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PATHOGENETIC CONCEPT AS THE BASIS OF THE DIAGNOSTIC-TREATMENT MODEL OF PURULENT-INFLAMMATORY DISEASES AND SEPSIS IN MEDICAL PRACTICE

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INTRODUCTION

Pathogenesis is the mechanism of the origin and development of diseases and their individual manifestations. It can be seen at different levels: from noticeable changes at the molecular level to disturbances in the body as a whole. Based on the results of the study of pathogenesis, it is possible to assess the prognosis of the disease and prescribe a reasonable treatment. The deep understanding of the pathogenesis is the key point in the development of a managing strategy for patients with various diseases. This makes it possible to develop the unique algorithm for the diagnostics of their diseases and a full-fledged treating strategy.

The understanding of the pathogenesis of sepsis is the key point in finding effective ways of its prevention and treatment. It develops when the body's response to the infection causes damage to its own organs and tissues and can lead to significant deterioration of a patient's health or even to death. As the WHO states, every year sepsis occurs in 30 million patients worldwide and kills 6 million patients. Regardless of various etiological factors of sepsis, the processes occuring in the bodis of those patients follow the same scenario.

According to the authors of the publications[1,2], patients with impaired skin integrity (wounds, burns, skin infections) are at risk of sepsis. The antigen in patients with burn shock is proteins of tissues, destroyed by a thermal agent that leads to the synthesis of pro-inflammatory cytokines. The cytokines interact with endothelial cells of the microcirculatory tract as well as they increase platelets, activate phagocytes, release prostaglandin E2, thromboxanes and platelet

[1] Modern definition of sepsis and septic shock in patients with deep burns / Surgery of Ukraine / G.P. Kozynets et al. 2017. № 1. P. 109–117. ISSN 1818-5398.

[2] Sorokina O.Y., Koval M.G. Screening and diagnosis of sepsis in patientssevere burns. *Emergency medicine*. Volume 16, № 1, 2020. p. 16–22. ISSN 2307-1230.

activating factor[3,4]. The difficulty of making differentiated diagnosis between systemic inflammatory response syndrome in patients with severe burns and sepsis is generally known.

In recent years, a lot of attention was paid to improve the diagnostics and treatment of patients with burn injuries. A particular emphasis should be placed on the feasibility of early surgical treatment with the proper restoration of skin integrity after a burn injury. It is characterized with significant volumes of damaged tissues, which should be eliminated, the activation of cellular and humoral phases of nonspecific resistance and the persistence of microflora. It should be noted that following endogenous intoxication which occurs in this disease, tissue repair in the area of inflammation and restoration of homeostasis is enormously complicated. Early surgical interventions for the prevention and treatment of wound infection, the restoration of anatomical structures and their rehabilitation are widely used. A separate domain is the study of a wound process and the impact of various drugs on it, as well as that of determining the optimal time of the plastic closure of wound defects[5,6,7].

But insufficent attention was paid to the problem of complications after burns, i.e. sepsis. The changes, occuring in patients with sepsis at the molecular level, are understood poorly. At the same time, they play a key role in understanding the processes, occurring in the human body during sepsis and allow the appointment of effective treatment. This problem is very relevant and needs solving.

The objective of the research is to create the pathogenetic concept as the basis of the diagnostic and treating model of purulent-inflammatory diseases and sepsis. Modern diagnostics of burn disease and sepsis, including that at the early stage, the optimal method of their treatment and the latest promising approach to control the treatment

[3] Shano V.P., Cherny V.I., Nesterenko A.N. Endotoxicosis, immune distress and multiorgan disorders: clinical and morphological justification of therapy from the standpoint of SIRS. *Pain, anesthesia and intensive care.* 2001. № 2. P. 45–47.

[4] Macrophage migration inhibitory factor mediates late cardiac dysfunction after burn injury. *Am. J. Physiol. Heart Circ. Physiol* / M.S. Willis et al. 2005. № 288. P. 795–804.

[5] Savchyn V.S. Features of reparative processes in patients with deep burns of the head and neck. *Archive of Clinical and Experimental Medicine.* 2014. № 23(2). P. 149–152.

[6] Boyarska G.M. Peculiarities of changes of phagocytic activity of neutrophilic granulocytes of peripheral and capillary blood of the zone of thermal damage in victims of severe burns. *Clinical surgery.* 2009. № 11/12. P. 18.7.

[7] Kovalenko O.N. Questions of infusion therapy of patients with burn shock. *Surgery of Ukraine*. 2014. № 2. P. 13–19.

process and improve treatment tactics will be offered. At the same time, the improvement of direct and long-term functional and cosmetic results of patients' surgical treatment remains the fundamental problem of modern combustiology.

1. Optimal treatment tactics for patients with burn injury as a method of preventing of purulent-septic complications and sepsis

This section will present the detailed analysis of current advances in combustiology. The results presented here are fundamentally important for solving the problem set in the research. It should be noted that significant progress has been done in this area over the last decade[8]. At the same time a number of important theoretical and practical problems remain insufficiently studied. The issues of the radicalism of early surgical interventions in patients with burns, the volume and time of their implementation, means of plastic wound closure, correction of general disorders of homeostasis are also debatable. The role of local and general disorders, which characterize the severity of injuries, is insufficiently elucidated and the dynamics of histoimmunological changes in wounds has not been under analysis.

The recovery of affected skin with deep and large burns is a difficult problem. Even during a favorable course of burn disease, this process lasts at least 1 or 2 months after injury. The loss of water, proteins, electrolytes happens through the surface of a burn wound while the wound itself remains a source of infection and intoxication and the main driving force of pathological changes occurring in the human body. Thus, an important component of treatment is the need for rapid and safe removal of necrotic tissue, the use of modern methods of antibacterial therapy, the correction of metabolic processes in time and the fastest recovery of lost skin. In addition to infusion therapy and surgical treatment, the use of skin substitutes for temporary closure of burn wounds is an important area of treatment. The important point is also the choice of the optimal recovery time of the skin in the short time after injury, when patients are not yet exhausted by a long treatment process and the regenerative properties of the body are still preserved.

[8] Kovalenko O.M. Pathogenetic substantiation of programs of surgical treatment of children with common burns and their influence on the course of wound process. Doctor's thesis. 2012. Kyiv: O. Bohomolets National Medical University. 298 p.

At the same time significant progress has been reached in combustiology lately. The concept of early surgical necrectomies of burn wounds with their primary plasticity is widespread. Means of the prevention and treatment of wound infection, the restoration of anatomical structures and non-surgical correction in the postoperative period are developed. Methods of medical and social rehabilitation of patients are improved. Considerable attention was also paid to the problems of the functional state of the internal organs, increasing the body's immunoreactivity and combating wound infection.

The authors[9] have proposed the method of collection, cryopreservation and lyophilization of xenografts from pig skin. Lyophilized xenografts are included in the State Register of Medical Devices and approved for use in medical practice in Ukraine in accordance with the Order of the Ministry of Health of Ukraine (11 May 1998, No. 115). Viable lyophilized xenografts with an area of 100, 200, 300 cm², made according to a special technology, are packed in bags and become ready for use. Their shelf life is 3 years. Lyophilized xenografts should be widely used as a skin substitute in the treatment of both superficial and deep burns, donor and scalped wounds, trophic ulcers. The mandatory element of wound treatment is to clean it, remove fragments of necrotic formations, disinfect the skin around the wound, wash the wound surface with antiseptic solutions and apply an aseptic dressing.

