Diet and Nutritional Interventions in Early Life

Subjects: Pediatrics | Gastroenterology & Hepatology

Contributor: Giulia Catassi, Marina Aloi, Valentina Giorgio, Antonio Gasbarrini, Giovanni Cammarota, Gianluca Ianiro

The infant gut microbiome plays a key role in the healthy development of the human organism and appears to be influenced by dietary practices through multiple pathways. First, maternal diet during pregnancy and infant nutrition significantly influence the infant gut microbiota. Moreover, breastfeeding fosters the proliferation of beneficial bacteria, while formula feeding increases microbial diversity. The timing of introducing solid foods also influences gut microbiota composition. In preterm infants the gut microbiota development is influenced by multiple factors, including the time since birth and the intake of breast milk, and interventions such as probiotics and prebiotics supplementation show promising results in reducing morbidity and mortality in this population.

Keywords: microbiome ; pediatrics ; diet

1. Introduction

The infant gut microbiome is the collection of microorganisms residing in the gastrointestinal tract of newborns and infants (i.e., children between 1 and 23 months of age) [1]. This microbial community is composed of different microorganisms, including bacteria, viruses, fungi, parasites, archaea, and other microbes. Bacteria are the most abundant and diverse group within the gut microbiome [2][3].

Generally, the human gut microbiome is fundamental in shaping the health and well-being of individuals throughout their lifespan [4]. The critical role of this microbial community is even more pronounced during infancy, the period that lays the groundwork for an individual's long-term health trajectory [5][6]. Multiple recent research works have underscored the significance of the gut microbiome in infants concerning different facets of health and illness [7][8], shedding light on the intricate interactions among microbial populations, nutrition, genetics, and the body's immune mechanisms [5][6].

The quantitative and qualitative composition of the gut microbiome is heavily dependent on the diet. This is particularly true during the first two years of life due to the many changes that take place during this period of life, including breast and/or formula feeding, weaning and gradual introduction of different solid foods [9][10][11].

2. Diet and Nutritional Interventions in Early Life

2.1. Milk Feeding in Early Life

The maturation of the gut microbiota in early life is deeply influenced by the methods of infant nutrition, which are breast milk and formula feeding [12]. The type of feeding significantly influences the composition and function of the infant gut microbiota mainly because of differences in nutrient composition, particularly related to the Human Milk Oligosaccharides (HMOs) [13].

2.2. Role of Breastfeeding in Shaping the Infant Gut Microbiome

The primary role of breast feeding in establishing a healthy infant gut microbiome has been increasingly recognized in recent years [5]. Breast milk contains different components, including proteins, fats, carbohydrates, and immunoglobulins [14]. A significant component of breast milk is the HMOs, such as GOS, which undergo only partial digestion in the small intestine, mainly reaching the colon [15]. In the colon, HMOs are fermented, largely by *Bifidobacteria*, resulting in the production of SCFAs [16] that inhibit the growth of opportunistic pathogens, specifically belonging to the Clostridiaceae, Enterobacteriaceae, and Staphylococcaceae families [17][18][19]. Sakurama and colleagues showed that *Bifidobacteria* produce an enzyme, lacto-N-biosidase, that contributes to the digestion of GOS [20]. As shown by Matsuki et al. [21], Bifidobacterium numbers increase, HMO content in stool decreases, and the levels of acetic and lactic acid increase in one-month-old infants. Consequently, HMOs exhibit a pronounced prebiotic impact by selectively fostering the growth of a *Bifidobacterium*-dense microbiota.

Bifidobacteria, particularly the *Bifidobacterium infantis*, exhibit a direct correlation with the levels of mucosal Immunoglobulin A (IgA) secreted by the gut [22]. Additionally, this bacterium is known for its anti-inflammatory properties.

Therefore, the synergy between HMOs and *Bifidobacteria* not only enhances the variety and equilibrium of the baby's intestinal microbiota but is also crucial in supporting the host's immune system and general well-being. Moreover, remnants of HMO metabolism, such as fucose, lactate, and 1,2 propanediol, as well as aromatic amino acid-derived co-HMO metabolism products like indolelactate and 4-hydroxypheyllactate, are typically present in breastfed (BF) infants [1] [23].

Additionally, human milk is also a source of bacteria that colonize the infant gut [24]. Mother-to-infant transmission studies, accounting for both cultured and non-cultured bacteria, provide strong evidence that this bacterial transfer takes place through breastfeeding [25][26]. This transmission has been verified by detecting the same bacterial strains in both maternal milk and the stool of breastfed infants [27]. Furthermore, research by Pannaraj and colleagues [28] suggests that bacterial transmission via breast milk has a more profound influence on the early bacterial colonization of a newborn than the bacteria from the areolar skin.

Human breast milk is comprised of a diverse array of microbiota, encompassing both skin-related and non-skin-related Gram-positive bacterial strains [29]. Notably, Streptococci (specifically *S. mitis* and *S. salivarius*) and coagulase-negative Staphylococci prevail in both human milk and stool of breastfed babies [30]. These microorganisms can compete with undesirable pathobionts, such as *Staphylococcus aureus*, for space and resources within the infant gut.

The origin of the microbial population in breast milk remains uncertain. The entero-mammary pathway theory suggests that immune cells selectively transport bacteria from the gut to the mammary gland [31]. This idea is supported by data indicating a resemblance in the bacterial profiles of a mother's feces and her breast milk [32]. This hypothesis is further supported by clinical studies finding probiotic strains previously ingested by the mother in her breast milk [33][34].

Infant feeding also influences significantly the host gene expression, as demonstrated by transcriptomic studies conducted on intestinal epithelial cells [35]. It has been observed that breastfeeding increases the transcription of genes related to immunological processes and metabolic functions [35]. Breastfeeding plays a key role in rectifying disruptions in the infant's gut microbiota resulting from cesarean birth, highlighting its essential function in forming a robust intestinal microbiota, regardless of the method of delivery [36].

2.3. Impact of Breastfeeding Duration and Exclusivity

The duration and exclusivity of breastfeeding are major drivers of infant gut microbiota composition [37]. Both exclusive breastfeeding (EBF), defined as the consumption of only breast milk without any additional formula milk, food, or drink, not even water, and its duration, shape specifically the infant gut microbiota [37][38][39][40]. A meta-analysis of seven studies revealed that during the first 6 months of life non-exclusively breastfed infants exhibited consistently higher gut bacterial diversity and microbiota age compared to exclusively breastfed infants [38]. Furthermore, relative abundances of Bacteroidetes and Firmicutes and their respective energy pathway were consistently higher in non-exclusively breastfed infants [38]. These differences persisted until 2 years of age. In the CHILD study [37], the relationship between exclusive breastfeeding and duration of EBF and the prevalence and relative abundance of different bacteria in the infant gut, represented by amplicon sequencing variants (ASVs), was analyzed, with notable differences in the overall relative abundance of ASVs at 3 and 12 months in exclusive vs. non-exclusive BF. In a recent work by Chichlowski [40], the gut microbiome of EBF infants was less diverse but more stable compared to formula-fed infants. *Bifidobacterium*, known for selectively using HMOs as growth substrates, was the dominant genus in the infants' stools at all points in time, regardless of EBF duration. Infants who experienced EBF for more than six months exhibited a greater relative abundance of *Bifidobacterium bifidum* compared to those who were EBF for less than three months [40].

Laursen identified a positive correlation between the duration of breastfeeding and the occurrence of *Bifidobacterium*, *Veillonella*, *Megasphaera*, *Haemophilus*, lactic acid bacteria, and Enterobacteriaceae. Conversely, longer breastfeeding duration had a negative effect on the abundance of *Lachnospiraceae* and *Ruminococcaceae*, bacteria known for breaking down complex carbohydrates [41].

