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Research Article

ELECTROLYTE AND WATER EXCRETION IN ARTERIAL HYPERTENSION. I. STUDIES IN NON-MEDICALLY TREATED SUBJECTS WITH ESSENTIAL HYPERTENSION [1]

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In a preliminary investigation it was reported that abnormally high rates of sodium excretion followed the infusion of hypertonic saline in untreated patients with essential hypertension (1). Furthermore, it was noted that several oral drugs commonly employed in the treatment of hypertension usually modified this pattern of renal sodium excretion. The present report describes further work on sodium excretion in hypertensive patients and in general agrees with previous reports of other authors (2, 3). In addition, it describes studies made in an attempt to clarify the disturbance of sodium excretion in hypertension and its relationship to renal function, renal hemodynamics, salt intake, and splanchnic sympathetic activity.

MATERIAL AND METHODS

The eight normotensive subjects in Group I had no history of hypertension and were considered normal with the exception of D. R. who had bronchial asthma in remission at the time of the study, and M. G. who had asymptomatic chronic pyelonephritis.

The nine subjects in Group II were known to have essential hypertension for at least five years. They were all compensated and had no history of congestive heart failure. However, five subjects in Group II had hypertensive heart disease, with an enlarged left ventricle as indicated by the electrocardiogram and chest roentgenogram.

The eight subjects in Group III, who also had essential hypertension without cardiac decompensation, had been surgically treated more than two years before the study with a bilateral thoracolumbar sympathectomy. Patient T. S., in addition, had had a total bilateral adrenalectomy for malignant hypertension. Four patients of the group had definite hypertensive heart disease.

Dietary intake of salt was not restricted. All hypertensive patients had been without antihypertensive drug treatment for at least three months prior to the study. The average surface areas of patients in the three groups were comparable.

All subjects were studied without sedative medication in the morning, in the post-absorptive state while lying supine. Throughout the study the subjects drank 100 ml. of water every half-hour. Urine was collected through an indwelling bladder (Foley) catheter. At the end of each collection the bladder was washed out with 20 ml. of distilled water and was then completely evacuated with air. After standard priming doses, a sustaining infusion containing inulin (3.3 per cent) and para-aminohippurate (1 per cent) in 3.5 per cent glucose in water was started and given at the rate of 1.2 ml. per minute by means of calibrated drip. Every 20 minutes arterial blood samples were obtained for the determination of inulin, para-aminohippuric acid, sodium, potassium and hematocrit. Following the control period which consisted of three to four urine collections, each one being for 10 to 15 minutes, 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 three urine collections were obtained in the "recovery" period at intervals of 15 minutes. In a few subjects following the "recovery" period, Pitressin® was injected intravenously in a single dose of 40 to 100 milliunits. After the injection three more urine collections were made in the "Pitressin®" period at intervals of 15 minutes.

Blood and urine concentrations of para-aminohippuric acid were measured by the method of Goldring and Chasis (4), and inulin was determined by the method of Roe, Epstein, and Goldstein (5). Serum and urinary sodium and potassium were determined by the internal standard flame photometer (lithium standard). The hematocrit was determined in Wintrobe tubes. Measurements of brachial arterial pressure were obtained with an electromanometer (Sanborn) and recorded by direct-writing oscillograph.

RESULTS

The renal responses to intravenous 5 per cent sodium chloride in the normotensive and hypertensive groups are summarized in Table I. The

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statistical analysis of the responses are given in Table II.

PAH clearance (renal plasma flow)

The control renal plasma flows in the hypertensive groups were not significantly different from those in the normotensive group. All three groups had significant increases in renal plasma flow during the infusion of 5 per cent sodium chloride. In only the non-splanchnicectomized hypertensive group were the increases significantly prolonged into the recovery period. Otherwise the changes in renal plasma flow during and following the saline infusion were not significantly different in the three groups.

Inulin clearance (glomerular filtration rate)

The glomerular filtration rates at rest did not differ significantly between the hypertensive and normotensive groups. During and following the saline infusion, the splanchnicectomized hypertensive group like the normotensive group had no significant increases in glomerular filtration rate although the *untreated* hypertensive group had small but significant increases in this function. Otherwise, the changes in glomerular filtration rate caused by the hypertonic saline were not significantly different in the groups.

