PHYSIOLOGICAL REGENERATION IN RAT KIDNEYS

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In rats weighing rom 113 to 227 g growth of the kidney is accompanied by hypertrophy of the parenchymal cells and not by an increase in the number of nuclei. The presence of dividing cells in the kidneys of these rats is evidence of regenerative processes in the organ.

The ability of the kidney to undergo physiological regeneration has not yet been settled, for many workers consider that mitoses discovered in the kidneys of adult animals are connected with growth, and not renewal, of the organ. Disagreement in the interpretation of results is explained by the fact that not all investigations conducted into this problem have been carried out on animals which grow throughout their life, so that if a low mitotic coefficient is found it is difficult to determine whether the existing mitoses are responsible purely for growth of the organ or, to some extent, for its renewal [2, 4-6]. For these reasons, results indicating that in rats of certain age groups growth of the kidney takes place purely on account of hypertrophy of its cells are interesting [8].

In this investigation we studied the ability of the kidney in rats of particular age groups to undergo physiological regeneration.

EXPERIMENTAL METHOD

Noninbred albino male rats of different age groups, weighing 55, 113, 180, 227, 280, 316, and 361 g respectively, were used in the experiment. The animals were killed by decapitation, ignoring the diurnal periodicity of mitosis, the kidneys were removed and weighed, and the right kidney was chopped up with scissors and homogenized in a Warren's homogenizer with a teflon pestle [8] in 10 ml 0.01N HCl, initially until all pieces of kidney visible to the naked eye had disappeared, and then for a further 2 min. The homogenate was poured into a beaker and further HCl added in the proportion of 10 ml acid per 100 ml weight of kidney. In each case the number of nuclei was counted in 2 Goryaev's chambers, in 5 large squares in each chamber. The mean was calculated and the results determined for the whole volume of homogenate. Very long spindle-shaped and also very small nuclei were not counted. Before the experiment began the time during which the organ had to be homogenized in order to obtain a standard number of nuclei was determined. For this purpose the minced kidney was homogenized in a standard volume of 0.01N HCl until all pieces of kidney visible to the naked eye had disappeared, and then after every 30 sec of homogenization (for 4 min) samples of 0.1 ml were taken and diluted, after which the number of nuclei was counted in 10 large squares of a Goryaev's chamber.

It will be seen from Fig. 1 that 2 min after the beginning of homogenization the number of nuclei remained constant (differences occuring between different points on the graph are not statistically significant). Measurements of this nature were made on 8 animals. Later in the investigation a standard duration of homogenization was used: 2 min after disappearance of pieces of kidney visible to the naked eye. The left kidney was fixed in 12% formalin, paraffin sections 5 μ in thickness were stained with hematoxylin-eosin and by Ross's method, and the mitotic coefficient was determined in promille in the renal cortex. By means of an Abbe drawing apparatus the epithelium lining the lumen of the proximal portions of the convoluted tubules was drawn and its height determined, and cells of the collecting tubules in the cortex were fully drawn and their area determined.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that in each successive age group the mean weight of the kidney was significantly higher than in the preceding group except for group 6 and 7. Together with the increase in

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TABLE 1. Age Changes in Kidneys of Sexually Immature and Mature Rats

Age group	Number of animals	Weight of rat (in g)	Weight of right kidney (in mg) (M ± m)	Number of nuclei in right kidney (millions)	Number of nuclei per mg	Mitotic coefficient (in %)
1-	6	54,8	310±14	161±6,5	519 554	—
2-	6	113,0	520±18	222±8,7	429 076	0,22
3-	5	180,0	748±40	249±10,0	334 197	0,89
4-	5	227,0	870±30	243±7,2	280 322	0,38
5-	5	280,0	1 110±50	321±20,0	289 463	0,29
6-	6	316,0	1 170±50	376±22,0	321 000	—
7-	6	361,0	1 255±30	369±21,0	294 000	—

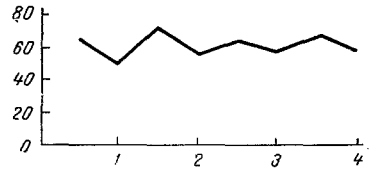

Fig. 1. Changes in number of nuclei in a standard volume of homogenate depending on duration of homogenization. Abscissa, duration of homogenization (in min), ordinate, number of nuclei.

