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ROLE OF BACTERIA IN INTESTINAL OBSTRUCTION PATHOPHYSIOLOGICAL PROCESSES

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Summary. *Intestinal obstructions cause proliferation of fecal type flora proximally from the point of obstruction. Pathophysiological processes, caused by fecal flora proliferation, in patients with simple mechanical obstruction result in metabolic disturbances (fat and B12 absorption disturbance), change in the gases volume and composition within the bowel above the obstruction point, and change in fluid and electrolytes flow through the bowel wall. Sepsis and septic shock, as the most serious complications of strangulation obstruction occur as a consequence of a host response to bacterial signal molecules. Endotoxin of Gram-negative bacteria and exotoxins, peptidoglycan, lipoteichoic acid and various exoenzymes of Gram-positive bacteria initiate the release of cytokines from the host cells. The underlying mechanism of sepsis syndrome is widespread vascular endothelial injury with fluid extravasation and microthrombosis promoted by cytokines. Vascular endothelial injury decreases oxygen and substrate utilization by the affected tissues and lead to the multi-organ disfunction syndrome.*

Key words: *Intestinal obstruction, sepsis, cytokines*

Introduction

Bacterial flora of a human gastrointestinal tract is a complex ecosystem comprised of aerobe and anaerobe bacteria. Bacteriological analyses show that there are more than 500 bacterial species in the intestinal tract of one individual (1).

Microflora of oral cavity is complex because it is exposed to continuous contamination. Oral cavity bacterial flora contains 40% of aerobe and facultatively anaerobe, and 60% of anaerobe bacterial species. Streptococcus, Lactobacillus, Neisseria and Staphylococcus species make most of aerobe and facultatively anaerobe flora. Most prevailing anaerobes are Bacteroides, Fusubacterium, Peptococcus, Peptostreptococcus and Veillonella parvula (2).

Bacteria from oral cavity reach stomach through esophagus with saliva and food. Stomach concentration of bacteria is usually lower than 10^3 bacteria per gram of stomach content (2,3). The low concentration of stomach bacteria is the result of gastric juice acidity, acting destructively on majority of bacteria and of antibacterial activity of gastric mucosa. Stomach dominant aerobe and facultatively anaerobe bacterial flora includes Streptococcus, Staphylococcus and Lactobacillus. Oral anaerobes, such as Peptostreptococcus, Fusobacterium and Bacteroides, may be present in a small number (1,3,4).

Bacterial flora of duodenum, jejunum and proximal ileum is similar to gastric flora. Bacteria concentration in small intestine proximal part does not usually exceed 10^4 bacteria per gram of contents (2,3,5).

Coliforms and anaerobe bacteria may be isolated from the gastric contents and proximal intestinum during their passage through this part of digestive tract, but in very low concentrations (2).

Distal ileum represents the transition zone between proximal intestinum microflora and colon microflora. Bacterial flora of distal ileum, besides Gram-positive aerobes and facultative anaerobes, contains coliform bacteria and anaerobes (Bacteroides, Bifidobacterium, Fusobacterium and Clostridium species) in significant concentrations. The concentration of bacteria in these intestine sections ranges from 10^5–10^9 bacteria per gram of intestinal contents (3,6,7).

Distally from ileocecal valvula, the flora is being significantly changed in view of domination and concentration of the present bacteria. Colon bacterial concentration ranges from 10^9-10^{12} per gram of feces (2). Bacteria make 30-40% of fecal masses. Anaerobe flora, composed of the species belong to the genera Bacteroides, Fusobacterium, Eubacterium, Clostridium, Bifidobacterium, Peptococcus and Peptostreptococcus make about 99% of colon bacterial flora. Clostridia, being the part of colon normal flora, are Cl. perfinges, Cl. hystoliticum, Cl. septicum, Cl. sordelli and Cl. difficile (1,3,4,5). The low redox potential and the path of intestinal contents within the colon ensure an optimum media for growth and multiplication of anaerobes. In aerobe flora coliforms are dominant (Escherichia coli, Citrobacter, Klebsiella, Enterobacter and Serratia) (1).

