CHANGES IN INTERNAL SECRETORY STRUCTURES OF THE KIDNEYS AND HETEROGENEITY OF THE MEDULLA IN RATS WITH ACUTE WATER AND SALT LOADING

B. N. Tsibel', A. Ya. Terner, L. Yu. Raevskaya, and L. S. Vasil'eva

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The concentrating power of the renal medulla is based on its functional heterogeneity, which has its morphological equivalents. The structural features distinguishing the parts of the nephron in different zones of the medulla are well known. Differences also have been noted in relations between fragments of the nephron and blood vessels in the outer and inner medulla, as well as zonal differences in structure of the medullary interstices [9, 11]. Differences in the structure and distribution of the renomedullary interstitial cells (IC), which play an important role in the concentrating function of the medulla and regulation of the blood pressure, have received less study [1, 2, 10, 13]. Some workers are of the opinion that the functional state of IC and synthesis of renal prostaglandins (PG) are linked with the lipid granule content of IC [3, 6, 15]. It has been shown that the number of lipid granules (LG) in IC in rats is determined by their distribution in the papilla, and that it can change depending on certain conditions and, in particular, on the presence of spontaneous genetic hypertension [4].

Considering the role of PG in transepithelial sodium transport in the papilla [10] and regulation of the renal blood flow [12], acute water and salt loading, which modulate PG synthesis [4], can serve as a model with which to study responses of IC and the distribution of LG in them. In view of the connection noted in the literature between PG synthesis and renin release [7, 8], the simultaneous investigation of IC and of the juxtamedullary apparatus (JMA) of the kidneys, appears to be interesting.

The aim of this Investigation was to study the structure and lipid granule content of IC in different zones of the medulla and the state of the JGA of the rat kidney during acute water and salt loading.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 150-180 g were used. Tap water and 0.9% and 2% sodium chloride solutions, in a quantity equivalent to 5-7% of body weight, was injected in to the animals' stomach through a tube. The animals were killed 1 and 2 h after injection of the fluids. In each series of the experiment and control group 10 animals were used. Osmolarity and sodium concentration, as well as plasma renin activity (PRA), were determined in the rats' blood plasma by radioimmunoassay. The juxtaglomerular index (JGI) was determined by a silver impregnation method [5] and the interstitial-cell index (ICI) in IC, namely the number of lipid drops (LG) in IC, calculated per cell, were determined by light-optical methods in sections through the kidneys IC were studied separately in the following zones of the medulla: outer medulla, center of the inner medulla, apex, and lateral zones (periphery of the papilla). The principle of the histotopographic investigation of IC in the rat medulla was described in more detail previously [4]. For electron-microscopic investigation, pieces were excised from these same parts of the medulla, fixed successively in solutions of glutaraldehyde and osmic acid, and embedded in Araldite. The sections were stained with uranyl acetate and lead citrate and examined in the 100-LM electron microscope.

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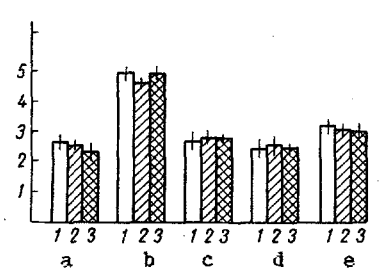

Fig. 1

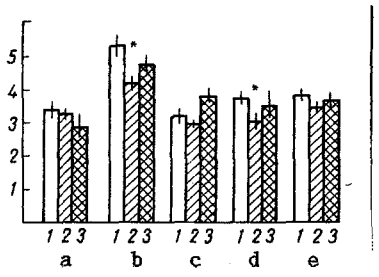

Fig. 2

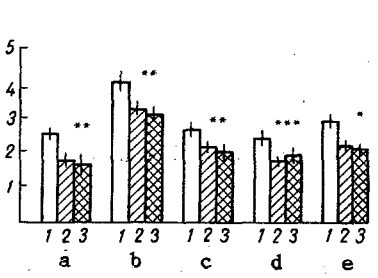

Fig. 3

Fig. 1. Index of lipid granule content of renomedullary cells (ICI) after water loading. Here and in Figs. 2 and 3: a) base of papilla, b) center; c) periphery, d) apex, e) renal papilla as a whole. 1) ICI in control; 2) ICI 1 month after loading; 3) ICI 2 h after loading.

Fig. 2. Index of lipid granule content of renomedullary cells (ICI) after loading with 0.9% sodium chloride solution, $*p < 0.02$.

Fig. 3. Index of lipid granule content of renomedullary cells after loading with 2% sodium chloride solution. $*p < 0.001$, $**p < 0.01$, $***p < 0.05$.

