Abstract

The current high level of medical care in the world, in particular in obstetrics and gynecology, creates the preconditions for the optimal preservation of women's reproductive health and quality of life. However, in low-income countries, the quality of care for pregnant women and women after labor needs to be significantly improved. Women’s poor education, insufficient awareness of the threatening signs of a fetus during pregnancy as well as the lack of awareness of contraception lead to a large number of unplanned pregnancies, short intervals between pregnancies that negatively affects women’s health. Such patients more often suffer from the anemia of pregnant women, late gestosis, fetoplacental insufficiency, fetal growth retardation. Also, the arsenal of diagnostic methods is not wide enough, and the untimely treatment of women leads to a complicated course of pregnancy and childbirth. Currently, infections are in the fourth rank in the structure of the world’s maternal mortality and account for 11%, and in low-income countries, septic shock is one of the leading dangers, despite significant progress in the prevention and treatment of purulent-septic complications in obstetrics. In all countries, there is an increase in cases of sepsis, and its treatment is accompanied by serious costs while maintaining high mortality [1]. But at first glance, paradoxical is the fact that in high-income countries, there is a tendency to increase the incidence of postpartum purulent-inflammatory diseases, despite the extremely high level of medical care. According to the studies [2], the incidence of severe sepsis with fatal consequences increases by 10% per year. The main risk factors are: late motherhood, obesity, pregnancy with chronic diseases, the use of assisted reproductive technologies and multiple pregnancies, high frequency of cesarean sections (operative delivery increases the risk of development of postpartum purulent-septic complications in 5-20 times).

Keywords: Pathogenetic Concept; Postpartum Purulent-Inflammatory Diseases; Method of Fluorescent Spectroscopy; Reproductive Health

Introduction

The definition of sepsis and septic shock has changed three times during the last 25 years; every four years, the international intensive care protocol was updated with the participation of leading organizations and experts. Thus, the urgency of the problem is obvious and requires doctors of all specialties of modern knowl-
edge for early timely detection and for early targeted treatment of sepsis and septic shock in obstetrics.

There is certain specificity in the formation of purulent-inflammatory diseases in pregnant women and women after the labor. On the one hand, the positive point is the young age of the woman, the absence of severe extragenital pathology in most cases, a well-developed algorithm for monitoring the health of pregnant women detect minimal violations of her health, the localization of the source of an infection in the pelvic cavity, availability for diagnosis and treatment, the sensitivity of the microflora to broad-spectrum antibacterial drugs.

At the same time, the course of postpartum purulent-inflammatory diseases in pregnant women is accompanied by atypical erased progress which is characterized by a discrepancy between nonspecific general manifestations and the severity of the local pathological process. Women are also characterized by physiological immunesuppression, increased white blood cell count, vascular endothelial dysfunction, increased levels of proinflammatory cytokines in childbirth, the presence of an inflammatory reaction in pregnancy complications (preeclampsia, eclampsia, premature birth).

In addition, during pregnancy there are characteristic physiological changes that level the informativeness of certain diagnostic criteria, in particular, tachycardia and tachypnea. Also, in obstetric sepsis, body temperature does not change significantly. If patients in the general population with sepsis have the specific disturbance of consciousness, drowsiness among pregnant women may be a sign of the physiological course of pregnancy. For ordinary patients with sepsis, edema or a positive fluid balance are typical. At the same time, the edema of pregnant women is also a frequent manifestation, which makes this indicator also uninformative in the diagnosis of obstetric sepsis. Hyperglycemia greater than 7 mmol/l without diabetes is typical for sepsis. In pregnant women, normal blood sugar levels should not change, but gestational diabetes is also a common phenomenon that can "mask" the clinical picture of sepsis and complicate its diagnosis [3].

In order to study effectively the changes that occur in the body during the development of septic conditions, it is at first advisable to study septic processes in other models, and then use the data to assess obstetric sepsis. As part of our research, we studied sepsis on in vitro models by examining blood serum (BS) when diluted with centrifuged and non-centrifuged bacterial culture of Staphylococcus aureus, and later we studied the serum of in surgical patients with purulent-septic diseases as well as sepsis patients and patients with burn injury, who have a high risk of developing septic complications. In fact, patients with burn injuries can be model objects for studying the peculiarities of serum changes in sepsis. The acquired knowledge can be effectively used for the in-depth understanding and interpretation of the results of the study of women in labor with postpartum purulent-inflammatory diseases.

In our opinion, in order to increase the level of medical care for women during pregnancy and in the postpartum period, it is necessary to carry out a set of effective interventions. On the one hand, clinical protocols should be improved and training courses for health professionals should be conducted, effective diagnostic methods should be developed and modern statistical methods should be used to evaluate the results of the study. On the other hand, which is especially important for low-income countries, it is also important to raise women’s awareness of need for timely registration and dispensary monitoring during pregnancy in order to increase their awareness of reproductive health, threatening signs during pregnancy, physiology and hygiene of the postpartum period. That’s why it is important to organize and conduct classes in the "School of Mothers" for pregnant women, and for women and couples it is also advisable to conduct classes in the "School of Responsible Parenthood". We cannot stay away from this important problem and take an active part in solving it, either. Our goal is to actually help doctors to understand and comprehend modern approaches to personal medicine and individual approach to each patient by using new modern diagnostic methods.

For the last 20 years, we have been developing and implementing the method of fluorescence spectroscopy (MFS) for the diagnosis of purulent-inflammatory diseases and sepsis in surgical practice [4-6] and women with postpartum endometritis [7-9], for patients with burn injury [10,11].

The aim of the research is to develop and implement the method of fluorescence spectroscopy for monitoring and assessing women during pregnancy, before childbirth and in the postpartum period in order to optimize, control and assess their condition.

