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MORPHOLOGICAL ASPECTS OF RABBIT LIVER DAMAGE DURING THYROIDECTOMY

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Abstract: Non-alcoholic fatty liver disease (NAFLD) is a prevalent metabolic disorder with significant links to obesity, diabetes, and atherosclerosis. This study explores the morphological changes in the liver following thyroidectomy in rabbits, establishing an experimental model for early-stage fatty liver disease. Forty female rabbits were divided into two groups: a control group (thyroid mobilization) and an experimental group (thyroidectomy). Liver samples were collected at 4 and 8 weeks post-surgery for histological analysis. By the 4th week, animals in the thyroidectomy group exhibited granular and hydropic dystrophy in hepatocytes, along with fine-droplet fatty degeneration and minimal chronic hepatitis. These changes were more pronounced by the 8th week, showing progressive necrotic and inflammatory processes and initial fibrosis signs. The findings suggest that primary hypothyroidism induced by thyroidectomy in rabbits closely mirrors the structural characteristics of NAFLD, providing insights into the pathogenesis and progression of fatty liver disease in hypothyroid conditions.

Keywords: Thyroidectomy, Rabbit liver, Fatty liver disease, Hypothyroidism, Hepatocyte dystrophy, Liver fibrosis, Chronic hepatitis, Protein dystrophy, Histopathology, Experimental model.

Introduction. Non-alcoholic fatty liver disease (NAFLD) is becoming one of the most common diseases in modern human populations. It is diagnosed in 10-30% of the population of European countries, while among people with obesity or diabetes mellitus its frequency reaches 57-74%. There is no longer any doubt about the connection between NAFLD and metabolic diseases such as diabetes mellitus, obesity, and atherosclerosis. This makes the study of this pathology relevant both in terms of their comorbid associations and taking into account the possible premorbid role of liver damage in their development.

Evidence-based diagnostics of NAFLD is based on histological detection of small- or large-droplet fatty degeneration of hepatocytes in liver biopsies, which is clinically expressed as steatosis, steatohepatitis and steatofibrosis, considered as a single stage-by-stage process. Various mechanisms of development of fatty degeneration of hepatocytes and addition of inflammatory phenomena with the outcome in organ fibrosis are discussed with more or less evidence. However, the trigger mechanisms of these reactions remain the least studied, including in connection with the diagnosis of NAFLD in humans only at the stage of already formed pathological conditions of the organ.

The above facts make the problem of studying morphological changes in the liver, starting from the early stages of NAFLD formation, very relevant, which, given the need to perform repeated invasive liver biopsies on patients, does not stand up to criticism from an ethical standpoint (the "benefit-harm" ratio). The way out of the situation seems to be the search for such an adequate experimental model of the development of fatty degeneration of the organ in laboratory animals, in which the initial "starting point" of dystrophic changes will be easily visible and their formation itself will occur quite quickly.

In this capacity, it makes sense to study the effect of thyroidectomy on the features of the formation of pathomorphological processes in the rat liver. The mechanism of biological action of thyroid hormones is realized through binding to nuclear receptors (TR) α and β at the genomic level, although their non-genomic effect (on the cell membrane, cytoplasm and mitochondria) is also known. Metabolic disorders observed when the thyroid function is switched off concern mainly carbohydrate and lipid metabolism. Sufficient evidence has been accumulated indicating a connection between thyroid status and insulin resistance. At the same time, data on its relationship with the morphofunctional state of the liver are presented mainly by isolated clinical observations of liver damage with a decrease in thyroid function [10-12].

Purpose of the study:to study the features of formation and morphological characteristics of liver damage in rabbits at different times after thyroidectomy as a reproducible model of experimental fatty liver disease.

Materials and methods. The study was performed on 40 laboratory female rabbits of a non-linear breed weighing 200-300 g. The animals were divided into 2 groups: 1st (research - 20 individuals), in which total thyroidectomy was performed; 2nd (control group - 10 individuals), in which thyroid gland mobilization was performed without thyroidectomy. Anesthesia was performed by inhalation of ether vapors by animals. After processing the surgical field, an incision was made in the skin and the edges of the wound were spread apart on holders. The muscles were spread apart using a blunt method, the trachea was exposed, opening access to the thyroid gland. Coagulation of the thyroid arteries was performed with an electrocoagulator, after which both lobes of the thyroid gland and the isthmus were excised with additional processing of the organ bed with a coagulator. The result of the manipulations performed was thyroidectomy, providing reliable primary (postoperative) hypothyroidism without the need for further monitoring of the animal's hormonal status. After the intervention was completed, the wound was sutured layer by layer with nylon threads. In control animals, thyroid mobilization was performed according to the method described above, but without removing the organ. After completion of the surgical intervention, animals of both groups were placed in cages and kept in standard vivarium conditions on a standard diet.

