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INFLUENCE OF REGIONAL LYMPHOTROPIC ANTIBACTERIAL THERAPY ON THE PROGRESSION OF PHLEGMONS IN THE MAXILLOFACIAL REGION

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The lymphatic system is a part of human circulatory system and is actively involved in providing the body's immune response. It repeats the vasculature, consisting of lymphatic capillaries, vessels, as well as evenly distributed lymphoid tissue, which is part of the lymph nodes and aggregate glands of the small intestine (Peyer's patches) and others. 100 patients with acute odontogenic inflammatory diseases of the maxillofacial region were examined. Patients received traditional drug treatment. In addition, we included regional lymphotropic antibacterial therapy to the main method of treatment. Regional lymphotropic administration of antibacterial drug in the treatment of phlegmons of the maxillofacial region leads to an accelerated onset of the second phase of the wound process development, more rapid detoxification of the body, a decrease in the number of complications, as well as the prevalence of pronounced positive lymphogram dynamics.

Key words: acute odontogenic inflammatory disease, maxillofacial region, lymphatic system.

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ВПЛИВ ЛІМФОТРОПНОЇ РЕГІОНАРНОЇ АНТИБАКТЕРІАЛЬНОЇ ТЕРАПІЇ НА ПЕРЕБІГ ФЛЕГМОН ЩЕЛЕПНО-ЛИЦЕВОЇ ДІЛЯНКИ

Лімфатична система входить до єдиної кровоносної системи людини і активно бере участь у забезпеченні імунної відповіді організму. Вона повторює судинну мережу, що складається з лімфатичних капілярів, судин, а також рівномірно розподіленої лімфоїдної тканини, що входить до структури лімфатичних вузлів і групові лімфатичні фолікули тонкої кишки (Пейєрові пляшки) та інші. Обстежено 100 пацієнтів з гострими запальними одонтогенними захворюваннями щелепно-лицевої ділянки. Хворі отримували традиційне медикаментозне лікування, додатково до основного методу лікування включали регіонарну лімфотропну антибактеріальну терапію. Регіонарне лімфотропне введення антибіотика при лікуванні флегмон щелепно-лицевої ділянки призводить до прискореного настання другої фази розвитку раневого процесу, більш швидкої детоксикації організму, зменшення числа ускладнень у хворих, а також переважання вираженої позитивної динаміки в лімфограмі.

Ключові слова: гострі запальні одонтогенні захворювання, щелепно-лицева ділянка, лімфатична система.

The article is a fragment of the research project: “Comprehensive treatment of patients with phlegmon of the maxillofacial region with influence on the reparative processes course”, state registration No. 0117U000398.

The lymphatic system is a part of human circulatory system and is actively involved in providing the body's immune response. It repeats the vasculature, consisting of lymphatic capillaries, vessels, as well as evenly distributed lymphoid tissue, which is part of the lymph nodes and aggregate glands of the small intestine (Peyer's patches) and others. According to the evidence of the world's lymphologists, lymphatic system is the main organ of the human immune system; it contains the vast majority of all lymphocytes [2, 4]. The lymphatic system is involved in all pathological processes in the macroorganism [8].

It plays one of the leading roles in purulent-inflammatory diseases [5, 6, 8], since the splitting and further movement of bacteria and toxins occurs through the lymphatic vessels and lymph nodes. A so-called accumulation of toxins is created there, so the endolymphatic administration of antibacterial immunoregulatory agents is pathogenetically justified [1, 9]. Antibacterial saturation by the lymphotropic route creates high concentrations of anti-inflammatory and other drugs on the routes of microorganisms and bacteroids movement, which contributes to a rapid immune response and the movement of antibacterial drugs to microorganisms, improves lymph rheology. This, in turn, unblocks inflamed lymph nodes, reduces the likelihood of their suppuration or necrosis of inflammatory infiltrates in the lymphatic system [8].

One of the many hallmarks of odontogenic infection is that the patient's body cannot cope on its own, without treatment, it cannot stop the flow of microorganisms from the source of infection. Moreover, this means that there is no hope for self-healing and complete elimination of the infectious focus. In the best case, the process becomes inveterate [3, 7].

The purpose of the study was to increase the effectiveness of phlegmon treatment in the maxillofacial area by influencing pathogenic factors, the administration of second antibacterial drug by the lymphotropic route.

