SCIENTIFIC REVIEWS AND LECTURES

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GUT MICROBIOME AND BREASTFEEDING OF CHILDREN

A review of the literature on studies of intestinal microflora in children is presented. Research in recent years demonstrates the importance of the impact of the gut microbiota on children's health. Contemporary ideas about the gut microbiome are considered. A brief description of the intestinal microflora composition and its impact on the health of the child is given.

Keywords: intestinal microflora, intestinal microbiome, microbiota, gastrointestinal tract, immune system.

Introduction. Currently, the intestinal microbiota is being thoroughly studied all over the world, as a significant influence of the state of the intestinal microflora on the health of children has been proven, and its dysfunction – dysbiosis leads to various pathological conditions.

This review presents the results of Russian and foreign studies on the state of the intestinal microbiome in young children.

Modern ideas about the gut microbiota appeared several years ago in connection with the emergence of molecular-genetic research methods, which made it possible to obtain new information about the composition of the intestinal microbiota in people of different ages. the formation of the intestinal microbiota in children is of a great interest, especially at an early age. In particular, this is caused by a change in the understanding of the microbiocenosis of various biotopes of the body and the appearance of previously unexplored bacterial species [3,5,10].

About thousand species of microorganisms live in the intestine, 90 percent of them are anaerobic [1,2,11,24,25,26].

According to the US National Institute of Health (NIH), only 10 percent of the cells that make up the human body are actually human cells, and the remaining 90 percent belong to bacteria inhabiting various human biotopes [3,4,15,16].

As you know, the intestine is the largest "immune organ" of a person, 80 percent of immunocompetent cells are located there. The formation of the intestinal microbiota is influenced by a number of factors, such as the gestation period, the method of delivery, the type of feeding. Unfavorable factors also have a great influence, especially in the early stages of ontogenesis, such as complicated pregnancy, violation of endoecology in the mother, changes in gestation, operative delivery, late application to the breast, artificial feeding, antibiotic therapy [2,16,19,28,29].

As a result of many studies, data indicating that microbial colonization expands rapidly after birth, and the composition of the microbiome varies especially strongly in early childhood have emerged. It was found that the microbiome in infancy contains vaginal, dermal, oral and fecal strains of the mother, while the intestinal microbiome of the child had the biggest similarity with the intestinal microbiome of the mother by 4 months of life [20,21,28,29].

In the postnatal period, the main influence on the composition of the intestinal microbiota is the method of feeding. Thus, breast milk contains a large number of bacteria, while the microbiota of breast milk is formed when microorganisms penetrate through the intestinal lymphoid tissue (enterological pathway) or by endocytosis due to increased permeability of the intestinal mucosa during childbirth. Probiotic bacteria predominate during breastfeeding, Enterobacteria predominate during artificial feeding [2,12,13,14].

Breastfeeding is believed to protect against the child from development of many diseases, including obesity, diabetes and autoimmune diseases such as asthma and allergies. According to a number of authors, the mechanism by which breast milk determines a child's predisposition to such diseases can be determined by a long-term effect on the intestinal microbiota [6,7,8,22,24]. In particular, as the only source of nutrition in the first 4-6 months of life, the composition of breast milk or formula determines the availability of nutrients for the intestinal microbiota in an infant, and can have a selective effect. The key difference between breast milk and artificial mixtures is the presence of prebiotics, oligosaccharides and antibodies that affect bacterial colonization. Breast milk contains bifidobacteria, streptococci, lactobacilli, which directly make up the microbiome of the baby's intestines. However, there is a great variability in the composition of breast milk depending on the state of health of the mother [27]. The composition of breast milk is dynamic, changes over time, and may also depend on the sex of the child or during illness. It remains to be determined whether the "main" group of breast milk components is responsible for the protective function. For premature infants, breast milk feeding mitigates some of the negative consequences affecting the formation of the intestinal microbiome [26,27].

