MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
SUMY STATE UNIVERSITY
ACADEMIC AND RESEARCH MEDICAL INSTITUTE

Eastern Ukrainian Medical Journal

116, Kharkivska st., Sumy 40007, Ukraine eumj.med.sumdu.edu.ua
e-mail: eumj@med.sumdu.edu.ua ISSN: 2663-5909 (print)/2664-4231 (online)

How to cite: Benedykt VV, Hnatiuk MS, Prodan AM, Verveha BM. Pathogenetic aspects of motor-evacuation disorders of the small intestine in acute generalized peritonitis and their treatment. *East Ukr Med J*. 2026;14(1):210-222. DOI: https://doi.org/10.21272/eumj.2026;14(1);210-222

ABSTRACT

Volodymyr V. Benedykt
https://orcid.org/0000-0002-7650-1771
Department of Surgery of the Faculty of Postgraduate Education, I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

Mykhailo S. Hnatiuk
https://orcid.org/0009-0008-5607-6123
Department of Clinical Anatomy and Operative Surgery, I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

Andrii M. Prodan
https://orcid.org/0000-0002-6052-192X
Department of Surgery of the Faculty of Postgraduate Education, I. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine

Bohdana M. Verveha
https://orcid.org/0000-0002-7463-5899
Department of Pathological Physiology, Department of Radiology and Radiation Medicine, State NonProfit Company "Danylo Halytsky Lviv National Medical University", Lviv, Ukraine

PATHOGENETIC ASPECTS OF MOTOR-EVACUATION DISORDERS OF THE SMALL INTESTINE IN ACUTE GENERALIZED PERITONITIS AND THEIR TREATMENT

Introduction. Despite the constant improvement of surgical techniques and intensive care methods, acute peritonitis is the main cause of mortality in surgical patients. One of the key pathogenetic factors in the development of multiple organ failure in acute generalized peritonitis is intestinal insufficiency syndrome, the main cause of which is intestinal paresis with impaired motor and evacuation functions due to the source of intoxication. Early diagnosis and correction of intestinal insufficiency syndrome affect the results of treatment of patients with abdominal sepsis and multiple organ failure.

Objective: To study the mechanisms of development of motor-evacuation disorders of the small intestine in acute generalized peritonitis and to develop pathogenetically based treatment tactics.

Materials and methods. Experimental modeling of acute inflammation of the peritoneum was performed on sexually mature non-linear white male rats (n=32) by intraperitoneal injection of 10 % filtered fecal suspension at a dose of 0.5 ml per 100 g of body weight. Animals of the control group were injected subcutaneously in 0.9 % NaCl solution. The experiment investigated the severity of endogenous intoxication, the activity of lipid peroxidation and the state of the antioxidant system in the blood of animals on the first, on the third, and on the seventh days after the administration of faeces suspension. A bacteriological examination of the parietal intestinal biotope and a histological study of the small intestine were performed, the bioenergetic state of the small intestine and the content of IgA-, IgG-, or IgM-producing cells were studied.

The results of diagnosis and treatment of 132 patients with acute generalized peritonitis who were inpatients in the surgical department of the Ternopil Municipal City Hospital No. 2 were analyzed, and a retrospective analysis of 50 patient records who died from peritonitis was

performed. The severity of peritonitis was determined according to Mannheim peritonitis index. The severity of endogenous intoxication was determined by the leukocyte intoxication index, the level of middleweight molecules in the blood, and the erythrocyte intoxication index. Intra-abdominal pressure was measured.

Results. Clinical manifestations of enteral insufficiency syndrome during experimental modeling of acute generalized peritonitis are accompanied by an increase in the concentration of thiobarbituric acid reactive substances and lipid-hydroperoxides in the blood of animals, a decrease in the activity of enzymatic and non-enzymatic antioxidants. A depletion of intestinal Adenosine triphosphate, and a decrease in the number of intestinal IgA-producing plasma cells against the background of dystrophic and necrobiotic lesions of epithelial cells were detected. The manifestation of acute inflammation of the peritoneum is characterized by quantitative and qualitative changes in the microbiota of the parietal intestinal biotope. A decrease in the number of *Escherichia coli* strains isolated in monoculture and an increase in the number of two-component and three-component microbial associations were revealed, among which *Escherichia coli*, *Enterobacter aerogenes*, *Enterococcus spp* and *Candida species* prevailed.

In patients with acute generalized peritonitis with a favorable course in the postoperative period, the dynamics of endogenous intoxication was studied and the influence of intra-abdominal pressure on the restoration of small intestine motility after surgical treatment was determined. The treatment tactics were optimized by performing intracavitary pneumomassage of the small intestine.

Conclusions: The main links in the pathogenesis of motor-evacuation disorders of the small intestine in peritonitis are endogenous intoxication, which is a trigger for the activation of lipid peroxidation processes, impaired immune defense of the small intestine mucosa, a decrease in the bioenergetic capabilities of myocytes, dystrophic and necrobiotic lesions of epithelial cells. The use of a complex of therapeutic measures aimed at early restoration of the motor-evacuation function of the small intestine and prevention of increased intra-abdominal pressure allows reducing the degree of intestinal insufficiency syndrome in the early stages of the postoperative period and preventing the development of abdominal sepsis.

Keywords: intestinal insufficiency syndrome, acute inflammation of the peritoneum, lipid peroxidation, endogenous intoxication, bacteriological examination of parietal intestinal biotope, morphological changes in the small intestine, intra-abdominal pressure, pneumomassage.

Corresponding author:
Bohdana Verveha, Department of Pathological Physiology, Department of Radiology and Radiation Medicine, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
e-mail: danaverveha@gmail.com

РЕЗЮМЕ

Володимир В. Бенедикт
https://orcid.org/0000-0002-7650-1771
Кафедра хірургії факультету післядипломної освіти, Тернопільський національний медичний університет імені І.Я.

ПАТОГЕНЕТИЧНІ АСПЕКТИ МОТОРНО-ЕВАКУАТОРНИХ ПОРУШЕНЬ ТОНКОЇ КИШКИ ПРИ ГОСТРОМУ ПОШИРЕНОМУ ПЕРИТОНІТІ ТА ЇХ ЛІКУВАННЯ

Актуальність. Не дивлячись на постійне вдосконалення техніки оперативних втручань та методів інтенсивної терапії, гостре запалення очеревини є основною причиною летальності у хворих хірургічного профілю. Одним із ключових патогенетичних

Горбачевського МОЗ України,
м. Тернопіль, Україна

Михайло С. Гнатюк
Кафедра оперативної хірургії та клінічної анатомії, Тернопільський національний медичний університет імені І.Я. Горбачевського МОЗ України, м. Тернопіль, Україна
https://orcid.org/0009-0008-5607-6123

Андрій М. Продан
https://orcid.org/0000-0002-6052-192X
Кафедра хірургії факультету післядипломної освіти, Тернопільський національний медичний університет імені І.Я. Горбачевського МОЗ України, м. Тернопіль, Україна

Богдана М. Вервега
https://orcid.org/0000-0002-7463-5899
Кафедра патологічної фізіології, кафедра радіології та радіаційної медицини, Державне некомерційне товариство "Львівський національний медичний університет імені Данила Галицького", м. Львів, Україна

факторів розвитку поліорганної недостатності при гострому поширеному перитоніті є синдром ентеральної недостатності, основною причиною якого є парез кишківника з порушенням його моторної та евакуаторної функцій внаслідок чого він стає джерелом інтоксикації. Рання діагностика та корекція синдрому ентеральної недостатності позитивно впливають на результати лікування пацієнтів з абдомінальним сепсисом та поліорганною недостатністю.

