SODIUM AND CATECHOLAMINE EXCRETION

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THE DEVELOPMENT of hypertension has been correlated with increased sympathetic activity and/or with increased vascular response to sympathetic stimulation or to catecholamine (= CA) administration. Hypertension also develops or is aggravated by loading with sodium and administration of mineralocorticoids (DOCA). Hypertension induced by Na-DOCA has been reported to be accompanied by increased turnover rate of CA in heart and reduced retention of CA (DE CHAMPLAIN *et al.*, 1969). However, this phenomenon was abolished by ganglion-blocking agents in spite of continued administration of Na-DOCA (DE CHAMPLAIN *et al.*, 1969). On the other hand, it is also unclear whether the kinetics of development of abnormal CA storage fit that of the increased blood pressure. We, therefore, set to study the rate of catecholamine secretion to clarify whether it was related to hypertension or to sodium administration.

The experiments were carried out in rats and in cats. Intragastric loading of 50 ml/kg of 0·15 M NaCl caused increased CA excretion in the urine (4·12 $\pm$ 0·49 μg/kg $\times$ 8 hr compared to 2·61 $\pm$ 0·30 in non-loaded rats and 2·51 $\pm$ 0·26 in rats loaded with an equivalent volume of water; $P < 0{\cdot}01$). Since intragastric loading involved handling of the animals and stress of the introduction of a gastric tube, in the next experiment rats were adapted to metabolic cages with food and water *ad lib.* and, after 10 days the water was switched for a solution of NaCl. Urinary CA excretion on the day of presentation of NaCl increased from 0·528 $\pm$ 0·043 μg/rat $\times$ 24 hr to 0·950 $\pm$ 0·060; $N = 10$, $P < 0{\cdot}001$, paired analysis). The possibility that passage of sodium through the gastrointestinal tract was the cause of increased CA excretion was eliminated because intra-peritoneal sodium-loading also resulted in a rise of CA excretion (from 2·61 $\pm$ 0·30 to 3·59 $\pm$ 0·30 μg/kg $\times$ 8 hr, $N = 10$, $P < 0{\cdot}05$).

The increased CA excretion caused by sodium-loading was abolished after treatment of the rats with a ganglion-blocking agent (Pentapyrrolidinium), thus suggesting that the effect of sodium was mediated through increased sympathetic activity rather than through a direct effect at adrenergic nerve terminals or on the storage mechanism in these nerve endings.

Although the effect of sodium loading on catecholamine excretion was evident within a short time (hours) the type of experiment described did not exclude the possibility that inactivation of CA was reduced rather than that secretion of CA was enhanced by the sodium load. Therefore, the effect of sodium loading was also studied in the cat with the technique of collection of adrenal vein blood. Intravenous infusion of NaCl, as shown in Fig. 1, resulted in immediate (within 10 min) increase of CA secretion from adrenal medulla. The secretion of CA following i.v. sodium loading increased by 7·51 $\pm$ 2·31 ng/kg $\times$ min from each adrenal at the peak.

In cats with bilateral cervical vagotomy infusion of 0·15 M NaCl caused an even greater increase of CA secretion from the adrenal gland (10·22 $\pm$ 3·86 ng/kg $\times$ min)

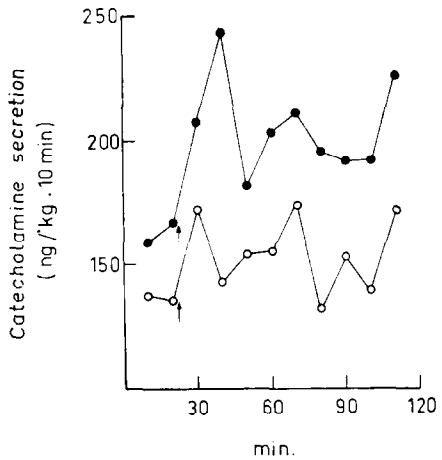

FIG. 1.—Effect of sodium loading on catecholamine secretion by the cat adrenal gland *in vivo*. Sodium infusion started at arrow and continued at the rate of 0·15 mEq/kg × min. ○———○ 0·15 M NaCl (11 experiments); ●———● 1·5 M NaCl (6 experiments).

and the fall in the secretion rate noted after the initial rise (Fig. 1) was abolished following vagotomy. This fall was, therefore, apparently due to hypervolemia.

The various experiments described indicate that sodium-loading can induce an immediate increase of CA secretion. These findings seem to raise doubt about the correlation of sodium and hypertension on the one hand, and sodium and catecholamines on the other hand, since hypertension follows only after long-term loading with sodium while the effect on catecholamines in our experiments seems to be immediate.

To further investigate this point a long-term experiment was performed with rats. The rats were placed in individual cages on food *ad lib.* and either water or 1·4% NaCl as drinking fluid. Catecholamine excretion in the urine was followed for two months. An immediate increase in CA excretion was observed on the day of switching from water to NaCl solution as drinking fluid (from 0·811 ± 0·102 to 1·285 ± 0·159 μg/rat × 24 hr, $P < 0{\cdot}05$). However, while the CA excretion in the control group (on H_2O) was constant throughout the 2 months, it increased gradually in the experimental group (on NaCl) to 3·914 ± 0·436 μg/rat × 24 hr. During the first two weeks the increase of CA excretion was mainly in norepinephrine but from one month onwards epinephrine excretion increased even more than norepinephrine. At the end of two months on NaCl no significant change in blood pressure was observed between the two groups. Tyrosine hydroxylase activity was increased fourfold in the adrenals of the NaCl-treated rats and cardiac endogenous catecholamines were significantly reduced (0·447 ± 0·028 compared to 0·534 ± 0·019 μg/g in hearts of the control group, $P < 0{\cdot}02$). These latter findings corroborate those reported for rats with Na-DOCA hypertension (DE CHAMPLAIN *et al.*, 1969). However, in our experiment no significant change of blood pressure accompanied these alterations of catecholamine storage and synthesis. Thus, again, there is an indication of a dissociation between the effect of sodium on catecholamines and its effect on blood pressure. Whether the effect of sodium on catecholamines is through a central mechanism or through other, as yet unidentified, mediators deserves further study.

REFERENCE

DE CHAMPLAIN J., KRAKOFF L. and AXELROD J. (1969) *Circulat. Res.* XXIV & XXV (Suppl. I), 75–92.