11883 P

Effects of Hypophysectomy on Some Renal Functions.*

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We have reported[1] that diodrast (D) and inulin plasma clearances are markedly reduced in hypophysectomized dogs. It was not determined whether the low D clearance was due to a low renal plasma flow (RPF) or to a diminished renal extraction of D, or to both. The present paper reports on the effects of "simple" hypophysectomy (section of stalk with removal of dependent gland) and of complete hypophysectomy (includes destruction of median eminence) on D plasma clearance, plasma D extraction, RPF, tubular extraction of D, maximum tubular excretory rate for D (D Tm), inulin clearance, filtration fraction and blood volume. It also reports on the question of glomerular intermittence after hypophysectomy, with the finding that intermittence does not occur. Since no certain difference in effects of simple and of complete hypophysectomy was observed on any of the processes studied, no distinction will be made in the present report: the effects are apparently due to loss of anterior lobe, although further observations are required before a final statement can be made. Six dogs have been studied; pre-hypophysectomy observations of most of the processes studied were made on the same animals.

Diodrast plasma clearance. In 15 post-hypophysectomy clearance periods on 3 dogs (K6, K10 and K11) taken at 7 to 93 days after operation, D plasma clearance has averaged 141 cc/min./M², where the normal was 258. The clearance of one completely hypophysectomized dog (K8) on the 4th postoperative day was 155, normal 222; a "simple hypophysectomy" dog (K9) on the 3rd day showed 191 cc/min./M², where normal had been 208. One dog (K1), with a normal clearance of 232, had a unilateral nephrectomy on 7/22/40 and a simple hypophysectomy on 7/26/40; on 9/4/40 her D clearance was 107. The kidney removed on 7/22/40 weighed 54 g, the remaining kidney at death on 9/30/40 weighed 52 g. These observations indicate that while hypophysectomy prevents renal hypertrophy it does not prevent a maintenance of normal D clearance per gram of kidney in the remaining kidney after uninephrectomy, *i.e.*, clear-

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1 White, H. L., and Heinbecker, P., *Am. J. Physiol.*, 1940, **130**, 464.

ance through remaining kidney was approximately half that of both kidneys while normal.

Plasma D extraction. Plasma D extraction has not been changed from normal by hypophysectomy, the values ranging from 0.71 to 0.85. While a number of post-hypophysectomy renal vein samples have shown anomalously low extractions, the probability of this has not been higher than in normals; an extraction less than 0.7 has been arbitrarily called anomalously low.

Renal plasma flow. RPF was determined as inulin plasma clearance/inulin plasma extraction and as D plasma clearance/plasma D extraction $\times$ 1.12 (12% of the D output is contributed by cells); the 2 methods usually agree within 8% and practically always within 10%. A completely hypophysectomized dog (K10), with a normal RPF of 374 cc/min./M^2, showed RPF of 224 on the 20th postoperative day. A simple hypophysectomy dog (K11), with a normal RPF of 268, showed 162 on the 7th postoperative day. If our present belief, that plasma D extraction is not altered by hypophysectomy, continues to be sustained on subsequent observations, it will then be permissible to determine RPF as D plasma clearance $\times$ 1.2 on dogs without renal explants, hypophysectomized as well as normal.

Tubular extraction of D. If the term "tubular extraction"[2] is modified to read

$$\frac{\text{tubular clearance of D}}{\text{RPF} - \text{glomerular clearance of D}}$$

it will give a better expression of the tubules' effectiveness in extracting D than does the original expression, tubular clearance of D/RPF. The new expression tells what fraction of the D presented to the tubules is extracted by the tubules, while the original expression tells what fraction of the D presented to the kidneys is extracted by the tubules. The former averaged 0.77 in 2 dogs (K10 and K11) while normal and 0.79 after hypophysectomy, indicating that the effectiveness of the tubules in extracting D at low rates is not affected by hypophysectomy.

Diodrast Tm. Diodrast Tm has averaged 18 mg iodine/min./M^2 on normals and 8 mg/min./M^2 at 7 to 26 days after hypophysectomy. In one experiment (K10) on the 26th postoperative day 3 Tm periods were run at a plasma I level of 23 mg %, with an average tubular output of 8.1 mg iodine/min./M^2; the next three periods were run at a plasma I level of 39 mg %, with an average tubular output of 7.7 mg/min./M^2. These findings show that the maximum

[2] White, H. L., *Am. J. Physiol.*, 1940, **130**, 582.

tubular excretory rate for D is significantly diminished by hypophysectomy and are in contrast with the absence of effect on tubular extraction of D at low rates of output.

