

Exploring the Infant Microbiome from Birth to Early Growth: Review

Aziza M. Amer ¹, Mohamed M. Amer ^{2*}

¹ Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt.

² Department of Poultry Diseases, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt.

***Corresponding Author:** Mohamed M. Amer., Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt.

Received Date: May 20, 2025; Accepted Date: April 10, 2025; Published Date: April 16, 2025

Citation: Aziza M. Amer, Mohamed M. Amer, (2025), Exploring the Infant Microbiome from Birth to Early Growth: Review, *Clinical Trials and Clinical Research*,4(2); DOI:10.31579/2834-5126/094

Copyright: © 2025, Mohamed M. Amer. This is an open access article distributed under the creative commons' attribution license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

The infant microbiome consists of trillions of microorganisms and is shaped by a combination of genetic, environmental, and dietary influences. Its development is vital for the infant's immune system and overall well-being, underscoring the necessity of comprehending these processes to enhance health outcomes.

The formation of the microbiome commences at birth, with infants encountering microorganisms during delivery, whether through vaginal birth or cesarean section. Research suggests that infants born vaginally acquire a microbiome that closely mirrors that of their mothers. The evolution of the infant microbiome is a multifaceted process that initiates at birth and continues to develop throughout the early years of life. This microbiome plays a pivotal role in health, affecting immune function, metabolism, resistance to pathogens, neurodevelopment, and long-term health outcomes. Gaining insight into its significance can guide strategies aimed at optimizing infant health and preventing diseases.

Investigating the infant microbiome from birth through early development highlights its essential function in influencing health and growth. Understanding the various factors that affect microbial colonization can lead to strategies that foster healthy microbiome development, potentially reducing health risks linked to microbial imbalances. Probiotic strains such as *Lactobacillus rhamnosus* GG, *Bifidobacterium bifidum*, and *Lactobacillus reuteri* have proven to be particularly effective for infants. Ongoing research in this field is crucial for uncovering the complexities of the microbiome, its effects on lifelong health, and for developing various strategies to promote well-being and minimize disease risk.

Keywords: microbiota; pregnancy; immunoglobulin; neurological health

Introduction

Infants are typically defined as children from birth until around one year of age, after which they are referred to as toddlers. The term originates from the Latin word "infantem," which translates to "babe in arms" as a noun and "unable to speak" as an adjective (CDCP, 2013; Maggie, 2022). Following birth, infants generally experience a weight loss of about 5% to 10% of their initial weight. By the time they reach two weeks of age, they should begin to gain weight rapidly. By four to six months, an infant's weight is expected to be double that of their birth weight. Growth tends to slow during the latter half of the first year. Between the ages of one and two, toddlers typically gain around 5 pounds (2.2 kilograms) (Onigbanjo et al., 2020). The infant microbiome, consisting of trillions of microbes, is essential for health and development from birth through early childhood, influencing immune and neurological health (Yang et al., 206; Frerichs and Niemarkt, 2024; Koren et

al., 2024). Maternal gut microbiota impacts fetal immune and neurodevelopment indirectly via microbiota-derived metabolites (Koren et al., 2023). These metabolites can cross the placenta during pregnancy, triggering a fetal immune response (Aburto and Cryan, 2024). Research indicates that the human fetal intestine has a diverse metabolome as early as 12 weeks gestation, with metabolites and metabolic pathways linked to neurodevelopment being particularly enriched (Li et al., 2020). Probiotic strains such as *Lactobacillus rhamnosus* GG, *Bifidobacterium bifidum*, and *Lactobacillus reuteri* have been identified as particularly effective for infants (Segers et al., 2014; Martinelli et al., 2020; Depoorter and Vandenplas, 2021). The field of microbiome interventions for infants is rapidly advancing, exploring various strategies to enhance health and mitigate disease risk.

