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Research Article

Sepsis: The New Approach to The Successful Solving of The Problem

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Abstract:

Background: The significant improvement of immediate and long-term functional results of treating of patients is the fundamental problem of modern medical science. A deep understanding of the pathogenesis is the key point in creating the management strategy for patients with various diseases. 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.

The aim of the research is to use the method of fluorescence spectroscopy in creating pathogenetic diagnostic and treatment model for the prevention and treatment of purulent-inflammatory diseases and sepsis.

Methods:

Stage 1 consisted of an in vitro study, Stage 2 covered - 100 patients with surgical purulent-inflammatory diseases (including 15 patients with sepsis), Stage 3 engaged 180 women with postpartum purulent-inflammatory diseases (main group), 40 women with uncomplicated course of the postpartum period (control group), Stage 4 involved 20 patients with burn injury (main group), 35 people with burn injury (comparison group). In addition to standard treatments, patients also underwent serum studies using the method of fluorescence spectroscopy.

Result(s): We have proposed the pathogenetic concept of diagnostic and treatment approach for purulent-inflammatory diseases and sepsis. As part of the method of fluorescence spectroscopy, thorough studies of the serum of patients with postpartum purulent-inflammatory diseases, of patients with a surgical profile, including sepsis, as well as burns trauma were conducted. A thorough analysis of the obtained results was provided.

Conclusion(s): Based on our proposed pathogenetic concept, the possible mechanisms of sepsis and effective methods of diagnosis, monitoring and prognosis for its spread are discussed in details. It is proposed to use the pathogenetic component of the treatment of purulent-inflammatory diseases and sepsis on the basis of the pathogenetic model, which has been developed by us.

Keywords: pathogenetic model; sepsis; method of fluorescence spectroscopy

Introduction

Sepsis occurs when the body's response to the infection causes damage to its own tissues and organs and can cause the significant deterioration of the patient's condition and even his death. It is estimated to affect more than 30 million people each year and can kill 6 million people [1]. This problem is quite typical for low- and middle-income countries. According to the WHO, sepsis occurs annually in 3 million newborns and 1.2 million of children [2]. One of ten maternity deaths is due to obstetric sepsis. 95% of maternal sepsis deaths occur in low- and middle-income countries [3]. 1 million newborns die each year from maternal infections, including maternal sepsis [4]. Over the past 25 years, the definition of sepsis and septic shock has changed three times; every four years the international intensive care protocol was updated with the participation of dozens of leading organizations and experts [5]. Thus, the urgency of the problem is obvious and requires modern knowledge from scientists and doctors for early diagnosis and timely, targeted treatment of sepsis and septic shock, including in obstetrics [6]. According to the 1991 definition at the conciliatory conference of the American College of Thoracic Surgeons and the Society for Critical Medicine (ACCP / SCCM) in Chicago (USA), sepsis is a systemic inflammatory response syndrome (SIRS), caused by a source of infection. In 2001, the working group understood the shortcomings of such a definition, but did not offer any alternative [7]. In 2016, criteria for the diagnosis of sepsis by rapid dynamic assessment of organ failure (qSOFA) were proposed. According to experts of this consensus [8], organ dysfunction caused by sepsis can be hidden. Thus, its presence should be considered in any patient with an infection.

