MINISTRY OF HEALTH OF UKRAINE

ODESA NATIONAL MEDICAL UNIVERSITY

Faculty *Medicine*

Department *Surgery, Radiological Diagnostics, Radiation Medicine, Therapy and Oncology*

APPROVED BY
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METHODOLOGICAL RECOMMENDATION FOR PRACTICAL CLASSES OF THE ACADEMIC DISCIPLINE

Faculty, course Medical 6th year

Academic discipline Surgery
(name of the discipline)

PRACTICAL CLASSES

Practical class № 2

Topic: "Systemic inflammatory response syndrome in surgical patients.
Pathogenesis, significance in various diseases and injuries.
Therapeutic tactics. Shock in surgical patients. Causes, diagnosis, treatment tactics"

Approved:

At the meeting of the Department of Surgery, Radiation Diagnostics, Radiation Medicine, Therapy and Oncology of Odesa National Medical University

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PRACTICAL CLASSES

Practical class № 2

Topic of the practical class:
'Systemic inflammatory response syndrome in surgical patients. Pathogenesis, significance in various diseases and injuries. Therapeutic tactics' - 2 hours.
'Shock in surgical patients. Etiology, diagnosis, treatment tactics.' - 4 hours

1. Relevance of the topic. The need for a clearer definition of severe diseases associated with infection and conditions that are clinically similar to severe infection, as well as the understanding that systemic inflammation, rather than infection, leads to the development of multiple organ failure, contributed to the approval of terminology at the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference in 1992, which has become the most widely used worldwide. R. Bone et al. proposed the term 'Systemic Inflammatory Response Syndrome' (SIRS), which includes complex changes in the systemic activation of the natural immune response, regardless of the cause. It was assumed that SIRS could be caused by local and systemic infection, severe trauma, burns, or sterile inflammatory reactions such as uninfected necrosis. The concept of SIRS was widely accepted in the scientific community, and shortly after the conference conclusions were published, almost all studies on severe infection used or mentioned the SIRS criteria.
The relevance of the topic is due to the high mortality rate in the development of shock, which, according to various sources, ranges from 25 to 50% of those suffering from shock.

Learning objectives:

2.1. Learning Objectives:

The student should learn to:
- to inform higher education students about: **I level**
a) Causes of development of shock states of different genesis;
b) principles of diagnosis of shock in surgical patients;
c) characteristic laboratory and clinical signs of shock in surgical patients;
d) directions in the choice of treatment of patients in shock states.
1. Identify anamnestic and clinical objective signs of diseases that led to the development of a systemic inflammatory response syndrome.
I**I level**
2. Basic principles of diagnosis of criteria for systemic inflammatory response syndrome and differential diagnosis of its causes.
a) classification of shock according to the etiopathogenetic aspects of the condition;
b) diagnostic criteria for the stages of shock;
c) principles of treatment of different types of shock;
3. Prescribe a plan of examination using laboratory, radiological, endoscopic methods of the third level of examination.
II**I level**

4. Provide emergency conservative care to patients with

systemic inflammatory response syndrome level III **level**

a) recognise certain types of the above pathology,

b) assess the severity of the patient's condition based on the results of the studies;

c) predict possible complications; III level

5.Determine indications for different methods of treatment of the syndrome systemic inflammatory response syndrome IV level

2.1. <u>Educational objectives:</u>

1. Formation of professionally significant personality of a doctor.

2. To emphasise the importance of different surgical schools in the development of modern methods of diagnosis and treatment of systemic inflammatory response syndrome.

3. Interdisciplinary integration.

№	Disciplines	To know	To be able to
I. Previous disciplines			
1.	Anatomy, histology	Structure of the vascular system, microcirculatory system, immunocompetent organs.	Be able to identify the main areas of development of pathological reactions in systemic inflammatory response syndrome.
2.	Physiology and pathophysiology	Features of blood circulation and microcirculation in systemic inflammatory response syndrome	Be able to interpret haemodynamic disorders in patients with systemic inflammatory response syndrome.
3.	Biochemistry	Biochemistry of immunological and mediator reactions in systemic inflammatory response syndrome.	Be able to interpret laboratory data in the diagnosis of systemic inflammatory response syndrome.
4.	Pharmacology	Mechanism of action of drugs used in the treatment of systemic inflammatory response syndrome.	Prescribe syndromic treatment for systemic inflammatory response syndrome.
5	Microbiology	Main pathogens of sepsis and systemic inflammatory reaction of bacterial origin	Conduct bacterioscopy of biopsy material and wound contents to determine the nature of the bacterial invasion
II. Intersubject integration			
1.	Sepsis in patients with acute surgical infection	Signs of acute surgical infection, its spread and manifestation in the form of a systemic reaction	Interpret the data of examination, objective examination of biochemical and bacteriological studies, ultrasound and endoscopic examination.
2.	Acute surgical diseases of the abdominal and thoracic organs	Know the main types of surgical pathology that can lead to systemic inflammatory response syndrome.	Take anamnesis, be able to find signs of acute surgical diseases during laboratory and instrumental examination.

3.	Gram-positive and gram-negative sepsis in surgical patients	Know the clinical picture, differential diagnosis and principles of treatment of various types of sepsis	Be able to examine a patient with sepsis, determine its cause, and prescribe treatment.
4.	Multiple organ failure in patients with surgical pathology	Know the features of the clinical picture and diagnosis of multiple organ failure.	To be able to make a differential diagnosis of diseases that have led to multiple organ failure, to prescribe further examination and syndromic treatment.

4. Lesson content.

Inflammation is one of the oldest typical defensive reactions to local damage inherent in mammals; its classic external signs have been known since ancient times. The evolution of views on the nature of inflammation throughout the history of human society largely reflects the development of fundamental general biological concepts of the body's response to injury. I.I. Mechnikov (1883) was the first to lay the foundations for the scientific development of the problem of inflammation, defining it as a protective concentration of phagocytes in the area of alteration. The technological revolution, the rapid development of molecular biology, immunology, biochemistry, and genetics have created the fundamental prerequisites for a significant advancement of knowledge on key medical issues. The synthesis of a huge amount of new data has allowed us to reach a qualitatively different level of understanding of inflammation as a general pathological process that underlies the pathogenesis of many critical conditions, including sepsis, severe burn and mechanical trauma, pancreatitis and others.

The main content of modern concepts of inflammation can be summarised as follows:

- Classical signs of local inflammation: hyperaemia, local temperature rise, edema, pain, associated with morphological and functional restructuring of endothelial cells of post-capillary venules, blood coagulation in them, adhesion and transendothelial migration of leukocytes, complement activation, kininogenesis, arteriolar vasodilation, mastocyte degranulation.

- A special place among inflammatory mediators is occupied by the cytokine network, which controls the processes of immune and inflammatory response. The main producers of cytokines are T cells and activated macrophages, as well as, to varying degrees, other types of leukocytes, post-capillary venular endothelial cells, platelets and various types of stromal cells. Cytokines primarily act in the inflammatory focus and in the territory of the responding lymphoid organs, performing a number of protective functions as a result.

- Small amounts of mediators can activate macrophages, platelets, release adhesion molecules from the endothelium, and produce growth hormone. The developing acute-phase reaction is controlled by pro-inflammatory mediators, interleukins: IL-1, IL-6, IL-8, tumour necrosis factor (TNF), as well as their endogenous antagonists, such as IL-4, IL-10, IL-13, soluble TNF receptors, etc., which are called anti-inflammatory mediators. By maintaining the balance of relations between pro- and anti-inflammatory mediators, under normal conditions, the

prerequisites for wound healing, destruction of pathogenic microorganisms, and maintenance of homeostasis are created.

Systemic adaptive changes in acute inflammation include stress reactivity of the neuroendocrine system; fever; release of neutrophils into the circulation from the vascular and bone marrow depots; increased leukocytopoiesis in the bone marrow; hyperproduction of acute phase proteins in the liver; and development of generalised forms of immune response.

- In case of severe local inflammation or failure of the mechanisms limiting its course, some of the cytokines: TNF-a, IL-1, IL-6, IL-10, TGF-b, INF-g can enter the systemic circulation, providing long-term effects. If the regulatory systems fail to maintain homeostasis, the destructive effects of cytokines and other mediators begin to dominate, leading to impaired permeability and function of the capillary endothelium, the onset of DIC syndrome, the formation of distant foci of systemic inflammation, and the development of organ dysfunction.

- The accumulation of proinflammatory cytokines in the blood and the realisation of their distal effects (at a distance from the primary focus of damage) are considered from the point of view of the systemic inflammatory response syndrome (SIRS). Thus, the concentration of certain pro-inflammatory cytokines in the blood usually does not exceed 5-20 pg/ml, and in the case of SIRS, it can increase 5-10 times or more. It is obvious that the nature of the damage can, in some cases, become systemic, and this circumstance fundamentally changes the essence of the inflammatory process as a whole.

According to V. Chereshnev et al. the fundamental differences between systemic and ‘classical’ inflammation are expressed in the development of a response to systemic alteration, and pro-inflammatory mechanisms in this case lose their protective basis for localising damage factors, and become the main driving force of the pathological process.

Terminology and clinical and laboratory criteria for systemic inflammation

SIRS - systemic inflammatory response syndrome. And in the first publications of the 90s in Russia, the authors used different translation options. In November 2001 in Moscow at an interdisciplinary conference on sepsis, a consensus was reached between Russian experts on the use of the Russian-language version of SIRS - ‘systemic inflammatory response syndrome’, which more accurately reflects the essence of the changes occurring in this pathological process. It is noteworthy that the formalisation of the concept of inflammation in the form of SIRS was somewhat accidental and was initially associated with an attempt to more accurately define the group of patients with sepsis during clinical trials, when the concept of sepsis syndrome emerged. The next step was a defining one - the 1991 conciliation conference of the American College of Chest Physicians\ Society of Critical Care Medicine, whose task was to develop a definition of sepsis, based on fundamental developments in the field of inflammation, formulated the concept of SIRS, emphasising its nonspecificity.

The SIRS diagnosis is based on the recording of at least two of the four clinical and laboratory parameters:

1) temperature > 38 °C or < 36 °C C; 2) heart rate > 90 beats/minute; 3) respiratory rate >
20 respiratory movements/minute or $_{RaCO2}$ < 32 mmHg; 4) peripheral blood leukocytes > ^{12x109}/L or < ^{4x109}/L or the number of rod-shaped cells more than 10.

