THE EFFECT ON RENAL EFFICIENCY OF LOWERING ARTERIAL BLOOD PRESSURE IN CASES OF ESSENTIAL HYPERTENSION AND NEPHRITIS

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In 1856 L. Traube (1) postulated that arterial pressure was elevated in cases of disease of the kidneys to overcome mechanical resistance against blood flow, thus compensating for the abnormal resistance and maintaining the efficiency of the kidneys as excretory organs. The "compensatory" theory has had many adherents, some of whom have generalized it to include hypertension of varied etiology.

The object of the present investigation was to compare the efficiency of excretion, when the blood pressure was at a high level, with that when it was reduced. It was hoped to bring evidence which would substantiate or refute the compensatory theory as applied to patients suffering from hypertension. The urea clearance test of Möller, McIntosh and Van Slyke (2) was used for the comparison.

METHOD

Two patients exhibiting extreme elevation of blood pressure and typical histories of the malignant phase of essential hypertension, two with moderate hypertension, and two suffering from hemorrhagic Bright's disease, were selected for this study. Throughout the control period of two months or more, and the experimental period of from three months to a year, blood pressures were taken at 9:30 A.M. with the patient confined to bed at all times. Control urea clearance tests were performed. The arterial blood pressure fell spontaneously in two cases (Numbers 1 and 6) sufficiently to be significant. Two patients (Numbers 3 and 4) received sodium thiocyanate by mouth in doses graduated from 65 mgm. to 260 mgm. given daily until the systolic blood pressure had fallen 80 mm. Hg or more (3, 4, 5, 6). Clearance tests were again run and the blood pressure again allowed to approach the original level by discontinuance of thiocyanate. One patient (Number 2) exhibited persistently elevated blood pressure for a period of at least five years. Intramuscular injection of aqueous colloidal sulfur (1 cc. 1:1000 solution) was associated with a sharp and prolonged fall in pressure to normal (7). The blood pressure

TABLE I

Effect of alteration of arterial blood pressure on renal efficiency as measured by the urea clearance test

Patient number	Date	Blood pressure	Corrected urine volume	Blood urea	Urea clearance		Treatment	Diagnosis
		mm. Hg	*cc. per minute*	*mgm. per cent*	*Successive hourly periods per cent of normal*	*Average per cent of normal*		
1	April 3	210/120	1.2 1.0	15.7	58.2 69.6	63.9	None	Essential hypertension
	October 10	118/116	4.5 4.1	6.4	70.2 67.1	68.6		
	October 23	150/100	4.5 4.1	6.9	68.0 70.4	69.2		
	November 9	190/120	4.2 4.0	8.8	62.2 59.6	60.9		
2	April 17 (1933)	204/110	.32 .73	19.6	16.6 24.9	20.7	None	Essential hypertension
	May 1 (1934)	230/124	1.9 2.3	24.7	38.3 41.3	39.8		
	May 7	220/120	1.3 2.2	21.9	29.2 29.7	29.4		
	June 8	138/92	2.3 3.4	16.5	36.3 30.4	33.4	Sulfur injection 1 c.c. 1 : 1000 Q.D.	
	June 11	128/88	3.9 2.7	19.4	42.1 34.6	38.3		
3	June 1	264/118	1.4 0.8	14.0	47.5 49.3	48.4	None	Malignant hypertension

TABLE I (*continued*)

Patient number	Date	Blood pressure	Corrected urine volume	Blood urea	Urea clearance		Treatment	Diagnosis
		mm. Hg	*cc. per minute*	*mgm. per cent*	*Successive hourly periods per cent of normal*	*Average per cent of normal*		
3	June 13	228/108	0.9 0.9	19.8	51.9 49.7	50.8		
	December 6	278/118	2.0 5.0	15.8	44.0 44.4	44.2		
	January 16	238/136	0.8 3.4	12.2	55.0 43.8	49.4	Thiocyanate	
	February 25	220/108	0.5 3.2 2.9	14.2	64.8 43.0 74.2	60.6	Thiocyanate	
	March 6	266/130	0.4 0.6	13.0	54.2 51.2	52.7		
	March 18	290/137	0.4 2.5	17.9	47.8 37.0	42.4		
	March 20	274/130	2.8 0.4	9.3	46.9 73.7	60.3		
	April 8	230/130	2.2 0.6	12.8	50.4 47.8	49.1	Thiocyanate	
4	January 25	300/163	1.0 3.4	15.4	53.5 58.0	55.7	None	Malignant hypertension

TABLE I (*continued*)

Patient number	Date	Blood pressure	Corrected urine volume	Blood urea	Urea clearance		Treatment	Diagnosis
		mm. Hg	*cc. per minute*	*mgm. per cent*	*Successive hourly periods per cent of normal*	*Average per cent of normal*		
4	January 31	250/154	2.0	13.2	50.0			
			4.4		62.6			
			7.4	11.8	52.4	59.6		
			5.3		63.4			
	February 8	240/150	1.8	11.8	67.0			
			2.3		63.6			
			9.2	11.8	73.6	65.3		
			8.5		69.3			
			4.4		63.2			
	February 25	220/132	2.0	11.2	71.6	77.9	Thiocyanate	
			6.4		84.2			
	March 18	200/120	2.0	16.7	61.1	68.9	Thiocyanate	
			5.0		76.8			
	April 3	220/122	1.8	10.8	71.2	75.7	None	
			3.9		80.3			
5	February 15 (1933)	188/104	1.0	14.5	50.6		None	Chronic nephritis
			1.7		52.2	46.4		
			4.3	17.0	42.2			
			4.3		42.5			
	March 9	210/106	3.2	24.8	50.0	52.5		
			1.2		55.0			
	November 2	160/102	1.8	16.5	45.0	49.3		
			3.9		53.7			
	February 10 (1934)	154/86	1.9	15.7	46.9	50.5		
			3.1		54.1			

