Alteration in Renal Na and H_2O Content Following Adrenalectomy.* (30326)

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The mammalian kidney elaborates a concentrated urine by virtue of the existence of a countercurrent multiplier system. It is presumed that one of the major factors involved in its operation is the rate at which Na is transported out of ascending limb fluid(1). Thus it is reasonable to assume that any substance which can alter that transport should also alter the maximum papillary concentration of Na which may be achieved. Adrenal cortical hormones are known to alter the rate of renal tubular sodium transport(1). If aldosterone acts on the ascending limb, it might be expected to affect the renal medullary gradient for Na. However, conflicting reports exist as to the effect of adrenalectomy on the renal countercurrent multiplier system(2,3,4, 5). The work presented here is an attempt to account for some of the apparent disagreements. Since these workers used different protocols and experimental procedures, comparison between their results is difficult. We therefore selected one protocol and varied experimental procedures as described below.

Methods. A total of 77 male Sprague-Dawley rats was used. All animals were kept in separate cages in an air-conditioned room (22°C) and fed Purina Lab Chow *ad lib.* Adrenalectomies were performed under sodium pentobarbital anesthesia as described by Grollman(6). The animals were then maintained for 10 days on one of the regimens as outlined in Table I. At time of the experiment the rats were again anesthetized with sodium pentobarbital. The left kidney was exposed by a ventral midline incision, quickly removed and cut in half along the long axis. Small pieces of tissue were carefully cut with a razor blade from the tip of the papilla, inner and outer zones of the medulla and cortex. The time interval between removal of the kidney and isolation of the tissue aliquots was between 1-1½ minutes. The samples were placed in tared aluminum pans and quickly weighed on a torsion balance to the nearest 0.01 mg. The wet weights of the tissue were approximately 10 mg (range 7.9-21 mg). After weighing, the sections were then dried at 105°C overnight and reweighed. Sodium concentrations were measured as previously described(7).

Results. Table II presents the results of all experiments. Only the values for the tip of papilla and cortex are given, since in all cases the sections from the middle and outer medulla had sodium concentrations intermediate to those presented.

Tip of papilla. The first 3 groups of animals may be considered as controls. There

TABLE I. Adrenalectomy Experiments and Controls.

Groups	Procedure	Replacement therapy: Drinking fluid (*ad lib*)	Replacement therapy: Hormone	Replacement therapy: Dose & route of admin
A.	Intact	Tap water	—	—
B.	"	.9% NaCl	—	—
C.	"	"	ADH*	50 milliunits /rat subcut
D.	Adx	"	—	—
E.	"	"	ADH	50 milliunits /rat subcut
F.	"	Tap water	Cortisone†	2 mg/rat/ day subcut
G.	"	"	Cortisone	2 mg/rat/ day subcut
			ADH	50 milliunits /rat subcut

* Antidiuretic hormone (Pitressin—Parke-Davis). Single dose given 3 hr prior to removal of kidneys.
† Saline suspension of cortisone acetate (Merck Sharp & Dohme).

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TABLE II. Concentration of Sodium and Per Cent Water of Renal Tissue.

Groups	No. of experiments	Papilla: Na, mEq/kg wet wt	Papilla: Na, mEq/100 g dry wt	Cortex: Na, mEq/kg wet wt	Cortex: Na, mEq/100 g dry wt	(Wet wt—Dry wt)/Wet wt × 100: Papilla	(Wet wt—Dry wt)/Wet wt × 100: Cortex
Control + tap water	10	215 ± 8	114 ± 3	70.0 ± 4	26.8 ± 1	81.3 ± .5	74.7 ±1.2
Control + saline	10	212 ± 10	118 ± 6	66.7 ± 2	25.6 ± 1	82.4 ± .6	74.3 ± .5
Control + saline + Pitressin	10	207 ± 19	109 ± 8	67.3 ± 6	25.1 ± 2	81.4 ± .6	74.0 ± .4
Adrenalectomized + saline	15	208 ± 13	115 ± 6	67.0 ± 3	26.6 ± 1	82.3 ± .5	74.9 ± .3
Adrenalectomized + saline + Pitressin	13	158 ± 12	97 ± 7	59.4 ± 4	22.5 ± 2	83.7 ± .5	73.4 ± .5
Adrenalectomized + cortisone (2 mg)	9	237 ± 16	131 ± 9	60.3 ± 4	23.3 ± 2	82.1 ± .4	74.3 ± .3
Adrenalectomized + cortisone (2 mg) + Pitressin	10	231 ± 20	118 ±11	62.0 ± 2	23.4 ± 1	80.9 ± .4	73.3 ± .5

All values represent the mean of each group ± one standard error of mean.

was no statistically significant difference in the concentration of Na between any of the first 3 groups. Addition of 0.9% NaCl to the drinking water or administration of Pitressin did not alter the concentration of Na in the papilla.

