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Blood Flow to the Kidney and Creatinine Clearance.*

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In a series of experiments carried out at the University Hospital, Minneapolis, by one of us (Medes) in collaboration with Dr. Hilding Berglund, it was demonstrated that creatinine clearance may be elevated in hyperthyroidism. In 20 cases of hyperthyroidism the clearance averages 196 ± 8.6 cc. per minute, as compared with a normal average of 173 ± 2.9 cc. per minute. In the former group the range extended from 111 to 338 cc. per minute, whereas in the latter group the highest value found in 60 tests was 296 cc. per minute. That increased blood flow through the kidneys might be one factor responsible for the increased creatinine clearance seemed probable, and the present investigation, undertaken at the suggestion of Dr. Berglund, is an attempt to evaluate this factor.

The thermo-stromuhr method of Rein¹ for measuring blood flow was used because it permits observations to be made under more nearly normal physiologic conditions.^{2, 3} All observations were made on dogs and limited to one kidney, the other having been removed 3 or more weeks prior to the measurement of blood flow. The unit was applied to the renal artery, employing the usual ether anesthesia and sterile technic. After the recovery of the animal observations were begun. The observations were made at intervals of about 15 minutes, and the average value throughout the period was estimated.

Creatinine clearance was measured by the method of Rehberg.⁴ Creatinine (1.5 to 2 gm., depending on the weight of the animal) was administered intravenously one hour before readings were started, and 150 to 250 cc. of water was given by stomach tube. All urine was removed by catheter, the bladder was flushed with several washings of physiologic sodium chloride solution and the

* Work done at the Institute of Experimental Medicine, The Mayo Clinic, Rochester, Minnesota.

¹ Rein, Hermann, *Z. f. Biol.*, 1928, **87**, 394. In: Abderhalden, Emil, *Handbuch der biol. Arbeitsmethoden*. Berlin, Urban and Schwarzenberg, 1929, **5**, 692.

² Baldes, E. J., Herrick, J. F., and Essex, H. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 1109.

³ Herrick, J. F., and Baldes, E. J., *Physics*, 1931, **1**, 407.

⁴ Rehberg, P. B., *Zentralbl. f. inn. Med.*, 1929, **50**, 367.

washings were added to the urine. Samples of blood were taken at the beginning and end of each period and the values were averaged. Plasma creatinine was determined by Folin's method. Unless the standard and unknown were of approximately the same concentration, the determination was repeated. Creatinine readings

TABLE I
Creatinine clearances and blood flow

Creatinine clearance control exper. cc. per min.	Days	Observation min.	Blood flow, cc. per min.	Creatinine clearance cc. per min.	Blood flow, % of maximum	Clearance, % of maximum
Dog 1. Wt. 9.7 kg.						
22.0, 21.1, 24.7 Aver.—22.6	1	38	90	19.1	83	80
		43	104	22.9	96	96
		43	105	23.3	97	97
		50	106	23.5	98	98
		46	108	23.9	100	100
		14 ³ / ₄	90	13.9	83	58
		18 ¹ / ₄	101	21.9	94	92
Dog 2. Wt. 14 kg.						
37.4, 36.2, 36.0, 36.6 Aver.—36.6	1	45	261	37.2	97	100
		80	245	33.1	91	89
		40	243	33.6	90	90
		77	269	37.3	100	100
		47	269	36.4	100	98
		60	269	36.3	100	97
		42	269	36.1	100	97
Dog 3. Wt. 11.3 kg.						
42.1, 37.3, 37.6 Aver.—39.0	1	40	130	37.5	90	89
		41	133	39.0	92	93
		36	143	41.0	99	98
		35	144	41.5	100	99
		30	144	42.0	100	100
Dog 4. Wt. 4.6 kg.						
26.8, 27.6, 29.4, 27.9 Aver.—27.9	1	48	115	12.4	63	75
		35	139	14.2	76	86
		32	140	15.2	77	92
		38	165	16.1	90	98
		37	183	16.5	100	100
	2	50	295	18.9	100	100
		38	185	16.1	63	85
		48	192	17.1	65	90
		56	287	18.6	97	98
		43	190	16.5	64	87
44	190	16.5	64	87		
49	198	17.5	67	93		
Dog 5. Wt. 12.7 kg.						
30.7, 34.3 Aver.—32.5	1	53	78	0.8	47	
		34	97	3.5	58	27
		28	128	9.8	77	76
		30	128	9.8	77	76
		31	167	12.9	100	100
	2	57	152	4.1	53	33
		61	244	9.2	85	75
		48	263	10.4	91	85
		44	263		91	
		40	263	10.5	91	85
55	288	12.3	100	100		

were corrected from a curve constructed, using the same set of reagents.

