REGENERATIVE PROCESSES IN THE KIDNEYS OF RATS IN LATE STAGES AFTER OPERATION

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In recently published investigations, the kidney has been studied in a state of regeneration or compensatory hypertrophy in the late postoperative period. The results obtained have not been consistent: some workers [3,6,7,9, 11) describe the gradual development of decompensation of the operated kidney, while others [1,2,10] describe its state as good, with no appreciable functional or morphological disturbances. In her previous experiments, the author showed [5] that after removal of 50% or 75% of the kidney tissue from rats, the residual kidney, which had undergone regeneration or compensatory hypertrophy, may appear morphologically and functionally defective, and the greater the amount of kidney tissue removed, the sooner can this be seen. However, 15 months after the removal of 75% of the kidney tissue from rats of the same age as in the author's experiments, G. G. Samsonidze [4] observed well marked repair processes in the regenerating kidney without any pathological changes. It may therefore be asked what determines the fate of the regenerating or the compensatorily hypertrophied kidney. In Samsonidze's experiments, the rats received only half the quantity of protein which they would have received had they been kept on the pellet diet received by the rats in the author's experiments. It was therefore suggested that the protein level in the pellet diet was excessively high for the rats after these operations, and this played an important role in the development of the pathological changes in the residual kidney. Evidence for this was given by experiments in which normal rats, kept on a high protein diet, developed degenerative changes in the kidneys.

In the present investigation, the effect of the diet on the state of the kidneys was studied at late periods after removal of a considerable proportion of the kidney tissue.

EXPERIMENTAL METHOD

The right kidney and $\frac{1}{2}$-$\frac{1}{3}$ of the left kidney were removed from noninbred male albino rats weighing 170-180 g (altogether about 75% of the kidney tissue was taken). Intact animals were used as controls. The total number of experimental and control animals was subdivided into two groups. The rats of group 1 received a standard pellet diet as normally given in the Institutions of the Academy of Medical Sciences of the USSR (18.53% protein, 4.25% fat, 51.74% carbohydrate), and the animals of group 2 received a natural diet consisting of porridge with meat, milk, grain, and vegetables (9.7% protein, 2.8% fat, 41.9% carbohydrates). During the month before they were sacrificed, the following investigations were made on six animals of each experimental and control group: the 24-h diuresis, the protein content in the urine (by Brandenberg's method modified by Larinova), the pH of the urine, the residue of the urine was analyzed, a water-loading test was performed, the urea concentration in the blood and urine was determined by a urease express method, and the concentration index was calculated. All the animals were sacrificed 8 months after the operation. The kidneys were fixed in 10% formalin solution. Paraffin sections, 7 μ in thickness, were stained with hematoxylin-eosin and by Mallory's method; sections cut on a freezing microtome were stained with Sudan III. The large and small diameter of the renal corpuscles was measured by means of a screw ocular micrometer, and their area was then calculated from the formula of an ellipse. The height of the epithelium of the convoluted tubules was also measured.

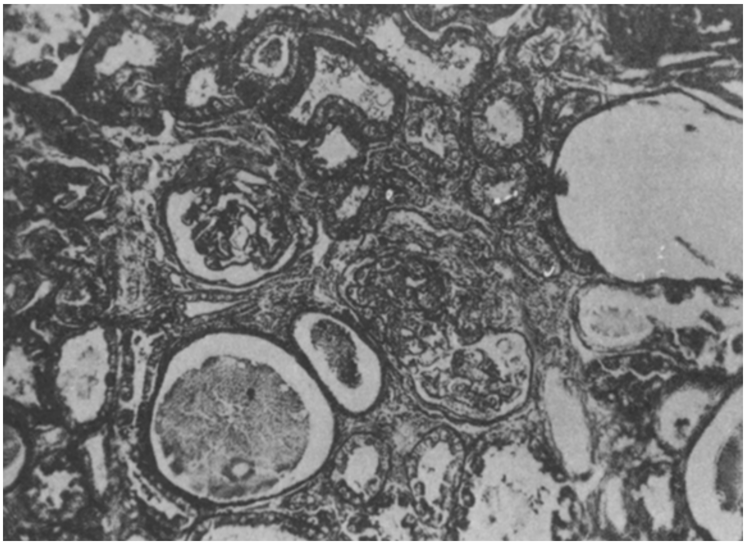

Fig. 1. Kidney of an experimental rat kept on a pellet diet, 8 months after operation. The hypertrophied renal corpuscles are replaced by connective tissue, and only isolated capillary loops remain; the lumen of the convoluted tubules is dilated and filled with masses of protein material. Mallory's stain. 200 ×.

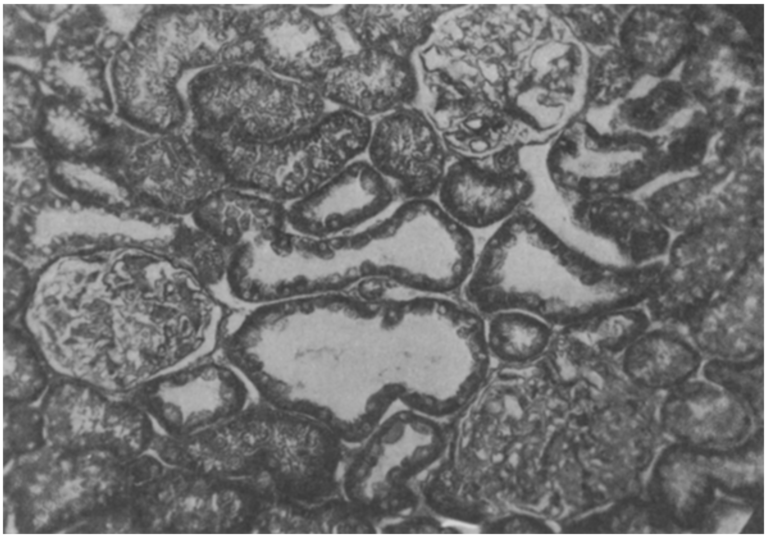

Fig. 2. Kidney of an experimental rat kept on a low protein diet, 8 months after operation. The renal tubules are hypertrophied, the lumen of certain convoluted tubules is dilated. Mallory's stain. 200 ×.