The animals were withdrawn from the experiment by overdosing on ether anesthesia in accordance with the requirements of the European Convention for the Protection of Experimental Animals 86/609 EEC at the 4th and 8th week of the experiment. The animals' livers were collected, and the trachea area in close topographic proximity to the thyroid gland was examined after thyroidectomy to assess the possibility of thyroid tissue regeneration. During these periods, the trachea had a normal structure, and no thyroid tissue growth was detected on it.

Histological processing of the obtained material was carried out according to standard methods. Staining of liver tissue micropreparations was carried out with standard (hematoxylin-eosin) and special dyes: Sudan III - to identify lipids and picrofuchsin according to Van Gieson - to identify connective tissue.

Results. The analysis of the experimental study results showed that the control group of animals at the age of 4-8 weeks exhibited a typical morphological structure of the liver. The organ is represented by lobules that do not have clear boundaries and are separated by a thin layer of connective tissue. The interlobular connective tissue of the rabbit liver is poorly developed. The parenchyma of the lobules is formed by hepatic beams located radially around the central vein. Hepatocytes have a polygonal shape, the cytoplasm looks granular and amphophilic with one, less often two nuclei of a regular round or elongated shape. The cytoplasm of hepatocytes contains glycogen, when stained with Sudan III, barely distinguishable lipid droplets located mainly perinuclearly are detected in single hepatocytes. Portal tracts are represented by triads: arteriole, venule and bile ducts. The stroma of the portal tracts contains single macrophages, histiocytes, lymphocytes and polymorphonuclear leukocytes. The sinusoidal capillaries inside the lobules are very small vessels, their walls are lined with endothelium. Leukocyte infiltrates and connective tissue fibers are not detected in the parenchyma.

In the study group of animals, by the 4th week after thyroidectomy, pronounced dystrophic processes were detected in the rat liver. All preparations showed a picture of protein (granular) dystrophy: hepatocytes looked enlarged in size, swollen, with many acidophilic protein granules in the cytoplasm, giving a coarse-granular appearance characteristic of this type of dystrophy. In some cases, the nucleus had a poorly distinguishable chromatin structure, in other cases only shadows of nuclei, stained bluish, were determined. The boundaries between cells were not clearly defined.

In addition to granular, hydropic dystrophy was detected: sharply swollen hepatocytes with optically empty and rarefied cytoplasm. The cell contours were well defined, the nuclei were located mainly centrally with karyopyknosis and karyolysis. Remnants of weakly eosinophilic granular cytoplasm were located around the nuclei or along the cell membranes. Hydropic dystrophy was found mainly in the pericentral parts of the lobule.

By the 4th week of the experiment, hepatocytes of all rats contained lipid droplets of various diameters, mainly small ones. When stained with Sudan III, small inclusions of neutral fat were clearly visible, located mainly perinuclearly, the cytoplasm of the cells seemed to be uniformly dusted with small grains that reacted to fat. At the same time, the nucleus remained in the center of the hepatocyte. This type of fatty degeneration is usually called fine-grained or dusty. In most liver tissue samples, other signs of dystrophic changes were present - weak staining of nuclei, disintegration of some cells. In all animals, fatty degeneration, having a diffuse nature, was somewhat more pronounced in the periportal zone. Fat vacuoles were detected in 1/3 of hepatocytes, which corresponds to the first degree of steatosis. According to A.I. Abrikosov et al., fine-grained obesity should be called degenerative, since the basis of the process in this case is damage to liver cells.

Already in the 4th week of the experiment, foci of inflammatory infiltration appeared in the liver tissue, more often in the periportal zone, represented by accumulations of lymphocytes and plasma cells, resembling the histological picture characteristic of chronic hepatitis with minimal activity (Fig. 1).

