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EXPERIMENTAL CHEMOTHERAPY OF BURNS AND SHOCK. VIII.¹

II. Electrolyte Changes in Tourniquet Shock²

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The importance of electrolytes in shock has been indicated by the effectiveness of isotonic sodium chloride solutions therapeutically and by the 800-percent increase in the toxicity of administered potassium in the shocked animal which was reported in part I of this paper.

The present section offers descriptive data on the electrolyte changes in animals shocked by a tourniquet method, and is divided into (a) tissue, (b) urine, and (c) serum studies. The magnitude of the changes in sodium, potassium, and fluid is presented and the possible role of these changes as toxic factors in shock is discussed.

TISSUE ELECTROLYTE STUDIES

In any description of the electrolyte picture in shock it is important to clarify first the changes occurring locally in a traumatized area. Numerous experiments concerned with this have been reported, but have usually involved studies of the blood or individual tissues (8, 17-23). In the present studies data are presented concerning the changes in sodium, potassium, and water occurring in the entire injured area following a fatal amount of trauma.

The tourniquet technique previously reported (3) was used on both hind legs of mice. This method offers a standardized reproducible form of fatal trauma, suitable for application to large numbers of mice. Analyses were made on the entire legs, thus including all of the traumatized area.

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² Part I of this paper was published in PUBLIC HEALTH REPORTS, 60: 373-381, April 6, 1945. The tables, figures, and references are numbered consecutively throughout the two papers.

METHODS

The sampling procedure for the legs consisted in tying the mouse onto a board, which was suddenly dropped into a freezing mixture of ether and solid CO_2 . Each entire leg was then cut off, using a large curved scissors. The incision was begun at the base of the tail with the curved cutting end directed outward. The amputation of the frozen legs was always made by the same individual and, as indicated below in table 2, gave reproducible results when pooled legs were used. Any excess ether was removed with filter paper, and the legs were immediately placed in a ground-glass stoppered weighing bottle. After reaching room temperature, the bottle was opened for 10 seconds to permit the escape of any residual ether vapor. It was then weighed ("wet weight") and dried at 110°C . to constant weight ("dry weight"). All mice had been weighed (within 0.1 gm. of exact weight) at the start of the experiment.

The results of pooled samples from groups of five animals using this technique are indicated in table 2. Similar agreement is found in water, potassium, and sodium analyses.

TABLE 2.—*Reproducibility of sampling technique. Weight of 2 legs per 15-gm. mouse*

Group	Number of animals pooled	Wet weight (gm.)
A.....	5	1.330
B.....	5	1.305
C.....	5	1.346
D.....	5	1.378
	5	1.348
	5	1.379
	5	1.358
	5	1.348

The use of pooled samples from a large group of homogeneous mice offers all of the advantages obtained from serial determinations upon a single animal, and, since each sample is an average of several animals, individual variations are reduced accordingly. In addition, the process of sampling has no influence on subsequent samples.

Albino mice of a National Institute of Health strain (average weight 15 gm.) were deprived of food, but not water, for 18 hours before each experiment. Previous diet had been Ralston dog pellets. No food or water was permitted after commencement of the experiment (except as specifically indicated in table 4). Only female mice were used.

Mice were selected alternately for controls and for tourniquet shock. Animals in both groups were lightly anesthetized with ether, and rubber bands were placed on both legs of the tourniquet-shocked group. The tourniquets were removed after 2 hours. Any animals showing abrasions or cuts resulting from chewing on the legs were discarded.

At the times desired (table 3) the tourniquet-shocked animals and

their respective controls were tied onto a board and dropped into the freezing mixture. Their legs were cut as described above, including the entire injured area, and pooled as indicated in table 3. Only living animals were used for the procurement of samples; any animals dying before the sampling time were discarded.

TABLE 3.—Tissue analyses of tourniquet-shocked and control mice (untreated). Values for weight and water (gm.) and for sodium and potassium (milliequivalent) expressed as the total amounts in both hind legs per 15-gm. mouse. Individual values are listed for experiment 3 to indicate the reproducibility of the method. Values for other experiments represent averages of multiple determinations

Experiment number	Number of animals	Type	Number hours after removal of tourniquet	Dry weight		Excess water in legs of shocked animals *		Potassium	Potassium decrease in legs of shocked animals	Sodium	Sodium excess in legs of shocked animals	Estimated sodium in excess water	Estimated sodium not in excess water
				Water	(gm.)	Percent body wt.							
1	16	Control		0.475	0.854			0.0850		0.0796			
	16	Shocked	2	.468	1.278	0.424	2.8	.0552	0.0298	.163	0.083	0.060	0.023
2	10	Control		.457	.866			.105		.0676			
	10	Shocked	1/2	.525	1.278	.412	2.7	.0936	.011	.134	.066	.068	.008
	10	Shocked	2	.531	1.339	.473	3.2	.0791	.026	.169	.101	.067	.034
	5	Shocked	4	.522	1.381	.515	3.4	.0748	.030	.186	.118	.073	.045
	3	Shocked	24		1.400	.534	3.6	.0608	.044	.187	.119	.076	.043
3	5	Control		.461	.917								
	5	Control		.448	.900			.097		.0665			
	5	Control		.464	.915			.102		.0724			
	15	Average control		.458	.911			.100		.0695			
	5	Shocked	1/2	.504	1.272	.361	2.4	.076	.024	.138	.069	.051	.018
	5	Shocked	1/2	.538	1.272	.361	2.4	.082	.018	.146	.077	.051	.026
	10	Average shocked	1/2	.521	1.272	.361	2.4	.079	.021	.142	.073	.051	.022
	5	Shocked	2	.532	1.350	.439	2.9	.073	.027	.178	.109	.062	.047
	5	Shocked	2	.548	1.405	.494	3.3	.069	.031	.174	.105	.070	.035
	10	Average shocked	2	.540	1.378	.467	3.1	.071	.029	.176	.107	.066	.041
5	Shocked	4	.512	1.552	.641	4.3	.075	.025	.212	.143	.091	.052	

Method of analyses.—After drying the legs to constant weight, they were ground and extracted with 0.75 normal nitric acid, according to the method of Lowry and Hastings (24). After separation of the extract an equal volume of 1.5 normal ammonium hydroxide was added to precipitate most of the large amount of calcium present from the bone.

Aliquots of the filtrate were ashed at 600° C. overnight in silica crucibles after the addition of 0.3 cc. of 1.5 normal sulfuric acid. Upon cooling, 0.2 cc. concentrated hydrochloric acid was added, and the crucible again dried on the steam bath. Potassium determinations were made by the chloroplatinic acid method (Shohl and Bennett (25) with modifications of Fenn (26)), and sodium by the uranyl zinc acetate method [(Butler and Tuthill (27)). The precipitate was stirred mechanically for 10 minutes as suggested by Manery and Hastings (28).].

The adequacy of the dilute nitric acid cation extraction, reported by Lowry and Hastings (24), was confirmed by analyses of standard muscle powders and by recovery of added potassium and sodium. The ammonium hydroxide precipitation likewise did not affect the accuracy of the analyses. This was checked further by analyses of dried ground muscle powder with which solid tribasic calcium phosphate had been mixed (1:3). Analyses of standard muscle powders and solutions were carried out during the experiments as checks on the procedures.

RESULTS

The results are tabulated in table 3 and figure 5. In all experiments the comparisons are made between the tourniquet-shocked

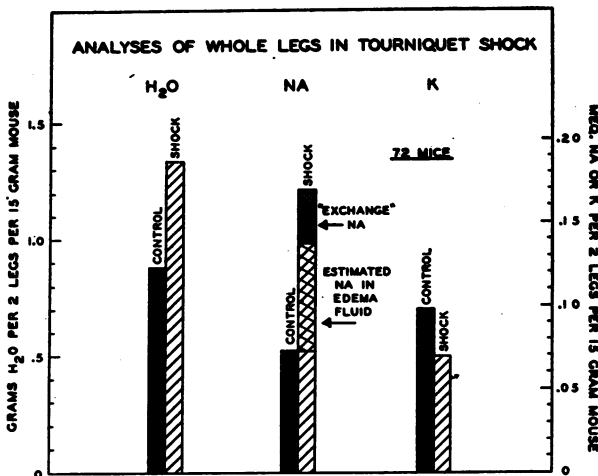


FIGURE 5.—Tissue changes in legs subjected to tourniquets for 2 hours. Analyses 2 hours after removal of tourniquets. Derived from data in table 3. Values are expressed as the total amount of water, sodium, and potassium in the two legs of a 15-gm. mouse.

animals and their specific controls. All values are expressed as the total amount of water, potassium, or sodium in the two hind legs (corrected to mouse weight of 15 gm.).

In all experiments a parallel tourniquet experiment from the same group of animals was conducted simultaneously for mortality data alone, without analyses. In all groups mortalities were greater than 80 percent.

By using both entire legs for the analyses, we have been able to obtain data on the total changes in the injured areas. These are the changes to which the rest of the body has to adjust. In all the experiments there was a considerable sodium and fluid loss into the injured area, and a considerable potassium loss from this area.

Fluid loss.—The fluid loss in 2 hours averaged 3 percent of the body weight. Our findings are consistent with the findings of Blalock,

Harkins, and others (29). Since our data were obtained by comparisons of normal and injured legs in different animals, this answers the objections of Moon (30) that the usual fluid loss experiments compare injured and uninjured legs in the same animal. Similar fluid loss changes have been reported by Haist and Hamilton (31) using plethysmographic methods.

