MORPHOLOGICAL CHANGES IN REGENERATING RAT KIDNEY AT LONG INTERVALS AFTER INJURY

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In previous publications [2, 3] it has been shown that after partial resection (from $^1/_3$ to $^1/_2$) of one kidney and complete removal of the other, restoration of the partially resected organ occurs. Regeneration of the kidney is a complex process [1] involving changes both at the injured surface and in the rest of the kidney, which is not directly affected by the injury (regeneration hypertrophy). We observed restorative processes over a 7-month period.

In the present study we followed the restorative processes for longer periods following injury, since changes in regenerating organs over long periods after injury have not been adequately studied.

METHOD

Experiments were performed on white male rats weighing 150-200 g. The left kidney was removed from each of 10 experimental animals, and $^1/_3$-$^1/_2$ of the right kidney was resected at the same time. Five rats served as controls. The convex portion opposite the hilum was removed in resection, by means of an incision parallel to the long axis of the organ. The part removed contained mainly cortical substance.

After the animals were sacrificed the kidneys were weighed, measured, and fixed in Bouin's fluid and in 10% formalin. Small pieces were imbedded in paraffin, and sections were stained with hematoxylin by Bemer's method, and with azocarmine and hematoxylin by Heidenhain's method.

The area of a median cross-section of the kidney and the areas occupied by cortical and medullary substance in this section were measured.

The areas of individual renal corpuscles were also determined, and the mean area for 50 corpuscles was calculated. In addition, the diameters of the convoluted tubules and collecting ducts and the heights of the tubule cells and renal corpuscles were measured by means of an ocular micrometer. For each of these quantities the mean of 50 measurements was calculated. Statistical analysis of the data showed that this number of measurements ensures that reproducible results will be obtained.

RESULTS

Table 1 presents data characterizing the changes in weight and size of the operated kidneys 15 months after operation, in comparison with results of previous experiments [2, 3] in which the changes were observed 3-7 months after operation.

Data for the control rats were obtained 15 months after the beginning of the experiment. The values found for these rats were not statistically different, in most cases, from those for control rats sacrificed after only three months. Consequently, in the further analysis of our data we proceeded on the basis that during the period of between 3 and 15 months no significant morphological changes took place in the kidneys of control rats, and we confined our attention to comparison with a single control.

Taking this into account, we may note that in contrast to the kidneys of control animals, those of experimental animals showed significant changes, which indicated that restorative processes were occurring, during periods long after the beginning of the experiment. The weights of the kidneys of experimental animals were 57% greater after 15 months than after 3 months. The relative weight particularly increased; it was more than twice as great for the experimental as for the control group. This indicated, to be specific, that the experimental animals did not grow as much as the controls. It is interesting that 15 months after the operation the width of the kidney was markedly increased, although just this dimension was reduced by the operation. As a result, the kidneys assumed a form similar to their original form, and the defect was erased to some extent. The area of the median section of the kidney was also significantly greater after 15 months than after 3 months.

TABLE 1

Weights and Dimensions of Right Kidneys of Experimental and Control Rats at Various Intervals After Start of Experiment

Time of examination	Weight of kidney		Dimensions of kidney (in mm)			Area of median section (in mm^2)	
	mg	% of body weight	length	width	thickness	total	cortex
After 3 months	1 552	0,63	21,5	8,7	10,3	56,2	50,5
After 7 months	1 756	0,65	23,2	9,0	10,8	58,4	53,1
After 15 months	2 439	0,93	23,5	13,1	11,8	63,7	58,7
Control	1 394	0,41	18,6	10,6	8,8	44,6	39,8

TABLE 2

Dimensions of Renal Corpuscles and Convoluted Tubules of Experimental and Control Rats

Time of examination	Renal corpuscles						Convoluted tubules					
	total number in section	number per mm^2	area (in μ^2)	maximum dimension of cavity (in μ)	number of nuclei in outer wall of Bowman's capsule	distance between nuclei (in μ)	diameter (in μ)	diameter of lumen (in μ)	area occupied by cells (in μ^2)	number of nuclei per cross-section	distance between nuclei (in μ)	height of cells (in μ)
After 3 months	139	2.8	6,206	8.2	18.6	13.1	46.5	21.9	1,716	7.2	9.4	11.6
After 7 months	147	2.8	6,563	7.1	19.5	12.6	43.6	16.0	1,437	8.1	9.0	12.0
After 15 months	128	2.3	11,387	6.6	21.9	11.7	44.0	12.0	1,796	8.9	8.7	14.1
Control	170	4.3	5,093	4.2	12.9	9.3	35.1	6.1	1,199	4.7	7.7	11.1

The changes in various parts of the kidney, as revealed by microscopic examination, are shown in Table 2.

