THE EFFECT OF "RICE DIET" ON PLASMA VOLUME AND EXTRACELLULAR FLUID SPACE IN HYPERTENSIVE SUBJECTS¹

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The treatment of hypertensive vascular disease with the "rice diet" of Kempner has been introduced in the past few years (1), and is receiving increasing interest from investigative and therapeutic points of view (2-5). This diet contains "in 2000 calories not more than 5 grams of fat and about 20 grams of protein derived from rice and fruit, and not more than 200 mgms. of chloride and 150 mgms. of sodium" (5a). In addition, it contains about 450 grams of carbohydrate and about 3000 mgms. of potassium (5b). The diet is, therefore, low in sodium chloride, fat, protein and other substances, and relative to its total electrolyte content, high in potassium.

Because of the well-known relationships between the extracellular fluid compartment and dietary sodium (6-10) a study of the plasma volume and extracellular thiocyanate space in patients on this diet seemed desirable. Interpretation of the data must be extended to include the possibility that other features of the diet, besides the low sodium content, might have had a modifying effect on the results obtained.

MATERIALS AND METHODS

This report deals with data obtained from 17 patients observed on this regimen over a period of 100 days. The group contains 16 patients with hypertensive vascular disease and one patient with coronary artery disease without hypertension. The patients studied were from the service of Dr. Walter Kempner.

The basis for selection of the patients was availability, absence of clinical heart failure, normal initial extracellular fluid volumes and absence of major renal damage as measured by urinalysis, Mosenthal test, serum non-protein nitrogen concentration, and ability to excrete phenolsulphonthalein. Strict observance of the diet was judged by urinary chloride excretion (1, 5a). All the patients were outpatients and were studied in the morning postabsorptive state. A preliminary rest period of 30 minutes in the recumbent position preceded each study. Serial observations were made before starting

the diet and at arbitrary points of three, six, 10, and 14 weeks thereafter.

Plasma volume and thiocyanate space were measured by a modification of the simultaneous method of Gregersen and Stewart (11) based upon the plasma dilution of T 1824 and the extracellular space dilution of sodium thiocyanate. Techniques were adapted to the Beckman spectrophotometer for the former and the photoelectric colorimeter for the latter. The method of Bowler (12) was used in determining serum thiocyanate. Fifteen mgms. of T 1824 and 16 cc. of 5 per cent sodium thiocyanate were introduced intravenously from calibrated syringes and samples were withdrawn from the contralateral arm through an indwelling needle left *in situ* in one of the antecubital veins. Samples were obtained at six minute intervals over a period of from 42 to 48 minutes. A disappearance curve was plotted for T 1824 in each case and extrapolated to zero time to obtain the point from which calculations were made. Corrections were made for imperceptible hemolysis in all samples (13).

The point of stabilization of the thiocyanate curve was taken to be the concentration at the time of maximal dilution. The space obtained from this measurement may be assumed to approximate the extracellular fluid space (14). The figure obtained by subtraction of the plasma volume from the volume of this space is referred to in the paper as the interstitial volume. Blood volume was calculated from the plasma volume as obtained above and the red cell volume obtained from the venous hematocrit reading. Hematocrit readings were made in Wintrobe tubes and the correction factor for trapped plasma was not calculated. Serum sodium levels were measured in the model 52A Perkin Elmer Flame Photometer. Each blood pressure measurement represents the mean of six daily casual recordings. The transverse diameter of the heart was measured from six foot chest films.

RESULTS

Table I shows that before starting the diet, the mean plasma volume of the group expressed in cc. per kilogram of body weight was 41 ± 4 which is comparable to Gregersen's (15) normal figures of 45 ± 4 . The total extracellular fluid in per cent of body weight was calculated but is not recorded in the table. The mean was 22 per cent ± 1.5 which is comparable to the value for the normal

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subjects of Lavietes, Bourdillon, and Klinghoffer (16). In the 17 patients listed, it will be seen the mean decrease in the plasma volume was 10 per cent ± 1.7 ,² and in the interstitial fluid volume, the mean decrease was 12 per cent ± 1.5 .² Both these figures are highly significant with $p < 0.01$. All percentage changes are expressed as the difference between the figures from the initial study and the mean of the figures obtained from the studies at the end of 10 and 14 weeks. Analysis of the individual cases shows that there was a decrease in both spaces in 13 cases, and in one of the spaces in the other four.

