



TASHKENT MEDICAL ACADEMY

100 TMA
ANNIVERSARY



Journal of Educational and Scientific Medicine



Issue 3 (1) | 2023



OAK.UZ
Google Scholar

Science Education Commission of the Cabinet
Ministry of the Republic of Uzbekistan

ISSN: 2181-3175

Why Does Surgical Infection Often Affect Diabetics? Literature review of recent data

B. D. Babadzhanov, A. O. Okhunov¹, S. S. Atakov, U. K. Kasimov, I. S. Sattarov, A. R. Bobobekov, N. Sh. Khudaibergenova, K. J. Matmuratov, Sh. A. Khamdamov, Sh. A. Bobokulova, F. M. Abdurakhmanov, K. Kh. Boboev, D. A. Korikhonov

ABSTRACT

The review article is devoted to the problem of the relationship between diabetes mellitus and surgical infection. It is known that patients with diabetes mellitus are most susceptible to the development of surgical infection. Moreover, the infectious process can affect both soft tissues and internal organs. And any process in patients with diabetes mellitus associated with a surgical infection proceeds especially, aggressively, and requires an individual approach that goes beyond the approved standards. However, until now Issues related to the causes and consequences of such a medical phenomenon as surgical infection in patients with diabetes mellitus remain controversial. Giving a review of the literature, we tried to draw a line on these controversial issues and identify specific areas that are important from the point of view of the characteristics of the pathogenesis of the onset and course of the disease. We hope that this review, enriched with modern literature sources, will allow researchers to look at this problem through the realities that occur in clinical practice.

Keywords: Diabetes mellitus, surgical infection, pathogenesis

Demetris first proposed the term "diabetes" back in the II century BC. Such a term, meaning "to pass through", was designated in connection with the presence of pronounced, the most striking symptoms of this disease in the form of polyuria and polydipsia [97].

It was only in the second half of the XVII century that T. Willis proved that urine in such patients can taste different, in particular, it can be sweet and not sweet. It was in such cases that he added the word "mellitus" to the term "diabetes", which in the combined form of the disease acquired a reflection of the meaning of "diabetes sweet as honey" [63].

Thanks to the results of M.Dobson's research, which proved the nature of the origin of the sweet taste of urine, the disease is known today as diabetes mellitus [9].

Surgical infection is one of the most serious complications in patients with diabetes Mellitus, exceeding its mortality complications such as hypo/hyperglycemic coma, diabetic nephropathy, diabetic retinopathy and cardiopathy. According to a number of authors, mortality in surgical infection in patients with diabetes mellitus ranges from 32.4% to 49.2%, and in case of complica-

¹ Department of General and Pediatric Surgery, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: general-surgery@mail.ru

tion of the process with sepsis and septic shock from 80% and higher [3,5,12,31,59].



Frederick Bunting (right) with his assistant Charles Herbert Best. In 1921, they first received and practically used insulin. Photo. Toronto, c. 1924.

The presented data, according to a number of authors, are due to the peculiarity of the course of surgical infection in patients with diabetes mellitus. Surgical infection in combination with diabetes mellitus aggravates the pathological process due to the formation of a vicious circle consisting not only of the relationship between micro and macroorganisms, but also a number of complex molecular biochemical and metabolic processes [1, 2, 4, 6, 7, 13, 14, 18, 19].

Surgical infection in patients with diabetes has a negative effect on metabolism, which is one of the leading factors in the pathogenesis of the underlying disease. Such an effect aggravates insulin deficiency, increases oxidative processes and acidosis. In turn, such disorders, along with microcirculation disorders on the background of angiopathy, worsen the wound healing process, reduces regenerative abilities in the lesion. Such a mechanism of the course of the disease in patients with diabetes mellitus known today as the "mutual burden syndrome" [89].

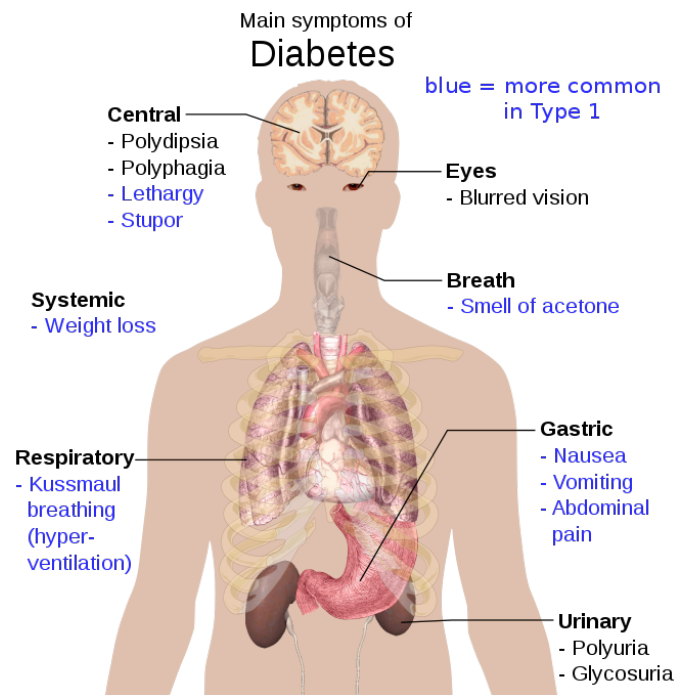
With the "mutual burden syndrome", significant violations in the immune defense occur in patients with diabetes mellitus [54].

The ongoing disorganization of metabolism, namely carbohydrate metabolism, leads to the development of hyperglycemia, glucosuria and a progressive decrease in glycogen in tissues [25]. In such cases, the liver, the main metabolic organ of a person and leading in the development of multiple organ failure syndrome, suffers first [28].

The occurring hypoinsulinemia slows down the process of synthesis of fatty acids from glucose and protein synthesis. Azoturia develops because of the progression of catabolic processes over anabolic ones in protein metabolism [26].

