THE EFFECT OF DIURETICS ON THE GENERAL BLOOD PRESSURE IN ANIMALS WITH CONSTRICTION OF THE RENAL ARTERIES *

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Since the days of Traube¹ a mechanical explanation for the high blood pressure of chronic renal disease has frequently been advocated, the original theory postulating increased peripheral resistance in the kidney itself as the cause. Failure of ligature of both renal arteries to raise the blood pressure materially was sufficient disproof of the theory in any such simple form. Various modifications of it have been suggested. Katzenstein² obtained a slight rise after incomplete occlusion of the renal arteries, and Alwens³ by compressing the kidneys in oncometers. In spite of the failure to produce any rise in blood pressure at all comparable to the hypertension of human nephritis, the obvious association of hypertension with those types of renal disease in which the renal arterial system is most compromised, in the absence of any other satisfactory explanation, has prevented the entire abandonment of the mechanical theory. Furthermore, clinicians have always been impressed with the compensatory nature of hypertension.

The following experiments were undertaken in the hope of affording further light on the tenability of Traube's theory under conditions of increased functional demand on the kidney. It was thought possible that, if the renal artery were narrowed, but not occluded, and then diuretic substances administered intravenously, the compensatory nature of hypertension might be revealed. Narrowing of the renal artery without obliteration was made possible by the aluminum band of Halsted.⁴ The diuretic substances used were sodium chlorid, urea and caffein, injected intravenously; in addition, the effect of epinephrin was tested. With an aluminum band placed about the renal artery, no increased flow through the kidney can occur as a result of mere local vasodilatation. If any reflex mechanism exists whereby diuretic substances can produce an increased flow through the kidney under these conditions, a rise in general blood pressure must occur. If, on the other hand, no rise in general blood pressure and no diuresis fol-

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1. *Gesammelte Abhandlungen*, Berlin, 1856, **2**, 290; **3**, 440.

2. *Virchows Arch. f. path. Anat.*, 1905, **182**, 327.

3. *Deutsch. Arch. f. klin. Med.*, 1910, **98**, 137.

4. *Bull. Johns Hopkins Hosp.*, 1905, **16**, 346.

lows, then the evidence for this particular view of the compensatory nature of hypertension would be lacking.

TECHNIC OF EXPERIMENTS

The experiments were performed as follows: As large a dog as obtainable was used and was anesthetized with paraldehyd. A cannula was then placed in the carotid artery and connected with a recording mercury manometer for the registration of the arterial pressure, and another cannula placed in the femoral vein for the injection of the solutions. The kidneys were next delivered through lumbar incisions and the renal arteries exposed. A cannula was inserted in the left ureter and connected with an electrical drop recorder. In Experiments 1 to 11 no further operative procedures were done at this time, but in Experiments 12 to 15 the right renal artery was now ligated.

A control period was then begun, arterial pressure and urine flow being recorded on a kymograph. When the blood pressure had become steady, the various solutions were injected into the femoral vein, a sufficient time being allowed to elapse between injections for the blood pressure curve to return to its former level, varying from ten minutes to one hour in different experiments. The speed of injection was as nearly uniform as possible. The aluminum band was then placed around the left renal artery with sufficient constriction to reduce markedly the pulsation distal to it, but not to abolish pulsation completely. In Experiments 1 to 11, ligature of the right renal artery was also performed. This operation sometimes required the administration of a small amount of ether.

After a second control period, the various solutions were again injected through the femoral cannula in the same volume and the same order as before. The dog was killed at the conclusion of the experiment before recovering from the anesthetic.

The solutions tested, and the volumes used, were as follows:

- 5 per cent. sodium chlorid solution, 10 to 20 c.c.
- 5 per cent. urea in 0.9 per cent. sodium chlorid solution, 10 to 20 c.c.
- 5 per cent. caffein solution 7.5 to 10 c.c.
- 1 in 50,000 epinephrin chlorid solution, 10 c.c.

The amount injected varied with the size of the dog. In the bulk of the experiments 15 c.c. of the sodium chlorid and of the urea solutions, and 10 c.c. of the caffein and the epinephrin solutions were used.

The experimental difficulties in adjusting the band so as to diminish, but not completely obstruct, the blood flow were considerable. A number of experiments had to be abandoned because of failure to accomplish this, or because of clotting in the cannula, or death of the dog before the conclusion of the tests. In addition, one of us (E. W. B.) was called to active military duty before sufficient experiments had been performed, and the other (K. H.) must assume the responsibility for the later experiments and for the opinions expressed in this paper.

In order to bring the results together in a clear manner, the blood pressure and urine-drop records have been measured on the tracings, and the figures from the eight successful experiments are given in tabular form. The blood pressure figures give the rise, represented by +, or fall, represented by —, in mean carotid pressure expressed

in mm. Hg. The urine is calculated as drops per hour, because of the extremely scanty secretion obtained in parts of the experiment. The two lines, before and after, refer to the observations made before the constriction of the left renal artery with the band, the right renal artery having been ligated previously.

TABLE 1.—DATA OF EXPERIMENTS

Experiment Number	Control Period: Urine, Drops per Hr.	Sodium Chlorid		Urea		Caffein		Adrenalin	
		Bl. Pr. Change in Mm. Hg	Urine, Drops per Hr.	Bl. Pr. Change in Mm. Hg	Urine, Drops per Hr.	Bl. Pr. Change in Mm. Hg	Urine, Drops per Hr.	Bl. Pr. Change in Mm. Hg	Urine, Drops per Hr.
2 Before.....	60					Sl. variations	420	+60	180
After.....	12					Unchanged	10	+40	15
8 Before.....	20	+2	50	+2	20	-6	20	+40	60
After.....	8	+2	8	+2	8	-5	8	+25	8
10 Before.....	60	+3	60	+2	60	-12	180	+23	120
After.....	6	+10	6	+2	6	-15	6	+25	6
11 Before.....	60	+10	120	+4	120	-20	360	+17	240
After.....	120	+7	240	+2	150	-15	120	+12	120
12 Before.....	40	+6	140	+4	180	-20	240	+12	180
After.....	30	+6	48	+3	45	-5	30	+14	30
13 Before.....	60	Sl. variations	180	Sl. variations	120	-27	420	+25	540
After.....	150	Sl. variations	180	Sl. variations	240	-32	600		
14 Before.....	90	+3	240	+3	240	-25	480	+20	300
After.....	150	Sl. variations	360	+3	360	-30	150	+19	150
15 Before.....	15	+5	60	+5	60	-25	45	+20	60
After.....	28	Sl. variations	60	Sl. variations	90	-15	60	+15	28

As may be seen at a glance, the results of these experiments as shown in the table are negative. They give no support to the view that hypertension in chronic renal disease is a compensatory mechanism, brought into play when the renal arterial stream-bed is narrowed, by chemical or reflex paths, to counteract the effect on excretion of the locally diminished blood flow. Their value is only that of negative evidence in general. They do not disprove the compensatory nature of hypertension, but show that its demonstration is not to be had by the experimental method employed. A similar study of animals in whom a constricting band had been left for a considerable period around the renal artery, simulating a chronic lesion, would be of interest, but external events prevented our undertaking it, as had been hoped.

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