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Diagnostic and Therapeutic Model of Sepsis and Purulent-Inflammatory Diseases

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Abstract

In this study, the method of fluorescence spectroscopy was used to improve the diagnostics and prediction of sepsis, pyo-inflammatory diseases and postpartum endometritis. At the first stage of the study, the researcher explored the fluorescence spectra of dilutions of serum with centrifuged and non-centrifuged bacterial culture (6-day crop sugar broth with Staphylococcus aureus), distilled water, 20% albumin and sugar broth. The focus was on the influence of treatment, including infusion therapy, on the fluorescence spectral characteristics of a patient's serum. At the second stage, the method of fluorescence spectroscopy was used for the diagnosis of sepsis *in vivo*. At the third stage, the analyst scrutinized the peculiarities of pregnancy, childbirth, and the postpartum period (totally, 40 parameters) in patients with postpartum pyo-inflammatory diseases and in the control group.

Keywords

Pyo-Inflammatory Diseases, Sepsis, Postpartum Endometritis, Method of Fluorescence Spectroscopy

1. Introduction

Despite an in-depth attention to the global epidemiological problem of sepsis, it has not been fully resolved yet. The focus has been on the selection of effective antibiotic regimens and other aspects of treatment. At the same time, the microscopic mechanisms of the aetiology and pathogenesis of sepsis have not been debated satisfactorily. It develops in over 30 million people annually and kills over 6 million out of them [1]. The prevalence of sepsis is the highest in low- and middle-income countries. Every year 3 million newborns and 1.2 million children suffer from sepsis [2]. Three out of ten deaths from neonatal sepsis are

likely to be caused by drug-resistant pathogens.

One tenth death due to pregnancy and childbirth is caused by maternal sepsis. In this case, 95% of maternal sepsis deaths occur in low- and middle-income countries [3]. One million newborns die every year due to maternal infections, including maternal sepsis [4].

Given the significant urgency of sepsis, particularly within the most recent thirty years, congresses and conferences were held around the world. Much attention is paid to the search for etiological factors, as well as the objective markers of the severity of patients' conditions (respiratory rate, heart rate, leukocyte level in the general blood test, etc.). There is enough adequate information on the pathogenetic factors of sepsis, but the molecular changes occurring at the molecular level are not well understood. This understanding is very important for explaining and exploring the pathogenetic component of treating sepsis. Treatment may not be as effective as necessary without the in-depth understanding of these aspects.

The recent achievements of medicine are closely linked to the successful development of biomedical research, in particular in the field of biological chemistry. Significant progress in these studies has made it possible to elucidate numerous complex mechanisms in the vital activities of the human body both in normal and pathological conditions. Today's methods of preventing and treating diseases involve the widespread use of biochemical research methods for their diagnosis, choice of drugs and treatment methods, as well as for monitoring the effectiveness of treatment.

The progress of studies and technology in the second half of the last century has led to the widespread use of physical methods for the diagnosis of diseases. Researches from the last few decades have shown that fluorescence spectroscopy is one of the most common and universal methods for studying biological tissues and liquids. In this paper, the main advantages of this method, such as high sensitivity, accuracy, expressiveness, will be used for the reliable diagnosis of sepsis and for the improvement of therapeutic tactics.

2. Literature Review

Due to the great significance of the sepsis problem, world congresses are dedicated to it. In 1991, the sepsis classification meeting in Chicago proposed the classification of sepsis based on the systemic inflammatory response syndrome to any inflammatory or non-inflammatory injury. The next definition of sepsis was discussed in 2001. The presence of clinical signs of systemic inflammatory response syndrome and suspected or proven infection at the time were the basis for the diagnosis of sepsis [5] [6] [7]. These criteria for the clinical diagnosis of sepsis and its classification, offered by the American College of Chest Physicians/Society for Critical Care Medicine (ACCP/SCCM), are still the basis for today's experts. But in recent years, additional information contributed to the understanding of this problem. Besides, clinicians needed clearer characteristics

to detect sepsis at the early stages of its development. So, at the 45th Orlando Intensive Care Congress in 2016, the Society of Critical Care Medicine and the European Society of Critical Care Medicine organized a working group of 19 specialists who gave a new definition of sepsis, *i.e.* Sepsis-3. According to their definition, sepsis is a life-threatening organ dysfunction caused by impaired regulation of the body's response to infection. The aim of the changes, proposed in 2016, was the acceleration of the diagnosis and improving the treatment of sepsis. In particular, clinical signs of sepsis are infection and organ failure due to the presence of this infection. The latter is measured according to the qSOFA scale, covering quick Sequential Organ Failure. It includes the impaired consciousness, systolic blood pressure less than 100 mm of mercury and respiratory rate greater than 22 per minute. However, the problem of sepsis still remains relevant and has not been resolved. Simple qSOFA criteria help to identify patients with suspected sepsis, but they don't offer effective diagnosis, including that at the preclinical level, and more effective treatment.

It should be noted that in the presence of pyo-inflammatory diseases, including sepsis, there is a blockage of serum albumin molecules by the products of bacterial metabolism, which leads to a significant decrease in the number of complete albumin molecules capable of performing their transport functions in the human body [8] [9]. The very increase in the number of inferior albumin molecules leads to an increase in the severity of the disease. Unfortunately, the aforementioned was beyond sepsis experts' attention. It suggests the need for intensive infusion therapy for patients with sepsis with a 20% solution of albumin. This process will help to replenish the body with complete albumin. It is an important pathogenetic component of treatment that, in combination with antibiotic therapy, can significantly increase its effectiveness.

Thus, the use of fluorescence spectroscopy enables the diagnostics of pyo-inflammatory diseases and sepsis, including those at their early stages, as well as controls the whole treatment process.

Therefore, the purpose of this paper is to build a diagnostic and therapeutic model of sepsis, based on the pathogenetic concept of the development of this pathology.

3. Data and Methodology

3.1. Data Source

The overall research was carried out from December 2001 to December 2018.

