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INFLUENCE OF CASEIN AND OTHER AGENTS ON THE PRODUCTION OF RENAL LESIONS IN RATS BY SULFADIAZINE AND ACETYLSULFADIAZINE ¹

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Renal lesions have been produced by sulfadiazine in experimental animals (1-3). In humans treated with sulfadiazine, similar lesions have been observed (4-8). The lesions generally have been attributed to the precipitation of insoluble drug in the tubules and lower urinary tract. Sodium bicarbonate, which increases the solubility of sulfadiazine by creating an alkaline medium (9), has been used clinically (10, 11) and experimentally (12). Urea has also been shown to increase the solubility of sulfonamides (13, 14) and to prevent renal lesions in rats fed acetylsulfapyridine (15). Since the completion of the present work, it has been reported (16) that diuresis from sodium chloride or "alkalinizing salt mixtures" was corrective in acute renal obstruction produced in rats by sulfadiazine administration.

Our interest in this problem arose from the observation, made in the course of nutritional experiments, that rats fed sulfadiazine-containing diets of low casein content (10 percent) for a 30-day period regularly developed unusually severe renal lesions. We have found that the incidence and severity of these lesions were reduced by increasing the casein content of the diet or by giving urea, sodium bicarbonate, or sodium chloride. Increased conjugation of sulfadiazine and high renal concentrations of conjugated sulfadiazine have been noted in connection with development of the lesions. This relationship between conjugated sulfadiazine and renal lesions has been studied further by the administration of acetylsulfadiazine.

METHODS

Albino rats of Wistar and Osborne and Mendel strains were weaned at about 22 days and fed one of several purified diets (table 1). In some experiments, rats were fed sulfonamide-containing diets at weaning while in other studies the rats first were fed control diet No. 836 for 1 or 3 weeks and then were fed the sulfonamide-containing diets. Food intake was always *ad libitum*. Water intake was either *ad libitum* or restricted.

¹From the Division of Physiology and the Pathology Laboratory, National Institute of Health.

TABLE 1.—Percentage composition of diets ¹

Diet No.	Sulfa- diazine	Acetyl- sulfa- diazine :	Potas- sium chloride	Sodium chloride	Sodium bicar- bonate	Urea	Casein (Snamco)	Sucrose
808	1						10	77
819							10	78
832	1						20	67
833	1					5	10	72
835	1				4		10	73
836							20	68
843	1			4			10	73
855		1					10	77
856		1				5	10	72
857		1			4		10	73
858		1		4			10	73
859		1					30	57
866	1						30	57
884	1		4				10	73
896		0.75					10	77.25
899		.50					10	77.50
900		.25					10	77.75
906		.50				5	10	72.50
907		.50		4			10	73.50
908		.50			4		10	73.50
909		.50					30	57.50
920	2				4		10	72
933	3				4		10	71
943	4				4		10	70

¹ Each diet included Crisco 8 percent, salt mixture No. 550 (17) 4 percent, and vitamins in the following amounts per 100 gm. of diet: 1 mg. of thiamine hydrochloride, 2 mg. of riboflavin, 1 mg. of pyridoxine hydrochloride, 4 mg. of calcium pantothenate, 2 mg. of niacin, 200 mg. of choline chloride, and 0.4 mg. of 2-methyl-1, 4-naphthohydroquinone diacetate. Twice weekly each rat was given an oral supplement of 0.25 cc. of corn oil containing 2,000 units of vitamin A and 200 units of vitamin D (Natola), and once weekly 3 mg. of α -tocopherol in ethyl laurate.

² The acetylsulfadiazine used in these studies was furnished through the courtesy of Dr. E. H. Northey and Mr. W. O. Brewer, Calco Chemical Division, American Cyanamid Co.

Litter mates of the same sex and closely comparable weight were always used in setting up experimental and control groups. The average weight of weanling rats was 36 gm. and that of 6-week-old rats was 120 gm.

The experimental period was usually 30 days. At the end of this period, surviving rats were decapitated. Animals which appeared moribund during this period also were decapitated in order to obtain fresh tissues for chemical and histologic study. Tissues were fixed in 3.7-percent aqueous formaldehyde, embedded in paraffin, sectioned, and stained with eosin-azure and van Gieson's picrofuchsin. The right kidney was usually used for histologic study and the left was weighed and used for determination of sulfadiazine concentration. In the present report, the renal lesions were graded "very slight to moderate" and "severe," depending upon the extent and degree of tubular dilatation, cast formation, epithelial degeneration, and the amount of neutrophil exudation and interstitial reaction.

Sulfadiazine was determined by the methods of Marshall and co-workers (18, 19). Tissues were homogenized in a Waring blender and filtrates were prepared as previously described for cecal contents (20). Values were expressed on the basis of wet weight. Determinations of the ratio of free to total sulfadiazine in the urine were made on small freshly voided specimens.

The term "conjugated sulfadiazine" is used in this report to denote the form of sulfadiazine which can be determined by the Bratton and Marshall method (18) only after hydrolysis.

litter mates fed the control, 10-percent casein-containing diet (No. 819) was 355 mgm. (range: 265–415 mgm.) (table 2). Upon inspection, the kidney surface appeared smooth but was completely covered with white specks less than 1 mm. in diameter. The intervening tissue appeared pale tan in color. In sagittal sections, white chalky streaks were noted in a radial pattern extending from papilla to cortex.

Histologically, the involvement was generally limited to collecting tubules, distal convoluted tubules, and the ascending limb of Henle's loop. The tubules were greatly dilated and contained casts and amorphous debris. In special preparations sulfadiazine and acetylsulfadiazine crystals were demonstrated in the dilated tubules. Their epithelium showed flattening, degeneration, or proliferation, and the surrounding interstitium often showed leucocyte infiltration and fibroblast proliferation. Glomerular and vascular lesions were not noted and deposition of calcium was rare.

Calculi and hydronephrosis were never observed grossly in association with these lesions. However, single or multiple bladder calculi were found in 11 rats in these studies in which these renal lesions did not occur.

Lesions noted in other tissues in these rats have been reported (22).

Pyuria was noted in all rats which developed lesions. Freshly voided, uncentrifuged urine usually contained 100 to 200 white blood cells per high power field (300 diameters). Red blood cells and casts were noted infrequently. Repeated microscopic examination of the urinary sediment in each of the 10 control rats (table 2) failed to reveal any abnormal elements.

Prevention of lesions.—Increase of the casein content of the diet from 10 to 20 or 30 percent, or inclusion of urea, sodium bicarbonate, or sodium chloride³ in the diet were noted to have preventive actions on the development of lesions (tables 2 and 3). Lesions were completely prevented in 6-week-old rats by each of these substances while in weanling rats only sodium bicarbonate was completely effective. In considering how these substances might act in preventing lesions, several factors have been studied. Some of these factors are food and drug intake, water intake and urine output, solubility of sulfadiazine and acetylsulfadiazine, and absorption of sulfadiazine.

Food intake was measured and from this the sulfadiazine intake was calculated. It was found generally to be less in the rats which developed lesions than in the rats in which the lesions were prevented (tables 2 and 3).

Water intake was either ad libitum or paired. When the intake was ad libitum (table 2), each of the preventive agents except sodium bicarbonate resulted in an augmented water intake. However, the water intake of individual rats within a group showed no correlation with the development of lesions. In another experiment, the water intakes of litter mates fed the urea-containing diet (No. 833) and the 20 percent casein-containing diet (No. 832) were restricted to the

³ Potassium chloride was also found to have a preventive action. No lesions were observed in four 6-week-old rats fed the potassium chloride-containing diet (No. 884) for the 30-day experimental period. The average values were 771 mg. for kidney weight, 48 mg. percent (free) and 18 mg. percent (conjugated) of sulfadiazine in the kidney, and 28 mg. percent (free) and 0 mg. percent (conjugated) of sulfadiazine in the blood.

intakes of the litter mates fed the basic experimental diet (No. 803) (table 2). As an added check, measurements of urine outputs were made and no significant differences between the various groups were found. It may be noted that the preventive actions of urea and casein were no less than and perhaps even superior to the preventive actions observed in the previous experiment when water intake was unrestricted and, therefore, greater. Thus the preventive actions could not be attributed to diuresis.

TABLE 3.—*Production and prevention of renal lesions in 6-week-old rats fed 1-percent sulfadiazine-containing diets for 30 days*

	Diet No. 803, 10-percent casein		Diet No. 833	Diet No. 835	Diet No. 843	Diet No. 866
	Lesions present	Lesions absent	Urea	Sodium bicar- bonate	Sodium chloride	30-per- cent casein
Number of rats.....	6	4	10	10	10	10
Weight gain in 30 days (gm. per rat).....	-20	+4	+2	+1	+7	+13
Food intake (gm./day).....	5.1	7.7	7.6	7.2	7.6	7.3
Water intake (cc./day).....	14.1	13.4	12.2	13.5	13.7	13.7
Blood sulfadiazine concentration (mgm. percent).	64	74	43	44	32	44
5 days (free).....	60	70	34	45	39	46
10 days (free).....	40	50	28	26	19	35
20 days.....	0	0	1	0	0	0
(free).....	52	50	33	21	23	25
(conjugated).....	0	0	0	0	0	0
30 days.....	55	27	34	26	33	33
6 days.....	52	20	28	27	28	33
Conjugated sulfadiazine fraction in urine (percent).	47	23	28	26	36	27
9 days.....	51	31	23	27	32	28
12 days.....	64	30	28	25	28	34
18 days.....	52	27	26	18	29	27
24 days.....	51	23	23	12	19	25
29 days.....	76	110	37	23	19	68
Kidney sulfadiazine concentration (mgm. percent).	201	5	1	0	4	2
Kidney weight (mgm.).....	989	586	667	601	593	658
Kidney lesions.....	0	4	10	10	10	10
absent.....	1	0	0	0	0	0
very slight to moderate.....	5	0	0	0	0	0
severe.....						

These 10 groups of 5 litter mates were prepared for 3 weeks after weaning on a 20-percent casein sulfadiazine-free diet (No. 836).

Water intake was "paired" for each group of litter mates during the 30-day experimental period.

The figures given here are average values.

