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Clinical and Microbiological Significance of the Specificity, Composition and Functional Differences of Dysbiosis in Children and Adults

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Annotation: The gut microbiota has a significant impact on the development, maturation and differentiation of the immune system. It has a significant impact on the mental and physical development of the child. Large-scale cohort studies can provide a more complete picture of the differences between people and more accurately characterize how the gut microbiota affects human physiology and disease processes. The formation of the intestinal microbiota begins in utero or immediately after birth, and by the age of three its composition completely changes and becomes the same as in adults. In childhood, it is very important to form a balanced gut microbiota, because dysbiosis can continue into adulthood. The human intestinal microbiota may play a fundamental role in the risk of developing diseases that can be programmed at an early age, and studies have shown that dysbiosis, or imbalance of the intestinal microbiota at an early age, is associated with specific disease outcomes in children or adults, including obesity, cardiovascular diseases, neurological disorders. disorders, atopic dermatitis, diabetes, asthma and other allergic diseases. In fact, it is extremely important to investigate the role of the human gut microbiota at an early age. Thus, research is currently focused on factors affecting the gut microbiota of infants. This review discusses the latest results of our

research on how various factors, such as the type of delivery, type of diet and medication, including antibiotics, affect the intestinal microflora of infants. It also discusses promising methods for preventing and restoring dysbiosis in children and adults.

Keywords: Human gut microbiome, Clostridium difficile, Bacteroides, Newborns, short bowel syndrome, celiac disease.

Introduction. The human gut microbiome is dynamic and is formed under the influence of many factors. The gut microbiota is located in the human gastrointestinal tract and performs an important function, including it has been proven to play an important role in the overall state of human health. Recent advances in next-generation sequencing have shown that dysbiosis, that is, an imbalance in the normal gut microbiota, is related to some diseases, because this imbalance can disrupt the symbiotic relationship between the host and the microbes associated with it [1,2,3]. A number of studies have found that changes in the composition of the gut microbiome are associated with various diseases of the gastrointestinal tract and gastrointestinal diseases in children and adults. Interest in the complex microbial community of the gut has increased due to these changes in the composition of the microbiome, known as dysbiosis, and their relationship to health and disease. At best, we still have only a superficial understanding of the relationship between the gut microbiota and health and disease. The main problem hindering progress in this area is our incomplete understanding of the composition and changes of the gut microbiome throughout human life [5,6,7,8]. Most microbiome studies today use a case-control scheme, which increases the sensitivity of the analysis to methodological problems. In addition, most studies tend to focus on specific diseases and phenotypes and have relatively small sample sizes. The study of large and well-characterized population groups can help us better understand the differences in the composition of the microbiome (according to stool or other sources) and its role in the etiology of chronic diseases [9,10,11,12,13]. These populations provide rich information about various physiological parameters, disease status, drug use, diet, and other "omic" data related to each participant. Until now, microbiome research has focused mainly on adults. However, it has been shown that the gut microbiome changes throughout a person's life, especially during development, and the most noticeable changes are observed in childhood. Interestingly, new evidence suggests that early changes in the gut microbiome are associated with an increased risk of developing diseases later in life, such as asthma and Crohn's disease. However, these studies were limited by the small sample size. If we want the dynamics of the microbiota to develop, studies of well-characterized cohorts of the population of different ages, including studies of pediatric cohorts, are necessary. So far, a complete description of the diversity, composition, and functional differences between children and adults in large, homogeneous, and representative cohorts has not been provided [1,2,4,9,11-17].

The main purpose of the presented manuscript is to conduct a brief analysis of the literature based on the conducted scientific studies of the clinical and microbiological substantiation of their functional differences in the composition of the microbiota in children and adults.

The specifics of the intestinal microbiota in children. Currently, it is known that the number of microorganisms in various parts of the body is greater than human cells, in a ratio of 1:1.3, and this affects the health of the host throughout life. Since the uterus is usually considered sterile, microbial colonization of the human body begins at birth. However, several studies have questioned this idea, finding bacteria in amniotic fluid, meconium, and placenta. These claims, however, are considered controversial. After the rupture of the fetal bladder, when the child goes

