Studies of the Control of Plasma Aldosterone Concentration in Normal Man

III. RESPONSE TO SODIUM CHLORIDE INFUSION

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ABSTRACT The peripheral plasma levels of aldosterone, renin activity, potassium, sodium, corticosterone, and cortisol were measured in six normal subjects four times daily—10 a.m., 2 p.m., 5 p.m., 11 p.m.—on 3 consecutive days. A constant daytime activity program was maintained throughout the study. After 5 days on a 10 mEq sodium/100 mEq potassium isocaloric intake, the mean upright 10 a.m. plasma renin activity was 1773±186 ng/100 ml per 3 hr and the mean plasma aldosterone, 81±14 ng/100 ml. These two parameters fell continuously throughout the day parallel to the fall in plasma cortisol and corticosterone. In response to 2 liters of normal saline infused from 10 a.m. to 2 p.m. on 2 consecutive days, plasma aldosterone levels fell significantly to 13±5 ng/100 ml at 2 p.m. after the 1st day's infusion and to 6±1 ng/100 ml at 2 p.m. after the 2nd. Plasma renin activity demonstrated a parallel fall to 368±63 ng/100 ml per 3 hr and 189±27 ng/100 ml per 3 hr at 2 p.m. on the 1st and 2nd days, respectively. There was no significant alteration in plasma levels of cortisol, corticosterone, potassium, or sodium on the 2 days of sodium loading in comparison with the control day. In an additional study, five normal supine subjects received 500 ml saline/hr for 6 hr. As in the 2 day study, plasma aldosterone and renin activity had parallel decrements at 1, 2, 4, and 6 hr after the start of the saline infusion. From these studies, it is concluded that plasma renin activity is the dominant factor controlling plasma aldosterone when sodium-depleted normal subjects are acutely repleted.

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INTRODUCTION

It has been demonstrated that administration of sodium to normal individuals either by increasing dietary sodium intake or by giving an intravenous load of saline decreases aldosterone secretion or excretion (1–6). The relationship between the response of the renin-angiotensin system and aldosterone to a sodium load has been less clearly defined. Several investigators have recently reported the response of plasma aldosterone to various sodium manipulations (7–9). However, well-controlled studies relating the rate of change of the renin-angiotensin system and plasma aldosterone levels and correlating these with sodium excretion, serum sodium, and potassium, and directly or indirectly with adrenocorticotropin (ACTH) secretion have not been reported. In order to clarify these relationships, the present study reports a carefully controlled evaluation in normal sodium-deplete subjects of the response of plasma renin activity, cortisol, corticosterone, aldosterone, sodium, and potassium to the infusion of normal saline.

METHODS

Protocol

Response to 2 days of saline infusion. Six normal subjects (4 males, 2 females) between the ages of 21 and 29 yr were studied on The Clinical Research Center of the Peter Bent Brigham Hospital. All subjects were normotensive, had normal physical examinations, and no evidence by history or laboratory testing for clinical disease. All denied the use of drugs. The experimental nature of the study was explained and informed consent obtained from each subject. The subjects were maintained on a constant activity pattern simulating normal daily activity, i.e., supine from 11:30 p.m., until 8 a.m.; up from 8 a.m. to 11:30 p.m. with one 300-yard walk at least hourly. All subjects ate a

TABLE I

*6 hr Sodium and Potassium Excretion Pattern in Response to Saline Infusion in Normal Subjects**

