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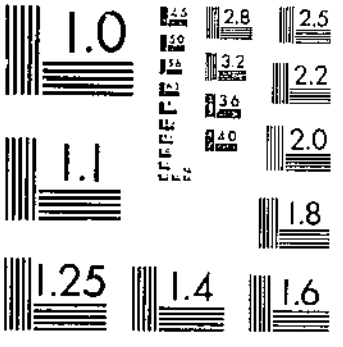

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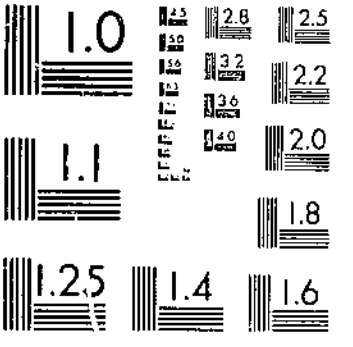

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Results of Treating Bovine Mastitis With Sulfonamides Containing Urea[1]

By W. W. Swett, *senior dairy husbandman*, R. R. Graves,[2] *head*, C. A. Matthews, *dairy husbandman, Division of Dairy Cattle Breeding, Feeding, and Management Investigations*; L. A. Burkey,[3] *bacteriologist, Division of Dairy Research Laboratories*; and P. C. Underwood, *veterinarian, Bureau of Dairy Industry, Agricultural Research Administration*

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INTRODUCTION

In October 1942, the Bureau of Dairy Industry began a survey of the extent of mastitis infection in its herd at the Agricultural Research Center, Beltsville, Md. At the same time it began a study of the effectiveness of sulfonamide preparations in the eradication and control of the disease. During the first 10 months' work, two sulfonamide preparations were used. One preparation was sulfanilamide in oil and the other was a combination of sulfanilamide and sulfadiazine in oil. The results obtained with these two preparations were reported[4] in August 1944, and in the same report a number of references were made to a sulfonamide containing urea, with which treatments had been begun in August 1943.

[1] Submitted for publication January 9, 1947.

[2] Retired March 30, 1946.

[3] Succeeded J. Frank Cone, market-milk specialist, who resigned May 15, 1944, after conducting the bacteriological work during the first 9 months.

[4] Swett, W. W., Graves, R. R., Matthews, C. A., Cone, J. Frank, and Underwood, P. C. A study of the effectiveness of sulfonamide preparations in the elimination of bovine mastitis. U. S. Dept. Agr. Tech. Bul. 884, 20 pp. 1944.

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Other investigators had reported [5 6] that certain kinds of bacteria appear to possess, or to acquire through contact, a high degree of resistance to sulfonamide preparations and that urea increases the solubility of sulfonamides, enhances their bacteriostatic action, and removes fastness of sulfonamide-resistant organisms.

The purpose of using sulfonamides containing urea was to determine whether or not such preparations would be substantially more effective than sulfanilamide or than a combination of sulfanilamide and sulfadiazine in eliminating udder infections. This bulletin gives the results obtained with sulfonamide-urea preparations in the Beltsville herd, from August 1943 to October 1944.

EXPERIMENTAL METHODS AND MATERIALS

Taking Milk Samples

In this study of sulfonamide-urea preparations, the procedures for taking milk samples and for making the laboratory tests were essentially the same as those described previously in reporting [7] the results obtained with sulfanilamide and sulfadiazine. In the subsequent discussion, these two drugs will be referred to as S and SD, respectively, and the preparation containing both drugs as S + SD. The sulfonamide-urea preparation will be referred to as SUG.

Milk samples were obtained from all cows as soon as practicable after the beginning of each lactation period. Samples were taken thereafter, at any time during the lactation, from cows showing swollen quarters, flakes in their milk, or any other mastitic condition. Milk samples for laboratory examination were taken just prior to the regular afternoon milking. First, the udder of the cow was wiped clean with a cloth wet in a solution containing about 200 p.p.m. of available chlorine. Then, the end of each teat was wiped off with a pledget of cotton wet with alcohol, particular attention being given to cleaning the teat orifice. A separate sample was drawn from each quarter of the udder into a sterile container, and each sample was marked with the number of the cow and the quarter from which it was taken. The samples were iced and sent to the laboratory the following day for examination.

Administering Treatment

Sulfonamide-urea preparations were administered by infusion to all udder quarters that showed infections that had not been treated previously, and also to infected quarters that had failed to respond to single or repeated treatments with other sulfonamide preparations. Except in unusual cases only the quarters known to be infected were treated. Ordinarily treatment was given once a day on 4 successive days. In lactating cows injections were made as soon as possible after milking, and the material was left in the udder until the next regular

[5] Strakosch, Ernest A., and Clark, W. G. beneficial effect of urea in topical sulfonamide therapy. Minn. Med. 26: 276–282. 1943.

[6] Tsuchiya, H. M., Tenenberg, D. J., Clark, W. G., and Strakosch, E. A. antagonism of anti-sulfonamide effect of methionine, and enhancement of bacteriostatic action of sulfonamide by urea. Soc. Expt. Biol. and Med. Proc. 50: 262–266. 1942.