According to the WHO, sepsis is the dangerous dysfunction of the internal organs caused by dysregulation of the body's response to infection. At the same time, insufficient attention was paid to the pathogenetic assessment of the development of purulent-septic complications, including sepsis. The issues of early diagnosis of purulent-inflammatory conditions, especially their monitoring and treatment, are not completely resolved. These issues need quick solution by using contemporary scientific approaches to the choice of diagnostic methods and optimization of treatment tactics. In this regard, in May 2017, the 70th session of the World Health Assembly adopted a resolution on sepsis on the basis of the report of the WHO Secretariat. According to it, the primary attention should be focused on improving early diagnosis, finding new markers and improving treatment tactics and monitoring of patients. Therefore, the aim of our research is to use the method of fluorescence spectroscopy in pathogenetic diagnostic and treatment model for the prevention and treatment of purulent-inflammatory diseases and sepsis. There is sufficient information about the pathogenetic factors of sepsis, but changes occuring at the molecular level are studied insufficiently. Their understanding is very important for understanding and development the pathogenetic component of treatment of sepsis. Without the in-depth understanding of these aspects, the diagnosis and treatment of sepsis may not be effective enough. Especially important is the detoxification function of albumin, which is especially evident in patients with moderate endogenous intoxication. Due to the changes in the conformation of its molecules, albumin interacts with hydrophobic molecules of endotoxins and promotes their excretion from the body. In patients with purulent-inflammatory diseases and sepsis with increasing endogenous intoxication, most of the binding centers of albumin molecules are blocked by the products of bacterial metabolism. Although the total concentration of albumin in the blood of patients may be within normal limits, its actual "effective concentration" is much lower [9]. This leads to the violation of the basic functions of the body and requires timely implementation of effective treatment measures.

For this aim, the pathogenetic concept of diagnostic and treatment model of purulent-inflammatory diseases and sepsis was created. It is based on the fact that albumin molecules have the ability to complex. In the diseases which are accompanied by endogenous intoxication, part of the albumin molecules in the blood of patients are blocked by toxins. 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. The new definition of sepsis is to define X* - the maximum minimum value of the concentration of normal albumin molecules in the case of presence of a septic condition. If X is more than X*, this ensures the viability of the organism to some extent. Then at X less X*, exitus letalis develops.

Materials and methods

Among the research methods, we used clinical, laboratory (general and biochemical blood tests, general urine test, examination for viral hepatitis B and C, syphilis and HIV), instrumental methods (bacteriological examination of the content of the uterine cavity, histologic analysis of metroaspirate, method of fluorescence spectroscopy (MFS), mathematical and statistical methods (logit regression and ROC analysis)). The study of biological objects by using the method of fluorescence spectroscopy makes it possible to detect pathological processes in living organisms, even at an early stage of their origin. The method of mathematical modeling has been used as well, including the simulation of changes of the characteristics of blood serum (BS) in patients with sepsis in vitro by diluting the BS with the bacterial culture of Staphylococcus aureus. The method of mathematical modeling was also used, including the simulation of changes of the characteristics of blood serum (BS) in patients with purulent-inflammatory diseases and sepsis in vitro. As part of the research were the stages of in vitro and in vivo studies. In vitro studies (stage 1) were conducted in 2001-2003 in the Ambulance Municipal City Clinical Hospital (Lviv). In vivo studies were conducted from 2001 to 2019 at three clinical bases: the Ambulance Municipal City Clinical Hospital (Lviv), Department of Gynaecology № 2 of Vinnytsia Council Clinical Hospital № 2 and the burn department of Lviv Communal City Clinical Hospital №8. The samples of BS of patients with purulent-inflammatory diseases and sepsis, covering the postpartum period, were the object of study. The study was designed by the following groups of patients. Stage 2 was performed from 2001 to 2008 and included studies of fluorescence spectra (FS) of BS of 100 patients, including 42 patients with aseptic pathology, 43 ones with preseptic pathology, 15 patients with sepsis and 40 healthy subjects of the control group. Stage was conducted from 2013 to 2019 on the basis of the Department of Gynaecology № 2 of Vinnytsia Council Clinical Hospital № 2 and included the study of 180 mothers with postpartum purulent-inflammatory diseases and 40 healthy mothers with uncomplicated postpartum period. Stage 4 was conducted from 2013 to 2019 on the basis of burn department of Lviv Communal City Clinical Hospital № 8. It included studies of *20 patients with burn trauma (main group)*, for which the study of the BS by the MFS was done, as well as 25 healthy individuals of the control group. Also within this stage, the study design included the presence of the comparison group (35 patients), for which we also used improved treatment tactics, developed on the basis of analysis and interpretation of the results of the study of BS of patients of the main group within the MFS. Luminescence is the result of the absorption of light by the system under study and is caused by the transition of its molecules from the energized state to the basic state. Fluorescence is the partial case of luminescence with $\tau < 10^{-7}$ seconds. The studies were supported by using the MDR-2 and MDR-12 optical monochromators. BS excitation was performed with a deuterium lamp DDS-400 with a light wavelength of 280 nm, which corresponds to the region of luminescence of human serum albumin. The main groups of the study were patients with purulent-inflammatory diseases and sepsis, which are characterized by endogenous intoxication, which according to our proposed pathogenetic model leads to the formation of two types of albumin molecules in the blood of patients. MFS made it possible to record changes in the structure of albumin molecules in the blood of patients and to shape new diagnostic criteria and treatment tactics on the basis of these results.