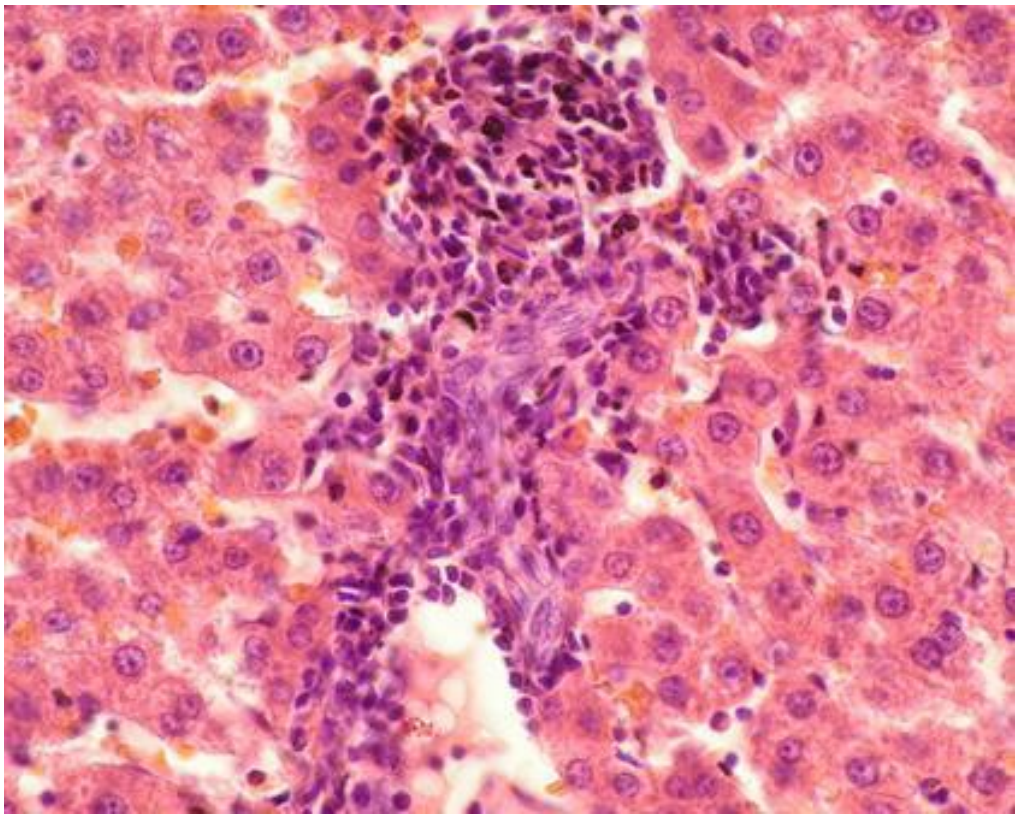

Fig. 1. Minimal hepatitis. Staining: Hematoxylin and eosin. Magnification ×40.

No signs of liver fibrosis were detected at this time. The histoarchitecture of the organ retained its normal structure. The expansion of the sinusoids was noteworthy, which is a sign of serous edema (Fig. 2).

