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## THE CHEMOTHERAPY OF BURNS AND SHOCK

### VI. STANDARDIZED HEMORRHAGE IN THE MOUSE.

### VII. THERAPY OF EXPERIMENTAL HEMORRHAGE<sup>1</sup>

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#### VI. Standardized Hemorrhage in the Mouse

In common with the problems of burns and trauma, investigations concerned with the early mortality following hemorrhage have been hindered by the lack of satisfactory methods. The chief difficulties have been the variable response of the experimental animal to the injury and the inability to employ a sufficient number of animals to equalize these variations; contributory factors such as the inadequate standardization of the animal, the injury, and environmental conditions, as well as lack of uniformity in the criteria of shock and the basis of evaluation of therapy, have resulted in many conflicting reports in the large literature in this field (1, 2, 3). Recent attempts to control these difficulties have been made (3, 4, 5, 6). Even here variations in susceptibility of unknown origin remain which render the control of conditions open to question unless simultaneous comparison is possible (7).

By the use of simple techniques in mice, permitting the study of large numbers of animals, and by employing mortality as the criterion, standardized conditions for the evaluation of therapy in burn and traumatic shock have been developed (8, 9). Where adequate groups of animals were employed, satisfactory reproducibility of results has been obtained.

The present report deals with an attempt to apply similar methods to the study of hemorrhage. It was found that the cut tails of mice or rats, immersed in warm oxalate solution, will bleed readily up to the point of death. This permits the study of measured hemorrhage

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upon a large number of unanesthetized animals during the course of one experiment, an important factor in obtaining uniform conditions.

#### METHOD

Mice are placed in glass tubes, one end of which is covered with wire screening, the other plugged with a stopper containing a hole at the periphery, through which the tail protrudes. An assortment of tubes has been prepared so that the proper size can be selected for the individual mouse. Tubes that are too large permit the animal to turn around, while if the tubes are too small there is interference with respiratory movements.

The tubes are placed upon a shelf built along the edge of a water bath 5 feet in length. They are conveniently held in place by rubber bands tacked to the shelf. The tails of the animals project into measuring cylinders held in place in the water bath by means of a rack. The cylinders are made of 10 cc. pipettes cut off at both ends, one end of which is annealed or tightly stoppered. The cylinders are filled with 1.3 percent sodium oxalate and adjusted to a given mark after the solutions have reached equilibrium with the temperature of the bath, which is kept at 43° C. by means of a thermoregulator. Temperature control of the bath is necessary in order to obtain accurate volumetric readings.

After placing the mouse in the holding tube the tail is dipped into a beaker of oxalate solution to compensate for any solution the tail would take up from the measuring cylinder. The tip of the tail is cut off with scissors, the animal fastened horizontally upon the rack with the tail placed in the cylinder so that the lower portion is submerged in the oxalate solution. When the amount of bleeding approaches the desired quantity, the tail is raised from the solution at frequent intervals for the purpose of reading the volume of bleeding above the original mark on the cylinder.

It is convenient to divide the animals into weight groups and to calculate the desired amount of bleeding for each group at the beginning of the experiment. As an example, all mice weighing between 16 and 17 gm. are placed together and the bleeding calculated on a basis of the average weight of the group, thereby facilitating the handling of a large number of animals. An interval of 1 minute is ordinarily allowed between the onset of hemorrhage in the different mice, and as the time required for bleeding is usually 5 to 15 minutes, this limits the number of mice under observation at a given time.

After the desired volume has been bled, the distal end of the tail is ligated with thread and the animal removed from its container and placed in a numbered jar. Between bleedings the measuring cylinders are stoppered with small corks.

The albino mice used in these experiments were 13- to 20-gm. females. Food was withheld for 18 hours, but care was taken to make water accessible up to the time of the first bleeding. The diet was Ralston dog pellets. No anesthesia was used. At least three people are needed for a large-scale experiment: one to handle the animals, one to observe and record bleeding volumes, and one to administer treatment. With this technique, as many as 90 mice can be studied in 1 day.

The above method may also prove useful for the study of standardized anemia or chronic blood loss in experiments upon small laboratory animals.

#### RESULTS IN NORMAL MICE

The majority of mice died at the completion of, or shortly after, a fatal hemorrhage; delayed mortality was irregular and infrequent (2.8 percent among 351 control animals). For the purpose of evaluating therapy, bleeding in two stages was therefore adopted. The first bleeding consisted of 2.25 percent of body weight, which was the maximum blood loss that could be sustained under these conditions without a high mortality. The second bleeding was begun 1 hour after the beginning of the first and in most experiments carried to a maximum of 5 percent of body weight. The final mortality includes any mice dying within 24 hours. Animals dying from the first bleeding were discarded, and comparison was made upon a basis of the bleeding volume and mortality resulting from the second bleeding. With uniform conditions and with an inbred strain of mice, the group mortality curves showed good agreement, although unexplained variations from day to day occur. Due to limitation in the supply of mice at the National Institute of Health, it was necessary to use outside sources, as a result of which greater variations were encountered. The control mortality curve represents an index of susceptibility, and since this is determined during each experiment, corrections for this variable can be made.

In this investigation, the therapeutic effect of a given agent was based upon at least 3 to 5 experiments, with a total of 40 or more mice in each treated group. Similar numbers of animals were employed in the control groups. While significant differences exist between individual experiments, a comparison of the composite control curves shows good agreement. The mortality in the composite groups at a blood loss of 4.5 percent body weight ranged from 62.5 to 82.5 percent, with a mean mortality among 302 mice of 75 percent. At a blood loss of 5 percent of body weight the mortality range was 91 to 100 percent, with a mean of 95.5 percent (fig. 1).<sup>2</sup>

<sup>2</sup> The error of sampling in proportions involving groups of 40 can be calculated from  $\sqrt{pq/n}$ . At 75 percent mortality, the range 2 S.E. equals 14 percent, while at 95 percent the range 2 S.E. equals 7 percent. Thus, the variation in our percent mortalities in the different control groups is within the range of chance variation.

In two groups of experiments comprising 39 mice each, the bleeding was stopped at 4 and 4.5 percent of body weight in order to estimate the total mortality at these points. At 4 percent blood loss the mean mortality was 31 percent, while at 4.5 percent it was 76.5 percent.

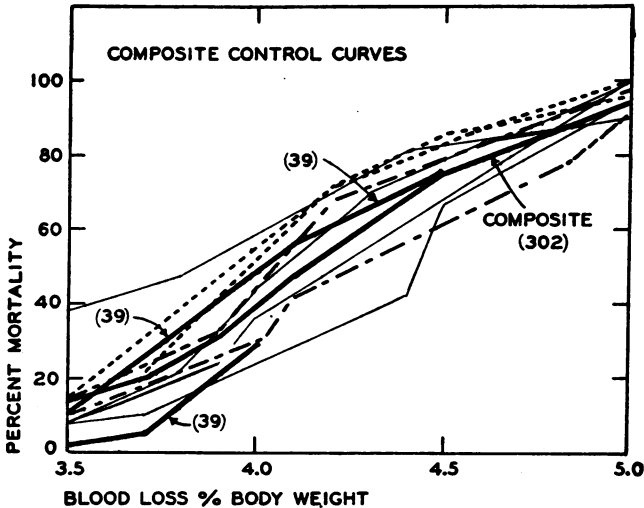


FIGURE 1.—The mortality curves of normal mice subjected to hemorrhage. Each curve represents 3 or more experiments with 25 to 50 mice. The heavy continuous lines present a summary of all untreated mice in which bleeding was terminated at 4 percent body weight (39 mice), 4.5 percent body weight (39 mice), and 5 percent body weight (302 mice). All curves are plotted from deaths which occur during the course of bleeding, except the end points which include any deaths within 24 hours.

Throughout these experiments, all animals dying as a result of the first bleeding (2.25 percent of body weight) are excluded from the series.

#### STATISTICAL TREATMENT

Statistical comparison of the data was made by converting the curves to straight lines by the probit method of Bliss as adapted for cumulative results (10). The bleeding volumes equivalent to 50 percent mortalities and their respective standard errors were determined for the different curves. From this the significance of their differences was calculated and expressed as P (probability) values.

#### VII. Therapy of Experimental Hemorrhage

Therapy was administered between the first and second hemorrhage. In the case of oral administration, it was given by stomach tube within a few minutes after completion of the first bleeding, in order to allow time for absorption. Intravenous therapy, through the tail veins, was given as nearly as possible between 20 minutes after the first bleeding and 20 minutes before the second, allowing 1 to 2 minutes for each injection. Because of the short period of time available for therapy, this was limited to one oral or intravenous dose.

An individual experiment comprised 30 to 45 mice which were taken in rotation for one or more forms of therapy or to serve as controls.

Under the conditions of these experiments it was necessary to administer treatment during the course of severe hemorrhage, rather than in the post-hemorrhagic shock state. The severity of the hemorrhage prior to treatment is evidenced by the fact that 10.5 percent of 1,360 mice died as a result of the first hemorrhage and were excluded from the analysis of the data.

Although treatment was given only during the course of the hemorrhage, the end point is based upon mortality, and it is probable that the method may offer a valid means of comparing the effectiveness of therapeutic procedures for later phases of hemorrhage, although specific information on this point is not available. In actual clinical practice the conditions we have employed are encountered frequently.

#### COMPARISON OF MOUSE SERUM WITH 0.9 PERCENT NaCl

In preliminary experiments it was shown that 0.8 to 1.0 cc. of 0.9 percent NaCl (5.0 to 6.0 percent body weight) administered orally is equal or superior to comparable intravenous therapy. Statistical

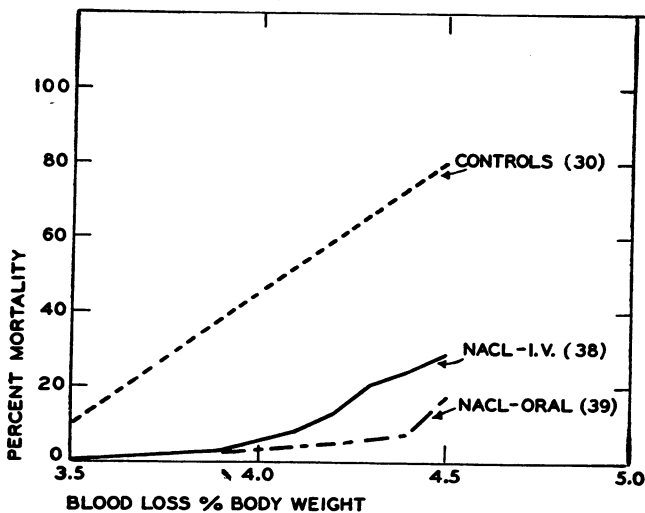


FIGURE 2.—Comparison of 0.9 percent NaCl orally and intravenously; 0.8 to 1 cc. given orally shortly after the first bleeding, and intravenously in two equally divided doses. In all subsequent experiments, therapy limited to one dose. The bleeding was terminated at 4.5 percent body weight. In all figures, numbers in parentheses refer to number of mice in each group.

analysis shows that the differences in response are not significant ( $P=0.7$ ), while with both routes the mortality curves are significantly ( $P=<0.001$ ) below the controls (fig. 2, table 4). All subsequent therapy with saline solutions has been limited to the oral route.

