# PANCREATIC MORPHOLOGY IN THYROID DISEASES IN WHITE MICE

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***https://doi.org/10.5281/zenodo.15306291***

***Abstract.*** *In our study, we examined white laboratory rats born to control and experimental mothers with hypothyroidism. Morphological analysis of the pancreas during various stages of postnatal ontogenesis revealed significant delays in the development and formation of individual components of the vascular wall compared to the control group.*

*From the first days of the experiment, changes in the arterial wall were observed in all experimental animals. The results demonstrate that morphological changes in pancreatic cells and their blood vessels occur in offspring born to mothers with hypothyroidism.*

***Key words:*** *pancreas, acinus, mercazolil, share*

# МОРФОЛОГИЯ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ ПРИ ЗАБОЛЕВАНИЯХ ЩИТОВИДНОЙ ЖЕЛЕЗЫ У БЕЛЫХ МЫШЕЙ

***Аннотация.*** *В нашем исследовании мы изучали белых лабораторных крыс, рожденных от контрольных и экспериментальных матерей с гипотиреозом. В результате морфологического анализа поджелудочной железы в разные периоды постнатального онтогенеза выявлены существенные изменения задержки развития и формирования отдельных компонентов сосудистой стенки по сравнению с контрольной группой.*

*С первых дней после начала эксперимента у всех подопытных животных отмечали изменения артериальной стенки. Полученные результаты показывают, что у потомства, рожденного от матерей с гипотиреозом, происходят морфологические изменения в клетках поджелудочной железы и ее кровеносных сосудах.*

***Ключевые слова:*** *поджелудочная железа, ацинус, мерказолил, доля*

**Introduction.** Hypothyroidism is a clinical syndrome resulting from a persistent deficiency of thyroid hormones or a reduction in their biological effects at the tissue level.

According to the World Health Organization, the prevalence of primary hypothyroidism in the population ranges from 0.2–1%, while latent primary hypothyroidism affects 7–10% of women and 2–3% of men. Within a year, 5% of latent hypothyroidism cases progress to overt hypothyroidism [1, 4, 8, 11, 17].

Hypothyroidism is the most common thyroid dysfunction, characterized by a gradual onset, subtle symptoms, and satisfactory well-being in mild to moderate cases. Symptoms may include fatigue, depression, or complications during pregnancy.

The prevalence of hypothyroidism is approximately 1%, rising to 2% in women of reproductive age and up to 10% in the elderly.

Thyroid hormone deficiency causes systemic changes in the body. These hormones regulate energy metabolism in cells, and their deficiency leads to reduced oxygen consumption, decreased energy expenditure, and impaired processing of energy substrates [2, 6, 9, 14, 18].

Hypothyroidism disrupts the synthesis of cellular enzymes dependent on energy, impairing normal cell function. In advanced cases, myxedema—edema of the mucous membranes—develops due to excessive accumulation of glycosaminoglycans, which increase tissue hydrophilicity and water retention [3, 7, 10, 15, 16].

In women, hypothyroidism is associated with reproductive system disorders, including irregular menstrual cycles (amenorrhea, dysfunctional uterine bleeding), and mastopathy.

Thyroid hormone deficiency can lead to infertility. While mild hypothyroidism may not prevent pregnancy, it increases the risk of spontaneous abortion or neurological disorders in offspring. Both men and women may experience reduced libido [5, 12, 13, 19].

The pancreas is highly susceptible to pathological influences from endogenous and exogenous stimuli, leading to functional impairments and systemic pathological processes.

Changes in pancreatic function often originate from alterations in its vascular and connective tissue stroma.

Thus, damage to the pancreas results in quantitative and qualitative changes in stromal vessels, the islets of Langerhans, and acini. These structural changes are accompanied by clinical symptoms of impaired pancreatic function.

**Purpose of the Research.** To investigate the nature of morphological changes in the pancreas in experimental thyroid disorders.

**Materials and Methods.** The study examined the pancreases of 80 sexually mature white laboratory rats divided into two groups.