EXPERIMENTAL RESULTS

One hour after water loading the osmolarity of the plasma fell to 277 ± 1.7 milliosmoles/liter and the plasma sodium level fell 131 ± 0.61 mmoles/liter, with a return to the control values after 2 h, PRA showed a tendency to rise (to 12.29 ± 2.35 mg/ml · h, compared with 7.79 ± 1.28 mg/ml · h in the control in this series; JGI fell to 59 ± 5.4 after 1 h, compared with 70 ± 5 in the control. Granules in cells of JGA were small, with indistinct, melting contours. IC differed in their structure of IC of the control group only by dilatation of the cisterns of the reticulum in some of the cells. Just as in the control, the larger number of LG was discovered in IC in the center of the internal medulla, and there were fewer of them in all the remaining zones (Fig. 1; Fig. 4a and b).

In the case of loading with 0.9% sodium chloride solution the osmolarity of the plasma and the sodium level were unchanged, whereas there was a significant increase in JGR (129 ± 10 after 1 h and 108 ± 13 after 2 h, 73 ± 4.7 in the control), which corresponded to reduction of PRA (2.74 ± 0.5 mg/ml · h after 1 h, 1.97 ± 0.5 mg/ml · h after 2 h, 7.1 ± 0.6 mg/ml · h in the control). For the papilla as a whole a tendency was noted for ICI to fall (reduction of the number of LG in IC); this decrease was more marked 1 h after loading and in the center of the papilla (4.25 ± 0.16, 5.41 ± 0.36 in the control), whereas in the peripheral zones and apex of the papilla sometimes an increase in the number of LG was observed (Fig. 2, Fig. 4c).

Electron-microscopy revealed changes of dystrophic and necrobiotic character in some renomedullary cells, whereas in others there was an increase in the quantity of euchromatin in the nuclei and widening of the reticulum (Fig. 4d). After loading with 2% sodium chloride solution osmolarity was increased (304 ± 2.3, 307 ± 2.1 milliosmoles/liter) and the plasma sodium level rose. JGI was increased at both times of observation (98 ± 1.7 and 101 ± 1.6, 64 ± 3.6 in the control). PRA fell until 2 h after loading (3.72 ± 0.31 mg/ml · h, whereas in the control in this series it was 4.87 ± 0.45 mg/ml · h). ICI was significantly reduced in all zones of the medulla (Fig. 3). On electron microscopy LG of increased density were found in IC. Degenerative and necrobiotic changes in the cells with swelling of the mitochondria, widening of the reticulum, pycnosis of the nuclei, and ruptures of the cytolemma were more marked 2 h after loading, but in other IC an increase in the euchromatin content and widening of the cisterns of the Golgi complex also were noted.

Thus changes in JGA were found to correspond to changes in PRA and were connected with the character of loading. In the case of water loading, reduction of plasma osmolarity was accompanied by a decrease in JGI and changes in the granules of the epithelioid cells, whereas in the case of loading with 2% sodium chloride solution, and an increase in plasma osmolarity, the changes were opposite in character. On loading with 0.9% sodium chloride the osmolarity of the plasma was unchanged, but JGI nevertheless was significantly increased, with a corresponding decrease in PRA. This may perhaps have been connected with

