INTERTUBULAR CELLS AND THEIR RELATIONSHIP TO THE RENAL CAMBIUM

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Intertubular cells (ITCs) of the human renal cortex (from fetuses, newborn infants, children aged 1-5 years, adults aged 40-70 years) were studied. In the developing kidneys (fetal, neonatal) ITCs account for between 21.4 and 12.6% of the total number of epithelial cells of the convoluted tubules, whereas in children after the age of 1 year and in adults they account for only 7.6%. As a result of the action of a nephrotoxic poison (ethylene glycol) and of severe hypoxia on the kidneys the ITCs are activated, they start to divide, and they account for 14.5% of the total number of epithelial cells of the convoluted tubules. The view is expressed that ITCs constitute a distinctive cambium of the renal tubules, formed by conversion of some cells of the metanephrogenic cord into a resting state.

KEY WORDS: intertubular cells; renal cambium.

Recent investigation have shown that the function of the nephron is closely linked with cells of the interstices of the kidneys [4, 10, 11, 13]. Information on the intertices of the renal cortex is extremely scanty and indefinite. Evidence has been obtained that remnants of the metanephrogenic tissue [1, 9], relatively undifferentiated mesenchymal elements [15], or "polypotent intertubular cells" [2] are present in the renal cortex. However, no detailed description has been given of the interstitial cells of the cortex. There is likewise no information in the literature on the role of these cells under normal and pathological conditions, although it is unlikely that the intestices of the renal cortex are limited to a supporting and trophic function.

In the course of a study of the pathomorphology of the kidneys in ethylene glycol poisoning [3] attention was directed to the cortical cells, whose localization, shape, and staining properties distinguish them from ordinary stromal cells.

EXPERIMENTAL METHOD

To study the properties of the intertubular cells (ITCs) human kidneys were used at the following periods: from fetuses at the 28th-32nd week of pregnancy – 10 cases; kidneys from full-term newborn infants dying from birth trauma – 6 cases; kidneys from children aged up to 5 years dying from acute respiratory diseases – 8 cases; kidneys from adults (aged 30-70 years) dying from acute coronary insufficiency – 10 cases. Besides these "intact" kidneys, kidneys also were used from persons dying from ethylene glycol poisoning (10 cases) and from uncompensated blood loss (6 cases). Pieces of kidneys were fixed in neutral formalin and in Carnoy's fluid and embedded in paraffin wax. Sections, 5-7 μ in thickness, were stained with hematoxylin–eosin, picrofuchsin, and Schiff's reagent, the argyrophilic fibers were impregnated by Gomori's method, and nucleoproteins were detected by Brachet's and Feulgen's reactions, lipids with Sudan III, and succinate dehydrogenase (SD) activity was determined in frozen sections by Nachlas' method. The ITCs were counted by counting 500 nuclei of the epithelium of the convoluted tubules and their ITCs and expressing the latter as a percentage of the whole. The numerical results were subjected to statistical analysis.

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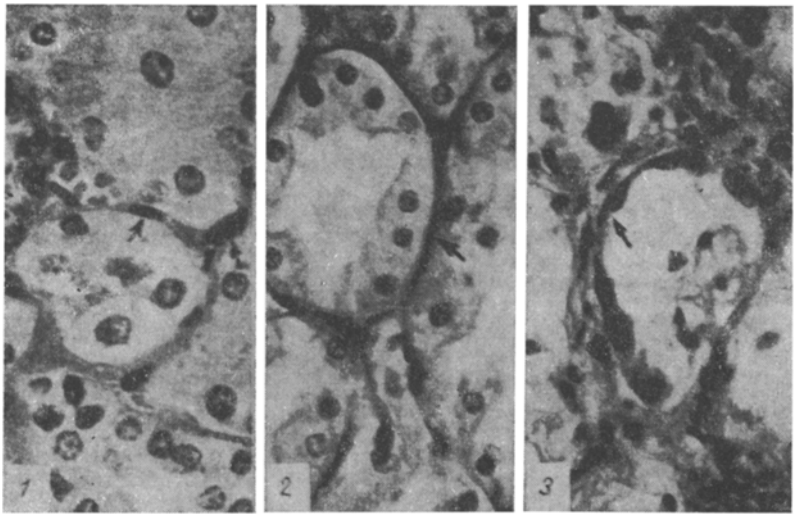

Fig. 1. Swelling of nuclei of ITCs in uncompensated blood loss (2nd day). Hematoxylin–eosin, 400x.

Fig. 2. Arrangement of ITCs in pairs (2nd day after poisoning with ethylene glycol). Hematoxylin–eosin 200x.

Fig. 3. Cells of ITC type in lumen of convoluted tubule (13th day after ethylene glycol poisoning). Hematoxylin–eosin, 200x.

