PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 147, 784-787 (1974)

Effect of Deoxycorticosterone on Organ Weights of Rats During Maturation (38438)

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It has been known for some time that injections of deoxycorticosterone (DOC) produces an increase in renal mass (1–5). One finds, however, that much information known about other forms of renal hypertrophy is not available concerning DOC-induced hypertrophy. For example, the immediate temporal changes giving rise to hypertrophy of the remaining kidney after unilateral renal extirpation are well known, as well as the age dependence of hypertrophy resulting from removal of a kidney (6–8) or induced by a high salt diet are known (9), the same relationship for DOC has not been described in any detail.

Recently, we have been involved in studies concerning the effect of DOC on renal function during development of the rat (10). As part of these studies, we were able to obtain information about the relatively short-term effects of the hormone on organ weights. It is the purpose of this communication to report these observations.

Methods. Wistar rats (Simonsen strain, Gilroy, CA) were used in these studies. Pregnant mothers were obtained and experiments were carried out on the offspring born in our own animal quarters. Starting at 15 days postnatally and at varying ages thereafter, DOC in sesame oil at a dosage level of 1 mg/100 g of body wt was administered daily by intramuscular injection. To prevent a potential bias resulting from possible genetic influences, both male and female siblings from the same litter were studied at different ages. Control animals were injected with carrier only. The animals were divided into two treatment periods. One group was studied at the end of either 4 or 5 days of injections; the other after 9 or 10 days.

On the day of experimentation, the animals were anaesthetized and clearance studies carried out using standard procedures for this laboratory (11). Results of the clearance studies are not reported here. At the end of the clearance studies, the animals were sacrificed and the kidneys, heart, spleen and liver were rapidly removed, blotted, and then weighed. Least square regression analysis and analysis of variance was carried out on the data generated by these studies on the IBM 360 Model 50 computer, using the statistical program "Statpack."

Results. One of the major problems that exists in making comparisons of organ growth in different animal populations is the question of whether organ weights are best related to age or body size. In Fig. 1, kidney weight as a function of body weight or age is plotted for control male animals along with comparative data for 9–10 day DOC treated male animals. When kidney weight is considered in terms of age dependence, one sees a great deal of scatter in addition to overlap between the experimental and control groups. On the other hand, when the data are normalized on the basis of weight, overlap and scatter are both reduced. In addition, a curvilinear relation between kidney weight and body weight becomes apparent. An analysis of variance was carried out on the three possible relations; kidney weight and age; kidney weight and body weight; and the double reciprocal relationship. Of the three, the double reciprocal relation between kidney weight and body weight indicates that a larger F value is obtained for the double reciprocal relations between kidney weight and body weight for all animal populations. The F values are two to ten times as large for the double reciprocal relationship as for either of the other relationships and indicate that the variance from the double reciprocal regression is far less than for other relations tested.

A comparable but not as definitive a relation-

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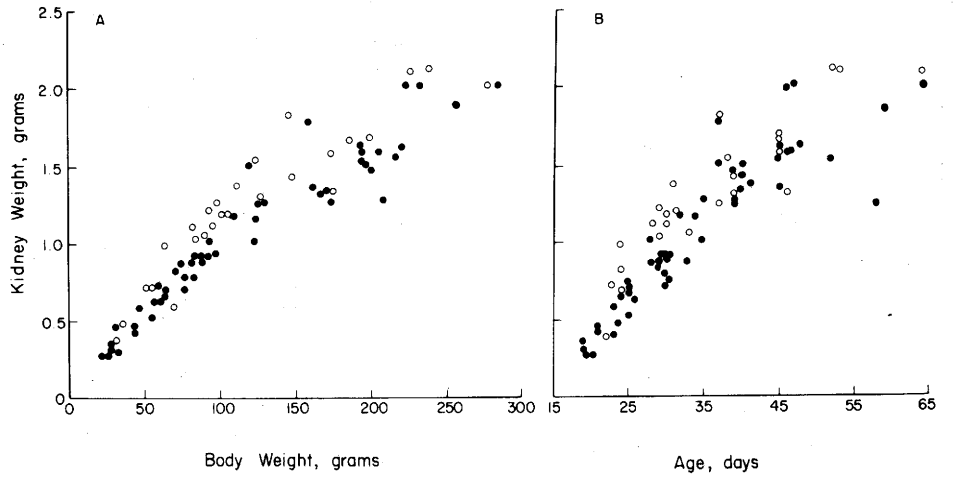

FIG. 1. Relationship between kidney weight and body weight (A) as well as kidney weight and age (B). Solid points represent data from control animals while open circles show data from animals treated with DOC 9 or 10 days.

ship is seen with heart weights and body weights. As with the kidney, one finds an increase in F values for the double reciprocal relationship, but not for all animal populations. As with the kidney, the F values are all larger for the double reciprocal relation except for 9–10 day DOC treated males. In this group F for the double reciprocal relationship is half as great as for the liver relation between heart weight and body weight. In the case of spleen and liver weights in relationship to body weight, as good a fit as any is obtained with a simple linear relationship. No sex dependence or effect of DOC on the relationships were detected.

In contrast to the absence of the effect of DOC on other organs, DOC causes renal hypertrophy. In Figs. 2 and 3, the least squares solution of the double reciprocal relationship is shown, as well as the standard error (shaded region) of the solution. Least squares results on the 4–5 day and 9–10 day treatment groups are shown by the broken lines. There is no difference in the extent of hypertrophy between the 4–5 day and the 9–10 day treatment groups. As can be seen in Figs. 2 and 3, the kidneys of the females are smaller than in males, and there is no sex dependence relative to the ability of the kidneys to undergo hypertrophy. Unlike other forms of hypertrophy (6–9), ability for DOC to induce hypertrophy is not influenced by age (or size) of the animal; rather the extent of hypertrophy seems to be related to absolute kidney weight.

