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BODY FLUID AND ELECTROLYTE COMPOSITION IN ARTERIAL HYPERTENSION. I. STUDIES IN ESSENTIAL, RENAL AND MALIGNANT HYPERTENSION *

By W. HOLLANDER,† A. V. CHOBANIAN and B. A. BURROWS with the technical assistance of VALENTINE BIKERMAN

(From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, the Radio-isotope and Medical Services, Boston Veterans Administration Hospital, and the Department of Medicine, Boston University School of Medicine, Boston, Mass.)

In previous studies in this laboratory it was found that the capacity to excrete sodium as indicated by the rate of excretion of an intravenously administered sodium load was significantly increased in essential and renal hypertension (1, 2). Sodium excretory capacity was reduced by antihypertensive therapy and was correlated significantly with the level of arterial pressure. However, the absence of a high degree of correlation, together with the ability of dietary sodium intake to influence the renal capacity to excrete sodium, suggested that in addition to an elevated blood pressure other factors such as an increase in body sodium and fluid volume might enhance sodium excretion in hypertensive individuals.

Studies in Cushing's syndrome and Addison's disease by other workers suggest that the level of adrenal cortical activity may influence not only the renal capacity to excrete sodium but also the arterial pressure as well as the body's content of fluids and electrolytes (3, 4). In line with these observations are recent reports indicating that an increase in aldosterone activity occurs in certain groups of hypertensive subjects (5–7).

To clarify the relationship of arterial hypertension to alterations in adrenal cortical function and in electrolyte and water metabolism, it was decided to study body fluid and electrolyte composition in various forms of hypertension, including that associated with primary aldosteronism (8). The present report describes the findings in essential, renal and malignant hypertension. The observations in primary aldosteronism are presented in a separate report (9).

CLINICAL MATERIAL AND METHODS

Radioisotope dilution studies were performed in untreated ambulatory hypertensive patients and normal subjects who were paired as to age, sex, height, weight and body build. The dietary intake of salt as indicated by history and urinary sodium excretion over a 24 hour period was "unrestricted" and comparable in the hypertensive and the control subjects.

The 20 subjects with essential hypertension had sustained elevations of blood pressure with grade I to III retinopathy (Keith-Wagener) but without complicating nitrogen retention or congestive heart failure. However, 8 of these subjects were found to have enlarged left ventricles on roentgenographic examination.

The 10 subjects designated as having "renal hypertension" had a history of kidney disease which antedated the onset of the hypertension. Included in the group were 5 subjects with bilateral chronic pyelonephritis, 2 with polycystic kidney disease and 3 with glomerulonephritis. Their fundi showed grade I to III retinopathy whereas their blood urea nitrogen levels were normal except in 2 subjects. The left ventricle was enlarged in 5 subjects but no patient had complicating congestive heart failure.

The 7 hypertensive subjects with complicating heart failure had enlargement of the left ventricle with symptoms and signs of pulmonary congestion but without clinically detectable peripheral edema. The decholin circulation time was prolonged in all subjects but only 1 had a definite elevation of venous pressure. Two of the subjects had nitrogen retention and all showed grade II to III hypertensive retinopathy.

All 10 subjects who had malignant hypertension had grade IV retinopathy (papilledema) as well as marked elevation of blood pressure. In the group there were 4 subjects with chronic bilateral pyelonephritis, 3 with essential hypertension, 2 with glomerulonephritis, and 1 with renal arterial occlusion. Most of the subjects complained of fatigability and exertional dyspnea. They also had nitrogen retention as well as an enlarged left ven-

