PRACA POGLĄDOWA

THE PEDIATRIC GUT MICROBIOME AND ITS ROLE IN CHILDHOOD DISEASES: FROM DEVELOPMENT TO THERAPEUTIC POTENTIAL

Mikrobiom jelitowy u dzieci i jego rola w chorobach wieku dziecięcego: od rozwoju do potencjału terapeutycznego

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Abstract

The gut microbiome plays a fundamental role in child development, influencing metabolic regulation, immune maturation, and neurodevelopment from early life onward. Increasing evidence links disturbances in gut microbial composition to pediatric disorders, including obesity, allergic diseases, autoimmune conditions, neurodevelopmental disorders, and gastrointestinal pathologies. This review summarizes current knowledge on the developmental trajectory of the pediatric gut microbiome, the major environmental and biological factors shaping its composition, and key disease-related microbial patterns described in recent literature. Particular attention is given to mechanisms involving immune modulation, intestinal barrier function, microbial metabolites, and the microbiota–gut–brain axis. Finally, the potential role of probiotics as a microbiome-targeted strategy is discussed, emphasizing both their therapeutic promise and existing limitations. Overall, the pediatric gut microbiome emerges as a modifiable determinant of health, warranting further longitudinal and interventional research.

Streszczenie

Mikrobiom jelitowy odgrywa fundamentalną rolę w rozwoju dziecka, wpływając na regulację metabolizmu, dojrzewanie układu odpornościowego oraz rozwój układu nerwowego od najwcześniejszych etapów życia. Coraz więcej dowodów wskazuje, że zaburzenia składu mikrobioty jelitowej są powiązane z występowaniem chorób wieku dziecięcego, w tym otyłości, chorób alergicznych, schorzeń autoimmunologicznych, zaburzeń neurorozwojowych oraz patologii przewodu pokarmowego. Niniejszy artykuł podsumowuje aktualny stan wiedzy na temat rozwoju mikrobiomu jelitowego u dzieci, głównych czynników środowiskowych i biologicznych kształtujących jego skład, a także charakterystycznych wzorców mikrobiologicznych związanych z chorobami, opisanych w najnowszym piśmiennictwie. Szczególną uwagę poświęcono mechanizmom obejmującym modulację odpowiedzi immunologicznej, funkcję bariery jelitowej, rolę metabolitów bakteryjnych oraz komunikację w osi mikrobiota–jelito–mózg. Na zakończenie omówiono potencjalną rolę probiotyków jako strategii terapeutycznej ukierunkowanej na mikrobiom, podkreślając zarówno ich obiecujące możliwości kliniczne, jak i ograniczenia. Ogólnie rzecz biorąc, mikrobiom jelitowy dzieci jawi się jako modyfikowalny czynnik warunkujący zdrowie, co uzasadnia potrzebę dalszych badań podłużnych i interwencyjnych.

Keywords: probiotics; gut microbiome; microbiota–gut–brain axis; immune system development

Słowa kluczowe: probiotyki; mikrobiom jelitowy; oś mikrobiota–jelita–mózg; rozwój układu odpornościowego

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Introduction

The gut microbiome is increasingly recognized as a central regulator of childhood development, influencing biological, cognitive, and emotional processes from birth through adolescence. Childhood encompasses four major stages – infancy, early childhood, middle childhood, and adolescence – and deviations from expected developmental milestones at any of these stages may indicate emerging health concerns. These include conditions such as malnutrition, obesity, neurodevelopmental disorders, including autism spectrum disorder (ASD), food allergies, and asthma. Growing evidence indicates that alterations in gut microbiota composition and function contribute to the onset and progression of many of these disorders, positioning the microbiome as a potentially modifiable determinant of pediatric health outcomes [1].

The pediatric gut microbiome is a complex ecosystem composed of bacteria, viruses, fungi, archaea, and parasites, with bacteria constituting the most abundant and diverse group. Although microbial interactions shape health across the lifespan, their influence is particularly critical during infancy, when key physiological processes are established. Recent research demonstrates that early-life microbial communities interact closely with nutrition, host genetics, and immune system maturation, collectively shaping both immediate and long-term health trajectories [2].

Environmental and physiological factors strongly influence the establishment and subsequent maturation of the gut microbiome. Although the existence of prenatal colonization remains debated, there is broad consensus that extensive microbial colonization begins after birth. Early gut communities are dominated by facultative anaerobes, which are gradually replaced by obligate anaerobes as the intestinal environment stabilizes. Compared with the adult microbiota, the infant microbiome is less diverse and more dynamic [1]. Key determinants of early microbial composition include delivery mode, feeding practices (breastfeeding versus formula feeding), antibiotic exposure, and environmental conditions [1, 2]. The introduction of solid foods marks a major ecological transition: populations such as *Proteobacteria* typically decline, while overall microbial diversity and functional stability increase. Throughout childhood, the microbiome becomes progressively more complex and resilient, and by adolescence it shifts toward a more adult-like profile characterized by reduced aerobic and facultative anaerobic populations and an expansion of obligate anaerobes [1].