Proposals to implement SIRS criteria into clinical practice immediately found both supporters and opponents. The main arguments in favour of the validity of these criteria were that they can be used to identify with high sensitivity the population of patients at risk of organ dysfunction and adverse outcome, determine indications for ICU admission, and assess the response to treatment. In turn, the sceptics' objections were based on the low specificity of the SIRS criteria, which, in their opinion, may significantly reduce clinical benefit.

Hundreds of publications in reputable journals, in which the authors use its criteria, prove the necessity and usefulness of the SIRS designation. The low specificity of the SIRS criteria served as an impetus for the development of approaches to the differential diagnosis of infectious and non-infectious genesis of the syndrome. In this regard, procalcitonin has received the most positive certification to date.

Systemic inflammatory response and organ dysfunction

The establishment of anaesthesiology and resuscitation as an independent speciality and the organisation of intensive care units have improved survival rates in the acute period of critical conditions. The flip side of this seemingly favourable trend was the increase in the population of patients with multiple organ dysfunction (MOD), which is now the main cause of death in ICUs. It turned out that in the genesis of MOD, regardless of the aggressive factor, the systemic inflammatory response syndrome plays a leading role.

According to current knowledge, the pathogenesis of organ dysfunction includes 10 consecutive steps.

1. Activation of systemic inflammation. The SIRS syndrome is formed against the background of microbial invasion, shock of any nature, ischaemia/hyperfusion, massive tissue damage, and bacterial translocation from the intestine.
2. Activation of initiating factors Systemic activating factors include coagulation proteins, platelets, mast cells, contact activation systems (bradykinin production) and complement activation.
3. Changes in the microcirculation system. Vasodilation and increased vascular permeability. In local inflammation, the purpose of these changes is to promote the penetration of phagocytes to the site of injury. In the case of activation of the SIRS, there is a decrease in systemic vascular tone and damage to the vascular endothelium at a distance from the primary focus.
4. Production of chemokines and chemoattractants. The main effects of chemokines and chemoattractants are marginalisation of neutrophils, release of proinflammatory cytokines (TNF-a; IL-1; IL-6) from monocytes, lymphocytes and some other cell populations that may activate the anti-inflammatory response.
5. Marginalisation (‘sticking’) of neutrophils to the endothelium in local inflammation, the chemoattractant gradient directs neutrophils to the centre of the lesion, whereas in the development of SIRS, activated neutrophils diffusely

infiltrate perivascular spaces in various organs and tissues.

6. Systemic activation of monocytes/macrophages.
7. Damage to the microcirculatory bed. The launch of the SIRS is accompanied by the activation of free radical oxidation processes and endothelial damage with local platelet activation at the site of injury.
8. Tissue perfusion disorders. Due to endothelial damage, decreased perfusion and microthrombosis in some areas of the microcirculation, blood flow can completely stop.
9. Focal necrosis. Complete cessation of blood flow in certain parts of the microcirculatory bed causes local necrosis. Especially vulnerable are the organs of the splanchnic basin.
10. Re-activation of inflammatory factors. Tissue necrosis resulting from SIRS, in turn, is a stimulus for its re-activation. The process of SIRS becomes autocatalytic, which maintains itself even in the conditions of radical rehabilitation of the infectious focus or bleeding control, elimination of another primary damaging factor.

Approaches to the treatment of systemic inflammation

Deciphering the process of SIRS has led to the development of new areas of therapy, in particular, the creation of highly specific drugs that limit the destructive effects of mediators. We are talking about monoclonal antibodies to key proinflammatory cytokines, their recombinant receptor antagonists and soluble receptors. To date, clinical trials have been conducted on the efficacy of the following: monoclonal antibodies to TNF-a and platelet-activating factor, IL-1 receptor antagonist and soluble TNF receptors p55\p75. The results were disappointing - no significant clinical effect was found. Moreover, a higher mortality rate was demonstrated in patients with septic shock when using one of the TNF antagonists. Apparently, the role of this cytokine in the fight against SIRS of an infectious nature remains poorly understood, as evidenced by the occurrence of infectious complications in patients with rheumatoid arthritis receiving anti-TNF.

Subsequently, encouraging results for patients with infectious SIRS have been obtained with the use of medications that have multiple targets to control the progression of systemic inflammation. In recent years, convincing evidence of efficacy has emerged in relation to stress doses of hydrocortisone in septic shock and activated protein C (APC) in severe sepsis.

One of the features of immunocompetent cells is the presence of receptors with high affinity for glucocorticosteroids (GCS). It has been established that the anti-inflammatory effect of GCS is manifested in supraphysiological doses.

The following mechanisms can be distinguished that exert anti-inflammatory effects

GCS:

- Inhibition of IL-12 production by macrophages and monocytes, the main

factor responsible for the differentiation and balance of lymphocytes in the Th1\Th2 direction;

- Inhibition of the production and activity of pro-inflammatory cytokines (IL-1, IL-2, IL-3, IL-6, IFN-g, TNF-a), chemokines, eicosanoids, bradykinin, adhesion molecules;

- Limiting the activity of nuclear factor (NF-kB);

- Stimulation of the synthesis of anti-inflammatory cytokines and factors (IL-1ra, soluble TNF receptor, IL-10, TGF-b);

- Inhibition of the formation of cyclooxygenase-2, inducible NO synthase (iNO);

- Activation of lipocortin synthesis, which limits the production of leukotrienes and phospholipase A2.

Thus, the demonstrated efficacy of hydrocortisone may be associated with limiting systemic inflammation by enhancing the natural compensatory mechanisms of the macroorganism in response to the resulting endogenous 'mediator explosion'. It should be emphasised that positive clinical effects have been proven only for hydrocortisone in doses of 200-300 milligrams/day, and only for patients with relative adrenal insufficiency.

The evidence base is gradually growing for intravenous immunoglobulins containing a combination of IGG and IGM (Pentaglobulin), one of the points of application of which is the neutralisation of pro-inflammatory cytokines. The effects of the infusion medium, antibiotics, parenteral nutrition products and even ALV have also been considered from the point of view of their impact on the process of systemic inflammation.

In the last few years, the concept of another pathological syndrome, Transfusion-related acute lung injury (TRALI), associated with the transfusion of blood components, has been formulated. The resulting pulmonary damage is caused by the action of substances released from leukocytes during the preparation and storage of IL-6, IL-8, TNF and lysophosphatidylcholine. Stimulation of the inflammatory response leads to an increase in the permeability of the alveolar-capillary membrane and the accumulation of fluid in the interstitium. In contrast to blood components, artificial colloids did not have a similar effect. Moreover, some of them had the opposite effect. The greatest anti-inflammatory effect was characteristic of hydroxyethyl starches with a molecular weight of 130,000 daltons and a substitution number of 0.4 and 3-7.5% NaCl solution.

The possibility of stimulation of cytokine generation by pulmonary macrophages with their subsequent penetration into the systemic bloodstream during high-volume mechanical ventilation (V=12 ml\kg) and the absence of this phenomenon during respiratory support with a volume limitation - V=6 ml\kg - was established. Very interesting data were obtained regarding statins. They have been shown to reduce leukocyte adhesion to the endothelium, reduce the content of IL-1, TNF, IL-6 and the expression of Toll-like receptors (TLR). Impressive results were obtained when analysing the outcomes in patients with sepsis and bacteremia who were taking and not taking statins. Mortality on statin therapy was 1.8% versus 23.1% in the control group (p=0.002). Higher survival rates with statins were recorded in patients who had undergone heart or lung transplantation.

New prospects are opening up in connection with the development of a group of drugs that block the mechanisms of intracellular signal transduction aimed at activating the synthesis of pro-inflammatory mediators. The first results of experimental studies on TAK-242, which inhibits TLR-4-mediated cytokine production; ethacrynic acid and ethylpyruvate, which block activation of the nuclear factor NF-kB, look encouraging.

Currently, according to the criteria of evidence-based medicine, those areas of sepsis therapy that have been successfully tested in large clinical trials can be recommended for clinical practice. These areas are listed below:

- Early diagnosis of sepsis
- Early and effective treatment of the infection site
- Correction of haemodynamics
- Additional therapy
- Ventilation with a low-pressure limit
- Control of glycaemic profile
- Adequate nutrition

A. Early diagnosis and initiation of sepsis therapy.

1. Treatment of severe sepsis and septic shock should be initiated as soon as this syndrome is diagnosed and cannot be delayed pending transfer to the ICU.

2. Targeted therapy of severe sepsis and septic shock begins with haemodynamic support until the following parameters are achieved

- Central venous pressure (CVP) 8-12 mmHg (108.8 -163.2 mmHg) (in ventilated patients, CVP up to 15 mmHg (204 mmHg) is acceptable)
- Mean arterial pressure ≥ 65 mmHg.
- Diuresis ≥ 0.5 ml/kg/hour
- Haemoglobin saturation with oxygen (saturation, SatO2) in the superior vena cava or mixed venous blood > 70%

3. Bacteriological cultures should be performed prior to the initiation of antibiotic therapy. All patients with sepsis should have a blood culture performed at least twice (one from a peripheral vein, one from a central venous catheter (no more than 48 hours old)). Cultures of other biological substrates such as urine, cerebrospinal fluid, sputum should be obtained before starting antibiotic therapy, but taking into account the clinical situation.

4. Diagnostic measures should be performed quickly to determine the source of infection and the causative microorganism. Clear and accurate diagnostic methods should be used; patients in serious condition should have the necessary tests performed on site in the ward.

5. The differential diagnosis between infectious and non-infectious etiology of the pathological process accompanied by the development of SIRS is made by a test to determine the level of procalcitonin (PCT). Procalcitonin is characterised by a short latency period (3 hours after infection), a long half-life (25-30 hours) and is a stable protein in vitro even at room temperature.

B. Early and effective treatment of the infection site.

1. Every patient with severe sepsis should be evaluated for the presence of an infection site, with an assessment of the possible association of sepsis with a potentially infected device (vascular catheter, urethral catheter, endotracheal tube, intrauterine device).

2. When choosing methods of debridement, it is necessary to weigh the pros and cons of the proposed intervention, assess the risk of complications, such as bleeding, fistula formation, etc. In general, the methods that are least traumatic for the patient should be used.

3. Simultaneously with the search for the source, a complex of initial therapy aimed at stabilising haemodynamics should be carried out. After identifying the source of severe sepsis or septic shock, the necessary measures to sanitise the focus should be taken as quickly as possible.

4. If an intravascular catheter is a potential source of sepsis, it should be removed immediately after other vascular access has been secured. The intravascular portion of the catheter to be removed is sent to the bacteriological laboratory. At the same time, blood is taken for culture; if the same pathogens are isolated from the blood and the catheter, angiogenic sepsis is diagnosed.

