Participation of Tissue Electrolytes and Water to the Spontaneous Hypertension in Rats

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Relationship between the electrolyte patterns in aorta, heart and serum, and the progression of hypertension in spontaneously hypertensive rat was studied. No significant differences in sodium, potassium and water contents in the tissues, and in electrolyte concentrations in the serum were found between the hypertensive rats at pre- or early-hypertensive phase and control rats of same ages. However, a marked increase in electrolyte and water contents in aorta and a decrease in concentration of potassium in the serum were observed in the hypertensive rats at the advanced phases. These results suggest that the disturbances in tissue electrolytes are not participant of the pathogenesis but of the marked progression of the hypertension.

THE close correlation between the occurrence of the hypertension and abnormal electrolyte pattern in the tissues prompted the study of the electrolyte pattern in the hypertensive condition. TOBIAN et al¹ have reported that the contents of sodium and water in renal artery and psoas muscle are higher in the hypertensive subjects than in the normal ones. From their further studies²⁻⁵ which demonstrated increased levels of sodium, potassium and water in the aorta of the various types of experimental hypertensive rats, they have suggested the possibility that the similar events in the arterioles could result in an increased peripheral vascular resistance in virtue of swelling of the vessel wall and narrowing of the vascular lumen. The increased levels of electrolytes in the mesenteric arteries of the hypertensive animals have also been demonstrated by KOLETSKY et al⁶ and HALPERN et al⁷. The slight elevation of sodium level in aorta of the desoxycorticosterone acetate (DOCA) hypertensive rat but not in the hypertensive rats of post-DOCA, renal or spontaneous origin⁸ and the significant elevation of the potassium level alone in aorta of the renal hypertensive rat⁹ suggest that the electrolyte pattern in the aorta is modified by the

progression of the hypertension.

In our preliminary study,¹⁰ the increased levels of sodium, potassium and water in the aorta were found in the hereditary dominant and spontaneously hypertensive rats (OKAMOTO and AOKI)^{11,12} at the ages of 23, 34 and 54 weeks. In order to analyze the correlation between the abnormal electrolyte pattern and progression of the hypertension, the levels of electrolytes in the aorta, heart and serum were estimated in the spontaneously hypertensive rats at the ages of 6 (pre-hypertensive phase) and 13 weeks (early-hypertensive phase) in comparison with those in the normotensive Wistar rats. In addition, the similar observations were made in the DOCA and dexamethasone hypertensive rats.

METHODS

Female spontaneously hypertensive and normotensive Wistar rats of specific pathogen-free derivation at the ages of 6, 13, 24 and 36 weeks were used. The hypertensive rats were of F₁₅ generation. The number of animals at the respective age was 10 except 8 hypertensive animals at the age of 6 weeks. The animals were maintained on the normal commercial diet (Nippon CLEA

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TABLE I BODY WEIGHT, BLOOD PRESSURE, HEART RATE AND SERUM ELECTROLYTES IN SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT PRE- AND EARLY-HYPERTENSIVE PHASES

Group	No. of Rats	Body Weight (g)	Blood Pressure (mmHg)	Heart Rate (beats/min)	Serum Electrolytes (mEq/l)	
					Na	K
Prehypertensive Phase (6 Weeks of Age)						
Control	10	116.1 ± 4.0	128.2 ± 4.8	434.4 ± 24.5	141.2 ± 3.0	3.815 ± 0.214
SH. Rat	8	120.0 ± 16.2	144.4 ± 8.5	435.0 ± 22.9	142.0 ± 2.8	3.875 ± 0.342
P Value		N.S.	0.001	N.S.	N.S.	N.S.
Early Hypertensive Phase (13 Weeks of Age)						
Control	10	200.7 ± 13.1	122.9 ± 9.8	456.4 ± 28.3	137.2 ± 3.2	3.664 ± 0.166
SH. Rat	8	182.6 ± 9.3	167.3 ± 7.2	446.2 ± 38.5	139.0 ± 2.7	3.767 ± 0.386
P Value		0.005	0.001	N.S.	N.S.	N.S.

