ALTERATIONS IN THE INTESTINAL WALL'S HISTOLOGICAL STRUCTURE UNDER CONDITIONS OF EXPERIMENTAL OBSTRUCTIVE ILEUS

[a]VALENTIN NEPOMNYASHCHY, [b]TAMARA TAMM,
[c]IVAN MAMONTOV, [d]OLENA SHAKALOVA,
[e]KONSTANTIN KRAMARENKO, [f]ANDREY USTINOV

[a,b,c,d,e,f]Kharkiv National Medical University, Kharkiv, Ukraine.
email: [a]doktor.nep@gmail.com, [b]tamm_ti@ukr.net,
[c]ivan.n.mamontov@gmail.com, [d]shakalovahelena@gmail.com,
[e]kakram1966@gmail.com, [f]drustinovkharkiv@gmail.com

Abstract: In 50-86% of cases, patients with obstructive ileus develop various types of purulent complications, which are the primary cause of fatalities. It is believed that these complications are caused by the microflora present in the lumen of the intestinal tube. The existing methods of preventing purulent complications in ileus, aimed at affecting the microorganisms residing in the intestinal lumen, have not reduced the number of purulent-septic complications. There arose a need to clarify the location of a potential source of purulent complications in acute intestinal obstruction (AIO). To this end, an experiment was conducted to study the dynamic changes in the histological structure of the intestinal wall during obstructive ileus over 48 hours. The experiment was carried out on 12 white rats. The animals were divided into two groups. The first group (control) consisted of four animals which underwent laparotomy under general anaesthesia without any intervention on the intestines. The second group consisted of eight animals, in which, after laparotomy, the lumen of the small intestine was ligated at the midpoint of its length to create a complete obstruction, and the laparotomy wound was tightly sutured. After the animals were withdrawn from the experiment, a histological examination of the intestinal wall was performed at 12, 24, 36, and 48 hours. The experiment results showed that no changes in the control group animals were detected in the abdominal organs during the indicated time frames. Examination of the histological structure of the intestinal wall showed that the average thickness of the mucous membrane was 0.45±0.05 mm, the muscle layer 0.05±0.10 mm and the ratio of villi height to crypt length was 2.5:1. Columnar enterocytes with a height of 31±0.5 microns, with a distinct striated border on the apical surface, were identified. In the group of animals with experimental ileus, after 12 hours, the intestinal lumen was found to have increased to 6-8 mm above the site of obstruction, and serous effusion was observed in the abdominal cavity. These signs progressed, and after 48 hours, the intestine above the obstruction site was 2.5 times larger than usual, bluish-purple in colour, and the amount of effusion in the abdominal cavity had increased and became cloudy. Histological examination of the control group revealed no structural abnormalities in the intestinal wall throughout the experiment. In the group of animals with experimental obstructive ileus, signs of purulent inflammation in the intestinal wall were already observed 12 hours after the onset of AIO. It was established that purulent inflammation of the intestinal wall begins on the mucosal side. The trigger for this phenomenon is removing the protective layer from the villi of the intestinal enterocytes. Over time, the inflammatory process progresses, spreading to the muscle layer and ultimately to the serosal layer. The observed inflammatory changes in obstructive ileus develop above the obstruction site and along the entire length of the afferent intestinal segment. Thus, based on the histological study, it was determined that the source of purulent complications in obstructive ileus may be the wall of the intact segment of the intestine located above the obstruction site.

Keywords: Obstructive ileus, Intestine, Experiment, Complications, Histological structure, Microorganisms.

1 Introduction

Postoperative mortality in patients with acute intestinal obstruction (AIO) exceeds 17% and currently shows no tendency to decrease (Van Maanen et al., 2019; Radzikhovskiy et al., 2012; Biliaieva et al., 2014; Usenko & Voitiv, 2019; Tamm et al., 2012, 2015; Rami Reddy & Cappell, 2017). One of the most common causes of adverse outcomes is purulent-septic complications, which develop in 50-86% of cases (Kondratenko, 2013; Radzikhovskiy et al., 2012; Biliaieva et al., 2014; Usenko & Voitiv, 2019; Tamm et al., 2012; Long et al., 2023), with postoperative peritonitis accounting for 35-56%, anastomotic failure for 6.2-17.5% (Usenko & Voitiv, 2019; Tamm et al., 2012, 2015; Amanova & Kuanyshev, 2019; Bordeianou, 2022; Griffiths & Glancy, 2020), and suppuration of postoperative wounds for 2.7-37.8%. Several publications suggest that the source of purulent-septic complications in patients with ileus is the microflora present in the intestinal lumen (Kondratenko, 2013; Bordeianou, 2022; Chen et al., 2012; Griffiths & Glancy, 2020; Hartmann et al., 2019; Edizsoy et al., 2020).