Normal intestinal flora has a significant role in physiological processes of digestion, like K vitamin synthesis, bile pigments and bile acids conversion, nutritional substances and digestion by-products absorption (1,8).

Mechanisms of bacterial proliferation regulation in the gastrointestinal tract

The bacterial flora proliferation degree, on various levels of gastrointestinal tract, is regulated by many factors originating from a host and microorganisms.

In oral cavity saliva acts inhibitory on a small number of bacterial species. Stomach, however, presents the main barrier for bacteria proliferation. The acid gastric contents and mucose antibacterial activity act destructively on most of the bacteria. In patients with achlorhydria and partial gastrectomia there is evidenced a greater number of bacteria in the stomach and small intestine (3).

Acidoresistant streptococci and lactobaciles reach small intestine in the greatest number. Unconjugated bile acids inhibit the bacteria growth in vitro, but their significant antibacterial activity in vivo has not been proven (4,9).

The most significant mechanism preventing bacterial population proliferation in the small intestine is a normal peristalsis of the small intestine, providing for mechanical elimination of bacteria to the colon and prevents small intestine bacterial colonization (10). Opposite to that, delayed passage of the bowel content in distal ileum, and particularly in the colon, ensures favourable environment for bacterial population proliferation.

The contents of normal bacterial flora and relation of some bacterial species is regulated by mutual bacterial interaction, as well, particularly in the colon. Bacteria may favor or inhibit the growth of other bacterial species by some of the following mechanisms: change of intraluminal Ph and redox potential, competition regarding the need for nutritional matters and bacteriocins production (8, 9). Aerobe and facultatively anaerobe bacteria, for example, by using oxygen, create optimal conditions for anaerobes growth and multiplication. In absence of these bacteria it is not possible for anaerobes to survive.

Many Gram-negative bacteria produce bacteriocins, plasmides coded protein substances, acting bactericidally to bacteria cells of the same or different species. The most significant bacteriocins in the intestinal tract are colicins produced by E. coli (11).

The role of bacteria in intestinal obstruction pathophysiological processes

Intestinal obstructions, compromitting peristalsis and conditioning the path of intestinal content, cause the flora proliferation of fecal type (colon type flora) proximally from the obstruction point (12). Bacteriological analyses have shown that, opposite to fecal flora, proximally to the obstruction point, the samples of intestinal content distally from the obstruction point, have got scanty flora or are even sterile (12). Bacteria concentration above the obstruction point ranges from 10^7–10^{11} bacteria per gram of bowel content. Anaerobe bacteria are dominant, and of aerobe, coliform bacteria (3).

Pathophysiological processes caused by proliferation of fecal flora may be differentiated in different forms of intestinal obstruction.

Pathophysiological processes in simple mechanical obstruction

Pathophysiological processes, induced by fecal flora proliferation, in patients with simple mechanical opstruction result in:

- metabolic disturbances,
- change of gases volume and composition in the bowel above the obstruction point,
- change of fluid and electrolytes flow through the bowel wall.

Metabolic disturbances Bacterial flora of fecal type in the small intestine results in metabolic disturbances, the most frequent of which are fat and B12 vitamin absorption disturbances. The role of bacteria in fat absorption disturbance is based on bacterial deconjugation of bile salts in the small intestine, resulting in reduced fat dissolubility, mal-absorbtion and steatorea (13). Some researches suggest that deconjugated bile salts inhibit reesterification or transportation of dissolved fatty acids by mucosa cells. Bacteroides, Bifidobacterium, Clostridium, Veillonella and Enterococcus species have got enzyme system responsible for bile salts deconjugation. Coliform bacteria do not take part in this process (14,15).

Bacterial proliferation syndrom in the small intestine is often associated to megaloblastic anemia due to B12 vitamin deficit. Bacterial cells bind B12 vitamin in the proximal small intestine, no matter if it is free or binded to colabin factor. It prevents vitamin B12 absorption in distal ileum. Many authors point to the significant role of anaerobe bacteria, particularly Bacteroides, in pathogenesis of B12 malabsorbtion (13,14).