All values are average and standard deviations of results in 8 hypertensive and 10 normotensive rats.

TABLE II ELECTROLYTES AND WATER CONTENTS, AND WEIGHT IN AORTA AND HEART OF SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT PRE- AND EARLY-HYPERTENSIVE PHASES

Group	No. of Rats	Aorta					Heart				
		Wt.	H ₂ O(%)	Na	K	Na/K	Wt.	H ₂ O(%)	Na	K	Na/K
Prehypertensive Phase (6 Weeks of Age)											
Control	10	7.11 ±0.26	66.34 ±1.06	276.3 ±12.3	139.7 ±3.3	1.977 ±0.101	84.61 ±4.92	76.50 ±0.30	154.7 ±5.8	331.0 ±4.7	0.4676 ±0.0131
SH. Rat	8	8.23 ±1.37	66.15 ±0.86	271.1 ±26.2	139.6 ±11.1	1.944 ±0.129	94.46 ±13.24	76.48 ±0.32	152.5 ±9.7	325.6 ±8.0	0.4683 ±0.0234
P Value		0.025	N.S.	N.S.	N.S.	N.S.	0.05	N.S.	N.S.	N.S.	N.S.
Early Hypertensive Phase (13 Weeks of Age)											
Control	10	9.75 ±0.54	65.15 ±0.79	271.6 ±15.9	134.1 ±8.1	2.032 ±0.151	122.6 ±9.0	76.18 ±0.38	152.3 ±8.7	332.9 ±4.3	0.4581 ±0.0304
SH. Rat	8	11.70 ±1.24	65.69 ±0.99	273.3 ±6.7	129.6 ±4.9	2.109 ±0.110	150.5 ±20.0	76.09 ±0.44	145.9 ±5.5	329.9 ±4.8	0.4426 ±0.0213
P Value		0.005	N.S.	N.S.	N.S.	N.S.	0.001	N.S.	N.S.	N.S.	N.S.

All values are average and standard deviations of results in 8 hypertensive and 10 normotensive rats.
Wt: Defatted dry weight (mg) Na and K contents: mEq/kg of defatted dry weight

CE-2) containing 0.3% sodium and tap water ad libitum at the room temperature of 24 ± 1°C. The development and progression of the hypertension in the spontaneously hypertensive rats kept under the same condition were described elsewhere.¹³

Male Wistar rats at the ages of 4 to 5 weeks and weighing 70 to 120 g had the right kidney

removed and concomitant implantation of a 25 mg pellet of DOCA subcutaneously in the back under anesthesia with methylhexital sodium, 100 mg/kg administered intraperitoneally. Control rats were only nephrectomized unilaterally. From next day until 17 days after the surgical procedure the animals were allowed free access to 1% saline. Thereafter, their drinking water was

TABLE III BODY WEIGHT, BLOOD PRESSURE, HEART RATE AND SERUM ELECTROLYTES IN SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT AGES OF 24 AND 36 WEEKS

SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT AGES OF 24 AND 36 WEEKS						
Group	No. of Rats	Body Weight (g)	Blood Pressure (mmHg)	Heart Rate (beats/min)	Serum Electrolytes (mEq/l)	
					Na	K
Advanced Hypertensive Phase (24 Weeks of Age)						
Control	10	239.7 ± 12.0	130.9 ± 7.2	434.4 ± 25.2	141.1 ± 1.4	3.786 ± 0.214
SH. Rat	10	209.4 ± 9.1	189.6 ± 23.0	502.8 ± 17.4	142.0 ± 1.4	3.370 ± 0.268
P Value		0.001	0.001	0.001	N.S.	0.005
Advanced Hypertensive Phase (36 Weeks of Age)						
Control	10	259.6 ± 30.8	123.0 ± 10.7	466.8 ± 28.5	139.5 ± 1.2	3.680 ± 0.204
SH. Rat	10	211.6 ± 10.0	186.9 ± 16.3	511.2 ± 26.0	139.8 ± 1.0	3.311 ± 0.258
P Value		0.001	0.001	0.005	N.S.	0.005

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.