In view of the demonstration by Blalock that the fluid loss extends above the traumatized area, it is very likely that our animals really exhibited changes that were greater than those we obtained. Furthermore, for all our analyses we used only living animals; it is very possible that electrolyte changes of greater magnitude would be found if terminal values were obtained.

Sodium analyses.—Sodium analyses at 2 hours showed an increase in the injured area of 0.097 milliequivalent sodium per mouse in addition to that already present. This is equivalent to approximately 25 percent of the total sodium in the extracellular space (32).

Similar local sodium findings have been reported by Fox and Keston (8) in burns and tourniquet shock, using radioactive sodium. Following the trauma, they observed a marked increase in radioactive sodium in the injured areas.

This loss of sodium into the injured area, together with the loss of fluid, indicates a marked extracellular dehydration in the other portions of the body. The possible significance of extracellular dehydration has been studied by numerous investigators (32-35).

If the sodium concentration in the edema fluid is estimated as 0.142 molar³ then only 0.065 milliequivalent of sodium is contained in the 0.46 gm. of edema fluid in the local area. As the total sodium increase in the same area is 0.097 milliequivalent, 0.032 milliequivalent of sodium (approximately one-third of the total sodium increase) is probably not accounted for by this edema fluid.

Potassium analyses.—Potassium analyses demonstrate a loss from the injured area of one-third of the total potassium content of the legs in a period of 2 hours, amounting to 0.028 milliequivalent potassium. (Tissue hemoglobin determinations indicate that the changes in red cell content in the injured area are too small to affect these potassium results significantly.)

It is of interest that this value for potassium loss is very similar to that portion of the sodium gained in the injured area which was not accounted for by the edema fluid. It is possible that in traumatized tissue, in addition to the edema fluid, there is an electrolyte redistribution with a sodium-potassium interchange. [Similar observations have been made by C. L. Fox, Jr. (personal communication).]

³ Sodium analyses were carried out on 5 pooled serums from 24 normal mice; the average sodium concentration was 154 milliequivalents per liter of serum (154, 154, 157, 152, 156).

Eichelberger and Hastings (36) in isolated muscle experiments have shown that during prolonged equilibration there is a loss of potassium from the muscle and a simultaneous gain in sodium. Manery and Solandt (19) demonstrated that injured muscle *in vivo* loses potassium and gains chloride. The role of anoxia in causing a potassium release from muscle has also been indicated by the work of Baetjer, Fenn, and others (22, 23) using blood potassium determinations.

Treated mice.—The tissue changes in treated ⁴ mice are listed in table 4, and show essentially the same potassium findings as those discussed for untreated animals. The injured areas show the increased swelling (H₂O) that occurs in treated animals. These experiments were carried out mainly to obtain values at later intervals for correlation with the urine experiments reported below.

TABLE 4.—*Tissues changes in tourniquet-shocked and control mice treated with isotonic sodium chloride. Values for weight and water are in grams and for potassium in milliequivalents per 15-gm. mouse*

Number of animals	Type	Interval after removal of tourniquet (hours)	Dry weight	Water	Excess water in legs of shocked animals	Potassium	Potassium decrease in legs of shocked animals	Ratio potassium/dry weight
5	Control		0.506	0.852		0.0865		0.17
5	Control		.532	.806		.0883		.17
10	Average control		.519	.829		.0874		.17
5	Shocked	4	.569	1.61	0.78	.0571	.0303	
5	Shocked	4	.543	1.43	.60	.0598	.0276	
10	Average shocked	4	.556	1.52	.69	.0585	.0290	
5	Control		.444	.711		.0789		.18
5	Control		.468	.730		.0829		.18
10	Average control		.456	.721		.0809		.18
5	Shocked	24	.492	1.32	.60	.0378	.0431	
5	Shocked	24	.503	1.57	.85	.0423	.0386	
10	Average shocked	24	.500	1.45	.73	.0401	.0409	
5	Control		.442	.625		.0665		.15
5	Control		.373	.591		.0657		.18
10	Average control		.408	.608		.0661		.16
5	Shocked	50	.472	1.62	1.01	.0337	.0324	
5	Shocked	50	.422	1.63	1.02	.0249	.0412	
10	Average shocked	50	.447	1.63	1.02	.0293	.0368	

The long starvation during the experiment produced a considerable decrease in the dry weight and potassium content of the controls, although the potassium:dry weight ratio remained approximately constant. However, as in all other experiments, all comparisons have been made only between a group subjected to tourniquet shock and a control group starved for the same period and receiving the same treatment.

⁴ Two and five-tenths cc. 0.154 molar sodium chloride the first day, and 2 cc. 0.15 molar sodium chloride containing 5 percent glucose the second day by stomach tube; no other food or fluid.

The analyses in tables 3 and 4 after different periods of shock indicate that the changes reported are progressive with the greatest rate of change in the early phase.

CONCLUSIONS

After 2 hours of untreated tourniquet shock:

There is a fluid loss into the injured area amounting to at least 3 percent of the body weight.

Sodium loss into this area is equivalent to at least 25 percent of the total sodium in the extracellular spaces. Only two-thirds of this sodium loss can be attributed to the edema fluid.

The injured area loses approximately one-third of its potassium content.

URINE ELECTROLYTE ANALYSES

The tissue electrolyte experiments describe the changes occurring in the injured tissue locally, and do not tell much about the changes in the rest of the body. Some indication of these changes may be obtained from urine balance studies. Stewart and Rourke (37), for example, used the urinary excretion of potassium as an index of the potassium changes in the dog after hemorrhage.

In these experiments urine studies have been made on shocked mice treated with isotonic sodium chloride solution. No urine analyses were carried out in untreated mice because lack of urine flow and early deaths precluded such observations. Data were obtained on pooled 24- and 48-hour urine samples from shocked animals kept in metabolism cages, and compared with the tissue electrolyte changes in treated mice already described (table 4).

METHODS

In these experiments the same principle of pooled specimens and strict comparison of shocked animals and their specific controls was used again.

Albino mice of the National Institute of Health strain were deprived of food but not water for 18 hours prior to commencement of the experiment. No food or water was permitted during the course of the study other than the specific therapy.

The mice were divided at random into groups of five. Some of these groups served as controls, while tourniquets were applied to the remainder for 2 hours.

Upon removal of the tourniquets the groups of control and tourniquet-shocked mice were placed in their respective cages, after the bladders had been emptied by abdominal pressure. (The cages were of the usual metabolic type with fine-mesh screen bottoms, and were set into large glass funnels.) At the same time, each animal (both in the tourniquet-shocked and in the control groups) received 1.5 cc. of

a 0.154-molar sodium chloride solution by stomach tube. Another 1 cc. was administered 2 to 3 hours later.

At the end of 24 hours, the bladders of the mice were again emptied, and this urine added to that in the collecting vessel. Since the actual volume of urine obtained was small, due partly to evaporation, the cage floors, funnels, and collecting vessels were thoroughly washed with 250 to 400 cc. of water each. The total washings plus the collected urines were saved for analyses.

Following this procedure, the mice were replaced in their respective cages, and treated by stomach tube with 1 cc. of a 0.151-molar sodium chloride solution containing 5 percent glucose. This treatment was repeated in 4 hours. At the end of 48 hours, urine and cage washings were again collected as described.

Aliquot portions of the total samples were analyzed for potassium and sodium, using the chloroplatinic acid (25) and uranyl zinc acetate (27) methods.

The diet prior to the experimental period in experiments 1 and 2 was Ralston dog pellets. Animals in experiment 3 received a semi-purified diet with added yeast. During the week preceding the experiment animals in experiment 4 were fed a highly purified diet,⁵ which was low in potassium and high in sodium. The total potassium content of this diet was <0.01 percent.

If any animal died during the experiment it was necessary to discard the entire cage, as the exact proportion of the urine which had been contributed by the dead mouse would be obscure. In experiment 4, after the long starvation, occasional deaths occurred both in the control and tourniquet-shocked animals at the end of the second day, and it was necessary, therefore, to discard most of these second-day urines.

RESULTS

The results of these analyses are tabulated in tables 5 and 6. The reproducibility of the technique within any one group of mice, using the pooled specimens from five mice, is indicated by comparisons of the various values within any individual experiment. The average results of experiments 1, 2, and 3 are graphically illustrated in figures 6 and 7.

All comparisons are made between a tourniquet group and a control group of the same experiment. Thus, the differences measured are in addition to any effects of starvation on the electrolyte balance, since the controls were subjected to identical conditions.

⁵ Diet for experiment 4: Purified casein 18.0 percent, cod liver oil 3 percent, olive oil 8 percent, cerelese 67 percent, salt mixture 4 percent. Into each 100 gm. of the diet was incorporated 1 mg. of thiamine hydrochloride, 1 mg. of pyridoxine hydrochloride, 4 mg. of calcium pantothenate, 2 mg. of niacin, 200 mg. of choline chloride, 0.001 mg. of biotin, and 0.4 mg. of 2-methyl-1,4 naphthoquinone. The salt mixture described by McCollum and Davis (28) was used, except for substitution of dibasic sodium phosphate for all the dibasic potassium phosphate usually included.

Sodium analyses.—The marked retention of the sodium administered to the shocked mouse is demonstrated in table 5 and figure 6. All of the sodium administered on the first day, and 72 percent of the sodium administered during the total 2-day period was retained by the shocked animals. Analyses of the control urines showed complete excretion of the administered sodium in the 48-hour period.