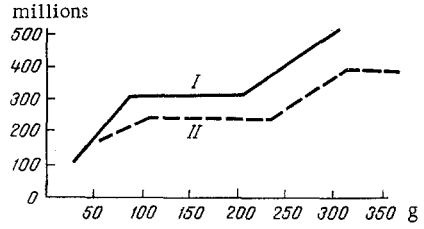

Fig. 2. Total number of nuclei in kidneys of rats of different ages from data in the literature [8] (I) and personal observations (II). Abscissa, weight of rat (in g), ordinate, number of nuclei (millions).

weight of the kidney in group 2, the number of nuclei in the kidney also increased, but later (groups 3 and 4), despite continuing growth of the kidney, the number of its nuclei remained unchanged except in group 5 (the difference between the number of nuclei in groups 5 and 6 is not statistically significant). Calculation of the number of nuclei per milligram kidney tissue shows that the increase in weight of the kidney in groups 2, 3, and 4 was accompanied by a decrease in the number of nuclei, evidence of the occurence of hypertrophy of the cells. Despite the constant number of nuclei in groups 2, 3, and 4, the mitotic coefficient was high (0.22-0.89%).

Repeated experiments are illustrated in Table 2. Just as in the earlier case, the increase in weight of the kidney in all age groups with an increase in weight of the rat was clearly defined, whereas the number of nuclei remained unchanged as the weight of the kidney increased from 620 to 745 mg. The decrease in the number of nuclei per milligram kidney tissue despite the increase in weight was also clearly defined, evidence of hypertrophy of the cell.

In rats of these three age groups no difference could be found in the height of the epithelial cells lining the proximal portions of the convoluted tubules. The area of the cells of the collecting tubules in the kidneys of rats of group 3 was increased compared with those of group 2 (P = 0.01). Mitoses were found in the kidneys of rats of all three age groups.

The results demonstrate that in male noninbred albino rats with body weight between 113 and 227 g the increase in weight of the kidney takes place purely on account of hypertrophy of the cells, confirming other observations [8] of the same phenomenon in kidneys of Sherman rats of both sexes with body weight from 80 to 200 g (Fig. 2). As the authors cited showed, it is connected with manifestation of activity of the sex hormones. In noninbread albino rats sexual maturity corresponds to the time of reaching a body weight of 100-110 g, when the vagina opens [1] and spermatogenesis is established [3]. Correspondingly, even in rats weighing 98 g, having almost reached sexual maturity, a subsequent increase in weight of the kidney is accompanied by a further increase in the number of its nuclei, whereas in sexually mature rats weighing 113 g, the increase in weight of the kidney takes place purely on account of hypertrophy of its cells. The existence of a definite mitotic coefficient in kidneys whose enlargement takes place purely by hypertrophy of the cells may be evidence that renewal of the kidney, rather than growth, is taking place. A study of the diurnal periodicity of mitotic activity in noninbred albino rats weighing 52 and 156 g, carried out jointly with R. I. Bogatova, showed that the mean mitotic coefficient for the 24-hour period in sexually mature male rats is actually higher than in immature animals. Even on the assumption that the mitotic coefficient in rats of these

TABLE 2. Age Changes in Some Indices of the Rat Kidney

Age group	Number of animals	Weight of rat (in g)	Weight of right kidney (in mg) (M ± m)	Number of nuclei in right kidney (millions) (M ± m)	Number of nuclei per mg	Height of epithelium (in μ)	Area of cell (in μ^2)	Mitotic coefficient (in ‰)
1-	10	95.8	476±8	187±3	394 074	9,7	133	0,17
2-	11	135,0	620±20	257±8	410 876	9,4	137	0,29
3-	6	190,0	745±50	251±8	336 918	9,5	149	0,28

age groups is the same [7], it may be supposed that in young, sexually mature rats the processes of renewal of the kidney are more intensive than in immature rats, and this again may partly be attributed to manifestation of activity of sex hormones at this period [8].

LITERATURE CTIED

1. R. I. Bogatova-Nikanorova, in: Proceedings of a Conference of Junior Research Workers of the Institute of Experimental Biology [in Russian], Moscow (1966), p. 21.
2. L. D. Liozner (Editor), Cell Renewal [in Russian], Leningrad (1966).
3. I. Claremont and B. Perey, Am. J. Anat., 100, 241 (1957).
4. J. L. Edwards and R. E. Klein, Am. J. Path., 38, 437 (1961).
5. C. P. Leblond and B. E. Walker, Physiol. Rev., 36, 255 (1956).
6. C. P. Leblond, Nat. Cancer Inst. Monogr., No. 14, 119 (1964).
7. E. Stocker, E. Teubner, and C. Rosenbusch, Verh. Dtsch. Path. Ges., 48, 295 (1964).
8. B. Zumoff and M. Pachter, Am. J. Anat., 114, 479 (1964).