TABLE IV ELECTROLYTES AND WATER CONTENTS, AND WEIGHT IN AORTA AND HEART OF SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT AGES OF 24 AND 36 WEEKS

SPONTANEOUSLY HYPERTENSIVE (SH) RAT AT AGES OF 24 AND 36 WEEKS											
Group	No. of Rats	Aorta					Heart				
		Wt.	H ₂ O(%)	Na	K	Na/K	Wt.	H ₂ O(%)	Na	K	Na/K
Advanced Hypertensive Phase (24 Weeks of Age)											
Control	10	11.93	67.23	274.5	127.7	2.156	142.5	76.36	144.7	321.6	0.4499
		±0.63	±0.65	±13.3	±7.9	±0.136	±10.7	±0.36	±10.1	±5.9	±0.0270
SH. Rat	8	16.64	69.17	275.4	140.0	1.975	201.5	76.18	140.3	326.5	0.4303
		±2.48	±1.01	±7.0	±9.5	±0.181	±38.3	±0.29	±7.0	±6.6	±0.0227
P Value		0.001	0.001	N.S.	0.01	0.025	0.001	N.S.	N.S.	N.S.	N.S.
Advanced Hypertensive Phase (36 Weeks of Age)											
Control	10	12.04	66.09	276.7	132.4	2.091	142.0	76.22	156.9	327.7	0.5195
		±1.10	±0.84	±13.2	±4.5	±0.109	±10.3	±0.28	±7.5	±9.0	±0.1487
SH. Rat	8	16.64	68.11	300.8	140.0	2.151	190.1	76.49	150.5	334.9	0.4498
		±2.05	±1.31	±10.4	±9.6	±0.155	±28.0	±0.20	±5.7	±8.5	±0.0206
P Value		0.001	0.001	0.001	0.05	N.S.	0.001	0.025	0.05	N.S.	N.S.

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.
Wt: Defatted dry weight (mg) Na and K contents: mEq/kg of defatted dry weight

exchanged for 1% saline and water in ratio of 1 to 2. This exchange during the late period derived from the previous observation that the maintenance of the steroid-treated animal on 1% saline alone resulted in the death of 12% animals on 17 days and the animals exhibited pronounced hypertension more than 190 mmHg 5 days before death. The 10 DOCA hypertensive and control

rats were used on 20 and 44 days after the surgical procedure.

Dexamethasone phosphate dissolved in physiological saline was injected subcutaneously in dose of 0.2 mg/kg/day to female Wistar rats weighing 130 to 150 g for 30 days. Twenty four hours after the last injection the animals were subjected to the experiment. Control rats were

given the same amount of physiological saline for 30 days. All animals in this series of experiment received no nephrectomy or a 1% saline to drink.

After blood for electrolyte analysis was sampled from the abdominal aorta under ether inhalation, the rats were sacrificed by bleeding. Immediately thereafter, the heart and aorta from the heart to the diaphragmatic level were extirpated. The fat and connective tissues and the coagulated blood attached to the heart and aorta were removed on the glass plate. The weighed tissues were dried at 80°C for 48 hours. The difference in weight of the tissues before and after drying was regarded as the water content. These tissue samples were defatted with ether for 48 hours and the weight of the redried samples was regarded as defatted dry weight. Sodium and potassium in the aorta and heart were extracted by standing at room temperature for 48 hours using concentrated nitric acid. The concentration of both cations in the supernatants of the extracts and in the serum was analyzed by flame photometry.

The systolic blood pressure in unanesthetized rats was measured once or twice a week following the microphonic method reported previously¹⁴ and heart rate was counted from the recording of the pulse waves picked up by a small microphone pick up apposed to the tail distal to a rubber cuff. The values of both parameters in the present report were taken one or two days before sacrifice of the animals.