The clinical data for this particular investigation were provided by the Lviv city clinical emergency hospital and the department of gynaecology at the Vinnytsia city clinical hospital. The luminescent laboratory of the department of experimental physics at the Ivan Franko National University of Lviv provided experimental data. The measurements were performed using the aperture monochromators MDR-2 and MDR-12.

The objects of the study were "spectral-fluorescence modelling of changes in

blood serum (BS) in sepsis *in vitro*" (dilution of BS by centrifuged and non-centrifuged crops (CP and NCP) of bacterial culture of Staphylococcus aureus), dilution of BS with distilled water, 20% solution of albumin, sugar broth, 100 patients with a surgical profile (15 of whom have sepsis), 75 women with postpartum endometritis and 40 control subjects (women with uncomplicated course of postpartum period).

Research methods are: clinical, laboratory, biochemical, instrumental methods, including the method of fluorescence spectroscopy (MFS), as well as mathematical and statistical methods.

3.2. Research Results

In the study, MFS was used to improve the diagnosis and prognosis of pyo-inflammatory diseases. 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. The results of the experiment were displayed in the graphical and numerical form and processed graphically and statistically.

This method is based on the peculiarities of changes in the characteristics of BS in pyo-inflammatory diseases and sepsis. In the presence of endogenous intoxication in the body, the interaction of albumin molecules with the products of bacterial metabolism due to the ability of albumin molecules to complex takes place. The total number of albumin molecules remains constant. At the same time, the number of complete albumin molecules in the serum samples decreases. These changes cannot be recorded by the methods used in the standard algorithm for the diagnosis of pyo-inflammatory diseases and sepsis. At the same time, the MFS allows us to record these changes. The luminescence (fluorescence) of albumin molecules is due to the presence of the amino-acid residues of tryptophan in it. In the healthy people of the control groups, FS of BS look like a λ-type curves with maximum fluorescence in the region of 330.1 - 335.1 nm. The main indicators used for the analysis in the conducted work are the values of fluorescence intensity If and the position of fluorescence maxima λ_{max}. In patients with purulent-septic complications, a decrease in the intensity of fluorescence is observed. This occurs due to the fact that some binding centres of albumin interact with the products of bacterial metabolism and give glow in the longer wavelength region. Therefore, when the septic process develops, there are changes in the spectral-fluorescence characteristics of BS immediately, which can be detected only with the help of MFS. Initially, these changes are accompanied by a decrease in the fluorescence intensity, and subsequently, a long-wave "septic peak" is formed. These changes are a negative prognostic sign. If the long-wave shift is greater and the "septic peak" is higher, the prognosis is worse for patients. In particularly critical cases, the major peak caused by complete albumin is reduced to minimum, and the patient has only a "septic peak" in the long-wave area. Then there is a risk of even exitus letalis. At the same time, as

patients improve, changes in the spectral-fluorescence characteristics of BS occur in reverse order: there is an increase in the fluorescence intensity of the main peak, and the "septic peak" gradually shifts into the short-wave region and gradually disappears.

In the first phase of the study, the dilutions of BS by non-centrifuged and centrifuged bacterial culture (6-day sowing on the Staphylococcus aureus sugar broth), distilled water, 20% donor albumin, and sugar broth were studied. The problem of the influence of therapeutic measures, in particular infusion therapy, on the spectral-fluorescence characteristics of BS patients was also discussed [10].

The dilution of BS with 20% donor albumin leads in the cases of low concentrations to the slight shift of λ_{max} and a slight increase of the intensity; at high concentrations, If and λ_{max} are virtually unchanged. These results are actually consistent with the spectral characteristics of a 20% donor albumin solution. We focused on the study of spectral-fluorescence features of the pathognomic pathogenic for sepsis pathological constellation serum + bacterium − the phenomenon of bacteremia. To assure the validity of our assertions, we created the fluorescence-spectral model of sepsis *in vitro* by breeding BS by non-centrifuged (NCF) and centrifuged (CF) bacterial culture of bacteria [10]. In the *in vitro* studies, the FS of 11 dilutions of serum by NCF and CF cultures of bacteria [10] were measured for two similar experimental series of dilutions with concentrations starting from 100% of the standard serum down to the pure bacterial cultures (NCF/CF, respectively) with an experimental step of 10% dilution. It has been proven that starting with 10% of bacterial culture content in BS (proportions that are appropriate to the clinical model of sepsis), there appeared in vivo shifting by 7 - 10 nm in the long-wave region that is typical for sepsis (**Figure 1**, **Figure 2**, **Table 1**, **Table 2**). It should be noted that the changes of FS of BS in the dilution of NCF and CF of bacteria have a specific character and form the basis for the development of MFS for the early diagnosis of sepsis by studying the spectral-fluorescent model of sepsis *in vivo*.

At the second stage, MFS was used for diagnosing sepsis in vivo for patients with inflammatory diseases, sepsis and patients with burn injury [11]. In the study of the spectral-fluorescence characteristics of BS in patients with purulent-septic complications, two probable qualitatively significant tendencies were recorded, namely: the shift of fluorescence band maxima for patients with pre-septic pathology and sepsis in long-wave region and a significant reduction in their intensities (maximum up to 70% - 80%) of the donor unit. Both vectors of change had no correlation with the standard laboratory-biochemical parameters of conventional control of these patients, but correlated properly with the integrated clinical criteria for the severity of the patient's condition and the phenomenon of verified bacteraemia [12]. It should be noted that the revealed changes in the spectral-fluorescence characteristics of BS in patients with sepsis in most cases were preclinical in nature: they were usually recorded 24 - 48

