TRANSLOCATION OF FLUID PRODUCED BY THE INTRAVENOUS ADMINISTRATION OF ISOTONIC SALT SOLUTIONS IN MAN POSTOPERATIVELY*

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During the past decade several papers from this clinic[1, 2, 3] have pointed out certain possible, undesirable complications attendant upon the unwise use of intravenous isotonic sodium chloride solution. It has been emphasized[3] that these dangers are increased many fold during the immediate postoperative period of the sick surgical patient. This concept is neither new nor original, since many authors[4] have directed attention to the potential toxicity of so-called "physiologic saline," especially when large amounts are administered.

Studies to determine the manner in which the human body handles large intravenous infusions of "salt" solutions were undertaken in patients undergoing combined abdominoperineal resections for carcinoma of the rectum. An explanation of the "salt intolerance" was sought in the excretions and retentions of sodium, chloride and water in the 30-hour period beginning with the operation. Solutions of various composition and tonicity were infused at regular intervals during this period.

The study was divided into five six-hour periods. The initial infusion was started at the beginning of the operation and the rate of administration was determined by the exigencies of the operation. The second infusion was started six hours after the first infusion. This, and subsequent infusions, were administered at approximate rates of 250 Ml. per hour for the smaller amounts and 400 Ml. per hour for the larger volumes.

Weighed dressings covered with oiled silk were applied to the anterior and posterior wounds. These dressings were changed and reweighed every 12 hours (three determinations of losses from wound drainage). In the balance studies, such losses were considered as an ultrafiltrate of plasma, since loss of blood was visibly small.

Urine was collected during the five periods and preserved with thymol and refrigeration. Two samples of blood, one with heparin and one under oil, were withdrawn before operation, at the end of operation, and at the end of the final infusion period. The urines were analyzed for specific gravity, p_H by glass electrode, potassium by the method of Fiske and Litarczek,[5] sodium by the method of Butler and Tuthill,[6] ammonia by the method of Folin and Bell,[7] chloride by the method of Logan,[8] sulfate by the method of Fiske,[10] phosphate by the method of Fiske and Subbarow,[10] total nitrogen by

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the micro-kjeldahl method of Pregl,[11] urea,[12] and carbon dioxide[13] by the methods of Van Slyke, and creatinin by the method of Popper.[14] Heparinized whole blood was analyzed for hematocrit by use of capillary tubes, for specific gravity by the method of Barbour and Hamilton,[15] and for hemoglobin by the photo-electric method of Evelyn.[16] Serum proteins were calculated from the specific gravity of the sera according to the formula of Weech.[17] Serum was analyzed for sodium, carbon dioxide content and chloride.

Blood loss during operation was estimated, and in almost all cases found to correspond to the average figures previously reported by this clinic.[18]

Procedure and Method of Calculation: The patients who served as subjects were selected only in that they were determined to be free of gross cardiovascular and kidney disease. They were prepared for operation by sulfasuccidine and Miles' regimen. If the hemoglobin was below 80 per cent, they were transfused before operation. The preanesthetic medication consisted of morphine in combination with barbiturates. Operations were performed under spinal anesthesia with either nupercaine or continuous procaine. Preoperatively, an indwelling catheter was introduced, which remained in place throughout the study.

All intake was by the intravenous route. The first five cases received 3,750 Ml. of 0.9 per cent NaCl in five equal infusions during the first 30 hours after operation. Three patients received 3,750 Ml. of 0.75 per cent NaCl plus 0.22 per cent $NaHCO_3$, an adjusted salt solution containing a physiologic amount of $NaHCO_3$ (26 mEq. per liter). One patient received 5,625 Ml. of 0.6 per cent NaCl, a solution physiologic with respect to chloride. Three patients received 7,500 Ml. of 0.45 per cent NaCl, and one patient, 7,500 Ml. of 0.375 per cent NaCl plus 0.11 per cent $NaHCO_3$.

In-put of sodium was kept constant at 578 mEq. except in the case of one patient, a small individual who received 80 per cent of the established infusion. Since the nutritional status of these patients with neoplastic disease could only be judged by body weight, and the preformed water contained in the water evaporated from lungs and skin and given off in the urine could only be guessed at, this preformed water has been ignored in the calculations of load of water. However, in Benedict's fasting subject, Levanzin, preformed water amounted to 585 Gm. during the first 24 hours of the fast.[19]

Water gained as a result of the breakdown of body protein was calculated from the urinary nitrogen by use of the factor 6.25 and the equation: water = 0.27 liters per 100 Gm. protein.[20] Insensible loss was estimated for all patients as 0.07 per cent of body weight per hour, as suggested by Adolph.[21] This value is based upon studies of normal individuals and in all probability is too conservative an estimate of losses by patients immediately postoperatively.

Water balance, thus, becomes in-put plus oxidative gain less the combined losses by way of the urine, wounds, lungs and skin. Sodium and chloride balances are calculated from in-put less urinary and wound losses.

Results: Table I summarizes the changes in the blood and serum of eight patients receiving the five types of infusion. There is evidence that all patients handled the infusions fairly efficiently with the probable exception of Patient St. The best examples of this efficiency are the small changes produced in the concentrations of sodium and chloride in the sera of the patients receiving large infusions of hypotonic solutions. Serum proteins are lowered in every case, regardless of the volume of solution infused.

