

ROLE OF A FUNCTIONAL LOAD IN ACTIVATION OF CELLS DURING REGENERATION OF THE MOUSE KIDNEY

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Activation of cells during reparative regeneration of organs may be expressed by an increase in the nucleic acid content of the cells, hypertrophy of the cells, or stimulation of their mitotic activity [1, 4]. The activation of cell division and growth during regeneration is associated with the influence of protein products of tissue breakdown and, probably, with a compensatory increase in the function of the organ [1-4, 8, 9, 10, 14]. In a previous communication it was shown that an activation reaction may arise in conditions which preclude the action of protein products of tissue breakdown. After removal of one paired organ, an increase in mitotic activity, an increase in the content of nucleic acids, and hypertrophy of the cells were observed in the residual intact organ [8].

Similar results have been obtained by other authors studying the phenomenon of compensatory hypertrophy [11-13, 15, 16]. It has been suggested that the action of tissue breakdown products is not the only factor causing activation of cells during regeneration. Another such factor in reparative regeneration may be a change in the functional activity of the organ.

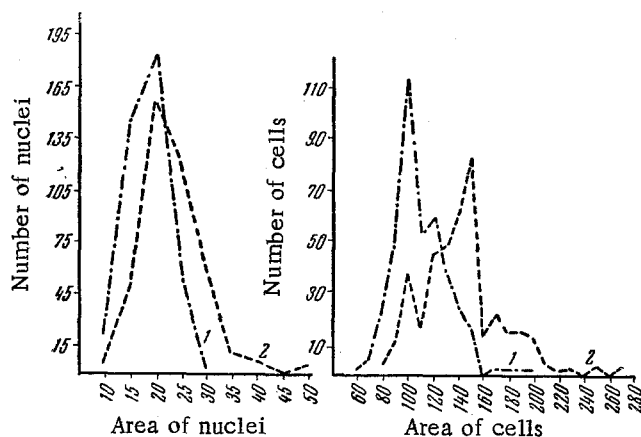


Fig. 1. Variance curves of the dimensions of the cells and their nuclei in the regenerating kidney following one-stage total and partial nephrectomy. 1) Control (regenerating kidney); 2) experiment (regenerating kidney, the second kidney having been removed).

The suggestion that a compensatorily increased function may act as a factor stimulating regeneration has been made before. For instance, I. A. Knorre [5] and G. G. Samsonidze [7], showed that processes arising in the regenerating kidney were considerably intensified if this organ was subjected to a doubled functional load as a result of removal of the opposite kidney. However, these investigations did not yield data concerning the cytological changes taking place in regeneration.

We have studied the activation of cell division and growth in conditions throwing an increased functional load on the organ.

EXPERIMENTAL METHOD

Experiments were conducted on albino mice aged $2\frac{1}{2}$ -3 months. In the first series of experiments one-third of the right kidney of the mice was resected. To produce a functional load, during the 21 days before operation the animals were given urea by mouth, twice a week, in a dose of 50 mg per mouse weighing 15-16 g. In a control group of mice one-third of the right kidney was resected, but the animals were not given urea. The mice were sacrificed 3 and 7 days after the operation. Histological investigation was carried out on both kidneys—the normal(left) and regenerating (right).

In a second series of experiments resection of one-third of the right kidney and total removal of the left kidney were performed in one stage. In a control group of mice only the one-third of the right kidney was resected. The mice were sacrificed 3 days after the operation. In a third series of experiments the left kidney was removed from the mice 8 days before resection of one-third of the right kidney. In a control group only partial resection of the right kidney was performed. The mice were sacrificed 3 days after the resection.

TABLE 1. Changes in Mitotic Activity of the Epithelium of the Kidney After One-Stage Partial Resection and Total Resection of the Opposite Organ

Group of animals	No. of animals	No. of mitoses	Coefficient of phases (K)	Area (in μ^2)	
				Of cells	Of nuclei
Resection of one kidney (control)					
Partially resected kidney	10	13.2	4.1	109.7	18.4
Intact kidney	10	13.9	3.9	123.4	19.25
Partial resection of kidney and total resection of opposite kidney (experiment)	6	42.6	4	141.5	22.9
			P < 0.001	P < 0.001	P < 0.001

TABLE 2. Changes in Mitotic Activity of the Epithelium of the Kidney After Partial Resection of One Kidney Preceded by Total Resection of the Paired Organ