2.4. Role of Formula Feeding in Shaping the Infant Gut Microbiome

Formula-fed (FF) infants show more diverse colonization compared to their breastfed counterparts [42]. Infants who are FF show a greater prevalence of *Clostridiales* and *Proteobacteria* in their gut microbiome [24]. Additionally, the gut microbiota of these infants tends to have a higher concentration of *Atopobium* and *Bacteroides* but less *Bifidobacteria* compared to

breastfed infants [43]. Formula feeding has also been observed to decrease the overall quantity of gut bacteria while simultaneously increasing the diversity within the gut microbiome [40][44].

This difference in microbiota composition is primarily attributed to the absence of HMOs and the increased protein content in formula milk. Infant formulas often contain supplemental FOS and/or GOS, but these are not as selective as HMOs [45]. They can stimulate the growth of various bacterial species, leading to a significantly different microbiota composition compared to that seen in breastfed infants [46][47].

Interestingly, the gut microbiota of FF infants, even when the formula contains GOS, show a predominance of proteolytic over saccharolytic metabolism [48][49]. This is evidenced by the elevated concentrations of protein breakdown byproducts [43]. Unfortunately, some of these metabolites can be converted in the liver into detrimental metabolites, such as p-cresol-sulfate and phenylacetateglutamine; these compounds can contribute to enterocyte toxicity, promote inflammation and increased gut permeability and disrupt normal metabolic functions by competing with other substances for sulfation in the liver, a pathway used to detoxify a variety of compounds [50][51].

2.5. How Changes in the Composition of Infant Formula Can Modulate Infant Gut Microbiota

Efforts to promote the development of a gut microbiome in FF infants that closely resembles that of a breastfed infant in order to emulate health advantages conferred by breast milk include the supplementation of infant formula with prebiotics, probiotics or symbiotics [52][53][54], which are synergistic combinations of both.

2.6. Prebiotics

Numerous research efforts have been conducted to explore the impact of prebiotic addition on the composition of the infant gut microbiome [45][55]. Research has demonstrated the advantages of enriching infant formula with HMOs like 2′ fucosyllactose and lacto-N-neotetraose [56]. The goal of this strategy is to replicate the positive impacts that breast milk has on the intestinal microbiota. Initial studies have shown promising results, as the gut microbiota of infants fed with HMO-supplemented formula showed a greater resemblance to that of breastfed infants [57]. These supplements not only support optimal growth in infants, but also promote the growth of beneficial *Bifidobacteria*, achieving a gut microbial composition closer to that of breastfed infants. The supplementation of infant formula with GOS and FOS can lead to an increased abundance of *Bifidobacteria* and lower fecal pH, mirroring attributes of breastfed infants [58].

Although infant formula products are engineered to replicate the macronutrient profile of human milk, currently, the majority of them do not incorporate substantial levels of prebiotics and/or probiotics, as reported by Salminen et al. in 2020 [59]. Babies fed with formula enhanced with HMOs exhibited increased *Bifidobacteria* and decreased *Enterobacteriaceae* and *Peptostreptococcaceae* [53]. A study by Borewicz [45] compared the fecal microbiota composition in infants who were breastfed with that of babies fed with an infant formula fortified with prebiotics (GOS and/or FOS) or receiving mixed feeding. These findings were compared with those from infants who were given conventional formulas. By next-generation sequencing analysis, this study demonstrated a bifidogenic effect of prebiotic-fortified formulas as compared to traditional formulas. Infants who were fed formulas fortified with prebiotics showed gut microbiota compositions that were more similar to those found in breastfed babies. This was not the case in formula-fed infants who were given formulas without any added prebiotics. This study also demonstrated lower bifidogenic activity in formulas combined with breastmilk feeding, suggesting a possible interference between the components of the two [45].

The addiction of bovine milk-derived oligosaccharides (MOS) to infant formula was evaluated in a three-arm RCT including a control group fed on regular cow milk-based formula, an experimental group receiving the same formula but with added MOS, and a reference group of exclusively breast milk-fed infants [60]. The overall gut microbiota composition in the experimental group showed more similarities with that of breast milk-fed infants than with the control group. *Bifidobacteria* were found in higher abundance in the experimental group compared to the control group. Moreover, infants born via cesarean in the experimental group also showed a microbiota composition that was more similar to breast milk-fed and vaginally born infants than to the control group infants. By the age of 4 months, counts of harmful bacteria, *Clostridioides difficile* and *Clostridium perfringens*, were significantly reduced in the experimental group than in the control group. The experimental group also showed twice the amount of fecal secretory IgA compared to the control group.

Two comprehensive systematic reviews carried out by Rao et al. [55] and Mugambi [61] examined the effects of adding prebiotics to formula milk. Both showed higher stool colony counts of *Bifidobacteria*, regardless of differences in dosage, duration of supplementation, and method of reporting results. However, three specific studies using supplementation with GOS, FOS or a GOS/FOS mix found no difference in *Bifidobacteria* levels between the infant formula-supplemented groups and their controls [62][63][64]. Prebiotic supplementation had an inconsistent impact on [63][64][65][66] while decreasing

the levels of *C. difficile* [67][68]. A double-blinded RCT comparing an infant formula supplemented with a symbiotic composed of bovine MOS and the probiotic *Bifidobacterium animalis* vs. the same formula alone caused a significant increase in *Bifidobacteria* abundance and lower microbiota diversity in the experimental group vs. controls, similarly to breastfed infant [69].

2.7. Probiotics

Currently, the most frequently examined and utilized probiotic species belong to the *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* genera [70][71]. Researchers are also exploring the potential application of bacteria extracted from breast milk to develop infant formulas that closely resemble the nutritional composition of natural breast milk [5]. Supplementation of the formula with *Bifidobacterium* species and/or lactic acid bacteria, such as *Lactobacillus* strains, is deemed secure and generally accepted [72][73][74] and may potentially enhance their immune response [75][76].

Studies investigating the effect of probiotic supplementation of infant formulas did not find a strong correlation between fecal *Bifidobacterium* concentration and *Bifidobacterium* supplementation [77][78][79]. *Bifidobacteria* colonization in the infant gut was indeed found to be unstable over time, most likely due to competition among members of the gut microbial [80][81]. This finding has been supported by a systematic review [66] of 12 RCTs, reporting that supplementation of probiotics did not increase the counts of *Bifidobacteria* or *Lactobacilli* nor decreased the levels of pathogens such as *Bacteroides* and *E. coli*. [61].

In a recent observational study, neonates undergoing varied probiotic administration for six months showed an elevation in stool *Bifidobacteria* levels only during the first week after birth, implying that probiotics might potentially expedite the initial colonization of this taxon, together with a concomitant reduction in the Enterobacteriaceae family, without differences in alpha diversity [82]. Regardless of the probiotic species, fecal *Lactobacillus* levels were higher in infants supplemented with a probiotic [82][83]. Another investigation revealed that healthy infants given formula supplemented with *Lactobacillus rhamnosus GG* (LGG) showed a greater frequency of *Lactobacilli* colonization compared to those who were fed with a standard formula [84]. Additionally, in very low birth weight infants, the supplementation of *Bifidobacterium breve* Bb12 favored gut colonization by the added bacteria and expedited the growth of *Lactobacilli* compared to those infants who did not receive the probiotic supplement [85].

To foster a beneficial gut microbiota, the most opportune time for administering probiotics is prior to the establishment and colonization of individual microbial taxa [86]. This crucial window is typically within the initial months of life. Nonetheless, the colonization timings vary across different microbial taxa [87]. Therefore, identifying these specific periods of opportunity for each taxon is of paramount importance. However, the optimal duration of probiotic supplementation required to guarantee a protracted beneficial impact on gut microbiota remains unclear.