Table II presents the urinary concentrations of potassium, sodium, chloride, and the ratios of sodium to chloride of all patients during the first 24 hours

TABLE I

CHANGES IN THE BLOOD AND SERUM OF EIGHT PATIENTS RECEIVING THE VARIOUS INFUSIONS

Patient—Infusion		Blood: Hematocrit Vol. %	Blood: Hemoglobin Gm. %	Blood: Specific Gravity	Serum: Protein Gm. %	Serum: Carbon Dioxide* Vol. %	Serum: Chloride mEq./l.	Serum: Sodium mEq./l.
Br ♂ 0.9% NaCl	Preop.	43.0	14.9	1.0556	6.12	60.1	101.3	137.7
	Postop.	40.0	12.4	1.0476	5.27	57.4	103.2	132.5
	30 hrs.	37.3	11.6	1.0438	3.35	48.9	108.7	136.8
St ♀ 0.75% NaCl+	Preop.	40.5	12.6	1.0501	6.19	58.4	104.2	136.9
0.22% $NaHCO_3$	Postop.	17.5	6.0	1.0283	3.20	55.2	115.4	143.8
	33 hrs.	16.2	6.8	1.0363	5.21	58.9	105.0	136.9
	Transfus.	25.3	8.2	1.0397	5.24	63.3	106.7	136.9
Vo ♂ 0.75% NaCl+	Preop.	43.9	14.2	1.0524	5.44	68.9	102.7	139.7
0.22% $NaHCO_3$	Postop.	51.5	15.4	1.0551	5.62	71.8	103.0	140.6
	30 hrs.	40.0	12.4	1.0494	5.03	64.0	104.3	140.6
Mo ♂ 0.6% NaCl	Preop.	43.4	14.6	1.0546	6.50	64.2	100.8	132.3
	Postop.	44.4	13.7	1.0521	5.85	58.8	102.7	130.6
	30 hrs.	36.9	12.1	1.0473	4.96	55.1	102.5	130.4
Hu ♂ 0.38% NaCl+	Preop.	50.7	15.7	1.0559	6.19	62.6	97.8	132.8
0.11% $NaHCO_3$	Postop.	44.8	13.5	1.0486	4.90	58.7	99.9	132.6
	30 hrs.	42.0	12.7	1.0486	4.76	56.5	99.9	126.7
Le ♂ 0.45% NaCl	Preop.	48.9	15.4	1.0585	6.25	63:8	102.3	138.3
	Postop.	47.0	14.2	1.0571	6.12	53.2	102.0	137.2
	30 hrs.	33.3	10.5	1.0435	4.86	53.5	95.8	120.8
Sm ♀† 0.45% NaCl	Preop.	47.3	15.2	1.0582	7.01	56.5	100.7	132.6
	Postop.	42.8	13.0	1.0512	5.58	59.3	101.7	134.3
	30 hrs.	45.9	12.5	1.0501	5.11	53.8	94.8	127.1
Re ♂ 0.45% NaCl	Preop.	50.5	16.4	1.0607	6.63	57.7	103.3	135.4
	Postop.	49.2	15.2	1.0507	6.50	66.7	101.0	138.2
	30 hrs.	28.3	9.5	1.0422	4.63	53.2	99.4	131.2

* Content.
† Patient Sm received 80% of the infusion.

postoperatively. It is noteworthy that the two patients receiving the adjusted salt solution and the hypotonic, adjusted salt solution were the only subjects who excreted sodium and chloride in ratios approximating that of an ultrafiltrate of plasma.

Table III summarizes the loads of sodium, chloride and water at the end of 30 hours' infusion for eight patients receiving the various infusions.

The complete data, except for blood changes, are presented in Figures 1 through 6. Loads of water, sodium and chloride, and urinary losses of sodium, chloride, potassium, phosphate, sulfate and nitrogen are charted as cumulative balances and losses throughout the 30-hour period. The nitrogen scale has been adjusted to correspond to the nitrogen to potassium ratio existing in tissue. As a result, Figures 1 to 6 stress the presence of "excess