Gut microbiota:

Gut microbiota consists of various microorganisms, including bacteria, yeast, and viruses. The microbial microbiome contains approximately 3.3 million active genes, significantly outnumbering the 22,000 human genes. The gut microbiota comprises organisms residing in the gastrointestinal tract, contributing to about 60% of the dry weight of feces, with 99% being anaerobic bacteria. While bacteria dominate the microbiome, the presence of viruses, archaea, and eukaryotes, although less abundant, is also noteworthy (Ursell et al., 2012). From a taxonomic perspective, bacteria are categorized into phyla, classes, orders, families, genera, and species. A limited number of phyla encompass over 160 species (Laterza et al., 2016). The primary gut microbial phyla include Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia, with Firmicutes and Bacteroidetes together accounting for 90% of the gut microbiota (Arumugam et al., 2011). The Firmicutes phylum includes more than 200 genera, such as *Bacillus*, *Lactobacillus*, *Clostridium*, *Enterococcus*, and *Ruminococcus*, with *Clostridium* making up 95% of this phylum. Bacteroidetes is primarily represented by genera like *Bacteroides* and *Prevotella*. The Actinobacteria phylum is less abundant, mainly represented by the *Bifidobacterium* genus (Arumugam et al., 2011; Rinninella et al., 2018). Through assembly and curation, researchers identified 10,000 viral species from 248 virus family-level clades (VFCs) in fecal viromes of 647 one-year-old children (Shah et al., 2025). Additionally, it has been observed that phages can influence the composition and function of the gut microbiota (Rasmussen et al., 2020; Liang et al., 2020). The composition and structure of gut microbiota are influenced by various host and microbial factors. Host factors include age, genetic background, overall health, dietary habits, medication use, intestinal pH, peristalsis, transit time, mucus secretions, mucous immunoglobulin, and tissue oxidation-reduction potentials. Microbial factors also play a significant role.

Bacterial Colonization:

The human fetus is believed to grow in a sterile environment devoid of bacteria (Dominguez-Bello et al., 2010). Following birth, the infant's gut is swiftly populated through a multifaceted process influenced by various interrelated factors, such as the delivery method and feeding type (Pannaraj et al., 2017). Right after birth, the newborn's intestinal microbiota is initially dominated by Enterobacteriaceae and Staphylococcus (Matsuki et al., 2016), which are subsequently supplanted by *Bifidobacterium* and certain lactic acid bacteria (Mitsuoka et al., 2014). This *Bifidobacterium*-rich microbiota, referred to as Bifidus flora, persists until complementary foods are introduced (Palmer et al., 2007; Vallès et al., 2014). In the immediate postnatal period, the first microorganisms to colonize the infant originate from the mother's microbiota, which can be found in the vaginal area, feces, breast milk, mouth, and skin, as well as from the surrounding environment (Matsumiya et al., 2002; Makino et al., 2011). The first year of life is crucial for development, as the microbiota becomes increasingly diverse and stable (Yatsunenkeno et al., 2012; Levin et al., 2016; Laursen et al., 2017). Initially low in diversity at birth, the microbiota evolves into a more intricate and adult-like composition by the age of 1 to 2 years (Stewart et al., 2018). During the early years, the gut microbiome consists of facultative anaerobic bacteria. However, in the following weeks, these initial colonizers are gradually replaced by conventional anaerobic bacteria, which ultimately dominate the intestinal microbiota (Clemente et al., 2012). As the infant nears weaning, the proportion of *Bacteroides* increases, leading to the competitive exclusion of *Bifidobacterium* within the gut microbiota. Post-weaning, the Bifidus flora is supplanted by adult-type microorganisms, primarily including *Bacteroides*, *Prevotella*, *Ruminococcus*, *Clostridium*, and *Veillonella* (Vallès et al., 2014). By the age of three, an infant's gut

microbiota closely resembles that of an adult (Yatsunenkeno et al., 2012). Various factors, including maternal nutrition, health conditions, and the use of antibiotics during pregnancy and childbirth, can significantly affect the infant's initial microbial profile (Taylor et al., 2012). The colonization of gut bacteria generally begins at birth. Infants delivered vaginally are exposed to their mother's vaginal and fecal microbiota, whereas those born through cesarean section may initially acquire bacteria from the skin (Dominguez-Bello et al., 2010). Once breastfeeding commences, breast milk introduces additional prebiotics. Colostrum, in particular, is abundant in human milk oligosaccharides (HMOs), which cannot be digested by human enzymes alone. The production of these oligosaccharides can represent up to ten percent of the total energy used in human milk synthesis (Bode, 2012) and supports the proliferation of beneficial gut microbes (Newburg et al., 2007; Thum et al., 2018). In vitro research indicates that HMOs selectively promote the growth of beneficial bacteria such as *Bifidobacterium longum* while inhibiting harmful pathogens like *Escherichia coli* and *Clostridium perfringens* (Yu et al., 2013; Kunz et al., 2017). The metabolic byproducts of HMOs, including lactate and short-chain fatty acids (SCFAs) produced by *Bifidobacterium longum* subspecies *infantis* (*B. infantis*), also suppress the growth of *E. coli* and *C. perfringens*. When cultivated on HMOs, *B. infantis* demonstrates a higher affinity for binding to intestinal epithelial cells and exhibits enhanced barrier-supporting and anti-inflammatory properties (Sela et al., 2011; Chichlowski et al., 2012). *B. infantis* has been shown to dominate the gut microbiota of breastfed infants, providing several benefits to the host, such as accelerating immune response maturation, modulating the immune system to reduce inflammation, enhancing intestinal barrier integrity, and increasing acetate production (Chichlowski et al., 2020).