2.8. Introduction of Complementary Foods

During the fourth month of life, the infant's renal and gastrointestinal systems reach physiological maturation, enabling them to process non-milk alimentary substances [88]. Upon reaching the sixth month, the nutritional and energetic benefits procured solely from breast milk become insufficient to meet the growing metabolic demands of the infant [89]. Thus, the inclusion of complementary food is needed for the appropriate somatic and neurodevelopmental trajectory [88][90].

The implementation of complementary feeding presents a heterogeneous pattern across Europe and worldwide. Certain European regions, exemplified by the UK and Sweden, adhere to the World Health Organization's endorsement of starting such feeding regimens from six months. However, other territories, including Belgium and Spain, advocate for the initiation of these diets between the fourth and sixth month, a strategy that is in alignment with the guidelines of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition [91]. According to this committee, the introduction of complementary alimentary substances should not precede the fourth month and should not be delayed beyond the sixth month, including those containing potential allergenic substances.

2.9. Diversity of Solid Food Introduction

Despite remarkable advancements in our knowledge of early-life gut microbial interaction and our growing understanding of the microbial capacity to metabolize various dietary compounds, the understanding of the effects of diet on gut microbiota during the complementary feeding period is still limited [92].

The shift from exclusive milk feeding to the inclusion of family foods in the infant's diet corresponds with substantial changes in the gut microbiota [93]. During this period, the alpha diversity increases, with a shift from *Bifidobacterium*-dominant community to *Bacteroidetes*- and *Firmicutes*-dominant communities [94]. For instance, there is a rapid decrease

in the population of *Bifidobacterium* species that can degrade HMO [95][96]. Simultaneously, there is a significant increase in diversity and the emergence of *Bacteroidaceae*, *Lachnospiraceae*, and *Ruminococcaceae* species, reflecting the more complex diet that comes with the introduction of fibers and new proteins [97][98]. A longitudinal study by Stewart et al. [99] reported a clear increase in gut microbial diversity after the introduction of solid foods. Further, this increased diversity correlated with enhanced immunological and metabolic development in infants, suggesting the potential health benefits of diverse solid food introduction. A recent study by Pannaraj et al. [28] provided similar findings, reporting the association of diversified solid food intake with the enrichment of specific microbial groups, particularly *Bifidobacterium* and *Bacteroides*.

Diverse solid foods act as new sources of microbiota-accessible carbohydrates, therefore stimulating the growth of beneficial taxa such as *Bifidobacterium*, *Lactobacillus*, and *Bacteroides* [100]. These microbes produce SCFAs, such as butyrate, propionate, and acetate, promoting a healthy gut environment and influencing the immune system [101]. The introduction of fruits and vegetables, rich in fermentable fibers, leads to an increase in beneficial microbes like *Bacteroides* and *Bifidobacterium* [102]. On the other hand, protein-rich foods like meats and eggs can stimulate proteolytic microbes such as *Clostridium* and *Streptococcus* [103]. Hence, the introduction of a diverse diet could ensure a balance between these microbes, leading to a more resilient and healthier gut microbiota.

Since gut microbes primarily derive their energy from dietary fibers and secondarily from proteins/peptides, these macronutrients are likely to have the greatest influence on the microbial composition [104][105]. The primary outputs of metabolizing dietary fiber include SCFAs like acetate, butyrate, and propionate [106][107]. High levels of acetate are generated during the initial stages of infancy, whereas the levels of butyrate and propionate start at a markedly reduced state, subsequently elevating as the infant grows older [9]. Correspondingly, the products of protein degradation, notably branched-chain fatty acids (BCFAs), remain essentially unobservable during the lactation period yet exhibit a parallel trajectory of augmentation with advancing age [41]. These changes align with the beginning of solid food intake and the end of breastfeeding [108]. In agreement with the typical gut microbiota developmental pattern, key species within the *Lachnospiraceae* and *Ruminococcaceae* families produce butyrate, while *Bacteroides* species are common propionate producers [109]. These species possess a comprehensive array of enzymes for breaking down dietary fibers into these SCFAs [110]. Moreover, certain species more abundant in older infants, such as *Bacteroides* and *Clostridium*, might employ a range of amino acids derived from dietary proteins to produce BCFAs [111]. Thus, complementary feeding might have a causative effect on microbiota composition and metabolism [13][112].

In a study of nine-month-olds infants, the diversity of gut microbiota was found to increase with the introduction of solid food, particularly fibers and protein, independent of whether the infants were breastfed or formula-fed [113]. A study by Marrs [114] suggests that the introduction of allergenic food, in conjunction with continued breastfeeding between 3 to 6 months of age, resulted in the increase of the overall gut microbiota Shannon diversity. Specifically, this diversification was characterized by the emergence of various microbial taxa, notably *Prevotellaceae* and *Escherichia/Shigella*. Of note, the presence of *Prevotella* has been linked with high-fiber diets [97].

Elevated protein intake has been associated with a heightened abundance of *Lachnospiraceae* and a decrease in saccharolytic organisms, such as those in the *Bifidobacteriaceae* family [115]. Simultaneously, the consumption of fiber was linked to an increase in the proportions of Prevotellaceae [116][117].

2.10. Timing of Solid Food Introduction

The timing of complementary food introduction is known to influence gut microbiota composition. A study by Bäckhed et al. [118] suggests that the delayed introduction of solid food could cause a lag in microbial maturation and increase susceptibility to allergies and obesity. On the other hand, an earlier introduction could expose infants to potential pathogens and allergens [119][120][121]. Hence, the timing of solid food introduction should balance between these risks and benefits.

Differding and coworkers found that the introduction of complementary feeding before 3 months of age can lead to enhanced microbial diversity and a higher concentration of fecal butyrate and that these effects may continue up to the age of 12 months [94]. In an RCT comparing traditional spoon feeding to a baby-led approach (involving self-feeding with complementary “finger foods”), the authors found that babies weaned through a baby-led approach were introduced to solid foods approximately 20 days beyond the initial six months (at the age of seven months) [122]. At this age, their consumption of both vegetables and fibrous nutrients was markedly reduced.

By contrast, Laursen and colleagues discovered that the length of time infants were breastfed had a greater influence on both the variety and the proportion of intestinal microbiota and their overall microbial richness at the age of nine months than when they began eating solid complements [93]. This conclusion aligns with the latest findings from Bäckhed et al.

[118], which indicate an increase in *Lachnospiraceae* populations correlating with increased consumption of household meals, as opposed to a decline in *Bifidobacteriaceae* numbers. This alteration likely mirrors the dietary shift from mother's milk, which is rich in *Bifidobacteriaceae*, to solid foods typical of late infancy that are abundant in fiber and protein, thus supporting the growth of *Lachnospiraceae* species [93].

In another study, Differding and coworkers [123] investigated how the timing of introducing complementary foods can significantly affect the infant's gut microbiota composition, in turn potentially impacting their gut health and overall nutrition: *Ruminococcus bromii*, which is able to digest resistant starches [124] was found in greater amounts in infants who were breastfed for less than four months and given complementary foods early. In infants fed with a diet rich in resistant starches, *R. bromii* could potentially outperform other commensal bacteria that are not as efficient in energy extraction, potentially causing a shift in metabolic processes and dysbiosis. Additionally, these infants had a reduced number of *Bifidobacterium animalis*, a dominant bacterial species in young gut ecosystems, which generally diminishes with the infant's growth and the onset of weaning [99][123]. An increased presence of *Bifidobacterium animalis* may be advantageous for the gastrointestinal health of infants, as indicated by a randomized controlled trial which demonstrated that its supplementation reduced the levels of fecal calprotectin (an indicator of gut inflammation) and decreased gastrointestinal leakiness in infants born before term [125].