Results of the research

The aim of the in vitro study stage was to study the changes of the spectral-fluorescent characteristics of BS [10-12], that occur in patients with purulent-inflammatory diseases and sepsis (dilution of BS by bacterial cultures of Staphylococcus aureus), diabetes mellitus (dilution of BS with sugar broth) and to study the effect of massive infusion therapy (dilution of BS with distilled water). Also, studies of FS of dilutions of BS with 20% albumin solution, the spectral-fluorescent characteristics of which were used in our studies as a reference. The main studied indicators were the fluorescence intensity (I_F) and the position of the fluorescence maximum (λ_{max}).

The dilution of BS with distilled water decrease the concentration quenching of albumin molecules and increase the fluorescence intensity, which is also typical because of the physiological increase of circulating blood volume (this situation occurs during pregnancy)[13].The FS dilutions of BS by bacterial culture (6-day culture of Staphylococcus aureus on sugar broth), starting with 20% of the content of centrifuged or non-centrifuged crops in BS allow to reproduce the proportions that are characteristic of FS of BS in sepsis in vivo. In this case, the fluorescence (I_F) intensity gradually decreases by more than 30% with an increase of the content of bacterial culture in the solution due to the blocking of normal albumin molecules by toxins. There is also a long-wavelength shift of the fluorescence bands (λ) of the dilutions (more than 10 nm). A

similar nature of the behavior of the spectral-fluorescent characteristics occurs for dilutions of BS with sugar broth. According to the pathogenetic concept in this case there is a blockade by sugar residues of full-fledged albumin molecules. In the case of dilutions of BS with 20% albumin solution, the fluorescent characteristics of these dilutions do not change. In vivo studies included the study of the spectral-fluorescent characteristics of BS in patients with purulent-inflammatory diseases and sepsis. Three main scenarios for the development of sepsis have been identified and described [12, 14]. We will dwell on two of them in more detail (Fig.1, 2). In patient with sepsis (Fig.1, table 1) BS of the fluorescence intensity decreased by 70%, and the long-wave shift of FS of BS reached 40 nm, which is consistent with the results of in vitro studies [10, 12] (dilution of BS by centrifuged and non-centrifuged cultures of bacteria). This long-wave (septic) peak (curve 1) is mainly due to the glow of "pathological" albumin molecules. The patient underwent the complete clinical and laboratory examination and was prescribed antibiotic and infusion therapy (8-10 liters daily). This case allows us to illustrate within the MFS the successful outcome of treatment of the patient with sepsis who was admitted to the hospital in serious condition. The patient underwent a complete clinical and laboratory examination, antibiotic and infusion therapy was prescribed in a volume of 8-10 liters daily. At the same time, the results of standard clinical and laboratory data were not informative enough. The patient underwent a thorough examination and surgery to remove the source of infection in the body (massive retroperitoneal pelvic phlegmon, which caused sepsis-epiduritis), He was also prescribed a complex infusion, antibacterial and anti-inflammatory therapy, which contributed to the progression of this patient. Undoubtedly, this was facilitated by her young age (33 years) and the absence of comorbidities. The survival of this patient in such a serious condition was possible due to X> X*. In this case, although the patient was admitted to the hospital not at the stage of formation of the septic condition, but on the background of its manifestation, MFS helped us to identify the septic peak (Figure.1, curve 1) and determine the rational choice of treatment tactics.