TABLE 5.—*Excretion of sodium in the urine of shocked and normal mice following sodium chloride therapy*¹

Experiment number	Previous diet ²	Type	First day (0.385 mEq. ³ administered)		Second day (0.302 mEq. ⁴ administered)		Total for 2 days (0.687 mEq. administered)	
			Sodium excreted (mEq.)	Percent retained	Sodium excreted (mEq.)	Percent retained	Sodium excreted (mEq.)	Percent retained ⁵
1.....	Normal stock.....	(Shocked.....)	0.015	100	0.148	37	0.163	75
		Control A.....	.396	-----	.274	-----	.670	-----
		Control B.....	.438	-----	.248	-----	.686	-----
		Average control.....	.417	-----	.261	-----	.678	-----
2.....	Normal stock.....	(Shocked A.....)	.007	100	.086	68	.093	91
		Shocked B.....	.022	100	.144	48	.166	81
		Average shocked.....	.015	100	.115	58	.130	86
		Control A.....	.440	-----	.290	-----	.71	-----
3.....	Semi-purified.....	Control B.....	.420	-----	.290	-----	.73	-----
		Average control.....	.430	-----	.290	-----	.72	-----
		(Shocked A.....)	.026	96	.148	41	.174	71
		Shocked B.....	.022	97	.153	39	.175	71
4.....	Potassium "free", purified high sodium.	Shocked C.....	.020	97	.121	50	.141	76
		Average shocked.....	.023	97	.141	43	.163	73
		Control A.....	.358	-----	.271	-----	.659	-----
		Control B.....	.400	-----	.270	-----	.670	-----
4.....	Potassium "free", purified high sodium.	Average control.....	.394	-----	.271	-----	.665	-----
		(Shocked A.....)	.070	100	-----	-----	-----	-----
		Shocked B.....	.082	100	-----	-----	-----	-----
		Shocked C.....	.081	100	.366	0	.447	55
4.....	Potassium "free", purified high sodium.	Shocked D.....	.089	100	-----	-----	-----	-----
		Average shocked.....	.081	100	-----	-----	-----	-----
		Control A.....	.472	-----	.352	-----	.824	-----
		Control B.....	.476	-----	-----	-----	-----	-----
4.....	Potassium "free", purified high sodium.	Average control.....	.474	-----	-----	-----	-----	-----

¹ All values are expressed as mEq. excreted per mouse, although they represent determinations on the pooled urines from 5 mice.

² All animals starved 18 hours before commencement and during the 2 days of the experiment.

³ Administered as isotonic NaCl (stomach tube).

⁴ Administered as isotonic NaCl in 5 percent glucose (stomach tube).

⁵ Percent retained = $\frac{\text{Na excreted by average control} - \text{Na excreted by shocked group}}{\text{Na administered}} \times 100$.

⁶ Analyses not reported on the second day were due to individual deaths in both control and shocked groups.

These results are similar to those already published by Fox (7, 8). Sodium and chloride balance studies in his burned patients showed this same marked retention. Similar findings for chlorides were published by Davidson in 1926 (39).

Potassium analyses.—During this same period of sodium retention the potassium excretion increased considerably in the shocked group (table 6, fig. 7). During this 2-day period the potassium excretion of the tourniquet group averaged 80 percent more than the control ex-

cretion. Experiment 4 (low potassium diet) was included to demonstrate this increase in the tourniquet excretion under conditions where that portion of the nonspecific potassium excretion (in both tourniquet-shocked and control groups) resulting from previous food in-

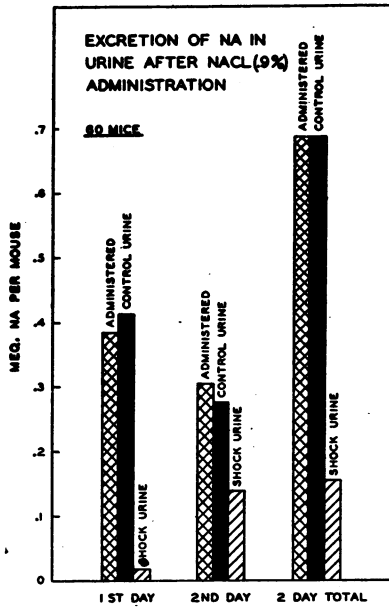


FIGURE 6.—Sodium excretion in normal and shocked mice. Averages of experiments 1, 2, and 3 (table 5).

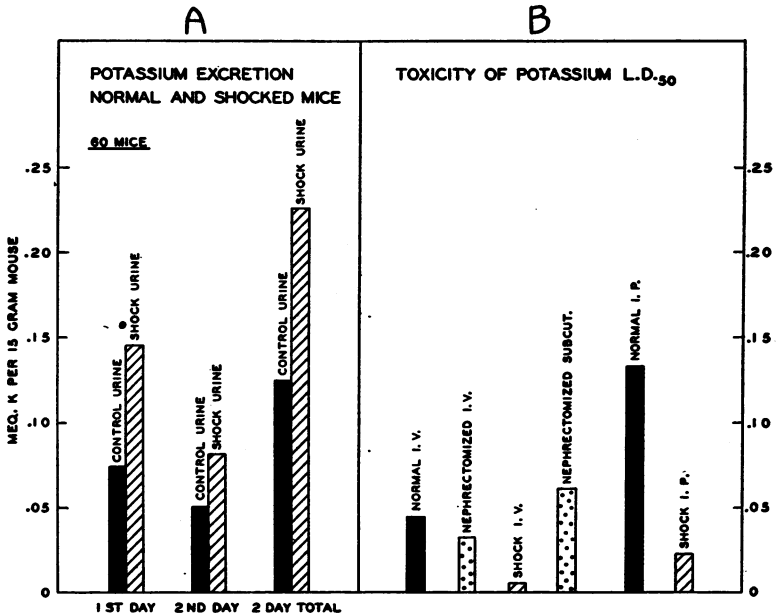


FIGURE 7.—A. Potassium excretion in normal and shocked mice. Averages of experiments 1, 2, and 3 (table 6). B. Toxicity data derived from figures 2 and 3 and text (see part I of this paper).

take are largely eliminated. Thus, on this low potassium intake, control excretion of potassium on the first day was 0.026 milliequivalent per mouse, while the tourniquet-shocked group excreted 0.069 milliequivalent per mouse in the same period, an increase of 166 percent.

TABLE 6.—*Excretion of potassium in the urine of shocked and normal mice following sodium chloride therapy. Analyses were performed on same urines as in table 5*¹

Experiment number	Previous diet ²	Type	First day ³		Second day ³		Total	
			Total potassium	Excess potassium (tourniquet-shocked group)	Total potassium	Excess potassium (tourniquet-shocked group)	Total potassium	Excess potassium (tourniquet-shocked group)
1.....	Normal stock.....	{ Shocked.....	0.175	0.126	0.068	0.023	0.243	0.143
		{ Control A.....	.064	-----	.048	-----	.112	-----
		{ Control B.....	.045	-----	.042	-----	.087	-----
		{ Average control.....	.055	-----	.045	-----	.100	-----
2.....	Normal stock.....	{ Shocked A.....	.144	.022	.105	.045	.249	.068
		{ Shocked B.....	.150	.028	.109	.049	.259	.078
		{ Average shocked.....	.147	.025	.107	.047	.254	.073
		{ Control A.....	.127	-----	.057	-----	.184	-----
		{ Control B.....	.116	-----	.062	-----	.178	-----
		{ Average control.....	.122	-----	.060	-----	.181	-----
3.....	Semi-purified.....	{ Shocked A.....	.099	.052	.070	.026	.169	.079
		{ Shocked B.....	.120	.073	.078	.034	.198	.108
		{ Shocked C.....	.117	.070	.060	.016	.177	.087
		{ Average shocked.....	.112	.055	.069	.025	.181	.091
		{ Control A.....	.046	-----	.042	-----	.088	-----
		{ Control B.....	.047	-----	.045	-----	.092	-----
4 ⁴	Potassium "free" purified high Na.....	{ Average control.....	.047	-----	.044	-----	.090	-----
		{ Shocked A.....	.073	.047	-----	-----	-----	-----
		{ Shocked B.....	.053	.027	-----	-----	-----	-----
		{ Shocked C.....	.061	.035	.069	.038	.130	.081
		{ Shocked D.....	.087	.061	-----	-----	-----	-----
		{ Average shocked.....	.069	.043	-----	-----	-----	-----
		{ Control A.....	.018	-----	.031	-----	.049	-----
		{ Control B.....	.034	-----	-----	-----	-----	-----
		{ Average control.....	.026	-----	-----	-----	-----	-----

¹ All values are expressed as mEq. excreted per 15 gm.-mouse, although they represent determinations on the pooled urines from 5 mice.

² All animals starved 18 hours before commencement and during the 2 days of the experiment.

³ Treated as in table 5.

⁴ Analyses not reported on the second day were due to deaths in both control and shocked groups.

⁵ Potassium content of diet < 0.01 percent.

The average 2-day total excretion of potassium (fig. 7) was 0.124 milliequivalent per mouse in the controls and 0.226 milliequivalent per mouse in the tourniquet-shocked group, a difference of 0.1 milliequivalent potassium per mouse. The magnitude of these potassium values for a 15-gm. mouse is indicated in figure 7, in which the toxicities of potassium are also illustrated. In view of the poor renal function of shocked animals, the data on potassium toxicity for nephrectomized mice ($L. D_{50} = 0.06$ milliequivalent potassium subcutaneously per 15-gm. mouse) is included.

It is thus demonstrated that the amount of potassium released and excreted in our experiments is toxic for an anuric animal. While it is obvious that, in view of difference in rate of administration, no exact correlation can be made, it seems possible from these data that the

potassium released in the body may be of sufficient magnitude to be an important factor in death from shock.