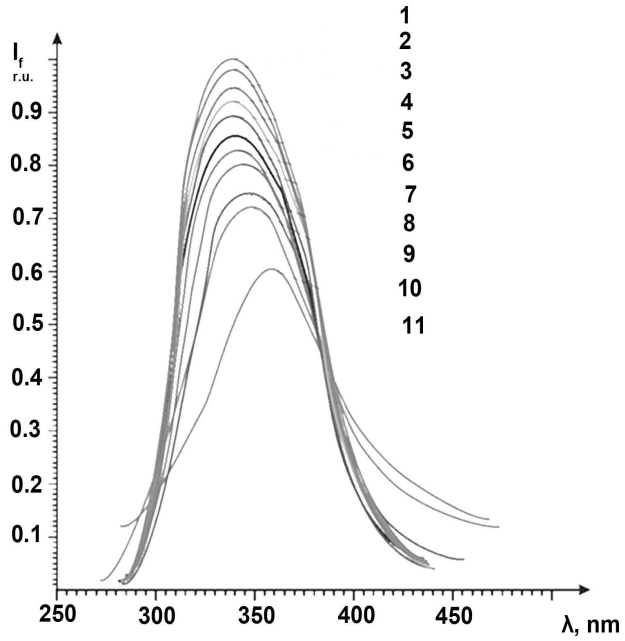

Figure 1. Effect of dilution non-centrifuged (NCF) crops on fluorescence spectra of donor blood serum (BS) (1—blood serum (BS); 2—90% BS; 3—80% BS; 4—70% BS; 5—60% BS; 6—50% BS; 7—40% BS; 8—30% BS; 9—20% BS; 10—10% BS; 11—CF crops). λ_{ex} = 280 nm.

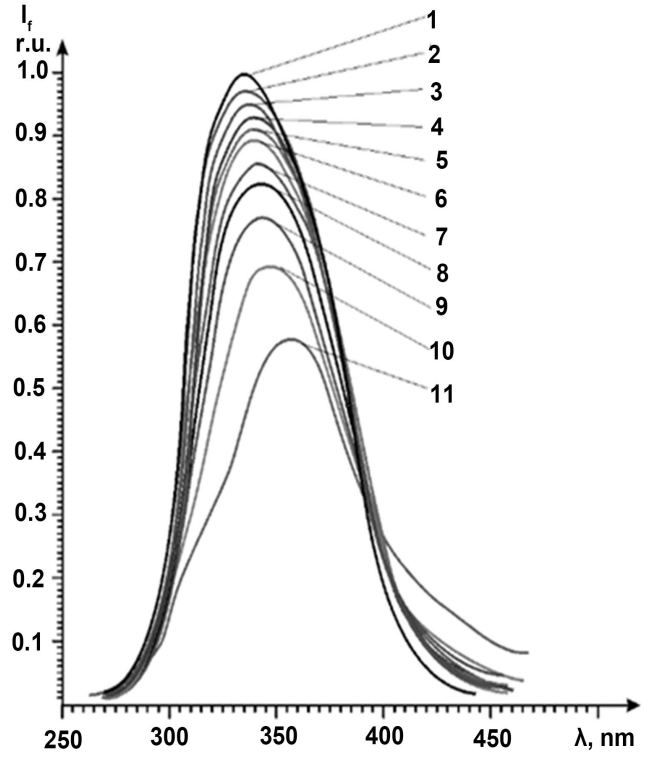

Figure 2. Effect of dilution centrifuged (CF) crops on fluorescence spectra of donor blood serum (BS) (1—blood serum (BS); 2—90% BS; 3—80% BS; 4—70% BS; 5—60% BS; 6—50% BS; 7—40% BS; 8—30% BS; 9—20% BS; 10—10% BS; 11—CF crops). λ_{ex} = 280 nm.

Table 1. Influence of dilution by non-centrifuged bacterial cultures on spectral-fluorescence characteristics of blood serum.

N	1	2	3	4	5	6	7	8	9	10	11
λ_{max} nm	339	339	339	339	339	340	341	344	347	348	358
I, r.u.	1.00	0.98	0.95	0.92	0.89	0.85	0.83	0.8	0.75	0.72	0.60

Table 2. Influence of dilution by centrifuged bacterial cultures on spectral-fluorescence characteristics of blood serum.

N	1	2	3	4	5	6	7	8	9	10	11
λ_{max} nm	335	335	337	340	340	340	341	343	343	347	357
I, r.u.	1.00	0.97	0.95	0.93	0.91	0.89	0.86	0.82	0.77	0.69	0.58

hours before the appearance of obvious clinical and laboratory signs of a significant change in the general somatic status of patients (Ukraine's Patent 76953) [13] [14]. At the same time, the structure of the excitation spectra of the fluorescence of donors and patients with sepsis is generally similar, but the patient's intensity of the excitation spectra is much lower than that of the donor.

Interesting are the results of the study of FS of BS in patients with pyo-inflammatory diseases. At first, we will present and discuss the results of individual, most revealing studies, in particular, of serial examinations of three patients with sepsis, for whom the dynamics of FS in different pathogenetic scenarios at different stages of the disease are studied. Figure 3 summarizes the results of a study of FS of the BS donor and patient (aged 33) with severe sepsis, which was treated in Lviv's city clinical emergency hospital. At the time of hospitalization, a critically difficult condition of the patient and verified bacteremia (blood seeding at the time of hospitalization: Staphylococcus aureus).

Figure 3 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 donor fluorescence band, and the fluorescence intensity (If) was 0.3 related unites (r.u.) from the donor If. This curve is, in fact, a septic peak, signalling a critical condition of the patient. The intensity of this curve in the region of 340 nm indicates a small amount of complete albumin in the BS of the patient. After surgical intervention and the elimination of the source of infection and intensive antiseptic therapy and prolonged bacteremia, the significant improvement and stabilization of the patient's condition were achieved: the analysis of the FS of the patient on the seventh postoperative day revealed that the shift of her band of fluorescence was significantly reduced and constituted $\Delta\lambda = 7$ nm (Figure 3, Table 3).