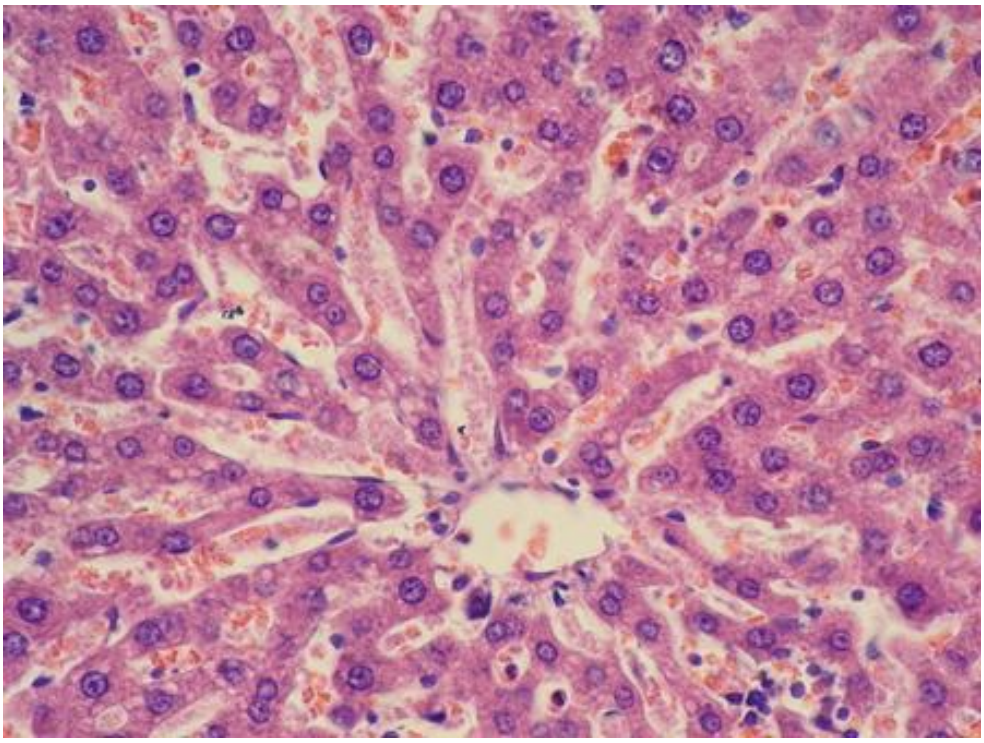

Fig. 2. Serous edema of the parenchyma. Staining: Hematoxylin and eosin. Magnification ×40.

Erythrocytes often formed columns, typical of stasis phenomena.

Thus, already in the 4th week of postoperative hypothyroidism, gross dystrophic changes were clearly observed in the liver of rats against the background of serous edema - protein-fat dystrophy with signs of chronic hepatitis with minimal activity.

On the 8th week of the experiment, pathological processes in the liver underwent a number of changes due to the progression of dystrophic disorders. Signs of protein dystrophy, while remaining, had a greater degree of expression. The cytoplasm of hepatocytes was sharply rarefied, coarsely granular, hypochromia of nuclei was determined. In most liver samples, hydropic dystrophy was detected, more pronounced than in the previous observation period. The cytoplasm of the cells is transparent, the emphasized contour of hepatocytes is characteristic due to well-distinguished membranes.

Against the background of persistent dust-like dystrophy of hepatocytes, cells were identified whose cytoplasm was completely filled with neutral fat (Fig. 3).

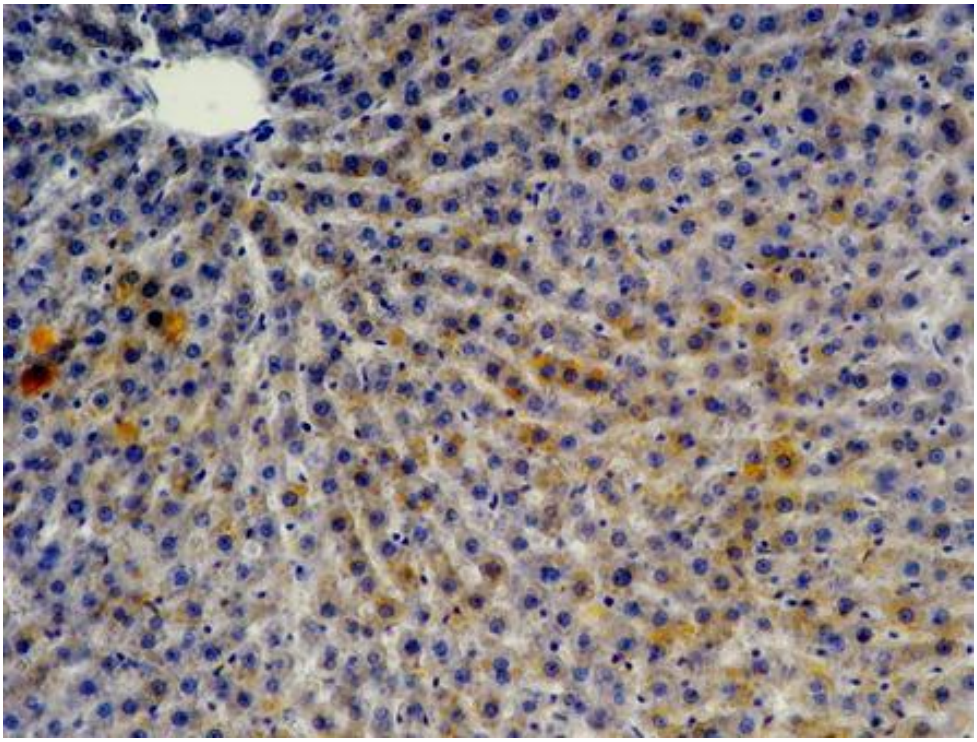

Fig. 3. Small droplet fatty degeneration. Stain: Sudan III. Magnification ×40.