It is possible that shocked animals which do not receive treatment and progress to death would exhibit more profound potassium change. Although it is known that sodium chloride administration influences potassium excretion (40), our method of comparing only tourniquet-shocked animals and control mice similarly treated would tend to minimize any such factor.

Comparison of these urine data on potassium (table 6) and the potassium content of the legs in the tissue analyses (table 4) indicates that at least half of the excess potassium excreted by the shocked animals was derived from sources other than the injured areas.

Adrenal insufficiency and shock.—In view of the frequent comparison made between the shock syndrome and adrenal insufficiency, it is very important to emphasize the contrast between the urinary picture just described and the usual urinary findings in adrenal insufficiency. The urines of the mice subjected to tourniquet shock show an increased excretion of potassium and a considerable retention of sodium, even though treated with large amounts of saline, as opposed to the low potassium and high sodium values reported for the urine in adrenal insufficiency (41).

Although the end results in the body (decreased sodium, increased potassium) may be similar, the urinary picture indicates that a difference in mechanism exists.

CONCLUSIONS

In urinary analyses of saline-treated shocked animals:

There is a marked retention of administered sodium.

There is a considerably increased excretion of potassium.

This increase in potassium excretion is above the usual toxic doses (intravenous or intraperitoneal) for normal, nephrectomized, and shocked animals.

This urinary picture contrasts sharply with the urine picture in adrenal insufficiency.

SERUM STUDIES

In the first section of this paper the marked toxicity of potassium for shocked animals was demonstrated. In view of these data, together with the tissue and urine analyses, it was deemed advisable to attempt to re-evaluate some of the experiments reported on this subject. Most of these (17-21) demonstrate that the blood potassium levels are higher in shocked than in normal animals, but point out that these shock values are usually not as high as the potassium levels necessary to kill a normal animal. On the basis of their blood studies, Scudder and Zwemer (18) have emphasized the importance of potassium in shock.

Under certain abnormal conditions, such as sodium depletion, fluid loss, or numerous toxic agents, a given amount of potassium may be

much more toxic than normally, and it is possible that deaths from potassium poisoning may occur at lower serum potassium levels under these conditions than are necessary to kill a normal animal. This is suggested by the antagonisms already demonstrated for sodium and potassium (2, 42, 43) and for calcium and potassium (44). Although this possibility is supported by the potassium toxicity experiments already discussed, a more direct evaluation, using serum potassium levels, is reported in this section. Rabbits were used for these serum studies because of the difficulty in getting adequate blood from shocked mice.

METHODS

Adaptation of the tourniquet technique to rabbits.—Initial attempts to apply rubber tubing to the thighs of 1- to 2-kg. rabbits were unsatisfactory because of the tendency of the tubing to slip down. A mechanical device was designed that permitted the rapid application of tourniquets high up on the thigh with only a small percentage of failures. This consisted of a brass cylinder 6.5 cm. in diameter and 5.5 cm. long, divided in half through the long axis, and held together at one end by small hinges which permitted the half cylinders to be opened and closed. Metal rods were soldered to the other end for use as handles.

Loops were made of rubber tubing (a wall thickness of 1/32 inch and an inside diameter of 1/8 inch) by tying together the ends of strips 20 inches in length. These strips were looped around the hinged end of the closed brass cylinder seven times. The leg of the rabbit was then drawn through the cylinder, which was pressed firmly against the body. While this pressure was applied the cylinder was opened by pulling the halves apart until the tubing slid from the cylinder onto the thigh of the rabbit. Occasionally the tourniquet failed to remain in place when the cylinder was removed, but it was usually possible to reapply it successfully.⁶

For the purpose of these experiments the tourniquets were allowed to remain in place for 2½ to 3 hours. All experiments were performed in a constant-temperature room at 22° to 24° C.

Serum analyses.—All rabbits were deprived of food for 17 hours prior to the experiments. Tourniquets were placed on both legs and removed after 2½ to 3¼ hours. These animals were divided into two groups, one control for mortality data and the other for potassium chloride injection. As in the mouse toxicity experiments in shock, it is very important to have a mortality control group, to be certain that the animals receiving potassium chloride die from the treatment and would not have died until later from the tourniquet shock. A

⁶ Canzenelli, Guild, and Rapport have currently described a method for tourniquet shock in rabbits (*Am. J. Physiol.*, 143: 97 (1945)).

third group of animals, without tourniquet application, were used for a study of the serum potassium and toxicity of potassium chloride in normal animals.

The potassium chloride was injected as an isotonic solution (0.150 molar) usually 1 to 1½ hours after removal of the tourniquets. As indicated in figure 8A, the potassium chloride was administered considerably before the animals would have died from the tourniquet shock alone.

At first, the potassium chloride was injected intravenously. However, considerable variations in the blood levels (table 7) occurred with different rates of administration, probably due in part to occasional addition of potassium chloride directly into the blood stream immediately before death. Consequently, intraperitoneal injections were employed in most of the experiments.

By the intraperitoneal route, normal animals received 100 cc. potassium chloride per kilo of body weight, while shocked animals were given 25 cc. per kilo. With these doses 31 of 36 normal animals and 25 of 26 shocked animals died. In the intravenous experiments the potassium chloride was administered into the ear vein at a uniform slow rate timed by a stop watch until the animal appeared near death, when the rate was decreased and care was taken not to administer more of the solution than needed.

Terminal blood samples were obtained in all animals by cardiac puncture immediately upon cessation of respiration and accompanying convulsions, but while the heart was still beating. No later specimens were included. No hemolysis occurred in the bloods.

In several of the experiments, the fluid remaining in the peritoneal cavity was measured after death.

RESULTS

The results are tabulated in table 7 (fig. 8B). The averages of the serum potassium at death in animals subjected to tourniquet shock given potassium chloride (13.2 ± 0.22 milliequivalent per liter with intraperitoneal injection) was in the same range as shocked animals not given potassium chloride (12.08 ± 0.35 milliequivalent per liter) even though the prompt death of the treated animals as compared with untreated controls indicated clearly that the animals were dying as a result of the potassium injection (fig. 8A).

These average terminal potassium concentrations in tourniquet-shocked animals, both with and without administered potassium chloride, were lower than the average potassium levels in normal

animals ⁷ dying after intraperitoneal injection of potassium chloride (16.58 ± 0.68 milliequivalent per liter). The distribution of these serum values is indicated in figure 8B.

TABLE 7.—Terminal serum potassium (mEq. per liter) in shocked rabbits and in normal and shocked rabbits following potassium chloride administration. Tourniquets were applied for 2½ to 2¾ hours. Isotonic potassium chloride was administered 1 to 1½ hours after tourniquet removal

No treatment	Treatment															
	Intraperitoneal administration of potassium chloride				Slow intravenous administration of potassium chloride				Fast intravenous administration of potassium chloride							
	Normal rabbits 100cc./kilo		Shocked rabbits 25cc./kilo		Normal rabbits		Shocked rabbits		Normal rabbits		Shocked rabbits					
Terminal serum K	Survival after injection (minutes)	Terminal serum potassium	Survival after injection (minutes)	Terminal serum potassium	Amount injected (cc.)	Duration of injection (minutes)	Terminal serum potassium	Amount injected (cc.)	Duration of injection (minutes)	Terminal serum potassium	Amount injected (cc.)	Duration of injection (minutes)	Terminal serum potassium	Amount injected (cc.)	Duration of injection (minutes)	Terminal serum potassium
12.1 ¹	2 60	13.9	25	11.6	66	33	10.4	3.8	18	13.3	38	6	16.2	0.7	3½	17.5
9.9 ¹	3 75	17.7	4	13.5	72	36	14.7	.4	2	13.6	54	18	21.2	3.0	3½	19.6
9.4 ¹	40	22.0	3	14.6	86	44	19.5	9.2	28	13.8	38	10	27.6	3.0	1½	12.2
11.2 ¹	60	19.4	16	14.0	92	63	18.8	7.0	12	15.3	18	5½	21.2	8.0	5	15.9
13.1 ¹	40	18.1	16	12.1	73	38	24.4	8.0	45	12.9	72	35	16.4	1.8	5½	13.9
12.8 ¹	39	15.3	5	12.9	35	18	27.0	31.0	38	13.0	8	3	15.0	1.0	5	18.3
10.9	53	24.9	13	12.7	66	33	15.2	10.0	52	12.0	68	33	37.8	4.0	6½	17.6
11.6	50	15.4	18	13.5	---	---	---	10.0	51	12.7	---	---	---	6.0	5	14.3
11.5	47	22.9	5	12.7	---	---	---	24.0	84	13.8	---	---	---	5.0	5½	18.6
12.4	35	14.2	27	11.2	---	---	---	---	---	---	---	---	---	---	---	---
10.7	60	16.6	11	12.7	---	---	---	---	---	---	---	---	---	---	---	---
14.3	60	19.7	18	15.4	---	---	---	---	---	---	---	---	---	---	---	---
13.3	50	14.4	24	12.2	---	---	---	---	---	---	---	---	---	---	---	---
13.0	41	13.6	45	11.8	---	---	---	---	---	---	---	---	---	---	---	---
12.7	34	12.1	9	13.7	---	---	---	---	---	---	---	---	---	---	---	---
14.3	23	13.3	20	12.1	---	---	---	---	---	---	---	---	---	---	---	---
	35	11.7	17	12.7	---	---	---	---	---	---	---	---	---	---	---	---
	40	21.4	17	13.2	---	---	---	---	---	---	---	---	---	---	---	---
	38	13.6	23	14.3	---	---	---	---	---	---	---	---	---	---	---	---
	50	19.3	22	13.1	---	---	---	---	---	---	---	---	---	---	---	---
	32	19.5	1	15.1	---	---	---	---	---	---	---	---	---	---	---	---
	35	12.6	23	14.4	---	---	---	---	---	---	---	---	---	---	---	---
	43	11.3	36	12.2	---	---	---	---	---	---	---	---	---	---	---	---
	46	14.7	12	14.7	---	---	---	---	---	---	---	---	---	---	---	---
	33	14.3	30	13.6	---	---	---	---	---	---	---	---	---	---	---	---
	43	19.3	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	50	16.7	---	---	---	---	---	---	---	---	---	---	---	---	---	---
	35	16.3	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Average	12.06	16.58	13.20	18.51	13.38	22.20	16.43									
Standard error	0.35	.68	.22	2.02	.28	2.83	.79									

¹ Tourniquet applied for 3 hours.