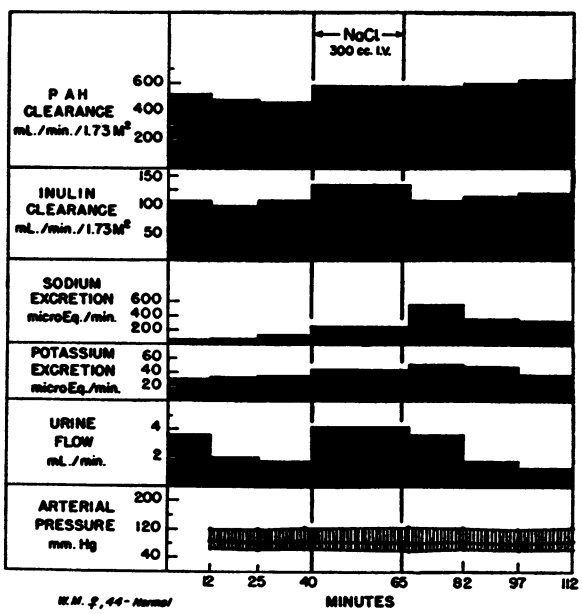

FIG. 1. RENAL RESPONSES TO INTRAVENOUS HYPERTONIC SALINE IN A NORMOTENSIVE INDIVIDUAL

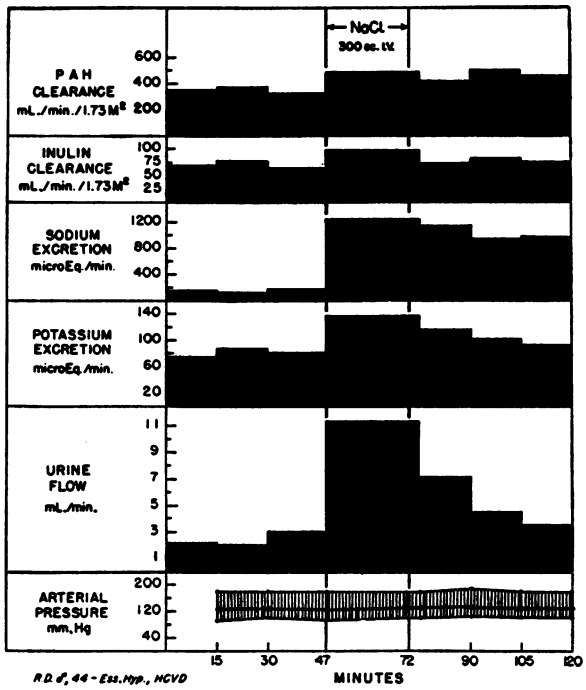

FIG. 2. RENAL RESPONSES TO INTRAVENOUS HYPERTONIC SALINE IN A SUBJECT WITH ESSENTIAL HYPERTENSION

Sodium excretion

The control sodium excretion in the untreated hypertensive group but not in the splanchnicectomized hypertensive group was significantly higher than in the normotensive group. Although all three groups showed significant increases in sodium excretion during and following the infusion of 5 per cent sodium chloride, the increases were significantly greater in the hypertensive groups than in the normotensive group (Figures 1, 2 and 3). Included in the splanchnicectomized hypertensive group was an adrenalectomized subject who also had an abnormally high rate of sodium excretion after the saline infusion (Figure 4). The mean increase in sodium excretion in the splanchnicectomized hypertensive group was not as great as in the non-splanchnicectomized hypertensive group.

Ratio of excreted sodium to filtered sodium (E/F sodium)

The calculated ratio of excreted sodium to filtered sodium (E/F sodium) both before and after

TABLE I

Renal excretion of hypertonic saline in normotensive individuals (Group I)