Studying the gut microbiota during childhood is particularly important because it differs substantially from the adult microbiome and plays a critical role in establishing metabolic pathways that may persist throughout life. Disruptions in early microbial development have been linked to metabolic disorders such as pediatric obesity, suggesting that interventions targeting early-life microbial dynamics may help prevent obesity and its associated comorbidities [3]. Understanding these mechanisms is essential not only for metabolic health but also for immune and neurodevelopmental maturation, underscoring the microbiome's multidimensional role in shaping pediatric health outcomes [2, 3].

Given the interplay between microbial maturation, metabolism, immune function, and neurodevelopment, examining the pediatric gut microbiome offers a unique opportunity for early interventions and preventive strategies. This review synthesizes current knowledge on the developmental trajectory of the pediatric gut microbiome, the factors influencing its composition, and its implications for metabolic, immune, and neurodevelopmental health, while identifying key knowledge gaps that require further investigation.

Methodology

This narrative review was based on a structured literature search conducted in PubMed, Scopus, and Google Scholar. The search focused on studies published within the past five years to ensure inclusion of the most recent and clinically relevant evidence reflecting current advances in microbiome research. Predefined keywords were used to identify publications related to pediatric gut microbiome development, disease associations, and probiotic interventions.

Approximately 50 articles were screened at the title and abstract level. Following full-text evaluation for relevance, 24 publications were included in the final narrative synthesis and are listed in the reference section. Eligible studies focused on pediatric populations and addressed microbiome-related mechanisms, disease associations, or therapeutic implications.

Given the narrative nature of this review, no formal risk-of-bias assessment tool was applied. Instead, study selection prioritized peer-reviewed publications in reputable journals that provided clear methodological descriptions and reported biologically or clinically plausible associations between gut microbiome alterations and pediatric health outcomes.

Factors shaping the pediatric gut microbiome

The development of the pediatric gut microbiome is a dynamic and highly sensitive process that begins before birth and continues throughout early childhood. This complex ecosystem is shaped by a combination of prenatal influences, perinatal exposures, nutrition, environmental interactions, and medical interventions. Because the gut microbiome plays a critical role in metabolic programming, immune maturation, and neurodevelopment, understanding the factors that modulate its early assembly is essential for promoting long-term health and preventing disease later in life [1].

Maternal influences and prenatal programming

The maternal gut microbiome plays a pivotal role in shaping fetal immune development even before birth. During pregnancy, the maternal microbiota undergoes physiological changes that parallel shifts in immune and metabolic function. Microbial components and metabolites, including short-chain fatty acids (SCFAs), lipopolysaccharides, bacterial DNA, and immune-active peptides, can cross the placental barrier and influence fetal immune programming [4].

Evidence suggests that immune education begins in utero and is partly regulated by maternal microbiota-derived molecules that interact with fetal immune cells, promoting immune tolerance and developmental priming. Although the existence of a true fetal microbiome remains debated, accumulating data support prenatal exposure to microbial products. Moreover, maternal infections – even those occurring prior to conception – may modulate immune outcomes in offspring, highlighting the long-lasting biological consequences of maternal microbial signaling [4].

After birth, breast milk continues this biologically mediated maternal microbial transfer by delivering live bacteria, metabolites, antibodies, and oligosaccharides that shape neonatal microbiota composition and immune maturation. Exclusive breastfeeding should therefore be regarded as a critical extension of maternal influence on early microbial assembly [4, 5].

Mode of delivery and initial colonization

The mode of delivery represents one of the earliest environmental determinants of microbial colonization. Vaginally delivered infants are exposed primarily to maternal vaginal and intestinal microbes, including species from the genera *Lactobacillus*, *Prevotella*, and *Bacteroides*. In contrast, infants born via cesarean section acquire a microbiota dominated by maternal skin and oral bacteria, resulting in delayed colonization by beneficial obligate anaerobes such as *Bacteroides* and *Bifidobacterium* [1].

These early microbial differences are not merely transient but have lasting implications for microbiome stability and immune development. Cesarean-born infants frequently exhibit reduced microbial diversity, delayed establishment of commensal taxa, and increased abundance of opportunistic pathogens such as *Klebsiella* and *Enterococcus* during infancy. Such alterations have been associated with an increased risk of immune dysregulation and metabolic disorders later in life [1].