Based on this, several methods of preventing purulent-septic complications have been proposed in practical medicine: nasointestinal intubation with the evacuation of the intestinal contents, intraoperative intestinal lavage, and trans-tube administration of antibacterial drugs (Usenko & Voitiv, 2019; Amanova & Kuanyshev, 2019; Edizsoy et al., 2020; Hartmann et al., 2019). It has been suggested that broad-spectrum antibacterial drugs should be administered parenterally, not therapeutically, but prophylactically. All these methods were proposed empirically, and some are pretty traumatic. For example, with nasointestinal intubation, desquamation of the intestinal mucosa occurs, and the procedure itself does not reliably reduce the number of purulent complications (Biliaieva et al., 2014; Amanova & Kuanyshev, 2019; Rami Reddy & Cappell, 2017; Long et al., 2023; Griffiths & Glancy, 2020; Edizsoy et al., 2020). The introduction of antibacterial drugs via a tube lacks evidence, and there is contradictory data regarding the choice of antibacterial drug type and dosage (Tamm et al., 2012, 2015).

Thus, the high mortality rates caused by the frequent development of purulent-septic complications in the postoperative period in patients with AIO necessitate clarification of the source of purulent complications in this patient category.

2 Literature review

Postoperative intestinal obstruction is a common occurrence and a significant clinical problem. Researchers are conducting studies to understand the mechanisms underlying obstructive ileus. It is widely studied in patients and experimental models on laboratory animals. A wide range of treatments has been tested to prevent or alter the course of this disorder (Edizsoy et al., 2020; Hartmann et al., 2019; Georgopoulos et al., 2020; Tamm et al., 2019; Wattchow et al., 2021).

Classically, ileus refers to a transit disruption, and most published studies have been conducted on postoperative patients (Ariès&Huet, 2020). Small bowel obstruction is one of the most common conditions in emergency surgical departments (Śmiechowicz, 2022; Markwart et al., 2020). Without addressing problematic intestinal segments, patients can develop multiple organ failure. Additionally, small bowel obstruction can cause significant structural and quantitative changes in the gut microbiota and disrupt the intestinal mucosal barrier (Mo et al., 2021; Bessard et al., 2024).

Modern experimental studies have shown that small bowel obstruction entails time-dependent damage to the mucosal epithelium. Simultaneously, molecular changes in the intestinal mucosal barrier occur as early as 3 hours after the onset of small bowel obstruction, with subsequent increased permeability. Initial intestinal hypermotility is followed by a reduction in peristalsis (Hartmann et al., 2019; Mavrigiannaki & Georgopoulos, 2024).

Excessive bacterial growth in the small intestine is associated with symptoms of functional gastrointestinal disorders, although the mechanisms remain poorly defined, and treatment involves nonspecific antibiotics. Changes in the microbiome composition indicate potential consequences for the functional capacity of the small intestine, particularly in the digestion of dietary carbohydrates and fibre. The study by Saffouri et al. (2019) found that a short-term shift to a low-fibre diet leads to altered intestinal permeability and gastrointestinal symptoms related to changes in microbial diversity.

It has been established that changes in gut microbiota may play an essential role in the pathogenesis of ileus. In a mouse model of partial significant bowel obstruction, changes in the microbiota composition were found, specifically a decrease in *Bacillota* and an increase in *Pseudomonadota* and *Bacteroidota* (Hegde et al., 2018). Moreover, complete small bowel obstruction leads to a reduction in Bacillota, an increase in Pseudomonadota, Verrucomicrobia, and Bacteroidota, and a disruption of the intestinal mucosal barrier (Mo et al., 2021).
As obstructive ileus progresses, the occlusion of the lumen leads to the accumulation of fluid and gas due to excessive bacterial

growth proximal to the site of obstruction. The intestinal wall gradually stretches, thickens, and eventually becomes paralysed due to the blockage, which can typically lead to complications such as enteritis, sepsis, and even complete intestinal obstruction. Small bowel obstruction can change the predominant bacterial groups in the intestine. Depleted functional profiles of the gut microbiota have been found in experimental studies by Wang et al. (2023). Therefore, characterising the microbial composition of the small intestine is essential, as this may allow for a more targeted antibiotic approach in patients with purulent-septic postoperative complications.

It has been shown that the intestinal barrier is altered after intestinal resection due to signalling through toll-like receptor 4 (TLR4) at the gut level. Excessive bacterial growth is associated with increased bacterial translocation, indicating changes in intestinal permeability. It has been found that barrier dysfunction, which leads to increased permeability, occurs through two main pathways: paracellular and transcellular. Paracellular permeability is regulated by intercellular complexes, namely desmosomes, adhesions, and tight junctions (TJs). In transcellular permeability, molecules are transported through intestinal epithelial cells via endocytosis, passive diffusion, or binding to specific membrane carriers (Courtney et al., 2021).

Experimentally induced acute obstructive ileus causes significant bacterial translocation in rats. In conditions of intestinal obstruction, the colonisation of the proximal part of the small intestine by intestinal flora occurs (Belyansky et al., 2002). Lipopolysaccharide, the main component of the outer membrane of gram-negative bacteria, is a potent endotoxin responsible for organ dysfunction during sepsis. It is present in the bloodstream in gram-negative infections and gram-positive and fungal infections, likely due to sepsis-related disruption of the intestinal barrier (Caroff & Novikov, 2020; Śmiechowicz, 2022). It has been established that disruption of the intestinal barrier function and subsequent translocation of microorganisms and their metabolic products play a critical role in developing septic complications in many systemic and intra-abdominal pathologies, such as after obstructive intestinal obstruction.