Patient Age	Sex	Diagnosis‡	Procedure	C_{PAH}	C_{IN}	UV	$U_{Na}V$	$U_{K}V$	$\frac{E}{F}$ Na*	$\frac{E}{F}$ K†	Hematocrit (arterial)
				ml./min./ 1.73 M.²	*ml./min./ 1.73 M.²*	*ml./min.*	*MicroEq./ min.*	*MicroEq./ min.*	%	%	%
V. B. 31	F	Normal	Control	447	90	2.9	155	90	1.2	25.6	42.0
			5% NaCl	519	97	2.7	260	88	1.8	22.0	38.0
			Recovery	572	90	1.5	366	81	2.7	23.7	38.4
J. M. 27	F	Normal	Control		106	3.4	84	233	0.5		42.5
			5% NaCl		100	2.0	184	158	1.2		37.8
			Recovery		106	1.5	243	223	1.5		38.2
D. R. 52	M	Bronchial asthma	Control	347	96	6.9	188	58	1.4	13.4	54.9
			5% NaCl	407	123	7.6	391	78	2.2	14.1	50.1
			Recovery	367	126	1.7	328	41	1.8	7.2	51.9
W. P. 32	F	Normal	Control	498	98	2.0	213	65	1.6	15.9	42.2
			5% NaCl	561	109	2.8	526	54	3.4	13.3	
			Recovery	504	100	4.1	599	40	4.4	10.0	38.4
W. M. 44	F	Normal	Control	481	102	2.5	98	33	0.7	8.1	36.3
			5% NaCl	575	130	4.2	244	43	1.3	8.5	32.3
			Recovery	598	112	2.3	425	46		10.5	33.9
J. K. 47	M	Normal	Control	505	98	6.3	60	84	0.5	24.6	46.0
			5% NaCl	579	99	7.9	218	94	1.5	26.4	41.5
			Recovery	451	94	1.1	376	61	1.1	21.3	41.7
M. G. 62	F	Chronic pyelonephritis	Control	182	54	2.6	81	43	1.6	18.1	48.4
			5% NaCl	211	57	3.3	319	60	3.9	23.9	43.0
			Recovery	234	56	1.8	306	59	3.8	24.0	44.4
C. J. 38	F	Normal	Control	632	101	11.3	101	90	0.7	22.6	42.7
			5% NaCl	598	91	12.5	168	52			
			Recovery	623	102	1.3	275	41	1.1	10.0	40.6
Renal excretion of hypertonic saline in individuals with essential hypertension (Group II)											
K. B. 35	M	Ess. hyp.	Control	565	126	6.3	617	145	3.5	23.0	46.5
			5% NaCl	744	130	12.8	2,290	137	12.1	20.3	42.6
			Recovery	789	135	7.7	1,561	152	7.9	21.6	43.2
R. D. 44	M	Ess. hyp. H.C.V.D.	Control	351	73	2.6	152	87	1.4	30.0	44.3
			5% NaCl	484	99	11.4	1,258	137	8.7	38.5	40.2
			Recovery	462	79	5.0	1,014	114	8.8	36.1	39.9
D. C. 36	F	Ess. hyp. H.C.V.D.	Control	309	81	12.4	601	77	5.5	23.8	40.3
			5% NaCl	303	80	10.5	706	68	6.2	21.3	34.9
			Recovery	355	85	5.9	1,131	76	9.5	22.3	37.4
D. F. 45	F	Ess. hyp.	Control	390	91	4.7	723	74	5.6	21.4	39.6
			5% NaCl	530	108	8.0	1,202	91	7.2	22.2	35.5
			Recovery	468	96	7.7	1,661	91	11.5	24.9	37.5

* $\frac{E}{F}$ Na = $\frac{\text{sodium excreted}}{\text{sodium filtered}}$.

† $\frac{E}{F}$ K = $\frac{\text{potassium excreted}}{\text{potassium filtered}}$.

‡ Ess. hyp. = Essential hypertension.

H.C.V.D. = Hypertensive cardiovascular disease.

§ Previously adrenalectomized.