Origins of the Infant Microbiome:

The development of the microbiome starts at birth. Infants encounter microorganisms during the delivery process:

1. In Utero Development: Recent research challenges the notion that the fetal environment is completely sterile. Studies have found bacteria present in amniotic fluid, meconium, and placental tissues, indicating that microbial exposure begins before birth (Aagaard et al., 2014).

2. Birth Method: The way an infant is delivered plays a crucial role in their initial microbial colonization. Infants born vaginally are generally exposed to their mother's vaginal and gut microbiota, while those delivered via cesarean section may acquire microbes from the skin and the surrounding hospital environment (Dominguez-Bello et al., 2010; Selma-Royo et al., 2020). Research has shown that cesarean delivery is linked to a lower diversity of gut microbiota in infants, which may have lasting health effects (Rahman et al., 2022).

3. Feeding Method:

a. **Breastfeeding:** Breast milk significantly contributes to the infant microbiome, providing not only essential nutrients but also prebiotics and beneficial bacteria that support the growth of specific gut microbiota (WHO, 2009; Martín-Rodríguez et al., 2022). The bacterium *B. infantis* has been found to dominate the gut microbiota of breastfed infants (Chichlowski et al., 2020).

b. **Formula Feeding:** Infants who are formula-fed typically exhibit a different microbial profile, often showing a higher prevalence of pathogenic bacteria (Bäckhed et al., 2015; Rahman et al., 2022).

Developmental Stages of microbiota:

Development infant of microbiota can be classified into 3 stages including:

1. Initial Colonization (0-6 Months):

The initial phase of colonization is characterized by a swift increase in bacterial populations, predominantly from the Bacteroidetes and Firmicutes phyla. This stage is essential for laying the groundwork for the gut microbiome (Yatsunenko et al., 2012). A study conducted by Ma et al. (2022) aimed to analyze the gut microbiota of healthy infants, focusing on the effects of delivery methods and feeding practices. The infants were exclusively breastfed or given specific formulas for over four months post-birth. The composition of fecal bacteria was assessed at 40 days, 3 months, and 6 months of age. Introduction of solid foods occurred between 4 to 6 months, which did not influence the microbiota prior to 4 months. Based on the delivery methods (vaginal delivery (VD) or cesarean section (CS)) and feeding types (breast-fed (br) or formula-fed (fo)), the infants were categorized into four groups: VD-br, VD-fo, CS-br, and CS-fo. The findings revealed that at 40 days, α diversity was lower in breast-fed infants compared to formula-fed infants. By 3 months, the α diversity was notably reduced in the CS-br group, although no significant differences were detected following the introduction of solid foods. *Bifidobacterium* was the most prevalent genus across all groups at each time point, followed by Enterobacteriaceae. At 40 days of age, the levels of *Bifidobacterium* were significantly higher in the CS-br group compared to the CS-fo group, while no notable differences were observed between the VD-br and VD-fo groups. By 3 and 6 months of age, the variations in *Bifidobacterium* levels among the groups had diminished. Additionally, at 40 days, the abundance of *Streptococcus* and *Enterococcus* was considerably lower in the br infants than in the CS-fo group. By 3 months, *Enterococcus* levels were significantly reduced in the CS-br group compared to the fo infants, although no significant difference was found for infants delivered via VD. The interplay between delivery methods and feeding types significantly influences the gut microbiota of infants. Breastfeeding and vaginal delivery may mitigate the potential negative effects of formula feeding or cesarean delivery on gut microbiota, fostering a more stable and advantageous gut environment for infants.

