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Development of Sarcoidosis after Successful Treatment of Itsenko–Cushing's Disease

Kurbanova Nozima Sabirdjanovna

Assistant of the Department of Endocrinology, Samarkand State Medical University

Vaxobov Sherzod Arslon o‘g‘li, Murtozov Bekzod Baxtiyorovich,
Musurmonov Baxtishod G‘ayrat o‘g‘li, Pardayev Lazizjon Ulfat o‘g‘li, Omonova Dilorom

Students of the Samarkand state Medical University

Abstract: Itsenko-Cushing's disease is a rare severe neuroendocrine disease caused by chronic overproduction of adrenocorticotropic hormone by a pituitary tumor. High concentrations of cortisol in the blood during endogenous hypercortisolism have an immunosuppressive and anti-inflammatory effect, as does systemic glucocorticosteroid therapy. This may help reduce the activity of the patient’s concomitant autoimmune inflammatory diseases. On the other hand, a decrease in cortisol levels during treatment of Cushing's disease may be associated with reactivation of the immune system, which increases the risk of relapse or onset of various autoimmune diseases. We present our own clinical case demonstrating the difficulties of diagnosing endogenous hypercortisolism in a young patient and the subsequent development of sarcoidosis that arose after successful surgical treatment of Itsenko-Cushing's disease.

Key points: sarcoidosis, hypercortisolism, Itsenko–Cushing's disease, glucocorticosteroids, Löfgren's syndrome, corticotropinoma.

RELEVANCE. Cushing's disease is a rare, severe neuroendocrine disease caused by chronic overproduction of adrenocorticotropic hormone (ACTH) by a pituitary tumor (corticotropinoma). Constant supraphysiological secretion of ACTH leads to excessive production of cortisol by the adrenal cortex and the development of endogenous hypercortisolism [1][2]. Characteristic symptoms of hypercortisolism include obesity, arterial hypertension, carbohydrate metabolism disorders, and decreased bone mineral density [3]. However, the combination of obesity, arterial hypertension and carbohydrate metabolism disorders occurs with a frequency of up to 20–30% in the general population as part of the metabolic syndrome [4–7]. The global community does not recommend screening for endogenous hypercortisolism in all individuals with obesity and diabetes mellitus due to the widespread prevalence of these diseases. However, the incidence of metabolic syndrome directly correlates with age, and the younger the patient with metabolic syndrome, the more justified is the exclusion of endogenous hypercortisolism. High concentrations of cortisol during endogenous hypercortisolism have immunosuppressive and anti-inflammatory effects, as well as therapy with systemic glucocorticosteroids. This can help reduce the activity of the patient’s concomitant autoimmune inflammatory diseases (for example, rheumatoid arthritis). On the other hand, a decrease in cortisol levels during treatment of Cushing's disease may be associated with reactivation of the immune system, which increases the risk of relapse or onset of an autoimmune disease. In the medical literature, there are few descriptions of cases of the onset or exacerbation of rheumatoid arthritis [8], atopic dermatitis, autoimmune thyroiditis [9], seronegative arthritis, retinal vasculitis [10], pemphigus [11], as well as sarcoidosis [12] after successful treatment of endogenous hypercorticism. We present our own clinical case demonstrating the difficulties of

diagnosing endogenous hypercortisolism in a young patient and the development of sarcoidosis that arose after surgical treatment of Itsenko-Cushing's disease.