The increased solubility of sulfadiazine and acetylsulfadiazine in alkaline media is well known (9). The average pH values of the urines of rats fed the sodium bicarbonate-containing diet (No. 835) were from 7.7 to 8.1, while those of rats on the basic experimental diet (No. 803) were from 6.6 to 6.7 (table 2). The preventive agents other than sodium bicarbonate did not elevate the urinary pH values above those of rats fed diet No. 803. However, it was found that sodium chloride depressed the in vitro solubilities of sulfadiazine and acetylsulfadiazine, while urea, as has been shown (14), increased them. The "salting out" effect of sodium chloride has been reported for other compounds such as benzoic acid (23, 24), phenol, and phenyl acetic acid (24). The preventive actions of all of these agents, therefore, cannot be accounted for entirely on the basis of an increased solubility.

In order to obtain a rough indication as to whether any of the preventive agents might interfere with absorption of sulfadiazine, determinations were made of the sulfadiazine concentration in cecal contents. Pooled samples of cecal contents from all rats in table 3 were used for this purpose. Sulfadiazine concentrations for the groups of rats fed the various diets expressed as grams sulfadiazine (free) per 100 gm. of wet cecal contents were as follows: 2.44 for the basic, experimental diet (No. 803), 0.95 for the urea-containing diet (No. 833), 0.56 for the sodium bicarbonate-containing diet (No. 835), 0.75 for the sodium chloride-containing diet (No. 843), and 0.96 for the 30 percent casein-containing diet (No. 866). From these data, there is no indication that these various agents depress the absorption of sulfadiazine. It has also been found possible to prevent in rats fed a 20-percent casein-containing diet (No. 836) the severe renal lesions which result from the subcutaneous administration of sulfadiazine (1 mgm. per gm. body weight per day) to rats fed a control, 10-percent casein-containing diet (No. 819).

TABLE 4.—*Preventive action of sodium bicarbonate in rats fed 2-, 3-, and 4-percent sulfadiazine-containing diets for 30 days*

	Diet No. 803	Diet No. 920	Diet No. 933	Diet No. 943
	Sulfadiazine, 1 percent; sodium bicarbonate, 0 percent	Sulfadiazine, 2 percent; sodium bicarbonate, 4 percent	Sulfadiazine, 3 percent; sodium bicarbonate, 4 percent	Sulfadiazine, 4 percent; sodium bicarbonate, 4 percent
Number of rats.....	18	5	5	5
Weight gain (gm. per rat per day).....	-0.23	+0.54	+0.63	+0.49
Blood sulfadiazine concentration (mgm. percent).....	64	38	39	55
{ 15 days (free).....	66	35	43	63
{ 30 days (free).....		0	0	
{ (conjugated).....				
Conjugated sulfadiazine fraction in urine (percent) ¹	65	23	20	19
Kidney sulfadiazine concentration (free).....	98	46	169	176
{ (conjugated).....	813	3	8	17
Kidney weight (mgm.).....	892	394	413	490
Kidney lesions.....	0	5	5	2
{ absent.....	0	0	0	3
{ very slight to moderate.....	5	0	0	0
{ severe.....				

¹ 3 rats in this group died during the experimental period.

² Determinations were made on 2 to 4 specimens obtained from each rat during the last 4 days of the experimental period.

³ These 3 lesions were all slight (±).

These rats were prepared for 1 week after weaning on a 20-percent casein, sulfadiazine-free diet (No. 836) and then placed on this experiment.

The figures given here are average values for all rats which survived the 30-day experimental period.

Effect of preventive agents on blood sulfadiazine levels.—Rats fed diets containing urea, sodium bicarbonate, sodium chloride, or higher levels of casein had much lower blood sulfadiazine levels than rats fed the basic, experimental diet (No. 803) (tables 2 and 3). This effect was noted when water intake was either ad libitum or restricted. The data in table 3 show that rats fed sodium bicarbonate, sodium chloride,

or extra casein in their diets had average blood-sulfadiazine concentrations of 21 to 25 mg. percent at 30 days, that rats fed the urea-containing diet (No. 833) had a concentration of 33 mg. percent, while rats given no protective agent (diet No. 803) had a concentration of 51 mg. percent. However, it is noteworthy that in this latter group the blood levels of rats which did not develop lesions were as high as the levels of rats that did develop lesions.

TABLE 5.—*Further studies on the preventive action of sodium bicarbonate in rats fed a 4-percent sulfadiazine-containing diet*

	Diet No. 803 Sulfadiazine 1 percent			Diet No. 943 Sulfadiazine 4 percent Sodium bicarbonate 4 percent		
Rat number.....	1	2	3	4	5	6
Weight gain in 30 days (gm. per rat).....	+3	-9	+2	+15	+13	+15
Percent of absorbed sulfadiazine recovered in urine.....	94	84	93	71	81	86
Urine sulfadiazine concentration (mgm. percent).....	84	102	96	281	329	247
Percent of recovered sulfadiazine in conjugated form.....	78	92	89	82	35	80
Blood sulfadiazine concentration (mgm. percent).....	48	47	48	23	10	25
Urine sulfadiazine concentration (mgm. percent).....	43	50	51	46	41	37
Liver sulfadiazine concentration (mgm. percent).....	2	5	1	0	0	0
Heart-lung sulfadiazine concentration (mgm. percent).....	28	33	30	23	22	23
Kidney sulfadiazine concentration (mgm. percent).....	0	0	0	0	0	0
Heart-lung sulfadiazine concentration (mgm. percent).....	37	40	40	32	34	30
Kidney sulfadiazine concentration (mgm. percent).....	0	3	0	0	0	0
Kidney weight (mgm.).....	53	64	66	211	92	82
Kidney lesions.....	139	172	246	0	0	0
	810	710	950	700	520	430
	Severe	Severe	Severe	Slight	Slight	None

¹ The heart and both lungs were determined as a single tissue specimen.

Rats Nos. 1, 2, and 3 were litter mates of the same sex and weight of rats Nos. 4, 5, and 6 respectively. They were prepared as in table 4. At the conclusion of the 30-day experimental period, urinary studies were made during a 5-day "balance" period. The rats were sacrificed following this 5-day period.

In order to test whether one of the preventive agents was effective in the presence of high blood sulfadiazine levels, diets were fed which contained sodium bicarbonate and higher percentages of sulfadiazine (table 4). It was not until sulfadiazine was incorporated in the diet (No. 943) at a 4-percent level that blood concentrations were reached which were comparable with concentrations obtained in feeding the diet No. 803 (containing 1 percent sulfadiazine but without sodium bicarbonate). Slight renal lesions were produced.

Conjugation of sulfadiazine as related to the development of lesions.—Increased conjugation of sulfadiazine (as indicated by the conjugated sulfadiazine fraction in the urine) was found in all rats which developed severe renal lesions, but was not found in rats which did not develop lesions. In rats with severe renal lesions the conjugated sulfadiazine fraction in the urine was in the neighborhood of 50 percent, while in rats with slight or no renal lesions it was about 25 percent (tables 3, 4, and 5). However, no relationship between the actual urinary concentration of conjugated sulfadiazine and the development of lesions was noted in studies with sodium bicarbonate (table 5).

High concentrations of the conjugated sulfadiazine fraction in the kidney were found to be associated invariably with the development of severe lesions and were not found in the absence of lesions. This relationship was noted without exception in all the data obtained in these studies (tables 2, 3, 4, and 5). Thus, in a group of rats fed the 4-percent sulfadiazine, 4-percent sodium bicarbonate-containing diet (No. 943) in which renal lesions were very slight or absent, the average concentrations of free and conjugated sulfadiazine were 176 and 17 mg. percent, respectively (table 4). A group of rats fed the basic experimental, 1-percent sulfadiazine-containing diet (No. 803) all developed severe lesions. In the kidneys of these rats, the average concentrations of free and conjugated sulfadiazine were 98 and 813 mg. percent, respectively. It was also noted in the individual values which went to make up the average values in tables 2, 3, and 4, that in some kidneys without lesions, the total sulfadiazine concentrations (with free sulfadiazine predominant) were higher than in some kidneys with lesions (with conjugated sulfadiazine predominant).

Recovery from lesions.—Histologic studies of early and late recovery stages in rats with severe renal lesions have been made and are reported elsewhere (21). The rats used in these studies had developed severe renal lesions after ingestion of the basic experimental, 1-percent sulfadiazine-containing diet (No. 803) for the 30-day experimental period starting from weaning. At the conclusion of the experimental period, unilateral nephrectomy was carried out. The rats recovered on a diet (No. 819) lacking in sulfadiazine but otherwise identical to diet No. 803. In these studies the earliest histologic evidence of recovery was a disappearance of casts. The dilated tubules resumed a normal appearance or collapsed and atrophied. Tubular atrophy was most marked just beneath the capsule and produced a pitted appearance. Interstitial edema and leucocyte infiltration disappeared. Interstitial fibrosis increased. In rats killed after 3 months' recovery on diet No. 819, the kidneys showed atrophy of as many as one-half of the subcapsular tubules and interstitial fibrosis of the cortex and medulla.

Recovery studies in the continued presence of sulfadiazine were also carried out in 13 rats with severe lesions. After unilateral nephrectomy, 2 rats were continued on the same basic experimental diet (No. 803), 5 on a urea-containing diet (No. 833), and 6 on a sodium bicarbonate-containing diet (No. 835). All the rats on diets No. 803 and No. 833 died within 5 days with no evidence of repair in the remaining kidney. Of the 6 rats fed the sodium bicarbonate-containing diet (No. 835), 3 died early, while 3 survived and were sacrificed 40 days later. By this time the acute lesions had disappeared and only residual stigmata (cortical scars, tubular atrophy) remained. Renal deposits of conjugated sulfadiazine were absent, conjugation was reduced by about 80 percent and the blood concentration was reduced by about 50 percent (table 6).

Renal lesions with sulfathiazole.—Feeding of sulfathiazole-containing diets has resulted in renal lesions similar to those produced by sulfadiazine. Of 24 rats fed a 1-percent sulfathiazole, 10-percent casein-containing diet (identical to diet No. 803 except that sulfathiazole replaced sulfadiazine), 22 died in an average of 8 days (range: 3–18 days). Slight to moderate renal lesions were observed in 11 of these rats. Of 12 litter mates fed a similar sulfathiazole-containing diet with the casein level raised to 25 percent, all but 1 survived the 30-day experi-

mental period and lesions were noted in only 2 rats. When urea (5 percent) was included in the 1-percent sulfathiazole, 10-percent casein-containing diet and fed to 4 rats, all survived the 30-day experimental period without evidence of renal lesions. When methionine (0.5 percent) was included in the 1-percent sulfathiazole, 10-percent casein-containing diet of 4 pair-fed litter mates, all died within 4 days and 2 of these had renal lesions.