2. Stabilization and Diversification (6-12 Months):

As infants begin to consume solid foods, the microbiome becomes more diverse, with increasing representation of various bacterial taxa. This diversification is shaped by dietary changes and environmental exposures (Korpela, 2021; Rutayisire et al., 2016).

3. Maturation (1-3 Years):

By the age of three, the infant microbiome resembles that of adults, characterized by increased stability and diversity. However, it continues to be influenced by diet, lifestyle, and exposure to pathogens (Faith et al., 2013).

Impact of Environmental Factors:

Numerous elements contribute to the formation of the infant microbiome. Key factors include the method of delivery, nutritional choices (such as breastfeeding versus formula feeding), the administration of antibiotics during birth or in early infancy, and exposure to various environmental factors, including pets and siblings. The use of antibiotics, in particular, can significantly disrupt the microbiome, reducing its diversity and potentially resulting in health complications (Rahman et al., 2022).

Interactions with family members, pets, and the surrounding environment introduce new microbial species, further influencing the microbiome's development. Early exposure to a variety of environments can foster a more robust microbiome (Lloyd-Price et al., 2016; Mahurkar et al., 2027). Research indicates that infants who grow up in households with pets or older

siblings often exhibit a more diverse gut microbiota (Lax et al., 2014). Additionally, exposure to different microbial environments, such as those found in rural versus urban areas, can affect the microbiome and may play a role in the development of allergies. Evidence suggests that residing in rural settings, where there is greater exposure to animals and a wider array of microbes, correlates with lower rates of allergies (Rook, 2010).

2. Antibiotic Use:

The use of antibiotics during pregnancy or in early infancy can disrupt the normal development of gut microbiota. Antibiotics can reduce microbial diversity and may lead to an increased risk of conditions such as obesity and allergies later in life (Jernberg et al., 2010). Antibiotic treatment during infancy can disrupt the normal development of the microbiome, leading to long-term consequences on health, including increased susceptibility to infections and allergies (Zimmermann and Curtis, 2020).

Components of the Infant Microbiome:

Infant gut microbiota including

a. Bacterial Components:

The gut microbiome of infants is predominantly characterized by the presence of *Bifidobacteria* and *Lactobacilli*. These beneficial microorganisms play a crucial role in digestion and the absorption of nutrients (Arrieta et al., 2014; Sarkar et al., 2021). As the infant matures, the microbiome becomes more diverse, influenced by changes in diet and exposure to the environment, which includes the introduction of bacteria from the mother's microbiome and the surrounding surroundings (Kapourchali and Cresci, 2020). The microbiota of infants mainly consists of various bacterial communities, including:

1. Bifidobacteria:

Bifidobacteria are among the first microorganisms to inhabit the gut of infants, particularly those who are breastfed, typically colonizing within days to weeks after birth and accounting for 40% to 80% of the gut microbiota (Tannock, 2002; Ling et al., 2016; Makino et al., 2015). These bacteria are transmitted from the mother through the vaginal canal, gastrointestinal tract, or breast milk (Duranti et al., 2017). Infants delivered vaginally tend to have higher levels of *Bifidobacterium* spp. compared to those born via cesarean section, although the differences in gut microbiomes become apparent only after five days and tend to diminish by the time the infant reaches 30 days of age (Chen et al., 2007; Milani et al., 2015; Wampach et al., 2017; Grönlund et al., 2011).

Reduced levels of *Bifidobacterium* spp. have been linked to chronic conditions such as asthma and obesity, as well as diminished responses to vaccines (Ly et al., 2011; Huda et al., 2014). Henrick et al. (2018) proposed that the decrease in *Bifidobacterium* spp. in developed nations may be a factor in the increasing prevalence of allergic and autoimmune disorders. The presence of these bacteria can also be influenced by factors such as diet, antibiotic consumption, and the onset of puberty (Voreades et al., 2014; Yatsunenko, 2012). Importantly, *B. infantis* is the dominant strain in the gut microbiota of breastfed infants, playing a crucial role in immune development, inflammation regulation, intestinal barrier enhancement, and acetate production (Underwood et al., 2015).

3. Bacteroides:

The initial establishment of *Bacteroides* in infants primarily occurs through maternal transmission during childbirth. Infants delivered vaginally generally exhibit higher concentrations of *Bacteroides*, as these bacteria are commonly found in the vaginal microbiota (Dominguez-Bello et al., 2010;

Fouhy et al., 2012). Additionally, human milk contains oligosaccharides that facilitate the proliferation of *Bacteroides* and other beneficial microorganisms (Underwood et al., 2013). Following birth, infants encounter various microbes from their environment, including those from caregivers and the home setting, which can further enhance the colonization of *Bacteroides* (Rautava et al., 2012).