CASE DESCRIPTION. Patient M. considered herself healthy until she was 28 years old, at this age her body weight was 80–85 kg with a height of 175 cm, body mass index (BMI) 27.1 kg/m², blood pressure 120–130/70–80 mm Hg ., menstruation began at the age of 12, the cycle was regular. At the age of 20 years and 24 years - pregnancies that occurred independently, ending in birth at term through the vaginal birth canal without complications.At the age of 28, during her third pregnancy, she gained 40 kg in weight, an increase in blood pressure to 150/120 mm Hg, excessive hair growth on the face and back, and the appearance of stretch marks on the abdomen and mammary glands were noted. During pregnancy I took enalapril 5 mg. By the end of pregnancy, the body weight was 120 kg with a height of 175 cm (BMI 39 kg/m²). The pregnancy ended with the urgent birth of a healthy child. After giving birth, the weight remained the same, the blood pressure remained elevated to 150/100 mm Hg, she periodically took enalapril 5 mg, and did not consult a doctor. At 30 years old, the patient noted that the menstrual cycle had not recovered after pregnancy, her body weight had increased by another 5 kg (BMI 40.8 kg/m2), and she was worried about recurrent furunculosis. I consulted a therapist with the above complaints, but no hormonal examination was carried out. A diagnosis of grade 3 obesity was made, all changes were interpreted as consequences of obesity, diet therapy was recommended - without any effect. Sibutramine was prescribed at a dose of 15 mg; within 3 months, while taking it, I lost 15 kg (body weight 110 kg), however, due to an increase in blood pressure, the drug was discontinued; after stopping the drug for 1 year, body weight gradually increased to 125–130 kg. At the age of 32, I consulted an endocrinologist at my place of residence. Based on the combination of obesity, arterial hypertension, menstrual irregularities, and hirsutism, endogenous hypercortisolism was suspected in a young patient. In addition, hormonal examination was indicated to exclude the secondary nature of arterial hypertension and clarify the endocrine causes of menstrual irregularities. Hormonal examination excluded thyroid dysfunction, hyperaldosteronism, acromegaly, hyperprolactinemia and pheochromocytoma; a significant increase in the excretion of free cortisol in daily urine was revealed - 635.2 nmol/day (100–379), which was the basis for a more thorough examination. At the age of 33, she was hospitalized in an endocrinology hospital; upon examination, her weight was 130 kg, height 175 kg, BMI 42.4 kg/m², subcutaneous fat was overdeveloped, redistributed according to the central type: waist circumference (WC) 144 cm, hip circumference (HC)) 124 cm, OT/VR 1.16. On the skin, attention was drawn to the presence of keloid scars at the site of boils; cyanotic striae on the anterior surface of the abdomen, mammary glands, 7–10 mm wide, up to 20 cm long; excessive growth of terminal type hair over the upper lip, chin, cheeks, linea alba, lower and upper extremities, sacrum, hirsut number on the Ferriman-Galwey scale 14 points (moderate hirsutism). Blood pressure is 180/120 mm Hg, heart rate is 82 beats/min, otherwise the circulatory system is without abnormalities. Examination of the respiratory, digestive and genitourinary systems was unremarkable. According to the algorithm for diagnosing endogenous hypercortisolism, at the first stage of the diagnostic search, to exclude/confirm hypersecretion of cortisol, 1 or 2 studies out of 3 possible are carried out: a study of the daily excretion of free cortisol in the urine, a small dexamethasone test, and determination of the level of free cortisol in saliva in the evening. The patient was found to have an increase in daily urinary excretion of free cortisol and no physiological suppression of cortisol production after taking 1 mg of dexamethasone (Table 1), which confirmed the presence of endogenous hypercortisolism and was the basis for continuing the examination. The first line of treatment for Cushing's disease is neurosurgical removal of the pituitary tumor [1], and therefore our patient underwent endoscopic transnasal adenomectomy. In the postoperative period, a decrease in blood pressure to 100–110/60–70 mmHg was noted. without taking antihypertensive therapy, muscle weakness, lack of appetite. The blood cortisol level in the morning was 64 nmol/l (119–618), which corresponded to secondary adrenal insufficiency, the development of which is a favorable prognostic marker for radical removal of corticotropinoma [1][2]. According to histological examination: basophilic pituitary adenoma with infiltration of adjacent glial tissue. According to immunohistochemical examination of the removed tumor tissue, the presence of corticotropinoma was confirmed: pronounced diffuse staining of the cell cytoplasm with antibodies