Wound cleaning is a mandatory element of wound treatment, the purpose of which is to remove fragments of necrotic formations, disinfect the skin around the wound, wash the wound surface with antiseptic solutions and apply an aseptic bandage. Wound epithelialization occurs directly under lyophilized xenoimplants. Freeze-dried lyophilized xenoimplants adsorb toxins from the wound surface, reduce the inflammatory process in the wound and revascularize areas of necrosis. Later, lyophilized xenoimplants fall off on their own after healing the wound.

In the process of treating deep burns in the traditional way, the local treatment of burn wounds is aimed at restoring microcirculation, creating antibacterial protection and stimulating reparative processes. After chemical necrectomy and wound cleansing, autodermoplasty should be performed[10]. This reduces pain, water, protein and electrolyte loss from the wound, prevents infection and promotes marginal and islet

[9] Bigunyak V.V., Luchanko P.I. Method of lyophilization of xenodermografts. Patent of Ukraine № 10737, 1993.

[10] The use of lyophilized xenografts to restore lost skin / V.V. Bigunyak et al. P. 127–12.

epithelialization. Under the removed xenoimplants, there are pure granulations which are ready to accept autografts. Along with the formation of granulation, tissue is an active course of epithelialization of the wound surface.

Deep burns with an area of more than 20% of the body's surface often have the following complications: sepsis, erosions and ulcers of the gastrointestinal tract. Immunosuppression, suppression of the cellular immune system and intoxication of the body are also characteristic. Consequently, the excision of necrotic tissue significantly improves the patient's condition due to the elimination of a source of infection and intoxication. An open wound surface of a large area leads to depletion of the compensatory capabilities of the human body. So, the technique of early necrectomy with xenodermoplasty prevents progressive intoxication from the affected areas and the development of infection in wounds, reduces the possibility of further progression of burns and leads to the restoration of the skin in the shortest possible time.

Summarizing the above provisions, one can state that the use of xenoimplants in complex therapy can improve the general condition of patients, sleep, appetite, normalize body temperature, reduce homeostasis, reduce plasma toxicity, accelerate the process of epithelialization of superficial and deep burns. But, despite the significant progress, made in recent years in the treatment of superficial burns, functional and cosmetic results in many cases remain unsatisfactory. Local complications develop at the site of burns, i.e. post-burn scars. They often lead to contractures and deformities of the joints, violation of peripheral and central blood circulation. The use of lyophilized xenoimplants in the complex treatment of patients with burn injuries is easy to use; it does not cause allergic reactions, but it reduces water, protein and electrolyte loss, creates a barrier for microorganisms, reduces pain, scarring and has a significant clinical effect.

Universal cell-mediated reactions of the extravascular phase of inflammation become specific in burn injury. At the same time, inflammation loses its adaptive value and acquires signs of a chronic one, stimulates the inclusion of the immunocompetent system into the pathological process[11,12]. This features lie, first of all, in massive

[11] Nagaichuk V.I., Kozynets G.P., Chornopyschuk R.M. Modern tactics of surgical treatment of patients with burns : монograph. Vinnytsia. 2019. 330 p.

[12] The experience of using lyophilized xenodermotransplants in the complex treatment of both superficial and deep burns / V.V. Bigunyak et al. Hospital Surgery, 1999. № 4.

endogenous intoxication, the depletion of factors of natural resistance and the disturbance of developing mechanisms of immunological reactivity and lead to the inability of an organism to produce an adequate adaptive-protective reaction of an inflammation[13,14] .

Thus, it is obvious that necrotized tissues in the wound are a source of infection and intoxication. Their self-rejection occurs within 3 weeks or more. Transplantation of skin flaps on the granulation surface of the wound often leads to their lysis. The cause of complications may be the microbial inoculation of granulation tissue. If there is an infection in the wound, it increases the influence of chemical inflammatory factors, increases the activation and proliferation of fibroblasts. This can cause the formation of immature collagen. The transplantation of split autografts on the granulation surface leads to rough scars, deformities and contractures.

The paper[15] analyzes 10-year experience of preventing and treating purulent-septic complications at the Center for Thermal Traumas and Plastic Surgery at the Municipal 8th City Clinical Hospital in Lviv. The clinical material consisted of 927 patients with the area of thermal lesions 10–75% of the body surface and aged from 4 to 75. The high risk of complications requires the search for a wide range of new treatments, the use of ultrasound and laser energy in the comprehensive treatment of victims. Burn wounds are the ideal environment for the reproduction of microorganisms before the formation of granulations, which create a barrier against the wound flora. On the one hand, granulating tissues are a haven for microbes and, on the other hand, they create protection against the bacterial invasion of surrounding tissues and bloodstream as a local defense mechanism. All patients underwent comprehensive treatment within the framework of this study: active surgical tactics along with intensive infusion-transfusion therapy, purposeful, adequate antibacterial therapy, the correction of immunological reactivity. In the framework of this study, the analysis of the microbial landscape of burn wounds has revealed that in 46.8%, the causative agent of the infectious

[13] Kozinets G.P., Povstyanoy H.E. Methods of action on the inflammatory reaction and anti-infective protection of burn wounds. *Ways to improve the treatment of burn wounds* : Mat. Republican seminar main specialists-combustiologists of RCD with the participation of leading specialists of Russia. Khmelnitsky. 1993. P. 5–7.

[14] Savchyn V.S. Features of the inflammatory response in burn injuries of the head and neck. № 2 part 2. 2014.

[15] Bik V.G., Galibey I.B., Savchyn V.S. Prevention and treatment of purulent-septic complications in combustiology. *Galician Medical Bulletin*. 2002. Vol. 9, № 3. P. 1–3.

process was Staphylococcus aureus; in 19.7%, Pseudomonas aeruginosa; in 10.5%, Escherichia coli; in 5.8%, Proteus; 2.9%, Klebsiella; 2%, Streptococcus; 0.4%, Spore saprophytes; 0.4%, Penicillium fungus. The ultrasonic cavitation of wounds (the simultaneous action of physical and chemical factors, low-frequency ultrasound and antiseptics: iodinol, iodopyrone, chlorhexidine bigluconate, betadine) was used to fight against infection in wounds during frequent, almost daily dressings. After cavitation, the number of colonies that grew during sowing from wounds in the nutrient medium decreased sharply. The above data allow us to conclude that the combination of low-frequency ultrasound with antiseptics is a reliable polyvalent factor that promotes wound healing. To optimize the course of the pre- and postoperative period, laser therapy and laser acupuncture with a helium-neon laser were used. The prevention of catheter-associated infection can be achieved by using silicone polyurethane catheters; strict adherence to a sepsis in combination with the high professionalism of the practitioner and strict adherence to the rules of catheter care are also necessary.

