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The Effect of Acute Adrenalectomy on Volume Natriuresis in the Rat[1] (37846)

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(Introduced by S. Solomon)

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A correlation between sodium balance and adrenal mineralocorticoid secretion, at least in part mediated by the renin–angiotensin system, can be regarded as established (1). Disturbances of sodium balance are usually associated with parallel alterations in extracellular fluid volume; acutely induced alterations in extracellular fluid volume are known to be followed by appropriate change in renal excretion of water and sodium (2). It would be logical if the natriuretic component of this renal response were partly under the control of aldosterone, and indeed changes in blood volume following infusion or hemorrhage lead to reciprocal change in blood levels of aldosterone or angiotensin (3). Although it has been repeatedly emphasized that the renal reaction to altered aldosterone level is too slow to account for the prompt natriuresis which occurs with plasma volume expansion by infusions, a reduced level could contribute to the developed response. However, many investigators have shown that the natriuretic response to plasma-expanding infusions is not prevented by simultaneous administration of mineralocorticoids (4). Even this does not exclude a participatory role of inhibited aldosterone secretion in short-term volume adjustments, as an initial high level of a hormone does not necessarily eliminate a response to lowering of this level, as has been reported (5) for the antidiuretic effect of vasopressin. Current emphasis on renal vascular factors as mediators of volume natriuresis (6), and the fact that this response is little altered by renal denervation (7), could suggest that adrenal catecholamine secretion rate might also play a part in renal volume responses. Unequivocal resolution of these questions would seem to depend on studies in adrenalectomized animals. Such studies in the dog have led to the conclusion that the adrenals are not essential to natriuretic response to plasma volume expansion (8). We have reexamined this conclusion by comparing the natriuresis following whole blood infusion in acutely adrenalectomized and in intact rats.

Methods. A group of six rats (Sprague–Dawley, anesthetized with Inactin, 100 mg/kg) was prepared exactly as described previously (9) except that, in addition to other minor surgical preparations, both adrenal glands were removed through lumbar incisions about 30 min before the experiment. Arterial and central venous blood pressures were monitored, and bladder urine collections were used for determining urine volume ($\dot{V}$), total sodium excretion ($U_{Na}\dot{V}$), and glomerular filtration rate as ^{3}H-inulin clearance; during the 20-min urine collection periods, a blood sample was obtained for measuring hematocrit and ^{3}H-inulin content. Over the fourth period, an infusion of whole blood from a normal donor rat was given intravenously in an amount equal to one-third of the estimated blood volume. The resultant measured changes in renal excretion and cardiovascular variables over

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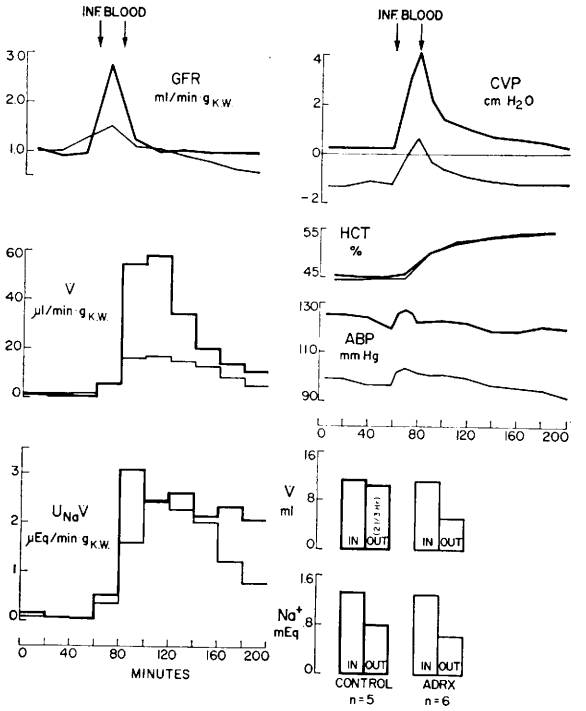

FIG. 1. Effect of acute adrenalectomy on renal volume response. Period averages for the two series of rats identified in the water and sodium balance graphs, lower right; in these, $\dot{V}_{IN}$ is taken as the volume of blood infused, Na^+_{IN} its plasma sodium content, $\dot{V}_{OUT}$ is the urine volume over the last 140 min, and Na^+_{OUT} its sodium content. Other plots give values over 20-min periods; GFR, glomerular filtration rate; $\dot{V}$ urine volume; $U_{Na}\dot{V}$, total sodium excretion; CVP, central venous mean pressure; ABP, arterial mean blood pressure.

the succeeding six periods were compared with data from the earlier series (9) of control rats with intact adrenals. These rats, sham-operated in the neck for comparison with a vagotomized group, underwent an amount of surgery comparable to that in the adrenalectomized series.

Results. Adrenalectomized rats exhibited lower arterial and central venous pressures than the control group (Fig. 1, Table I) but had similar renal function and hematocrit values. The whole-blood infusion produced a transient rise in blood pressure and a sustained hemoconcentration quite similar to these changes in control rats, but the increase in central venous pressure was clearly less.

The adrenalectomized rats responded to infusion with a small and transient increase in glomerular filtration rate (GFR), fol-

TABLE I. Mean Values for Measured Variables Averaged over Preinfusion Hour, C, and over Postinfusion Hour, E, with SEM.

