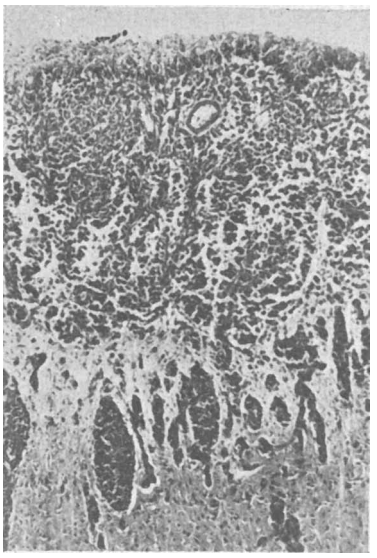

FIG. 2. Mouse Sarcoma 37, 14 days after transplantation to subdural space of guinea pig.

By the end of the 1st week a solid layer of tumor tissue was present in the subarachnoid space, and rows of tumor cells infiltrated the brain along the perivascular spaces. Areas of necrosis and fibrosis were present in the upper layers of the tumor. The animal sacrificed on the 11th day showed an ovoid polypoid meningeal mass measuring 1.1 x 0.8 x 0.4 cm, lying upon and depressing the brain surface (Fig. 1). On the 14th and the 18th day there was deep invasion of the brain with gross extension to the proximity of the ventricle and thick cuffs of tumor cells around the cerebral vessels (Fig. 2). The tumor of the animal sacrificed on the 18th day measured 1.5 x 1.0 cm over its surface and extended 0.4 cm into the brain tissue. This is 3 to 4 times larger than the largest size obtained in this laboratory following transplantation of this tumor to the anterior chamber and several hundred times larger than the average size. The last surviving animal with subdurally transplanted tumor developed a gait disturbance during the 3rd week and died 21 days after transplantation. The autopsy showed hemorrhage and necrosis of the brain and abundant well preserved tumor tissue. No lesions of note were seen in the other viscera.

Summary. Mouse Sarcoma 37 was transplanted to the subdural space of 14 guinea pigs. Evidence of growth was present in all animals sacrificed between the 2nd and 18th day after transplantation. One animal died at the end of the third week, apparently as the result of invasion of the brain by tumor tissue. The pattern of growth in the meninges and brain was similar to that previously observed in the anterior chamber of the eye of guinea pigs, but, after the 9th day the mass of tumor tissue in the brain was greater than that in the eye for comparable periods. There was no evidence of regression of tumor in the brain in contrast with tumor transplanted to the anterior chamber, which usually begins to regress by the end of the 2nd week.

Since this paper was submitted for publication, H. S. N. Greene published an excellent paper on "The Transplantation of Tumors to the Brain of Heterologous Species," *Cancer Research,* 1951, v11, 529.

Received July 9, 1951. P.S.E.B.M., 1951, v78.

Depressor Effect of Potassium Restriction on Blood Pressure of the Rat. (18978)

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Although there is ample evidence(1,2) that an adequate intake of potassium is necessary for the structural integrity of the cardiovascular system, almost no hemodynamic studies

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of the potassium deficient animal have been made. Recently, however, in a preliminary communication(3) we reported the occurrence of hypotension in a group of rats placed upon a diet containing only 0.01% potassium. In the present report these preliminary studies have been extended, and the influence of sodium intake upon the depressor effect of potassium restriction also investigated. The results of these studies not only confirm the preliminary finding concerning the hypotensive effect of potassium restriction, but also suggest that the lowering of the blood pressure can be prevented by the simultaneous restriction of sodium in the diet.

Methods. Male rats (Long-Evans strain), 45 days old, were used in all experiments. Variations in either the potassium or sodium intake were made by adding known amounts of either cation to an otherwise basic diet, as described by Follis *et al.*(2), consisting of known and fixed amounts of carbohydrate, fat, protein, salts, and vitamins. These values were checked by analysis using the flame photometer method. Blood pressure readings were taken by the microphonic method(4) before the experiment and then once weekly for 7 weeks. All rats were killed 8 weeks after the beginning of the experiment. The heart, kidneys and adrenal glands of the various groups of rats were removed and weighed (dry and wet). Histological studies also were made of the same organs.

Results. A. *Effect of dietary potassium restriction upon blood pressure of rats.* Twenty-nine rats were placed upon the basic diet containing 0.01% potassium and 0.4% sodium. Twenty-four of these rats were living at the end of the 7-week period. The average weight of the group at the beginning and end of the experimental period was 124 g (range: 96 to 177) and 162 g (range: 108 to 222), respectively. The average initial blood pressure of the group was 104 mm Hg (S.E. mean: ±2.3). The average pressure slowly decreased until at the end of the 7th week the average pressure was 84 mm Hg (S.E. mean: ±2.1). The rats appeared to be in fairly good health, but when they were held in the hand it was apparent that they were asthenic and had poor muscle tonus. Although they moved about freely, they lacked vigor.

A control group of 29 rats was given the same diet containing, in addition, 0.6% potassium. These rats gained much more weight; their average initial weight of 113 g (range: 101 to 128 g) increased to 234 g (range: 201 to 273). The course of their blood pressure measurements also was different. Thus, the average initial pressure of 105 mm Hg (S.E. mean: ±1.9) increased significantly over 7 weeks to a final reading of 113 mm Hg (S.E mean: ±2.1), as might be expected in growing rats.