Both reduced amino acids absorption and reduced level of serum proteins may be observed in patients with bacteria proliferation in the small intestine. Bacteria, using amino acids for their metabolic needs, may account for these disturbances. In patients with reduced serum protein level, there has been detected higher level of indol in proximal small intestine, which is the product of triptophan bacterial decomposition Increased production of urea in this patients is the result of proteins bacteral decomposition to amonia and its conversion to urea (14).

Carbohydrates absorption disturbance has been recorded based on reduced absorption of D xylose and the presence of higher quantity of carbohydrates bacterial metabolism decomposition products, detected in patients jejunal aspirate (16).

Besides the indicated mechanisms by which bacteria compromise absorption, it is significant to point out that infiltered mucose has got reduced absorption capacity in patients with bacterial proliferation (17).

Change of gases volume and composition. The bowel proximal to the point of obstruction becomes progressively distended with accumulated gas and liquids. Bacteria have got the role in intraluminal production of gases, although their role in the change of gas volume above the obstruction point is not primary. Production of gases is the result of carbohydrates and/or proteins bacterial fermentation. Bacteria are primarily account-

able for hydrogen, carbon-dioxide and methane production. However, the quantity of these gases above the obstruction point is low. Nitrogen dominates, originating from swallowed air (12).

Change in fluid and electrolytes flow through the bowel wall. The role of microbial flora in fluid and electrolytes flow through the bowel wall has been proven experimentally. Heneghan (1981.) observed abundant secretion of water and electrolytes into the ileum lumen and their absorption disturbance proximally from the obstruction point in dogs with abundant bacterial flora. Opposite to that, in dogs, not infected by bacteria, the increased exudation has not been recorded (18). This study shows that bacteria may have the role in increased exudation of fluids and electrolytes in infiltered mucosa absorption disfunction, as well. Participation of bacteria in increased exudation of fluid may be explained by toxins production. Endotoxin of Gram-negative bacteria results in increased capillary permeability (19). Some kinds of type A Clostridium perfigens produce enterotoxin acting on the bowel wall mucous membrane and effect fluids exudation into the bowel lumen (13).

The increased bacterial population, however, probably plays an insignificant role in simple mechanical obstruction as long as the bowel wall maintains its integrity.

Pathophyisiological processes in strangulation obstruction

The role of bacteria in strangulation obstruction pathophysiological processes is in direct correlation with bowel wall integrity disturbance. Namely, ischemic or hemorrhagic bowel wall infarction result in anoxia and necrosis of the bowel wall, providing ideal conditions for bacterial growth and multiplication, particularly for anaerobe bacteria. Moreover, necrotic tissue has no blood supply, and therefore no phagocytes, complement, or antibody to protect it. Therefore, devitalized tissue represents a defect in host defence. Bacteria proliferate and invade the bowel wall. Six hours after the strangulation, maximum number of bacteria is achieved proximally from the obstruction (20). Quantitative bacteriological studies indicated that proximally from the obstruction point, dominant bacteria are Bacteroides, Clostridium and coliforms (12).

By bacterial proliferation and invasion of the bowel wall, the wall vascular permeability is still being increased. Fluid transudation through the bowel wall results in free peritoneal fluid accumulation. Bacterial toxins and certain microbial molecules transudation is performed along with the fluid through the bowel wall into the peritoneal cavity (20,21). The toxins and bacterial molecules would then pass via the peritoneal lymphatics into the bloodstream. The presence of toxins in the free peritoneal fluid is confirmed by a biological experiment (22).

Bacteria, invading the bowel wall also cause microvascular thrombosis in the wall, which favours necrosis development (23). In case of bowel wall perforation occurrence, due to necrosis, the intestinal content floods the peritoneal cavity and peritonitis is being developed.