to ACTH was noted (Ki-67 expression was not assessed in this case). To compensate for adrenal insufficiency, the patient was prescribed hydrocortisone at a replacement dose of 15 mg/day (in 2 doses - 10 mg in the morning and 5 mg in the afternoon). While taking hydrocortisone, her health improved, her appetite returned to normal, weakness disappeared, and her blood pressure stabilized at 120/80 mmHg. Over the next 3 months, there was a regression of symptoms of hypercortisolism: body weight decreased by 15 kg, the redistribution of subcutaneous fat became more uniform, stretch marks decreased in size and paled, less intense hair growth on the face and body was noted, and the menstrual cycle was restored. The patient continued therapy with hydrocortisone at a dose of 15 mg/day. 4 months after surgical treatment, the patient's body temperature increased to 37.6–37.8°C, arthralgia began to bother her, general and muscle weakness, and nausea appeared. A few days after the increase in body temperature, a typical picture of erythema nodosum appeared on the skin of the legs, for which the patient was hospitalized in a therapeutic hospital. At the initial examination, height 175 cm, body weight 115 kg, BMI 38 kg/m², waist circumference 130 cm, hip circumference 131 cm, WC/VR 1; the skin is of normal color, in the left and right subclavian areas there are dense dark brown formations with a diameter of 0.5–1 cm, on the anterior surface of the abdomen there are light pink striae about 0.5 cm wide. Auscultation of the lungs - hard breathing, wheezing were not listened to. Examination of the circulatory, digestive and genitourinary systems was unremarkable. CT scan of the chest (Fig. 2, 3) revealed multiple small-focal opacities in the pulmonary parenchyma of lymphogenous distribution, a few reticular opacities, thickening of the peribronchovascular interstitium and enlargement of the lymph nodes of the mediastinum and roots of the lungs, i.e. a symptom complex highly specific for the acute form of sarcoidosis. Laboratory data confirmed the activity of systemic inflammation: erythrocyte sedimentation rate (ESR) 42 mm/h (0–20), the level of C-reactive protein (CRP) was increased to 7.23 mg/l (normal 0.01–4.99) . Blood calcium levels were within normal limits. Differential diagnosis was carried out with respiratory tuberculosis and lymphoproliferative diseases; the results of the examination of the patient and assessment of the course of the disease made it possible to exclude these diseases.

Considering the presence of typical clinical and radiological symptoms of the acute course of sarcoidosis and the lack of data for other possible causes of lung damage, morphological verification of the diagnosis was not performed. Complaints of muscle weakness and nausea in a patient after a recent adenomectomy for Cushing's disease were regarded as decompensation of adrenal insufficiency due to associated systemic inflammation. The dose of hydrocortisone was increased to 25 mg/day (10 mg in the morning, 10 mg at lunch and 5 mg in the evening), during which nausea and weakness stopped. Subsequently, over several months, gradual disappearance of erythema nodosum was noted. During dynamic CT of the chest, performed one year after the diagnosis of sarcoidosis, focal shadows and enlargement of the intrathoracic lymph nodes persisted but did not progress, which indirectly confirmed the diagnosis of sarcoidosis; There was a positive trend in ESR and CRP indicators. The patient continued taking hydrocortisone at a dose of 25 mg/day. Subsequently, communication with the patient was severed due to a change of residence.