**Methodology**

The clinical research center for this particular investigation was the Department of Gynecology №2 of Vinnytsia Council Clin-
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The luminescent laboratory of the Department of Experimental Physics, Ivan Franko Lviv National University was an experimental research centre. The overall research was carried out from 2015 to 2019. We used the clinical-anamnestic method, clinical, laboratory, instrumental and statistical diagnostic methods to diagnose the health status of women during pregnancy, childbirth and in the postpartum period. In women with postpartum purulent-inflammatory diseases vacuum aspiration of the walls of the uterine cavity was performed, followed by histopathological examination of the metroaspirate. In addition to standard diagnostic methods, we also additionally used the method of fluorescence spectroscopy (MFS) (Patent for the model UA 76953 from 25.01.2013 and Patent for the model UA133472 from 10.04.2019) [12,13].

The investigation was carried out using monochromators MDR-2 and MDR-12. BS stimulation was done under wavelength of 280 nm. The choice of this particular wavelength can be supported by the fact, that it detects albumin molecules, which undergo conformational changes during purulent-inflammatory diseases. The main focus of this study was to investigate the BS and involved the following patient cohorts: 40 pregnant women, 170 patients with postpartum purulent-inflammatory diseases and 40 patients with uncomplicated course of the postpartum period. The research was carried out according to the Human Research Ethics protocol (fragment from protocol №11 of the Bioethics Committee of National Pirogov Memorial Medical University, Vinnytsia, from 19.11.2015).

Data analysis

Among the statistical research methods we used the method of logistic regression and ROC-analysis. In terms of medical research, logistic regression helps to derive a model, based on dependency between characteristics of a particular disease and its prognostic factors; this model is a cornerstone of the timely and correct diagnosis. Another potential use of this model is the evaluation of potential risk factors in clinical practice. Additionally, statistical data assessment was carried out using ROC-analysis (Receive Operating Characteristics), which is an alternative method to determine significance of clinical tests. ROC-analysis is the final stage of establishing the most efficient model; it enables determination of cut-off threshold as well helps in devising the most viable model of prognosis [14].

Results

Spectral analysis is one of the most important methods for studying the structure of matter and physical processes, which take place in it, including at the molecular level. Luminescence occurs due to the absorption of light by the system under study due to the transition of its molecules from the excited state to the ground state. The absorption and radiation processes are presented in more details in figure 1.

In the initial state (it is also called the ground, unexcited state), the molecule (atom) occupies the energy position with the lowest energy (Figure 1a). The absorption of light transfers the system from the ground state to the excited states, which, along with the electron state, also have vibrational energy due to the oscillation of molecules. Therefore, such states are also called electron-oscillating (Figure 1b). Due to the oscillating motion, the electronic energy of the molecule turns into oscillating; the molecule loses its energy and for about 10-12 seconds relaxes to the lowest excited state (Figure 1c). The molecule transitions from this lowest excited state to the ground state are accompanied by radiation - luminescence (Figure 1d).

According to the afterglow duration, $\tau$ luminescence is divided into two types: fluorescence if $\tau < 10^{-7}$ seconds, i.e. the extinction of luminescence occurs very quickly (for the eye, instantly); phosphorescence if $\tau > 10^{-4}$ seconds. In this case, the extinction occurs relatively slowly and is often clearly visible to the naked eye). As part of our own research, we studied radiation with short attenuation times, that is fluorescence.

Before discussing the results of the study of BS of patients with purulent-septic complications in the framework of MFS, we briefly dwell on the basic ideas of the pathogenetic concept of diagnostic

and treatment model of purulent-inflammatory diseases and sepsis. It is based on the fact, that in diseases that are accompanied by endogenous intoxication, part of the albumin molecules in the blood of patients is blocked by toxins. As a result, there are two types of albumin molecules in their blood: normal and blocked by toxins (pathological). It is established that the spectral-fluorescent characteristics of the serum of patients with purulent-inflammatory diseases and sepsis are universal markers of the severity of their condition. At the same time their changes are registered for 24-48 hours before emergence of obvious clinical and laboratory signs of the general somatic condition of patients. The peculiarities of the behavior of these markers for various specific diseases are illustrated. At the same time, most of the currently available methods make it possible to diagnose the disease in the presence of an already developed clinical picture. The results of the influence of various factors on the spectral-fluorescent characteristics of the serum of patients are analyzed. In order to overcome optimally endogenous intoxication in patients, it is proposed to use an infusion of albumin solution.

Albumin molecules have the ability to complex. In diseases that are accompanied by endogenous intoxication, parts of their binding centers become blocked by toxins. As a result, these albumin molecules lose the ability to perform their basic functions, namely transport and detoxification. And although the total concentration of albumin in the body may be within normal limits, its actual "effective" concentration can be significantly reduced. Note that the determination of the "effective" concentration of albumin cannot be performed by modern conventional diagnostic methods, which are currently widely used in the laboratories of health care facilities. Given the pathogenetic changes of albumin molecules in endogenous intoxication, an effective point of pathogenetic treatment is the use in complex therapy of infusions of albumin solution. At the same time, infusion of albumin solution impairs the synthesis of endogenous albumin in the human body. However, without this infusion in the presence of endogenous intoxication, the body will not be able to overcome the infection on its own.

To diagnose, monitor and correct the treatment process, the method of fluorescence spectroscopy is proposed. The clinical base of the study at the first and second stages was the purulent-septic center of the Municipal City Clinical Ambulance Hospital in Lviv (Ukraine). The experimental base of luminescent research at all stages was the luminescence laboratory of the Department of Experimental Physics of the Ivan Franko National University of Lviv. The study was performed by using optical monochromators MDR-2 and MDR-12. As a source of exciting light, a deuterium lamp DDS-400 with a continuous radiation spectrum in the region $\lambda = 200-420$ nm was used. The excitation of the blood serum was performed with light with a wavelength of 280 nm, which corresponds to the glow region of human serum albumin. The main characteristics, that we study are the fluorescence intensity ($I_\lambda$) and the position of the maximum fluorescence band ($\lambda_{\text{max}}$) of the BSBS of patients is a mixture of normal (concentration $X$) and blocked by toxins (concentration $1-X$) molecules of albumin.