TABLE I—*Continued*

Patient Age	Sex	Diagnosis‡	Procedure	C_{PAH}	C_{IN}	UV	$U_{Na}V$	$U_{K}V$	$\frac{E}{F}$ Na*	$\frac{E}{F}$ K†	Hematocrit (arterial)
				ml./min./ 1.73 M²	*ml./min./ 1.73 M²*	*ml./min.*	*MicroEq./ min.*	*MicroEq./ min.*	%	%	%
I. P.			Control	467	131	4.8	765	104	4.5	22.6	43.3
42	M	Ess. hyp.	5% NaCl	659	142	13.0	2,387	211	11.3	42.4	39.8
		H.C.V.D.	Recovery	624	133	12.2	2,364	163	12.1	35.8	41.0
C. C.			Control	458	106	8.0	250	78	1.6	17.4	38.3
48	F	Ess. hyp.	5% NaCl	643	128	8.2	1,340	143	7.0	28.5	
		H.C.V.D.	Recovery	625	132	9.3	1,726	128	8.7	22.4	38.0
R. O.			Control	322	79	9.1	141	121	1.2	40.3	40.1
50	M	Ess. hyp.	5% NaCl	338	79	8.0	975	139	8.0	51.7	37.8
		H.C.V.D.	Recovery	320	85	4.1	802	80	6.5	26.1	
W. M.			Control	443	127	8.4	216	153	1.2	31.6	46.1
40	M	Ess. hyp.	5% NaCl	518	148	9.6	686	229	3.1	38.7	44.3
			Recovery	464	131	8.6	1,276	214	6.8		
			Pitressin® 40 milliunits	494	131	7.4	1,032	299	5.4	50.7	44.7
J. W.			Control		60	3.9	522	72	6.2	30.0	39.5
50	M	Ess. hyp.	5% NaCl		78	14.5	1,682	106	14.5	35.9	37.4
		H.C.V.D.	Recovery		60	7.3	1,467	74	16.5	30.9	
			Pitressin® 80 milliunits		68	10.9	1,711	98	17.2	28.7	38.4
Renal excretion of hypertonic saline in splanchnicectomized individuals with essential hypertension (Group III)											
V. V.			Control	537	118	1.9	176	57	1.5	12.1	39.4
37	F	Ess. hyp.	5% NaCl	756	138	6.7	1,013	85	4.9	15.4	36.8
		H.C.V.D.	Recovery	760	129	5.1	1,092	70	5.7	13.6	37.7
I. R.			Control	402	103	1.5	137	119	0.9	23.1	44.3
49	M	Ess. hyp.	5% NaCl	457	120	5.6	754	182	4.2	30.3	41.6
		H.C.V.D.	Recovery	451	118	5.3	867	147	5.1	25.0	41.7
A. G.			Control	527	100	7.8	599	50	4.4	12.5	36.5
36	F	Ess. hyp.	5% NaCl	567	106	17.0	1,530	60	10.0	13.8	34.6
			Recovery	471	89	6.7	1,270	52	10.0	13.9	
T. S.§			Control	108	28	2.5	292	37	7.3	25.5	49.0
49	M	Ess. hyp.	5% NaCl	160	40	7.2	948	74	16.5	43.0	46.2
		H.C.V.D.	Recovery	110	33	6.1	867	64	18.7	42.1	46.8
A. L.			Control	425	119	12.7	1,164	82	6.9	18.7	44.9
60	M	Ess. hyp.	5% NaCl	381	103	14.3	1,758	87	11.4	26.4	41.8
		H.C.V.D.	Recovery	438	115	8.8	1,614	79	10.0	20.3	
			Pitressin® 40 milliunits	450	119	7.4	1,402	98	2.6		43.4
N. K.			Control	374	72	2.4	262	81	2.5	28.8	52.7
49	F	Ess. hyp.	5% NaCl	550	83	6.0	746	127	5.9	40.3	49.0
		H.C.V.D.	Recovery	508	87	7.8	1,051	125	8.1	36.8	
			Pitressin® 100 milliunits	537	97	8.0	1,182	130	8.1	31.3	49.1
R. T.			Control	332	84	1.5	209	87	1.8	20.7	42.1
40	M	Ess. hyp.	5% NaCl	441	97	4.8	871	114	6.2	23.5	38.2
			Recovery	455	97	6.2	1,205	107	8.5	22.6	41.0
N. I.			Control	322	83	5.2	39	32	0.3	8.8	47.5
58	M	Ess. hyp.	5% NaCl	395	78	5.1	848	74	7.5	21.1	44.0
			Recovery	407	96	5.9	913	77	6.6	17.9	44.8