In most preparations, a picture of chronic hepatitis with a minimal degree of activity was noted, however, at the indicated time after thyroidectomy, its severity was greater than at 4 weeks.

The search for signs of fibrosis in rabbit liver tissue on preparations stained according to Van Gieson showed the proliferation of connective tissue, the expansion of large portal tracts due to thickening of the stroma, and the formation of connective tissue strands from the triads to the central vein.

Discussion. After thyroidectomy in laboratory animals with established primary postoperative hypothyroidism, changes are detected in the liver that almost completely reproduce the structural characteristics of NAFLD in metabolic syndrome. Already in the 4th week of postoperative hypothyroidism in rats, there is a clear picture of a combination of diffuse fine-droplet fatty degeneration with protein (granular) and hydropic degeneration of hepatocytes, as well as foci of inflammatory infiltration mainly in the periportal zone. The phenomena of protein degeneration progress by the 8th week of the experiment simultaneously with the appearance of initial signs of organ fibrosis.

The above-mentioned regularities, detected at the early stage of NAFLD modeling, force us to re-evaluate the set of pathogenetic mechanisms of its development. The revealed diffuse small-drop fatty liver degeneration in rats with primary postoperative hypothyroidism can be interpreted as a consequence of developing insulin resistance against the background of complete loss of thyroid function. In conditions of insulin resistance, the flow of free fatty acids (FFA) through the portal system of the liver increases and, as a result, neutral fat accumulates in the cytoplasm of hepatocytes.

The protein dystrophy of hepatocytes detected in experimental animals requires understanding from the point of view of the mechanism associated with a decrease in the synthesis of proteins by the liver, including those that are part of lipoproteins, as a result of which the mechanism of lipid elimination from hepatocytes slows down.

The causes of granular dystrophy are hypoxic conditions, as well as various infections and intoxications. However, the fact of their presence is excluded by the conditions of the present experiment, respectively,

the leading factor of protein dystrophy is hypoxia, the presence of which in hypothyroidism is confirmed by numerous studies.

Against the background of protein dystrophy, the synthesis of lipoproteins (LDL, VLDL) is disrupted, which transport cholesterol, triglycerides and phospholipids from the liver to peripheral tissues and ensure the elimination of fatty inclusions from hepatocytes, as well as HDL, which exhibit antiatherogenic properties. The detection of a combination of lipid and protein metabolism disorders can be considered as a morphological substrate of atherogenic dyslipidemia, observed in most cases in patients with hypothyroidism.

The imbalance of anabolic and catabolic components of protein metabolism, including those related to transport and structural proteins, characteristic of hypothyroidism, contributes to an increase in the susceptibility of cells to external influences (impaired transmembrane exchange between the cell and tissue fluid). In addition, there is a decrease in tissue sensitivity to the effects of catecholamines, which aggravates the imbalance of metabolic processes.

Hydropic dystrophy revealed in animals in the experiment is essentially a reflection of disturbances in water-electrolyte and protein metabolism, resulting in a change in intracellular colloid-osmotic pressure. This pathological process occurs with damage to hepatocyte membranes and destabilization of organelle membranes, primarily with activation of lysosome hydrolytic enzymes and rupture of intramolecular bonds with the addition of water, therefore hydropic dystrophy should be considered as a manifestation of focal colliquative necrosis.

In addition to necrotic processes, inflammatory-proliferative processes are detected in the liver of experimental animals already on the 4th week after thyroidectomy. Such changes are observed in advanced stages of metabolic disorders characterized by disruption of cell homeostasis, and indicate the potential for the development of hepatitis and even cirrhosis only under the influence of endogenous factors.