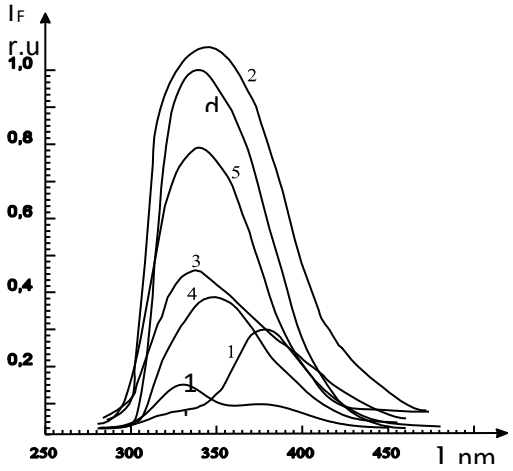

Figure 1: Fluorescence spectra of blood serum of septic patient: 1 – 28.12.; 1′– 02.01.; 2 – 04.01.; 3 – 12.02.; 4 – 19.03. 5 – 04.06. and donor of BS (340 nm – «normal peak», 380nm – « septic peak»).

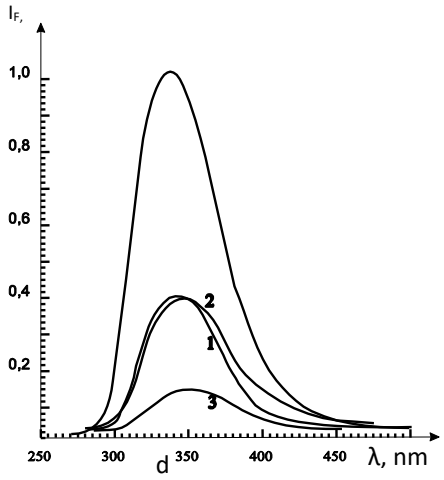

Figure 2. FS of BS of patient 3 with sepsis and diabetes: 1 - 03.06; 2 – 05.06; 3 – 06.06 and donor BS. λex =280 nm.

N	d	1	1′	1′	2	3	4	5
Date	28.12.	28.12.	02.01.	02.01.	04.01.	12.02.	19.03.	04.06.
λ_{max}, nm	340	380	380	345	345	337	349	340
I_F, r.u.	1.0	0.3	0.09	0.15	1.07	0.46	0.39	0.79

Table 1: Changes in the spectral -fluorescent characteristics of the serum of a patient with sepsis

N	d	1	2	3
Date	03.06	03.06	05.06	06.06
λ_{max} , nm	338	342	347	351
I_F, r.u.	1.0	0.41	0.40	0.15

Table 2: Changes in the spectral - fluorescent characteristics of the serum of person 2 with sepsis

Suppression of bacteremia helped to reduce the number of pathological albumin molecules in the patient's blood. This also contributed to the process of restoring the synthesis of endogenous albumin by the liver. This was mainly due to the young age of the patient. The next measurement of the FS of BS on the 4 January (Figure. 1, curve 2) showed the increase of fluorescence up to 1.07 I_F. It was unexpectedly at first glance. In fact, this process was expected. As a result of an in-depth analysis of the described above situation (growth of X), we modeled the fluorescence curve on 2 January (curve 1′). The right maximum indicates a decrease in the concentration of pathological albumin, and the left - a certain increase in the concentration of the complete albumin in the patient's blood. Subsequent studies of the