Patient	Day	Urine sodium				Urine potassium			
		7 a.m.–1 p.m.	1–7 p.m.	7 p.m.–1 a.m.	1–7 a.m.	7 a.m.–1 p.m.	1–7 p.m.	7 p.m.–1 a.m.	1–7 a.m.
		mEq				*mEq*			
1	Control	<1	<1	2	<1	21	32	28	8
	Saline d/1	<1	3	10	3	24	19	20	8
	Saline d/2	2	46	72	57	17	31	29	31
2	Control	1	1	1	<1	20	20	21	8
	Saline d/1	2	3	9	7	25	26	25	5
	Saline d/2	19	58	85	88	42	39	25	11
3	Control	<1	<1	<1	<1	28	27	24	9
	Saline d/1	<1	1	6	1	28	23	21	9
	Saline d/2	15	43	102	19	43	64	22	7
4	Control	1	2	2	1	19	33	21	15
	Saline d/1	5	54	95	13	28	46	31	11
	Saline d/2	42	159	70	11	33	50	12	6
5	Control	<1	<1	<1	<1	25	44	21	6
	Saline d/1	2	8	5	<1	52	32	19	5
	Saline d/2	30	89	75	11	53	51	20	6
6	Control	4	1	3	1	48	9	11	12
	Saline d/1	10	56	41	10	21	20	18	64
	Saline d/2	81	90	90	22	31	20	14	9
Mean ±SEM	Control	1±1	1±0.5	2±0.5	1±0.5	27±4	28±5	21±2	10±1
	Saline d/1	2±1	21±11	28±15	6±2	30±5	28±4	24±2	17±9
	Saline d/2	32±11	81±18	82±5	35±13	37±5	43±6	20±3	12±4
Mean ±SEM 24 hr total	Control	5±1				85±4			
	Saline d/1	57±28				97±9			
	Saline d/2	230±20				111±9			

* Control diet 10 mEq Na/100 mEq K.

constant 10 mEq sodium/100 mEq potassium, 2500 ml, isocaloric diet divided into three meals a day and a snack at bedtime. On the day of admission, 400–500 ml of blood was drawn from each subject in a sterile acid citrate dextrose blood bank container and maintained in the blood bank for reinfusion later in the study.

After they had achieved metabolic balance (usually on the 5th or 6th day), blood was obtained for sodium, potassium, hematocrit, total protein, plasma cortisol, corticosterone, aldosterone, and peripheral renin activity (PRA)[1] upright at 10 a.m., 2 p.m., 5 p.m., and 11 p.m. on 3 consecutive days and at 8 a.m. on the 4th day except no PRA was obtained at 11 p.m. An equal volume of blood was replaced with each sampling. On the 2nd and 3rd study days, 2 liters of 0.9% sodium chloride was infused between 10 a.m. and 2 p.m.

Response during saline infusion. Five sodium-deplete normal subjects (age 21–28 yr) were studied on an identical 10 mEq Na/100 mEq K diet. When in balance, they were kept supine and infused with normal saline for 6 hr at the same rate as in the 2 day study, i.e., 500 ml/hr. Samples for Na, K, PRA, and aldosterone were obtained before, and 1, 2, 4, and 6 hr during the infusion. An equal volume of blood was replaced with each sampling.

Laboratory procedures

All blood samples were immediately spun and the plasma separated and frozen until time for assay. The samples for PRA were drawn using EDTA as the anticoagulant and the samples for corticosterone, cortisol, and aldosterone used sodium heparin as the anticoagulant. Sodium and potassium in urine and serum were measured by flame photometry using lithium as an internal standard.

The plasma aldosterone, corticosterone, and cortisol were measured by displacement analysis techniques as previously reported by this laboratory (10). In brief, the plasma is extracted with methylene chloride, chromatographed in a Bush 5 system, and the three steroids eluted. The corticosterone and aldosterone are determined by radioimmunoassay using antibodies specifically directed against them. The cortisol is measured by a competitive protein-binding method similar to that described by Nugent and Mayes (11). The levels found in the plasma of adrenalectomized subjects are below the sensitivity of the method for cortisol and corticosterone, and at the 2 pg/4 ml level for aldosterone. The sensitivity of the cortisol assay system is 0.2 ng/binding tube; for the corticosterone assay, 0.02 ng/binding tube; and for the aldosterone, 0.002 ng/binding tube. The coefficient of variation is between 7 and 11% at a level 10 times the sensitivity for the three assays. Recovery of added steroid from each assay is the same, ranging from 85 to 110%. The cortisol, corticosterone, and aldosterone values in 12 samples were compared with a double isotope derivative method previously used (8) which produced a correlation coefficient of 0.99 with a P value of correlation < 0.001 for all three steroids.