5. After sanitation of the primary focus, the doctor should constantly remember and conduct a diagnostic search for secondary foci, primarily pneumonia, angiogenic infection, urinary infection.

C. Antibiotic therapy

1. All patients with severe sepsis and septic shock should receive systemic antibiotic therapy.

2. Incorrect choice of antibiotics worsens the results of sepsis treatment by 2 times, but the effectiveness of therapy depends on the adequacy of surgical sanitation of the primary focus by 80%.

3. As a rule, at the initial stage of treatment of a patient with sepsis, in the absence of bacteriological diagnosis, empirical antibiotic therapy is prescribed, which depends on

- the spectrum of suspected pathogens depending on the location of the primary focus;
- pharmacokinetic characteristics of antibacterial drugs that ensure penetration and activity in the infection site;
- previous antibiotic therapy;
- level of resistance of nosocomial pathogens according to microbiological monitoring of the hospital;
- conditions of sepsis occurrence - community-acquired or nosocomial;
- severity of infection, assessed by the APACHE II scale, in the presence of multiorgan failure - SOFA scale.

5. Recommendations for empirical antibiotic therapy

Nature of infection	1st line products	Alternative products

Out-of-hospital Sepsis, severe sepsis	Amoxicillin/clavulanate +/- aminoglycoside Cefotaxime + metronidazole Ceftriaxone + metronidazole	Ampicillin/sulbactam +/- aminoglycoside Ticarcillin/clavulanate Pefloxacin + Metronidazole Moxifloxacin
Out-of-hospital septic shock	Cefoperazone/sulbactam Cefepime + metronidazole	Imipenem Meropenem Moxifloxacin
Nosocomial Sepsis, severe sepsis	Cefepime +/- metronidazole Cefoperazone/sulbactam	Imipenem Meropenem Ciprofloxacin + metronidazole Ceftazidime + metronidazole
Nosocomial septic shock	Imipenem Meropenem	Cefepime +/- metronidazole Cefoperazone/sulbactam +/- amikacin Ciprofloxacin + metronidazole +/- amikacin

a. Antibiotic therapy (ABT) should be started within the first hour if severe sepsis is diagnosed. Antibiotics are administered intravenously.

b. All patients should receive an adequate dose of antibiotic, taking into account possible organ dysfunction. The presence of renal or hepatic impairment usually requires a change in dose and dosing regimen. This must be taken into account to achieve maximum benefit with minimal toxicity.

i. Renal function can be assessed by creatinine clearance

$$\text{Creatinine clearance in men (mL/min)} = \frac{(140 - \text{age(years)}) \times \text{ideal (estimated) body weight (kg)}}{0.8 \times \text{serum creatinine } (\mu\text{mol/l})}$$

Creatinine clearance in women = 0.85 x creatinine clearance in men

a) Estimated body weight of a man (kg) = 50 + 0.91 * (Height (cm) - 152.4)
b) Estimated body weight of a woman (kg) = 45.5 + 0.91 * (Height (cm) - 152.4)

c. Antibiotic therapy should always be reassessed after 48-72 hours, based on the microbiological and clinical data obtained, with the aim of prescribing a narrow-spectrum antibiotic (to prevent the development of resistance, increase the effectiveness of ABT, and reduce costs). A positive result in naturally sterile material (blood, cerebrospinal fluid, cavity contents, puncture specimen) is a guide to action in one hundred per cent of cases. When examining a non-sterile specimen, bacteriological monitoring is performed, and after obtaining the results, the clinically significant one

is selected and therapy is adjusted. Bacteriological material from drains is not taken due to lack of information.

d. In case of nosocomial (hospital-acquired) infection, in case of isolation of specific microorganisms, the antibiotic regimen should be reviewed:

- Staphylococcus aureus resistant to methicillin (oxacillin), vancomycin or linezolid, or rifampicin + ciprofloxacin;
- Enterococcus faecalis resistant to ampicillin or Enterococcus faecium - vancomycin or linezolid;
- Fungi of the genus Candida - fluconazole or amphotericin B;
- In case of infection caused by P. aeruginosa - antipseudomonas cephalosporins (ceftazidime, cefepime) or meropenem. In case of low level of resistance, other drugs with antisinusoidal activity (imipenem, amikacin, ciprofloxacin, ticarcillin/clavulanate) may be prescribed in the hospital
- E. coli ESBL+ and Kl. Pneumoniae ESBL+ requires carbapenems as an alternative to cefepime, cefoperazone/sulbactam
- Acinetobacter - cefoperazone/sulbactam, carbapenems

e. Antibiotic therapy of sepsis is carried out until the patient's condition is stable and the main symptoms of the infection disappear. Due to the absence of pathognomonic signs of bacterial infection, it is difficult to establish absolute criteria for stopping antibiotic therapy. Usually, the question of discontinuing antibiotic therapy is decided individually based on a comprehensive assessment of the patient's condition. In general, the criteria for the adequacy of antibiotic therapy can be presented as follows:

- stable normalisation of body temperature;
- positive dynamics of the main symptoms of infection;
- no signs of a systemic inflammatory reaction;
- normalisation of the gastrointestinal tract function;
- normalisation of the number of leukocytes in the blood and the leukocyte formula;
- negative haemoculture.

Preservation of only one sign of bacterial infection (fever or leukaemia) is not an absolute indication for continuing antibiotic therapy. An isolated subfebrile temperature (maximum daytime temperature of 37.9°C) without chills and changes in the peripheral blood may be a manifestation of postinfectious asthenia or non-bacterial inflammation after surgery and does not require continuation of antibiotic therapy. So does the persistence of moderate leukocytosis (9-12x109/L) in the absence of a left shift and other signs of bacterial infection.

f. If the diagnostic search proves that the current clinical syndrome is due to non-infectious causes, then ABT should be discontinued to prevent the development of resistance and superinfection by other microorganisms.

6. Infusion therapy

a. During the first 6 hours of treatment of severe sepsis and septic shock, the following indicators should be achieved:

i. Central venous pressure (CVP) of 8-12 mmHg (108.8 - 163.2 mmHg) (in ventilated patients, CVP up to 15 mmHg (204 mmHg) is acceptable)

ii. Mean arterial pressure ≥ 65 mmHg.

iii. Diuresis ≥ 0.5 ml/kg/hour

iv. Haemoglobin saturation with oxygen (saturation, SatO2) in the superior vena cava or mixed venous blood > 70%

Infusion therapy may consist of natural or artificial colloids or crystalloids. There is no evidence for one type of infusion medium over the other. However, due to the much larger volume of redistribution of crystalloids compared to colloids, a much larger number of crystalloids is required to achieve the final result, which can lead to tissue edema. Therefore, the approximate recommendations for the qualitative composition of the infusion programme in patients with severe sepsis are colloids/crystalloids - 1:3, with septic shock - 1:2 and may vary depending on the clinical situation. The colloidal preparations of choice are solutions of modified gelatin ('Gelofusin') and hydroxyethyl starch preparations ('Hemohes').

b. The rate of infusion therapy in patients with suspected hypovolaemia is 500-1000 ml of crystalloids or 300-500 ml of colloids per 30 minutes and may be repeated after assessment of response (increase in blood pressure, diuresis rate) and tolerability (no evidence of intravascular fluid overload). Infusion therapy should be carried out with careful assessment of volemia, and given venodilation and capillary leakage syndrome, aggressive infusion therapy may be required for a long time (up to 24 hours). The fluid balance at this time is always positive, the calculation of the need for infusion therapy is relative, taking into account clinical manifestations and monitoring results

c. In the absence of coronary artery disease, acute blood loss, correction of anaemia is recommended only if the haemoglobin level is less than 70 g/l (recommended haemoglobin levels are 70-90 g/l).

d. The use of fresh frozen plasma to correct laboratory abnormalities in the haemostatic system in the absence of bleeding or planned procedures with a risk of bleeding is not recommended. It is not recommended to transfuse fresh frozen plasma to replenish the volume of circulating fluid (safer and more cost-effective means are available) or for parenteral nutrition. In accordance with Order of the Ministry of Health of the Russian Federation No. 363 of 25 November 2002, the indications for transfusion of FFP are:

- acute disseminated intravascular coagulation syndrome (DIC), which complicates the course of shocks of various genesis (septic, haemorrhagic, haemolytic) or caused by other causes (amniotic fluid embolism, crash syndrome, severe trauma with tissue destruction, extensive surgery, especially on the lungs, blood vessels, brain, prostate), massive transfusion syndrome.

- Acute massive blood loss (more than 30% of the circulating blood volume) with the development of haemorrhagic shock and DIC syndrome;

- liver diseases accompanied by a decrease in the production of plasma factors coagulation factors and, accordingly, their deficiency in the circulation (acute fulminant hepatitis, liver cirrhosis);

- overdose of indirect anticoagulants (dicoumarin and others);
- during therapeutic plasmapheresis in patients with thrombotic thrombocytopenic purpura (Moscovitz disease), severe poisoning, sepsis, acute DIC syndrome;
- coagulopathies caused by a deficiency of plasma physiological anticoagulants.

In patients with severe sepsis, platelet mass should be transfused when the platelet count is less than 5*109/L, regardless of the presence of a bleeding clinic. If the platelet count is 5-30*109/litre, the platelet mass is transfused if there is a risk of bleeding. For surgical interventions or invasive procedures, a platelet counts of 50*109/L or more is required.

7. Vasopressors

a. Fluid therapy is a fundamental aspect of haemodynamic support in patients with septic shock, and ideally, correction of volemia should always precede the administration of vasopressors. Vasopressor therapy should be initiated if hypotension and hypoperfusion persist despite adequate infusion therapy. Vasopressor therapy may be required for a short time, even in the presence of signs of hypovolaemia in the setting of ongoing infusion therapy. At a mean arterial pressure below 70 mmHg, the mechanism of vascular tone autoregulation is disrupted and perfusion begins to depend linearly on mean arterial pressure, so it is important to achieve adequate perfusion by administering vasopressors and achieving a MAP ≥ 70 mmHg (MAP = (Adsist + 2*Addiast)/3)

b. All sympathomimetics should be administered via a central venous catheter. There is no evidence for the superiority of one vasopressor drug over another, and norepinephrine, epinephrine and dopamine can all be used to correct hypotension in sepsis. Dopamine is used in the absence of contraindications (primarily cardiac arrhythmias) at a dose of up to 10 μg/kg/min; if hypotension persists or cardiac arrhythmias occur during dopamine titration, epinephrine is the drug of choice.

c. Low doses of dopamine for renal protection (renal doses) should not be used in the treatment programme for severe sepsis.