$$\Delta E_i \cdot \text{ is the difference between the energies of the excited and ground states of normal albumin, and } \Delta E_i, \text{ respectively, } \cdot \text{ for albumin molecules, blocked by toxins. } \Delta E_a \geq \Delta E_i.$$ Note that for patients with purulent-septic complications, the main characteristics that are studied for them $I(X)$ and $\lambda_{\text{max}}(X)$, depend from $X$ and are determined by the following relations:

$$I(X) = I_{a,X} + I_{X} \cdot (1-X)$$

$$\lambda_{\text{max}}(X) = \lambda_{\text{max}} + a \cdot X' + \lambda_{\text{max}}' \cdot (1-X)$$

$$I_{a,X}, I_{X}, \lambda_{\text{max}}, \lambda_{\text{max}}' \cdot \text{ are appropriate characteristics for normal and pathological albumin molecules.}$$

The study included some stages. At the first stage, the fluorescence spectra of BS of 100 surgical patients with purulent-inflammatory diseases were studied. Among them there were 16 patients with sepsis. Figure 2 presents the results of the study of the fluorescence spectra of the BS of the donor and the patient with severe sepsis, caused by purulent epididymitis of the lumbar-sacral spine and massive retroperitoneal intrapelvic phlegmon. She was treated in the hospital from 28 December 2001 till 15 April 2002. At the time of hospitalization (28 December 2001) she was in a critically serious condition with verified bacteraemia (blood culture of 28 December 2001 - Staphylococcus aureus). This figure shows that the maximum of the fluorescence band of the patient’s BS is shifted to the long-wavelength region by $\Delta \lambda = 40$ nm (curve 1) relative to the fluorescence band of the donor, and the fluorescence intensity was 0.3 $I_\lambda$ of the donor’s BS. This contribution is connected with the glow of albumin molecules, blocked by toxins. At the same time, in the region of $\approx 335$ nm, the luminescence intensity, mainly due

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to the contribution of full-fledged albumin molecules, is very small. This indicates that the predominant contribution to the intensity of the BS of this patient in a serious condition is made by pathological albumin molecules.

It is important to note, that the survival of patients in such a serious condition is possible only when \( X \geq X^* \) (\( X^* \) - the limit value of the concentration of complete albumin in the blood, which ensures the survival of patients with sepsis). After surgical treatment and intensive antiseptic therapy and ongoing bacteraemia (blood culture of 4 January 2002 - *Staphylococcus aureus*), a significant improvement and stabilization of the patient’s condition was noted:

- Analysis of the fluorescence spectra of the patient’s BS on the seventh postoperative day revealed that the shift of her fluorescence band changed significantly and was \( \Delta \lambda = 7 \) nm (Figure 2, curve 2). At the same time, the intensity of the patient’s fluorescence band increased significantly and quite unexpectedly to \( 1.07 I_F \).

Because of subcompensated changes in the absolute quantitative and qualitative content of BS proteins at the time of examination (biochemical studies on 2-4 January 2002: total protein and protein fractions were at the lower limit of normal), the rapid increase in the fluorescence band of the BS of patient in this case cannot be interpreted by absolute hypoproteinemia that typically causes a weakening of the concentration quenching of fluorescence, which is characteristic of protein fluorescence.

The only possible explanation for the phenomenon of increasing fluorescence band intensity of the BS of this patient registered above may be the presence of transient hypervolemia during this period of treatment: the volume of daily intravenous infusions during this treatment period was 8-10 liters. Under such circumstances, a natural increase in the fluid component of the BS leads to pseudohypoproteinemia - a laboratory phenomenon which is not a standard biuret reaction and can be differentiated from true hypoproteinemia only by special techniques and the normogram of Phillips and van Slyke.

Note, that due to the lack of experience in studying the process of recovery of patients in septic conditions, the unique opportunity to obtain valuable information about the behavior of spectral-fluorescence characteristics within six days after December 28, 2001 was lost. At this time the patient obtained treatment, which helped her to come out of severe condition 1, namely the intensity of peak 1 decreased significantly, and the peak at \( \lambda \approx 335 \) nm appeared. It is most likely, that the patient went from this state to state 2. This was connected with a decrease of the concentration of pathological albumin molecules and an increase of the number of normal ones.

Further studies of the fluorescence spectra of this patient showed, that bacteremia was not overcome. Although (see Figure 2, curves 3,4) the long-wave septic peak disappeared only a further long process of treatment under the influence of complex therapy led to a significant suppression of bacteremia and a significant improvement in the patient’s condition (Figure 2, curve 5) and she was discharged from the hospital in satisfactory condition.

In our opinion, the forced excessive therapeutic dilution of the blood during this period caused a weakening of the concentration quenching of the fluorescence of the BS of this patient and caused

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Table 1: Changes of the spectral-fluorescent characteristics of the patient 1 with sepsis.

**Figure 2:** Fluorescence spectra of blood serum of septic patient: 1 - Dec. 12; 2 - Jan. 4; 3 - Feb. 12; 4 - Mar. 19. 5 - June 4 and donor of BS (340 nm - “normal peak”, 380nm - “septic peak”).

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an increase in the intensity of the fluorescence bands of her BS. Undoubtedly, the above-mentioned significant increase in the intensity of the fluorescence band of her BS from 4 January 2002 was influenced by the weakening of septic symptoms.

Thus, according to our studies of the fluorescence spectra of the BS of the above patient, the decrease of intensity and shift of the fluorescence band are connected to the presence of advanced septic process and correlate with integrated indicators of clinical severity and bacteremia. The dynamics of changes in the spectral-fluorescent characteristics of the BS of the mentioned patient quite objectively reflects the course of sepsis and correlates with the effectiveness of treatment tactics. It is important that for the first time we obtained fundamental results for the fluorescence spectra of a patient with sepsis and studied the dynamics of their changes during the recovery. They became a reference point for our further studies of the fluorescence spectra of BS of patients with purulent-inflammatory diseases and sepsis. They became a reference point for our further studies of the fluorescence spectra of BS of patients with purulent-inflammatory diseases and sepsis.

