VOLUME REGULATION IN RENAL INSUFFICIENCY CAUSED BY A DECREASE IN MASS OF THE RENAL PARENCHYMA

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With an increase in the extracellular fluid volume renal excretion of sodium increases as a result of the arrival of an increased quantity of natriuretic hormone (NUH) in the blood stream [8, 10]; however, the problem of the site of formation of this hormone has not yet been solved [3, 6]. It has been suggested that NUH may be formed in the kidneys [4, 9]. Meanwhile evidence has been obtained that blood plasma and urine of patients with renal failure can potentiate sodium excretion [2, 5]. Accordingly it was decided to study the ability of animals with a reduced mass of functioning nephrons to excrete sodium after expansion of the extracellular space and to examine the role of NUH in this response.

EXPERIMENTAL METHOD

Experiments were carried out on 152 albino rats weighing 110-140 g. Three-quarters of the mass of the renal parenchyma was removed from the animals 2 weeks before the investigation began. Volume regulation was studied in the animals after the volume of their extracellular fluid had been increased by intravenous injection of isotonic NaCl solution, by infusion of a 0.45% NaCl solution into the stomach (salt loading), or by the same procedure with tap water (water loading). In all experiments the liquid, warmed to body temperature, was introduced in a dose equivalent to 3% of body weight. For the intravenous injection of fluid the animals were anesthetized with pentobarbital (40 mg/kg), but experiments with water and salt loading were performed on unanesthetized animals. For the next 2 h hourly portions of urine were collected from all the animals and the sodium concentration in them was determined by flame photometry. Besides diuresis and sodium excretion, the concentration of NUH in the blood plasma and urine also was determined by a method devised by Yu. I. Ivanov [7] in the writer's laboratory; glomerular filtration was determined by endogenous creatinine, and the volume of the extracellular space (using sodium thiocyanate) and the intravascular fluid volume (by means of Evans' blue) also were determined. Animals undergoing mock operations served as the control. The experimental results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Two weeks after removal of three-quarters of the mass of the kidneys glomerular filtration was only 35% of its initial level, whereas sodium excretion was increased from 0.16 ± 0.011 to 0.22 ± 0.012 μmole/min/kg body weight ($P < 0.002$), due to a decrease in the reabsorbed sodium fraction from 99.88 ± 0.06 to $99.63 \pm 0.013\%$ ($P < 0.001$).

To study this phenomenon the role of NUH as the possible cause of this inhibition of reabsorption was investigated. First experiments were carried out to study sodium excretion after expansion of the extracellular space by various methods. The data in Table 1 show that regardless of the method by which the fluid volume was increased, sodium excretion was increased in both the control and the partially nephrectomized animals. In the control period sodium excretion by each functioning nephron of the experimental animals exceeded its value in rats undergoing the mock operation. After expansion of the extracellular space, however, nephrons of the reduced kidney excreted an even greater quantity of sodium not only during the first hour, but also, and more especially, during the second hour, when this difference became more considerable.

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TABLE 1. Effect of Increase in Fluid Volume on Sodium Excretion in Rats 2 Weeks after Partial Nephrectomy (M ± m; n = 10)

Experimental conditions	After mock operation		After partial nephrectomy	
	I	II	I	II
Intravenous injection of 0.85% sodium chloride solution				
Control period	1,2±0,14	0,6±0,07	1,7±0,16*	2,3±0,41*
After increase in fluid volume				
1 h	6,2±1,22	1,9±0,37	7,8±1,80	7,5±1,80*
2 h	3,8±0,57	1,6±0,25	8,6±1,08*	11,4±1,40*
Salt loading				
Control period	1,3±0,08	0,6±0,09	1,6±0,18	2,4±0,27*
After increase in fluid volume				
1 h	3,3±0,37	1,1±0,13	4,1±0,48	4,5±0,53*
2 h	1,9±0,40	0,9±0,17	3,8±0,43*	5,4±0,61*
Water loading				
Control period	0,9±0,09	0,4±0,04	1,4±0,14*	2,2±0,21*
After increase in fluid volume				
1 h	3,2±0,45	1,1±0,16	3,6±0,30	4,3±0,36*
2 h	1,7±0,21	0,8±0,10	3,4±0,43*	5,3±0,72*

*Here and in Table 2, changes statistically significant ($P < 0.05$).

Legend. I) μmoles/h, II) mmoles/100 ml glomerular filtrate/h.