fluorescence spectra of this patient showed, that the bacteremia was not completely overcome (Fig. 1, curves 3,4), although the long-wave septic peak disappeared. At that time, the patient's body continued the competition between bacteremia and the compensatory properties of her body in combination with complex therapeutic measures. Only a further long process of treatment under the influence of complex therapy led to the significant suppression of bacteremia and notable improvement of the patient's condition (Fig.1, curve 5). At the time of treatment of this patient the pathogenetic model had not yet developed, and therefore, unfortunately, no infusion therapy with a solution of donor albumin was prescribed. We are convinced, that this procedure could significantly accelerate the healing process of this patient. The second scenario clearly demonstrates the behavior of the spectral-fluorescent characteristics of another person with sepsis (Fig. 2). This person was admitted to the hospital at the beginning of the formation of the septic condition in her body. Therefore, the study of the FS of BS did not reveal a two-peak structure, because a pathological "septic" peak in the region of 380 nm has not been formed yet. But there was the decrease in the fluorescence intensity of the BS, which persisted for some time against the background of ongoing bacteremia. After surgery on the background of intensive antibacterial and anti-inflammatory therapy, the patient's condition remained unchanged for three days. Unfortunately, this scenario was not so optimistic. This patient had another comorbidity - diabetes. In this case, there were two types of pathological albumin molecules: blocked by toxins and blocked by increasedamount of glycosylated albumin. The condition of this patient suddenly deteriorated within one day after surgery on the background of intensive antibiotic therapy, which can be explained by the presence of the number of severe comorbidities and her advanced age. The patient died as a result of an advanced process of generalization of infection and multiple organ failure. However, such a severe disease scenario, presented in Fig. 2, does not deprive us the opportunity to discuss another, in our opinion, the scenario of treatment of this patient, starting from 3 June, which, unfortunately, was not implemented. It could be implemented (Table 3) starting from 3 June if the pathogenetic concept of the development of purulent-inflammatory diseases and sepsis at that time had been proposed. According to this scenario, the patient had to obtain 3 June 200 ml of albumin solution and continue daily infusion of 150 ml of albumin until complete recovery. Although this did not give a complete guarantee of the patient's recovery, the procedure had to be performed, giving the patient the last chance to survive. The scenario of such a variant of the treatment process for patient 2 in the possible case of her recovery is presented in table 3.

N	d	1	2	3	4	5
Date	03.06	03.06	05.06	07.06	09.06	11.06
λ_{max}, nm	338	342	347	345	340	338
I_F, r.u.	1.0	0.41	0.40	0.38	0.43	0.51

Table 3: Changes in the spectral -fluorescent characteristics of the serum of person 2 with sepsis

Particular attention should be also paid to the urgency of this problem, especially in high-income countries due to the growing number of pregnant women with obesity and diabetes, which contributes to an increased risk of postpartum purulent-septic complications. Obesity can affect negatively a woman's health, cause insulin resistance, dyslipidemia, hormonal and psychological problems and also sexual problems during menopause [15]. About 6% of albumin molecules in the BS of healthy donors are glycosylated. At the same time, in patients with diabetes mellitus due to the presence of hyperglycemia 9-12% of albumin molecules are glycosylated [13]. Therefore, it is possible that patients with diabetes have a tendency to develop purulent-septic processes in the body and their long course. It is logical to hypothesize that "sugar-laden albumin" is not able to bind and eliminate completely toxic products from the body, which leads to a deepening of endogenous intoxication. Therefore, pregnant women with diabetes are at risk for the formation of postpartum purulent-inflammatory diseases. If the medical institution is not able to control the treatment process within the MFS, it is necessary to conduct a detailed monitoring of the patient's health and in case of deterioration to carry out additional examinations and use appropriate treatment tactics and use infusions of 20% albumin solution. Also it is necessary to conduct detailed monitoring of the course of diabetes in the patient. Figure. 3 and tables 4,5 present the results of research in the dynamics of FS of the BS of the patient with severe postpartum endometritis. In the same figure and in tables 4-5 for comparison the corresponding results for the third of the above-mentioned persons with sepsis, who was treated in 2002 also are depicted. She had a complicated somatic and gynecological anamnesis. 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 examination were revealed. She had risk factors for emerging postpartum endometritis. This patient showed a significant decrease in fluorescence intensity up to 0.35 r.u. and a noticeable long-wavelength shift of the fluorescence band. As the condition of this patient was satisfactory, she underwent manual vacuum aspiration of the walls of the uterine cavity. After this procedure and antibacterial and uterotonic therapy, the patient's condition improved. It is very important to choose the optimal time for manual vacuum aspiration. On the one hand, it should be carried out in a timely manner, without delay, and on the other hand, it is necessary to stabilize the patient's condition by this time and start effective anti-inflammatory and antibacterial therapy at the normal body temperature.