Undoubtedly, the considerable increase in the fluorescence band intensity of its BS mentioned above was connected with the decrease in septic symptoms. Our *in vitro* studies of the spectral-fluorescence characteristics of standard

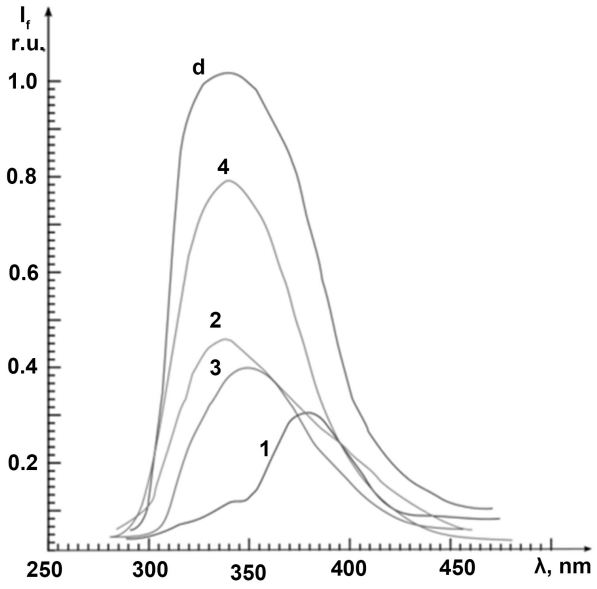

Figure 3. Fluorescence spectra of serum in Patient 1 with sepsis: 1—28.12; 2—04.01; 3—12.02; 4—19.03; 5—04.06 and donor of BS (d). *λ*ex = 250 nm.

Table 3. Changes in spectral-fluorescence characteristics of serum of a patient with sepsis.

N	control group	1	2	3	4	5
λ_{max} nm	340	380	345	337	349	340
I, r.u.	1.0	0.3	1.07	0.46	0.39	0.79

dilutions of the donor BS with distilled water (**Figure 4**, **Table 4**) clearly confirmed the correctness of our supposed explanation of the reported phenomenon of increase in the fluorescence band of this patient's fluorescence (**Figure 3**, 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 fluorescence bands. An additional confirmation of this assumption is the fact that after a change in the mode of infusion therapy associated with the reduction of septic symptoms and the dominance of the cardiovascular disorders regular for this stage, in the absence of significant changes in laboratory biochemical parameters, a decrease in the intensity of the fluorescence to 0.39 r.u. was observed and exceeded the baseline (**Figure 3**, curves 3, 4 relative to curve 1).

Later, under the influence of intensive complex therapy, a gradual improvement of the patient's condition with corresponding dynamics of changing spectral-fluorescence characteristics of her BS was observed: the gradual increase of fluorescence band intensity and the reverse shift of its maximum in the spectral region 337 nm (**Figure 3**, curves 3 - 5). The significant approximation of the fluorescence parameters of the patient's BS to the corresponding indicators of

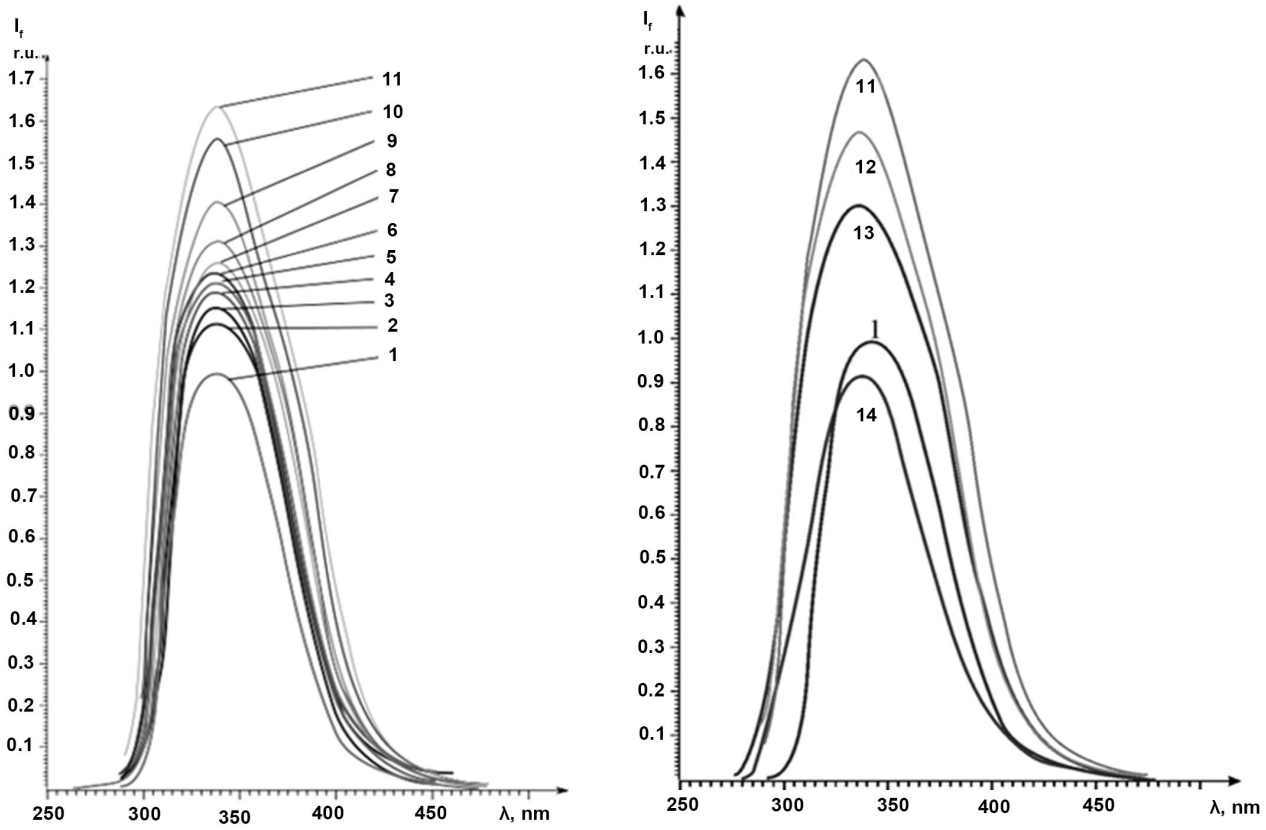

Figure 4. Effect of dilution with distilled water (DW) on the fluorescence spectra of donor blood serum (BS) (1—BS; 2—90% BS; 3—80% BS; 4—70% BS; 5—60% BS; 6—50% BS; 7—40% BS; 8—30% BS; 9—20% BS; 10—10% BS; 11—5% BS; 12—DW:If = 0).