In three of these latter patients (G.P., T.E., and C.C.J.), although the total extracellular fluid decreased, there was no significant decrease in the plasma volume, and in fact, in the case of C.C.J., there was a gradual increase to 105.4 per cent of the original figure. C.C.J.'s hematocrit dropped from 47.5 to 35.5 over the 100 day period and it

is felt the plasma volume changes are a reflection of this. In the fourth of these patients, W.L., both the plasma volume and interstitial volume had decreased at the time of the three week study but in the succeeding weeks, interstitial volume rose to the prediet figure but the plasma volume remained low.

Shown also in Table I are the decreases in plasma and extracellular fluid volume over the 10-14 week period relative to weight changes during the same period. It will be seen that the mean figures for plasma volume and interstitial fluid volume, expressed in cc. per kilogram of body weight, show no change.

That the decrease in extracellular fluid volumes is not a simple function of the weight change is suggested in Figure 1 in which weight changes are plotted against fluid changes. The r values for each period of observation, except the three week period, are such that no positive correlation can be established. At the three week period, correlation is of limited significance. In addition, this

TABLE I
Clinical and experimental observations on 17 patients on "rice diet"

Patient	Diagnosis	Age	Sex	Wgt. (kgm.)		Absolute P.V. (cc.)			Absolute IFS (cc.)			Vols. rel. to wgt. (cc. per kgm.)			
						Before diet	After diet	% diff.	Before diet	After diet	% diff.	P.V.		IFS Vol.	
				Before diet	After diet							Before diet	After diet	Before diet	After diet
H. B. R.	HCVD	54	M	79.5	74.6	3430	2925	-16.0	14,150	12,175	-14.0	42.9	39.2	178.0	163.2
M. F.	ASHD	57	M	76.0	65.0	2905	2535	-13.0	11,640	10,520	-9.6	38.2	39.0	153.1	161.8
G. P.	HCVD	46	F	55.0	51.8	2155	2135	-1.0	10,130	9,850	-2.8	39.2	41.2	184.1	190.1
M. S.	HCVD	56	F	71.0	62.3	2930	2360	-19.7	13,665	10,870	-20.5	41.3	37.9	192.5	174.5
C. L.	HCVD	61	M	82.8	77.7	3910	3380	-13.6	15,605	14,005	-10.2	47.1	43.5	188.5	180.2
L.S.	HVD	48	F	49.5	45.4	2085	1895	-9.2	9,507	8,395	-11.7	45.4	41.7	207.1	184.9
C. C. J.	HCD	61	M	76.8	67.3	2755	2915	+ 5.4	13,980	12,400	-11.3	36.0	43.3	182.0	184.2
W. L.	HCVD	66	M	84.0	77.0	3505	3245	-7.4	15,188	15,150	-0.3	41.7	42.1	180.8	196.7
T. E.	HCVD	51	M	78.0	73.7	3070	3107	+ 1.2	13,290	12,425	-6.5	39.4	42.1	170.3	168.5
S. G.	HCVD	51	M	97.0	83.1	3450	2920	-15.3	18,895	13,740	-27.3	35.6	35.1	194.7	165.3
N. E.	HCVD	48	M	69.0	61.4	2930	2220	-24.3	12,425	10,905	-12.2	42.5	36.1	180.0	177.6
J. S.	HCVD	40	M	68.5	67.3	2830	2640	-6.8	12,695	11,845	-6.7	41.6	39.2	185.3	176.0
A. A.	HCVD	59	M	69.6	65.5	3225	2935	-9.1	14,670	11,940	-18.6	46.0	44.8	210.7	182.2
P. M.	HCVD	42	M	83.2	75.0	3685	3180	-13.7	16,515	15,150	-8.3	44.4	42.4	198.5	202.0
F. C. L.	HCVD	58	M	76.4	70.5	2735	2500	-11.3	14,215	12,510	-12.0	36.0	35.4	186.0	177.4
H. G.	HCVD	56	M	60.0	54.5	2550	2300	-10.0	12,405	10,645	-14.2	42.0	42.2	206.7	195.3
L. M.	HCVD	42	F	79.5	65.0	2550	2290	-10.1	11,510	9,775	-15.0	32.0	35.2	144.7	150.3
Mean				73.7	66.9	2985	2675	-10.2	13,555	11,900	-11.8	40.6	40.0	184.9	178.2
S. D.								7.3			6.5				
S. E.								1.7			1.5				

P. V.—Plasma volume

IFS—Interstitial fluid or total extracellular fluid — plasma volume

Before diet—Initial study

After diet—Mean of studies at 10 and 14 weeks

TABLE I (continued)