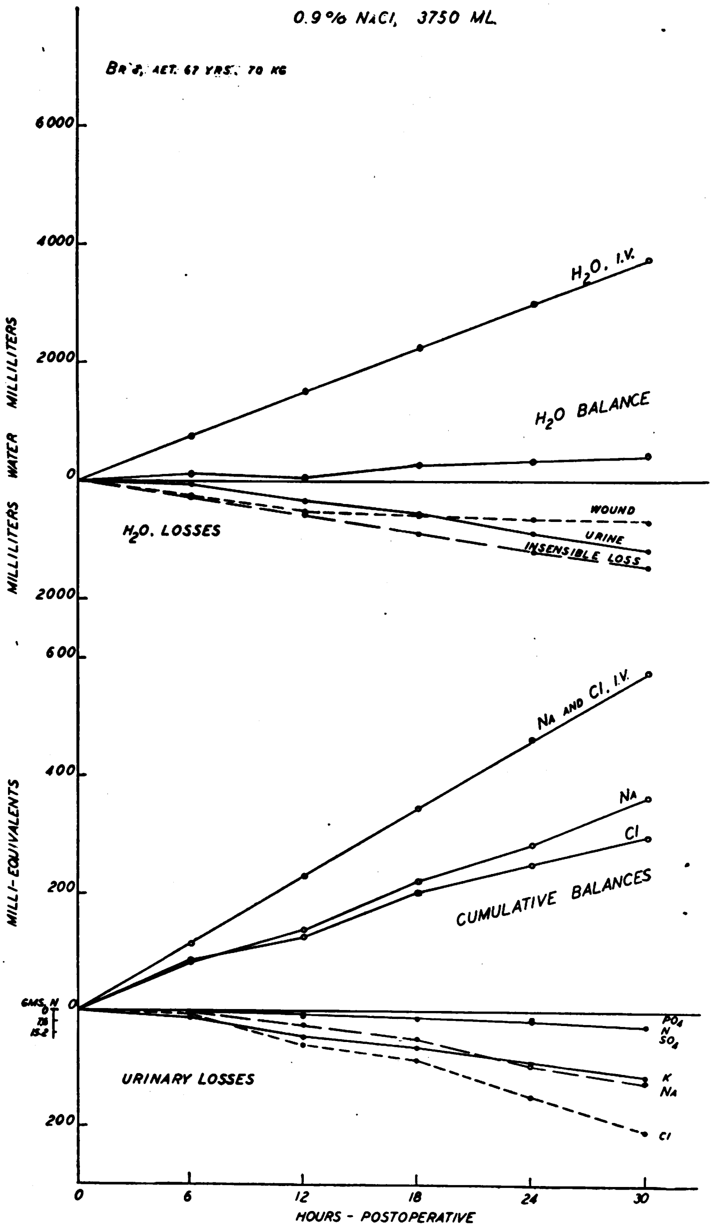

FIG. 1.—Cumulative balances of water, sodium and chloride, and losses of water and urinary constituents of patient Br., m., No. 565,142, who received 3750 Ml of 0.9% NaCl in five equal infusions during 30 hours following combined abdominoperineal resection for carcinoma of the rectum. The patient was not prepared for operation by Mile's regimen because of a cecostomy performed 19 days before. Operation was performed under continuous procaine spinal. Postoperative course was uneventful, except for a mild, transitory hypotension lasting for six hours after operation.

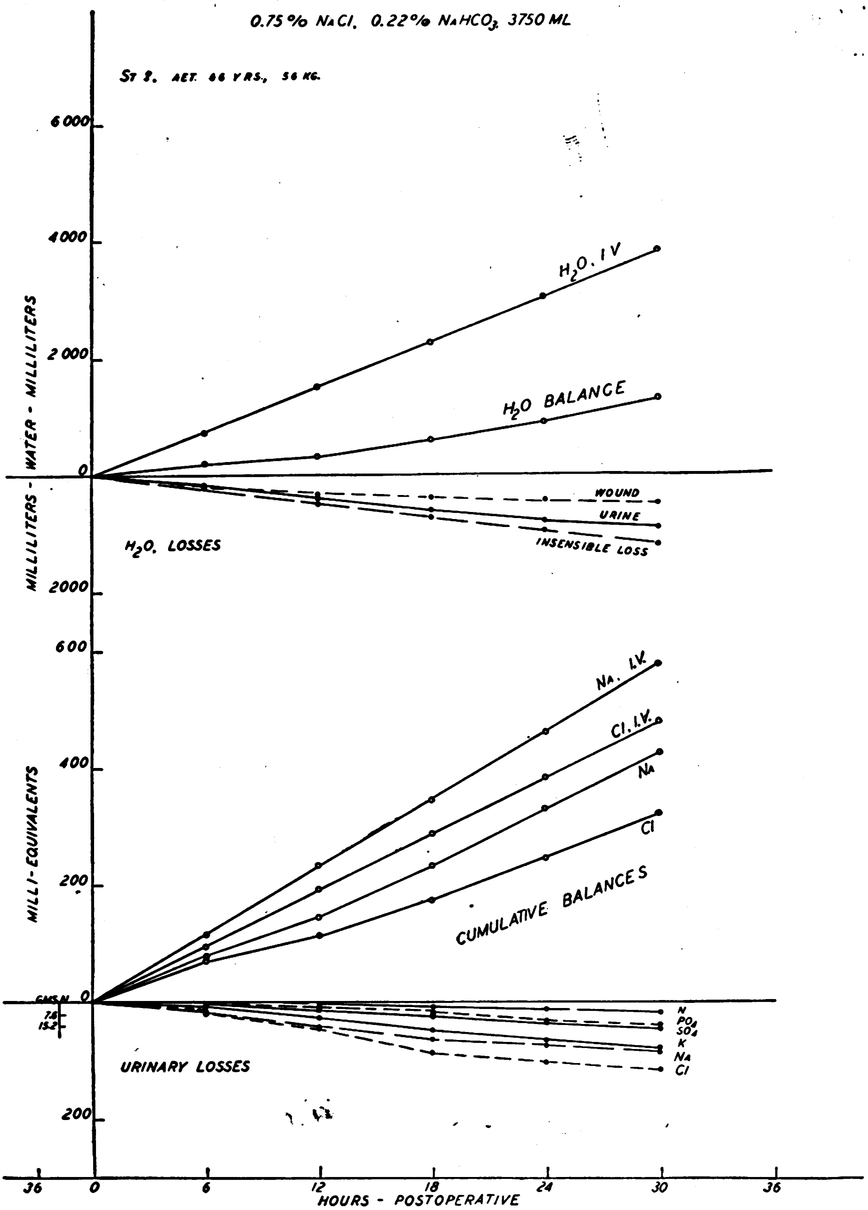

FIG. 2.—Cumulative balances of water, sodium and chloride, and losses of water and urinary constituents of patient St., f., No. 563,726, who received 3750 Ml. of 0.75% NaCl plus 0.22% $NaHCO_3$ during 30 hours following combined abdominoperineal resection. Operation was performed under continuous procaine spinal anesthesia. There was marked hypotension during the operation, and the postoperative course was characterized by tachycardia and hypotension. The patient received a transfusion of 500 Ml. of blood at the end of the infusion period.

potassium" excreted by all the patients studied. Judging from the losses of Levanzin, about 40 mEq. of the potassium are due to starvation. The remainder may be attributed in part to tissue trauma, in part to the infusion of 34 Gm. of salt. As shown by Gamble,[22] the addition of extracellular electrolytes causes a large transfer of intracellular water to the extracellular compartment. The removal of intracellular electrolyte follows in order to