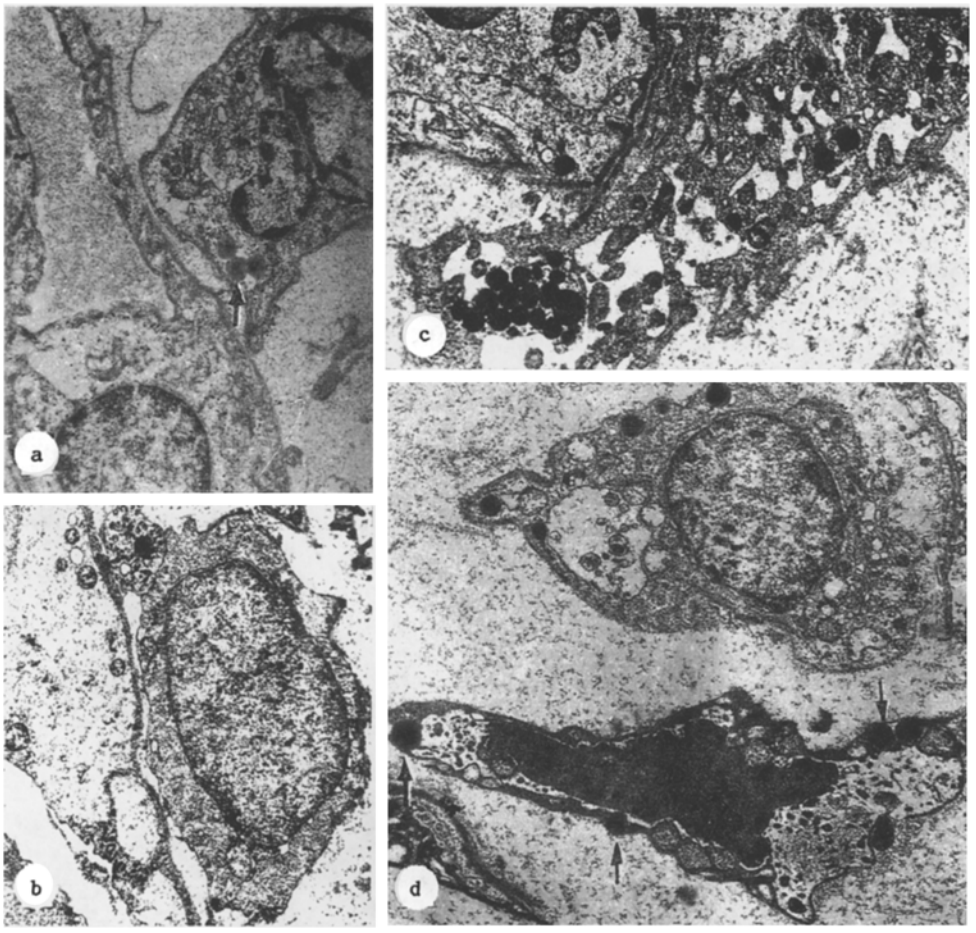

Fig. 4. Some structural features of renomedullary cells (IC) in different zones of papilla and changes in structure after salt loading. a) IC in center of papilla (control). LG of average density (arrow), cell nucleus segmented, well marked heterochromatin; b) IC in apex of papilla. Euchromatin predominates in nucleus of IC, no LG visible in cell. In adjacent process of another IC, dense LG can be seen (arrow); c) concentration of LG in process of IC in apex of papilla after loading with physiological saline; d) IC in center of papilla after loading with physiological saline: on right — pycnotic nucleus in IC, coagulation of cytoplasmic structures, LG around periphery of cell (arrow); on left — dilated cisterns of endoplasmic reticulum in IC, LG at periphery of cell.

an increase in the sodium intake and an increase in plasma volume. The morphological and functional changes in the renin-angiotensin system described above were aimed at preserving water and electrolyte homeostasis and were less marked in the case of water loading. Changes in IC also were least marked with water loading, and with salt solution loading a decrease in the lipid granule content was found, chiefly in the center of the papilla, where the IC contained the largest number of LG, and with an increase in plasma osmolarity the number of LG decreased in the remaining zones of the papilla. If we accept the view that the lipid granule content of IC corresponds to storage of PG precursors [2, 3, 6], the decrease in the number of LG in IC accompanying an increase in the sodium chloride content might be connected with increased synthesis of PG, for many of the medullary PG possess a natriuretic action, In this case, the decrease in the quantity of PG precursors found in LG and, specifically, in the central zone of the papilla, where vessels and loops of juxtamedullary nephrons are present, with which IC are in contact, becomes explicable. However, a more complex process evidently takes place and it is essential to take into account changes in osmolarity of the medullary interstices, with which a tendency toward redistribution of LG in the zones of the papilla and dystrophy and necrobiosis of some IC, as well as correlation between PG synthesis and angiotensin II formation, are perhaps connected. Significant correlation was not found in the series of experiments described above between the morphometric parameters of IC and JGA studied.

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CHANGES IN PHAGOCYTIC ACTIVITY IN COMPLICATED EXPERIMENTAL WOUNDS

V. V. Zakharov, A. V. Nikolaev, Ch. R. Ragimov, L. A. Mamedov, A. P. Khokhlov, A. B. Shekhter, N. D. Egorova, and V. A. Sitarov

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An increase in the number of postoperative septic complications, which cannot always be prevented, and difficulties in their treatment are among the urgent problems of modern surgery [2, 7]. The mechanism of formation of a suppurative inflammatory process in postoperative wounds is mainly dependent on a disturbance of phagocytosis [6]. Phagocytic cells, on contact with foreign bodies or microorganisms, actively take up oxygen and generate superoxide anion-radicals ($O_2^{\cdot-}$), from which are formed hydroxyl radicals ($^{\cdot}OH$). which possess high bactericidal and also destructive actions, initiating lipid peroxidation (LPO) [10, 13, 14]. Protection against excessive intensification of LPO is effected both by the antioxidative system of the tissues and by phagocytic cells, which secrete antioxidants, especially ascorbic acid, into the intercellular space [17]. The latter substance can eliminate free radicals in accordance with the following scheme: ascorbic acid + $2O_2^{\cdot-}$ + $3H_2$ → dehydroascorbate + $2H_2O_2$, converting toxic oxygen radicals into less toxic. Ascorbic acid also protects glutathione and protein SH-groups against oxidation and is thus an additional factor in antioxidative protection [15, 19].

Hence the interest of the study of the role of ascorbic acid and LPO products on phagocytic activity in the formation of the septic focus.

I. M. Sechenov First Moscow Medical Institute.

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