TABLE 6.—*Influence of sodium bicarbonate on recovery from renal lesions*

Rat number.....	Diet No. 803 Before recovery period ¹ sul- fadiazine 1 percent			Diet No. 835 After recovery period ² sul- fadiazine 1 percent sodium bicarbonate 4 percent		
	7	8	9	7	8	9
Blood sulfadiazine concentration (mgm. percent) (free).....	56	73	64	35	24	36
Conjugated sulfadiazine fraction in urine (percent).....	³ 72	³ 44	³ 59	⁴ 9	⁴ 13	⁴ 13
Kidney sulfadiazine concen- (free).....	32	24	42	18	9	9
tration (mgm. percent). (conjugated).....	141	86	201	18	9	18
Kidney weight (mgm.).....	695	540	710	405	540	630
Kidney lesions.....	severe	severe	severe	none	none	none

¹ These values were obtained at the conclusion of the 30 day experimental period on diet No. 803. Unilateral nephrectomy was performed at this time and diet No. 835 was fed.

² These values were obtained 40 days after unilateral nephrectomy.

³ Average of 5 daily determinations from the twenty-sixth to the thirtieth experimental days.

⁴ Average of 5 daily determinations from the sixty-sixth to the seventieth experimental days.

ACETYLSULFADIAZINE

Production of lesions.—Administration of acetylsulfadiazine in a 10-percent casein-containing diet (No. 855) resulted in more severe renal lesions and shorter survival than the administration of sulfadiazine in such a diet (No. 803). Diets were fed which contained acetylsulfadiazine at levels of 0.25, 0.50, 0.75, and 1.00 percent (table 7).

TABLE 7.—*Production of renal lesions in 6-week-old rats fed 0.25-, 0.50-, 0.75- and 1.00-percent acetylsulfadiazine-containing diets*

	Diet No. 900, 0.25 per- cent	Diet No. 899, 0.50 per- cent	Diet No. 898, 0.75 per- cent	Diet No. 855, 1.00 per- cent
Number of rats.....	6	6	6	6
Number of rats surviving the 30-day experimental period.....	6	6	5	2
Weight gain (gram per rat per day).....	+1.3	0	-1.4	-3.2
Blood sulfadiazine concentration (free).....	2	9	14	17
(mgm. percent). (conjugated).....	3	8	13	17
Muscle sulfadiazine concentration (free).....		3	6	7
(mgm. percent). (conjugated).....		4	6	6
Liver sulfadiazine concentration (free).....		5	8	10
(mgm. percent). (conjugated).....		6	10	10
Cecal contents sulfadiazine concen- (free).....	18	50	69	116
tration (mgm. percent). (conjugated).....	131	469	1,068	1,849
Kidney sulfadiazine concentration (free).....	0	10	19	34
(mgm. percent). (conjugated).....	43	259	368	514
Kidney weight (mgm.).....	930	1,277	1,541	1,878
Kidney lesions.....	absent.....	0	0	0
very slight to moderate.....	3	0	0	0
severe.....	2	6	5	2

The figures given here are average values for rats which survived the 30-day experimental period.

Of 12 rats fed the 1-percent acetylsulfadiazine-containing diet (No. 855), only 2 survived the 30-day experimental period. The lesions observed in these 2 rats and in some of those dying as early as 13 days after starting the experiment were of extreme severity (tables 7 and 8). Even at a level of 0.5 percent (diet No. 899), acetylsulfadiazine appeared to be as effective as 1-percent sulfadiazine (diet No. 803) in the production of severe renal lesions (compare data in table 3 with data in tables 7 and 9).

TABLE 8.—*Effects of preventive agents on the production of renal lesions in 6-week-old rats fed 1 percent acetylsulfadiazine-containing diets*

	Diet No. 855, 10 percent casein	Diet No. 856, urea	Diet No. 857, sodi- um bicar- bonate	Diet No. 858, sodi- um chlo- ride	Diet No. 859, 30 percent casein
Number of rats.....	6	6	6	6	6
Number of rats surviving the 30-day experimental period.....	0	1	4	0	0
Survival in days (range).....	10-20	5-16	11	8-13	8-13
Kidney sulfadiazine con- centration (mgm. per cent.).....	19	15	11	13	17
{free.....	707	467	418	324	200
{conjugated.....					
Kidney lesions.....	1	5	4	4	2
{very slight to moderate.....					
{severe.....	5	1	2	2	4

These 6 groups of 5 litter mates were prepared for experiment as in table 3.

Water intake was "paired" for each group of litter mates.

The figures given here are average values.

Values for the concentration of acetylsulfadiazine in cecal contents (table 7) in rats fed varying amounts of the drug are of the same order of magnitude as values reported for sulfadiazine under somewhat similar conditions (20). This finding suggests that the greater renal toxicity of acetylsulfadiazine is not due to greater intestinal absorption.

The blood concentrations of total sulfadiazine were much lower in rats fed acetylsulfadiazine than in rats fed a similar amount of sulfadiazine. About 50 percent of the total sulfadiazine in the blood was in the free form. In liver and muscle tissues, the free form also constituted about 50 percent of the total drug concentration. Since less than 10 percent of the urinary sulfadiazine was found to be in the free form (table 9), the relatively high ratios of free to conjugated compound in the blood and other tissues are probably due to the more rapid renal clearance of the conjugated compound. It is noteworthy that, despite very low blood concentrations, severe renal lesions were developed in most rats.

Anatomically these renal lesions were similar to those seen with sulfadiazine. It was noted, however, that with acetylsulfadiazine more tubules were involved and the inflammatory changes were more marked. Leucocytes were more numerous both in the tubules and in the interstices. Tubular epithelium showed more degeneration. The most extreme renal damage of the entire study was encountered in rats given acetylsulfadiazine.

TABLE 9.—*Effects of preventive agents on the production of renal lesions in 6-week-old rats fed 0.5 percent acetylsulfadiazine-containing diets*

		Diet No. 899, 10 per cent casein	Diet No. 906 urea	Diet No. 908, sodium bicarbonate	Diet No. 907, sodium chloride	Diet No. 909, 30 per cent casein
Number of rats.....		6	16	6	16	6
Blood sulfadiazine concentration (mgm. percent).	10 days..	(free).....	4.4	2.0	0.4	1.7
		(conjugated).....	4.9	2.0	1.1	2.5
	20 days..	(free).....	7.0	2.6	1.0	4.5
		(conjugated).....	11.7	4.5	3.5	4.8
	30 days..	(free).....	8.9	3.2	1.3	2.3
		(conjugated).....	10.5	1.4	8	1.3
Heart-lung sulfadiazine concentration ¹ (mgm. percent).		(free).....	5.6	1.7	1.0	1.3
		(conjugated).....	7.0	1.1	6	8
Conjugated sulfadiazine fraction in urine ² (percent)		93-99	97-100	95-99	97-99	97-99
Kidney sulfadiazine concentration (mgm. percent).		10	6	0	2	0
		(conjugated).....	277	362	101	106
Kidney weight (mgm.)		1,096	891	666	820	737
Kidney lesions.....	absent.....	0	0	0	0	1
	very slight to moderate.....	0	1	6	2	3
	severe.....	6	3	0	1	2

These 6 groups of 5 litter mates were prepared for experiment as in table 3.

Water intake was "paired" for each group of litter mates.

The figures given here are average values for all rats which survived the 30-day experimental period.

¹ Two rats in this group died during the experimental period.

² Three rats in this group died during the experimental period.

³ The heart and both lungs were determined as a single tissue specimen.

⁴ These figures represent the range of averages of values obtained 5, 10, 15, 20, and 25 days after start of the experiment.

Prevention of lesions.—Casein, urea, sodium bicarbonate, and sodium chloride, each of which were found to have some effectiveness in prevention of the renal lesions caused by sulfadiazine were tested in similar dietary concentrations for their effectiveness in prevention of lesions caused by acetylsulfadiazine.

One-percent acetylsulfadiazine-containing diets were fed to 5 groups of 6-week-old litter mate rats (6 per group) (table 8). The basic, 10-percent casein-containing diet (No. 855) was fed to one group. A urea-containing diet (No. 856) was fed to a second group, a sodium bicarbonate-containing diet (No. 857) to a third group, a sodium chloride-containing diet (No. 858) to a fourth group, and a 30-percent casein-containing diet (No. 859) to the remaining group. Poor appetite and weakness were noted early. Only 5 of 30 rats survived the 30-day experimental period. Four of the five rats were in the sodium bicarbonate-fed group and one was in the urea-fed group. Renal lesions were noted in all rats and no significant influence could be attributed to any of the 4 agents studied. Early death with the resultant lack of time for the full development of lesions made comparisons difficult.

One-percent acetylsulfadiazine-containing diets were fed to five groups of weanling rats (five per group). The experimental conditions were the same as for 6-week-old rats. The toxicity of the drug for weanlings was greater than for the 6-week-old rats. None of the rats survived the 30-day experimental period. Twenty-one of the twenty-five rats died within 15 days. The remaining four rats, all of which were in the sodium bicarbonate-fed group, died after 26 to 29 days. As with the 6-week-old rats, renal lesions were noted in all the animals.

Five-tenths percent acetylsulfadiazine-containing diets were fed to five groups of 6-week-old rats (6 per group) (table 9). Here too, the conditions, except for the acetylsulfadiazine content of the diets, were the same as in the experiments with 1-percent acetylsulfadiazine-containing diets. Most rats survived the 30-day experimental period. As in a previous experiment (table 7), severe renal lesions were noted in all rats fed the basal, 10-percent casein-containing diet (No. 899). Sodium bicarbonate was effective in preventing the development of severe renal lesions but ineffective in preventing the development of milder ones. The 30-percent casein-containing diet (No. 909) appeared to have some degree of protective action. Only two of six rats had severe lesions, three had milder ones, and one rat had no lesions. In the group fed urea and sodium chloride, some of the rats did not survive the experimental period and the data are inadequate for determining any preventive effect.

The conjugated sulfadiazine fraction in the urine determined at 5-day intervals during the 30-day experimental period was from 93 to 97 percent of the total drug (table 9). Since the amount of deacetylation (as judged by the excretion of free sulfadiazine) was so small, the present data are not adequate for determining whether the various agents had any significant influence on deacetylation.