TABLE I

Essential hypertension *

Subject	Sex	Age	Body wt	BSA	BP	Fundi	BUN	Serum osm.	ECF (S³⁵O₄ space)	Naₛ	Kₛ	Naₑ/ body wt	Kₑ/ body wt
		yrs	kg	m²	mm Hg	grade	mg %	mOsm/L	% body wt	mEq/L	mEq/L	mEq/kg	mEq/kg
W.M.	M	49	76.3	1.92	205/135	III	14	296	15.3	137	3.5	33.5	45.6
M.S.	M	49	71.8	1.83	225/125	II	22	281	13.8	141	3.6	41.3	49.0
V.W.	F	32	65.0	1.72	255/150	II	13	288	13.1	144	4.1	37.1	30.9
M.D.	F	36	70.5	1.72	195/125	II	13	288	13.8	142	4.3	33.1	29.9
R.D.	F	48	50.8	1.58	195/110	II	17	286	14.7	147	3.7	38.0	32.6
H.L.	F	44	65.4	1.61	220/115	II	9	288	14.0	144	4.2	33.8	28.0
M.S.	F	55	67.7	1.65	245/130	II	13	290	14.7	138	3.8	29.5	27.7
J.W.	M	46	83.2	2.00	205/110	II	14	291	14.6	141	3.6	45.1	44.1
M.H.	F	36	85.9	2.04	180/110	I	15	286	12.4	142	4.1	39.3	35.7
A.L.	M	50	67.8	1.77	235/145	III	17	283	16.2	141	3.9	41.5	42.1
D.C.	M	58	86.3	1.95	195/125	III	19	288	14.0	144	4.7	38.1	38.2
M.M.	F·	60	99.5	1.98	230/130	III	20	297	15.1	141	4.2	33.9	26.1
C.A.	F	34	104.5	2.10	180/125	I	10	288	11.3	146	3.9	26.5	25.4
M.D.	F	46	76.8	1.83	215/125	II	13	281	14.7	145	4.5	35.1	30.3
H.B.	F	47	55.3	1.55	185/110	II	18	283	14.7	142	4.4	39.9	36.9
B.C.	M	36	85.9	2.04	175/115	II	14	290	12.7	144	4.2	32.3	35.1
H.B.	M	35	74.1	1.95	180/125	II	19	287	14.3	140	4.5	36.0	43.2
R.M.	F	53	63.3	1.59	180/120	II	16	302	13.9	140	4.2	42.1	30.4
G.H.	M	54	79.3	1.94	175/110	I	16	296	14.7	141	3.8	45.7	33.7
M.M.	F	49	69.1	1.71	175/100	II	12	286	14.2	142	4.2	39.3	36.5
						Control							
J.D.	M	52	74.5	1.89	120/80	0	18	286	15.8	139	4.0	41.2	39.9
J.L.	M	48	70.4	1.88	105/70	0	8	285	14.3	137	4.5	41.8	52.9
M.D.	F	33	66.4	1.76	105/65	0	12	279	15.9	138	4.3	38.0	35.0
J.M.	F	34	70.9	1.76	120/80	0	10	280	13.8	140	3.9	36.3	38.2
S.R.	F	45	49.5	1.50	125/75	0	17	289	17.0	140	4.2	36.7	43.2
A.J.	F	43	66.3	1.65	100/65	0	8	288	16.1	143	3.8	37.8	34.7
G.H.	F	56	66.1	1.69	125/80	0	15	284	14.8	143	4.1	34.5	32.4
A.F.	M	49	81.8	1.91	125/75	0	13	297	16.5	146	4.8	37.7	38.3
M.E.	F	37	86.8	2.00	130/75	0	8	283	15.3	139	4.2	29.5	28.8
E.H.	M	48	66.6	1.75	125/80	0	19	289	14.0	140	4.3	42.0	40.5
S.P.	M	62	85.0	1.95	125/80	0	14	288	16.5	140	4.4	35.6	32.8
M.E.	F	62	95.5	2.03	130/80	0	18	292	13.5	140	4.5	32.6	26.7
E.V.	F	39	108.9	2.13	135/85	0	12	288	10.1	139	4.1	29.6	27.1
N.R.	F	43	73.6	1.83	135/85	0	7	283	14.6	140	3.9	30.7	32.6
M.M.	F	41	52.0	1.51	115/75	0	10	277	14.3	137	3.6	34.8	33.4
T.M.	M	33	88.2	2.06	120/75	0	17	287	13.5	145	4.5	35.2	42.9
H.T.	M	36	74.5	1.97	120/75	0	13	290	14.8	144	4.5	42.8	40.0
E.K.	F	49	66.8	1.61	100/60	0	12	287	14.2	140	4.5	33.9	30.4
H.D.	M	52	80.3	1.95	115/80	0	11	287	15.0	141	4.4	39.8	39.1
T.M.	F	49	70.5	1.70	130/70	0	14	286	14.1	138	3.5	32.6	32.3

* BSA =body surface area. BP =blood pressure. BUN =blood urea nitrogen. Osm. =osmolality. ECF =extracellular fluid volume. Naₛ =serum sodium. Kₛ =serum potassium. Naₑ =exchangeable sodium. Kₑ =exchangeable potassium.