Table 4. Influence of dilution by with distilled water on spectral-fluorescence characteristics of blood serum.

N	1	2	3	4	5	6	7	8	9	10	11	12	13	14
λ_{max} нм	338	338	337	337	337	337	338	339	338	338	338	336	336	338
I, в.о.	0.99	1.11	1.15	1.19	1.21	1.24	1.26	1.31	1.40	1.56	1.63	1.47	1.30	0.92

the donor BS was revealed 2.5 months later after her leaving hospital. Thus, according to our studies of the BS of the above-mentioned patient, the decrease in the intensity and the shift of the fluorescence band take place due to the presence of an advanced septic process and correlates with the integral indicators of the severity of the clinical condition and bacteremia. The dynamics of changes in the FS of the BS objectively reflect the course of sepsis and correlate with the effectiveness of therapeutic tactics.

Remarkable was also the results of the study of the FS of BS of another person with severe sepsis, who was treated at Lviv's city clinical emergency hospital. The major difference between these two cases is that, due to the timely hospitalization and early surgical elimination of the source of the infection, the septic process was considerably lower that was much reflected in the dynamics of changes in the spectral fluorescence (Figure 5, Table 5).

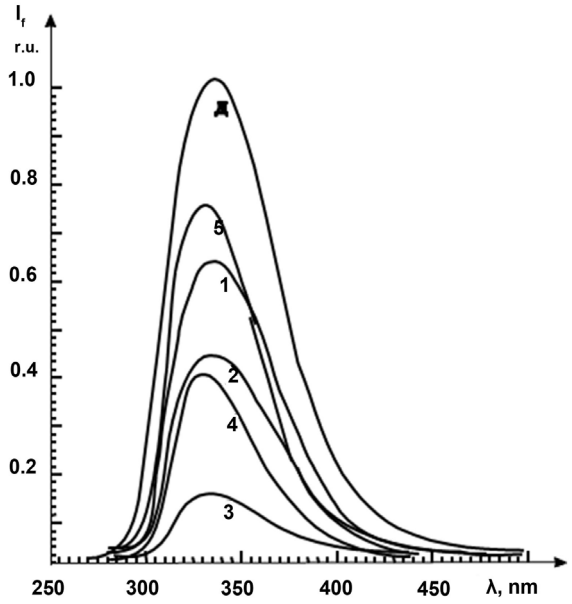

Figure 5. FS of BS in Patient 2 with sepsis: 1—03.06; 2—05.06; 3—06.06; 4—07.06; 5—10.06 and donor of BS. λ_{ex} = 280 nm.

Table 5. Changes in the spectral-fluorescence characteristics of serum of a person 2 with sepsis.

N	control group	1	2	3	4	5
λmax, nm	336	336	334	333	330	331
I, r.u.	1.0	0.64	0.44	0.16	0.41	0.76

Analyzing the results in this figure, one can conclude that after eliminating the source of the infection background by an intensive antibiotic therapy, this patient with clinically insignificant course of sepsis during a certain period experienced bacteremia (Klebsiella pneumonia) (curves 1-3). At this stage of treatment, the decrease in fluorescence band intensity reached maximum (0.16 If) only at the end of the bacterioemic period. Subsequently, during the gradual recovery of the person under study, there was a significant increase in the fluorescence intensity of the BS up to 0.75 If (**Figure 5**, curve 5).

Noteworthy are the results of studies of the spectral-fluorescence characteristics of BS in patient with sepsis and diabetes (**Figure 6**, **Table 6**).

The patient's condition during the observation period was steadily worsening, despite surgery and intensive antibiotic therapy, which may well be explained by the presence of a number of serious comorbidities and her older age. It should be remarked that the negative dynamics of the condition of this patient is reflected by the unfavourable dynamics of the parameters of the spectral-fluorescence characteristics of her BS: a constant decrease in the intensity of fluorescence bands (**Figure 5**, curves 1, 2, 3). The patient died as a result of an advanced process of generalizing infection and multiple organ failure.

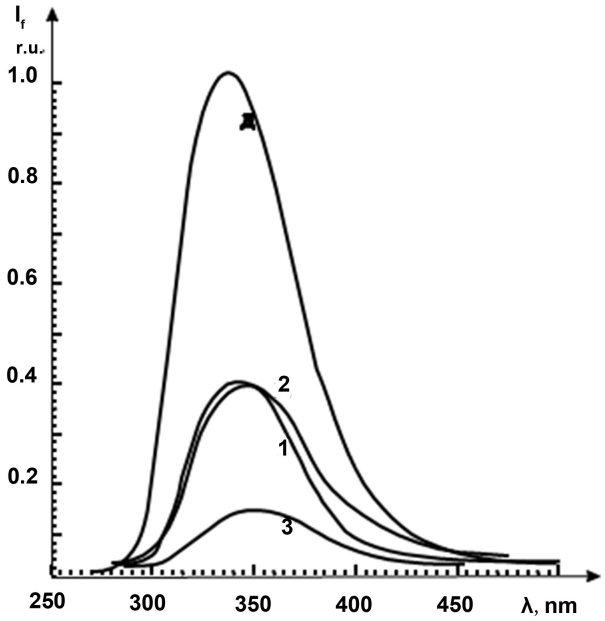

Figure 6. FS of BS of patient 3 with sepsis and diabetes: 1—03.06; 2—05.06; 3—06.06 and donor BS. λ_{ex} = 280 nm.

Table 6. Changes in the spectral-fluorescence characteristics of serum of a person 3 with sepsis.

