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# FEATURES OF THE COURSE OF THE WOUND PROCESS IN PATIENTS WITH DIABETIC FOOT SYNDROME

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The main cause of amputations in diabetes mellitus is an infectious-necrotic process on the foot. The aim of the study was to investigate the features of the wound process in patients with diabetic foot syndrome. 56 patients with purulent surgical pathology were examined. The main group consisted of patients with diabetes. The control group consisted of patients without diabetes with purulent pathology of the lower extremities. The clinical picture of the wound process, cytological changes and pH were studied. Patients with diabetes are characterized by early acidosis with a severe course of the wound process, and fluctuations in wound pH led to a change in the cytological picture. Such patients have a protracted first phase of the wound process, frequent complications. In severe cases, the wound process in patients with diabetes mellitus is polyphasic-discordinated, with several phases of the wound process.

**Key words**: diabetic foot syndrome, wound process, cytology, pH.

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# ОСОБЛИВОСТІ ПЕРЕБІГУ РАНЕВОГО ПРОЦЕСУ У ХВОРИХ НА СИНДРОМ ДІАБЕТИЧНОЇ СТОПИ

Основною причиною ампутацій при цукровому діабеті є інфекційно-некротичний процес на фоні ран та виразок стопи. Метою дослідження було вивчити особливості перебігу ранового процесу у хворих із синдромом діабетичної стопи. Обстежено 56 хворих з гнійною хірургічною патологією. Основну групу склали хворі з синдромом діабетичної стопи. Контрольну групу склали хворі без діабету з гнійною хірургічною патологією нижніх кінцівок. Вивчали клінічну картину ранового процесу, цитологічні зміни та pH рани. Для хворих на цукровий діабет характерний ранній ацидоз з важким перебігом раневого процесу, коливання pH рани призводять до зміни цитологічної картини. У хворих з синдром діабетичної стопи спостерігається затяжна перша фаза та часті ускладнення ранового процесу з його декомпенсацією. У важких випадках рановий процес у хворих на цукровий діабет має поліфазно- дискординантний характер, з наявністю в рані одночасно декількох фаз раневого процесу.

**Ключові слова:** синдром діабетичної стопи, рановий процес, цитологія, pH.

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The problem of diabetes mellitus (DM) is currently relevant in most countries of the world. The increase in the number of patients with diabetes mellitus leads to an increase in the number of complications of this disease [14, 15]. One of them is diabetic foot syndrome (DFS), which develops in more than 10 % of patients and almost 70 % of them require surgical treatment [6, 14].

Foot ulcers and their complications are an important cause of morbidity and mortality in diabetes mellitus. About a third of patients with DM are hospitalized with complications of DFS [9, 13]. The number of lower limb amputations per 100 thousand people with DFS in Europe ranges from 1.5 (Iceland) to 34.5 (Belgium). In the USA and Canada, this figure ranges from 3.3 to 7.5 [14, 15]. Often, the occurrence of purulent-inflammatory and destructive lesions of the foot leads not only to the loss of the lower limb, but also to the death of the patient [2, 14]. Mortality in Europe 5 years after limb amputation due to DFS ranges from 44.5 to 77.0, and in the USA it reaches 72.0 per 100 thousand people [15].

Polyneuropathy and increased pressure in the supporting zones of the foot contribute to the development of ulcers of the foot and toes [8, 14]. The main cause of amputations in DFS is an infectious-necrotic process in the foot, developing against the background of wounds, cracks and ulcers [4, 10, 12].

The severity of the wound process in diabetes mellitus is due to the fact that the wound cleansing phase is excessively delayed, and the regeneration phase often does not occur at all [1, 12]. Therefore, the study of the characteristics of the course of the wound process in DFS is of great importance for the prevention and proper treatment of complications of DFS in order to reduce the number of lower limb amputations and mortality.

**The purpose** of the study was to establish to the features of the course of the wound process in patients with DFS, taking into account the results of clinical, pH–metric and cytological studies.