The effects of the various agents in depressing the sulfadiazine blood concentration are clearly shown (table 9) both with the free form as in earlier experiments (table 3) and with the conjugated form. Values for drug concentrations in the heart and lungs were lower but showed the same pattern as the blood values.

DISCUSSION

Reduction of the casein content of a sulfadiazine-containing diet to a level of 10 percent has permitted the uniform production of severe renal tubular lesions. These lesions are similar in general character to those reported in experimental animals (1-3) and observed in man (4-8) following the administration of sulfadiazine. Sodium bicarbonate, sodium chloride and urea, in addition to casein, have been found to exert a preventive action on the development of these renal lesions. The preventive effect of these agents is another illustration of the need for consideration of dietary factors in the interpretation of pharmacologic data (25-27).

High concentrations of sulfadiazine in the blood have been noted along with the development of lesions. These high levels have been greatly reduced by the agents which exert preventive actions on the development of lesions. However, it appears likely that even if the magnitude of the blood concentration exerts an important influence on the development of renal lesions, there are other significant factors as well. In some rats with high blood levels lesions have not de-

veloped (table 3), and lesions have been prevented by sodium bicarbonate when the administration of large doses of sulfadiazine resulted in high blood values (table 4). In addition, extremely severe lesions were developed by the administration of acetylsulfadiazine even though relatively low blood concentrations were achieved (table 9).

The reduction of blood levels by sodium bicarbonate and sodium chloride may be explained in part by an increase in renal clearance as shown for sulfamerazine in dogs (28, 29). Clinical studies (30) have also indicated some depression of blood level and increased urinary excretion of sulfadiazine after the oral administration of sodium bicarbonate. Reduction of blood concentration of sulfanilamide by increasing the casein content of the diet has been reported in rats (25, 26) and mice (31). It appears suggestive that this casein effect may be accounted for to some extent by the action of urea which results from its catabolism.

The influence of the preventive agents on the therapeutic effectiveness of sulfadiazine as a result of the decrease in sulfadiazine concentration has not been determined in these studies. It is of interest to note that Rosenthal has found an impairment in the therapeutic effectiveness of sulfanilamide when the casein content of the diet was increased (31).

Increased conjugation of sulfadiazine and high renal concentrations of conjugated sulfadiazine have been noted whenever a severe lesion has developed, but were not found in the absence of a lesion. Although isolation and identification of the conjugated sulfadiazine fraction has not been made in these studies, it is probable that it consists largely of acetylsulfadiazine. The administration of acetylsulfadiazine under the same conditions as sulfadiazine has indicated this conjugated compound to be far more toxic both in regard to the production of renal lesions and the survival of the animals. This greater toxicity of acetylsulfadiazine is in accord with data reported in studies on rats (2) and with data contained in clinical reports (4, 6, 11). It is noteworthy that, unlike other acetylated sulfonamides, acetylsulfadiazine is more soluble than the free compound.

The same agents (sodium bicarbonate, sodium chloride, urea, and casein) which reduced the sulfadiazine blood levels also decreased the degree of conjugation and the renal concentration of conjugated sulfadiazine. Although there may be an important causal relationship between blood level and conjugation, it appears that other factors may also be operative.

It seems clear that the final development of renal lesions may be governed by a number of factors. The results of the present studies have suggested important influences by blood level and conjugation. While the value of increasing the solubility of the drug in the tubules has been confirmed, it has also been shown that sodium chloride,

despite its "salting out" effect on both sulfadiazine and acetylsulfadiazine is effective in the prevention of renal lesions. It appears likely too that other significant factors, not considered here, are operative in the production of renal lesions by sulfadiazine.

SUMMARY AND CONCLUSIONS

Sulfadiazine (1 percent) in a purified diet of low casein content (10 percent) fed to rats for 30 days has resulted in the uniform production of severe renal lesions.

Casein, urea, sodium bicarbonate, and sodium chloride have been found to exert preventive actions on the development of these renal lesions, despite restriction of water intake. Sodium bicarbonate was found to be the most effective of these agents under the specific conditions of this study.

The blood sulfadiazine concentration has been reduced by each of the preventive agents mentioned. The magnitude of the blood sulfadiazine concentration may influence the production of these renal lesions, but there appear to be other significant factors as well.

In experiments with sodium bicarbonate, severe renal lesions have been prevented, even when high blood sulfadiazine concentrations resulted from the feeding of a 4-percent sulfadiazine-containing diet.

Increased conjugation of sulfadiazine and high renal concentration of conjugated sulfadiazine have been noted to be associated invariably with these severe lesions and have never been noted when lesions were prevented.

Acetylsulfadiazine, despite its greater solubility and lower blood concentration than free sulfadiazine, was found to be far more toxic than free sulfadiazine as judged by the incidence and severity of renal lesions and by survival.

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PUBLIC HEALTH IN GREENLAND¹

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THE COUNTRY

Greenland, a Danish possession and the world's largest island; has an area of approximately 840,000 square miles (published estimates vary widely) and a population of 18,000. The native Eskimos make up over 90 percent of the population, the other residents of the country being principally Danish officials and employces. The principal settlements are located along the southwest and west coasts.

The interior of the land is buried beneath a vast ice cap which covers the entire island except for a narrow coastal zone, comprising approximately 40,000 square miles, or an area roughly equal to that of Tennessee. On the whole, vegetation in the coastal areas is very scanty. In certain sections of the southern west-coast region a few low-growing shrubs are found and a luxuriant growth of grass and flowering plants carpets some of the protected valleys during the summer season.

Greenland was discovered by the Norsemen in the tenth century. They established colonies at several places, which existed for several hundred years, but these settlements disappeared from the historical scene well over 200 years before the beginning of the modern period in the island's history. This period dates from the first of the eighteenth century when Danish missionary groups settled in Greenland and the present capital, Godthaab, was founded by the missionary Hans Egede in 1721.

The Danes have worked unceasingly in behalf of the interests of the natives and in Greenland they have written a bright page in the record of European colonial administration. The Greenlandic language has been reduced to writing and is employed by pastors, teachers, and officials in their daily intercourse with the Eskimos. Schools and churches have been maintained throughout the country and the regional industries have been protected and developed. Not least among the accomplishments of the Danish administration has been the establishment of a complete health program to care for the needs of the native population.

¹ This report is based on information gained in conversations with the Governor of Greenland and members of the American Consular Staff at Godthaab in the spring of 1943; upon recent personal correspondence with the Chief Medical Officer of the Greenland Public Health Service, Dr. Sylvester M. Saxtorph; and upon observations of a general nature which were made in 1943 when the writer was serving as the ship's surgeon on the U. S. C. G. cutter *Tahoma*, attached to the Greenland Patrol.

TUBERCULOSIS—THE MAJOR PUBLIC HEALTH PROBLEM

Tuberculosis is the major public health problem in Greenland, as it also is in Iceland. The disease has existed in both of these islands for centuries and is believed to have been present in Greenland long before the Danish colonization, which suggests that it was introduced into the country by the Norsemen who came to Greenland from Iceland, a land that has no native Eskimo population. The high incidence of the disease among the Eskimos probably is partly due to a constitutional racial weakness in the natives; but doubtless other factors, such as overcrowding in family living quarters, are also important in favoring the spread of the infection. The death rate from tuberculosis is very high. In 1937 there were 99 deaths in the west coast of Greenland, which would place the annual death rate from tuberculosis for the entire population at approximately 550 per 100,000. During the same year 280 deaths from other causes were recorded for the same area.

The Greenlandic Government maintains 17 hospitals along the coast and these have a total of about 350 beds, giving 19.4 hospital beds per thousand population (United States, 9.7 per thousand population). Dr. Saxtorph estimates that 80 percent of the hospital beds are assigned to tuberculosis patients and states that as many as possible of all active cases of the disease receive hospital treatment. Pneumothorax collapse therapy is carried out regularly in all the hospitals, and occasional thoracoplastic operations are performed. Phrenic nerve interruption has been widely used in the past but more recently this operation has been abandoned in Greenland (in line with the general policy in most European countries) as being a none-too-effective procedure. Through the untiring efforts of the Danish physicians, and the liberal use of public funds to support the country's health program, conditions with respect to tuberculosis control in Greenland are now much better than they were in other years.

VENEREAL DISEASES WELL CONTROLLED

Syphilis does not exist among the native population due to the strict regulations governing visitors and employees coming from other countries to Greenland. Despite colorful tales told by some returning members of American service units that have been in the Greenland area, it is doubtful that many of the members of these units have had any opportunity for social intercourse with the natives. Our American authorities are particularly careful to see that the laws of the country governing relations of foreigners with the Eskimos are strictly obeyed by our troops, coastguardsmen, and civilian employees in accordance with the agreements upon which we entered Greenland in 1941.

A few cases of gonorrhea are reported scattered along the coast but

the disease is not a serious health problem. The natives are cooperative in seeking treatment, and the complications which are so often seen among female patients in other countries are seldom reported among the Eskimo women.

OTHER COMMUNICABLE DISEASES

Measles (rubeola) has never occurred in Greenland and German measles (rubella) likewise is not reported from this country.

Smallpox (variola) vaccination is obligatory and all the native children are inoculated at an early age. From the lack of any reports to the contrary, one would judge that this program has been generally successful in preventing outbreaks of smallpox among the natives.

OCCUPATIONAL DISEASES AMONG CRYOLITE MINERS

For several generations the cryolite mines at Ivigtut ("plentiful grass") have been worked by Danish employees. This mineral, which is comparatively rich in fluorine, is used in the production of aluminum. Workers exposed to cryolite dust may ingest enough of it in a year or two to cause chronic fluorine poisoning, leading to the occurrence of "mottled enamel" or to generalized osteosclerosis, depending on the degree of exposure (1). The measures taken to protect the miners at Ivigtut against the cryolite dust appear to have been adequate to guard them against fluorine poisoning, for repeated examinations of these men, including X-ray studies, have never revealed any signs of occupational disease among the miners. Since the natives are not employed in the mines they are not exposed to any of the possible hazards of this work.

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NATIONAL INSTITUTE OF HEALTH RESEARCH FELLOWSHIPS

The Public Health Service announces the creation of National Institute of Health research fellowships, after July 1, 1945.

The junior research fellowships will be available to those holding master's degrees in the sciences (such as physics, chemistry, entomology, etc.) allied to public health, from an institution of recognized standing. The stipend will be \$2,400 per annum.

The senior research fellowships will be available to those holding a doctor's degree in one of the sciences allied to public health. The stipend will be \$3,000 per annum.