The negative dynamics of the morphological picture of the rat liver, recorded under conditions of postoperative hypothyroidism for 8 weeks, characterized by further progression of dystrophic, necrobiotic and inflammatory-proliferative processes, convincingly proves the connection between the morphofunctional state of the liver and thyroid status.

Conclusions

1. An experiment with thyroidectomy in rabbits reproduces the morphological picture of fatty liver degeneration, corresponding to the main characteristics of changes inherent in non-alcoholic fatty liver disease, convincingly proving the relationship between the morphofunctional state of the organ and thyroid status.
2. In the early stages after the development of postoperative hypothyroidism in the liver of experimental animals, a combination of fatty and protein dystrophy of hepatocytes with manifestations of colliquative necrosis, hepatitis with minimal activity and initial signs of liver fibrosis occurs.
3. With increasing time after thyroidectomy, progression of dystrophic and necrotic processes in hepatocytes is observed, as well as the consistent appearance of signs of transformation of steatosis into steatohepatitis and steatofibrosis of the liver.
4. Experimental data on the structural features of the liver make it possible to clarify some morphological and pathogenetic aspects of the formation of fatty liver disease in primary (postoperative) hypothyroidism in order to optimize diagnostic and therapeutic approaches to the management of this category of patients.

Literature

1. Sh, O. F., Ikhtiyarova, G. A., Xudoyqulova, F. S., & Abdieva, N. U. (2023). EFFECTIVE AND EXPRESS METHOD FOR DIAGNOSING THE CERVICAL AND VAGINA DISEASES IN REPRODUCTIVE AGE WOMEN.
2. Abdieva, N. (2024). CONDITION OF BREAST TISSUEAND THE RISK OF DEVELOPING BREAST CANCER IN PATHOLOGICAL SECERATION SYNDROME. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(4), 161-170
3. Abdieva, N. (2024). THE ROLE OF GENETIC PREDICTORS OF METABOLIC DISORDERS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME CONCOMITANT WITH CERVICAL NEOPLASIA. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(3), 50-54.
4. Abdiyeva Nigina Ulugbekovna. (2024). ENDOSCOPIC-MORPHOLOGICAL CHARACTERISTICS OF BACKGROUND DISEASES OF THE CERVIX. *Лучшие интеллектуальные исследования*, *14*(4), 120–129.
5. Abdiyeva Nigina Ulugbekovna. (2024). ENDOSCOPIC-MORPHOLOGICAL CHARACTERISTICS OF BACKGROUND DISEASES OF THE CERVIX. *Лучшие интеллектуальные исследования*, *14*(4), 120–129. Retrieved from http://web-journal.ru/index.php/journal/article/view/3052.
6. Abdieva, N. U. (2024). THE ROLE OF CYTOKINES IN THE DEVELOPMENT OF CERVICAL ECTOPIA AND ITS PREVENTION. *Valeology: International Journal of Medical Anthropology and Bioethics (2995-4924)*, *2*(9), 112-119.
7. Farida Farkhodovna, K. ., Umida Rakhmatulloevna, N. ., & Mokhigul Abdurasulovna, B. (2022). ETIOLOGY OF CHRONIC RHINOSINUSITIS AND EFFECTIVENESS OF ETIOTROPIC TREATMENT METHODS (LITERATURE REVIEW). Новости образования: исследование в XXI веке, 1(4), 377–381. извлечено от https://nauchniyimpuls.ru/index.php/noiv/article/view/1367
8. Numonova, A., & Narzulayeva, U. (2023). EPIDEMIOLOGY AND ETIOPATHOGENESIS OF CHF. Наука и инновация, 1(15), 115-119.
9. Орипова Озода Олимовна, Самиева Гулноза Уткуровна, Хамидова Фарида Муиновна, & Нарзулаева Умида Рахматуллаевна (2020). Состояние плотности распределения лимфоидных клеток слизистой оболочки гортани и проявления местного иммунитета при хроническом ларингите (анализ секционного материала). Academy, (4 (55)), 83-86.
10. Umida Rakhmatulloevna Narzulaeva, & Xamrayeva Muxlisa Farmon qizi. (2023). ETIOPATHOGENESIS OF HEMOLYTIC ANEMIA. Web of Medicine: Journal of Medicine, Practice and Nursing, 1(1), 1–4. Retrieved from https://webofjournals.com/index.php/5/article/view/26
11. Нарзулаева, У. Самиева, Г., & Насирова, Ш. (2023). Гемореологические нарушения на ранних стадиях гипертензии в жарком климате. Журнал биомедицины и практики, 1(1), 221–225. https://doi.org/10.26739/2181 -9300-2021-1-31
12. Umida Rakhmatulloevna Narzulaeva. (2023). Important Aspects of Etiology And Pathogenesis of Hemolytic Anemias. American Journal of Pediatric Medicine and Health Sciences (2993-2149), 1(7), 179–182. Retrieved from https://grnjournal.us/index.php/AJPMHS/article/view/817
13. Нарзулаева, У. Р., Самиева, Г. У., & Насирова, Ш. Ш. (2021). ИССИҚ ИҚЛИМДА КЕЧУВЧИ ГИПЕРТОНИЯ КАСАЛЛИГИНИНГ БОШЛАНҒИЧ БОСҚИЧЛАРИДА ГЕМОРЕОЛОГИК БУЗИЛИШЛАР. ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ, 6(1).

