SUBMICROSCOPIC CHANGES IN CELLS OF THE RENAL TUBULES DUE TO HYPERTHERMIA

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After exposure of rats to hyperthermia at 42° for 3 h, reactive and destructive changes in the ultrastructures, especially the mitochondria, develop in the cells of the nephron. The mitochondria swell and increase in volume, while the electron density of the matrix is reduced and folding of the outer limiting membrane appears. The swollen mitochondria undergo partial or complete lipid degeneration. Local destructive processes, isolated by the membrane, develop in the cytoplasm of the nephron cells.

Under hyperthermic conditions, the kidneys play an important role in regulating the water and salt balance of the organism [5,8]. Changes in kidney function during hypothermia take the form of a reduction in diuresis, the intensive elimination of potassium and calcium from the body, and changes in the rate of filtration of inorganic salts by the tubules of the nephron [5,7]. Conflicting data have been obtained for the morphology of the kidney under the influence of hyperthermia. Some workers [12,14] consider that as well as vascular disturbances (hyperemia, stasis, hemorrhages), necrotic lesions develop in all parts of the nephron. Others [11,15,16] have described the development of destructive changes only in the cells of the distal portion of the nephron – "distal nephron nephrosis."

There is no information in the literature on submicroscopic changes in the kidney cells during hyperthermia.

In this investigation, ultrastructural changes were studied in the cells of the proximal and distal portions of the nephron in animals exposed to hyperthermia.

EXPERIMENTAL METHOD

The investigation was carried out on adult male albino rats weighing 200-210 g, using the method adopted in the author's laboratory. The rats were heated to 42° for 3 h in a special chamber. The rectal temperature of the intact rats varied between 34.8 and 36.3°, and after the end of the experiment between 39 and 41°.

Pieces of kidney tissue from the control and experimental animals were fixed in 1% osmium tetroxide by Caulfield's method, and embedded in Vestopal and Epon. Ultrathin sections were cut on the UMTP-1 and LKB ultramicrotomes, and contrasted with lead citrate by Reynolds' method. Electron micrographs were obtained in the UÉMV-100 electron microscope at a voltage of 75 kV.

EXPERIMENTAL RESULTS

According to personal data and those of other workers [1,10,17,19], the proximal portion of the nephron consists of a single layer of prismatic cells characterized by a brush border on their apical surface. This border consists of a system of microvilli of distinctive structure, providing a considerably increased absorbing surface of the cell. The microvilli lie 0.01 μ apart and the spaces between them are filled with homogeneous, electron-dense intercellular substance. Numerous spherical vacuoles are present in the apical part of the cells, surrounded by a single-layered smooth membrane. The cytoplasmic membrane at the base of the cell forms folds penetrating deeply into its body, between which lie mitochondria of various sizes (from 0.9 to 2.5 μ) and shapes, creating a characteristic picture of basal striation in the optical microscope (Fig. 1). Numerous mitochondria are also present in the perinuclear zone. The matrix of the mitochondria is of average electron density, and the crystae are oriented both parallel and perpendicular

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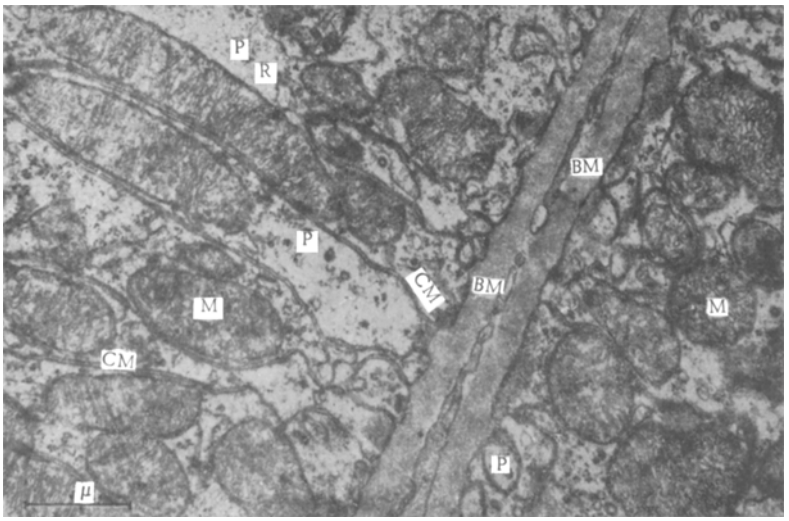

Fig. 1. Basal part of cells of proximal portion of nephron from the kidney of an intact rat. Mitochondria (M), ribosomes (R), polysomes (P), cytoplasmic membrane (CM), basement membrane (BM). Epon, 21,000 times.