In general, the pathogenesis of reducing the resistance of the body of a diabetic patient before surgical infection can be explained by the following factors: hyperglycemia, decreased trophic cells and tissues, hypovitaminosis and electrolyte imbalance, decreased immunity, hypoxia in tissues because of microcirculation disorders [99].

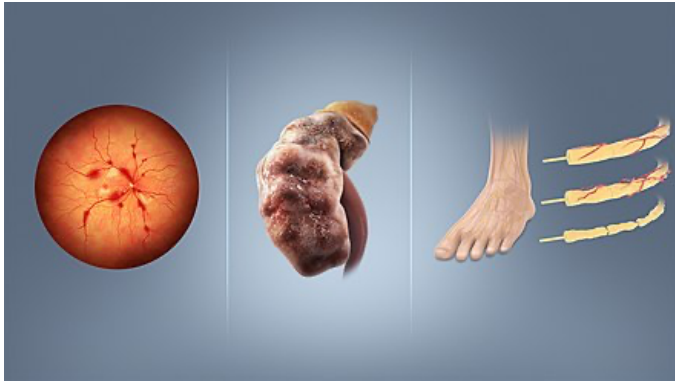
Stable hyperglycemia leads to an increase in glucose concentration in sweaty skin secretions, which accordingly creates a favorable breeding ground for microorganisms of any habitat category (both for pathogenic and conditionally pathogenic infections). Due to metabolic disorders and a decrease in glycogen in the tissues, the nutrition of cells and tissues of the body is disrupted. All this happens against the background of a violation of the immune mechanisms of the body's defense against infection. In addition to the above, tissue hypoxia due to a violation of the microcirculatory system also applies [43].



Overview of the most significant symptoms of diabetes

Internal organs in patients with diabetes are affected by surgical infection as well due to the presence of a number of characteristic pathological processes de-

scribed above. Such disorders are commonly referred to as stereotypical disorders of metabolic processes [94].



Retinopathy, nephropathy, and neuropathy are potential complications of diabetes

Intensive processes of glycogen breakdown in the liver and violation of the acid-base state led to the development of progressive acidosis. At the same time, surgical interventions, and especially the use of general anesthesia, aggravates the process of acidosis, since in patients with diabetes mellitus, the microcirculatory process in the tissues in the internal organs is initially disrupted [16, 50].

These disorders are aggravated with the development of blood loss of varying degree and with hypovolemic condition, which are one of the leading pathogenetic factors in the aggravation of the purulent-inflammatory process [60].

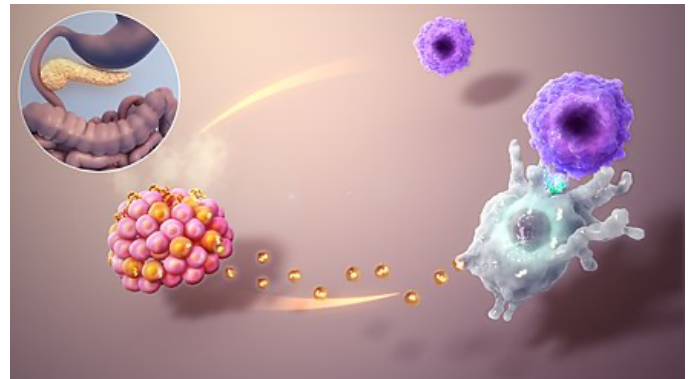
As for the development of electrolyte imbalance and acid-base state, it should be noted such a fact as its development in acute inflammatory diseases of internal organs in favor of acidosis. On the other hand, hyperglycemic state, and metabolic acidosis, against the background of diabetic nephropathy and renal insufficiency, can contribute to the development of water-electrolyte balance disorders. Aggravating factors may also be the consequences of the surgical pathology itself, for example, blood loss during operations, dehydration, due to indomitable vomiting, etc. [15].

Even in conditions of correction of hyperglycemia, in severe forms of diabetes mellitus, the need for oxygen by tissues and organs becomes prohibitively high. Prolonged increase in oxygen tension and its consumption increases vascular permeability due to the development of endothelial dysfunction in the capillary system of the microcirculatory bed. The destruction of the subendothelial space, due to the exudation of proteins and fatty acids, accelerates the process of atherogenesis, aggravat-

ing angiopathy, which is the leading factor determining the relationship between damage and tissue regeneration[11].

Developing acidosis in tissues and dehydration contribute to the accumulation of oxygen in hemoglobin, which leads to secondary hypoxia in tissues [62].

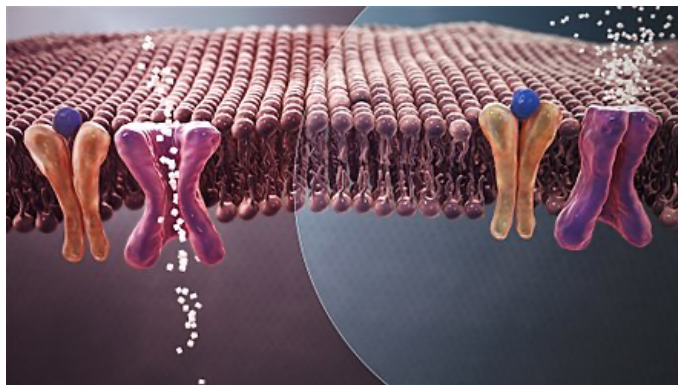
Patients with diabetes mellitus are characterized by the presence of blood clotting disorders in the direction of hypercoagulation. The main link in these pathological processes is a violation of the rheological properties of blood. Hyperglycemia and hyperlipidemia provoke an increase in the viscosity of blood plasma in diabetes mellitus. Accordingly, due to the slowing of blood flow, endovascular aggregation of platelets and other shaped elements, mostly erythrocytes, occurs. Aggregated shaped elements get along provoking the development of the syndrome of the same name. The level of fibrinogen in the blood increases against the background of a decrease in free heparin. There is a high-risk of developing thrombotic complications. At the same time, violation of the rheological properties of blood leads to disorganization of the microcirculatory bed and aggravation of trophic disorders in tissues and internal organs [17].