From the aspect of various bacterial kinds multiplication cycle, the development of peritinitis has a bi-phase course (14,21). The first phase is characterized by the domination of Gram-negative aerobe flora (E. coli, Enterobacter, Proteus, Pseudomonas and others) which is the result of quicker biological cycle of these bacteria multiplication. Anaerobes are present, as well, but their intensive multiplication starts later, once the aerobes using oxygen had provided anaerobic conditions. The second phase is characterized by anaerobe infection. Anaerobe flora is polymorphic with dominance of Clostridium and Bacteroides species.

Localised tissue infection may then lead to microbial invasion of the bloodstream. Bacteremia and local or systemic spread of microbial molecules and toxins lead to the development of sepsis and eventually septic shock (23,24,25). However, the primary role in sepsis development is to be attributed to local and systemic spreading of toxins and other microorganisms' products, and not to the invasion of microorganisms into the blood. Blood cultures yield bacteria in approximately 20 to 40 percent of cases of severe sepsis and 40 to 70 percent of cases of septic shock (23,25,26).

Sepsis and septic shock Sepsis with the septic shock occurs as the result of the host response to bacterial signal molecules, such as endotoxin of Gram-negative bacteria and exotoxins, peptidoglycan, lipotheichoic acid, certain polysaccharides and various exoenzymes of Gram-positive bacteria (21,24,25). The most common bacteria involved in development of sepsis after strangulation obstruction are shown in Table 1.

Endotoxin is the most potent and best-studied Gram-negative bacterial signal molecule. It represents lipopolysaccharide complex (LPS), situated within the external mucous membrane of bacteria cell wall. Lipopolysaccharide consists of A lipid (toxic component) and polysaccharide (accountable for antigen group bacterial species specificity). Lipid A is constant among the bacterial species which belong to Enterobacteriaceae family (27).

Of the anaerobic Gram-negative organisms only Fusobacteria possess an endotoxin which is chemically identical to and biologically as potent as the endotoxin of coliform bacteria (21). Bacteroides species have lipopolysaccharide which significantly differs from lipopolysaccharides of species belonging to Enterobacteriaceae family. It has no typical A lipid, that being the reason for its extremely low endotoxic activity (28). Owing to that, clostridia play primary role in intoxication, regardless of high Bacteroides concentration in the intestinal content (21). Apart from exotoxin, Clostridium species trigger host response by other components, as well, such as peptidoglycan, lipoteichoic acid, certain polysaccharides and exoenzymes.

Toll-like receptors (TLRs) have an essential role in the innate recognition of microbial signal molecules and in triggering acquired immunity. So far, ten mammalian Toll-like receptors (TLR1-TLR10) have been identified. Individual TLRs recognise distinct structural components of pathogens. TLR4 recognizes LPS, but TLR2 peptidoglycan from Gram-positive bacteria, lipoprotein and lipopeptides (29).

Table 1. Putative mediators of sepsis

Mediators	Effects
TNF	PNM: ↑release from bone marrow, ↑migration, ↑transendothelial passage, ↑metabolic activation. MPH activation, ↑cytotoxicity, ↑lymphokine production. Endothelial cell: ↑surface antigen, ↑procoagulant activity, ↑vascular proliferation. Fibroblast: ↑cytokine production, ↑collagen synthesis. Fever, hypotension, vascular leak, anorexia.
IL 1	PNM: ↑marrow release, ↑influx to injury site, ↑transendothelial passage, ↑metabolic activation. MPH activation, ↑cytotoxicity. T cell: activation and ↑lymphokine production. Endothelial cell: ↑procoagulant activity, ↑vascular permeability and metabolic activation. Fiver, anorexia, weight loss, nitrogen loss.
IL 2,4,6,8	Hypotension, capillary leak, decreased myocardial contractility, leukocyte, chemotaxis, synthesis of proteins by the liver (e.g. fibrinogen).
Hageman factor	Coagulation, fibronolysis.
Complement cascade	Neutrophil chemotaxis, neutrophil aggregation, capillary leak.
Endorphins	Hypotension.
Leucotrienes thromboxane	Platelet aggregation, neutrophil adhesion, capillary leak, decreased myocardial contractilit
Prostaglandins	Hypotension, neutrophil adhesion to endothelium, fever, muscle aches, muscle proteolysis.
Bradykinin	Hypotension, capillary leak.
Serotonin	Pulmonary hypertension, capillary leak.
Histamine	Hypotension, capillary leak.
Platelet-activating factor	Hypotension, capillary leak, platelet aggregation, leukocyte activation, decreased myocardial contractility.
Phagocyte products-lysosomal proteins, oxygen free radicals	Endothelial cell damage, capillary leak.
Myocardial depressant factor	Decreased myocardial contractility.
Endothelin 1	Vasoconstriction, especially in the kidney.
Endothelial relaxing factor (nitric oxide)	Hypotension.