Infant nutrition and microbial maturation

Among all postnatal influences, infant feeding practices exert the strongest selective pressure on microbiome composition. Breastfed infants typically harbor microbiota enriched in *Bifidobacterium*, *Lactobacillus*, and other species capable of metabolizing human milk oligosaccharides (HMOs) – complex carbohydrates that selectively nourish beneficial microbes [2, 5].

In contrast, formula feeding is associated with greater microbial diversity and accelerated maturation toward an adult-like microbial profile. Although increased diversity is conventionally regarded as beneficial, premature microbial maturation may promote low-grade inflammation and metabolic dysregulation during a critical developmental window [2, 5]. The duration and exclusivity of breastfeeding further shape microbial trajectories in a dose-dependent manner [6]. Discontinuation of breastfeeding induces a marked ecological shift characterized by increased representation of *Firmicutes* and fiber-fermenting taxa typical of the adult microbiome [2, 5].

Beyond taxonomic changes, the functional capacity of the microbiome evolves in parallel. Breastfeeding is associated with enrichment of metabolic pathways involved in carbohydrate utilization, fatty acid synthesis, and vitamin production. In contrast, the microbiota of formula-fed infants is characterized by enhanced bile acid metabolism and amino acid turnover – features indicative of microbial functional maturity [2, 5].

Antibiotic exposure and microbial disruption

Antibiotic administration during early life constitutes one of the most disruptive influences on microbiome development. Exposure is consistently associated with decreased microbial diversity and persistent structural changes in microbial communities. Broad-spectrum antibiotics, particularly macrolides and penicillins, disproportionately deplete beneficial taxa such as *Bifidobacterium* and *Lactobacillus*, thereby compromising SCFA production and immune regulation [7].

Macrolide exposure – especially to azithromycin – has been linked to sustained loss of alpha diversity and depletion of *Akkermansia muciniphila*, a bacterium associated with intestinal barrier integrity and anti-inflammatory effects. Antibiotic treatment is also associated with reductions in regulatory immune-inducing taxa, including *Clostridium* clusters IV and XIVa, which contribute to regulatory T-cell induction [7].

In addition, early antimicrobial exposure promotes the emergence of antimicrobial resistance through selective pressure on microbial populations and perturbation of microbial gene expression. Among neonates treated empirically for suspected early-onset sepsis, alterations in microbiome composition and resistome persistence have been documented months after treatment cessation. Narrow-spectrum regimens, such as penicillin combined with gentamicin, appear to exert fewer ecological effects and are increasingly favored when treatment is unavoidable [8].

Prematurity and hospital-associated colonization

The microbiome development of preterm infants differs fundamentally from that of term neonates. Instead of maternal microbial seeding, premature infants are predominantly colonized by microorganisms originating from the hospital environment, including opportunistic and antibiotic-resistant strains [7].

Distinct fungal colonization patterns also characterize this population, with *Candida* species dominating early development before transitioning toward *Saccharomyces* species following dietary diversification. Gastrointestinal immaturity further compromises microbial establishment. Structural abnormalities – including shortened villi and crypts, decreased mucus and antimicrobial peptide production, increased gut permeability, and impaired motility – foster an intestinal environment unfavorable to obligate anaerobes and susceptible to dysbiosis [7].

Collectively, these vulnerabilities increase the risk of infectious complications, necrotizing enterocolitis, and long-term metabolic and immunological consequences,

underscoring the need for targeted microbial interventions in neonatal care settings [7].

Diet and environmental influences across childhood

Beyond infancy, diet remains a dominant force shaping microbial ecology. Diets high in saturated fat, refined sugar, and animal protein – the so-called Western diet – are associated with reduced microbial diversity and enrichment of taxa linked to obesity, cardiovascular disease, and metabolic syndrome [3].

In contrast, carbohydrate-rich dietary patterns support a *Prevotella*-dominant enterotype associated with improved metabolic functions. Data from the Integrative Human Microbiome Project demonstrate that microbial composition shifts dynamically in disease states such as inflammatory bowel disease and diabetes, emphasizing the central role of nutrition in modulating microbial resilience [3].

Environmental exposures further influence microbial assembly. Children raised in households with siblings or domestic animals exhibit greater microbial diversity, consistent with increased microbial exchange and enhanced immune training through environmental contact [1].