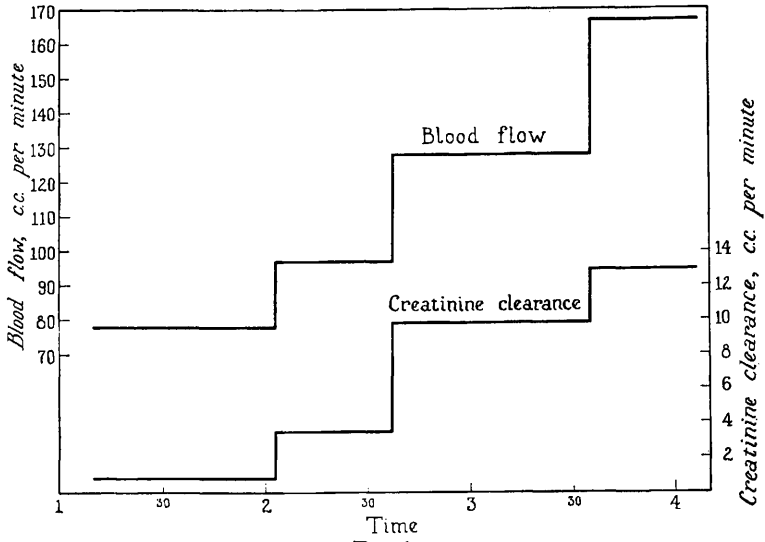


FIG. 1.

Parallelism between creatinine clearance and blood flow. The changes are typical for the first day of observation.

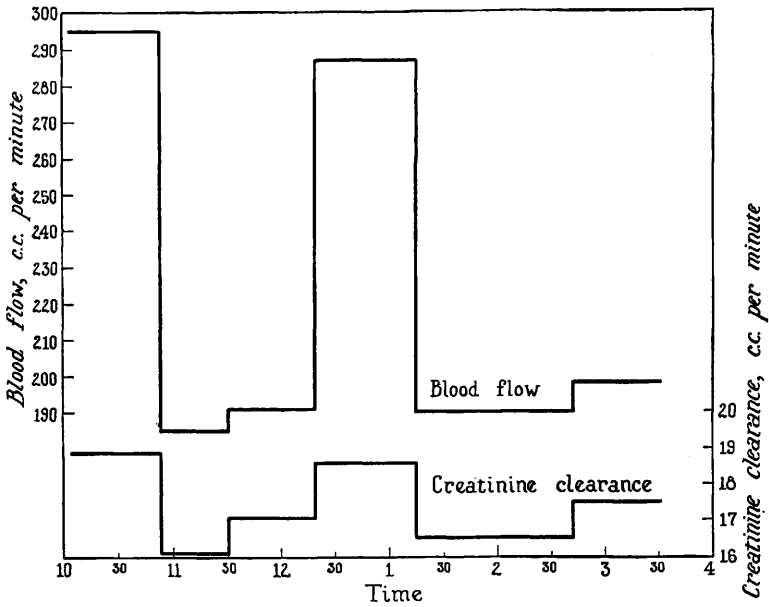


FIG. 2.

Parallelism between creatinine clearance and blood flow. The second day of an experiment. The increase between 12:00 and 1:00 follows a period of exercise.

At the close of the experiment the animal was killed, the position of the unit checked and the renal artery and kidney were examined grossly for possible injuries. In questionable cases sections of the kidney were examined microscopically.

A general parallelism has been found to exist between the blood flow and creatinine clearance (Table I, Fig. 1 and 2). Where the creatinine clearances approximate the values formed during the control periods (Exp. 1, 2 and 3) there seems to be almost a direct proportionality. However, the changes in blood flow were slight. In cases in which the fluctuations in blood flow were large and in which the creatinine clearances failed to return to their preoperative level, there is no direct proportionality (Fig. 1 and 2).

Observations made on the day of the operations showed a gradual increase in blood flow and creatinine clearance (Fig. 1). When the dogs recovered slowly the first period of observation showed a condition of marked oliguria with a scarcely measurable creatinine clearance and an appreciable blood flow. This instance of minimal creatinine clearance, in spite of an appreciable blood flow is in contrast to another observation (not recorded in the table): Creatinine clearance and blood flow diminished simultaneously and ultimately ceased during the second day of the experiment when the dog suddenly became nauseated. On exploration, it was found that the artery had become obstructed because of displacement of the unit applied to the blood vessel, which probably occurred during the retching accompanying vomiting. In this case in which the oliguria was caused by occlusion of the artery, both blood flow and creatinine clearance were measurable until anuria occurred.

Summary and Conclusions. A series of experiments was undertaken to study the relation between creatinine clearance and blood flow. The thermo-stromuhr method of measuring blood flow was used because it permits such observations without the complicating factor of anesthesia. All observations were made on unilateral nephrectomized dogs. A general parallelism but not a direct proportionality between the blood flow to the kidney and the creatinine clearance was observed.