The use of vasopressin may be considered in patients with refractory shock who remain hypotensive despite adequate fluid therapy and high doses of conventional vasopressors.

8. Inotropic therapy

a. In patients with low cardiac output that persists despite adequate infusion therapy, Dobutamine may be used to increase cardiac output. If hypotension persists on the background of the ongoing therapy, Dobutamine should be combined with vasopressors.

9. Corticosteroids

a. Intravenous corticosteroids (hydrocortisone (SOLU-CORTEF) 200-300 milligrams/day divided into 3-4 doses or as a continuous infusion for 7 days) are

recommended in patients with septic shock who, despite adequate fluid therapy, still require vasopressors to maintain adequate blood pressure.

b. Corticosteroid doses greater than 300 milligrams/day should not be used in the treatment programme for patients with severe sepsis and septic shock.

c. In the absence of a septic shock clinic, corticosteroids should not be used to treat patients with sepsis. There are no contraindications for basic therapy of the underlying or background disease (including pulse therapy)

10.Recombinant human activated protein C.

a. One of the characteristic manifestations of sepsis is systemic coagulation disorders (activation of the coagulation cascade and inhibition of fibrinolysis), which ultimately lead to hypoperfusion and organ dysfunction. Recent studies have shown the effectiveness of replacement therapy with recombinant human activated protein C in patients with severe sepsis.

b. Activated protein C is recommended for use in high-risk patients (APACHE II ≥ 25, sepsis-induced multiple organ failure, septic shock or sepsis-induced RDSV). Absolute contraindications related to the risk of bleeding or if the risk of relative contraindications is higher than the expected benefit of activated protein C administration.

11.Artificial lung ventilation

a. Mechanical ventilation is indicated for all patients with septic shock. In addition to normalising oxygen transport and reducing respiratory work, it has been shown that mechanical ventilation can reduce the rate of development of the septic cascade, which increases dramatically in hypoxia.

The type of respiratory support in patients with severe sepsis depends on the degree of hypoxia and organ dysfunction. The presence of adequate consciousness, absence of high respiratory effort, severe tachycardia (heart rate up to 120 per minute), normalisation of venous blood return and SaO2>90% against the background of oxygen support for spontaneous respiration may well allow refraining from transferring to mechanical ventilation, but assessment of organ dysfunction in the dynamics is mandatory. All doubts about the adequacy of respiratory support should be resolved in favour of mechanical ventilation.

b. High tidal volumes should be avoided in sepsis-induced acute lung injury (ALI)/acute respiratory distress syndrome (ARDS), which can cause high plateau pressures. The respiratory volume is calculated at the rate of 6-8 ml/kg of ideal (estimated) body weight, with a guaranteed volume of minute ventilation to maintain SaO2/SpO2=88-95%. The end-expiratory plateau pressure should be maintained at less than 30 cmHg by manipulating not only the tidal volume but also the respiratory cycle duration (Ti)

c. Moderate hypercapnia is acceptable in patients with Hg/HDP if the ventilation parameters are set to minimise plateau pressures and tidal volumes.

d. Positive end-expiratory pressure should prevent lung tissue collapse. One approach to determining the appropriate level of PEEP (positive end-expiratory pressure) is to set the appropriate level of PEEP based on the FiO2 level required to maintain adequate oxygenation. Some experts select the PEEP based on compliance (obtaining the highest level of compliance that reflects the process of recruitment (recruitment is the process of restoring lung tissue lightness by involving collapsed alveoli in gas exchange).

FiO2	0.3	0.4	0.4	0,5	0,5	0,6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	20-24

a. Patients on mechanical ventilation should have the head end of the bed elevated by 30-45 degrees for prophylaxis, and a combination of pharmacological and mechanical prophylaxis is recommended.

b. The recommended sedation regimens are intermittent bolus sedation or continued prolonged administration with daily interruption/reduction of the infusion rate with awakening and, if necessary, re-titration. Administration of the drug in the form of a prolonged infusion has a less significant effect on haemodynamics

c. Muscle relaxants to synchronise the patient with the respirator are used only as a last resort. If muscle relaxants are required, on-demand bolus administration is recommended.

d.Weaning from the respirator should be timely, and respiratory rehabilitation in ventilated patients should begin when the following criteria are met:

I. The patient is conscious;

II. Hemodynamics is stable (without vasopressors);

III.No other potentially dangerous conditions have developed;

IV. Low levels of plateau pressure and the required positive end-expiratory pressure;

V. FiO2 levels that can be provided by a face mask or nasal cannulas.

If the spontaneous breathing attempt is successful, extubation should be considered.

12.Glycaemic control.

a. After initial stabilisation of patients with severe sepsis, it is necessary to maintain a glycaemic level not exceeding 8.3 mmol/l. Hyperglycaemia is corrected by infusing insulin intravenously through a dosing unit. Glycaemia control is performed every 2 hours, after glycaemia stabilisation - control in 4 hours.

b. In patients with severe sepsis, the glycaemic control strategy should include a nutritional protocol with preference for enteral access.

13.Nutritional support

a. The development of multiple organ failure syndrome in sepsis is usually accompanied by hypermetabolism. In this situation, energy needs are met by the destruction of the patient's own cellular structures, which exacerbates existing organ dysfunction and increases endotoxemia. Therefore, nutritional support is an extremely important component of treatment.

b. Nutritional support may be provided by enteral, parenteral or combined means, depending on the clinical situation.

c. The inclusion of early enteral nutrition in the intensive care complex prevents the translocation of microflora from the intestine, the development of dysbiosis, increases the functional activity of the enterocyte and the protective properties of the mucous membrane, reducing the degree of endotoxemia and the risk of secondary infectious complications.

d. The calculation of the amount of nutritional support shall be based on the ideal (estimated) body weight:

i. Protein 1.5-2.5 g/kg/day
ii. Fat 0.5-1.5 g/kg/day
iii. Glucose 2-6 g/kg/day
iv. Energy 30-35 kcal/kg/day (B:F:E=20%:30%:50%)
v. Calculation of energy required for utilisation of 1 gram of parenterally administered amino nitrogen - 150 kcal per 1 gram of amino nitrogen.

e. To monitor the nutritional status, it is necessary to evaluate the level of total protein, blood urea and daily urinary urea excretion (in patients without signs of renal insufficiency) in the dynamics, which will allow to calculate the actual protein requirement and assess the level of metabolism:

f. Nutritional support for septic shock:

1. It is carried out after achievement of the goals of initial targeted therapy (correction of hypovolaemia, correction of hypoxaemia, absence of signs of hypoperfusion and microcirculatory disorders (if signs of hypoperfusion persist, the priority direction of therapy is haemodynamic support);

2. Enteral nutrition only to prevent atrophy of the gastrointestinal mucosa, translocation and development of SLE (20 ml/hour).

3. The main volume of nutrient supplementation is parenteral.

14.Prevention of deep vein thrombosis

a. Patients with severe sepsis should be prophylactically treated for deep vein thrombosis with low molecular weight heparin or low doses of unfractionated heparin. In patients who have contraindications to the use of heparin (such as thrombocytopenia, severe coagulopathy, ongoing bleeding, or fresh intracranial haemorrhage), mechanical prophylaxis (special graduated compression stockings, intermittent compression devices) is indicated, with the presence of peripheral vascular disease being a contraindication. In high-risk patients (for example, a history of severe sepsis and deep vein thrombosis)

15. Prevention of stress ulcers

Stress ulcer prophylaxis should be performed in all patients with severe sepsis. H2-blockers are more effective than sucralfate (Venter) and similar drugs. Proton pump inhibitors have not been compared with H2 blockers, so their relative effectiveness is unknown. They show similar results in their ability to raise gastric pH.

5. Plan and organisational structure of the lesson

№	Main stages of the lesson, their function and content	Learning objectives in terms of learning levels	Methods of control and training	Methodological support materials	Time min
1	2	3	4	5	6
	Preparatory stage				
1.	**Organisation of the lesson**				5 min
2.	**Setting learning objectives and motivating the topic**				10 min
3.	**Control of the initial level of knowledge, skills and abilities.**				
	1.Etiopathogenesis of systemic inflammatory response syndrome	II	Level II methods		
	2. Physiology and biochemistry of local and systemic inflammatory reactions.	II	1. Individual oral interview. 2. Written theoretical questionnaire.	Level II tasks Tables, Slides.	
	3.Clinical picture of systemic inflammatory response syndrome in surgical patients	II	3. Solving typical problems.	Video recordings	
	4.Algorithm of examination of patients	II			60
	5. Differential diagnosis of the cause of systemic inflammatory response syndrome.	II		Equipment, X-rays, Medical history	
	6. Interpretation of examination data - blood tests - general, biochemical, coagulogram, endoscopic, radiological	III	1. Solving atypical situational problems		
	7.Principles of conservative therapy of systemic inflammatory response syndrome	III	2. Prescribing treatment for a patient		
	8. Surgical treatment of patients with systemic inflammatory response syndrome in patients with surgical pathology.	II			
1	2	3	4	5	6

Main stage					
4.	**Developing professional skills and abilities**				
	1.Master the methods of objective examination of patients with systemic inflammatory response syndrome in patients with surgical pathology.	III	Method of forming practical training skills	Teaching equipmen t - indicative maps	130 min.
	2. Supervise a patient with systemic inflammatory response syndrome 3. Participate in the clinical eview of an intensive care unit atient with systemic nflammatory response yndrome	III	A method of developing skills: a) Professional training in solving atypical problems	Atypical tasks in the form of: patient, medical history, test case studies, business games, bandaging	
	4.Perform dressing on the patient in the postoperative period	III			
Final stage					
5.	**Control and correction of the level of professional skills**	III	Method of control: Individual control of practical skills	Equipment	60
6.	**Summing up the results of the lesson**				3 min.
7.	**Homework, educational literature on the topic**			Indicative map of independ ent work with literature	2 min.

6. Materials for methodological support of the lesson

Control materials for the preparatory stage of the lesson.

Questions.

1. Classical signs of local inflammation
2. Pathophysiology of the inflammatory response in the human body, the role of cellular humoral and vascular links in the development of the inflammatory process.
3. Signs of generalisation of the inflammatory process and signs of systemic inflammatory response syndrome.
4. Causes of systemic inflammatory response syndrome in patients with surgical pathology.
5. Diagnosis and differential diagnosis of the causes of systemic inflammatory response syndrome.