Gut microbiome and childhood diseases

Neurodevelopmental and neurological disorders (ASD and related conditions)

Both the gut microbiome and the central nervous system undergo rapid and dynamic development during early childhood. Accumulating evidence suggests that intestinal microorganisms play a fundamental role in shaping neurodevelopmental trajectories during this critical period [9–13]. Communication between the gut and the brain is mediated by the microbiota–gut–brain axis (MGBA), a bidirectional network integrating neural, immune, endocrine, and metabolic pathways [9, 12].

Several complementary mechanisms are involved in early-life gut–brain signaling. Microbial metabolites – particularly SCFAs and tryptophan-derived compounds – modulate blood–brain barrier integrity, microglial maturation, and neuroinflammatory pathways. These metabolites also influence systemic and intestinal immune tone, including cytokine production and T-cell differentiation, thereby impacting neuroimmune development. Additionally, the vagus nerve and the enteric nervous system transmit neural signals from the gastrointestinal tract to brainstem and cortical regions, enabling rapid bidirectional communication between the gut and the central nervous system [9, 11, 12].

Dysregulation of the MGBA has been implicated in multiple neurodevelopmental, psychiatric, and neurodegenerative disorders. Disruption of gut–brain communication has been associated with mood disorders, Alzheimer's disease, and autism spectrum disorder (ASD) [13]. In children with ASD, recurring alterations in gut microbiota composition include an increased abundance of *Clostridium* species and reduced representation of *Bifidobacterium*. Certain *Clostridium* species are capable of producing neurotoxic and pro-inflammatory metabolites that may enter systemic circulation and influence neurological function. Given the relative instability of the pediatric microbiome, early childhood appears to represent a sensitive window during which microbiota-targeted interventions may exert long-term neurodevelopmental effects [12].

Emerging evidence also links the MGBA to rare pediatric neurological disorders. In pediatric-onset leukodystrophies, microbiome disturbances may contribute to neuroinflammation, immune dysregulation, and altered metabolic signaling, thereby influencing disease progression and neurological outcomes [10]. Similarly, in neonates with necrotizing enterocolitis, disruption of gut–brain communication has been associated with subsequent neurodevelopmental impairment, potentially mediated through inflammatory signaling and altered microbial metabolite profiles [11].

Although much of the mechanistic insight originates from preclinical research, an increasing number of observational studies in pediatric cohorts support a clinically relevant role of the gut microbiome in neurodevelopment. However, further longitudinal and interventional studies are required to determine causality and evaluate the therapeutic potential of microbiome-modifying strategies in pediatric neurological and neurodevelopmental conditions [9–13].

While numerous studies report alterations in gut microbiota composition in children with neurodevelopmental disorders, most human data remain associative. Evidence is largely derived from cross-sectional or case–control studies, whereas causal relationships are primarily supported by preclinical models. Consequently, direct causality between microbiome alterations and neurodevelopmental outcomes in children has not yet been firmly established.

Importantly, findings across studies are not fully consistent. Variability in reported microbial signatures may reflect differences in age at sampling, dietary patterns, gastrointestinal comorbidities, medication use, and analytical methodologies, complicating direct comparison between cohorts.

Key knowledge gaps remain regarding the temporal stability of microbiome alterations, critical developmental windows of vulnerability, and the long-term neurodevelopmental impact of microbiome-targeted interventions in pediatric populations.

Allergic diseases and atopic disorders

Disruption of the gut microbiome is increasingly recognized as a significant contributor to allergic disease development in children [14–16]. Studies in atopic dermatitis (AD) report pronounced differences in gut microbial composition between affected and healthy children, characterized by reduced microbial diversity and shifts in dominant taxa [14]. In many cases, these alterations precede clinical manifestations, suggesting that dysbiosis may contribute to disease initiation rather than arise solely as a consequence of inflammation [14, 15].

The gut and skin microbiota function as interconnected ecosystems that modulate immune responses. Children with AD commonly exhibit reduced levels of *Lactobacillus* and *Bifidobacterium* and increased abundance of *Clostridium* species and *Staphylococcus aureus*. Experimental data support the immunoregulatory role of *Lactobacillus* species in attenuating allergic inflammation [14].

Across pediatric allergic conditions, gut dysbiosis frequently involves an increased Firmicutes-to-Bacteroidetes ratio together with overrepresentation of *Ruminococcus gnavus*. This species has been identified as a major contributor to allergic phenotypes. Disruption of intestinal epithelial integrity associated with dysbiosis facilitates antigen translocation into systemic circulation, promoting abnormal immune activation and increasing allergic susceptibility [16].

Microbial metabolites, particularly SCFAs derived from dietary fiber fermentation, are critical for maintaining epithelial integrity and immune tolerance. Reduced fecal SCFA concentrations have been consistently reported in allergic children, and depletion of microbial genes related to fiber metabolism has been associated with an elevated risk of allergic sensitization [16].