TABLE II

Mean data and statistical analysis

	Control	5% NaCl	5% NaCl − Control	p	Recovery	Recovery − Control	p
			PAH clearance *ml./min./1.73M.²*				
Normotensive group	442 ± 54	493 ± 53	+51 ± 16	0.02	478 ± 53	+37 ± 25	0.2
Hypertensive group	413 ± 31	527 ± 54	+114 ± 27	<0.01	513 ± 55	+100 ± 28	<0.01
Mean difference*	−29 ± 62	+34 ± 76	+63 ± 32		+35 ± 76	+63 ± 37	
p	0.6	0.7	0.07		0.6	0.1	
Splanchnicectomized hypertensive group	378 ± 48	463 ± 61	+85 ± 29	0.02	450 ± 62	+72 ± 31	0.06
Mean difference*	−63 ± 72	−29 ± 81	+34 ± 33		−28 ± 82	+35 ± 40	
p	0.4	0.7	0.3		0.7	0.4	
			Inulin clearance *ml./min./1.73M.²*				
Normotensive group	93 ± 6	101 ± 8	+8 ± 5	0.2	98 ± 7	+5 ± 4	0.2
Hypertensive group	97 ± 9	110 ± 9	+13 ± 3	<0.01	104 ± 10	+7 ± 2	0.03
Mean difference*	+4 ± 10	+9 ± 12	+5 ± 6		+6 ± 12	+2 ± 4	
p	0.7	0.4	0.3		0.6	0.7	
Splanchnicectomized hypertensive group	88 ± 10	95 ± 10	+7 ± 4	0.1	95 ± 10	+7 ± 3	0.08
Mean difference*	−5 ± 12	−5 ± 13	0 ± 6		−3 ± 13	+2 ± 5	
p	0.7	0.7	>0.9		0.8	0.7	
			$U_{Na}V$ *MicroEq./min.*				
Normotensive group	123 ± 20	289 ± 42	+166 ± 29	<0.01	365 ± 39	+242 ± 32	<0.01
Hypertensive group	443 ± 84	1391 ± 207	+948 ± 176	<0.01	1444 ± 154	+1001 ± 115	<0.01
Mean difference*	+320 ± 86	+1103 ± 211	+782 ± 179		+1080 ± 159	+759 ± 119	
p	<0.01	<0.01	<0.01		<0.01	<0.01	
Splanchnicectomized hypertensive group	360 ± 129	1058 ± 133	+699 ± 52	0.01	1110 ± 89	+750 ± 64	<0.01
Mean difference*	+237 ± 130	+770 ± 140	+532 ± 60		+745 ± 98	+508 ± 72	
p	0.09	0.01	0.01		0.01	0.01	
			$U_{K}V$ *MicroEq./min.*				
Normotensive group	87 ± 22	78 ± 13	−9 ± 11	0.5	74 ± 22	−13 ± 7	0.1
Hypertensive group	101 ± 10	140 ± 17	+39 ± 13	0.02	121 ± 16	+20 ± 11	0.1
Mean difference*	+14 ± 24	+62 ± 22	+48 ± 17		+47 ± 27	+33 ± 13	
p	0.6	0.01	0.02		0.1	0.03	
Splanchnicectomized hypertensive group	68 ± 10	100 ± 14	+32 ± 7	<0.01	90 ± 12	+22 ± 6	<0.01
Mean difference*	−19 ± 24	+22 ± 19	+41 ± 13		+16 ± 25	+35 ± 10	
p	0.4	0.3	<0.01		0.5	0.01	
			UV *ml./min.*				
Normotensive group	4.7 ± 1.1	5.4 ± 1.3	+0.6 ± 0.4	0.1	1.9 ± 0.3	−2.8 ± 1.3	0.08
Hypertensive group	6.7 ± 1.0	10.7 ± 0.8	+4.0 ± 1.6	0.03	7.5 ± 0.8	+0.8 ± 1.4	0.6
Mean difference*	+2.0 ± 1.5	+5.3 ± 1.5	+3.4 ± 1.6		+5.6 ± 0.9	+3.6 ± 2.0	
p	0.2	<0.01	0.05		<0.01	0.08	
Splanchnicectomized hypertensive group	4.4 ± 1.4	8.3 ± 1.6	+3.9 ± 1.0	<0.01	6.5 ± 0.4	+2.0 ± 1.1	0.1
Mean difference*	−0.3 ± 1.8	+2.9 ± 2.1	+3.3 ± 1.0		+4.6 ± 0.6	+4.9 ± 1.8	
p	0.9	0.2	<0.01		<0.01	0.02	
			Mean arterial pressure *mm. Hg*				
Normotensive group	87 ± 2	89 ± 3	+2 ± 3	0.6	89 ± 2	+2 ± 2	0.4
Hypertensive group	144 ± 5	144 ± 5	0 ± 2	>0.9	144 ± 5	0 ± 1	>0.9
Mean difference*	+57 ± 6	+55 ± 6	−2 ± 4		+55 ± 5	−2 ± 2	
p	<0.01	<0.01	0.6		<0.01	0.5	
Splanchnicectomized hypertensive group	152 ± 11	156 ± 12	+3 ± 3	0.3	151 ± 11	−1 ± 2	0.6
Mean difference*	+66 ± 11	+67 ± 12	+1 ± 4		+62 ± 11	−3 ± 3	
p	<0.01	<0.01	0.8		<0.01	0.3	

* Refers to the difference between the normotensive and the designated hypertensive group.