6. Sepsis, differences from systemic inflammatory response syndrome, causes of occurrence, clinical symptoms.
7. The main causes of sepsis, clinic and diagnosis of endotoxic shock.
8. Multiple organ dysfunction and multiple organ failure as manifestations of systemic inflammatory response syndrome.
9. Prediction of the development of multiple organ failure in patients with systemic inflammatory response syndrome and planning of complex syndromic therapy of this condition.

Sepsis classification

Pathological process	**Clinical and laboratory signs**
Systemic inflammatory response syndrome (SIRS) is a systemic reaction of the body to the effects of various strong stimuli (infection, trauma, surgery, etc.).	It is characterised by two or more of the following: - temperature >38°C or <36°C - Heart rate >90/min - Respiratory rate >20/min or hyperventilation (RaCo2 (32 mmHg)) - White blood cells >12(^{109}/ml or <4(^{109}/ml, or immature forms >10%)
Sepsis is a syndrome of systemic inflammatory response to microbial invasion	The presence of a focus of infection and 2 or more signs of systemic inflammatory response syndrome
Severe sepsis	Sepsis combined with organ dysfunction, hypotension, and tissue perfusion disorders. The latter is manifested, in particular, by an increase in lactate concentration, oliguria, and acute impairment of consciousness
Septic shock	Sepsis with signs of tissue and organ hypoperfusion and arterial hypotension, which is not eliminated by infusion therapy and requires the administration of catecholamines
Additional definitions	
Multiple organ dysfunction syndrome	Dysfunction in 2 or more organ systems
Refractory septic shock	Arterial hypotension that persists despite adequate infusion, inotropic and vasopressor support

Diagnostic criteria for sepsis

Infection suspected or confirmed in combination with several of the following criteria:

Common criteria
Hyperthermia, temperature >38.3°C

Hypothermia, temperature <36°C Heart rate >90/min (>2 standard deviations from the normal age range) Tachypnoea Disturbance of consciousness Need for infusion support (>20 ml/kg per 24 hours) Hyperglycaemia (>7.7 mmol/l) in the absence of diabetes mellitus
Criteria for inflammation
Leukocytosis > $^{12/109}$/l **Leukopenia** < $^{4/109}$/l Shift towards immature forms (>10%) with normal leukocyte count C-reactive protein content >2 standard deviations from the norm Procalcitonin content >2 standard deviations from the norm
Haemodynamic criteria
Arterial hypotension: SBP <90 mmHg, SBP <70 mmHg, or SBP decrease of more than 40 mmHg (in adults) or SBP decrease of at least 2 standard deviations below the age-related norm. Saturation SVO2 >70% Cardiac index > 3.5 $^{l/min/m2}$
Criteria for organ dysfunction
Arterial hypoxaemia PaO2/FiO2 <300 Acute oliguria <0.5 ml/kg (hourly Increase in creatinine by more than 44 μmol/l (0.5 mg%). Coagulation disorders: APTTb >60 sec or Mnos >1.5 Thrombocytopenia < ^{100x109}/l Hyperbilirubinaemia > 70 mmol/l Intestinal paresis (absence of intestinal noise)
Indicators of tissue hypoperfusion
Hyperlactatemia >1 mmol/l Symptom of slow capillary refill, marbling of the extremities

Surgical treatment of sepsis

Effective intensive care of sepsis is possible only with complete surgical rehabilitation of the infection site and adequate antimicrobial therapy. Surgical treatment should be aimed at adequate sanitation of purulent and inflammatory foci. Methods of surgical intervention include:

1. drainage of purulent cavities
2. removal of foci of infected necrosis
3. removal of internal sources of contamination - colonised implants (artificial heart valves, vascular or joint prostheses), foreign bodies temporarily inserted into tissues or internal environment of the body for therapeutic purposes (tubular drains and catheters), as well as removal or proximal disconnection (diversion) of the flow of contents of hollow organ defects considered as sources of infection.

Definition of the term ‘shock’

Shock is a pathological process that develops in response to the impact of extreme stimuli, which is accompanied by a progressive disruption of vital functions of the nervous system, blood circulation, respiration, metabolism and other functions. In fact, it is a disruption of the body's compensatory reactions in response to injury.

Shock is an acute generalised haemodynamic disorder with a tendency to worsen, leading to an increasing oxygen deficit in cells and, at first, reversible and later irreversible cellular damage.

Causes of shock

According to the pathogenesis, shock is divided into:

- hypovolaemic
- cardiogenic
- traumatic
- septic
- anaphylactic;
- neurogenic;
- combined (combining elements of different shocks).

In the practice of a surgeon, hypovolemic and septic shock are the most commonly encountered conditions;

Hypovolaemic shock

This type of shock occurs due to a rapid decrease in the volume of circulating blood, which causes a drop in the filling pressure of the circulatory system and a decrease in the venous return of blood to the heart. As a result, the blood supply to organs and tissues is impaired and ischaemia develops.

Causes

The volume of circulating blood can decrease rapidly for the following reasons:

a) Blood loss. External or internal blood loss (e.g. after injuries, surgeries, gastrointestinal bleeding, blood clotting disorders);

b) plasma loss (e.g., burns, peritonitis, tissue damage, intestinal obstruction)

c) fluid loss by the body without appropriate replenishment (e.g. in case of diarrhoea, vomiting, intestinal fistulas, excessive sweating, diabetes mellitus and diabetes insipidus) leads to a disorder of water and electrolyte metabolism such as hypovolaemic hypernatremia.

Fluid and electrolyte imbalance:

- In *acute pancreatitis*: acute hypovolaemia and hypovolaemic shock. Dehydration.
- In case of *intestinal obstruction*: acute hypovolaemia and dehydration are formed due to fluid loss and their deposition in the intestinal lumen. The total volume of fluid lost can be very large. Losses are isotonic in nature, quickly leading to disturbances in central and peripheral haemodynamics, initially in the form of hypovolaemic shock.
- In peritonitis: severe isotonic dehydration and hypovolaemic shock require urgent anti-shock measures. Total fluid loss in the absence of replacement therapy reaches 4-6 litres or more.

Septic shock is a decrease in pressure caused by sepsis (hypotension: blood pressure less than 90 mmHg) with adequately replenished blood volume and the impossibility of raising blood pressure above 90 mmHg by using sympathomimetics. Comparative

characteristics of haemodynamic disorders in different types of shock (Appendix 1)
Diagnosis

Shock syndrome is diagnosed in the presence of acute cardiac and circulatory dysfunction in a patient, which is manifested by the following signs

- cold, wet, pale cyanotic or marbled skin;
- sharply slowed blood circulation in the nail bed;
- anxiety, blackout;
- dyspnoea
- oliguria
- tachycardia;
- reduction in blood pressure amplitude and its decrease.

The clinical classification divides shock into four stages according to its severity.

Shock of the first stage.

Consciousness is preserved, the patient is contactable, slightly inhibited. Systolic blood pressure (BP) exceeds 90 mm Hg, pulse is rapid.

Shock of the second stage.

Consciousness is preserved, the patient is inhibited. Systolic blood pressure is 90-70 mm Hg, pulse is 100-120 beats per minute, weak filling, shallow breathing.

Shock of the third degree.

The patient is adynamic, lethargic, unresponsive to pain, and answers questions unambiguously. The skin is pale, cold, with a cyanotic tint. Breathing is shallow, frequent. Systolic blood pressure is below 70 mm Hg, pulse is more than 120 beats per minute, thready, central venous pressure (CVP) is zero or negative. Anuria (absence of urine) is observed.

Shock of the fourth stage is manifested clinically as one of the terminal conditions.

There are three levels of isotonic dehydration (V. Hartig):

Level I (deficit of about two litres): fatigue, tachycardia, weakness, apathy, anorexia, tendency to orthostatic collapse, normal blood pressure in the supine position;
Level II (deficit of about four litres): apathy, anorexia, vomiting, falling blood pressure even in the supine position;
Level III (deficit of 5-6 litres): confusion, shock, systolic blood pressure in the supine position below 90 mmHg.

Assessment of blood loss severity

In 1982, the American College of Surgeons established 4 classes of bleeding, depending on the amount of blood loss and clinical symptoms

class	Clinical symptoms	Volume of	In ml.
		blood loss	

l	Tachycardia at rest and during the transition from horizontal to vertical position (orthostatic), increased blood pressure, signs of peripheral vasoconstriction	15%	750-1250
ll	Orthostatic hypotension (more than 15 mm Hg), pallor	20-25%	1250-1750
lll	Arterial hypotension in the supine position, anxiety, pallor, cold sweat, oliguria	30-40%	More than 1750
lV	Impaired consciousness, collapse, organ failure	More than 40%	More than 2000

Clinical manifestations of hypovolemia

Clinical manifestations	Volume of blood loss (% of body weight)		
	5%	10%	15%
Mucous membranes	dry	very dry	exceedingly dry
consciousness	norm	norm	confusingly
Orthostatic changes in blood pressure and heart rate	minor	moderate	expressed
Blood pressure at rest	normal	lowered	low
Resting heart rate	normal or slightly higher	increased	severe tachycardia
diuresis	slightly reduced	reduced	significantly reduced

Gravimetric method.

Intraoperative blood loss is determined by the difference in the weight of blood-soaked and dry napkins, tampons, balls, diapers, and gowns. The resulting value is increased by 50% and summed with the volume of blood in the bank of the electric suction device. The error of the method is 10-15%.

For an approximate assessment of the severity of blood loss, the Algover-Bruber index, the so-called shock index, can be calculated (the ratio of heart rate to systolic blood pressure)

- 0,54 - 0
- 0.78 - 10-20% -0,5-1,0l
- 0,99 -21-30% - 1,0 - 1,5l.
- 1,11 - 31-40% - 1,5- 2,0l.
- 1.38 - 41-50% - more than 2.0 litres
- more than 1.5 - more than 50%

Pulse rate

Heart rate 90-100 beats/min - 10-20%.
Heart rate up to 120 beats/min - 21-30%.
Heart rate up to 140 beats/min 31-40%
Heart rate more than 140 beats/min -41% and more

Systolic blood pressure

Systemic blood pressure more than 100 mm Hg - 10-20%
Systemic blood pressure less than 10 mm Hg - 21-30%
Systemic blood pressure less than 70 mm Hg - 31-40%
Systemic blood pressure less than 50 mm Hg - more than 41%

The classification according to Kulakov et al. 1998 reflects the severity of blood loss more accurately.