DISCUSSION. Cushing's disease is characterized by increased levels of cortisol in the blood due to the synthesis of ACTH by the pituitary tumor, which is accompanied by the same biological effects as therapy with systemic glucocorticosteroids. High cortisol levels contribute to the development of immunosuppression and, in addition to increasing the risk of bacterial infections, can mask existing autoimmune diseases. With successful surgical treatment of Itsenko-Cushing's disease, a rapid decrease in cortisol levels occurs, which leads to a decrease in the negative effects of hypercortisolism, including a weakening of the anti-inflammatory and immunosuppressive effects. This, in turn, creates the preconditions for the emergence or progression of the patient's existing inflammatory immunopathological processes, including those that determine the development of sarcoidosis. Sarcoidosis is currently considered as a disease of unknown etiology, in which the formation of non-caseating granulomas occurs in various organs and tissues, activation of T-lymphocytes, macrophages and other immunocompetent cells, which is accompanied by increased synthesis of pro-inflammatory cytokines and chemokines. Sarcoidosis of the lungs and intrathoracic lymph nodes is most often detected. Sarcoidosis can debut as an acute inflammatory disease, for

example in the form of Löfgren's syndrome (erythema nodosum, arthritis, fever, enlarged intrathoracic lymph nodes). Systemic glucocorticosteroids, suppressing the inflammatory activity of the disease, are effective in the treatment of most cases of acute sarcoidosis, however, short-term use of these drugs is associated with an increased likelihood of relapse and the formation of a chronic progressive form of the disease, which, along with the known side effects of steroids, limits their use in Löfgren's syndrome [13][14]. The risk of relapse of sarcoidosis may be especially high during the first months after completion of a short course of glucocorticosteroid therapy, which is a consequence of the insufficient duration of the immunosuppressive effect of treatment, which did not lead to the disappearance, but only to a decrease in the activity of the self-inducing immunopathological process. Rebound hypocortisolism that occurs after cessation of systemic glucocorticosteroid therapy can also contribute to the activation of inflammation. In drawing clinical parallels between exogenous and endogenous hypocortisolism, it is worth mentioning the small amount of data currently available to support the above-mentioned concept. Cases described in the literature of the occurrence or exacerbation of various autoimmune diseases (thyroiditis, rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, seronegative arthritis, retinal vasculitis, Graves' disease, sclerosing pancreatocholangitis, atopic dermatitis, psoriasis, pemphigoid, vitiligo, as well as sarcoidosis [8 –12][15–18]) after removal of corticotropinoma, adrenal adenoma or ectopic adenoma remain few in number. These diseases debuted or worsened at different times (from 1 month to several years) after surgical treatment, so it is difficult to talk about a cause-and-effect relationship in all cases. The occurrence of acute and primarily chronic forms of sarcoidosis, according to data summarized by Noreña-Rengifo B. et al. (2019) [19], most often observed within 5 months after treatment, but in two cases these changes occurred after 12 and 72 months. In the case we presented, 4 months after successful neurosurgical treatment of Itsenko–Cushing's disease, the patient developed symptoms of acute sarcoidosis (Löfgren's syndrome). Hydrocortisone therapy, which the patient was receiving at that time (at a dose of 15 mg/day), could not prevent the development of systemic inflammation, since the dose of glucocorticosteroids approximately corresponded to the average daily need for these hormones and did not have immunosuppressive properties. Relief of symptoms of Löfgren's syndrome was observed when the dose of hydrocortisone was increased to 25 mg/day. This dose of glucocorticosteroids is higher than the doses that patients receive after surgical treatment of Itsenko-Cushing's disease for replacement purposes. However, in the present case, a high dose of glucocorticosteroids was due to the need for immunosuppressive therapy due to the development of sarcoidosis. Löfgren's syndrome involves the presence of a symptom complex including erythema nodosum, arthritis, fever and radiological changes in the form of hilar lymphadenopathy [20]. On CT of the chest in Löfgren's syndrome, it is possible to visualize damage to the pulmonary parenchyma due to its involvement in sarcoidosis. Along with the enlargement of intrathoracic lymph nodes characteristic of Löfgren's syndrome, a CT scan of the lungs in our patient revealed interstitial changes in the pulmonary parenchyma (fine-focal and reticular shadows) that did not disappear for more than 1 year, which indicates the transformation of the acute form of sarcoidosis into a chronic one [20] . Laboratory tests for Löfgren's syndrome reveal signs of increased acute-phase indicators of inflammation in the blood (ESR, CRP). Indicators of pulmonary function, pulmonary diffusion, and the results of exercise tolerance tests in Löfgren's syndrome, as a rule, correspond to normal values and are not a method for diagnosing the disease, so these studies were not carried out in this patient.