Figure 3 presents the results of the study of another person with sepsis. Due to the timely hospitalization and early surgical elimination of the source of infection, the progress of the septic process was much lower. Therefore, at the time of hospitalization there was only a significant decrease in the intensity of fluorescent spectra of BS, but the "septic" peak was absent, which was a good prognostic sign (Figure 3).

Nevertheless, after elimination of the source of infection on the background of intensive antibiotic therapy of this patient with a clinically mild course of sepsis for some time there was bacteremia - Klebsiella pneumoniae (curves 1-3). Note, that the decrease of the intensity of the fluorescence bands reached a maximum (0.16 $I_f$) only at the end of the bacteremic period. Subsequently, with the gradual recovery of the mentioned person, there was a significant increase in the fluorescence intensity of the BS up to 0.75 $I_f$ (Figure 3, curve 5).

Based on the analysis of the results of the study of FS of BS and the clinical features of sepsis in both of the above cases, we recorded a similar nature of the dynamics of the disease in the "postbacterial" period. At the same time, the study of the spectral-fluorescent characteristics of the BS of these patients, allowed to trace clearly the nature of the disease to recovery in contrast to

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Table 2: Changes of the spectral-fluorescent characteristics of the patient 2 with sepsis.

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Table 3: Changes of the spectral-fluorescent characteristics of the patient 3 with sepsis.

The second stage of our research was a series of in vitro experiments. In particular, the study of the spectral-fluorescent characteristics of BS dilutions with distilled water, 20% albumin solution, sugar broth, non-centrifuged and centrifuged bacterial cultures of *Staphylococcus aureus* [15]. Let us focus on the most important of the results. The dilution of BS with distilled water causes an increase of the fluorescence intensity of BS (Figure 5). However, the position of the maxima of the fluorescence bands does not change. Changes in fluorescence spectra during the dilution of BS with distilled water have a specific character and form the basis for the development of the fluorescent method to diagnose various diseases accompanied by hypoproteinemia and hypoalbuminemia and various treatments (study of the effects of infusion therapy). This made it possible to model the effect of infusion therapy on the spectral-fluorescence characteristics of BS of patients.

A similar effect was observed with massive infusion therapy (Figure 2, curve 2). Our in vitro studies of the bacteria of standard dilutions of the donor BS with distilled water (see Figure 5) confirmed the correctness of our suggested explanation of the registered phenomenon of fluorescence intensity increase of the BS of the patient with sepsis (Figure 2, curve 2). After all, the decrease in the content of BS in the samples after the addition of distilled water also leads to a significant increase in the intensity of the fluorescence bands.

It is important, that the dilution of BS with albumin solution has small effect on the spectral-fluorescence characteristics of these solutions. However, the position of the fluorescence bands does not change. Changes of fluorescence spectra, when diluting BS with distilled water have a specific character and form the basis for the development of a fluorescent method to diagnose various diseases accompanied by hypoproteinemia and hypoalbuminemia and to study the effects of infusion therapy. This made it possible to simulate the effect of infusion therapy on the spectral-fluorescent characteristics of BS of patients.

The detected effect of changing of the spectral-fluorescent characteristics of dilutions of BS by bacterial culture is due to the influence of bacteria and products of their metabolism on the molecules.

Note that patients with diabetes have elevated levels of glycosylated albumin in the blood serum. In healthy people it’s level is 6%, but in patients with diabetes - 9%. Therefore, albumin molecules in patients with diabetes have fewer free binding centers, which impair the detoxification function in these patients and leads to a prolonged course of purulent-septic conditions. This case is a clear evidence of this. The old age and a number of comorbidities further worsened the prognosis, leading to the development of exitus lethalis.

The patient’s condition deteriorated steadily during the follow-up period, despite surgery and intensive antibiotic therapy that may be explained by the presence of a number of severe comorbidities and her advanced age. The negative dynamics of this patient’s condition is reflected by the unfavorable dynamics of the parameters of the spectral-fluorescent characteristics of her BS: a constant decrease in the intensity of the fluorescence bands (Figure 4, curves 1, 2, 3). Unfortunately, the mentioned patient died as a result of the advanced process of the generalization of infection and multiorgan failure. The dynamics of changes in the spectral-fluorescent characteristics of the BS of patients with sepsis objectively reflects the clinical features of the disease, which significantly depends on the quality of diagnosis and correlates with the effectiveness of treatment tactics.

To illustrate the above considerations, we present the results of the studies of the spectral-fluorescent characteristics of the BS of the patient with sepsis and diabetes mellitus (Figure 4, Table 3). The patient's condition deteriorated steadily during the follow-up period, despite surgery and intensive antibiotic therapy that may be explained by the presence of a number of severe comorbidities and her advanced age. The negative dynamics of this patient’s condition is reflected by the unfavorable dynamics of the parameters of the spectral-fluorescent characteristics of her BS: a constant decrease in the intensity of the fluorescence bands (Figure 4, curves 1, 2, 3). Unfortunately, the mentioned patient died as a result of the advanced process of the generalization of infection and multiorgan failure. The dynamics of changes in the spectral-fluorescent characteristics of the BS of patients with sepsis objectively reflects the clinical features of the disease, which significantly depends on the quality of diagnosis and correlates with the effectiveness of treatment tactics.

of albumin of BS. Changes of the fluorescence spectra of BS during dilution of BS by bacterial cultures (Figure 6, 7) have a specific character and form the basis for the development of a fluorescent method for early diagnosis of sepsis by studying the spectral-fluorescence model of sepsis in vivo. The behavior of the spectral-fluorescent characteristics of dilutions of BS with sugar broth has a similar character.

**Figure 5:** Effect of dilution with distilled water (DW) on the fluorescence spectra of donor blood serum (BS) (1 - BS, 2 - 90% BS, 3 - 80% BS, 4 - 70% BS, 5 - 60% BS, 6 - 50% BS, 7 - 40% BS, 8 - 30% BS, 9 - 20% BS, 10 - 10% BS, 11 - DW: If = 0).