through the first stage of colonization by microorganisms, going down the birth canal, sterility disappears. Until about the age of three, the composition of the microbiome changes rapidly after childbirth, when it becomes as diverse and complex as in adults [5-11]. Many factors influence the diversity and amount of microbiota in the intestines of infants at an early age, as we will discuss below. A mother shares microbes and microbial metabolites with her child during pregnancy, childbirth and breastfeeding. This shows how important the mother's health is during pregnancy. Due to changes in the composition of the maternal microbiome, a high maternal body mass index increases the child's vulnerability to obesity and diabetes later in life. There is a correlation between the amount of *Bacteroides*, *Clostridium* and *Staphylococcus* in stool and higher body mass index and obesity in mothers; on the other hand, the amount of *Bifidobacterium decreased*. In addition, infants with a normal body mass index had low levels of *Akkermansia muciniphila*, *Staphylococcus* and *Clostridium difficile* during pregnancy. During pregnancy, metabolites in the mother's intestine can enter the body of the developing embryo and fetus. In a recent study involving mice, short-chain fatty acids produced in the intestine penetrate the placenta and affect the differentiation and metabolism of embryonic organs by acting on G-protein-related receptors. The first thing a newborn receives from his mother is breastfeeding [7-16]. In addition, during this process, a microbiota is formed in the intestines of a newborn. The newborn is first exposed to the milk microbiome and then to maternal milk factors such as breast milk oligosaccharides, antimicrobial factors and secretory IgA (sIgA). WHO recommends that infants should only be fed breast milk during the first six months of life. Several studies have been conducted comparing the effects of formula and breast milk on the microbiome of newborns in order to understand the effects of feeding on newborns. Despite the fact that bifidobacteria are the most common bacteria in both milk and formula, the microbiota of breastfed infants is more stable and homogeneous. In addition, breast milk has been found to prevent diarrhea, necrotizing colitis, allergies and celiac disease [18,19, 20, 21].

Features of the structure of the intestinal microbiota in adults. The adult human body contains 100 trillion intestinal bacteria, including more than 1,000 species, and approximately 160 species in a fecal sample, which exceeds the number of somatic cells in a ratio of 1.3:1. Commensal bacteria live in the colon, oral cavity, male and female genital tract, respiratory system and on human skin. The formation of the baby's gut microbiota begins quickly after birth with exposure to microbes from the mother's birth canal, the biota of the mother's skin and the environment. The microbiota then develops into an adult-like gut microbiota. Adult gut microbiota were more likely to contain firmicutes such as Lactobacillales and Clostridiales, while Actinobacteria such as Bifidobacteriales were more common in samples taken from children aged one year. After weaning, the number of actinobacteria in children decreased, and by the age of three, the intestinal microbiota became more similar to the intestinal microbiota of adults [5,11,14,15,16,20]. The microbial composition of the body varies significantly depending on the state of health and disease. "Microbiota" and "microbiome" are synonymous, but "microbiota" refers to organisms living in a particular environment, and "microbiome" refers to microorganisms and their genome in that particular environment. The microbiome contains about 3.3 million active genes, while humans have 22,000 genes. The organisms living in the intestine are called mycobiotes, which make up about 60% of its dry mass; 99% of them are anaerobic bacteria. Although bacteria make up the majority of the microbiome, viruses, archaea and eukaryotes are less common, but they also need to be taken into account [1,4,5,9,11].

Factors affecting the gut microbiota in children and adults. As already mentioned, it is very important to form a healthy intestinal microbiota in infancy, since the intestinal microbiota changes dramatically during the first three years of life, acquiring a composition characteristic of an adult, and dysbiosis that develops at an early age can persist until adulthood. The mother's microbiota in the intestines and intestines, the method of delivery, the type of feeding, the use of antibiotics and other drugs, the duration of pregnancy, the presence of siblings and pets, as well as regional differences in nutrition and sanitary conditions are some of the factors affecting the intestinal

microflora of newborns and infants. In this article, we review new data on the effect of these factors on the gut microbiota in children, paying special attention to the type of feeding, delivery and antibiotics [3-12]. Scientists have found clear differences between the gut microbiome of children and adults, including differences in microbiota diversity and the number of *Firmicutes and Bacteroidetes*. These changes were associated with predicted shifts in functional properties, including energy metabolism, antibiotic production, and the production of essential B vitamins. These observations are probably related to the development of the interaction of the human gut microbiome with age. Since both the GenR and RS cohorts have been thoroughly studied, scientists have presented two valuable data sets here to study the possible relationship of the human stool microbiome with lifestyle, environmental factors, as well as with health and diseases. In addition, since the genotypes of the participants in both groups were determined, it was possible to study the relationship between the genetics of the host and its microbiome [18,21,24,27]. Environmental factors in adults, especially unhealthy diet and medication intake, are the most important factors negatively affecting the gut microbiota. Since genetic factors are relatively stable, they probably do not play such a big role in the increase in the number of these diseases [25,26,28].