Various extracellular and intracellular pathways are involved in endotoxin perception, and it is believed that non-canonical caspase-mediated pyroptosis activation plays a significant role in sepsis pathophysiology. Endotoxin induces specific pathological changes in several organs, contributing to poor outcomes (Nguyen et al., 2021; Śmiechowicz, 2022; Radocchia et al., 2021).

The current issue is finding ways to prevent and overcome purulent-septic complications in the postoperative period in patients with ileus. In their study, Hartmann et al. (2021) found that preoperative mechanical bowel preparation prevents permeability and leukocyte infiltration of the intestinal wall in the early phase of postoperative intestinal obstruction in mice. Meanwhile, Hegde et al. (2018) demonstrated that antibiotic destruction of the microbiota had little effect on changes in inflammation, motility, or bacterial translocation associated with obstruction.

Thus, postoperative intestinal obstruction causes pathophysiological changes in mucosal permeability and intestinal inflammatory immune response. Moreover, obstruction disrupts the small intestine's biocenosis and pronounced dysbacteriosis of the large intestine.

Research aim: To examine the dynamics of the histostructure of the intestinal wall in experimental obstructive ileus to clarify the localisation of the source of purulent-septic complications.

To achieve the goal of the study, the following research tasks were determined:

- To simulate obstructive ileus in white rats under experimental conditions;
- To study the histostructure of the intestinal wall using the model of obstructive ileus;
- To identify the specific morphological changes in the wall of the small intestine during experimental obstructive ileus;
- To determine the causes of purulent-septic complications in obstructive ileus.

3 Materials and methods

The experiment was carried out on 12 white rats. The animals were divided into two groups. The first group (control) consisted of 4 animals, which underwent laparotomy under general anaesthesia, following aseptic rules, without any intervention on the intestines. After this, the wound was tightly sutured. The second group consisted of 8 animals, where, after laparotomy, a ligature was used to tie off the intestinal lumen at the midpoint, and the laparotomy wound was tightly sutured (S.A. Shalimov, 1984). In each group, the animals were withdrawn from the experiment after 12, 24, 36, and 48 hours by administering a lethal dose of anaesthetic. All manipulations in the experiment were carried out by international requirements for experimental research (Geneva, 2004) and the Law of Ukraine "On the Protection of Animals from Cruelty" dated 21.02.2006, No. 3477.

After the animals were withdrawn from the experiment, during the autopsy, the condition of the intestinal loops was evaluated: their serous cover, diameter, the presence of effusion in the abdominal cavity, quantity, and nature. In the second group of animals, two fragments of the small intestine weighing 1 gram each were taken, one of which was located 1 cm above the obstruction site and the other 1 cm below the border of the duodenum. In the obtained biopsy samples, the dynamics of the intestinal histostructure were studied at 12, 24, 36, and 48 hours. In the control group, histostructure analysis of 2 biopsy samples of the intestinal wall was also performed at these time points after laparotomy. The identified changes in the control group and the group with obstructive ileus were then compared.

4 Results

After the animals in the control group were withdrawn from the experiment, no abnormalities were found during the inspection of the abdominal organs at the specified time points.

In animals with induced acute ileus, after 12 hours, an expansion of the intestinal segment up to 6-8 mm above the obstruction site was observed in the abdominal cavity, with the serous membrane appearing shiny. Below the ligature, the small intestine was collapsed. A small amount of serous fluid was present in the abdominal cavity.

After 24 hours, the intestine above the ligature remained the same size but had a cyanotic tint, while below the ligature, the intestinal lumen was collapsed, with a shiny serous membrane. After 36 hours, in the group of animals with obstructive ileus, the nature of the effusion in the abdominal cavity became cloudy with an unpleasant odour. The intestine above the ligature had acquired a bluish-purple colour. The segment of the intestine below the ligature had slightly expanded but retained its standard colour. After 48 hours of ileus in the animals, dark spots appeared on the intestine above the obstruction against the background of a dull serous membrane. The fluid in the abdominal cavity became cloudy with a colibacillaryodour and a mixture of fibrin.

Histological examination of the intestinal biopsies at the specified time points showed that the thickness of the small intestine's mucosal wall in the control group was 0.5±0.02 mm. In contrast, the thickness of the unchanged muscular layer was 0.95±0.01 mm. The ratio of villi height to crypt length in the mucous membrane was 2.5:1. Cylindrical cells predominated in the crypts, among which goblet cells were also found. Paneth cells (5.0±1.0 per crypt) were located in the deep sections of the crypts. Among the cylindrical cells of the crypts, cells with mitotic figures were found, comprising 4.5 ± 0.5 per crypt.

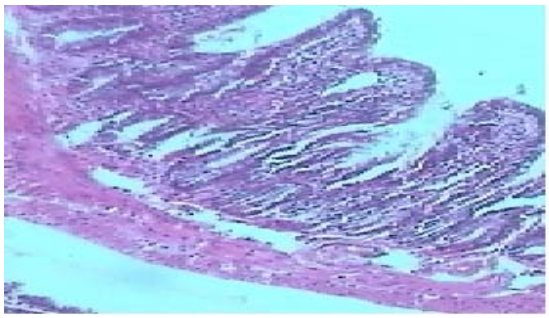

Figure 1. Histostructure of the intestinal wall villi under normal conditions: the apical surface is covered with cylindrical epithelium, and a distinct striated border is visible.Staining H&E x 100

In the epithelial covering of the villi, there are intraepithelial lymphocytes of 161.0±17.4 per 1000 epithelial cells. In the lamina propria of the mucosa, loose fibrous connective tissue predominates, containing 16.0 ± 4.5 small lymphocytes per villus (Figure 2).