² 67 cc. per kilo potassium chloride intraperitoneally.

³ 80 cc. per kilo potassium chloride intraperitoneally.

⁴ Potassium chloride administered 1¾ to 2¾ hours after tourniquet removal.

⁷ In the previous section we have repeated the demonstration of Schechter (15) and Darrow and co-workers (16) that solutions introduced into the peritoneal cavity tend to assume the electrolyte composition of a serum ultrafiltrate during absorption. In the present experiments, following death resulting from the intraperitoneal administration of isotonic potassium chloride to normal animals, approximately 85 percent of the administered fluid can be recovered. The sodium concentrations in three of these recovered fluids were 66, 57, and 65 milliequivalents per liter. It is thus very likely that the "normal" animals really develop a sodium deficit while the potassium chloride is being absorbed, and in this respect are abnormal. The shocked group received smaller amounts of potassium chloride solution and died after a shorter interval, thus permitting less opportunity for such an exchange to occur.

These data suggest that care must be taken in comparing potassium concentrations in shocked animals with those found in normal animals. It is possible that a given level of potassium in a shocked animal is more significant than the same level in normal animals. Winkler (45) has pointed out that the volumes of distribution for potassium are possibly changed in such abnormal conditions as adrenalectomy.

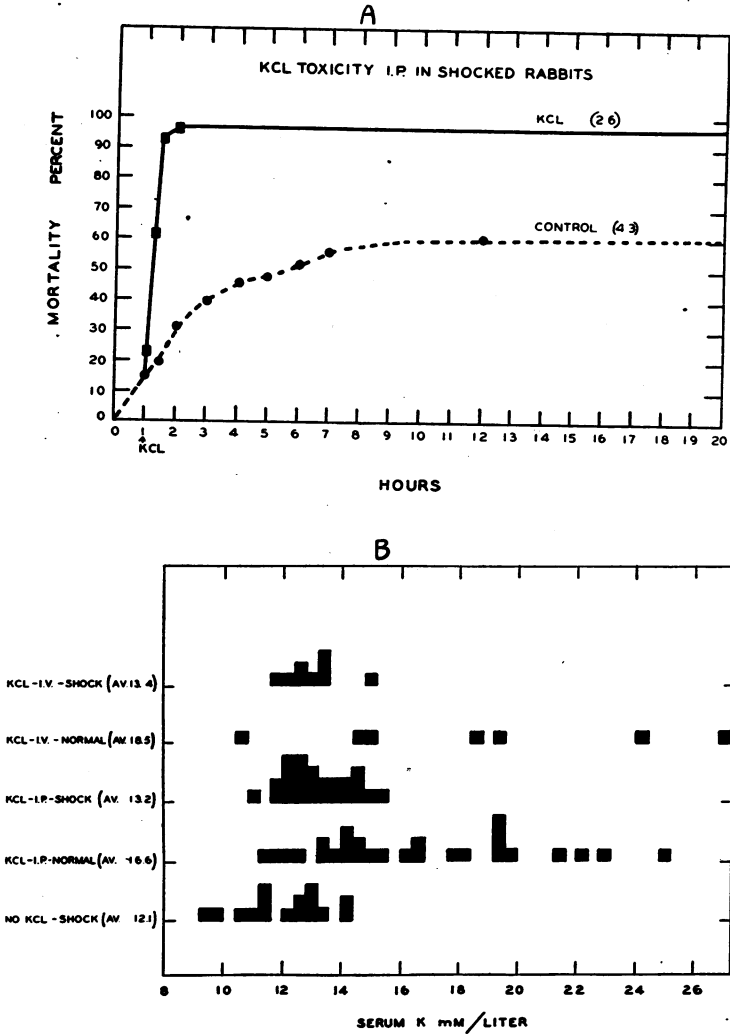


FIGURE 8.—A. Composite curves illustrating the method employed for studying deaths after administration of isotonic potassium chloride intraperitoneally in shocked rabbits. Death from the drug, which occurred soon after potassium chloride administration, was easily distinguished from death due to shock (control curve). Tourniquet application 2¼ to 2¾ hours; potassium chloride injected 1 hour after removal of tourniquet. B. Distribution of terminal serum potassium values in shocked rabbits, and in normal and shocked rabbits following potassium chloride administration. Each unit square represents one animal (data from table 7).

All the values discussed here are terminal values obtained immediately upon cessation of respiration and accompanying convulsions. The exact timing of these determinations may be very important, in view of the demonstration by Winkler and Hoff (20) that serum potassium rises rapidly upon sudden acute anoxia.

CONCLUSIONS

A tourniquet technique for rabbits is described.

The increased toxicity of administered potassium for shocked mice reported above is confirmed for rabbits.

Shocked animals dying as a result of potassium administration have terminal serum potassium levels approximately the same as shocked animals dying without potassium treatment. These values are less than terminal potassium levels in normal rabbits dying after potassium administration.

It is possible that the state of the animal is important in evaluating the importance of different levels of serum potassium concentrations.

GENERAL DISCUSSION

An attempt has been made to measure quantitatively the extent of fluid and sodium accumulation, and the amount of potassium liberated from the entire injured area following a standardized fatal degree of trauma in mice.

In additional experiments in which death was prevented by sodium therapy, quantitative information was obtained on the total amount of potassium excreted and the quantity of sodium retained by the body for 48 hours subsequent to the trauma.

The extent of these changes has made it clear that all three factors, fluid, sodium and potassium, are of a magnitude which may be considered important in the mechanism of shock and in influencing mortality. This does not preclude other factors from contributing to these effects.

In an effort to evaluate the significance of these changes in their effect upon mortality, it was established that the shocked animal exhibited a high degree of sensitivity to administered potassium. It is believed that this abnormal sensitivity is brought about by the three factors we have studied, potassium liberation, sodium depletion, and fluid loss, as well as some possibly unknown factors.

On the basis of these various findings, possible mechanisms for the beneficial effect of isotonic sodium chloride in therapy may be postulated.

It is probable that a major effect of the administration of sodium chloride solution is the replenishment of the dehydrated extracellular

compartment, which results from the electrolyte and fluid shifts subsequent to the injury. It seems likely that the isotonic sodium chloride solution would also serve as a source for any further edema fluid forming in the injured area, thus preventing any further drain on the extracellular stores of the rest of the body.

It has already been shown (2, 42, 43) that the administration of sodium chloride can counteract the action of fatal doses of potassium chloride. It is thus possible that the sodium chloride solution used in shock therapy may also act to counteract the toxic action of the excess potassium present.

GENERAL SUMMARY

The sodium, water, and potassium changes in the tissues and urines of mice in tourniquet shock are described.

Toxicity data, indicating the marked sensitivity of shocked animals to administered potassium are presented.

Shocked animals were very sensitive to the additional sodium and fluid losses caused by intraperitoneal administration of glucose.

A tourniquet method for producing shock in rabbits is described. The averages of terminal serum potassium values were similar in rabbits dying in shock and in shocked rabbits killed by potassium chloride administration. In normal animals killed by potassium chloride the average values were higher.

The importance of potassium in shock, together with the fluid and sodium changes, is discussed.

Possible mechanisms for the therapeutic action of isotonic sodium chloride are suggested.

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DEATHS DURING WEEK ENDED MARCH 17, 1945

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

	Week ended Mar. 17, 1945	Corresponding week, 1944
Data for 93 large cities of the United States:		
Total deaths.....	9,622	9,532
Average for 3 prior years.....	9,505
Total deaths, first 11 weeks of year.....	107,463	113,204
Deaths under 1 year of age.....	663	679
Average for 3 prior years.....	648
Deaths under 1 year of age, first 11 weeks of year.....	7,022	6,985
Data from industrial insurance companies:		
Policies in force.....	67,133,456	66,373,891
Number of death claims.....	15,439	13,891
Death claims per 1,000 policies in force, annual rate.....	12.0	10.9
Death claims per 1,000 policies, first 11 weeks of year, annual rate.....	10.9	11.5

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 MARCH 24, 1945

Summary

The current total of 225 cases of meningococcus meningitis, although less than the weekly figure for any of the past 6 weeks and approximately only 40 percent of that for the corresponding week last year, is 2½ times the 5-year median. Five States which reported more than 10 cases each are as follows (last week's figures in parentheses): New York 32 (36), Pennsylvania 12 (16), Ohio 14 (13), Michigan 11 (4), California 20 (27). The total for the year to date is 3,016, as compared with 6,637 and 5,231, respectively, for the corresponding periods of last year and 1943 and a 5-year median of 842.

Of the total of 28 cases of poliomyelitis reported for the current week as compared with 25 last week and a 5-year median of 24, 5 were reported in New York, 4 in Texas, 3 in California, and 16 in 11 other States. The cumulative total of 426 cases, as compared with 277 for the corresponding period last year and a 5-year median of 311, is more than was reported in the first 12 weeks of any other year since 1928.