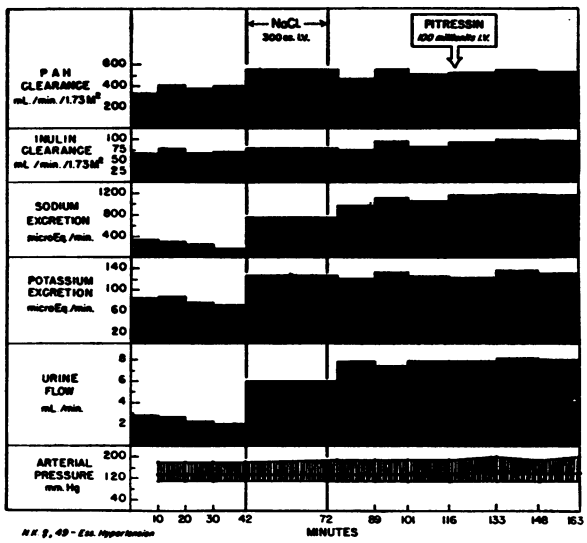

FIG. 3. RENAL RESPONSES TO INTRAVENOUS HYPERTONIC SALINE IN SPLANCHNICECTOMIZED HYPERTENSIVE SUBJECT

the infusion of saline was significantly higher in the hypertensive groups than in the normotensive group. The increases in this ratio after the infusion, which were significant in all groups, were likewise significantly greater in the hypertensive groups than in the normotensive group.

Correlations of sodium excretion

In analyzing the groups all together (Table III), sodium excretion before and after the saline infusion was significantly correlated (statistically) with the control arterial pressure. Increases in sodium excretion following intravenous 5 per cent sodium chloride were likewise significantly correlated with changes in renal plasma flow but not with changes in glomerular filtration rate, however. They were not significantly correlated with the control renal plasma flow or with the control glomerular filtration rate.

In analyzing the small groups separately, the control sodium excretion did not show a significant statistical correlation with the control arterial pressure. Increases in sodium excretion produced by the saline infusion also were not correlated with the control arterial pressure, renal plasma flow and glomerular filtration rate, or with the changes in these functions which occurred after the infusion of saline.

Potassium excretion

The control excretion of potassium in the hypertensive groups was not significantly different from that in the normotensive group. During and following the infusion of 5 per cent saline, the average potassium excretion in the normotensive group decreased slightly but insignificantly whereas in both hypertensive groups it increased slightly. The latter increases were statistically significant except for those in the untreated hypertensive group during the saline infusion.

Ratio of excreted potassium to filtered potassium (E/F potassium)

The calculated ratio of excreted potassium to filtered potassium (E/F potassium) during the control period was significantly higher in the untreated but not in the splanchnicectomized hypertensive group than in the normotensive group. This ratio did not change in the normotensive

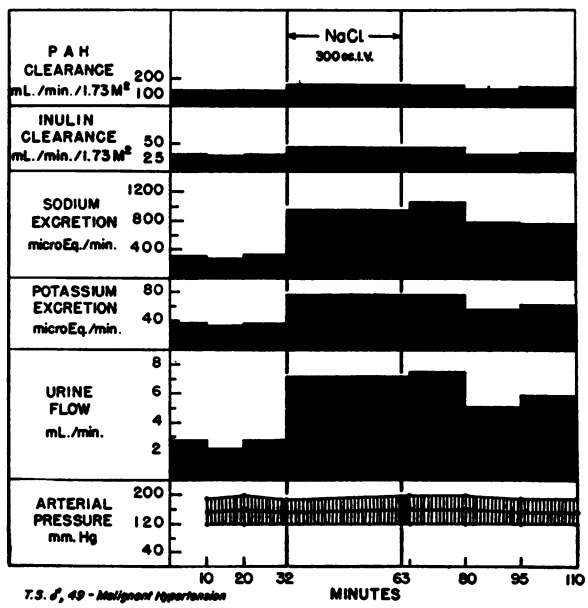

FIG. 4. RENAL RESPONSES TO INTRAVENOUS HYPERTONIC SALINE IN A SPLANCHNICECTOMIZED AND ADRENALECTOMIZED HYPERTENSIVE SUBJECT

The subject, who was maintained on 25 mg. of oral cortisone and 5 mg. of a DOCA linguet daily, had an abnormaly high rate of sodium excretion following the infusion of 5 per cent NaCl even though the renal plasma flow and glomerular filtration rate were markedly reduced.

TABLE III

Correlations of sodium excretion

ΔNa excretion* correlated with:	r†	p‡
Control Na excretion	0.301	0.2
Control mean B.P.	0.532	<0.01
Control PAH clearance	0.165	0.5
Control inulin clearance	0.237	0.3
ΔPAH clearance*	0.541	<0.01
ΔInulin clearance*	0.226	0.3
Control Na excretion correlated with control mean B.P.	0.436	0.03

* Changes in function following saline infusion.
† r = Coefficient of correlation.
‡ p = Probability.

group during the infusion but it increased significantly in the hypertensive groups and was significantly higher in these groups than in the control group. In the recovery period the E/F potassium continued to be significantly higher in the non-splanchnicectomized hypertensive group than in the normotensive group.

