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Influence of Hemorrhage and of Albumin Injections upon the Sodium Concentration of Human Plasma.*†

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The purpose of this paper is to present data on the change in concentration of plasma sodium following phlebotomy in 4 normal subjects as well as on the changes in plasma sodium concentration after injections of salt-poor human albumin and/or concentrated plasma in several patients with malnutrition and hypoalbuminemia. The latter were part of a larger group in which other effects of administering salt-poor albumin and concentrated plasma were studied and reported.[1]

Methods. Control blood samples were drawn without stasis from the antecubital vein with the subject in the supine position. All succeeding specimens were obtained from the opposite arm. Clotting was prevented by moistening the barrel of the syringe with a small amount of a commercial heparin solution. After thorough mixing the samples were transferred to hematocrit tubes 8 mm in diameter and centrifuged at 3,000 r.p.m. for 40 minutes, after which the supernatant plasma was carefully removed. One cc of the plasma thus obtained was diluted to 100 cc and thoroughly mixed. A Perkin-Elmer flame photometer was used for making the sodium determinations. A standard solution for calibration contained 50 parts of sodium, as sodium chloride, per million (50 mg per liter) in distilled water. This solution read 100 on the machine. Intermediate values were obtained with standard solutions of concentrations varying from 0 to 50 mg per liter. The calibration curve deviated only slightly from a straight line. Readings of the unknown samples were recorded and corresponding sodium concentrations were determined from the curve. Frequent resettings of the zero and standard were made while performing each determination. Five readings were recorded for each sample and the average used as the most accurate value. The maximum range noted in the 5 readings was about 1.5 scale divisions, the average deviation $\pm$ 1 division, equivalent to approximately $\pm$ 1 milliequivalent of sodium. The flame photometer determinations on 3 samples of plasma were checked by gravimetric methods. Agreement within 2 milliequivalents was obtained. For a complete discussion of use and limitations of the flame photometer for such purpose the reader is referred to the paper of Held.[2]

Findings. Sodium concentrations, determined in 7 normal males 23 to 49 years of age, at intervals of 5, 10, 15, 20, 60, 120, and 180 minutes, showed little variation. The concentrations ranged from 143 to 157 milliequivalents per liter in the several subjects. The extreme differences noted in the 2 to 6 successive samples drawn from the same subject were only 1 to 5 milliequivalents per liter. The average normal value of 147 milliequivalents per liter is in close agreement with the figure of 144 milliequivalents per liter reported by Marinis, Muirhead, Jones and Hill.[3]

Effect of Phlebotomy. In 4 normal young men the plasma sodium concentration was measured before, immediately after and at intervals of ½, 1, 2, 3, and 24 hours after rapid removal of 500 cc of blood. The sodium concentration fell significantly in each instance. These data are recorded in Fig. 1. In one subject the plasma potassium was simul-

* The serum albumin used in this study was processed by the American National Red Cross from blood which it collected from volunteers.

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1 Elman, R., Kelly, F. J., and Simonsen, D. H., in press.

