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MORPHOLOGICAL CHANGES IN THE ULTRASTRUCTURE OF THE GASTRIC MUCOSA IN THE LATE STAGES OF HYPOTHYROIDISM

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The ultrastructure of rat gastric mucosa was studied by electron microscopic examination on days 50, 100, and 150 after thyroidectomy. It was established that as hypothyroidism develops, dystrophic-destructive changes become pronounced in chief and parietal cells on days 50 and 100, while the latter is combined with compensatory changes in mucous cells. Endocrine cells are more resistant to the lack of thyroid hormones. On day 150, destructive and dystrophic changes predominate in all structural components of mucous cells, and decompensation comes to the fore.

Key words: hypothyroidism, rats, stomach, mucous membrane, electron microscopy.

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МОРФОЛОГІЧНІ ЗМІНИ УЛЬТРАСТРУКТУРИ СЛИЗОВОЇ ОБОЛОНКИ ШЛУНКУ НА ПІЗНІХ СТАДІЯХ ГІПОТИРЕОЗУ

Методами електронномікроскопічного дослідження була вивчена ультраструктура клітин залоз слизової оболонки шлунку щурів на 50, 100 та 150 добу після тиреоектомії. Встановлено, що по мірі розвитку гіпотиреозу в головних та парієтальних клітинах на 50 та 100 добу набувають виразності дистрофічно-деструктивні зміни, тоді як в слизових клітинах останні поєднуються з компенсаторними. Ендокринні клітини є більш стійкими до нестачі гормонів щитоподібної залози. На 150 добу в усіх структурних компонентах клітин слизової оболонки переважають деструктивно-дистрофічні зміни, і на перший план виходить декомпенсація.

Ключові слова: гіпотиреоз, щурі, шлунок, слизова оболонка, електронна мікроскопія.

The study is a fragment of the research project "Morphological features of rat organs under conditions of experimental exogenous influence", state registration No. 0122U000491.

Diseases of the thyroid gland occupy the first place among diseases of the endocrine system. Recently, there has been a rapid increase in the pathology of the thyroid gland in the population of Ukraine. At the same time, if earlier doctors observed an increased amount of thyroid hormones, then recently, there has been a decrease in their amount in the body. Autoimmune thyroiditis is now the main cause of this disease, but until recently, it was considered the consequence of the accident at the Chernobyl nuclear power plant [1]. Insufficiency of thyroid hormones in the body leads to a violation of water and electrolyte exchange, all types of metabolism, causing morphofunctional and biochemical changes in various organs and systems, particularly in the digestive system. It contributes to developing gastritis, peptic ulcer disease, atherosclerotic changes in microvessels, and other diseases [3, 6]. These diseases, for which hypothyroidism is an obligatory risk factor, lead to the formation of necrotic changes in the stomach, which often becomes the direct cause of death of patients with this pathology.

Unfortunately, insufficient literature is devoted to morphofunctional changes in the stomach under hypothyroidism conditions and during its correction [2, 7]. Their study, considering clinical and laboratory data, would become a theoretical basis for understanding the pathogenesis of gastrointestinal diseases in hypothyroidism development of adequate methods of diagnosis, treatment, and prevention [5, 8].

Previously, we conducted electron microscopic studies of gastric gland cells early after thyroidectomy on the 14th and 35th day of observation, which showed the staged development of changes in the ultrastructural organization of the glands of the gastric mucosa of rats in the dynamics of the development of hypothyroidism. In the early stages (14 days), against the background of reactive changes, apoptosis processes were expressed, experienced mainly by mucous neck and parietal cells. Endocrine cells undergo the least changes and are more stable in the early stages of postoperative hypothyroidism. As hypothyroidism develops (35 days), signs of compensatory and adaptive processes appear in some cells (gastric chief and parietal cells), while dystrophic processes are more pronounced in mucous cells. At the same time, the number of apoptotic cells was significantly reduced.

The purpose of the study was to examine the ultrastructural changes in all types of cells of the mucous membrane of the rats' stomach in the late period after thyroidectomy.