Мета. Вивчити механізми розвитку моторно-евакуаторних порушень тонкої кишки при гострому поширеному перитоніті та розробити патогенетично обґрунтовану тактику лікування.

Матеріали та методи. Експериментальне моделювання гострого запалення очеревини проведено на статевозрілих нелінійних білих щурах-самцях (n=32) шляхом введення у черевну порожнину 10 % профільтрованої калової суспензії в дозі 0,5 мл на 100 г маси тварини. Тваринам контрольної групи підшкірно вводили 0,9 % NaCl. В експерименті досліджували вираженість ендогенної інтоксикації, активність вільнорадикального окиснення ліпідів та стан антиоксидантної системи у крові тварин на першу, третю та сьому доби від моменту введення калової суспензії. Проводили бактеріологічне дослідження пристінкового кишкового біотопу та гістологічне дослідження тонкої кишки, вивчали біоенергетичний стан тонкої кишки та вміст плазматичних клітин-продуцентів IgA, Ig M та Ig G.

Проведено аналіз результатів обстеження та лікування 132 хворих на гострий поширений перитоніт, які перебували на стаціонарному лікуванні у хірургічному відділенні КНП “Тернопільська комунальна міська лікарня №2”, та здійснено ретроспективний аналіз 50 медичних карт стаціонарних хворих, які померли від перитоніту. Тяжкість перитоніту визначали за Мангеймським індексом перитоніту. Вираженість ендогенної інтоксикації оцінювали за допомогою визначення лейкоцитарного індексу інтоксикації, кількості молекул середньої маси та еритроцитарного індексу інтоксикації. Проводили вимірювання інтраабдомінального тиску.

Результати та обговорення. Клінічні прояви синдрому ентеральної недостатності впродовж експериментального моделювання гострого поширеного перитоніту супроводжуються збільшенням вмісту у крові тварин активних продуктів тіобарбітурової кислоти та гідропероксидів ліпідів, зниженням активності ензимної та неензимної ланок антиоксидантної системи. Виявлено зменшення вмісту АТФ у стінці тонкої кишки та зниження кількості плазматичних клітин-продуцентів IgA на фоні дистрофічних та некробіотичних уражень епітеліоцитів. Перебіг гострого запалення очеревини характеризується кількісними та якісними змінами мікробіоти пристінкового кишкового біотопу. Верифіковано зменшення кількості штамів *Escherichia coli*, виділених у монокультурі, та збільшення кількості двокомпонентних та трикомпонентних мікробних асоціацій серед яких переважали *Escherichia coli*, *Enterobacter aerogenes*, Enterococcus spp та *Candida species*.

У хворих на гострий поширений перитоніт із сприятливим перебігом у післяопераційному періоді вивчено динаміку ендогенної інтоксикації та визначено вплив інтраабдомінального

тиску на відновлення моторики тонкої кишки після хірургічного лікування. Оптимізовано тактику лікування проведенням внутрішньопорожнистого пневмомасажу тонкої кишки.

Висновки: Основними ланками патогенезу моторно-евакуаторних порушень тонкої кишки при перитоніті є ендогенна інтоксикація, що є тригером активації процесів пероксидного окиснення ліпідів, порушення імунного захисту слизової оболонки тонкої кишки, зменшення біоенергетичних можливостей міоцитів, дистрофічних та некробіотичних уражень епітеліоцитів. Застосування комплексу лікувальних заходів, спрямованих на раннє відновлення моторно-евакуаторної функції тонкої кишки та попередження підвищення інтраабдомінального тиску, дозволяє знизити ступінь синдрому ентеральної недостатності в ранні терміни післяопераційного періоду та попередити розвиток абдомінального сепсису.

Ключові слова: синдром ентеральної недостатності, гостре запалення очеревини, пероксидне окиснення ліпідів, ендогенна інтоксикація, бактеріологічне дослідження пристінкового кишкового біотопу, морфологічні зміни тонкої кишки, інтраабдомінальний тиск, пневмомасаж.

***Автор, відповідальний за листування**:*
Богдана Вервега, кафедра патологічної фізіології; кафедра радіології та радіаційної медицини, Львівський національний медичний університет імені Данила Галицького, м. Львів, Україна;
e-mail: danaverveha@gmail.com

INTRODUCTION

A crucial and often unsuccessful aspect of modern surgery is the treatment of patients with acute generalized peritonitis (AGP). This disease attracts the attention of all surgeons providing emergency medical care. In recent years, despite the use of modern antibacterial drugs and minimally invasive methods of diagnosis and treatment of AGP, there has been no pronounced trend towards a decrease in mortality [1, 2, 3]. Treatment of a patient with AGP requires choosing the optimal surgical approach [4]. For many years, the efforts of the medical community have been aimed at finding more effective diagnostic methods and pathogenetically based surgical treatment methods [5].

The severity of the condition in patients with AGP is determined by intestinal failure syndrome (IFS), which includes intestinal paresis and increased intraintestinal pressure [6]. Against this background, inflammatory changes in the intestinal wall develop, leading to impaired microcirculation and intestinal wall trophism. The barrier function of the intestinal mucosa is disrupted, which contributes to the translocation of endotoxins and bacteria into the hemo- and lymphocirculation system.

Actually, the translocation of bacteria and their toxins from the lumen of the gastrointestinal tract into the blood contributes to the transformation of the intestine into a source of endotoxicosis, leading to generalization of infection with subsequent dysfunction of target organs [7]. The cause of the multiple organ dysfunction syndrome (MODS) in AGP is also intra-abdominal hypertension, which enhances the processes of tissue destruction due to compression ischemia and microcirculatory disorders in the intestinal wall and parenchymal organs [8].

For a more profound understanding of the pathogenesis of acute peritonitis, it is relevant to study morphological changes in the small intestine due to paresis, as well as the pathophysiological mechanisms underlying bacterial translocation in IFS, which is one of the main mechanisms of AGP development.

Our work aimed to study the mechanisms of development of motor-evacuation disorders of the small intestine in acute generalized peritonitis and to develop a pathogenetically based treatment approach.