TABLE 2. Excretion of NUH (in conventional units/min/100 ml glomerular filtrate) and Its Concentration in the Intravascular Space (in conventional units/100 g body weight) of Rats 2 Weeks after Partial Nephrectomy (M ± m)

Experimental conditions	NUH excretion		Quantity of NUH in intravascular space	
	after mock operation	after partial nephrectomy	after mock operation	after partial nephrectomy
Control period	8,4±0,35	50,1±4,67*	28,4±1,30	35,8±2,06*
After increase in fluid volume				
1 h	75,4±5,08	181,3±16,51*	52,6±2,80	56,0±2,90
2 h	35,3±3,32	217,0±24,86*	31,3±1,98	41,6±2,71*

It can be tentatively suggested that after partial nephrectomy NUH formation is stimulated, just as in the control animals. To test this hypothesis special experiments were carried out. It will be clear from Fig. 1 that after an increase in the fluid volume the concentration of NUH in the blood plasma increased in both groups of animals. At the same time, a higher NUH concentration was observed in the blood plasma of the partially nephrectomized rats, both in the control period and after the increase in fluid volume (mainly at the second hour). Data showing the hourly excretion of NUH with the urine also are given in Fig. 1 (below); they show that in the control period the partially nephrectomized animals excreted more NUH than animals undergoing the mock operation. After expansion of the extracellular space, NUH excretion increased in both groups of animals. During the 2 h of the investigation the total NUH excretion with the urine was about equal in the two groups. After partial nephrectomy, however, the mass of functioning renal parenchyma, determined by the creatinine clearance method [1], allowing for compensatory hypertrophy was only one-third of their mass in rats undergoing the mock operation. Accordingly the NUH excretion by each remaining nephron of the reduced kidney was considerably greater (Table 2).

The NUH content in the intravascular space of the partially nephrectomized rats was increased in the control period and at the second hour of the experiment (Table 2). Since the volume of the extracellular space (the preoperative body weight of the animals of the two groups was about equal) in the rats with a reduced mass of renal parenchyma was 36.2 ± 0.51 ml, whereas in the animals undergoing the mock operation it was 37.5 ± 0.47 ml ($P > 0.05$), and since the NUH concentrations in the blood plasma of these animals were 8.6 ± 0.66 and 5.0 ± 0.41 conventional units ($P < 0.001$) respectively, the NUH concentration in the extracellular space of the animals with a reduced kidney was naturally greater than in animals undergoing the mock operation.

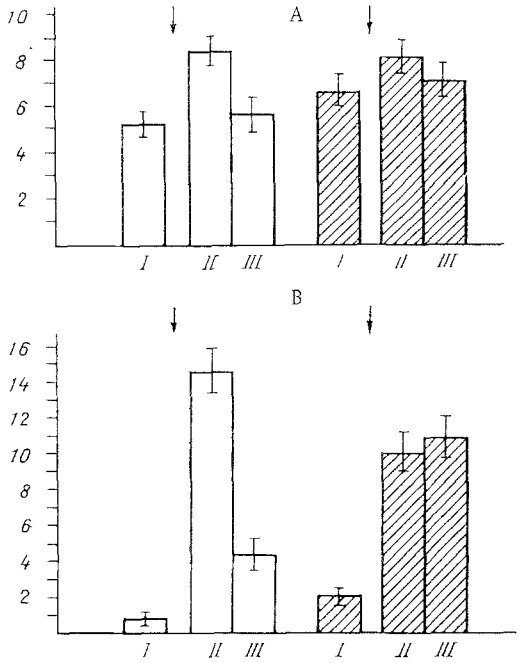

Fig. 1. Concentration of NUH in blood plasma (A) and its excretion (B) in rats undergoing mock operation and rats with reduced mass of renal parenchyma, before and after volume loading. Abscissa, stages of investigation: I) NUH concentration (A) and hourly excretion of NUH (B) before volume loading, II) the same when tested 1 h after volume loading, III) the same 2 h after volume loading; ordinate: A) NUH concentration (in conventional units/ml), B) NUH excretion (in conventional units/h). Unshaded columns) control; shaded columns) experiment.

NUH production thus increased by a greater degree in the partially nephrectomized rats in the period before the increase in fluid volume than in animals undergoing the mock operation. After expansion of the extracellular space NUH formation increased in both groups of animals. Because of the considerable decrease in mass of the renal parenchyma, NUH excretion by each active nephron of the residual kidney was increased, especially after expansion of the extracellular space. The more marked sodium excretion by nephrons of the reduced kidney was evidently connected with this fact also. Moreover the results give reasons for doubting that the kidneys are the site of formation of NUH.

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