PRA was measured by a modification of the Boucher method as previously described (12). Statistical analyses were performed by the Student t test and least squares

[1] *Abbreviation used in this paper:* PRA, plasma renin activity.

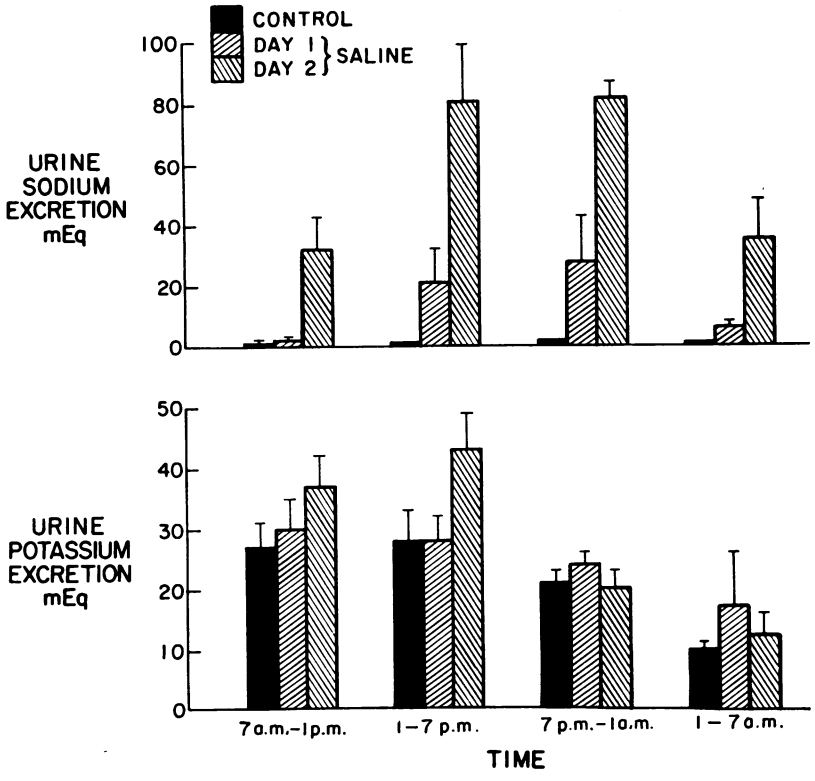

FIGURE 1 Urine sodium and potassium excretory response to saline infusion (2 liters 0.9% NaCl from 10 a.m. to 2 p.m.) in normal subjects on a 10 mEq sodium/100 mEq potassium diet.

regression analysis as described by Snedecor and Cochran (13), utilizing a General Electric 635 computer. The results are expressed as mean ± standard error of the mean, and significance as $P < 0.02$ unless otherwise indicated. Nonsignificant differences were those with $P > 0.05$.

RESULTS

Response to 2 days of saline infusion. When 2 liters of normal saline was infused, the mean weight of the subjects increased 1.5±0.1 kg on the 1st day and 0.3±0.2 kg on the 2nd day. Accompanying this was a significant increase in the mean 24 hr urine sodium excretion from 5±1 to 57±28, and then to 230±20 mEq on the 1st and 2nd days, respectively. Mean potassium excretion also increased from 85±4 to 97±9 and then to 111±9 mEq (Table I, Fig. 1). Using the paired *t* test, the mean potassium excretion on the 2nd day but not the 1st day was significantly greater than in the control period. During the first 6 hr urine collection on the 1st day of saline load, there was no significant change in urine sodium excretion, even though this period encompassed most of the time of the saline infusion. However, there was a significant increase at each succeeding time interval and on the 2nd day of saline load, each 6 hr urine sodium excretion was significantly greater than the corresponding 6 hr urine on the 1st day of saline loading. Potassium excretion did not alter significantly on the 1st day of saline load and only increased significantly over control levels during the 1–7 p.m. period on the 2nd day.