MATERIALS AND METHODS

The retrospective clinical study included the results of the examination and treatment of 132 patients with AGP who were inpatients in the Surgical Department of the Ternopil Municipal City Hospital No. 2 during 2019–2024. To verify the diagnosis, clinical and laboratory and instrumental research methods were used. The severity of peritonitis was determined by the Mannheim Peritonitis Index [9]. The degree of

endogenous intoxication was assessed by determining the leukocyte intoxication index (LII) [10], the number of middle molecules (MMs) [11], and the erythrocyte intoxication index [12]. Intra-abdominal pressure was measured according to Kron et al. [13].

In addition, we conducted a retrospective analysis of 50 medical records of inpatients who died from AGP.

The experimental study was conducted on white non-linear rats (n=32), which were kept in a vivarium in accordance with the "Standard Rules for the Design, Equipment, and Maintenance of Experimental Biological Clinics (Vivaria)". The experiments were conducted in accordance with the provisions of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986); Council of Europe Directive 86/609/EEC (1986); Law of Ukraine No. 3447 – IV "On the Protection of Animals from Cruelty"; General Ethical Principles of Animal Experiments, adopted by the First National Congress of Ukraine on Bioethics (2001), which was confirmed by the conclusion of the Bioethics Committee of the Danylo Halytsky Lviv National Medical University (Minutes No. 8 of November 23, 2020; Minutes No. 6 of June 22, 2021).

Animals were divided into two groups: the main group (n=24) and the control group (n=8). In the main group of animals with simulated AGP, the study was conducted on the first, third, and seventh days after fecal suspension administration. These terms correspond to the reactive, toxemic, and terminal stages of peritonitis. Experimental animals of the studied groups were sacrificed by euthanasia with an overdose of sodium thiopental (100 mg/kg of body weight). Rats in the control group were subcutaneously injected with 0.9% NaCl. Acute generalized peritonitis was simulated by injecting 10% filtered fecal suspension into the abdominal cavity at a dose of 0.5 ml per 100 g of animal weight. Fecal suspension was obtained by mixing isotonic solution and cecal contents of three intact animals and filtering it twice through a double layer of gauze.

To determine the intensity of lipid peroxidation (LPO) and the state of the antioxidant system, the content of active products of thiobarbituric acid (TBA-AP) and lipid hydroperoxides (LOOHs) in the blood was determined. The state of the antioxidant system was assessed by the activity of superoxide dismutase, catalase, reduced glutathione, and ceruloplasmin. Superoxide dismutase was determined in blood serum using a method based on the reduction of nitrotetrazolium by superoxide radicals formed due to the reaction between phenazine metasulfate and the reduced form of nicotinamide dinucleotide; catalase activity was determined using the reaction with ammonium molybdate [14]. The content of reduced glutathione was determined by the interaction of Ellman's reagent with free SH groups; and the level of ceruloplasmin was determined by the oxidation reaction of para-phenylenediamine [14].

For histological examination, fragments of the small intestine were collected, fixed in 10% formaldehyde solution, dehydrated in alcohols of increasing concentration, embedded in paraffin; sections were prepared and stained with hematoxylin-eosin. To detect plasma cells producing IgA, IgM, and IgG, microtome sections of the intestine were treated with monospecific antisera against the indicated immunoglobulin classes, conjugated to fluorescein isothiocyanate; for this purpose, the direct Koons method was used with appropriate controls. Using a Lumam P-8 fluorescent microscope, plasma cells that gave a specific glow in fluorescent light were counted per 1 mm² of the mucous membrane of the studied organ.

Bacteriological studies were performed by sampling the parietal intestinal biotope into a sterile test tube, taking culture on a nutrient medium, isolating a pure culture, and identifying aerobic and anaerobic microorganisms using highly selective media. Based on the data obtained, the frequency of certain pathogens and their associations (%) was calculated.

The concentration of adenosine triphosphate (ATP) in the muscular coat of the small intestine was determined using the ion exchange chromatography method [15].

Statistical analysis of the indicators was performed using standard computer programs (Statistica Version 6, StatSoft, Inc., SPSS Statistics 17.0) with determination of the arithmetic mean (M) and standard error of the arithmetic mean (m). In all cases, differences between groups were considered significant if the p-value < 0.05 (ANOVA).

RESULTS

In animals with AGP, an increase in the level of TBA-AP was detected on the first, third, and seventh days by 32.6%, 100.0% ($p<0.01$), and 285.8% ($p<0.001$), respectively, compared to the controls (Table 1), which indicated the activation of LPO. The content of LOOHs on the first day increased by 3.9 times ($p<0.001$), on the third day – by 2.5 times ($p<0.001$), and on the seventh day – by 2.2 times ($p<0.01$) compared to animals in the control group.

The activity of superoxide dismutase in the group of rats with AGP on the first day of the experiment decreased by 9.9% ($p<0.05$), on the third day – by 19.0% ($p<0.001$), and on the seventh day – by 31.0% ($p<0.001$) compared to the control group of animals (Table 2), which was a manifestation of a decrease in antioxidant protection secondary to increased oxidative

stress. Catalase activity increased by 50.0% on the first day of the experiment, which could be explained by the protective-compensatory reaction of the rat organism to endogenous intoxication caused by AGP. On the third day of experimental modeling of acute peritoneal inflammation, catalase activity increased by 11.1% and decreased by 44.4% on the seventh day compared to the controls (p<0.001).

Table 1 – Indicators of lipid peroxidation activity in the blood of rats with acute generalized peritonitis (M±m)

Parameter	Control group (n=8)	Experimental group		
		Day 1 (n=8)	Day 3 (n=8)	Day 7 (n=8)
TBA-AP, mmol/l	1.90±0.12	2.52±0.29	3.80±0.50 p<0.01	7.33±0.76 p<0.001
LOOHs, units	1.26±0.12	4.91±0.29 p<0.001	3.16±0.33 p<0.001	2.78±0.37 p<0.01

Note: p – significance of the difference vs. the control group of animals

Table 2 – Indicators of antioxidant system activity in the blood of rats with acute generalized peritonitis (M±m)

Parameter	Control group (n=8)	Experimental group		
		Day 1 (n=8)	Day 3 (n=8)	Day 7 (n=8)
Superoxide dismutase activity, units	57.2 ± 1.7	51.5 ± 1.1 p<0.05	46.3 ± 0.9 p<0.001	39.5 ± 0.6 p<0.001
Catalase activity, mkat/l	0.18 ± 0.01	0.27 ± 0.01 p<0.001	0.20 ± 0.01	0.10 ± 0.01 p<0.001
Reduced glutathione, mM/L	2.72 ± 0.01	2.19 ± 0.02 p<0.001	2.02 ± 0.05 p<0.001	1.91 ± 0.04 p<0.001
Ceruloplasmin, g/l	0.23 ±0.02	0.36 ± 0.01 p<0.001	0.29 ± 0.01 p<0.001	0.17 ± 0.01 p<0.001

Note: p – significance of the difference vs. the control group of animals

The concentration of reduced glutathione in the blood of animals with AGP decreased throughout the entire observation period. Thus, on the first day of the experiment, the difference vs. the controls was 19.5%, on the third day – 25.7%, and on the seventh day – 29.8%, respectively. This confirms the gradual depletion of the antioxidant system.