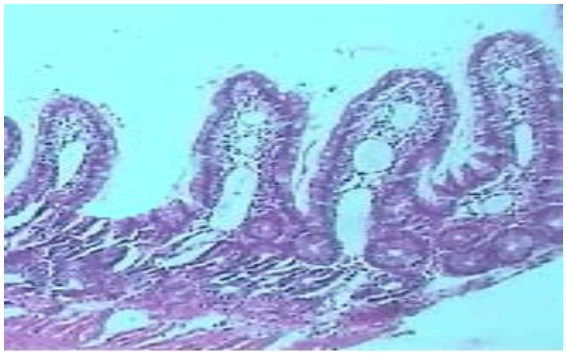

Figure 2. Histostructure of the intestinal wall under normal conditions: the lamina propria of the mucosa is represented by loose connective tissue containing small lymphocytes and plasma cells. Staining H&E x 100

The analysis of morphological changes in the wall of the small intestine during obstructive ileus, based on the observation periods in animals, showed the following dynamics. Twelve hours after the formation of acute intestinal obstruction (AIO), a morphological examination of the wall of the afferent section of the intestine showed an increase in the thickness of the villi to 0.135±0.014 mm, and the ratio of villi height to crypt length decreased by half, amounting to 1.9:1. The height of the brush-border enterocytes decreased to 28.7±0.5 µm. It should be noted that during this period, the thickness of the muscle layer did not change and remained 0.95±0.02 mm.

At the same time, the brush border of the enterocytes was difficult to trace in most of the villi, and focal bacterial accumulations were found on the epithelial surface. Goblet cells were found only in the basal sections of the villi, and their ratio to brush-border enterocytes in the epithelial lining was 1:3. The number of mitoses detected per crypt was 5.6±0.2, and the number of Paneth cells increased to 5.7±0.1.

The mucosal structure's cellular composition changed towards an increase in the number of intraepithelial lymphocytes, which amounted to 185.0±29.0 per 1000 epithelial cells at this time point. The oedema of the villi's lamina propria was so pronounced that the oedematous fluid, in some areas, separated them from the covering epithelium. Among the lymphocytes, numerous neutrophilic leukocytes, sometimes clustered, appeared and were also detected in the epithelial covering of the villi (Figure 3).

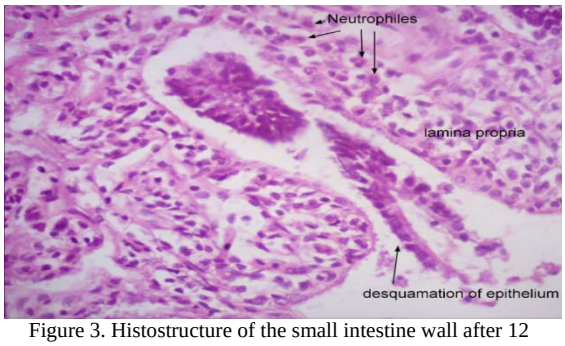

Figure 3. Histostructure of the small intestine wall after 12 hours: epithelial desquamation, pronounced oedema of the villi stroma, lymphocytic-leukocytic infiltration of the villi stroma, as well as congestion of the microvessels. Staining with haematoxylin and eosin, x180

After 24 hours, the thickness of the intestinal mucosal wall decreased to 0.35±0.06 mm, which was associated with the progressive increase in the diameter of the intestinal segment above the obstruction site. Furthermore, the thickness of the villi sharply increased, with the epithelial covering removed from their surface (Figure 4). At the same time, abundant bacterial colonies were found on the surface of the villi.

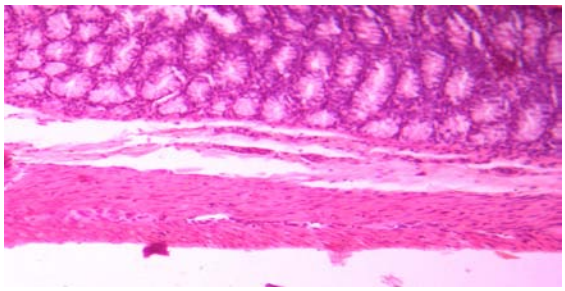

Figure 4. Histostructure of the intestinal mucosa after 24 hours: partial detachment of the covering epithelium, lymphocytic-leukocytic infiltration of the villi stroma, and leukostasis in the vessels. Staining H&E x180

After 36 hours of mechanical ileus, the degenerative process in the mucosa was most significantly pronounced. This manifested as an almost complete absence of the villi covering epithelium and the presence of a large number of bacteria (Figure 5), with the imbibition of the villi stroma by polymorphonuclear leukocytes and the penetration of microflora into the submucosal layer (Figure 6).