Autoimmune attack in type 1 diabetes.

In patients with diabetes mellitus, the protein composition of the blood changes. The pathogenesis of these disorders occurs because of a lack of insulin. The latter contributes to the depression of protein synthesis due to inhibition, against the background of increased catabolic processes, especially in skeletal muscles. The reserve sources of proteins are progressively depleted, which is inevitable against the background of the absence of carbohydrates in cells, stimulates an active oxidative process due to aminoacids. This process takes place to ensure normal energy aerobic metabolism. Inhibition of anabolic processes in patients with surgical infection on the background of diabetes mellitus is clinically mani-

festated by slowing down regenerative and strengthening neurobiotic processes [8].

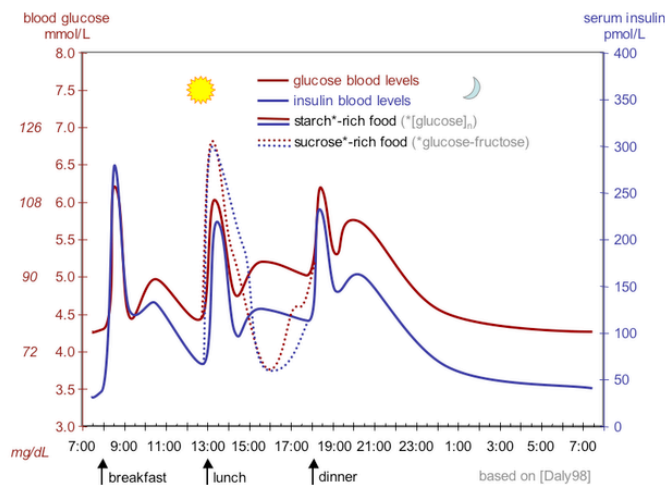


Reduced insulin secretion or weaker effect of insulin on its receptor leads to high glucose content in the blood.

In patients with diabetes mellitus, the hormonal balance is disturbed, between insulin and ant insulin hormones. This leads to disorders not only of carbohydrate and protein, but also of fat metabolism. In diabetes mellitus, the process of lipolysis prevails over lipogenesis, because of which the level of free fatty acids in the blood increases. The main part of fatty acids is oxidized in the liver to ketone bodies. The resulting ketosis, manifested by hyperketonemia and ketonuria, worsens metabolic acidosis and leads to dehydration of the body. The duration of this pathological process determines the timing of the development of fatty liver dystrophy. In other words, the freer fatty acids enter the liver, the earlier fatty hepatitis develops. The level of very low-density lipoproteins increases which are the basis of the pathogenetic link of thermogenesis diabetic angiopathy [58].

Surgical infection in patients with diabetes mellitus occurs against the background of pronounced immunological processes. Such disorders are characterized by both humoral and cellular imbalance of immunity. Glycosylated immune proteins lose their ability to bind antigens against the background of chemotaxis depression and phagocytosis by granulocytes. Violation of the functions of leukocytes occurs due to insufficient energy intake for them. In particular, ascorbate, which does not enter fibroblasts and leukocytes due to stable hyperglycemia. The activity of leukocytes decreases which does not allow them to penetrate into the lesion. In addition, a decrease in the activity of neutrophils and macrophages leads to a slowdown in the purification of non-viable and necrotic tissue elements of foci of destruction [51].

Regression of the purulent-inflammatory process is significantly hindered in patients with diabetes mellitus due to impaired proliferation of endotheliocytes. Slowing down the reorganization of connective tissue, scar formation and a decrease in the intensity of epithelialization, during surgical infection in patients with diabetes mellitus, also occurs as a result of a decrease in the synthesizing activity of cells responsible for the deposition of collagen and its strength. Such a pathological relationship is caused by a violation of cellular and humoral immunity, lengthening the phases of the regenerative process, translating an acute destructive process into a sluggish one [30].

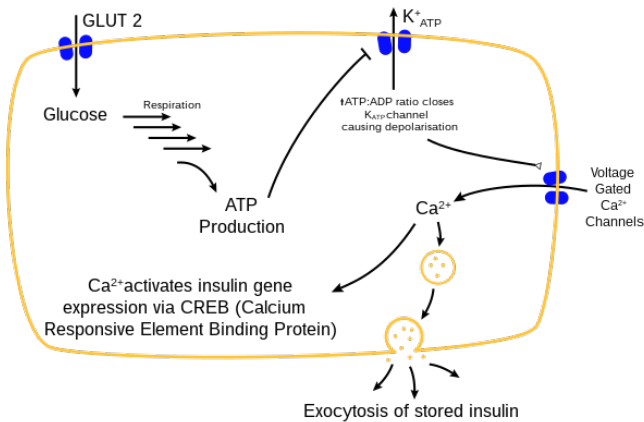


The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals. One of the effects of a sugar-rich vs a starch-rich meal is highlighted.

The course of surgical infection in patients with diabetes mellitus depends on various factors, both internal and external, which are based on hyperglycemia, violation of protein and carbohydrate metabolism, virulence of microbial flora. Changes in the rheological properties of blood, slowing down the rate of wound healing, disruption of collagen synthesis, suspension of contraction of the injury zone, violation of phagocyte chemotaxis - all this determines the features of the course of surgical infection in patients with diabetes mellitus [29].

Inhibition of phagocytic and bactericidal activity of granulocytes, inhibition of neutrophil migration through the vascular wall and inhibition of chemotaxis, reduction of the ability of neutrophils to adhere to the vascular endothelium in the area of injury - all this forms the basis of mechanisms for reducing the phagocytic function of

neutrophils, as well as their ability to kill microorganisms [57].



Mechanism of insulin release in normal pancreatic beta cells. Insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose.