Ceruloplasmin is known to protect lipid-containing biostructures from damaging effects by intercepting free radical oxygen species. In addition, it inactivates free radicals formed in macrophages and leukocytes during phagocytosis and activation of lipid peroxidation processes in the focus of inflammation. In rats with AGP, an increase in ceruloplasmin levels was detected on the first and third days of the experiment by 56.5% and 26.1%, respectively, which indicated a protective and compensatory reaction to endogenous intoxication. On the seventh day of the experiment, a 26.1% decrease in this indicator relative to the control group was observed, which could be explained by the elimination of excessive superoxide anion radicals from the blood.

The course of acute peritoneal inflammation was accompanied by activation of lipid peroxidation and a decrease in the activity of the enzymatic and non-enzymatic antioxidant systems. At the same time, functional activity was significantly impaired and ATP synthesis in the muscular membrane of the small intestine was reduced. Thus, on the first day of the experiment, a 1.4-fold decrease in ATP concentration was detected in animals with simulated AGP compared to the control group. On the third and seventh days, the ATP content decreased by 1.8 and 2.4 times compared to the controls, indicating impaired mucosal permeability under the influence of reactive oxygen metabolites.

During histological examination of the small intestine in the experimental group of animals on the first day of AGP development, the integrity of the epithelial lining was observed, along with a decrease in the number of goblet cells and intraepithelial lymphocytes (Fig. 1). The number of macrophages and mast cells in the lamina propria of the mucosa slightly

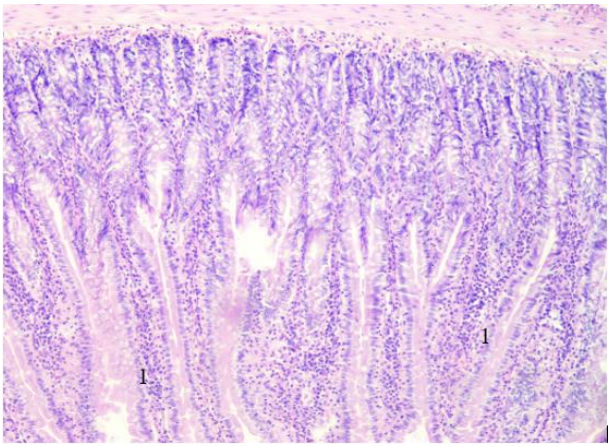

Figure 1 – Histological structure of the small intestine wall in an animal with acute generalized peritonitis (Day 1). Inflammatory infiltration of the villi (1). Hematoxylin and eosin staining; ×200

increased. The vessels became full of blood, but without manifestations of perivascular hemorrhages. In the stroma of the glandular component, pronounced inflammatory infiltration, mainly lymphocytic and plasmacytic, was noted in individual areas, with a significant number of eosinophilic leukocytes. Damage to the microcirculatory bed was characterized by pronounced morphological changes. Semi-thin sections showed marked hyperemia of capillaries and venules, and in some places, rouleaux of erythrocytes were observed.

On the third day of AGP, an increase in the height and number of epithelial cells was observed, as well as a tendency to increased volumetric density of intracellular organelles. On the seventh day, increased permeability of the mucous membrane vessels was observed in the wall of the small intestine, accompanied by significant villous stroma swelling and focal hemorrhages. Columnar epithelial cells underwent dystrophic and necrobiotic changes. In the cytoplasm, predominantly hyaline-droplet and hydropic dystrophy developed. This culminated in desquamation and exposure of the basement membrane, leading to multiple erosions. In the lamina propria of the mucosa, focal hyperplasia of lymphoid structures was visualized (Fig. 2) in combination with increased exudative inflammation, which confirmed an increase in the number of neutrophilic leukocytes in the exudate.

Similar manifestations were also visualized in the serosa, as evidenced by edema and increased cellular infiltration. The mucosal villi were dilated and shortened due to diffuse lymphocytic and histiocytic infiltration of the stroma. The villi capillaries were paretically dilated and caused multiple diapedetic hemorrhages. Focal necrosis of the surface epithelium was detected.

Certain morphometric changes were observed in all layers of the small intestine wall, mainly expressed on the seventh day of development of experimental AGP. Thus, the thickness of the mucous membrane was 87.5% greater than in the control group. The muscular layer was thinned by 32.8%, and the submucosa was 3.3 times thicker than in the controls.

At the same time, on the seventh day of AGP development, a 36.3% decrease in the number of IgA-producing plasma cells was observed in the small intestinal mucosa, while the number of IgM- and IgG-producing plasma cells increased by 3.3 and 2.8 times, respectively, compared to the control group.

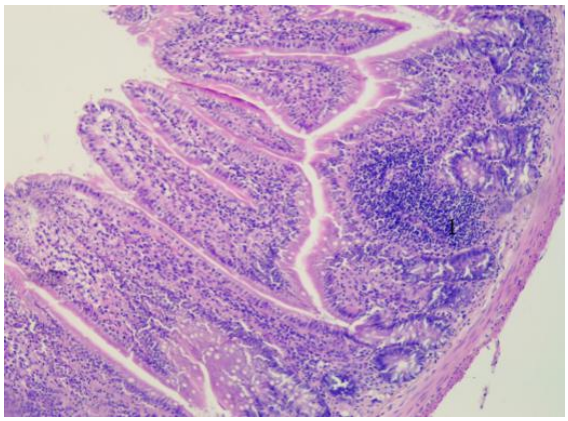

Figure 2 – Histological structure of the small intestine wall in an animal with acute generalized peritonitis (Day 7). Focal hyperplasia of lymphoid tissue (1) is visualized in combination with increased exudative inflammation. Hematoxylin and eosin staining; ×200

The frequency of detection of microorganisms isolated from the parietal intestinal biotope of rats with AGP is shown in Figure 3. Among the detected microorganisms, representatives of the genera *Escherichia coli* (75.0%), *Enterobacter* (16.7%), and *Enterococcus* (16.7%) predominated. Monoinfection was identified in 41.7% of cases, and associations of pathogens in 58.3%. Two-component microbial associations were isolated in 54.2% of cases, and three-component associations – in 4.2%. Among all isolated cultures, gram-negative microorganisms accounted for 69.2% (27/39), gram-positive microorganisms – 23.1% (9/39), fungi of *Candida species* – 7.7% (3/39).