[7] See footnote 4, p. 1.

milking. The milk containing the residue of the injected preparation was discarded. In dry cows the injections usually were made on 4 successive days and all of the injected material was left in the udder.

The stock material was agitated thoroughly before treatment was begun, in order to insure uniform distribution of the sulfa drugs throughout the mixture. Usually a small quantity was transferred to a sterilized can with a lid, to permit easier handling and more complete dispersion of the suspended ingredients by agitation. If a number of cows were being treated, the can was set in a bucket of hot water in order to maintain a temperature that would facilitate easy handling.

A 50-cc. glass and metal serum syringe with Luer type nozzle fitting was used. Injection cannulas having as large a bore as possible and still being small enough to allow easy access into the teat canal were used. A sterilized cannula was used for each quarter treated. Following the injection the quarter was massaged upward for the purpose of distributing the injected material through the cistern and into the larger milk ducts.

Milk samples were taken from all treated udders, approximately 10 days after treatment, to determine the effectiveness of the treatment.

Various Formulas Tried

As the supply of sulfadiazine was exhausted and replenishment was not feasible at the time this study was being conducted (because of wartime demands for the drug by the armed forces) sulfadiazine was not included in the preparations containing urea.

Considerable experimental work was carried on in an effort to obtain a sulfonamide preparation containing urea that would be reasonably stable and that would not be injurious to mammary tissues. Various carrying agents were tried. Uninfected quarters of the udders of a number of cows were injected experimentally with preparations containing different concentrations of urea to determine their tolerance by mammary tissues. In these tests, glycerin alone or mixtures of glycerin and mineral oil were used as carriers. It was found that a preparation containing a high concentration of equal parts of sulfanilamide and urea in glycerin was injurious to udder tissues. This was indicated by hardening of the treated quarters, discoloration and changes in consistency and reaction of the milk, and marked increases in leucocyte counts. Injections of sterile glycerin produced no unfavorable reaction, which showed glycerin was not the offending ingredient. Long usage had shown that sulfanilamide is readily tolerated by the udder. Preparations containing a lower proportion of urea, when injected into other uninfected quarters, proved less irritating.

Two infected quarters were treated with a preparation containing sulfanilamide and urea (in the proportion of 680 gm. of sulfanilamide to 120 gm. of urea) in a carrier consisting of 800 cc. of glycerin and 400 cc. of mineral oil. Four other quarters were treated with a similar preparation containing 1,000 cc. instead of 800 cc. of glycerin. In nearly every instance the milk became yellow about 24 hours after the first injection and continued to be yellow until about 2 days after the last injection. Some flocculation appeared at various times in the milk from all treated quarters. The treated quarters showed a slight full-

ness on the day following the second injection. None of the cows exhibited any rise in temperature or other unfavorable reaction except as noted. The bacteriologist who examined milk samples before and after treatment reported that two showed a distinct increase in leucocyte count, one a decrease, and three no significant change.

The material was too thick and heavy for easy administration, so a preparation was made up which contained the same proportion of sulfanilamide and urea (680 and 120 gm., respectively) in a carrier of 1,000 cc. of glycerin and 700 cc. of mineral oil. This was used in treating eight infected quarters. Comparative leucocyte counts were not made. The same changes occurred as before in the color and consistency of the milk. Otherwise no unfavorable results were observed in any of the cows. This material also was too thick and heavy for easy administration.

A preliminary survey showed that the infecting organisms had been eliminated from 9 (64.3 percent) of the 14 infected quarters treated. The udders tolerated the material satisfactorily. Some cows produced milk at a higher level after treatment than before; some at a lower level. The average decline in milk production was between 4 and 5 percent, which is approximately the same as was reported [8] when cows were treated with S and S+SD and not significantly greater than might be expected in untreated cows during the half-month period represented. These preliminary results appeared to justify a continuation of the study of sulfonamide preparations containing urea.

In order further to facilitate administration, the formula was changed slightly in September 1943. The new preparation consisted of sulfanilamide and urea in the proportion of 350 gm. to 50 gm., respectively, mixed in a Waring blendor with 500 cc. of glycerin. Some difficulty was experienced in making the injections, even with this less-concentrated material, but preparations made according to this formula were used in all subsequent cases until October 1944, which marked the termination of treatments with sulfonamides containing urea.

The technique of administering the sulfanilamide-urea preparation was essentially the same as for the S and the S + SD preparations except that it was necessary, because of its thicker consistency, to have the material at a higher temperature (approximately body temperature) at the time of injection.

Dosage

During the early part of the experiment a dosage of 50 cc. was used in each treated quarter at each daily injection. Later the standard dose was increased to 75 cc. In persistent cases this was raised still further to 100 cc. or 125 cc. It is estimated that each 50-cc. dose contained approximately 22.15 gm. of sulfanilamide and 3.17 gm. of urea. The larger doses, of course, contained correspondingly greater quantities of each ingredient. This material appears to have had a concentration of sulfanilamide approximately 50 percent higher than the S and S+SD preparations most extensively used in previous studies of mastitis in this herd.

[8] See footnote 4, p. 1.