For two decades, the authors of this paper kept to the principle of active surgical tactics, which involved the earliest possible start of surgical treatment, the maximum reduction of intervals between repeated dermoplasties, ensuring independent, uncomplicated healing of donor wounds during 10–12 days. Stage necrectomies were performed after 6–10 days, preferably every other day. Necrotic scab was excised simultaneously on the area of not more than 10% of the body surface. Hemostasis was also performed: the electrocoagulation of blood vessels, the application of dry bandages. The use of enzymes and keratolytics, which produce the proteolysis of necrotic tissues (40% salicylic ointment), was also promising. For the local treatment of wounds, they recommended the use of antiseptics, Ukrainian ointments on hydrophilic and combined bases like “Levosin”, “Levomekol”, “Oflocaine”, “Nitacid”, “Myramistin”. The use of sorbents is also relevant. It should be noted that over a few past decades, the immune resistance of the population of Ukraine, especially the poor, has decreased in 8–10 times. This contributes to the increase in mortality from burn injuries by 1.5–2 times. Therefore, it is advisable in such cases to use immunotherapy with immunoglobulins. Summarizing the above, it should be noted that adequate treatment in the acute period of burn disease should include the use of modern detoxification methods, effective antibacterial therapy taking into account the susceptibility of the pathogen and active

surgical tactics using lyophilized xenoderm implants in the treatment of energy and ultrasound. Transfusion therapy, immunocorrection and immunomodulation should be also the integral part of treatment.

In general, the use of various antimicrobial drugs, antibiotics, expansion and scope of surgical interventions and invasive manipulations, as well as the use of drugs with pronounced immunosuppressive effects in medical technologies during the twentieth century have caused a significant change in the etiological structure of surgical infections. Of particular note is the significant growth of "opportunistic flora", in particular gram-negative bacteria. Pseudomonas auruginosa is specially noted among them. It is an aerobic gram-negative bacterium which has a low need for nutrients that determines its ability to survive even in the case of absence of sufficient nutrients (in anaerobic conditions). This microorganism is able to survive in solutions of disinfectants (furacillin, diocin) and is sensitive to drying, chlorine-containing disinfectants and high temperatures. Pseudomonas auruginosa never infects unaffected tissues, but is very likely to infect compromised tissues. This microorganism is quite resistant to antibiotics.

The authors[16] analyzed the results of treating 45 patients with postoperative wound infections, caused by Pseudomonas auruginosa. The initial testing of patients included standard assessment of the severity of their general condition, clarification of anamnestic data, physical and laboratory-biochemical examination. Vulnerological examination included assessment of the color, volume and nature of the exudate on the bandages, the nature of changes in the perifocal and wound tissues. Bacteriological examination was conventional, starting with the initial collection of material during the first dressing and consisted of culturing on standard media and identifying the microflora of wound exudate, determining its sensitivity to antibiotics by diffusion into agar from standard disks. These clinical and vulnerological studies were performed every day; general laboratory tests, every other day during the first 10 days of observation; biochemical ones, on the day of the initial examination and at the final stage of treatment within the study. Very peculiar are local tissue changes in the defeat of Pseudomonas auruginosa that is manifested in the wound by the presence of a significant amount of green-blue liquid exudate with a specific nauseating-sweet odor, fibrin layering, edema and the “slipping”

[16] Postoperative wound infections caused by Pseudomonas auruginosa: evaluation of therapeutic efficacy of Ceftazidime-KMP / I.D. Gerych et al. *Clinical antibiotic therapy*. 2003. № 5. P. 29–36.

of granulation tissue, the appearance of punctate or focal necrosis. The studies show that the use of monoantibiotic therapy Ceftazidine-KMP has absolute clinical (93.3%) and bacteriological (91.1%) efficacy that makes it possible to use it as a drug of choice in the treatment of infections, caused by Pseudomonas auruginosa.

The correct choice of the method of early necrectomy (at day 35) and xenodermoplasty followed by autodermoplasty in combination with effective antibiotic therapy was also presented in the paper[17]. The study was performed in 14 children aged from 2 to 18 with deep facial burns. At the same time, there is no single tactic among combustiologists to treat children with deep burns of the head, including the face. Some authors (L. Anishchenko, 1994, H. Kozynets, 2000) prefer the method of treatment, which consists of transplanting autodermotransplants to granulation wounds that ebanles skin transplantation on day 17^{h}–21 and leads to the stages of burn toxemia and septicotoxemia with all possible complications. Since the 1980s abroad (Iapgekouis, Vygke), and since 1996 in Ukraine (M. Povstianyi, V. Bihunyik, V. Nahaichuk, V. Taran, O. Kovalenko), early excision of necrotic tissues has been applied much more widely, when lyophilized xenodermotransplants are used as a temporary wound dressings.

It should be emphasized that a burn wound, especially on the face, differs from other wounds, because it is covered with necrotic tissue, which is nutrient medium for microorganisms. The penetration of microorganisms into the body is one of the essential mechanisms of burn disease. Virulent flora enters the vascular bed and can cause various purulent complications, bacteremia, septicemia. This is especially true in case of severe immunosuppression, especially in children with severe burns.

Obviously, necrotized tissues in the wound are the source of infection and intoxication. Their self-rejection occurs within 3 weeks or more. The transplantation of skin flaps on the granulation surface of the wound often leads to their lysis. The cause of complications may be microbial inoculation of granulation tissue. If there is an infection in the wound, it increases the influence of chemical inflammatory factors, increases the activation and proliferation of fibroblasts. This can lead to the formation of immature collagen, while the transplantation of split autografts on the granulation surface leads to rough scars, deformities and contractures. The authors of this paper performed an early necrectomy during days

[17] Early necrectomy for deep facial burns in children for prevention of purulent complications / V.S. Savchyn et al. 2002.

3–6 after the burn. An early excision of a deep necrotized scab on the face is advisable, as necrotized tissue is the gateway to infection and their removal prevents the occurrence of purulent-septic complications. Also, early necrectomy can reduce the preoperative period, the wound healing period and the duration of inpatient treatment. In turn, a fresh wound bed is better perceived by a full-layer autodermatograft. Dermo-epidermal necrectomy was performed after reaching the level of Hb 100 g/l, H-32, total protein 55 g/l, diuresis 1 ml/kg/ hour. Thus, early surgical treatment of children with deep facial burns gives the best cosmetic functional effect and is economically justified.

According to the research18, facial burns can cause scarring of the neck (14.6%), inversion of the lip (4.9%), microstomy (3.7%), inversion of the eyelid (3.7%) and combined contractures that combine the above types of scar lesions.

According to the results of the research[19], it is advisable to perform the non-contact infrared thermometry of burn wounds in order to determine the depth of the burn wound. This allows us to predict the depth of the burn, which is based on the difference between local, perifocal temperature and the temperature of the homologous area of the body surface 24 hours after the injury. The temperature difference of homologous segments (ΔT) above 1°C is a clear boundary for the presence of dermal burns. It was revealed that the limit temperature for deep dermal burns was 34°C. The presence of wound temperature less than 34°C and a temperature gradient $\Delta T \geq 2°C$ indicates the presence of deep dermal burns. The pH difference of homologous segments (ΔpH) less than 2 units is a clear sign of superficial dermal burns; difference $\Delta pH \geq 3$ units indicates the presence of deep dermal burns 16–24 hours after injury. During the surgical treatment of deep dermal burns, it is expedient to apply wound coverings differently: at wound indicators $pH \geq 9.0$ units and wound temperature $T \leq 33.6°C$.