EXPERIMENTAL RESULTS

Remnants of the metanephrogenic cord were detected in the subcapsular zone of the fetal kidneys. Cells of this cord also were found in comparatively wide intertubular spaces and they had flattened hyperchromic nuclei and a narrow border of basophilic cytoplasm. The content of nucleoproteins in the cells varied, and no SD or lipids were detected. Flattened cells (of the metanephrogenic type) also were found inside the tubules, among cubical cells. The basement membranes of the tubules consisted of fragments of very thin argyrophilic fibers, and sometimes the membranes themselves could not be revealed by the PAS reaction. Because of the discontinuity of structure of the basement membrane, cells of the metanephrogenic cord could penetrate inside the tubule. Some of the convoluted tubules had distinctly formed basement membranes, readily detectable by the PAS reaction. These tubules were closely packed together and no flattened cells could be seen inside them. However, cells with greatly flattened hyperchromic nuclei and very little cytoplasm were constantly found between the tubules. Often the cytoplasm of the ITCs could not be revealed by ordinary staining methods and, for that reason, the cells appeared to be immured in the ground substance of the basement membranes of the convoluted tubules. The ITCs had a tendency to lie in pairs or in chains. In fetal kidneys they accounted for 21.4 ± 2.0% of the total number of epithelial cells of the convoluted tubules ($P = 0.05$).

In the neonatal kidneys the metanephrogenic cord was absent in the subcapsular zone and definitive convoluted tubules and glomeruli lay next to the capsule. In this zone groups of cells similar to cells of the metanephrogenic band were found. Nearly all the convoluted tubules were closely packed together; their basement membranes consisted of comparatively thin argyrophilic fibers. The membranes were detectable over the whole length of the tubules by the PAS reaction, but they varied in thickness. Flattened and "immured" ITCs were seen in all fields of vision (magnification 200x), but not in every tubule. These cells occurred both singly or as discrete clusters. In the neonatal kidneys ITCs accounted for 12.6 ± 1.0% of the total number of cells of the convoluted tubules ($P = 0.05$).

The kidneys of children aged 1-5 years had a subcapsular zone free from glomeruli, and all the convoluted tubules were closely packed together. The basement membranes were well impregnated with silver and they showed up with the PAS reaction. ITCs were not visible in all fields of vision and they occurred singly and in groups of two or three cells. Often the nuclei of the ITCs lay with one pole next to the capillary wall. The ITCs accounted for 7.6 ± 1.6% of the number of epithelial cells of the convoluted tubules ($P = 0.05$). In adult human kidneys ITCs occurred singly or two or three at a time. In some fields of vision no ITCs were present. As a rule, ITCs were either immured in the ground substance of the basement mem-

branes or they lay against the capillary wall. The long axis of the flattened nucleus of such cells was perpendicular to the capillary wall, a characteristic feature of pericytes [6], but no pericytes have been described in the renal capillaries [14, 17]. Neither SD nor lipids were detected in the cytoplasm of the ITCs. In the adult human kidneys ITCs accounted for 7.6 ± 0.8% of the total number of epithelial cells of the convoluted tubules ($P = 0.05$).

The response of the ITCs to exposure of the kidney to nephrotoxic poison (ethylene glycol) and to severe hypoxia (uncompensated blood loss) was characteristic. After the first few days the nuclei of the ITCs swelled (Fig. 1), their DNA content increased, and often a central constriction appeared around the nuclei. ITCs began to be found in every tubule, often as chains of two or three cells (Fig. 2). The number of ITCs increased and they accounted for 14.5 ± 1.5% of the total number of epithelial cells of the convoluted tubules ($P = 0.05$).

In the later stages after exposure to the harmful factor (7th-13th days) flattened cells with hyperchromic and pale nuclei, resembling swollen ITCs, began to be found in the lumen of the convoluted tubules (Fig. 3). No basement membranes could be seen under these cells and weak SD activity was detected only in a few cells.

The results of these investigations, together with those of investigation of the kinetics of cell populations of the developing kidney [7], justify definite conclusions regarding the nature of the ITCs. The formation of this unique "proliferative reserve" during embryogenesis of the kidneys [7] can be regarded as the switching of some cells of the metanephrogenic cord into a resing state (the R-period), in which the cells may remain for an indefinitely long time [5, 16]. The cells come out of the resting state in response to the action of certain stimuli [8]. The morphological properties of the ITCs correspond to those that are characteristic of nonfunctioning cells in the R-period [12]. Activation of ITCs in hypoxia and during the action of a nephrotoxic poison on the kidneys indicates that these cells bear a certain relationship to compensatory and adaptive reactions that come into effect if the tubular epithelium is injured. From this standpoint the ITCs can be regarded as a special type of cambium of the renal tubules.

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