TABLE 1.—Comparison of mouse serum *i. v.* with whole blood *i. v.* and with 0.9 percent NaCl orally in hemorrhage. Hemoglobin concentration and hemoglobin lost per gm. mouse are estimated upon the shed blood

Experiment number	Therapy	Routes	Number mice	Percent body weight bled								Mortality (Percent)	Average weight (gm.)	Hemoglobin concentration, per cent (gm.)	Hemoglobin lost per gm. mouse (mg.)
				2.5-3.5	3.6-3.9	4.0-4.2	4.3-4.5	4.6-4.8	4.9-5.1	4.9-5.1	4.9-5.1				
1A	Plasma 0.5 cc.	<i>i. v.</i>	15			1				2	2	33.3	17.6	13.0	6.4
1B	Serum 0.5 cc.	<i>i. v.</i>	10			1				3	2	60			
1C	do.	<i>i. v.</i>	15	1	5	1	3			3	1	93.3			
1A	NaCl 0.5 cc.	oral	16			1				5	2	50	17.4	12.0	5.9
1B	do.	do.	10			2				2	2	60			
1C	do.	do.	15		1	4	6	1		1	2	93.3			
1A	Controls		20	2	5	4	3	1		1	2	85	18.5	13.9	6.0
1B	do.		20	5	4	4	7	3		3	95				
1C	do.		10	3	5	2					100				
2A	Serum 0.5 cc.	<i>i. v.</i>	10	2						1	5	80	17.5	11.6	5.8
2B	do.	<i>i. v.</i>	9	1		1				1	44.4				
2C	do.	<i>i. v.</i>	9			2				2	1	44.4	18.1	11.0	5.3
2D	do.	<i>i. v.</i>	11			1				1	2	27.3			
2E	do.	<i>i. v.</i>	11	1			2			1	4	72.7	18.3	11.4	6.1
2A	Whole blood 0.5 cc.	<i>i. v.</i>	10									0	17.7	14.7	7.5
2B	do.	<i>i. v.</i>	10									0			
2C	do.	<i>i. v.</i>	11	1			1			2	1	45.5	17.0	14.3	7.3
2D	do.	<i>i. v.</i>	9							1	3	11			
2E	do.	<i>i. v.</i>	9			1				1	3	44.4	18.2	12.9	6.6
2A	Controls		10			2	4			4	4	100	17.5	13.5	6.0
2B	do.		10	1		2	6			1	3	100			
2C	do.		10			2	1			2	3	90	17.0	12.5	5.4
2D	do.		10	3	1	2	3			1	1	100			
2E	do.		10			3	3			3	1	100	17.3	13.4	6.0

In this and all subsequent tables experiments with the same number indicate that they were run simultaneously.

In most of the studies mouse serum rather than plasma has been employed because the use of anticoagulants is avoided and because the serum, when processed as in previous experiments (8), has proved of uniformly low toxicity. Intravenous injection of 1 cc. is tolerated without symptoms.

A comparison of 0.5 cc. of serum (3.0 to 3.6 percent body weight) orally and intravenously shows a lower mortality by the latter route although the results are not statistically significant ( $P=0.3$ ) (fig. 3,

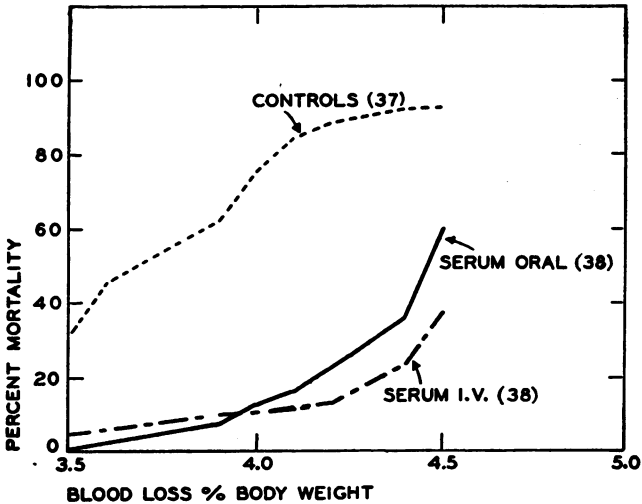


FIGURE 3.—Comparison of 0.5 cc. of mouse serum administered orally and intravenously. Bleeding terminated at 4.5 percent body weight. Thirty-eight mice in each treated group.

table 4). By both routes the mortality curves are significantly ( $P < 0.001$ ) lower than the controls.

All important comparisons are based upon experiments in which the agents to be compared and the controls were tested simultaneously. Three such experiments, comprising a total of 40 mice treated with 0.5 cc. serum, 41 with 0.5 cc. of saline, and 50 controls show an equal effectiveness for serum and saline in reducing mortality (fig. 4, table 1). A summary of all experiments in which 0.5 cc. serum intravenously was employed, when compared with those employing 0.5 cc. of saline orally, shows, at a blood loss of 4.5 percent, a mortality of 28 percent in 128 mice receiving serum, 22.7 percent in 119 mice given saline, and 73.5 (125 mice) and 75.5 percent (130 mice) in their respective controls. At 5 percent blood loss the mortalities for these groups are 55.5 percent for serum (90 mice), 68 percent for saline (81 mice), and 91.5 percent (100 mice) and 88.5 percent (95 mice) for their respective controls.

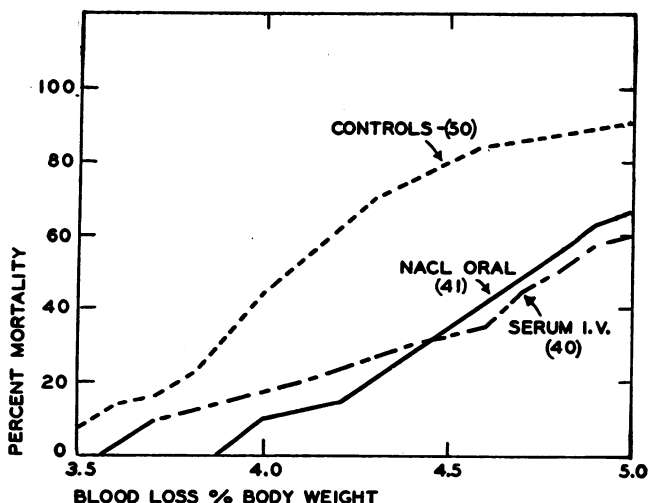


FIGURE 4.—The similar therapeutic effects of 0.5 cc. mouse serum i. v. and 0.5 cc. of 0.9 percent NaCl orally.

COMPARISON OF WHOLE BLOOD WITH SERUM

The view is generally held, supported by laboratory evidence, that plasma can in large measure replace whole blood in the treatment of hemorrhage (11, 12, 13).

Whole blood was obtained immediately prior to our experiments by decapitating large mice and collecting the blood in a receptacle con-

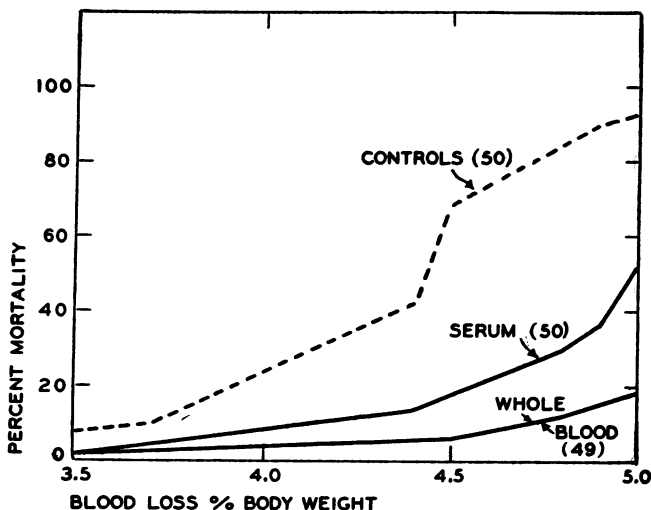


FIGURE 5.—Comparison of 0.5 cc. whole blood i. v. with 0.5 cc. serum i. v.

taining sufficient ammonium citrate (this salt used in order to avoid Na and K) to give a final concentration of 2.1 mg. per cc. In one series heparinized blood and plasma were used. The blood was fil-



tered through sterile gauze before use; all samples were tolerated by normal mice in doses up to 1 cc. intravenously.

In a group of three experiments with 49 mice receiving 0.5 cc. whole blood intravenously, 50 mice receiving 0.5 cc. serum intravenously, and 50 controls, the mortality at 5 percent body weight blood loss was 18 percent for whole blood, 52 percent for serum, and 92 percent among the controls (fig. 5, table 1).

Because of the inaccuracy in statistical treatment of mortality curves where only a small percentage of animals die, and which there-

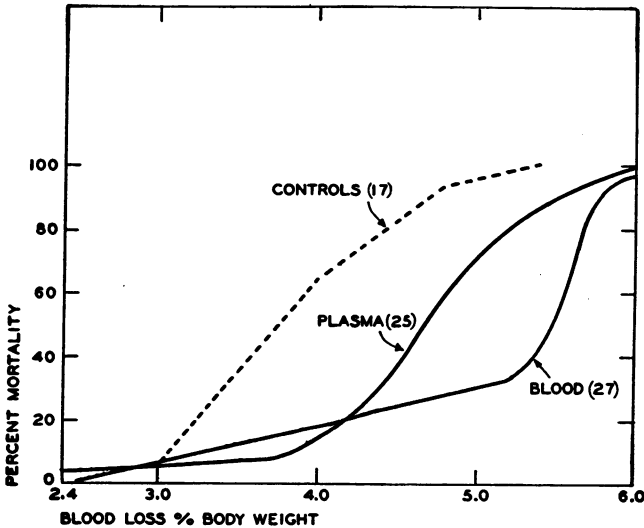


FIGURE 6.—Comparison of 0.5 cc. heparinized blood with plasma i. v., in which bleeding was continued until death of all animals.

fore represent only a limited part of the complete curve, an experiment was carried out for comparison of whole blood with heparinized plasma wherein the bleeding was carried to the death of all animals. In this way complete mortality curves were obtained (fig. 6).