TABLE II

"Renal" hypertension

Subject	Diagnosis*	Sex	Age	Body wt	BSA	BP	Fundi	BUN	Serum osm.	ECF (S³⁵O₄ space)	Naₛ	Kₛ	Naₑ/ body wt	Kₑ/ body wt
			yrs	kg	m²	mm Hg	grade	mg %	mOsm/L	% body wt	mEq/L	mEq/L	mEq/kg	mEq/kg
J.W.	Pyelo.	M	50	78.9	1.95	205/125	III	33	296	16.0	140	5.0	39.6	34.7
V.C.	Pyelo.	F	43	53.6	1.51	185/125	II	13	287	13.0	139	3.9	32.4	40.8
A.G.	Pyelo.	F	32	68.6	1.73	170/110	II	16	283	13.8	141	4.4	39.4	32.4
G.A.	Pyelo.	F	46	70.0	1.81	180/115	I	21	287	12.5	143	3.9	37.5	32.7
B.R.	Pyelo.	F	38	63.6	1.72	255/180	II	17	292	12.2	134	3.6	30.6	34.6
G.R.	Polycyst.	M	24	87.6	2.10	150/110	II	14	287	13.0	139	3.9	32.4	40.8
M.C.	Polycyst.	F	45	65.8	1.61	195/135	II	23	283	16.2	141	4.3	42.9	32.8
M.M.	Neph.	F	28	60.1	1.71	200/125	II	13	288	15.6	144	4.0	33.1	31.0
G.T.	Neph.	M	46	82.0	1.95	175/115	III	20	288	15.4	140	4.8	35.9	49.1
A.G.	Neph.	F	55	73.1	1.73	195/125	II	20	289	14.1	143	4.0	31.0	30.9
						Control								
H.B.	Normal	M	52	80.3	1.95	115/80	0	11	287	15.0	141	4.4	39.8	39.1
M.M.	Normal	F	41	52.0	1.51	115/75	0	10	277	14.3	137	3.6	34.8	33.4
J.M.	Normal	F	34	70.9	1.76	120/80	0	10	280	13.8	140	3.9	36.3	38.2
N.R.	Normal	F	43	73.6	1.83	135/85	0	7	283	14.6	140	3.9	30.7	32.6
M.D.	Normal	F	33	66.4	1.76	105/65	0	12	279	15.9	138	5.3	38.0	35.0
H.G.	Normal	M	26	85.0	2.03	125/85	0	17	297	14.7	145	4.2	38.7	36.4
A.J.	Normal	F	43	66.3	1.65	100/65	0	8	288	16.1	143	3.8	37.8	34.7
F.W.	Normal	F	25	62.5	1.73	125/85	0	9	290	14.9	140	4.3	39.1	42.4
A.F.	Normal	M	49	81.8	1.91	125/75	0	13	297	16.5	146	4.8	37.7	38.3
T.M.	Normal	F	49	70.5	1.70	130/70	0	14	286	14.1	138	3.5	32.6	32.3

* Pyelo. =chronic pyelonephritis, bilateral. Polycyst. =polycystic kidney disease. Neph. =glomerulonephritis.

tricle with a prolonged decholin circulation time but without peripheral edema.

Radioactive sodium (Na^{24})[1] and radioactive potassium (K^{42})[1] were given orally in tracer doses of 80 and 125 μc respectively; 22 to 24 hours after the administration of the isotopes, serum and urine samples were obtained for the measurements of specific activity which were used for calculating exchangeable sodium (Na_e) and exchangeable potassium (K_e) (10, 11). Urine was also collected during the equilibration period for determination of sodium and potassium content and radioactivity excreted. After the first blood and urine samples were obtained, radiosulfate ($S^{35}O_4$)[2] in a dose of 50 μc was administered intravenously with a calibrated syringe. Twenty minutes after the injection, serum and urine were obtained for the determination of radiosulfate space (12).