As is evident from the data in Table 2, the number of renal corpuscles in the regenerating kidneys is less than normal. Thus, the number of renal corpuscles is not completely restored by the regeneration process. The area of the corpuscles is a different matter, especially if the increased dimensions of the kidney are taken into account. It is true that the area of each corpuscle increases even in the kidneys of control animals. It increases from 4338 to 5093 μ^2 during the experiment – i.e., it parallels the age of the animal. This increase is statistically significant (P = 0.01). But in the experimental rats the in-

cant (P = 0.01). But in the experimental rats the increase in corpuscular area is significantly greater than that due to age. This increase is particularly marked in the last five months, when the corpuscle area increases by 73%. The increase in corpuscle area is not connected with an increase in the width of the space between capsule and glomerulus. The latter dimension falls in the late experimental periods, although it remains greater than for the control rats. Along with this, the number of nuclei in the outer wall of Bowman's capsule increases; this increase is statistically significant (P = 0.003).

The changes in the renal tubules are of a different sort from those in the corpuscles. It was not possible to detect further hypertrophy of the tubules as the experiment continued. In fact, the tubule diameters even decreased somewhat, from 46.5 to 44 μ; but in this case the difference was not statistically significant. The reduction in the tubule diameter was accompanied by a considerable diminution in the size of the tubule lumen (from 21.9 to 12 μ), while the area occupied by cells—i.e., the area of the tubular wall—increased (from 1716 to 1796 μ^2).

We previously observed [2] that during the first three months following injury, an increase in tubule diameter occurs in the regenerating kidney, which is partially explained by an increase in the diameter of the lumen. As is apparent from the data obtained in the present study, the changes occurring in the tubule in subsequent experimental periods are different in character. A certain amount of change in the form of the cells in the tubule wall must be noted. The distances between the nuclei of those cells change slightly, becoming 8.7 instead of 9.4 μ. The height of the cells increases considerably, from 11.6 to 14.1 μ; this change is statistically significant (P = 0.000). There are more cells per tubule cross-section, to judge from the fact that the number of nuclei found in a tubule cross-section increases from 7.2 to 8.9; this increase is statistically significant (P = 0.005). It will be recalled that in the control rats no such changes could be observed. These data refer to the convoluted tubules. We found similar changes in the collecting ducts of the cortex and medulla of kidneys that had regenerated, and therefore we did not make a separate study of these data.

Our results permit us to conclude that in the injured kidney, where about $\frac{1}{3}$ predominantly cortical substance was removed, accompanied by removal of the opposite kidney, restorative processes continue for long periods after injury (from the third to the 15th month after operation). The weight and size of the regenerating kidney increase, and its form changes. Apparently the restorative processes take place primarily in the renal corpuscles, which undergo considerably hypertrophy. As for the renal tubules, their diameters are unchanged; as a result, it is hard to see how they could contribute to the change in the kidney size. It is possible that the tubules increase in length, since we did not take the length of the tubules into consideration in our experiments. But this is unlikely, since the increase in cross-sectional area of the kidney was caused exclusively by an increase in the area of its cortical layer. In view of this we must suppose that the area occupied by the collecting ducts in the medulla does not increase, and since the changes in the collecting ducts are of the same type as those in the convoluted tubules, we can suppose that the convoluted tubules do not increase in length. This argument should be tested experimentally. It should be noted that at the long-time intervals, changes occur in the renal tubules. They take the form of an increase in the number of cells in the tubule wall and a thickening of this wall, with a resulting decrease in the diameter of the lumen. We are justified in regarding these changes as restorative.

Further analysis shows that these changes occur as a result of an increase in the number of cells—i.e., cellular hyperplasia. Cell dimensions do not diminish during the experiment. Cells in the kidneys of experimental animals remain hypertrophied—their dimensions are greater than those of the corresponding cells in the control animals. This shows that the phenomenon of cellular hypertrophy may be of a lasting and stable character.

SUMMARY

Complete removal of the left kidney and resection of $^1/_3$ to $^1/_2$ of the right kidney were performed simultaneously in mature rats. The experiment then lasted for 15 months. Regenerative processes continued long after injury, as shown by comparison with the changes observed 3 months and 8 months after operation. The size and weight of the kidney increased. This increase results from enlargement of the renal corpuscles. The lumen of Bowman's capsule becomes smaller, while the thickness of its outer wall increases. The diameter of the convoluted tubules and collecting ducts does not increase, but the thickness of their walls does, causing a reduction in the size of the lumen. The cells in the tubular wall become taller. These restorative processes occur as a result of cellular hyperplasia, and the cells are larger than in control animals.

LITERATURE CITED

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* Original Russian pagination. See C. B. Translation.