# RENAL FUNCTIONING DURING REGENERATIVE HYPERTROPHY

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When one kidney is affected by nephrolithiasis, tuberculosis, or malignancy the surgeon must resect it [1, 2, 5, 11, 12]. Clinicians have long been interested in the reserve functional capacities of a single kidney.

Detailed experimental studies have been made of the morphological changes in a single kidney after resection [4, 6, 8, 10]. The process which occurs in the kidney after resection is called regenerative hypertrophy. Little research has been done on renal functioning during regenerative hypertrophy [7, 10].

We studied the functioning of the glomerules and tubules of a single hypertrophied kidney after resection.

## EXPERIMENTAL METHOD

The experiments were conducted on 4 dogs with ureters opening into the anterior abdominal wall. The functioning of the intact kidneys was investigated and one kidney was then removed. The functioning of the remaining kidney was studied over a period of 8 months. Two dogs were later subjected to successive (8 and 10 months after the nephrectomy) reaction of both poles of the remaining kidney and one pole was resected in two others. Renal functioning was determined after each stage of the operation. Glomerular filtration and water resorption in the tubules were studied with insulin, while renal plasma flow and maximum tubule secretion were determined with diodrast. For purposes of comparison the experimental results were calculated per square meter of body surface. The experiment lasted 13 months.

## EXPERIMENTAL RESULTS

In all 4 dogs diuresis averaged 3.56 $ml/min/m^2$ for the intact right kidney. After removal of the opposite kidney diuresis increased to 6.01 $ml/min/m^2$. Oliguria and hematuria were noted during the first two days after resection of one pole of the single hypertrophied kidney. The residual nitrogen content of the blood increased (to 57.4-60.2 mg-%). After 3-4 days diuresis averaged 4.19 $ml/min/m^2$ for the resected kidney. Urine production increased progressively and reached 6.38 $ml/min/m^2$ at the end of the 2nd month, i. e., exceeded that of the hypertrophied kidney before resection. Inhibition of diuresis was observed after resection of the second pole. After 3-4 days urine production reverted to 4.68 $ml/min/m^2$, gradually increasing to 5.5-6.2 $ml/min/m^2$ over the next 3 months; this was 155-174.4% of the urine production of the intact kidney (Figs. 1 and 2). Judging from diuresis, the function of a single kidney is completely restored after resection of both poles. However, diuresis does not characterize the change in renal functioning sufficiently well.

The functioning of the glomerular apparatus was evaluated from the change in glomerular filtration, renal blood flow, and the quantity of the filtration fraction. Glomerular filtration by the right kidney averaged 47.9 $ml/min/m^2$ before nephrectomy in all 4 dogs. Eight months after removal of 1 kidney filtration by the hypertrophied kidney had risen to 65.9 $ml/min/m^2$. Glomerular filtration decreased to 51.9 $ml/min/m^2$ during the first few days after resection of one pole of the single kidney and remained at this level for 2-3 weeks. It began to increase gradually at the end of the 1st month, but reached the level of the hypertrophied kidney (67.1 $ml/min/m^2$) only at the end of the 2nd month. Filtration dropped sharply, to 34.5 $ml/min/m^2$, after resection of the 2nd pole. It then gradually rose for 3 months after this operation, but reached only 40.6 $ml/min/m^2$, or 84.6% of the glomerular filtration of the intact kidney.

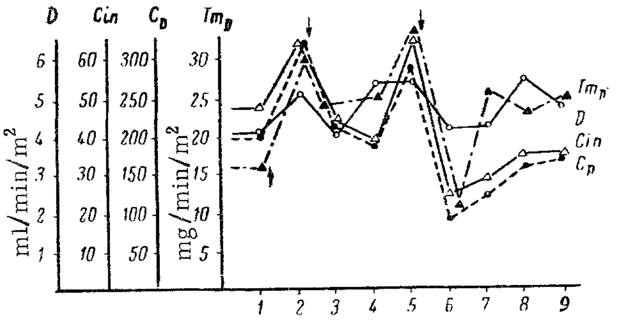


Fig. 1. Functioning of the right kidney of the dog Tsygan after removal of the left kidney (arrow pointing upward) and resection of the poles of the right kidney (arrows pointing downward). Along the ordinate D represents diuresis, $C_{in}$ is the index of insulin clearance, $C_D$ is the index of diodrast clearance, and $Tm_D$ is the maximum tubule secretion as determined with diodrast. Along the abscissa: 1)Functioning of intact kidney; 2) after removal of left kidney; 3) during first few days after resection of upper pole of right kidney; 4 and 5) during 1st and 2nd months after resection; 6) during first few days after resection of lower pole; 7, 8, and 9) during 1st, 2nd, and 3rd months after resection of lower pole.

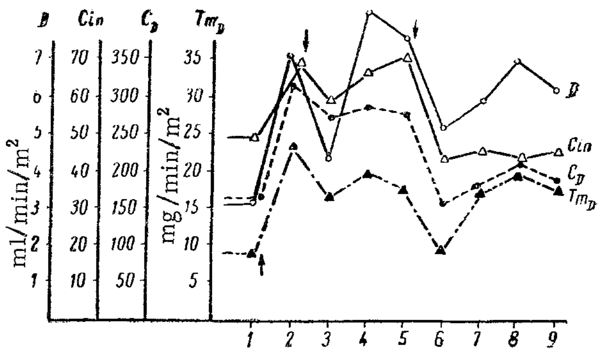


Fig. 2. Functioning of right kidney of the dog Kashtanok after removal of the left kidney (arrow pointing upward) and resection of the poles of the right kidney (arrows pointing downward). The key is the same as for Fig. 1.