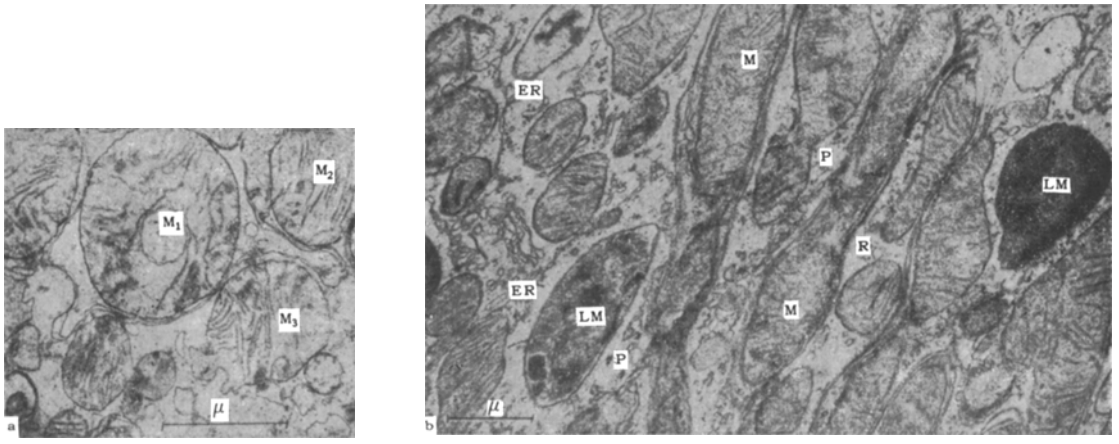

Fig. 2. Reactive and destructive changes in mitochondria in cells of the proximal (a) and distal (b) tubules of the nephron of a rat after exposure to hyperthermia at 42°. Annular (M_1) and swollen (M_2) mitochondria, folds of outer membrane of mitochondria (M_3), and lipid degeneration of mitochondria (LM). Endoplasmic reticulum (ER), ribosome (R), polysomes (P). Vestopal, 29,000 × (a) and 21,000 × (b).

to the long axis of the mitochondria. The Golgi apparatus lies mainly in the perinuclear region and consists of a system of paired membranes, forming a few tubules and also vacuoles of different sizes. The endoplasmic reticulum is feebly developed and consists of a few tubules and vesicles bounded by smooth membranes. Only in places are ribonucleoprotein granules (ribosomes) carried by the outer membrane of individual cisterns. Free ribosomes and polysomes are scattered in the cytoplasm of the cells. The nucleus with its finely granular karyoplasm lies in the basal part of the cell.

The ultrastructural organization of the cells in the distal portion of the nephron differs in some respect from the structure of cells of the proximal tubule. The apical surface of the cells of the distal portion likewise carries microvilli, but they are few in number, shorter and wider, and they lie 0.3-0.4 μ apart. The cytoplasmic membrane of the basal part of the cell forms very deep invaginations, as a result of which each mitochondrion apparently lies in the hollow between its folds. The cells of the distal tubule are rich in mitochondria which are greatly elongated, sometimes up to 5 μ in length. The nucleus is of the ordinary structure and lies in the central part of the cell.

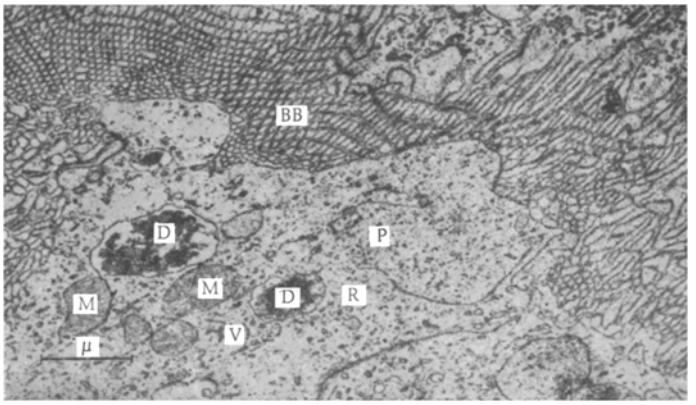

Fig. 3. Changes in a cell of the proximal tubule of a nephron produced by hyperthermia in a rat. Areas of degenerated cytoplasm (D) can be seen at the base of the brush border (BB). Vacuoles (V), polysomes (P), ribosomes (R), Vestopal, 21,000 ×.