References

1. Tanaka, M.; Nakayama, J. Development of the gut microbiota in infancy and its impact on health in later life. Allergol. Int. 2017, 66, 515–522.
2. Turroni, F.; Milani, C.; Duranti, S.; Lugli, G.A.; Bernasconi, S.; Margolles, A.; Di Pierro, F.; Van Sinderen, D.; Ventura, M. The infant gut microbiome as a microbial organ influencing host well-being. Ital. J. Pediatr. 2020, 46, 16.
3. Mehta, S.; Huey, S.L.; McDonald, D.; Knight, R.; Finkelstein, J.L. Nutritional Interventions and the Gut Microbiome in Children. Annu. Rev. Nutr. 2021, 41, 479–510.
4. Kho, Z.Y.; Lal, S.K. The Human Gut Microbiome—A Potential Controller of Wellness and Disease. Front. Microbiol. 2018, 9, e01835.
5. Davis, E.C.; Castagna, V.P.; Sela, D.A.; Hillard, M.A.; Lindberg, S.; Mantis, N.J.; Seppo, A.E.; Järvinen, K.M. Gut microbiome and breast-feeding: Implications for early immune development. J. Allergy Clin. Immunol. 2022, 150, 523–534.
6. Yang, I.; Corwin, E.J.; Brennan, P.A.; Jordan, S.; Murphy, J.R.; Dunlop, A. The Infant Microbiome: Implications for Infant Health and Neurocognitive Development. Nurs. Res. 2016, 65, 76–88.
7. Ahearn-Ford, S.; Berrington, J.E.; Stewart, C.J. Development of the gut microbiome in early life. Exp. Physiol. 2022, 107, 415–421.
8. Kapourchali, F.R.; Cresci, G.A.M. Early-Life Gut Microbiome—The Importance of Maternal and Infant Factors in Its Establishment. Nutr. Clin. Pract. 2020, 35, 386–405.
9. Di Profio, E.; Magenes, V.C.; Fiore, G.; Agostinelli, M.; La Mendola, A.; Acunzo, M.; Francavilla, R.; Indrio, F.; Bosetti, A.; D'Auria, E.; et al. Special Diets in Infants and Children and Impact on Gut Microbioma. Nutrients 2022, 14, 3198.
10. Layuk, N.; Sinrang, A.W.; Asad, S. Early initiation of breastfeeding and gut microbiota of neonates: A literature review. Med. Clínica Práctica 2021, 4, 100222.
11. Homann, C.M. Evaluating the Relationship between Dietary Intake at the Time Immediately before and after the Introduction of Solid Foods and the Gut Microbiome in Full-Term Infants: A Longitudinal Study. Published Online 2020. Available online: https://macsphere.mcmaster.ca/handle/11375/25499 (accessed on 25 July 2023).
12. Rey-Mariño, A.; Francino, M.P. Nutrition, Gut Microbiota, and Allergy Development in Infants. Nutrients 2022, 14, 4316.
13. Laursen, M.F.; Bahl, M.I.; Michaelsen, K.F.; Licht, T.R. First Foods and Gut Microbes. Front. Microbiol. 2017, 8, 356.
14. Ballard, O.; Morrow, A.L. Human milk composition: Nutrients and bioactive factors. Pediatr. Clin. N. Am. 2013, 60, 49–74.
15. Cuxart, I.; Coines, J.; Esquivias, O.; Faijes, M.; Planas, A.; Biarnés, X.; Rovira, C. Enzymatic Hydrolysis of Human Milk Oligosaccharides. The Molecular Mechanism of Bifidobacterium Bifidum Lacto-N-biosidase. ACS Catal. 2022, 12, 4737–4743.
16. Lawson, M.A.E.; O'neill, I.J.; Kujawska, M.; Javvadi, S.G.; Wijeyesekera, A.; Flegg, Z.; Chalklen, L.; Hall, L.J. Breast milk-derived human milk oligosaccharides promote Bifidobacterium interactions within a single ecosystem. ISME J.

2019, 14, 635–648.

17. Laursen, M.F. Gut Microbiota Development: Influence of Diet from Infancy to Toddlerhood. Ann. Nutr. Metab. 2021, 77 (Suppl. 3), 21–34.
18. Fukuda, S.; Toh, H.; Hase, K.; Oshima, K.; Nakanishi, Y.; Yoshimura, K.; Tobe, T.; Clarke, J.M.; Topping, D.L.; Suzuki, T.; et al. Bifidobacteria can protect from enteropathogenic infection through production of acetate. Nature 2011, 469, 543–547.
19. Sakurama, H.; Kiyohara, M.; Wada, J.; Honda, Y.; Yamaguchi, M.; Fukiya, S.; Yokota, A.; Ashida, H.; Kumagai, H.; Kitaoka, M.; et al. Lacto-N-biosidase Encoded by a Novel Gene of Bifidobacterium longum Subspecies longum Shows Unique Substrate Specificity and Requires a Designated Chaperone for Its Active Expression. J. Biol. Chem. 2013, 288, 25194–25206.
20. Wada, J.; Ando, T.; Kiyohara, M.; Ashida, H.; Kitaoka, M.; Yamaguchi, M.; Kumagai, H.; Katayama, T.; Yamamoto, K. Bifidobacterium bifidum Lacto-N-Biosidase, a Critical Enzyme for the Degradation of Human Milk Oligosaccharides with a Type 1 Structure. Appl. Environ. Microbiol. 2008, 74, 3996.
21. Matsuki, T.; Yahagi, K.; Mori, H.; Matsumoto, H.; Hara, T.; Tajima, S.; Ogawa, E.; Kodama, H.; Yamamoto, K.; Yamada, T.; et al. A key genetic factor for fucosyllactose utilization affects infant gut microbiota development. Nat. Commun. 2016, 7, 1–12.
22. Wickramasinghe, S.; Pacheco, A.R.; Lemay, D.G.; Mills, D.A. Bifidobacteria grown on human milk oligosaccharides downregulate the expression of inflammation-related genes in Caco-2 cells. BMC Microbiol. 2015, 15, 1–12.
23. Saturio, S.; Nogacka, A.M.; Alvarado-Jasso, G.M.; Salazar, N.; Reyes-Gavilán, C.G.d.L.; Gueimonde, M.; Arboleya, S. Role of Bifidobacteria on Infant Health. Microorganisms 2021, 9, 2415.
24. Boudry, G.; Charton, E.; Le Huerou-Luron, I.; Ferret-Bernard, S.; Le Gall, S.; Even, S.; Blat, S. The Relationship between Breast Milk Components and the Infant Gut Microbiota. Front. Nutr. 2021, 8, 629740.
25. Yang, L.; Sakandar, H.A.; Sun, Z.; Zhang, H. Recent advances of intestinal microbiota transmission from mother to infant. J. Funct. Foods. 2021, 87, 104719.
26. Ferretti, P.; Pasolli, E.; Tett, A.; Asnicar, F.; Gorfer, V.; Fedi, S.; Armanini, F.; Truong, D.T.; Manara, S.; Zolfo, M.; et al. Mother-to-Infant Microbial Transmission from Different Body Sites Shapes the Developing Infant Gut Microbiome. Cell Host Microbe 2018, 24, 133–145.e5.
27. Yassour, M.; Jason, E.; Hogstrom, L.J.; Arthur, T.D.; Tripathi, S.; Siljander, H.; Selvenius, J.; Oikarinen, S.; Hyöty, H.; Virtanen, S.M.; et al. Strain-Level Analysis of Mother-to-Child Bacterial Transmission during the First Few Months of Life. Cell Host Microbe 2018, 24, 146–154.e4.
28. Pannaraj, P.S.; Li, F.; Cerini, C.; Bender, J.M.; Yang, S.; Rollie, A.; Adisetiyo, H.; Zabih, S.; Lincez, P.J.; Bittinger, K.; et al. Association Between Breast Milk Bacterial Communities and Establishment and Development of the Infant Gut Microbiome. JAMA Pediatr. 2017, 171, 647–654.
29. Notarbartolo, V.; Giuffrè, M.; Montante, C.; Corsello, G.; Carta, M. Composition of Human Breast Milk Microbiota and Its Role in Children's Health. Pediatr. Gastroenterol. Hepatol. Nutr. 2022, 25, 194–210.
30. Guo, W.; Liu, S.; Khan, M.Z.; Wang, J.; Chen, T.; Alugongo, G.M.; Li, S.; Cao, Z. Bovine milk microbiota: Key players, origins, and potential contributions to early-life gut development. J. Adv. Res. 2023. ISSN 2090-1232.
31. Selvamani, S.; Dailin, D.J.; Gupta, V.K.; Wahid, M.; Keat, H.C.; Natasya, K.H.; Malek, R.A.; Haque, S.; Sayyed, R.Z.; Abomoelak, B.; et al. An Insight into Probiotics Bio-Route: Translocation from the Mother's Gut to the Mammary Gland. Appl. Sci. 2021, 11, 7247.
32. Rodríguez, J.M. The Origin of Human Milk Bacteria: Is There a Bacterial Entero-Mammary Pathway during Late Pregnancy and Lactation? Adv. Nutr. 2014, 5, 779.
33. Simpson, M.R.; Avershina, E.; Storrø, O.; Johnsen, R.; Rudi, K.; Øien, T. Breastfeeding-associated microbiota in human milk following supplementation with Lactobacillus rhamnosus GG, Lactobacillus acidophilus La-5, and Bifidobacterium animalis ssp. lactis Bb-12. J. Dairy Sci. 2018, 101, 889–899.
34. Bergmann, H.; Rodríguez, J.M.; Salminen, S.; Szajewska, H. Probiotics in human milk and probiotic supplementation in infant nutrition: A workshop report. Br. J. Nutr. 2014, 112, 1119–1128.
35. Komatsu, Y.; Kumakura, D.; Seto, N.; Izumi, H.; Takeda, Y.; Ohnishi, Y.; Nakaoka, S.; Aizawa, T. Dynamic Associations of Milk Components With the Infant Gut Microbiome and Fecal Metabolites in a Mother–Infant Model by Microbiome, NMR Metabolomic, and Time-Series Clustering Analyses. Front. Nutr. 2022, 8, 813690.
36. Liu, Y.; Qin, S.; Song, Y.; Feng, Y.; Lv, N.; Xue, Y.; Liu, F.; Wang, S.; Zhu, B.; Ma, J.; et al. The Perturbation of Infant Gut Microbiota Caused by Cesarean Delivery Is Partially Restored by Exclusive Breastfeeding. Front. Microbiol. 2019, 10,