Materials and methods. All procedures carried out in the study involving human subjects were in accordance with the ethical standards of the institutional and/or national research committee, as well as the Declaration of Helsinki of 1975 and its revision in 1983. The patients gave written informed consent to the study.

We carried out diagnostics and combination therapy of 100 patients with odontogenic phlegmons who were hospitalized at the Department of Surgical and Therapeutic Dentistry of the SI “Zaporizhzhya Medical Academy of Post-Graduate Education, MOH of Ukraine” in the Department of Maxillofacial Surgery Municipal Non-Profit Enterprise of Zaporizhzhya City Council “City Hospital of Urgent and Emergency Medical Care” in 2016-2017. The patients were divided into 2 groups. Group 1 – 45 patients, who were treated with Ceftriaxone (Darnitsa, Ukraine) by intramuscular administration. Group 2 – 55 patients, whose treatment consisted of both a typical method and local lymphatic administration of Gentamicin (Darnitsa, Ukraine) antibacterial drug.

Upon admission to the hospital, all patients underwent a comprehensive examination. Surgical treatment was performed according to the generally accepted method under the general or topical anesthesia. Cytological control of the wound condition as a criterion of treatment efficacy was carried out in two stages: 1 – after the incision and drainage of the purulent focus, 2 – on the 5th-7th day of treatment. In the postoperative period, the wound was sponged daily with antiseptic solutions and proteolytic enzymes were injected into it on the 3rd day.

The patients received conventional antibacterial and anti-inflammatory therapy and underwent correction of the water-electrolyte balance. The complex of the treatment process included physiotherapy.

From the first hours of hospitalization, all patients received antibiotic therapy. When choosing the sites for the lymphotropic administration of antibacterial drugs, we proceeded from the regional principle based on the lymphatic system structure in the maxillofacial region, taking into account the anatomical and physiological principle of lymphatic drainage (fig. 1).

For a targeted effect on the inflammatory process in the mandibular body region as well as in the adjacent sublingual, submandibular, pterygomaxillary and submasticatory cellular spaces, the antibacterial drug was injected strictly subcutaneously 1 cm below and laterally to the mastoid process of the temporal bone on the side of inflammation.

In the mental region, preparations were injected submucosally into the region of the mandibular nerve exit from the mandible on both (Fig. 2) sides by the method of subperiosteal anesthesia.

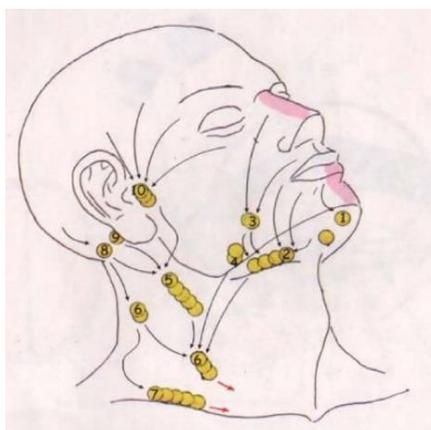


Fig. 1. Scheme of the anatomical and physiological lymphatic drainage of the maxillofacial region (MFR).



Fig. 2. Scheme of antibacterial drug administration by regional lymphotropic route in the lymphatic drainage region.

To influence the infectious and inflammatory process in the maxillary bone, upper lip, infraorbital, zygomatic, and buccal regions, we injected lymphotropic antibacterial drugs subcutaneously into the nasolabial fold on the side of inflammation. Penetration of the drug into the spongy substance of the maxillary bone was performed during its lymphotropic injection into the nasolabial fold. With the spread of the inflammatory process in the parotidomasseteric region or the parotid salivary gland parenchyma, lymphotropic antibiotic drugs were injected subcutaneously under the base of the tragus.

It is possible to administer simultaneously an antibacterial drug from several points based on the severity of the inflammatory process. The course of lymphotropic antibacterial therapy was 5-7-10 days.

For the treatment of patients with phlegmons of the maxillofacial region, regional lymphotropic antibacterial therapy was used as an additional method of administering medicinal substances to the main principle of treatment. Ceftriaxone was chosen as the main antibacterial drug. In addition, gentamicin was administered lymphotropically as the second antibacterial drug.

The distribution of patients was carried out by their gender and age (table 1). The most common population in the hospital are patients of working age, from 20 to 40 years old (90.9 %).