Bacteroides serve several essential functions within the gastrointestinal tract of infants. They are crucial for the early establishment of the gut microbiome (Matharu et al., 2022). These bacteria play a significant role in the digestion of complex carbohydrates and dietary fibers, thereby supporting nutrient absorption (Martens et al., 2011).

4. *Escherichia coli* (E.coli) as a Component of Infant Gut Biota:

Some strains of bacteria are advantageous and support gut health, while others can be harmful (Kaper et al., 2004). *E. coli* is crucial for the formation and upkeep of the infant gut microbiota. Its early presence facilitates metabolic processes and the development of the immune system, thereby enhancing the infant's overall health. While certain *E. coli* strains are well-known for causing foodborne illnesses, many others are benign and play an essential role in the gut microbiota, especially in infants (Nataro and Kaper, 1998). The development of gut microbiota in infants is vital for their growth and health, affecting various physiological functions and the maturation of the immune system. The infant gut microbiome starts to form at birth, shaped by factors such as the delivery method (vaginal or cesarean), maternal health, and feeding practices. *E. coli* is among the first bacteria to colonize the gastrointestinal tract of newborns (Fouhy et al., 2012). Research indicates that *E. coli* can be found in the feces of infants within the initial days of life (Martinez et al., 2016). Infants born vaginally typically acquire *E. coli* strains from the birth canal, whereas those delivered by cesarean section may experience a delay in colonization of *E. coli* and other beneficial bacteria due to limited exposure to maternal microbes (Dominguez-Bello et al., 2010). In a study examining the prevalence of uropathogenic lineages in Swedish infants and enteropathogenic lineages in Pakistani infants, Nowrouzian et al. (2019) analyzed ExPEC and EPEC strains of *E. coli* belonging to B2 phylogenetic subgroups/STCs that colonize these populations. A total of 120 gut commensal *E. coli* B2 strains were collected from Swedish infants ($n = 87$) and 19 from Pakistani infants ($n = 12$), which were categorized into B2 subgroups. The presence of bundle-forming pili and intimin adhesin was assessed in the EPEC lineages. Previous research had established the virulence markers of ExPEC and the duration of strain persistence in the microbiota. The findings revealed that 84% of the strains from Swedish infants and 47% from Pakistani infants were classified into one of the ten primary B2 subgroups ($P = 0.001$). Among the Swedish strains, the predominant B2 subgroups included IX/STc95 (19%), II/STc73 (17%), VI/STc12 (13%), and III/STc127 (11%), each exhibiting unique sets of ExPEC virulence markers. In contrast, EPEC lineages with limited ExPEC characteristics represented 47% of the Pakistani B2 strains, while only 7% of the Swedish B2 strains fell into this category. The distribution of B2 subgroups within the phylogenetic group varied significantly between the two populations. Uropathogenic B2 subgroups were more prevalent in the gut microbiota of Swedish infants, whereas EPEC lineage 1 strains were more commonly found in the intestines of Pakistani infants. Additionally, ExPEC virulence genes were found to be more widespread among Swedish strains compared to their Pakistani counterparts. The absence of exposure to maternal vaginal and fecal microbiota may result in a delayed colonization of *E. coli* and other beneficial bacteria (Dominguez-Bello et al., 2010). Breast milk is rich in prebiotics that support the growth of beneficial bacteria, including *E. coli*, whereas infants who are formula-fed may develop a different microbial profile, often associated with a higher occurrence of

potentially harmful strains (Bäckhed et al., 2015). *E. coli* plays a vital role in various metabolic processes within the gut. It participates in carbohydrate fermentation and the synthesis of SCFAs such as acetate, propionate, and butyrate, which are essential for maintaining gut health and can affect systemic inflammation (Morrison and Preston, 2016). Additionally, *E. coli* aids in the education of the immune system, fostering tolerance to non-harmful antigens while enabling effective responses to pathogens (Round and Mazmanian, 2009). It is crucial for caregivers to maintain proper hygiene and food safety practices to reduce the risk of exposure to harmful strains, particularly among vulnerable groups such as infants (Nataro and Kaper, 1998). The colonization of *E. coli* in infants generally commences shortly after birth. Research indicates that *E. coli* can be identified in the feces of infants within the first week of life, with a notable increase in diversity and abundance in the subsequent months (Martinez et al., 2016). The prevalence of *E. coli* in infants is influenced by geographic location, health status, and environmental conditions. In healthy infants, studies have reported a high occurrence of *E. coli* within the gut microbiota. One study involving a cohort of infants found that *E. coli* was present in over 90% of fecal samples during the first year of life (O'Sullivan et al., 2016).

