COMPENSATION AND ADAPTATION IN THE KIDNEY AFTER HYDRONEPHROTIC TRANSFORMATION

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There are data in the literature on the stages, the character of the course, and the essential features of the pathological changes arising in the parenchyma of the kidney and its tubular and vascular formations during hydronephrotic transformation (HT) [3, 4, 7, 9]. However, the restoration of morphological and functional relations when disturbed in the kidney after experimental occlusion of the ureter has so far received little study [1, 8, 10, 11, 12].

We used a complex approach to the study of pathological and reparative changes in the kidney after temporary HT, studying them at intervals in the course of an experiment in order to establish the threshold of its reversibility.

EXPERIMENTAL METHOD

Experiments were carried out on 30 noninbred adult albino rats of both sexes. Under pentobarbital anesthesia and with sterile precautions, after a midline laparotomy the left ureter was ligated in its proximal third with a silk ligature on the 1st, 3rd, 7th, 10th, 15th, and 30th days. The ligature was removed after 1-3 days and the ureter was massaged. Recovery of its patency was judged by the decrease in volume of the renal pelvis, by the

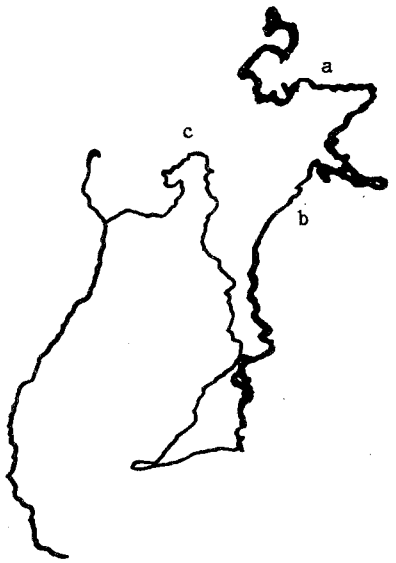

Fig. 1. Superficial nephron of rat kidney on 30th day after recanalization of ureter occluded for 3 days. a) Convoluted part of proximal end of tubule of nephron is not straightened; b) straight part of proximal part of tube of nephron; c) distal part. Stained with osmium and hematoxylin. 16×.

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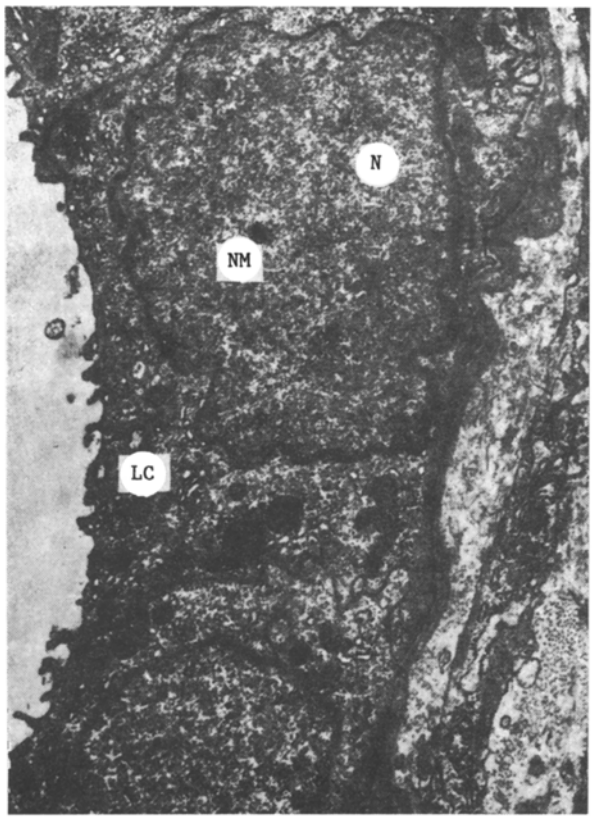

