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MORPHOLOGY OF THE PANCREAS UNDER EXPERIMENTAL STRESS CONDITIONS

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Objective: to assess the nature of morphological and morphometric changes in the pancreas during experimental stress. **Materials and methods:** white laboratory rats were used in the experiments under stress conditions. To achieve the goal of the study, the pancreas of 60 sexually mature white laboratory rats was studied. White laboratory rats were divided into 2 groups. The first group consisted of intact adult rats in the control group. In our second group, the laboratory rats were placed in a special maze cage, and an experimental stress model was called. This stress model was continued after the rats became pregnant and gave birth to their offspring. **Results:** The pancreatic acini of experimental rats under stress retained their shape, but in some exocrinocytes, structural disorders, loss of basal basophilia, and hyperchromic state of the nuclei were detected. In some cases, the nucleoli disappeared, and an increase in the number of zymogen granules was observed in the cytoplasm. This is associated with a violation of the release of the secretory content of the granules. At the same time, mild edematous changes occurred in the connective tissue surrounding the excretory ducts. **Conclusion:** the appearance of choroid tumors observed in the connective tissue of this gland. In addition, the intensity of signs of destruction of the terminal secretory part of the lobes decreased, and at the same time the number and height of the pancreas in the lobes decreased.

Keywords: pancreas, stress, pancreatic lobe, acinus.

Relevance. Undoubtedly, stress reactions are considered a complex adaptational process that ensures the body's adaptation to the effects of various environmental factors. This process is carried out through the mutually integrated activity of many functional systems, and in this, the nervous system plays a leading regulatory role. At the same time, the long-term or excessively strong effect of stress factors can strain the body's adaptive mechanisms, leading to the development of structural and functional damages in various organs and systems [1, 5, 8, 12, 20].

Deep study of these issues has important significance for the scientifically based application of biologically active substances with corrective properties in practice. The body's resistance under stress conditions, cellular immunity indicators, cortisol amount, lipid and phospholipid metabolism, as well as the normalization of these changes have not been analyzed in detail [3, 11, 18, 22].

Currently, scientific views on the biological role of low-molecular metabolites of natural origin, which have high multi-vector biological activity, are being reconsidered. Their active participation in metabolic processes, as well as their immunomodulatory and antistressor properties, arouse special scientific interest [2, 4, 9, 14, 23].

The effect of stress on the organism of laboratory animals has been widely covered in many experimental studies. The scientific works of some authors [6, 10, 15] are devoted to studying the morphofunctional changes emerging in the pancreas under the influence of stress factors with different etiologies and the use of biologically active substances for the purpose of correcting them. However, a unified scientific view regarding the character of morphological, ultrastructural, and functional changes developing in the pancreas has not been formed, and this condition is mainly explained by the diversity of stress models and the duration of stress effects.

For instance, a decrease in the concentration of adenylate cyclase in the blood of rats under chronic stress conditions has been determined [7, 13, 17]. Along with this, while a decrease in the levels of glucose, growth hormone, and adrenocorticotropic hormone was observed, no significant change in the amount of corticosterone, insulin, and C-reactive protein was recorded [16]. Some researchers [24] emphasize that periodic stress causes β-cell hyperplasia, and also over time causes a decrease in the number of β-cells and an increase in the proliferation of α-cells in the pancreas.

The activation of anaerobic glycolysis in β-cells under stress conditions is considered as one of the universal metabolic response mechanisms. The strengthening of the glycolysis process is an important manifestation of compensatory metabolic reconstruction aimed at maintaining energy supply against the background of increasing ATP-dependent processes in cells. This condition has been confirmed by the results of a number of experimental studies [19, 21]. Despite this, the issue of studying the morphological changes developing in the pancreas under stress conditions remains one of the urgent scientific problems even today.

Materials and Methods

The researches were carried out on sexually mature female Wistar line rats with a body weight of 180-220 g. The animals were kept in standard vivarium conditions, at a temperature of 20-22 °C, in a 12-hour light/dark regime, and were provided with the opportunity for free access to drinking water and food. During the experiment, the rats were given standard briquetted combined food intended for laboratory animals. In our second group, after the laboratory rats were placed in a special maze cage, an experimental stress model was induced. This stress model was continued after the rats became pregnant and after their offspring were born. After the baby rats were born, they were euthanized by decapitation method on the 3rd, 7th, 14th, 21st, and 30th days. For histological examinations, tissue samples were taken from the head, body, and tail parts of the pancreas.

