89**: 215-240. 1947.

5. Berridege, N. J. Penicillin in Milk. III. The Effect of Low Concentrations of Penicillin on the Rate of Acid Production by Starter Cultures. J. Dairy Research **23**: 348-354. 1956.

6. Bradfield, A. Effect of Mastitis Curatives on Cheese Making. Proc. 28th Ed. Conf. Vermont Dairy Plant Operators and Milk Distributors. pp. 23-25. 1949.

7. Bradfield, A. The Effect of Mastitis Curatives on Cheese Making. Can. J. Comp. Med. Vet. Sci. **14**: 127. 1950.

8. Bradfield, A., Resi, L. A. and Johnstone, D. B. The Presence of Aureomycin in Milk and its Effect on Cheese Making and Starter Activity. J. Dairy Sci. **35**: 51-58. 1952.

9. Broggler, H. Juncher, H. O. and Magnusson, I. Nogle undersøglser over anvendeligheden af penicillinholdig maelk. Maanedsskr. Dyrlaeger **62**: 217-223. 1951.

10. Bryan, C. S. Problems Created for the Dairy Industry by Antibiotic Mastitis Treatments. J. Milk and Food Tech. **14**: 161-162. 1951.

11. Chapman, H. R. The Addition of Penicillinase to Milk of Cows Receiving Penicillin. Dairy Ind. **21**: 970-971. 1956.

12. Churchill, E. S., Drury, A. R., Lewis, B. D., Frank, C. L. and Bryan, C. S. A Report on the Modified Phosphatase Method of Detecting Antibiotic Substances in Milk. Milk Plant Monthly **40** (4): 28-31. 1951.

13. Claybaugh, G. A. and Nelson, F. E. The Effect of Antibiotics in Milk: A Review. J. Milk and Food Tech. **14**: 155-160. 1951.

14. Dumais, R. L'effect nuisible de la penicilline dans ce lait sur les ferments lactiques et le fromage Cheddar. Quebec Lait **10**: 14-16. 1951.

15. Erskine, D. Dermatitis caused by Penicillin in Milk. Lancet **1**: 431-432. 1958.

16. Galesloot, T. E. Invloed van penicilline op de morfologie van yoghurt-en zuurselbacterien. Een methods on snel te kunnen vaststellen of penicilline de waarschijnlijke oorzaak is geweest van een gerende zuurvorming in yoghurt en zuursel. Ned. Milk Zuivetijdschr. **10**: 64-70. 1956.

17. Hargrove, R. E., Walter, H. E., Malkames, J. P. Jr., and Maskell, K. J. The Effect of Penicillin and Streptomycin on Swiss Cheese Starters. J. Dairy Sci. **33**: 401. 1950.

18. Harmon, L. G. Antibiotics in Milk. Texas J. Sci. **3**: 167-179. 1951.

19. Havmand, H. C., Jepsen, A. and Overby, A. J. Two Years of Collective Mastitis Campaign in Cooperative Dairies with Practical Control of Penicillin-induced Starter Failures by Use of Penicillinase or Penicillin Resistant Starter. Roy. Vet. and Agr. Coll., Copenhagen, Den. Bull. 47. 1955.

20. Hunter, G. J. E. A note on the Effect of Penicillin in the Reductase Test for Milk Quality. J. Dairy Research **16**: 149-151. 1949.

21. Hunter, G. J. E. The Effect of Penicillin on Lactic Streptococci. J. Dairy Research **16**: 39-45. 1949.

22. Hunter, G. J. E. The Effect of Penicillin in Milk on the Manufacture of Cheddar Cheese. J. Dairy Research **16**: 235-241. 1949.

23. Jepsen, A. and Overby, A. J. The Disturbing Effect of Penicillin Milk in the Dairy Industry and Proposals of Some Technical Methods for the Elimination of Failures. Studies on the Inactivation of Penicillin by Means of Penicillinase. Ned. Melk Zuitveltijdschr. **5**: 157-185. 1951.

24. Johns, C. K. Differences in Sensitivity of Lactic Starters to Antibiotics. J. Dairy Sci. **36**: 1241-1247. 1953.

25. Johns, C. K. and Desmaris, J. G. The Effect of Residual Penicillin in Milk on the Dye Reduction Tests for Quality. Can. J. Agr. Sci. **33**: 91-97. 1953.

26. Johnstone, D. B. Effect of Aureomycin Upon Acid Production by Cheese Starters. Bacteriol. Proc. p. 26. 1950.

27. Kästli P. Störungen in der Milchverarbeitung durch die Mastitis - behandlung mit Penicillin. Schweiz. Arch. Tierheilk. **90**: 685-695. 1948.