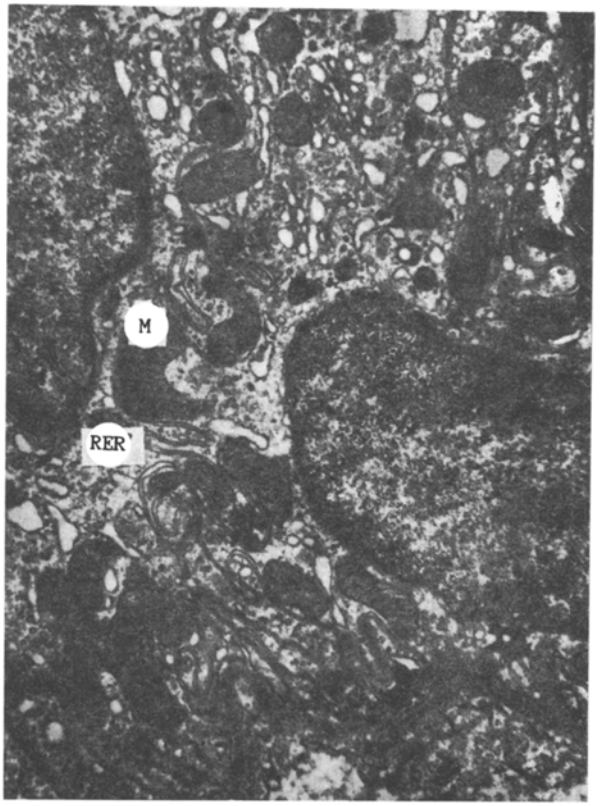

Fig. 2

Fig. 3

Fig. 2. Repair processes in organelles of epitheliocytes of collecting tubule after removal of the cause of HT lasting 10 days. Functional strain on the nucleus (N) with many evaginations of the nuclear membrane (NM), widening of the profiles of the lamellar complex (LC), and an increase in the number of free ribosomes in the cell cytoplasm. 11,000×.

Fig. 3. Signs of hypertrophy and hyperplasia of intracellular structures of distal part of tubule of nephron during recovery period after 7 days of HT. Dilatation of cisterns of rough endoplasmic reticulum (RER), and of lamellar complex (LC), budding of mitochondria (M). 15,000×.

passage of urine, and by the peristaltic movements of the ureter. At the later stages of occlusion as indicated above the ureter was excised at the site of ligature and a polyethylene tube was inserted into both ends of it, and secured by sutures [6]. Material for light- and electron-microscopic investigation was taken on the 30th day after recanalization of the ureter. The method of microdissection [2] was used to determine changes in the length, shape, and spatial arrangement of the nephrons.

Changes in the parameters of the urinary tubules were analyzed by measuring their external diameter, the thickness of their wall, and the diameter of their lumen. Micromorphometry of the renal corpuscles and of their glomeruli was carried out. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Microdissection studies in the recovery period (on the 30th day) after 1 day of HT showed little change in the length and thickness of the isolated nephrons (Fig. 1). In serial sections stained with fuchselin and picrofuchsin, the external diameter of the collecting tubules was reduced (to 35.66 ± 0.65 μ from 43.7 ± 0.30 μ). The area of the epitheliocytes in transverse section was 597.23 ± 23.13 μ^2 compared with 544.75 ± 14.31 μ^2. Later (3 days) the medulla of the macerated kidney was somewhat condensed, and the papilla remained flattened. There was a significant decrease in the external diameter (35.36 ± 0.21 μ compared with 48.97 ± 0.33 μ) and the lumen of the collecting tubules (18.98 ± 0.93 compared with 37.69 ± 0.41 μ) in HT [5]. The epitheliocytes lining them preserved their usual structure, except that a few of them showed signs of hypertrophy and partial destruction.

In the later stages of HT (7-10 days), followed by restoration of the passage of urine, on the 30th day the lumen of individual collecting tubules remained moderately dilated (57.31 ± 1.67 μ compared with 61.36 ± 0.65 μ). The area of the epithelium lining them was increased (699.71 ± 37.13 compared with 615.26 ± 29.33 μ). The epitheliocytes of the tubules at this period were in different morphological and functional states. Besides cells with the characteristic normal ultrastructure, there were also regenerating cells with pale cytoplasm, and with very few mitochondria, with clearly defined cristae and contours of their membranes. The dark cells which had undergone trophy during development of HT remained flattened in the recovery period (on the 30th day). However, their nuclei were enlarged, they occupied the whole of the cytoplasm, and their outlines were uneven, with numerous invaginations and evaginations. The nucleoli were distinctly outlined. The rough endoplasmic reticulum was condensed and consisted of a large number of small vesicles and tubules, with a fair number of ribosomes on their membranes. The lamellar complex was well developed. The mitochondria were oval and spherical in shape and small in size. Single primary lysosomes were seen. Microvilli on the apical surface were more numerous (Fig. 2).

