Effect of Hypophysectomy on Size of Remaining Kidney after Ureteroduodenostomy and Contralateral Nephrectomy. (19768)

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This study was prompted by an examination of the adrenal glands of a number of dogs and rats that Drs. M. A. Block, K. G. Wakim and F. C. Mann had used in another investigation. They had removed one kidney and had transplanted the ureter of the remaining kidney into the duodenum of each animal. In every animal, the adrenal glands and the remaining kidney were appreciably heavier than those of control animals. This observation inspired an inquiry into the possible factors responsible for the increased size of these organs. Among the various possibilities, the influence of the hypophysis cerebri was considered to be the most probable. Consequently, experiments were designed to test the validity of this idea.

Method of study. Seven adult dogs, both males and females, weighing from 8 to 14 kg, were used. The pituitary body was approached by the transbuccal procedure. The operation was done with the animals anesthetized with pentobarbital sodium and with the usual sterile technic. In 4 of the 7 dogs, the pituitary body was successfully removed, while in the remaining 3 it was not removed because of difficulties with hemorrhage at the time of operation. In these 3 dogs, the pituitary body was found intact at necropsy. These dogs served as control animals.

The most reliable criterion of hypophysectomy is the absence of the pituitary body upon macroscopic and microscopic examination. In the 4 cases in which hypophysectomy was successful, no traces of the pituitary body were found grossly or upon microscopic examination of sections of the tissue removed from the site of the organ. In animals living more than 21 to 28 days after hypophysectomy, additional evidence of the absence of the pituitary body was shown by the size and histologic appearance of such structures as the adrenal cortex, thyroid gland and gonads.

In from 12 to 43 days after hypophysectomy, the left kidney was removed from each of the 7 animals and served as a control for the study of the remaining kidney. The operation was done with ether anesthesia, and the usual sterile precautions were followed. The kidney was removed through a midline incision of the abdominal wall. Immediately after its removal, the kidney was incised on its outer border and was placed in a 10% solution of formalin, and was weighed 24 hours later, after removal of all excess tissues.

The ureteral transplantation, which was done according to the method described by Beaver and Mann(1), was performed immediately after the left kidney had been removed. In cases in which hypophysectomy was performed, the kidney was not removed until 5 to 40 days had passed.

Histologic preparations were made of all the kidneys, adrenal glands, thyroid glands and gonads, and serial sections were made of all tissue found at postmortem on the floor of the sella turcica and in the region of the attachment of the hypophysis cerebri.

Dogs 1, 2 and 4 of the hypophysectomized group and dog 3 of the nonhypophysectomized group (Table I) were found dead, but, since their deaths were discovered before postmortem changes occurred, their kidneys and other organs were given the same treatment as those of the other animals in the series.

The percentage increase in the weight of the remaining kidney was calculated by use of the following formula:

$$\%\ \text{enlargement of remaining kidney} = \frac{K_2w - K_1w \times 100}{K_1w}$$

in which K_2w equals the weight of the remaining kidney and K_1w equals the weight of the control kidney.

Results. Evaluated according to the formula, the remaining kidneys of the control dogs or the dogs in which the hypophysis

TABLE I. Effect of Hypophysectomy on Size of Remaining Kidney after Transplantation of Its Ureter into Duodenum and Removal of Contralateral Kidney.

		Hypophysectomized dogs								
		Body wt, kg			Wt of kidneys				Period of survival, days	
Dog	Sex	Before hypophysectomy	Before abdominal operation	Final	Left, g	Right, g	Difference, g	Difference, %	After abdominal operation	After hypophysectomy
1	♂	9.9	9.5	9.5	32	39	7	21.8	7	12
2	♂	10.5	10.25	9.25	33	39	6	18.2	4	10
3	♂	14.2	12.4	11.2	27	40	13	48.1	3	43
4	♀	12.25	13	13	24	27	3	12.5	8	37
Mean		11.7	11.2	10.7	29	36.25	7.25	25.15	5.5	25.5