DISCUSSION OF RESULTS

Number and Nature of Infections Treated

Sulfonamide preparations containing urea were administered to 100 quarters of cow udders. Fifteen quarters have been omitted from consideration here, either because it was not possible to obtain adequate milk samples after treatment and the results consequently could not be determined, or because the nature of the infection or the cause of mastitis in the udder could not be determined.

Of the 85 quarters for which results were obtainable, 56 (65.88 percent) were infected with streptococci, 5 (5.88 percent) with staphylococci, 22 (25.88 percent) with pseudomonades, and 2 (2.35 percent) with coliform bacteria. As compared with reports from other sources, this is a very high proportion of pseudomonadal infections and a correspondingly low proportion of streptococcal infections. The following analyses of results are based on the 85 quarters for which the nature of the infection and the results of the treatments were definitely determined. The first 14 infected quarters treated with urea preparations made according to various formulas and containing different proportions of glycerin and mineral oil are included in the total of 85 quarters. Despite the fact that these earliest preparations contained some mineral oil, all of the sulfanilamide-urea preparations contained sulfanilamide, urea, and glycerin. Thus for brevity in the following discussions they will be referred to from time to time as SUG.

Effectiveness of Sulfanilamide-Urea Preparations

At the outset attention should be called to the fact that a direct, unqualified comparison of the results obtained with SUG cannot be made with those obtained with S or S+SD. In the first place, differences in refinement of methods of identification may have altered the apparent incidence of the various species of infecting organisms. Furthermore, a considerable number of the quarters treated with SUG had failed previously to respond favorably to the administration of from one to seven treatments with S or S+SD. In these cases of previous failure the infective organisms may have been of an initially resistant strain, they may have acquired resistance to sulfonamides through repeated treatments, or the site of the infection in the udder and tissue changes resulting from the infection may have prevented unrestricted action of the drugs on the organisms. At any rate, the inclusion of such cases in determining the effectiveness of any subsequent form of treatment may be expected to make the results appear in a less favorable light. These cases of previous failure on S and S+SD have been studied separately from those in which SUG was used only on previously untreated infections. The two groups are compared with each other. Then the two separate groups and the combined results for all SUG treatments are compared with the results previously reported for S and S+SD. The summarized data for all of these comparisons are given in table 1.

TABLE 1.—*Effectiveness of sulfanilamide-urea preparations (SUG) compared with that of the sulfanilamide and sulfadiazine preparations (S and S+SD)*

Nature of infection	Quarters treated	Quarters cleared of infection	
	Number	*Number*	*Percent*
QUARTERS TREATED WITH S OR S+SD			
Streptococci	91	73	80. 22
Staphylococci	10	9	90. 00
Pseudomonades	18	10	55. 55
Coliform bacteria	6	5	83. 33
All types	125	97	77. 60
QUARTERS TREATED WITH SUG (AFTER PREVIOUS FAILURE WITH S OR S+SD)			
Streptococci	12	6	50. 00
Staphylococci			
Pseudomonades	6	4	66. 67
Coliform bacteria	1	1	100. 00
All types	19	11	57. 89
QUARTERS TREATED WITH SUG (NO PREVIOUS TREATMENT WITH S OR S+SD)			
Streptococci	44	29	65. 91
Staphylococci	5	4	80. 00
Pseudomonades	16	13	81. 25
Coliform bacteria	1	1	100. 00
All types	66	47	71. 21
ALL QUARTERS TREATED WITH SUG			
Streptococci	56	35	62. 50
Staphylococci	5	4	80. 00
Pseudomonades	22	17	77. 27
Coliform bacteria	2	2	100. 00
All types	85	58	68. 24

INFECTIONS THAT PREVIOUSLY HAD FAILED TO RESPOND TO S OR S+SD

Of the 85 quarters treated with SUG, 19 had failed to respond favorably to previous infusions of S or S+SD. Five had failed to respond to 1 treatment, 1 to 2 treatments, 1 to 3 treatments, 1 to 4 treatments, 6 to 5 treatments, 3 to 6 treatments, and 2 to 7 treatments.

In reporting the results obtained with S and S+SD[9] it was shown that, taking all types of infection together, almost 94 percent of the quarters that responded at all were cleared of infection by the first, second, or third treatment. It would appear that favorable results from subsequent treatment with SUG could not be expected in the case of nearly two-thirds of the 19 quarters that had failed on S or S+SD

[9] See footnote 4, p. 1.

because of the large number of unsuccessful treatments they had received. However, 11 of the 19 (57.89 percent) responded favorably to SUG—6 on the first treatment, 2 on the second, and 3 on the fourth. Some of the quarters that had shown the greatest resistance to S or S+SD responded quickly when treated with SUG. For example, the 6 that responded to the first treatment with SUG included 3 that had failed on 1 treatment, 1 that had failed on 3, 1 that had failed on 5, and 1 that had failed on 6. The 2 that were cleared by the second SUG treatment had received 5 and 7 previous treatments wihout success. The 3 that required 4 SUG treatments had previously failed on 1, 2, and 6 treatments with S or S+SD. These 11 quarters had received an average of 3.45 treatments with S or S+SD. They were cleared of infection by an average of 2.00 treatments with SUG.