**Materials and methods.** In 2020–2024, we conducted a comprehensive examination and treatment of 56 patients with purulent surgical pathology in Poltava City Hospital No. 2, No. 3 and Medical Center

*"*Medion*"*. The first (main) group (27 patients) consisted of patients with diabetic foot syndrome II B, III A-III B stage for Meggitt-Wagner. To exclude the influence of limb ischemia on the course of the wound process, only patients with the neuropathic form of diabetic foot were selected for the main group. The second (control) group (29 patients) consisted of patients who had purulent surgical pathology of the lower extremities; however, they did not have diabetes mellitus. In patients of both groups, a study of the course of the wound healing process was conducted by examining the clinical picture, cytological changes in the wound and pH on days 1, 7–8, 12–14, 23 after surgery.

**Results of the study and their discussion.** The average area of ulcerative defects in patients in the main group was 5.2±0.3 $cm^2$, they were localized in areas of greatest pressure when walking. The average area of wounds in patients in the control group was 7.3±0.5 $cm^2$.

According to Doppler measurements and ultrasound examination of the arteries of the lower extremities, the main blood flow in the segment of the arteries of the legs was preserved in all patients of the main group.

Stage II B according to Wagner was detected in 9 (33.3 %) patients of the main group. Stage III A according to Wagner was detected in 12 (44.4 %) patients and Stage III B was detected in 6 (22.2 %) patients of the main group.

7 (24.1 %) patients in the control group had infected wounds of the lower extremities of various etiologies with incipient phlegmon, 9 (31.1 %) patients had an abscess, 8 (27.6 %) – had phlegmon of the lower extremity, and 5 (17.2 %) patients had osteomyelitis of the foot bones.

Patients of both groups were prescribed basic drug therapy, which included compensation of carbohydrate metabolism in patients of the main group, antibacterial therapy, taking into account the sensitivity of the microflora, metabolic therapy, symptomatic therapy, local treatment.

In order to identify the characteristics of the course of the wound process in patients with purulent-necrotic lesions of DFS, we conducted cytological studies, as well as studies of the pH of the wound contents in 27 patients of the main group and in 29 patients of the control group at 1, 7–8, 12–14, 23 days after surgery. Local clinical signs of the wound process, the presence of intoxication, body temperature, and indicators of general clinical and laboratory examinations were taken into account.

It was found that in the majority of patients in the main and control groups on the 1st day after surgery, the pH tended to varying degrees of acidosis, which in 17 out of 27 patients in the main group and in 15 out of 29 patients in the control group (Table 1) was of an uncompensated nature (pH 5.0–5.5), which indicated the severity of the destructive process. The clinical manifestations of the inflammation phase were also corresponding: with sharp swelling, hyperemia, progressive infiltration of the wound edges, pain on palpation against the background of a sharp deterioration in general health and distinct changes in blood tests (leukocytosis up to $16\times10^9$/l), accelerated ESR (25–60 mm/h). In patients with a higher wound pH, the inflammatory response was weaker. Analysis of the results of cytological studies in acidosis (pH 5.5–6.0) revealed in all preparations a large number of neutrophils, most of which were in the stage of regeneration with nuclear fragmentation and blurred cytoplasm. In this case, degenerative phagocytosis predominated.

Two preparations revealed macrophages with weakened functional activity, the presence of bacteria in the cytoplasm and the absence of digestive vacuoles. This confirms the degenerative-inflammatory type of cytogram in patients with decompensated acidosis.

The inflammatory-regenerative and regenerative type of cytogram was not detected in the patients of the main and control groups on the first day after the operation. As we can see, in the main group there were patients with a degenerative-inflammatory type of cytogram, and in the control group – with an inflammatory type (Table 1).