Patient	Absolute B.V. (cc.)			Plasma proteins				Arter. press. (mm. mercury)		T.D. heart (cm.)	
				Level (gms.%)		Tot. circ. (gms.)					
	Before diet	After diet	% diff.	Before diet	After diet	Before diet	After diet	Before diet	After diet	Before diet	After diet
H. B. R.	6070	4690	— 22.7	6.9	6.5	237	190	160/100	122/74	17.0	14.0
M. F.	5555	4535	— 18.4	7.7	7.9	224	200	134/84	104/66	13.0	12.0
G. P.	3720	3380	— 9.1	7.3	7.0	157	149	210/115	185/115		
M. S.	5220	3930	— 24.7	7.2	7.2	211	170	242/108	170/86	19.5	15.5
C. L.	6660	6145	— 7.7	6.5	6.2	254	210	180/110	144/96	12.5	12.5
L. S.	3500	3105	— 11.3	7.0	7.7	146	146	145/102	136/92	11.0	11.0
C. C. J.	5260	4675	— 11.1	6.1	7.0	168	204	154/84	120/76	13.5	13.0
W. L.	6550	5940	— 9.3	6.8	6.8	238	221	196/116	130/90	14.0	12.5
T. E.	5455	5085	— 6.8	7.2	7.2	221	224	180/110	140/86	17.0	15.5
S. G.	6900	5685	— 17.6	7.7	7.7	266	225	162/119	116/80	14.5	13.0
N. E.	5640	4225	— 25.1	7.2	6.7	211	149	210/110	118/108	14.0	13.0
J. S.	5560	4445	— 20.1	7.0	6.4	198	169	180/110	134/90		
A. A.	5450	4770	— 12.5	7.2	7.2	232	211	224/112	196/96	15.0	14.5
P. M.	7020	5485	— 21.9	7.2	6.7	265	207	180/120	144/100	17.0	15.0
F. C. L.	5040	4585	— 9.0	6.7	6.5	183	162	222/128	180/104	15.5	14.5
H. G.	4905	4380	— 10.7	7.2	7.2	184	166	208/140	210/120	15.0	12.5
L. M.	4050	3640	— 10.1	6.5	6.8	166	156	180/100	136/94	14.5	11.0
Mean	5445	4630	— 14.6	7.02	6.97	209	186				
S.D.			6.3								
S.E.			1.5								

figure shows that although weight loss was fairly constant throughout the total period of observation, extracellular fluid loss was most marked in the first three to six weeks and thereafter the volume became relatively fixed.

FIG. 1. FIGURE SHOWING LACK OF CORRELATION BETWEEN WEIGHT AND EXTRACELLULAR FLUID LOSS OF PATIENTS ON RICE DIET.

Individual figures represent changes between observations.

That this series is different from other suffering weight loss is shown by comparing it with the group of individuals studied by Henschel and his associates (17). Their subjects voluntarily underwent a "European starvation diet" for about six months with consequent loss of about one-fourth of their body weight. These individuals had surprisingly constant absolute plasma volume and interstitial fluid volume with large increases relative to weight.

Table I shows also that the mean decrease in blood volume of 15 per cent $\pm 1.5^3$ was slightly higher than the decrease in plasma volume over the same period. This is a reflection of the decrease in peripheral venous hematocrit. The danger of calculating the red cell volume from venous hematocrit under varying conditions has been pointed out (18). These studies are not helpful in determining the cause of the fall in hematocrit. Since this is an unusual diet, it may be related to some deficiency. The point remains open for further study.

Total plasma proteins before starting the diet and at the end of the 14 week period are shown in Table I. As Kempner has reported (5a),

³ Standard error.

TABLE II

Sodium concentration in extracellular fluid of seven patients before and after three weeks of "rice diet" with net decrease due to volume change

Patient	First study		Second study		Net change in extracellular sodium in meq.
	Serum Na in meq./L.	Total E.C.F.	Serum Na in meq./L.	E.C.F.	
G. P.	142.6	12,290	144.3	12,620	+ 69
C. L.	146.0	19,512	144.4	18,390	-193
W. L.	146.0	18,695	139.1	17,465	-300
L. S.	139.5	11,595	142.6	10,855	- 70
J. W.	139.1	15,715	142.6	13,335	-288
C. C. J.	140.8	16,735	140.8	14,955	-252
T. E.	144.3	16,360	144.3	15,640	-104
Mean					-163

there is no significant change in the level. However, in view of the volume change, there was a mean decrease in total circulating plasma protein of 11 per cent.

In seven of the patients in the series, measurement of the serum sodium concentration was made previous to starting the diet, at the time of the initial study, and three weeks later at the time of the second study. Results are shown in Table II. In all cases, concentrations obtained were within normal limits. However, in view of the volume changes in all cases except G.P., there was a mean loss of sodium from the extracellular phase of 163 meq. This again re-emphasizes the importance of volume in the interpretation of any serum or blood chemistry determination.