Although most available evidence is associative, experimental studies provide support for causality. Selected members of the *Clostridia* class have been shown to improve gut barrier integrity and reduce allergen sensitivity, while microbiota transfer from healthy infants protects against allergic responses in animal models [16]. In contrast, increased abundance of *Clostridium* species has been reported in pediatric asthma, and early colonization with this genus has been associated with a higher risk of allergic disease development [17].

Most human studies linking gut microbiome alterations to pediatric allergic diseases are observational and therefore demonstrate associations rather than definitive causality. Experimental models provide supportive mechanistic evidence; however, translation of these findings to human pediatric populations remains limited.

Conflicting results have been reported regarding the role of specific taxa, including members of the *Clostridium* genus, which have been associated with both protective and adverse immune effects depending on timing, strain specificity, and host context.

Further research is required to define strain-specific effects, optimal timing for microbial modulation, and the durability of microbiome-related immune programming across childhood.

Obesity and metabolic dysregulation

Growing evidence indicates that the gut microbiome plays a critical role in metabolic regulation, energy homeostasis, and immune function, and that disturbances in microbial composition are strongly associated with the development of childhood obesity [3,18–19]. Experimental studies in animal models provide compelling evidence for causality. Transplantation of fecal microbiota from obese donors into germ-free mice has been shown to induce metabolic traits characteristic of obesity, including increased adiposity and altered energy regulation. Similarly, gut microbiota derived from mice that developed obesity following early antibiotic exposure induced comparable metabolic alterations in recipient germ-free animals. Moreover, microbial communities from obese hosts exhibit enhanced capacity for dietary energy extraction, and transfer of these communities results in increased fat deposition in previously lean recipients [3].

The gut microbiome is also involved in endocrine regulation and metabolic signaling. In children with obesity accompanied by central precocious puberty, gut microbial profiles differ significantly from those of normal-weight peers. These alterations include an increased abundance of *Firmicutes* and a reduction of *Bacteroidetes*, as along with elevated levels of *Alistipes*, *Klebsiella*, and *Sutterella*, and decreased representation of beneficial genera such as *Anaerostipes*, *Bacteroides*, and *Bifidobacterium*. Such compositional changes have been linked to disruptions in inositol metabolism and SCFA production, contributing to impaired metabolic regulation and excess adiposity [19].

The microbiome further influences neuroendocrine regulation through its interaction with metabolic pathways. SCFAs produced by bacterial taxa such as *Ruminococcus* and *Roseburia* modulate leptin gene expression via activation of free fatty acid receptors, thereby affecting hypothalamic signaling and pubertal timing. Notably, microbial profiles in girls with coexisting obesity and precocious puberty differ from those observed in children with either condition alone, suggesting a distinct microbial pattern associated with combined pathology [19].

Emerging evidence suggests that gut microbiota dysregulation may represent a biological link between obesity and asthma. Children with obesity-related asthma exhibit heightened immune dysregulation and persistent low-grade inflammation, and both clinical and experimental studies have reported microbial disturbances in individuals affected by both conditions. However, disease-specific microbial signatures remain insufficiently characterized, and further clinical research is required to define precise associations [18].

Evidence for a causal role of the gut microbiome in obesity is strong in experimental animal models; however, pediatric human studies remain predominantly associative. Although consistent microbial patterns have been described in children with obesity, causality cannot be inferred due to the observational nature of most available data.

Reported microbial signatures in pediatric obesity vary substantially across studies, likely reflecting differences in age, pubertal status, diet, ethnicity, and methodological approaches, underscoring the heterogeneity of obesity-associated microbiome profiles.

Major knowledge gaps include the identification of disease-specific microbial signatures, clarification of bidirectional host–microbiome interactions, and determination of whether microbiome modulation can sustainably influence metabolic outcomes in children.

Autoimmune diseases (T1D, celiac disease)

Type 1 diabetes (T1D) results from complex interactions between genetic predisposition and environmental factors, with the gut microbiome increasingly recognized as a major contributor to disease pathogenesis. Significant alterations in microbial composition and function have been observed in association with islet autoimmunity and progression to clinical disease [20].

Reported microbial changes include reduced SCFA production, altered bile acid and tryptophan metabolism, and increased intestinal permeability, collectively promoting immune dysregulation. Functional remodeling of the microbiome during disease progression is further characterized by decreased bile acid metabolism and increased biosynthesis of inflammatory components such as lipopolysaccharides [20].