TABLE II

URINARY EXCRETION OF POTASSIUM, SODIUM AND CHLORIDE IN 24 HOURS POSTOPERATIVELY

Patient—Infusion	Urine Volume Ml.	Potassium mEq./l.	Sodium mEq./l.	Chloride mEq./l.	Ratio Na:Cl	Comment
Br ♂ 0.9% NaCl (3000 Ml.)	886	97.9	105.2	165.0	0.64	Miles' regimen not used. Wound loss: 630 Gm.
Ke ♂ 0.9% NaCl (3000 Ml.)	579	92.5	94.6	147.3	0.64	Infusion in one dose postoperatively
Br ♀ 0.9% NaCl	891	117.4	93.8	135.2	0.69	First day
(3000 Ml.)	831	80.1	25.1	53.9	0.47	Infection, 2nd day
Mo ♀ 0.9% NaCl (3000 Ml.)	944	54.8	168.0	216.1	0.78	
Li ♀ 0.9% NaCl (3000 Ml.)	990	46.3	187.6	232.6	0.81	500 Ml. blood postoperatively
Fe ♂ 0.75% NaCl+ 0.22% $NaHCO_3$	1230	116.7	168.0	154.3	1.09	First day
(3000 Ml.)	1380	81.0	154.8	150.5	1.03	Second day
St ♀ 0.75% NaCl+ 0.22% $NaHCO_3$ (3000 Ml.)	735	87.0	98.0	126.0	0.78	Wound loss: 395 Gm.
Vo ♂ 0.75% NaCl+ 0.22% $NaHCO_3$ (3000 Ml.)	1070	129.2	120.7	81.3	1.48	Wound loss: 610 Gm.
Mo ♂ 0.6% NaCl (4500 Ml.)	1186	100.6	91.0	124.8	0.73	Wound loss: 665 Gm.
Hu ♂ 0.38% NaCl+ 0.11% $NaHCO_3$ (6000 Ml.)	895	101.3	138.3	112.1	1.23	Wound loss: 400 Gm.
Le ♂ 0.45% NaCl (6000 Ml.)	1170	129.5	121.2	141.5	0.86	Wound loss: 1375 Gm.
Re ♂ 0.45% NaCl (6000 Ml.)	491	106.5	15.2	52.5	0.29	Wound loss: 1826 Gm.
Sm ♀ 0.45% NaCl (4800 Ml.)	1321	72.1	95.4	102.1	0.93	Wound loss: 991 Gm.

preserve normal ionic concentration during the period of stress created by the load of salt. However, this explanation is scarcely adequate to account for the excess potassium in those cases receiving the large infusions which provided sufficient water. From Table II, it is evident that loss of potassium can be correlated with the volume of urine excreted.

Figure 1, Patient Br, ♂, 3,750 Ml. of 0.9 per cent NaCl, describes a very small balance of water at the end of 30 hours, a large load of sodium and chloride, a moderate loss of fluid from the posterior wound. The urinary excretion of chloride exceeded that of sodium.

Figure 2, Patient St, ♀, 3,750 Ml. of 0.75 per cent NaCl and 0.22 per cent $NaHCO_3$, indicates a greater load of water and a greater load of sodium and chloride, but the actual retention concentrations are less than those of

Figure 1. More chloride than sodium is lost in the urine, but the difference is small.

Figure 3, Patient Mo, ♂, 5,625 Ml. of 0.6 per cent NaCl, describes a positive load of water, a marked diuresis after 24 hours (a fact established by Bayliss and Fee[23] for 0.6 per cent NaCl in dogs), a minimal loss from wounds, large urinary "excess potassium" and a greater excretion of urinary

TABLE III

THIRTY-HOUR LOADS OF SODIUM, CHLORIDE AND WATER

Patient—Infusion		In-put mEq. or Ml.	Oxidative Water Ml.	Urine mEq. or Ml.	Excretion Wound mEq. or Ml.	Insensible Loss Ml.	Load mEq. or Ml.
Br 0.9% NaCl	Na	577.5		119.6	93.0		364.9
	Cl	577.5		205.0	72.6		299.9
	H_2O	3750	161	1174	694	1470	573
St 0.75% NaCl+	Na	579.5		85.8	65.5		428.2
0.22% $NaHCO_3$	Cl	481.0		118.1	49.5		323.4
	H_2O	3750	94	885	450	1180	1329
Vo 0.75% NaCl+	Na	579.5		158.0	110.6		310.9
0.22% $NaHCO_3$	Cl	481.0		112.6	86.9		281.5
	H_2O	3750	218	1320	790	1640	218
Mo 0.6% NaCl	Na	577.5		189.0	120.2		268.3
	Cl	577.5		239.6	92.3		245.6
	H_2O	5625	200	2416	855	1470	1084
Hu 0.38% NaCl+	Na	577.5		263.5	119.7		194.7
0.11% $NaHCO_3$	Cl	577.5		212.8	90.5		177.7
	H_2O	7500	204	1495	905	1470	3834
Le 0.45% NaCl	Na	577.5		227.3	201.6		148.6
	Cl	577.5		264.5	152.9		150.1
	H_2O	7500	194	2130	1390	1510	2664
Sm 0.45% NaCl	Na	462.0		200.3	187.4		73.8
	Cl	462.0		225.6	142.2		85.5
	H_2O	6000	216	2044	1293	1010	1869
Re 0.45% NaCl	Na	577.5		10.9	375.8		190.8
	Cl	577.5		25.9	285.1		266.4
	H_2O	7500	79	506	2592	1470	3011

chloride. At the end of 48 hours, the patient had received 200 Ml. of orange juice and 250 Ml. of water, the sodium load was reduced to 164 mEq., the chloride load to 116 mEq. and the water load to —38 Ml.

