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THE INFLUENCE OF MICRONUTRIENT DEFICIENCY AND GUT MICROBIOTA ON IMMUNE RESPONSE: THE ROLE OF MICROBIOTA AND ITS METABOLITES

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Annotation

Micronutrients are substances necessary for the normal functioning of the body. An important component of the body's defense system is a healthy gut microbiota. This article reviews current scientific approaches to correcting micronutrient deficiency and modulating the microbiota to improve the functional state of the immune system in children and adolescents, using the examples of Multi-Tabs® vitamin-mineral complexes and Bifiform® probiotics.

Introduction

Micronutrients (vitamins, macro- and trace elements) are essential components of human nutrition. These compounds regulate physiological and biochemical processes underlying the vital functions of the body.

Child nutrition is a cornerstone of health and normal development. As Hippocrates stated: "We are what we eat. Disease is a result of improper nutrition, habits, and lifestyle." According to the World Health Organization (WHO), 60% of deaths are directly related to poor nutrition.Vitamin deficiency, a risk factor for a number of diet-related diseases, is caused by unbalanced diets, impaired absorption of vitamins and trace elements due to gastrointestinal, liver, or thyroid pathologies, living in ecologically unfavorable areas, diabetes, and the intake of anti-vitamins (such as anti-tuberculosis drugs, antidepressants, sulfonamides, indirect anticoagulants, etc.).Vitamin deficiency can also result from increased demands during periods of rapid growth, recovery, active sports, mental stress, or infections.

A multicenter study conducted by the Scientific Center for Children's Health and the Russian Medical Academy of Continuous Professional Education, involving more than 2,000 children from seven regions, revealed deficiencies in fruits, vegetables, and meat in the diet of children aged six months to three years, along with limited consumption of baby food and excessive intake of "adult" products and sweets.

Parental surveys of children aged 6–36 months showed that 55% of children aged 6–12 months rarely consume meat, with this proportion increasing with age to 77.6% in children aged 24–36 months.

A similar trend was observed for vegetable consumption: 58.4% of children aged 6–12 months eat vegetables daily, decreasing to 35.4% in children aged 24–36 months. At the same time, the consumption of sweets sharply increases with age—from 51% at 6–12 months to 80.4% at 24–36 months.

The nutritional situation of school-aged children is even more concerning. According to parental surveys, children often consume foods high in animal fats and trans fats (confectionery,

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processed meat products, baked goods, chips, popcorn, mayonnaise, etc.) at home, while their diets are deficient in fresh vegetables, fruits, dairy products, and fish. Nearly half of the children consume fast food once a month, and one in ten several times a month.

Vitamin deficiency increases with age. Experts estimate that adolescents from age 14 consume less meat, milk, and fish. Low or absent fish intake leads to vitamin D deficiency.

Studies of vitamin status among children in various Russian regions, as reported in the National Program for Optimizing Vitamin and Mineral Intake (2017), indicated low levels of vitamins B6, B1, B2 (24–53%), vitamin C (27%), vitamin A (36%), and vitamin E (47%).

According to the Biotic Medicine Center, a survey of 30,000 Russian children and adolescents revealed deficiencies in macro- and trace elements (zinc, copper, manganese, boron, selenium) in most participants.

A study conducted by the Russian Medical Academy of Continuous Professional Education on daily calcium intake in adolescents (2014–2015) showed reduced intake compared to the norm (1,200 mg) in adolescents with both normal (700–800 mg) and reduced bone mineral density (425 mg).

Statistically significant differences were observed between baseline levels of essential elements such as zinc, manganese, and boron and normal values, with increases after three months of vitamin-mineral complex supplementation.

Over the past decades, food quality has changed due to soil depletion, leading to insufficient mineral content in plants. Harvesting vegetables, fruits, and greens before full ripeness prevents the accumulation of nutrients. Animal husbandry practices, long transport and storage, and food processing reduce the content of bioactive compounds.

Vitamins D, A, E, C, B6, B9, and trace elements such as zinc, selenium, copper, boron, and magnesium play significant roles in the immune response.

