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# Modern View on the Problems of the Diagnosis and Treatment of Purulent-inflammatory Diseases and Sepsis in Obstetrics and Gynecological Practice

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The preservation of women's reproductive health and the birth of healthy children remains the fundamental problem of contemporary medical science. In the process of pre-pregnancy training, pregnancy, childbirth and the postpartum period there are a number of provoking factors that can cause a negative impact at any of these stages. The proper assessment and thorough analysis of the nature of these risks will provide the individual approach for each pregnant woman and woman in labour. This approach corresponds essentially to the modern principles of the personnel medicine and the world standards.

Over the past 30 years, under the auspices of the WHO, a lot of attention has been paid to the diagnosis and treatment of sepsis. However, significant efforts of physicians did not lead, unfortunately, to the expected success. In May 2017, the WHO adopted the very important resolution, according to which it was recommended to focus the main attention on the improving of the diagnosis, finding new markers, improving the treatment tactics and monitoring the condition of patients with purulent-septic complications during the treatment. Thus, the very relevant problem of medical science became the search for modern effective methods for the diagnosis of purulent-inflammatory diseases and sepsis in obstetric and gynaecological, surgical practices, including burn injury, especially their monitoring and treatment.

According to the WHO, every tenth death during pregnancy and childbirth is associated with the obstetric sepsis. At the same time,

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about 95% of cases occur in middle- and low-income countries. One million new-borns die each year from purulent-septic complications. In high-income countries there is the significant increase of surgical activity in obstetrics, which contributes to the increased incidence of postpartum purulent-inflammatory diseases and sepsis. In high-income countries women usually plan pregnancy after building a successful career in the late reproductive age. However, at this time most of them have extragenital pathology, including severe forms. Also relevant is the problem of infertility and the use of assisted reproductive technologies and induced multiple pregnancies, which create additional burdens on the body of pregnant women. In addition, in high-income countries, the problem of increasing of the incidence of obesity and diabetes is certainly relevant to the occurrence of postpartum purulent-septic complications, including postpartum endometritis (PE) and sepsis.

Modern advances in medicine are closely linked to the successful development of the biomedical and physical research methods. Methods of disease prevention and treatment involve the widespread use of the biochemical and other methods for their diagnosis, selection of drugs and treatment methods, as well as monitoring of their effectiveness. But, unfortunately, most modern laboratory, microbiological and instrumental research methods are representative on the background of already manifesting signs of the pathological processes. Thus, it would be extremely important to have the method with the high sensitivity and the ability to make the reliable diagnosis at the preclinical stage, as well as to allow

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the prognostic assessment of the disease during the treatment. Advances in science and technology in the second half of the last century have led to the widespread use of physical methods for the diagnosis of various diseases.\_Studies of the recent decades have testified [1,2] that the method of fluorescence spectroscopy (MFS) is one of the most common and universal methods of studying of biological tissues and fluids. Luminescent analysis is actually the method of studying of the luminescent characteristics of various objects. This method is also widely used in various fields of science and economy, in paleontology, defectoscopy, geology, for sanitary assessment of product quality and for monitoring of the purity of the environment (water, air).

In the study of biological objects, in particular of blood serum (BS), MFS allows to detect pathological processes in living organisms at an early stage of their development, without destroying the organisms themselves. The main advantages of this method are the combination of high sensitivity and expressiveness with the possibility of non-destructive control of biological objects and environments. These characteristics that lead to the increased interest to the MFS as the important and promising method of early diagnosis of various diseases.

The aim of the research is to develop the pathogenetic approach to the diagnosis, monitoring and management of the treatment process and prognosis within the MFS for the patients with purulentseptic diseases. Its high diagnostic value, accuracy, expressiveness and sensitivity allow to create the modern concept of diagnosis, monitoring and efficient treatment for patients with purulent-inflammatory diseases and sepsis and in patients with burn trauma.

Fluorescence spectra (FS) were investigated via the excitation of BS samples by light with the wavelength of 280 nm, corresponding to the luminescence region of human serum albumin. Thus, when forming a sample of patients in order to study their FS, it is important to include patients with the pathology with changes in the protein composition of the BS. The main markers, which we investigated within the MFS, were the fluorescence intensity (I  $_F$ ) and the position of the fluorescence maximum ( $\lambda_{max}$ ). Within the framework of MFS, new and very important results were obtained, which helped to study and justify the basic patterns of behaviour of spectral-fluorescent characteristics (I  $_F$ ,  $\lambda_{max}$ ) for patients with purulent-inflammatory diseases, sepsis [3,4], postpartum purulent-inflammatory diseases [5,6] and burn injury in the dynamics [7-9]. In order to conduct an adequate assessment and interpreta-

tion of the obtained experimental data for these characteristics in various diseases, including the dynamics during treatment, a series of studies "*in vitro*" was conducted by dilutions of BS by distilled water, 20% donor albumin, sugar broth, non-centrifuged and centrifuged bacterial culture [2,4,10]. This made it possible to study the changes of the spectral-fluorescent characteristics of the BS of patients as a result of treatment.