RESULTS

I. Spontaneously hypertensive rats at the pre- and early-hypertensive phases

As shown in Table I, the estimated mean values of the systolic blood pressure of rats at the pre-hypertensive and early-hypertensive phases were 144 and 167 mmHg, respectively, and were significantly ($P < 0.001$) higher than those in the control Wistar rats, although the value of 144 mmHg was not considered to indicate a hypertensive state. Heart rate and the concentrations of electrolytes in the serum of the hypertensive rats at the both phases were within normal range. The contents of electrolytes and water in the aorta and heart were also not affected by the progress of the hypertension at the early phase although the defatted dry weights were found to be significantly ($P < 0.05$) increased (Table II). The mean body weight of the hypertensive rats was somewhat less than that of the control animals, throughout the observation ages.

II. Spontaneously hypertensive rats at the ages of 24 and 36 weeks

At the ages of 24 and 36 weeks the average blood pressure in the hypertensive rats was 190 and 187 mmHg, respectively. The blood pressure in 2 to 4 animals at either age was more than 200 mmHg. In association with the rise of blood pressure the heart rate was also increased ($P < 0.005$). The concentration of potassium alone in the serum was found to be markedly decreased ($P < 0.005$) at the ages (Table III). The markedly increased ($P < 0.001$) level of sodium in the aorta but not in the serum was demonstrated in the hypertensive rats at the age of 36 weeks, while the increases in contents of potassium ($P < 0.05$) and water ($P < 0.001$) in the aorta were found in the hypertensive rats at both ages. Accordingly, this resulted in a decrease ($P < 0.025$) of the sodium/potassium ratio only at the age of 24 weeks. The content of the electrolytes in the heart was not markedly affected by the progression of the hypertension. The level of sodium in the heart of the animals at the age of 36 weeks was somewhat lowered ($P < 0.05$). However, the weight ($P < 0.001$) as well as the water content ($P < 0.025$) of the heart were found to be increased (Table IV).

III. DOCA hypertensive rats

The blood pressure of the male Wistar rats 20 and 44 days after the implantation of the DOCA pellet was 198 and 240 mmHg, respectively. At the same time period the control animals removed of the right kidney and received the daily administration of saline showed somewhat elevated blood pressure. Although no significant difference in body weight was observed between the DOCA hypertensive rats and the control rats, as shown in Table V, the heart rate in the former animals was slightly decreased ($P < 0.025$). Potassium concentration in the serum of the hypertensive rats was markedly decreased ($P < 0.001$). The electrolyte patterns in the aorta and heart of the hypertensive rats in Table VI demonstrated the marked increase ($P < 0.001$) in water content and weight as well as the increase ($P < 0.025$) in content of sodium and potassium in the aorta. A slight but not significant increase in sodium, decrease in potassium and marked increase ($P < 0.001$) in weight and water content were observed in the heart of the hypertensive rats. Such changes of the electrolyte and water patterns in the aorta and heart were more marked in the rats of 44 days after the pellet implantation than in

TABLE V BODY WEIGHT, BLOOD PRESSURE, HEART RATE AND SERUM ELECTROLYTES IN DOCA HYPERTENSIVE (DH) RAT

Group	No. of Rats	Body Weight (g)	Blood Pressure (mmHg)	Heart Rate (beats/min)	Serum Electrolytes (mEq/l)	
					Na	K
20 Days after Pellet Implantation						
Control	10	150.2 ± 9.1	136.3 ± 14.1	496.8 ± 17.2	143.6 ± 0.9	3.531 ± 0.262
DH. Rat	10	151.5 ± 11.8	197.6 ± 15.0	462.0 ± 34.5	143.4 ± 0.9	2.934 ± 0.184
P Value		N.S.	0.001	0.025	N.S.	0.001
44 Days after Pellet Implantation						
Control	10	265.1 ± 13.9	145.7 ± 6.7	472.9 ± 31.7	143.5 ± 1.6	3.928 ± 0.325
DH. Rat	10	245.0 ± 31.8	240.2 ± 4.6	435.2 ± 33.6	144.6 ± 1.8	3.286 ± 0.453
P Value		N.S.	0.001	0.025	N.S.	0.005

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.