For Na^{24} and K^{42} determinations, 4-ml aliquots of serum and urine were prepared in duplicate in Lusteroid test tubes and assayed in well-type sodium iodide and plastic phosphor[3] scintillation counters. By employing simultaneous equations the contribution of Na^{24} and K^{42} to the total activity of each sample was calculated (13). For $S^{35}O_4$ determinations, after the Na^{24} and K^{42} had decayed, serum proteins were precipitated with 10 per cent trichloroacetic acid and 1-ml aliquots of the supernatant were dried by infrared lamps in Pyrex planchets[4] with wafers of lens paper to ensure even distribution. Urine samples were similarly prepared without protein precipitation. S^{35} radioactivity was counted with a thin window Geiger-Mueller tube. Standards for the radiosulfate counting were made with an aliquot of the patient's serum obtained before radiosulfate administration to correct for the water content of the serum samples. Correction was made for the Gibbs-Donnan effect by multiplying the serum value by 0.9. Sodium and potassium were measured in urine and plasma with a lithium internal-standard flame photometer. Total solute concentration of the serum was determined by freezing point depression using a Fiske osmometer and sodium chloride standards of known osmolality. Results were expressed as serum osmolality without correcting for the contribution of serum proteins to the freezing point depression. Although serum water content was not directly determined, the "exchangeable" sodium and potassium values, calculated respectively from the specific activities of sodium and potassium in the serum and urine, were not significantly different.

Renal studies identical with those previously described (1) were also carried out in 5 of the patients with malignant hypertension. On the day of the test no medication was given. The subjects were studied in the morning in the postabsorptive state while lying supine. Urine was collected through an indwelling bladder

1 Kindly supplied by Dr. A. K. Solomon, Dept. of Biophysics, Harvard Medical School, Boston, Mass.

2 Obtained from Oak Ridge National Laboratory, Oak Ridge, Tenn.

3 Obtained from Baird-Atomic, Cambridge, Mass.

4 Obtained from Tracerlab, Boston, Mass.

TABLE III

Hypertension with mild heart failure *

Subject	Diagnosis	Sex	Age	Body wt	BSA	BP	VP	CT	Fundi	BUN	Serum osm.	ECF ($S^{35}O_4$ space) % body wt	Nas	Ks	Nae/ body wt	Ke/ body wt
			yrs	kg	m²	mm Hg	mm H₂O	sec	grade	mg %	mOsm/L	% body wt	mEq/L	mEq/L	mEq/kg	mEq/kg
R.C.	Es. hyp.	M	50	64.4	1.70	235/135	55	25	II	21	289	20.2	141	3.5	50.9	36.0
E.W.	Es. hyp.	F	44	50.0	1.47	230/135	75	30	II	19	285	26.1	142	3.5	51.0	34.0
E.H.	Es. hyp.	M	51	63.8	1.81	170/115	60	21	II	16	285	20.9	141	3.7	49.4	36.0
S.L.	Es. hyp.	F	48	39.5	1.35	245/145	85	23	II	19	271	20.2	134	4.0	45.0	35.6
R.W.	Pyelo.	M	63	88.6	2.11	185/125	75	28	III	30	303	16.8	142	3.7	46.8	31.5
M.S.	Pyelo.	F	55	45.7	1.40	255/135	155	31	III	90	325	18.1	142	5.0	50.5	34.4
E.G.	Neph.	M	58	61.4	1.72	230/130	100	26	II	20	280	17.0	139	4.0	51.5	34.7
							Control									
E.H.	Normal	M	48	66.6	1.75	125/80	60	12	0	19	289	14.0	140	4.3	42.0	40.5
S.R.	Normal	F	45	49.5	1.50	125/75	60	14	0	17	289	17.0	140	4.2	36.7	43.2
J.W.	Normal	M	49	65.9	1.81	115/75	45	10	0	11	293	16.2	140	3.7	42.6	34.2
A.L.	Normal	F	50	37.5	1.31	115/75	50	16	0	12	287	15.1	138	3.9	39.0	40.4
S.P.	Normal	M	62	85.0	1.95	125/80	85	17	0	14	288	16.5	140	4.4	35.6	32.8
M.A.	Normal	F	60	42.0	1.38	100/60	60	13	0	10	285	14.2	139	4.3	41.4	36.6
I.F.	Normal	M	54	61.4	1.71	130/75	70	15	0	14	291	15.3	142	4.6	44.6	39.8

* VP = venous pressure. CT = circulation time (decholin). Es. hyp. = essential hypertension. Pyelo. = chronic pyelonephritis, bilateral. Neph. = glomerulonephritis, subacute.