598.

37. Fehr, K.; Moossavi, S.; Sbihi, H.; Boutin, R.C.; Bode, L.; Robertson, B.; Yonemitsu, C.; Field, C.J.; Becker, A.B.; Mandhane, P.J.; et al. Breastmilk Feeding Practices Are Associated with the Co-Occurrence of Bacteria in Mothers' Milk and the Infant Gut: The CHILD Cohort Study. Cell Host Microbe 2020, 28, 285–297.e4.
38. Ho, N.T.; Li, F.; Lee-Sarwar, K.A.; Tun, H.M.; Brown, B.; Pannaraj, P.S.; Bender, J.M.; Azad, M.B.; Thompson, A.L.; Weiss, S.T.; et al. Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations. Nat. Commun. 2018, 9, 1–13.
39. Li, Y.; Ren, L.; Wang, Y.; Li, J.; Zhou, Q.; Peng, C.; Li, Y.; Cheng, R.; He, F.; Shen, X. The Effect of Breast Milk Microbiota on the Composition of Infant Gut Microbiota: A Cohort Study. Nutrients 2022, 14, 5397.
40. Chichlowski, M.; van Diepen, J.A.; Prodan, A.; Olga, L.; Ong, K.K.; Kortman, G.A.M.; Dunger, D.B.; Gross, G. Early development of infant gut microbiota in relation to breastfeeding and human milk oligosaccharides. Front. Nutr. 2023, 10, 1003032.
41. Laursen, M.F.; Sakanaka, M.; von Burg, N.; Mörbe, U.; Andersen, D.; Moll, J.M.; Pekmez, C.T.; Rivollier, A.; Michaelsen, K.F.; Mølgaard, C.; et al. Bifidobacterium species associated with breastfeeding produce aromatic lactic acids in the infant gut. Nat. Microbiol. 2021, 6, 1367–1382.
42. Hascoët, J.; Hubert, C.; Rochat, F.; Legagneur, H.; Gaga, S.; Emady-Azar, S.; Steenhout, P.G. Effect of formula composition on the development of infant gut microbiota. J. Pediatr. Gastroenterol. Nutr. 2011, 52, 756–762.
43. Ma, J.; Li, Z.; Zhang, W.; Zhang, C.; Zhang, Y.; Mei, H.; Zhuo, N.; Wang, H.; Wang, L.; Wu, D. Comparison of gut microbiota in exclusively breast-fed and formula-fed babies: A study of 91 term infants. Sci. Rep. 2020, 10, 1–11.
44. Fabiano, V.; Indrio, F.; Verduci, E.; Calcaterra, V.; Pop, T.L.; Mari, A.; Zuccotti, G.V.; Cokugras, F.C.; Pettoello-Mantovani, M.; Goulet, O. Term Infant Formulas Influencing Gut Microbiota: An Overview. Nutrients 2021, 13, 4200.
45. Borewicz, K.; Suarez-Diez, M.; Hechler, C.; Beijers, R.; de Weerth, C.; Arts, I.; Penders, J.; Thijs, C.; Nauta, A.; Lindner, C.; et al. The effect of prebiotic fortified infant formulas on microbiota composition and dynamics in early life. Sci. Rep. 2019, 9, 1–13.
46. Hill, C.J.; Lynch, D.B.; Murphy, K.; Ulaszewska, M.; Jeffery, I.B.; O'shea, C.A.; Watkins, C.; Dempsey, E.; Mattivi, F.; Tuohy, K.; et al. Evolution of gut microbiota composition from birth to 24 weeks in the INFANTMET Cohort. Microbiome 2017, 5, 1–18.
47. Béghin, L.; Tims, S.; Roelofs, M.; Rougé, C.; Oozeer, R.; Rakza, T.; Chirico, G.; Roeselers, G.; Knol, J.; Rozé, J.C.; et al. Fermented infant formula (with Bifidobacterium breve C50 and Streptococcus thermophilus O65) with prebiotic oligosaccharides is safe and modulates the gut microbiota towards a microbiota closer to that of breastfed infants. Clin. Nutr. 2021, 40, 778–787.
48. He, X.; Parenti, M.; Grip, T.; Lönnerdal, B.; Timby, N.; Domellöf, M.; Hernell, O.; Slupsky, C.M. Fecal microbiome and metabolome of infants fed bovine MFGM supplemented formula or standard formula with breast-fed infants as reference: A randomized controlled trial. Sci. Rep. 2019, 9, 11589.
49. Chow, J.; Panasevich, M.R.; Alexander, D.; Boler, B.M.V.; Serao, M.C.R.; Faber, T.A.; Bauer, L.L.; Fahey, G.C. Fecal Metabolomics of Healthy Breast-Fed versus Formula-Fed Infants before and during In Vitro Batch Culture Fermentation. J. Proteome Res. 2014, 13, 2534–2542.
50. Roager, H.M.; Stanton, C.; Hall, L.J. Microbial metabolites as modulators of the infant gut microbiome and host-microbial interactions in early life. Gut Microbes 2023, 15, 2192151.
51. Yao, Q.; Li, H.; Gao, Y.; Zheng, N.; Delcenserie, V.; Wang, J. The Milk Active Ingredient, 2′-Fucosyllactose, Inhibits Inflammation and Promotes MUC2 Secretion in LS174T Goblet Cells In Vitro. Foods 2023, 12, 186.
52. Lemoine, A.; Tounian, P.; Adel-Patient, K.; Thomas, M. Pre-, pro-, syn-, and Postbiotics in Infant Formulas: What Are the Immune Benefits for Infants? Nutrients 2023, 15, 1231.
53. Holst, A.Q.; Myers, P.; Rodríguez-García, P.; Hermes, G.D.A.; Melsaether, C.; Baker, A.; Jensen, S.R.; Parschat, K. Infant Formula Supplemented with Five Human Milk Oligosaccharides Shifts the Fecal Microbiome of Formula-Fed Infants Closer to That of Breastfed Infants. Nutrients 2023, 15, 3087.
54. Zhang, B.; Li, L.Q.; Liu, F.; Wu, J.Y. Human milk oligosaccharides and infant gut microbiota: Molecular structures, utilization strategies and immune function. Carbohydr. Polym. 2022, 276, 118738.
55. Rao, S.; Srinivasjois, R.; Patole, S. Prebiotic supplementation in full-term neonates: A systematic review of randomized controlled trials. Arch. Pediatr. Adolesc. Med. 2009, 163, 755–764.
56. Dinleyici, M.; Barbieur, J.; Dinleyici, E.C.; Vandenplas, Y. Functional effects of human milk oligosaccharides (HMOs). Gut Microbes 2023, 15, 2186115.