28. Katznelson, H. and Hood, E. G. Influence of Penicillin and other Antibiotics on Lactic Streptococci in Starter Cultures Used in Cheddar Cheese Making. J. Dairy Sci. **32**: 961-968. 1949.

29. Katznelson, H. and Hood, E. G. Penicillin in Relation to Acid Production in Milk by Starter Cultures Used in Cheddar Cheese Making. Science **109**: 490-491. 1949.

30. Krienke, W. A. Drugs, Mastitis and Acid Starters. Am. Milk Rev. 12 (6): 54, 56. 1950.

31. Krienke, W. A. Effects of Various Drugs in Milk from Mastitis-Treated Cows. Southern Dairy Prod. J. **47** (5): 37, 132-134. 1950.

32. Lemoigne, M. Sanchez, G. and Girard, H. Caracterisation de la pencilline et de la streptomycine dans le lait. Lait **33**: 15-16. 1953.

33. Marth, E. H. and Ellickson, B. E. Antibiotic Residues in Milk and Milk Products. J. Milk and Food Tech., **22**: 3, 1959.

34. Meewes, K. H. and Paslawski, S. Untersuchungen über den Einfluss keimhemmender Substanzen auf Milchsäurebakterien. Kiel. milchwirtsch. Forschungsber. **3**: 543-549. 1951.

35. Moeller-Madsen. A. and Bendtsen, G. Nogle antibiotica's haemmende virkning paa almindelige syrevaekker, *Streptococcus thermophilus og Thermobacterium helveticum* Danish Gov't. Research Institute on Dairy Ind. Bull. 105, p. 72. 1956.

36. Neal, C. E. and Calbert, H. E. The Use of 2, 3, 5-Triphenyltetrazolium Chloride as a Test for Antibiotic Substances in Milk. J. Dairy Sci. **38**: 629-633. 1955.

37. Overby, A. The Effect of Various Antibiotics in Milk Following Intramammary Infusion. Nord. Veterinärmed. **4**: 993-1004. 1952.

38. Scott, R. Destruction of Starter Activity by Penicillin. Dairy Ind. **15**: 1260-1262. 1950.

39. Shahani, K. M. The Effect of Heat and Storage on the

Stability of Aureomycin in Milk, Buffer and Water. J. Dairy Sci. **40**: 289-296. 1957.

40. Shahani, K. M. and Harper, W. J. Differences in the Acid Production and Phosphorus Metabolism of Oxytetracycline Sensitive and Resistant Organisms. Appl. Microbiol. **6**: 9-14. 1958.

41. Shanhani, K. M. and Harper, W. J. The Development of Antibiotic Resistance in Cheese Starter Cultures. Milk Prod. J. **49**: 15-16, 53-54. 1958.

42. Stoltz, E. I. and Hankinson, D. J. Antibiotics and Lactic Acid Starter Cultures. Appl. Microbiol. **1**: 24-29. 1953.

43. Stoltz, E. I. and Hankinson, D. J. The Effects of Antibiotics in Milk on the Human Intestinal Coliform Bacteria. J. Milk and Food Tech. **17**: 76-78. 1954.

44. Treccani, V. Methodo rapido per la determinazione degli antibiotici nel latte destinato al caseificio. Ann. Microbiol. **5**: 93-97. 1953.

45. Trembath, R. H. Effect of Penicillin in Milk on Starter Cultures. Australian J. Dairy Technol. **5**: 143-146. 1950.

46. Ullberg, S. Antibiotica i Mjolk. En snab bestammings metod. Nord. Veterinarmed. **4**: 1061-1077. 1952.

47. Vickers, H. R., Bagratuni, L. and Alexander, Suzanne. Dermatitis caused by Penicillin in Milk. Lancet **1**: 351-352. 1958.

48. Welch, H. Problems of Antibiotics in Food as the Food and Drug Administration Sees Them. Am. J. Pub. Health **47**: 701-705. 1957.

49. Wessner, P. Penicillin in Cheesemilk and Its Inactivation with Penicillinase. Intern. Dairy Congr. Proc., 13th Congr. **3**: 1121-1129. 1953.

50. Whitehead, H. R. and Lane, D. J. The Influence of Penicillin on the Manufacture and Ripening of Cheddar Cheese. J. Dairy Research **23**: 355-360. 1956.

51. Wilkowske, H. H. and Krienke, W. A. Influence of Penicillin on the Lactic Acid Production of Certain Lactobacilli. J. Dairy Sci. **34**: 1030-1033. 1951.