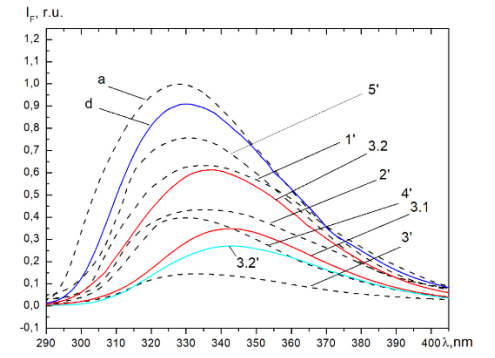

Figure 3: Fluorescence spectra of serum of the woman after childbirth with endometritis in dynamics (3.1 - 14.02.2015; 3.2 - 17.02.2015, 3.2′- 17.02.2015), a woman with uncomplicated course of postpartum period (2), patient with sepsis (1′ ,2′, 3 ′, 4′, 5′) and 20% donor albumin (a).

№	Albumin	2	3.1	3.2	3.2′	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_{max}, nm	330.1	330.1	343.1	337.1	343.1	335.2	335.2	334,1	331,6	331
I_F, r.u.	1.0	0.91	0.35	0.61	0.27	0.63	0.43	0.16	0.40	0.76

Table 4

№	Albumin	3.1	3.2	3.3	3.4	3.5	1′	3′	4′	5′
Date	14.02	14.02	17.02	20.02	22.02	25.02	3.06	6.06	7.06	10.06
λ_{max}, nm	330.1	343.1	348.2	339.0	336	334	335.2	334,1	331,6	331
I_F, r.u.	1.0	0.35	0.27	0.38	0.55	0.68	0.63	0.16	0.40	0.76

Table 5

After the correction of the treatment in the next experiment, the marked increase in I_F of BS of this patient to 0.61 r.u. and the long-wavelength shift of the fluorescence band was leveled. Nevertheless, without correcting treatment tactics on February 14 the patient's condition could in principle deteriorate (curve 3.2′) with the subsequent transition to the septic condition (curve 3′), as in the above-mentioned patient with sepsis. It is very important to monitor the treatment process within the MFS as well as to monitor closely patients' health. Curve 3.2′ could be obtained by us within the MFS. In this case, the correction of treatment tactics with infusions of 100-150 ml of 20% albumin solution several times until recovery was done. This scenario of the disease of the above-mentioned patient is presented in Table 5. We analyzed two possible scenarios of the treatment process for the above-mentioned patient with postpartum endometritis. The first scenario is optimal, because in the second case, the disease could progress. In this case, the chances of full recovery would be much lower. Without the use of MFS, it would be difficult to expect a successful completion of the treatment process.In low-income countries, it is necessary to conduct available research methods, including the ultrasonographic examination of the pelvic organs to assess the condition of the uterine cavity objectively. If necessary, invasive procedures (the manual vacuum aspiration of the walls of the uterine cavity or hysteroscopy) and infusions of 100-150 ml of 20% albumin solution of at a time, which can dramatically change patients' health in many cases, are scheduled.Nevertheless, as based on the analysis of the results of treatment at our clinical base at the Gynaecological Department No. 2 over 300 patients with postpartum purulent-inflammatory diseases for 6 years, no case of septic complication was detected. This can be explained by the high qualification of medical staff and the use of modern treatment tactics and diagnostic methods, including MFS. Otherwise, due to doctors' low qualifications, it is difficult to hope for a positive result in the treatment of women with postpartum purulent-inflammatory diseases.Fig. 4 presents the results of research in the dynamics of fluorescence spectra, and Table 6 shows data for the spectral-fluorescent characteristics of the BS of the patient with the burn injury (area of the burn surface 38%), who was admitted to the hospital on 27 June 2015 [16]. He was immediately prescribed appropriate treatment, including antibiotic therapy and infusion therapy with 2-3 liters daily.

