COMPARISON OF THE EFFECTS OF FUNCTIONAL LOADING AND UNILATERAL NEPHRECTOMY ON EARLY POSTNATAL GROWTH OF THE KIDNEY

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UDC 612.65'46-063

The effects of functional loading and unilateral nephrectomy on early postnatal growth of the kidney were compared. Significant differences were found between the cellular mechanisms of adaptation to those two factors. After unilateral nephrectomy differentiation of the nephrons took place more rapidly and was accompanied by reduced proliferative activity of the nephrogenic cells, by contrast with the effects of functional loading. On the other hand, the effects of functional loading and unilateral nephrectomy on differentiated cells of the proximal tubules were similar in character: hyperplasia and hypertrophy. Compensatory hypertrophy of the kidney cannot be regarded as a result of functional loading alone.

No general agreement has yet been reached on the mechanism of compensatory processes. Among the factors bringing about restoration, functional loading has been named by one group of workers [5-7] although others give preference to humoral factors [2, 3].

Since the structural formation of the kidney is mainly complete after the first 2 weeks of postnatal life [1-4], the writers postulated that differences or similarities in the mechanisms of adaptation to functional loading and to unilateral nephrectomy might be reflected in this process.

EXPERIMENTAL METHOD

Experiments were carried out on 40 newborn rats divided into four equal groups. As functional loading, the rats of group 1 received injections of 0.3 ml of "uremic serum," obtained as described previously [4], twice a day for the first 7 days after birth. The animals of group 2 were injected similarly with the serum of intact adult rats (control to group 1). Left-sided nephrectomy was performed on the rats of group 3 on the 2nd day after birth; group 4 consisted of intact control animals. All the experimental rats were killed 7 days after birth, after which their right kidneys were fixed in toto in AAF fluid and embedded in paraffin wax. The total number of glomeruli was counted in sections cut strictly transversely relative to the hilum of the kidney, stained with hematoxylin-eosin; the areas of the nephrogenic zone, the zones of formed nephrons, the medullary and papillary zones, and the cells and nuclei of the proximal tubules were determined, and the nucleo-cytoplasmic ratio was calculated. The mitotic index was counted in 10,000-12,000 cells separately in the nephrogenic zone and in the epithelium of the proximal portion of the nephron and expressed per 1000 cells. Statistical analysis of the data was carried out by the Fisher – Student method.

EXPERIMENTAL RESULTS

Under the influence of functional loading induced by administration of uremic serum, the total area of cross section of the kidney increased on account of enlargement of the zone of formed kidney structures (Table 1). Little change was found in the size of the nephrogenic zone or of the medullary zone with the papilla.

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Laboratory for Biophysical Problems, Department of Histology, Tashkent Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 5, pp. 30-32, May, 1974. Original article submitted June 25, 1973.

TABLE 1. Dimension of Various Zones of the Kidney (M ± m)

Group of animals	Total area of kidney	Area of nephrogenic zone	Area of formed kidney structure	Area of medullary zone + papilla
	Conventional units			
Injection of uremic serum	276,2±5,9	41,7±1,3	145,5±4,9	69,0±3,2
Injection of normal serum	254,1±4,2	40,8±1,3	124,4±3,3	88,9±2,3
Left-sided nephrectomy	317,4±4,7	14,95±0,81	198,2±3,9	104,2±2,1
Control	217,3±2,9	51,1±1,4	96,9±2,5	69,3±0,4

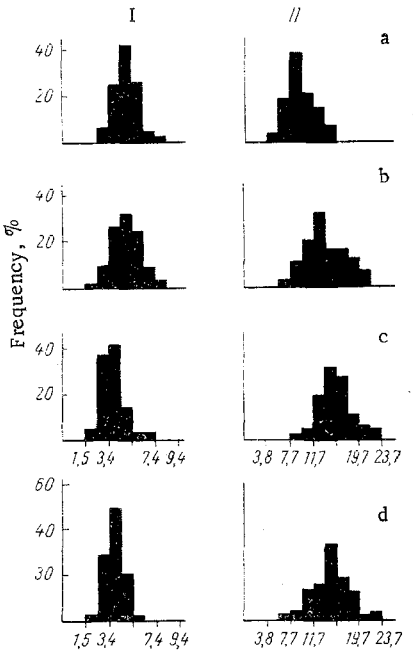

Fig. 1. Histogram of distribution of areas of nuclei and cytoplasm of cells from the proximal tubules of the kidney during functional loading and after unilateral nephrectomy. Abscissa, area of cross section of nuclei and cytoplasm of cells in conventional units; ordinate, frequency of occurrence of nuclei and cytoplasm of cells with particular areas (in %); a) control; b) injection of normal serum; c) injection of uremic serum; d) left-sided nephrectomy. I) Nucleus, II) cytoplasm.

After left-sided nephrectomy the total area of cross section of the kidney increased on account of intensive growth of the zone of formed structures accompanied by a sharp decrease in the area of the nephrogenic (undifferentiated) zone. The area of the medullary zone with the papilla also increased.

Analysis of the changes in area of the various zones of the kidney during functional loading by uremic serum and after left-sided nephrectomy revealed significant differences in the character of the response of the kidney in young rats to these two factors. Functional loading with uremic serum led to an increase in area of the formed structures only, whereas compensatory hypertrophy also was accompanied by a reduction in size of the undifferentiated zone; i.e., it evidently led to the more rapid differentiation of the nephrogenic cells. This hypothesis was confirmed by the results of counting the number of glomeruli per unit area of cross section relative to the hilum of the kidney. Whereas functional loading with uremic serum caused no change in the number of formed glomeruli (nephrons) in the section (99.6 ± 0.61 compared with 98.1 ± 0.63 in the control with normal serum), during compensatory hypertrophy their number was increased by more than one-third (107.8 ± 0.55 compared with 74.6 ± 1.05 in the control).

Changes in mitotic activity taking place in the nephrogenic (undifferentiated) zone under the influence of uremic serum and after unilateral nephrectomy were characteristic. Whereas during compensatory hypertrophy the mitotic index was sharply reduced (1.20 ± 0.10 compared with 6.10 ± 0.02 in the control), during functional loading with uremic serum it was almost unchanged (5.95 ± 0.07 compared with 5.86 ± 0.07 in the control with normal serum).

Both functional loading with uremic serum and unilateral nephrectomy led to hypertrophy of the cells and their cytoplasm in the formed tubules of the proximal portion of the nephron, accompanied by a decrease in size of the nuclei and a considerable reduction in the nucleo-cytoplasmic ratio (Fig. 1). A significant increase in the mitotic index was found in the epithelium of the proximal tubules both during functional loading with uremic serum (5.18 ± 0.03 compared with 4.82 ± 0.07 in the control with normal serum) and after unilateral nephrectomy (6.27 ± 0.27 compared with 3.54 ± 0.05 in the control). It can be concluded from these observations that functional loading with uremic serum and unilateral nephrectomy produced similar effects on differentiated cells of the proximal tubules. This effect consisted essentially of hyperplasia and hypertrophy of the cells with a reduction in the nucleo-cytoplasmic ratio.

It can be concluded from this general assessment of the effect of functional loading with uremic serum and of unilateral nephrectomy on early postnatal development of the kidney that these factors are by no means identical. Unlike functional loading with uremic serum, unilateral nephrectomy had a marked stimulant effect on differentiation of the nephrogenic cells.

Compensatory hypertrophy of the kidney evidently cannot be regarded as the result of functional loading alone.

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