57. Natividad, J.M.; Marsaux, B.; Rodenas, C.L.; Rytz, A.; Vandevijver, G.; Marzorati, M.; Van den Abbeele, P.; Calatayud, M.; Rochat, F. Human Milk Oligosaccharides and Lactose Differentially Affect Infant Gut Microbiota and Intestinal Barrier In Vitro. Nutrients 2022, 14, 2546.

58. Ben, X.M.; Zhou, X.Y.; Zhao, W.H.; Yu, W.L.; Pan, W.; Zhang, W.L.; Wu, S.M.; Beusekom, C.M.; Schaafsma, A. Supplementation of milk formula with galacto-oligosaccharides improves intestinal micro-flora and fermentation in term infants. Chin. Med. J. Engl. 2004, 117, 927–931.

59. Salminen, S.; Stahl, B.; Vinderola, G.; Szajewska, H. Infant Formula Supplemented with Biotics: Current Knowledge and Future Perspectives. Nutrients 2020, 12, 1952.

60. Estorninos, E.; Lawenko, R.B.; Palestroque, E.; Sprenger, N.; Benyacoub, J.; Kortman, G.A.M.; Boekhorst, J.; Bettler, J.; Cercamondi, C.I.; Berger, B. Term infant formula supplemented with milk-derived oligosaccharides shifts the gut microbiota closer to that of human milk-fed infants and improves intestinal immune defense: A randomized controlled trial. Am. J. Clin. Nutr. 2022, 115, 142–153.

61. Mugambi, M.N.; Musekiwa, A.; Lombard, M.; Young, T.; Blaauw, R. Probiotics, prebiotics infant formula use in preterm or low birth weight infants: A systematic review. Nutr. J. 2012, 11, 58.

62. Giovannini, M.; Verduci, E.; Gregori, D.; Ballali, S.; Soldi, S.; Ghisleni, D.; Riva, E. Prebiotic effect of an infant formula supplemented with galacto-oligosaccharides: Randomized multicenter trial. J. Am. Coll. Nutr. 2014, 33, 385–393.

63. Xia, Q.; Williams, T.; Hustead, D.; Price, P.; Morrison, M.; Yu, Z. Quantitative analysis of intestinal bacterial populations from term infants fed formula supplemented with fructo-oligosaccharides. J. Pediatr. Gastroenterol. Nutr. 2012, 55, 314–320.

64. Vivatvakin, B.; Mahayosnond, A.; Theamboonlers, A.; Steenhout, P.G.; Conus, N.J. Effect of a whey-predominant starter formula containing LCPUFAs and oligosaccharides (FOS/GOS) on gastrointestinal comfort in infants. Asia Pac. J. Clin. Nutr. 2010, 19, 473–480.

65. Salminen, S.; Endo, A.; Isolauri, E.; Scalabrin, D. Early Gut Colonization With Lactobacilli and Staphylococcus in Infants: The Hygiene Hypothesis Extended. J. Pediatr. Gastroenterol. Nutr. 2016, 62, 80–86.

66. Salvini, F.; Riva, E.; Salvatici, E.; Boehm, G.; Jelinek, J.; Banderali, G.; Giovannini, M. A specific prebiotic mixture added to starting infant formula has long-lasting bifidogenic effects. J. Nutr. 2011, 141, 1335–1339.

67. Holscher, H.D.; Faust, K.L.; Czerkies, L.A.; Litov, R.; Ziegler, E.E.; Lessin, H.; Hatch, T.; Sun, S.; Tappenden, K.A. Effects of prebiotic-containing infant formula on gastrointestinal tolerance and fecal microbiota in a randomized controlled trial. JPEN J. Parenter. Enteral. Nutr. 2012, 36 (Suppl. 1), 95S–105S.

68. Huet, F.; Abrahamse-Berkeveld, M.; Tims, S.; Simeoni, U.; Beley, G.; Savagner, C.; Vandenplas, Y.; Hourihane, J.O. Partly Fermented Infant Formulae With Specific Oligosaccharides Support Adequate Infant Growth and Are Well-Tolerated. J. Pediatr. Gastroenterol. Nutr. 2016, 63, e43–e53.

69. Simeoni, U.; Berger, B.; Junick, J.; Blaut, M.; Pecquet, S.; Rezzonico, E.; Grathwohl, D.; Sprenger, N.; Brüssow, H.; Szajewska, H.; et al. Gut microbiota analysis reveals a marked shift to bifidobacteria by a starter infant formula containing a synbiotic of bovine milk-derived oligosaccharides and Bifidobacterium animalis subsp. lactis CNCM I-3446. Environ. Microbiol. 2016, 18, 2185–2195.

70. Das, T.K.; Pradhan, S.; Chakrabarti, S.; Mondal, K.C.; Ghosh, K. Current status of probiotic and related health benefits. Appl. Food Res. 2022, 2, 100185.

71. Fijan, S. Microorganisms with Claimed Probiotic Properties: An Overview of Recent Literature. Int. J. Environ. Res. Public Health 2014, 11, 4745.

72. Gil-Campos, M.; López, M.; Rodriguez-Benítez, M.V.; Romero, J.; Roncero, I.; Linares, M.D.; Maldonado, J.; López-Huertas, E.; Berwind, R.; Ritzenthaler, K.L.; et al. Lactobacillus fermentum CECT 5716 is safe and well tolerated in infants of 1–6 months of age: A Randomized Controlled Trial. Pharmacol. Res. 2012, 65, 231–238.

73. Scalabrin, D.; Harris, C.; Johnston, W.; Berseth, C. Long-term safety assessment in children who received hydrolyzed protein formulas with Lactobacillus rhamnosus GG: A 5-year follow-up. Eur. J. Pediatr. 2017, 176, 217–224.