The total of 6,624 cases of scarlet fever, as compared with 7,356 for the corresponding week last year and a 5-year median of 4,269, is more than reported for the corresponding week of any year, except 1944, since 1937. More than half of the current total occurred in the Middle Atlantic and East North Central areas. The cumulative total is 68,094, as compared with 69,087 for the same period last year and a 5-year median of 48,344.

Only 4 cases of smallpox were reported for the week (in 4 States), as compared with 20 cases last week and a 5-year median of 19. The total to date is 118, as compared with 152 for the period last year and a 5-year median of 319.

A total of 355 cases of dysentery (all forms) was reported for the week, as compared with 436 last week and 254 for the corresponding week last year. The total to date is 7,794, as compared with 3,414 for the corresponding period last year. The increase for the current period is accounted for in most part by cases reported in Texas.

Deaths registered for the week in 93 large cities of the United States totaled 9,602, as compared with 9,622 last week, 9,605 for the corresponding week last year, and a 3-year (1942-44) average of 9,570. The cumulative figure is 117,065, as compared with 122,809 for the same period last year.

Telegraphic morbidity reports from State health officers for the week ended March 24, 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, meningococcus		
	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44
	Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944	
NEW ENGLAND												
Maine.....	0	1	0	1	2	2	1	319	151	2	5	1
New Hampshire.....	2	0	0	0	0	1	0	10	29	1	0	0
Vermont.....	0	0	0	0	1	0	7	155	39	0	0	0
Massachusetts.....	5	3	1	0	0	0	143	782	782	2	11	8
Rhode Island.....	1	1	0	0	18	0	4	234	143	2	3	0
Connecticut.....	2	1	0	0	2	4	138	502	349	4	7	2
MIDDLE ATLANTIC												
New York.....	12	15	19	13	16	12	121	3,427	2,413	32	56	20
New Jersey.....	6	2	2	6	10	15	61	1,515	1,515	5	20	3
Pennsylvania.....	12	9	10	3	9	0	143	940	1,206	12	27	8
EAST NORTH CENTRAL												
Ohio.....	11	6	6	10	22	16	39	2,487	634	14	37	1
Indiana.....	7	3	8	10	7	36	37	315	262	5	9	5
Illinois.....	8	14	17	1	61	35	91	1,092	1,092	10	44	3
Michigan ¹	10	10	3	0	6	6	86	1,127	904	11	35	5
Wisconsin.....	0	5	3	55	85	85	28	2,316	1,058	4	8	1
WEST NORTH CENTRAL												
Minnesota.....	3	7	5	3	3	2	17	1,467	214	3	11	1
Iowa.....	12	1	3	0	0	0	31	239	239	0	1	0
Missouri.....	6	4	4	11	3	5	6	414	414	6	27	3
North Dakota.....	1	0	0	12	28	9	6	146	61	0	0	0
South Dakota.....	0	2	2	0	1	1	23	55	14	1	0	0
Nebraska.....	3	2	2	15	1	3	26	110	110	0	2	0
Kansas.....	1	5	5	2	4	11	23	863	760	5	7	1
SOUTH ATLANTIC												
Delaware.....	0	1	0	0	0	0	29	6	7	2	1	0
Maryland ²	3	8	3	2	4	8	80	1,076	196	3	5	5
District of Columbia.....	0	0	0	0	3	2	19	153	91	1	2	2
Virginia.....	4	2	6	442	480	501	85	1,355	692	10	37	4
West Virginia.....	1	2	4	8	3	49	51	447	280	6	7	2
North Carolina.....	7	8	8	0	7	68	46	1,899	1,028	9	13	2
South Carolina.....	6	0	3	260	515	559	22	524	259	0	7	2
Georgia.....	3	5	6	10	51	84	29	428	216	3	11	2
Florida.....	4	2	2	0	5	10	35	385	178	7	15	1
EAST SOUTH CENTRAL												
Kentucky.....	5	2	3	0	82	38	9	89	137	6	5	5
Tennessee.....	6	3	3	50	74	96	135	218	218	8	33	3
Alabama.....	12	3	5	104	62	264	16	462	462	5	8	4
Mississippi ²	4	2	2	0	0	0	0	0	0	8	6	1
WEST SOUTH CENTRAL												
Arkansas.....	5	5	5	46	105	114	34	202	177	2	5	1
Louisiana.....	2	6	6	47	60	10	42	334	120	3	6	3
Oklahoma.....	5	2	5	68	141	143	44	89	74	0	2	2
Texas.....	20	37	37	1,021	964	1,243	650	2,003	1,359	5	11	2
MOUNTAIN												
Montana.....	0	1	2	22	17	14	11	194	53	1	4	0
Idaho.....	1	0	0	0	0	0	1	50	92	0	0	0
Wyoming.....	0	2	2	0	20	20	16	114	86	0	0	0
Colorado.....	4	2	9	14	41	23	16	367	266	0	1	0
New Mexico.....	5	0	1	3	18	15	4	79	79	0	0	1
Arizona.....	2	3	2	137	106	165	15	357	122	2	0	0
Utah ²	0	0	1	29	204	22	116	30	266	0	0	0
Nevada.....	0	0	0	0	0	0	0	1	10	0	0	0
PACIFIC												
Washington.....	4	1	1	4	34	6	241	212	291	4	6	3
Oregon.....	36	1	1	16	30	30	52	98	438	1	8	0
California.....	31	23	16	14	85	152	1,226	2,584	1,127	20	47	6
Total.....	272	212	271	2,429	3,379	4,016	4,065	32,271	24,632	225	550	90
12 weeks.....	3,713	3,002	3,509	48,726	37,797	144,942	28,015	272,325	184,225	3,016	6,637	842

¹ New York City only.
² Period ended earlier than Saturday.

Telegraphic morbidity reports from State health officers for the week ended March 24, 1945, and comparison with corresponding week of 1944 and 5-year median

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever ⁴		
	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44	Week ended—		Median 1940-44
	Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944		Mar. 24, 1945	Mar. 25, 1944	
NEW ENGLAND												
Maine.....	0	0	0	97	64	12	0	0	0	0	1	0
New Hampshire.....	0	0	0	3	13	13	0	0	0	0	0	0
Vermont.....	1	0	0	17	10	7	0	0	0	0	0	0
Massachusetts.....	2	0	0	390	443	368	0	0	0	0	2	0
Rhode Island.....	0	0	0	19	15	16	0	0	0	0	0	0
Connecticut.....	0	0	0	107	129	78	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York.....	5	1	0	89 ¹	646	587	0	0	0	5	5	4
New Jersey.....	2	0	0	230	295	295	0	0	0	0	1	1
Pennsylvania.....	2	1	1	797	689	377	0	0	0	6	3	3
EAST NORTH CENTRAL												
Ohio.....	0	0	0	447	490	261	1	1	1	1	2	2
Indiana.....	0	0	0	186	244	186	1	1	2	5	3	3
Illinois.....	1	0	0	482	532	520	1	0	1	1	1	1
Michigan ²	0	0	0	209	283	283	0	0	1	0	3	3
Wisconsin.....	0	0	0	307	461	148	0	1	0	1	0	0
WEST NORTH CENTRAL												
Minnesota.....	0	0	0	137	208	82	0	0	0	0	1	0
Iowa.....	0	0	0	120	168	60	1	0	0	0	0	0
Missouri.....	0	0	0	82	161	125	0	0	2	2	4	2
North Dakota.....	0	0	0	28	45	16	0	0	0	0	0	0
South Dakota.....	0	0	0	11	27	24	0	1	0	0	0	0
Nebraska.....	0	0	0	99	102	34	0	0	0	0	0	0
Kansas.....	1	1	1	87	106	96	0	0	0	0	3	1
SOUTH ATLANTIC												
Delaware.....	0	0	0	15	23	16	0	0	0	0	0	0
Maryland ²	0	0	0	291	230	81	0	0	0	0	0	0
District of Columbia.....	0	0	0	51	155	23	0	0	0	0	0	0
Virginia.....	1	1	0	149	159	43	0	0	0	0	1	2
West Virginia.....	0	0	0	54	96	42	0	0	0	2	6	2
North Carolina.....	2	0	0	111	28	26	0	0	0	1	2	2
South Carolina.....	0	0	0	6	9	8	0	1	0	0	1	1
Georgia.....	0	0	1	58	21	15	0	0	0	3	3	3
Florida.....	0	0	0	7	15	8	0	0	0	1	4	4
EAST SOUTH CENTRAL												
Kentucky.....	0	0	0	53	63	81	0	0	0	1	3	1
Tennessee.....	2	1	0	86	64	64	0	1	1	2	0	1
Alabama.....	1	0	0	14	12	16	0	0	0	1	0	2
Mississippi ²	1	0	0	22	22	6	0	0	0	1	1	2
WEST SOUTH CENTRAL												
Arkansas.....	0	0	0	16	15	6	0	0	1	0	2	2
Louisiana.....	0	1	0	13	13	10	0	0	0	4	10	3
Oklahoma.....	0	0	0	16	18	18	0	1	1	2	0	1
Texas.....	4	4	2	94	81	49	0	0	2	3	9	8
MOUNTAIN												
Montana.....	0	0	0	9	58	22	0	0	0	0	0	0
Idaho.....	0	0	0	48	37	5	0	0	0	0	0	0
Wyoming.....	0	0	0	10	17	9	0	0	0	0	0	0
Colorado.....	0	0	0	71	60	46	0	0	0	0	0	0
New Mexico.....	0	0	0	23	14	6	0	0	0	5	1	1
Arizona.....	0	0	0	54	15	13	0	0	0	0	0	0
Utah ²	0	0	0	30	149	42	0	0	0	0	0	0
Nevada.....	0	0	0	1	1	1	0	0	0	0	0	0
PACIFIC												
Washington.....	0	1	0	100	361	47	0	1	1	0	1	1
Oregon.....	0	0	0	48	151	18	0	0	0	1	1	1
California.....	3	3	3	388	340	177	0	0	0	0	3	3
Total	28	14	24	6,624	7,356	4,269	4	8	19	50	75	75
12 weeks.....	426	277	311	68,094	69,067	48,344	118	152	319	674	891	907

¹ Period ended earlier than Saturday.