Of the eight that failed when treated with SUG after previous failures with S or S+SD, three received two treatments, two received three, one received four, and two received five treatments with SUG. In this group all but one had received from four to seven unsuccessful treatments with S or S+SD. The eight that failed to respond to both sulfonamides received an average of 4.75 treatments with S or S+SD and an average of 3.25 treatments with SUG.

The 8 that failed to respond apparently were infected with highly resistant organisms or were in some way protected from the action of the sulfonamides. On the other hand, the results with the 11 that responded—most of them rather quickly—may indicate that urea increased the effectiveness of the sulfonamide, or that changing from one sulfonamide preparation to another may have been beneficial.

Twelve of the 19 quarters (63.16 percent) that failed to respond to S or S+SD were infected with streptococci. This percentage is not materially different from the one for the entire group of 85 quarters (65.88 percent). They had received an average of 4.75 treatments with S or S+SD. Only 6 of the 12 (50.0 percent) subsequently responded to SUG treatments. Six quarters infected with pseudomonades had received an average of 3.00 treatments with S or S+SD. Four of the six (66.7 percent) responded to SUG. One quarter containing coliform bacteria that had failed to respond to 1 treatment with S+SD cleared as a result of 1 treatment with SUG.

Only 50 percent of the streptococcal infections that previously had failed were cleared with SUG (table 1). This is definitely lower than the percentage for S or S+SD. Considering this low percentage and the number of treatments they had received previously, it appears that the streptococcal infections in the group were particularly resistant. On the other hand, the percentage of effectiveness was higher for pseudomonadal infections (66.7 percent) than in the group treated only with S or S+SD, and also for coliform infection (100 percent) although only one such quarter was treated with SUG.

QUARTERS NOT PREVIOUSLY TREATED WITH S OR S+SD

The results for the 66 quarters infused with SUG that had not been treated previously with S or S+SD were somewhat more favorable. In this group 47 (71.21 percent) responded to infusions of SUG as compared with 57.89 percent for those that had failed on S or S+SD.

Infections by streptococci accounted for 44 of the 66 previously untreated quarters (66.7 percent); staphylococci accounted for 5 (7.6 percent); pseudomonades for 16 (24.2 percent); and coliform bacteria for 1 (1.5 percent). These percentages are not significantly different from those for the entire group of 85 quarters to which SUG was administered.

The SUG treatment was successful in eliminating 29 of the 44 streptococcal infections (65.91 percent), 4 of the 5 staphylococcal infections (80 percent), 13 of the 16 pseudomonadal infections (81.25 percent), and the 1 coliform infection from 1 quarter (100 percent). Except for the coliform infections, the results of which are the same in both cases, these percentages are all higher than the corresponding ones for infections that had failed to respond previously to S and S+SD.

Compared with the results reported previously for S and S+SD, however, the percentage is distinctly lower for streptococcal infections and much higher for pseudomonadal infections. The differences for staphylococcal and coliform infections are not very significant because of the small numbers of quarters treated.

It is noteworthy that in the case of these previously untreated infections, which presumably represent a condition comparable with that which existed when S and S+SD were used, the effectiveness of SUG was 71.21 percent for all types of infections. This is lower than the effectiveness of S and S+SD for all types of infections (table 1).

ALL INFECTIONS TREATED WITH SUG

It has been pointed out that SUG infusions were more highly effective in eliminating previously untreated infections than in eliminating infections that had failed to respond to S or S+SD. Obviously, the results for all SUG treatments (both groups combined) would tend to be intermediate between them.

The organisms were eliminated by SUG infusions from 35 of the 56 quarters infected with streptococci (62.50 percent), from 4 of the 5 infected with staphylococci (80.00 percent), from 17 of the 22 infected by pseudomonades (77.27 percent), and from both of the quarters infected by coliform bacteria (100 percent). Comparative percentages are given in table 1 to show the results for all S and S+SD and for all SUG infusions. Considering the number of cases involved, the decrease in percentage of efficiency in eliminating streptococcal infections and the increase in efficiency in eliminating pseudomonadal infections are the most striking results shown by the table. For all types of organisms combined, the percentage of efficiency is significantly lower for SUG than for S or S+SD (68.24 and 77.60 percent, respectively).

Attention is called to the fact that the proportion of streptococcal infections was lower in the group treated with SUG than in the group treated with S and S+SD (65.88 and 72.80 percent, respectively). The effectiveness of the SUG treatment also was lower. The proportion of pseudomonadal infections was definitely higher in the group treated with SUG (25.88 as compared with 14.40 per-

cent) and the effectiveness of the SUG treatment was considerably higher than that of S and S+SD. The lower effectiveness of SUG for streptococcal infections and the higher effectiveness of SUG for pseudomonadal infections occurred both in the group that previously had failed to respond to S or S+SD and in the group that previously was untreated.