TABLE VI ELECTROLYTES AND WATER CONTENTS, AND WEIGHT IN AORTA AND HEART OF DOCA HYPERTENSIVE (DH) RAT

Group	No. of Rats	Aorta					Heart				
		Wt.	H ₂ O(%)	Na	K	Na/K	Wt.	H ₂ O(%)	Na	K	Na/K
20 Days after Pellet Implantation											
Control	10	8.63 ± 0.88	66.83 ± 1.07	285.5 ± 9.9	143.4 ± 10.0	2.002 ± 0.157	97.1 ± 9.5	76.49 ± 0.25	144.6 ± 5.6	338.6 ± 12.7	0.4272 ± 0.0212
DH. Rat	10	11.81 ± 1.10	69.96 ± 1.72	303.5 ± 18.1	157.8 ± 9.0	1.927 ± 0.119	133.9 ± 10.2	77.11 ± 0.32	149.1 ± 6.0	336.9 ± 7.9	0.4430 ± 0.0123
P Value		0.001	0.001	0.025	0.005	N.S.	0.001	0.001	N.S.	N.S.	N.S.
44 Days after Pellet Implantation											
Control	10	12.09 ± 0.99	66.91 ± 0.50	271.8 ± 10.3	130.2 ± 4.1	2.091 ± 0.103	156.9 ± 10.1	76.45 ± 0.37	143.4 ± 13.0	342.0 ± 9.8	0.4196 ± 0.350
DH. Rat	10	18.97 ± 1.72	70.27 ± 1.13	304.7 ± 12.1	154.0 ± 9.1	1.993 ± 0.112	227.5 ± 17.0	76.83 ± 0.25	150.6 ± 6.3	331.4 ± 9.7	0.4450 ± 0.0200
P Value		0.001	0.001	0.001	0.001	N.S.	0.001	0.025	N.S.	0.05	N.S.

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.

Wt: Defatted dry weight (mg) Na and K contents: mEq/kg of defatted dry weight

the rats of 20 days.

IV. Dexamethasone hypertensive rats

The blood pressure of the Wistar rats treated with dexamethasone was 150 mmHg one week, and 183 mmHg 30 days, thereafter. The body weight gain was markedly depressed ($P < 0.001$) by the treatment (Table VII). The daily food intake was depressed by 10% and the daily water-

intake by 30%. The heart rate was found to be increased ($P < 0.01$). In contrast to the spontaneously and DOCA hypertensive rats, the serum potassium in the dexamethasone hypertensive rats was somewhat elevated ($P < 0.05$), while the contents of sodium and water in the aorta were decreased ($P < 0.025$). On the other hand, the water and electrolyte patterns in the heart of the dexamethasone hypertensive rats were markedly

TABLE VII BODY WEIGHT, BLOOD PRESSURE, HEART RATE AND SERUM ELECTROLYTES IN DEXAMETHASONE HYPERTENSIVE (DxH) RAT

DEXAMETHASONE HYPERTENSIVE (DxH) RAT						
Group	No. of Rats	Body Weight (g)	Blood Pressure (mmHg)	Heart Rate (beats/min)	Serum Electrolytes (mEq/l)	
					Na	K
Dexamethasone 0.2 mg/kg/day s.c. for 30 Days						
Control	10	202.0 ± 18.0	139.9 ± 6.7	487.8 ± 20.8	142.5 ± 2.5	3.533 ± 0.167
DxH. Rat	10	167.3 ± 8.2	182.6 ± 10.6	515.6 ± 18.8	142.2 ± 3.0	3.740 ± 0.247
P Value		0.001	0.001	0.01	N.S.	0.05

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.