Adrenalectomy alone did not result in significant changes in the concentration of sodium. However, if Pitressin was administered to adrenalectomized rats maintained on 0.9% NaCl in the drinking water, the concentration of Na was reduced significantly ($P < .05$) below that of the control given saline and Pitressin. In addition, the percent water of the tissue increased significantly ($P = .05$). However, no such changes were evident if adrenalectomized rats were maintained on 2 mg of cortisone per day.

Cortex. The only statistically significant alteration in cortical concentrations was a reduction in tissue hydration in the adrenalectomized rats maintained on 0.9% NaCl given Pitressin. The percent water was reduced from 74.9% to 73.4% ($P = .02$).

Discussion. In our hands, adrenalectomy did not reduce the concentration of sodium in the papilla below that of intact animals. Our results appear to differ from those of others. Guinnebault and Morel(2) and Kessler *et al*(5) reported that the sodium concentration in the papilla was reduced following adrenalectomy. Crabbe and Nichols(3) reported a reduction in the concentration of sodium when expressed as mEq/l of tissue water, but not when expressed as mEq/100 g dry weight. In contrast, Platts(4) was unable to demonstrate any alteration in sodium concentration or tissue hydration in adrenalectomized animals.

We believe that the apparent disagreement between these results may be partially explicable on the basis of the difference in the experimental protocols and the level of circulating ADH. Kessler *et al*(5) maintained their rats on 0.3% NaCl while we used 0.9% NaCl. Although it is not entirely clear why this should account for the difference in results, it is possible that such rats suffered mild volume depletion due to salt loss. Injection of Pitressin into intact animals, or adrenalectomized animals maintained on cor-

tisone had no effect on the papillary concentration of sodium. However, injection of Pitressin into adrenalectomized animals which did not receive adrenal hormones, resulted in a large decrease in the papillary concentration of sodium. This reduction in concentration of sodium was statistically significant when expressed on a dry weight or wet weight basis.

The paradoxical effect of Pitressin in the adrenalectomized animal is somewhat difficult to explain. However, a possibility exists which we believe is likely to be responsible for the changes noted. Adrenalectomized animals generally show a reduction in renal blood flow if not given adrenal hormones(8). Such a reduction in blood flow is not enough to alter the efficiency of the countercurrent multiplier system significantly. ADH also reduces medullary blood flow(9). It seems to us that this reduction imposed on an animal already having reduced blood flow could easily embarrass the countercurrent multiplier system. Severe restrictions in renal blood flow have been shown to reduce the ability of the kidney to form a concentrated urine(10).

The increase in tissue hydration may also be related to reduced medullary blood flow. If the flow were reduced enough the medullary tissue might suffer a reduction in metabolic rate sufficient to cause swelling of the cells. Naturally it is not possible from the present data to determine if the increase in tissue water is due to intracellular swelling or to extracellular changes. It is important to note that Pitressin in the adrenalectomized animal did not increase cortical hydration, but reduced it. This is consistent with the finding that ADH alters medullary blood flow alone(9).

Summary. It appears that the conflicting reports in the literature regarding the effects of adrenalectomy on the concentration of water and electrolytes in the kidney may be due to different levels of circulating ADH in the animal at the time of experiment, or to differences in the protocols of the several sets of experiments.

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Tissue Catecholamine Levels in Prolonged Oligemic Hypotension.* (30327)

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Stress situations have been shown to result in high circulating levels of catecholamines (1), presumably accompanied by depletion of tissue stores(2). *A priori* one might expect that such depletion would affect all organs indiscriminately. On the other hand, one could formulate a working hypothesis to the effect that not all organs suffer equally as a consequence of the imposed stress situation

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