Urine flow

The control urine flow was not significantly different in the groups. During the infusion of saline there was no significant change in urine flow in the normotensive group whereas in the hypertensive groups there was a significant increase in urine excretion. In the recovery period the mean urine flow in the normotensive group decreased but this decrease just lacked statistical significance at the 5 per cent level. In both hypertensive groups, however, the urine flow in the recovery period did not change significantly from the control urine flow and was significantly higher than that in the control group. Pitressin® in a single intravenous dose of 40 to 100 milliunits in four hypertensive subjects (W. M., J. W., A. L., and N. K.) did not decrease urine flow in the recovery period suggesting that the sustained flow was due to an osmotic diuresis caused by an increased sodium excretion (Figure 3).

Arterial hematocrit

The arterial hematocrit at rest was not significantly different in the groups. After the infusion of hypertonic saline, it significantly decreased in all three groups. Although the decrease in hematocrit during the infusion was significantly greater in the normotensive than in the hypertensive group, the hematocrit was not significantly different in the groups during and following the infusion.

Arterial pressure

The mean arterial pressure before and after the saline infusion was significantly higher in the hypertensive groups than in the normotensive group. The changes in mean arterial pressure produced by the infusion were insignificant in all the groups.

Pulse rate

The average pulse rate at rest and after the saline infusion was not significantly different in the groups and did not change significantly.

Sodium intake and sodium excretion

In Table IV the effect of altering the sodium content of the diet on the excretion of sodium in response to intravenous 5 per cent sodium chloride is summarized.

During sodium restriction a slight and consistent reduction in weight but not in blood pressure occurred. Associated with the changes in diet and weight, the increases in sodium excretion following the infusion of 300 ml. of 5 per cent saline were reduced and were not as great as those found during an unrestricted salt diet. However, sodium excretion was not necessarily reduced to normal by salt restriction in the hypertensive subjects since it remained unequivocally high in at least one (A. L.) of the three subjects. Normotensive subject E. H., who was placed on an 18-gram salt diet, developed slight peripheral edema and a weight gain of six pounds. While on this diet, sodium excretion in response to intravenous hypertonic saline was greater than that observed during a 10-gram salt diet and approached the values found in hypertensive individuals. To determine whether acute increases in body fluid and sodium might augment the excretory response to hypertonic saline in normotensive subjects, isotonic saline was infused at the rate of 22 ml. per minute in patients H. D. and P. G. prior to the administration of 5 per cent sodium chloride. The prior expansion of the extracellular fluid volume

with 1,000 to 1,700 ml. of saline in both subjects, however, failed to augment sodium excretion in response to intravenous 5 per cent sodium chloride.

DISCUSSION

In both the normotensive and hypertensive groups the increases in sodium excretion produced by the infusion of hypertonic saline were associated with increases in the calculated load of filtered sodium. Although the latter changes were not measureably different between the groups, the increases in sodium excretion were greater in both the splanchnicectomized and the non-splanchnicectomized hypertensive groups than in the normotensive group. The differences in sodium

TABLE IV

The effect of salt intake on the excretion of sodium

Patient Age	Sex	Daily NaCl intake	Duration	Weight	Blood pressure	Procedure	$U_{Na}V$	UV
		Gms.	*days*	*pounds*	*mm. Hg*		*MicroEq./min.*	*ml./min.*
W. P.						Control	871	3.7
65	M	15	14	162.0	180/110	5% NaCl (300 ml.)	1,127	6.8
						Recovery	2,048	10.7
						Control	81	2.0
		2	10	160.0	170/120	5% NaCl (300 ml.)	221	9.3
						Recovery	303	2.5
A. L.						Control	1,064	6.5
45	M	15	14	158.2	250/150	5% NaCl (300 ml.)	1,640	11.2
						Recovery	1,740	11.5
						Control	40	1.8
		2	10	156.0	240/145	5% NaCl (300 ml.)	525	4.2
						Recovery	560	3.5
I. C.						Control	242	7.2
58	F	10	10	140.0	190/110	5% NaCl (300 ml.)	836	8.7
						Recovery	878	4.9
						Control	101	5.9
		2	10	139.0	190/110	5% NaCl (300 ml.)	424	9.1
						Recovery	343	2.7
E. H.						Control	206	6.7
42	F	10	9	165.5	130/80	5% NaCl (300 ml.)	331	4.7
						Recovery	326	1.5
						Control	9	4.8
		1	7	162.5	130/76	5% NaCl (300 ml.)	24	2.7
						Recovery	15	0.6
						Control	235	10.2
		18	6	168.5	126/74	5% NaCl (300 ml.)	569	9.4
						Recovery	939	3.1
H. D.						Control	117	10.1
29	F	10	5	114.5	110/70	5% NaCl (300 ml.)	267	1.4
						Recovery	442	2.0
						Control	214	3.2
		10	5	114.2	110/60	0.9% NaCl (1,000 ml.)	152	4.5
						5% NaCl (300 ml.)	348	2.9
						Recovery	481	1.9
P. G.						Control	393	2.9
22	F	10	7	161.5	120/70	5% NaCl (300 ml.)	586	5.8
						Recovery	589	1.9
						Control	106	4.7
		10	5	162.0	118/74	0.9% NaCl (1,700 ml.)	166	4.1
						5% NaCl (300 ml.)	340	2.7
						Recovery	323	1.1