When diluting the BS by bacterial cultures of *Staphylococcus aureus* (Figure 6, Figure 7) $I_f$ gradually decreases with increasing content of bacterial culture in solution. There is also a long-wave shift of the fluorescence bands ($\lambda_{max}$) of these dilutions. The detected effect of changing of the spectral-fluorescent characteristics of dilutions of BS by bacterial culture is connected with the influence of bacteria and products of their metabolism on the molecules of serum albumin of the BS.

At the third stage of the study, the main task was to develop the optimal treatment tactics and methods of effective control of the treatment process for the 25 patients with burn injuries and 40 patients of control group. The clinical base of the study was the burn department of Lviv Communal City Clinical Hospital No 8. The research lasted in 2015-2019. The comparison group consisted of 25 patients in serious condition, whose BS was not tested by using MFS. But for these patients a modified treatment regimen was used, as well as for patients of the main group. After all, as mentioned above, burn patients can be a standard for studying the features of the spectral-fluorescent characteristics of the BS of patients with purulent-inflammatory diseases and sepsis.

The most optimal approach for the detection of septic conditions in patients is the study of the spectral-fluorescent characteristics of the BS in the frame of the method of fluorescence spectroscopy. There is a high risk of septic condition in burns in two cases, namely: with a large area and depth of burns and inadequate treatment at the initial stage of the disease. Therefore, the key thesis of successful treatment is a comprehensive approach to prevention of the development of bacteremia through early surgical treatment and comprehensive therapy. The fundamental idea of the successful completion of the treatment process is constant monitoring of it within the method of fluorescence spectroscopy with the possibility of its correction. In the treatment process, the intensity of the fluorescence and position of the fluorescence maximum are of fundamental importance. The lower the fluorescence intensity, the...
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Figure 7: Effect of dilution centrifuged (CF) crops on fluorescence spectra of donor blood serum (BS) (1 - blood serum (BS) 2 - 90% BS 3 - 80% BS, 4 - 70% BS, 5 - 60% BS, 6 - 50% BS, 7 - 40% BS, 8 - 30% BS, 9 - 20% BS, 10 - 10% BS, 11 - CF crops). λ_{ex}=280 nm.

higher the probability of a septic condition and the more likely is exitus letalis.

The results of the research of fluorescence spectra of the patient with the burn injury with the burn surface area 28%, who was hospitalized in February 2017, in the dynamics, are presented in Figure 8, and the data for the spectral-fluorescent characteristics of his BS are depicted in table 3.

He was immediately given appropriate treatment, including antibiotic and infusion therapy of up to 3 liters daily, as well as infusions of 10% donor albumin (February 6 and 10) in amount 100 ml. The condition of this patient was much more severe than the previous one. Despite intensive treatment, his condition deteriorated markedly during the first 5 days. This is evidenced by the decrease in fluorescence intensity and a slight long-wavelength shift (Figure 8, curves 8.1, 8.2). Compared with the previous patient in this case, most likely, there was a more noticeable endogenous intoxication. Therefore, the correction of the treatment process was performed for him, including the infusion of 10% solution of donor albumin (February 15, 18, 26 and March 2 in the amount 100-150 ml). It is obvious that the intake of a sufficient amount of albumin significantly improved the work of the body’s detoxification systems with the subsequent normalization of the body’s synthesis of endogenous albumin. As a result, the fluorescence intensity of the patient’s BS gradually increased, and the long-wave shift leveled off. After that, the patient was discharged from the hospital in a satisfactory condition. Without correction of the treatment process, the patient’s condition could have deteriorated (Figure 8, curve 8.3′) towards a subsequent transition to the severe septic condition, as it was as in case of the patient with sepsis.

Figure 8: FS of BS of patient 8 with a burn trauma, who was hospitalized in Communal City Clinical Hospital №8, Lviv in 2017 in the dynamics during treatment (8.1 - 9.02., 8.2 - 14.02., 8.3 - 22.02., 8.3′ - 22.02., 8.4 - 27.02., 8.5 - 03.03., 8.6 - 10.03., 8.7 - 31.03.), and a patient with sepsis, who was treated in 2002 in Ambulance Hospital (1′ - 3.06., 2′ - 5.06; 3′ - 6.06; 4′ - 7.06, 5′ - 10.06) and 20% albumin solution (a).λ_{ex}=280 nm.

Our results for the spectral-fluorescence characteristics of the above-mentioned patient with burn injury correlate well with the corresponding results (Figure 8, curves 1′-5′) for a patient with sepsis, treated in hospital in 2002. Regardless of the etiological factors of sepsis, the pathogenetic mechanisms of septic complications are unified. Serum albumin molecules have the ability to complexation. In case of the presence of endogenous intoxication

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Table 4: Changes of the spectral-fluorescent characteristics of the patient 8 with burn trauma.

in the body, they are blocked by the products of bacterial metabolism. Understanding the microscopic mechanisms of the theory of pathological albumin formation is the basis for the development of pathogenetic treatment tactics [16].

It is obvious, that the intake of a sufficient amount of albumin has allowed to improve significantly body’s detoxification systems with the subsequent normalization of the synthesis of endogenous albumin. As a result, the fluorescence intensity of the patient’s BS gradually increased, and the long-wave shift leveled off. After that, the patient was discharged from the hospital in satisfactory condition. Note, that without the correction of the treatment process, the patient’s condition could deteriorate further (Figure 8, curve 8.3′) with subsequent transition to a severe septic condition, as was in the case with a patient with sepsis in this figure. Note, that our results for the spectral-fluorescence characteristics of the above-mentioned patient with burn injury correlate well with the corresponding results (Figure 8, curves 1′-5′) for a patient with sepsis who was treated in hospital in 2002. Regardless of the etiological factors of sepsis, the pathogenetic mechanisms of septic complications are unified. In the case of the presence of endogenous intoxication in the body, aluminum molecules are blocked by the products of bacterial metabolism. Understanding the microscopic mechanisms of the theory of pathological albumin formation is the basis for the development of pathogenetical treatment tactics. Therefore, the key thesis of successful treatment is a comprehensive approach to prevention of the development of bacteremia through early surgical treatment and comprehensive therapy. The fundamental idea of successful completion of the treatment process is constant monitoring within the method of fluorescence spectroscopy of the treatment process with the possibility of its correction.