In many of the quarters treated with SUG the milk sample obtained following the first treatment was off-color—usually pink and having the appearance of being bloody. This condition occurred in samples of milk which showed low as well as high leucocyte counts and was irrespective of the type or the seriousness of the infection. The condition was temporary and apparently was not associated with any injurious effect on the udder.

Number of Treatments Required to Eliminate Infections

In reporting the results obtained with S or S+SD [10] it was shown that for all infections treated 93.81 percent of the quarters that were cleared of infections responded to one of the first three treatments. The percentages for the various types of infections that responded to the first three treatments were 91.78 for streptococci, 100 for staphylococci, 100 for pseudomonades, and 100 for coliform bacteria.

Table 2 shows the total number of quarters cleared of infection and the percentage of the total that was cleared by the first, second, or third treatment with S or S+SD and with SUG. As in table 1 the infections treated with SUG are divided into two groups—those that previously had failed to respond to S or S+SD and those that previously were untreated. All percentages are based on the total number of infections that were eliminated.

In the group of infections that previously had failed to respond to S or S+SD but that were eliminated by SUG, the average effectiveness of the first treatment was low for all types combined. The proportion eliminated by the first three treatments was 72.73 percent as compared with 93.81 percent for those eliminated by S or S+SD.

In the group previously untreated that were eliminated by SUG, the effectiveness of the first treatment was higher than for either of the foregoing groups for streptococcal infections. For staphylococcal infections the first treatment was relatively effective but only 75 percent responded to three treatments. For pseudomonadal infections the first treatment was lower than when S or S+SD was used but much higher than in the group that previously had failed to respond to S or S+SD. However, the second treatment eliminated the rest. The one coliform infection was eliminated by the first treatment. Results for all types of infection combined were higher for the first, for the first two, and for the first three treatments than for either of the foregoing groups. Three treatments eliminated 97.87 percent in this group as compared with 93.81 percent for those effectively treated with S or S+SD, and 72.73 percent for those that responded to SUG after having failed previously.

The first three treatments with SUG were more highly effective than the first three treatments with S or S+SD, in the case of streptococcal infections. They were less effective in the case of staphylococ-

[10] See footnote 4, p. 1

TABLE 2.—*Total number of quarters cleared by all treatments with sulfonamide preparations (S or S+SD, and SUG) and the number and percentage of the total cleared by the first, second, or third treatment*

TREATED WITH S OR S+SD

Infecting organism, quarters cleared by all treatments, and sequence of treating	Quarters cleared by each of first three treatments		Cumulated proportion of total quarters cleared
	Number	*Percent*	*Percent*
Streptococci (73 quarters cleared by all treatments):			
First treatment	47	64. 38	64. 38
Second treatment	17	23. 29	87. 67
Third treatment	3	4. 11	91. 78
Staphylococci (9 quarters cleared by all treatments):			
First treatment	6	66. 67	66. 67
Second treatment	2	22. 22	88. 89
Third treatment	1	11. 11	100. 00
Pseudomonades (10 quarters cleared by all treatments):			
First treatment	9	90. 00	90. 00
Second treatment	0	----------	90. 00
Third treatment	1	10. 00	100. 00
Coliform bacteria (5 quarters cleared by all treatments):			
First treatment	3	60. 00	60. 00
Second treatment	0	----------	60. 00
Third treatment	2	40. 00	100. 00
All types (97 quarters cleared by all treatments):			
First treatment	65	67. 01	67. 01
Second treatment	19	19. 59	86. 60
Third treatment	7	7. 22	93. 81

TREATED WITH SUG (AFTER PREVIOUS FAILURE WITH S OR S+SD)

Streptococci (6 quarters cleared by all treatments):			
First treatment	4	66. 67	66. 67
Second treatment	1	16. 66	83. 33
Third treatment	0		83. 33
Pseudomonades (4 quarters cleared by all treatments):			
First treatment	1	25. 00	25. 00
Second treatment	1	25. 00	50. 00
Third treatment	0		50. 00
Coliform bacteria (1 quarter cleared by all treatments):			
First treatment	1	100. 00	100. 00
Second treatment			
Third treatment			
All types (11 quarters cleared by all treatments):			
First treatment	6	54. 55	54. 55
Second treatment	2	18. 18	72. 73
Third treatment	0	----------	72. 73

TREATED WITH SUG (NO PREVIOUS TREATMENT WITH S OR S+SD)

Infecting organism, quarters cleared by all treatments, and sequence of treating	Quarters cleared by each of first three treatments		Cumulated proportion of total quarters cleared
	Number	*Percent*	*Percent*
Streptococci (29 quarters cleared by all treatments):			
First treatment	25	86. 21	86. 21
Second treatment	3	10. 34	96. 55
Third treatment	1	3. 45	100. 00
Staphylococci (4 quarters cleared by all treatments):			
First treatment	3	75. 00	75. 00
Second treatment	0	----------	75. 00
Third treatment	0	----------	75. 00
Pseudomonades (13 quarters cleared by all treatments):			
First treatment	10	76. 92	76. 92
Second treatment	3	23. 08	100. 00
Third treatment	----------	----------	----------
Coliform bacteria (1 quarter cleared by all treatments):			
First treatment	1	100. 00	100. 00
Second treatment	----------	----------	----------
Third treatment	----------	----------	----------
All types (47 quarters cleared by all treatments):			
First treatment	39	82. 98	82. 98
Second treatment	6	12. 77	95. 74
Third treatment	1	2. 13	97. 87