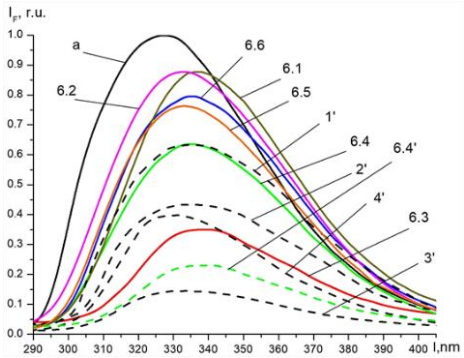

Figure 4: FS of BS of patient 6 with a burn injury, who was hospitalized in Communal City Clinical Hospital №8, Lviv in 2015 in dynamics during treatment (6.1 - 3.07., 6.2 - 8.07., 6.3 - 13.07., 6.4 -17.07., 6.4′ -17.07., 6.5 - 20.07., 6.6 - 24.07.) and a patient with sepsis, who was treated in 2002 in Ambulance hospital (1 ′ - 03.06., 2 ′ - 05.06., 3 ′ - 06.06., 4 ′ - 07.06., 5 ′ – 10.06) and 20% albumin solution (a), ex = 280 nm.

№	a	6.1	6.2	6.3	6.4	6.4’	6.5	6.6	1’	2’	3’	4’	5’
Date	3.07	3.07	8.07	13.07	17.07	17.07	20.07	24.07	3.06	5.06	6.06	7.06	10.06
λ_{max}, nm	327	336.1	332.2	341.1	335.1	341.1	333.1	335.1	335.2	335.2	334.1	331.6	331
$I_{F, r.u.}$	1	0.88	0.88	0.35	0.64	0.27	0.76	0.80	0.63	0.43	0.14	0.4	0.76

Table 6

Staphyloccus aureus 10^5 and Pseudomonas aeruginosa 10^6 were verified on the basis of microbiological examination. Due to infusion therapy, the fluorescence intensity of BS was not significantly reduced during the first 6 days (I_F = 0.88 r.u.), which correlated with the results of in vitro studies. No shift of BS of fluorescence spectra to the long-wavelength region was detected, despite the verification of two pathogens in the patient. The studies of the fluorescence spectra of this patient's BS on 13 July 2015 (Figure. 4, Curve 6.3) showed a significant decrease of its I_F up to 0.35 r.u. and a shift of the fluorescence spectra in the long-wavelength region by 9 mm. The d eterioration of this patient's clinical condition was also revealed. This indicated the deepening of endogenous intoxication. The treatment process was corrected, including the use of 100 ml of 20% donor albumin solution infusion for 8 times on different days. The subsequent sampling of the BS revealed a gradual normalization of the

spectral-fluorescent characteristics of the patient's BS (see Table 6). Therefore, he was discharged from the hospital in satisfactory condition on 24 July 2015. Figure 4 shows that the spectral-fluorescence characteristics of this patient are qualitatively correlated with the corresponding results of the patient with sepsis, presented in the same figure by dashed curves (Curves 1′-5′). This patient was treated in the hospital in 2002. Without the correction of the treatment process, the condition of the patient with the burn injury could continue to deteriorate (Fig. 4, Curve 6.4′) with subsequent transition to the severe septic condition, as it was in the case with the patient with sepsis. In order to correct the treatment process of the patient with the burn injury, the information about the behavior of the spectral-fluorescent characteristics of the patient with sepsis was significant (Curve 3′). It is important that the behavior of the spectral-fluorescent characteristics of the patients with sepsis, including burn injury, is determined by the contributions of two types of albumin molecules: complete and "blocked by toxins". Figure 1 shows that most of the albumin molecules of the patient with severe sepsis (Curve 1) are blocked by toxins (long-wave peak). Only a small number of complete molecules of albumin provide support the vital functions of the patient's body (fluorescence in the region of 330 nm). In such a serious condition of the patient, the synthesis of albumin is very slow. However, if this patient (Fig. 1) had been given the infusion of 20% albumin solution, the additional peak in the region of 330-345 nm could have appeared in her fluorescence spectrum, which could have led to the improvement in her condition. But this is only our assumption. For this patient, the possible changes in the fluorescence spectrum during infusion of 20% albumin solution were not proved. This may be the subject of our further studies of the spectral-fluorescence characteristics in patients with severe sepsis and with severe burn injury. Regardless of the etiological factors of sepsis, the pathogenetic mechanisms of septic complications are unified. Patients with severe burns are model objects for studying the patterns of behavior of the spectral-fluorescent characteristics of patients with sepsis. Serum albumin molecules have the ability to complex. In the case of presence of endogenous intoxication in the body, they are blocked by the products of bacterial metabolism. Understanding of the microscopic mechanisms of the theory of pathological albumin formation is the basis for the development of pathogenetical treatment tactics. The most optimal approach for the detection of septic conditions in patients is the study of spectral-fluorescent characteristics of BS with the method of fluorescence spectroscopy. There is the high risk of septic condition in patients with burn injury in two cases: with the large area and depth of burns and inadequate treatment at the initial stage of the disease. Consequently, the key thesis of the successful treatment is the comprehensive approach to the prevention of the development of bacteremia through early surgical treatment and comprehensive therapy. The fundamental idea of the successful completion of the treatment is its constant monitoring within the method of fluorescence spectroscopy of the treatment process with the possibility of its correction. The intensity and position of the fluorescence maximum are the important parameters in the treatment process. The lower the fluorescence intensity and a more noticeable long-wave shift, the higher is the probability of exitus letalis.