The age of patients in all groups ranged from 18 to 65 years (mean age was 39.8 ± 12.7 years). There were no significant differences in the gender and age composition of the studied groups (the mean age of patients in the main group was 38.4 ± 12.1 years, in the comparison group – 41.3 ± 13.1 , $p=0.32$).

All 100 patients included in the comparison group by the etiological factor of the purulent-inflammatory process of the maxillofacial region had teeth affected by the extensive caries.

Table 1

Distribution of patients with phlegmons of the maxillofacial region depending on gender and age

Gender	Age (years)				Total
	15-20	21-40	41-60	61 and older	
Male	6	43	9	2	60
Female	7	22	10	1	40

In particular, from the topographic classification of phlegmons of the maxillofacial region, the purulent-inflammatory process can spread to one, two or more regions. Purulent-inflammatory diseases of the maxillofacial region are focalized (fig. 3) in the submandibular, parotideomasseteric and parapharyngeal regions and mouth floor. In 63 patients, the spread of acute purulent-inflammatory process was observed in two or more anatomical cellular spaces.

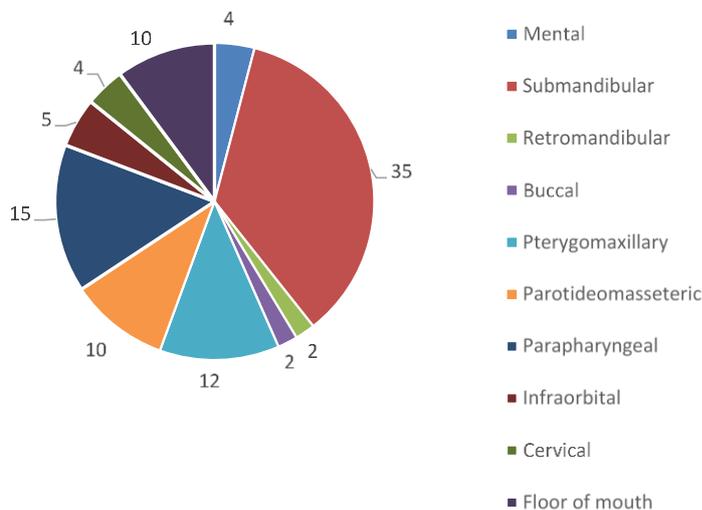


Fig. 3. The location of the inflammatory process in the anatomical cellular spaces.

In 63 patients, the spread of acute purulent-inflammatory process was observed in two or more anatomical cellular spaces. In 17.3 % of patients with odontogenic phlegmons of the maxillofacial region, a torpid stage of the disease was observed with blurred clinical signs in comparison with general and local signs of the inflammatory process and the absence of positive dynamics for the performed antibacterial therapy.

58 (58.3 %) patients had concomitant somatic diseases, such as chronic diseases of the digestive system, ENT organs and bronchopulmonary system.

Before hospitalization, 57 (57 %) patients did not seek medical help, self-medicated, and also used antibacterial drugs without a doctor's prescription. 43 (43 %) patients were on an outpatient appointment with a dental surgeon at the place of residence before being sent to the hospital. They were treated with anti-inflammatory therapy and antibacterial drugs. The course of the inflammatory process from the first clinical symptoms to hospitalization in the vast majority (87 %) of patients was more than 3 days. In these patients, lymphotropic therapy accelerated the resolution of the inflammatory process and led to the recovery in a shorter time.

The indices of a clinical blood analysis, which was taken upon admission to the hospital, convincingly show the development of inflammatory processes in patients. At the time of hospitalization, no hemogram of different white blood cell (WBC) counts was observed between the comparison groups.

In 86 (86 %) patients, red blood cells did not exceed normal values, and only in 14 (14 %) patients their value was $4 \times 10^{12}/l$. Hemoglobin indices in 24 (24 %) patients was less than 120 g/l, while in the remaining 76 (76 %) patients it was within the normal range.

The changes in the values in the WBC differential were different. In 35 (35%) patients, the WBC count was within the normal range, in 7 (7 %) patients had leukopenia less than $4 \times 10^9/l$, and only 58 (58 %) patients had leukocytosis of more than $11 \times 10^9/l$. An increase in the number of stab neutrophils up to 7-8 %, and in segmented neutrophils – up to 70 %, was also observed only in 45 (45.5 %) patients.