ALL QUARTERS TREATED WITH SUG

Streptococci (35 quarters cleared by all treatments):			
First treatment	29	82. 86	82. 86
Second treatment	4	11. 43	94. 29
Third treatment	1	2. 86	97. 14
Staphylococci (4 quarters cleared by all treatments):			
First treatment	3	75. 00	75. 00
Second treatment	0		75. 00
Third treatment	0		75. 00
Pseudomonades (17 quarters cleared by all treatments):			
First treatment	11	64. 71	64. 71
Second treatment	4	23. 53	88. 24
Third treatment	0		88. 24
Coliform bacteria (2 quarters cleared by all treatments):			
First treatment	2	100. 00	100. 00
Second treatment			
Third treatment			
All types (58 quarters cleared by all treatments):			
First treatment	45	77. 59	77. 59
Second treatment	8	13. 79	91. 38
Third treatment	1	1. 72	93. 10

cal and pseudomonadal infections, the same for coliform infections, and almost the same (93.10 percent and 93.81 percent, respectively) for all types of infections combined, as compared with those treated effectively with S or S+SD.

There was a tendency, except in the case of pseudomonadal infections, for the first treatment with SUG to eliminate a higher percentage of the susceptible organisms than when S or S+SD was used. For all types of infections combined, the lowest response to first treatment was in the group that previously had failed to respond to S or S+SD, indicating that even the infections in this group that finally were eliminated by SUG probably were relatively more resistant than the others.

Results of Treating Acute Mastitis

Acute mastitis is not a definite condition and the term often is loosely used as there are many degrees and various manifestations of acuteness. The presence of flakes in the milk or other mild changes in the appearance of the milk usually are not considered as indicating an acute condition. On the other hand, hot or hard quarters, especially when accompanied by a sudden marked reduction in the quantity of milk secreted and in its physical consistency, are classed as acute or clinical cases.

There were four acute cases that failed to respond to S or S+SD and later were treated with SUG. Three were pseudomonadal infections and one was streptococcal. Only one of the four received two treatments of S or S+SD. Three of the four responded favorably to SUG; one on the first treatment and two on the fourth.

Among the 66 infections not previously treated with S or S+SD, there were 14 cases of acute mastitis. Two of these followed severe injury to the udder. There were 2 other cases of infection accompanying injury that were not classed as acute. One responded and one did not.

Six of the 14 acute cases (42.9 percent) were cleared of infection—all by the first treatment. Four of these were pseudomonadal infections and 2 were streptococcal. The 8 that failed included 2 cases of severe teat injury. Five of the 8 were streptococcal infections and 3 were pseudomonadal. Four of the 8 failed on only 1 treatment, 3 on 2 treatments, and 1 on 5 treatments.

From the results shown it appears that the probability of success in treating acute mastitis is less favorable than in treating nonacute cases, although it is recognized that a higher percentage of cleared infections might have resulted if some had received additional treatments. On the other hand, the administration of sulfonamides in some cases could not have been continued further because the disease progressed rapidly and the quarters became "blind" and impervious to injections. In two of these, hot water was applied to the udder to relieve the acute symptoms, although this presumably cannot be credited entirely with elimination of the offending organisms.

Effectiveness in Treating Dry Cows

Many research workers and practitioners have reported better results from treating cows for mastitis while dry than during lactation. The previous report of results with S or S+SD showed that only three

of the eight quarters treated while dry were cleared of infection, but pointed out that the relatively low percentage of favorable results could not be considered as an indictment of dry treatment since all of those that failed had failed repeatedly to respond during lactation.

SUG was used in treating 76 lactating and 9 dry quarters. Fifty-three (69.74 percent) of the lactating quarters were cleared of infections—41 by the first treatment, 7 by the second, 1 by the third, and 4 by the fourth—an average of 1.40 treatments. The 23 that failed to respond favorably received an average of 2.22 treatments.

Five of the nine nonlactating quarters (55.56 percent) were cleared of infection—four by the first treatment and one by the second—an average of 1.20 treatments. Despite the lower percentage of eliminations for dry quarters (55.56 percent) than for lactating quarters (69.74 percent), unqualified conclusions cannot be drawn because of the small number of data.

In the first place, 3 of the 9 quarters that were treated while dry (33 percent) previously had failed to respond to S or S+SD, as compared with 16 of the 76 (21 percent) treated during lactation. Thus a higher proportion of those treated dry may have been more resistant. In both the lactating and the dry groups those that previously had failed had been given an average of 4.00 treatments with S or S+SD. All of the three previous failures subsequently were cleared of infection when treated dry. They received an average of only 1.33 treatments with SUG. Only 7 of the 16 previous failures (43.75 percent) were subsequently cleared of infection when treated during lactation. They had received an average of 2.86 treatments with S or S+SD and required an average of 2.00 treatments with SUG to eliminate the infection.