On the first day of experimental AGP development, monoculture was detected in 62.5% of cases, and two-component microbial associations in 37.5% (Table 3). *Escherichia coli* was the dominant pathogen – it was isolated from all monocultures and from associations with *Staphylococcus spp.* (12.5%) and *Enterococcus spp.* (12.5%). In one case, the association was represented by *Enterobacter aerogenes* and *Streptococcus spp.*

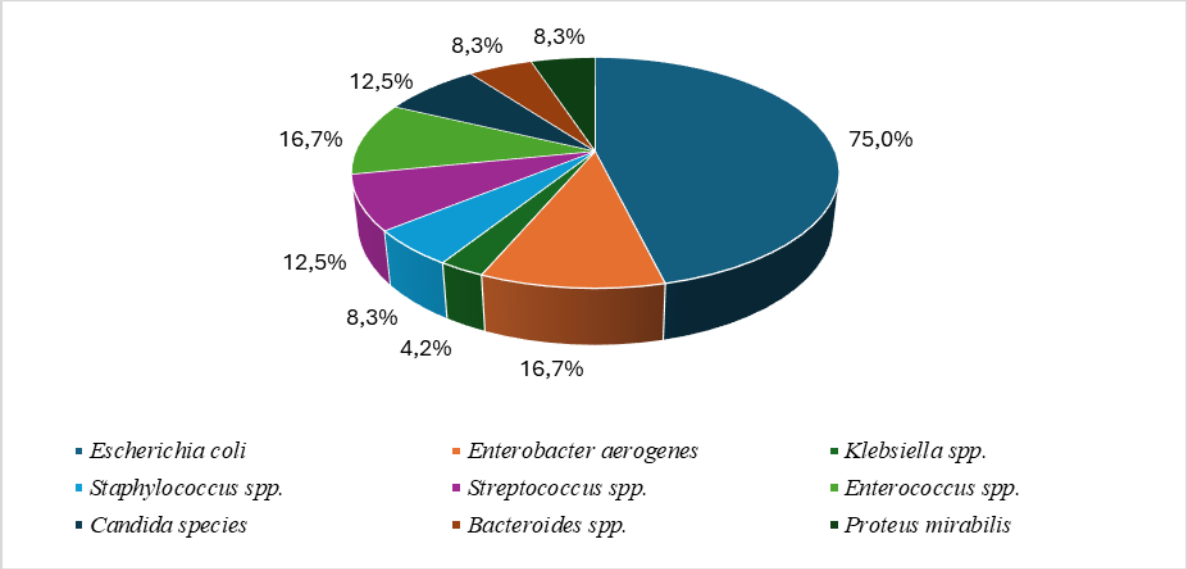

Figure 3 – Percentage distribution of isolated microorganisms of the parietal intestinal biotope in animals with acute generalized peritonitis

Table 3 – Composition of isolated microflora of the parietal intestinal biotope of animals with acute generalized peritonitis

Type of microorganism	**Frequency of isolation of microorganism strains, %**					
	Day 1		Day 3		Day 7	
	n=8	%	n=8	%	n=8	%
Escherichia coli	7	87.5	6	75.0	5	62.5
Enterobacter aerogenes	1	12.5	1	12.5	2	25.0
Klebsiella spp.	-	-	-	-	1	12.5
Staphylococcus spp.	1	12.5	1	12.5	-	-
Streptococcus spp.	1	12.5	1	12.5	1	12.5
Enterococcus spp.	1	12.5	1	12.5	2	25.0
Candida species	-	-	1	12.5	2	25.0
Bacteroides spp.	-	-	1	12.5	1	12.5
Proteus mirabilis	-	-	1	12.5	1	12.5

On the third day of experimental AGP, monoculture was identified in 50.0% of cases. Among the two-component associations of microorganisms, *Escherichia coli* and cocci were more common (75.0%). In one case, the association was represented by *Enterobacter aerogenes* and *Proteus mirabilis.*

A lower frequency of *Escherichia coli* monocultures (25.0%) was found on the seventh day of experimental AGP. Two-component associations were cultured in 62.5% of cases, three-component microbial associations – in 12.5%. Microorganism associations consisted of gram-negative bacilli, among which *Escherichia coli* and *Enterobacter aerogenes* predominated, and gram-positive cocci, among which *Enterococcus spp.* predominated. In 25.0% of cases, associations of *Candida species* and *Escherichia coli* were cultured. The three-component microbial associations were represented by *Candida species, Escherichia coli,* and *Enterobacter aerogenes.* Associations of *Proteus mirabilis* and *Bacteroides spp.* were detected in only 12.5% of cases. This confirms the assumption that colonization of the small intestine by bacteria of the *Enterobacteriaceae* family contributes to endotoxemia in acute peritonitis, and an increase in the number of yeast-like fungi of the genus *Candida* may indicate decreased nonspecific resistance, impaired phagocytic

immune reactions, and decreased synthesis of secretory immunoglobulin A.

Endogenous intoxication in AGP potentiates the activation of lipid peroxidation processes, disruption of the immune defense of the small intestinal mucosa, reduction of the bioenergetic capabilities of myocytes, destruction of membranes, which leads to changes in morphological structures and morphometric relationships with the phenomena of local circulatory disorders. All this, taken together, causes dysfunction of myocytes and enterocytes, leading to overstretching of the intestine and the development of dynamic intestinal obstruction.

Thus, the pathogenesis of motor-evacuation disorders of the small intestine in AGP, taking into account the results of our studies, is shown in Figure 4.

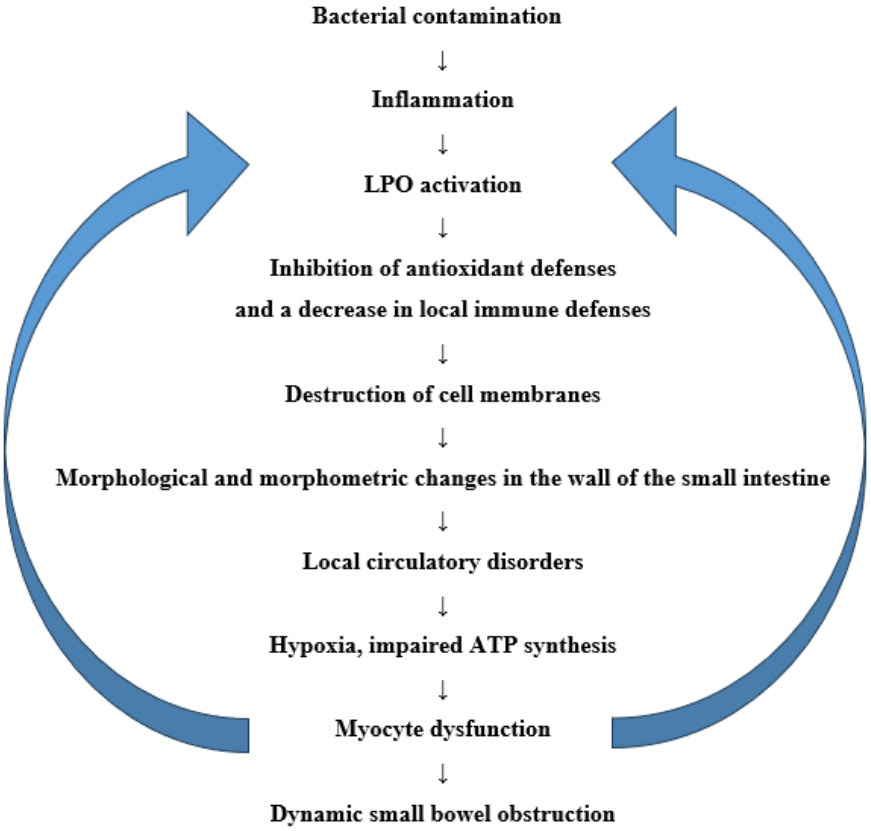

Figure 4 – Pathogenesis of motor-evacuation disorders of the small intestine in experimental acute generalized peritonitis