The obtained laboratory data were carried out in the International System of Units and processed by the methods of variation statistics according to the Mann-Whitney U-test using the MedStat package and the EZR v.1.35 statistical package (Saitama Medical Center, Jichi Medical University, Saitama, Japan 2017), which is a graphical interface to RFSC (The R Foundation for Statistical Computing, Vienna, Austria).

Results of the study and their discussion. As a result of the study, it was found that in 17.3 % of patients with odontogenic phlegmons of the maxillofacial region, a torpid stage of

At the same time, there was a decrease in the content of lymphoid cells in all patients: severe lymphopenia (5–15 %) was observed in 41 (40.5 %) patients, 14 (14.1 %) patients showed a decrease in their number (up to 20–30 %). In 20 (20.3 %) patients, the number of lymphoid cells did not cross their lower limit of normal (15–20%), and only in 25 (25 %) patients the level of lymphocytes was within the physiological limits (table 2). A decrease in the number of lymphocytes with a low number of WBC proves that this is one of the signs of a torpid disease course.

Table 2

Hematological parameters in practically healthy individuals and patients with phlegmons of groups 1 and 2 during hospitalization

Index	Healthy individuals (n=20)	Group 1 (n=45)	Group 2 (n=55)
Red blood cells, ($10^{12}/l$)	4.64±0.06	4.31±0.08*	4.27±0.08*
Hemoglobin, (g/l)	141.0±1.7	132.6±2.8*	134.7±2.1*
Blood Colour Index (RU)	0.91±0.01	0.89±0.01	0.89±0.01
White Blood Cells, (10^9)	5.88±0.14	11.02±0.4*	12.48±0.4*
Stab Neutrophils, (%)	3.05±0.29	8.53±0.74*	9.69±0.61*
Segmented Neutrophils, (%)	61.18±0.74	64.48±1.65*	66.09±1.44*
Lymphocytes, (%)	28.09±0.6	18.82±1.4*	16.72±1.2*
Monocytic Cells, (%)	5.45±0.38	6.04±0.4	5.03±0.2
ESR mm/hour	6.0±0.6	29.2±1.7*	28.2±1.5*

Note: * – significant differences from the group of healthy individuals ($p < 0.05$).

Thus, 40.5 % of patients had hematological signs of impaired immune response, which indicates the inflammation development, unfavorable for the patient's rapid recovery.

ESR indices were the evidence of the low clinical activity of the inflammatory process. In 33 (33.5 %) patients these values did not exceed 20 mm/h, in 45 (53.2 %) patients their values were in the range of 20–40 mm/h, and only in 22 (22.2 %) patients they were above the physiological range of 40 mm/h.

The observation results showed a positive dynamics in the treatment of group 2 patients with the regional administration of the second antibacterial drug in addition to the main method of treatment. Namely, there was a decrease in the length of their hospital stay in comparison with the patients of the first group. Already on the 4th day, a positive dynamics was noted in the results of blood tests (an increase in the number of RBC, ESR decrease, a decrease in the number of WBC, etc.), a decrease in the symptoms of general intoxication of the body and a decrease in signs of local inflammation were also observed. The wound cleared up and granulations appeared there three days earlier. The normalization of body temperature in patients of the group 2 took place 3–4 days earlier, the body temperature in the group 1 patients was accompanied by periodic rises. In the second group of patients, simultaneously with the normalization of body temperature, the general status improved, sleep and appetite returned to normal.

When injected intramuscularly, the drug enters the bloodstream from the lymph sinuses. The antibacterial drug enters the bloodstream from the lymphatic system periodically, in small doses, while maintaining a positive concentration of the antibiotic in the lymphatic system and a longer stay in the bloodstream. This explains the preservation of a high concentration of the antibacterial drug in soft tissues in the inflammatory process region in comparison with the same intramuscular administration.

When using this method of introducing antibacterial drugs, we identified three types of complications: infiltrate formation, skin necrosis, and allergic reactions.