These fellowships will offer an opportunity for study and research at the Institute or some other institution of higher learning, in association with highly trained specialists in the candidate's chosen field.

Letters of inquiry should be addressed to The Director, National Institute of Health, Bethesda 14, Md.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES

April 22–May 19, 1945

The accompanying table summarizes the prevalence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in the Public Health Reports under the section "Prevalence of disease." The table gives the number of cases of these diseases for the 4 weeks ended May 19, 1945, the number reported for the corresponding period in 1944, and the median number for the years 1940–44.

DISEASES ABOVE MEDIAN PREVALENCE

Diphtheria.—Diphtheria incidence continued at a comparatively high level. For the 4 weeks ended May 19 there were 816 cases reported as compared with 769 for the corresponding period in 1944 and a 1940–44 median of 780 cases. Increases over last year, as well as over the 5-year median, were reported from the West North Central, South Atlantic, East and West South Central, and Pacific sections. In the New England and Mountain sections the incidence was about normal, while in the Middle Atlantic and East North Central sections the incidence was relatively low.

Meningococcus meningitis.—The number of cases (704) of meningococcus meningitis reported for the current 4 weeks was only about 45 percent of the number reported in 1944, but it was more than twice the 1940–44 median for the same weeks. Each section of the country showed a decline from the 1944 incidence, but the New England section alone showed a decline from the 1940–44 median. While the number of cases remains high in relation to normal years, it is evident that the 1943–44 epidemic is subsiding.

Poliomyelitis.—The incidence of poliomyelitis still remains somewhat above the seasonal expectancy. For the 4 weeks ended May 19 there were 136 cases reported, which was almost twice the 1940–44 median for the corresponding period. Of the total cases, Texas reported 39, New York 20, South Carolina 11, California 7, and Florida 5 cases, but no other State reported more than 4 cases for the 4-week period. For the country as a whole the current incidence is the highest for this period since 1939 when 149 cases were reported.

Scarlet fever.—This disease, while less prevalent than in 1944, was still above the normal seasonal expectancy. For the 4 weeks ended May 19 there were 19,001 cases as compared with a 5-year median of 15,612 cases for this period. Each section of the country reported a lower incidence than in 1944, but the number of cases fell below the median expectancy in only one section, the East South Central.

Number of reported cases of 9 communicable diseases in the United States during the 4-week period April 22-May 19, 1945, the number for the corresponding period in 1944, and the median number of cases reported for the corresponding period, 1940-44

Division	Current period	1944	5-year median	Current period	1944	5-year median	Current period	1944	5-year median
	Diphtheria			Influenza ¹			Measles ²		
United States.....	816	769	780	5,246	5,210	5,650	19,070	104,755	104,755
New England.....	26	27	26	90	78	12	1,358	8,080	8,080
Middle Atlantic.....	85	96	120	25	28	81	2,229	14,927	14,927
East North Central.....	73	117	144	200	323	510	2,593	19,422	19,422
West North Central.....	93	53	73	59	102	102	869	7,512	7,512
South Atlantic.....	153	142	142	1,207	1,399	1,972	968	14,683	7,852
East South Central.....	71	57	58	121	388	388	449	2,260	2,260
West South Central.....	155	120	124	2,868	2,245	2,156	2,267	15,429	6,894
Mountain.....	51	58	50	611	403	461	1,522	3,724	4,324
Pacific.....	109	99	67	65	244	290	6,815	18,700	7,313
	Meningococcus meningitis			Polliomyelitis			Scarlet fever		
United States.....	704	1,636	336	136	103	73	19,001	25,698	15,612
New England.....	34	83	48	5	6	1	2,023	2,252	1,458
Middle Atlantic.....	156	401	97	21	5	8	5,282	6,049	4,590
East North Central.....	133	412	22	12	6	7	4,756	7,115	4,189
West North Central.....	49	154	14	6	6	4	1,621	2,684	1,141
South Atlantic.....	86	189	74	24	16	16	1,692	2,425	819
East South Central.....	71	133	32	12	7	11	507	642	638
West South Central.....	67	106	34	45	26	11	480	658	319
Mountain.....	15	29	5	1	3	5	765	1,087	437
Pacific.....	93	129	31	10	28	22	1,895	2,786	771
	Smallpox			Typhoid and paratyphoid fever			Whooping cough ³		
United States.....	38	48	93	281	345	377	10,548	7,061	15,291
New England.....	0	0	0	9	20	27	1,144	577	1,110
Middle Atlantic.....	0	0	0	38	29	51	2,193	1,008	2,896
East North Central.....	18	16	35	41	39	39	1,516	913	3,367
West North Central.....	2	8	14	9	10	15	304	343	673
South Atlantic.....	1	4	7	51	71	71	1,629	1,467	1,586
East South Central.....	2	6	14	39	40	42	351	468	673
West South Central.....	10	4	14	68	70	57	1,841	1,172	1,623
Mountain.....	4	1	5	16	9	18	523	536	620
Pacific.....	1	9	9	10	57	25	1,767	577	2,103

¹ Mississippi and New York excluded; New York City included.

² Mississippi excluded.

DISEASES BELOW MEDIAN PREVALENCE

Influenza.—The number of cases (5,246) of influenza reported during the 4 weeks ended May 19 was about the same as that reported for the corresponding period in 1944 and only slightly below the 1940-44 median. While the number of cases in the New England section was not large, it was more than 7 times the 5-year median. In the Mountain section the number of cases (611) was 1.3 times the median, but in all other sections the incidence was relatively low.

Measles.—This disease continued at a low level, the number of cases (19,070) reported for the current 4-week period being the lowest in the 17 years for which these data are available. The 1940-44 median for the corresponding weeks is approximately 105,000 cases. The situation is favorable in all sections of the country, each section reporting an unusually low incidence.

Smallpox.—The number of cases (38) of smallpox was the lowest on record for this period of the year. The incidence dropped below even the previous year, when 48 cases were reported for these same weeks, and it was less than one-half of the seasonal median. Fifteen of the cases occurred in Indiana, and 4 each in Louisiana and Texas; no more than 2 cases were reported from any other State.

Typhoid and paratyphoid fever.—The incidence of this disease reached a new low level. For the 4 weeks ended May 19 there were 281 cases reported as compared with 345 in 1944 and a 1940–44 median of 377 cases. The West South Central section reported an increase over the median; in the East North Central and Mountain sections the disease was about normal; and in all other sections the incidence fell below the normal seasonal expectancy.

Whooping cough.—The number of reported cases (10,548) of whooping cough was about 1.5 times the number reported for this period in 1944, but it was only about 70 percent of the preceding 5-year median (approximately 15,300 cases). In the New England, South Atlantic, and Mountain sections the disease was about normal, but in all other sections the incidence was comparatively low.

MORTALITY, ALL CAUSES

For the 4 weeks ended May 19 there were 36,279 deaths from all causes reported by 93 large cities to the Bureau of the Census. The preceding 3-year average for the same weeks was 36,028 deaths. The number of deaths for the first 2 weeks of the current period was less than the 3-year average, but during the third week the number was 2 percent higher than the average, and during the fourth week it was 5 percent above the average.

INCIDENCE OF HOPITALIZATION, APRIL 1945

Through the cooperation of the Hospital Service Plan Commission of the American Hospital Association, data on hospital admissions among members of Blue Cross Hospital Service Plans are presented monthly. These plans provide prepaid hospital service. The data cover hospital service plans scattered throughout the country, mostly in large cities.

Item	April	
	1944	1945
1. Number of plans supplying data.....	69	80
2. Number of persons eligible for hospital care.....	12,002,748	16,954,625
3. Number of persons admitted for hospital care.....	96,306	149,184
4. Incidence per 1,000 persons, annual rate, during current month (daily rate×365).....	97.8	107.1
5. Incidence per 1,000 persons, annual rate for the 12 months ended April 30.....	104.0	103.7
6. Number of plans reporting on hospital days.....	17	21
7. Days of hospital care per case discharged during month ¹	8.27	7.89

¹ Days include entire stay of patient in hospital whether at full pay or at a discount.

DEATHS DURING WEEK ENDED MAY 19, 1945

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended May 19, 1945	Correspond- ing week, 1944
Data for 92 large cities of the United States:		
Total deaths.....	9,097	8,816
Average for 3 prior years.....	8,652	-----
Total deaths, first 20 weeks of year.....	187,832	194,523
Deaths under 1 year of age.....	536	617
Average for 3 prior years.....	559	-----
Deaths under 1 year of age, first 20 weeks of year.....	12,311	12,421
Data from industrial insurance companies:		
Policies in force.....	67,307,972	66,545,578
Number of death claims.....	13,633	12,919
Death claims per 1,000 policies in force, annual rate.....	10.6	10.2
Death claims per 1,000 policies, first 20 weeks of year, annual rate.....	11.0	10.9

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED MAY 26, 1945

Summary

The total of 44 cases of poliomyelitis reported for the current week, as compared with 47 last week, includes 17 cases in Texas (last week 24), 4 cases each in New York and California, and 18 cases in 10 other States. The total for the corresponding week last year was 39, and the median number for the corresponding weeks of the past 5 years is 28. The total for the first 21 weeks of the year is 741 cases, as compared with 499 for the same period last year, which is also the 5-year median. The largest numbers of cases in Texas have been reported in three widely separated counties—Hidalgo, Harris, and Haskell. Up to May 19, cases had been reported in 33 counties of the State.

For the third consecutive week the incidence of meningococcus meningitis increased. The total number of cases reported currently is 182, as compared with 174 last week and a 5-year median of 81. For the corresponding weeks of last year and 1943 the totals were, respectively, 332 and 423. Of the current total, 100 cases occurred in 6 States, as follows (last week's figures in parentheses): New York 26 (26), New Jersey 11 (11), Illinois 23 (14), Missouri 17 (2), Virginia 10 (1), California 13 (19). The total for the year to date is 4,695, as compared with 10,609 and 10,276, respectively, for the corresponding periods of the epidemic years of 1944 and 1943, and a 5-year median of 1,648 for the period.

Slight increases occurred during the week in the incidence of measles and scarlet fever. The current figure for measles, 5,335, however, is less than half the least number reported for the corresponding week of the past 5 years, but the total for the week for scarlet fever, 4,679 cases, is slightly more than that for any corresponding week since 1937. To date the incidence of whooping cough is almost 40 percent above that for last year, while both smallpox and typhoid fever are below last year's low figures.