CONCLUSION. This observation complements the available information on extremely rare cases of the development of sarcoidosis after successful treatment of endogenous hypercortisolism. The results of observation of our patient confirm the concept of the immunosuppressive effect of high concentrations of endogenous cortisol on current or emerging autoimmune processes and the increased likelihood of developing a systemic inflammatory disease against the background of a decrease in blood cortisol levels to physiological levels.

References:

1. Shernazarov F, Tohirova J, Jalalova D. TYPES OF HEMORRHAGIC DISEASES, CHANGES

IN NEWBOENS, THEIR EARLY DIAGNOSIS. Science and innovation. 2022;1(D5):16-22.

2. Zhalalova DZ. The content of endothelin and homocysteine in blood and lacrimal fluid in patients with hypertensive retinopathy Web of Scientist: International Scientific Research Journal. ISSUE. 2022;2:958-963.
3. D.Jalalova, X.Raxmonov, F.Shernazarov. THE ROLE OF C-REACTIVE PROTEIN IN THE PATHOGENESIS OF VISUAL VASCULAR DISEASES IN PATIENTS WITH ARTERIAL HYPERTENSION. SAI. 2022;1(8):114-121. doi:10.5281/zenodo.7335637
4. D.Jalalova, X.Raxmonov, F.Shernazarov. SIGNIFICANCE OF ENDOTHELIAL DYSFUNCTION IN THE DEVELOPMENT OF RETINOPATHY IN PATIENTS WITH AH AND WAYS OF ITS CORRECTION. SAI. 2022;1(8):101-113. doi:10.5281/zenodo.7335616
5. Shernazarov F, Zuhridinovna JD. MICROCIRCULATION DISORDERS IN THE VASCULAR SYSTEM OF THE BULBAR CONJUNCTIVA IN THE INITIAL MANIFESTATIONS OF CEREBRAL BLOOD SUPPLY DEFICIENCY. Science and innovation. 2022;1(Special Issue 2):515-522.
6. D.Jalalova, N.Normatova, F.Shernazarov. GENETIC MARKERS FOR THE DEVELOPMENT OF DIABETIC RETINOPATHY. SAI. 2022;1(8):919-923. doi:10.5281/zenodo.7443019
7. Нарбаев А, Джураева З, Курбонова Н, Кувондиков Г, Давранова А, Содиков С. Особенности изучения многофакторного управления сахарным диабетом 2 типа. *Журнал проблемы биологии и медицины*. 2017;(4 (97)):78-79.
8. Хамраев Х, Содиков С, Хамраева Д, Собирова Д. Клинико-функциональное состояние печени у больных с сахарным диабетом. *ЖПБМ*. 2018;(1 (99)):189-191.
9. Содиков С, Каримова Н, Каримова З. Реабилитация больных пожилого возраста сахарным диабетом 2-типа. *ЖПБМ*. 2017;(4 (97)):105-106.
10. Хамидова МН, Исматова ИФ, Бердиеров ЖШ, Негматова ГШ, Даминов АТ. САХАРНЫЙ ДИАБЕТ И COVID-19. *Eurasian Journal of Medical and Natural Sciences*. 2022;2(13):190-204.
11. Шухратовна СД, Кахрамонович ЮУ, Махмудович КТ. Структурные изменения сосудисто-стромального комплекса щитовидной железы при эутиреоидной и токсических формах зоба. *Научный журнал*. 2019;(10 (44)):67-69.
12. Собиржоновна КН, Саллохидинович СС, Акбаровна ОМ. Эпидемиологический Статус И Факторы Риска Сахарного Диабета На Сегодняшний День. *Miasto Przyszłości*. 2023;32:212-219.
13. Salimova DE, Daminnov AT. A CLINICAL CASE BASED ON THE EXPERIENCE OF TREATING HYPERTENSION IN A PATIENT WITH TYPE 2 DIABETES MELLITUS, OBESITY AND VITAMIN D DEFICIENCY. *Educational Research in Universal Sciences*. 2023;2(12):150-154.
14. Takhirovich DA. ASSESSMENT OF HEARING FUNCTION IN INDIVIDUALS WITH TYPE 2 DIABETES. *American Journal of Pediatric Medicine and Health Sciences (2993-2149)*. 2023;1(9):124-126.
15. Qahramonov FA, Amirov BY, Tursunboyeva LI, Daminov AT. Autoimmun tireoidit bilan kasallangan bemorlardagi funksional buzilishlarning differensional diagnostikasida qalqonsimon bez zichligini aniqlash. *Science and Education*. 2023;4(3):82-86.
16. Nazira K, Siddikovna TG, Davranovna DA, Takhirovich DA, Tulkinovich OS. Cardiovascular complications in patients who have had covid on the background of diabetes mellitus 2. *1*. 2021;2(3):37-41.
17. Choriyev S, Gadoeva Z, Mardonova F, Jurakulov F, Hafizov S, Daminov AT. Changes in the