74. Maldonado-Lobón, J.; Gil-Campos, M.; Maldonado, J.; López-Huertas, E.; Flores-Rojas, K.; Valero, A.; Rodríguez-Benítez, M.; Bañuelos, O.; Lara-Villoslada, F.; Fonollá, J.; et al. Long-term safety of early consumption of Lactobacillus fermentum CECT5716: A 3-year follow-up of a randomized controlled trial. Pharmacol. Res. 2015, 95–96, 12–19.

75. Rautava, S.; Kalliomäki, M.; Isolauri, E. Probiotics during pregnancy and breast-feeding might confer immunomodulatory protection against atopic disease in the infant. J. Allergy Clin. Immunol. 2002, 109, 119–121.

76. Maldonado, J.; Cañabate, F.; Sempere, L.; Vela, F.; Sánchez, A.R.; Narbona, E.; López-Huertas, E.; Geerlings, A.; Valero, A.D.; Olivares, M.; et al. Human milk probiotic Lactobacillus fermentum CECT5716 reduces the incidence of gastrointestinal and upper respiratory tract infections in infants. J. Pediatr. Gastroenterol. Nutr. 2012, 54, 55–61.

77. Horigome, A.; Hisata, K.; Odamaki, T.; Iwabuchi, N.; Xiao, J.Z.; Shimizu, T. Colonization of Supplemented Bifidobacterium breve M-16V in Low Birth Weight Infants and Its Effects on Their Gut Microbiota Weeks Post-administration. Front. Microbiol. 2021, 12, 610080.

78. Yan, W.; Luo, B.; Zhang, X.; Ni, Y.; Tian, F. Association and Occurrence of Bifidobacterial Phylotypes Between Breast Milk and Fecal Microbiomes in Mother–Infant Dyads During the First 2 Years of Life. Front. Microbiol. 2021, 12, 669442.

79. Alander, M.; Mättö, J.; Kneifel, W.; Johansson, M.; Kögler, B.; Crittenden, R.; Mattila-Sandholm, T.; Saarela, M. Effect of galacto-oligosaccharide supplementation on human faecal microflora and on survival and persistence of Bifidobacterium lactis Bb-12 in the gastrointestinal tract. Int. Dairy J. 2001, 11, 817–825.

80. Lin, C.; Lin, Y.; Zhang, H.; Wang, G.; Zhao, J.; Zhang, H.; Chen, W. Intestinal 'Infant-Type' Bifidobacteria Mediate Immune System Development in the First 1000 Days of Life. Nutrients 2022, 14, 1498.

81. Frese, S.A.; Hutton, A.A.; Contreras, L.N.; Shaw, C.A.; Palumbo, M.C.; Casaburi, G.; Xu, G.; Davis, J.C.C.; Lebrilla, C.B.; Henrick, B.M.; et al. Persistence of Supplemented Bifidobacterium longum subsp. infantis EVC001 in Breastfed Infants. mSphere 2017, 2, e00501–e00517.

82. Quin, C.; Estaki, M.; Vollman, D.M.; Barnett, J.A.; Gill, S.K.; Gibson, D.L. Probiotic supplementation and associated infant gut microbiome and health: A cautionary retrospective clinical comparison. Sci. Rep. 2018, 8, 1–16.

83. Alcon-Giner, C.; Dalby, M.J.; Caim, S.; Ketskemety, J.; Shaw, A.; Sim, K.; Lawson, M.A.; Kiu, R.; LeClaire, C.; Chalklen, L.; et al. Microbiota Supplementation with Bifidobacterium and Lactobacillus Modifies the Preterm Infant Gut Microbiota and Metabolome: An Observational Study. Cell Rep. Med. 2020, 1, 100077.

84. Vendt, N.; Grünberg, H.; Tuure, T.; Malminiemi, O.; Wuolijoki, E.; Tillmann, V.; Sepp, E.; Korpela, R. Growth during the first 6 months of life in infants using formula enriched with Lactobacillus rhamnosus GG: Double-blind, randomized trial. J. Hum. Nutr. Diet 2006, 19, 51–58.

85. Li, Y.; Shimizu, T.; Hosaka, A.; Kaneko, N.; Ohtsuka, Y.; Yamashiro, Y. Effects of bifidobacterium breve supplementation on intestinal flora of low birth weight infants. Pediatr. Int. 2004, 46, 509–515.

86. van Best, N.; Trepels-Kottek, S.; Savelkoul, P.; Orlikowsky, T.; Hornef, M.W.; Penders, J. Influence of probiotic supplementation on the developing microbiota in human preterm neonates. Gut Microbes 2020, 12, 1–16.

87. Milani, C.; Duranti, S.; Bottacini, F.; Casey, E.; Turroni, F.; Mahony, J.; Belzer, C.; Delgado Palacio, S.; Arboleya Montes, S.; Mancabelli, L.; et al. The First Microbial Colonizers of the Human Gut: Composition, Activities, and Health Implications of the Infant Gut Microbiota. Microbiol. Mol. Biol. Rev. 2017, 81, e00036-17.

88. Abate, A.D.; Hassen, S.L.; Temesgen, M.M. Timely initiation of complementary feeding practices and associated factors among children aged 6–23 months in Dessie Zuria District, Northeast Ethiopia: A community-based cross-sectional study. Front. Pediatr. 2023, 11, 1062251.

89. Berti, C.; Socha, P. Infant and Young Child Feeding Practices and Health. Nutrients 2023, 15, 1184.

90. Campoy, C.; Leis, R. Methods of introduction of complementary feeding in the first year of life. An. Pediatría Engl. Ed. 2023, 98, 247–248.

91. Fewtrell, M.; Bronsky, J.; Campoy, C.; Domellöf, M.; Embleton, N.; Mis, N.F.; Hojsak, I.; Hulst, J.M.; Indrio, F.; Lapillonne, A.; et al. Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. J. Pediatr. Gastroenterol. Nutr. 2017, 64, 119–132.

92. Tang, M.; Matz, K.L.; Berman, L.M.; Davis, K.N.; Melanson, E.L.; Frank, D.N.; Hendricks, A.E.; Krebs, N.F. Effects of Complementary Feeding With Different Protein-Rich Foods on Infant Growth and Gut Health: Study Protocol. Front. Pediatr. 2021, 9, 793215.

93. Laursen, M.F.; Andersen, L.B.B.; Michaelsen, K.F.; Mølgaard, C.; Trolle, E.; Bahl, M.I.; Licht, T.R. Infant Gut Microbiota Development Is Driven by Transition to Family Foods Independent of Maternal Obesity. mSphere 2016, 1, e00069-15.

94. Differding, M.K.; Benjamin-Neelon, S.E.; Hoyo, C.; Østbye, T.; Mueller, N.T. Timing of complementary feeding is associated with gut microbiota diversity and composition and short chain fatty acid concentrations over the first year of life. BMC Microbiol. 2020, 20, 56.

95. McKeen, S.; Roy, N.C.; Mullaney, J.A.; Eriksen, H.; Lovell, A.; Kussman, M.; Young, W.; Fraser, K.; Wall, C.R.; McNabb, W.C. Adaptation of the infant gut microbiome during the complementary feeding transition. PLoS ONE 2022, 17, e0270213.

96. Tang, M.; Frank, D.; Hendricks, A.; Ir, D.; Krebs, N. Protein Intake During Early Complementary Feeding Affects the Gut Microbiota in U.S. Formula-fed Infants (FS04-03-19). Curr. Dev. Nutr. 2019, 3 (Suppl. 1), nzz048.FS04-03-19.

97. Fu, J.; Zheng, Y.; Gao, Y.; Xu, W. Dietary Fiber Intake and Gut Microbiota in Human Health. Microorganisms 2022, 10, 2507.