Group 1 (control) consisted of 30 healthy rats. Group 2 (experimental) included 50 female rats treated with 0.5 mg of mercazolil per 100 g of body weight for 14 days to induce hypothyroidism, followed by 0.25 mg per 100 g for one month.

After pregnancy and delivery, the experimental mothers continued receiving 0.25 mg of mercazolil per 100 g during lactation. Blood samples from the tail veins of mothers and offspring were analyzed for thyroid hormone levels.

Offspring were euthanized by decapitation on days 3, 7, 14, 21, and 30 post-birth.

Pancreatic tissues from the head, body, and tail were collected for histological examination. Tissues were fixed in 10% formalin, dehydrated in alcohol, and embedded in paraffin. Histological sections (8–12 µm) were stained with hematoxylin-eosin.

All experiments and euthanasia complied with the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1985).

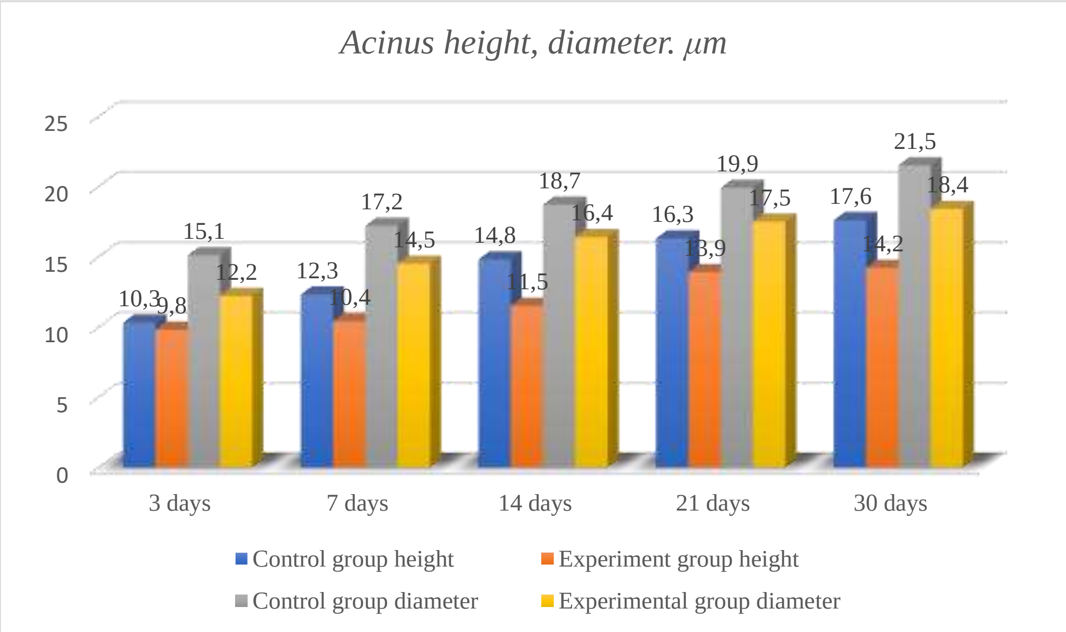
Sections (8–10 µm) were prepared using a rotary microtome and stained with hematoxylin-eosin following standard methods [Volkova O.V., Yeletsky Yu.K., 1982].

**Results.** In 3-day-old rat pups, no histological differences were observed compared to the control group. The connective tissue capsule, acini, islets of Langerhans, blood vessels, and α- and β-cells showed no changes. Acini were pyramidal or oval in shape.

In 7-day-old rat pups, the histological structure remained largely similar to the control group. The organ's delicate stroma was covered by a connective tissue capsule dividing the gland into lobes, with acini as the structural unit. Acini were pyramidal, oval, or polygonal, with a wide base and narrowed apex.

The islets of Langerhans and blood vessel walls were unchanged, with capillary diameters of 3.3±0.2 µm. However, α-cells were slightly enlarged (area: 96,495.7±342.53 $nm^2$), with a reduced nuclear-cytoplasmic index (0.52±0.06). α-cells were less damaged than β-cells due to a denser cytoplasmic membrane.