E. coli present in the infant gut is generally divided into two main types: commensal (non-pathogenic) and pathogenic strains:

- a. Commensal *E. coli*: These strains are vital components of the gut microbiota, contributing significantly to metabolic functions and the development of the immune system. They assist in nutrient absorption and the production of essential vitamins (Morrison and Preston, 2016).
- b. Pathogenic *E. coli*: In contrast, pathogenic strains can lead to gastrointestinal diseases and are further classified into several categories. Enterotoxigenic *E. coli* (ETEC) is associated with diarrhea in infants and travelers, producing toxins that result in fluid loss. Enteropathogenic *E. coli* (EPEC) is linked to infant diarrhea, as it adheres to intestinal cells and disrupts their normal function. Shiga toxin-producing *E. coli* (STEC) is notorious for causing severe gastrointestinal illnesses and can result in hemolytic uremic syndrome (HUS), a serious complication (Nataro and Kaper, 1998). Additionally, certain environmental conditions, such as inadequate sanitation and contamination, can heighten the risk of encountering these harmful strains (Kaper et al., 2004).

5. Enterococcus bacteria in the gut of infants:

Enterococcus species are gram-positive cocci that form a part of the normal gut microbiota in humans and various mammals. Notably, *Enterococcus faecalis* and *Enterococcus faecium* are significant for gut health, exhibiting both beneficial and pathogenic characteristics. These species typically begin to colonize the gut of infants shortly after birth. Research has shown that Enterococcus can be identified in the feces of newborns within the initial days of life (Favier et al., 2002). The colonization process is affected by multiple factors, including the mode of delivery and feeding methods. Infants delivered vaginally are exposed to their mother's microbiota, which includes Enterococcus, during the birthing process. Conversely, infants born via cesarean section often present a different microbial profile, resulting in variations in the timing and diversity of Enterococcus colonization (Dominguez-Bello et al., 2010). Breastfeeding has been demonstrated to support the establishment of beneficial gut bacteria, including Enterococcus. Breast milk contains prebiotics that foster the growth of these bacteria, while formula-fed infants may show different patterns of colonization (Bäckhed et al., 2015). Enterococcus species are frequently detected in the feces of healthy infants, with studies indicating that they can represent a substantial portion of the gut microbiota during the first year of life (O'Sullivan et al.,

2016), often reaching levels that are comparable to or even surpass those of other dominant gut bacteria (Penders et al., 2006).

Enterococcus can cause various infections, such as urinary tract infections and bacteremia (O'Brien et al., 2015). While commensal strains of *Enterococcus* may play a role in nutrient metabolism and the development of the immune system, certain opportunistic strains are linked to infections, especially in individuals with weakened immune systems (Lebreton et al., 2014). The types of *Enterococcus* found in the infant gut include:

a. *Enterococcus faecalis*: This species is one of the most prevalent *Enterococcus* types in the infant gut and is typically regarded as a commensal bacterium.

b. *Enterococcus faecium*: Another frequently identified *Enterococcus* species in the infant microbiome, which includes both commensal and opportunistic strains (Weinstein et al., 1997).

c. *Enterococcus avium*: This species is less commonly found in the infant gut compared to *E. faecalis* and *E. faecium*. Although most *Enterococcus* strains are benign, some can develop antibiotic resistance, complicating treatment for infections. *Enterococcus faecium* has been particularly noted for its association with multidrug-resistant infections in clinical environments (Leclercq, 2001).