2 Held, P. M., *J. Biol. Chem.*, 1947, **167**, 499.

3 Marinis, T. P., Muirhead, E. E., Jones, F., and Hill, J. M., *J. Lab. and Clin. Med.*, 1947, **32**, 1208.

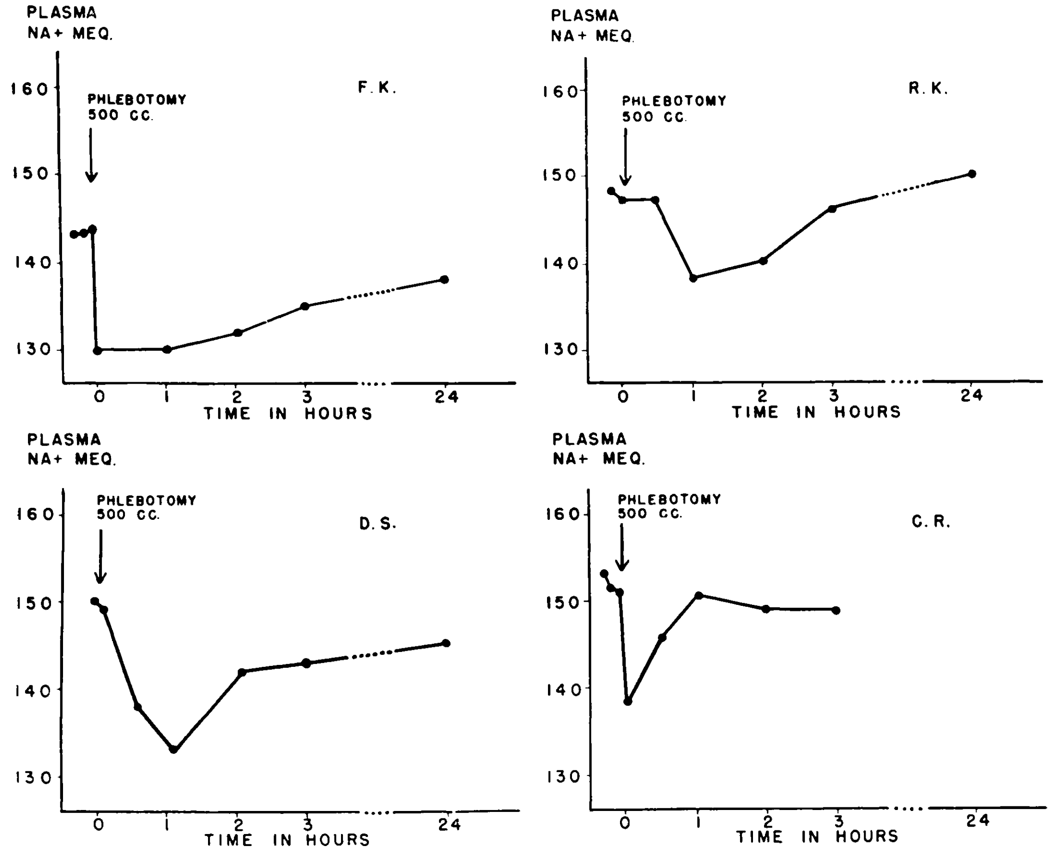

Fig. 1.
Fall in Serum Sodium Following Phlebotomy.
The 4 curves shown above represent observations on 4 healthy donors bled 500 cc. Note the constant drop in the plasma sodium concentration with its return to normal varying from 1 to 3 or more hours.

taneously determined, but no change was noted.

Effect of Injection of Albumin and of Plasma. In 5 patients having malnutrition, hypoalbuminemia and edema, the plasma sodium concentration was measured before, immediately after, and at intervals of 1, 3, 6, and 24 hours after the infusion of either 25% salt-poor human albumin or concentrated plasma.‡ (Table I) Four patients were given 7 injections of albumin; 1 patient received albumin on one occasion and concentrated plasma 2 days later; one patient received concentrated plasma alone. Following 5 of the 7 albumin injections, the plasma sodium concentration fell significantly, the maximum decrease occurring immediately after infusion (at which time the plasma volume showed its maximum increase).[2] In one case (B.P., Table I) in which plasma potassium concentration was simultaneously determined, no significant change was found. In the 2 patients receiving concentrated plasma the plasma sodium content increased significantly, the highest value being obtained 3 hours after injection in both. Immediately after plasma infusion the plasma volume was increased maximally, as with albumin, and at this time the plasma sodium concentration had changed little, or not at all.

‡ Two 500 cc units of Red Cross lyophilized plasma were dissolved in 1 unit (500 cc) of distilled water. The sodium content was determined by us to be 3.80 g per 500 cc; that of the 25% albumin solution was recorded by the manufacturer as 0.3 g per 100 cc.

TABLE I.
Plasma Sodium Concentration (Milli-equivalents per liter) Before and at Various Intervals Following the Injection of Salt-poor Human Albumin and Double Strength Plasma in Patients with Malnutrition.

Subject	Age	Sex	Diagnosis	Injection	Plasma Na+ concentration (meq.) Before	After	1 hr	3 hr	6 hr	24 hr	Max. decrease (meq)
B.E.	71	M	Carcinoma head of pancreas	Albumin (50 g)	150	138	150	156	147		12
				” ” ”	150	149	148	149	142		8
G.H.	45	F	Non-tropical sprue	” ” ”	137	123				144	14
				” ” ”	144	130				131	14
B.P.	48	M	Cirrhosis	” ” ”	136	137	137	141		145	
				” ” ”	143	130	146			147	13
E.R.	75	M	Carcinoma of pancreas	” ” ”	149	139.5	139.5	141.5	143.5	144	9.5
G.S.	71	M	Cirrhosis	Plasma (470 cc double strength)	141	140	141	148	139	141	
				Plasma (285 cc double strength)	138	142	141	148		138	

Discussion. The fall we observed in the plasma sodium concentration following either hemorrhage or the injection of 25% salt-poor human albumin solution is assumed to be a part of the hemodilution process and thus resolves itself ultimately to a discussion of the source of the fluid that enters the circulation following such procedures.