Table 1

**Wound environment and cytogram type in patients of the main and control group on the 1st day after surgery**

| Type cytograms | The main group (n=27) | | | The control group (n=29) | | |
|---|---|---|---|---|---|---|
| | Abs. | % | pH of the wound | Abs. | % | pH of the wound |
| Necrotic | 3 | 11.1 % | 5.0–5.5 | 2 | 6.9 % | 5.0–5.5 |
| Degenerative-inflammatory | 14 | 51.9 % | 5.5–6.0 | 13 | 44.8 % | 5.5–6.0 |
| Inflammatory | 10 | 37.0 % | 6.0–6.5 | 14 | 48.3 % | 6.0–6.5 |

In the stage of subcompensated acidosis (pH 6.0–6.5), which was found in 10 (37.0 %) patients of the main group and in 14 (48.3 %) patients of the control group, a cytological picture corresponding to the inflammatory type was noted, when the entire field of vision is occupied by neutrophilic leukocytes with a

decrease in the number of degenerative forms and satisfactory phagocytosis. In most cases, phagocytosis was complete. An increase in the number of macrophages and an increase in their activity were revealed, bacteria, remnants of melted leukocytes, digestive vacuoles with clear contours were found in the cytoplasm. Virtually all preparations contained fibroblasts, polyblasts, and single epithelial cells in small quantities.

According to clinical signs, after surgical interventions (opening of abscesses, necroctomies) in 17 (62.9 %) patients of the main group, the body temperature rose to 37.5–39ºC, in 6 (22.2 %) – increased pain, in 19 (70.4 %) – feeling improved, pain decreased, in 4 (14.8 %) – a deterioration of the local status was observed, which required additional revision of the wound with necrectomy. In the control group, an increase in temperature was observed in 11 (37.9 %) patients, and in 2 (6.9 %) patients a worsening of the wound condition was observed.

The cytological pattern in such patients corresponded to the necrotic and degenerative-inflammatory types of the cytogram, which were characterized by an intense purulent-inflammatory process with the presence of a large number of neutrophils, a significant part of which (60 %) was in the stage of degeneration with fragmentation of the nuclei, indistinctness of the cytoplasm. Cellular detritus, nuclear and cytoplasmic fragments, single eosinophils were determined in the preparations. In 7 (25.9 %) patients of the main group, degenerative phagocytosis occurred, in 5 (18.5 %) – incomplete phagocytosis.

On the 7th–8th day after the operation, 7 (25.9 %) patients of the main group (Table 2) observed an exacerbation of the wound process caused by secondary necrosis in the wounds, which was accompanied by an increase in body temperature above 38ºC, increased pain in the area of the foot wounds, and the appearance of edema and hyperemia of its edges, purulent or purulent is separated. A decrease in the pH of the wound medium (5.5–6.0) with a degenerative-inflammatory and inflammatory type of cytogram was noted, in which neutrophils, macrophages with incomplete phagocytosis appeared, and the number of fibroblasts decreased. In 3 (11.1 %) patients, a discoordination of the cellular reaction was observed, which was manifested by a mismatch between the cytological picture, the pH of the wound medium and the phase of its course. In these conditions, in the regeneration phase, clinical, pH–metric and cytological signs of several phases of the wound process were revealed. We tentatively defined this variant of the course of the wound process as polyphasic- discordinated, which is an indicator of its decompensation. An inflammatory type of cytogram was observed in 13 (48.2 %) patients of the main group.

Repeated surgical interventions and adequate conservative therapy significantly improved the patients' condition. At the same time, the main clinical symptoms regressed, the pH of the wound environment increased (6.0–7.0) in wound prints, a decrease in the number of degenerative forms of neutrophils, activation of phagocytosis, and the appearance of polyblasts at different stages of transformation were observed.

On days 7–8 after surgery, the necrotic type of cytogram was not detected in patients in the control group; in the majority of patients – 16 (55.2 %) there was an inflammatory-regenerative type of cytogram (Table 2).