TABLE VIII ELECTROLYTES AND WATER CONTENTS, AND WEIGHT IN AORTA AND HEART OF DEXAMETHASONE HYPERTENSIVE (DxH) RAT

DEXAMETHASONE HYPERTENSIVE (DXH) RAT											
Group	No. of Rats	Aorta					Heart				
		Wt.*	H ₂ O(%)	Na	K	Na/K	Wt.*	H ₂ O(%)	Na	K	Na/K
Dexamethasone 0.2 mg/kg/day s.c. for 30 Days											
Control	10	4.56	66.72	265.0	147.9	1.793	58.16	76.25	151.1	353.0	0.4283
		±0.47	±0.85	±9.6	±7.7	±0.068	±2.72	±0.46	±10.7	±6.2	±0.0306
DxH. Rat	10	5.73	65.70	254.5	149.1	1.712	68.29	75.94	141.2	366.9	0.3854
		±0.42	±0.86	±8.3	±6.7	±0.108	±3.19	±0.33	±10.1	±9.9	±0.0287
P Value		0.001	0.025	0.025	N.S.	N.S.	0.001	N.S.	0.05	0.005	0.005

All values are average and standard deviations of results in 10 hypertensive and normotensive rats.

Wt*: Defatted dry weight (mg)/body weight 100g

Na and K contents: mEq/kg of defatted dry weight

modified, resulting in decrease ($P < 0.005$) of sodium/potassium ratio caused by decrease ($P < 0.05$) in sodium and increase ($P < 0.005$) in potassium (Table VIII). Marked increase ($P < 0.001$) in the relative weight of the aorta and heart per 100 g body weight was observed, though these organs did not show marked change in absolute weight.

DISCUSSION

The rise of blood pressure in the spontaneously hypertensive rats progressed with age and growth, and this was associated with cardiac, renal, and vascular complications.¹⁵ TAKATSU¹⁶ has studied the relationship between the electrolyte metabolism and genetic factors in the spontaneously hypertensive rats, and he observed that positive metabolic balance of sodium and consequently the presumed accumulation of sodium in the body per se were not directly related with the progression of the hypertension. In our laboratory, it was found that there were no sig-

nificant differences in the urinary excretion of sodium and potassium between the spontaneously hypertensive and normotensive Wistar rats from 5 to 20 weeks of age (unpublished work), and daily oral administration of 10 mg/kg of hydrochlorothiazide to spontaneously hypertensive rats at the pre- and early-phases did not prevent the progressive rise in blood pressure.¹⁴ Recently LOUIS et al.¹⁷ reported that the spontaneously hypertensive rats were relatively insensitive to changes in dietary sodium intake. No significant abnormality in the water and electrolyte patterns in the aorta, heart and serum confirmed in the present experiment at the early phase of hypertension excludes the involvement of the tissue electrolyte disturbances in the pathogenesis of the hypertension.

Increase in the peripheral vascular resistance due to abnormality in the electrolyte pattern in the arteriolar wall has been suggested by TOBIAN et al.¹⁸ The sodium ion imbalance between the extracellular and intracellular spaces was postu-

lated by FRIEDMAN et al.^{19,20} to produce a persistent contraction of the vascular smooth muscles. Further, the authors²¹ have reported a significant increase in the ion-binding capacity by the cellular and paracellular matrices in the arterial wall of the renal or DOCA hypertensive rats. The same increase was already found 2 to 4 days after the administration or the ligation of the renal artery. These evidences suggest that the abnormal change of the electrolyte pattern in the vessel wall is a prerequisite for the manifestation and development of these hypertension.