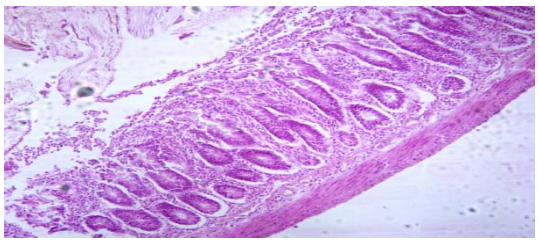

Figure 5. Histostructure of the villi after 36 hours: pronounced oedema of the stroma and almost complete destruction of the epithelial covering, combined with extensive microbial colonisation. Staining H&E x180

The thickness of the intestinal mucosal wall at this time decreased to 0.22±0.13 mm. At the same time, markedly dilated microvessels with leukocyte margination, erythrocyte sludging phenomena, and leukocytic-fibrin thrombi were observed in the submucosal layer and serous membrane.

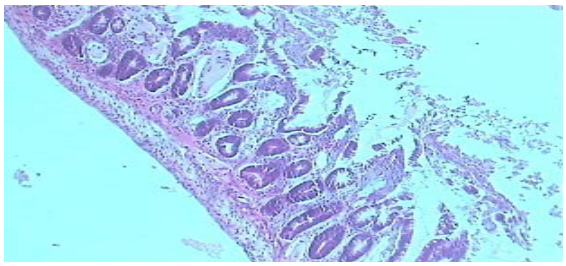

Figure 6. Histostructure of the small intestine mucosa after 36 hours: total desquamation of the villi epithelium, along with many bacterial colonies and neutrophilic leukocytes with translocation into the submucosal layer. Staining H&E x100

After 48 hours of mechanical ileus, it was practically impossible to determine the thickness of the villi in the studied animals due to total desquamation of the covering epithelium, pronounced imbibition of the stroma by polymorphonuclear leukocytes, a large number of microbial colonies on the mucosal surface, and "penetration" of some of them into the submucosal layer.

Ulcerative defects were identified, involving significant destruction of a large part of the muscular layer of the intestine, surrounded by a dense leukocytic perifocal infiltrate (Figure 7).

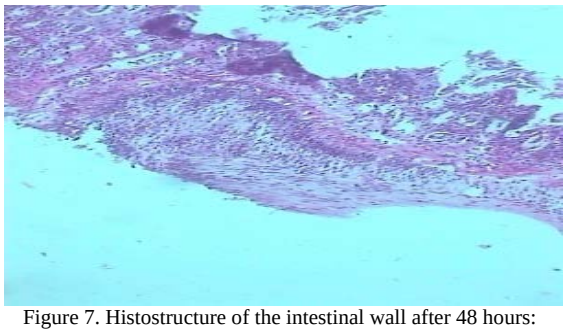

Figure 7. Histostructure of the intestinal wall after 48 hours: ulcerative defect of the intestinal wall. Staining with haematoxylin and eosin, x100

The serous membrane of the intestine was markedly oedematous with focal-diffuse leukocytic infiltrates. Leukocytic-fibrin thrombi were found in its vessels. On the surface of the serous membrane, massive deposits consisting of fibrinous-leukocytic debris mixed with a large number of bacterial colonies were localised. Their presence indicates a breach in the integrity of the intestinal wall. It is worth noting that some vessels of the serous membrane also contained bacterial colonies in their lumen.

In two animals of this group, after 48 hours, purulent-inflammatory destruction of the intestinal wall was most pronounced, with destruction of all its layers (Figure 8) and multiple ulcerative-necrotic defects.

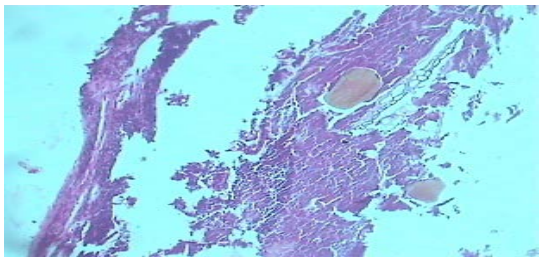

Figure 8. Histostructure of the intestinal wall after 48 hours: total necrosis of a section of the intestinal wall. Staining with haematoxylin and eosin, x100

5 Research discussion

A global study on the epidemiology of intestinal obstruction from 1990 to 2019 showed that intestinal obstruction is a common acute surgical disease, with an increase in incidence from 56.9% to 86.7% respectively (Long et al., 2023). The authors claim that elderly people are at higher risk of morbidity and mortality, and overall, intestinal obstruction "places a significant burden on modern healthcare systems." The rate of hospitalisation for ileus in the USA is 350,000 per year, with 65% due to adhesions, 10% due to hernias, 5% due to tumours, and 20% from other causes (Rami Reddy & Cappell, 2017).

Analysis of the literature data shows that the leading cause of mortality in patients with obstructive ileus is the development of various purulent complications. Many authors believe the source of purulent complications is the microflora in the intestinal lumen. In this regard, methods of preventing purulent complications by affecting the microflora in the intestinal lumen have been proposed (Kondratenko, 2013; Usenko & Voitiv, 2019). Introducing these proposed methods of prevention of purulent-septic complications (PSC) in acute intestinal obstruction (AIO) into clinical practice has not reduced the number of these complications or improved treatment outcomes.

