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

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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-

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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].

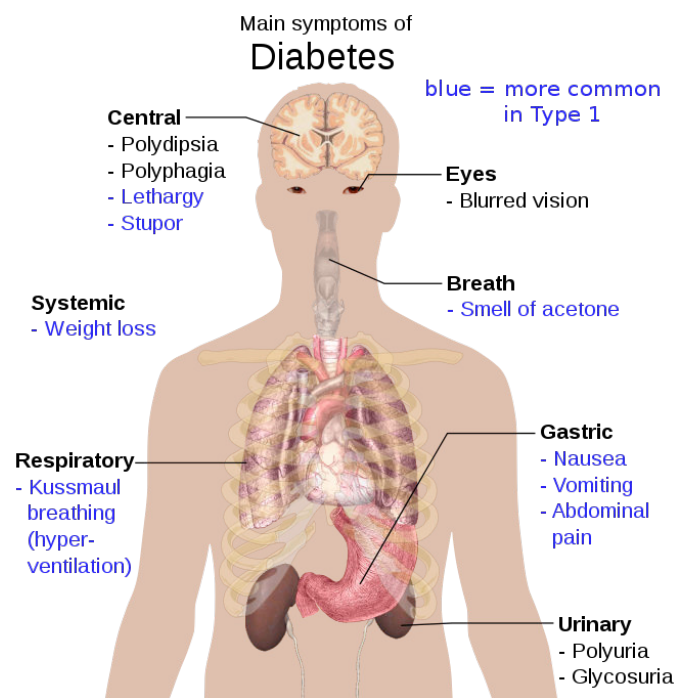
With the "mutual burden syndrome", significant violations in the immune defense occur in patients with diabetes mellitus [54].

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].

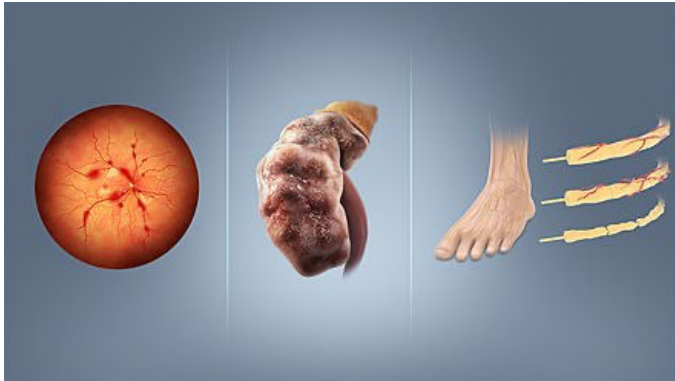
Stable hyperglycemia leads to an increase in glucose concentration in sweaty skin secretions, which accordingly creates a favorable breeding ground for microorganisms of any habitat category (both for pathogenic and conditionally pathogenic infections). Due to metabolic disorders and a decrease in glycogen 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].

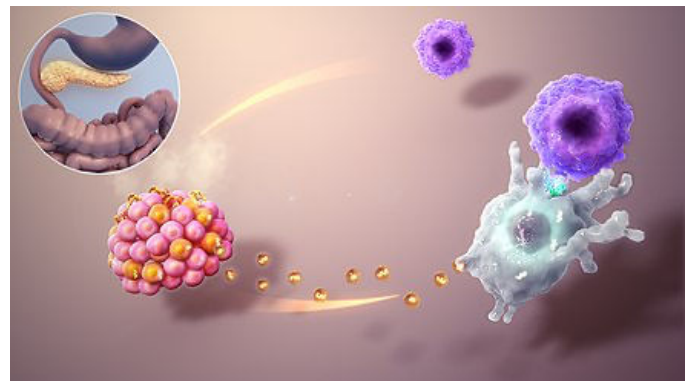
As for the development of electrolyte imbalance and acid-base state, it should be noted such a fact as its development in acute inflammatory diseases of internal organs in favor of acidosis. On the other hand, hyperglycemic state, and metabolic acidosis, against the background of diabetic nephropathy 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].

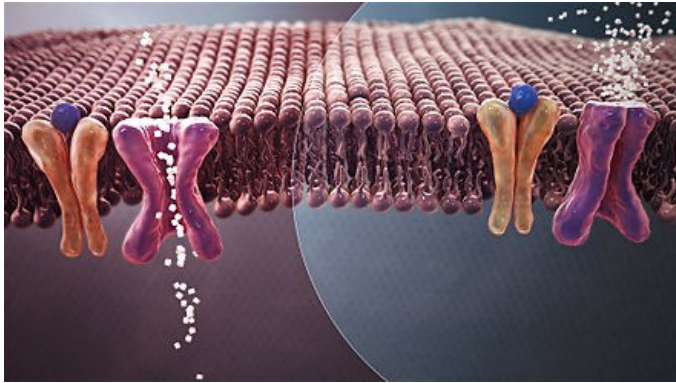
Patients with diabetes mellitus are characterized by the presence of blood clotting disorders in the direction of hypercoagulation. The main link in these pathological processes is a violation of the rheological properties of blood. Hyperglycemia and hyperlipidemia provoke an increase in the viscosity 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 amino acids. 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].

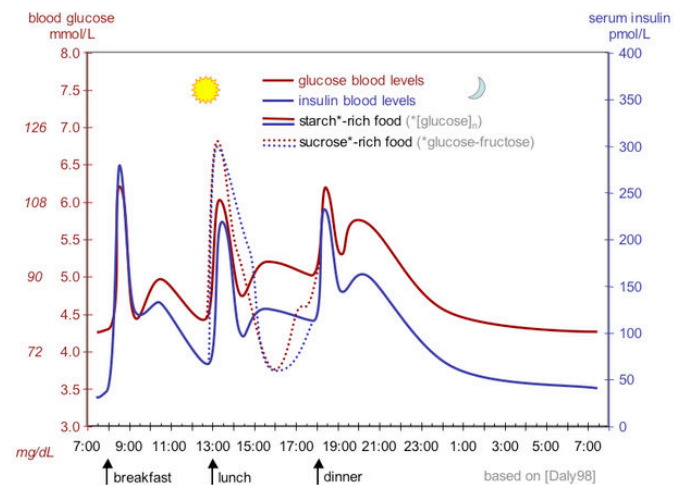


Reduced insulin secretion or weaker effect of insulin on its receptor leads to high glucose content in the blood.

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].

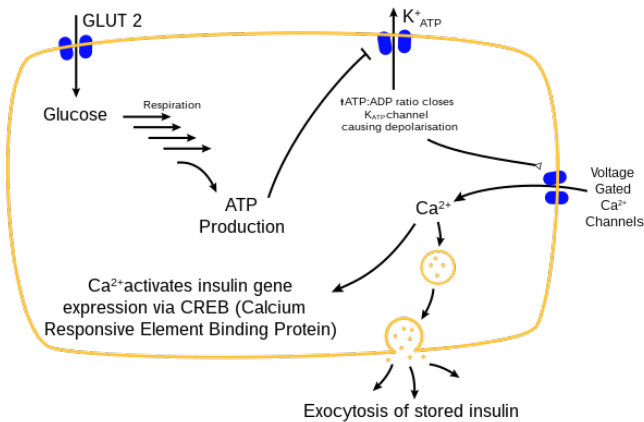


The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals. One of the effects of a sugar-rich vs a starch-rich meal is highlighted.

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.

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