The higher percentage of previous failures that cleared and the smaller number of treatments required when treated dry as compared with those treated during lactation might be interpreted as favoring treatment during the dry period despite the lower percentage of all treated quarters cleared by treatment when dry. Furthermore, eight of the nine quarters treated while dry were infected with streptococci, for which the average efficiency in all quarters was only 62.50 percent for SUG. Apparently there is no significant increase in efficiency to be derived from treating during the dry period. On the other hand, there appears to have been no ill effects from treating during the dry period, and it would seem to be advisable to treat an infected quarter while dry rather than wait until the next lactation period. At any rate, delaying the administration of treatment for an extended period until the cow becomes dry would appear to be an undesirable practice unless the treatment itself were known to interfere seriously with milk secretion.

Effect of SUG Treatments on Milk Production

It was shown in a previous study [11] that treatments with S or S+SD had no significant depressing effect on milk production. The average level of production for a 10-day period after the termination of treatment was only 4.21 percent lower than for a 10-day period before treatment was begun. This decline was considered to be little if any

[11] See footnote 4, p. 1.

TABLE 3.—*Changes in daily milk production averages by cows treated with S or S+SD, and with SUG*[1]

Stage of lactation	Lactation periods represented	Average daily milk production[2]			Change from pretreatment average daily milk production			
		Before treatment	During treatment	After treatment	During treatment		After treatment	
	Number	*Pounds*	*Pounds*	*Pounds*	*Pounds*	*Percent*	*Pounds*	*Percent*
TREATMENT WITH S OR S+SD								
1 to 3 months	27	44. 58	42. 81	42. 48	−1. 77	−3. 96	−2. 10	−4. 71
3 to 6 months	9	23. 99	23. 99	24. 41			+. 42	+1. 74
6 to 9 months	10	26. 62	24. 86	24. 81	−1. 76	−6. 61	−1. 81	−6. 80
9 to 12 months	7	25. 00	22. 90	23. 95	−2. 10	−8. 41	−1. 05	−4. 20
All months	53	35. 11	33. 60	33. 63	−1. 51	−4. 30	−1. 48	−4. 21
TREATMENT WITH SUG								
1 to 3 months	24	37. 38	34. 39	35. 35	−2. 99	−7. 99	−2. 0[3]	−5. 43
3 to 6 months	7	27. 39	24. 08	25. 09	−3. 31	−12. 08	−2. 30	−8. 40
6 to 9 months	3	25. 31	22. 59	22. 36	−2. 72	−10. 75	−2. 95	−11. 66
9 to 12 months	4	21. 38	19. 85	21. 24	−1. 43	−7. 13	−. 14	−. 64
All months	38	32. 90	30. 03	30. 95	−2. 87	−8. 73	−1. 95	−5. 94

[1] For each sulfonamide, only the first treatment during a lactation period is included. Treatments administered during clinical or acute mastitis are omitted.

[2] With few exceptions the pretreatment average is for 10 days, the treatment period is for 4 days, and the posttreatment is for 10 days. Time from midpoint of pretreatment to midpoint of posttreatment period is, therefore, approximately 14 days.

greater than the expected decline for the same period in a group of untreated cows.

A similar study was made to ascertain the effect of SUG treatments on level of production. As in the previous study, cows treated during acute mastitis were omitted from the production comparisons. In the case of any cow that received more than one treatment during one lactation, the first one affording a comparison of producing levels was used. Data are given for 34 cows treated with SUG in 38 lactation periods. The effect of SUG on milk production is compared with that of S or S+SD in table 3.

The SUG preparation seems to have had a more depressing effect than the S or S+SD preparations during the 4-day period of treatment. The decrease from the pretreatment average for this 4-day period was 8.73 percent for SUG and 4.30 percent for S or S+SD. The difference between the average production after the termination of treatment and the average before treatment was begun was greater in the case of SUG than in the case of S or S+SD, but the difference was not so marked as during the 4-day treatment period. Decreases in average production were 1.95 pounds (5.94 percent) for SUG and 1.48 pounds (4.21 percent) for S or S+SD.

In the case of cows treated with SUG the pretreatment production averages ranged from 7.50 to 61.73 pounds daily for individual cows. Production averages for the period before, during, and after treatment were respectively 32.90, 30.03, and 30.95 pounds daily. These averages are all lower than the corresponding ones for cows treated with S or S+SD.

The average daily production after treatment was lower than the pretreatment average in 29 cases and higher in 9. The tendency to maintain or to increase production was not confined to any stage of lactation or level of production. The 9 cows that showed increases after treatment included the one with the highest and also the one with the lowest production average. Three of the 9 were in the first 3 months of lactation, 2 were in lactation from 3 to 6 months, and 2 from 9 to 12 months. The average daily production of the 9 cows before and after treatment was 32.04 and 33.21 pounds, respectively. Both of these averages are close to the averages for the entire group of 38 lactation periods.

Little significance can be attached to the average declines for different stages of lactation because of the uneven distribution of cows in the various stage groups.