Pathogenesis is the mechanism of the 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 management of 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 of etiological factors of the mentioned diseases, processes in the bodies of the respective patients occur according to a similar scenario.

There is sufficient information about the pathogenetic factors of sepsis, but changes occurring at the molecular level are studied insufficiently. Their understanding is very important for understanding and developing the pathogenetic component of treating sepsis.\_It is known that in the presence of low concentrations of toxin molecules, albumin molecules are able to perform properly their transport and detoxification functions. The pathogenetic concept of diagnostic and treatment model of purulent-inflammatory diseases and sepsis is proposed in this article in order to explain the changes that occur in the body in patients with sepsis [11].

This concept is based on the fact that albumin molecules have the ability to complex. In patients with purulent-inflammatory diseases and sepsis with increasing endogenous intoxication, most of the binding centres of albumin molecules are blocked by the products of bacterial metabolism. As a result, there are two types of albumin molecules in their blood: normal (concentration: X) and blocked by toxins: pathological (concentration: 1-X). So, pathological albumin molecules lose the ability to perform their basic functions, namely transport and detoxification. In the case of presence of endogenous intoxication, the spectral-fluorescent characteristics are functions of the concentration of normal albumin molecules X: I  $_F$  (X),  $\lambda_{max}$ (X). At the same time, their behavior with changes in the concentration of toxins for patients with purulent-septic diseases can be registered with the help of MFS [2,4,6]. However, even within

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this method, it is difficult to obtain detailed information about the behavior of markers  $I_F(X)$ ,  $\lambda_{max}(X)$  at high concentrations of toxins (small values of X). At small values of X there is such a critical value of X\*, that at X<X\* exitus letalis becomes.

In [3,4,11], the behaviour of the spectral-fluorescent characteristics of the BS of the patient with sepsis was studied for 5 months in the dynamics during the treatment until the complete recovery. In the severe condition of the patient, the fluorescence spectrum of her BS clearly shows the two-peak structure [11]: in the region of 340 nm - «normal» peak and in the region of 380 nm - «septic» peak. This contribution was received, when X>X, the patient with sepsis continued to live because she was young and had no comorbidities. The septic peak is associated with pathological albumin molecules. When the patient's condition improves, the septic peak gradually disappears. When the patient's condition is approaching septic, we [11] proposed to use the traditional methods of treatment (surgical, etiotropic - antibiotic, infusion therapy) as well as the pathogenetic treatment infusion of donor albumin solutions. This procedure replenishes the level of complete albumin in the blood of critically ill patients for improving transport and detoxification functions.\_The glycosylation of albumin molecules in patients with diabetes significantly worsens the condition of patients with purulent-septic diseases [3,4]. In our analysis of the treatment process of 200 patients with postpartum purulent-inflammatory diseases, no patients with severe purulentinflammatory diseases were identified. One of the most likely explanations for this fact may be the high level of qualification of medical staff, as well as the use of MFS to monitor the treatment process [6]. MFS and the method of logit-regression have the high diagnostic value and they also allow to perform prognostic assessment of the disease during the treatment [5].

At the same time, we found a septic peak for the first time [3,4,11] within the MFS.\_However, its behavior in low X (X>X<sup>\*</sup>) was not studied in detail. This problem can be solved by studying *«in vitro»* the corresponding changes of the spectral-fluorescent characteristics of the BS of patients with sepsis at significant concentrations of pathological albumin molecules. For this study, it would be necessary to obtain experimental samples of dilutions of BS by centrifuged and non-centrifuged cultures of bacteria with high concentrations of toxins.

We have mentioned that the problem of sepsis was relevant in obstetric practice and not only in low-income countries. Now we shall illustrate the importance of using MFS to monitor the condition of women in labour and in the postpartum period, including in patients with purulent-septic complications.