Conclusions

The significant improvement of the functional results of treating patients is the fundamental problem of medical science. The study of the biological objects with the method of fluorescence spectroscopy makes it possible to detect pathological processes in living organisms at different stages of their development. The main and very significant advantage of this method is the combination of high sensitivity and expressiveness with the possibility of non-destructive control of biological objects. The deep understanding of pathogenesis is the key point in creating the strategy of the treatment tactics of patients with various diseases. Obtaining the information about the mechanisms of origin and evolution of purulent-inflammatory diseases and sepsis is extremely important for the rapid search for the effective ways to treat them. This is why we have proposed the pathogenetic concept of diagnostic and therapeutic approach for purulent-inflammatory diseases and sepsis. It is based on the fact that in patients with these diseases part of the albumin molecules in the BS are blocked by the products of bacterial metabolism, i.e. toxins. These pathological molecules of albumin are unable to perform their main functions: transportation and detoxification. Even in healthy people, about 6% of albumin molecules in the blood are glycosylated. At the same time in patients with diabetes mellitus, 9-12% of them are glycosylated. So, the sum of the concentrations of pathological and glycosylated albumin molecules together forms concentration X. As a result, the sum of the concentrations of pathological and glycosylated albumin molecules is concentration X. The new definition of sepsis is to define X*, i.e. the maximum minimum concentration of albumin in patients with sepsis. If X>X*, it ensures the viability of the organism in patients with this disease (X –is the concentration of normal albumin molecules in patients with this disease). If X< X*, exitus letalis may occur. Within the MFS, thorough studies of the spectral-fluorescent characteristics of BS of patients with postpartum purulent-inflammatory diseases, patients with surgical profile and burn injury as well as sepsis were conducted. It is established that the studied characteristics were universal markers of the severity of the patients' condition. At the same time their changes were 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 purulent-inflammatory diseases and sepsis were illustrated. The viability of patients with sepsis can be ensured if there is the sufficient concentration of normal albumin in their blood (X> X*). It was proposed to use infusions of 20% albumin solution in order to overcome endogenous intoxication. In this case, the control and monitoring of the treatment process of patients, especially in serious condition, can be properly provided within the MFS. It is connected with the fact that we can clearly assess the effects of bacteremia and treatment by applying patients' fluorescent characteristics, and we can control and adjust the treatment process. It is very important to analyze our proposed different scenarios of the treatment process in detail. Maybe this can help to implement some of the scenarios. We have analyzed in detail the various scenarios for the development of purulent-inflammatory diseases and sepsis and offer alternative scenarios, which can be implemented without the use of MFS. During the pandemic of COVID-19, there were difficulties in using MFS in the treatment process, in particular for patients with burn injury. The analysis of the obtained results of the treatment of patients with burn disease [16] with the use of MFS helped to treat successfully over 35 patients with burn injuries.

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