An increase in blood viscosity and the tendency of erythrocytes to aggregation significantly affect the course of the wound process. All this happens due to changes in the electrostatic properties of red blood cells and a decrease in their deformation properties. Glycosylated hemoglobin is formed, which forms a stronger bond with oxygen and promotes the development of tissue hypoxia, especially in the affected area of surgical infection. A special inflammatory process is formed that characterizes the predominance of the necrotic process over the purulent one. The formation of extensive foci of necrosis does not tend to be limited and proceeds against the background of a violent general reaction [56].

Metabolic disorders and disorganization of the microcirculatory bed led to an elongation of both phases of the course of the wound process. The purulent-inflammatory process is widespread and is characterized by a lesion of the regional lymphatic system[101].

With the development of the exudation phase, the migration of leukocytes to the focus of the inflammatory process slows down. There is insufficient purification of the inflammatory focus from necrotic tissues due to the low activity of neutrophils and macrophages. There is an accumulation of potassium salts in the cells, which disrupt chemotaxis and reduce the oxygen demand by leukocytes. In addition to this, hypoglycemia, ketoacidosis, and the above metabolic factors, during the exudation phase, reduce the macrophage activity of leukocytes. At the same time, during the transition of the inflammatory process to the next phase, the formation of both

connective tissue and angiogenesis slows down. The process of reorganization of connective tissue, scar formation and epithelialization proceed significantly slowly [24].

A characteristic feature of the course of the purulent-inflammatory process in patients with diabetes mellitus is the aggravation of the local inflammatory process due to ketoacidosis, energy imbalance, immune disorders and hemorheology. There are shifts in the hemostasis system to the extent that may exceed the compensatory response reserves. They are simply depleted due to the effects of catabolism products, metabolites, microbes and their waste products, as well as excessively high activity of kinins. The resulting vicious circle leads to insulin deficiency, exacerbating diabetes mellitus. The activity of proteolytic enzymes leads to the breakdown of tissues and stimulates the necrobiotic process. In such conditions, even a minor purulent-inflammatory focus can cause decompensation of diabetes mellitus against the background of inflammatory acidosis and destruction of insulin by proteolytic enzymes [10].

Thus, a number of metabolic processes that aggravate the course of the underlying disease and create conditions for a more severe variant of the destructive process determines the course of the purulent-inflammatory process in patients with diabetes mellitus. Clinicians designate these changes as they are active course of the purulent-inflammatory process, which determines the features of the course of surgical infection in patients with diabetes mellitus.

Conflict of Interest - The authors state that they have no conflict of interest.

Financing - independent.

REFERENCES:

1. Anaerobic infection in surgical practice: Methodological manual / R. G. Avanesyan, Y. A. Spesivtsev, M. V. Lyubimov, et al. – St. Petersburg: St. Petersburg State Pediatric Medical University of the Ministry of Health of the Russian Federation, 2021. – 28 p.
2. Biochemical parameters of blood serum of patients with periprosthetic infection of the hip joint in carbohydrate metabolism disorders / E. L. Matveeva, A. G. Gasanova, A. M. Ermakov // Genius of orthopedics. – 2022. – T. 28, No 2. – P. 200-203.
3. Eryukhin I. A., Shlyapnikov S. A. Sepsis and diabetes: pathogenetic parallels and crossroads. – 2008. – V. 8, No 1. – P. 223-229.
4. Zemlyanoy A. B., Zelenina T. A., Salukhov V. V. Parallels of antibiotic resistance features of diabetic foot syndrome