Defects in intestinal barrier proteins and alterations in exocrine pancreatic function have been identified in both individuals with T1D and in genetically predisposed children prior to disease onset, suggesting that intestinal dysfunction may precede autoimmune processes. Moreover, gut microbiome structure has been associated with glycemic control, disease duration, and vascular complications, indicating that microbial variability contributes to interindividual differences in clinical outcomes [20].

Gastrointestinal disorders (IBD, functional constipation)

Inflammatory bowel disease

The gut microbiome is a central factor in the pathogenesis of inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis [13, 21, 22]. Pediatric IBD is characterized by reduced microbial diversity, decreased *Firmicutes*, and increased *Enterobacteriaceae* [21, 22].

Loss of beneficial taxa, including *Faecalibacterium prausnitzii* and *Bifidobacterium*, is frequently observed, while pro-inflammatory bacteria including *Escherichia coli* are enriched. Microbiome composition varies with disease severity, with microbial profiles during remission more closely resembling those of healthy controls compared to those seen during active disease [21, 22].

Ruminococcus gnavus has been linked to severe disease phenotypes and increased inflammatory activity. Mechanistic evidence suggests that this organism promotes inflammation through TLR4-mediated induction of tumor necrosis factor-α (TNF-α) [21]. Although establishing causality remains challenging, family and twin studies suggest that microbial profiles correlate more strongly with disease state than with shared genetic background. Inflammation itself may also perpetuate dysbiosis by altering the intestinal metabolic environment [22].

Functional constipation

In functional constipation (FC), accumulating evidence suggests that gut microbiota dysregulation contributes to altered intestinal motility [23, 24]. SCFAs, particularly butyrate, have been proposed as modulators of bowel motility, although findings remain inconsistent and causality has not been established [23].

Comparative studies have demonstrated significant microbial differences between children with FC and healthy controls, including reduced *Firmicutes* and increased abundance of *Actinobacteria* and *Bifidobacterium* in specific subgroups [24]. Although mechanistic pathways remain incompletely defined, these findings support a contributory role of dysbiosis in pediatric FC [23, 24].

Potential use of probiotics in pediatric disease management

Interest in probiotics has expanded substantially in recent years, coinciding with increased recognition of the gut microbiome as an active regulator of immune, metabolic, and neurodevelopmental processes in children. Although probiotics are often discussed as a heterogeneous group, clinical effects appear to be strain-specific, not class-wide. The most consistent evidence in pediatric populations has been reported for selected strains, particularly *Lactobacillus rhamnosus* GG, *Bifidobacterium infantis*, *Bifidobacterium breve*, and *Saccharomyces boulardii*. In contrast, results for other strains and multi-strain formulations remain variable, underscoring the importance of strain-level characterization when interpreting clinical outcomes [12–24].

Currently, the strongest clinical evidence supports probiotic use in the prevention and management of acute infectious diarrhea, antibiotic-associated diarrhea, and necrotizing enterocolitis in preterm infants. For other indications, including allergic diseases, obesity, autoimmune disorders, and neurodevelopmental conditions, available data remain limited and largely heterogeneous, with inconsistent clinical endpoints and modest effect sizes.

One of the most consistently reported effects of probiotics is the stabilization of intestinal epithelial integrity. Selected strains of *Bifidobacterium*, *Lactobacillus*, and specific members of the *Clostridia* class have been shown to strengthen tight junctions and reduce gut permeability, thereby limiting the systemic translocation of microbial products and dietary antigens. Preservation of mucosal barrier function is particularly relevant in conditions characterized by chronic inflammation or immune dysregulation, such as allergic diseases, type 1 diabetes, and inflammatory bowel disease (IBD) [16, 20, 21, 23].

In addition to their barrier-related effects, probiotics exert immunomodulatory activity by influencing cytokine production, promoting regulatory T-cell differentiation, and attenuating pro-inflammatory pathways. Bacterial metabolites, most notably SCFAs such as butyrate, contribute to immune tolerance and epithelial health. Impairment in microbial metabolic activity has been reported across several pediatric disease states, including obesity, allergic disorders, and autoimmune diseases, indicating that functional restoration of the microbiome may represent a therapeutically relevant target [16,18–22].

Neurodevelopmental and neurological disorders

The microbiota–gut–brain axis provides a mechanistic framework through which probiotics may influence neurodevelopmental outcomes. Microbial metabolites regulate neuroimmune crosstalk, blood–brain barrier integrity, and microglial maturation during critical windows of early development. Altered abundance of *Clostridium* and *Bifidobacterium* species has been reported in children with autism spectrum disorder and related neuropsychiatric conditions, supporting the hypothesis that targeted modulation of microbial composition may influence neurological function [9–13].

