Renomedullary Deficiency. A Contributory Factor in the Pathogenesis of Experimental Renal Hypertension[1]

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Summary. The results indicate that renomedullary deficiency induced by renal artery clipping might contribute to the development of renal hypertension.

It has long been recognized that the kidney exhibits an endocrine-like antihypertensive function[3] which has been associated with the cells of the renal medulla[4–10]. Thus, renomedullary transplantation has resulted in the lowering of blood pressure in various forms of experimental hypertension[6, 8–10], and antihypertensive substances have been isolated from the renal medulla[5, 7]. In addition, experiments in rats with hereditary hydronephrosis have shown that the presence of medullary tissue is essential for the preservation of normal blood pressure in animals subjected to the hypertensive stimulus of salt overload[10, 11]. The purpose of the present study was to investigate the role of the renal medulla in the pathogenesis of one-kidney renal hypertension.

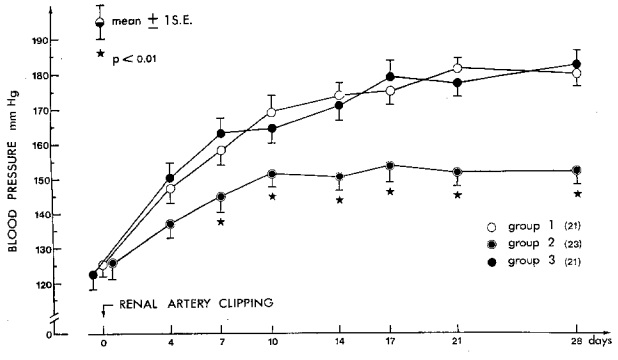

Fig. 1. Blood pressure in unilaterally nephrectomized hydronephrotic rats after renal artery clipping. Group 1, normal kidney remaining; group 2, hydronephrotic kidney plus subperitoneal autotransplant of renal medulla; group 3, hydronephrotic kidney plus renocortical autotransplant. Number of animals studied is shown in parentheses.

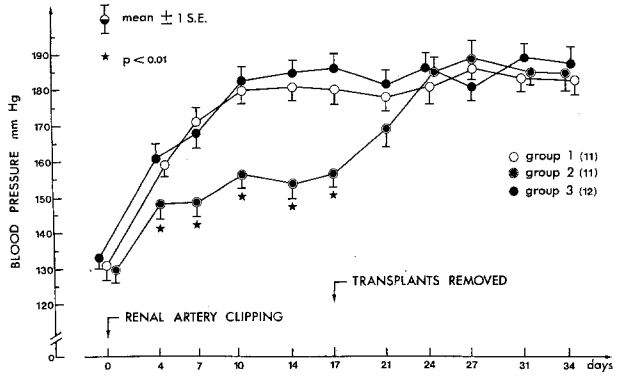

Fig. 2. Blood pressure in renal hypertensive hydronephrotic rats after removal of autotransplants. Group 1, normal kidney remaining; group 2, hydronephrotic kidney plus renomedullary autotransplants; group 3, hydronephrotic kidney plus renocortical autotransplant. Number of animals studied is shown in parentheses.

Methods. Experiments were performed in 2- to 2.5-month-old (200–250 g) male Memorial Research Center/Hydronephrosis (MRC/H)[11] rats with unilateral hydronephrosis. The animals were given a standard diet and tap water ad libitum. Diagnosis of kidney disease was made by i.v. pyelography[12] and verified at autopsy. The only rats used were those which exhibited 'moderate hydronephrosis'[13] characterized by a dilated renal pelvis containing 1 to 2 ml of urine, almost total destruction of the medulla, and moderate damage to the cortex.

The animals were divided into 3 groups and unilaterally nephrectomized. Rats in the first group had the normal kidney remaining and received no transplants. Rats from the 2nd and 3rd groups were left with the hydronephrotic kidney and received subperitoneal autotransplants of renal medulla and cortex, respectively. To this end, the medulla from the removed kidney, or a piece of the renal cortex of comparable size, was cut into pieces (approximately 1 mm in diameter) which were then placed in a subperitoneal 'pocket' in the abdominal wall. 2 weeks after the surgery initial measurements of systolic blood pressure (tail-cuff)[10] were made in all animals, while serum urea and creatinine concentrations were determined in 10 rats from each group[10].