EXPERIMENTAL RESULTS

The mean weight of the kidneys in the rats of group 1 was 85.6%, and in the rats of group 2, 77.5% of the weight of both kidneys of the control animals; the differences were not statistically significant. The shape of the kidneys was not restored, and a scar was present at the site of injury.

Histological investigation of the kidneys of the control rats revealed no significant changes.

In five of the eight rats of group 1 receiving a high protein diet, considerable pathological changes were observed in the kidneys (Fig. 1). The interior of the Bowman's capsules of some of the renal corpuscles were filled with

Clinical Indices of Renal Function in Experimental and Control Rats 7 Months after Beginning of Experiment

Animals	24-h diuresis (in ml)	Protein concentration in urine (‰)	Blood urea concentration (in mg%)	Urea concentration in urine (in mg%)	Concentration index
Control	4.0	0.22	47.1	777.0	9.0
Receiving pellet diet	7.0	1.46	228.73	989.64	5.6
Receiving natural diet	4.8	0.44	119.19	764.04	7.4

exudate, the capillary loops of the glomeruli were palm-shaped, and the walls of the Bowman's capsules were thickened. Some renal corpuscles were found which were completely or partially replaced by connective tissue, and only isolated capillary loops remained. Sometimes the connective tissue had replaced the whole nephron. The renal corpuscles unaffected by sclerosis were greatly hypertrophied and their area was almost twice that in the control animals (experimental 21 970 μ^2, control 10 053 μ^2). The lumen of the convoluted tubules was dilated to three times that of the controls, and in some cases cysts were formed and their lumen was filled with masses of protein. The mean height of the epithelium of the convoluted tubules was slightly increased, but not in all animals; besides an increase in the height of the epithelium and the appearance of stratified epithelium in some cases, other cases were observed with atrophy of the tubular epithelium, mostly associated with a sharp increase in the size of the lumen. In two rats of this group, the changes described above were observed, but the lumen of the tubules was not so sharply dilated and no cysts were formed. In one rat, the pathological changes were limited to an increase in the thickness of the walls of the Bowman's capsules of certain renal corpuscles, dilation of the lumen of some convoluted tubules, and proliferation of the connective tissue around certain nephrons. Two rats of group 1 died six months after the operation, before the end of the experiment. No significant changes were found in their internal organs. Histological investigation of the residual kidney revealed marked nephrosclerosis and hyalinosis of many of the renal corpuscles. In one of these rats, marked fatty degeneration of the epithelium of the convoluted tubules was observed.

In the rats of group 2 receiving a natural, low-protein diet, pathological changes were observed in three cases, in the form of an increase in the thickness of the walls of Bowman's capsules, lobulation of the glomeruli, and partial or complete replacement of the renal corpuscles by connective tissue. In four rats of this group, the only changes observed were thickening of the walls of some Bowman's capsules and dilatation of the lumen of some convoluted tubules (Fig. 2). In one rat of group 2, no pathological changes were seen. None of these animals died in the late postoperative period, and none developed severe nephrosclerosis with dilatation of the lumen of the convoluted tubules and cyst formation. As in group 1, the renal corpuscles were hypertrophied, but only 75% compared with the controls (S = 17 541 μ^2; the difference between the areas of the renal corpuscles in the animals or groups 1 and 2 is statistically significant, $P < 0.05$). Seven months after the operation, the 24-h diuresis was increased in three rats receiving a high-protein diet, and in five rats protein was present in the urine, while in four animals hyaline casts appeared in the urinary sediment. In six animals, the blood urea was raised, and in six animals the reaction of the kidney to a water load was modified (diuresis began 2-3 h after administration of water and reached a maximum after 3-4 h) (see table).

In the rats of group 2 receiving a low-protein diet, the 24-h diuresis and protein concentration in the urine was increased in only one case, and a sharp increase was observed in the level of the blood urea. The concentration index was higher and the reaction of the residual kidney to water loading was modified to a lesser degree.

The results show that the regenerative processes developing in the kidneys of rats after removal of 75% of the renal tissue do not always produce a lasting result and may be replaced by the morphological and functional insufficiency of the organ. This is most marked in rats receiving a high-protein diet, and is much less obvious in animals receiving a low-protein diet. On the assumption that, after removal of 75% of the renal tissue, decomposition of the partly resected kidney is associated with an increased functional load, it may be postulated that lowering the protein content of the diet of the rats after operation, by minimizing the load on the residual kidney, postpones the development of its decompensation. Such an explanation,of course, must be treated with great care for two reasons: first, the development of decompensation after removal of a large quantity of kidney tissue may be due not only to the increased function of the partially resected kidney, but also with inadequacy of the blood supply and nerve supply of the hypertrophied and hyperfunctioning nephrons, and second, with an increase in the protein content of the diet of the rats after operation, besides an increase in the specific functional load, the possibility of other, as yet unknown, factors (for example, toxic) acting on the kidney cannot be ruled out. Another factor to be borne in mind is the fact that animals receiving a pellet diet eat it dry, and this causes detachment of the cells of the renal epithelium [12].

The conflicting results given in the literature are evidently due to differences in the diet of the experimental animals. Too little attention has been paid to this factor, yet it plays a fundamental role in determining the stability of the regenerative processes in the partially resected kidney.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**