Table 2

**Wound environment and type of cytogram in patients the main and control group on the 7–8th day after the operation**

| Type cytograms | The main group (n=27) | | | The control group (n=29) | | |
|---|---|---|---|---|---|---|
| | Abs. | % | pH of the wound | Abs. | % | pH of the wound |
| Necrotic | 2 | 7.4 % | 5.0–5.5 | 3 | 10.3 % | 5.5–6.0 |
| Degenerative-inflammatory | 7 | 25.9 % | 5.5–6.0 | 10 | 34.5 % | 6.0–7.0 |
| Inflammatory | 13 | 48.2 % | 6.0–7.0 | 16 | 55.2 % | 6.5–7.5 |
| Inflammatory-regenerative | 5 | 18.5 % | 6.5–7.5 | 3 | 10.3 % | 5.5–6.0 |

On days 12–14 after surgery, patients in the main group showed an increase in the pH of wound secretions and corresponding changes in the cytological picture of early prints. Thus, in 5 (18.5 %) patients of the main group, decompensated acidosis (pH 5.5–6.0) persisted, which was cytologically characterized by a degenerative-inflammatory type of cytogram. 11 of the 27 examined patients of the main group had subcompensated acidosis (pH 6.0–6.5), 10 had compensated acidosis (pH 6.5–7.5) with an inflammatory-regenerative type of cytogram. The latter observed a decrease in the number of degenerative forms of neutrophils from 60 % (at pH 5.5–6.0) to 20 % (at pH 6.0–6.5) and an increase in the number of macrophages and polyblasts.

As the pH of the wound environment increased, degenerative-inflammatory, inflammatory and inflammatory-regenerative types of cytograms were observed, which were characterized by a further decrease in the number of degenerative forms of neutrophils with normalization of their structure and increased segmentation of nuclei in relation to surgical treatment of purulent-necrotic lesions. An increase

in the number of mononuclear elements, profibroblasts, macrophages, and actively functioning microphages was revealed. The clinical picture in these patients was characterized by decreased pain in the wound, improved well-being, a significant decrease in purulent discharge from wounds, and intensified processes of their cleansing.

In one patient of the main group with a severe course of purulent-necrotic lesions of DFS after radical surgical treatment of a purulent focus, the clinical course of the wound process was characterized by the absence of an inflammatory reaction from the edges of the wound, the presence of serous-purulent discharge and pale granulations, and the cytological state was characterized by a certain amount of detritus bacteria, the presence of single degenerative neutrophils, macrophages, polyblasts, fibroblasts. The regenerative type of cytogram was not observed in patients of the main group on days 12–14 after surgery.

By 12–14 days after surgical treatment, five patients in the control group were discharged for outpatient treatment. In other patients, the necrotic and degenerative-inflammatory type of cytogram was not determined. The vast majority of patients – 14 (68.0 %) had a regenerative type of cytogram.

On days 22–24 after surgery, studies were carried out in 25 (92.6 %) patients of the main group, since 2 patients were discharged for outpatient treatment. In 2 patients of the main group, subcompensated acidosis with an inflammatory type of cytogram was detected, and in 8 patients, compensated acidosis with an inflammatory-regenerative type was detected. In 15 (60 %) patients of the main group, the pH level of the wound environment ranged from 7.5–8.0. In the wound, regenerative processes with an inflammatory-regenerative and regenerative type of cytogram predominated, the main indicators of which were polyblasts and fibroblasts.

On the 23rd day in the postoperative period, we did not observe a necrotic and degenerative-inflammatory type of cytogram in patients of the main group.

In most patients, there was a decrease in the number of neutrophils, macrophages, a significant number of fibroblasts, polyblasts, and epithelial cells against the background of completed phagocytosis, which corresponds to the regenerative type of cytogram.

Analysis of clinical observations and studies of wound pH, as well as cytological data, indicate that changes in these indicators correspond to the phases of the wound process: inflammation, regeneration and scar organization. It is characteristic that at a certain pH level there is a corresponding cytological indicator. Thus, the maximum number of neutrophils is detected at a pH of the wound environment equal to 5.5–6.0, and reaches 60–80 %, gradually decreasing as the wound environment increases. At pH 8.0–9.0, isolated degenerative forms of neutrophils occur. Macrophages are present in wounds regardless of the nature of the pH of the wound environment, but their number reaches a maximum at pH 6.5–7.5, that is, in the phase of cleansing the wound from dead cells and non-viable tissues. Polyblasts were most active at pH 6.0–7.5 in all phases of healing, and in minimal quantities at pH 5.0–5.5. Fibroblasts are most active at pH above 6.5. Their maximum number is detected at pH 7.0–7.5 and decreases with granulation and epithelization of the wound. The activity of epithelial cells manifests itself at a pH of 7.0–8.5; they were not detected in the sharply acidic reaction of the wound environment.