Statistical analysis of these results reveals that whole blood is significantly better than plasma ( $P = < 0.001$ ).

In that part of the curve corresponding to the previous experiments, the results are in agreement; the mortality at 5 percent blood loss was 30 percent for the whole blood, 72 percent for plasma, and 96 percent for the controls.

#### COMPARISON OF WHOLE BLOOD WITH SALINE

Since serum and saline give approximately similar results, it is to be expected that whole blood would be superior to saline; it remained to be determined whether several times the volume of salt solution orally would equal the effect of a given volume of blood given intravenously. While the amount of blood that can be injected intrave-

nously within a short time is limited, a considerably larger amount of saline can be administered orally without hazard. Apart from this, the availability of whole blood and of facilities for its administration is often limited in military and civilian emergencies.

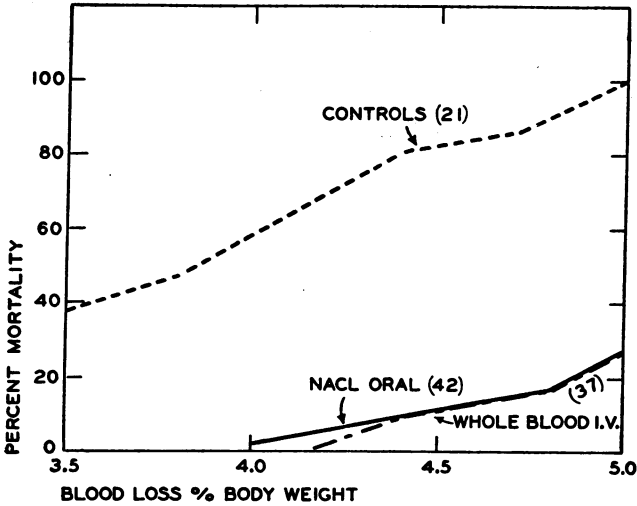


FIGURE 7.—The identical response of 0.5 cc. of whole blood i. v. and 0.9 to 1.4 cc. of saline orally.

Three experiments were performed, including 37 mice receiving 0.5 cc. of whole blood intravenously (3.0 to 3.6 percent body weight), 42 mice receiving 0.9 to 1.4 cc. of saline (8 percent of body weight) orally, and 21 controls. Equal degrees of effectiveness were obtained

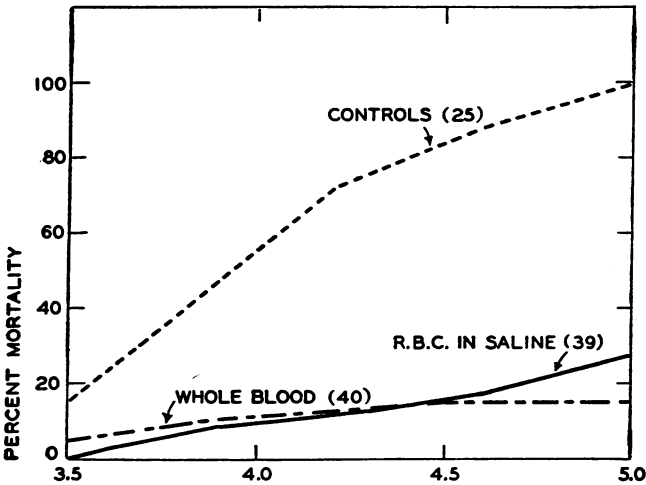


FIGURE 8.—The similar effects of 0.5 cc. of whole blood i. v. to 0.5 cc. of erythrocytes suspended in saline, i. v.

under these conditions for saline and whole blood; the mortality at 5 percent blood loss was 26.5 percent for blood, 28 percent for saline, and 100 percent for the controls (fig. 7, table 2).

TABLE 2.—Whole blood 0.5 cc. i. v. compared with an equal amount of red cell suspension in saline i. v., and with approximately three times this quantity of saline orally (8 percent body weight=1.2 to 1.6 cc. per mouse)

Experiment number	Therapy	Route	Number mice	Percent body weight bled							Mortality (percent)	Average weight (gm.)	Hemoglobin concentration, percent (gm.)	Hemoglobin lost per gm. mouse (mg.)
				Deaths										
				2.5-3.5	3.6-3.9	4.0-4.2	4.3-4.5	4.6-4.8	4.9-5.1					
3 A	Whole blood 0.5 cc.	i. v.	16			1	1	1	4	43.8	17.0	15.0	7.4	
3 B	do.	i. v.	12					1		8.3				
3 C	do.	i. v.	9				2		1	33.3				
3 A	NaCl 8 percent body weight	oral	17			2	1	2	1	35.3	16.6	11.5	5.5	
3 B	do.	do.	11						1	9				
3 C	do.	do.	14			1	1		5	50				
3 A	Controls		8	2	2	2				100	16.8	13.5	5.6	
3 B	do.		8	2	1	1	2	1	1	100				
3 C	do.		5	3	2					100				
4 A	Whole blood 0.5 cc.	i. v.	9							0				
4 B	do.	i. v.	13	2			2			46.1				
4 C	do.	i. v.	18							0				
4 A	RBC in saline 0.5 cc	i. v.	10			1			1	20				
4 B	do.	i. v.	14				2	2	1	50				
4 C	do.	i. v.	15			1	1			13.3				
4 A	Controls		8	3	3	3	3		2	100				
4 B	do.		8	2	2	3	1			100				
4 C	do.		9	2	4	2		1		100				

In other experiments in which similar doses of whole blood and of saline were employed, but done upon different days, the results show good agreement with those obtained above. Eighty-nine additional mice receiving 0.5 cc. (3 to 3.6 percent body weight) of blood intra-

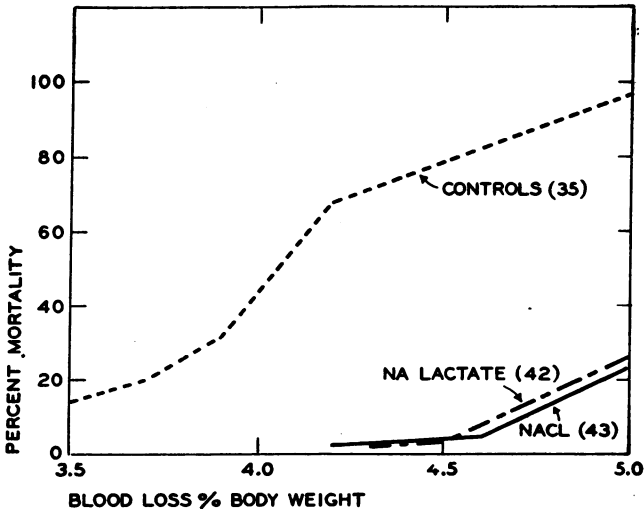


FIGURE 9.—The identical effects of equimolar solutions of NaCl (0.9 percent) and sodium lactate (1.75 percent). Oral administrations of 8 percent body weight in both cases.

venously (figs. 5 and 8, tables 1 and 2) had a final mortality of 16.6 percent, as compared with 85 mice receiving 8 percent body weight of saline orally (fig. 9, table 3) with a final mortality of 25 percent.

It must be concluded that the erythrocytes contribute an important effect in the prevention of death from hemorrhage. Within certain limits, a similar degree of effectiveness can be obtained by increasing the dosage of salt solution orally.

#### COMPARISON OF WHOLE BLOOD WITH ERYTHROCYTES SUSPENDED IN SALINE

Whole blood was obtained as described; a measured portion was centrifuged, the plasma removed, the red cells washed twice with 0.9 percent saline, and finally made up to the original volume with saline.

These experiments comprised 40 mice receiving 0.5 cc. of whole blood intravenously, 39 mice receiving 0.5 cc. of red cell suspension intravenously, with 25 controls. A similar degree of therapeutic effectiveness was obtained for both agents (fig. 8, table 2).

Since in the erythrocyte suspension plasma is replaced by saline, these results are in agreement with those described above which show an equal response for saline and serum. The results are of practical interest in view of the large quantities of erythrocytes made available by the current blood donations for preparation of plasma.

TABLE 3.—Comparison of 0.9 percent sodium chloride and 1.75 percent sodium lactate orally in doses of 8 percent body weight. Also, the relative effects in hemorrhage of NaCl, KCl, and H<sub>2</sub>O. In experiments 6A and 6B, the bleeding was stopped at 4.5 percent body weight

Experiment number	Therapy	Route	Number mice	Percent body weight bled							Mortality (Percent)	Average weight (gm.)	Hemoglobin concentration, percent (gm.)	Hemoglobin lost per gm. mouse (mg.)
				Deaths										
				2.5-3.5	3.6-3.9	4.0-4.2	4.3-4.5	4.6-4.8	4.9-5.1					
5A	NaCl 8 percent body weight	oral	10							3	30	16.8	11.7	6.0
5B	do.	do.	16			1		2		3	31	17.0	11.9	6.0
5C	do.	do.	17					1		3	29.4			
5A	Na lactate 8 percent body weight	do.	10				1	1		2	40	16.2	12.1	6.0
5B	do.	do.	16				1	2		6	56.3	17.0	11.7	6.8
5C	do.	do.	16					1		1	12.5			
5A	H <sub>2</sub> O 8 percent body weight	do.	10		3	1	2	2		1	90	15.9	12.8	5.6
5B	do.	do.	16		2	4	2	4		3	94	17.0	12.2	5.5
5A	Controls		10		1	6	1	1			100	16.2	13.4	5.3
5B	do.		17		4	5	1	4		1	100	17.2	13.2	5.6
5C	do.		8		1	2	2	2		1	87.5			
6A	H <sub>2</sub> O 8 percent body weight	oral	9		1	1	2	2			34.4	18.3	12.9	6.3
6B	do.	do.	20		2	4	6	1			60	19.7	13.2	5.6
6C	do.	do.	13		1	1	1	1		3	46	17.2	12.9	6.3
6A	Controls		9		3	4	1				100	18.3	13.7	6.0
6B	do.		14		6	3					78.5	20.1	15.2	5.9
6C	do.		15		1	5	6	2			100	17.0	14.1	6.4
7A	NaCl 0.5 cc.	oral	10			1	1	1		5	70	15.6	12.7	6.3
7B	do.	do.	10			1	1	1		5	80	16.2	12.2	6.0
7C	do.	do.	10			1	1	2		3	70	15.0	11.1	5.4
7D	do.	do.	10			1	1	1		6	70			
7A	KCl 0.5 cc.	do.	10		1	1	1	2		1	70	15.8	12.1	5.4
7B	do.	do.	10		1	1	1	2		4	100	15.4	12.1	5.5
7C	do.	do.	10		2	1	4	2		2	90	14.5	11.6	5.1
7D	do.	do.	10		1	2	3	3			90			
7B	H <sub>2</sub> O 0.5 cc.	do.	10		1	1	2	2		6	100	15.4	11.9	5.5
7C	do.	do.	11		1	1	1	1		4	82	15.0	11.1	5.3
7D	do.	do.	10		2	1	2	2		2	100			
7A	Controls		15		3	1		3		3	80	14.7	13.7	6.5
7B	do.		10		1	1	2	1		2	100	15.4	12.7	5.7
7C	do.		10		1	3	3	3		3	100	15.1	13.2	5.4
7D	do.		10		2	1	2	2		2	100			

<sup>1</sup> Half of these used. This represents determinations on half the animals used.