Plasma aldosterone had a diurnal rhythm with the mean 10 a.m. upright level (81±14 ng/100 ml) significantly greater than both the mean 5 p.m. (56±15 ng/100 ml) and 11 p.m. (32±8 ng/100 ml) (Fig. 2, Table II). On the 1st day of saline loading, the postsaline (2 p.m.) plasma aldosterone (13±5 ng/100 ml) was significantly less than the 10 a.m. and the control day 2 p.m. value. Similarly, the 5 p.m. (16±3 ng/100 ml) and the 11 p.m. (10±2 ng/100 ml) levels were both significantly less than on the control day. On the 2nd day of saline loading, the plasma aldosterone value fell significantly to even lower levels so that by 11 p.m. it was 4±1 ng/100 ml (Fig. 2, Table II).

The mean 10 a.m. upright PRA (1773±186 ng/100 ml per 3 hr) also fell significantly ($P < 0.05$) during the control day. On the 1st day of saline loading, there was a significant decrease in the postsaline 2 p.m. (368±63 ng/100 ml per 3 hr) and 5 p.m. (461±35 ng/100 ml per 3 hr) values. The values fell significantly further on the 2nd day of saline load showing a pattern similar to that for aldosterone.

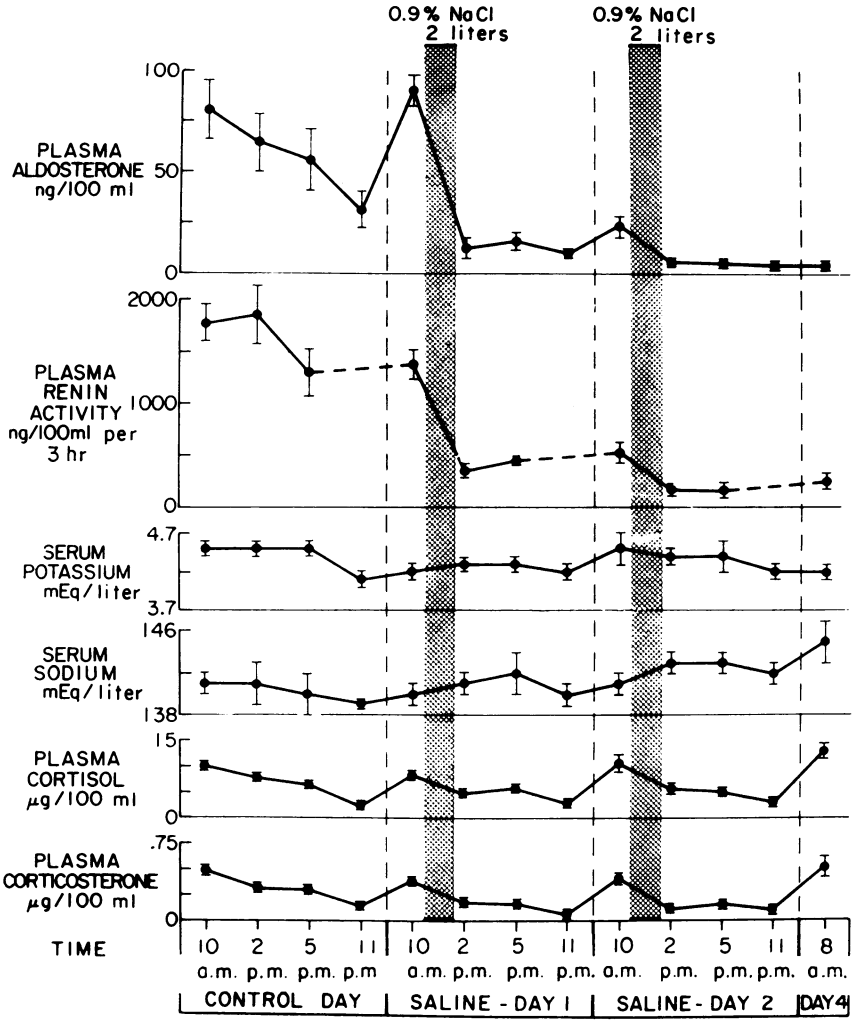

FIGURE 2 Response of plasma aldosterone, renin activity, cortisol, and corticosterone, and serum sodium and potassium to saline infusion in normal subjects on a 10 mEq sodium/100 mEq potassium diet.

In contrast, plasma levels of cortisol showed a normal diurnal variation on each of the 3 days without significant daily differences. The mean 10 a.m. values varied from 8.5±0.8 to 10.7±1.5 µg/100 ml. On all 3 days, there was a significant fall to 11 p.m. values which