thyroid gland in the long period after a new coronavirus infection. *Science and Education*. 2023;4(12):102-106.

18. Kamalov T, Bahriev N, Yuldashev U, Sabirova D. CLINICAL AND HORMONAL CHARACTERISTICS OF PRIMARY HYPOGONADISM IN PRESCHOOL BOYS. *MedFarm*. 2019;10(9). doi:10.32743/2658-4093.2019.9.10.188
19. Daminov AT, Yuldoshev B, Murodullo I, Naimova N. CLINICAL CASE OF PRIMARY HYPOTHYROIDSIS. *Educational Research in Universal Sciences*. 2024;3(3 SPECIAL):135-138.
20. Daminov AT, Norkulov A, Turamudov R, Zayniddinova D. CLINICAL OBSERVATION OF SEVERE ITSENKO-CUSHING DISEASE. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):549-556.
21. Daminov A, Khaydarov O, Hasanova M, Abdukakhorova R. COMPLICATIONS OF GLUCOCORTICOID THERAPY IN PATIENTS DIABETES SURVIVED COVID-19. *Евразийский журнал медицинских и естественных наук*. 2023;3(4):197-200.
22. Takhirovich DA, Corners SJA, Shukhratovna NG, Shukhratovna SG, Zaynuddinovna MG. COURSE OF COVID-19 IN PATIENTS WITH DIABETES MELLITUS. *Web of Scientist: International Scientific Research Journal*. 2022;3(02):73-76. doi:10.17605/OSF.IO/B6FU2
23. Shukhratovna NG, Erkinovna SD, Suxrobovna XM, Ikromovna AZ. DIABETES MELLITUS, ISCHEMIC HEART DISEASE AND ARTERIAL HYPERTENSION. *PEDAGOG*. 2022;5(5):381-386.
24. O'g'li SOS, O'g'li RSO, Taxirovich DA. DIFFUZ TOKSIK BUQOQ. *Лучшие интеллектуальные исследования*. 2023;4(1):131-133.
25. Negmatova GS, Toshimova GT qizi, Abdiyev LS o'g'li, Daminov AT. EFFECTIVENESS OF CORRECTION OF DYSLIPIDEMIA IN ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1 SPECIAL):269-274.
26. G.Sh N, D.e S, Oybekovma XS, Qamariddinovna XA, O'g'li BJA. ENDOCRINE GLANDS, STRUCTURE, AGE FEATURES, FUNCTIONS. *PEDAGOG*. 2022;5(5):341-345.
27. Sobirjonovna KN. FACTORS DETERMINING THE CLINICAL SIGNIFICANCE OF DEPIPTIDYL PEPTIDASE 4 INHIBITORS IN THE TREATMENT OF PATIENTS WITH TYPE 2 DIABETES MELLITUS. *World Bulletin of Public Health*. 2022;8:67-72.
28. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. FAMILY FORM OF NEPHROGENIC X-LINKED DIABETES INSUPLIUS. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):703-710.
29. Daminov AT, Djabbarova D, Abduvohidova N, Furkatova D, Farxodova S, Ibragimova P. Features of bone tissue remodeling in patients with type 2 diabetes mellitus. *Science and Education*. 2023;4(11).
30. Daminov Abdurasul Takhirovich RSU. FEATURES OF THE CLINIC, REHABILITATION, TREATMENT OF AUTOIMMUNE THYROIDITIS IN THE CONDITIONS OF THE IODINE-DEFICIENCY REGION. Published online April 12, 2023. doi:10.5281/ZENODO.7820412
31. Shuhratovna NG, Shukhratovna SD. Features of the course of autoimmune hepatitis in children as a variant of autoimmune polyglandular syndrome. *Asia Journ of Multidimensi Resear (AJMR)*. 2020;9(7):89. doi:10.5958/2278-4853.2020.00228.1
32. Erkinovna SD. Features of the Course of Diabetes Mellitus Type 2 with Arterial Hypertension. *JournalNX*. Published online 2020:460-461.
33. Negmatova GS, Xakimova GD qizi, Abdiyev LS o'g'li, Daminov AT. FEATURES OF THE