Figures 4 and 5 are presented to contrast the paths of excretion of large volumes of fluid. Both patients received 7,500 Ml. of 0.45 per cent NaCl. Patient Le, ♂, Figure 4, showed a large load of water, a marked increase in the loss from wounds, a diuresis after 24 hours, a greater urinary excretion of chloride than of sodium, and the smallest load of NaCl of the patients charted. Patient Re, ♂, Figure 5, was hypotensive after the operation. The volume of urine excreted was very small, the quantity of sodium and chloride negligible. Such massive losses of fluid from the posterior wound occurred that the final loads of sodium, chloride and water were not unlike those of Figure 4.

Figure 6, Patient Hu, ♂, 7,500 Ml. of 0.375 per cent NaCl and 0.11 per cent $NaHCO_3$, shows the largest water retention of the group and a pronounced urinary loss of both sodium and chloride, with sodium predominating.

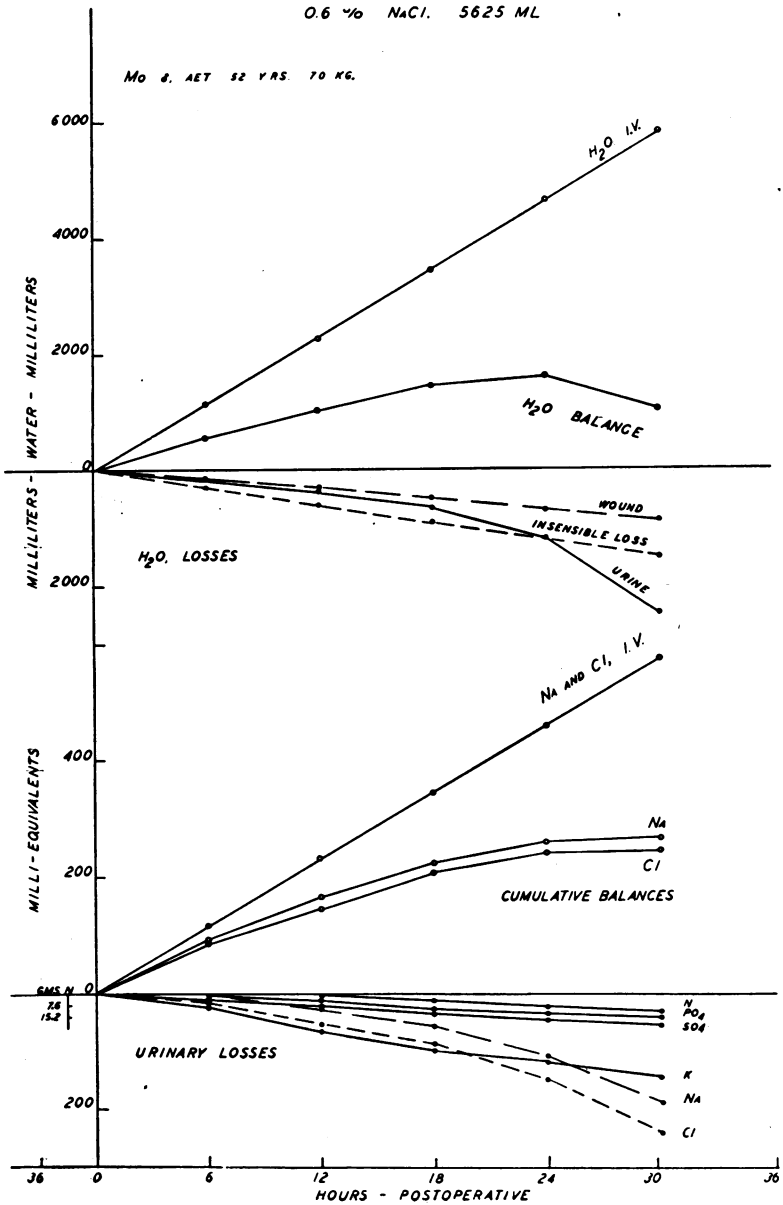

FIG. 3.—Cumulative balances of water, sodium and chloride, and losses of water and urinary constituents of patient Mo., m., No. 568,132, who received 5625 Ml. of 0.6% NaCl during 30 hours following combined abdominoperineal resection. Operation was performed under continuous procaine spinal anesthesia. Hypotension did not develop, and the postoperative condition of the patient was excellent.