MPH-macrophages, PNM-polymorphonuclear leukocyte, ↑increase, IL-interleukin, TNFα-tumour necrosis factor

After being released into the bloodstream, LPS is captured immediately by LPS-binding protein, a specific lipid transfer protein that delivers LPS to CD14 present on the surface of macrophages. CD14 lacks a transmembrane domain and so is incapable of transducing signals, which suggests that other molecules must be responsible for LPS signaling. TLR4 is essential for LPS signaling (29). The interaction of LPS with TLR4 requires another molecule MD-2 which associates with the extracellular domain of TLR4 (30).

Stimulation of macrophages by LPS through the TLR4 signaling pathways induces the production of the tumor necrosis factor-α (TNFα) or cachetin. TNFα stimulates the macrophages to produce interleukin-1 (IL-1). TNFα and IL-1 act synergistically on macrophages and on other cells, particularly neutrophils, monocytes and endothelial cells to produce a variety of additional mediators, as well as additional TNFα (21,23,31,32,33). In fact, once sepsis is underway, the endothelial cell may be the key cell, both as target and effector. Putative mediators of sepsis and their effects are shown in the Table 2.

Table 2. The most common bacteria involved in development of sepsis after strangulation obstruction

	Aerobes	Anaerobes
Gram-positive	Enterococcus	Clostridium Peptostreptococcus Bifidobacterium Peptococcus
Gram-negative	Escherichia coli Enterobacter Proteus Pseudomonas	Bacteroides Fusobacterium

The most important biological effects of LPS-induced host immune response are:

- increased vascular permeability (the effect of TNFα, IL-2, IL-4, IL-6, IL-8, complement cascade, serotonin, histamine, platelet activating factor-PAF, phagocyte products-lysosomal proteins and oxygen free radicals);
- extensive microvascular thrombosis or disseminated intravascular coagulation-DIC (the effect of IL-1, TNFα, Hageman factor);
- vasodilatation (the effect of activated neutrophiles released bradikinin and macrophages released nitrogen-oxides);
- decrease myocardial contractility (the effect of IL-2, IL-4, IL-6, IL-8, leukotriens and thromboxane, PAF);
- fever (the effect of TNFα, IL-1) (20,23,34,35).

Sepsis leaves no organ or system untouched. In protracted cases of sepsis one organ after another may fail. This condition is called the multi-organ dysfunction syndrome (MODS) (23,25,35). The probable underlying mechanism of this syndrome is widespread vascular endothelial injury. Leukocyte-derived mediators and platelet-leukocyte-fibrin thrombi contribute to this injury. TNFα promotes intravascular coagulation initially by inducing blood monocytes to express tissue factor

(lipoprotein) that binds to factor VIIa to form an active complex that can convert factors X and IX to enzymatically active forms. The result is activation of both extrinsic and intrinsic clothing pathways, culminating in the generation of fibrin. Also, the vascular endothelium itself seems to play an active role in the vascular endothelial injury. TNFα induce vascular endothelial cells to produce and release cytokines, procoagulant molecules, PAF, endothelium-derived relaxing factor (nitrite oxide) and other mediators. These mediators can also promote increased vascular permeability, microvascular thrombosis and disseminated intravascular coagulation (DIC). Moreover, vascular integrity may be damaged by neutrophil enzymes and toxic oxygen metabolites so that local hemorrhage ensues (2,23,25).