RULES FOR INSULIN INJECTION TECHNIQUES IN ELDERLY AND SENILE PATIENTS WITH DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1 SPECIAL):259-264.

34. Takhirovich DA, Zafarovna KM, Isroilovna IS. FEATURES OF TYPE 1 DIABETES IN CHILDREN WHO HAVE COVID-19. *American Journal of Pediatric Medicine and Health Sciences (2993-2149)*. 2023;1(9):121-123.
35. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. FEATURES OF VITAMIN-D METABOLISM IN PATIENTS WITH DIABETIC NEPHROPATHY. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):681-689.
36. Xudoyorov S, Mirkomilova M, Burxonov U, Sayfieva G, Sheralieva N, Daminov AT. Fourniers gangrene in modern conditions. *Science and Education*. 2023;4(12):107-117.
37. Alimovna KN, Sobirjanovna KN, Abdurasul D, Tulkinovich OS. GROWTH HORMONE FOR THE TREATMENT OF HEREDITARY DISEASES IN CHILDREN. 10.
38. Negmatova .G.Sh, D.e S, Qizi MZO, Mannobovich MS, Orifjonovich MM. HERPETIC MENINGITIS. *PEDAGOG*. 2022;5(5):346-348.
39. Ahrorbek N, Myungjae L, Jungjae L, et al. Hormonal Regulation. *Texa Jour of Mutl Stud*. 2023;25:39-43.
40. Ismoilova SI. Impact of vitamin D deficiency on the risk of developing type 1 diabetes. *Science and Education*. 2023;4(3).
41. Даминов АТ, Хакбердиева В, Жаникулов С, Муродхонов С. КЛИНИЧЕСКИЙ СЛУЧАЙ ПЕРВИЧНЫЙ ГИПОТИРЕОЗ. *Educational Research in Universal Sciences*. 2024;3(3 SPECIAL):131-134.
42. Мизамова МАК, Эшпулатова ГНК, Эшмуродова ЗНК, Салимова ДЭ. Осложнения акромегалии, связанные со здоровьем, текущие и перспективные варианты лечения. *Science and Education*. 2023;4(4):187-195.
43. Takhirovich DA, Zafarovna KM, Isroilovna IS. NEVROLOGIYADA ENDOKRIN O`ZGARISHLAR. *SO‘NGI ILMIY TADQIQOTLAR NAZARIYASI*. 2023;6(12):417-422.
44. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. PRETIBIAL MYXEDEMA: PATHOGENETIC FEATURES AND CLINICAL ASPECTS. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):695-702.
45. Negmatova GS, Salimova DE. Qandli diabet 2-tipning arterial gipertenziya bilan birgalikda kechish xususiyatlari va ularni davolash usullari. *Science and Education*. 2023;4(2):516-519.
46. Taxirovich DA, J T, O E, I A. QANDLI DIABET-2 TIPI BOR BEMORLARDA COVID-19 KASALLIGINI GLUKOKORTIKOIDLAR BILAN DAVOLASH DINAMIKASINI BAHOLASH. *Gospodarka i Innowacje*. 2023;34:78-81.
47. G.Sh N, D.e S, Alisherovich BA, Erkin R is the son of S, Bektash U is the son of S. RELATIONSHIP BETWEEN DIABETIC NEPHROPATHY AND CARDIAC DISORDERS IN PATIENTS WITH TYPE 2 DIABETES. *PEDAGOG*. 2022;5(5):337-340.
48. Daminov AT, Sa’dullayeva SM qizi, Ismoilova SI qizi. SAMARQAND VILOYATIDA QANDLI DIABET ASORATLARI UCHRASH CHASTOTASI. *Educational Research in Universal Sciences*. 2024;3(3 SPECIAL):139-142.
49. Shukhratovna NG, Erkinovna SD, O‘g‘li IBI, Qizi ADD. THE ROLE OF GASTROINTESTINAL HORMONES IN THE PATHOLOGY OF THE DIGESTIVE SYSTEM. *PEDAGOG*. 2022;5(6):408-412.
50. Ulugbekovna NP, Bakhtiyorovna RI, Almosovich RA, Takhirovich DA. Thyroid Diseases during Pregnancy and their Impact on Maternal and Fetal Outcomes. *American Journal of*