excretion therefore appeared to be due to a difference in the renal tubular handling of sodium. Abnormally high rates of sodium excretion in hypertensive individuals have also been reported to occur during mannitol diuresis (6), suggesting that the hypertensive renal response is not a specific one to the elevated serum sodium produced by intravenous 5 per cent sodium chloride but is a non-specific response to an increase in the effective osmotic pressure of the serum.

The lack of a high degree of correlation between the level of the blood pressure and the renal excretory response to a 5 per cent sodium chloride suggests that in addition to the arterial pressure other factors operate to enhance sodium excretion in patients with essential hypertension. Green and Ellis have been able to relate the renal response of hypertensive individuals to an elevated control sodium excretion (7), but in the present study this relationship was not found to be consistent. Control sodium excretion was considerably higher in untreated hypertensive than in normotensive individuals, but in splanchnicectomized hypertensive subjects the control sodium excretion was not significantly different from that of normotensive subjects. Although these findings indicate that an elevated control sodium excretion is not necessary for large increases in sodium excretion to occur after intravenous 5 per cent sodium chloride, the greater increases of sodium excretion in the untreated hypertensive group than in the sympathectomized hypertensive group suggest that it is capable of augmenting the excretory response to hypertonic saline.

By altering the sodium content of the diet in a small number of hypertensive and normotensive individuals, similar directional changes in sodium excretion following the infusion of 5 per cent sodium chloride appeared to result. These observations might be interpreted to indicate that the excretion of sodium is a function of total body sodium. However, the failure to augment sodium excretion by the prior expansion of the extracellular fluid volume with isotonic saline does not support this hypothesis. Luetscher and Curtis' studies (8) suggest that the observed changes in sodium excretion might be the result of an alteration in adrenal cortical activity. Green and Ellis have presented evidence that significant differences in dietary salt intake may actually exist between normotensive and hypertensive individuals and may account for their different excretory responses to intravenous hypertonic saline (7). The findings in the present study, however, indicate that sodium excretion may be abnormal in hypertensive subjects even though their dietary salt intake is normal.

Primary as well as secondary changes in adrenal cortical activity may affect the renal responses to intravenous 5 per cent sodium chloride. Burnett has found that non-hypertensive patients with adrenal cortical insufficiency (Addison's disease) have an impaired excretory response to intravenous hypertonic saline which is partially corrected by steroid treatment (9). On the other hand, Birchall, Tuthill, Jacobs, Trautman, and Findley have observed that in adrenal cortical hyperfunction (Cushing's syndrome) sodium excretion is abnormally high following an infusion of hypertonic saline. By pre-treating a normotensive individual with cortisone, the same investigators were able to augment sodium excretion following intravenous 5 per cent sodium chloride (3). Although the level of adrenal cortical activity appears to be capable of affecting sodium excretion, the observations in an adrenalectomized hypertensive patient, T. S., who had an increased capacity to excrete sodium while on replacement steroid therapy, suggests that the hypertensive response to intravenous 5 per cent sodium chloride does not necessarily depend upon an increase in adrenal function.

SUMMARY

Both splanchnicectomized and non-splanchnicectomized hypertensive individuals have an increased capacity to excrete sodium as indicated by their excretion of sodium following the infusion of 300 ml. of 5 per cent sodium chloride. The capacity to excrete sodium was significantly correlated with the systemic arterial pressure but not with the control sodium excretion, renal plasma flow and glomerular filtration rate. However, the lack of a high degree of correlation between blood pressure and sodium excretion suggests that additional factors operate to enhance sodium excretion in individuals with essential hypertension. Some of the factors considered were dietary so-

dium intake, extracellular fluid volume, total body sodium and adrenal cortical function.

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