be assumed that in the presence of a low sodium content in the diet, the potassium in the tissues is retained sufficiently to prevent the development of hypotension. Biochemical studies will be required to prove this point.

Summary. (1) Dietary restriction of potassium was found to lead to the occurrence of hypotension in the rat. (2) This depressor effect of potassium deprivation was prevented by simultaneous dietary withdrawal of sodium.

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Effect of Variation of Potassium Intake on Pressor Activity of Desoxycorticosterone. (18979)

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Although the chronic administration of DCA may induce hypertension in various animals, it occurs regularly in the rat only if rather large doses are administered to younger animals(1). Furthermore, hypertension occurs uniformly only when additional sodium is given and when renal damage or uninephrectomy has been accomplished(1-3). Even under many of these conditions, certain investigators have not been able to produce a significant hypertension(1,3,4). Sayers(1) concluded that "the impression is gained that DCA must act in combination with as yet unknown factors in the production of pathological lesions in experimental animals." One of the possible factors responsible for the irregularity in the frequency, intensity, and persistence of the hypertension induced by DCA is the potassium loss induced by this steroid(5). For loss of this cation has been found in our laboratory to produce a marked hypotension in both the normotensive(6,7) and the hypertensive(8) rat. In other words, DCA may initiate one or more mechanisms to elevate the blood pressure, yet also initiate one (*e.g.* the loss of potassium) to decrease the blood pressure.

In view of the latter possibility, it was thought worthwhile to study the effect of DCA in the rat deprived of potassium and in the rat fed an excess of this same cation. The results of the study indicated that the effects of DCA on the blood pressure were far more profoundly influenced by experimental variation of the potassium intake than that of sodium.

Effect of DCA on rats deprived of potassium. Methods. A group of 24 six-weeks-old male rats (Long-Evans) was deprived of potassium by placing them on a potassium-deficient diet(8). At the end of 8 weeks, 8 of these potassium-deficient rats were given DCA in benzyl alcohol† (4 mg) 3 times a week by

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subcutaneous injection. Eight more were treated in the same fashion, except that they also drank sodium chloride solution (1%). The remaining 8 rats received no DCA but were maintained on the potassium-deficient diet as controls. Systolic blood pressures were taken weekly by means of the microphonic manometer(9).

Results. The rats deprived of potassium had an average blood pressure of 84 mm Hg (range: 60 to 98 mm) at the end of the 8-week period of feeding a potassium-deficient diet. The administration of DCA induced an even more marked depressor response, the average blood pressure falling to 65 mm Hg (range: 50 to 80 mm) within one week. Marked loss of weight occurred in these animals, all of which died in less than 3 weeks. Moreover, those rats drinking saline solution showed a more marked decline in blood pressure, to an average of 60 mm Hg, and even greater toxicity, death occurring in all by the end of the first week. In the control potassium-deficient rats, the average blood pressure remained at the same hypotensive levels; moreover, no loss of weight or mortality occurred in this group.

Effect of excess potassium compared to excess sodium in intact rats given DCA. Methods. Sixteen 6-weeks-old male rats (Long-Evans) were divided into 2 groups. The first group of 8 was fed a normal diet but received potassium chloride (1%) to drink. The remaining 8 rats were fed the same diet but received sodium chloride (1%) to drink. DCA in benzyl alcohol (4 mg) was administered 3 times a week by subcutaneous injection to all of the rats. Blood pressures were obtained at weekly intervals.

Results. As Fig. 1 shows, both groups of rats exhibited an increase in blood pressure following DCA injections. However, those DCA-treated rats drinking KCl solution showed an increasingly higher degree of hypertension in sharp contrast to those drinking NaCl solution which demonstrated a decline in blood pressure starting at the sixth week and eventually becoming normotensive.