Most patients in the control group were discharged for outpatient treatment by 23 days after surgery. Only 7 patients out of 29 remained. Only one of them had an inflammatory-regenerative type; 6 (85.7 %) had a regenerative type of cytogram.

Analysis of the course of the wound process indicates significant fluctuations in the pH of the wound environment in patients with DFS. Early acidosis with a slow increase in the pH of the wound environment, characteristic of patients with purulent-necrotic lesions, is, in our opinion, associated with a severe, cascading course of the wound process with frequent exacerbations and relapses.

Thus, a comparative analysis of clinical manifestations, cytological, pH–metric picture in patients of the main group for DFS in comparison with patients with purulent surgical infection without diabetes mellitus indicates a slower and more complicated course of the wound process with a tendency to its decompensation in DFS. Also, the course of the wound process when it is severe in patients with DFS has a polyphase-discordinated character, which is based on the simultaneous presence of several phases of the wound process with a corresponding cytological picture in the wound. The polyphasic-discordinated nature of the course of the wound process in patients with purulent-necrotic lesions indicates decompensation of the wound process.

In patients with DFS without ischemia, the infectious process underlies purulent-necrotic lesions [2, 10]. Trophic changes in the skin and soft tissues create favorable conditions for the development of infection on the foot, inhibit regenerative processes, which has a decisive effect on the results of treatment [7, 11]. We agree with the point of view that the addition of a purulent-necrotic process against the background of diabetes mellitus significantly worsens the course of the underlying disease with the development of mutual aggravation syndrome [5, 12].

Local changes in DFS are characterized by the development of a widespread process without a tendency to delimitation. Lesions of the foot tissues in such patients are characterized by unclear demarcation boundaries with the formation of a significant zone of tissue in a state of necrobiosis [1, 7, 9]. Therefore, even radical operations do not exclude the possibility of repeated interventions [10, 14].

Our analysis of the results of clinical, pH–metric, cytological studies and their comparison with the control group of patients indicates a longer course of the wound process in patients with DFS, even if it is uncomplicated, which is explained by severe acidosis, prolonged wound cleansing, slow blast transformation of cells and negatively affects wound healing.

One of the unfavorable factors in the course of a diabetic wound is a long period of its cleansing, which is a harbinger of a delayed onset of the second and third periods of the wound process [1, 2, 3]. A long first period of the wound process with the appearance of new foci of necrosis leads to the fact that the second and third periods of the wound process in a patient with diabetes mellitus do not occur at all [2, 9, 14].

So, the link that can be used to reduce the number of amputations in diabetes can be considered the protracted first phase of the wound process. The first three weeks for a patient with diabetes can be fatal without the development of the second phase of the wound process. The impossibility of the onset of the second phase of the wound process: the proliferation phase leads to the inevitability of limb amputation [4, 9, 10]. The extreme slowness of the wound cleansing process is evidenced by the cytological picture in the main group on the first day after surgery, with a pronounced degenerative-inflammatory process: a sufficient number of inflammatory cells, detritus and the absence of regenerative cells.

Analysis of the course of the wound process indicates significant fluctuations in the pH of the wound environment in patients with diabetes. Early acidosis with slow elimination of the wound environment, typical for patients with purulent-necrotic lesions, in our opinion, is associated with a severe, cascading course of the wound process with frequent relapses. A wide range of fluctuations in the pH of the wound environment in patients with DFS leads to corresponding changes in cells, which is manifested by a protracted inflammatory process and an extension of the wound cleansing period.