During a retrospective analysis of 50 medical records of deceased patients, it was found that the cause of death in 41 patients (82.0%) was MODS and bacterial-toxic shock; in 5 (10.0%) – pulmonary embolism, in 3 (6.0%) – cerebral pathology, in one patient (2.0%) – progression of pulmonary heart failure with the development of DIC syndrome. 4 patients (8.0%) were hospitalized in the reactive stage of peritonitis, 18 (36.0%) – in the toxic stage, and 28 (56.0%) – in the terminal stage. The Mannheim peritonitis index averaged 27.34 points.

Among the causes of mortality in this group, MODS was the most common. One of the main factors in the pathogenesis of this pathological condition is IFS. It was found that upon admission to the clinic, 36 (72.0%) patients had no intestinal motility, and 14 (28.0%) had decreased peristalsis. At the end of treatment, intestinal motility was absent in 41 (82.0%) patients, hypoperistalsis – in 6 (12.0%), and normal motility – in only 3 (6.0%). Therefore, as MODS progresses, small intestinal motility is usually absent, which contributes to worsening of organ and body system dysfunction. Intubation of the pathologically altered small intestine is necessary and mandatory in the treatment of this syndrome. Traditional methods of closing the abdominal cavity that are used nowadays are not always appropriate and effective, as they lead to increased intra-abdominal pressure and do not always allow for adequate sanitation of the abdominal cavity. This is indicated by the high mortality rate on the first, second, fourth, and fifth days after surgery (Fig. 5).

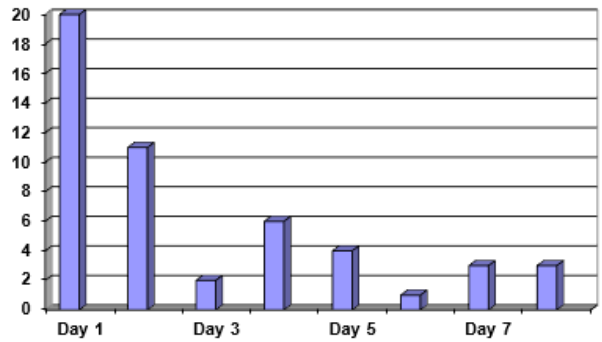

Figure 5 – Mortality in the postoperative period in patients with acute generalized peritonitis

A fatal outcome in operated patients occurred in the first two days in 31 (64.6%) cases, and on the fourth or fifth day in 10 (20.8%) cases. Thus, post-operative death of patients with AGP usually occurs due to MODS secondary to intoxication caused in most cases by functional obstruction of the small intestine. In a later period, 7 (14.6%) patients died as a result of decompensation of existing concomitant diseases.

Intubation of the small intestine was performed in only 14.6% of operated patients, while 20.8% of operated cases ended with laparostomy.

A study of patients with AGP with a favorable postoperative course yielded the following results. LII in patients before the operation was 5.26 ± 0.17 units, on the first day – 6.27 ± 0.21 units, on the third day – 3.66 ± 0.11 units, and only on the sixth-eighth day this indicator approached the normal level. On the first day after surgery, the adsorption capacity of erythrocyte membranes was (56.40 + 1.97)%, on the third day – (50.48 + 1.82)%, on the fifth day – 1.8 times less, and at discharge – 2.2 times less compared to the preoperative value. In 90% of cases, intestinal peristalsis was detected only at the end of the fourth day, and spontaneous gas passage was observed in almost 70% of patients on the sixth or seventh day.

Taking into account the results of the experimental study of acute peritonitis, a retrospective analysis of medical records of deceased patients with AGP, and data on the disease course in those who recovered, we applied the following algorithm of providing medical care to these patients. The use of these measures, according to the authors, can improve the treatment outcomes in patients with AGP and depends on the actions of the surgeon.

Before the operation, decompression of the digestive canal was performed against the background of intensive drug therapy aimed at correcting the patient's homeostasis, with the mandatory administration of antioxidants and concentrated glucose solutions; to reduce the intensity of intoxication, laparoscopic drainage or microlaparotomy under local anesthesia for drainage of the abdominal cavity was performed. During this period of time, along with intensive therapy, broad-spectrum antibiotics were administered intravenously.

After eliminating the source of peritonitis, lavage and drainage of the abdominal cavity, the operation was completed with intestinal decompression and, if necessary, a laparostomy was performed (in the terminal stage of AGP with the clinical picture of anaerobic peritonitis, for the prevention of compartment syndrome with severe dynamic obstruction of the small intestine).

In the postoperative period, along with the generally accepted correction of homeostasis and immune disorders, it will be advisable to carry out a set of measures aimed at the early restoration of the motor-evacuation function of the gastrointestinal tract.

To improve the functional state of the small intestine and its stimulation, from the first or second day after surgery, we used intracavitary pneumomassage of the small intestine against the background of parenteral administration of ATP solutions, concentrated glucose solutions, “Essentiale”, antioxidants, and calcium preparations, which are a necessary substrate for myocyte contraction.

We have developed a method for stimulating the motility of the digestive tract [16], namely the small intestine, in patients with AGP, which allows us to directly influence the rhythm drivers of peristalsis of the digestive tract in a “pulsating mode”. Thus, periodic irritation of the organ during the proposed method simulates the physiological conditions of food's effect on mechanoreceptors. The advantages of the method in patients with functional postoperative intestinal obstruction also include stimulation of motor function, increased bioelectrical capacity and redox processes in the tissues of the small intestine, improvement of the microcirculatory bed, and impact on microbial flora.

In 18 (13.6%) patients with AGP, the operation was completed with laparostomy. In 13 cases, this method was used during primary surgery, in 5 cases – during relaparotomy in patients with postoperative peritonitis. In seven cases, during relaparotomy, open intubation of the small intestine was performed using an end enterostomy after forced resection of the distal part of the organ using the proposed method [17] due to the ineffectiveness of closed antegrade decompression in unresolved AGP.