14. Нарзулаева, У., Самиева, Г., Лапасова, З., & Таирова, С. (2023). Значение диеты в лечении артериальной гипертензии. Журнал биомедицины и практики, 1(3/2), 111–116. https://doi.org/10.26739/2181-9300-2021-3-98
15. Xalimova, Y. S. (2024). Morphology of the Testes in the Detection of Infertility. *Journal of Science in Medicine and Life*, *2*(6), 83-88.
16. Халимова, Ю. С. (2024). Морфологические Особенности Поражения Печени У Пациентов С Синдромом Мэллори-Вейса. *Journal of Science in Medicine and Life*, *2*(6), 166-172.
17. Salokhiddinovna, X. Y. (2023). Anemia of Chronic Diseases. *Research Journal of Trauma and Disability Studies*, *2*(12), 364-372.
18. Salokhiddinovna, X. Y. (2023). MALLORY WEISS SYNDROME IN DIFFUSE LIVER LESIONS. *Journal of Science in Medicine and Life*, *1*(4), 11-15.
19. Salohiddinovna, X. Y. (2023). SURUNKALI KASALLIKLARDA UCHRAYDIGAN ANEMIYALAR MORFO-FUNKSIONAL XUSUSIYATLARI. *Ta'lim innovatsiyasi va integratsiyasi*, *10*(3), 180-188.
20. Халимова, Ю. С. (2024). КЛИНИКО-МОРФОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ВИТАМИНА D В ФОРМИРОВАНИЕ ПРОТИВОИНФЕКЦИОННОГО ИММУНИТА. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(3), 86-94.
21. Saloxiddinovna, X. Y. (2024). CLINICAL FEATURES OF VITAMIN D EFFECTS ON BONE METABOLISM. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 90-99.
22. Saloxiddinovna, X. Y. (2024). CLINICAL AND MORPHOLOGICAL ASPECTS OF AUTOIMMUNE THYROIDITIS. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 100-108.
23. Saloxiddinovna, X. Y. (2024). MORPHOFUNCTIONAL FEATURES BLOOD MORPHOLOGY IN AGE-RELATED CHANGES. *Лучшие интеллектуальные исследования*, *14*(4), 146-158.
24. Saloxiddinovna, X. Y. (2024). CLINICAL MORPHOLOGICAL CRITERIA OF LEUKOCYTES. *Лучшие интеллектуальные исследования*, *14*(4), 159-167.
25. Saloxiddinovna, X. Y. (2024). Current Views of Vitamin D Metabolism in the Body. *Best Journal of Innovation in Science, Research and Development*, *3*(3), 235-243.
26. Saloxiddinovna, X. Y. (2024). MORPHOFUNCTIONAL FEATURES OF THE STRUCTURE AND DEVELOPMENT OF THE OVARIES. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(4), 220-227.
27. Saloxiddinovna, X. Y. (2024). Modern Views on the Effects of the Use of Cholecalciferol on the General Condition of the Bod. *JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH*, *3*(5), 79-85.
28. Abdurashitovich, Z. F. (2024). APPLICATION OF MYOCARDIAL CYTOPROTECTORS IN ISCHEMIC HEART DISEASES. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *39*(5), 152-159.
29. Abdurashitovich, Z. F. (2024). ASTRAGAL O'SIMLIGINING TIBBIYOTDAGI MUHIM AHAMIYATLARI VA SOG'LOM TURMUSH TARZIGA TA'SIRI. *Лучшие интеллектуальные исследования*, *14*(4), 111-119.

