STUDY OF CREATININE SOLUTION BY THE ARREST OF DIURESIS (STOP-FLOW) TEST

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Excretion of exogenous and endogenous creatinine in the urine was studied by the stop-flow method. The creatinine/inulin ratio was found to be increased in the proximal portions of the nephron. After the flow of urine had been stopped, creatinine appeared in the urine sooner than inulin. This indicates that creatinine is secreted in the proximal portions of the nephron. Creatinine secretion was unaffected either by changes in the pH of the urine or by administration of probenecid. Furthermore, the dynamics of the pH along the nephron was unaffected by administration of creatinine. This suggests that creatinine transport in the renal tubules takes place by noionic diffusion. Exogenous and endogenous creatinine could not be distinguished either by the volume of secretion or by its localization.

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Creatinine is widely used along with inulin to study the rate of glomerular filtration. According to reports in the literature, tubular secretion participates in the excretion of exogenous creatinine in rats [1]. and dogs [3, 4]. No data concerning the secretion of endogenous creatinine could be found in the accessible literature.

Tubular transport of exogenous and endogenous creatinine was studied in the investigation described below by the method of arrest of diuresis (the stop-flow method).

EXPERIMENTAL METHOD

Thirty dogs weighing 10-25 kg were prepared by the method described in [2]. The left ureter was catheterized through an incision in the abdominal wall in an acute experiment. A 5% solution of urea and 0.1% inulin in physiological saline was infused into the femoral vein at the rate of 15-20 ml/min. In the experiments with exogenous creatinine, this substance was added to the infused solution at the rate of 1.2 g/liter. After a high level of osmotic diuresis (5-10 ml/min) had been obtained, control samples of urine and blood were taken and the catheter was clamped for 5 min. At the end of occlusion, 25-30 samples of urine (each of 0.7-0.8 ml) were collected in special tubes in the course of 1.5-2 min. Blood was taken for analysis in the middle of the occlusion period. The secretion of substances transported in the nephron as ions is known to be changed considerably by a change in the pH of the urine [2]. Probenecid (and its analogous Soviet preparation ethamide) inhibits the renal secretion of substances possessing acid properties. It was therefore decided to investigate the character of creatinine secretion under the influence of changes in the pH of the urine and administration of probenecid. To modify the pH of the urine 0.15M $NaHCO_3$ solution was injected instead of 5% urea. The effect of probenecid (30 mg/kg, intravenously) on tubular secretion of creatine also was studied. The localization of changes in the concentrations of the substances was determined from the volume of urine collected after removal of the clamp from the catheter. It was assumed that the increase in concentration of inulin due to reabsorption of water is observed in the distal portions of the nephron, corresponding to a total volume of urine collected of 2-8 ml [2]. The proximal portion of the nephron, according to data in the literature [2-4], corresponds to a total volume of urine of 10-20 ml.

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TABLE 1. Corrected Creatinine Clearance (M ± t)

Region of nephron	Exogenous								Endogenous	
	5% urea	P	0,15 M urea	$NaHCO_3$	P	Probenecid	P	5% urea	P
Control	1,05±0,07(19)		1,04±0,06(8)			1,28±0,12(5)		1,03±0,05(6)	
Distal tubules	1,06±0,07(19)	>0,5	1,04±0,06(8)		>0,5	1,31±0,12(5)	>0,5	1,2±0,11(6)	>0,5
Proximal tubules	1,47±0,07(19)	<0,01	1,3±0,1(8)		<0,05	1,69±0,12(5)	<0,01	1,78±0,2(6)	<0,01

Note. Number of observations given in parentheses.

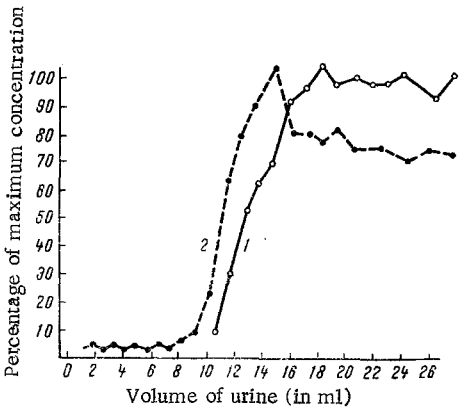

Fig. 1. Dynamics of inulin (1) and creatinine (2) concentrations in the urine following their injection in the period of arrest of diuresis.

In a separate series of experiments, only 5% urea solution was infused into the animals, the catheter was clamped, and 6 min later a solution containing 1 g inulin and 0.8 g creatinine was injected intravenously. The clamp was taken from the catheter 2 min later and samples of urine collected as described above. In this case the appearance of inulin in the urine indicated restoration of normal ultrafiltration processes in the glomeruli [2]. The time of appearance of the test substances in the urine was also determined from the volume of urine collected after the end of occlusion.

Each sample of urine and blood was analyzed for creatinine (by Folin's method and inulin (by Schreiner's method). The ratio between the concentrations of the two substances in the urine and blood (U/B) and also the ratio between the creatinine clearance and the inulin clearance (U/B for creatinine/ U/B for inulin), the inulin-corrected creatinine clearance, to eliminate the effect of reabsorption of water on creatinine transport, were calculated for each sample of urine; the pH of the urine was determined with a type LPU-01 potentiometer.

The experimental results were subjected to statistical analysis. The mean corrected creatinine clearance was calculated for each sample of urine. The values of these indices for each experimental sample were compared with the corresponding indices obtained during the period of free flow of urine (control).

EXPERIMENTAL RESULTS

Location of Creatinine Secretion. Along the length of the distal tubules the corrected clearance of both exogenous and endogenous creatinine was not significantly different from the control. In the proximal portions of the nephron, an increase in the creatinine/inulin ratio on the average to 1.47 was observed. The difference compared with the control was significant in both cases with a volume of urine of 12-18 ml (Table 1). This points to the location of creatinine secretion in the proximal tubules. The location of creatinine secretion corresponds to that of renal transport of p-aminohippurate (PAH) [2-4]. No significant difference was found between exogenous and endogenous creatinine as regards either the volume of secretion (Table 1) or its localization.

After injection of inulin and creatinine in the period of arrested flow of urine, creatinine appeared in the urine sooner than inulin (Fig. 1). Inulin appeared when the volume of urine was 13.1 ± 0.67 ml, and creatinine at 10.3 ± 0.85 ml ($P < 0.02$). These results confirm the conclusion that creatinine is secreted in the proximal portions of the nephron.

Character of Creatinine Secretion. The change in pH of the urine after injection of 0.15 M $NaHCO_3$ did not affect creatinine secretion. Probenecid likewise had no effect on creatinine transport (Table 1), a result which did not confirm data in the literature showing that creatinine secretion is inhibited by probenecid [4]. These findings suggest that creatinine differs from PAH in the mechanism of its active transport in the renal tubules. Probably nonionic diffusion takes place in this case. This hypothesis is supported by the absence of differences in the pH dynamics along the nephron whether creatinine was injected or not.

The small volume of creatinine secretion and the slight differences between its clearance in whole urine and the inulin clearance do not evidently prevent the use of this substance for the study of filtration and water reabsorption in the nephron.

LITERATURE CITED

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