Materials and methods. The study was performed on 35 white female Wistar rats weighing 180–200 g. Keeping and all manipulations with animals were carried out in full accordance with the guidelines of the General Ethical Principles of Animal Experiments approved by the First National Congress on Bioethics (Kyiv, 2001) with strict compliance with the requirements of the European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, the provisions of the methodological recommendations of the Preclinical Study of Medicines. Animals underwent total thyroidectomy under ketamine anesthesia [4]. Stomach body sections of 30 rats 50, 100, and 150 days after thyroidectomy and 5 intact animals were the material for electron microscopic examination. Fragments of stomach bodies were fixed in 2.5 % glutaraldehyde solution with additional fixation in 1 % OsO_4 Miloning buffer. Ultrathin sections were contrasted with solutions of uranyl acetate and lead citrate. The preparations were examined under a PEM-125K electron microscope.

Results of the study and their discussion. On the 50th day after thyroidectomy, the lumen of cells of the gastric glands does not contain vacuoles, which were observed earlier after thyroidectomy. Still, there are remnants of apoptotic cells and cellular detritus. Signs of active biosynthetic processes characterize chief cells. Their nuclei acquire a slightly irregular shape due to the formation of invaginations, which increases the cell surface. The cytoplasm contains a lot of free ribosomes and polysomal complexes, tubules of the endoplasmic reticulum with ribosomes attached to them, the Golgi apparatus, mitochondria of different sizes and shapes with an intact matrix, and cristae. Zymogen granules in clusters are observed in the apical part of the chief cells and separate structures in the perinuclear zone. Parietal cells have a rounded nucleus with evenly distributed chromatin in the nucleoplasm. The increase in giant mitochondria with a well-preserved structure, which occupies most of the cytoplasm volume, attracts attention. Some mitochondria tightly adhere to the karyolemma and form invaginations. Intracellular tubules of the endoplasmic reticulum fill the cytoplasm in large numbers and appear as small, rounded structures.

In contrast to the chief and parietal cells, in which compensatory and adaptive processes come to the fore, mucous neck cells undergo further dystrophic changes. Compared to the previous period of observations, their number is decreasing, and those observed have changed mainly according to the “dark” type. Their sizes are reduced. In some of them, individual organelles can still be distinguished, but most cells can be identified only by the content of mucous granules. This gives reason to believe that the above-described dark mucocytes reflect different stages of apoptosis, which become significantly pronounced 50 days after the operation.

Endocrine cells of the glands of the gastric mucosa at this time of observation are found in small numbers. We identified mainly embryonic stem (ES) cells and mixed -type cells. Their morphological structure is generally preserved. In the cytoplasm of these cells, a small amount of diffusely located electron-dense granules of mostly rounded shape and small size is observed.

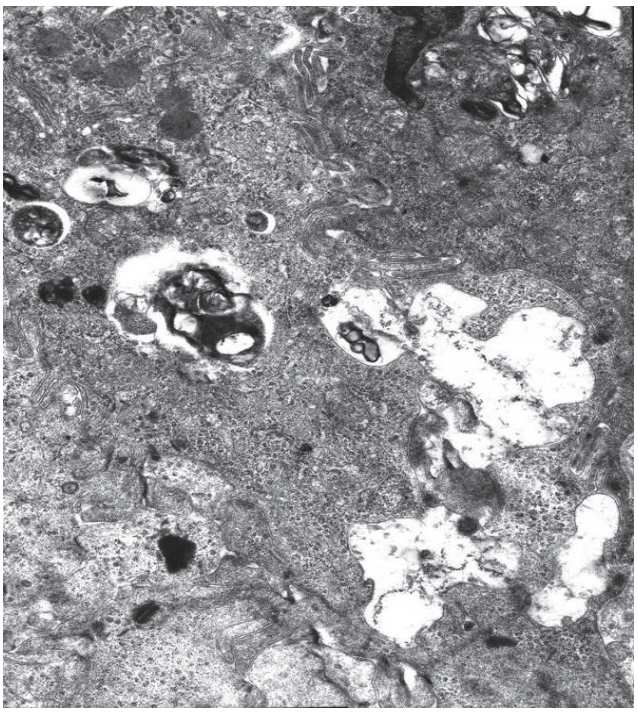
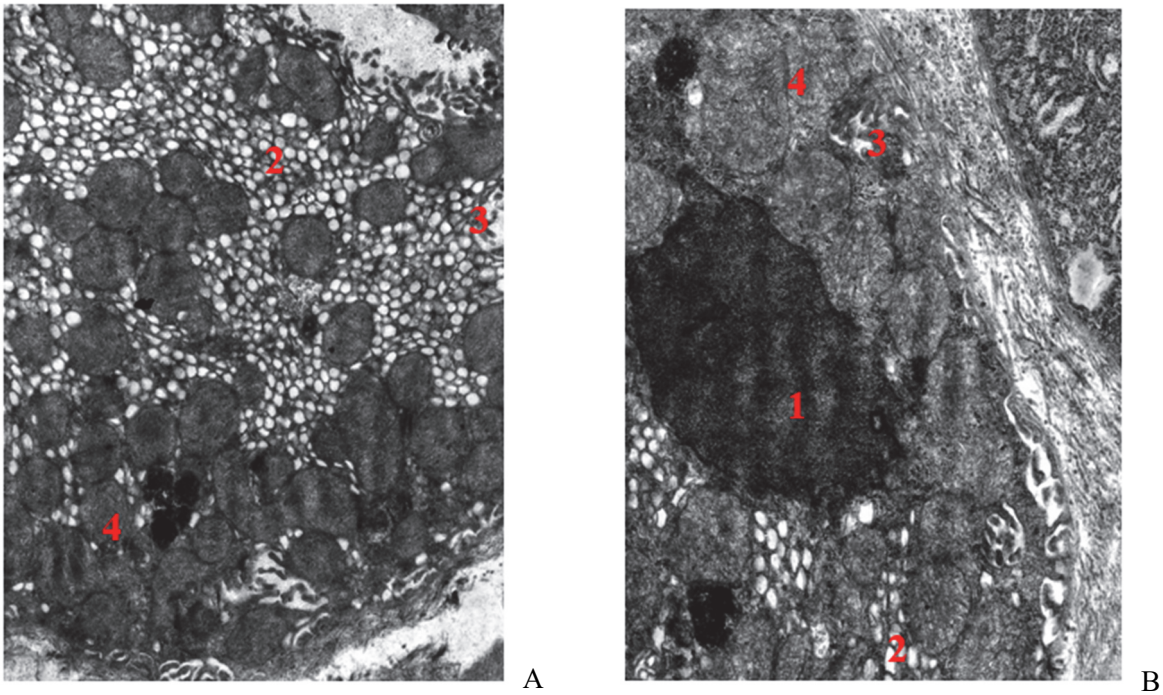