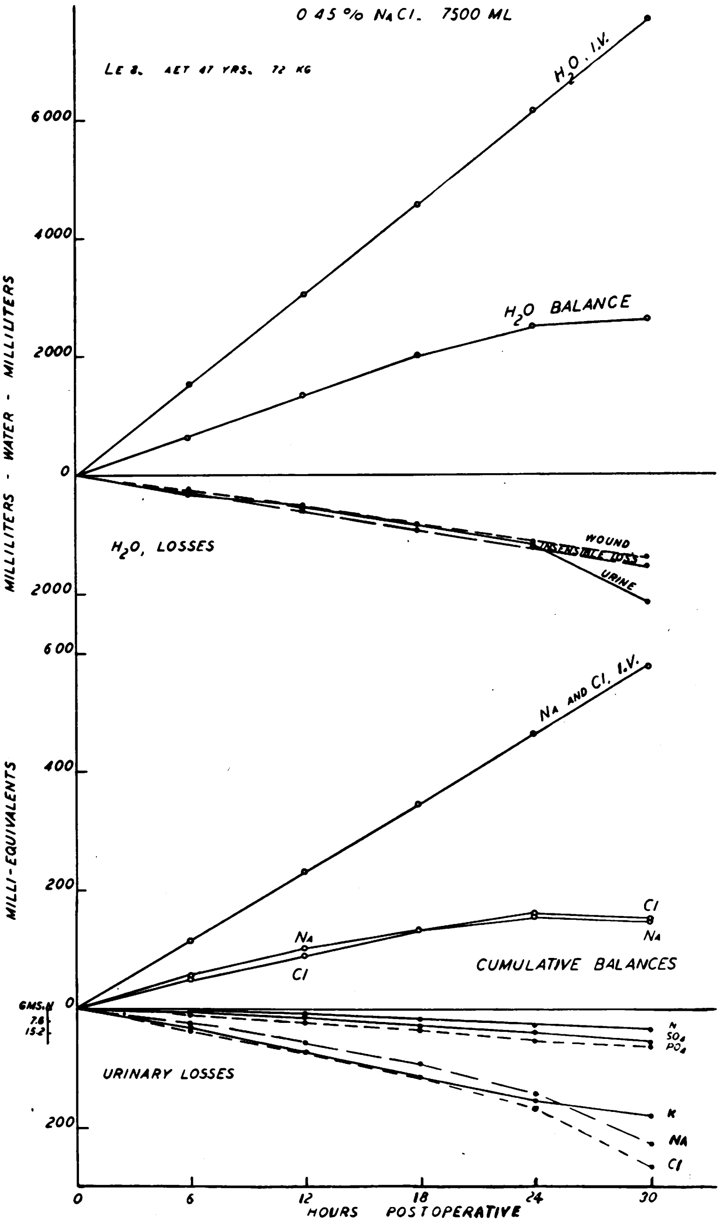

FIG. 4.—Cumulative balances of water, sodium and chloride, and fluid and urinary losses of patient Le., m., No. 564,071, who received 7500 Ml. of 0.45% NaCl during 30 hours following combined abdominoperineal resection. The operation was performed under nupercaine spinal anesthesia. Operative and postoperative courses were uneventful.

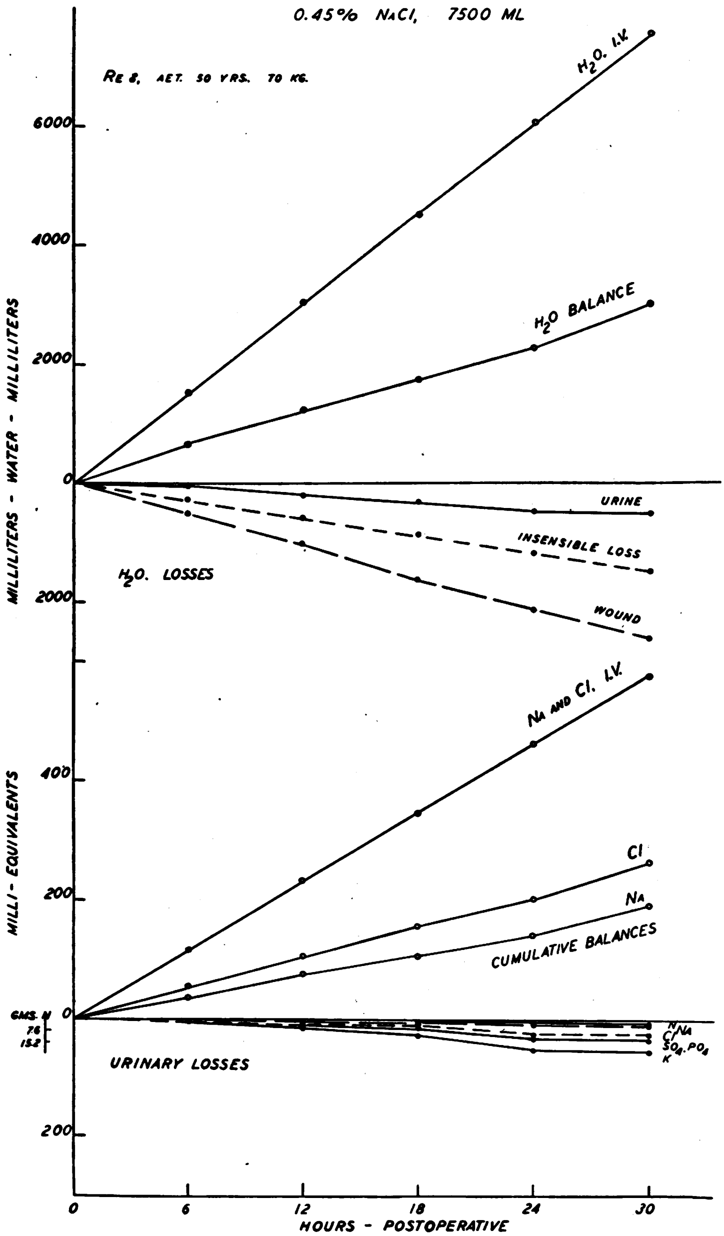

FIG. 5.—Cumulative balances of water and sodium and chloride, and fluid and urinary losses of patient Re., m., No. 562,197, who received 7500 Ml. of 0.45% NaCl during 30 hours following operation. An uneventful operation was followed by a prolonged period (12 hours) of hypotension, very low pulse pressure, tachycardia and oliguria. The entire postoperative course was characterized by a very marked transudation from the posterior wound.