<sup>2</sup> Bled to 4.5 percent body weight.

## COMPARISON OF SODIUM CHLORIDE WITH SODIUM LACTATE

Previous results in the chemotherapy of burn shock (8) have shown an equal response with equimolar solutions of several sodium salts—chloride, lactate, succinate, acetate, and bicarbonate. Chloride and lactate were also of equal effectiveness in traumatic shock in mice (9). Dr. C. L. Fox, Jr. (14) has chosen sodium lactate for the oral therapy of burn shock in man because of its palatability and its effect in combating acidosis. Promising clinical results have been reported by him.

In four experiments a comparison was made between 0.9 percent NaCl and 1.75 percent (equimolar) sodium lactate orally in doses of 8 percent body weight (fig. 9, table 3).

Equal responses were obtained: a final mortality of 28 percent with NaCl (43 mice) and 30 percent with lactate (42 mice). These findings indicate that, in common with burn and traumatic shock, the therapeutic effects of NaCl are primarily a function of the sodium ion.

## KCL AND WATER

In previous work upon burn shock in mice, it was found that water was without benefit, if not actually harmful. Isotonic solutions of KCl were harmful, as evidenced by a decrease in survival time in compar-

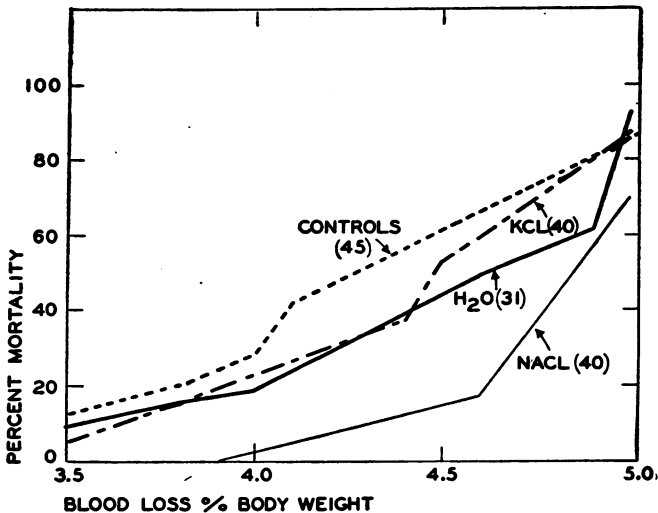


FIGURE 10.—Comparison of NaCl, KCl, and water orally in doses of 0.5 cc. per mouse (3 to 3.6 percent body weight).

ison with controls, and by the fact that KCl, when added to NaCl, antagonized the curative action of the latter (8). These findings are of value in an understanding of the mechanism of the response to saline; they indicate a therapeutic effect specific for the sodium ion,

and are not inconsistent with the possibility of potassium as a toxic factor in shock, a possibility suggested by Scudder (16) and investigated by others (16, 17, 18).

KCl was administered orally in 1 percent solution, equimolar to 0.9 percent NaCl. Doses of 0.5 cc. (3 to 3.6 percent body weight) were used, representing approximately one-fifth of the L.D.<sub>50</sub> of KCl orally (8). In four experiments with 40 mice no appreciable difference ( $P=0.21$ ) was observed from the control mortality curve (fig. 10, table 3).

In quantities of 3.0 to 3.6 percent body weight, water by mouth gives a mortality curve in hemorrhage that does not deviate significant-

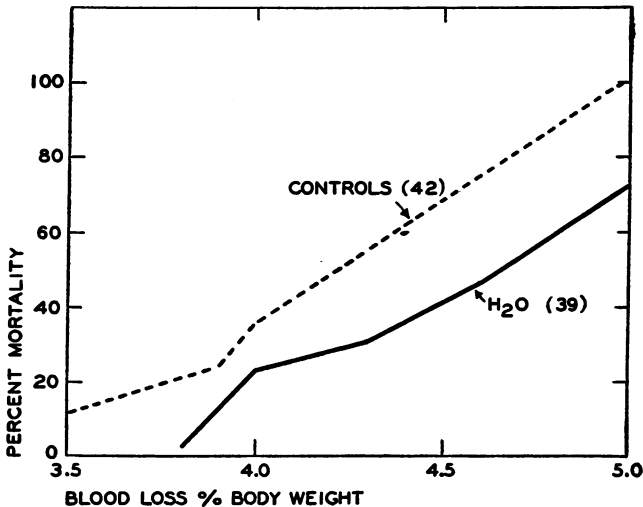


FIGURE 11.—The effect of water orally in amounts of 8 percent body weight.

ly ( $P=0.25$ ) from the control (fig. 10, table 3). With doses of 8 percent body weight the final mortality among 39 mice was 72 percent as compared with 100 percent for 42 controls (fig. 11, table 3). Statistical analysis shows this difference to be significant ( $P=0.003$ ). The interpretation of the results with KCl and water, when corrected for hemodilution and blood loss, will be discussed below.

#### COMPARISON OF ISOTONIC WITH HYPERTONIC SALINE

A series of preliminary tests were made in which 0.9 percent NaCl orally was compared with equivalent doses (7 percent body weight) of 1.8 percent NaCl and with half (3.5 percent body weight) the dose of 1.8 percent NaCl. In this way both the volume and the strength of the solutions were varied in the same experiment.

No significant difference between the three treatments was noted (fig. 12, table 4). This somewhat contradictory result may be taken

to indicate that two opposite influences are involved. The lack of added benefit from increased quantities of 1.8 percent NaCl may be due to the deleterious action of large doses of hypertonic solutions in the presence of blood loss. Similar results were previously obtained in burn shock (8). The experiments do suggest that within certain limitations hypertonic solutions of saline are effective; a more extensive investigation is required to establish these limitations.

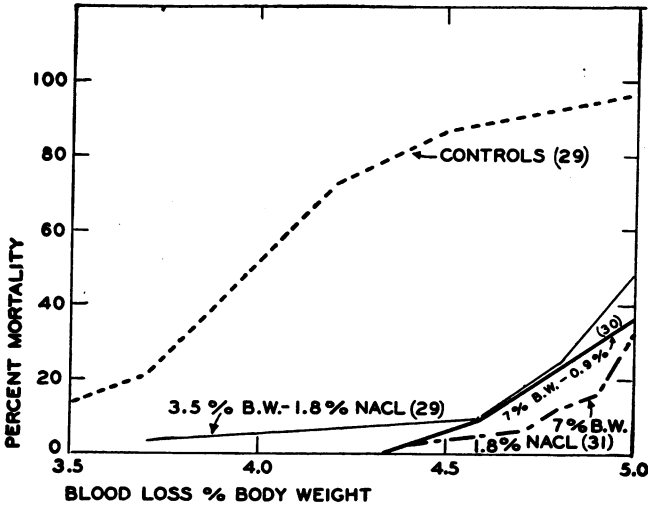


FIGURE 12.—Comparison of 0.9 percent and 1.8 percent NaCl in doses of 7 percent body weight, and 1.8 percent NaCl in doses of 3.5 percent body weight. All treatment given orally.

**CORRELATION OF THERAPEUTIC RESPONSE WITH HEMOGLOBIN LOSS AND HEMODILUTION**

Hemoglobin determinations were made upon the majority of bloods obtained. The total blood collected from both first and second bleedings was used. In a given experiment the samples from the control group and from each treated group were pooled for these estimations, which were carried out by the acid hematin method with a photoelectric colorimeter.

Since the volumes of blood loss and weights of the animals were known, it was possible to calculate the average hemoglobin concentration in the shed blood, and the average amount of hemoglobin lost per gram of mouse for each group.

The results of these studies are summarized in table 5. It is seen that all forms of fluid therapy except whole blood were attended by hemodilution when compared with their respective controls.



TABLE 4.—*The relative effects of isotonic and hypertonic NaCl. Also comparisons of oral with i. v. NaCl and oral with i. v. serum. In these latter experiments bleeding was stopped at 4.5 percent body weight*

Experiment number	Therapy	Route	Number mice	Percent body weight bled							Mortality (percent)	Average weight (gm.)	Hemoglobin concentration, Percent (gm.)	Hemoglobin lost, Per gm. mouse (mg.)
				2.5-3.5	3.6-3.9	4.0-4.2	4.3-4.5	4.6-4.8	4.9-5.1	Deaths				
8 A	0.9 percent NaCl	oral	20				2	4	7	65				
8 B	7 percent body weight	do.	10					1	1	20				
8 A	1.8 percent NaCl	do.	21				1	3	7	52.4				
8 B	7 percent body weight	do.	10						2	20				
8 A	1.8 percent NaCl	do.	19		1		1	4	8	73.7				
8 B	3.5 percent body weight	do.	10					1	2	30				
8 A	Controls		19	3	5	6	3		2	100				
8 B	do.		10	1	4	2	1		1	90				
9 A	NaCl 1 cc.	i. v.	18				4	1		144.4	16.8	12.9	5.8	
9 B	do.	i. v.	10				1			120	18.7	11.9	5.3	
9 C	NaCl 0.8 cc.	i. v.	10		1		1	1		130	15.8	10.5	4.7	
9 A	NaCl 1 cc.	oral	19		1		1			110.5	16.9	14.1	6.4	
9 B	do.	do.	10			1	3			140	18.6	12.2	5.4	
9 C	NaCl 0.8 cc.	do.	10				1			110	16.0	11.9	5.4	
9 A	Controls		14	2	6	3				178.6				
9 B	do.		16	1	3	4		5		181.2				
9 C	do.		16	1	3	4				155	15.1	12.1	5.5	
10 A	Serum 0.5 cc.	i. v.	20	1		2	8			110	16.2	13.3	6.2	
10 B	do.	i. v.	10				1			137.5	15.3	12.7	4.3	
10 C	do.	i. v.	8	1				2						
10 A	do.	oral	19		1	2	11	2		184	15.0	12.5	5.5	
10 B	do.	do.	10			1	1			120	15.9	12.5	5.6	
10 C	do.	do.	9		2	1	4	1		188.8	14.9	12.5	5.0	
10 A	Controls		18	4	7	6	1			1100	15.4	15.4	5.3	
10 B	do.		10	1	2	4				170	17.1	12.8	5.4	
10 C	do.		9	4	5	6				1100	17.1	11.8	4.2	

<sup>1</sup> Bled to 4.5 percent body weight.