Discussion. The quantitative relationship of organ weight to body weight will have to be defined if hypotheses about the regulatory processes governing organ growth are to have meaning. Thus, a linear relationship shows parallel growth rates and may indicate a direct link between regulation of organ weight and body weight. On the other hand, a double reciprocal relationship indicates a limiting value and could possibly reflect suppression of organ growth as related to the size of the organ *per se* or to body weight. One of the problems associated with

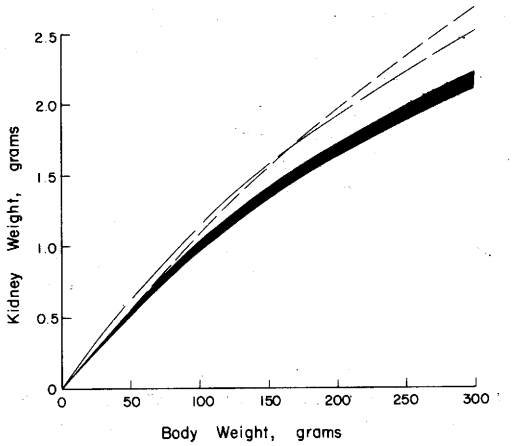

FIG. 2. Relationship between kidney weight and body weight in control and DOC treated male animals. Solid region shows the relationship for control animals with the area representing one standard error around the least squares solution. Short dashed line shows the least squares solution for 4–5 day DOC treated animals, while that of long dashes shows the relationship for 9–10 day treated animals.

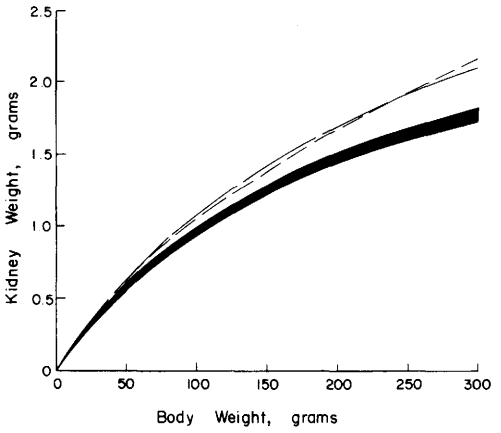

FIG. 3. Same relationships as in Fig. 2 for the female rats. Symbolism is the same as in Fig. 2.

defining the exact relationship is the fact that a linear relationship often provides a statistically significant description in terms of establishing a statistically significant relationship. For all correlations, the smallest F value was 58 for a sample size of 29, thereby indicating a high level of correlation. The best fit, however, is determined when equations are obtained which minimize the deviations from the least squares curve.

In the case of the kidney weight relationship to age or body weight, different curves have been reported over the weight ranges used in this study. A linear dependence (12) as well as the curvilinear one found here (13–16) have been reported. It has been argued that all the organs examined show a decreasing curvilinear relationship sometime during development (16), but only the heart is fitted to advantage by the double reciprocal relationship in this study.

Although a sex dependence of control kidney weight to body weight has been found, it is unlikely that this relationship is a result of differences in body composition as, for example, in body fat. If such were the case, a sex dependence for other organs would be evident and such is not seen. It is unlikely that the sex difference is a simple consequence of the differences in sex hormones, since estradiol and progesterone as well as testosterone exert renotropic action (1–4). Irrespective of the sex difference of control kidney weights, the extent of DOC-induced hypertrophy is not sex dependent, nor does it seem to be dependent on the size (age) of the animal. In contrast, renal hypertrophy induced by unilateral renal extirpation (6–8) or by high salt diet (9), as well as the hyperplasia following nephrectomy (17, 18) all are age dependent.

With respect to DOC-induced hypertrophy, it is quite extensive after only 4 days of treatment and no difference is found between 4 and 9 days of treatment. Although Goss and Rankin (19) as well as Moraski (20) described an increase in mitotic counts in DOC-treated animals within a few days of starting treatment, studies reporting changes of kidney weight in relation to body weight have been three weeks in duration of treatment (20) or longer (2).

Another confounding factor involved in previous studies of the effect of DOC on organ weights is that in some papers, treatment was so long as to produce hypertension (6) or salt intake was also increased (20, 21), thus preventing a study of the effect of DOC alone. In previous studies, an effect of DOC in increasing heart weight has been described (5, 22). This observation was not confirmed in these short-terms studies, nor was the report of DOC-induced hypertrophy of the liver (3). It may be argued that it takes more time for DOC to exert its effect on the heart. It also is likely that the cardiac hypertrophy resulted from blood pressure changes rather than being a direct effect of the hormone.

Summary. Organ weights of control and DOC-treated rats have been determined for animals of different ages and body weights. The relationships between kidney weight and body weight as well as heart weight and body weight are best fitted by hyperbolic functions. Males have larger kidneys than females for comparable body weights, but DOC-induced hypertrophy of the kidney is independent of sex. The extent of hypertrophy after 4 days is as great as after 9 days of DOC treatment. Organ weight to body weight relationships for heart, spleen and liver are independent of sex or DOC treatment.

This work was partially supported by grants from the National Science Foundation (GB 35637X) and from the National Institutes of Health (AM 16171). We wish to thank Lucy Moore, April Kopp and Stephan Foster for their expert help in carrying out these studies.

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Received May 20, 1974. P.S.E.B.M., 1974, Vol. 147.