Deaths recorded for the week in 93 large cities of the United States totaled 9,033, as compared with 9,202 last week, 8,638 for the corresponding week last year, and a 3-year (1942-44) average of 8,600. The cumulative figure is 199,034, as compared with 205,326 for the first 21 weeks of last year.

Telegraphic morbidity reports from State health officers for the week ended May 26, 1945, and comparison with corresponding week of 1944, and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, men- ingococcus		
	Week ended—		Med- ian 1940- 44	Week ended—		Med- ian 1940- 44	Week ended—		Med- ian 1940- 44	Week ended—		Med- ian 1940- 44
	May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944	
NEW ENGLAND												
Maine.....	0	0	0	—	—	—	0	207	97	0	1	1
New Hampshire.....	0	0	0	—	—	—	7	4	28	0	0	0
Vermont.....	0	0	0	—	—	—	17	39	88	0	0	0
Massachusetts.....	4	3	3	—	—	—	286	982	998	6	16	3
Rhode Island.....	0	0	0	26	9	—	4	9	60	0	1	0
Connecticut.....	0	0	0	2	—	2	117	437	437	1	8	4
MIDDLE ATLANTIC												
New York.....	10	22	19	13	11	16	143	614	888	26	52	9
New Jersey.....	1	2	3	5	2	2	64	925	990	11	18	2
Pennsylvania.....	12	11	9	—	1	1	504	600	1,143	9	20	9
EAST NORTH CENTRAL												
Ohio.....	5	7	9	7	12	12	94	412	412	6	17	3
Indiana.....	7	1	3	6	2	4	49	46	162	4	3	2
Illinois.....	7	13	16	1	9	9	299	419	419	23	23	1
Michigan ¹	6	4	4	1	3	2	288	886	886	4	35	3
Wisconsin.....	3	2	2	24	4	37	73	2,122	1,644	2	7	1
WEST NORTH CENTRAL												
Minnesota.....	4	0	2	2	—	—	15	476	476	2	5	1
Iowa.....	2	1	2	—	—	—	76	226	268	3	7	1
Missouri.....	1	2	5	—	1	1	40	159	189	17	12	3
North Dakota.....	1	0	0	7	—	—	1	15	15	0	0	0
South Dakota.....	1	0	0	—	—	—	6	9	37	0	2	0
Nebraska.....	5	0	0	2	1	1	19	16	37	0	2	0
Kansas.....	6	5	3	—	1	1	49	220	377	1	4	0
SOUTH ATLANTIC												
Delaware.....	1	0	0	—	—	—	1	8	20	0	0	0
Maryland ²	9	8	5	1	3	3	38	290	290	4	5	5
District of Columbia.....	0	0	0	—	—	—	6	147	92	1	0	0
Virginia.....	4	5	5	51	38	59	30	440	286	10	9	9
West Virginia.....	3	0	3	10	3	4	3	98	51	1	0	0
North Carolina.....	2	3	3	—	9	4	31	615	557	4	4	3
South Carolina.....	8	12	5	155	180	180	26	243	141	2	2	2
Georgia.....	1	2	3	6	6	8	13	62	142	1	5	1
Florida.....	2	1	1	—	—	3	14	168	168	3	7	0
EAST SOUTH CENTRAL												
Kentucky.....	3	2	2	1	25	4	42	74	113	1	3	0
Tennessee.....	2	3	3	12	8	10	69	44	133	3	3	2
Alabama.....	3	5	5	9	46	21	7	135	135	2	10	2
Mississippi ³	3	6	2	—	—	—	—	—	—	2	7	3
WEST SOUTH CENTRAL												
Arkansas.....	0	3	3	16	10	16	38	45	75	6	1	1
Louisiana.....	5	0	1	5	2	2	249	34	27	2	4	2
Oklahoma.....	2	8	3	26	16	19	26	240	98	0	1	0
Texas.....	30	36	16	568	421	389	457	2,281	900	9	17	8
MOUNTAIN												
Montana.....	0	0	0	4	—	2	16	74	81	0	0	0
Idaho.....	0	0	0	—	—	—	21	19	40	2	0	0
Wyoming.....	1	0	0	—	—	3	4	82	82	0	0	0
Colorado.....	9	5	7	17	9	20	26	114	208	0	1	1
New Mexico.....	0	7	2	—	4	2	9	106	87	0	0	0
Arizona.....	4	4	2	33	40	55	10	80	80	0	1	0
Utah ³	0	0	0	4	4	5	226	52	134	0	0	0
Nevada.....	0	1	0	—	—	—	5	9	0	0	0	0
PACIFIC												
Washington.....	6	8	2	—	—	1	285	274	502	1	1	1
Oregon.....	3	1	2	5	3	6	69	0	137	0	2	0
California.....	13	18	11	10	11	55	1,463	3,378	734	13	16	8
Total.....	189	211	199	1,009	884	884	5,335	17,935	19,116	182	332	81
21 weeks.....	5,726	4,786	5,590	62,406	332,541	164,062	69,471	521,500	422,963	44,666	10,609	1,648

¹ New York City only.

² Period ended earlier than Saturday.

³ Correction: Louisiana, week ended May 5, meningococcus meningitis 6 cases (instead of 2).

Telegraphic morbidity reports from State health officers for the week ended May 26, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Polio-myelitis			Scarlet fever			Smallpox			Typhoid and para-typhoid fever ¹		
	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44
	May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944		May 26, 1945	May 27, 1944	
NEW ENGLAND												
Maine.....	0	0	0	40	34	13	0	0	0	0	0	0
New Hampshire.....	0	0	0	26	0	3	0	0	0	0	0	0
Vermont.....	0	0	0	10	6	5	0	0	0	0	0	0
Massachusetts.....	0	0	0	317	286	197	0	0	0	1	7	3
Rhode Island.....	1	0	0	20	7	7	0	0	0	0	1	0
Connecticut.....	0	0	0	57	58	58	0	0	0	0	1	0
MIDDLE ATLANTIC												
New York.....	4	4	1	739	448	448	0	0	0	2	4	5
New Jersey.....	0	0	0	116	237	237	0	0	0	1	3	1
Pennsylvania.....	1	1	1	567	464	384	0	0	0	8	8	8
EAST NORTH CENTRAL												
Ohio.....	3	1	1	332	371	213	1	0	0	1	0	3
Indiana.....	3	0	0	90	38	39	0	2	1	2	2	2
Illinois.....	0	0	0	312	275	269	1	0	2	2	3	4
Michigan ²	0	0	0	325	327	267	0	0	0	0	1	1
Wisconsin.....	0	0	0	244	292	149	0	1	2	0	0	0
WEST NORTH CENTRAL												
Minnesota.....	0	1	0	87	125	52	0	0	0	0	0	0
Iowa.....	0	0	0	34	156	42	0	0	1	0	0	1
Missouri.....	1	0	0	49	61	58	0	0	1	0	5	3
North Dakota.....	0	0	0	31	32	5	0	0	0	1	0	0
South Dakota.....	0	0	0	8	11	6	0	0	0	0	0	0
Nebraska.....	0	0	0	59	11	9	1	0	0	0	0	0
Kansas.....	0	1	1	59	51	51	0	0	0	1	1	0
SOUTH ATLANTIC												
Delaware.....	0	0	0	4	8	8	0	0	0	0	0	0
Maryland ³	0	0	0	132	122	49	0	0	0	0	2	3
District of Columbia.....	0	0	0	30	82	14	0	0	0	0	0	0
Virginia.....	1	1	1	62	55	25	0	0	0	3	0	3
West Virginia.....	0	0	0	32	67	34	0	0	0	1	3	3
North Carolina.....	0	1	0	72	20	14	0	0	0	2	4	2
South Carolina.....	3	0	0	14	5	5	0	0	0	3	4	1
Georgia.....	1	0	0	23	16	12	0	0	0	2	5	9
Florida.....	0	5	1	6	3	3	0	0	0	3	3	3
EAST SOUTH CENTRAL												
Kentucky.....	0	1	0	42	49	36	0	0	0	1	11	5
Tennessee.....	0	0	0	29	26	26	0	0	0	5	4	4
Alabama.....	1	2	1	12	8	8	0	0	0	3	2	1
Mississippi ²	0	2	0	7	4	2	0	1	1	2	2	2
WEST SOUTH CENTRAL												
Arkansas.....	1	0	0	8	4	4	0	0	1	3	1	1
Louisiana.....	0	9	1	12	1	4	0	3	0	1	6	6
Oklahoma.....	0	0	0	20	14	12	1	0	0	1	3	3
Texas.....	17	4	1	69	57	36	0	0	1	3	7	7
MOUNTAIN												
Montana.....	0	0	0	16	25	14	0	0	0	1	0	0
Idaho.....	0	0	0	18	21	10	0	0	0	1	0	0
Wyoming.....	0	0	0	3	6	6	0	0	0	0	0	0
Colorado.....	0	1	0	39	29	20	0	0	0	1	0	0
New Mexico.....	0	0	0	11	11	7	0	0	0	0	0	0
Arizona.....	0	1	0	48	24	10	0	0	0	1	0	0
Utah ²	0	0	0	18	43	20	3	0	0	1	0	0
Nevada.....	0	0	0	1	1	0	0	0	0	0	0	0
PACIFIC												
Washington.....	3	0	0	51	124	37	0	0	0	1	0	0
Oregon.....	0	0	1	26	90	10	0	0	0	0	1	1
California.....	4	4	5	352	160	117	0	0	0	0	18	6
Total.....	44	39	28	4,679	4,365	3,218	7	7	34	58	113	113
21 weeks.....	741	499	469	112,805	128,239	82,496	216	241	536	1,242	1,603	1,700

¹ Period ended earlier than Saturday.

² Including paratyphoid fever reported separately as follows: Massachusetts 1; New York 1; South Carolina 1; Florida 2; Texas 1; Montana 1.

³ Correction: Florida, poliomyelitis, week ended April 28, 4 cases (instead of 5); week ended May 5, 8 cases (instead of 0), all in Palm Beach County; Ohio, smallpox, week ended May 19, 0 (instead of 1).

Telegraphic morbidity reports from State health officers for the week ended May 26, 1945, and comparison with corresponding week of 1944 and 5-year median—Con.