Morphological analysis revealed minor changes, including vascular dilation, increased microvessel and venous plexus permeability, and extravasation of the liquid blood component into surrounding connective tissue.




By day 14, pancreatic stroma exhibited increased edema, particularly in perivenular and pericapillary spaces. Collagen fibers were swollen, loose, and showed stratification and surface disorganization of the connective tissue matrix.

The average capillary diameter in the exocrine parenchyma was 4.8±0.1 µm ($p \leq 0.05$).

Capillary walls were dilated, with stroma showing erythrocyte accumulation and tissue edema (Fig. 1).

The average area of Bhujayra nuclei in pancreatic islets decreased (14,865.4±96.3 nm² in controls vs. 12,698.4±133.2 nm² in hypothyroid rats; $p<0.05$). β-cell nuclei exhibited karyopyknosis and karyolysis.

Endocrine cells showed significant structural changes: α-cell area decreased by 8.5% (92,110.6±145.6 nm² vs. 100,567.2±312.5 nm² in controls), while nuclear area increased (35,546.5±179.4 nm² vs. 32,500.2±98.6 nm² in controls). α-cell nuclei had enlarged nuclear pores and reduced electron density.

The nuclear-cytoplasmic index of α-cells increased to 0.57±0.02 (0.54±0.02 in controls).

Secretory granule area in α-cells increased, but granule diameter decreased from 22.7±0.9 nm to 18.4±0.5 nm, indicating morphological maturation.

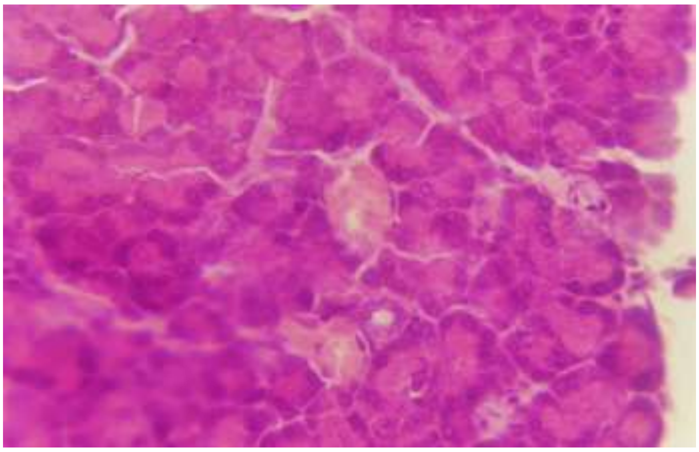


***Fig 1.*** *Rat pancreas on the 14st day of the experiment. Red blood cell aggregation and tissue edema. Stained with hematoxylin and eosin. X: 10x40.*

By day 21, vascular disorders persisted, with increased vascularity, blood stasis, diapedetic perivascular hemorrhages, and intensified edema (Fig. 2). Capillary diameter in the exocrine parenchyma increased to 6.1±0.3 μm (5.15±0.4 μm in controls). Exocrine cells showed significant structural changes, with blood cell congestion in vessels and leukocyte accumulation in the gland parenchyma (Fig. 3). α-cell area decreased by 8.5% (92,110.6±145.6 nm² vs. 100,567.2±312.5 nm² in controls), while nuclear area increased (35,546.5±179.4 nm² vs. 32,500.2±98.6 nm² in controls).

The nuclear-cytoplasmic index of α-cells rose to 0.57±0.02 (0.54±0.02 in controls). Secretory granule area increased, but granule diameter decreased from 22.7±0.9 nm to 18.4±0.5 nm.