The early excision of necrotic tissue and delayed autodermoplasty is recommended for patients with deep dermal burns. Autodermoplasty can be postponed until the patient's condition is compensated. Delayed autodermoplasty should be performed in patients with common dermal

[18] Post-burn scar contractures of the head and neck: the current state of the problem / V.S. Savchyn et al.

[19] Kovalenko A.O. Candidate's dissertation “Improvement of surgical treatment of patients with dermal burns through the use of wound dressings”. Kyiv, 2018. 14.01.03 surgery. 186 p.

lesions, because it give us an opportunity to remove a significant portion of necrotic tissue in the early post-trauma, while closing the wound with temporary coatings that helps to reduce intoxication syndrome and microbial load on the patient's body.

At the same time, the transplantation of autodermotransplants for early granulation (granulation on day 5–7) promotes engraftment without loss of autologous skin and without scarring. In the treatment program of patients with widespread dermal burns in the first phase of the wound process, it is advisable to include wound dressings, in particular xenodermoimplants. The use of wound dressings leads to the change in the alkaline reaction of the wound surface in patients with dermal burns to acid that stimulates the healing process. The shift of the pH of the wounds to the alkaline side at all stages of the wound process is a sign of an unfavorable course.

2. Features of changes in albumin molecules in purulent-inflammatory diseases and sepsis

Serum albumin composes 60% of total plasma proteins. It plays an important role in maintaining oncotic pressure. It is also involved in metabolic processes and transports of various chemicals. Albumin is a polypeptide, which consists of 585 amino acids with molecular weight 66.000-69.000 Da. Albumin synthesis occurs exclusively in the liver at the rate of 0.2 g / kg per day. This provides regular replenishment of albumin in the body, which is regulated by osmoreceptors and is inversely proportional to the level of colloid-oncotic pressure.

The detoxification function of albumin is important. Due to the changes of the conformation of its molecules, albumin interacts with hydrophobic molecules of endotoxins and promotes their excretion from the body. Albumin synthesis may decrease under the influence of infusion of synthetic colloids and albumin. It is also slowed by the influence of stress, sepsis, starvation, hyperthermia, and in elderly people. Hormones insulin, cortisone, testosterone, ACTH, growth factors and thyroid hormone can increase the rate of albumin synthesis by hepatocytes. The half-life of endogenous albumin is 21 days, and that of exogenous albumin is 12 hours. Albumin is mainly an extracellular protein. 40% of albumin is contained in blood plasma, and 60% in the depo (40% in the skin, 20% in the muscles of the internal organs)[20].

[20] Dziuba D.O., Galushko O.A. Albumin and gelatin solutions. Acute and urgent conditions in the doctor's practice. 2016. 6 (63). P. 15–18.

Albumin enters the interstitium through pores in the endothelium of the capillars and returns to the bloodstream along with the lymph flow. One cycle lasts 15–18 hours.

Albumin molecules are able to complex. Diseases, which are accompanied by endogenous intoxication, are characterized with impaired ability of albumin to perform its functions, bacause some of its binding centers are blocked by toxins. This leads to the deterioration of detoxification capabilities of the body. Although the total concentration of albumin in the body may be within normal limits, its actual "effective" concentration is much lower. Because of the pathogenetic changes of albumin molecules in patients with endogenous intoxication, the effective component of pathogenetic treatment is the use in complex therapy infusions of albumin solution. As mentioned above, the infusion of albumin solution reduces the synthesis of endogenous albumin, but without this infusion, the body will not be able to overcome the infection in case of the presence of endogenous intoxication. Currently, two aspects of solving the problem of purulent-septic complications of burn injuries are fundamentally important, namely: the possibility of their early diagnosis and the risk assessment of sepsis. After all, a successful solution of this problem can significantly reduce the level of mortality.

In order to resolve successfully this fundamentally important issue, we need to look for new ways. Owing to the use of physical research methods, it is possible to improve significantly modern diagnostic algorithms and offer new ways to solve the problem of early diagnosis and prognosis of diseases, including purulent-septic complications and sepsis.

3. Method of fluorescence spectroscopy. The own experience of its use for the diagnostics and monitoring of patients with purulent-inflammatory diseases and sepsis

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 Fig.1.

In the initial state (it is also called the ground, unexcited state), the molecule (atom) occupies the energy position with the lowest energy (Fig.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 (Fig.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 (Fig. 1c). The molecule transitions from this lowest excited state to the ground state are accompanied by radiation – luminescence (Fig. 1d).

According to the afterglow duration, τ 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.

The fundamentally important advantages of the method of fluorescence spectroscopy (MFS) are its simplicity, expressiveness, high sensitivity and accuracy, as well as its ability to control effectively biological objects and environments. Thus, the use of this method is very promising for improving diagnostics in medical practice. Within the framework of MFS, it is possible to study the spectral-fluorescent characteristics of biological objects both in normal and in various pathological conditions. In medical practice since 2000, we have been using this method to study the blood serum (BS) and urine of patients, including those with purulent-septic complications and sepsis. The study included several stages.

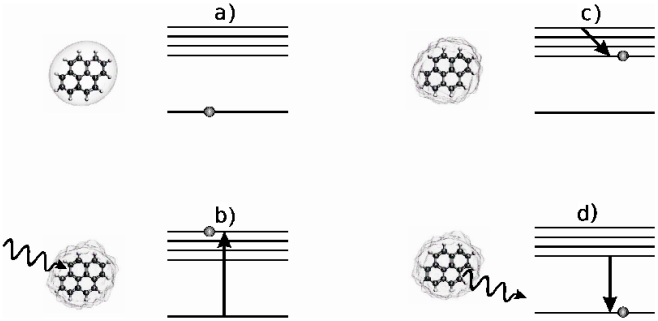

Fig. 1. Scheme of luminescence of molecule in the case of irradiation with light

At the first stage, the behavior of the spectral-fluorescent characteristics of the BS of 100 surgical patients with purulent-inflammatory diseases and sepsis and 40 donors were studied [21] [22].

The clinical basis of the study at this stage was the purulent-septic center of Lviv's municipal clinical hospital of emergency medical services (Ukraine). The experimental base of luminescent research 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 λ = 200–420 nm was used. The excitation of the BS was performed with light with a wavelength of 280 nm, which corresponds to the glow region of human serum albumin. The main indicators, used for the analysis of fluorescence spectra of BS, were the fluorescence intensity (I_F) and the position of the maximum fluorescence band (λ_{max}). BS of patients is a mixture of normal (concentration X) and blocked by toxins (concentration 1-X) molecules of albumin.

For purulent-inflammatory diseases, three characteristic types of changes of the spectral-fluorescent characteristics of BS, which correspond to aseptic, preseptic and septic pathologies, were identified.

Now we shall dwell in detail on the results of the study within the MFS of the excitation fluorescence spectra of the patient with sepsis and the donor (Fig. 2). The structure of the fluorescence excitation spectra of the patient with sepsis and the donor are generally similar, but the patient's intensity of fluorescence of BS is much lower, than that of the donor.

Fig. 3 and table 1 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 epiduritis of the lumbosacral 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). 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

[21] Prospects for the diagnosis of sepsis and purulent-septic complications: the method of fluorescence spectroscopy. *Bulletin of the Ukrainian Medical Dental Academy* / I.D. Gerych et al. 2009. V. 9. № 1. P. 248–256.