Vascular endothelial injury, with fluid extravasations and microthrombosis, decrease oxygen and substrate utilization by the affected tissue and lead to the organ malfunction. The most important affected organs are:

Lung: Increasing alveolar capillary permeability results in an increased pulmonary fluid content, which decreases pulmonary compliance and interferes with oxygen exchange. Progressive diffuse pulmonary infiltrates, decreasing compliance, and arterial hypoxemia signal the development of the adult respiratory distress syndrome (ARDS) (23,25,34,36).

Gastrointestinal tract: Hemorrhagic necrosis of the mucosa occurs, probably at least in part because of ischemia. Loss of mucosal integrity can lead to hemorrhage (25, 34).

Kidney: Acute renal failure due to acute tubular necrosis occurs.

Liver: Stasis of bile, focal necrosis, and jaundice are common.

Endocrine and metabolic effects: Sepsis is a catabolic state, with massive proteolysis, lipolysis, and glycogenolysis. Stress hormones (cortisol, catecholamines, glucagon) circulate in high levels. Oxygen metabolism is deranged: an abnormally high fraction of the oxygen sent to the tissues is returned to the heart unused, either because some vascular beds are not perfused or because some cells are too metabolically impaired to use the oxygen delivered to them. Either way, in the absence of a functioning Krebs cycle, glycolysis proceeds at a high rate and pyruvic acid formed is reduced to lactic acid, resulting in lactic acidosis (23,25).

Heart: Depression of myocardial function, manifested as increased and diastolic and systolic ventricular volumes with a decreased ejection fraction, develops within 24 h in most patients with advanced sepsis. Cardiac output is maintained because ventricular dilation permits a normal stroke volumen. In survivors, myocardial function returns to normal over several days (23,34).

Septic shock usually results from a severe decrease in systemic vascular resistance, a generalized maldistribution of blood flow, and functional hypovolemia that is due, at least in part, to diffuse capillary leakage of intravascular constituents. Other factors that may decrease effective intravascular volume include dehydration from antecedent disease or insesible fluid losses, vomiting or diarrhea, and polyuria. While myocardial disfunction may contribute to hypotension, refractory hypotension is usually due to a low systemic vascular resistance, and death results from refractory shock or the failure of multiple organs rather than from cardiac disfunction per se (23,34,35).

Sepsis is the most severe complication of intestinal obstruction. It occurs as the result of the host response to certain microbial molecules. Prevention of septic shock implies due time administration of antibiotic therapy (even before getting the microbiological finding). Owing to that, the knowledge of the most frequent carriers of sepsis and their sensitivity to antibiotics is extremely important. The new approach in sepsis therapy and septic shock prevention includes administration of drugs that neutralize bacterial endotoxin (monoclonal anti-endotoxin antibodies, non toxic lipid A analogs, a polymyxin B-dextran conjugate that binds endotoxin) and those, neutralizing cytokines such as recombinant IL-1 receptor antagonist, genetically engineered soluble receptors for TNFα, and monoclonal antibodies to TNFα. Unfortunately, in the recent clinical trials these agents failed to prevent the death of patients with sever sepsis or septic shock (23,37,38).