On restoration of the passage of urine in the later stages of HT (15-30 days) the collecting tubules in most histological preparations still had a dilated lumen (43.31 ± 1.18 μ), containing accumulations of albuminous masses. The date of the epitheliocytes varied. Some were totally destroyed, others had pycnotic nuclei and pale cytoplasm, rich in vacuoles, and swollen mitochondria, and contained numerous lysosomes and albuminous droplets. Only solitary cells were close to normal in appearance. On the 30th day after HT lasting 1-3 days, most epitheliocytes in the distal part of the tubules of the nephrons and the thin part of the loop preserved their normal ultrastructure.

In the recovery period (on the 30th day) after 7-10 days of HT, depending on the state of the epitheliocytes of the distal part of the tubules of the nephron, four different groups of them can be distinguished. In the first and largest group, cells were close were to their original appearance. In the second group the nuclei were irregular in shape, with invaginations and evaginations of the nuclear membrane. Chromatin granules occupied a marginal situation in the nucleoplasm. Cisterns of the endoplasmic reticulum were dilated and there were a few granules on their membranes. The lamellar complex consisted of a few large vesicles. The mitochondria were swollen with a translucent matrix and reduced cristae. In the third group of epithelocytes disintegration of the intracellular structures was observed, whereas in the fourth group there were signs of intracellular hypertrophy, in the form of enlargement of the nuclei, and an increase in the number and volume of cisterns of the endoplasmic reticulum. The lamellar complex was hypertrophied and the number and size of the mitochondria increased (Fig. 3). In the reovery period after 15-30 days of occlusion of the ureter, most epitheliocytes showed signs of hydropic degeneration, with colliquative necrosis in places.

In the proximal part of the tubules of the nephrons in the recovery period after HT for 1-3 days most of the epitheliocytes were unchanged, In some cells signs of hyperplasia and hypertrophy of the intracellular structures predominated. On the 30th day after removal of the ligature from the ureter, after occlusion lasting 30 days, in the overwhelming majority of cells with a brush border evidence of karyopycnosis and disintegration of the organelles were observed, with the appearance of autophagolysosomes and albuminous droplets in the cytoplasm.

After 1-3 days of HT most glomeruli of the renal corpuscles showed little change. On restoration of the passage of urine after the late stages (15-30 days) of HT they remained deformed. The capillaries in them had collapsed. Marked proliferation of interstitial connective tissue was observed in the cortex. The components of the filtration-reabsorption barrier showed atrophic changes.

The experimental results showed that after 1-3 days of HT, followed by recanalization of the ureter (30th day), the tubular and vascular formations of the kidney had not undergone any appreciable morphological changes. After longer occlusion of the ureter (more than 15 days) marked destructive changes predominated in the kidney, and were accompanied by replacement of the parenchymatous structures by connective tissue.

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AUTORADIOGRAPHIC STUDY OF HUMAN EPIDERMOCYTES CULTURED IN A LOW CALCIUM MEDIUM

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Since the 1950s biologists and clinicians have displayed increased interest in the development of transplantation of tissues, especially the skin. It was Medawar who first showed that the epithelial cells of human skin can be cultured. However, growth of a large mass of epithelial cells, which would be necessary, for example, to cover burned areas, still presents great difficulties. These difficulties can be explained by the fact that, despite the evident therapeutic importance of transplantations of cultured epidermis, world wide there are only a few clinics in which this method of treatment of burns is used [3, 9]. The basic difficulty is that 4-5 days after seeding, epidermocytes grow more slowly and undergo differentiation. To intensify multiplication of epidermocytes, several stimulators and methods of culture have been suggested [4, 5, 7, 8], but none of them has solved the problem to a significant degree. The search for stimulators of cell division and inhibitors of differentiation therefore continues. Research by Hennings and co-workers [6] has shown that reducing the calcium ion concentration in the nutrient medium to 0.04-0.05 mM stimulates division of epidermocytes obtained from the skin of newborn mice. In the present experiments with epidermocytes isolated from adult human skin multiplication of the cells in medium with a higher calcium concentration was stimulated. The results of these experiments are described below.

EXPERIMENTAL METHOD

Small pieces of skin pinch grafts obtained during autologous skin grafting operations on burned patients were used as material. The pieces were treated with 0.25% trypsin solu-

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