Studies of the microbiota of young children have focused on the number and diversity of specific bacterial flora. In one of the studies, it was found that breastfed children have a large number of bifidobacteria, and the microbiome of children feeding on the mixture was more diverse [9,12,13]. Another study showed that with natural feeding in the intestinal microbiome of a child, the number of actinobacteria increases and the number of proteobacteria decreases than in children who are artificially fed [14]. In a prospective study, overweight children aged 7 years had a lower content of bifidobacteria and a higher colonization of Staphylococcus aureus in infancy, compared with children with normal weight. This study proved that immunoglobulins obtained from breast milk stimulate the immune function of the intestine and the composition of the intestinal microbiome, which provides additional evidence for the mechanisms linking breastfeeding with immunoprotection. It was also found that in a population at risk of malnutrition (insufficient intake of essential trace elements), lower levels of sialylated oli-

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gosaccharides in breast milk are associated with a slowdown in the growth of young children, and their inclusion in the diet of laboratory animals caused an increase in body weight. This confirms the association of body height and weight with the gut microbiome [10,11].

According to many authors, a number of additional studies are required, but the data obtained emphasize the period of early childhood as a critical period when microbial dysbiosis can lead to overweight in later life. The components of breast milk form the microbiome of the baby's intestine and can provide lifelong protection against obesity and other metabolic diseases [16].

Recent studies show that microbial transfer from mother to fetus already occurs in the womb. Microbes were found in the placenta, amniotic fluid, fetal cell membrane, umbilical cord blood and meconium [17].

Breastfeeding provides the newborn with its own microbiota, as well as prebiotic, immunological and other microbiota-forming compounds that can indirectly change the composition of colonization in the newborn. Therefore, the diverse composition of breast milk can be considered as a selective biofactor for achieving the diversity of the intestinal microbiota and, consequently, as a determining factor of health [21].

A number of studies have proven that breast milk contains 102-104 viable bacteria per milliliter, thus, it can directly affect the establishment of the neonatal microbiota [22]. Lactobacilli, staphylococci, enterococci and bifidobacteria are transferred through breast milk [21]. The microbiota of breast milk also develops during the entire period of breastfeeding. Thus, the colostrum microbiota is more diversed than later breast milk [15]. Colostrum contains a large number of staphylococci, lactic acid bacteria and streptococci [21]. A month after the birth of a child, the number of staphylococci decreases sharply, while lactic acid bacteria are still numerous. Breast milk oligosaccharides are structurally complex sugars, unique in composition. They are indigestible, do not provide energy, but serve as prebiotics, which are substrates for the fermentation processes of intestinal microbes, inducing their growth and activity of beneficial bacteria [22]. The composition of breast milk oligosaccharides is regulated by the genetic status of the fucosyltransferase-2 secretor and other factors, including the stage of lactation, maternal health and ethnicity [4]. In addition, oligosaccharides favor the growth of bifidobacteria [4,22,23]. The maturation of the breast milk microbiota occurs in parallel with the evolution of the intestinal microbiota of the newborn [7].

Translocation of microbes, microbial nucleic acids and bacterial lipopolysaccharides from the intestine into the bloodstream occurs regularly [26]. According to several authors, the origin of bacteria in breast milk is still being discussed. Some researchers suggest that breast milk bacteria originate from maternal skin, since some bacteria contained in breast milk are present on adult skin [18,20]. However, most studies suggest that translocation of maternal intestinal bacteria into the mammary gland is the main pathway. Dendritic cells and macrophages can capture live commensal bacteria from the intestinal lumen and transfer to mesenteric lymph nodes. From there, the bacteria can circulate to other organs, including the mammary glands [23]. Also, the method of delivery can affect the transfer of bacteria to the mammary glands. The same studies have proved that during cesarean section, the microbiota of breast milk is the most diverse, but contains fewer bifidobacteria [18,23].

The role of breast milk for the development of the baby's gut microbiota is very important and is the main tool for the development of the immune system.

Thus, a review of studies conducted on this topic shows that there is significant evidence of a connection between the composition of the baby's gut microbiome and the mother's breast milk. However, there are currently no large-scale studies on the possibilities of the influence of breast milk factors in the formation of the intestinal microbiota of a child. In the future, along with determining the dynamics of the microbiome over time, there is a need for randomized interventional studies that would study ways to regulate the formation of the microbiota of young children and possible subsequent programming of the immune response.