Vitamin D acts from the first phase of the immune response. In innate immunity, it reduces dendritic cell maturation, inhibits synthesis of pro-inflammatory cytokines (TNF-α, IL-6, IL-12, IL-23), and antigen presentation, promoting macrophage differentiation and antimicrobial peptide production. In adaptive immunity, vitamin D modulates T lymphocytes and antibody production. Expression of hundreds of genes is regulated by vitamin D, confirming its immunomodulatory effect.

Vitamin A (retinol) is a typical anabolic vitamin, particularly important for fetal development. Retinol participates in cellular proliferation and differentiation of immune cells, activating cytotoxic functions of T cells and macrophages, crucial for antiviral defense. The gut microbiota converts dietary vitamin A into its active form (retinoic acid), and the microbiota's condition influences levels of vitamins A and K in the body. Vitamin C has multiple functions, enhancing resistance to respiratory infections. Deficiency impairs interferon production, disrupts cellular immunity, and slows antibody synthesis. Vitamin E is a potent antioxidant that protects cells from free radical damage. It supports rapid immune cell reproduction and

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immunoglobulin synthesis, improving tissue respiration. The immune system depends on the combined presence of multiple vitamins affecting its functional state.

Macro- and trace elements are also crucial. Deficiency suppresses the activity of immune cells involved in both innate and adaptive immunity. Correcting deficiencies restores immune competence. Zinc deficiency impairs leukocyte chemotaxis, natural killer activity, and phagocytosis, induces lymphocyte apoptosis, and blocks Th1 responses by reducing anti-inflammatory cytokines. Zinc is essential for immune cell proliferation, activation, and vitamin D receptor functionality. Selenium, a strong antioxidant, enhances immune response in combination with vitamins E and C, boosting macrophage activity, interferon synthesis, and antibody production. Copper and boron also influence immunity. Copper modulates Th1 responses via transcription factors and enzyme activation. Boron supports antibody production, natural killer cells, and cytotoxic T lymphocytes. Copper and boron participate in adaptive immunity, while vitamins D, A, E, C, zinc, selenium, and magnesium affect both innate and adaptive immunity, acting synergistically. Single nutrients cannot achieve the same immunomodulatory effects. Even with balanced nutrition, vitamin deficiency can reach 30%, as food vitamin content has decreased two- to threefold. Therefore, regular use of multivitamin complexes (MVCs) is often necessary.

MVCs, such as Multi-Tabs®, provide age-appropriate supplementation and are essential for Russian populations with near-year-round deficiencies. Factors to consider include composition, micronutrient doses, and absence of artificial additives.

Multi-Tabs® Baby contains essential vitamins (A, C, D) for infants, especially those with perinatal risk factors, limited maternal diet, formula feeding, or absorption disorders. Multi-Tabs® Malysh (1–4 years) provides water- and fat-soluble vitamins without sugar, colors, or preservatives. Multi-Tabs® Malysh Calcium Plus adds calcium and osteogenic nutrients. Multi-Tabs® Junior is for children 4–11 years, and Multi-Tabs® Immuno Plus, containing LGG probiotic and immunomodulatory nutrients, is for adolescents 18+ and adults. According to the National Program (2017), prophylactic MVC use involves double doses (100–200% of recommended intake) for 3–4 weeks, followed by maintenance doses (30–50%) and standard age-appropriate doses.

Influence of Microbiota and Its Metabolites on Immune Response

Insights into the microbiota were greatly advanced by the Human Metagenome Project. The microbiome includes 1 million genes and 40,000 microbial species, compared to only 23,000 human genes. The gut microbiota weighs 1–3 kg and has a memory capacity of 100,000 terabytes.

Humans can be classified into three enterotypes based on gut microbiota composition: Bacteroides-dominated, Prevotella-dominated, and Ruminococcus-dominated.

Gut microbiota performs metabolic, protective, and epigenetic functions. Its protective role operates on three levels: microbial antagonism and quorum sensing, influence on the intestinal barrier, and modulation of the immune system.