Allergic and immune-mediated diseases

In pediatric allergic disease, probiotics are being investigated for their capacity to support immune maturation and promote oral tolerance. Reduced levels of *Bifidobacterium* and selected *Clostridia* have been associated with amplified allergic inflammation, whereas restoration of these taxa is linked to improved immune regulation [14–16]. Experimental studies further indicate that early-life microbial modulation may influence long-term susceptibility to allergic disease through immune-programming mechanisms [16].

Obesity and metabolic regulation

Potential metabolic effects of probiotics include modulation of energy extraction from the diet, regulation of lipid metabolism, and interaction with endocrine pathways. Gut microbial activity influences leptin signaling and SCFA production, both of which contribute to adiposity regulation and pubertal timing. Distinct microbial patterns observed in children with coexisting obesity and precocious puberty suggest that microbiota composition may contribute to metabolic heterogeneity within pediatric obesity and may inform individualized therapeutic approaches [18, 19].

Autoimmune diseases

In autoimmune conditions such as type 1 diabetes and pediatric IBD, probiotics may support restoration of disease-associated dysbiosis by enhancing colonization resistance and modulating inflammatory cascades. Alterations in bile acid metabolism, increased lipopolysaccharide production, and disruption of epithelial defenses have been reported in both disorders, reinforcing the concept that microbial intervention may help re-establish intestinal homeostasis and immune balance [20–22].

Functional gastrointestinal disorders

In functional gastrointestinal disorders, including pediatric functional constipation, modulation of the gut microbiota may influence motility patterns through fermentation processes and SCFA production. Distinct microbial signatures have been identified in constipated children compared with healthy controls, providing further rationale for microbiota-oriented therapeutic strategies in this population [23, 24].

Interpretation of probiotic efficacy in pediatric populations is complicated by substantial heterogeneity across studies. Variability in probiotic strains, dosing regimens, treatment duration, age at intervention, and clinical outcome measures limits comparability between trials. In addition, many studies involve small sample sizes, short follow-up periods, and lack mechanistic validation, collectively reducing the strength of clinical inference.

Translation of probiotic research into routine pediatric practice remains challenging. The absence of standardized formulations, limited regulatory oversight, and inconsistent reporting of strain-specific effects hinder clinical decision-making. Furthermore, interindividual variability in baseline microbiome composition may influence therapeutic response, suggesting that a uniform probiotic approach may not be universally effective. As a result, despite promising experimental and clinical findings, evidence-based implementation of probiotics in pediatric care remains limited.

Conclusion

The pediatric gut microbiome plays an essential role in shaping metabolic, immune, and neurodevelopmental outcomes from infancy through adolescence. Accumulating evidence indicates that disruptions in microbial maturation are associated with a broad spectrum of childhood diseases, including obesity, allergic disorders, autoimmune conditions, neurodevelopmental abnormalities, and gastrointestinal pathologies.

Environmental exposures, maternal health, mode of delivery, feeding practices, antibiotic use, and dietary patterns collectively influence microbial assembly during critical developmental windows. When these processes are perturbed, long-term consequences for immune balance, metabolic regulation, and neurological development may arise.

Probiotics represent a promising tool for microbiome modulation in pediatric populations, with potential applications across multiple disease categories. Their effects include enhancement of epithelial barrier integrity, immune regulation, and restoration of microbial metabolic capacity. However, current evidence is limited by heterogeneity in probiotic strains, dosing regimens, and clinical outcome measures.

Future research should prioritize well-designed randomized controlled trials, longitudinal cohort studies, and mechanistic investigations to establish causality and define optimal intervention strategies. A deeper understanding of strain-specific effects and developmental timing will be necessary to translate microbiome science into evidence-based pediatric therapies.

References

1. Ronan V, Yeasin R, Claud EC. Childhood development and the microbiome: the intestinal microbiota in maintenance of health and development of disease during childhood. Gastroenterology, 2021; 160(2): 495–506. doi: 10.1053/j.gastro.2020.08.065
2. Catassi G, Aloi M, Giorgio V, et al. Role of diet and nutritional interventions in shaping the infant gut microbiome. Nutrients, 2024; 16(3): 400. doi: 10.3390/nu16030400