ranged from 2.4±0.6 to 3.2±0.8 µg/100 ml. Corticosterone showed a similar diurnal change; however, in contrast to the cortisol determinations, the mean 2 p.m. plasma corticosterones immediately after the saline load 175± 39 and 132±34 ng/100 ml) were both significantly less ($P < 0.05$ and $P < 0.02$) than the 2 p.m. level on the control day (321±62 ng/100 ml) by paired t analysis.

Mean serum potassium did not show any significant alterations on the 3 days, the 11 p.m. tended to be less than the rest of the values and was significantly so in comparison with the 10 a.m. value on the control day and the 2nd day of saline load. Serum sodium values did not significantly change during the course of the study; however, the values on the 2nd day of saline load tended to be higher than on the 1st and the control days (see Table II, Fig. 2). Both total protein and hematocrit fell by 15–20% in response to the saline infusion.

Plasma aldosterone levels were significantly correlated with renin activity ($P < 0.001$) with an index of determination of 0.87 and a correlation coefficient of 0.93. Aldosterone was not significantly correlated with plasma cortisol, serum potassium, or serum sodium, and the correlation of aldosterone with corticosterone was of marginal significance ($P < 0.05$), (correlation coefficient 0.53, index of determination 0.28).

Response during saline infusion. The mean 24 hr urine excretion of sodium and potassium rose from 10±1

TABLE II

Response of Plasma Aldosterone, Corticosterone, Cortisol, and Renin Activity, and Serum Potassium to Acute Saline Infusion