B. *Effect of sodium intake upon hypotension induced by dietary potassium restriction.* In view of the above depressor effect induced by the dietary restriction of potassium, it was considered important to determine the possible influence of concomitant alterations in the sodium intake upon this response. Therefore, one group of 21 rats was placed upon low potassium diet (0.01%), which also contained a low sodium content (0.04%). The weight and blood pressure of both groups were followed weekly for 7 weeks. An actual fall in weight occurred in the group of rats maintained upon the low sodium-low potassium diet. Thus, the average initial weight was 117 g (range: 89 to 164) and the average final weight was 111 g (range: 73 to 178). No fall occurred in the blood pressures of these

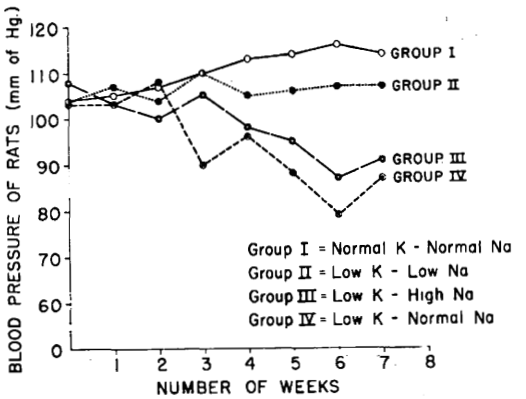

FIG. 1.

3. Freed, S. C., and Friedman, M., *Science,* 1950, v112, 788.

4. Friedman, M., and Freed, S. C., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 670.

TABLE I. Average Wet and Dry Weight of Kidneys, Heart and Adrenals in Potassium Deficient Rats.*

Diet K	Diet Na	No. rats	Kidneys Wet, g	Kidneys Dry, g	Kidneys W/D ratio	Heart Wet, g	Heart Dry, g	Heart W/D ratio	Adrenals Wet, g	Adrenals Dry, g	Adrenals W/D ratio
Low	Normal	10	1.36	.32	4.3	.38	.08	4.6	.017	.010	1.7
"	Low	17	1.12	.28	4	.41	.10	4.1	.027	.014	1.8
"	High	19	1.32	.33	4	.40	.095	4.2	.020	.008	2.5
Controls		6	.82	.27	3	.39	.12	3.3	.018	.010	1.8

* Calculated per 100 g body wt.

rats over the period of the experiment. Thus, the initial average pressure was 104 mm Hg (S.E. mean: ± 1.6) and at the end of 7 weeks the average pressure was 107 mm Hg (S.E. mean: ± 4.5) The animals, however, presented the same general appearance of asthenia observed in the previously described group of rats which were restricted *only* in their potassium intake. Twenty-two rats placed upon a low potassium diet containing a high sodium content (0.70%) exhibited relatively little gain in weight (increase of 130 to 142 g over the 7-week period). The fall in blood pressure was somewhat less than that found in rats receiving a normal amount of sodium in their low potassium diet. Their average initial pressure was 108 mm Hg (S.E. mean: ± 2.2) and at the end of 7 weeks it was 91 mm Hg (S.E. mean: ± 3.1).

C. *Pathological changes following dietary potassium restriction.* The heart, kidneys and adrenal glands of the various groups of rats were examined histologically at the end of 7 weeks. Rats placed upon diets low in potassium but normal or high in sodium invariably exhibited foci of necrosis and cellular infiltration in the myocardium. These lesions were found chiefly in the subendocardial area of the left ventricle. Although all of the potassium deficient rats exhibited these lesions, no correlation could be found between the severity of histological change and degree of depressor effect. Rats placed upon a diet not only low in potassium, but also low in sodium did not exhibit degenerative changes in the myocardium.

From Table I, it can be noted that kidneys of the animals on low potassium diets with varying sodium content were heavier than normal. This increased weight, however, was due to a greater water content, as indicated by the essential equivalence of the dry weights to that of the control group. The reverse relationship occurred with the heart weights, the wet weights being comparable to the controls, but the dry weights being somewhat decreased. This latter suggests the possibility that rats on the low potassium diets had a decreased myocardial mass. The adrenal glands of the rats on the low potassium-high sodium diet were apparently edematous while those on the low potassium-low sodium diet were possibly hypertrophic. These results are essentially in confirmation of the findings of Kornberg and Endicott(5) who reported widespread edema in rats on a low potassium diet.

Discussion. The foregoing observations strongly suggest that drastic restriction in the rat's intake of potassium leads to a gradual fall in the animal's blood pressure. The exact mechanism responsible for the observed hypotension is still not known. However, the general inanition resulting from potassium deprivation cannot be held responsible, because control animals either partially starved(3) or those markedly emaciated from feeding on the diet low in sodium as well as potassium did not exhibit any significant change from normal in their blood pressure. Moreover, no correlation could be found between the severity of the myocardial necrosis occurring in the potassium deficient rat and degree of hypotension. Studies concerning the mechanism of the lowering of blood pressure are being pursued. The prevention of the depressor effect of the potassium deficient diet by the withdrawal of dietary sodium was an interesting, but not necessarily a surprising, phenomenon. It is well known that sodium displaces potassium in the tissues(6). It can

5. Kornberg, A., and Endicott, K. M., *Am. J. Physiol.*, 1946, v145, 291.

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.

The authors wish to express their gratitude for the valuable assistance of Dr. Sanford O. Byers.

Received July 13, 1951. P.S.E.B.M., 1951, v78.

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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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† We are grateful to Dr. Abbott E. Allen of the Schering Corp. for generous supplies of DCA used in these studies.