- infections at inpatient and outpatient stages of treatment. – 2022. – T. 16, No 6. – P. 234-242.
5. Changes in the structure of pathogens of surgical infection in patients with diabetes mellitus depending on the strategy of their treatment / R. P. Terekhova, Y. S. Paskhalova, G. E. Skladan, et al. // Wounds and wound infections. Journal named after prof. B.M. Kostyuchenko. – 2015. – V. 2, No 3. – S. 22-29.
 6. Infection in vascular surgery and metabolic syndrome: coincidence or relationship? / N. I. Glushkov, M. A. Ivanov, A. S. Artemova, et al. // Cardiology and cardiovascular surgery. – 2017. – T. 10, No 1. – S. 56-61.
 7. Knyazevskaya E. E., Yakhina V. V. Endovascular technologies in the treatment of patients with neuroischemic form of diabetic foot syndrome // Bulletin of medical Internet conferences. – 2014. – V. 4, No 4. – P. 430.
 8. Korobova V. Yu., Omelchuk K. L. Metabolic disorders in gestational diabetes mellitus // Student Science - 2016: Materials of the forum dedicated to the 80th anniversary of the birth of the Honored Scientist of the Russian Federation, Professor A. V. Papayan, St. Petersburg, April 15–16, 2016. – St. Petersburg: St. Petersburg State Pediatric Medical University, 2016. – P. 78.
 9. Kostyakov S.E., Demyanenko A.N. Historical prerequisites for the discovery of insulin. Bulletin of the Smolensk State Medical Academy. – 2013. – Volume. 12, № 3. – P. 90-97.
 10. Morphological changes in periodontal tissues in simulated diabetes mellitus in the experiment / V. I. Beda, E. V. Kuzenko, S. M. Germanchuk // Dentistry. Aesthetics. Innovation. – 2017. – V. 1, No 2. – P. 259-266.
 11. Metabolic disorders in diabetes mellitus / L. Novikova, T. N. Semenova, K. A. Pashkov, D. Yu. – 2022. – № 22(417). – P. 567-571.
 12. Experience in the treatment of purulent surgical infection in patients with diabetes mellitus / M. M. Magomedov, M. G. Nakhbarova, G. M. Gamzatov, Z. A. Amirlaeva // Modern aspects of surgical endocrinology: Proceedings of the XXV Russian symposium with the participation of therapists-endocrinologists, dedicated to the 85th anniversary of the clinics of the Samara State Medical University, Samara, October 01–03, 2015 / Under the general editorship of I.V. Makarov, T.A. Britvin. – Samara: Limited Liability Company "Etching", 2015. – P. 446-450.
 13. Features of diagnostics, surgical tactics and restorative operations for necrotizing soft tissue infections in patients with diabetes mellitus / M. Kh. Nabiev, Sh. Yusupova, A. T. Azimov, T. B. Boronov // Bulletin of Avicenna. – 2018. – T. 20, No 1. – P. 97-102.
 14. Pathogen-specific molecular imaging and molecular testing methods in the prognosis of the complicated course of diabetic foot syndrome, amputation risk and patient survival / M. A. Zorkaltsev, V. D. Zavadovskaya, T. V. Saprina, et al. // Bulletin of Siberian Medicine. – 2022. – T. 21, No 3. – P. 166-180.
 15. Poteshkina N. G., Mirina E. Yu. Correction of metabolic disorders in type 2 diabetes mellitus // breast cancer. – 2010. – T. 18, No 9. – P. 608-612.
 16. Starostina E. G. Acute decompensation of metabolism in diabetes mellitus. Problems of endocrinology. – 1998. – T. 44, No 6. – S. 32-39.
 17. Fedoseev E. N., Shapovalova O. O., Shamrova E. A. Experimental study of sorption properties of erythrocytes. Medical Sciences. – 2019. – № 1. – S. 71-75.
 18. Khalikova O. M., Kasymov U. K. Features of diagnostics of surgical infections of soft tissues in diabetes mellitus // Young scientists in solving actual problems of science: Proceedings of the VIII International Scientific and Practical Conference., Vladikavkaz, June 22, 2018. – Vladikavkaz: "Vesta", 2018. – P. 165-167.
 19. Characteristics of background pathology in patients with inflammatory diseases of the face and neck against the background of diabetes mellitus / M. A. Gubin, S. V. Ivanov, A. L. Gromov, N. Yu. – 2017. – № 2. – S. 45-48.
 20. A combination of diabetes mellitus and acute purulent-destructive lung diseases solving the problems of diagnosis and treatment. / A.O. Okhunov, Sh.A. Khamdamov // World Bulletin of Public Health, 2023, #19, P.127-135. Retrieved from <https://scholarexpress.net/index.php/wbph/article/view/2149>
 21. A new method of treating pneumonia complicated by an abscess in patients after COVID-19 / A.K. Shadmanov, J. Mirshaval, A.O. Okhunov, Sh.A. Bobokulova // Journal of Education and Scientific Medicine, 2023, 1(2), P. 2-9. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/421>
 22. About predatory publishing – what it is and how to recognize it? / F.L. Azizova, A.O. Okhunov, N.Sh. Khudaibergenova // Journal of Educational and Scientific Medicine – 2023 – V.1, #3. – P.45-55.
 23. Aktivnost monoooksigenaznoy i nitregicheskoy sistem v mikrosomax pecheni pri deystvii na organizm induktorov i ingibitorov lekarstvennogo metabolizma / S.A.Sayfulaeva, A.O.Oxunov, A.S. Komarin, et al. // Vrach-aspirant - 2012 - # 59 (4). - S. 73-78. [in Russian]
 24. American Diabetes Association. Diagnosis and classification of diabetes mellitus. // Diabetes Care. – 2009. - #32. – P.62-67.
 25. Bailes B.K. Diabetes mellitus and its chronic complications. // AORN J. – 2002. - #76(2). – P.266-276.
 26. Bielka W., Przekaz A., Pawlik A. The Role of the Gut Microbiota in the Pathogenesis of Diabetes. // Int. J. Mol. Sci. – 2022. - #23(1). – P.480.
 27. Bobokulova Sh.A., Okhunov A.O. Acute purulent-destructive lung diseases as consequences of endotheliitis after COVID-19. Journal of Education and scientific medicine, 2022, 2(3), 56-61. Retrieved from <https://journal-s.tma.uz/index.php/jesm/article/view/360>