TABLE IV

Malignant hypertension *

Subject	Diagnosis	Sex	Age	Body wt	BSA	BP	VP	CT	Fundi	BUN	Serum osm.	ECF ($S^{34}O_4$ space)	Na_s	K_s	Na_e/body wt	K_e/body wt
			yrs	*kg*	*m²*	*mm Hg*	*mm H₂O*	*sec*	*grade*	*mg%*	*mOsm/L*	*% body wt*	*mEq/L*	*mEq/L*	*mEq/kg*	*mEq/kg*
M.D.	Ren. art. occl.	F	55	46.8	1.44	245/150	55	21	IV	22	285	21.1	139	3.4	48.5	35.1
J.H.	Es. hyp.	F	28	60.5	1.69	195/135	75	28	IV	44	294	22.6	140	3.3	53.1	38.8
D.D.	Es. hyp.	M	35	85.4	2.00	210/145	75	27	IV	27	303	20.7	138	5.0	51.0	42.3
R.N.	Es. hyp.	M	50	78.7	2.00	215/130	65	15	IV	22	320	16.6	144	4.2	32.9	30.2
I.M.	Neph.	F	34	85.9	2.04	240/150	40	16	IV	45	301	11.6	141	4.2	36.6	28.0
A.M.	Neph.	F	40	51.5	1.49	205/125	145	30	IV	20	293	24.1	140	4.8	67.0	29.9
E.H.	Pyelo.	M	40	75.3	2.02	210/135	45	18	IV	46	310	18.9	143	5.0	47.0	37.1
L.S.	Pyelo.	F	28	41.4	1.38	230/140	50	19	IV	35	345	14.0	142	4.4	42.9	43.3
R.M.	Pyelo.	M	45	69.8	1.73	205/135	70	25	IV	51	321	21.0	137	3.5	49.5	43.7
D.C.	Pyelo.	M	55	76.5	1.82	255/145	60	15	IV	20	288	14.2	143	4.7	38.3	34.2
							Control									
R.T.	Normal	F	56	47.2	1.50	115/75	50	13	0	17	288	16.0	142	4.4	36.9	43.1
F.W.	Normal	F	25	62.5	1.73	125/85	55	16	0	9	290	14.9	140	4.3	39.1	42.4
T.M.	Normal	M	33	88.2	2.06	120/75	30	14	0	17	287	13.5	145	4.5	35.2	42.9
H.D.	Normal	M	52	80.3	1.95	115/80	45	13	0	11	287	15.0	141	4.4	39.8	39.1
M.E.	Normal	F	37	86.8	2.00	130/75	60	12	0	8	283	15.3	139	4.2	29.5	28.8
M.M.	Normal	F	41	52.0	1.51	115/75	75	11	0	10	277	14.3	137	3.6	34.8	33.4
H.T.	Normal	M	36	74.5	1.97	120/75	65	18	0	13	290	14.8	144	4.5	42.8	40.0
A.A.	Normal	F	32	39.9	1.41	105/65	65	15	0	12	289	14.4	140	4.7	41.3	42.0
E.H.	Normal	M	48	66.6	1.75	125/80	60	12	0	19	289	14.0	140	4.3	42.0	40.5
S.D.	Normal	M	53	75.0	1.85	115/65	55	10	0	15	285	16.1	142	4.4	39.6	38.1

* Ren. art. occl. = renal artery occlusion.   Neph. = glomerulonephritis, subacute.   Pyelo. = chronic pyelonephritis, bilateral.