Patient	Age	Sex	Time:	Control day 10 a.m.	Control day 2 p.m.	Control day 5 p.m.	Control day 11 p.m.	1st day saline 10 a.m.	1st day saline 2 p.m.	1st day saline 5 p.m.	1st day saline 11 p.m.	2nd day saline 10 a.m.	2nd day saline 2 p.m.	2nd day saline 5 p.m.	2nd day saline 11 p.m.	2nd day saline 8 a.m.
1	22	M	*Aldosterone	87	41	37	23	90	13	21	19	47	8	8	5	4
			*Corticosterone	434	220	—	122	281	168	194	93	344	161	130	60	177
			‡Cortisol	9.8	6.9	8.5	1.1	8.9	4.6	4.3	1.6	6.8	4.8	3.7	1.7	9.0
			§Renin	2500	2670	2470	—	1440	320	514	—	790	091	100	—	100
			‖Potassium	4.6	4.4	4.6	4.0	4.2	4.5	4.2	4.1	4.8	4.8	4.7	4.6	4.5
2	21	F	Aldosterone	133	126	136	69	115	15	27	6	28	4	4	—	4
			Corticosterone	676	396	569	118	460	139	189	22	471	112	83	—	335
			Cortisol	9.4	7.7	7.1	3.9	7.6	6.0	5.4	1.9	7.7	4.4	4.5	—	9.1
			Renin	1860	740	1130	—	1100	230	500	—	420	310	180	—	340
			Potassium	4.7	4.7	4.8	4.6	4.7	4.3	4.4	4.5	4.4	4.3	4.0	—	4.4
3	22	M	Aldosterone	—	75	47	19	70	22	16	11	15	7	4	2	3
			Corticosterone	282	138	136	69	390	122	172	12	177	29	84	10	238
			Cortisol	6.7	—	5.7	0.95	6.1	3.3	5.3	0.7	7.8	2.3	3.7	0.2	13.4
			Renin	1864	1900	1280	—	920	230	340	—	320	210	150	—	123
			Potassium	4.5	4.3	—	3.8	4.3	4.2	4.3	4.0	4.1	4.3	4.0	4.4	4.2
4	21	M	Aldosterone	35	33	18	11	—	6	8	6	11	5	7	4	2
			Corticosterone	352	425	222	84	338	64	59	39	583	69	142	129	599
			Cortisol	12.4	9.3	5.2	2.0	8.2	3.3	8.8	5.6	14.6	6.5	4.9	4.0	16.1
			Renin	1490	2000	970	—	1478	473	400	—	617	163	205	—	434
			Potassium	4.4	4.5	4.4	4.1	3.9	4.4	4.2	3.9	4.4	4.3	3.9	4.1	—
5	20	M	Aldosterone	79	43	39	31	82	9	16	9	11	6	6	6	7
			Corticosterone	666	185	339	313	419	183	—	42	366	128	372	332	1482
			Cortisol	13.1	9.2	6.3	—	12.2	6.9	6.8	4.3	10.7	6.4	6.1	5.1	18.3
			Renin	1000	—	790	—	1675	—	—	—	150	200	115	—	—
			Potassium	4.5	4.7	4.1	3.8	4.2	4.1	4.6	4.8	5.1	4.3	5.5	3.9	4.2
6	29	F	Aldosterone	72	67	60	41	96	11	9	8	24	5	—	4	4
			Corticosterone	571	564	244	176	447	371	236	183	529	290	162	81	359
			Cortisol	9.3	6.6	4.8	3.8	7.7	4.6	5.0	4.8	16.4	10.3	7.8	3.9	12.2
			Renin	1923	1891	1180	—	1645	585	549	—	820	159	320	—	317
			Potassium	4.3	4.2	4.5	4.3	4.0	4.5	4.0	3.9	4.0	4.4	4.0	3.9	3.9
	Mean ±SEM		Aldosterone	81 ±14	64 ±13	56 ±15	32 ±8	91 ±7	13 ±5	16 ±3	10 ±2	23 ±5	6 ±1	6 ±1	4 ±1	4 ±1
			Corticosterone	497 ±62	321 ±62	302 ±66	148 ±33	389 ±26	175 ±39	170 ±27	65 ±29	412 ±55	132 ±34	162 ±40	122 ±50	532 ±182
			Cortisol	10.1 ±0.9	7.9 ±0.5	6.3 ±0.5	2.4 ±0.6	8.5 ±0.8	4.8 ±0.5	5.9 ±0.6	3.2 ±0.8	10.7 ±1.5	5.8 ±1.0	5.1 ±0.6	3.0 ±0.8	13 ±1.4
			Renin	1773 ±186	1840 ±277	1303 ±222	—	1376 ±139	368 ±63	461 ±35	—	520 ±100	189 ±27	178 ±30	—	263 ±58
			Potassium	4.5 ±0.1	4.5 ±0.1	4.5 ±0.1	4.1 ±0.1	4.2 ±0.1	4.3 ±0.1	4.3 ±0.1	4.2 ±0.1	4.5 ±0.2	4.4 ±0.1	4.4 ±0.2	4.2 ±0.1	4.2 ±0.1