N	control group	1	2	3
λmax, nm	338	342	347	351
I, r.u.	1.0	0.41	0.40	0.15

The above results indicate three most likely scenarios for sepsis. The dynamics of changes in the spectral-fluorescence characteristics of BS in patients with sepsis objectively reflect the clinical features of the disease, which significantly depends on the quality of diagnosis and correlates with the effectiveness of therapeutic tactics. MFS makes us able to use effective therapeutic tactics and correlate its correction depending on the change of the patient's condition. It should be noted that the first stage of the disease significantly reduces the intensity of fluorescence of the BS, which is associated with an increase in the number of defective albumin molecules in the BS, blocked by toxins. Therefore, an important element of therapeutic tactics for pyo-inflammatory diseases, including sepsis, is the infusion of 20% solution of albumin, which allows to replenish the amount of complete albumin in the patient's blood.

At the third stage, the peculiarities of the course of pregnancy, childbirth and the postpartum period (40 parameters in all) were analyzed in 75 women in postpartum period of the main group with postpartum endometritis and 40 people of the control group with the uncomplicated course of the postpartum period. MFS (of Ukraine's Patent 133472) was also used for the diagnosis of postpartum pyo-inflammatory diseases [15]. Extragenital pathology, gynecolog-

ical diseases, risk of miscarriage, complicated pregnancy, colpitis, the presence of TORCH infection, childbirth duration over 12 hours, presence of anomalies of childbirth, foetal distress, age of up to 35, length of stay in hospital within 3 - 5 days, decrease in fluorescence intensity and the presence of a long-wave shift are the reliable prognostic factors for the development of postpartum endometritis (PE) [16] [17].

It has been shown that in patients with PE, the decrease in the fluorescence intensity and the shift of the λ_{max} of the FS of BS into the long-wavelength region correlates with the severity of the disease. At the same time, it has been found that the spectral-fluorescence parameters of BS in patients are dynamic indicators that respond immediately to any—even minimal—changes in their clinical status and are integral characteristics of the health of the human body (**Figures 7-10** and **Tables 7-10**).

Figure 7 presents the results of a study of the FS of the BS of a woman 60 with PE, which was hospitalized in the gynaecological department on the 13th day of the postpartum period.

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 for home in a satisfactory condition.

Quite interesting are the results of the study of the FS of the BS of the woman after labour, depicted in **Figure 8**. This patient was treated 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 24 days of her postpartum period. After the vacuum aspiration of the uterine cavity walls on 02 February 2015, the endometrial histological study revealed endometritis [16] [17].

Table 7. Spectral-fluorescence characteristics of patient with postpartum endometritis (60) and a patient with sepsis (1', 3', 4').

N	albumin	control group	60	60'	60''	1'	3'	4'
λmax, nm	330,1	330.1	337.1	337.1	336.1	376.8	339.8	349.5
I, r.u.	1	0.91	0.54	0.51	0.69	0.29	0.45	0.39

Table 8. Spectral-fluorescence characteristics of patient with postpartum endometritis (61) and a patient with sepsis (1', 3', 4').

N	albu min	2	61	61'	61"	61"	1'	3'	4'
λmax, nm	330.1	330.1	339.1	339.1	336.1	329	376.7	339.8	349.5
I, r.u.	1	0.91	0.56	0.53	0.72	0.88	0.29	0.45	0.39

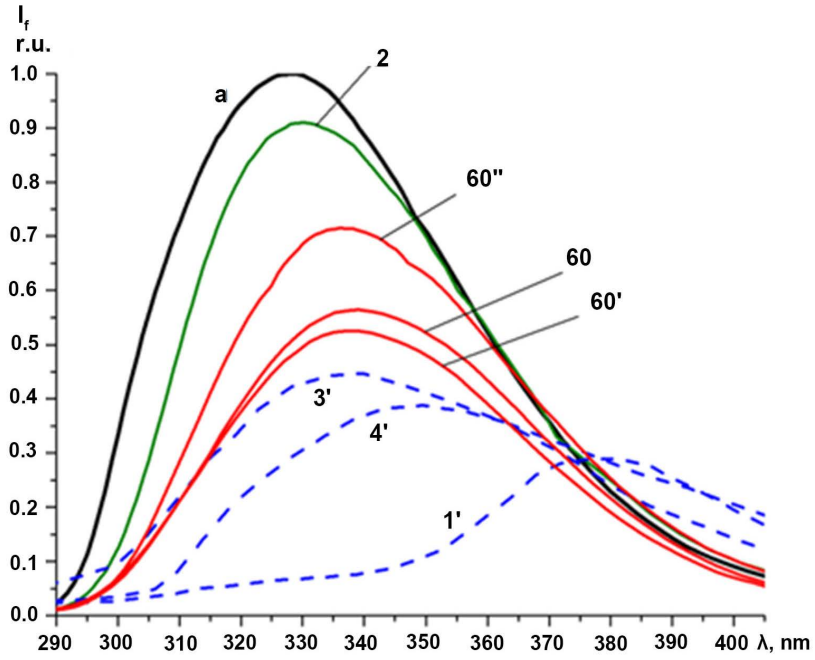

Figure 7. Fluorescence spectra of blood serum in the patient with postpartum endometritis in dynamics (60—24.02.2015; 60'—26.02.2015, 60"—29.02.2015), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see **Figure 3**) and 20% donor albumin (a) (λ_{ex} = 280 nm).

Within four days, there took place a decrease in the fluorescence intensity of the BS of the patient from 0.56 r.u. (curve 61) to 0.53 (curve 61') followed by the normalization of its condition as a result of effective antibiotic therapy (curves 61" and 61'"). As a result, we observed a positive dynamics of changes in the spectral-fluorescence characteristics of Patient 61's BS, which reflects the dynamics of the healing process.