Figures 9-10 present the results of the studies of fluorescent spectra of pregnant women (Figure 9: pregnant women 1-4) and (Figure 10: pregnant women 5-10). These figures show that among pregnant women, there is an increase of the fluorescence intensity of their BS up to 30% as compared with the spectral-fluorescence characteristics of the 20% albumin solution used as a reference. During pregnancy, women have a physiological increase in circulating blood volume, but the level of protein in it is almost unchanged. Due to this, physiological hypoproteinemia occurs, and the mutual concentration quenching the luminescence of albumin molecules decreases. Therefore, the intensity of serum fluorescence increases. An additional confirmation of this fact is also the results of the study of the fluorescence spectra of dilutions of BS with distilled water (see Figure 5), which also demonstrates a similar effect. Thus, the dilution of BS with distilled water can be used as model objects to study hypoproteinemia, as well as to assess the impact of infusion therapy on the human’s body.

Figure 9: Fluorescence spectra of the serum of pregnant women (1-10) and 20% solution of donor albumin (a) ($\lambda_{\text{ex}} = 280$ nm).

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Some results of the study of fluorescence spectra of the BS of women with uncomplicated course of the postpartum period are presented on Figures 11-12. It was found that among women of this group there was almost no noticeable shift of $\lambda_{\text{max}}$ (the value of this indicator ranged from 330 to 377 nm). The intensity of fluorescence is in the range of 0.81-1.31 r.u. compared with $I_F$ of 20% of donor albumin. The observed increase in $I_F$ is probably related to the phenomena of relative hypoproteinemia in them, which continues to persist in the postpartum period. This information is very important in the analysis of our results of the study of fluorescent spectra of BS of women in the main group with postpartum purulent-inflammatory diseases. Note that the average value of $I_F$ in women of the control group is 0.96 r.u., and the average value of $\lambda_{\text{max}}$ in this group was 333 nm.

Figures 13-19 shows, for example, the results of the study of the fluorescence spectra of BS of women of the main group with postpartum purulent-inflammatory diseases. In general, for patients of the main group there is a decrease of the intensity of serum fluorescence, which according to our pathogenetic concept, is associated with the blocking of some albumin molecules by toxins, which leads to the decrease of the concentration of complete albumin in the BS.

Quite interesting are the results of the study of the fluorescent spectra of the BS of Patient 60 after labour, depicted in Figure 13 and in Table 5. She was hospitalized in the gynaecological department on the 13th day after the childbirth. This patient had a gynaecological disease (cervix erosion), and an episiotomy was performed during the labour. In the postpartum period, mild anaemia and 3rd-degree vaginal cleanliness were revealed. The ultrasound diagnostics also showed an anomaly of uterine development with enlarged cavity with hyperechogenic content. Three blood samples were taken to see the dynamics. The fluorescence intensity of BS was slightly decreased for the second sample (curve 60'). She had some complaints (general weakness, fever up to 39.5°C). At that time, the vacuum aspiration of the walls of the uterine cavity was performed for therapeutic purposes. As a result, the patient’s condition improved (curve 60''), and subsequently, she left the hospital in a satisfactory condition.

The importance of the study of fluorescent spectra of BS of Patient 61 after childbirth in the dynamics is depicted in Figure 14 and in Table 6. This patient was treated for mycoplasmosis and extragenital pathology (chronic bronchitis). There was the threat of a premature childbirth at the 32nd week of her pregnancy. There was a 1st-degree rupture of the cervix during the delivery.

During the analysis of vaginal output, bacterial vaginosis was detected. Complaints, i.e. the lower abdominal pain and fever up to 38°C in the patient, appeared on the 23rd day of the postpartum period. Patient 61 was admitted to the gynaecological department on the 24th day of her postpartum period. After the vacuum aspiration of the uterine cavity walls, the endometrial histological study revealed endometritis.

**Figure 13:** Fluorescence spectra of blood serum in patient with postpartum endometritis in dynamics (60 - 24.02.2015, 60' - 26.02.2015, 60'' - 29.02.2015), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see Figure 2) and 20% donor albumin (a) \(\lambda_{ex} = 280\ \text{nm}\).

**Figure 14:** Fluorescence spectra of blood serum in patient with postpartum endometritis in dynamics (61 - 2.02.2015, 61' - 4.02.2015, 61'' - 6.02.2015, 61''' - 30.04.2015), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see Figure 2) and 20% donor albumin (a) \(\lambda_{ex} = 280\ \text{nm}\).

<table>
<thead>
<tr>
<th>N</th>
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<th>60''</th>
<th>1'</th>
<th>3'</th>
<th>4'</th>
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<tr>
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<td>336,1</td>
<td>376,8</td>
<td>339,8</td>
<td>349,5</td>
</tr>
<tr>
<td>(I, r.u.)</td>
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<td>0,91</td>
<td>0,54</td>
<td>0,51</td>
<td>0,69</td>
<td>0,29</td>
<td>0,45</td>
<td>0,39</td>
</tr>
</tbody>
</table>

**Table 5:** Spectral-fluorescent characteristics of the patient with postpartum endometritis (60) and a patient with sepsis (1', 3', 4').

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The classic form of endometritis occurs on day 3-5, and in the erased form on day 8-10 of the postpartum period. After manual vacuum aspiration for the next two days, there was a decrease in the fluorescence intensity of the BS from 0.56 r.u. (curve 61) to 0.53 r.u. (curve 61') with subsequent normalization as a result of effective antibiotic therapy of the patient (curves 61'' and 61'''). Thus, we recorded a positive dynamics of changes of the spectral-fluorescent characteristics of the BS of Patient 61, which qualitatively reproduces the recovery scenario of a patient with sepsis (curves 1', 3', 4').