TABLE V

Sodium excretion in malignant hypertension

Subject	Procedure	C_{PAH}	C_{IN}	V	$U_{Na}V$	U_KV
		ml/min/1.73 m^2		*ml/min*	*μEq/min*	
M.D.	Control	261	95	7.5	111	38
	5% NaCl (300 ml i.v.)	353	115	9.9	850	107
	Recovery	310	101	5.3	855	86
D.D.	Control	225	60	3.8	322	70
	5% NaCl (300 ml i.v.)	265	75	14.6	1,581	105
	Recovery	247	62	7.5	1,467	74
R.N.	Control	255	71	2.9	235	91
	5% NaCl (300 ml i.v.)	290	78	8.9	1,161	129
	Recovery	289	80	8.0	1,297	144
A.M.	Control	374	73	2.4	236	84
	5% NaCl (300 ml i.v.)	550	83	6.0	746	127
	Recovery	522	92	7.5	1,117	128
D.C.	Control	305	81	5.4	301	75
	5% NaCl (300 ml i.v.)	333	85	5.3	706	68
	Recovery	357	87	5.9	1,131	76

catheter. Following the "control" period which consisted of 3 to 4 urine collection periods of 10 to 15 minutes each, 300 ml of 5 per cent sodium chloride was administered intravenously at the rate of 10 to 12 ml per minute. At the end of the infusion a urine collection designated as "5 per cent NaCl" was made. Thereafter at least 3 additional urine collections were obtained in the "recovery" period at intervals of 15 minutes. The measurements of para-aminohippuric acid and inulin clearances, and concentrations of sodium and potassium in the urine and serum were made by methods previously reported (1).

RESULTS

The measurements of body fluid and electrolytes in hypertensive and control subjects are summarized in Tables I to V. The statistical analyses of these findings are given in Table VI.

Essential hypertension. Exchangeable sodium per kilogram of weight and the radiosulfate space expressed as percentage of body weight were not significantly different in the hypertensive and control groups. Although serum sodium and blood urea nitrogen were slightly but significantly elevated in the hypertensive as compared with the control group, serum osmolality was not significantly different in the two groups. Intracellular and extracellular exchangeable sodium, as calculated from the radiosulfate spaces and serum sodium values, also did not show a significant difference in the groups (p > 0.4). Serum potassium and total exchangeable potassium per kilogram of

weight were not significantly different in the hypertensive and control groups.

Hypertension associated with bilateral renal disease. Serum sodium, serum osmolality, radiosulfate space and exchangeable sodium in the "renal hypertensive group" were not significantly different from the values obtained in the control group. Exchangeable potassium and serum potassium were also comparable in the groups.

Hypertension complicated by mild heart failure. Exchangeable sodium and radiosulfate spaces were significantly higher in the seven hypertensive subjects who had mild heart failure without clinically detectable peripheral edema than in the control group. The increase in exchangeable sodium averaged 9 mEq per kg weight or 22 per cent of the values in the control group, whereas the mean increase in the $S^{35}O_4$ space was 4.4 per cent of body weight, or 29 per cent of control values. However, serum sodium and osmolality did not differ significantly in the two groups. The mean serum potassium and exchangeable potassium were slightly reduced as compared with the control values. These differences in serum potassium were not statistically significant, but those in exchangeable potassium were significant at the 5 per cent level.

Malignant hypertension. The group with malignant hypertension as compared with the control group had significant elevations of exchangeable