The intra-abdominal pressure has an equally important influence on the development of multiple organ failure. With an uncomplicated course of AGP, the value of this indicator on the first day after surgery was 12.75±2.12 mm Hg, while with restoration of motor-evacuator function of the small intestine, this

value was 8.50±1.40 mm Hg ($p<0.05$). Determination of intra-abdominal pressure is a prognostic criterion that complements the assessment of the postoperative period course.

Early restoration of the motor-evacuator function of the small intestine (on average, on the second or third day) contributes to a significant reduction in the level of general intoxication. Thus, the value of LII in patients with AGP was almost 2.9 times lower, and the concentration of MSM was 1.9 times lower than the preoperative value.

Thus, decompression and evacuation of the intestinal contents, prevention of increased intra-abdominal pressure by using laparostomy during surgery if indicated, as well as early drug correction of the motor-evacuator function of the small intestine make it possible to use the digestive tract as a system for body detoxification in a patient with AGP and to begin early enteral nutrition in order to accelerate recovery in the early postoperative period.

Conducting intracavitary pneumomassage using ATP solutions, concentrated glucose solutions, “Essentiale”, antioxidants, and calcium preparations, along with standard therapy, allows restoring small intestinal motility in 2-3 days after surgery, which makes it possible to transfer patients to enteral nutrition, reduce the manifestations of IFS, and prevent the occurrence of abdominal sepsis.

DISCUSSION

The changes in oxidant-antioxidant reaction indicators in the process of complex treatment of patients with AGP are of great practical importance, as they are indicators of the treatment efficacy and allow choosing the correct treatment approach [18]. The results of our studies confirm that the development of experimental AGP is accompanied by the activation of free radical lipid oxidation, and the detected changes in the levels of TBA-AP and LOOHs are of a multidirectional nature and depend on the observation period. The obtained data on the changes in the main indicators of the antioxidant system observed in the blood of rats indicate the active participation of the glutathione system, catalase, and superoxide dismutase in detoxification processes. The results of our work are consistent with the data of Mammadova E. T., who indicated oxidative stress as a key link in multiorgan dysfunction in peritonitis [19].

As AGP progresses in the abdominal cavity, efferent impulses coming from the enteroreceptors of the affected peritoneum and mesentery cause a decrease in volumetric blood flow in the mesenteric basin and impaired microcirculation in the intestinal wall, along with inhibition of the motor function of the small intestine. Our histological study of the small intestine in animals with AGP verified the increase in dystrophic and necrobiotic changes in columnar epithelial cells secondary to microcirculatory vessels' reaction during the reactive, toxemic, and terminal stages of acute peritoneal inflammation. Similar to our results, Adilbekova D. et al. [20] also reported that in the pathogenesis of small intestinal lesions, changes in the vessels of the microcirculatory bed are of great importance, which subsequently lead to impaired cell trophism, tissue hypoxia, damage to cellular elements, impaired cellular metabolism, deficiency of energy and plastic materials, and accumulation of metabolic products in cells and tissues. Microcirculatory disorders of the mucous and submucosal layers of the small intestinal wall are a morphological manifestation of intestinal failure; they characterize the severity of inflammation in the small intestine and the clinical prognosis of the disease [21].

We found that as degenerative changes in the small intestine wall increase, ATP formation in the muscularis mucosa of the small intestine decreases, especially in the terminal stage of AGP. This finding confirms the hypoxic origin of bioenergetic disorders associated with intestinal ischemia [6]. The concentration of ATP in the intestinal wall determines mucosal permeability in vivo. Increased permeability may be due to intra-abdominal hypertension and microflora activity. Translocation of bacteria and their toxins from the lumen of the gastrointestinal tract into the blood contributes to the transformation of the intestine into a source of endotoxicosis, leads to generalization of infection with subsequent dysfunction of target organs, and determines the further course of the disease and its outcome. A number of studies support the idea that AGP is a disease of polymicrobial etiology with a high quantitative composition of *Enterococci, Escherichia coli, Enterobacteriaceae, Candida spp* [22], and *Escherichia coli* and *Enterococcus faecium* [23]. We found that the progression of acute peritoneal inflammation was accompanied by quantitative changes in the microbiota of the parietal intestinal biotope, namely, an increase in the number of two-component and three-component microbial associations. Our work demonstrated that qualitative changes in the intestinal microbiocenosis were characterized by a decrease in the number of *Escherichia coli* strains isolated in monoculture and an increase in the number of strains of *Enterobacter aerogenes, Enterococcus spp.,* and *Candida species*.

Against the background of the identified morphological changes in the small intestine, we observed a decrease in the level of Ig-A producing plasma cells, which indicated a violation of the mucosal defense and favorable conditions for microbial adhesion. The growth of IgM and IgG-producing

plasma cells confirmed the activation of the secondary humoral response.

At the clinical stage, we found that in 72% of deceased patients, intestinal motility was absent, which correlated with the severity of MODS. This is consistent with the data of Klingensmith and Coopersmith (2016), who considered the gut as a "driver of multi-organ dysfunction" in critical conditions [24].

The use of intestinal decompression and intracavitary pneumomassage in our study contributed to improved motility and reduced intoxication levels in clinically favorable cases, which confirmed the effectiveness of physiological stimulation of intestinal peristalsis as part of pathogenetic therapy [16].

Thus, the results of the study demonstrate the multifactorial pathogenesis of motor-evacuation disorders in AGP and confirm the feasibility of using a comprehensive approach to early diagnosis and treatment of intestinal failure syndrome.

CONCLUSIONS

1. Clinical manifestations of intestinal failure syndrome in experimental peritonitis are accompanied in the early stages by an increase in endogenous intoxication, activation of lipid peroxidation, and impaired immune defense of the small intestinal mucosa against the background of dystrophic and necrobiotic lesions of epithelial cells.

2. To prevent the occurrence of increased intra-abdominal pressure in the postoperative period, it is necessary to use surgical methods of reducing intra-abdominal pressure: intestinal decompression and laparostomy (in the terminal stage of AGP with the clinical picture of anaerobic peritonitis, for the prevention of compartment syndrome with severe dynamic obstruction of the small intestine).

The use of intracavitary pneumomassage against the background of drug correction (administration of ATP solutions, concentrated glucose solutions, "Essentiale", antioxidants, and calcium preparations as a necessary substrate for myocyte contraction) contributes to the improvement of the functional state of the small intestine and the early restoration of the passage of chyme through the digestive canal in patients with acute generalized peritonitis.