Inulin clearance and filtration fraction. In 3 dogs (K9, K10 and K11) while normal, inulin clearance has averaged 84 cc/min./M^2 and filtration fraction (average of inulin clearance/D RPF and of inulin extraction) 0.27; at 3 to 26 days after hypophysectomy inulin clearance has averaged 55 and filtration fraction 0.26. The drop in glomerular filtration rate parallels the drop in RPF.

Blood volume. Plasma volumes were determined essentially according to Gibson and Evelyn.[3] Plasma and blood volumes in normals have averaged 60 and 115 cc/kilo, respectively; in hypophysectomized dogs they have averaged 48 and 92 cc.

Discussion. The present findings indicate that the low D plasma clearance of hypophysectomized dogs means a low RPF rather than a low extraction of D. A low RPF would not, however, explain a low D Tm, which should remain normal even with a low RPF, provided sufficient D is presented to the tubules, if the normal excretory capacity of the tubules for D is maintained. That sufficient D is being presented to the tubules in these experiments is proved by the experiment on K10 cited under Diodrast Tm, in which the rate of tubular output of D was not increased on raising the plasma I level from 23 to 39 mg %.

Two possible explanations of the low D Tm suggest themselves. The first is that, on the average, fewer nephrons are being supplied with blood in the hypophysectomized than in the normal animal (glomerular intermittence). This possibility appears to be excluded by the finding that the picture of ink-injected kidneys of 3 hypophysectomized dogs was the same as that in normal dogs, which seems best explained on the view that all the glomeruli are open all the time.[4] The second possibility is that the tubular mechanism for excreting D is deficient in hypophysectomized dogs, and this seems to be the correct one. Since the tubular extraction of D at low plasma levels is not affected, the findings may be interpreted as evidence that some hypothetical substance concerned in the tubular excretion of D[5] is deficient in quantity but is of normal quality. Further observations will reveal whether D Tm returns toward normal late after hypophysectomy.

Since the fall in RPF occurs with an unchanged filtration fraction

[3] Gibson, J. G., 2nd, and Evelyn, K. A., *J. Clin. Invest.*, 1938, **17**, 153.

[4] White, H. L., *Am. J. Physiol.*, 1939, **128**, 159.

[5] Shannon, J. A., *Physiol. Rev.*, 1939, **19**, 63.

and in the absence of glomerular intermittence, the renal vasoconstriction appears to involve all parts of the renal vascular tree uniformly. The arterial blood pressure in these animals is only slightly lowered. The fall in blood volume, which is probably accompanied by a fall in cardiac output, also must be partially responsible for the fall in RPF.

11884

Technic for Demonstrating Antibodies Against Tuberculin in Experimental Animals with Sensitized Collodion Pellets.*

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A method for utilizing suspensions of sensitized collodion pellets for determining the presence of specific antibodies in blood sera has recently been described by Cannon and Marshall.[1] Such a procedure appeared to offer a technic for studying the development of antibodies against tuberculin in tuberculous infection and in experimental procedures in which killed tubercle bacilli were used for immunization. It is the purpose of this paper to report the results obtained in testing the blood sera of such experimental animals with suspensions of collodion pellets sensitized with commercial old tuberculin.

Following the method described by Cannon and Marshall[1] a supply of collodion pellets was prepared. A suspension of these pellets having a turbidity-factor of 244 (Summerson-Klett photoelectric colorimeter with a No. 66 filter) was mixed with an equal amount of a 5% (by volume) solution of commercial old tuberculin. The mixture was allowed to stand overnight at a temperature of 4°C. The pellets were recovered and washed in double-distilled water by centrifuging and resuspending them 3 times. The final suspension of sensitized pellets was diluted to equal a standard suspension having a turbidity-factor of 154. Serial dilutions of the serum to be tested were made in saline solution so that the volume in each tube was 0.5 cc. To each dilution was added 0.5 cc of the suspension of sen-

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1 Cannon, P. R., and Marshall, C. E., *J. Immunol.*, 1940, **38**, 365.