CLINICAL OBSERVATIONS

During the first three to six weeks on the diet, complaints of weakness, anorexia, and mild memory impairment were not uncommon. Despite the rather limited fluid intake on the regimen (1) there were no complaints of thirst. Instances of improvement in effort tolerance and decrease in headache were common. Complaints of mild dizziness on standing and the finding of some postural hypotension occurred in 12 of the 17 cases. This latter usually occurred between the third and tenth weeks but without simple time relationship to the changes in body fluid. The postural hypotension disappeared and was not present in any of the subjects at the end of the 14th week.

Table I shows changes in arterial pressure and the size of the heart. It will be seen there is no simple quantitative relationship between these and

the changes in blood volume, *e.g.*, case N.E. has a decrease of 25 per cent in his blood volume with only a very slight decrease in mean arterial pressure. Contrariwise, case T.E. had no change in plasma volume and only 7 per cent in blood volume, but blood pressure fell from moderate elevation to within normal limits. The data also show that there is no simple quantitative relationship between changes in blood volume and transverse diameter of the heart.

DISCUSSION

The volume of the body fluids varies with the body content of the osmotically active electrolytes. In the case of the extracellular fluid space sodium plays the dominant role (19, 20). Marked alterations in one direction or another, either of intake or output of sodium, are reflected in extracellular fluid volume changes in the same direction provided the organism is capable of making these changes. These changes in fluid volume allow relatively constant concentrations of electrolytes in spite of a relatively large change of total electrolyte content of the body.

In certain pathological states such as Addison's disease, where loss of renal sodium control is a fundamental feature, total extracellular fluid is reduced. Induced "hypochloremia" by sweating (21) with replacement of water loss also causes a reduction in the volume of extracellular fluid. With large increases in dietary sodium, Gamble, Darrow and others have shown the extracellular fluid volume to expand. In complete fasting (6) and on pure glucose diets (7), the extracellular fluid volume contracts.

Although the "rice diet" has other unusual features which might have influenced the data, it is presumed that the low sodium intake with the loss of body sodium is the fundamental factor, and the explanation for the results obtained.

It is usually stated that under most conditions, dietary sodium is adequate to maintain constant fluid volumes. These data would indicate that in an average group of hypertensive patients, a daily intake of about 150 mgms. is insufficient. As there are no comparable data on healthy people, one can draw no conclusions concerning normal minimal requirements. Since 16 of these subjects had hypertensive vascular disease for a greater or lesser period of time and the 17th subject had other vas-

cular disease, it is possible that their renal sodium conserving mechanisms were altered as compared to normals.

It appears that there may be physiological significance to what would seem to be minor variations of a low salt diet. Perera and Blood (22), in a study of a similar group of patients who received 250–350 mgms. of sodium daily for periods of two weeks, found no change in the plasma volume. Comparing that fact with these present data would suggest that absolute sodium balance in hypertensive vascular disease is achieved somewhere between these two figures.

The data would also indicate that after a period of about three weeks, some form of sodium equilibrium is reached because the volumes become and remain relatively constant, and Kempner has reported (5a) that the serum sodium level is maintained. Presumably, this again is related to some alteration in base conserving mechanisms of the kidney. Whether or not these mechanisms are related to the renal functional changes, *i.e.*, decrease in glomerular filtration rate which McCance (21) has described in experimental salt depletion, or to decrease in renal plasma flow and glomerular filtration rate which Chasis and his colleagues (3) have described in this diet, or hormonal influences, is entirely speculative and awaits further investigation. The subjective clinical findings of anorexia, weakness, mild memory impairment and the finding of mild postural hypotension would be in keeping with the clinical picture of sodium depletion. The cardiovascular effects of sodium depletion of a greater magnitude than found in the present series has been well described (23). The fact that there is no simple correlation between blood volume changes and blood pressure and heart size changes is not surprising in view of the other variables of the regimen which are known to have these effects, *e.g.*, moderate weight loss, rest and encouragement; and also because of the other factors of the diet which must have measurable effects on body metabolism.

CONCLUSIONS

1. Both plasma volume and extravascular thio-cyanate space show highly significant decreases over a 14 week period in patients on the "rice diet" of Kempner.

2. Blood volume estimated from the plasma volume and venous hematocrit shows a greater decrease than can be accounted for by plasma volume changes.

3. Although total plasma protein concentration remains at constant levels, there is a significant decrease in total circulating protein. Similarly there is a decrease in total extracellular sodium.

4. Patients initially do have symptoms usually ascribed to sodium depletion. These are not present at the end of the 14 week period. There is no simple relationship between fluid volume changes and reported clinical results.

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