Blood density	Hematocrit (g/l)	Blood loss volume (ml)	Nv(g/l)
1057-1054	0,44-0,40	Up to 500	65-62
1053-1050	0,38-0,32	1000	61-50
1049-1044	0,30-0,22	1500	59-48
Less than 1044	Less than 0.22	More than 1500	Less than 43

Classification of blood loss (Brusov1998)

By type	1. Trauma (wound, operating) 2. Pathological (diseases, pathological processes) 3. Artificial (exfusion, therapeutic bloodletting)
By speed of development	Acute (more than 7% of the BV/h) Subacute (5-7% of the BV/h) Chronic (less than 5% of the BV/h)

By volume	Small (0.5-10% of the BV) Medium (11-20% of the BV) Large (21-40% of the BV) Massive (41-70% of the BV) Fatal (more than 70% of the BV)
By the degree of hypovolaemia and the possibility of shock	Mild - BV deficit 10-20%, GO deficit less than 30% - no shock, skin cold, pale, dry. Diuresis is more than 30 ml/hour. BUN - 38-32%, Hb - 80-90 g/l, AI 0.8-1.2, level
the possibility of shock	fibrinogen, platelets, platelet time, fibrinolytic activity is normal or slightly higher than normal. BV deficiency 15-20% (1000 ml) Moderate - BV deficit 21-30%, GO deficit 30-45%, shock occurs with prolonged hypovolaemia. Agitation, anxiety, cold sweat. Diuresis is less than 25-30 ml/h. Ht - 30-22%, Hb - 70-80 g/l, INR 1.3-2.0, fibrinogen, platelet count, platelet time, fibrinolytic activity is higher than normal. BV deficiency 25-30% (1500-2000 ml) Severe - BV deficiency 31-40%, GO deficiency 46-60%, shock is inevitable Extremely severe - BV deficit more than 40%, GO deficit more than 60%, shock, terminal condition. pale skin, sticky sweat, anuria. Ht less than 22%, Hb less than 70 g/l, INR more than 2.0, fibrinogen, platelet count, platelet time, fibrinolytic activity are reduced. Coagulopathy of consumption is replaced by fibrinolysis. BV deficiency is more than 35% (more than 2 litres).

A very important and sensitive criterion for hypovolaemia is the value of the CVP. With the loss of 100 grams of blood, the CVP decreases by 0.7 cmHg, i.e. for every 1 litre of blood, the CVP decreases by 7 cmHg.

Determination of the volume of blood loss based on the value of the CVP

CVP cm. H_2O.	BV deficit (%)
+4,0	Less than 10%
+2,0	11-20%
0	21-25%
-2,0	26-30%
- 4,0	More than 30%

Average amount of traumatic and surgical blood loss

Traumatic blood loss:

- haematoma in a hip fracture - 1.5-2 litres
- Increase in hip volume up to 1 cm. – 1l
- increase in thigh volume up to 2 cm. – 2l

- haematoma in case of tibia fracture - 0.5-1.5 litres
- Increase in the volume of the shoulder or lower leg up to 2 cm -1 litre
- open skull wound up to 2 litres
- closed skull wounds - up to 0.3 litres
- fracture of the forearm bones - 0.2-0.5 litres
- spinal fracture 0.5 - 1.5 litres
- fracture of the 1st rib -0.2-0.5 litres
- haemothorax 1.5-2.0 litres
- abdominal trauma - 2 litres and more
- scalped wound the size of a palm - 0.5 litres
- fracture of the pelvic bones - 2-3 litres and more
- peritoneal haematoma - lower haemorrhage (from the pelvic cavity to L5) - 250-500 ml
- medium haemorrhage of L5-L2 - 1-1.5 litres.
- large haemorrhage L2-th12 - 2-3 litres.

Operative blood loss

- thoracotomy - 0.7-1.0 litres
- amputation of the lower leg - 0.7 -1.0 litres
- osteosynthesis of large bones 0.5 -1.0 litres
- gastric resection - 0.4 -0.8 litres
- gastrectomy - 0.8-1.4 litres
- resection of the colon 0.8-1.5 litres
- caesarean section - 0.5-0.6 litres

Septic shock

Clinical signs of the septic shock phases

Clinical signs	Hyperdynamic phase of septic shock	hypodynamic phase of septic shock
Consciousness	Inadequacy, euphoria, motor agitation	Confusion, soporas, coma
skin	Dry, warm, hyper-permeable	Pale, with a marble tint, cold. Acrocyanosis
temperature	Hyperthermia with chills	Hypothermia
respiration	Vesicular or hard, tachypnea up to 30 per minute.	Diffuse wet rales, tachypnea more than 30 per min.
BLOOD PRESSURE	Normal or slightly reduced	Severe hypotension
HEART RATE	Tachycardia up to 110 per minute	More than 120 per min.
diuresis	25 ml/h	Less than 10 ml/h

acid-base balance	Compensated metabolic acidosis	Decompensated metabolic acidosis

Stages:

Early septic shock (hyperdynamic) stage ('warm shock') - blood pressure less than 90 mmHg (or 40 mmHg less than normal) within 1 hour despite therapy. Symptoms:

- Chills and fever.
- Oliguria.
- Tachycardia
- Arterial hypotension.
- Increased pulse pressure (due to a decrease in total peripheral vascular resistance)
- The skin of the extremities is warm, dry, pink (good blood circulation persists until the hour when there is no hypovolaemia).
- Mental disorders (inappropriate behaviour, agitation, confusion)
- Hyperventilation and respiratory alkalosis

Late (hypodynamic) stage *('cold shock').* Improper treatment and and the development of infection lead to the transition of septic shock to the next stage
- 'cold' shock. Clinical picture: hypovolaemic shock with signs of severe infection. Refractory septic shock for more than one hour despite appropriate therapy. The mortality rate is alarmingly high - 50-80%.

Minimal control in case of shock

In short-term and uncomplicated shock, for example, in shock accompanied by blood volume deficit, a small measurement programme that can be implemented in the simplest conditions is usually sufficient. This programme includes measurements of blood pressure using a cuff, CVP using a skin-inserted catheter into the superior vena cava, respiratory rate, hourly diuresis and assessment of blood flow in the skin (colour, temperature, capillary filling).

Treatment

Main means:

- ***It is important to eliminate the cause of shock as soon as possible, and even to ensure that the function of the main vital organs can be controlled:***
- Stop external bleeding (pressure dressing, pressure on the vessel)
- In case of internal bleeding, urgent surgical intervention is necessary.
- In the presence of sepsis, antibiotics are prescribed, and surgical intervention is required to eliminate the infection.
- In case of myocardial ischaemia, oxygen inhalation and medication are indicated
- Blood is drawn to determine haematocrit, arterial blood gases, potassium and lactate, blood type, Rh factor and individual compatibility, and the causative agent of the infection (culture). Only the necessary tests are performed.
- Insertion of a Foley catheter to monitor diuresis.
- A nasogastric tube is inserted for diagnosis (bleeding from the upper gastrointestinal tract) or treatment (prevention of aspiration and acute gastric

distension).

- Perform an ECG, chest X-ray, urinalysis with microscopic examination of sediment.

Infusion therapy

1. Bleeding control (temporary and permanent) and pain relief

2. Low-volume infusion therapy. A method of emergency infusion of small volumes of hypertonic solutions, which is a bolus infusion of 4-6 ml/kg of hypertonic-hyperoncotic solutions into a peripheral vein for 2-5 minutes. The most effective is the administration of 7.5% sodium chloride and HES medications - 6% reformane, 10% reformane plus, 6% stabizol - in equal proportions (1:1)

It should be noted that the infusion rate depends on the severity of the shock

1st degree shock - 50-60 ml/min.

2nd degree shock - 100 ml/min.

3rd degree shock - 200-300 ml/min.

4th degree shock - 200-500 ml/min.

If the blood pressure is not determined, the infusion rate should be 200-500 ml/min for 5-7 min. The blood pressure is determined, and then the infusion is carried out at such a rate that the blood pressure is not lower than 80-90 mmHg!

1) Regardless of the severity of the shock, it is necessary to catheterise the central vein and infusion should be performed under the control of the central venous pressure! To ensure a high infusion rate, several veins (or femoral artery) should be catheterised, paying attention to the catheter capacity!

2) Catheterise the bladder

3) Insert a nasogastric tube

4) Complete blood count, blood group, Rh factor, blood biochemistry

Low-volume infusion therapy programme

Blood loss (ml)	Crystalloids (mg/kg)	Volume correctors (10% reformate plus) Ml/kg	Blood products (ml/kg)
Up to 700	15-40	6-9	-
700-1500	25-50	7-10	-
1500-2000	25-50	15-20	Erythromass 8-10
More than 2000	25-50	20-25	Erythromass 8-10, albumin 8-10

Scheme of low-volume infusion therapy (Chornyi et al., 2001)

BV deficit	Hek (hydroxyethyl starch)	7,5% Nacl	Crystalloids
Up to 10%	10% hydroxyethyl starch 500 ml	2 ml/kg	1.5-2 times more than the amount of blood loss
Up to 20%	10% reformate 6-8 ml/kg or 4-6 ml/kg	2 ml/kg	6-8 ml/kg to 20 ml/kg
21-40%	6% stabizol 8-10 ml/kg	4 ml/kg	20 ml/kg
More than 40%	6% stabizol 10-15 ml/kg	4 ml/kg	20-25 ml/kg

In hypovolemic and septic shock, it is necessary to **start reimbursement of BV** ***as early as possible*****.**

1. Two large-diameter catheters (J 18G) are inserted into the peripheral or central veins. In septic shock, the measurement of CVP is more important than in hypovolaemic shock.

2. Administer 1000 - 2000 ml of Ringer's solution with lactate for 10-15 minutes. Then switch to 0.9% NaCl and continue the infusion until satisfactory tissue perfusion is achieved (criteria: diuresis of more than 0.5-1.0 ml/kg/min, mean arterial pressure above 65-70 mm Hg, elimination of metabolic acidosis).

3. If infusion therapy fails to stabilise the patient's condition or if the improvement is temporary, a blood transfusion is necessary. It is best to use whole blood that matches the recipient's blood group and Rh factor and has been tested for individual compatibility. It usually takes 45 minutes to collect such blood.

The principal therapy ***for isotonic dehydration***, according to the severity, involves restoring the volume of extracellular fluid by administering balanced saline solutions containing sodium and chlorine (see Appendix 5).