For the purpose of conducting morphological studies, tissue fragments of the pancreas were extracted and fixed in a 10% neutral formalin solution. Subsequently, the preparations were dehydrated through increasing concentrations of ethyl alcohol (70°, 80°, 90°, and 96°) and embedded in paraffin blocks. From the prepared paraffin blocks, histological sections with a thickness of 8-12 μm were prepared and stained by the hematoxylin-eosin method. The experiments and the processes of euthanizing the animals were carried out in accordance with the requirements of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1985). Histological sections with a thickness of 8-10 μm were prepared using a rotary microtome and stained with hematoxylin-eosin by a standard method (Volkova O.V., Yeletskiy Yu.K., 1982).

Results and Discussion

Microscopic examination of the pancreas of the rats in all experimental groups showed that this organ consists of an exocrine part represented by acini, an excretory duct system, and an endocrine part composed of islets of Langerhans containing β-cells that carry out insulin secretion. In the control group rats, it was observed that the pancreas was divided into distinct lobules with the help of connective tissue septa, and its parenchyma mainly consisted of pancreatocytes with an acinar structure. The islets of Langerhans, which are considered the endocrine part of the gland, were diffusely located throughout the parenchyma, forming small clusters of cells with a light-staining cytoplasm and nucleus (Figure 1).

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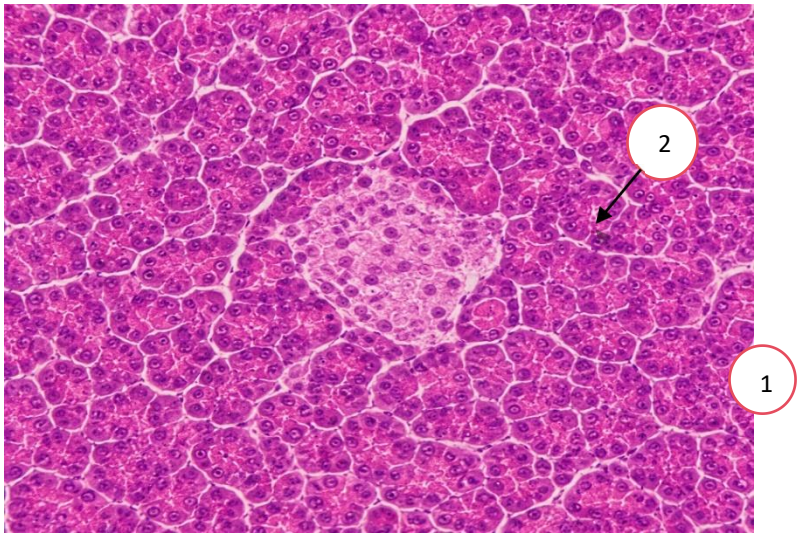
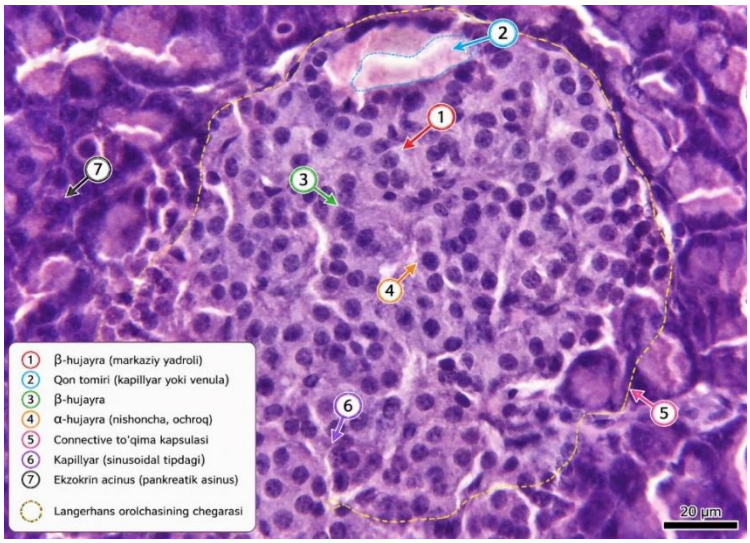