TABLE 5.—A summary of the effects of various therapeutic agents upon hemoglobin concentration, total hemoglobin lost, and mortality. Determinations carried out upon shed blood

Therapy	Number mice	Average weight (gm.)	Hemoglobin concentration, percent (gm.)	Hemoglobin lost per gm. mouse (mg.)	5 percent mortality (percent)
NaCl 8 percent body weight, oral.	53	16.5	11.7	5.8	37
Controls.....	26	16.7	13.34	5.46	100
NaCl 1 cc., i. v. <sup>1</sup> .....	38	17	12.0	5.4	34
NaCl 1 cc., oral <sup>1</sup> .....	39	17	13.0	5.9	18
Controls <sup>1</sup> .....	16	14.9	13.1	5.1	81
NaCl 0.5 cc., oral.....	46	15.7	12.0	5.9	65
KCl 0.5 cc., oral.....	30	15.2	11.9	5.33	87
Controls.....	55	16.3	13.4	5.96	90
H <sub>2</sub> O 8 percent body weight.....	31	16.8	12.7	5.85	72
Controls.....	33	16.8	13.7	5.85	100
H <sub>2</sub> O 8 percent body weight <sup>1</sup> .....	29	19.0	13.1	5.82	55
Controls <sup>1</sup> .....	23	19.3	14.5	5.94	86
H <sub>2</sub> O 0.5 cc., oral.....	21	15.2	11.5	5.4	91
Controls.....	20	15.2	12.95	5.55	95
Serum 0.5 cc., i. v.....	65	17.9	11.7	5.85	48.5
Controls.....	70	17.6	13.3	5.83	94.3
Serum 0.5 cc., i. v. <sup>1</sup> .....	38	15.2	12.5	5.43	39.5
Serum 0.5 cc., oral <sup>1</sup> .....	38	15.2	12.5	5.4	68
Controls <sup>1</sup> .....	37	16.3	13.8	5.06	92
Whole blood 0.5 cc., i. v.....	65	17.3	14.4	7.3	25
Controls.....	58	17.2	13.1	5.74	98

<sup>1</sup> Bled to 4.5 percent body weight.

In eight salt (3 to 3.6 percent body weight) therapy experiments, the average hemoglobin concentration was 12.3 gm. per 100 cc. (S.E. 0.6), while the paired controls had an average hemoglobin concentration of 13.5 (S. E. 0.4). In eight serum or plasma therapy experiments, the average hemoglobin concentration was 12.3 (S. E. 0.1), while the paired controls had an average hemoglobin concentration of 13.5 (S. E. 0.6). In seven groups treated with water, the average hemoglobin concentration was 12.4 (S. E. 0.3), while the control groups had an average of 13.6 (S. E. 0.3). In all cases, the individual treatment values were lower than those of the paired controls (table 5).

While these observations are of a preliminary nature due to the limited number of observations, certain differences in respect to mechanism are suggested. That hemodilution is not the sole factor in the therapeutic response is shown by the lack of correlation between the mortality results and hemodilution.

In animals treated with salt the mortality is lower than in the controls, even though the hemoglobin losses are substantially the same. This is particularly true with the large doses of salt, in which the mortality is markedly decreased, even though the loss of hemoglobin is at least as great, and possibly greater, than the controls. This marked decrease in mortality is far greater than could possibly be explained by the magnitude of the dilution. Although the number of hemoglobin

determinations is too small to treat adequately statistically, the direction of the findings is the same in all of the separate experiments.

When water is given, a similar degree of hemodilution occurs, but the therapeutic response is less even though the total hemoglobin loss is no greater than the controls. When the mortality curves for water are corrected for hemodilution the values coincide with the controls; this indicates that the beneficial effects of water can be explained entirely on the basis of hemodilution.

In three groups in which KCl was given, although hemodilution was present, the animals died at a rate equal to the controls from a hemoglobin loss less than the controls. The data, however, are insufficient for adequate statistical evaluation.

Following the administration of whole blood, the hemoglobin content increases. As expected, the animals are able to sustain a considerably greater hemoglobin loss than any other group and still have a low mortality.

#### DISCUSSION

The acute mortality in the mouse as a result of hemorrhage has shown certain similarities in the response to therapy to that of burns and trauma. It must be concluded from these common results that specific electrolytes and fluid are of greater importance than the plasma proteins in influencing the early survival of these animals from an extent of injury that is fatal to the controls. In all experiments the effects of serum or plasma therapy can be duplicated by equivalent volumes of an isotonic solution of NaCl. Evidence that this is a specific effect of an electrolyte is presented in that it is shared by all sodium salts that we have tested, that the potassium ion is ineffective or deleterious, and that water has little or no effect. The existence of a disturbance in sodium metabolism is further shown by the observation of Fox (14) that in clinical burns treated with large doses of sodium lactate orally, most of the administered sodium is retained in the body for 2 or more days; his experiments with radio-active sodium indicate that most of this sodium is accumulated in the injured area.

In all three types of injury, highly significant responses are not obtained until the dosage of saline by mouth approaches 10 percent of body weight. This fact must be considered in accounting for much of the negative evidence that has been reported in the literature, where saline therapy has been limited to smaller quantities, administered intravenously. Many experimenters in this field have compared saline with plasma or serum by intravenous routes (2, 3, 13, 19, 20). While there is no uniformity in these published results, they are to a large measure in disagreement with our own; some of the workers, however, have reached conclusions similar to ours (21, 22). As mentioned at the beginning of this paper, the handicaps

under which most previous investigation has been carried out, and the wide variety of conditions and criteria employed, have contributed largely to this confusion.

Oral therapy has been found at least equal to intravenous administration in burns and trauma as well as hemorrhage. This is an important consideration in view of the large quantities of fluid that seem indicated, and in the possible application of these results to emergency conditions where intravenous medication is not always available, and where time is a large factor in the value of therapy. It should be emphasized that in conditions of collapse, where gastrointestinal absorption may be poor, or where death may be imminent, intravenous therapy should also be used.

It is not surprising that the red cells contribute an effect in hemorrhage beyond that produced by serum or saline, since administration of whole blood or red cells in saline approaches a more complete repair of the injury than is otherwise attained. An evaluation of therapy with whole blood in the acute mortality from burns or trauma has not yet been done.

The applicability to man of the results we have obtained in the various forms of trauma in the mouse can be decided only by clinical trial. Here again the problems of comparative evaluation of therapy are greater than in the laboratory. Even though the best criteria available are employed, it is believed that no valid conclusions can be drawn except from a large number of observations under conditions as uniform as possible.

#### CONCLUSIONS

A method is described whereby large numbers of unanesthetized small laboratory animals can be subjected simultaneously to standardized hemorrhage.

Fatal hemorrhage in two stages was carried out in mice and therapy administered between bleedings.

Oral therapy with 0.9 percent NaCl is equal to intravenous administration. When given in quantities equivalent to 8 percent of body weight, the majority of animals will survive hemorrhage fatal to controls.

Administration of equal quantities of saline by mouth and mouse serum intravenously produces an identical therapeutic effect. Sodium chloride and sodium lactate in equimolar solutions give equivalent results. Water orally in large amounts brings about a slight reduction in mortality; smaller quantities of water or 1 percent KCl are without effect.

These results, along with those previously published on burn and traumatic shock, indicate that administration of specific electrolytes

and fluid is of greater significance in therapy than administration of plasma proteins.

Whole blood is superior to saline or serum. The response to whole blood intravenously can be equaled by three times the volume of saline given orally. Erythrocytes suspended in saline are as effective as equal volumes of whole blood. These findings indicate the importance of red cells in the therapy of hemorrhage.

The results are analyzed in relation to hemodilution and to hemoglobin loss.

The experimental evidence would seem to justify the clinical trial of sodium salts administered in isotonic solution in part or entirely by mouth in amounts up to 10 percent of body weight, in the treatment of burn shock, traumatic shock, and hemorrhage. In war casualties, particularly where intravenous medication is not immediately available, the procedure may be of value as a first-aid measure.

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### DEATHS DURING WEEK ENDED MAY 6, 1944

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

	Week ended May 6, 1944	Correspond- ing week; 1943
<b>Data for 93 large cities of the United States:</b>		
Total deaths .....	8, 922	9, 516
Average for 3 prior years .....	8, 722	-----
Total deaths, first 18 weeks of year .....	178, 684	181, 060
Deaths under 1 year of age .....	630	636
Average for 3 prior years .....	569	-----
Deaths under 1 year of age, first 18 weeks of year .....	11, 367	12, 578
<b>Data from industrial insurance companies:</b>		
Policies in force .....	66, 457, 823	65, 513, 811
Number of death claims .....	11, 928	12, 180
Death claims per 1,000 policies in force, annual rate .....	9.4	9.7
Death claims per 1,000 policies, first 18 weeks of year, annual rate .....	11.0	10.5

# PREVALENCE OF DISEASE

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

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## UNITED STATES

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### REPORTS FROM STATES FOR WEEK ENDED MAY 13, 1944

#### Summary

A total of 420 cases of meningococcus meningitis was reported for the week, as compared with 382 last week, 449 for the next earlier week, 485 for the corresponding week last year, and a 5-year (1939-43) median of 54. Decreases were recorded only in the Middle Atlantic, South Atlantic, and West South Central areas. Nine States reporting more than 15 cases each (last week's figures in parentheses) are as follows: *Increases*—Massachusetts 16 (8), New Jersey 21 (16), Illinois 29 (22), Michigan 28 (13), Missouri 19 (15), California 43 (25); *decreases*—New York 45 (50), Pennsylvania 25 (40), Ohio 28 (31). The total for the year to date is 9,885, as compared with 9,305 for the same period last year and a 5-year median of 941.

Of a total of 37 cases of poliomyelitis reported, as compared with 14 last week and a 5-year median of 22, 10 occurred in California and 4 each in South Carolina and Louisiana. A total of 131 cases has been reported since April 1, as compared with 143 for the same period last year.