In a review of the literature we have found but one report on the changes in serum sodium and potassium following hemorrhage. Stewart and Rourke[6] reported that in 4 normal dogs bled 2 to 3.5% of their body weight, samples drawn 12 hours after the hemorrhage showed a fall in serum sodium, potassium and protein concentration, and variable concentrations of the chloride, carbon dioxide and non-protein nitrogen. These changes occurred whether the animals were allowed fluids by mouth or not. Our subjects were given neither food nor fluids by mouth during the first hour. They remained in bed until the ½ hour samples had been drawn and were then permitted to be up and about. After the one-hour sample was drawn food and fluids were permitted *ad libitum.* The data presented herein in normal human subjects confirm Stewart and Rourke's findings in dogs.

Ashworth, Muirhead and Hill[4] studied the effect of concentrated citrated and defibrinated dog and human plasma on the serum sodium and potassium concentration of normal dogs. They found no change in the samples drawn 15, 20, 60 minutes and 4 hours after injection. Since the plasma volume (dye method) as well as the extracellular fluids (thiocyanate method) increased after infusion, without change in serum sodium concentration, these authors concluded that the fluid added to the circulation was derived from the intracellular space. We observed an increase in the serum sodium concentration 3 hours after the injection of concentrated citrated plasma in 2 patients.

Heyl, Gibson and Janeway[5] in their study of the effect of concentrated solutions of

4 Ashworth, C. T., Muirhead, E. E., and Hill, J. M., *Am. J. Physiol.*, 1942, **136**, 194.

5 Heyl, J. T., Gibson, J. G., 2nd, and Janeway, C. A., *J. Clin. Invest.*, 1943, **22**, 713.

human and bovine serum albumin on the blood volume after acute blood loss in normal men, reported no change in the serum or urinary potassium concentration, but their albumin solutions were not salt-poor. In 5 of the 7 patients in whom we injected salt-poor albumin a significant fall in plasma sodium occurred. In the single patient in whom potassium was measured, no change was noted. It should be emphasized that the fall in sodium concentration was most marked immediately after infusion, at which time the plasma volume had increased by a volume more than 3 times that of the fluid injected. The magnitude of the fall in sodium concentration was much less than could be accounted for by hemodilution with a sodium-free solution, hence the fluids responsible for the dilution probably contained sodium but in lower concentration than in plasma.

Because intracellular fluid is poor in sodium and rich in potassium, it is logical to assume that much of the diluting fluid must have come from this source, in which case one might expect a rise in plasma potassium. The latter was measured in 2 cases, but no change was found. However, renal clearance of potassium is so rapid that this discrepancy may not be significant. Indeed, Stewart and Rourke,[6] in the experiments cited earlier, found an increase in potassium output in the urine after hemorrhage. The red cells themselves might be assumed to be the source of the diluting fluid, but this could be true only if a rapid two-way shift of fluid were involved, inasmuch as no change in the size of red cells was observed after the injection of albumin.[2]

Summary. 1. Following phlebotomy in each of 4 normal male subjects, there was a transient fall in the plasma sodium concentration.

2. Following injections in 4 patients of a 25% solution of salt-poor human albumin solution, a similar fall in the plasma sodium concentration was noted.

3. It is concluded that sodium-poor fluid is added to the plasma, presumably from the intracellular space, following hemorrhage, as well as following injection of salt-poor human albumin.

6 Stewart, J. D., and Rourke, G. M., *J. Clin. Invest.*, 1936, **15**, 697.

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Environmental Conditions Which Initiate Sweating in Resting Man.

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During the course of studies[1,2,3] on the influence of environmental conditions upon the rate of water loss from the skin of man, observations were made to learn the environmental temperature and relative humidity which would initiate sweating in normal man.

Eleven subjects of both sexes, varying in ages from 12 to 59 years, were permitted to rest quietly on a hospital type of bed in an air-conditioned room. They were clothed only in a cotton gown. The rate of water loss from the skin of the epigastrium and volar surface of the right forearm was determined by a method previously described.[4]

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1 Burch, George, and Winsor, Travis, *J. Clin. Invest.*, 1944, **23**, 937.

2 Winsor, Travis, and Burch, George E., *Arch. Int. Med.*, 1944, **74**, 428.

3 Burch, George E., and Winsor, Travis, *Arch. Int. Med.*, 1944, **74**, 437.

4 Burch, George E., and Sodeman, William A., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 190.