28. Chromogranin A and its role in the pathogenesis of diabetes mellitus. / Z. Herold, M. Doleschall, A. Kovessdi, et al. // *Endokrynol. Pol.* – 2018. - #69(5). – P.598-610.
29. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: part I. / F. Paneni, J.A. Beckman, M.A. Creager, F. Cosentino // *Eur. Heart J.* – 2013. - #34(31). – P.2436-2443.
30. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. / Y. Li, Y. Liu, S. Liu, et al. // *Signal Transduct. Target. Ther.* – 2023 - #8(1). – P.152.
31. Diagnosis of infection in the foot in diabetes: a systematic review. / E. Senneville, B.A.Lipsky, Z.G.Abbas, et al. // *Diabetes Metab. Res. Rev.* – 2020. - #36. – P. 3281.
32. Differential diagnosis of necrotizing fasciitis. / A.O. Okhunov, D. N. Korikhonov, et al. // *British Medical Journal* – 2023 - #3.1.
33. Differentiated approaches to the diagnosis and treatment of acute lung abscesses in patients who have had COVID-19. / A. O. Okhunov, Sh. A. Bobokulova // *British Medical Journal* – 2023 - #3.1.
34. Difficult aspects of treatments patients with acute lung abscesses who survived COVID-19 / S.S. Atakov, Sh.A. Bobokulova, U.K. Kasimov, et al. // *Journal of Education and scientific medicine, 2023, (1), 57-60.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/292>
35. Effektivnost primeneniya tunnelnoy abdominoplastiki v sochetanii s liposaktsiey pri esteticheskoy xirurgicheskoy korrektsii razlichnykh variantov deformatsii peredney bryushnoy stenki / X.F. Asadov, A.O. Oxunov, D.A. Oxunova, et al. // *Vrach-aspirant* – 2012 - № 50 (1.1), S. 199-205. [in Russian]
36. Endovascular methods for correcting angiopathy of the diabetic foot syndrome in patients after COVID-19 / Okhunov A.O. // *16th European Diabetes and Endocrinology Congress* – 2022, P.12-15.
37. Errors and causes of ineffectiveness of primary operations for phlegmons of the face and neck. / A.O.Okhunov, K.Kh.Bobojev, O. A.Bobokhodjaev, et al. // *Journal of Education and Scientific Medicine, 2023, 1(2), P. 30-38.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/422>
38. Etiological factors leading to purulent mediastinitis. / A.O. Okhunov, & K.Kh. Bobojev. // *World Bulletin of Public Health, 2023, 18, 118-125.* Retrieved from <https://scholar-express.net/index.php/wbph/article/view/2081>
39. Etiology and pathogenesis of primary purulent mediastinitis. / A. O. Okhunov, K. Kh Bobojev. // *British Medical Journal* – 2023 - #3.1.
40. Evaluation of the effectiveness of various methods of treatment of acute purulent-destructive lung diseases in patients with diabetes mellitus. / A.O. Okhunov, Sh. A. Khamdamov // *British Medical Journal* – 2023 - #3.2.
41. Fargals in the treatment of necrotic infections of soft tissues on the background of diabetes mellitus / Kasimov U.K., et al. // *Open Access Repository* – 2023 - 4.02: 63-73.
42. Features of the educational program in foreign universities: the example of the medical college of the University of Central Florida, USA / A.K. Shadmanov, Z Kawell, A.O. Okhunov // *Journal of Educational and Scientific Medicine* – 2023 – V.2, #2. – P.2-9. Publisher: <https://journals.tma.uz/index.php/jesm/article/view/440>
43. Gomes B.F., Accardo C.M. Immunoinflammatory mediators in the pathogenesis of diabetes mellitus. // *Einstein (Sao Paulo).* – 2019. - #17(1). – P.4596.
44. How does lipid peroxidation affect the development of pneumosclerosis: experimental justification / I. Marupov, Sh. Bobokulova, A. Okhunov, et al. // *Journal of Education and Scientific Medicine, 2023, 1(1), P. 2-7.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/368>
45. How to treat acute purulent-destructive lung diseases if they are sequels to COVID-19: problems and ways to solve them / Sh.A. Bobokulova, Sh.A. Khamdamov, D. Korikhonov, et al. // *Journal of Education and Scientific medicine, 2023, 1(1), 47-55.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/394>
46. Improvement of treatment methods of acute purulent destructive pulmonary diseases considering the non-respiratory function of lungs. / A. O.Okhunov, Sh. A. Bobokulova // *湖南大学学报 (自然科学版) 48.8 (2021): P. 313-319.*
47. Influence of granulocyte-colony-stimulating factor on the cytological picture of the wound in patients with purulent-inflammatory diseases of soft tissues on the background of diabetes mellitus. / Okhunov A. // *Research Square; 2022.* DOI: 10.21203/rs.3.rs-2304237/v1.
48. Intensivnost perekisnogo okisleniya lipidov v legkix pri eksperimentalnom pnevmoskleroze / I.A. Ziyakulov, A.O. Oxunov, O.T. Sattarov, A.S. Komarin // *Vrach-aspirant.* – 2011. - №47 (4.2). - S.330-335. [in Russian]
49. Intestinal peptides and their main role in the pathogenesis of type 2 diabetes mellitus / P. Azizova, Sh. Razzakov, et al. // *Journal of Education and scientific medicine, 2022, #2(3), P.95-100.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/362>
50. Jin Q., Ma R.W. Metabolomics in Diabetes and Diabetic Complications: Insights from Epidemiological Studies. // *Cells.* – 2021. - #10(11). – P.2832.
51. Kaur R., Kaur M., Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: molecular insights and therapeutic strategies. // *Cardiovasc. Diabetol.* – 2018. - #17(1). – P.121.
52. Khamdamov Sh.A., Okhunov A.O. Immediate results of endovascular and little invasive methods of treatment of lung purulent diseases with diabetes mellitus. *Journal of Education and scientific medicine, 2022, (2), P. 63-65.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/274>
53. Kliniko-morfologicheskaya xarakteristika novogo sposoba modelirovaniya ostrogo gnoyno-destruktivnogo zabolovaniya legkix / A.O.Oxunov, Sh.A. Xamdakov et al. //