Decreases occurred in the incidence of both measles and scarlet fever. Totals reported are 25,812 for measles and 6,162 for scarlet fever, as compared with 26,067 and 6,672, respectively, for last week, and respective 5-year medians of 22,632 and 3,823.

The current incidence of diphtheria, influenza, smallpox, and whooping cough is below that for last week and the corresponding 5-year median. A total of 86 cases of typhoid fever was reported, as compared with 67 last week and a 5-year median of 100. Of the current total, 19 were reported in California and 12 in Texas.

Deaths recorded for the week in 92 large cities of the United States totaled 9,044, as compared with 8,874 last week and a 3-year (1941-43) average of 8,614. The total for the year to date is 186,531, as compared with 189,350 for the same period last year.

Telegraphic morbidity reports from State health officers for the week ended May 13, 1944, and comparison with corresponding week of 1943 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 1939-43	Week ended—		Median 1939-43	Week ended—		Median 1939-43	Week ended—		Median 1939-43
	May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943	
<b>NEW ENGLAND</b>												
Maine.....	1	0	0	1	1	229	34	127	1	2	1	
New Hampshire.....	0	0	0	-----	-----	5	42	38	2	4	0	
Vermont.....	1	0	0	-----	-----	66	251	142	0	0	0	
Massachusetts.....	2	0	4	-----	-----	971	1,669	1,048	16	30	5	
Rhode Island.....	0	2	1	18	1	54	52	93	1	12	0	
Connecticut.....	1	0	0	1	3	600	491	422	5	4	0	
<b>MIDDLE ATLANTIC</b>												
New York.....	9	16	20	15	10	1,555	3,383	2,320	45	70	7	
New Jersey.....	7	4	4	5	10	1,192	2,329	759	21	42	1	
Pennsylvania <sup>1</sup> .....	10	5	13	1	3	937	2,096	1,329	25	34	4	
<b>EAST NORTH CENTRAL</b>												
Ohio.....	5	19	10	9	8	433	519	497	28	15	1	
Indiana.....	8	6	6	7	1	179	490	219	11	7	1	
Illinois.....	3	32	30	16	26	685	1,870	445	29	14	2	
Michigan <sup>2</sup> .....	3	3	4	2	2	902	3,782	661	28	24	1	
Wisconsin.....	13	1	1	34	28	2,687	2,320	1,401	13	3	0	
<b>WEST NORTH CENTRAL</b>												
Minnesota.....	0	0	2	-----	-----	605	379	293	3	3	0	
Iowa.....	3	2	2	1	1	223	183	246	1	1	0	
Missouri.....	4	2	2	2	2	226	494	251	19	33	2	
North Dakota.....	1	1	1	-----	25	9	87	139	21	3	0	
South Dakota.....	0	0	1	-----	-----	1	19	63	6	1	0	
Nebraska.....	1	0	1	2	22	4	80	173	173	2	0	
Kansas.....	3	0	5	1	-----	4	465	542	542	5	7	
<b>SOUTH ATLANTIC</b>												
Delaware.....	1	0	0	-----	-----	13	117	9	1	2	0	
Maryland <sup>3</sup> .....	6	1	1	11	8	464	263	263	13	13	5	
District of Columbia.....	0	0	1	2	-----	194	123	123	3	2	0	
Virginia.....	3	2	5	93	141	141	849	326	326	12	19	
West Virginia.....	5	2	4	11	1	10	313	159	88	2	9	
North Carolina.....	8	6	5	4	8	6	878	280	356	6	18	
South Carolina.....	1	15	4	184	39	213	388	127	100	0	1	
Georgia.....	3	2	3	10	35	46	59	175	175	6	2	
Florida.....	3	3	1	27	12	11	295	136	166	2	9	
<b>EAST SOUTH CENTRAL</b>												
Kentucky.....	3	5	5	1	20	8	113	167	120	7	21	
Tennessee.....	2	1	2	29	63	42	92	376	181	14	9	
Alabama.....	4	2	4	24	47	47	238	205	149	9	8	
Mississippi <sup>4</sup> .....	8	1	5	-----	-----	-----	-----	-----	10	8	2	
<b>WEST SOUTH CENTRAL</b>												
Arkansas.....	2	2	3	35	8	21	161	98	120	4	0	
Louisiana.....	4	2	3	1	-----	3	31	88	67	2	3	
Oklahoma.....	1	6	6	28	44	44	408	91	153	1	0	
Texas.....	0	22	22	472	267	335	2,915	432	991	10	15	
<b>MOUNTAIN</b>												
Montana.....	2	1	2	-----	9	9	118	134	134	4	0	
Idaho.....	0	0	0	-----	-----	-----	80	44	44	1	8	
Wyoming.....	0	0	0	1	7	1	153	178	80	1	0	
Colorado.....	3	7	7	12	25	23	170	583	424	5	3	
New Mexico.....	0	0	0	1	8	6	143	23	27	1	0	
Arizona.....	7	1	1	25	24	55	118	10	73	0	1	
Utah <sup>5</sup> .....	0	0	0	-----	34	6	68	252	252	0	1	
Nevada.....	0	0	0	-----	-----	-----	-----	13	4	0	1	
<b>PACIFIC</b>												
Washington.....	1	5	1	-----	1	-----	236	620	620	4	4	
Oregon.....	0	0	0	8	65	12	158	237	237	0	5	
California.....	19	8	8	66	65	53	4,947	1,218	1,218	43	17	
Total.....	161	187	216	1,150	1,072	1,386	25,812	27,776	22,632	420	485	
19 weeks.....	4,345	4,926	5,255	330,757	71,140	143,546	480,447	398,642	351,766	9,885	9,305	

See footnotes at end of table.



Telegraphic morbidity reports from State health officers for the week ended May 13, 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Polio-myelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever <sup>4</sup>		
	Week ended		Median 1939-43	Week ended		Median 1939-43	Week ended		Median 1939-43	Week ended		Median 1939-43
	May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943		May 13, 1944	May 15, 1943	
<b>NEW ENGLAND</b>												
Maine.....	0	0	0	52	9	9	0	0	0	2	0	0
New Hampshire.....	0	0	0	6	2	5	0	0	0	0	0	0
Vermont.....	1	0	0	8	9	9	0	0	0	0	0	0
Massachusetts.....	0	1	0	345	483	191	0	0	0	1	1	1
Rhode Island.....	1	0	0	7	35	14	0	0	0	0	0	0
Connecticut.....	0	0	0	83	99	67	0	0	0	0	0	2
<b>MIDDLE ATLANTIC</b>												
New York.....	0	0	1	504	619	573	0	0	0	3	9	6
New Jersey.....	0	0	0	276	154	261	0	0	0	1	0	1
Pennsylvania.....	0	0	0	684	343	402	0	0	0	3	3	5
<b>EAST NORTH CENTRAL</b>												
Ohio.....	1	2	0	576	125	297	0	15	0	2	1	3
Indiana.....	0	0	0	169	66	82	0	0	1	4	2	2
Illinois.....	0	1	1	389	202	340	2	0	2	2	0	2
Michigan <sup>2</sup> .....	0	0	0	300	134	263	0	1	2	6	1	1
Wisconsin.....	0	1	1	318	357	131	1	0	1	0	0	2
<b>WEST NORTH CENTRAL</b>												
Minnesota.....	0	0	0	137	49	49	0	0	1	0	2	1
Iowa.....	0	0	0	166	56	56	0	6	9	0	0	1
Missouri.....	0	0	0	161	171	65	0	0	3	2	2	1
North Dakota.....	0	0	0	58	4	5	0	0	0	0	1	1
South Dakota.....	0	0	0	16	7	12	0	0	0	0	0	0
Nebraska.....	0	0	0	34	25	24	0	0	0	0	0	0
Kansas.....	1	0	0	63	78	54	0	0	0	0	2	2
<b>SOUTH ATLANTIC</b>												
Delaware.....	0	0	0	7	5	5	0	0	0	0	0	0
Maryland <sup>1</sup> .....	0	0	0	215	154	51	0	0	0	0	0	1
District of Columbia.....	0	0	0	119	18	12	0	0	0	0	0	0
Virginia.....	1	0	0	80	38	30	0	0	0	1	2	2
West Virginia.....	0	0	0	102	26	26	1	1	0	4	0	1
North Carolina.....	2	0	0	31	16	16	0	1	0	1	1	2
South Carolina.....	4	0	1	5	8	3	0	0	0	0	1	2
Georgia.....	1	0	0	27	15	11	0	0	0	2	5	5
Florida.....	2	0	2	4	3	4	0	0	0	1	1	4
<b>EAST SOUTH CENTRAL</b>												
Kentucky.....	1	1	0	91	32	48	0	0	0	0	1	4
Tennessee.....	0	0	0	63	28	55	0	0	0	3	4	4
Alabama.....	1	0	0	7	7	8	0	0	0	1	1	1
Mississippi <sup>2</sup> .....	2	4	1	5	9	1	0	0	0	3	0	3
<b>WEST SOUTH CENTRAL</b>												
Arkansas.....	0	2	0	7	12	7	0	0	0	0	1	2
Louisiana.....	4	0	0	3	1	5	0	0	0	8	5	5
Oklahoma.....	0	0	0	15	16	16	0	0	1	1	0	2
Texas.....	2	2	1	155	58	37	1	1	1	12	2	7
<b>MOUNTAIN</b>												
Montana.....	0	0	0	36	8	18	0	0	0	0	0	0
Idaho.....	0	0	0	59	90	7	0	0	0	1	1	1
Wyoming.....	0	0	0	16	55	14	0	0	0	0	0	0
Colorado.....	0	0	0	60	62	34	0	0	0	1	0	1
New Mexico.....	0	0	0	14	10	6	0	0	0	1	0	0
Arizona.....	1	3	0	18	9	7	0	0	0	1	1	1
Utah <sup>1</sup> .....	0	0	0	71	45	20	0	0	0	0	0	0
Nevada.....	0	0	0	2	2	0	0	0	0	0	0	0
<b>PACIFIC</b>												
Washington.....	2	0	0	178	31	31	3	0	0	0	0	2
Oregon.....	0	0	0	115	12	13	0	0	0	0	1	1
California.....	10	11	3	305	166	143	3	0	0	19	3	4
Total.....	37	28	22	6,162	3,963	3,823	11	25	33	86	54	100
19 weeks.....	426	483	436	118,430	75,724	75,724	224	501	856	1,376	1,083	1,507

See footnotes at end of table.