30. Abdurashitovich, Z. F. (2024). MORPHO-FUNCTIONAL ASPECTS OF THE DEEP VEINS OF THE HUMAN BRAIN. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(6), 203-206.
31. Abdurashitovich, Z. F. (2024). THE RELATIONSHIP OF STRESS FACTORS AND THYMUS. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(6), 188-196.
32. Abdurashitovich, Z. F. (2024). MIOKARD INFARKTI UCHUN XAVF OMILLARINING AHAMIYATINI ANIQLASH. *ОБРАЗОВАНИЕ НАУКА И ИННОВАЦИОННЫЕ ИДЕИ В МИРЕ*, *36*(5), 83-89.
33. Rakhmatova, D. B., & Zikrillaev, F. A. (2022). DETERMINE THE VALUE OF RISK FACTORS FOR MYOCARDIAL INFARCTION. *FAN, TA'LIM, MADANIYAT VA INNOVATSIYA JURNALI| JOURNAL OF SCIENCE, EDUCATION, CULTURE AND INNOVATION*, *1*(4), 23-28.
34. Toxirovna, E. G. (2024). QANDLI DIABET 2-TIP VA KOMORBID KASALLIKLARI BO'LGAN BEMORLARDA GLIKEMIK NAZORAT. *TADQIQOTLAR. UZ*, *40*(3), 48-54.
35. Toxirovna, E. G. (2024). XOMILADORLIKDA QANDLI DIABET KELTIRIB CHIQARUVCHI XAVF OMILLARINI ERTA ANIQLASH USULLARI. *TADQIQOTLAR. UZ*, *40*(3), 63-70.
36. Toxirovna, E. G. (2024). DETERMINATION AND STUDY OF GLYCEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH COMORBID DISEASES. *TADQIQOTLAR. UZ*, *40*(3), 71-77.
37. Tokhirovna, E. G. (2024). COEXISTENCE OF CARDIOVASCULAR DISEASES IN PATIENTS WITH TYPE 2 DIABETES. *TADQIQOTLAR. UZ*, *40*(3), 55-62.
38. Toxirovna, E. G. (2024). GIPERPROLAKTINEMIYA KLINIK BELGILARI VA BEPUSHTLIKKA SABAB BO'LUVCHI OMILLAR. *Лучшие интеллектуальные исследования*, *14*(4), 168-175.
39. Tokhirovna, E. G. (2024). MECHANISM OF ACTION OF METFORMIN (BIGUANIDE) IN TYPE 2 DIABETES. *JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH*, *3*(5), 210-216.
40. Tokhirovna, E. G. (2024). THE ROLE OF METFORMIN (GLIFORMIN) IN THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*, *4*(4), 171-177.
41. Qilichovna, A. M., & Nematilloyevna, X. M. (2024). METABOLIK SINDROMI VA QON BOSIMI BOR BEMORLARDA O'ZGARISH XUSUSIYATLARI BAHOLASH: Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari. *Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari*, *6*(4), 187-196.
42. Qilichovna, A. M., & Nematilloyevna, X. M. (2024). TIBBIYOT TILI HISOBLANMISH LOTIN TILINI SAMARALI O'RGANISH OMILLARI: Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari. *Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari*, *6*(4), 197-206.
43. Tog'aydullayeva, D. D. (2024). Embrional Davrda Gemopoez Va Unda Jigar Va Taloqning Roli. *Journal of Science in Medicine and Life*, *2*(6), 132-134.
44. Tog'aydullayeva, D. D. (2024). Occurrence of Combination Diseases in Ischemic Heart Disease and Metabolic Syndrome and their Diagnosis. *Journal of Science in Medicine and Life*, *2*(6), 126-131.
45. Tog'aydullayeva, D. D. (2024). Occurrence of Combination Diseases in Ischemic Heart Disease and Metabolic Syndrome and their Diagnosis. *Journal of Science in Medicine and Life*, *2*(6), 126-131.