The proposed methods and treatments in the clinic should generally be based on experimental evidence. Numerous studies have shown that the intestinal mucosa is the first to suffer during mechanical ileus (Tamm et al., 2012; Griffiths & Glancy, 2020; Edizsoy et al., 2020). In an experiment aimed at reducing mucosal damage during obstructive ileus, Edizsoy et al. (2020) offered animals food with probiotics. A feature of the experiment was that after 24-48 hours, the animals were re-operated, and the ileus was resolved by removing the ligature. Probiotic food was then introduced. The experiment noted that bacterial translocation was observed in the groups of animals without probiotics and, to a lesser extent, in those animals that received probiotics. The authors believe that further research is necessary.

Studies on experimental obstructive small bowel ileus have shown that changes in the barrier properties of the intestinal mucosa occur as early as 3 hours after the onset of obstruction, progressing over time. This is confirmed by increased permeability to protein molecules and decreased intestinal peristalsis (Edizsoy et al., 2020; Hartmann et al., 2019).

A targeted study of the microflora dynamics and the histostructure of the intestinal wall in obstructive ileus above the obstruction site was reflected in the works of Tamm et al. (2012, 2015). The authors did not examine the histostructure of the entire afferent segment of the intestine. In this regard, confirming or clarifying the dynamics of the histostructure of the intestinal wall, in which the passage of chyme is disrupted under the influence of microflora without treatment, is of particular interest.

A progressive experimental obstructive ileus model was used to study the stages of morphological changes in the intestinal wall. One link in the pathogenesis of acute intestinal obstruction (AIO) in obstructive ileus is the decolonisation of saprophytic microflora located in the lumen of the intestinal tube (Van Maanen et al., 2019).

In studying the histostructure of the intestinal wall in a model of obstructive ileus, it was found that as early as 12 hours after the development of intestinal obstruction, signs of progressive inflammation appear in the wall above the obstruction site, primarily manifesting in the mucosa (Tamm et al., 2012). This process occurs in the segment located directly above the obstruction site and at a distance from it, below the duodenum. Initially, the protective layer, which acts as a barrier for microorganisms, is removed from the surface of the villi. After that, abundant bacterial colonies appear on their surface, penetrating the villi stroma. This process is accompanied by forming a lymphocytic infiltrate containing segmented neutrophils. At the same time, oedema occurs in the submucosal layer of the intestine, where dilation of microvessels and the appearance of leukostasis at the margins are observed. The presence of bacteria and leukocytic-lymphocytic infiltration of the villi stroma at this stage indicates the onset of purulent

inflammation located directly within the thickness of the intestinal wall. During histological examination, signs of purulent inflammation were found throughout the entire segment of the intestine located above the obstruction site.

After 24 hours, the intestinal wall's inflammation becomes purulent, and after 36 hours, phlegmonous-purulent inflammation spreads through the entire thickness of the wall, reaching the muscular layer. The purulent-degenerative processes in the intestinal wall, which progress over time, lead to phlegmonous inflammation and microabscesses, with the involvement of the muscular layer while the serous membrane remains unaffected.

After 48 hours, areas of destruction of all layers of the intestinal wall appear, forming fibrinous-purulent peritonitis on the serous membrane.

Repeated experimental results showed that in obstructive ileus, the inflammation that develops in the intestinal wall spreads along the entire length of the intestine located above the obstruction site. As the obstruction progresses, phlegmonous enteritis develops in the afferent section of the intestine.

The authors who studied the histostructure of the intestinal wall in experimental obstructive ileus also found similar changes (Tamm et al., 2012, 2015). However, they studied biopsies directly above the obstruction site from the intestinal wall. Our research showed that the purulent inflammatory process occurs throughout the proximal section of the intestine, up to the obstruction site.

The process of purulent inflammation directly in the intestinal wall begins after removing the brush border, which performs a protective function. Within 36 hours, purulent inflammation spreads from the mucosa to the submucosal and muscular layers. The serous membrane was not involved in the inflammatory process during this time. However, by 48 hours of experimental ileus, histological examination revealed signs of purulent inflammation on the serous membrane. Thus, in progressive obstructive ileus, the source of purulent-septic complications is the microflora located within the inflamed intestinal wall rather than in the lumen of the intestinal tube. Why is this important? Because in patients with obstructive ileus, the target for antibacterial drugs should be the wall, not the intestinal lumen.

It can be assumed that after eliminating the cause of obstructive ileus, the source of purulent complications will be the phlegmonously altered intestinal wall, not the microflora in the intestinal lumen.

6 Conclusion

1. In the experiment with obstructive ileus, the protective mucous membrane layer is initially removed along the entire length of the intestinal section located above the obstruction site. As a result, the saprophytic microflora in the lumen of the intestinal tube penetrates its wall, transforming into pathogenic microflora and causing purulent inflammation.
2. Phlegmonous enteritis, which develops in the intestinal wall above the obstruction site in obstructive ileus, spreads through the entire wall thickness within 48 hours, involving all layers, including the serous membrane. After the cause of mechanical ileus is eliminated, the remaining section of the phlegmonously altered intestinal wall may serve as a source of purulent-septic complications.