After manual vacuum aspiration during the next two days, there was a decrease in the fluorescence intensity of the BS from 0.56 ppm. (curve 61) to 0.53 (curve 61') followed by its normalization as a result of effective antibiotic therapy (curves 61' and 61'"). Thus, we recorded the positive dynamics of the change in the spectral-fluorescence characteristics of the BS of Patient 61, which qualitatively reproduces the scenario of recovery of the patient for sepsis (curves 1', 3', 4').

Quite informative are the results of the study of the spectral-fluorescence characteristics of the BS of another woman with endometritis after the childbirth,

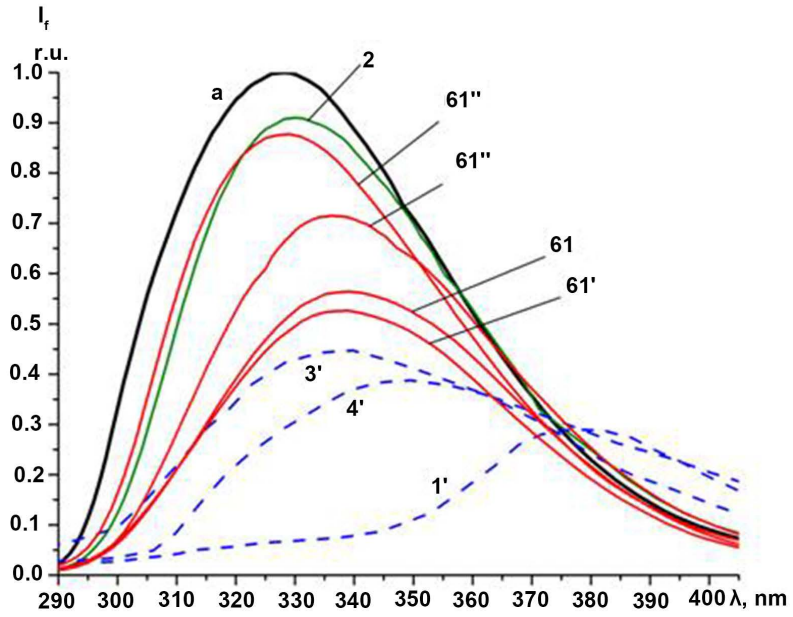

Figure 8. Fluorescence spectra of blood serum in patient with postpartum endometritis in dynamics (61—2.02.2015; 61'—4.02.2015, 61"—6.02.2015, 61'"—30.04.2015), women with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (see **Figure 3**) and 20% donor albumin (a) (λ_{ex} = 280 nm).

shown in **Figure 9** and **Table 9**. She had a complicated somatic anamnesis (transferred pleurisy in 2013, urolithiasis), chronic adnexitis. In childbirth, the anhydrous period duration was 6 hours 30 minutes. In the postpartum period, anemia, proteinuria, 3rd-degree purity of the vagina and the expansion of the uterine cavity according to ultrasound were revealed.

After the manual vacuum aspiration of the walls of the cavity of the uterus of Patient 62, antibacterial and uterotonic therapy was performed. We investigated the FS of the BS as of 15 July 2015 and revealed a significant decrease in the fluorescence intensity to 0.35 r.u. and a noticeable long-wave shift of its band (curve 62). In the following experiment, a marked increase of If of BS of this patient was recorded up to 0.6 r.u. and the shift into the shortwave region (see curve 62') was fixed. The results of the FS of BS are also present in the picture (see 1', 3', 4', **Figure 3**).

Figure 10 and **Table 10** present the FS of the BS of two more women with postpartum endometritis. It should be noted that the growth of If of Patient 69 from 0.59 r.u. (curve 69) to 0.96 r.u. (curve 69') correlates with the improvement of her condition during treatment. In the initial study of the FS of the BS of Patient 70 revealed a considerable decrease of If of BS (curve 70). After the vacuum aspiration on 20 February 2014 and the following treatment, the patient's condition improved significantly. This is evidenced by the results of the study of the FS of her BS (curve 70').

This makes it possible on the basis of the detailed information on the spectral-fluorescence parameters of the BS of patients to prescribe them effective treatment on time and to preserve the reproductive health of women in

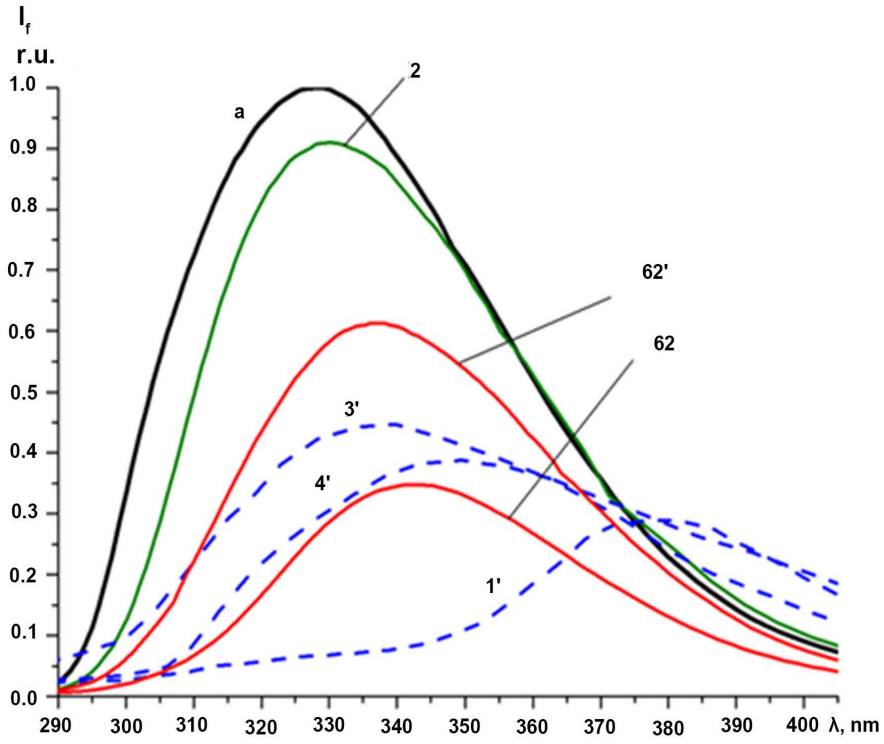

Figure 9. Fluorescence spectra of blood serum in the patient with postpartum endometritis in dynamics (62—14.02.2015; 62'—17.02.2015), the woman with uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') (See **Figure 3**) and 20% donor albumin (a) (λ_{ex} = 280 nm).