Thus, the analysis of clinical manifestations, cytological, pH–metric picture in patients of the main group according to DFS in comparison with patients with purulent infection without diabetes mellitus indicates a slower and more complex course of the wound process with a tendency to its decompensation in DFS. The course of the wound process in patients with DFS in severe cases has a polyphasic-discordinated nature, with the simultaneous presence of several phases of the wound process with a corresponding cytological picture in the wound. This nature of the course indicates decompensation of the wound process, which requires an appropriate correction of the treatment program for this category of patients.

## Conclusions

1. The course of the wound process in patients with DFS is slow, with a protracted first phase of the wound process, frequent complications and a tendency to decompensation.

2. The course of the wound process when it is severe in patients with DFS has a polyphase-discordinated character, which is based on the simultaneous presence of several phases of the wound process with a corresponding cytological picture in the wound.

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## PREDICTION OF ADVERSE OUTCOMES IN HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN TERM NEWBORNS

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The purpose of the study was to identify and predict adverse outcomes in term neonates diagnosed with hypoxic-ischemic encephalopathy a total of 120 children, aged from birth to one year. The study cohort was divided into two groups: the main group (90 patients with hypoxic-ischemic encephalopathy), and the control group (30 healthy children without a history of asphyxia). To develop a predictive model, logistic regression analysis was employed, a robust statistical method designed to explore and quantify the relationships between dependent and independent variables. A total of 67 independent variables (predictors) were identified, encompassing anamnestic, clinical, and laboratory-instrumental parameters. Using multiple variable selection methods (Enter, Forward, Backward, and Wald-based approaches), we identified key predictors that contribute significantly to the prognosis of these neonates. The high classification accuracy achieved across all methods (ranging from 93.3 % to 96.7 %) demonstrates its potential in clinical settings for predicting neonatal outcomes.

**Key words**: neonates, hypoxic-ischemic encephalopathy, predictive model, logistic regression analysis, outcomes.

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## ПРОГНОЗУВАННЯ НЕСПРИЯТЛИВИХ НАСЛІДКІВ ПРИ ГІПОКСИЧНО-ІШЕМІЧНІЙ ЕНЦЕФАЛОПАТІЇ У ДОНОШЕНИХ НОВОНАРОДЖЕНИХ

З метою дослідження з виявлення та прогнозування несприятливих наслідків у доношених новонароджених з діагнозом гіпоксично-ішемічна енцефалопатія, було обстежено 120 дітей віком від народження до одного року. Досліджувана когорта була розділена на дві групи: основну (90 пацієнтів з гіпоксично-ішемічною енцефалопатією) та контрольну (30 здорових дітей без асфіксії в анамнезі). Для розробки прогностичної моделі було використано логістичний регресійний аналіз – надійний статистичний метод, призначений для вивчення та кількісної оцінки взаємозв'язків між залежними та незалежними змінними. Усього було виявлено 67 незалежних змінних (предикторів), що охоплюють анамнестичні, клінічні та лабораторно-інструментальні параметри. Використовуючи методи множинного відбору змінних (Enter, Forward, Backward та Wald-based підходи), ми виявили ключові предиктори, які вносять значний внесок у прогноз цих новонароджених. Висока точність класифікації, досягнута всіма методами (від 93,3 до 96,7 %), демонструє її потенціал у клінічних умовах для прогнозування неонатальних результатів.

**Ключові слова:** новонароджені, гіпоксично-ішемічна енцефалопатія, прогностична модель, логістичний регресійний аналіз, результати.

Hypoxic-ischemic encephalopathy (HIE) is a leading contributor to neonatal mortality and long-term morbidity. Approximately 25 % of neonates diagnosed with HIE develop severe and irreversible neurodevelopmental impairments, such as intellectual disabilities, cerebral palsy, epilepsy, and sensorineural deficits. The primary etiology of neonatal HIE is perinatal asphyxia, often resulting from complications such as umbilical cord entanglement or abnormalities in amniotic fluid, which can lead to fetal distress, asphyxia, and hypoxia [2, 10].

The global incidence of hypoxic-ischemic encephalopathy is estimated to range from 1 to 3 per 1,000 live births in developed countries and from 2.3 to 30.6 per 1,000 live births in developing countries.