² Corrected reports, poliomyelitis: Ohio, week ended February 17, 0; West Virginia, week ended March 10, 0.

⁴ Including paratyphoid fever reported separately, as follows: Massachusetts 2; New York 1; Georgia 2; Louisiana 1.

Telegraphic morbidity reports from State health officers for the week ended March 24, 1945, and comparison with corresponding week of 1944 and 5-year median

Division and State	Whooping cough			Week ended Mar. 24, 1945							
	Week ended—			Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever	Undulant fever
	Mar. 24, 1945	Mar. 25, 1944	Median 1940-44	Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine.....	131	13	37	0	0	0	0	0	0	0	0
New Hampshire.....	0	1	3	0	0	0	0	0	0	0	0
Vermont.....	19	45	38	0	0	0	0	0	0	0	0
Massachusetts.....	240	97	189	0	1	0	4	0	0	0	1
Rhode Island.....	19	9	14	0	1	0	0	0	0	0	0
Connecticut.....	50	27	57	0	0	0	0	0	0	0	0
MIDDLE ATLANTIC											
New York.....	232	130	368	1	14	0	1	0	0	0	7
New Jersey.....	101	45	93	0	0	0	0	0	0	0	0
Pennsylvania.....	197	100	263	0	2	0	1	0	0	0	2
EAST NORTH CENTRAL											
Ohio.....	173	75	167	0	0	0	0	0	0	0	1
Indiana.....	8	5	37	0	0	0	0	0	0	0	0
Illinois.....	55	45	114	4	0	0	4	0	0	0	7
Michigan ¹	100	43	199	0	0	0	0	0	0	0	1
Wisconsin.....	56	69	101	0	0	0	0	0	0	0	0
WEST NORTH CENTRAL											
Minnesota.....	16	21	38	3	0	0	0	0	0	0	1
Iowa.....	3	11	19	0	0	0	0	0	0	0	12
Missouri.....	22	12	27	0	0	0	0	0	0	0	1
North Dakota.....	1	2	8	0	0	0	0	0	0	0	0
South Dakota.....	1	1	2	0	0	0	0	0	0	0	0
Nebraska.....	3	31	27	0	0	0	0	0	0	0	0
Kansas.....	38	30	39	0	0	0	0	0	0	0	5
SOUTH ATLANTIC											
Delaware.....	4	0	6	0	0	0	0	0	0	0	0
Maryland ¹	50	36	91	0	0	0	1	0	0	0	1
District of Columbia.....	8	2	14	0	0	0	0	0	0	0	0
Virginia.....	109	74	48	1	0	38	0	0	0	0	0
West Virginia.....	23	11	27	0	0	0	0	0	0	0	0
North Carolina.....	171	170	152	0	0	0	0	0	0	3	0
South Carolina.....	46	75	57	1	5	0	0	0	0	0	0
Georgia.....	19	10	18	0	2	0	0	4	12	5	5
Florida.....	22	27	20	5	1	0	0	0	6	1	1
EAST SOUTH CENTRAL											
Kentucky.....	18	68	68	0	2	0	0	0	0	0	0
Tennessee.....	168	10	29	0	0	0	0	1	0	5	5
Alabama.....	14	25	37	2	0	0	0	1	2	2	2
Mississippi ¹				0	0	0	0	2	2	2	0
WEST SOUTH CENTRAL											
Arkansas.....	28	4	8	2	2	2	0	0	0	0	2
Louisiana.....	2	0	4	0	0	0	0	0	0	2	0
Oklahoma.....	12	10	22	0	0	0	0	0	0	0	0
Texas.....	261	189	255	12	166	56	0	0	12	9	9
MOUNTAIN											
Montana.....	4	9	8	0	0	0	0	0	0	0	0
Idaho.....	4	0	9	2	0	0	0	0	0	0	0
Wyoming.....	12	7	1	0	0	0	0	0	0	0	0
Colorado.....	32	38	20	0	0	0	0	0	0	0	0
New Mexico.....	2	1	11	0	0	0	0	0	0	0	0
Arizona.....	34	31	31	0	0	18	0	0	0	0	0
Utah.....	27	39	46	0	0	0	0	0	0	4	4
Nevada ¹	0	0	0	0	0	0	0	0	0	0	0
PACIFIC											
Washington.....	18	63	72	0	0	0	0	0	0	0	1
Oregon.....	24	14	18	0	0	6	0	0	0	0	18
California.....	374	101	319	2	6	0	2	0	0	0	5
Total.....	2,951	1,826	3,685	35	202	120	13	0	8	39	91
Same week 1944.....	1,826			41	168	45	11	0	12	24	52
Average 1942-44.....	3,188			30	145	44	11	1	14	24	38
12 weeks: 1945.....	29,090			330	5,916	1,550	86	4	226	614	1,014
1944.....	22,109			317	2,352	745	126	2	125	475	483
Average 1942-44.....	38,806		47,025	276	1,889	567	114	6	192	475	374

¹ Period ended earlier than Saturday.

² 5-year median, 1940-44.

WEEKLY REPORTS FROM CITIES

City reports for week ended March 17, 1945

This table lists the reports from 89 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	Pollomyelitis 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	0	2	0	1	0	0	2
New Hampshire:												
Concord.....	0	0	0	0	0	0	3	0	4	0	0	0
Vermont:												
Barre.....	0	0	0	0	0	0	0	0	0	0	0	0
Massachusetts:												
Boston.....	0	0	0	0	67	3	16	0	92	0	0	42
Fall River.....	0	0	0	0	1	1	1	0	4	0	0	3
Springfield.....	0	0	0	0	0	1	1	0	11	0	0	1
Worcester.....	0	0	0	0	7	0	12	0	20	0	0	17
Rhode Island:												
Providence.....	0	0	0	3	0	0	3	0	19	0	0	36
Connecticut:												
Bridgeport.....	0	0	0	0	1	0	0	0	5	0	0	2
Hartford.....	0	0	1	0	34	1	1	0	25	0	0	0
New Haven.....	0	0	0	0	0	0	3	0	6	0	0	10
MIDDLE ATLANTIC												
New York:												
Buffalo.....	0	0	0	0	1	0	7	0	17	0	0	0
New York.....	22	0	4	3	24	31	74	2	358	0	3	108
Rochester.....	0	1	0	0	15	0	6	0	10	0	0	29
Syracuse.....	0	0	0	0	0	1	1	0	5	0	0	27
New Jersey:												
Camden.....	0	0	0	0	1	1	2	0	1	0	0	1
Newark.....	0	0	0	0	5	0	7	0	26	0	0	8
Trenton.....	0	0	0	0	2	0	1	0	11	0	0	0
Pennsylvania:												
Philadelphia.....	0	0	2	2	84	7	31	0	121	0	0	61
Pittsburgh.....	0	0	3	2	1	2	14	0	39	0	0	9
Reading.....	0	0	0	0	3	0	2	0	6	0	0	0
EAST NORTH CENTRAL												
Ohio:												
Cincinnati.....	1	0	0	1	4	2	9	0	20	0	0	14
Cleveland.....	2	0	2	1	10	8	6	0	72	0	0	47
Columbus.....	0	0	0	0	1	0	5	0	9	0	0	2
Indiana:												
Fort Wayne.....	0	0	0	0	0	0	1	0	7	0	0	1
Indianapolis.....	2	0	0	0	4	1	9	0	30	0	0	1
South Bend.....	0	0	0	0	0	0	0	0	7	0	0	1
Terre Haute.....	0	0	0	0	2	0	2	0	6	0	0	0
Illinois:												
Chicago.....	0	0	2	1	42	16	31	0	176	0	0	20
Springfield.....	0	0	0	0	2	0	2	0	5	0	0	10
Michigan:												
Detroit.....	6	0	1	54	3	16	0	0	97	0	0	22
Flint.....	0	0	0	3	0	7	0	0	9	0	0	3
Grand Rapids.....	0	0	0	4	0	1	0	0	8	0	0	0
Wisconsin:												
Kenosha.....	0	0	0	0	0	0	0	0	2	0	0	4
Milwaukee.....	0	0	0	2	0	3	0	0	61	0	0	1
Racine.....	0	0	0	1	0	0	0	0	7	0	0	12
Superior.....	0	0	0	0	0	0	0	0	2	0	0	1
WEST NORTH CENTRAL												
Minnesota:												
Duluth.....	1	0	0	0	0	0	5	0	10	0	0	0
Minneapolis.....	2	1	0	2	2	7	0	0	27	0	0	5
St. Paul.....	1	0	1	2	0	6	0	0	4	0	0	6
Missouri:												
Kansas City.....	0	0	2	1	2	11	0	0	18	0	0	1
St. Joseph.....	0	0	0	2	0	0	0	0	20	0	0	0
St. Louis.....	10	0	4	0	4	3	9	0	48	0	0	11

See footnotes at end of table.