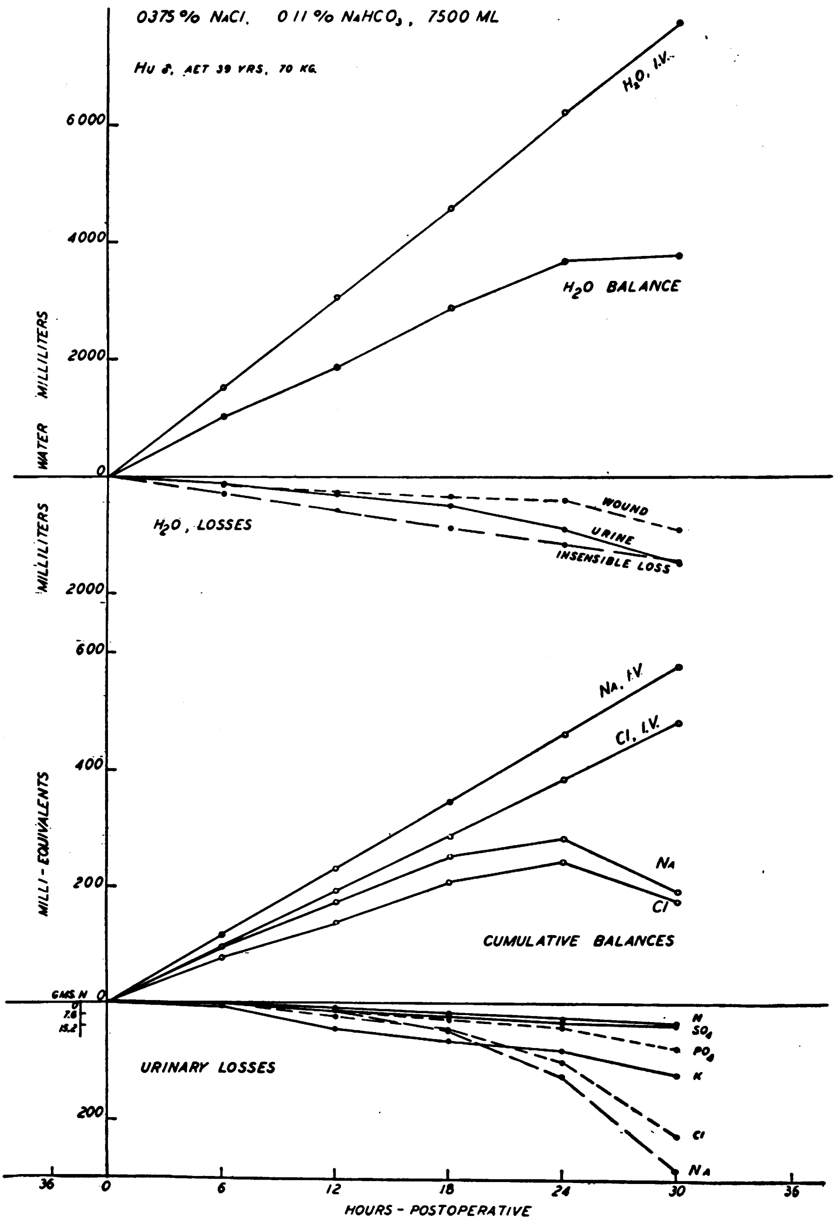

FIG. 6.—Cumulative balances of water and sodium and chloride, and fluid and urinary losses of patient Hu., m., No. 568,596, who received 7500 Ml. of 0.38% NaCl plus 0.11% $NaHCO_3$ during 30 hours following operation. Mild hypotension developed during the operation, 60/40. The postoperative course was satisfactory.

The loss from wounds is small, in contrast to the patients receiving 0.45 per cent NaCl. At the end of 48 hours, the patient had reduced the sodium load to —10 mEq., the chloride load to zero, and the water load to 2,770 Ml.

Table IV divides the patients into a so-called physiologic salt group (physiologic sodium or physiologic chloride) and an hypotonic group. The loads at 30 hours are computed as per cent of in-put. Basic differences are