References

1. Berg RD. The indigenous gastrointestinal microflora. Trends Microbiol 1996; 4:430-5.
2. Eisenstein B, Schaechter M. Normal Microbial Flora. In: Schaechter M, Engleberg NC (eds), Microbial Disease. Lippincott Wiliams&Wilkins, Philadelphia, 1999: 11-17.
3. Simon GL, Gorbach SL. Intestinal flora in health and disease. Gatroenterology 1984; 86: 174-93.
4. Guarner F, Malagelada JR. Gut flora in health and disease. Lancet 2003; 361: 512-9.
5. Wells CL, Barton RG, Wavatne CS, et al. Intestinal bacterial flora, intestinal pathology, and lipopolysaccharide-induced translocation of intestinal bacteria. Circ Shoch 1992; 37: 117-23.
6. Hooper LV, Wong MH, Thelin A, et al. Molecular analysis of commensal host-microbial relatins hips in the intestine. Science 2001; 291: 881-4.
7. Husebye E, Hellstrom PM, Sungler F, et al. Influence of microbial species on small intestinal myoelectric activity and transit in germ-free rats. Am J Physiol Gastrointest Liver Physiol 2001; 280: 368-80.
8. Klein AD. Microbial Growth. In: Prescott LM, Harley JP, Klein AD. Microbiology. McGraw-Hill Education, New York, 2002: 113-33.
9. Hooper LV, Gordon JI. Commensal host-bacterial relation hips in the gut. Science 2001; 292: 1115-18.
10. Nieuwenhuijs VB, Verheem A, Duijvenbode-Beumer H, et al. The role of interdigestive small bowel motility in the regulation of gut microflora, bacterial overgrowth, and bacterial translocation in rats. Ann Surg 1998; 228: 188-93.
11. Schaechter M, Eisenstein B, Engleberg NC. Genetics of Bacterial Pathogenesis. In: Schaechter M, Engleberg NC (eds), Microbial Disease. Lippincott Wiliams&Wilkins, Philadelphia, 1999: 39-51.
12. Fielding PL, Welch Jp. Intestinal Obstruction. Churchill Livingstone, New Jork, 1987: 32-9.
13. Ding LA, Li JS. Intestinal failure: Pathophisiological elements and clinical diseases. World J Gastroenterol 2004; 10(7): 930-33.