Telegraphic morbidity reports from State health officers for the year ended May 13, 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Whooping cough			Week ended May 13, 1944								
	Week ended		Median 1939-43	Anthrax	Dysentery			Encephalitis, infectious	Leprosy	Rocky Mt. spotted fever	Tularaemia	Typhus fever
	May 13, 1944	May 15, 1943			Ambic	Bacillary	Unspecified					
<b>NEW ENGLAND</b>												
Maine.....	14	52	30	0	0	0	0	0	0	0	0	0
New Hampshire.....	1	13	13	0	0	0	0	0	0	0	0	0
Vermont.....	3	1	31	0	0	0	0	0	0	0	0	0
Massachusetts.....	88	151	204	0	0	31	0	0	0	0	0	0
Rhode Island.....	6	16	16	0	0	0	0	0	0	0	0	0
Connecticut.....	46	48	51	0	0	0	0	0	0	0	0	0
<b>MIDDLE ATLANTIC</b>												
New York.....	116	260	346	0	0	8	0	0	0	0	0	0
New Jersey.....	48	135	135	0	0	0	0	0	0	2	0	0
Pennsylvania.....	83	280	307	0	0	1	0	0	0	0	0	0
<b>EAST NORTH CENTRAL</b>												
Ohio.....	52	82	218	0	1	0	0	0	0	0	0	0
Indiana.....	12	83	55	0	0	0	0	0	0	0	0	0
Illinois.....	13	128	128	0	0	31	0	0	0	0	0	0
Michigan <sup>1</sup> .....	62	291	199	0	1	1	0	0	0	0	0	0
Wisconsin.....	38	248	138	0	1	0	0	0	0	0	0	0
<b>WEST NORTH CENTRAL</b>												
Minnesota.....	11	91	48	0	4	1	0	0	0	0	0	0
Iowa.....	3	59	26	0	0	0	0	0	0	0	0	0
Missouri.....	19	50	44	0	0	0	1	0	0	0	0	0
North Dakota.....	1	12	11	0	0	0	0	0	0	0	0	0
South Dakota.....	5		0	0	0	0	0	0	0	0	0	0
Nebraska.....		16	7	0	0	0	0	0	0	0	0	0
Kansas.....	28	68	42	0	0	0	0	0	0	0	0	0
<b>SOUTH ATLANTIC</b>												
Delaware.....		2	1	0	0	0	0	0	0	0	0	0
Maryland <sup>2</sup> .....	50	107	102	0	0	0	2	1	1	0	0	1
District of Columbia.....	3	38	20	0	0	0	0	0	0	0	0	0
Virginia.....	65	145	55	0	0	0	17	0	0	0	2	1
West Virginia.....	16	61	46	0	0	0	0	0	0	0	0	0
North Carolina.....	97	175	175	0	0	0	0	0	0	1	1	7
South Carolina.....	83	62	62	0	0	0	0	0	0	0	0	0
Georgia.....	16	60	56	0	0	3	3	0	0	0	3	10
Florida.....	51	34	12	0	1	0	2	0	0	0	0	4
<b>EAST SOUTH CENTRAL</b>												
Kentucky.....	66	13	59	0	0	7	0	0	0	0	0	0
Tennessee.....	20	78	62	0	0	0	0	0	0	0	0	0
Alabama.....	48	100	51	0	0	0	0	0	0	0	0	11
Mississippi <sup>3</sup> .....											6	2
<b>WEST SOUTH CENTRAL</b>												
Arkansas.....	8	44	21	0	0	6	0	0	0	0	0	0
Louisiana.....	2	2	10	0	0	0	0	0	0	0	1	0
Oklahoma.....	16	33	14	0	0	0	0	0	0	0	0	0
Texas.....	220	494	300	0	5	374	0	1	0	0	2	34
<b>MOUNTAIN</b>												
Montana.....	1	25	14	0	0	0	0	0	0	1	0	0
Idaho.....	7	2	10	0	0	0	0	0	0	0	1	0
Wyoming.....	15	5	5	0	0	0	0	0	0	3	0	0
Colorado.....	45	21	27	0	0	0	0	0	0	0	1	0
New Mexico.....	8	18	23	0	0	0	0	0	0	0	0	0
Arizona.....	10	9	28	0	0	0	59	0	0	0	0	0
Utah <sup>4</sup> .....	43		50	0	0	0	0	0	0	0	1	0
Nevada.....	1	3	3	0	0	0	0	0	0	0	0	0
<b>PACIFIC</b>												
Washington.....	22	35	49	0	0	0	0	0	0	0	0	0
Oregon.....	13	52	29	0	0	0	0	0	0	0	0	0
California.....	115	431	431	0	0	4	0	2	0	0	0	0
<b>Total</b> .....	<b>1,690</b>	<b>4,183</b>	<b>3,820</b>	<b>0</b>	<b>13</b>	<b>467</b>	<b>84</b>	<b>2</b>	<b>1</b>	<b>7</b>	<b>18</b>	<b>70</b>
19 weeks.....	34,214	76,786	76,445	17	496	4,426	1,304	209	12	22	199	792
19 weeks, 1943.....				26	560	3,761	873	211	9	56	316	867

Alaska: Chickenpox 26, measles 1, German measles 8, whooping cough 3.

<sup>1</sup> New York City only. <sup>2</sup> Psittacosis: Pennsylvania, 1 case. <sup>3</sup> Period ended earlier than Saturday.

<sup>4</sup> Including paratyphoid fever cases reported separately as follows: Massachusetts 1, New York 1, Georgia 1, Florida 1, Louisiana 1 (week ended May 6: Massachusetts 2, Connecticut 1, Virginia 1, South Carolina 2, Florida 2, Tennessee 1, California).

## WEEKLY REPORTS FROM CITIES

City reports for week ended April 29, 1944

This table lists the reports from 86 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	Polymyellitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
<b>NEW ENGLAND</b>												
New Hampshire:												
Concord.....	0	0		0	3	0	1	0	2	0	0	0
Vermont:												
Barre.....	0	0		0	2	0	0	0	0	0	0	0
Massachusetts:												
Boston.....	0	0		1	203	4	23	0	62	0	0	12
Fall River.....	1	0		0	49	0	1	0	3	0	0	0
Springfield.....	0	0		0	39	0	0	0	37	0	0	5
Worcester.....	0	0		0	7	0	7	0	50	0	0	7
Rhode Island:												
Providence.....	1	0		0	80	1	2	0	7	0	0	8
Connecticut:												
Bridgeport.....	0	0		0	34	0	0	0	5	0	0	0
Hartford.....	0	0		1	9	0	2	0	28	0	0	0
New Haven.....	0	0	1	0	98	1	3	0	4	0	0	4
<b>MIDDLE ATLANTIC</b>												
New York:												
Buffalo.....	0	0		0	3	1	7	0	18	0	0	0
New York.....	9	1	3	1	1,005	36	78	0	322	0	2	24
Rochester.....	0	0		1	9	3	6	0	5	0	0	1
Syracuse.....	0	0		1	12	1	1	0	9	0	1	3
New Jersey:												
Camden.....	0	0		1	0	1	4	0	38	0	0	0
Newark.....	0	0	1	0	265	3	4	0	30	0	0	4
Trenton.....	0	0		0	7	0	3	0	13	0	0	0
Pennsylvania:												
Philadelphia.....	0	0	2	2	67	10	22	0	112	0	0	13
Pittsburgh.....	0	0		0	19	4	15	0	21	0	0	6
Reading.....	0	0		1	5	0	1	0	3	0	0	0
<b>EAST NORTH CENTRAL</b>												
Ohio:												
Cincinnati.....	1	0		1	35	10	6	0	65	0	0	2
Cleveland.....	2	0	6	1	65	9	9	0	121	0	0	11
Columbus.....	0	0		0	72	0	4	0	7	0	0	12
Indiana:												
Fort Wayne.....	0	0		0	0	0	3	0	5	0	1	0
Indianapolis.....	1	0		0	85	1	3	0	52	0	0	9
South Bend.....	0	0		0	1	0	0	0	6	0	0	0
Terre Haute.....	0	0		1	1	0	2	0	3	0	0	1
Illinois:												
Chicago.....	2	0	3	2	137	20	29	1	163	0	0	5
Springfield.....	0	0		0	39	0	5	0	9	0	0	1
Michigan:												
Detroit.....	4	0	2	1	128	8	21	0	146	0	2	21
Flint.....	0	0		0	3	0	3	0	3	0	0	0
Grand Rapids.....	0	0		0	21	1	1	0	5	0	0	0
Wisconsin:												
Kenosha.....	0	0		0	219	0	0	0	0	0	0	1
Milwaukee.....	0	1		0	156	4	6	0	61	0	0	17
Racine.....	0	0		0	41	0	1	0	7	0	0	3
Superior.....	0	0		0	5	0	0	0	22	0	0	0
<b>WEST NORTH CENTRAL</b>												
Minnesota:												
Duluth.....	0	0		0	119	1	2	0	11	0	0	0
Minneapolis.....	0	0		0	205	0	5	0	32	0	0	5
St. Paul.....	1	0		0	244	0	4	0	34	0	0	7
Missouri:												
Kansas City.....	0	0		0	96	2	3	0	38	0	0	4
St. Joseph.....	0	0		0	2	0	0	0	6	0	0	0
St. Louis.....	0	0	1	0	89	17	10	0	56	0	1	0
Nebraska:												
Omaha.....	0	0		0	96	0	3	0	25	0	0	4
Kansas:												
Topeka.....	0	0		0	70	0	2	0	1	0	1	3
Wichita.....	0	0	1	0	36	1	5	0	7	0	0	1