Division and State	Whooping cough			Week ended May 26, 1945							
	Week ended—		Median 1940-44	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever	Undulant fever
	May 26, 1945	May 26, 1944		Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine.....	25	2	24	0	0	0	0	0	0	0	1
New Hampshire.....	4	0	4	0	0	0	0	0	0	0	0
Vermont.....	24	5	13	0	0	0	0	0	0	0	1
Massachusetts.....	156	57	161	0	1	0	0	0	0	0	2
Rhode Island.....	20	5	18	0	0	0	0	0	0	0	0
Connecticut.....	77	39	39	0	0	0	0	0	0	0	3
MIDDLE ATLANTIC											
New York.....	210	102	270	4	4	0	1	0	0	0	6
New Jersey.....	117	57	172	2	1	0	0	0	0	0	0
Pennsylvania.....	221	70	238	0	0	0	0	0	0	0	2
EAST NORTH CENTRAL											
Ohio.....	132	64	145	0	0	0	0	0	0	1	0
Indiana.....	30	4	32	0	0	5	0	0	0	0	0
Illinois.....	39	33	106	0	1	0	0	1	1	0	8
Michigan ¹	44	51	279	4	1	0	0	0	0	0	7
Wisconsin.....	31	60	111	0	0	0	2	0	0	0	3
WEST NORTH CENTRAL											
Minnesota.....	14	20	40	1	0	1	0	0	0	0	8
Iowa.....	3	11	28	0	0	0	0	0	0	0	10
Missouri.....	16	21	21	0	0	0	0	0	0	0	12
North Dakota.....	4	0	3	0	0	0	0	0	0	0	0
South Dakota.....	0	5	5	0	0	0	0	0	0	0	0
Nebraska.....	4	0	6	0	0	0	0	0	0	0	0
Kansas.....	19	43	63	0	0	0	0	0	1	0	6
SOUTH ATLANTIC											
Delaware.....	1	0	1	0	0	0	0	0	0	0	0
Maryland ²	55	54	106	0	0	0	0	2	0	0	1
District of Columbia.....	14	4	10	0	0	0	0	0	0	0	0
Virginia.....	54	104	89	0	0	23	0	0	1	0	1
West Virginia.....	10	21	26	0	0	0	0	1	0	0	0
North Carolina.....	182	147	165	0	0	0	0	0	1	0	0
South Carolina.....	60	91	89	2	17	0	0	0	0	6	0
Georgia.....	12	13	35	1	5	2	0	0	0	14	2
Florida.....	7	22	24	2	1	1	0	0	0	9	0
EAST SOUTH CENTRAL											
Kentucky.....	58	80	80	0	0	0	0	0	1	0	1
Tennessee.....	27	16	65	0	0	0	0	1	3	0	0
Alabama.....	35	26	35	0	0	0	0	0	0	11	2
Mississippi ³				0	0	0	0	0	0	2	0
WEST SOUTH CENTRAL											
Arkansas.....	2	5	32	0	5	0	0	0	3	2	0
Louisiana.....	7	2	5	2	0	0	2	0	0	5	4
Oklahoma.....	10	7	22	0	1	0	0	0	0	0	0
Texas.....	250	263	374	11	337	71	1	0	0	31	15
MOUNTAIN											
Montana.....	2	1	4	0	0	0	0	0	2	0	0
Idaho.....	2	0	3	0	0	0	0	0	0	0	1
Wyoming.....	3	1	3	0	0	0	0	2	0	0	0
Colorado.....	35	21	19	0	0	0	0	0	0	0	2
New Mexico.....	3	4	22	1	0	0	0	0	0	0	0
Arizona.....	15	16	23	0	0	14	0	0	0	0	0
Utah ⁴	43	72	66	0	0	0	0	0	1	0	0
Nevada.....	0	0	0	0	0	0	0	1	0	0	0
PACIFIC											
Washington.....	24	8	57	0	0	0	0	0	0	0	0
Oregon.....	27	5	20	0	0	0	0	0	0	0	0
California.....	412	90	378	3	1	0	1	0	0	0	9
Total.....	2,540	1,722	3,805	33	375	117	7	8	14	81	107
Same week, 1944.....	1,722			25	571	117	10	16	10	64	70
Average, 1942-44.....	3,185			25	330	90	11	19	14	735	
21 weeks: 1945.....	52,392			628	8,879	2,404	140	50	331	1,084	1,867
1944.....	37,697			534	5,446	1,549	225	46	221	942	1,220
Average, 1942-44.....	67,811		780,538	510	3,808	1,176	210	784	327	748	

¹ Period ended earlier than Saturday.

² Correction: Louisiana, week ended May 5, typhus fever 4 cases (instead of 3).

³ 5-year median, 1940-44.

⁴ Leprosy: Illinois, 1 case.

WEEKLY REPORTS FROM CITIES

City reports for week ended May 19, 1945

This table lists the reports from 90 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland.....	0	0		0	0	0	2	0	1	0	0	16
New Hampshire:												
Concord.....	0	0		0	2	0	0	0	2	0	0	0
Vermont:												
Barre.....	0	0		0	4	0	0	0	0	0	0	2
Massachusetts:												
Boston.....	1	0		1	92	3	8	0	60	0	0	26
Fall River.....	0	0		0	3	0	0	0	5	0	0	1
Springfield.....	0	0		0	0	0	0	0	18	0	0	0
Worcester.....	0	0		0	8	0	3	0	16	0	0	5
Rhode Island:												
Providence.....	0	0		0	9	0	2	0	4	0	0	10
Connecticut:												
Bridgeport.....	0	0		0	0	0	2	0	5	0	0	0
Hartford.....	0	0		0	64	0	0	0	12	0	0	0
New Haven.....	0	0		0	3	1	1	0	0	0	0	7
MIDDLE ATLANTIC												
New York:												
Buffalo.....	0	0		0	4	2	2	0	12	0	0	0
New York.....	10	1	1	3	45	15	52	4	276	0	3	69
Rochester.....	2	0		0	14	1	1	0	16	0	0	19
Syracuse.....	0	0		0	1	0	2	0	9	0	0	37
New Jersey:												
Camden.....	0	0	1	0	1	0	4	0	4	0	1	0
Newark.....	0	0		0	5	4	2	0	28	0	0	11
Trenton.....	0	0	1	0	6	0	0	0	5	0	0	0
Pennsylvania:												
Philadelphia.....	0	0	3	2	311	3	22	0	84	0	3	85
Pittsburgh.....	0	0	1	0	3	6	11	0	32	0	1	6
Reading.....	1	0		0	8	0	3	0	23	0	0	1
EAST NORTH CENTRAL												
Ohio:												
Cincinnati.....	0	0		1	7	0	8	1	13	0	0	3
Cleveland.....	2	0	2	0	9	1	6	0	64	0	0	49
Columbus.....	1	0		0	4	0	2	0	5	0	0	1
Indiana:												
Fort Wayne.....	0	0		0	0	0	2	0	7	0	0	0
Indianapolis.....	1	0	4	0	28	0	3	0	21	0	0	1
South Bend.....	0	0		0	0	0	0	0	1	0	0	0
Terre Haute.....	0	0		0	2	0	2	0	5	0	0	0
Illinois:												
Chicago.....	1	0	1	1	183	10	16	0	106	0	0	12
Springfield.....	0	0		0	0	1	2	0	11	0	0	0
Michigan:												
Detroit.....	3	0	3	0	133	0	13	0	108	0	0	11
Flint.....	0	0		0	5	0	0	0	9	0	0	2
Grand Rapids.....	0	0		0	7	0	1	0	14	0	0	1
Wisconsin:												
Kenosha.....	0	0		0	1	0	0	0	14	0	0	2
Milwaukee.....	0	0		0	8	0	1	0	58	0	0	3
Racine.....	0	0		0	4	0	0	0	3	0	0	0
Superior.....	0	0		0	9	0	0	0	0	0	0	1
WEST NORTH CENTRAL												
Minnesota:												
Duluth.....	0	0		0	0	0	1	0	11	0	0	1
Minneapolis.....	0	0		0	0	0	7	0	20	0	0	1
St. Paul.....	0	0		0	2	0	3	0	7	0	0	3
Missouri:												
Kansas City.....	2	0		0	10	0	11	0	18	0	0	0
St. Joseph.....	0	0		0	1	0	0	0	5	0	0	0
St. Louis.....	0	0		0	13	1	8	0	20	0	1	15

City reports for week ended May 19, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococ- cus, cases	Pneumonia deaths	Pollomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL— continued												
North Dakota:												
Fargo.....	0	0		0	0	0	1	0	3	0	0	0
Nebraska:												
Omaha.....	3	0		0	33	0	2	0	18	0	0	1
Kansas:												
Topeka.....	1	0		0	1	0	0	0	12	0	0	0
Wichita.....	0	0		0	4	1	4	0	12	0	0	1
SOUTH ATLANTIC												
Delaware:												
Wilmington.....	1	0		0	0	1	1	0	1	0	0	0
Maryland:												
Baltimore.....	12	0	1	1	6	4	6	0	65	0	2	47
Cumberland.....	0	0		0	0	0	0	0	4	0	0	0
Frederick.....	0	0		0	2	0	0	0	0	0	0	0
District of Columbia:												
Washington.....	2	0		0	11	0	8	0	34	0	0	8
Virginia:												
Lynchburg.....	0	0		0	2	0	0	0	2	0	0	0
Richmond.....	0	0		0	9	0	4	0	9	0	0	1
Roanoke.....	0	0		0	0	0	0	0	7	0	0	0
West Virginia:												
Charleston.....	0	0		0	0	0	0	0	1	0	0	0
Wheeling.....	0	0		0	0	0	0	0	0	0	0	0
North Carolina:												
Raleigh.....	0	0		0	9	0	1	0	0	0	0	8
Wilmington.....	0	0		0	1	0	0	0	0	0	0	2
Winston-Salem.....	0	0		0	0	0	0	0	8	0	0	6
South Carolina:												
Charleston.....	0	0	1	0	0	0	0	2	0	0	0	0
Georgia:												
Atlanta.....	0	0	2	1	0	0	2	0	10	0	2	0
Brunswick.....	0	0		0	1	0	0	0	0	0	0	0
Savannah.....	0	0	1	1	0	1	1	0	0	0	0	0
Florida:												
Tampa.....	1	0		0	0	1	1	0	1	0	0	2
EAST SOUTH CENTRAL												
Tennessee:												
Memphis.....	0	0		1	47	2	5	0	7	0	1	3
Nashville.....	0	0		0	0	0	4	0	3	0	0	3
Alabama:												
Birmingham.....	0	0	1	0	0	2	1	0	6	0	0	0
Mobile.....	1	0		0	0	5	2	0	0	0	0	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock.....	0	0		1	0	0	0	0	0	0	0	0
Louisiana:												
New Orleans.....	3	0	3	0	22	3	5	0	6	0	0	4
Shreveport.....	1	0		0	0	0	7	0	0	0	0	0
Texas:												
Dallas.....	2	0		0	11	0	4	1	5	0	0	2
Galveston.....	0	0		0	0	0	2	0	0	0	0	0
Houston.....	0	0		0	0	0	4	4	3	0	0	2
San Antonio.....	0	0		0	0	0	6	2	0	0	0	2
MOUNTAIN												
Montana:												
Billings.....	0	0		0	1	0	0	0	6	0	0	0
Great Falls.....	0	0		0	1	0	0	0	0	0	0	1
Helena.....	0	0		0	0	0	0	0	4	0	0	0
Missoula.....	0	0		0	4	0	1	0	0	0	0	0
Idaho:												
Boise.....	0	0		0	0	0	0	0	0	0	0	0
Colorado:												
Denver.....	1	0		1	4	0	3	0	23	0	0	14
Pueblo.....	0	0		0	2	0	0	0	2	0	0	7
Utah:												
Salt Lake City.....	0	0		0	98	0	0	0	6	0	0	9