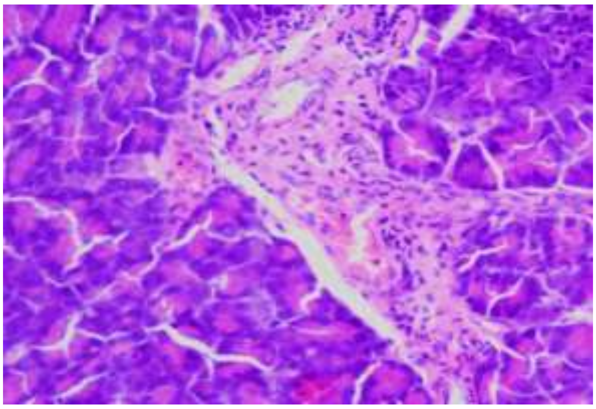


***Fig 2.*** *Rat pancreas on the 21st day of the experiment. Diapedetic hemorrhages, increased edema intensity. Stained with hematoxylin and eosin. X: 10x40.*

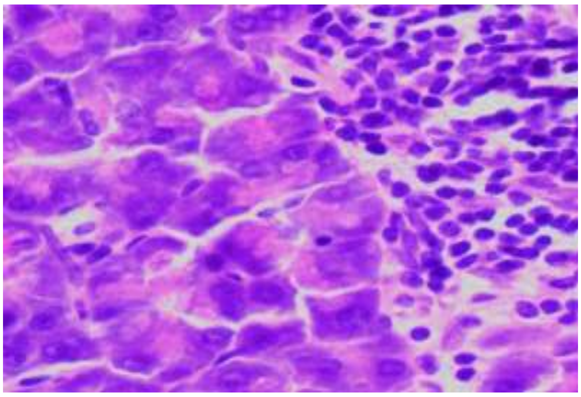


***Fig 3.*** *Rat pancreas on the 21st day of the experiment. Blood cell stagnation in the vessels and accumulation of leukocytes in the gland parenchyma. Stained with hematoxylin and eosin. X: 10x40*

By day 30, interstitial edema intensified and spread throughout the pancreas, peaking in perivenular spaces. Edema caused collagen fiber swelling, separation, and defibrillation (Fig. 4). Each pancreatic lobe was supplied by interlobular arterioles (diameter: 39.4±2.7 µm), branching from five arterioles per lobule. Intralobular precapillary arterioles formed a capillary network around the lobule, transitioning into postcapillary venules (diameter: 56.6±4.2 µm).

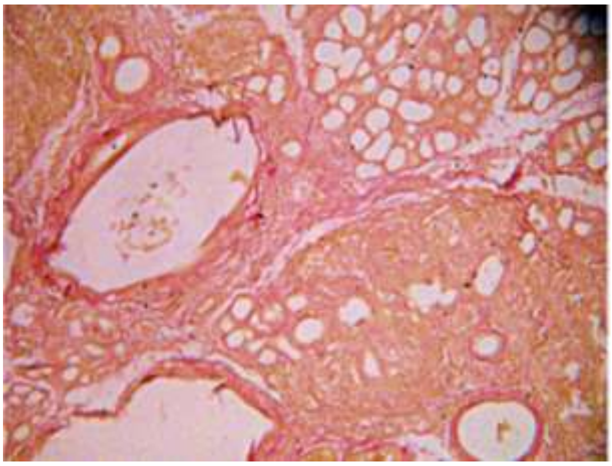


***Fig 4.*** *Rat pancreas on the 30th day of the experiment. Swelling of collagen fibers, dilation of pancreatic ducts. Stained with Van Gieson.*

The perivascular space was narrow or absent in some areas, separating islet capillaries from exocrine parenchyma capillaries. Islet capillaries showed thinned endothelial cytoplasm, numerous fenestrae, and pinocytic vesicles, indicating high functional activity. Interlobular arterioles and capillaries exhibited dilation, cytoplasmic vacuolization, eosinophilic nuclei, and karyolytic nuclei.

**Conclusion.** In the experimental hypothyroidism model, the pancreatic stroma exhibited dystrophic, destructive, and atrophic changes, diffuse edema, and fibrosis. The earliest signs of hypothyroidism appeared on days 7–14, peaking by day 21. Hypothyroidism induced hypertrophic changes in the protein-synthesizing apparatus of pancreatic islet cells, increasing granule synthesis by 1.5 times. The lack of significant changes in acinocyte secretion (granule number and secretion intensity) may reflect differential sensitivity between exocrine and endocrine cells.

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