[22] Fluorescence spectroscopy: possibilities of application in medical practice / I.D. Gerych et al. Lviv : Liga-Press, 2015. 366 p.

to the fluorescence band of the donor, and the fluorescence intensity was $0.3*I_F$ 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 330 nm, luminescence intensity due 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. The obtained result for the spectral-fluorescent characteristics of the BS at this time indicates a severe septic condition of the patient.

Note, that the survival of the patients in such a serious condition is possible only if $X \geq X^*$ (X^*– is the limit value of the concentration of complete albumin, enough to ensure 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 (Fig. 3, 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 of 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 pseudohypo-proteinemia – 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[23].

[23] Ostapiuk L. Diagnostic and Therapeutic Model of Sepsis and Purulent-Inflammatory Diseases. *International Journal of Clinical Medicine.* 2019. Vol. 10. P. 577-595. https://doi.org/10.4236/ijcm.2019.1011047.

Undoubtedly, the above-mentioned significant increase in the intensity of the fluorescence band of its BS of 4 January 2002 was influenced by a decrease of septic symptoms.

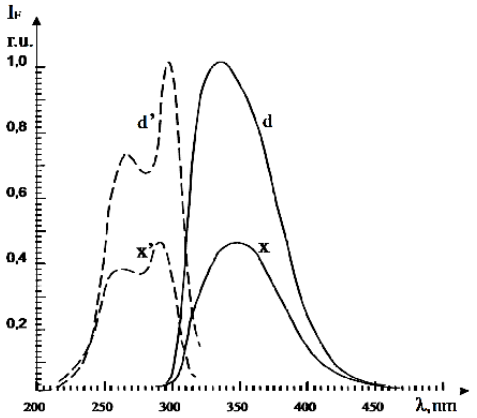

Fig. 2. Fluorescence spectra of blood serum of donor (d) and a person with sepsis (x) (λ_{ex}= 280 nm) and excitation spectra of fluorescence bands with λ_{max} = 340 nm of blood serum of donor (d ') and person with sepsis (x')

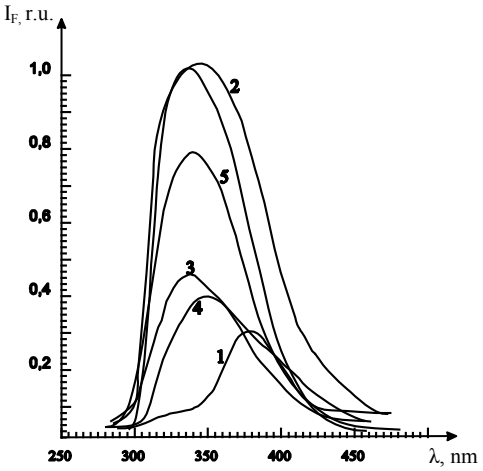

Fig. 3. Fluorescence spectra of blood serum of septic patient: 1 – 28.12; 2 – 04.01; 3 – 12.02; 4 – 19.03 5 – 04.06 and donor of BS (340 nm – «normal peak», 380nm – « septic peak»)

Table 1

N	d	1	2	3	4	5
Date	28.12	28.12	04.01	12.02	19.03	04.06
λ_{max}	340	380	345	337	349	340
I_F	1.0	0.3	1.07	0.46	0.39	0.79

Further studies of the fluorescence spectra of this patient showed, that bacteremia was not overcome, although (see Fig.3, curves 3,4) the long-wave septic peak disappeared. This indicated the significant decrease of albumin molecules, blocked by toxins in the BS of this patient. Only the further long process of treatment led to the essential suppression of bacteremia and the significant improvement of the patient's condition (Fig.3, curve 5). After the complex therapy she was discharged from the hospital in the satisfactory condition.

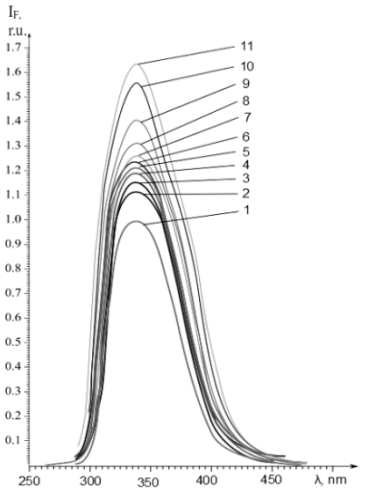

Fig. 4. The effect of dilution with distilled water on the fluorescence spectra of donor blood serum (1 – BS, 2 – 90% BS, 3 – 80% BS, 4 – 70% BS, 5 – 60% BS, 6 – 50% BS, 7 – 40% BS, 8 – 30% BS, 9 – 20% BS, 10 – 10% BS, 11 – 5% BS). λex=280 nm

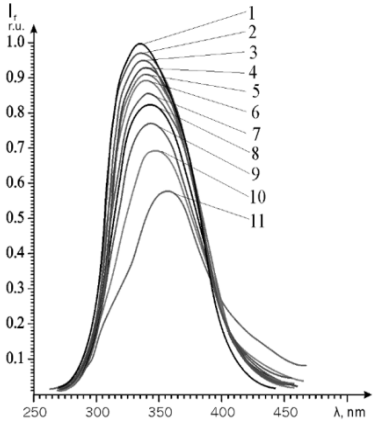

Fig. 5. Effect of dilution centrifuged crops on fluorescence spectra of donor blood serum (BS) (1 – blood serum (BS) 2 – 90% BS 3 – 80% BS, 4 – 70% BS, 5 – 60% BS, 6 – 50% BS, 7 – 40% BS , 8 – 30% BS, 9 – 20% BS, 10 – 10% BS, 11 – CF crops). λ_{ex} =280 nm

The above-mentioned reductions of the fluorescence bands of the patient's BS are connected with the presence of the advanced septic process and correlate with the integrated indicators of the severity of the clinical condition and bacteraemia. 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.

The detected changes in the spectral-fluorescent characteristics of BS in patients with sepsis in most of them were pre-manifest: they were usually recorded 24-48 hours before the appearance of obvious clinical and laboratory signs of significant change in the general somatic status of patients. The results, obtained with the help of MFS, are significantly ahead of the results of other research methods, which are now routinely widely used for diagnosis in health care facilities.

We were first to obtain the fundamental result for the fluorescence spectra of the patient with severe sepsis and study the dynamics of its changes during the process of recovery. It will be the guide in our further studies of the fluorescence spectra of BS in patients with purulent-inflammatory diseases and sepsis. Our results for the spectral-fluorescence characteristics of two more patients with sepsis for convenience will be discussed later in the analysis of the corresponding results for patients with burns with purulent-septic complications.

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. 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 (Fig. 4)[24]. 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.

[24] Modelling Changes in Blood Serum at Different Diseases and Therapeutic Measures. Biomedical and Biosocial Anthropology / O.V. Bulavenko et al. 2013. 20. 8–14.

A similar effect was observed with massive infusion therapy (Fig. 3, curve 2). Our in vitro studies of the bactaeria of standard dilutions of the donor BS with distilled water (see Fig. 4) confirmed the correctness of our suggested explanation of the registered phenomenon of fluorescence intensity increase of the BS of the patient with sepsis (Fig, 3, curve 2).