City reports for week ended May 19, 1945—Continued

	Diphtheria cases	Etiophthalmis, infectious, cases	Influenza		Measles cases	Meningitis, meningococ- cus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle.....	0	0	-----	0	20	1	8	0	17	0	0	8
Spokane.....	0	0	-----	0	3	0	1	0	5	0	0	0
Tacoma.....	0	0	-----	0	26	0	0	0	6	0	0	6
California:												
Los Angeles.....	2	0	3	0	76	4	5	0	55	0	0	28
Sacramento.....	0	0	-----	0	15	1	0	0	12	0	0	7
San Francisco.....	2	0	-----	0	175	2	5	0	43	0	0	11
Total.....	56	1	29	14	1,593	76	297	14	1,528	0	14	575
Corresponding week, 1944.....	70	-----	54	20	4,913	-----	326	-----	1,826	2	15	321
Average, 1940-44.....	60	-----	56	19	5,605	-----	345	-----	1,495	1	17	1,044

¹ 3-year average, 1942-44.

² 5-year median, 1940-44.

Anthrax.—Cases: Philadelphia, 1.

Dysentery, amebic.—Cases: New York, 5; Atlanta, 2; San Antonio, 1.

Dysentery, bacillary.—Cases: Buffalo, 2; New York, 6; Detroit, 1; Charleston, S. C., 15; Atlanta, 1; Nashville, 1; Los Angeles, 3.

Dysentery, unspecified.—Cases: Cincinnati, 5; San Antonio, 24.

Leprosy.—Cases: San Antonio 1.

Rocky Mountain spotted fever.—Cases: Washington, 1; Lynchburg, 2.

Tularemia.—Cases: Wichita, 1; Lynchburg, 1; New Orleans, 1.

Typhus fever, endemic.—Cases: Tampa, 1; Houston, 3.

Rates (annual basis) per 100,000 population, by geographic groups, for the 90 cities in the preceding table (estimated population, 1943, 34,394,800)

	Diphtheria case rates	Etiophthalmis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Pollomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England.....	2.6	0.0	0.0	2.6	484	10.5	47.1	0.0	322	0.0	0.0	175
Middle Atlantic.....	6.0	0.5	3.2	2.3	184	14.3	45.8	1.9	226	0.0	3.7	101
East North Central.....	4.9	0.0	6.1	1.2	243	7.3	34.1	0.6	267	0.0	9.0	52
West North Central.....	11.9	0.0	0.0	0.0	127	4.0	73.6	0.0	251	0.0	2.0	44
South Atlantic.....	26.2	0.0	8.2	4.9	67	11.4	39.2	3.3	232	0.0	6.5	121
East South Central.....	5.9	0.0	5.9	5.9	277	53.1	70.8	0.0	94	0.0	6.9	35
West South Central.....	17.2	0.0	8.6	2.9	95	8.6	50.3	20.1	40	0.0	0.0	29
Mountain.....	7.9	0.0	0.0	7.9	874	0.0	31.8	0.0	326	0.0	0.0	246
Pacific.....	6.3	0.0	4.7	0.0	498	12.7	30.0	0.0	218	0.0	0.0	95
Total.....	8.5	0.2	4.4	2.1	242	11.6	45.1	2.1	232	0.0	2.1	87

PLAGUE INFECTION IN SAN BENITO COUNTY, CALIF.

Plague infection has been reported proved in tissue from a ground squirrel, *C. beecheyi*, shot on April 17, 1945, on a ranch 7 miles east and 3 miles south of Tres Pinos, San Benito County, Calif.

TERRITORIES AND POSSESSIONS

Hawaii Territory

Plague (rodent).—A rat found on April 16, 1945, in Honokaa area, Honokaa, Hamakua District, Island of Hawaii, T. H., was proved positive for plague on April 22, 1945.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended May 5, 1945.—During the week ended May 5, 1945, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		22		132	283	57	40	50	114	698
Diphtheria		3	3	20	1	2			1	30
Dysentery, bacillary				3						3
German measles		12		13	13	2	6	37	36	119
Influenza		21			24	2	27		18	92
Measles		2	4	107	142	20	66	47	512	900
Meningitis, meningococcus				2	3					5
Mumps		6		137	84	42	15	186	38	508
Poliomyelitis				1		3				4
Scarlet fever		6	14	97	74	11	5	16	14	237
Tuberculosis (all forms)		9	9	73	51	13		26	58	239
Typhoid and paratyphoid fever			1	5				1		7
Undulant fever				3	3			1		7
Veneral diseases:										
Gonorrhea		28	4	116	149	24	44	22	61	448
Syphilis		11	6	102	99	14	8	7	19	266
Whooping cough		3		177	32	4	3	14	9	242

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during the current year. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

(Few reports are available from the invaded countries of Europe and other nations in war zones.)

Plague

Bolivia—Santa Cruz Department.—Information dated May 18, 1945, states that plague has been reported in Santa Cruz Department, Bolivia, as follows: Agudita, 3 cases, 2 deaths; Guadalupe, 3 cases, 1 death; Hornos, 15 cases, 12 deaths; Quebrada del Zorro, 14 cases, 9 deaths; Vallegrande, 26 cases, 10 deaths. For the month of April 1945, 4 additional cases of plague were reported in Lagunillas.

Ecuador.—For the month of April 1945, 3 cases of plague with 1 death were reported in Chimborazo Province, and 2 cases of plague were reported in Loja Province, Ecuador.

Egypt.—For the two weeks ended May 12, 1945, 4 cases of plague were reported in Port Said, Egypt. For the week ended May 12, 1945, 1 fatal case of plague was reported in Ismailiya, Egypt.

France—Corsica—Ajaccio.—For the week ended May 19, 1945, 2 cases of plague were reported in Ajaccio, Corsica, France, the first confirmed case occurring on May 17.

Madagascar.—Plague has been reported in Madagascar as follows: March 21–31, 1945, 12 cases; April 11–20, 1945, 11 cases.

Morocco (French).—For the period May 1–10, 1945, 6 cases of plague were reported in the region of Casablanca, French Morocco.

Smallpox

British East Africa—Tanganyika.—For the week ended April 14, 1945, 137 cases of smallpox with 1 death were reported in Tanganyika, British East Africa.

French Guinea.—For the period May 1–10, 1945, 200 cases of smallpox were reported in French Guinea.

Venezuela.—For the month of April 1945, 69 cases of smallpox with 2 deaths were reported in Venezuela. States reporting the highest incidence are as follows: Federal District, 39 cases, 1 death; Bolivar, 10 cases; Miranda, 5 cases, 1 death; Aragua, 5 cases. Two cases were reported in the port of La Guayra and 1 case in Puerto Cabello.

Typhus Fever

Bulgaria.—For the week ended April 28, 1945, 68 cases of typhus fever were reported in Bulgaria.

Chile.—For the month of March 1945, 57 cases of typhus fever were reported in Chile. Provinces reporting the highest incidence of the disease are as follows: Antofagasta, 18 cases; Tarapaca, 13 cases; Santiago, 13 cases; Concepcion, 11 cases.

Ecuador.—For the month of April 1945, 51 cases of typhus fever with 3 deaths were reported in Ecuador. Provinces reporting the highest incidence of the disease are as follows: Imbabura, 14 cases; Loja, 8 cases, 1 death; Tungurahua, 5 cases.

Iraq.—For the week ended May 12, 1945, 32 cases of typhus fever were reported in Iraq.

Italy—Messina Province—Capizzi.—Information dated May 18, 1945, states that during the past two weeks 35 cases of typhus fever were reported in Capizzi, Messina Province, Italy.

Morocco (French).—For the period May 1–10, 1945, 388 cases of typhus fever were reported in French Morocco, including 3 cases in Casablanca and 6 cases in Rabat.

Turkey.—For the week ended May 19, 1945, 79 cases of typhus fever were reported in Turkey, including 1 case in Ankara, 2 cases in Seyhan, and 4 cases in Zonguldak.

Venezuela.—For the month of April 1945, 15 cases of typhus fever with 1 death were reported in Venezuela, including 4 cases, 1 death in Apure State, 3 cases in Anzoategui State, 2 cases in Merida State, and 1 case in the airport of Maturin.

Yellow Fever

Brazil.—Deaths from jungle type of yellow fever have been reported in Brazil as follows: Goiaz State—Anapolis, March 8-16, 1945, 2, April 9-15, 2; Chagas, February 22, 1; Goiania, March 5, 1; Grimpas, February 28, 1; Itaberaí, February 23, 1; Morrinhos, March 1, 1; Neropolis, February 16, 1; Piracanjuba, March 11, 1; Pires do Rio, February 27, 1; Pontalina, March 7, 1; Sylvania, March 1-31, 2; Sussuapara, February 21, 1, March 19, 1; Vianopolis, March 1, 1; Minas Geraes States—Camelia, April 8, 1; Campina Verde, April 21, 1; Folhados, April 15, 1; Guaratinga, March 2, 1; Ituiutaba, March 19, 1, Apr. 3-22, 3; Joao Pinheiro, February 20, 1; Paracatu, February 26, 1, March 23-27, 2; Santana de Patos, April 4, 1.

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