The data in table 3 show that in general the decline in production was very slightly greater on an average, both in pounds and in percentages, for the cows treated with SUG than for those treated with S or S+SD, but in neither case can the decline be considered excessive.

A statistical analysis of the data showed that the decline in milk yield following treatment with SUG was not significantly different from the decline following treatment with S or S+SD.

SUMMARY AND CONCLUSIONS

During the period from August 1943 to October 1944 a sulfonamide consisting of sulfanilamide, urea, and glycerin (SUG) was used in treating 85 infected quarters of the udders of cows in the dairy herd of the Bureau of Dairy Industry at Beltsville, Md.

The object of the study was to determine the effectiveness of a sulfonamide preparation containing urea as a practical means of eliminating and controlling mastitis in a dairy herd and, so far as possible, to compare its effectiveness with that of sulfonamide preparations (S and S+SD) previously used in the same herd, that did not contain urea.

An absolute evaluation of the effectiveness of adding urea to sulfonamides cannot be made because in SUG the sulfadiazine was omitted, glycerin was substituted for mineral oil as a vehicle, the concentration of sulfanilamide was increased, and in many cases the dosage also was higher. Nevertheless, a fairly reliable comparison of the effectiveness of SUG and of S or S+SD in the practical control of mastitis in a herd would be possible save for the fact that some of the infections treated with SUG had failed previously to respond to S or S+SD, and may have been more resistant.

Of the 85 quarters studied 65.9 percent contained streptococci, 5.9 percent staphylococci, 25.9 percent pseudomonades, and 2.4 percent coliform bacteria. This is a much higher proportion of pseudomonadal infections than existed in the same herd during the study of S or S+SD or than ordinarily is reported from other sources. The proportion of streptococcal infections is correspondingly low.

Nineteen quarters previously had failed to respond favorably to S or S+SD despite repeated treatments in most of them. Eleven (57.89 percent) of these were cleared of infection by SUG. This is a relatively low percentage, which seems to indicate high resistance on the part of some of the infecting organisms, but the impressive thing about the results in this group is the quick response of some of the persistent cases when the change to SUG was made. There is some indication here that urea may have increased the effectiveness of the sulfonamide or else that a change from one sulfonamide to another may have been beneficial.

The effectiveness of SUG was definitely higher in the 66 previously untreated infections (71.21 percent) than in the 19 that had failed to respond to S or S+SD (57.89 percent). However, the average for the 66 previously untreated infections was lower than the average for 125 infected quarters treated with S or S+SD (77.60 percent). In this group the SUG was much less effective than S or S+SD in treating streptococcal infections but much more highly effective in treating pseudomonadal infections.

For the entire group of treatments with SUG the percentage of effectiveness was notably lower than for S or S+SD in streptococcal infections and much higher in pseudomonadal infections. Both sulfonamides were highly effective against staphylococcal and coliform infections. For all types of infections the percentage was somewhat lower for SUG (68.24 percent) than for S or S+SD (77.60 percent).

As was shown previously with S or S+SD, there is little to be gained in most cases by administering more than three treatments. Of the infections which responded to S or S+SD, 93.81 percent were eliminated by the first three treatments, and of those that responded to SUG, 93.10 percent were eliminated by the first three. For all types of infections combined, the response to the first treatment was higher for SUG than for S or S+SD.

The prospect of success seems to be less favorable in treating cases of acute mastitis than in treating nonacute cases. However, the acute cases that responded to SUG were cleared of infection by the first treatment.

The percentage of infections eliminated by SUG was lower for treatments administered during the dry period than for those given during lactation. There is some indication, however, that treatment during the dry period gave better results in cases that previously had failed when treated with S or S+SD. The data are limited and the results of the comparison are not conclusive.

The effect of SUG treatments on milk production was studied in 38 lactation periods of 34 cows. The decrease in production from the average for the 10 days before treatment to the average for the 10 days after treatment was very slightly greater, on an average, for the cows treated with SUG than for those treated with S or S+SD. In neither case, however, can the decline be considered excessive or significantly greater than the decline to be expected during a similar period in untreated udders.

The average percentage of efficiency for streptococcal infections and for all types of infections combined—both in cases that previously had failed on S or S+SD and in cases previously untreated—was relatively lower for SUG: the reduction in milk production between pretreatment and post-treatment periods was very slightly greater in cases treated with SUG; the heavy consistency of the material added somewhat to the effort involved in administering it; and off-color milk was observed in many of the quarters for a few days following the first treatment with SUG, but apparently the condition was not associated with any injurious effect on the udder.

On the other hand, the SUG preparation showed a markedly higher efficiency than the S or S+SD preparations in eliminating pseudomonadal infections and very good results in treating staphylococcal and coliform infections: there was some indication that it had merit as a follow-up on some resistant infections that had failed to respond to other sulfonamides; and for all types of infections combined, a greater proportion of the infections that proved susceptible to treatment were cleared by the first treatment with SUG than was the case when S or S+SD was used. To what extent these more desirable qualities of SUG may be attributable to the higher concentration of sulfanilamide and the larger doses used cannot be ascertained. All things considered, SUG does not appear to have proved superior, if in fact equal, to S or S+SD.

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