TABLE I (*continued*)

Patient number	Date	Blood pressure	Corrected urine volume	Blood urea	Urea clearance		Treatment	Diagnosis
		mm. Hg	*cc. per minute*	*mgm. per cent*	*Successive hourly periods per cent of normal*	*Average per cent of normal*		
5	February 23	150/90	1.9 2.3	18.2	47.7 47.3	47.5		
	March 5	160/98	.9 .7	32.2	64.2 56.4	60.3		
	March 23	136/80	1.2 1.9	14.8	59.9 42.8	51.4	Denervated right kidney	
	March 27	132/80	1.3 1.9	12.9	75.9 48.4	62.1		
6	March 11	194/110	0.45 1.0	46.3	13.5 14.9	14.2	None	Terminal stage of hemorrhagic Bright's disease
	March 21	174/100	0.67 0.90	61.3	12.6 13.0	12.8		
	April 4	160/100	0.68 1.0	113.0	9.4 10.5	9.9		
	April 7	146/82	1.2 1.0	114.0	9.5 10.2	9.3		
	September 27	138/86	1.6 1.8	105.0	11.3 11.9	11.6		
	October 28	122/78	1.1 1.0	147.3	9.8 9.6	9.9		
	March 1	154/94	0.67 1.0	43.3	11.7 8.0	9.8		
	April 2	168/102	1.1 1.5	130.0	7.7 8.2	7.9		

in one patient (Number 5) fell after denervation of one kidney was performed. The results are presented in the following table.

The blood pressure figures represent the blood pressure at the time the clearance was performed, also the approximate level for days or weeks previous to or following the test.

DISCUSSION

Whether reduction in blood pressure occurred spontaneously or resulted from sodium thiocyanate, colloidal sulfur injections, or unilateral renal denervation, no significant change in the clearance resulted. Nor did the clearance change when the pressure returned to its original level. It must be concluded that sodium thiocyanate and sulfur in the dosage employed and unilateral renal denervation had no detrimental effect on renal function.

Reid (8) found that administration of nitrites in therapeutic doses did not diminish the ability of the kidneys to concentrate urea in the urine, after its administration. The diuresis which ordinarily follows administration of 15 grams of urea is usually reduced by drugs of the nitrite series. Large doses of nitrite cause intolerance to the drug long before the stage of suppression of urine excretion.

CONCLUSIONS

1. The efficiency of the kidneys, as measured by the urea clearance test, is not altered by a marked fall in arterial blood pressure occurring spontaneously, or induced by sodium thiocyanate administered by mouth, or colloidal sulfur administered intramuscularly, in patients suffering from essential hypertension.

2. Sodium thiocyanate or colloidal sulfur in the dosage employed and over short periods of time does not appear to have a detrimental action on the kidneys of patients suffering from essential hypertension.

3. Fall in arterial blood pressure occurring spontaneously or as the result of renal denervation in patients suffering from chronic Bright's disease also caused no change in renal efficiency.

4. The abnormal elevation of blood pressure in these cases does not appear to assist in maintenance of renal efficiency. This evidence does not support the compensatory theory of the cause of hypertension in patients suffering from nephritis or essential hypertension.

BIBLIOGRAPHY

1. Traube, L., "Ueber den Zusammenhang von Herz und Nierenkrankheiten." Hirschwald, Berlin (1856), p. 59. Also Gesammelte Beitrg., 1878, **3**, 164.
2. Möller, E., McIntosh, J. F., and Van Slyke, D. D., Study of urea excretion. II. Relationship between urine volume and the rate of urea excretion by normal adults. J. Clin. Invest., 1928, **6**, 427.

3. Pauli, W., Ueber Ionenwirkungen und ihre therapeutische Verwendung. München med. Wchnschr., 1903, **50**, 153.
4. Nichols, B. J., The pharmacologic and therapeutic properties of the sulphocyanates. Am. J. M. Sc., 1925, **170**, 735.
5. Gager, L. T., The incidence and management of hypertension with a note on sulphocyanate therapy. J. A. M. A., 1928, **90**, 82.
6. Goldring, W., and Chasis, H., Thiocyanate therapy in hypertension. I. Observations on its toxic effects. II. Its effect on blood pressure. Arch. Int. Med., 1932, **49**, 321 and 934.
7. Rusznyák, S., Die schwefelbehandlung der arteriellen hypertonie. Klin. Wchnschr., 1924, **3**, 272.
8. Reid, C., The effect on renal efficiency of lowering the blood pressure in cases of high blood pressure. Quart. J. Med., 1925–26, **19**, 411.