Immediately after exposure of the rat to hyperthermia for 3 h at 42°, reactive and destructive changes in the cell ultrastructures were observed in the proximal and distal portions of the nephron. The latter were more marked in the mitochondria. Changes in some mitochondria also took the form of swelling and a decrease in the electron density of the matrix, some of them becoming annular in shape. The inner membranes in such mitochondria usually retained their normal structure, but were more loosely arranged. The outer membrane of some mitochondria formed folds or lobular invaginations, and in places its outlines were indistinct (Fig. 2a). The changes described in the ultrastructure of the mitochondria were reversible and reactive in character. Not all mitochondria of the cells from the proximal and distal portions of the nephron, it will be noted, reacted equally to external hyperthermia, but a considerable proportion of them retained their normal structure (Fig. 2b).

Besides reactive changes, destructive changes were also observed in the internal structure of the mitochondria, varying in their severity. In some mitochondria the cristae lost their regular arrangement and lay haphazardly, some of them being destroyed. In other mitochondria all cristae disappeared, the matrix became clear, and they had the appearance of pale vacuoles. Some mitochondria underwent partial or complete lipid degeneration (Fig. 2 b). In some mitochondria areas of degeneration could be seen, while other areas retained their normal structure. In others the matrix became coarse and uneven, with foci of rarefaction and condensation in the form of large osmiophilic granules. Completely degenerated mitochondria had the appearance of massive homogeneous and strongly osmiophilic bodies.

Similar reactive and destructive changes in the mitochondria have been found in the kidneys, central nervous system, and other organs after exposure to various external agents such as x rays, external heating, anoxia, and so on [2-4,18]. The changes observed in the structure of the mitochondria probably lead to a disturbance of the permeability of their membranes, of the transport of ions, and oxidative phosphorylation, and to the de-integration of many intracellular processes, [6].

After hyperthermia, submicroscopic changes were also found in a number of other structures of the cells in the proximal and distal parts of the nephron. Under normal conditions the gap between the folds of invaginating cytoplasmic membranes (extracellular spaces) is very narrow and has the appearance of thin tubules about 0.02 μ in diameter. In the experiments with hyperthermia, the extracellular spaces were greatly widened to attain a diameter of 0.1 μ, probably due to intensive reabsorption of water by the nephron tubules [9] and reflecting an increased functional load on the kidneys under hyperthermic conditions.

In addition, local degenerative processes developed in the apical, perinuclear, and basal parts of the cells of the proximal and distal tubules of the nephron. In some parts of the cells, fragmentation of the membranes of the endoplasmic reticulum and partial loss of ribosomes were observed (Fig. 2b). In more severe cases, the developing foci of destruction, including degenerated mitochondria, fragments of membranes of the endoplasmic reticulum, and other breakdown products, were separated from the remaining areas of the cytoplasm by a membrane. On electron micrograms these local foci of degeneration appeared as finely granular disintegration of the ultrastructures or as denser osmiophilic bodies (Fig. 3). The

development of local foci of destruction has been described in cells of the nephron tubules following partial ligation of the renal vein, and also in other organs exposed to various procedures. Usually high activity of acid phosphatase and of other hydrolytic enzymes is observed in these foci [13].

Changes affecting the nucleus were found in some cells. The nuclear membrane became irregular and in some places formed deep invagination. Chromatin was condensed mainly near the nuclear membrane, the nucleoplasm was clear, and the nucleus appeared optically empty.

Hence, after exposure of rats to hyperthermia at 42° for 3 h, reactive and destructive changes of nonspecific character developed in the cells of the proximal and distal portions of the nephron. The results thus obtained agree with those described by other workers [12,15] who observed lesions affecting cells of the nephron under the optical microscope, but they do not agree with the observations of those investigators [11,15,16] who described optical changes in hyperthermia only in the cells of the distal portion of the nephron.

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