City reports for week ended April 22, 1944—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcal, cases	Pneumonia deaths	Pollomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
<b>SOUTH ATLANTIC</b>												
Delaware:												
Wilmington.....	0	0		0	0	3	1	0	1	0	0	0
Maryland:												
Baltimore.....	19	0	3	3	404	5	15	0	115	0	2	17
Cumberland.....	0	0		0	0	0	0	0	0	0	0	0
Frederick.....	0	0		0	0	0	0	0	4	0	0	0
District of Columbia:												
Washington.....	0	0	2	0	229	4	6	0	191	0	0	5
Virginia:												
Lynchburg.....	0	0		0	2	0	1	0	6	0	0	0
Richmond.....	0	0	2	1	61	0	2	5	0	0	0	1
Roanoke.....	0	0		0	14	0	1	0	0	0	0	9
West Virginia:												
Wheeling.....	0	0		0	21	1	1	0	10	0	0	0
North Carolina:												
Wilmington.....	0	0		1	38	0	1	0	0	0	0	5
Winston-Salem.....	0	0		0	32	0	0	0	5	0	1	0
South Carolina:												
Charleston.....	0	0		0	29	0	2	0	0	0	0	0
Georgia:												
Atlanta.....	0	0		0	5	3	1	0	16	0	0	0
Brunswick.....	0	0		0	1	0	0	0	0	0	0	0
Savannah.....	0	0		0	0	0	1	0	0	0	0	0
Florida:												
Tampa.....	2	0	6	0	3	1	2	0	2	0	0	1
<b>EAST SOUTH CENTRAL</b>												
Tennessee:												
Memphis.....	0	0	1	1	31	7	1	0	58	0	0	8
Nashville.....	0	0		0	13	0	1	0	8	0	0	0
Alabama:												
Birmingham.....	0	0	3	1	21	0	1	0	6	0	0	1
Mobile.....	0	0		1	1	1	1	0	0	0	0	0
<b>WEST SOUTH CENTRAL</b>												
Arkansas:												
Little Rock.....	0	0		0	21	1	2	0	0	0	0	1
Louisiana:												
New Orleans.....	1	0	3	1	33	3	5	2	6	0	0	0
Shreveport.....	0	0		0	0	1	3	0	0	0	1	0
Texas:												
Dallas.....	3	0		0	213	3	2	0	7	0	0	2
Galveston.....	0	0		0	3	0	1	0	0	0	0	0
Houston.....	1	0		1	14	1	5	0	2	0	0	0
San Antonio.....	1	0		0	21	2	4	0	2	0	0	0
<b>MOUNTAIN</b>												
Montana:												
Billings.....	0	0		0	11	0	0	0	1	0	0	0
Great Falls.....	0	0		0	5	1	1	0	3	0	0	0
Helena.....	0	0		0	5	0	0	0	0	0	0	0
Missoula.....	0	0		0	19	0	1	0	2	0	0	0
Idaho:												
Boise.....	0	0		0	2	0	0	0	1	0	0	0
Colorado:												
Denver.....	2	0	1	1	99	0	3	0	21	0	1	2
Pueblo.....	0	0		0	13	0	1	0	1	0	0	1
Utah:												
Salt Lake City.....	0	0		0	17	0	0	0	29	0	0	3
<b>PACIFIC</b>												
Washington:												
Seattle.....	0	0		1	45	1	6	0	54	0	0	1
Spokane.....	0	0		0	10	1	2	0	16	0	0	1
Tacoma.....	0	0		0	17	0	1	0	35	0	0	0

## City reports for week ended April 22, 1944—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								
California:												
Los Angeles.....	4	0	5	1	463	6	10	0	27	0	0	10
Sacramento.....	1	0	---	0	26	0	2	0	4	0	0	2
San Francisco.....	0	0	2	1	130	3	6	1	48	0	0	11
Total.....	56	2	48	29	5,955	187	400	9	2,337	0	13	275
Corresponding week, 1943.....	68	---	84	0	4,438	---	470	---	1,514	1	0	1,149
Average, 1943.....	67	---	108	125	76,122	---	1,376	---	1,526	4	16	1,190

<sup>1</sup> 3-year average.

<sup>2</sup> 5-year median.

*Dysentery, amebic.*—Cleveland 1, St. Louis 1, Birmingham 1.  
*Dysentery, bacillary.*—New York 2, Detroit 1, Charleston, S. C., 10, Atlanta 1, Los Angeles 3.  
*Dysentery, unspecified.*—Baltimore 1, San Antonio 7.  
*Typhus fever, endemic.*—Richmond 1, Wilmington, N. C., 3, Charleston, S. C., 1, Savannah 3, Tampa 1, Mobile 3, New Orleans 1, Houston 1, San Antonio 2.

## Rates (annual basis) per 100,000 population, by geographic groups, for the 86 cities in the preceding table (estimated population, 1942, 34,546,900)

	Diphtheria case rates	Encephalitis, 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.....	5.2	0.0	2.6	5.2	1,355	15.5	100.8	0.0	512	0.0	0.0	93
Middle Atlantic.....	4.0	0.4	2.7	3.1	623	26.4	63.1	0.0	256	0.0	1.3	23
East North Central.....	5.9	0.6	6.4	3.5	590	31.0	54.5	0.6	395	0.0	1.8	49
West North Central.....	2.0	0.0	4.0	0.0	1,898	41.6	67.4	0.0	416	0.0	4.0	48
South Atlantic.....	36.9	0.0	22.8	8.8	1,476	29.8	59.7	8.8	614	0.0	5.3	67
East South Central.....	0.0	0.0	23.8	17.9	393	47.6	23.8	0.0	429	0.0	0.0	54
West South Central.....	17.6	0.0	8.8	5.9	897	32.4	64.7	5.9	50	0.0	2.9	9
Mountain.....	16.1	0.0	8.1	8.0	1,378	8.0	48.4	0.0	468	0.0	8.1	48
Pacific.....	8.8	0.0	12.3	5.2	1,211	19.3	47.3	3.3	322	0.0	0.0	44
Total.....	8.5	0.3	7.3	4.4	901	28.3	60.5	1.4	353	0.0	2.0	42

TERRITORIES AND POSSESSIONS

Hawaii Territory

*Plague (rodent).*—Rodents found in Paauhau area, Hamakua District, Island of Hawaii, T. H., have been proved positive for plague as follows: April 10, 1 mouse; April 13, 1 rat; April 14, 1 rat.

Panama Canal Zone

*Notifiable diseases—March 1944.*—During the month of March 1944, certain notifiable diseases were reported in the Panama Canal Zone and terminal cities as follows:

Disease	Panama		Colon		Canal Zone		Outside the Zone and terminal cities		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Chickenpox.....	8		7		6		2		23	
Diphtheria.....	7						1		8	
Dysentery (amebic).....							2	1	2	
Dysentery (bacillary).....			1		2				3	
German measles.....	3				13				16	
Leprosy.....							1	1	1	1
Malaria <sup>1</sup> .....	10		4		66		46	5	126	5
Meningitis, meningococcus.....	1	1							1	1
Mumps.....	8		3		19		6		36	
Paratyphoid fever.....	2						2		4	
Pneumonia.....		11		5	31	1		4	31	21
Tuberculosis.....		22		6	5	1		4	25	33
Typhoid fever.....							2	1	2	1
Typhus fever.....							1		1	
Whooping cough.....					2				2	

<sup>1</sup> 47 recurrent cases.

<sup>2</sup> Reported in the Canal Zone only.

Virgin Islands of the United States

*Notifiable diseases—January–March 1944.*—During the months of January, February, and March 1944, cases of certain notifiable diseases were reported in the Virgin Islands as follows:

Disease	January	February	March	Disease	January	February	March
Chickenpox.....		1	4	Mumps.....			1
Filariasis.....	9	6	11	Pellagra.....			1
Gonorrhoea.....	16	8	12	Schistosomiasis.....		1	
Hookworm disease.....	4	6	2	Syphilis.....	15	20	12
Lymphogranuloma inguinale.....		1		Tuberculosis.....	5	1	2
Malaria.....	2	1		Typhoid fever.....		1	
				Typhus fever.....	1		

## FOREIGN REPORTS

### CANADA

*Provinces—Communicable diseases—Week ended April 15, 1944.*—During the week ended April 15, 1944, 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		40	7	148	201	40	16	58	80	590
Diphtheria	2	5	2	40	3	1	1		1	55
Dysentery				5						5
German measles		21		93	66	10	44	24	24	282
Influenza	1	14	1		32	4	1		21	74
Measles		60	11	1,020	588	264	55	157	28	2,183
Meningitis, meningococcus				3	3				4	10
Mumps	1	9	1	181	154	67	14	47	42	516
Poliomyelitis								2		2
Scarlet fever		13	8	63	230	88	7	99	90	598
Tuberculosis (all forms)		6	1	325	40	11	11	12	20	426
Typhoid and paratyphoid fever				28	2			30	1	61
Undulant fever				1	2				2	5
Whooping cough		25		52	40	4	11	17	7	156

### CUBA

*Provinces—Notifiable diseases—4 weeks ended April 22, 1944.*—During the 4 weeks ended April 22, 1944, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana <sup>1</sup>	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	2	1	6	4		10	23
Chickenpox		11				3	14
Diphtheria	1	21	3	2		2	29
Leprosy						1	1
Malaria	13	4	9	9	5	249	289
Measles	4	28	15			2	49
Poliomyelitis			1				3
Scarlet fever		2			1		4
Tetanus, infantile			1			1	1
Tuberculosis	18	14	28	44	15	47	166
Typhoid fever	12	59	3	20	18	35	147
Yaws						1	1

<sup>1</sup> Includes the city of Habana.

## FINLAND

*Notifiable diseases—February 1944.*—During the month of February 1944, cases of certain notifiable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis.....	20	Paratyphoid fever.....	96
Chickenpox.....	521	Pneumonia.....	2,334
Conjunctivitis.....	23	Poliomyelitis.....	8
Diphtheria.....	1,453	Puerperal fever.....	34
Dysentery.....	6	Rheumatic fever.....	244
Gastroenteritis.....	1,428	Scabies.....	2,335
Gonorrhoea.....	505	Scarlet fever.....	953
Hepatitis, epidemic.....	520	Syphilis.....	390
Influenza.....	3,854	Typhoid fever.....	34
Laryngitis.....	58	Vincent's angina.....	6
Measles.....	6,522	Whooping cough.....	764
Mumps.....	340		

### 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

*Egypt.*—Plague has been reported in Egypt as follows: Port Said, week ended April 29, 1944, 2 cases, 1 death; Suez, week ended April 15, 1944, 7 cases, 5 deaths.

*India—Calcutta.*—For the week ended April 15, 1944, 2 cases of plague with 1 death were reported in Calcutta, India.

#### Smallpox

*India.*—Smallpox has been reported in India as follows: Bombay, week ended April 8, 1944, 227 cases, 53 deaths; Calcutta, week ended April 22, 1944, 340 deaths.

#### Typhus Fever

*Guatemala.*—For the month of March 1944, 280 cases of typhus fever with 43 deaths were reported in Guatemala. The Departments reporting the highest incidence of this disease are as follows: El Quiche, 36 cases; Guatemala, 90 cases, 16 deaths; Huehuetenango, 26 cases, 7 deaths; Quezaltenango, 42 cases, 7 deaths; San Marcos, 26 cases, 7 deaths.

*Hungary.*—For the week ended April 8, 1944, 80 cases of typhus fever were reported in Hungary.

*Iraq.*—Typhus fever has been reported in Iraq as follows: weeks ended March 18, 1944, 26 cases, 2 deaths; March 25, 1944, 49 cases, 3 deaths.