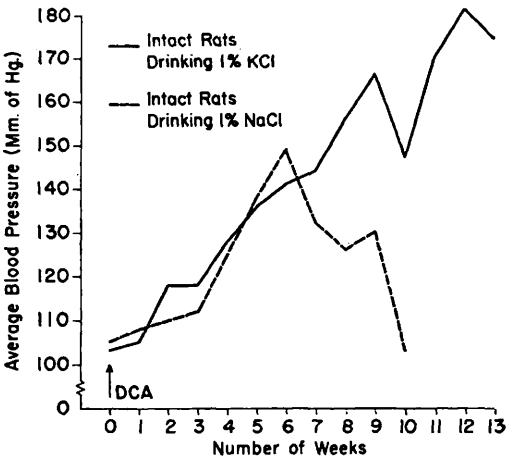

FIG. 1. The effect of DCA on intact rats given supplemental potassium or sodium.

The gain in average weight was greater in those rats given the excess potassium (178 to 315 g) than in those drinking sodium chloride solution (184 to 273 g). Deaths, as well as gross and microscopic evidence of toxicity were noted only in the latter group.

Discussion. The results of the preceding studies indicate that the pressor effect of DCA can be either abolished or accentuated in the normal rat with intact kidneys by the removal or addition, respectively, of potassium to the dietary intake of the experimental animal. Indeed, DCA was found to exert a further depressor effect in rats previously made potassium-deficient. Since it was shown previously that potassium deprivation has a depressor effect in both normotensive and hypertensive rats(6,8), this depressor effect of DCA may well be related to the loss of potassium which occurs during administration of this steroid(5). The loss of potassium occasioned by DCA is intensified by the concomitant administration of excess sodium(10) and would seem responsible for the more marked hypotension which occurred in the rats previously made potassium-deficient, as well as for the decline which followed the initial elevation of the blood pressure in the intact rats drinking saline (Fig. 1).

It is significant that when excess potassium

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was given, sustained hypertension developed in older rats with intact kidneys, and with relatively small dosage of DCA. Moreover, none of the latter rats died during the experimental interval, nor was gross evidence of toxicity observed in these animals, confirming the protective action of potassium in the DCA-treated animal(10-12).

Although most all of the pressor and toxic actions of DCA heretofore have been studied in reference to the cation, sodium, the importance of potassium in this same relation cannot be overlooked. Indeed, both these, as well as our earlier findings(8), strongly suggest that the presence of adequate amounts of the latter cation is essential for the development of hypertension in the rat, whether the latter is induced by the administration of DCA or by interference with renal hemodynamics.

Summary. Significant hypertension was produced by DCA in intact, older rats given excess potassium, in contrast with the failure of hypertension to persist in similarly treated rats but receiving excess sodium. Potassium deficiency abolished the pressor action of DCA in rats. The results of these studies also indicated that the effects of DCA on the blood pressure were far more profoundly influenced by experimental variation of the potassium intake than that of sodium.

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Work Performance of Adrenalectomized Rats Given Cortisone and 17-hydroxycorticosterone by Continuous Intravenous Injection. (18980)

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The biologic activity per unit weight of 17-hydroxycorticosterone has been found to be greater than that of 17-hydroxy-11-dehydrocorticosterone (cortisone) when assayed by the Ingle work-test(1,2) and by the liver glycogen deposition test(2). All biologic assays of the adrenal cortical steroids have been based upon the response to intermittent injection. Since there are some differences in the physical properties of the steroids the possibility must be considered that the apparent differences in potency are based upon differences in the rate of absorption from the site of injection or in the speed of inactivation of the compound after it enters the body fluids. Accordingly we have determined the biologic response per unit weight of 17-hydroxycorticosterone and of cortisone by administering each steroid by continuous intravenous injection to rats under the conditions of the Ingle work-test. In these experiments 17-hydroxycorticosterone had approximately twice the potency of cortisone.

Methods. Male rats of the Sprague-Dawley strain were maintained on Archer Dog Pellets until they reached a weight of 200 ± 2 g. The work test was carried out according to Ingle(3). The animals were anesthetized with phenobarbital sodium and cyclopal sodium and were subjected to the stimulation of muscle immediately following removal of both adrenal glands and both kidneys. The quadriceps muscle of the left hind leg was weighted with 100 g. A Nerve Stimulator, Model B, Upjohn, was used to deliver 5 pulses per second. The duration of each pulse was 20 milliseconds and the intensity was 20 milliamperes. The distance the weight was lifted was recorded on automatic work adders. Each recorder revolution represented approxi-

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