Figure 15 and table 7 present a number of results of FS of BS of women in labor with postpartum endometritis (PE). In the case of Patient 69, anemia was diagnosed during pregnancy; episiotomy and episioraphy were performed in childbirth; in the postpartum period anemia, proteinuria, IV degree of vaginal purity and bacterial vaginosis were detected. This woman was hospitalized in the postpartum period in the gynecology department twice: with purulent endometritis and episiotomy wound and with late postpartum hemorrhage. Patient 70 had a complicated gynecological history (one abortion), complicated pregnancy (threat of abortion in the first trimester, late preeclampsia of pregnant women), complications of childbirth (weakness of labor activity).

From the fifth day of the postpartum period, the woman’s body temperature rose to 39.8 °C, and on the 7th day she was hospitalized in the gynecological department. In the postpartum period, this woman was diagnosed with grade III vaginal cleanliness, and after manual vacuum aspiration of the walls of the uterine cavity when sowing its contents revealed Enterococcus faecalis $10^3$ CFU/ml, sensitive to amoxicillin and gatifloxacin.

The results of the study of the spectral-fluorescent characteristics of the BS of several other patients with postpartum endometri-(see Figure 2) and 20% donor albumin (a) ($\lambda_{ex}=280$ nm).

Table 6: Spectral-fluorescent characteristics of the patient with postpartum endometritis (61) and a patient with sepsis (1', 3', 4').

<table>
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<tr>
<th>N</th>
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<td>336,1</td>
<td>329</td>
<td>376,7</td>
<td>339,8</td>
</tr>
<tr>
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<td>0,56</td>
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<td>0,72</td>
<td>0,88</td>
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</table>

Figure 15: Fluorescence spectra of blood serum in patient with postpartum endometritis (68-71), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see Figure 2) and 20% donor albumin (a) ($\lambda_{ex}=280$ nm).

Figure 16: Fluorescence spectra of blood serum in patient with postpartum endometritis (78-83), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see Figure 2) and 20% donor albumin (a) ($\lambda_{ex}=280$ nm).

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Table 7: Spectral-fluorescent characteristics of the patient with postpartum endometritis (68-71) and a patient with sepsis (1′, 3′, 4′).

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<tr>
<th>N</th>
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<td>376.8</td>
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<td>0.29</td>
<td>0.45</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Table 8: Spectral-fluorescent characteristics of the patient with postpartum endometritis (68-71) and a patient with sepsis (1′, 3′, 4′).

<table>
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<td>376.8</td>
<td>339.8</td>
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<tr>
<td>I_{F}, r.u.</td>
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<td>0.78</td>
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<td>0.81</td>
<td>0.75</td>
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Extragenital pathology (biliary dyskinesia of the hypertensive-hypokinetic type) also occurred, and TORCH infection was detected. In childbirth, the anhydrous period was 6 hours and 20 minutes.

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Figure 17 and table 9 present the results of the study of FS of BS of two women with lochometra and endometritis. Patient 57 had a burdened gynecological history (chronic adenexitis). Episotomy and episioraphy were performed during childbirth. In the postpartum period, the results of laboratory tests revealed anemia of mild degree and III degree of vaginal cleanliness. During the treatment, this patient had an increase in fluorescence intensity, which correlated with the clinical improvement of her condition and the normalization of her body temperature. Instead, in Patient 58, who was diagnosed with anemia and proteinuria in the postpartum period, manual vacuum aspiration of the walls of the uterine cavity was performed on February 2, 2015. As a result, over the next two days there was a decrease in the fluorescence intensity of the BS from 0.61 r.u. (curve 58) to 0.59 (curve 58′) with subsequent normalization of the condition as a result of effective antibiotic therapy of this patient (curve 58″).

### Table 9: Spectral-fluorescent characteristics of the patient with postpartum endometritis (57-58) and a patient with sepsis (1′, 3′, 4′).

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<td>0,70</td>
<td>0,61</td>
<td>0,59</td>
<td>0,73</td>
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</tbody>
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The results of research in the dynamics of fluorescence spectra of the BS of the patient with severe postpartum endometritis are depicted in Figure 15. The data of the spectral-fluorescent characteristics are also depicted in Table 11. The corresponding results of the patient with sepsis who was treated in 2002 are also depicted in Figure 15 for comparison.

Figure 18 and Table 10 depict the results of the study of FS of BS of two more patients with postpartum endometritis. Patient 69 had a complicated somatic anamnesis (transferred pleurisy in 2013, urolithiasis), aggravated gynecological anamnesis (chronic adenexitis). In childbirth, the anhydrous period was 6 hours and 30 minutes. In the postpartum period, anemia, proteinuria and the third degree of vaginal cleanliness were revealed. The dilation of the uterine cavity was detected by ultrasound. She had risk factors for postpartum endometritis.

### Table 10: Spectral-fluorescent characteristics of the patient with postpartum endometritis (69-70) and a patient with sepsis (1′, 3′, 4′).

<table>
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<th>69′</th>
<th>70</th>
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<td>376,7</td>
<td>339,8</td>
<td>349,5</td>
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<tr>
<td>I_{F} r.u.</td>
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<td>0,64</td>
<td>0,29</td>
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</table>

The woman had a complicated somatic anamnesis (transferred pleurisy in 2013, urolithiasis), aggravated gynecological anamnesis (chronic adenexitis). In childbirth, the anhydrous period was 6 hours and 30 minutes. In the postpartum period, anemia, proteinuria and the third degree of vaginal cleanliness were revealed. The dilation of the uterine cavity was detected by ultrasound. She had risk factors for postpartum endometritis.

### Figure 19: Fluorescence spectra of serum of a woman after childbirth with endometritis in dynamics (6.1 - 14.02.2015; 6.2 - 17.02.2015, 6.2′- 17.02.2015), a woman with uncomplicated course of postpartum period (2), patient with sepsis (1′, 2′, 3′, 4′, 5′) and 20% donor albumin (a).

