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THE ROLE OF INTESTINAL MICROFLORA AND PROBIOTICS IN THE DEVELOPMENT OF IMMUNITY IN INFANTS

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In recent years, pediatricians and epidemiologists have noted the emergence of some unfavorable trends in the health of the child population, namely: an increase in allergic and autoimmune diseases, obesity, type 2 diabetes, and chronic nonspecific intestinal diseases.

The search for the causes and mechanisms of development of these diseases has revealed a number of factors that increase the risk of developing many pathological conditions. Among risk factors, changes in the composition of the intestinal microbiota (IMB) occupy one of the first places [3]. It has been proven that the development of atopy, obesity, and nonspecific inflammatory bowel diseases is often preceded by a change in the composition of the intestinal microflora (IMF).It is assumed that the violations of the composition of the Intestinal Microflora are based on modern principles of sterile management of childbirth, the widespread prevalence of surgical delivery, a significant prevalence of urogenital infections in mothers, the use of antibiotic therapy in pregnant women, children and mothers, a decrease in the prevalence and duration of breastfeeding. The nature of the IMF of a newborn baby depends on the microflora of the mother, the nature of childbirth, the environment and nutrition [5].

To date, convincing evidence has emerged of impaired IMF in children born by cesarean section. As can be seen from, normalization of the composition of IMF during surgical delivery is achieved only by the 6th month of life [1]. The same study showed that a decrease in the level of bifidobacteria (BB) in the stool of children is accompanied by an increase in the level of clostridia and bacteroides. A meta-analysis of data from various studies on the effect of operative delivery on the subsequent health of children showed a significantly higher incidence of morbidity in infants born by cesarean section. Antibiotic therapy is often used in the early postnatal period, sometimes without sufficient justification. In the work of S. Nutten [2] it was shown that the use of broad-spectrum antibiotics for 7 days is accompanied by gross changes in the IMF: a sharp decrease in the number of BD and lactobacilli (LB), up to their complete disappearance, replacement of healthy microflora with antibiotic-resistant strains, increased activity of mast cells and increased risk development of atopy. Violation of the composition of IMF reduces

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the capabilities of the intestinal protective barrier, in particular by reducing the antimicrobial function of Paneth cells [8]. There is now reliable evidence that disturbances in the composition of IMF in infancy due to antibiotic therapy are an important factor predisposing to the development of chronic inflammatory bowel diseases in the future. An additional factor that adversely affects the composition of IMF is artificial feeding.

Healthy IMF plays a decisive role in the formation and maturation of the immune response in infants. First of all, commensal bacteria are the first antigen to enter the baby's intestines, and the reaction of the innate immune system when encountering bacteria determines the direction of the immune response. The entry of pathogenic bacteria into the body is accompanied by activation of the nuclear factor and the release of pro-inflammatory cytokines. In the work of L. O'Mahony [4], in a clinical setting, the difference in the immune response of peripheral blood lymphocytes to contact with commensal and pathogenic flora was demonstrated: the commensal flora did not increase the production of proinflammatory cytokines, while the pathogenic flora induced active production of TNFα, IL12 and inflammatory processes. In an unfavorable situation, this process can be protracted and repeated in the future. The entry of commensal bacteria into the baby's body (during passage through the mother's birth canal, with BM) does not lead to activation of the nuclear factor and the production of inflammatory cytokines [7].

The appearance of T-regulatory cells secreting IL10, TGFβ, which have tolerogenic properties and soften the activity of the immune response, is observed. According to Rooks [10], this is due to the fact that in the process of thousands of years of human evolution, his body began to perceive LB and BB as "old friends", therefore the entry of these bacteria does not activate the synthesis of pro-inflammatory cytokines. At the same time, the absence of "old friends" disrupts the processes of immunoregulation and the development of tolerance in the baby's body. The task of commensal bacteria is to initiate, educate, and train the infant's immune system, and their absence becomes a risk factor for the development of autoimmune and allergic diseases in the child. Another mechanism by which commensal bacteria influence infant protection is through increased production of sIgA in the intestine. Most sIgA, as well as other immunoglobulins, is produced by intestinal plasma cells. The protective properties of sIgA, as a first line of defense, are due to its ability to prevent adhesion and penetration of pathogens [9].

The second line of defense is associated with the ability of sIgA to penetrate the epithelial cells of the intestinal mucosa and affect the replication cycle of viruses located intracellularly. SIgA, unlike other immunoglobulins, functions as a specific immunological barrier, binding antigens on the surface of the epithelium and preventing their penetration into the body, thereby reducing the activity of the

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immune response, reducing the likelihood of both inflammatory and allergic processes [6]. An important mechanism for protecting the gastrointestinal tract is maintaining the integrity of the intestinal mucosal barrier to prevent penetration by pathogens. In recent years, the possibility of beneficial modulation of the BMP of a formula-fed infant using infant formula enriched with probiotics has been widely discussed in the medical literature. The ability of probiotic bacteria to modulate the infant's immune system through several mechanisms has now been established [11]:

maintaining the integrity of the intestinal epithelial barrier:

increasing the mucin layer to prevent pathogen penetration;

reducing the possibility of increasing the permeability of the barrier to pathogens;

increased protection of epithelial cells by the release of stress-regulating proteins;

regulation of the functions of antigen-presenting cells by reducing their excessive activation;

ensuring the readiness of the immune system for an adequate response of a healthy body and suppressing the pro-inflammatory orientation of the immune response during the disease process;

formation of immunological tolerance.

At the same time, it is emphasized that infant formula probiotics must satisfy three main criteria: 1) stability in the product and when passing through the aggressive environment of the stomach and intestines; 2) effectiveness proven in clinical trials; 3) absolute safety for an infant receiving VHI from birth.

The theoretical and clinical data obtained allow us to speak about the effectiveness and necessity of using probiotics in the nutrition of children deprived of mother's milk from birth. The safety of probiotics is assessed for each specific strain and type of probiotic.

Currently, data have been obtained on the safety of using a number of probiotics in baby food, which include B. lactis, B. longum, L. rhamnosus and some others. The safety claim for B. lactis is based on extensive research into its properties. To date, the genome of B. lactis has been isolated and well studied, which lacks unfavorable metabolic characteristics and virulence potential. B. lactis does not have any negative effect on the parietal mucus layer, maintaining a high adhesion ability. There are numerous studies confirming the beneficial effects of B. lactis on the intestinal barrier and immunity.

Over the past 15 years, infant formula with B. lactis has been widely used in infant nutrition, and no side effects have been found with its use. Products containing B. lactis are consumed annually worldwide, and there are no

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documented cases of bacteremia or infection associated with the use of dairy products or infant formula fortified with B. lactis. No adverse effects have been reported in clinical trials of products containing B. lactis, including studies of full-term and preterm infants and infants born to HIV-infected mothers.

Thus, the use of probiotics in VHI from birth in the absence of breastfeeding will help develop a healthy immune system for the baby and reduce the risk of developing chronic inflammatory diseases.

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