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The mucosa-associated microbiota forms biofilms embedded in an extracellular matrix of polysaccharides, proteins, nucleic acids, and lipids. Denser biofilms resist colonization by foreign microbes.

Mucins, secreted by goblet cells, form a mucus layer that prevents direct bacterial contact with epithelium. Paneth cells secrete antimicrobial peptides (defensins). Microbes produce signaling molecules (autoinducers) that regulate species abundance.

Healthy microbiota prevents pathogen adhesion. Dysbiosis, with reduced microbial diversity and thinning mucus, allows pathogens to breach the epithelium and trigger inflammation ("leaky gut").

The epithelial barrier is normally impermeable to microbes. Tight junction proteins (occludins) and zonulin regulate intercellular space. Dysfunction increases pathogen penetration.

M cells capture antigens and present them to immune cells. The gut-associated lymphoid tissue (GALT) contains nearly all immune cells, including pattern-recognition receptors (Toll-like and Nod-like), macrophages, granulocytes, and natural killer (NK) cells.

Dendritic cells guide T-cell differentiation via cytokine production. Adaptive immunity involves T and B lymphocytes responding to specific pathogens.

Microbial metabolites penetrate the mucus layer and can trigger inflammation or promote immune tolerance. Bifidobacteria dominate the infant gut, preventing NF-kB activation and maintaining immune homeostasis. The microbiota shapes the immune system, regulating both short- and long-term responses. Factors influencing infant gut microbiota include delivery mode, gestational age, antibiotic use, and feeding type. A healthy microbiota supports immunity, prevents pathogen adhesion, stimulates secretory IgA and mucus production, promotes tight junction protein synthesis, and ensures immune tolerance. Dysbiosis reduces microbial diversity, increases pro-inflammatory microbes, and decreases tolerogenic species, leading to chronic inflammation. A European analysis of the quality of corresponding organic probiotics showed that only 13.8% of the declared strains were actually present. Probiotics with the same composition may differ in manufacturing technology and effectiveness. When choosing a probiotic, preference should be given to products with proven efficacy and safety. BiFiForm® meets these requirements – it is a probiotic brand designed to support gastrointestinal health while considering age-related and individual needs.

BiFiForm® Baby is a probiotic for children from the first days of life (0–2 years), containing a complex of beneficial bacteria that help normalize intestinal microflora. BiFiForm® Baby is supplied in bottles with dosing pipettes.

BiFiForm® is a probiotic for normalizing microflora in adults and children older than two years. BiFiForm® comes in enteric-coated capsules. The capsule's dual-layer protective shell ensures that the full complex of beneficial probiotic bacteria reaches the intestines.

BiFiForm® Baby contains probiotic strains such as *Bifidobacterium animalis* subsp. *lactis* BB-12 and *Streptococcus thermophilus* TH-4. Importantly, BB-12 and TH-4 are recognized as safe

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strains. They have received GRAS (Generally Recognized as Safe) status and have been approved by the U.S. Food and Drug Administration (FDA). Clinical studies confirming the probiotic's efficacy support its use in children for the prevention and treatment of acute infectious diarrhea, antibiotic-associated diarrhea, functional disorders, and for the development of a healthy immune system.

Conclusion

To prevent and correct micronutrient deficiencies in children and adolescents, vitamin-mineral complexes (VMCs) are used. Multi-Tabs® is a modern complex of vitamins, minerals, and trace elements for children and adults, characterized by proven efficacy, safety, and ease of use.

Probiotics with proven efficacy and safety are used to normalize gut microflora in children to support a healthy immune system and reduce the risk of inflammatory diseases. BiFiForm® is a probiotic brand designed to support gastrointestinal health with age-specific and individual considerations. BiFiForm® Baby is recommended for children from birth to two years, and BiFiForm® for children over two years and adults.

The combined use of BiFiForm® and Multi-Tabs® ensures supplementation of vitamins, macro- and micronutrients, synthesis of certain vitamins in the gut (e.g., vitamin K and B-complex), and a multifaceted effect on the child's immune system, thanks not only to the balanced Multi-Tabs® complexes but also to the immunogenic action of probiotics and the maintenance of gut microbiota balance.

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