- Vestnik nauki i obrazovaniya - 2018. - № 9 (9 (45)), S. 89-93. [in Russian]
54. Lalla E., Papapanou P.N. Diabetes mellitus and periodontitis: a tale of two common interrelated diseases. // *Nat. Rev. Endocrinol.* – 2011. - #7(12). – P.738-748.
55. Learning curves and impact of previous operative experience on performance on a virtual reality simulator to test laparoscopic surgical skills / T.P. Grantcharov, L. Bardram, P. Funch-Jensen, et al. // *The American Journal of Surgery.* – 2003 - #185 (2) - P:146–149.
56. Linking RAGE and Nox in diabetic micro- and macrovascular complications. / C. Koulis, A.D. Watson, S.P. Gray, et al. // *Diabetes Metab.* – 2015. - #41(4). – P.272-281.
57. Lower extremity arterial disease in patients with diabetes: a contemporary narrative review. / M. Nativel, L. Potier, L. Alexandre, et al. // *Cardiovasc. Diabetol.* – 2018. - #17(1). – P.138.
58. Macrovascular Complications of Type 2 Diabetes Mellitus. / M. Viigimaa, A. Sachinidis, M. Toumpourleka, et al. // *Curr. Vasc. Pharmacol.* – 2020. - #18(2). – P.110-116.
59. Management of necrotizing fasciitis in diabetic patients. / A. Gürlek, C. Firat, A.E. Oztürk, et al. // *J. Diabetes Complications.* – 2007. - #21(4). – P.265-271.
60. Meta-Inflammation and Metabolic Reprogramming of Macrophages in Diabetes and Obesity: The Importance of Metabolites. / S. Russo, M. Kwiatkowski, N. Govorukhina, et al. // *Front Immunol.* – 2021. - #12. – P. 746.
61. Metabolicheskaya aktivnost mikrosom slizistoy obolochki kulti jeludka posle rezektsii porajennogo yazvennim protsessom uchastka gastroduodenalnoy zoni / A.O. Oxunov, S.A. Sayfullaeva, I.S. Sattarov et al. // *Vrach-aspirant* - 2010. - Tom. 39. - №2.1. - S.131-140. [in Russian]
62. Metabolomics Signatures in Type 2 Diabetes: A Systematic Review and Integrative Analysis. / Y. Sun, H.Y. Gao, Z.Y. Fan, et al. // *J. Clin. Endocrinol. Metab.* – 2020. - #105(4). – P.240.
63. Milestones in the history of diabetes mellitus: The main contributors. / M.Karamanou, A.Protoyerou, G.Tsoucalas, et al. // *World J. Diabetes.* – 2016. - #7(1). – P.1-7.
64. Morphological aspects of wounds in patients with purulent inflammation of soft tissues in diabetes mellitus and under the influence of granulocyte-colony-stimulating factor / U.I. Pulatov, R.I. Israilov, A.O. Okhunov et al. // *Journal of Education and scientific medicine, 2022, 2(3), 43-50.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/363>
65. Morphological characteristics of a new experimental model of chronic renal failure in the background of diabetic nephropathy. / Shadmanov A.K., Okhunov A.O., Abdurakhmanov F. M. // *Journal of Education and scientific medicine, 2022, 2(3), 68-76.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/364>
66. Morphological Characteristics of Intestinal Vessels of Animals with an Experimental Model of Diabetes Mellitus Type 2 Complicated by Microangiopathy. / Okhunov A., et al. // *Indian Journal of Forensic Medicine & Toxicology* 14.4 (2020): P. 7348-7353.
67. Necrotizing fasciitis: difficulties on the way to diagnosing tactics. / Korikhonov D., Boboev K., Abdurakhmanov F. // *Journal of Education and Scientific Medicine, 2023, 2(1), P. 28-34.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/389>
68. Nerespiratornaya funktsiya legkix pri ix gnoynovospalitelnyx zabolevaniyax / O.T.Sattarov, Yo.X.Azizov, A.O. Oxunov, et al. // *Vrach-aspirant.* - 2011. - №44 (1.1). - S.205-210. [in Russian]
69. New approaches to improve autodermaplasty results / F.M. Abdurakhmanov, Sh.A. Khamdamov, D. Korikhonov, et al. // *Journal of Education and Scientific Medicine, 2(1), P. 22-27.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/387>
70. New approaches to treating lung abscesses as covid-19 sequels. / Okhunov A.O, Bobokulova Sh. A. // *World Bulletin of Public Health, 2023 - #19, P.101-107.* Retrieved from <https://scholarexpress.net/index.php/wbph/article/view/2281>
71. New pedagogical technologies in teaching surgery / A.O. Okhunov, N.Sh. Khudaibergenova, S.S. Atakov, et al. // *Journal of Education and scientific medicine, 2022, 1(3), 8-11.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/316>
72. Okhunov A. Influence of granulocyte-colony-stimulating factor on the cytological picture of the wound in patients with purulent-inflammatory diseases of soft tissues on the background of diabetes mellitus. *Research Square; 2022.* DOI: 10.21203/rs.3.rs-2304237/v1.
73. Okhunov A.O. Endovascular methods for correcting angiopathy of the diabetic foot syndrome in patients after COVID-19 // *16th European Diabetes and Endocrinology Congress – 2022, P.12-15.*
74. Okhunov A.O. Prediction and prevention of sepsis in patients with necrotizing fasciitis on the background of diabetes mellitus // *42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA, 2023, April 11-14, P.39.*
75. Okhunov A.O. SMART TEXTBOOK: a New Level in the Modern Educational Process. *Journal of Education and scientific medicine, 2022, 2(3), 11-18.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/337>
76. Okhunov A.O., Abdurakhmanov F.M. Prolonged intraarterial catheter therapy for diabetic gangrene of the lower limb // *42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA April 11-14, 2023 – P.38*
77. Okhunov A.O., Boboev K.Kh., Bobokhodjaev O. A. Errors and causes of ineffectiveness of primary operations for phlegmons of the face and neck. // *Journal of Education and Scientific Medicine, 2023, 1(2), P. 30-38.* Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/422>