Fig. 1. The gastric mucosa of a rat 100 days after thyroidectomy. Myelin-like structures in the chief cell. Electronic micrograph. Magn. – 9600.

Between the glands' cells, wandering white blood cells in different parts of the gastric mucosa contain many vacuoles with granules. In some places, these vacuoles occupy the entire volume of the cytoplasm.

100 days after thyroidectomy, although there are signs of compensatory and adaptive processes, they are somewhat redistributed among the cells of the glands of the mucous membrane. In the chief and parietal cells, where these processes became most pronounced after 50 days, next to cells containing well-developed endoplasmic reticulum tubules, Golgi complex, ribosomes, and polysomal complexes, increases in the size and number of mitochondria, i.e., functionally active cells, are observed destructively dystrophically changed cells, which are characterized by the presence of myelin-like structures in the chief cells (Fig. 1).

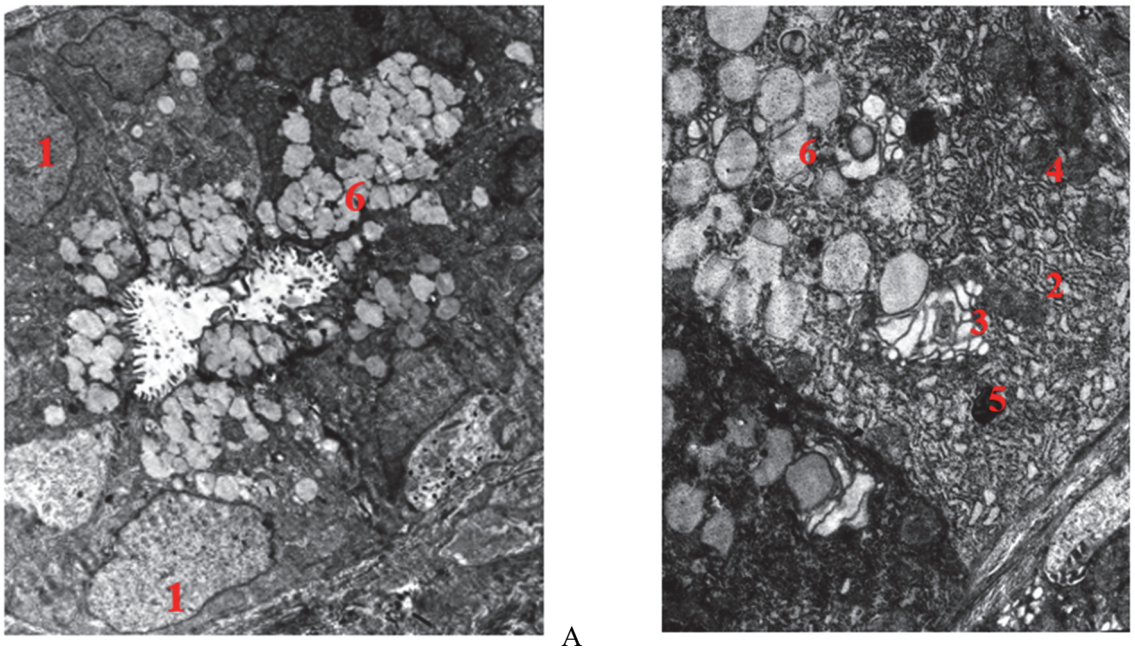
Parietal cells are characterized by electron-dense nuclei and mitochondria, a decrease in the number of intracellular tubules (Fig. 2).