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PREDICTION OF THE RISK OF DEVELOPING DESTRUCTIVE FORMS OF ACUTE CHOLECYSTITIS

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The number of patients suffering from cholelithiasis continues to grow steadily all over the world. Acute cholecystitis is one of the most dangerous complications of cholelithiasis is. The mortality rate in this complication largely depends on the degree of destructive changes in the biliary tract and ranges from 4 to 26%. In addition to the high mortality rate, acute cholecystitis is characterized by a significant percentage of both preoperative and postoperative complications. At the same time, in acute cholecystitis, there are no clear recommendations that would allow making a timely correct decision on the tactics of patient management. Often, clinicians resort to conservative treatment and are late with the operation. Currently, we are looking for methods that would allow us to predict the risk of developing destructive forms of acute cholecystitis in a timely manner. In some cases, on the contrary, there is an underestimation of contraindications, especially in somatically burdened patients, and unjustified surgical activity. Along with this, there is no consensus on the timing of surgical intervention In this review, the main methods for predicting the development of destructive forms of acute cholecystitis are considered. The new stage of diagnosis of diseases and predicting complications is characterized by the introduction of various mathematical models in an inextricable relationship with the accumulated diagnostic knowledge. Various methods are proposed based on the creation of mathematical models and programs for predicting acute calculous cholecystitis in emergency patients. Numerous studies have been devoted to the development of a point system for predicting destructive processes in the gallbladder. The algorithm of using these methods in patients with acute cholecystitis is presented, as well as the prospects for further search for effective methods for predicting the destruction of the gallbladder, acceptable for use in a wide clinical practice. At the same time, the problem of predicting the risk of developing this complication remains relevant. There is a need to search for new methods that would allow predicting the risk of developing destructive forms of acute cholecystitis at an early stage of the disease and determining the most rational treatment tactics. The number of patients suffering from cholelithiasis continues to grow steadily all over the world. One of the most dangerous complications of cholelithiasis is acute cholecystitis. The mortality rate in this complication largely depends on the degree of destructive changes in the biliary tract and ranges from 4 to 26%. In addition to the high mortality rate, acute cholecystitis is characterized by a significant percentage of both preoperative and postoperative complications. At the same time, in acute cholecystitis, there are no clear recommendations that would allow making a timely correct decision on the tactics of patient management. Often, clinicians resort to conservative treatment and are late with the operation. Currently, we are looking for methods that would allow us to predict the risk of developing destructive forms of acute cholecystitis in a timely manner. In some cases, on the contrary, there is an underestimation of contraindications, especially in somatically burdened patients, and unjustified surgical activity. Along with this, there is no consensus on the timing of surgical intervention In this review, the main methods for predicting the development of destructive forms of acute cholecystitis are considered. The new stage of diagnosis of diseases and predicting complications is characterized by the introduction of various mathematical models in an inextricable relationship with the accumulated diagnostic knowledge. Various methods are proposed based on the creation of mathematical models and programs for predicting acute calculous cholecystitis in emergency patients. Numerous studies have been devoted to the development of a point system for predicting destructive processes in the gallbladder. The algorithm of using these methods in patients with acute cholecystitis is presented, as well as the prospects for further search for effective methods for predicting the destruction of the gallbladder, acceptable for use in a wide clinical practice. At the same time, the problem of predicting the risk of developing this complication remains relevant. There is a need to search for new methods that would allow predicting the risk of developing destructive forms of acute cholecystitis at an early stage of the disease and determining the most rational treatment tactics.

Keywords: cholelithiasis, acute cholecystitis, prognosis, destructive forms, cholelithiasis, diagnosis.

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Treatment of acute cholecystitis is a difficult problem for clinicians. This is primarily due to high morbidity and a significant percentage of deaths. In recent years, there has been a steady increase in patients with cholelithiasis all over the world and reaches 10-15% in the adult population. According to American researchers, 6.3 million men and 14.2 million women aged 20-74 years suffer from cholelithiasis in the USA [29]. In Italy, according to the results of