After the basal measurements were completed, a silver clip (0.2 mm) was placed on the renal artery of the remaining kidney[14] in all animals and the blood pressure was monitored for the next 28 days. In a second experiment, the transplants (groups II and III) were removed or sham surgery was performed (group I) 17 days after renal artery clipping and the blood pressure was monitored

[1] Acknowledgments. The authors are grateful to Dr. B. B. Lozzio for constant help and encouragement. Supported by the American Heart Association grant No. 74–831.

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Systolic blood pressure (BP) and serum urea (BUN) and creatinine (Cr) concentrations in uninephrectomized rats before and after renal artery clipping

Groups	Before clipping			28 Days after clipping		
	BP (mmHg)	BUN (mg/dl)	Cr (mg/dl)	BP (mmHg)	BUN (mg/dl)	Cr (mg/dl)
I	125 ± 3[a]	13.8 ± 0.1	0.55 ± 0.04	173 ± 4[c]	23.5 ± 0.4[c]	1.00 ± 0.06[c]
II	125 ± 2	16.6 ± 0.1[b]	0.69 ± 0.04[b]	152 ± 2[b, c]	24.1 ± 0.9[c]	1.05 ± 0.07[c]
III	121 ± 3	17.3 ± 1.0[b]	0.70 ± 0.05[b]	172 ± 4[c]	25.4 ± 2.5[c]	1.14 ± 0.08[c]

10 animals in each group. [a] Mean ± 1 SE. [b] $p < 0.05$ when compared to group I. [c] $p < 0.01$ when compared to the basal value for the same group.

for another 17 days. At the end of the experiments, plasma urea and creatinine concentrations were determined in 10 animals from each group, all rats were killed, and the transplants were removed and examined as previously described[10]. All animals included in the study met the following criteria: 1. histological evidence of successful transplantation; and 2. systolic blood pressure at the beginning of the study below 140 mm Hg. The criterion for hypertension was BP > 149 mm Hg (3 SD above the mean blood pressure of 598 animals of this strain). Results are expressed as mean ± 1 SE.

Results and discussion. No significant difference in the average body weight was observed between the groups at any time. Serum urea and creatinine concentrations are shown in the Table. The characteristics of the autotransplants of both renal medulla and cortex were consistent with those described earlier[10]. The morphological features of the renomedullary transplants in the present case were consistent with those shown to protect against hypertension[9, 10].

The results of the present study (Figure 1) have shown that transplantation of the renal medulla, but not of renal cortex, abolishes the blood pressure rise in the course of renal hypertension. Moreover, after transplant removal, the blood pressure in group II rose within 1 week to the level found in groups I and III (Figure 2), a finding that further suggests antihypertensive actions by renomedullary tissue. The presented data are in close agreement with the previous reports on the antihypertensive effect of renomedullary transplants in one-kidney renal hypertension[8].

The finding of particular interest was that after renal artery clipping the time course of blood pressure increase and the final level of blood pressure reached were similar in rats from groups I (with normal medulla inside the clipped kidney) and III (with almost completely atrophied medulla). However, the presence of medullary tissue outside of the clipped kidney (group II) protected the animals against hypertension. These results suggest that renal artery clipping interferes in some way with the antihypertensive function of the renal medulla. Thus, the development of renal hypertension apparently involves clip-induced renomedullary deficiency as well as the known roles of the renin-angiotensin system and sodium and water retention[15, 16]. In quantitative terms this contribution may be on the order of 20–30 mm Hg, thus representing about one half of the total blood pressure rise in the present case.

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Sodium Pump: its Importance to Intercellular Communication in Heart Fibres[1]

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Summary. The effect of ouabain on the electrical coupling of canine Purkinje cells was investigated. It was found that the glycoside decreases cell communication through an increase in junctional resistance, what supports the view[2] that the sodium pump has an important role on the control of cell communication.

Previous observations from our laboratory[2, 3] have shown that the injection of sodium ions into a heart or liver cell (De Mello, unpublished) produces electrical uncoupling. These observations are probably explained by the increment of the intracellular calcium concentration which follows the raise of the intracellular sodium content[4, 5]. Evidence has been presented that calcium is, indeed, involved in the control of junctional permeability in epithelia[6] and in cardiac Purkinje fibers[7, 8]. In support of this idea is our recent finding that the injection of sodium ions into a cardiac Purkinje cell, immersed in low calcium solution, had a small effect on cell communica-

[1] This work was supported by Grant No. HL-10897 from the National Heart and Lung Institute, Bethesda, Maryland; from the P.R. Heart Association and from the General Research Support Grant.

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