Blood loss replacement scheme by V.Brusov

The level of	Blood loss (%)	Total transfusion volume	Components of blood replacement and
blood replacement	BV)	(in % of TO THE BV)	their ratio in the total volume
I	10	200-300	Crystalloids (monotherapy) or with colloids (0.7+0.3)
II	20	200	Crystalloids + colloids (0.5+0.5)

III	21-40	180	albumin, colloids, crystalloids (0,3+0,1+0,3+0,3)
IV	41-70	170	Erythrocyte mass, plasma, colloids, crystalloids (0,4+0,1+0,25+0,25)
V	71-100	150	Erythrocyte mass, plasma, colloids, crystalloids (0,5+0,1+0,2+0,2)

Treatment of septic shock

Emergency treatment measures:

1. Respiratory support - if the $_{paO2}$ is below 60 mmHg or cyanosis is noted, immediately start oxygen therapy: supply of a gas mixture with 50% oxygen. $_{paO2}$ should be at least 90%;
2. Hemodynamic support - normalisation of BV, followed by vasopressor therapy, the indicators for which are

a. Absence of hypovolaemia (CVP 12-15 mmHg)

b. Average blood pressure of 60 mmHg. c. Oliguria

For this purpose, dopamine is used (routine use in severe sepsis - renoprotective effect -5 μg /kg/min). In cases of refractory hypotension, adrenaline and ephedrine are prescribed.

Glucocorticoids can be effective in refractory septic shock. In this case, hydrocortisone is prescribed in a dose of 100 mg 3 times a day for 5-10 days.

3. Antibacterial therapy

Without detection, removal or drainage of the infection focus, treatment of sepsis is unpromising!

Intensive care of septic shock.

1. Monitoring of vital functions

- BLOOD PRESSURE
- HEART RATE
- pulse
- Respiratory rate
- blood saturation
- body temperature
- CVP
- haemoculture and laboratory parameters: Hb, erythrocytes, leukocytes, Ht, protein and its fractions, glucose
- transaminases, bilirubin, azotemia
- homeostasis state: coagulogram, BUN, electrolytes (potassium, sodium, chlorine, calcium)
- central haemodynamics parameters (by means of integral body rheography according to M. Tyshchenko or pulmonary artery catheterisation with Swan-Ganz catheter) - stroke volume, cardiac index, total peripheral vascular resistance, pulmonary capillary stiffness, BV, oxygenation of mixed venous blood

- diuresis

2. Maintaining adequate gas exchange

- oxygen therapy
- intubation (increase in RaO2 more than 350 mmHg, decrease in RaO2 below 70 mmHg, decrease in RaO2/FiO2 ratio less than 180 mmHg, increase in RaO2 more than 50 mmHg, obtained on the background of 100% oxygen inhalation)

Dosing of antihypoxants in the treatment of septic shock

antihypoxants	dosing
Glutamic acid	200 mg for 24 hours 2.0-2.5 g per kg
Fumarate (mafusol) Vit. B1	25-50 mg per 24 hours
Calcium pongamate	200-400 mg per 24 hours
Mildronate Sodium	1000 mg for 24 hours
thiopental Unithiol	1-3 g per 24 hours
Solcoseril Sodium	500-1000 mg per 24 hours
thiosulfate	1000 mg/24 hours
Glucocorticosteroids	3000 mg/24 hours
Piracetam	30 mg/kg for prednisolone 8-12 g/24 hours
Dalargin	1 mg bolus, then 0.36 mg/kg /24 h 50-100 mg/24 h 800-1400 mg/24 h in/m
Cytochrome c Vit. E GHB	100-120 mg/kg
amtysol	600 mg/24 h

3. Stabilisation of haemodynamic parameters

1. Infusion therapy

1.1. Hypertonic solutions - sodium chloride 7.5% IV pg. In a dose of 4 ml / kg

1.2. Crystalloids (Ringer's solution, lactasol, acesol) - 7-10 ml/kg for 20-30 minutes.

1.3. Colloids: dextrans (polyglucin), gelatin (gelafusin), HEC (infusol).

The ratio of colloids: crystalloids is 2:1

1.4. Polyionic solution 800-1200 ml for 2-3 hours (glucose solution 25% - 400 ml, potassium chloride solution 7.5% - 25 ml, calcium chloride solution 10% - 6 ml, magnesium sulfate solution 25% - 3 ml, insulin

% - 3 ml, insulin 24 units)

Evaluation of efficacy: blood pressure, blood pressure, blood pressure.

1.5. If necessary - vasodilators: droperidol IV 1-4 mg/kg, nitroglycerin 5-10 mg/min. Up to 200 mg/min.. nitroprusside 1-4 μg/kg/min.. contraindications before administration of vasodilators

uncorrected hypovolaemia, central blood pressure below 10 cmHg.

2. Inotropic support

A. Dopamine in the dose: 1. 2-5 mcg/kg/min... (effect on dopapreceptors) - increases blood flow in mesenteric, coronary, renal vessels.

2. 5-10 mcg/kg/min (effect on B-adrenoceptors) - increases heart function.

3. 20 mcg/kg/min (stimulation of A-adrenoceptors) - increases total vascular resistance

B. Dobutamine in a dose of 2.5-20 μg/kg/min - increases heart rate, does not affect the total vascular resistance

3. Vasopressors

3.1 Norepinephrine: 0.15-0.25 μg/kg/min.

3.2 Adrenaline: from 1.4 μg/min. Up to 5-10 μg/min.

4. Phosphodiesterase inhibitors

Amnion: 0.5-1.5 mg/kg - loading dose; 1.0 mg/kg - maintenance dose (bolus)
10-30 μg/kg/min - for 2-3 hours continuously, maintenance dose,
10.0 mcg/kg. - daily dose

Milrion (short-acting): loading dose - 50 mcg/kg. Bolus over 10 minutes, maintenance dose - 0.4-0.8 mcg/kg/min. The maximum daily dose is 0.13 mg/kg.

5.Correction of microcirculatory disorders Rheopolyglucin: 400- 800 ml/day. Dipyridamole: 50-100 mg 2-3 times / day Complamine : 300-600 mg. in a cap. Heparin therapy.

4. **Delineation of the mediator 'explosion'**

4.1 Inhibition of TNF production

Pentoxifylline (trental, allopurinol): 100-300 mg. i.v. on the physical.

4.2 Influence on systemic proteolysis

Protease inhibitors: Gordox - 200-400 IU IV, Contrical, trazylol - 80,000-200,000 units per day.

4.3. Influence on free radicals and lipid peroxidation Antioxidants - scavengers: ascorbic acid -1 g/day; Unitiol - 5.0-7.0 m g/kg 2-3 times a day.

4.4. Effects on nitric oxide

Methylene blue: 1 day of septic shock with cardiac index greater than 3.5 l/min*m2 and MAP of 8-12 mm. Hg. Hg - a loading dose of 3 mg/kg, bolus; then (by dosing) for 4 hours: 1 hour - 0.25 ml/hour, 2 hours - 0.5

ml/h, 3 hours - 1.0 ml/h, 4 hours - 2.0 ml/h.

4.5. Immunoglobulins and immunomodulators

Pentaglobulin (Ig G, Ig M) - 5-8 ml/kg on the first day, 4 ml/kg on the 3rd day, Intraglobulin (Ig G) - 2.5 ml/kg IV for 2-3 days.

Roncoleukin - 1-2 million IU. IU + 4-8 ml of 10% albumin solution + 400 ml. Physiotherapy. Saline at a rate of 80-120 ml/hour. For 4-5 hours.

Galavit - by mouth, 200 mg, then 100 mg2-3 times a day for 7 days.

4.6. Glucocorticosteroids

IV bolus up to 30 mg/kg of the patient's body weight followed by prednisolone for 10-15 minutes.

4.7. Cyclooxygenase inhibitors Thrombaxan, prostaglandins, prostacyclin

Toxic oxygen radicals, NSAIDs: ketorolac (90 mg/day), diclofenac (150 mg/day).

4.8. Opioid receptor antagonists Naloxone - 0.4-1.2 mg.

5. Antibacterial therapy

6. Extracorporeal detoxification

- Hemosorption

- Plasmapheresis
- Hemodialysis
- Hemofiltration

7. Anaesthetic support in patients with septic shock

Surgery for removal or active drainage of the primary focus should be short, as simple as possible, less traumatic and reliable.

The method of choice in such situations is total intravenous anaesthesia with controlled ventilation.

Criteria for the effectiveness of the therapy:

- warm, dry, pink skin, white spot symptom < 2 sec;
- increase and stabilisation of blood pressure;
- reduction of heart rate;
- positive values of central venous pressure;
- increase in pulse pressure;
- restoration of hourly diuresis to 0.5 ml/kg/hour;
- increase in blood haemoglobin level to 90-100 g/l and haematocrit over 30%

Features of diagnosis and intensive care of haemorrhagic shock in the elderly and senile

The course of hypovolaemic shock is malignant. With moderate blood loss in these patients, a hypodynamic phase of circulatory disorders is observed (in young people, on the contrary, a hyperdynamic phase).

The shock index has little information value.

Features of intensive therapy

Features of diagnosis and intensive therapy of burn shock.

Burn shock (BS) is a pathological process that occurs during thermal injury, resulting in disorders of microcirculation, central haemodynamics, water and electrolyte metabolism, renal function, gastrointestinal tract and central nervous system. In terms of pathogenesis, it is largely a hypovolaemic shock.

Differences in burn shock

1. A clear dependence of the development and severity of BS on the area and depth of the skin burn (the larger the area of the burn, the higher the likelihood of severe shock). In case of incomplete IT, BS can be restored
2. Torpidity (persistence and duration of the course). Despite timely and adequate treatment, BS can last for more than 72 hours or more
3. It is characterised by significant changes in water spaces with the subsequent development of prolonged edema in the burn area.
4. The blood pressure in the case of BS does not decrease immediately after the burn injury and is not important as an indicator of the severity of shock.

Features of BS in the elderly and senile.

1. Against the background of age-related changes in the body and concomitant diseases (hypertension, coronary heart disease, diabetes mellitus, etc.), minor burns can cause severe BS.

2. In most cases, there is a syndrome of mutual burden
3. Burn injury can exacerbate the course of concomitant diseases, which are frequent causes of death in this category of patients.
4. The clinical picture of BS is dominated by disorders caused by the state of compromised systems
5. Arterial hypotension occurs rapidly, ECG shows signs of myocardial ischaemia, oligoanuria.

Diagnosis of burn shock

The area of the burned surface is assessed according to the 'rule of nines' and the Lund I Browder diagram. Depending on the severity index of the lesion, shock of varying degrees can occur.