Normal subjects on a 10 mEq sodium/100 mEq potassium diet received 2 liters of normal saline intravenously from 10 a.m. to 2 p.m. on 2 consecutive days.
* ng/100 ml.
‡ μg/100 ml.
§ ng/100 ml per 3 hr.
‖ mEq/liter.

and 64±5 to 193±20 and 69±4 mEq/24 hr, respectively, in response to the 3 liters of saline. The mean control plasma aldosterone (66±7 ng/100 ml) fell significantly after 1 hr (36±8 ng/100 ml) and continued to fall throughout the infusion to a level of 7±1 ng/100 ml at 6 hr. PRA also fell significantly during the infusion. Furthermore, plasma aldosterone was significantly correlated with PRA ($P < 0.001$) with an index of determination of 0.73 and correlation coefficient of 0.86. (Table III).

Serum sodium did not change during the infusion (140±1 mEq/liter at the beginning and 138±2 mEq/liter at the end). Serum potassium remained unchanged (4.3—4.4 mEq/liter) until the 6 hr point when it fell to 4.1±0.2 mEq/liter.

DISCUSSION

In the present studies, an infusion of normal saline was associated with parallel changes in PRA and aldosterone, both during and after the infusion. While on the control

TABLE III

Acute Response of PRA and Aldosterone to 0.9% Sodium Chloride Infusion in Normal Supine Sodium-Deplete Man (10 mEq Na/100 mEq K diet)

Subject		Time from start of infusion (hr) 0	1	2	4	6
7	*Aldosterone	58	35	23	9	11
	‡Renin	1652	546	753	400	280
8	Aldosterone	57	32	21	11	7
	Renin	1186	467	560	514	444
9	Aldosterone	80	40	36	10	4
	Renin	1714	1082	738	418	273
10	Aldosterone	86	61	38	19	—
	Renin	2768	1278	835	518	316
11	Aldosterone	51	10	9	5	7
	Renin	1922	1050	870	—	—
Mean ±SEM	Aldosterone	66 ±7	36 ±8	25 ±5	11 ±2	7 ±1
	Renin	1850 ±260	885 ±160	750 ±55	460 ±30	330 ±40

The sodium chloride was infused at a rate of 500 ml/hr for 6 hr.
* ng/100 ml.
‡ ng/100 ml per 3 hr.

day, changes in renin activity and aldosterone were coincidental with changes in plasma cortisol and corticosterone, during the 2 days of saline infusion this was not the case except for the transient fall in the corticosterone levels immediately following the saline infusion. There also was no correlation of plasma aldosterone with serum sodium or potassium. These findings support the concept that renin activity is the dominant factor in the control of aldosterone with acute volume expansion in normal sodium-deplete man.

Other investigators have not always found a close association between renin activity and aldosterone secretion (7, 14–17). Since experimental design and methodologic differences could explain some of these reports, the present study was designed to carefully control other factors which could alter the level of renin activity or aldosterone and thereby artifactually produce dissociation between them. These controls have been detailed in a previous publication (8) and include rigorous control of dietary intake of sodium and potassium, of hemorrhage due to sample collection, of activity, and of the relationship of sampling to meal times. The absolute plasma aldosterone and renin activity values are similar to what we have previously reported and in reasonable agreement with other investigators when one considers variations in dietary intake of sodium and potassium (7, 8, 16, 17).

Two previous studies have described the relationship of plasma aldosterone to acute sodium repletion. Kem, Weinberger, Mayes, and Nugent studied the response of nine normal subjects to intravenous infusion of 2 liters of normal saline similar to that used in the present study (9). They also showed a significant fall in plasma aldosterone and a parallel fall in renin activity in their subjects. However, their study did not control dietary sodium and potassium before the infusion, and therefore, is not exactly comparable with the present study. It is of interest that all of our normal subjects would have been classified by their criteria as having primary aldosteronism. Presumably, this is a reflection of the higher potassium and lower sodium intake before saline infusion in our subjects, and the fact that our subjects were hemorrhaged as well as sodium depleted before the saline was administered. This illustrates the difficulty of determining a precise screening procedure for primary aldosteronism without having some indication of dietary intake before volume expansion.

