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ELECTROLYTE PATTERN OF THE AORTA IN THE SPONTANEOUSLY HYPERTENSIVE RATS

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It is well known that increase in the peripheral arteriole resistance is mainly responsible for the elevation of arterial blood pressure in hypertensive disease. Tobian and Binion (1) had suggested that biochemical changes in the arteriolar wall play an important part in this respect. Later they reported that amounts of sodium (Na), potassium (K) and water of the aortas in rats with various types of experimental hypertension were elevated (2). In 1963, Okamoto and Aoki (3) succeeded in separating a colony of Wistar rats with 100% incidence of spontaneous hypertension and named these animals "spontaneously hypertensive (SH) rats". The involvement of such biochemical changes of the blood, heart and aorta in pathogenesis of the hypertension of the SH rats was investigated in this report.

The SH and same strain normotensive (N) rats of 23, 34 and 54 weeks of age were divided into 6 groups consisting of ten rats in each. The blood, heart and thoracic aorta (from heart to diaphragm) of the animals were removed under ether anesthesia for Na and K analysis. Aorta was dissected free of adventitia, then heart and aorta were swabbed free of blood with analytic grade filter paper. After tissues were weighed, dried, defatted and extracted with nitric acid, Na and K in the extract were analyzed by use of a flame photometer. Systolic blood pressure was previously determined indirectly following a tail cuff method in unanesthetized condition.

The average values of blood pressure were 178.4, 174.6 and 184.3 mmHg in the SH rats of 23, 34 and 54 weeks of age, and 136.1, 139.1 and 132.7 mmHg in the N rats of the same ages, respectively. Fig. 1 illustrates the weight and water content per fresh tissue, the electrolytes content per kg dry defatted weight and Na/K ratio in the aorta. In comparison with N rats, the aorta of the SH rats showed significant elevation in weight, and water, Na and K contents, and reduction in Na/K ratio. Especially, water and K contents in the aorta were strikingly increased in the SH rats irrespective of age. In the heart these elevated changes were observed

FIG. 1. The average and standard deviations of weight, contents of water, Na and K, and Na/K ratio of the aorta in the spontaneously hypertensive and normotensive rats of 23, 34 and 54 weeks of age. Closed column shows the value of hypertensive rats, and open column shows the value of normotensive rats. **: $P < 0.001$ *: $P < 0.05$

only in the SH rats of 34 weeks of age. The serum levels of Na were similar in both rats, but K levels were somewhat lower in the SH rats than in the N rats. However, the reduction was significant ($p < 0.05$) only in the rats of 34 weeks of age.

The aortas of these rats, which had been hypertensive for more than three months, were hypertrophic and sclerotic macroscopically. The Na/K ratio in the aorta of the SH rats was lower than that of the N rats. Freed *et al.* (4) reported that Na/K ratio of arterial tissue had an inverse correlation to blood pressure levels. Barr *et al.* (5) showed that increase of intracellular K in arterial strips elevated basal arterial tone. Friedman *et al.* observed that K in the rat aorta was almost confined to cell compartment (6). The ionic changes of the

aorta observed in this studies, therefore, probably contribute to the maintenance of the hypertension of the SH rats, provided the similar changes occur in the arterioles.

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A PHARMACOLOGICAL EVIDENCE FOR THE EXISTENCE OF INTRACARDIAC SYMPATHETIC GANGLIA IN THE RABBIT

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It has been discussed for many years whether there exist intracardiac sympathetic ganglia or not. Present experiments were performed to throw light on this problem, through an investigation of effects of hexamethonium (C_6) on cardiac responses to sympathetic nerve stimulation. Rabbit hearts were isolated with bilateral stellate ganglia still attached (1), cannulated as Langendorff's preparations, and perfused at the rate of 10 to 12 ml/min with Krebs bicarbonate solution (perfusion medium) bubbled with 95% O_2 and 5% CO_2 maintained at 30°C in external medium in the same conditions as perfusion medium. Venous effluent was collected for 6.5 minutes during nerve stimulation. Noradrenaline (NA) released in venous effluent was measured fluorometrically (2). Bilateral ganglia were stimulated 6 times through fluid electrodes (1), each for 30 seconds at the interval of 30 seconds, with supramaximal rectangular pulses of 3.5 msec duration at a frequency of 30 cps, as described by Huković and Muscholl (3). Sympathetic nerve stimulation was repeated in the same preparation 2 times at interval of 30 minutes. First period of nerve stimulation released NA of 50.0 to 962.4 ng in total effluent in 12 cases. With 2nd period of stimulation NA output decreased by $34.5 \pm 3.5\%$, which described as 100% in Fig. 1-A.

Huković and Muscholl (3) reported no effects of C_6 on NA output released by nerve stimulation in rabbit's heart. In the present experiment, however, perfusion of C_6 5×10^{-6} (g/ml) 30 minutes before 2nd period of nerve stimulation decreased significantly NA output by 48% compared to the corresponding output of control hearts, as shown in Fig. 1-A. Administration of C_6 5×10^{-6} in external medium did not produce a significant decrease in NA output, ruling out the possibility that C_6 leaked from perfusion medium to external medium attacked stellate ganglia directly. On the other hand, C_6 did not alter positive ino- and chrono-tropic responses of the heart to sympathetic nerve stimulation. From these results, it seems likely that there might exist intracardiac sympathetic ganglia, of which postganglionic fibers might innervate possibly localized areas unrelated with atrial and ventricular myocardium.