Our clinical data evidenced the significant changes in the immune status in 17.3 % of patients with phlegmons of the maxillofacial region and neck. In the course of traditional antibacterial therapy, the general status stabilization in 40 (88 %) patients of group 1 was noted on the 4–5th day after surgery, in 5 (12 %) patients – on the 4–5th day after the revision of the wounds and elimination of leakages in the hidden cellular tissue spaces. The reduction in pain syndrome occurred on the 5th day. Observing a weakly expressed inflammatory response to the treatment, there were no signs of limiting the process of the group 1 patients for a long time. In 17 (37.7 %) patients, pyorrhea decreased on days 6–7; scanty, flaccid granulations formed in the wound on days 8–9. The mean number of days spent in the hospital of the group 1 patients was 13.21 ± 1.3 days.

In 5 (12 %) patients, recovery took a longer time, since several interfascial spaces and anatomical regions were involved (table 3). Serous-purulent fluid persisted against the background of already formed granulation tissue; up to 6–7 days, infiltration of soft tissues along the wound periphery did not diverge until 8–9 days. A decrease in the pyorrhea amount in 4 (8.8 %) patients was observed on the 8th day, fine-grained granulations appeared on the 7th day, complete cleansing of the wound and convergence of the edges were noted on the 10th day. The mean hospital stay for these patients was 12.34 ± 1.1 days, since these patients had a concomitant diabetes mellitus. The dynamics of clinical manifestations in patients of the group 1 was more pronounced.

Comparative characteristics of clinical indices in patients with phlegmons of the maxillofacial region

Index	Group 1 (n=45)	Group 2 (n=55)
General status improvement, (days)	4.7±0.6	2.4±0.7
Pain syndrome reduction, (days)	4.2±0.4	2.5±0.8
Purulent fluid reduction, (days)	6.2±0.7	3.4±0.6*
Granulations appearance, (days)	5.5±0.9	3.2±0.5*
Wound cleansing, (days)	8.2±0.8	6.2±0.7*
Inpatient day, (days)	12.7±1.2	9.5±0.6*

Note: * – statistically significant differences from the control group ($p < 0.05$).

Clinical picture improvement and general status stabilization in 53 (96.4 %) patients of group 2 took place on the third day after surgery, in 43 (95.6 %) patients of group 1 – on 4.7 ± 0.6 days ($p > 0.05$), the intensity of pain syndrome decreased on average by 4.2 ± 0.4 days ($p > 0.05$).

In 48 (87.3 %) patients of group 2, pyorrhea was absent after $3.4 \pm 0.6^*$ days ($p > 0.05$), the formation of granulations – after $3.2 \pm 0.5^*$ days ($p > 0.05$), and complete cleansing and convergence of the wound edges – after $6.2 \pm 0.7^*$ days ($p > 0.05$). In 4 patients of groups 1 and 2, the healing time of the postoperative wound was longer: the cessation of pyorrhea was noted after 6.2 ± 0.7 days ($p > 0.05$), the onset of granulations – after 5.5 ± 0.9 days ($p > 0.05$), complete cleansing and marginal convergence of the wound – after 12.7 ± 1.2 days ($p > 0.05$) (table 3).

Before hospitalization, patients did not seek medical help from a doctor, they were self-medicated, and they also used antibacterial drugs without a doctor's prescription, which in turn made it difficult to treat inflammatory diseases in the hospital, since microorganisms were weakly sensitive to antibiotic therapy.

Before hospitalization, patients did not seek medical help, self-medicated, and used antibacterial drugs without a doctor's prescription, which, in turn, made it difficult to treat inflammatory diseases in the hospital, since microorganisms were weakly sensitive to antibacterial therapy.

The expediency of topical regional application of antiproteinase drugs has been experimentally and clinically proven. In conditions of impaired venous outflow, the most effective is the administration of drugs into the regional arterial bed. For this purpose, the artery is isolated and catheterized, and the sequential administration of drugs (anticoagulants, antispasmodics), which improve the rheological properties of blood, is carried out. However, the sequential administration of these drugs does not always allow to normalize venous outflow quickly and effectively. In addition, with this method of administration, these drugs do not have the necessary anti-inflammatory properties, which are sufficient to stop the perifocal inflammatory response and do not provide the delivery of the antibiotic directly to the inflammation focus [6].

The observation results showed a positive dynamics of treatment of the group 2 patients with the regional administration of the second antibacterial drug in addition to the main method of treatment due to the creation of an antibiotic depot in the regional lymph nodes and an increase in the duration of the therapeutic dose action in the inflammation focus region [9].