Pediatric Medicine and Health Sciences (2993-2149). 2023;1(8):188-190.

51. Ismoilov JA, Egamberdiyeva YK kizi, Mahmamuradova NN, Daminov AT. TIME-RESTRICTED NUTRITION AS A NEW STRATEGY FOR THE THERAPY OF OBESITY AND COMORBID CONDITIONS. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):660-667.
52. Takhirovich DA, Nasimova D, Xushvaqtova B, Aliyeva N, Mirabror B. QUALITY OF MEDICAL CARE PROVIDED TO CHILDREN WITH TYPE 1 DIABETES MELLITUS. *PEDAGOG*. 2024;7(3):16-22.
53. Xoldorov X, Omonov F, Jumayev I, Daminov AT. TYPE 1 DIABETES AS A RISK FACTOR FOR BONE HEALTH IN CHILDHOOD. *Results of National Scientific Research International Journal*. 2023;2(8):131-135.
54. Daminov AT, Xurramova S, Islomov A, Ulashev M, Ikramov R, Mirzakhakimov P. Type 2 diabetes and bone mineral density in postmenopausal women. *Science and Education*. 2023;4(11).
55. Berkinov A, Safarov F, Tursunova S, Daminov AT. VITAMIN D STATUS IN SENIOR RESIDENTS OF SAMARKAND REGION. *Results of National Scientific Research International Journal*. 2023;2(8):136-140.
56. Taxirovich DA, Ulugbekovna RN, Abduxalimova YJ. STATUS AND PROSPECTS FOR THE FIGHT AGAINST DIABETES MELLITUS. *Educational Research in Universal Sciences*. 2024;3(1):4-9.
57. Davranova A. QALQONSIMON BEZ PATOLOGIYASI BO'LGAN O'SMIR QIZLARDA HAYZ DAVRINING BUZILISHINI O'ZIGA XOSLIGI. *Евразийский журнал медицинских и естественных наук*. 2022;2(8):113-115.