AUTHOR CONTRIBUTIONS

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

FUNDING

Nil.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

REFERENCES

1. Špička P, Chudáček J, Řezáč T, Vomáčková K, Ambrož R, Molnár J, Klos D, Vrba R. Prognostic significance of comorbidities in patients with diffuse peritonitis. *Eur Surg*. 2022;54:309–316. https://doi.org/10.1007/s10353-022-00780-w
2. Pathak A, Agrawal V, Sharma N, Karan K, Bagla Ch, Fouzdar A. Prediction of mortality in secondary peritonitis: a prospective study comparing p-POSSUM, Mannheim Peritonitis Index, and Jabalpur Peritonitis Index. *Perioper Med (Lond)*. 2023;12(1):65. https://doi.org/10.1186/s13741-023-00355-7
3. Mesa IO, Ferrer RH, Mora BR, Matos RYA, Travieso PG. Morbidity and mortality due to secondary peritonitis in the surgery service. *Revista Cubana de Cirugía*. 2019;58(2):1-13. Retrieved from: https://www.medigraphic.com/pdfs/cubcir/rcc-2019/rcc192f.pdf
4. Inukai K, Usui A, Yamada M, Amano K, Mukai N, Tsunetoshi Y, Nakata Y, Yokota J. Open abdominal management for perforative peritonitis with septic shock: a retrospective analysis on usefulness of a standardized treatment protocol. *Eur J Trauma Emerg Surg*. 2021;47:93–98. https://doi.org/10.1007/s00068-019-01132-2
5. Moroz P, Kotelban A. New approaches to the treatment of acute peritonitis. *Experimental and Clinical Medicine* [Internet]. 2022Jun.30 [cited 2025Feb.4];91(2):38-3. Retrieved from: https://ecm.knmu.edu.ua/article/view/777
6. Serban C, Toma A, Constantin B, Tocu G, Tudorascu I, Mihalache D, Bulgaru F, Mihailov R, Trus C, Popazu C, Voicu D. Unraveling the Mechanisms of Intestinal Insufficiency in Acute Peritonitis: A Comprehensive Overview. *Preprints*. 2024; 2024020184. https://doi.org/10.20944/preprints202402.0184.v1
7. Clements TW, Tolonen M, Ball CG, Kirkpatrick AW. Secondary Peritonitis and Intra-Abdominal Sepsis: An Increasingly Global Disease in Search of Better Systemic Therapies. *Scand J Surg*.

2021;110(2):139-149. https://doi.org/10.1177/1457496920984078. PMID: 33406974.
8. Benedyct V, Prodan A, Bahrii V, Dzhyvak V. A Modern View of the Causes and Mechanisms of the Development of Acute Disseminated Peritonitis. *J Educ Health Sport*. 2022;12:206-212. https://doi.org/10.12775/JEHS.2022.12.04.018.
9. Linder MM, Wacha H, Feldmann U, Wesch G, Streifensand RA, Gundlach E. Der Mannheimer Peritonitis-Index. Ein Instrument zur intraoperativen Prognose der Peritonitis [The Mannheim peritonitis index. An instrument for the intraoperative prognosis of peritonitis]. *Chirurg*. 1987 Feb;58(2):84-92. German. PMID: 3568820.
10. Kalf-Kalif YYa. On the leukocyte intoxication index and its practical significance. *Medical practice*. 1941;1:31-35.
11. Gabrielyan NI, Lipatova VI. [Experience in the use of middle molecule content in blood as a diagnostic criterion in children with kidney diseases]. *Lab. Delo*. 1984; 3(19):138-140.
12. Togaybayev AA, Kurguzkin AV, Rikun IV. [The method of diagnosis of endogenous intoxication]. *Lab. Delo.* 1988;9:22-24.
13. Kron IL, Harman PK, Nolan SP. The measurement of intra-abdominal pressure as a criterion for abdominal re-exploration. Ann Surg. 1984 Jan;199(1):28-30. https://doi.org/10.1097/00000658-198401000-00005. PMID: 6691728; PMCID: PMC1353253.
14. Vlizlo VV, Fedoruk RS, Ratych IB. *Laboratorni metody doslidzhen' u biolohii, tvarynnytstvi ta veterynarnii medytsyni* [Laboratory methods of investigation in biology, stock-breeding and veterinary]. Lviv: Spolom Publ., 2012, 764 p.
15. Cohn WE, Carter CE. The separation of adenosine polyphosphates by ion exchange and paper chromatography. J.Amer.Chem.Soc.1950;2:4273-4275. https://doi.org/10.1021/ja01165a506
16. Benedykt VV. Patohenetychne obhruntuvannia medykamentoznoi stymuliatsii motoryky travnoho kanalu pislia operatsii u khvorykh na hostru neprokhidnist' tonkoi kyshky [Pathogenetic Substantiation of Drug Stimulation of Gastrointestinal Motility after Surgical Treatment in Patients with Acute Small-Bowel Obstruction]. *Halyts'kyi likars'kyi visnyk*. 2016;3(23):6-8.
17. Benedykt VV, inventor. *Sposib enterostomii* [Enterostomy method]. Ukrainian patent, no. 55573, 2003.
18. Bilyayeva OO, Karol IV, Kryzhevsky VV, Osadcha OI. Dynamics of indicators of oxidant-antioxidant reactions in the postoperative period in patients with disseminated peritonitis. *Paediatric Surgery (Ukraine)*. 2024;1(82): 18-26. https://doi.org/10.15574/PS.2024.82.18.
19. Mammadova ET. Endogenous intoxication indicators in advanced peritonitis and their correction. *Klinicheskaia khirurgiia.* 2021;1-2:39-44. doi: https://doi.org/10.26779/2522-1396.2021.1-2.39
20. Adilbekova DB, Abdurazzakov KS, Baimakov SR, Akhmedova SM. Morphological Aspects of Intestinal Failure in Experimental Peritonitis And Correction. *Texas Journal of Medical Science.* 2023;18:63-69. https://doi.org/10.62480/tjms.2023.vol18.pp63-69
21. Liesnyi VV, Liesna AS, Filonenko VO. Morfolohichna kharakterystyka syndromu enteral'noi nedostatnosti pry rozlytomu perytoniti [Morphological characteristic of the syndrome of enteral insufficiency in diffuse peritonitis syndrome]. *Kharkivs'ka khirurhichna shkola*.2018;90(3):22–26.
22. Steinbach CL, Töpper C, Adam T, Kees MG. Spectrum adequacy of antibiotic regimens for secondary peritonitis: a retrospective analysis in intermediate and intensive care unit patients. *Ann Clin Microbiol Antimicrob*. 2015; 14:48. https://doi.org/10.1186/s12941-015- 0110-4.
23. Mačiulienė A, Maleckas A, Kriščiukaitis A, et al. Predictors of 30-Day InHospital Mortality in Patients Undergoing Urgent Abdominal Surgery Due to Acute Peritonitis Complicated with Sepsis. Med Sci Monit. 2019; 25:6331-6340. https://doi.org/10.12659/MSM.915435
24. Klingensmith NJ, Coopersmith CM. The Gut as the Motor of Multiple Organ Dysfunction in Critical Illness. *Crit Care Clin*. 2016;32(2):203-212. https://doi.org/10.1016/j.ccc.2015.11.004

Received 15.02.2025

Accepted for publication 27.03.2025

Published 30.03.2026