A B

Fig. 2. The gastric mucosa of a rat 100 days after thyroidectomy. Nucleus (1), tubulovesicles (2), intracellular tubules (3), and mitochondria (4) in parietal cells. Electronic micrograph. Magn. A – 12000, B – 21000.

At the same time, mucous neck cells, in which destructive processes prevailed during the previous observation period, demonstrate a mosaic ultrastructural organization (Fig. 3). Moreover, functionally active cells predominate. That is, compensatory and adaptive processes are expressed in them 100 days after the operation. Such mucous cells contain a nucleus with chromatin evenly distributed throughout the nucleoplasm, well-preserved Golgi complexes, EPR tubules, and mitochondria in the basal part of the cytoplasm. Mucous granules, rounded in shape, form a cluster in the apical part. Other cells have initial signs of dystrophic and destructive processes: edema of the tubules of the Golgi complex, fragmentation of EPR, and accumulation of electron-dense material in the cytoplasm of partially destroyed granules. Electron-dense mucous cells with nuclei in various stages of pyknosis and cells in the final stages of apoptosis are also observed.



A B

Fig. 3 The gastric mucosa of a rat 100 days after thyroidectomy. Functionally active nucleus (1), endoplasmic reticulum tubules (2), Golgi complex (3), mitochondria (4), lysosomes (5), mucus granules (6) in mucous neck cells. Electronic micrograph. Magn. A – 9600; B – 12000.

During this observation period, we detected 2 types of endocrine cells in the glands of the mucous membrane of the stomach: ES and EPR cells. ES cells are found in small numbers, as in the previous follow-up period. In their cytoplasm, there are small electron-dense granules of rounded shape, the number of which increases. The appearance of microfilaments in the cytoplasm of ES cells attracts attention.

On the 150th day of observation, destructive-dystrophic changes prevail in all structural components. Compensatory processes break down, and decompensation comes to the fore.

Thus, in the early periods of observation (35 days), we noted pronounced apoptosis processes, mainly in parietal and mucous neck cells. Later (50 days), the chief and parietal cells somewhat adapt to the lack of thyroid hormones, which correlates with the researchers' data [2, 7]. However, in mucous neck cells, adaptation processes occur somewhat later (100 days).

However, at a later observation time, irreversible destructive-dystrophic changes are observed in all cells of the gastric glands, leading to necrosis and organ dysfunction [5, 9].

We note the relative resistance of endocrine cells to hypothyroidism, which can be explained by their connection and dependence on the central organs of the endocrine system [10].

Conclusions

1. The conducted electron microscopic analysis showed that as hypothyroidism develops (50 days), signs of compensatory and adaptive processes appear in some cells (gastric chief and parietal cells). In contrast, dystrophic processes are more pronounced in mucous cells. At the same time, the number of apoptotic cells was significantly reduced.

2. At the later stages (100 days), dystrophic-destructive ones become pronounced in the chief and parietal cells against the background of adaptation processes, while in mucocytes, the latter alternate with compensatory ones. Endocrine cells are also more resistant to thyroid hormone deficiency in the late stages of postoperative hypothyroidism, although they also show changes in both adaptive and destructive plans.

Mucous and parietal cells were the most sensitive to the lack of thyroid hormones.

3. After the 150th day of observation, destructive-dystrophic changes prevail in all structural components. Compensatory processes break down, and decompensation comes to the fore.

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