Group		Arterial blood pressure (mm Hg)	Central venous pressure (cm H_2O)	Heart rate (beats/min)	Urine volume (μl/ min·$g_{K.W.}$)	Sodium excretion (μEq/ min·$g_{K.W.}$)	GFR (ml/ min·$g_{K.W.}$)
Control	C	124 ± 1	0.2 ± .1	364 ± 5	1.48 ± .08	0.10 ± .02	0.96 ± .05
	E	122 ± 2	1.2 ± .2	341 ± 4	48.85 ± 4.41	2.70 ± .24	1.07 ± .04
Adrenal-ectomized	C	101 ± 1	−1.2 ± .3	400 ± 4	2.16 ± .17	0.07 ± .006	1.10 ± .07
	E	99 ± 1	−0.8 ± .3	380 ± 4	16.23 ± 1.59	2.08 ± .16	1.03 ± .06

lowed by a progressive decline not seen in control rats. The diuretic response in adrenalectomized rats was much smaller ($P < .0001$) than in control animals, but the natriuretic response was comparable in magnitude ($P > .05$) except for some decline during the last two periods of the experiment. Excretion of the added fluid volume was therefore impaired by adrenalectomy, but the natriuretic component of the renal volume response was not obviously different, during the 100 min after expansion commenced, between animals with and without adrenal glands.

Discussion. It has previously been established that the renal response to blood infusion in the rat is due to vascular expansion, as it does not occur if the donor blood is simply exchanged with that of the recipient animal (10). The diuretic component of the response, but not the natriuretic component, has been shown to be largely dependent on the integrity of the vagi (9); this finding is consistent with the Gauer–Henry hypothesis (2) that the diuresis of volume expansion is due in part to inhibition of vasopressin secretion as a reflex response to stimulation of atriovenous receptors with vagal pathways.

A hypodynamic circulatory system is an early development after adrenalectomy (11) and is suggested in our rats by relative hypotension of both high- and low-pressure systems. The similar hematocrit values in the two groups of animals, both before and soon after expansion, imply, however, that the transcapillary partition of extracellular fluid was similar. Vascular distensibility was presumably greater in the adrenalectomized rats if this is reflected by the smaller rise in central venous pressure on infusion. As this pressure is one factor upon which the discharge rate of left atriovenous receptors depends, one should expect that diuresis due to inhibition of vasopressin secretion would be less, as was observed. The arterial hypotension would also have had an opposing reflex influence on such an inhibition (12).

The natriuretic component of the volume response was not obviously depressed by the lower vascular pressures in the adrenalectomized rats, although the later fall in this excretory reaction may have been related to the declining filtration rate. An alternative possibility is that inhibition of aldosterone secretion in intact rats may only manifest itself in a later stage of the natriuresis (as it outlasts the diuretic response in control rats) and that this contribution is missing in the adrenalectomized group. This interpretation is consistent with the earlier observation that the humoral component of the volume natriuretic mechanism, isolated by cross-circulation experiments in the rat, was attenuated if the infused partner was acutely adrenalectomized (13). However, the major early part of the volume natriuresis was not significantly different in character or magnitude in the present experiments whether or not the animal was adrenalectomized. It seems clear, then, that neither inhibition of aldosterone secretion nor reduced liberation of medullary catecholamines can account for the natriuresis of short-term renal correction of increased blood volume. Other factors must be invoked, and even where such factors have been shown to include a humoral component (13–16), an extraadrenal source is likely or has been established (13, 14).

1. Davis, J. P., In "The Adrenal Cortex" (A. B. Eisenstein, ed.), p. 203. Little, Brown and Co., Boston (1967).

2. Gauer, O. H., Henry, J. P., and Behn, C., Ann. Rev. Physiol. 32, 547 (1970).

3. Gross, F., Brunner, H., and Ziegler, M., Rec. Progr. Hormone Res. 21, 119 (1965).

4. de Wardener, H. E., Brit. Med. J. 3, 676 (1969).

5. Ledsome, J. R., and Mason, J. M., J. Physiol. (London) 221, 427 (1972).

6. Earley, L. E., and Daugharty, T. M., New Eng. J. Med. 281, 72 (1969).

7. Pearce, J. W., and Lichardus, B., Can. J. Physiol. Pharmacol. 45, 689 (1967).

8. Levinsky, N. G., Ann. NY Acad. Sc. 139, 295 (1966).

9. Veress, A. T., and Pearce, J. W., Can. J. Physiol. Pharmacol. 50, 463 (1972).

10. Pearce, J. W., Lichardus, B., Sonnenberg, H., and Veress, A. T., Proc. 4th Int. Congr. Nephrol. Vol. 2, p. 80, Stockholm (1969).

11. Lefer, A. M., and Verrier, R. L., J. Clin.

Pharmacol. Ther. **11**, 630 (1970).

12. Share, L., Amer. J. Physiol. **208**, 219 (1965).

13. Sonnenberg, H., Pearce, J. W., and Veress, A. T., J. Clin. Invest. **51**, 2631 (1972).

14. Tobian, L., Coffee, K., and McCrea, P., Trans. Ass. Amer. Physicians **80**, 200 (1967).

15. Kaloyanides, G. J., and Azer, M., J. Clin. Invest. **50**, 1603 (1971).

16. Bengele, H. H., Houttuin, E., and Pearce, J. W., Amer. J. Physiol. **223**, 69 (1972).

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