18% each, perineum - 1%.

Assessment of burn severity

Degree of burn	Diagnostic criteria	Damage severity index
I	Erythema (redness and swelling of the skin)	1 unit
II	Flinthenia (hyperaemia and swelling of the skin with epidermal detachment and blistering, with increased skin sensitivity) sensitivity is increased)	1 unit
III a	Dermal burns or partial necrosis of the skin (the burn surface is pink, the scab is light yellow or brown, sensitivity is reduced)	2 units
III b	Total skin necrosis (the burned surface is whitish, the scab is dense, dark red or grey-brown, no sensitivity)	3 units
IV	Necrosis of the skin and deeper tissues	4 units

According to the severity, BS is divided into:

a) Mild AOD - DSI from 10 to 30 units, lasts 24-36 hours.
b) Medium severity BS - DSI from 31 to 60 units, lasts 36-48 hours.
c) Severe BS - DSI from 61-90 units, lasts 64 hours.
d) Extremely severe BS -DSI more than 90 units, lasts up to 72 hours. And more

<u>Intensive care in case of burn shock</u>

Objectives of intensive therapy for burn shock:

1. Compensation for the volume of fluid lost.
2. Maintenance of circulating fluid that is lost.
3. Reducing the formation of edema.
4. Normalisation and restoration of acid-base balance.

5. Restoration of electrolytes and plasma proteins.
6. Increase in perfusion of organs and tissues.

The sequence of priority manipulations in case of burn shock is as follows:

1) Ensure patency of the upper airway.
2) Central vein catheterisation and initiation of infusion therapy.
3) Anaesthesia.
4) Application of dressings to the burned surface (local treatment of burns).
5) Catheterisation of the bladder.
6) Insertion of a probe into the stomach.

Infusion therapy

Burn shock severity	Ratio of reformate, 0.9% sodium chloride solution, 5% glucose solution			
	1 day	2 days	3 days	4 days
Light degree	0:1:0	0:1:1	-	-
Medium severity	0,5:1:0	0,5:0,5:2	0,5:0,5:2	0,5:0,25:2,25
Severe degree	1:1:0	1:0,5:1,5	1:0,5:1,25	1:0,25:1,75
Extremely difficult degree	1,5:1:0	1:0,5:1,5	1:0,5:1,75	1:0,25:1,75

Glucose solutions should not be used in the first 24 hours, as they penetrate the intercellular space and increase edema. Albumin is also contraindicated in the first day of burn shock.

When drawing up an infusion therapy plan, the following should be taken into account:

In case of burns of more than 30% of the body surface, the plasma output into the interstitial space is 4 ml/(kg*h), and the sodium loss is : 0.5-0.6 mEq*kg*% of the burn surface.

It should be remembered that vascular permeability is impaired immediately, but hypovolaemia becomes clinically important after 6-8 hours! As a result of heat loss and evaporation through the burn surface, the following is lost

- for adults - (ml/h) = (25+% burn) * body area (m2)
- for children - (ml/h) = (35 +% of burn) * body area (m2)

In case of a major burn injury, due to hypovolaemia, haemoconcentration occurs in 4-6 hours and persists for 24-48 hours despite adequate therapy!

Anaesthesia and sedation (narcotic analgesics, stadol 2 mg intramuscularly).

Prevention of thromboembolic complications (fraxiparin, trental, rheopolyglucin, etc.).

Prevention of septic complications (antibiotic therapy - maxipim 2 grams every 12 hours, amikin 15 mg/kg per day with an interval of 8-12 hours).

Ensuring systemic oxygen transport and correction of hypoxaemia (oxygen therapy, perfluorane, etc.).

Perfluorane dosage depending on the degree of burn shock (Usenko L., 1999)

Hypercaloric diet through parenteral (infesol and others) or enteral nutrition (berlamin modular and others).

The calculation of calories should be as follows:

1800 kcal/m2 of body surface /day (physiological requirement)

2200 kcal/m2 of the burn surface /day (additional costs of the burn)

It should be remembered that the basic energy requirement for an adult is 25-40 kcal/kg/day. To cover the energy requirement, it is necessary to multiply this value by the metabolic activity factor, which in severe burns is 2.

Correction of metabolic acidosis (sodium bicarbonate solution, etc.). Prevention of stress ulcers (omez, contraloc, elk, quamatel, etc.).

Criteria for the effectiveness of intensive care in burn shock.

1. Restoration of the patient's consciousness
2. Stabilisation of central and peripheral haemodynamics
3. Normalisation of breathing (Sat O2 more than 90%)
4. Restoration of renal function (diuresis at least 1 ml/kg/hour)
5. Achievement of haemodilution (Ht=33-38%)
6. Maintenance of colloidal osmotic pressure (total protein is more than 60 g/l)

6.2. Control materials for the final stage of the lesson.

Situational tasks

1. During the conservative treatment of acute pancreatitis, the patient developed hypotension, tachycardia, fever up to 39°C, tachypnoea.
What are the surgeon's actions?

Answer model: Immediately start treatment of endotoxic shock.

2. A 45-year-old patient with widespread peritonitis due to destructive cholecystitis has a decrease in diuresis of less than 0.5 ml/kg body weight per hour. What does this indicate and what are your actions?

Answer model: This indicates the development of multiple organ failure (primarily renal). It is necessary to intensify syndromic therapy of the systemic inflammatory response syndrome (correction of circulating fluid volume, normalisation of blood pressure and vascular tone, stimulation of diuresis).

3. A 32-year-old patient with a history of peptic ulcers developed a shock state with a decrease in blood pressure, tachycardia, tachypnea and fever. What does this indicate? What should the surgeon do?

Answer model: The patient has a perforated ulcer with peritonitis and endotoxic shock. Urgent surgical treatment with stabilisation of the patient's condition on the operating table is indicated.

6.3. Materials for methodological support of self-study of higher education applicants

№	Main tasks (to learn)	Instructions (to name)
1.	Biochemical and pathophysiological mechanisms of the inflammatory process.	Mechanisms of development of local and systemic inflammatory reactions in the body.
2.	Clinical signs of multiple organ failure syndrome	Signs of impaired cardiovascular, urinary, respiratory, liver, blood clotting system function and metabolic changes
3.	Syndromic diagnosis of the main manifestations of systemic inflammatory response syndrome	Objective examination Laboratory tests Instrumental examinations
4.	Conservative therapy of systemic inflammatory response syndrome	Syndromic therapy for individual disorders of various systems and organs
5.	Indications for surgical intervention in systemic inflammatory response syndrome	-the presence of a surgical infection - massive tissue damage Ischaemia of organs or individual tissues with necrotic changes.
6.	Surgical methods of treatment	those aimed at eliminating the cause of the systemic inflammatory response syndrome

Situational tasks

1. Patient H., 55 years old, was admitted to the surgical department with complaints of weakness, dizziness, widespread pain throughout the abdomen, more in the epigastric region, nausea, repeated vomiting, fever. Tachycardia is noted, with a pulse rate of 120/min, tachypnea - up to 40/min, leukocytosis - 18 G/l. What could be the reason for the development of systemic inflammatory response syndrome in this case?

Answer model: Acute destructive pancreatitis.

2. Patient T., 38 years old, complained of acute weakness, fever up to 39 °C, palpitations with a pulse rate of 112/min, shortness of breath. There was a drop in blood pressure to 80/50 mm Hg, leukocytosis - 15 G/l. A week ago she was treated in hospital for acute paraproctitis with opening and drainage of an abscess in the pararectal tissue. What is the most likely diagnosis?

Answer model: Systemic inflammatory response syndrome. Sepsis with endotoxic shock due to inadequate drainage of the abscess.

3. Patient K., 36 years old, is being treated in the intensive care unit on the third day after surgical treatment of acute appendicitis with widespread peritonitis. The patient has fever up to 38.7 °C, tachycardia up to 120 beats/minute, tachypnea - more

than 40/minute, and a decrease in the level of leukocytes in the peripheral blood to 2.7 G/l. What is your diagnosis?

Answer standard: Systemic inflammatory response syndrome. Sepsis, probably caused by gram-negative bacterial flora.

Materials for the main stage of the class

1.What is the systemic inflammatory response syndrome?

a) A systemic inflammatory response of the whole body in response to infection, trauma or other stressors

b) Local inflammation that is limited to one organ

c) Chronic inflammation with a gradual deterioration of the condition

d) The body's reaction to allergens

2.Which of the following are the main criteria for the diagnosis of systemic inflammatory response syndrome?

a) Fever (temperature > 38°C) or hypothermia (temperature < 36°C)

b) Hyperaemia and swelling in the wound area

c) Increased platelet count

d) Normal heart rate and blood pressure

3.Which of the following conditions is a common cause of a systemic inflammatory response in surgical practice?

a) Sepsis

b) Anaemia

c) Chronic bronchitis

d) Vitamin deficiency

4. Which molecules play a key role in the pathogenesis of systemic inflammatory response syndrome?

a) Cytokines (e.g. IL-1, TNF-α)

b) Thyroid hormones

c) Lipids

d) Glucose

5. What mechanism of disorders can lead to organ dysfunction in the systemic inflammatory response syndrome?

a) Activation and release of pro- and anti-inflammatory cytokines

b) Increase in the level of hemoglobin

c) Reduced activity of antioxidant enzymes

d) Decrease in the level of calcium in the blood

6.Which of the following conditions is most likely to cause the development of systemic inflammatory response syndrome?

a) Severe burns

b) Influenza

c) Mild headache

d) A small scratch

7.In which of the following conditions can the systemic inflammatory response syndrome progress to septic shock?

a) In the absence of adequate antibacterial therapy

b) In case of vitamin deficiency

c) With normal blood glucose levels

d) In case of increased potassium levels in the blood

8. Which of the following conditions can worsen the manifestations of the systemic inflammatory response syndrome in a patient with trauma?

a) Concomitant infection

b) Moderate fluid intake

c) Regular exercise

d) Normal body temperature

9.Which of the following methods is important in the early treatment of systemic inflammatory response syndrome?

a) Early and adequate use of antibiotics

b) Surgical intervention without prior preparation

c) Use of corticosteroids without prior diagnosis

d) Use of antiviral drugs

10. Which of the following measures helps to prevent the development of systemic inflammatory response syndrome in a surgical patient?

a) Effective antibacterial prophylaxis

b) Increasing the level of glucose in the blood

c) Prophylactic administration of anticoagulants

d) Change of diet

Literature:

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