78. Optimization of the educational process at the Department of general surgery / A.O. Okhunov, N.Sh. Khudayberganova, U.K. Kasimov, et al. // Journal of Education and scientific medicine, 2023, (1), P. 98-101. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/303>
79. Optimizatsiya rezultatov lecheniya gnoyno-nekroticheskix porajeniy myagkix tkaney na fone saxarnogo diabeta / B.D. Babadjanov, U.K. Kasimov, J.X. Otajonov, et al. // Vrach-aspirant. - 2009. - №5. - S.375-382. [in Russian]
80. Otsenka effektivnosti G-KSF (Filgrastim) pri lechenii gnoyno-vospalitelnix porajeniy myagkix tkaney na fone saxarnogo diabeta / U.K.Kasimov, B.D.Babadjanov, A.O.Oxunov, et al. // Vrach-aspirant – 2012 - № 50 (1.1). - S. 185-194. [in Russian]
81. Otsenka endotelialnoy disfunktsii pri diabeticheskoy angiopatii / I.A. Ziyakulov, A.O. Oxunov, O.T. Sattarov, et al. // Vrach-aspirant. - 2011. - №46 (3). - S.46-53. [in Russian]
82. Play to Become a Surgeon: Impact of Nintendo Wii Training on Laparoscopic Skills / D. Giannotti, G. Patrizi, G. Di Rocco, et al. // PLOS ONE. – 2013 - #8 (2) – P:57372.
83. Possibilities of modern physical methods of antisepsis in the treatment of acute lung abscesses in patients with diabetes mellitus / Sh. A. Khamdamov, F.M. Abdurakhmanov, Sh.A. Bobokulova, et al. // Journal of Education and Scientific Medicine, 2023, 1(1), P. 37-46. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/395>
84. Principles of diagnosis and treatment of acute purulent-destructive lung diseases. / A.O. Okhunov, K.Kh. Boboev, A.F. Valijonov, et al. // World Bulletin of Public Health, 2022, #7, 1-2. Retrieved from <https://scholarexpress.net/index.php/wbph/article/view/526>
85. Programma prognozirovaniya razvitiya tyajelogo sepsisa na fone nekroticheskogo fastsiita / O.T.Sattarov, A.O.Oxunov, Yo.X. Azizov, et al. // Vrach-aspirant. - 2011. - № 48 (5.2). - R. 314-322. [in Russian]
86. Prolonged intraarterial catheter therapy for diabetic gangrene of the lower limb / Okhunov A.O., Abduralhmanov F.M. // 42-Annual Meeting of the Surgical Infection Society, Westlake Village, CA April 11-14, 2023 – P.38
87. Purulent-destructive lung diseases, pathogenesis, and modern principles and treatment / Sh.A. Khamdamov, Sh.A. Bobokulova, D. Korikhonov, et al. // Journal of Education and Scientific Medicine, 2023, #2(1), P. 57-66. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/406>
88. Recommendations for the organization of distance education on the example of the use of electronic books. / Shadmanov A.K., Okhunov A.O. // Journal of Education and Scientific medicine, 2022, #2(3), P.7-10. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/336>
89. Reestablishment of recipient-associated microbiota in the lung allograft is linked to reduced risk of bronchiolitis obliterans syndrome. / D.L. Willner, P. Hugenholtz, S.T. Yerkovich, et al. // Am. J. Respir. Crit. Care Med. – 2013. - #187(6). – P.640-647.
90. Role and place of technologies webinar in cooperation of the educational process of the branches of the Tashkent medical academy / A.O. Okhunov, N.Sh. Khudaibergenova, S.S. Atakov, et al. // Journal of Education and scientific medicine, 2022, (2), 73-76. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/278>
91. Sepsis / A.O.Oxunov, B.D.Babadjanov, U.I. Pulatov, et al. // Patent izobreteniya DGU 04057 - 2016. [in Russian]
92. Shadmanov A.K., Okhunov A.O. Recommendations for the organization of distance education on the example of the use of electronic books. Journal of Education and Scientific medicine, 2022, 2(3), 7-10. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/336>
93. Shadmanov A.K., Okhunov A.O., Abdurakhmanov F. M. Morphological characteristics of a new experimental model of chronic renal failure in the background of diabetic nephropathy. Journal of Education and scientific medicine, 2022, 2(3), 68-76. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/364>
94. Sheehan L., Nieweglowski K., Corrigan P. The Stigma of Personality Disorders. // Curr. Psychiatry Rep. – 2016. - #18(1). – P. 11.
95. Sostoyanie aktivnosti monoooksigenaz slizistoy obolochki jeludka pri ushivanii perforativnix yazv s ispolzovaniem amnioticheskoy tkani / Sh.E. Ataxanov, R.I.Raximov, A.S.Komarin, et al. // Vrach-aspirant. - 2009. - № 1. - S.4-10. [in Russian]
96. Sovershenstvovanie metodov lecheniya kriticheskoy ishemii nijnix konechnostey na fone diabeticheskoy angiopatii / A.O. Oxunov, I.S. Sattarov, B.B. Janabaev, et al. // Vrach-aspirant. - 2009. - № 32 (5). - S. 382-388. [in Russian]
97. The Discovery of Insulin: An Important Milestone in the History of Medicine. / I. Vecchio, C. Tornali, N.L. Bragazzi, M. Martini // Front Endocrinol (Lausanne). – 2018. - #9. – P.613.
98. The microbiological environment of wounds and skin in patients with purulent-inflammatory diseases of soft tissues / W.S. Jonson, A.O. Okhunov, S.S. Atakov, et al. // Journal of Educational and Scientific Medicine – 2023 – V.2, #2. – P.72-81.
99. The panel of circulating cytokines in patients with type 2 diabetes and different patterns of chronic kidney disease / V. V. Klimontov, A. I. Korbut, N. B. Orlov, M. V. Dashkin // Diabetologia. – 2020. – Vol. 63, #1. – P. 413.
100. The role and place of nitroxidergic regulation of the endothelial system in the pathogenesis of acute lung abscess. / A. O. Okhunov et al. // Medical & Clinical Research 7.12 (2022): P. 1-6.

101. The Utility of Exosomes in Diagnosis and Therapy of Diabetes Mellitus and Associated Complications. / Y. Sun, Q. Tao, X. Wu, et al. // *Front Endocrinol (Lausanne)*. - 2021. - #12. - P.756581.
102. Translational medicine: a new way from the experimental laboratory to clinical practice. / Shadmanov A.K., Okhunov A.O. // *Journal of Education and scientific medicine*, 2023, (1), 2-7. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/282>
103. Treatment of acute lung abscesses considering their non-respiratory function in patients with diabetes. / Okhunov A. O., et al. // *Indian Journal of Forensic Medicine and Toxicology* 14.4 (2020): P. 7465-7469.
104. Ways to achieve positive results of dermaplasty in patients with diabetic foot syndrome. / Okhunov A. O., and F. M. Abdurakhmanov. // *British Medical Journal* – 2023 - #3.1.
105. What Do You Know About the Royal College of Physicians (London, UK)? Results of the Visit / A.K. Shadmanov, A.O. Okhunov, Sh.A. Bobokulova // *Journal of Educational and Scientific Medicine* – 2023 – V.1, #3. – P.2-10.
106. What do you need to know about the origin of purulent mediastinitis? / K. Kh. Boboyev, D.N. Korikhonov, A. O. Okhunov, F. M. Abdurakhmanov // *Journal of Education and Scientific Medicine*, 2023, 2(1), P. 15-21. Retrieved from <https://journals.tma.uz/index.php/jesm/article/view/385>