When diluting the BS by bacterial cultures of Staphylococcus aureus (Fig. 5) I_F gradually decreases with increasing content of bacterial culture in solution. There is also a long-wave shift of the fluorescence bands (λ_{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.

Changes of the fluorescence spectra of BS during dilution of BS by bacterial cultures have a specific character and form the basis for the development of the fluorescent method for early diagnosis of sepsis by studying the spectral-fluorescent model of sepsis in vivo (Fig. 3)[25].

At the third stage, the spectral-fluorescent characteristics of the BS of 170 new mothers with postpartum purulent-inflammatory diseases and 40 new mothers of the control group with uncomplicated post-partum perriod were studied[26]. A detailed study of the behavior of spectral-fluorescent characteristics of the BS of patients with postpartum endometritis was carried out. The control of the medical process and its correction, if necessary, were carried out. The effect of infusion of 20% albumin solution on the spectral-fluorescence characteristics of the BS of patients with postpartum endometritis was studied in the dynamics. It was revealed that no septic complications were found among patients with endometritis. Based on the use of statistical research methods (logit regression and ROC analysis), a reliable prognostic model of postpartum purulent-inflammatory diseases was

[25] Method for Early Diagnosis of Septic Complications by the Method of Fluorescence Spectroscopy / Gerych I.D. et al. Pat. № 76953 Ukraine A61B 17/00 G01N 33/48, G01N 21/64 ; Applicant and Patentee: Pirogov Vinnytsia National Medical University. № 201207441; stat. 19.06. 2012; publ. 25.01.2013, Bull. № 2.

[26] Justification of the feasibility of using the fluorescence spectroscopy method in the complex diagnosis of postpartum endometritis / O. Bulavenko et al. *Women's Health.* 2016. Vol. 3. P. 71–75.

elaborated[27,28]. Despite the presence of the large sample of patients with postpartum purulent-inflammatory diseases, only one patient with complicated form of postpartum endometritis was identified.

4. Assessment of the risk of sepsis, monitoring and control of the treatment process in patients with burn injuries

At the fourth 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 patients with burn injuries. The clinical base of the study was the burn department of Lviv Communal City Clinical Hospital No 8. The research lasted in 2015-2019. Two groups of patients and a control group were formed. The main study group consisted of 20 patients with flame burns and boiling water burns, including head and neck burns. The control group consisted of 25 healthy individuals (donors) without chronic diseases. For patients and donors within the MFS, a study of samples of their BS was conducted. The comparison group consisted of 25 patients in serious condition, whose BS was not tested by using MFS. But therapeutic tactics with donor albumin solution was also used for these patients. In this study, the classification of burns depending on the etiological factor, depth, area and location of the lesion was used for both groups of patients. In the course of the research, we also discussed clinical and anamnestic data and analyzed the spectral-fluorescent characteristics of the BS of patients of the main group, obtained dynamically within the framework of MFS. All the patients in the hospital underwent the appropriate surgical treatment of affected burn surfaces, followed by wound closure with lyophilized xenografts. The wounds were epithelialized partly under dry skin, partly under dry necrosis and applicators. Residual wounds were epithelialized under dry applicators. Patients also received anti-inflammatory treatment, antibiotic and infusion therapy, including with the use of albumin solution and

[27] A Prognostic Model of the Development of Postpartum Purulent-Inflammatory Diseases. *International Journal of Clinical Medicine* / O. Bulavenko et al. 2020. Vol. 12. P. 32–42. URL: https://doi.org/10.4236/ijcm.2020.112004.

[28] Bulavenko O.V., Ostapiuk L.R., Rud V.O. A new approach to the diagnosis of sepsis and purulent-inflammatory diseases. Conceptual options for the development of medical science and education : Collective monograph. Lublin : Poland, 2020. 677 p. P. 35–62.

desensitizing therapy[29,30,31,32].The main regularities of the behavior of the spectral-fluorescent characteristics of the BS of patients with burn trauma were studied and the problems of their treatment were discussed. However, at the same time, the problem of purulent-septic complications in patients with burns was not discussed.

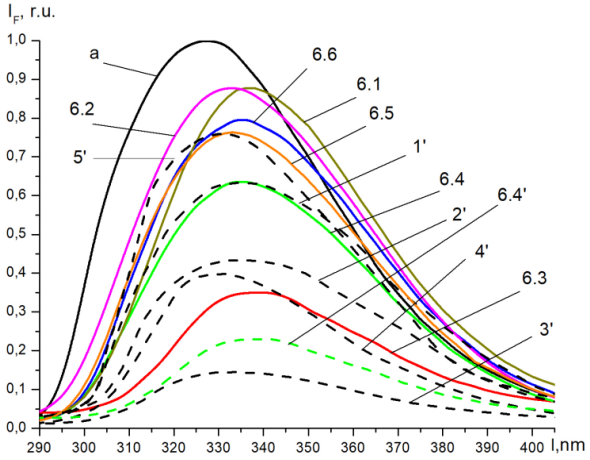

Fig. 6. Fluorescence spectra of BS of patient 6 with a burn injury, who was hospitalized in Communal City Clinical Hospital № 8, Lviv in 2015 in dynamics during treatment (6.1 – 3.07., 6.2 – 8.07., 6.3 – 13.07., 6.4 –17.07., 6.4' -17.07., 6.5 – 20.07., 6.6 – 24.07.) and a patient with sepsis, who was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

[29] Approbation of the method of fluorescence spectroscopy for the diagnosis of endogenous intoxication for the patients with burn injury / V.S. Savchyn, L.R. Ostapiuk, A.S.Voloshinovskii.*Clinical Surgery.* 2016. Vol. 6. P. 68–70.

[30] A new look at the diagnosis of endogenous intoxication in patients with burn injury. *Journal of Hospital Surgery* / V.S. Savchyn et al. 2019. № 1. P. 20–24. URL: https://doi.org/10.11603/2414-4533.2019.1.9907.

[31] The New Approach to the Diagnostics and Treatment of Endogenous Intoxication in Patients with Burn Injury. *International Journal of Clinical Medicine* / S. Zaporozhan et al. 2020. 11. 375–388. doi: 10.4236/ijcm.2020.116033

[32] Zaporozhan S., Savchyn V., Ostapiuk L., Tuziuk N. The new model of diagnostics, treatment and prevention of purulent-septic complications in patients with burn injury. *Challenges of medical science and education: an experience of EU countries and practical introduction in Ukraine : Collective monograph.* Wloclawek : Poland, 2020. 340 p. P. 107–141.

Table 2

№	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}	327	336.1	332.2	341.1	335.1	341.1	333.1	335.1	336	334	333	330	331
I_F	1	0.88	0.88	0.35	0.64	0.27	0.76	0.80	0.64	0.44	0.16	0.41	0.76

Now we shall discuss the results of the study of the spectral-fluorescent characteristics of the BS of patients with burn injury with septic complications. Fig. 6 presents the results of the research in the dynamics of fluorescence spectra, and Table 2 contains data for the spectral-fluorescent characteristics of the BS of the patient with burn injury with the area of the burn surface 38%, admitted to the hospital on 27 June 2015. He was immediately prescribed appropriate treatment, including antibiotic therapy and infusion therapy with the volume of 2–3 liters daily. Staphyloccus aureus 10^5 and Pseudomonas aeruginosa 10^6 were verified on the basis of a microbiological study.