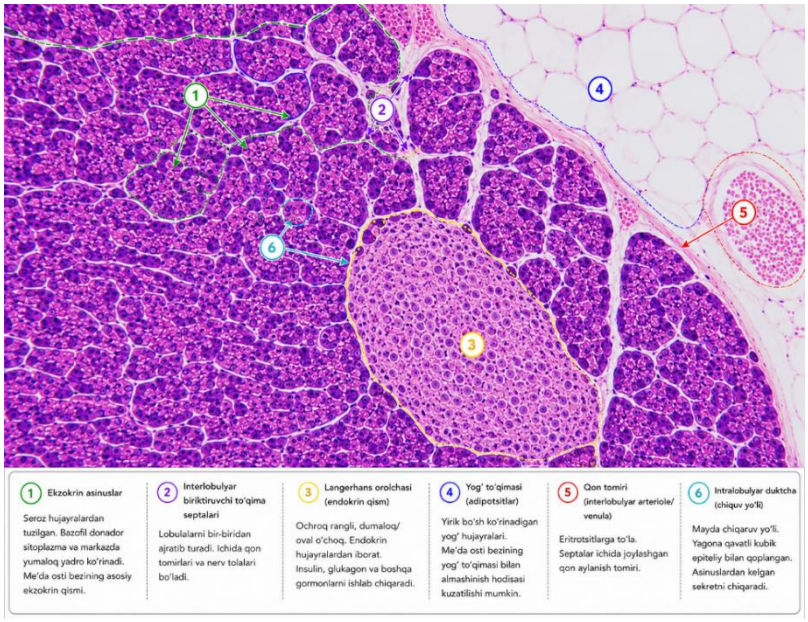
Figure 1. Histological structure of the pancreas of control group rats. 1 - pancreatic acinus cell, 2 - islet of Langerhans. Hematoxylin-eosin. X: 40x10.

The basal part of the acinar cells is characterized by strong basophilia, and this condition is explained by the well-developed granular endoplasmic reticulum in the cells. And in the apical part of the cells, oxyphilic staining secretory zones rich in zymogen granules were determined. Centroacinar cells were mainly located in the central part of the acini, morphologically distinguished from other cells by the relatively lighter staining of their cytoplasm and nucleus. As is known, the islets of Langerhans are considered a complex endocrine structure consisting of α-, β-, PP-, and δ-cells. The main part of the endocrine apparatus is formed by β-cells, and they are usually located in the central part of the islets, while α-cells are mainly found in the peripheral zones. While α-, β- and δ-cells synthesize the hormones glucagon, insulin and somatostatin respectively, PP-cells produce pancreatic polypeptide.



As a result of the morphometric assessment of the diameter of the islets of Langerhans of the pancreas of the rats in all studied groups, significant changes were recorded. In particular, the area

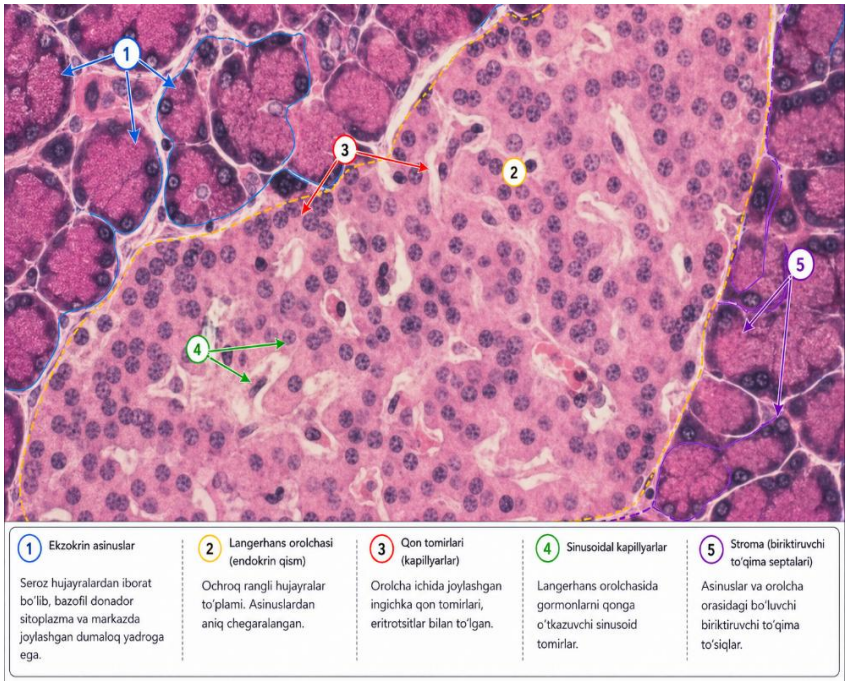
occupied by the islets of Langerhans constituted 255.13 μm², and it was determined that this indicator was higher by 73.25 μm² relative to the rats in the control group.