98. Gómez-Martín, M.; Saturio, S.; Arboleya, S.; Herrero-Morín, D.; Calzón, M.; López, T.; González, S.; Gueimonde, M. Association between diet and fecal microbiota along the first year of life. Food Res. Int. 2022, 162, 111994.

99. Stewart, C.J.; Ajami, N.J.; O'brien, J.L.; Hutchinson, D.S.; Smith, D.P.; Wong, M.C.; Ross, M.C.; Lloyd, R.E.; Doddapaneni, H.; Metcalf, G.A.; et al. Temporal development of the gut microbiome in early childhood from the TEDDY study. Nature 2018, 562, 583–588.

100. Neri-Numa, I.A.; Pastore, G.M. Novel insights into prebiotic properties on human health: A review. Food Res. Int. 2020, 131, 108973.

101. Suriano, F.; Nyström, E.E.L.; Sergi, D.; Gustafsson, J.K. Diet, microbiota, and the mucus layer: The guardians of our health. Front. Immunol. 2022, 13, 953196.

102. Simpson, H.L.; Campbell, B.J. Review article: Dietary fibre–microbiota interactions. Aliment. Pharmacol. Ther. 2015, 42, 158.

103. Wu, S.; Bhat, Z.F.; Gounder, R.S.; Ahmed, I.A.M.; Al-Juhaimi, F.Y.; Ding, Y.; Bekhit, A.E. Effect of Dietary Protein and Processing on Gut Microbiota—A Systematic Review. Nutrients 2022, 14, 453.

104. Calatayud, M.; Van den Abbeele, P.; Ghyselinck, J.; Marzorati, M.; Rohs, E.; Birkett, A. Comparative Effect of 22 Dietary Sources of Fiber on Gut Microbiota of Healthy Humans in vitro. Front. Nutr. 2021, 8, 700571.

105. Makki, K.; Deehan, E.C.; Walter, J.; Bäckhed, F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. Cell Host Microbe 2018, 23, 705–715.

106. Huang, Z.; Boekhorst, J.; Fogliano, V.; Capuano, E.; Wells, J.M. Impact of High-Fiber or High-Protein Diet on the Capacity of Human Gut Microbiota To Produce Tryptophan Catabolites. J. Agric. Food Chem. 2023, 71, 6956–6966.

107. Murga-Garrido, S.M.; Hong, Q.; Cross, T.-W.L.; Hutchison, E.R.; Han, J.; Thomas, S.P.; Vivas, E.I.; Denu, J.; Ceschin, D.G.; Tang, Z.-Z.; et al. Gut microbiome variation modulates the effects of dietary fiber on host metabolism. Microbiome 2021, 9, 1–26.

108. Singh, V.; Lee, G.; Son, H.; Koh, H.; Kim, E.S.; Unno, T.; Shin, J.H. Butyrate producers, "The Sentinel of Gut": Their intestinal significance with and beyond butyrate, and prospective use as microbial therapeutics. Front. Microbiol. 2023, 13, 1103836.

109. Tsukuda, N.; Yahagi, K.; Hara, T.; Watanabe, Y.; Matsumoto, H.; Mori, H.; Higashi, K.; Tsuji, H.; Matsumoto, S.; Kurokawa, K.; et al. Key bacterial taxa and metabolic pathways affecting gut short-chain fatty acid profiles in early life. ISME J. 2021, 15, 2574–2590.

110. Alsharairi, N.A. Therapeutic Potential of Gut Microbiota and Its Metabolite Short-Chain Fatty Acids in Neonatal Necrotizing Enterocolitis. Life 2023, 13, 561.

111. Akhtar, M.; Chen, Y.; Ma, Z.; Zhang, X.; Shi, D.; Khan, J.A.; Liu, H. Gut microbiota-derived short chain fatty acids are potential mediators in gut inflammation. Anim. Nutr. 2022, 8, 350–360.

112. Cong, X.; Xu, W.; Janton, S.; Henderson, W.A.; Matson, A.; McGrath, J.M.; Maas, K.; Graf, J. Gut Microbiome Developmental Patterns in Early Life of Preterm Infants: Impacts of Feeding and Gender. PLoS ONE 2016, 11, e0152751.

113. Gondolf, U.H.; Tetens, I.; Michaelsen, K.F.; Trolle, E. Dietary habits of partly breast-fed and completely weaned infants at 9 months of age. Public Health Nutr. 2012, 15, 578–586.

114. Marrs, T.; Jo, J.H.; Perkin, M.R.; Rivett, D.W.; Witney, A.A.; Bruce, K.D.; Logan, K.; Craven, J.; Radulovic, S.; Versteeg, S.A.; et al. Gut microbiota development during infancy: Impact of introducing allergenic foods. J. Allergy Clin. Immunol. 2021, 147, 613–621.e9.

115. Hughes, R.L.; Holscher, H.D. Fueling Gut Microbes: A Review of the Interaction between Diet, Exercise, and the Gut Microbiota in Athletes. Adv. Nutr. 2021, 12, 2190.

116. Li, L.; Ryan, J.; Ning, Z.; Zhang, X.; Mayne, J.; Lavallée-Adam, M.; Stintzi, A.; Figeys, D. A functional ecological network based on metaproteomics responses of individual gut microbiomes to resistant starches. Comput. Struct. Biotechnol. J. 2020, 18, 3833–3842.

117. Cronin, P.; Joyce, S.A.; O'toole, P.W.; O'connor, E.M. Dietary Fibre Modulates the Gut Microbiota. Nutrients 2021, 13, 1655.

118. Bäckhed, F.; Roswall, J.; Peng, Y.; Feng, Q.; Jia, H.; Kovatcheva-Datchary, P.; Li, Y.; Xia, Y.; Xie, H.; Zhong, H.; et al. Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life. Cell Host Microbe 2015, 17, 690–703.

119. Caffarelli, C.; Di Mauro, D.; Mastrorilli, C.; Bottau, P.; Cipriani, F.; Ricci, G. Solid Food Introduction and the Development of Food Allergies. Nutrients 2018, 10, 1790.
120. Koukou, Z.; Papadopoulou, E.; Panteris, E.; Papadopoulou, S.; Skordou, A.; Karamaliki, M.; Diamanti, E. The Effect of Breastfeeding on Food Allergies in Newborns and Infants. Children 2023, 10, 1046.
121. Du Toit, G.; Foong, R.X.M.; Lack, G. Prevention of food allergy—Early dietary interventions. Allergol. Int. 2016, 65, 370–377.
122. Leong, C.; Haszard, J.J.; Lawley, B.; Otal, A.; Taylor, R.W.; Szymlek-Gay, E.A.; Fleming, E.A.; Daniels, L.; Fangupo, L.J.; Tannock, G.W.; et al. Mediation analysis as a means of identifying dietary components that differentially affect the fecal microbiota of infants weaned by modified baby-led and traditional approaches. Appl. Environ. Microbiol. 2018, 84.
123. Differding, M.K.; Doyon, M.; Bouchard, L.; Perron, P.; Guérin, R.; Asselin, C.; Massé, E.; Hivert, M.; Mueller, N.T. Potential interaction between timing of infant complementary feeding and breastfeeding duration in determination of early childhood gut microbiota composition and BMI. Pediatr. Obes. 2020, 15, e12642.
124. Xiao, L.; Wang, J.; Zheng, J.; Li, X.; Zhao, F. Deterministic transition of enterotypes shapes the infant gut microbiome at an early age. Genome Biol. 2021, 22, 243.
125. Szajewska, H.; Guandalini, S.; Morelli, L.; Van Goudoever, J.B.; Walker, A. Effect of Bifidobacterium animalis subsp lactis supplementation in preterm infants: A systematic review of randomized controlled trials. J. Pediatr. Gastroenterol. Nutr. 2010, 51, 203–209.