Due to the infusion therapy, the fluorescence intensity of BS during the first 6 days did not decrease significantly (I_F = 0.88 r.u.) that correlated with the results of in vitro studies. There was also no shift in the fluorescence spectra of the BS in the long-wavelength region, despite the verification of two pathogens in the patient.

The examination of the fluorescence spectra of the BS of this patient on 13 June 2015 (Fig. 6, curve 6.3) showed a significant decrease in its I_F to 0.35 r.u. and a shift of the fluorescence band in the long-wavelength region by 9 nm. The deterioration of this patient’s clinical condition was also revealed. This indicated the deepening of endogenous intoxication in him. The treatment process was corrected by using the infusion of 20% donor albumin solution (100 ml 8 times on different days). Subsequent sampling of BS revealed a gradual normalization of the spectral-fluorescent characteristics of the BS of the patient (see table 2).

Therefore, he was discharged from the hospital in a satisfactory condition on 24 of July 2015. Figure 6 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 Lviv’s municipal clinical hospital of emergency medical services in 2002. Without the correction of the treatment process, the condition of the above-mentioned patient with burn injury could continue to deteriorate (Fig. 6, curve 6.4′) with subsequent transition to a severe

septic condition, as it was in case of the patient with sepsis. The behavior of the spectral-fluorescent characteristics of patients with sepsis, even after burn injuries, is determined by the contributions of two types of albumin molecules: complete and “blocked by toxins”. Fig. 3 shows that most of the albumin molecules of the patient with severe sepsis (curve 1) are blocked with toxins (long-wave peak). Only a small number of complete molecules of albumin provides support for the vital functions of the patient's body (fluorescence in the region of 330 nm). Earlier it was noted that in such a serious condition of the patient the synthesis of albumin was very slow. However, if this patient (Fig. 3) had been given an infusion of 20% albumin solution, a more noticeable peak in the fluorescence spectra could have appeared in the region of 330 nm that would lead to the improvement of her condition. But this is only our assumption. Strictly speaking about this patient, it was not proven what changes would occur in the fluorescence spectrum during the infusion of 20% albumin solution. This may be the subject of our further studies of the spectral-fluorescent characteristics of patients with sepsis after a burn injury in such a severe condition.

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 Fig. 7, and the data for the spectral-fluorescent characteristics of his BS are depicted in Table 3.

He was immediately given appropriate treatment, including anti-biotic 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 (Fig. 7, curves 7.1, 7.2). 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 (Fig. 7, curve 7.3′) towards a subsequent transition to the severe septic condition, as it was as in case of the patient with sepsis.

Our results for the spectral-fluorescence characteristics of the above-mentioned patient with burn injury correlate well with the corresponding results (Fig. 7, 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 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.

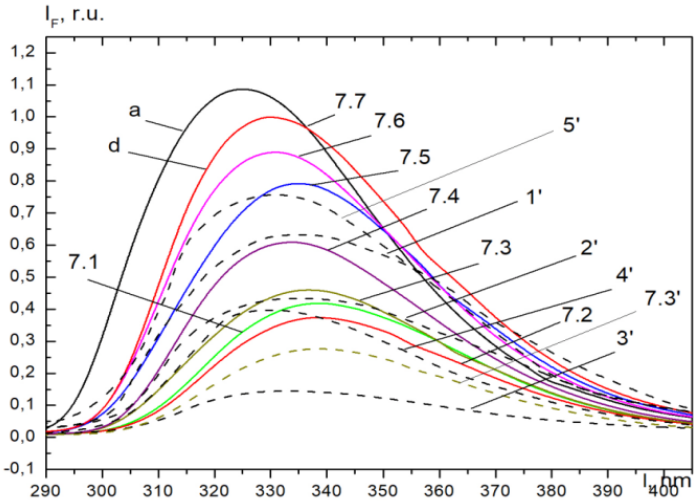

Fig. 7. Fluorescence spectra of BS of patient 7 with a burn trauma, who was hospitalized in Lviv Communal City Clinical Hospital No 8 in 2017 in the dynamics during treatment (7.1 – 9.02., 7.2 – 14.02., 7.3 – 22.02., 7.3′ – 22.02., 7.4 – 27.02., 7.5 – 03.03., 7.6 – 10.03., 7.7 – 31.03), and a patient with sepsis, who was treated in 2002 in Lviv's municipal clinical hospital of emergency medical services (1 ′ – 3.06., 2 ′ – 5.06; 3 ′ – 6.06; 4 ′ – 7.06, 5 ′ – 10.06) and 20% albumin solution (a), λex = 280 nm

Table 3

№	a	d	7.1	7.2	7.3	7.3’	7.4	7.5	7.6	7.7	1′	2′	3′	4′	5′
Date	9.02.	9.02	9.02	14.02	22.02	22.02	27.02	03.03	10.03	31.03	3.06	5.06	6.06	7.06	10.06
λ_{max}	330.1	333.1	335.1	339.1	337	337	334	335.1	331.1	332.0	336	334	333	330	331
I_F	1	1	0.41	0.37	0.46	0.27	0.61	0.79	0.89	0.95	0.64	0.44	0.16	0.41	0.76

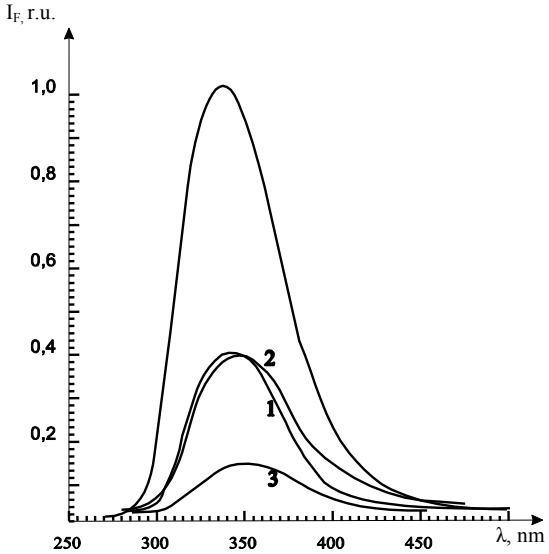

Fig. 8. Fluorescence spectra of BS of patient with sepsis and diabetes: 1 – 03.06; 2 – 05.06; 3 – 06.06 and donor BS. λ_{ex} =280 nm

Table 4

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

The most optimal approach for the detection of septic conditions in patients is the study of the spectral-fluorescent characteristics of their BS in the frame of the method of fluorescence spectroscopy. There is a high risk of septic condition in patients with burn injuries in two cases: in

patients with the large area and depth of burn trauma and in the case of inadequate treatment at the initial stage of the disease. Therefore, the key thesis of successful treatment is the comprehensive approach to prevent the development of bacteraemia owing to the 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. In the treatment process, the intensity and position of the maximum fluorescence of the BS of patients are the indicators of fundamental importance. The lower the fluorescence intensity, the higher the probability of exitus letalis.