		Nonhypophysectomized dogs								
		Body wt, kg			Wt of kidneys				Period of survival, days	
Dog	Sex	Initial	Before abdominal operation	Final	Left, g	Right, g	Difference, g	Difference, %	After abdominal operation	After transbuccal operation
1	♂	11.5	11.5	10.25	25	57	32	128	14	37
2	♂	8.4	8.4	7.5	20	44	24	120	7	13
3	♀	9.5	9.5	9.7	22	37.5	15.5	70	6	32
Mean		9.8	9.8	9.15	22.3	46.1	23.8	106	9	27.3

cerebri was intact were much larger and heavier than those of the hypophysectomized dogs. The increase in weight of the kidneys of the control nonhypophysectomized dogs ranged from 70 to 128% as compared to 12.5 to 48.1% for the hypophysectomized animals. The mean percentage difference was 106 in the control group as compared to 25.15% in the hypophysectomized dogs (Table I). This difference is highly significant statistically ($T = 4.9$, with 5 D.F.: $P < 0.01$).

The control kidneys of the hypophysectomized dogs were smaller than those of the nonhypophysectomized dogs. The remaining kidneys were the same in appearance. They had a dilated ureter and pelvis and accentuated renal capsular vessels. The kidneys of the hypophysectomized dogs were affected to a lesser degree than those of the nonhypophysectomized dogs (Fig. 1).

The control, or the left kidney, of the hypophysectomized dogs showed diminished capsular space, and many of the renal tubules seemed to have narrow lumina.

The remaining kidneys of the nonhypophysectomized dogs showed degeneration of the renal tubular cells with marked dilatation of their lumina. In the remaining kidneys of the hypophysectomized dogs, the same changes were seen, but to a lesser degree.

The adrenal glands (Fig. 2), gonads and the thyroid glands appeared smaller, and showed changes consistent with the ablation of the pituitary body in dogs living more than 3 or 4 weeks after hypophysectomy.

Comment. The results of the experiments on nonhypophysectomized dogs in which one kidney was removed and the ureter of the other was transplanted into the duodenum are very similar to those reported by Bollman and Mann(2), and by Block, Wakim and Mann(3). The former authors reported a 60 to 100% increase in weight of the kidney within 9 days, and the latter authors reported a 63.5 to 190.0% increase within 72 to 220 hours. In this study, the increase in the weight of the remaining kidney ranged from 70 to 128% in the nonhypophysectomized dogs in 6 to 14 days as compared to 12.5 to 48.1% in hypophysectomized dogs within 3 to 8 days.

In considering these striking results in the hypophysectomized group of animals, an inquiry can be made as to the possible relation of changes in body weight of the animals to the changes in the weight of the kidneys. Since there was an increase in the body weight of 1 dog and a decrease in the body weight of another, and since there was little change in the other 2 dogs, there is not much basis for further pursuit of this point.