Figure 1 presents the results of research in the dynamics of FS, and table 1 shows the data of the spectral-fluorescent characteristics of the BS of the patient with severe PE. The same figure and table 1 for comparison also show the corresponding results for one of the persons with sepsis who was treated in 2002. The somatic and gynecological anamnesis was complicated in this woman in postpartum period. During the childbirth, the anhydrous period was 6 hours and 30 minutes. In the postpartum period, anemia, proteinuria, the 3rd degree of vaginal cleanliness, dilation of the uterine cavity were detected according to ultrasound. So, she had risk factors for PE. This patient within the MFS showed the significant decrease in fluorescence intensity to 0.35 r.u. and the noticeable long-wavelength shift of the fluorescence band. This patient underwent manual vacuum aspiration (MVA) of the uterine wall. After this procedure and antibacterial and uterotonic therapy, the patient's condition improved. The very important point was to choose the optimal time for the MVA. After all, on the one hand, it should be carried out in a timely manner without delay, and on the other hand, by this time it is necessary yet to stabilize the patient's condition and begin effective anti-inflammatory and antibacterial therapy at normal body temperature. After correction of treatment in the next experiment, a marked increase of I \_ to 0.61 r.u. was recorded and the long-wavelength shift of the fluorescence band was leveled. After that, the patient was discharged from the hospital in satisfactory condition.



**Figure 1:** Fluorescence spectra of blood serum of woman with postpartum endometrities in the dynamics (6.1 - 14.02.2015; 6.2 - 17.02.2015), woman with uncomplicated postpartum period (2), patient with sepsis (1',2', 3', 4', 5') and 20% donor albumin (a) ( $\lambda_{ex}$  = 280 nm).

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**Figure 2:** Fluorescence spectra of blood serum of woman with complicated postpartum endometrities in the dynamics (6.1 - 14.02.2015; 6.2 - 17.02.2015, 6.3 - 20.02.2015, 6.4 - 22.02.2015, 6.5 - 25.02.2015), woman with uncomplicated postpartum period (2), patient with sepsis (1',2', 3', 4', 5') and 20% donor albumin (a) ( $\lambda_{ex}$ = 280 nm).

Otherwise, it is possible to reach a septic state. We illustrate in figure 2 and in table 2 another more unfavorable treatment scenario for the patient whose previous successful treatment scenario is presented in figure 1. Without the correction of treatment tactics (14.02.), the patient's condition could in principle worsen (curve 6.2) with the subsequent possible transition to the septic state (curve 3'), as in the person with sepsis depicted in this figure. It is very important to monitor the treatment process within the MFS and to monitor closely the health of patients. Subsequently, by prescribing infusions of 100-150 ml of 20% albumin solution and monitoring the patient's health within the MFS and correction of the treatment process, the patient's treatment process was completed (Figure 2, curves 6.3-6.5). In this case, the chances of full recovery would be much lower. In the above scenarios for the treatment of patients with purulent-septic diseases is very important to use MFS, which provides clear control and correction of the treatment process. If the MFS had not been used for monitoring and the medical process had not been corrected on February 17, her health could have become significantly more complicated and there could have been no chance for recovery. Without the use of

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Nº	Albumin	2	6.1	6.2	6.2′	1′	2′	3′	4′	5′
Date	14.02	14.02	14.02	17.02	17.02	3.06	5.06	6.06	7.06	10.06
λ <sub>max</sub> , nm	330.1	330.1	343.1	337.1	343.1	335.2	335.2	334,1	331,6	331
I <sub>F</sub> , r.u.	1	0.91	0.35	0.61	0.27	0.63	0.43	0.16	0.40	0.76

Table 1

Nº	Albumin	2	6.1	6.2	6.3	6.4	6.5	1′	3′	4′	5′
Date	14.02	14.02	14.02	17.02	20.02	22.02	25.02	3.06	6.06	7.06	10.06
λ <sub>max</sub> , nm	330.1	330.1	343.1	348.2	339.0	336	334	335.2	334.1	331.6	331
I <sub>F</sub> , r.u.	1	0.91	0.35	0.27	0.38	0.55	0.68	0.63	0.16	0.40	0.76



MFS, it would be difficult to expect the successful completion of the treatment process [6,12]. If it is not possible to monitor the condition of patients within the framework of MFS, it is necessary to monitor clearly the state of their health, to prescribe infusion solutions of donor albumin in case of its deterioration, to carry out surgical, etiotropic, pathogenetic and symptomatic treatment. But in this case we cannot guarantee the successful completion of the treatment process.

#### **Conclusions**

The pathogenetic concept of the diagnostic and treatment approach to purulent-septic diseases has been presented. In-depth studies of the spectral-fluorescent characteristics of the blood serum of patients with purulent-inflammatory diseases were conducted within the MFS. It helped reveal that these characteristics were universal markers of the patient's condition. At the same time,

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their changes were registered 24-48 hours before the appearance of obvious clinical and laboratory signs of their general somatic condition. The obtained results were illustrated for two possible scenarios of the postpartum purulent-inflammatory diseases.

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