TABLE VI

Mean data and statistical analyses

	Age (yrs)	Body wt (kg)	BSA (m²)	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	BUN (mg %)	Serum osm. (mOsm/L)	ECF (S³⁵O₄ space) (% body wt)	Na_s (mEq/L)	K_s (mEq/L)	Na_e/body wt (mEq/kg)	K_e/body wt (mEq/kg)
Control	45.9 ± 2.0*	74.7 ± 3.1	1.83 ± 0.04	120 ± 3	75 ± 2	12.8 ± 0.8	286 ± 1.0	14.7 ± 0.3	140 ± 0.6	4.2 ± 0.1	36.2 ± 0.9	36.1 ± 1.4
Es. hyp.	45.6 ± 1.9	74.9 ± 3.0	1.82 ± 0.04	202 ± 6	121 ± 3	15.2 ± 0.8	289 ± 1.2	14.1 ± 0.2	142 ± 0.6	4.1 ± 0.1	37.1 ± 1.1	35.1 ± 1.5
Mean difference	+0.3 ± 2.7	+0.2 ± 4.3	−0.01 ± 0.1	+82 ± 7	+46 ± 12	+2.4 ± 1.1	+3 ± 1.6	−0.6 ± 0.4	+2 ± 0.8	−0.1	+0.9	−1.0 ± 2.1
P	>0.9	>0.9	>0.9	<0.01	<0.01	0.04	0.1	0.2	0.04	0.1	0.5	0.6
Control	39.5 ± 3.0	70.9 ± 3.1	1.78 ± 0.1	120 ± 3	76 ± 2	11.1 ± 0.9	286 ± 2	15.0 ± 0.3	141 ± 1	4.1 ± 0.1	36.6 ± 0.9	36.2 ± 1.0
Renal hyp.	40.7 ± 3.2	70.3 ± 3.3	1.78 ± 0.1	191 ± 9	126 ± 6	19.0 ± 1.9	288 ± 1	14.3 ± 0.5	141 ± 1	4.2 ± 0.1	35.8 ± 1.3	36.0 ± 1.8
Mean difference	+1.2 ± 4.4	−0.6 ± 4.5	0 ± 0.1	+71 ± 9	+50 ± 7	+7.9	+2 ± 0.5	−0.7 ± 0.5	0	+0.1 ± 0.2	−0.8 ± 1.6	−0.3 ± 2.1
P	0.8	0.9	0.9	<0.01	<0.01	<0.01		0.2	>0.9	0.6	0.6	>0.9
Control	52.6 ± 2.4	58.3 ± 6.2	1.63 ± 0.1	119 ± 4	74 ± 4	13.8 ± 1.2	289 ± 1	15.5 ± 0.4	140 ± 1	4.2 ± 0.1	40.3 ± 1.2	38.2 ± 1.4
Hyp. & C.H.F.†	52.7 ± 2.4	59.1 ± 6.1	1.65 ± 0.1	221 ± 12	131 ± 4	30.7 ± 10.0	291 ± 7	19.9 ± 1.2	140 ± 1	3.9 ± 0.2	49.3 ± 0.9	34.6 ± 0.6
Mean difference	+0.1 ± 3.4	+0.8 ± 8.7	+0.02	+102 ± 12	+57 ± 5	+16.9 ± 10	+2 ± 7	+4.4 ± 1.3	0	−0.3 ± 0.2	9.0 ± 1.5	−3.6 ± 1.5
P	>0.9	>0.9	0.9	<0.01	<0.01	0.1	0.7	<0.01	>0.9	0.2	<0.01	0.04
Control	41.3 ± 3.3	67.3 ± 5.3	1.77 ± 0.1	118 ± 6	75 ± 3	13.1 ± 1.2	286 ± 6	14.8 ± 1.3	141 ± 0.7	4.3 ± 0.2	38.1 ± 1.3	39.0 ± 1.5
Malig. hyp.	41.0 ± 3.2	67.2 ± 5.1	1.76 ± 0.1	221 ± 6	139 ± 3	33.2 ± 3.9	306 ± 6	18.5 ± 1.3	141 ± 1.0	4.2 ± 0.2	46.7 ± 3.1	35.4 ± 1.6
Mean difference	−0.3 ± 4.6	−0.1 ± 7.3	−0.01 ± 0.9	+102 ± 7	+64 ± 3	+20.1 ± 4.1	+20 ± 6	+3.7 ± 1.3	0	−0.1 ± 0.2	+8.6 ± 3.3	−3.6 ± 2.2
P	>0.9	>0.9	>0.9	<0.01	<0.01	<0.01	<0.01	0.02	0.8	0.7	0.02	0.1

* Standard error.
† Hyp. & C.H.F. =hypertension with complicating congestive heart failure. Malig. hyp. =malignant hypertension.

sodium per kilogram of weight and of radiosulfate space expressed as percentage of body weight. The increases in the exchangeable sodium and the radiosulfate spaces were comparable and averaged 22 and 25 per cent above control values. These changes did not occur consistently in the group but appeared to occur only when there was also a prolonged decholin circulation time. Serum sodium was comparable in the normotensive and hypertensive groups, whereas serum osmolality was significantly elevated in the hypertensive group in association with nitrogen retention. Neither serum potassium nor exchangeable potassium was significantly different in the groups, although the mean exchangeable potassium was lower in the hypertensive than in the control group by 3.6 mEq per kg of weight.