3. Akagbosu CO, Nadler EP, Levy S, Hourigan SK. The role of the gut microbiome in pediatric obesity and bariatric surgery. Int J Mol Sci, 2022; 23(23): 15421. doi: 10.3390/ijms232315421
4. Ianiro G, Tilg H, Gasbarrini A, Cammarota G. Maternal gut microbiome in pregnancy: implications for immune development. Nat Rev Gastroenterol Hepatol, 2023; 20(2): 77–94. doi: 10.1038/s41575-023-00864-2
5. Donovan SM, Wang M, Li M, et al. Gut microbiome and breastfeeding: implications for immune development. J Allergy Clin Immunol, 2022; 150(3): 523–534. doi: 10.1016/j.jaci.2022.07.014
6. McDonnell L, Gilkes A, Ashworth M, et al. Association between antibiotics and gut microbiome dysbiosis in children: systematic review and meta-analysis. Gut Microbes, 2021; 13(1): 1–18. doi: 10.1080/19490976.2020.1870402
7. Sarafidis K, Pateras K, Kampouri M, et al. Probiotics and the gut microbiome in preterm infants. Gut Microbes, 2023; 15(1): 2201160. doi: 10.1080/19490976.2023.2201160
8. Reyman M, van Houten MA, Watson RL, et al. Effects of early-life antibiotics on the developing infant gut microbiome and resistome: a randomized trial. Nat Commun, 2022; 13(1): 893. doi: 10.1038/s41467-022-28525-z
9. Wang Q, Yang Q, Liu X. Microbiota–gut–brain axis and neurodevelopmental disorders. Proc Nutr Soc, 2023; 82(Suppl 1): E284. doi: 10.1093/procel/pwad026
10. Vaia Y, Bruschi F, Tagi VM, et al. Microbiota gut-brain axis: implications for pediatric-onset leukodystrophies. Front Nutr, 2024; 11: 1417981. doi: 10.3389/fnut.2024.1417981
11. Wang Y, Hang C, Hu J, et al. Role of gut–brain axis in necrotizing enterocolitis-related neurodevelopmental impairment. Front Neurosci, 2023; 17: 1059552. doi: 10.3389/fnins.2023.1059552
12. Romano K, Shah AN, Schumacher A, et al. The gut microbiome in children with mood, anxiety, and neurodevelopmental disorders: an umbrella review. Gut Microbiome (Camb), 2023; 4: e18. doi: 10.1017/gmb.2023.16
13. Person H, Keefer L. Psychological comorbidity in gastrointestinal disease: update on the brain–gut–microbiome axis. Prog Neuropsychopharmacol Biol Psychiatry, 2020; 110: 110209. doi: 10.1016/j.pnpbp.2020.110209
14. Liu Y, Du X, Zhai S, et al. Gut microbiota and atopic dermatitis in children. BMC Pediatr, 2022; 22: 323. doi: 10.1186/s12887-022-03390-3
15. Akagawa S, Kaneko K. Gut microbiota and allergic diseases in children. Allergol Int, 2022; 71(3): 301–309. doi: 10.1016/j.alit.2022.02.004
16. De Filippis F, Paparo L, Nocerino R, et al. Specific gut microbiome signatures and the associated pro-inflammatory functions are linked to pediatric allergy and acquisition of immune tolerance. Nat Commun, 2021; 12: 5958. doi: 10.1038/s41467-021-26266-z
17. Al-Mutairi AM, Alharbi AS, Aljohani AS, et al. Paediatric asthma and the microbiome: systematic review. Microorganisms, 2023; 11(4): 939. doi: 10.3390/microorganisms11040939
18. Hu M, Zhao X, Liu Y, et al. Gut microbiota in childhood obesity and asthma. Front Microbiol, 2023; 14: 1264356. doi: 10.3389/fmicb.2023.1264356
19. Wang LY, Qin X, Liu H, et al. Gut microbiota in childhood obesity and precocious puberty. BMC Microbiol, 2024; 24: 461. doi: 10.1186/s12866-024-03461-8
20. Blok L, Hanssen N, Nieuwdorp M, Rampanelli E. Gut microbiome in type 1 diabetes: microbiota–metabolite interactions. Metabolites, 2024; 14(2): 138. doi: 10.3390/metabo14020138
21. Fitzgerald RS, Sanderson IR, Claesson MJ. Pediatric inflammatory bowel disease and its relationship with the microbiome. Microb Ecol, 2021; 82(4): 833–844. doi: 10.1007/s00248-021-01697-9
22. Jauregui-Amezaga A, Smet A. Microbiome in inflammatory bowel disease. J Clin Med, 2024; 13(16): 4622. doi: 10.3390/jcm13164622
23. Avelar Rodriguez D, Popov J, Ratcliffe EM, Toro Monjaraz EM. Functional constipation in children and gut microbiome. Front Pediatr, 2020; 8: 595531. doi: 10.3389/fped.2020.595531
24. Zhao H, Lu X, Ye Y, et al. Dysbiosis of gut microbiota in children with functional constipation and damp-heat constitution: a cross-sectional multi-omics analysis. Sci Rep, 2025; 15: 42256. doi: 10.1038/s41598-025-26439-6