Dysbiosis. It seems that the state of the intestinal microbiota plays a crucial role in how children with short bowel syndrome (ShBS) develop. Serious complications, such as excessive bacterial growth in the small intestine and inflammation of the intestinal mucosa, can be caused by changes in the microbiota. This can lead to long-term dependence on parenteral nutrition, which increases the risk of liver failure and sepsis. The composition of the intestinal microbiome of children with ShBS is unknown. We present the first study of the gut microbial community profile of children with Schwachman syndrome. Dysbiosis, or imbalance of the gut microbiota, is associated with numerous health problems. Dysbiosis is associated with an increased risk of gastrointestinal diseases such as inflammatory bowel disease, irritable bowel syndrome and necrotic enterocolitis. It is also associated with allergic diseases, diabetes, obesity, cardiovascular diseases, autism spectrum disorders and sudden infant death syndrome. We believe that children with Kawasaki disease and idiopathic nephrotic syndrome may also have dysbiosis [14-21].. Many childhood diseases, such as autism, growth retardation, eating disorders, celiac disease, necrotizing enterocolitis, Helicobacter pylori infection, functional disorders of the gastrointestinal tract in children, inflammatory bowel diseases and much more, are associated with dysbiosis. Allergic diseases such as atopic dermatitis, allergic rhinitis and asthma can also cause dysbiosis. In addition, dysbiosis can affect the progression and development of immune and cardiovascular diseases, including heart failure. Probiotic supplements can help in the treatment of these diseases. However, we still need more in-depth research. In this review, we examined how the microbiota plays an important role in the development and treatment of common childhood diseases [1,12,14,17,18,20].

Discussion. More than 1000 species of microorganisms colonize the intestines. Currently, there is evidence that colonization of the intestine begins in the womb; bacteria have been found in the amniotic fluid, placenta and meconium of healthy newborns. Newborns born naturally have the microbiota of the mother's vagina, and newborns born by caesarean section have the microbiota of the mother's skin. Then, with each change in the baby's diet, the microbiota gradually changes. This begins with a simple newborn microbiota with a predominance of facultative anaerobic bacteria such as Streptococci, Enterobacteria and enterobacteria, and continues with a complex adult microbiota in the first few years of life, which is more diverse and capable of vitamin biosynthesis and polysaccharide digestion [1-5,18,19,20]. Intestinal mycobiota plays an important role in the immunological, metabolic, structural and neurological processes of the body. Human physical and mental health is also highly dependent on the gut microbiota. The intestinal microbiota has a significant impact on the normal and physiological development of the intestine. It also promotes the development and differentiation of the intestinal mucosa, as well as the immune system. It limits the reproduction of pathogenic and potentially pathogenic microbes,

fights them and suppresses their ability to penetrate and spread into the ecosystem. Some strains of the microbiota can produce bacteriocins, antimicrobial substances that prevent other bacteria from multiplying [14, 15, 18, 19,21,24]. The type and amount of microbiota in the human gut vary greatly. Many factors related to bacteria and the human body affect how bacteria colonize the intestine. Age, genes, general health, nutrition, medication, pH, peristalsis and time of passage of food through the intestine, mucous secretions containing immunoglobulins, and the redox potential of tissues are all factors affecting the human body. Nutrient availability, bacterial interaction or antagonism, and bacterial adhesion are all microbial factors. The microbiota in the intestine varies depending on its characteristics [22, 23, 25, 26, 27]. Dysbiosis is common in many childhood diseases such as autism, growth retardation, eating disorders, celiac disease, necrotizing enterocolitis, *Helicobacter pylori* infection, functional disorders of the gastrointestinal tract in children, inflammatory bowel diseases and many other disorders of the gastrointestinal tract.The differences in dysbiotic conditions from dysbiosis in children to dysbiosis in adults hm differ between them, as does the structure of the composition of the microbiota. In children, dysbiotic conditions affect to varying degrees the growth development or mental activity of children, as well as the activity of certain organs. And in adults, this can provoke the development of severe pathologies in many organs and systems. In particular, these include serious pathologies associated with neurodegenerative, autoimmune, and sepsis formation [27, 28, 29, 30, 31].

Conclusion. Thus, the microorganisms inhabiting the human body are closely related to each other. The intestine is the main habitat of this microbiota, because it creates a favorable environment for the vital activity of bacteria. The microbiota of a child develops both in childhood and adolescence. The gut microbiota of children and adolescents may differ in the relative content of genera, despite the fact that they are similar to adults in terms of the number of detectable species. Their intestinal microbiota contains more *Bifidobacterium spp., Faecalibacterium spp*. and representatives of the *Lachnospiraceae* than the adult gut microbiota, which contains more Bacteroides spp. Intestinal dysbiosis is also a potential pathogenic factor contributing to the development of various childhood diseases both in the gastrointestinal tract and beyond. This can lead to the development of severe pathologies in many organs and systems in adults, including serious pathologies associated with neurodegenerative, autoimmune, and sepsis formation. In children, dysbiotic conditions affect growth, development, or mental activity to varying degrees, as well as the activity of certain organs. The structure of the composition of the microbiota varies between dysbiosis in children and dysbiosis in adults.

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