An impairment in sodium excretory capacity, as indicated by the rate of sodium excretion following a rapid infusion of 300 ml of 5 per cent sodium chloride (Table V), was not demonstrable in five subjects with malignant hypertension, including three who had prolonged circulation times and increases in exchangeable sodium and extracellular fluid volume. The rate of sodium and potassium excretion in these five subjects was similar to that previously reported in uncomplicated hypertensive subjects and considerably higher than that found in normotensive subjects (1).

DISCUSSION

A number of conflicting reports have appeared concerning body fluid and electrolyte composition in arterial hypertension. Grollman and Shapiro have reported a slight but significant increase in the radiosulfate space in essential hypertension (14). In addition to an expanded extracellular fluid space, Ross has observed an increase in total exchangeable sodium in hypertensive subjects (15). In contrast to these observations, some other workers have found extracellular fluid volume and exchangeable sodium to be normal in arterial hypertension (16, 17). The current results suggest that the apparent discrepancies in these reports might be due to differences in selection and classification of the hypertensive subjects.

In the present study exchangeable sodium and extracellular fluid volume were not found to be significantly elevated in uncomplicated essential hy-

pertension. Exchangeable potassium also was not significantly altered in this form of hypertension. The latter finding is in sharp contrast to the marked reduction in exchangable potassium found in hypertension associated with primary aldosteronism (9). Hypertension associated with renal disease also appeared to be characterized by a normal body sodium, potassium and radiosulfate space. These observations indicate that the increased capacity of hypertensive subjects to excrete sodium is not due to an expanded extracellular fluid volume nor to an increase in body sodium as was previously considered (1, 2).

In contrast to uncomplicated hypertension, hypertension complicated by congestive heart failure was accompanied by an increase in both exchangeable sodium and radiosulfate space. These changes in body sodium and fluid volume were not clinically detectable in the early stages of heart failure, since they occurred without peripheral edema or weight gain during an unrestricted dietary salt intake. An elevated radiosulfate space has likewise been observed by Walser, Duffy and Griffin in mild heart failure without peripheral edema (16). The present and previous studies indicate that these alterations in body composition may also occur without a demonstrable impairment in sodium excretory capacity (18–20). In view of these observations it is possible that the increases in body sodium and extracellular fluid volume found by Ross in a group of subjects with severe hypertension might have been due to complicating subclinical heart failure.

An increase in body sodium and extracellular fluid volume also occurred in the malignant phase of hypertension without clinically detectable edema or an impairment in sodium excretory capacity. Since this accelerated form of hypertension was frequently complicated by severe vascular disease as well as by heart failure, it is not entirely clear whether the changes in body sodium and fluid volume were related to the hypertension itself or to the complications of the disease. However, it appears that body sodium may remain normal at the onset of malignant hypertension but may increase as the hypertension becomes complicated by severe cardiovascular disease, especially congestive heart failure. Complicating heart failure, which sometimes is clinically difficult to recognize in its early stages, may also account for the marked increase in aldosterone activity reported in severe and malignant cases of hypertension (5, 6). It is unlikely, however, that an augmented aldosterone activity per se is responsible for the changes in body fluids and electrolytes in malignant hypertension and congestive heart failure, since salt and water retention is usually greater whereas potassium depletion is considerably less in these conditions than in primary aldosteronism.

CONCLUSIONS

1. In uncomplicated essential and renal hypertension, exchangeable sodium (Na^{24} space), exchangeable potassium (K^{42} space), extracellular fluid volume ($S^{35}O_4$ space), and serum osmolality were not significantly different from the values obtained in control subjects.

2. In hypertension complicated by heart failure, even of a mild degree without clinically detectable peripheral edema, exchangeable sodium and radiosulfate space were significantly elevated, whereas exchangeable potassium was slightly reduced.

3. In malignant hypertension, exchangeable sodium and radiosulfate space were also significantly increased while exchangeable potassium was slightly reduced.

4. These body fluid and electrolyte patterns are significantly different from those found in the hypertension associated with primary aldosteronism.

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