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Effects on Blood Pressure of Injections of Urine Extracts of Normal and Hypertensive Individuals.

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Recent investigations indicate that the ischemic kidney contains more pressor substances than the normal kidney.[1, 2] Therefore, it appeared of interest to investigate further the possibility of an increased excretion of pressor substances in the urine of hypertensive individuals. Abelous and Bardier[3] demonstrated the presence of pressor substances in normal urine. This was substantiated by Bain[4] who, in addition, found that the urine of hypertensive individuals gave only slight, if any, pressor effect and concluded that these individuals retained the pressor substances. More recently Bohn and Hahn[5] by a modification of Bain's method reported the presence of pressor substances in the urine of pale hypertensive cases but that these materials were virtually absent in the urine from red hypertensive and normal individuals.

For these experiments, 24-hour urine samples were collected daily from 2 individuals (one male and one female) with essential hypertension having normal renal function and exhibiting a blood pressure of 200 mm Hg. Normal urine was obtained daily from students in the laboratory. The urine was extracted the same day according to the method of Bohn and Hahn by which the final residue was dissolved in Ringer-Locke's solution.

In an attempt to establish comparable test conditions, all the blood pressure tests were made on one normal unanesthetized dog which was carefully trained for blood pressure work.* Damshek and Loman's[6] intra-arterial blood pressure method was employed and

1 Harrison, T. R., Blalock, A., and Mason, M. F., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 38.

2 Prinzmetal, M., and Freidman, B., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 122.

3 Abelous, J.-E., and Bardier, E., *C. R. Soc. Biol.*, 1908, **64**, 596, 848.

4 Bain, W., *Lancet*, 1910, Apr. 30, 1190; *ibid.*, 1911, May 27, 1409; *Quart. J. Exp. Physiol.*, 1914, **8**, 229.

5 Bohn, H., and Hahn, F., *Z. f. Klin. Med.*, 1933, **123**, 558.

* Grateful acknowledgment is due to Dr. W. M. Parkins for the blood pressure determinations.

6 Damshek, W., and Loman, J., *Am. J. Physiol.*, 1932, **101**, 140.

the mean pressures determined in the femoral artery.[7] Injections were made into the jugular vein, always using the same quantity (10 cc) regardless of the urine equivalent. The injection period was 30 seconds in every case.

The initial tests were made with 10 liter concentrates, but later experiments showed that 1 to 2 liter quantities were quite satisfactory to compare the normal and hypertensive urines with this test animal. Four typical comparative tests exhibiting the similarity of the pressor activity of the urine extracts are shown in Table I. Generally, the pressure rose immediately on injection and reached its peak in 1 to 3 minutes, but in a few cases there was a short latent period. This rise was followed by a gradual decline and return to normal pressure. The effect varied between 5 and 15 minutes as determined from the time of injection. The cases surpassing 10 minutes were usually the ones that exhibited the initial latent period. An initial depression of pressure was observed in only one case. A series of tests were made using 1 liter urine equivalents as this provided the most sensitive range and blood pressure effects varying from 0 to 40 mm Hg were obtained. Although 2 extracts of normal urine gave no pressor activity the average of 24 mm Hg compared favorably with a 32 mm Hg average for hypertensive urine.

One extract was tested on an adrenalectomized dog being maintained on cortical hormone and a blood pressure rise of 40 mm Hg resulted with a 2 liter equivalent of hypertensive urine.

Bain obtained only slight pressor responses from hypertensive urine. An extract of his ether soluble fraction was prepared from 1500 cc of hypertensive urine which, on injection, produced a 40 mm Hg rise in pressure. This compared with the results obtained with the normal urine. Further treatment of the alcohol soluble fraction of Bohn and Hahn's method was attempted and it was found that neither filtration through permutit nor ether extraction would remove the pressor substances. The pressor activity was not destroyed after 7 days at room temperature.

Abelous and Bardier[8] were not able to find pressor substances in normal dog urine and therefore Bohn and Hahn's method was used in extracting dog urine. Twenty-four-hour samples were collected from 2 dogs with normal blood pressures and the extracts tested on 3 trained unanesthetized dogs. The concentration of urine was found to vary daily and thus the pressor activity of identical urine equivalents showed little agreement (Table I). However, the

[7] Parkins, W. M., *Am. J. Physiol.*, 1934, **107**, 518.

[8] Abelous, J.-E., and Bardier, E., *C. R. Soc. Biol.*, 1908, **65**, 63.

TABLE I.
Effects on Blood Pressure of Unanesthetized Dog of Injections of Urine Extracts.

Normal pressure, mm Hg.	Max. pressure, mm Hg.	Total rise, mm Hg.	Period effective, min	Urine equivalent injected*	Urine used
Effects of Urine Extracts of Normal and Hypertensive Individuals.					
94	144	50	10	4 l	Hypertensive
98	148	50	12	4 "	Normal
96	124	28	15	800 cc	Hypertensive
94	114	20	10	800 "	Normal
98	130	32	8	1 l	Hypertensive
98	132	34	7	1 "	Normal
98	136	38	5	1 "	Hypertensive
98	128	30	6	1 "	Normal
Effects of Dog Urine Extract.					
96	128	32	6	1 l	Normal
96	131	35	6	1 "	"
92	100	8	5	1 "	"
94	104	10	4	1 "	"
98	108	10	4	1 "	"
96	114	18	5	1 "	"
98	108	10	5	1 "	"
98	—	0	—	1 "	"
94	132	38	6	1 "	"

*10 cc injected in 30 seconds in each case.

activity of one extract when tested on 2 dogs would produce relatively the same effect and indicated that pressor substances are present in normal dog urine.

Summary. Although Bohn and Hahn found pressor substances in hypertension and Bain found this material only in the normal, the results of these experiments indicated that no significant differences in the amount of pressor substances, other than possible normal variations, existed between the urine of normal individuals and the urine of the 2 essential hypertensive individuals that were tested. Furthermore, the normal dog was found to excrete pressor substances in variable quantities.

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The Unidentified Base in Gelatin.

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Van Slyke and Hiller[1] reported evidence that the phosphotungstate precipitate obtained from hydrolyzed gelatin contained amino acid

[1] Van Slyke, D. D., and Hiller, Alma, *Proc. Nat. Acad. Sci.*, 1921, **7**, 185.