Literature:

1. Amanova, D. E., & Kuanyshev, S. R.: The phenomenon of bacterial translocation in acute mesenteric ischaemia: a modern view of the problem. *Journal of Kazakhstan Karaganda*, 2019, 1(90), 23–35.
2. Belyansky, L. S., Sayenko, V. F., Furmanov, J. A., & Churilova, T. J.: Bacterial translocation as a cause for septic complications in obstructive colonic ileus. *Acta chirurgica Belgica*, 2002, 102(2), 75–77. https://doi.org/10.1080/00015458.2002.11679270
3. Bessard, A., Cardaillac, C., Oullier, T., Rolli-Derkinderen, M., Neunlist, M., & Venara, A.: Alterations of Prostanoid Expression and Intestinal Epithelial Barrier Functions in Ileus. *Gastrointestinal Surgery*, 2024, 296, 65–173. https://doi.org/10.1016/j.jss.2023.12.018
4. Biliaieva, O. O., Radzikhovskyi, A. P., Ivanchenko R. V., & Miroshnychenko A. P.: Microjejunostomy for intestinal obstruction, its feasibility as a method of enteral nutrition in the early postoperative period. *Clinical Surgery*, 2014, 11, 11–15.
5. Bordeianou, L., & Yeh, D. D.: Etiologies, clinical manifestations, and diagnosis of mechanical small bowel obstruction in adults. *UpToDate. Literature review current through*, 2022. 69 p.
6. Caroff, M., & Novikov, A.: Lipopolysaccharides: Structure, Function and Bacterial Identification. OCL., 2020, 27, 31. https://doi.org/10.1051/ocl/2020025
7. Chen, X. L., Ji, F., Lin, Q., Chen, Y. P., Lin, J. J., Ye, F., Yu, J. R., & Wu, Y. J.: A prospective randomised trial of transnasal ileus tube vs nasogastric tube for adhesive small bowel obstruction. *World journal of gastroenterology*, 2012, 18(16), 1968–1974. https://doi.org/10.3748/wjg.v18.i16.1968
8. Courtney, C. M., Onufer, E. J., McDonald, K. G., Steinberger, A. E., Sescleifer, A. M., Seiler, K. M., Tecos, M. E., Newberry, R. D., & Warner, B. W.: Small Bowel Resection Increases Paracellular Gut Barrier Permeability via Alterations of Tight Junction Complexes Mediated by Intestinal TLR4. *The Journal of surgical research*, 2021, 258, 73–81. https://doi.org/10.1016/j.jss.2020.08.049
9. Edizsoy, A., Yılmaz, E., Çevikel, M. H., Yenisey, Ç., Sakarya, S., & Meteoğlu, İ.: Gut mucosa in the rats exposed temporary mechanical obstruction fed with probiotic. *Turkish journal of trauma & emergency surgery: TJTES*, 2020, 26(6), 833–842. https://doi.org/10.14744/tjtes.2020.30269
10. Georgopoulos, I., Mavrigiannaki, E., Stasinopoulou, S., Renieris, G., Nikolakis, G., Chaniotakis, I., Tiniakos, D., & Papaconstantinou, I.: Experimental Models of Partial Intestinal Obstruction in Young Mice: Establishment, and Evaluation. *The Journal of surgical research*, 2020, 252, 206–215. https://doi.org/10.1016/j.jss.2020.03.007
11. Griffiths, S., & Glancy, D. G.: Intestinal obstruction. *Surgery (United Kingdom)*, 2020, 38(1), 43–50. https://doi.org/10.1016/j.mpsur.2019.10.014
12. Hartmann, L., Arndt, M., Hahn, E. M., Mueller, M. H., Kreis, M. E., & Hering, N. A.: Effect of bowel preparation on intestinal permeability and inflammatory response during postoperative ileus in mice. *Surgery*, 2021, 170(5), 1442–1447. https://doi.org/10.1016/j.surg.2021.05.014
13. Hartmann, L., Zhao, X., Macheroux, T., Kasparek, M. S., Kreis, M. E., & Mueller, M. H.: Time-Dependent Alterations of Gut Wall Integrity in Small Bowel Obstruction in Mice. *The Journal of surgical research*, 2019, 233, 249–255. https://doi.org/10.1016/j.jss.2018.07.038
14. Hegde, S., Lin, Y. M., Golovko, G., Khanipov, K., Cong, Y., Savidge, T., Fofanov, Y., & Shi, X. Z.: Microbiota dysbiosis and its pathophysiological significance in bowel obstruction. *Scientific reports*, 2018, 8(1), 13044. https://doi.org/10.1038/s41598-018-31033-0
15. Kondratenko, P. G.: *Guide to clinical surgery. Differential diagnostics and treatment of surgical diseases.* Donetsk, 2013. 752 p.
16. Long, D., Mao, C., Liu, Y., Zhou, T., Xu, Y., & Zhu, Y.: Global, regional, and national burden of intestinal obstruction from 1990 to 2019: an analysis from the Global Burden of Disease Study 2019. *International journal of colorectal disease*, 2023, 38(1), 245. https://doi.org/10.1007/s00384-023-04522-6
17. Markwart, R., Saito, H., Harder, T., Tomczyk, S., Cassini, A., Fleischmann-Struzek, C., Reichert, F., Eckmanns, T., & Allegranzi, B.: Epidemiology and burden of sepsis acquired in hospitals and intensive care units: a systematic review and meta-analysis. *Intensive care medicine*, 2020, 46(8), 1536–1551. https://doi.org/10.1007/s00134-020-06106-2
18. Mavrigiannaki, E., & Georgopoulos, I.: *Experimental Animal Models for Studying Intestinal Obstruction.* IntechOpen, 2024. https://doi.org/10.5772/intechopen.115008.