The blood flow of the intact right kidney averaged 179.8 ml/min/m$^2$ in all 4 dogs. It reached 314.6 ml/min/m$^2$ 8 months after removal of the opposite kidney. Blood flow decreased to 242.5 ml/min/m$^2$ during the first few days after resection of one pole and persisted at this level for 1 month. It increased slightly (to 279.4 ml/min/m$^2$) only during the 2nd month. It decreased even more sharply, to 126.2 ml/min/m$^2$, after removal of the 2nd pole and then gradually rose to 191.9 ml/min/m$^2$, or 106.7% of the blood flow of the intact kidney.

The vascular functions of a single hypertrophied kidney (blood flow and filtration) thus decreased in direct proportion to the mass of renal parenchyma removed, increasing slightly after repeated resection.

The filtration fraction of the intact right kidney averaged 23.3% in all 4 dogs. It remained almost unchanged (21.5%) after removal of the opposite kidney and resection of the poles of the remaining kidney. This indicated uniform dilatation of the incoming and outgoing glomerular arterioles during regenerative hypertrophy.

The state of the renal tubules was evaluated from their water resorption and the secretory capacity of their epithelium. An averaged 43.35 ml/min/m$^2$ of water was resorbed in the tubules of the intact right kidney in all 4 dogs. Resorption rose to 59.93 ml/min/m$^2$ 8 months after removal of the opposite kidney. It decreased to 47.7 ml/min/m$^2$ after resection of one pole of the remaining hypertrophied kidney and remained at this level for 1 month. During the 2nd month it rose to 60.7 ml/min/m$^2$, i.e., reached the level exhibited by the hypertrophied kidney before resection. Water resorption dropped sharply, to 29.89 ml/min/m$^2$, after removal of the 2nd pole. Over the next 3 months of observation it rose very slowly to 35.05 ml/min/m$^2$, or 80.8% of the resorption level for the intact kidney. The decrease in resorption is explained by the increase in diuresis following repeated resection of the solitary kidney. The drop in resorption was greater than that in filtration. This is strikingly shown by the ratio of the quantity of water resorbed to the filtration level (in %): while this ratio averaged 92.4% for the intact kidney, it had mean value of 85.6% for the repeatedly resected solitary kidney.

The maximum secretion of the tubule epithelium of the intact kidney averaged 12.3 mg/min/m$^2$ in all 4 dogs. It rose to 27.05 mg/min/m$^2$ over 8 months after removal of the opposite kidney. Tubule secretion decreased to 20.3 mg/min/m$^2$ during the first few days after resection of one pole of the single hypertrophied kidney, but regained its prior level (25.03 mg/min/m$^2$) over the next 2 months. It dropped sharply, to 10.35 mg/min/m$^2$, after resection of the second pole of the solitary kidney, but subsequently rose progressively to 21.3 mg/min/m$^2$, or 173% of the tubule secretion of the intact kidney.

Tubule functioning is thus altered in a somewhat different manner than glomerulus functioning in regenerative hypertrophy. Water resorption drops considerably, but the tubule secretion of the solitary kidney is intensified to a greater extent after resection than vascular functions.

Analysis of the results obtained shows that all renal functions are inhibited during the first 2 days after resection of an isolated kidney. Renal functioning remains at a low level over the next 2-3 weeks and begins to increase only toward the end of the 1st month. During the 2nd month it reaches a level characteristic of the hypertrophied kidney before resection. After repeated resection of the solitary kidney its functioning, gradually increasing, reaches the level exhibited by the intact kidney, but never achieves that exhibited by the hypertrophied kidney.

All this indicates the great reserve capacities of the hypertrophied kidney, which would seem to have exhausted its compensatory capabilities. However, these reserve capacities are not unlimited. In the dog Damok both poles of the solitary kidney (approximately half the organ) were simultaneously resected. Regenerative hypertrophy did not develop after this operation. The animal died after 3 days, exhibiting symptoms of uremia (the residual nitrogen content of the blood rose to 107.8 mg-%).

In experiments on rats G. G. Samsonidze [6] established that there are substantial morphological differences in the course of compensatory and regenerative hypertrophy: in regeneration the malpighian corpuscles and tubules are enlarged primarily as a result of cellular hyperplasia and partially as a result of cellular hypertrophy, while in compensatory hypertrophy this enlargement is caused principally by cellular hypertrophy.

Comparison of renal functioning during regenerative and compensatory hypertrophy [3] clearly reveals the difference in their functional course. During compensatory renal hypertrophy functioning is already sharply elevated during the first few days after removal of the opposite kidney. After resection of the solitary kidney its functioning fails to improve for 2-3 weeks and reaches the preresection level only during the 2nd month. This is apparently the result of two factors. The first is the trauma incurred by the kidney during resection. We know from morphological works [9] that a resection wound in the kidney requires a month to heal completely. This trauma probably inhibits the development of regenerative hypertrophy in the remaining nephrons. The second factor may be described as follows. The reserve capacities of the solitary kidney are almost exhausted during compensatory hypertrophy and after resection its functioning increases gradually, apparently as a result of prolonged morphological and functional reorganization of the remaining cellular elements.

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