In accord with the progression of the age and hypertension in the spontaneously hypertensive rats, the contents of potassium, water and then sodium in the aorta were found progressively to increase, as were found in the DOCA hypertensive rats but not in the dexamethasone hypertensive rats. This indicates that the marked progression of the hypertension produces abnormal electrolyte pattern in the vessels or on the contrary the latter event per se accelerates the hypertension. The assumption that the excessive liberation of the mineral-corticoids results in the abnormal electrolyte pattern in the tissues is supported by the following evidences in the spontaneously hypertensive rat: 1) the area of glomerular zone of the adrenal cortex increases from early phase of the hypertension and markedly at the age of 4 to 5 months;²² 2) the functional activation of the glomerular zone is demonstrated histochemically from age of 5 to 7 months;²³ and 3) the hyperfunction of the hypothalamic nuclei which were assumed to bear the function of the ACTH activators is demonstrated enzyme-histochemically.²⁴ SOKABE^{25,26} reported that the renin contents in kidneys of the spontaneously hypertensive rats at the prehypertensive (5 weeks of age) and early hypertensive (11 weeks of age) stages were not significantly different from those in controls. However, the renin activity gradually decreased with the progression of the hypertension. Therefore, the activation of the renin-angiotensin aldosterone system seems to be not responsible for the abnormal electrolyte pattern in the spontaneously hypertensive rats.

HOLLANDER et al.²⁷ have found in the dogs with the ligated aorta that the "hypertensive segment" of the aorta above the ligation shows a significant elevation of sodium, chlorine and water, while the "hypotensive segment" below it shows the levels within normal range. The concomitant increased level of acid mucopolysaccharide in the hypertensive segment produced by

the hypertensive process is regarded to be responsible for the accumulation of the electrolytes and water. However, in the present experiments the contents of water and sodium in the hypertrophic aorta of the dexamethasone hypertensive rats were found to be decreased. Therefore, it is unlikely that the increase of electrolyte and water contents in the aorta of the spontaneously hypertensive rats at the age of 24 and 36 weeks occurred directly as the result of the rise in blood pressure. As mentioned above, since the spontaneously hypertensive rats in the advanced phase exhibit the vascular, renal and cardiac complications¹⁵ and the other hypertensive diseases,¹² it would seem that the abnormal electrolyte pattern in the tissues of the hypertensive rats derive from the secondary cardiovascular changes or the unknown factor(s), except for the excessive liberation of mineral-corticoids, as has been previously mentioned.

FREED et al.²⁸⁻³⁰ have shown that the administration of cortisone or prednisolone in the adrenalectomized rats or the hypotensive potassium-deficient rats results in the rise of blood pressure, the decrease in the sodium contents of aorta and heart, and the decrease in sodium/potassium ratio in the tissues. The dexamethasone hypertensive rats in the present experiment showed the decrease in sodium alone in the aorta, and decrease in sodium and sodium/potassium ratio and increase in potassium in the heart. On the other hand, the DOCA hypertensive rats showed the increase in sodium and potassium in the aorta and no significant changes in the heart, and the sodium/potassium ratio in the tissues was not affected. These results suggest that DOCA and dexamethasone have a different effect related to electrolyte metabolism in the aorta and cardiac tissues. Therefore, more works are required to elucidate the mode of action of dexamethasone responsible for the development of hypertension.

SUMMARY

Relationship between the electrolyte patterns in the aorta, heart and serum and the progression with age of hypertension in the spontaneously hypertensive rats was studied. No significant differences in sodium, potassium and water contents in the aorta and heart, and in electrolyte concentrations in the serum were found between the spontaneously hypertensive rats at pre- (6 weeks of age, with systolic blood pressure of 144 mmHg) or early-hypertensive (13 weeks of age, 167 mmHg) phase and normotensive Wistar rats

of same ages (128 and 123 mmHg). However, a marked increase in electrolyte and water contents in the aorta and a decrease in the concentration of potassium in the serum were observed in the hypertensive rats at the ages of 24 and 36 weeks whose blood pressure was more than 180 mmHg. Similar but more marked electrolyte imbalances were observed in the desoxycorticosterone hypertensive rats but not in the dexamethasone hypertensive rats. These results suggest that the disturbances in tissue electrolytes are not participant of the pathogenesis of the spontaneous hypertension but of the marked progression of the hypertension and that it may derive from the excessive liberation of mineral-corticoids and/or secondary vascular changes.

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