14. Keusch TG, Acheson D. Digestive System. In: Schaechter M, Engleberg NC (eds), Microbial Disease. Lippincott Wiliams&Wilkins, Philadelphia, 1999: 519-33.
15. Prescott LM, Harley JP, Klein AD. Microbial Metabolism. In: Prescott LM, Harley JP, Klein AD (eds), Microbiology. McGraw-Hill Education, New York, 2002: 153-72.
16. Riordan SM, Mciver CJ, Duncombe VM, Bolin TD, Thomas MC. Factors influencing the 1 gram C-D-xylose breath test for bacterial overgrowth. Am J Gastroenterol 1995; 90: 1455-60.
17. Barbara G, Stranghellini V, Brandi G, et al. Interactions between commensal bacteria and gut sensorimotor function in health and disease. Am J Gastroenterol 2005; 100: 2560-68.
18. Heneghan JB, Robinson JW. Intestinal obstruction in germfree dogs. In: Sasaki S. Rcent advances in germfree research. Procedings of the VIIth international symposium on gnotobiology. Tokyo: Tokai University Press, 1981: 379-84.
19. Cullen JJ, Caropreso DK, Ephgrave KS. Effect of endotoxin on canine gastrointestinal motility and transit. J Surg Res 1995; 58: 90-5.
20. Heinzelmann M, Scott M, Lam T. Factors predisposing to bacterial invasion and infection. Am J Surg 2002; 183: 179-90.
21. Heemken R, Gandawidjaja L, Hau T. Peritonitis: pathophysiology and local defense mechanisms. Hepatogastroenterology 1997; 44: 927-36.
22. Foster WC, Hausler RW. Studies on acute intestinal obstruction. II Acute strangulation. Arch Intern Med 1924; 34: 697-713.
23. Munford R. Sepsis and Septic Schock. In: Fauci A, Braunwald E, Isselbecher K (eds), Principles of Internal Medicine. McGraw-Hill Education, New York, 1998: 776-80.
24. Macfie J, O'Boyle C, Mitchell CJ, et al. Gut origin of sepsis: A prospective study investigating associations between bacterial translocation, gastric microflora, and septic morbidity. Gut 1999; 45: 223-8.
25. Whitnack E. Sepsis. In: Schaechter M, Engleberg NC (eds), Microbial Disease. Lippincott Wiliams&Wilkins, Philadelphia, 1999: 589-595.
26. Talaro KP, TalaroA. Gram-Negative Sepsis and Endotoxic Shock. In: Prescott LM, Harley JP, Klein AD. Microbiology. McGraw-Hill Education, New York, 2002: 604-8.
27. Rietschel ET, Kirikae T, Schade FU, et al. Bacterial endotoxin: molecular relations hips of structure to activity and function. FASEB 1994; 8: 217-25.
28. Tally FP. Bacteroides and Abscesses. In: Schaechter M, Engleberg NC (eds), Microbial Disease. Lippincott Wiliams& Wilkins, Philadelphia, 1999: 170-175.
29. Akira S. Mammalian Tool-like receptors. Curr Opin Immunol 2003; 15: 5-11.
30. Shimazy R, Akashi S, Ogata H, et al. MD-2, a moleculethatconfernslipopolysaccharideresponsiveness on Toll-like receptor 4.J Exp Med 1999; 189: 1777-1782.
31. Beutler B, Poltorak A. Sepsis and evolution of the innate immune response. Crit Care Med 2001; 29: S2-S7.
32. Vassalli P. The pathophysiology of tumor necrosis factor. Ann Rev Immunol 1992; 10: 411-52.
33. Dinarello CA, Wolff SM. The role of interleukin-1 in disease. N Engl J Med 1993; 328: 106-13.
34. Barber A, Shires GT. Shock. In: Schwartz SI, Shires GT, Spencer FC (eds), Principles of Surgery. McGraw-Hill Education, New York, 1999: 101-121.
35. Madl C, Druml W. Gastrointestinal disorders of the critically ill. Systemic consequences of ileus. Best Pract Res Clin Gastroenterol 2003: 17: 445-56.
36. Baldwin RE, Rice CL. Adult Respiratory Distress Syndrome. In: Chields TW (ed), General Thoracic Surgery. Lea&Febiger, Philadelphia, 1989: 474-482.
37. Lynn WA, Cohen J. Adjunctive therapy for septic shock: a review of experimental aproaches. Clin Infect Dis 1995: 20: 143-158.
38. Dinarello CA. The proimflammatory cytokines interleukin-1 and tumor necrosis factor and treatment of the septic shock syndrome. J Infect Dis 1991; 163: 1177-9.

ULOGA BAKTERIJA U PATOFIZIOLOŠKIM PROCESIMA INTESTINALNIH OPSTRUKCIJA

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Kratak sadržaj: *Intestinalne opstrukcije dovode do proliferacije flore fekalnog tipa proksimalno od mesta opstrukcije. Patofiziološki procesi, uzrokovani proliferacijom fekalne flore, kod bolesnika sa prostom mehaničkom opstrukcijom dovode do metaboličkih poremećaja (poremećaja u absorpciji masti i vitamina B12), promena u volumenu i sastavu gasova u crevu iznad mesta opstrukcije i promena u protoku tečnosti i elektrolita kroz zid creva. Sepsa i septički šok, kao najozbiljnije komplikacije strangulacione opstrukcije, nastaju kao posledica imunskog odgovora domaćina na bakterijske produkte. Endotoksin Gram-negativnih bakterija i egzotoksini, peptidoglikan, lipoteihoična kiselina i različiti egzoenzimi Gram-pozitivnih bakterija pokreću oslobađanje citokina iz ćelija domaćina. Citokini uzrokuju oštećenje endotela krvnih sudova sa ekstravazacijom tečnosti i mikrotrombozom, što predstavlja osnovni patofiziološki mehanizam septičnog sindroma. Oštećenje endotela krvnih sudova smanjuje dopremanje kiseonika i supstrata do zahvaćenih tkiva i dovodi do sindroma disfunkcije organa.*

Ključne reči: *intestinalne opstrukcije, sepsa, citokini*