Blair-West et al. (15) have previously reported a dissociation of aldosterone from renin activity and angiotensin II levels during correction of sodium deficiency in normal sheep. Sodium deficiency was produced by means of a parotid fistula and correction of the sodium deficit by oral administration of approximately 400–600 mEq of sodium bicarbonate. From 30 min to 6 hr after the ingestion of the sodium bicarbonate, aldosterone levels had fallen to a much greater extent than renin activity or angiotensin II. In contrast, in the present study, both during an infusion of sodium chloride on a single day and before and after infusing sodium chloride on 2 consecutive days, there was no dissociation of renin activity and aldosterone. This was true as early as 60 min after starting the infusion and as late as 3 hr after its completion. The difference between their results and our own may be due to different experimental designs and/or to species differences. A major difference between the two studies was the method used to produce sodium deficiency. In the present study, dietary intake of sodium was restricted; in the studies in sheep, noncompensated losses of fluids and electrolytes through a parotid fistula was used. The present study may, therefore, have produced a more selective sodium deficiency in comparison with other electrolytes than the sheep study. Secondly, the differences could be related to the route of administration of the sodium ion. In the present study, sodium chloride was given intravenously as opposed to oral administration of sodium bicarbonate in the sheep study. The gastrointestinal absorption of the sodium ion may bring into play other factors controlling aldosterone secretion besides the renin-angiotensin system, as has been proposed for the differences in insulin response to orally vs. intravenously administered glucose. Thirdly, the sodium repletion was more gradual in the present study. The sheep rapidly drank the total sodium load within minutes. In contrast, sodium chloride in the hu-

man study was infused at a constant rate over a 4 hr period.

There were several alterations in potential factors which could independently suppress aldosterone secretion in the sheep study that were not present in the human study. These differences may in part account for the disparity between the results of the two studies. In the initial sheep studies, serum potassium levels fell significantly during the course of the study. It has been shown in several species (18–20) that a fall in serum potassium will cause a rise in renin activity and a fall in aldosterone. This could explain the difference since there was no significant change in serum potassium levels in the present study. However, in a subsequent publication (21), Blair-West et al. showed that a concomitant infusion of potassium which prevented the fall in serum potassium did not significantly alter the dissociation with oral sodium loading of sheep.

Secondly, the sheep drank the sodium bicarbonate solution very rapidly so that a significant increase in serum sodium occurred. The same group has previously shown (22) that significant increases in sodium concentration in the sheep can to a small extent decrease aldosterone secretion. In contrast, there was no change in serum sodium concentration in the present study. Another explanation for the difference could be a transient degree of alkalosis in the sheep due to the large bicarbonate load given although this cannot be evaluated since pH measurements were not given.

Finally, the difference may reflect a fundamental difference in the control of aldosterone secretion between man and sheep. For example, the sheep has an exquisitely sensitive salt appetite so that a sodium deficit is both precisely and rapidly corrected when a sodium solution is offered (23). This is uncommon in normal man. This could be associated with an altered responsiveness of the glomerulosa cell to the renin-angiotensin system in comparison with other known or unknown control factors.

In summary, in normal sodium-deplete man (as opposed to sheep), there is no dissociation of plasma levels of renin activity and aldosterone in response to acute intravenous sodium repletion. The data suggest that plasma aldosterone is under the dominant control of renin activity in these circumstances. This is critically important since in some diseases, a dissociation between PRA and aldosterone secretion has been reported with sodium repletion (24–26). Results of the present study would suggest that in these diseases other factors are influencing the levels of PRA and/or aldosterone.

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