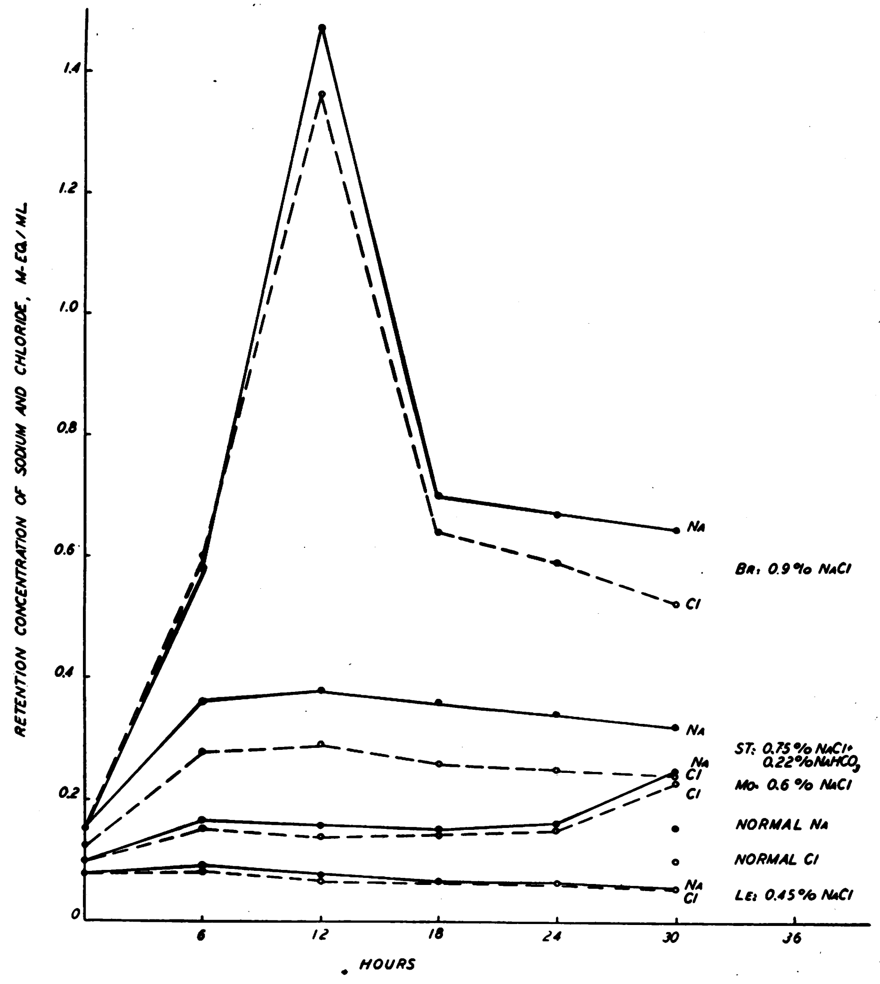

FIG. 7.—Calculated retention concentrations of sodium and chloride, mEq. per Ml. of four patients receiving isotonic salt solution, adjusted isotonic salt solution, isotonic chloride and hypotonic salt solutions, plotted against time after operation in hours.

found in the marked retention of salt with respect to water in the physiologic salt group, and the retention of water over salt in the hypotonic group.

Figure 7 describes the same findings graphically by plotting retention concentrations of sodium and chloride against time in hours. The graph reveals no tendency of the human kidney to convert the volume of infused fluid to a retained concentration of 0.102 mEq. per Ml. as found by Wolf[24] for the dog, and again emphasizes the inability of the human kidney to concentrate urine so well as the dog.

DISCUSSION.—Contrary to animal experiments, surgical patients cannot be considered to have a zero salt and water load at the start of the operation. Varying degrees of hydration and salt balance must exist, especially if the patient has been prepared for operation by Miles' regimen, as in the present series. However, the retention concentrations of Patient Br indicate strongly that there is little need for 27 Gm. of salt. The average loss of blood at these operations indicates a need of about 2 Gm. of salt. The urine, at best,

TABLE IV

THIRTY-FOUR LOADS OF SODIUM, CHLORIDE AND WATER, PER CENT OF IN-PUT

Patient	Infusion	Sodium Per Cent	Chloride Per Cent	Water Per Cent
Br ♂	0.9% NaCl	63	52	15
St ♀	0.75% NaCl+0.22% $NaHCO_3$	74	67	35
Vo ♂	0.75% NaCl+0.22% $NaHCO_3$	27	23	5
Mo ♂	0.6% NaCl	46	43	19
Average, isotonic solutions		53	46	19
Hu ♂	0.38% NaCl+0.11% $NaHCO_3$	34	37	50
Le ♂	0.45% NaCl	26	26	34
Sm* ♀	0.45% NaCl	16	19	30
Re ♂	0.45% NaCl	33	46	40
Average, hypotonic solutions		27	32	39

* Sm received 80% of the infusion.

excretes 7 Gm. of the excess; the losses from the anterior and posterior wounds accommodate an additional 5 Gm. There remains an excess of 13 Gm. of salt which serves only to embarrass a water balance already strained by the exigencies of operation and sequelae.

The hypothesis that the excretion rate of a substance is ordinarily proportional to load is untenable in the case of these surgical patients. The normal kidney is able to concentrate chloride taken orally to the extent of 0.29 to 0.33 mEq. per Ml.[25] In spite of heavy salt loads, no patient approximated this value. As a result of increasing salt load and increasing hypertonicity of the extracellular compartment, osmotic relationships can only be maintained by a shift of water from intracellular to extracellular space. Loads of salt created by the isotonic solutions require a transfer of approximately two liters of intracellular water within 30 hours after operation. The edema, a symptom of postoperative salt intolerance, may result not so much from the retention of water with salt as from the shifting of water from the intracellular to the extracellular space. It is unknown how much dehydration the cells can undergo before function breaks down and ceases. The brain cells are especially sensitive to change and the disorientation so often seen in cases of salt intolerance may be a symptom of this fluid shift.

SUMMARY AND CONCLUSIONS

Salt solutions of various composition and tonicity were administered to men and women undergoing major surgical operations. The rates of excretion of the urinary constituents were determined. Losses of sodium, chloride and water from the posterior and anterior wounds were estimated by use of weighed dressings. Cumulative balances of water, sodium and chloride were calculated.

1. The injection of "isotonic sodium chloride" solutions was attended by an average retention of 53 per cent of the sodium, 46 per cent of the chloride, and 19 per cent of the water 30 hours after the operation. Such retentions of salt indicate a withdrawal of approximately two liters of fluid from the intracellular compartment in order to maintain isotonicity.

2. The infusion of hypotonic solutions resulted in the average retention of 27 per cent of the sodium, 32 per cent of the chloride, and 39 per cent of the water during the same postoperative period. Extra water is thereby provided for excretory function of skin and lungs, and the intracellular compartment is not involved.

3. The human kidney, under the conditions of these experiments, does not elect to guard a "physiologic saline" solution.

4. If intravenous infusion is indicated in the postoperative care of the surgical patient, hypotonic solutions, 0.45 per cent NaCl, or better, 0.38 per cent NaCl plus 0.11 per cent $NaHCO_3$, should replace the "isotonic" solutions commonly in use.

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