Group of animals	No. of animals	No. of mitoses	Coefficient of phases(K)	Area (in μ^2)	
				Of cells	Of nuclei
Intact mice	5	6.2	1.76	81.2	12.85
Resection of one kidney (control)					
Partially resected kidney	10	11.2	2.2	114.4	17.0
Intact kidney.	10	10.7	2.13	106.6	15.45
Partial resection of kidney and total resection of opposite kidney (experiment)	12	25.5	2.4	159.6	22.1
			P < 0.001	P < 0.001	P < 0.001

The mitotic activity and the dimensions of the cells and nuclei were determined in sections of the kidney. Dividing cells in the epithelium of the main divisions of the nephron were counted. The degree of mitotic activity was judged by the number of dividing cells in a constant area (3.3 mm^2) and by the coefficient of phases. The cross sectional areas of the cells and nuclei were determined by drawing their projections on a screen and subsequent planimetry. Two hundred cells were measured in the investigated organ. Kidneys from two animals were taken from each group of experiments for measurement.

EXPERIMENTAL RESULTS

Information concerning the effect of urea loading on the processes of reparative regeneration of the kidney may be found in the literature [6]. To study the effect of a functional load on the mitotic activity of the cells dur-

ing regeneration of the kidney we repeated the experiments involving administration of urea. The experiments were repeated several times, varying the period of administration of the urea and the time of sacrifice. However, these experiments did not yield definite results. Neither significant changes in mitotic activity nor hypertrophy of the cells and nuclei could be observed.

More demonstrative results were obtained from experiments in which one kidney was totally resected and the other partially resected in one stage. The results of these experiments showed that in the control and experimental mice resection of the kidney caused an increase in the mitotic activity and dimensions of the cells. However, these changes were more marked in the animals left with only one kidney, which carried a greater functional load created by the conditions of compensatory hypertrophy. The number of cells showing mitotic division increased approximately $3-3\frac{1}{2}$ times (Table 1).

Analysis of the variance curves (Fig. 1) reveals a fairly large number of large cells and nuclei and the almost total disappearance of small cells in the animals undergoing one-stage total and partial nephrectomy. The variance curves are sharply displaced to the right. Similar results were obtained in the experiments in which unilateral nephrectomy preceded partial resection of the other kidney. The partial resection of the paired (right) organ took place 8 days after total removal of the left kidney. The results of these experiments also showed that in the animals of the experimental group the mitotic activity rose to twice its level in the kidney of the animals not undergoing removal of the left kidney in addition (Table 2).

Similar changes were observed during measurement of the areas of the cells and nuclei. The variance curves showed a marked shift of the curve of the experimental group to the right (Fig. 2).

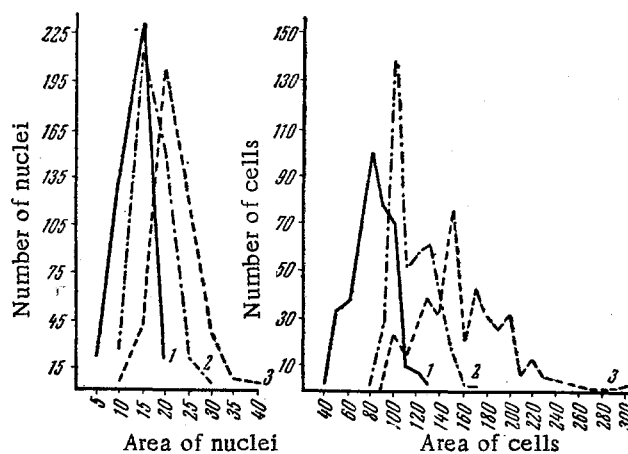


Fig. 2. Variance curves of the dimensions of the cells and their nuclei in the regenerating kidney following preliminary removal of the left kidney. 1) Normal; 2) control (regenerating kidney); 3) experiment (regenerating kidney, the second kidney having been removed at a preliminary operation).

Hence, after preliminary unilateral nephrectomy, activation of cell division and growth in the residual partially resected kidney was more marked than when regeneration took place in the presence of the intact paired organ.

SUMMARY

The effect of increased function, caused by urea loading and nephrectomy, on regeneration of the partially resected kidney was studied. After partial resection of one kidney, the other being intact, administration of urea did not affect mitotic activity. If, in addition, the opposite kidney was removed beforehand or at the same time, mitotic activity and the dimensions of the cells increased in the partially resected kidney to a greater degree than when an intact kidney was present.

The increased mitotic activity of the cells during reparative regeneration of the kidney after nephrectomy is associated with the compensatorily increased function of the organ. An increased functional load is an important factor causing stimulation of regeneration.

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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.