19. Mo, J., Gao, L., Zhang, N., Xie, J., Li, D., Shan, T., & Fan, L.: Structural and quantitative alterations of gut microbiota in experimental small bowel obstruction. *PloS one*, 2021, 16(8), e0255651. https://doi.org/10.1371/journal.pone.0255651
20. Nguyen, M., Pallot, G., Jalil, A., Tavernier, A., Dusuel, A., Le Guern, N., Lagrost, L., Pais de Barros, J. P., Choubley, H., Bergas, V., Guinot, P. G., Masson, D., Bouhemad, B., & Gautier, T.: Intra-Abdominal Lipopolysaccharide Clearance and Inactivation in Peritonitis: Key Roles for Lipoproteins and the Phospholipid Transfer Protein. *Frontiers in immunology*, 2021, 12, 622935. https://doi.org/10.3389/fimmu.2021.622935
21. Radocchia, G., Neroni, B., Marazzato, M., Capuzzo, E., Zuccari, S., Pantanella, F., Zenzeri, L., Evangelisti, M., Vassallo, F., Parisi, P., Di Nardo, G., & Schippa, S.: Chronic Intestinal Pseudo-Obstruction: Is There a Connection with Gut Microbiota? *Microorganisms*, 2021, 9(12), 2549. https://doi.org/10.3390/microorganisms9122549
22. Radzikhovskiy, A. P. et al.: *Intestinal Obstruction.* Kyiv: Phoenix, 2012, 503 p.
23. Rami Reddy, S. R., & Cappell, M. S.: A Systematic Review of the Clinical Presentation, Diagnosis, and Treatment of Small Bowel Obstruction. *Current gastroenterology reports*, 2017, 19(6), 28. https://doi.org/10.1007/s11894-017-0566-9
24. Saffouri, G. B., Shields-Cutler, R. R., Chen, J., Yang, Y., Lekatz, H. R., Hale, V. L., Cho, J. M., Battaglioli, E. J., Bhattarai, Y., Thompson, K. J., Kalari, K. K., Behera, G., Berry, J. C., Peters, S. A., Patel, R., Schuetz, A. N., Faith, J. J., Camilleri, M., Sonnenburg, J. L., Farrugia, G., … Kashyap, P. C.: Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. *Nature communications*, 2019, 10(1), 2012. https://doi.org/10.1038/s41467-019-09964-7
25. Śmiechowicz, J.: The Rationale and Current Status of Endotoxin Adsorption in the Treatment of Septic Shock. *Journal of clinical medicine*, 2022, 11(3), 619. https://doi.org/10.3390/jcm11030619
26. Tamm, T. I., Bogun, Ye. A., Nepomnyashchiy, V. V., Bardyuk, A. Ya., Ustinov, A. T., Gvozdik, Yu. A.: Stages of phlegmonous enteritis development as a source of purulent-septic complications in obturation intestinal obstruction. *Modern surgery and coloproctology*, 2012, 2(2), 98–102.
27. Tamm, T. I., Nepomnyashchiy, V. V., Shakalova, Ye. A., & Dvornik, I. A.: Prevention of purulent complications in mechanical bowel obstruction (experimental study). *Clinical Surgery*, 2015, 3, 65–79.
28. Tamm, T. I., Nepomnyaschy, V. V., Shakalova, O. A., Barduck, A. Ya.: Intestine wall histostructure peculiarities with peritonitis and mechanical intestine obstruction (experimental study). *Biomedical and Biosocial Anthropology*, 2019, 36, 27–34. https://doi.org/10.31393/bba36-2019-05
29. Usenko, O. Yu., & Voitiv, Ya. Yu.: Undifferentiated connective tissue dysplasia in patients with anastomotic suture failure of the hollow digestive organs. *Clinical Surgery*, 2019, 86(6), 3–7. https://doi.org/10.26779/2522-1396.2019.06.03
30. Van Maanen, J., Turaihi, H., Denevan, P., &Thambi-Pillai, T.: Overview and Management of Small Bowel Obstruction versus Ileus: A Primer for All Physicians. *South Dakota medicine: the journal of the South Dakota State Medical Association*, 2019, 72(5), 226–231.
31. Wang, Y., Zhang, M., Jiang, L., Gong, Y., Liu, K., & Zhang, T.: Alterations of gut microbiota in a mouse model with partial small intestinal obstruction. *Frontiers in microbiology*, 2023, 14, 1242650. https://doi.org/10.3389/fmicb.2023.1242650
32. Wattchow, D., Heitmann, P., Smolilo, D., Spencer, N. J., Parker, D., Hibberd, T., Brookes, S. S. J., Dinning, P. G., & Costa, M.: Postoperative ileus-An ongoing conundrum. *Neurogastroenterology and motility*, 2021, 33(5), e14046. https://doi.org/10.1111/nmo.14046

Primary Paper Section: A

Secondary Paper Section: AM, FQ