This patient showed a significant decrease in fluorescence intensity to 0.35 r.u. and a noticeable long-wavelength shift of the fluorescence band. After the manual vacuum aspiration of the uterine wall, antibacterial and uterotonic therapy, the patient’s condition significantly improved. This is evidenced by the results of a study of the FS of her BS (at 70′).

condition improved. After the correction of treatment in the next experiment, a marked increase in \( I_1 \) of BS of this patient to 0.6 r.u. was recorded, and the long-wavelength shift of the fluorescence band was leveled. Without the correction of treatment tactics, the patient’s condition could deteriorate in principle (curve 6.2′) with subsequent transition to a septic state (curve 1′), as in the abovementioned patient with sepsis. Due to the proper level of treatment of patients with endometritis (even in severe form), septic condition is almost unattainable. For the correction of medical tactics, it would be possible to prescribe 100-150 ml of 20% solution of albumin infusions once. In low-income countries with improper treatment, septic condition is possible, but even here we may avoid mortality by making appropriate adjustments to treatment. If in our case the patient had passed to a state of 6.2′, the prescription of up to 150-200 ml of albumin several times would have helped to ensure her recovery. The main thing is to monitor the treatment process within the MFS and examine closely the health status of patients. Without the correction of treatment using the infusion of albumin solution, there is a high probability of transition this patient to the septic state.

A detailed study of the behavior of the spectral-fluorescent characteristics of the BS of many other patients with postpartum endometritis was also performed. The control of the medical process was carried out. The dynamics of the infusion of 20% albumin solution on the spectral-fluorescent characteristics of the BS of patients with postpartum endometritis was studied and the treatment process was monitored. It was found that it was the only case of the complicated postpartum endometritis among the 170 patients with postpartum endometritis.

Based on the use of statistical research methods (logit regression and ROC analysis), a reliable prognostic model of postpartum purulent-inflammatory diseases was created. Despite the presence of a large sample of patients with postpartum purulent-inflammatory diseases, only one patient with complicated postpartum endometritis was identified.

### Table 11: Spectral-fluorescent characteristics of the patient with postpartum endometritis (69-70) and a patient with sepsis (1′, 3′, 4′).

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### Conclusions

Pathogenesis is a mechanism of origin and development of diseases and their individual manifestations. It can be considered at different levels: from noticeable changes at the molecular level to disturbances in the body as a whole. Understanding pathogenesis is very important for the formation of management strategies for patients with various diseases. In particular, information about the mechanisms of origin and development of purulent-inflammatory diseases and sepsis is essential for finding effective ways to prevent and treat them. Regardless the etiological factors of the mentioned diseases, the processes that occur in the bodies of the respective patients occur in a similar scenario. The examination of biological objects in the frame of the method of fluorescence spectroscopy make it possible to detect pathological processes in living organisms at an early stage of their development. The main advantages of this method are the combination of high sensitivity and expressiveness with the possibility of non-destructive control of biological objects. We have proposed a pathogenetic concept of diagnostic and treatment approach for purulent-inflammatory diseases and sepsis. It is based on the fact that these diseases are accompanied with the changes of the part of the albumin molecules in the serum, which are blocked by toxins. These pathological albumin molecules are not able to perform their main functions, i.e. transportation and detoxification.

In the framework of the method of fluorescence spectroscopy, we performed the research, including in the dynamics, of the blood serum of patients with postpartum purulent-inflammatory diseases, patients with surgical profile and burns, including sepsis. It has been established that the spectral-fluorescent characteristics of the serum of these patients are universal markers of their condition. The behaviour of these markers depends on the concentration of normal albumin molecules of the blood of patients. At the same time their changes are registered for 24-48 hours before emergence of obvious clinical and laboratory signs of the general somatic status of patients. The behavior of these markers, including...

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**Citation:** Ostapiuk Lesia, et al. “Problems and Challenges to Women’s Reproductive Health in the 21st Century”. *Acta Scientific Women’s Health Special Issue* 3 (2021): 70-87.
in the dynamics, for purulent-inflammatory diseases and sepsis is illustrated. Patients can be in a serious condition as long as their blood has a sufficient concentration of normal albumin \( X^* \), which ensures the viability of the body. In the case of \( X \) less than \( X^* \) the compensatory capacity of the organism is exhausted and its result is exitus letalis.

We have proposed the unique promising approach to the diagnosis and control of the treatment process and the correction and modification of treatment tactics within the method of fluorescence spectroscopy. Fundamentally important for overcoming endogenous intoxication is the use of antibiotic therapy and infusion of albumin solution. The results of in vitro studies obtained by us are very important for the organization of a proper treatment process. They demonstrate the important role of infusion therapy in complex treatment, including the use of antibacterial drugs. Especially important for overcoming endogenous intoxication is the use of infusion of albumin solution.

Using the method of fluorescence spectroscopy is very important for the organization of the treatment process in obstetrics and gynecology. Our studies show that the serum of more than 250 patients was studied in the framework of the method of fluorescence spectroscopy, a significant part of which was studied in dynamics. Only one patient among them had a condition close to septic. Owing to the proposed method of fluorescence spectroscopy, all patients were successfully treated. It is very important to evaluate and analyze the results of the study using statistical methods of logit regression and ROC analysis. They enable not only to assess the quality of the results of the study, but also to establish reliable prognostic factors for the occurrence of postpartum purulent-inflammatory diseases. And within the observation of patients during pregnancy, childbirth and in the postpartum period, attention should be paid to the correction of these factors, if it is possible (IJCM reference). If there are qualified specialists, if possible, this method should be used. In case of absence of equipment, only improved treatment tactics to ensure the proper therapeutic effect, even in severe diseases.

Fundamentally important is the use of the method of fluorescence spectroscopy to organize the treatment of burns. The serum of patients with burns is a very valuable model object to demonstrate the treatment of patients with sepsis. On their example, we can study a wide range of behaviour of spectral-fluorescent markers of purulent-inflammatory diseases and sepsis.

**Prospects of the results**

The results of the following investigation could be used in the prognosis of the risks of development of postpartum endometritis and septic complications in medical practice.

**Bibliography**


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Problems and Challenges to Women’s Reproductive Health in the 21st Century


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