Therefore, according to the study results, it can be argued that the proposed comprehensive treatment approach in patients with odontogenic phlegmons of the MFR (group 2) contributed to the acceleration of reparative processes, a reduction in the inflammation duration and faster wound healing (8.5 ± 1.2 day, $p \leq 0.05$ bed days) [8].

An important component of the successful and prospective treatment of MFR's phlegmons is the connection of biologically concepts and compliance with modern treatment methods using a sound approach to the provision of emergency care [8].

Conclusions

1. Regional lymphotropic administration of antibiotic antibacterial drug in the treatment of phlegmons of the maxillofacial region and neck leads to an accelerated manifestation of the second phase of the wound process development, more rapid detoxification of the body, a decrease in the number of complications, as well as the prevalence of pronounced positive lymphogram dynamics.

2. Studies have shown that a small-molecule antibacterial drug administered regionally into the lymphatic system accumulates in higher concentrations in various organs and tissues in comparison with the main antibacterial drug of a broad spectrum when administered intramuscularly.

3. When comparing the results of treatment of patients with focalized forms of purulent-inflammatory diseases of the maxillofacial region, the groups revealed a decrease in the dynamics of the disease course and the patient's recovery by at least two times.

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INCIDENCE OF OBSTETRIC AND EXTRAGENITAL PATHOLOGY IN VARIOUS-LEVEL OBSTETRIC INSTITUTIONS IN AZERBAIJAN

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The purpose of the work was to study the incidence of obstetric and extragenital pathology in various maternity institutions of the Republic of Azerbaijan for the period 2012-2014: in perinatal centers and district maternity hospitals. The study of obstetric and extragenital pathology in obstetric institutions of various levels of the Azerbaijan Republic for the period 2012-2014 showed that oedema and proteinuria without hypertension were found to 1.2 times more often in women admitted to obstetric regional institutions of the 2nd level, premature rupture of membranes – 4 times more often, urinary tract infection and 4.7 times more often than hospitalized in institutions of the 3rd level. At the same time, in pregnant women hospitalized in level 3 institutions in 2012-2014, clinical manifestations of FNP were 1.1 times more common, and pelvic organ pathologies were 5.6 times more common than in district maternity hospitals (level 2).

Key words: prenatal period, risk group, obstetric pathology, extragenital pathology, hospitalization, perinatal centers.

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ЧАСТОТА АКУШЕРСКОЇ ТА ЕКСТРАГЕНІТАЛЬНОЇ ПАТОЛОГІЇ В РІЗНОРІВНЕВИХ РОДОДОПОМІЖНИХ УСТАНОВАХ АЗЕРБАЙДЖАНУ

Метою роботи було вивчення частоти акушерської та екстрагенітальної патології в різних пологових установах Азербайджанської Республіки за період 2012-2014 років: у перинатальних центральних та районних пологових будинках. Вивчення частоти акушерської та екстрагенітальної патології в акушерських установах різного рівня Азербайджанської Республіки за період 2012-2014 років показало, що набряки та протеїнурія без артеріальної гіпертензії зустрічались у 1,2 рази частіше у жінок, госпіталізованих в районні акушерські установи 2-го рівня, передчасний розрив плідної оболонки – в 4 рази частіше, інфекції сечовивідних шляхів – в 4,7 рази частіше, ніж у госпіталізованих в установи 3-го рівня. Натомість, у вагітних, госпіталізованих в установи 3-го рівня в 2012-2014 роках, клінічні прояви ФНП зустрічались в 1,1 рази частіше, а патології тазових органів – в 5,6 разів частіше, ніж у районних пологових будинках (2-й рівень).

Ключові слова: допологовий період, група ризику, акушерська патологія, екстрагенітальна патологія, госпіталізація, перинатальні центри.

This work is a fragment of the doctoral dissertation “Clinical and pathogenetic features of perinatal losses in the conditions of transition to modern criteria of live birth”

With a combination of extragenital and obstetric pathology, the most unfavorable outcomes of labor are noted: the frequency of preterm labor increases, the risk of untimely discharge of amniotic fluid increases, the frequency of labor abnormalities, acute fetal hypoxia increases, and, as a result, the frequency of pathological labor increases [2, 3, 4, 8]. The development of rational tactics for the management of pregnancy and childbirth, as well as the correct choice of terms and methods of delivery based on a