City reports for week ended March 17, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, 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	2	0	0	0	3	0	0	0
Nebraska:												
Omaha.....	1	0	0	0	16	0	4	0	19	0	0	2
Kansas:												
Topeka.....	0	0	0	0	0	0	2	0	6	0	0	3
Wichita.....	0	0	0	0	3	0	3	0	2	0	0	1
SOUTH ATLANTIC												
Delaware:												
Wilmington.....	1	0	0	0	0	0	3	0	5	0	0	0
Maryland:												
Baltimore.....	6	0	2	0	4	2	10	0	124	0	0	27
Cumberland.....	0	0	0	0	0	0	0	0	7	0	0	0
Frederick.....	0	0	0	0	0	0	0	0	2	0	0	0
District of Columbia:												
Washington.....	0	0	0	0	10	1	7	0	63	0	0	2
Virginia:												
Lynchburg.....	0	0	0	0	0	0	1	0	4	0	0	0
Richmond.....	0	0	1	0	4	3	2	0	19	0	0	0
Roanoke.....	0	0	0	0	5	0	0	0	5	0	0	0
West Virginia:												
Charleston.....	0	0	0	0	0	0	0	0	0	0	0	0
Wheeling.....	0	0	0	0	39	1	1	0	0	0	0	0
North Carolina:												
Raleigh.....	0	0	0	0	9	0	0	0	1	0	0	6
Wilmington.....	0	0	0	0	0	0	1	0	1	0	0	13
Winston-Salem.....	0	0	0	0	3	0	2	0	14	0	0	1
South Carolina:												
Charleston.....	0	0	4	0	35	0	1	0	3	0	0	1
Georgia:												
Atlanta.....	2	0	3	0	0	0	3	0	22	0	0	1
Brunswick.....	0	0	0	0	2	0	1	0	0	0	0	0
Savannah.....	0	0	3	3	1	0	1	0	0	0	0	0
Florida:												
Tampa.....	0	0	0	0	1	0	1	0	1	0	0	0
EAST SOUTH CENTRAL												
Tennessee:												
Memphis.....	0	0	0	2	100	2	21	0	6	0	0	4
Nashville.....	0	0	0	0	0	1	4	0	3	0	0	2
Alabama:												
Birmingham.....	0	0	2	0	1	0	11	0	4	0	0	0
Mobile.....	0	0	0	2	0	0	5	0	1	0	0	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock.....	0	0	0	0	20	0	3	0	4	0	1	0
Louisiana:												
New Orleans.....	2	0	3	1	18	3	4	1	6	0	0	2
Shreveport.....	0	0	0	0	0	0	9	0	1	0	0	0
Texas:												
Dallas.....	0	0	1	1	2	0	0	0	7	0	0	0
Galveston.....	0	0	0	0	0	0	2	0	1	0	0	0
San Antonio.....	3	0	0	1	0	1	10	0	3	0	0	1
MOUNTAIN												
Montana:												
Billings.....	1	0	0	0	0	0	0	0	3	0	0	0
Great Falls.....	0	0	0	0	1	0	0	0	1	0	0	0
Helena.....	0	0	0	0	1	0	0	0	0	0	0	0
Missoula.....	0	0	0	0	1	0	0	0	0	0	0	0
Idaho:												
Boise.....	0	0	0	0	1	0	0	0	0	0	1	0
Colorado:												
Denver.....	1	0	2	1	5	0	5	0	23	0	0	14
Pueblo.....	0	0	0	0	0	0	3	0	11	0	0	0
Utah:												
Salt Lake City.....	0	0	0	0	45	0	1	0	5	0	0	12

City reports for week ended March 17, 1945—Continued

	Diphtheria cases	Etiophallitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Polomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle.....	1	0	-----	0	26	0	6	0	25	0	0	3
Spokane.....	0	0	-----	0	0	0	3	0	2	0	0	0
Tacoma.....	1	0	-----	0	10	1	1	0	10	0	0	1
California:												
Los Angeles.....	4	0	7	2	40	4	4	0	54	0	0	31
Sacramento.....	0	0	1	1	9	0	2	0	0	0	1	8
San Francisco.....	0	0	-----	0	98	2	4	0	49	0	1	21
Total.....	70	2	47	28	901	105	458	3	1,946	0	10	674
Corresponding week, 1944.....	59	-----	162	46	8,860	-----	484	-----	2,485	0	15	322
Average, 1940-44.....	65	-----	287	145	9,307	-----	508	-----	1,788	1	14	916

¹ 3-year average, 1942-44.
² 5-year median, 1940-44.

Dysentery, amebic.—Cases: Pittsburgh 1; Cincinnati 1; Los Angeles, 1; San Francisco 2.
Dysentery, bacillary.—Cases: Providence 1; New York, 2; St. Louis 1; Charleston, S. O., 3; Los Angeles, 1; San Francisco, 1.
Dysentery, unspecified.—Cases: San Antonio, 7; Helena, 5; Denver, 2; San Francisco, 2.
Typhus fever, endemic.—Cases: Tampa, 1; Mobile, 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 89 cities in the preceding table (estimated population, 1943, 53,958,100)

	Diphtheria case rates	Etiophallitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Polomyelitis 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.....	0.0	0.0	2.6	0.0	295	13.1	109.8	0.0	489	0.0	7.8	295
Middle Atlantic.....	10.2	0.5	4.2	3.2	63	10.4	67.1	0.0	275	0.0	1.4	112
East North Central.....	6.7	0.0	2.4	2.4	78	18.2	55.9	0.0	315	0.0	0.0	85
West North Central.....	29.8	2.0	8.0	6.0	64	13.9	93.5	0.0	312	0.0	0.0	58
South Atlantic.....	14.7	0.0	21.2	4.9	185	11.4	55.6	0.0	443	0.0	0.0	83
East South Central.....	0.0	0.0	11.8	23.6	596	17.7	342.0	0.0	83	0.0	0.0	35
West South Central.....	18.9	0.0	15.1	11.3	151	15.1	105.7	0.0	58	0.0	0.0	11
Mountain.....	15.9	0.0	15.9	7.9	429	0.0	71.5	0.0	342	0.0	7.9	207
Pacific.....	9.5	0.0	12.7	4.7	289	11.1	31.6	0.0	221	0.0	3.2	101
Total.....	10.8	0.3	7.2	4.3	139	16.2	70.5	0.5	300	0.0	1.5	104

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended March 3, 1945.—
During the week ended March 3, 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		1	1	101	258	39	22	76	134	632
Diphtheria	2	3	5	20	1	7	19			57
Dysentery:										
Bacillary				1					4	5
Unspecified					1					1
German measles		1		33	12		2	7	14	69
Influenza		31			171	2			30	234
Measles		1	5	161	61	5	10	29	333	605
Meningitis, meningococcus				4	9					13
Mumps		1		286	162	58	28	163	31	729
Scarlet fever		9	6	80	109	22	10	61	47	344
Tuberculosis (all forms)		8	4	160	42	16		18	26	274
Typhoid and paratyphoid fever			4	15	2					21
Undulant fever				1				1		2
Venereal diseases:										
Gonorrhoea		15	29	87	147	40	31	38	43	430
Syphilis		19	6	163	104	14	3	11	14	334
Whooping cough		9		161	55	4	11	26	24	290

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

Ecuador—Chimborazo Province.—For the month of February 1945, plague was reported in Chimborazo Province, Ecuador, as follows: Pungala, 1 case, 1 death; Rio Blanco, Quimiag Parish, 1 case, 1 death.

Madagascar.—For the period February 11–20, 1945, 10 cases of plague were reported in Madagascar.

Morocco (French).—For the period March 1–10, 1945, 12 cases of plague were reported in the interior of French Morocco.

Smallpox

Belgian Congo.—For the week ended January 13, 1945, 200 cases of smallpox were reported in Belgian Congo.

India—Calcutta.—For the week ended February 24, 1945, 379 cases of smallpox with 298 deaths were reported in Calcutta, India.

Nigeria.—For the week ended February 10, 1945, 156 cases of smallpox, with 21 deaths were reported in Nigeria.

Venezuela.—For the week ended March 17, 1945, smallpox (alastrim) was reported in Venezuela as follows: Caracas, 55 cases; La Guayra, 13 cases; San Felix, 6 cases; Santa Teresa, 6 cases.

Typhus Fever

Algeria.—For the period February 11–20, 1945, 137 cases of typhus fever were reported in Algeria. For the period February 21–28, 1945, 58 cases were reported.

Ecuador.—For the month of February 1945, 28 cases of typhus fever with 5 deaths were reported in Ecuador, including 19 cases of typhus fever with 2 deaths reported in Quito.

Egypt.—For the week ended February 17, 1945, 598 cases of typhus fever with 48 deaths were reported in Egypt.

Moldavia.—According to unofficial information, during the last week of February 1945, an epidemic of typhus fever was reported in Moldavia.

Morocco (French).—For the period March 1–10, 1945, 365 cases of typhus fever were reported in French Morocco including 170 cases reported in Casablanca region, 57 cases in Fez region, 54 cases in Marrakesh region, and 52 cases reported in Rabat region.

Turkey.—For the week ended March 17, 1945, 90 cases of typhus fever were reported in Turkey.

Yellow Fever

Gold Coast—District of Avenopeme Keta.—On March 18, 1945, 1 case of suspected yellow fever, terminating fatally on March 22, was reported in the District of Avenopeme Keta, Gold Coast.

Peru—Cuzco Department—Quincemil (vicinity of).—Information dated March 20, 1945, states that 1 confirmed case of yellow fever occurred in the vicinity of Quincemil, Cuzco Department, Peru.