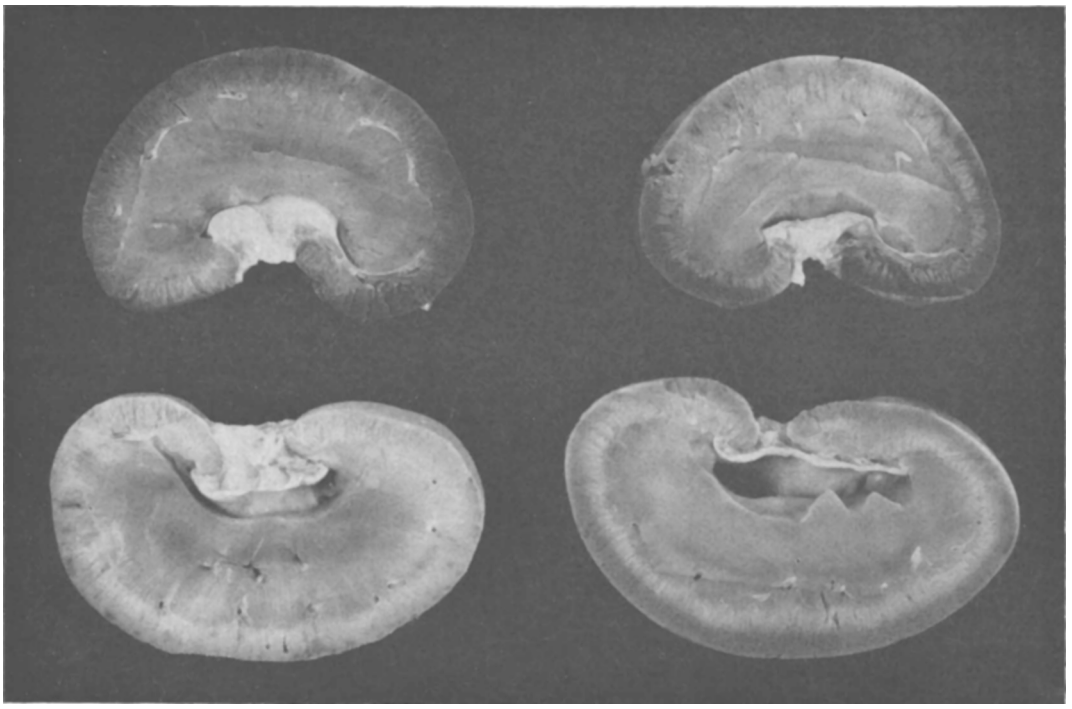

FIG. 1. Control kidney (above) and the remaining kidney (below) of hypophysectomized dog (left) and nonhypophysectomized dog (right). One may compare the dilatation of the renal pelves of the two kidneys.

If the position is taken that an explanation of the results resides in the lack of the hypophysis cerebri, and if this position is accepted, it may legitimately be asked whether it is a specific and direct effect due to a lack of a renotropic principle or whether the effect is indirectly mediated through one or another or through a combination of many of the endocrine glands or is due to the lack of the renotropic effect of the pituitary "tropes." That there may be a direct pituitary influence (renotropic) on the kidney has been suspected [Selye(4)] but never demonstrated. The results of the present study seem to point to such a mechanism.

FIG. 2. Adrenal glands of hypophysectomized dog (left) and intact animal (right) with the pituitary body removed at necropsy. One may compare the cortices of the 2 adrenal glands. (Thirty-seven days after hypophysectomy.)

In the absence of the pituitary body, the size of the kidney was found to be smaller than the control in dogs [Brown(5); Dandy and Reichert(6)] and in rats [Smith(7); McQueen-Williams and Thompson(8); Selye (4) and Astarabadi and Essex(9)]. Opinions in regard to the occurrence of compensatory hypertrophy in the absence of the pituitary body are controversial, but the consensus presented by Houssay(10) is that the pituitary body is considered important but not essential for the compensatory renal hypertrophy and, perhaps, it is the summation effect of all the pituitary hormones which plays the role and not a special renotropic hormone. However, the factors contributing to the increase in the size of the remaining kidney following transplantation of its ureter into the duo-

denum with contralateral nephrectomy has been discussed by Wakim, Block and Mann (11), and the evidence might be interpreted to indicate that the kidney was not carrying on efficient physiologic functions.

Under the condition of hypophysectomy in animals, and hypopituitarism in man, disturbance in renal physiology has been reported. For instance, the kidney showed marked depression of water diuresis in man [Slessor(12) and Robertson(13)], and similar findings in dogs have been reported by White(14); Lane and de Bodo(15); Earle, de Bodo, Schwartz, Farber, Kurtz and Greenberg(16); de Bodo, Schwartz, Greenberg, Kurtz, Earle and Farber(17), although White found that the somatotropic hormone restored the depressed function of the kidney of the hypophysectomized dog to normal and even caused hyperactivity.

From the evidence available, it would seem that the hypophysis cerebri must influence both the size and function of the kidney but through what mechanism is not clearly and completely understood.

Summary. Hypophysectomy was performed on adult male and female dogs by using the buccal approach. The left kidney which was removed through a midline abdominal incision served as a control, and the ureter of the right kidney was transplanted to the duodenum. The remaining kidney was removed 3 to 14 days later, and its weight and cytologic structure were compared with those of the control kidney.

The remaining kidneys of the nonhypophysectomized dogs weighed an average of 106% more than the control kidneys. This is in contrast to a 25.15% average increase in the weight of the remaining kidneys over the control kidneys of the hypophysectomized dogs.

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