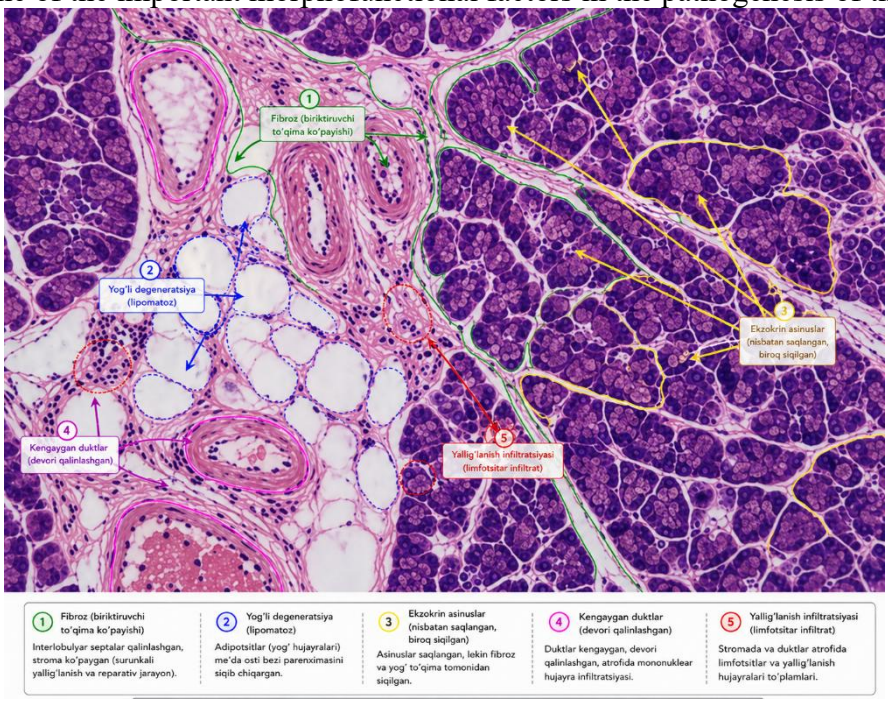
During the microscopic examination of the pancreas preparations of the experimental group rats, structures of various levels of the excretory duct system, including small intralobular ducts starting from the acini, interlobular ducts, as well as the main pancreatic duct, were determined. The exocrine part was characterized by being composed of protein-secreting acinar cells having a pyramidal shape and round nuclei.

In the central part of the acini, in some cases, centroacinar cells forming the initial segments of the pancreatic excretory system were observed. In all studied groups, the clear zonality of the acinar cells was recorded: while the basal part of the cells was stained strongly basophilic, the apical part manifested an oxyphilic characteristic due to the presence of secretory granules.

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Along with this, a significant decrease in the number of β-cells in the endocrine apparatus of the pancreas, as well as the development of destructive-dystrophic changes in them, was recorded as one of the important morphofunctional factors in the pathogenesis of the diabetic condition.



Significant structural changes occurred in the endocrine cells. The average area of β-cell nuclei decreased and underwent karyopyknosis. The area of the α-cell decreased by 8.5% relative to the control group. The nucleus of the α-cell acquired enlarged pores and lesser electron density. In the

α-cell, the area of secretory granules increases, but the diameter of the granules decreases from 22.7±0.9 nm to 18.4±0.5 nm.

As a result of morphometric researches, the diameter of the pancreatic acini reaches 11.4±0.3 μm, and their height reaches 2.15±0.18 μm. Relative to the control group in terms of the diameter and height of the acinus cell, in the experimental group the acinus diameter lagged behind in growth by up to 3%, and the height by up to 12%.

Conclusion. The results of the research showed that experimental stress led to changes connected with the changing of the structural composition of the pancreatic stroma of rats, interlobular connective tissue to form the structural components of fibrous tissue, as well as the appearance of choroid edema observed in the interlobular connective tissues. In addition, the intensity of signs of destruction of the terminal secretory part of the lobules decreased, and at the same time the number and height of the pancreas in the lobules decreased. It was determined that this is connected with the delay of the division process of the pancreas and the weakening of the secretory process. The thickening of the arrangement of insulocytes was observed in the islets of the endocrine part of the gland lobules.

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