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 (Fig.8, table 4), who was treated at Lviv's municipal clinical hospital of emergency medical services in 2002.

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 (Fig.8, curves 1, 2, 3).

In conclusion, it is important to note that the dynamics of changes in the spectral-fluorescent characteristics of the BS of patients with sepsis during treatment objectively reflects the clinical features of the disease. Successful completion of the treatment process significantly depends on the quality of diagnosis and monitoring and correlates with the effectiveness of treatment tactics. For successful and effective management of the treatment process within the MFS, it is very important to have portable equipment for the study of fluorescence spectra, as well as reliable financial support of the treatment process. If the septic process becomes uncontrollable and cannot be treated, the probability of patient's survival is low.

In conclusion, we would like to concentratre on the problems that need to be solved in order to improve properly the treatment process of patients with burn injuries to prevent the development of the septic process. It is necessary to conduct a clinical and laboratory examination of the patient, prescribe antibiotic therapy, infusion therapy, including the use of albumin solution. It is fundamentally important to carry out

early surgical treatment to prevent the development of endogenous intoxication of the body. It is important to sow bacteria in order to verify and study their sensitivity to antibiotic therapy. The authors[33] demonstrated the effectiveness of the fluorescent method for the diagnosis of bacterial contamination of wounds on the basis of a multicentric study. The accuracy of this method was higher than standard modern research methods, which are widely used in the routine practice of health care facilities. In this study, the fluorescent method allowed in 69% cases to change the treatment tactics and improve the provision of medical services to patients.

In the critical situation, the fluorescence intensity of albumin molecules is of fundamental importance. The most fundamental is the registration in time of the threatening moment which requires a rapid correction of treatment tactics. If the choice of antibiotic was not correct, it is necessary to replace antibiotics in accordance with the results of the determination of sensitivity according to the antibioticogram. In healthy people, up to 6% (average 4–5.8%) of albumin molecules are glycosylated, while in patients with diabetes such molecules are more than 9% (9–12%). The albumin glycosylation of more than 12% indicates the presence of decompensated diabetes mellitus. This reduces the amount of albumin, which is able to perform a detoxifying function, which slows down the healing process of wounds in patients with diabetes. Such patients have a predisposition to the prolonged course of purulent-septic complications and the likelihood of exitus letalis (Fig. 8).

Thus, in this section, based on the results of the study of septic complications of patients with surgical profile, the successful experience of using MFS to diagnose, control and improve the treatment of patients with sepsis after burn injury was illustrated. It is shown that the experience and skills, gained in this case, significantly helped to improve treatment tactics in the presence of septic complications in patients with burn injuries. Fundamentally important in the future are thorough studies within the MFS of different scenarios of the development of septic complications in severe forms of burns.

[33] Lam Le et al., 2020; Published by Mary Ann Liebert, Inc. Advances in Wound Care Volume 00 Number 00 DOI: 10.1089/wound.2020.1272

CONCLUSIONS

Delayed and unsatisfactory burn treatment at the initial stage can lead to sepsis and mortality. The pathogenetic concept of the diagnostic and treatment model of purulent-inflammatory diseases and sepsis is based on the fact that in patients with the diseases, accompanied by endogenous intoxication, part of the albumin molecules in the patient's blood is blocked by toxins. As a result, there are two types of albumin molecules in the blood of patients: normal and blocked by toxins. This causes the deterioration of the detoxification capabilities of the body. It is proposed to use the method of fluorescence spectroscopy for diagnosis, especially at the early stage, monitoring and correcting the treatment process. It has been established that the spectral-fluorescent characteristics of the serum of patients with purulent-septic complications were universal markers of the severity of the patients' condition. At the same time, some changes of the spectral-fluorescent characteristics of the patients' blood serum were registered 24–48 hours before the emergence of obvious clinical and laboratory signs of the patients' general somatic condition.

In order to overcome optimally endogenous intoxication, it is proposed to use infusions of albumin solution to increase the content of complete serum albumin in patients with endogenous intoxication. It is shown, that the scenarios of sepsis, including sepsis, which developed as a complication of burn disease, depend on the severity of the disease. The features of the pathogenesis of sepsis do not depend on its etiological factors.

SUMMARY

Burns occupy a leading place in the structure of injuries. Despite the introduction of modern advances in resuscitation and intensive care into medical practice, the mortality of patients with widespread burns remains quite high. A fundamentally important point is the surgical restoration of the skin after injury. The pathogenetic concept of the diagnostic and treating model of purulent-inflammatory diseases and sepsis is presented. The method of fluorescence spectroscopy was used for its implementation. It is shown that the spectral-fluorescent characteristics of the blood serum of patients with purulent-inflammatory diseases and sepsis are universal markers of the severity of their condition.

The influence of various factors on these markers during the treatment was analysed. The changes studied in patients with septic conditions in most cases were premanifest: they were usually recorded 24–48 hours

before the appearance of obvious clinical and laboratory signs of general somatic status of patients. It is recommended to use infusions of albumin solution in order to overcome endogenous intoxication in patients during treatment. Regardless the etiological factors of sepsis, the pathogenetic mechanisms of septic complications are unified.

The aim of the research is to create the pathogenetic concept as the basis of the diagnostic and treating model of purulent-inflammatory diseases and sepsis. Modern diagnostics of burn disease and sepsis, including that at the early stage, the optimal method of their treatment and the latest promising approach to control the treatment process and improvement of treatment tactics have been designed. At the same time, the fundamental problem of contemporary combustiology is the improvement of immediate and long-term functional and cosmetic results of patients' surgical treatment. The successful solution can significantly help prevent patients, including those with burns, from the septic condition.

The study was conducted from January 2001 to December 2019 and included 4 stages. The first two of them were performed on the basis of the purulent-septic centre of Lviv's Municipal City Clinical Emergency Hospital. The third stage was performed on the basis of Gynecological Department No 2 of Vinnytsia's City Clinical Maternity Hospital No 2, and the fourth on the basis of the City Center for Thermal Traumas and Plastic Surgery at the 8th City Municipal Clinical Hospital in Lviv. The experimental base at all the stages of the research was the luminescence laboratory of the Department of Experimental Physics of the Ivan Franko National University of Lviv. The research was performed by using the optical monochromators MDR-2 and MDR-12. As a source of exciting light, the deuterium lamp DDS-400 with a continuous radiation spectrum in the region λ = 200-420 nm was used. The excitation of BS was performed with light with a wavelength of 280 nm, which corresponds to the glow region of human serum albumin. The main characteristics under study were fluorescence intensity (I_F) and the position of the maximum fluorescence band (λ_{max}) of BS. The objects of the study were samples of BS of patients in main and control groups. In case of the endogenous intoxication of the body, conditions for the formation of albumin molecules with altered physico-chemical properties are created. Albumin binding centers are blocked by the products of bacterial metabolism, and this "pathological" albumin is unable to perform its functions, including transportation and detoxification.

The pathogenetic concept as the basis of the diagnostic and treating model of purulent-inflammatory diseases and sepsis is devised. The method of fluorescence spectroscopy was used to diagnose burns and sepsis. A prospectful approach to control the treatment process as well as correct and modify treatment tactics is proposed. In particular, the important role of donor albumin solution infusion in the treatment of the above-mentioned diseases has been established.

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