Table 9. Spectral-fluorescence characteristics of patient with postpartum endometritis (61) and a patient with sepsis (1', 3', 4').

N	albumin	2	62	62'	1'	3'	4'
λmax, nm	330.1	330.1	343.1	337.1	376.7	339.8	349.5
I, r.u.	1	0.91	0.35	0.61	0.29	0.45	0.39

childbirth. Further systematic studies of the FS of BS in the framework of MFS in patients with pyo-inflammatory diseases will make MFS an effective method of diagnosis in obstetrics and gynaecology and in medical practice in general.

It should be noted that in pyo-inflammatory diseases, including sepsis, there are changes in structures of albumin molecules and a decrease in the level of complete albumin in BS, capable of performing its functions, including detoxification. Therefore, the pathogenetic components of the treatment of these diseases are antibiotic therapy and infusion therapy with albumin solutions to replenish the amount of complete albumin in BS. According to the latest International Guidelines for the treatment of severe sepsis and septic shock, experts propose to use albumin in large volumes for infusion-transfusion therapy [18] [19] [20] [21].

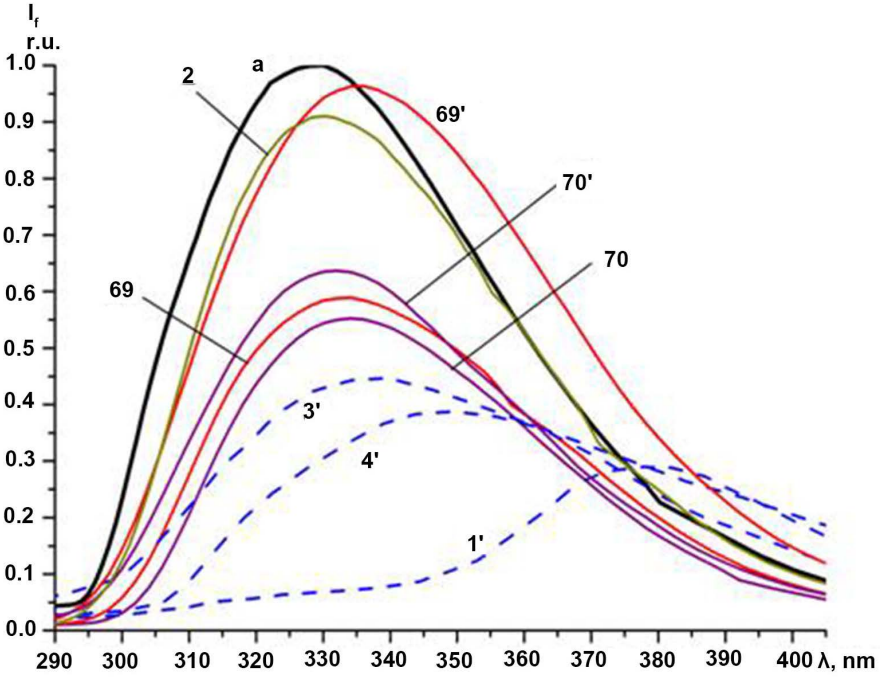

Figure 10. Fluorescence spectra of blood serum in the patient with postpartum endometritis in dynamics (69—20.02.2014; 69'—10.03.2014., 70—20.02.2014; 70'—24.02.2014.), uncomplicated course of postpartum period (2), patient with sepsis (1', 3', 4') and 20% donor albumin (a) (λ_{ex} = 280 nm).

Table 10. Spectral-fluorescence characteristics of patients with postpartum endometritis (61) and a patient with sepsis (1', 3', 4').

N	albu min	2	69	69'	70	70'	1'	3'	4'
λmax, nm	330.1	330.1	334.1	336.1	334.1	332	376.7	339.8	349.5
I, r.u.	1	0.91	0.59	0.96	0.55	0.64	0.29	0.45	0.39

4. Conclusions

1) It has been established that the bacterial culture dilution of BS, starting with 20% of the content of centrifuged or non-centrifuged cultures of bacterial culture in serum, makes possible the *in vitro* reproduction of proportions consistent with the clinical model of sepsis *in vivo*. A decrease in the fluorescence intensity of BS dilutions by over 30% and a long-wave shift of the FS maximum of over 10 nm were detected.

2) A method for diagnosing sepsis and pyo-inflammatory diseases is first proposed. Three plausible scenarios for sepsis were identified. It has been shown that the structure of FS BS is an effective marker of the severity of the disease, which can assess quickly and qualitatively the threat of critical purulent-septic complications as well as monitor the treatment process.

3) The spectral-fluorescence characteristics of BS in childbirth with PE were under study.

Fluorescence spectroscopy makes it possible to perform diagnostics at the preclinical stage, to assess quickly and qualitatively the threat of critical purulent-septic complications and to monitor the treatment process. The spectral-fluorescence characteristics of BS are found to be reliable markers for the diagnosis of pyo-inflammatory diseases in obstetric and gynaecological practices. The study of their dynamics enables them to prescribe the effective treatment on time and to prevent the development of obstetric sepsis.

4) In pyo-inflammatory diseases, including sepsis, there may happen the blockage of albumin molecules by the products of bacterial metabolism, which leads to a significant decrease in their ability to perform transport functions. The infusion therapy with a 20% solution of albumin will help to replenish patients' body with complete albumin. It is an important component of pathogenetic treatment that, along with antibiotic therapy, can significantly increase its effectiveness. The method of fluorescence spectroscopy will effectively monitor the treatment process.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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