6. *Helicobacter pylori* infection:

Helicobacter pylori (*H. pylori*) is a flagellated, spiral-shaped, Gram-negative bacillus that inhabits the human gastric mucosa, leading to an inflammatory response in the gastric lining, as well as the potential development of gastric and/or duodenal ulcers, intestinal metaplasia, or even gastric cancer (Patel and Underwood, 2018). The characteristics of *H. pylori* infection in children differ from those in adults, particularly in terms of prevalence, complication rates, diagnostic challenges, and a higher incidence of antibiotic resistance. In developing countries, the prevalence of *H. pylori* in children is significantly higher at 20%, compared to just 0.5% in developed nations (Kalach et al., 2017). Furthermore, *H. pylori* infection in children is associated with an increased risk of gut colonization by *Prevotella*, *Clostridium*, *Proteobacteria*, and *Firmicutes*, whereas uninfected children tend to have a higher presence of *Bacteroides*. These alterations in gut microbiota linked to *H. pylori* infection may contribute to the onset of chronic gastrointestinal diseases and antibiotic resistance (Yap et al., 2016). The incorporation of probiotics containing *L. acidophilus*, *L. casei* DN-114001, *L. gasseri*, *Bifidobacterium infantis* 2036, or *Lactobacillus reuteri* Gastrus, has shown similar beneficial effects during *H. pylori* treatment (Emara et al., 2014). Various studies have indicated that specific probiotic strains may exhibit inhibitory effects against *H. pylori*, while others can mitigate the side effects of antibiotic therapy, thereby enhancing the rate of *H. pylori* eradication (Sharma, 2020).

b. Viral components:

Large-scale investigations into the composition and structure of the early life virome remain limited, and studies on the human virome face significant challenges due to the vast amount of unexplored viral diversity, often referred to as the viral 'dark matter' issue (Aggarwala et al., 2017). Recent research has identified three new caudoviral families within human gut metagenome data (Benler et al., 2021). Additionally, the notable gut phage family Crassviridae has been reclassified as the viral order Crassvirales (Yutin et al., 2021), which is part of the newly proposed viral class Caudoviricetes, encompassing caudoviruses (Koonin et al., 2020). Recent findings indicate that transferring gut viral content from healthy individuals can effectively treat recurrent *Clostridioides difficile* infections (Ott et al.,

2017), reduce diet-induced obesity (Rasmussen et al., 2020), and prevent necrotizing enterocolitis in preterm infants (Brunse et al., 2022). While the underlying mechanisms remain unclear, they likely involve the modulation of gut microbiota composition through viral infections, as the majority of gut viruses are bacteriophages that specifically target bacteria (Shkoporov and Hill, 2019). A recent study by Shah et al. (2025) thoroughly examined the viral diversity in fecal viromes from 647 one-year-old children participating in the Copenhagen Prospective Studies on Asthma in Childhood 2010, an unselected cohort of healthy mother-child pairs in Denmark. Through assembly and curation, the study identified 10,000 viral species across 248 virus family-level clades (VFCs), with the majority (232 VFCs) being previously unidentified and belonging to the Caudoviricetes viral class.

c. Bacteriophages:

Certain phages have the potential to induce chronic infections, resulting in the persistent release of viral particles (Hobbs and Abedon, 2016). In response, bacteria employ various defense mechanisms (Bernheim and Sorek, 2020), including the clustered regularly interspaced short palindromic repeat (CRISPR)–Cas systems. This adaptive immune strategy involves the storage of DNA records (spacers) from previous viral infections within a chromosomal CRISPR array, enabling bacteria to fend off future phage assaults (Sorek et al., 2008).

Phages can also influence the composition and functionality of the gut microbiome (Rasmussen et al., 2020; Liang et al., 2020) and may provoke immune responses in the human host (Fluckiger et al., 2020; Górski et al., 2018; Dufour et al., 2019), indicating a complex interaction that could affect host health. The initial documentation of the viral metagenome (virome) in the infant gut dates back over ten years (Breitbart et al., 2008), with recent findings highlighting the impact of cesarean delivery and formula feeding on the infant virome (McCann et al., 2018).

In a study by Shah et al. (2025) examined the viral diversity in fecal viromes from 647 one-year-old children and identified 79% of the phages using CRISPR spacers found in bacterial metagenomes from the same children. Notably, *Bacteroides*-infecting crAssphages were outnumbered by previously uncharacterized phage families targeting *Clostridiales* and *Bifidobacterium*. The lifestyles of phages were consistent at the viral family level, comprising 33 virulent and 118 temperate phage families, with virulent phages being more abundant, while temperate phages exhibited greater prevalence and diversity.

Role of the Microbiome in Early Growth:

The infant microbiome not only affects immune function but also contributes to metabolic processes that influence growth and development. Microbial metabolites, such as SCFAs, are produced during the fermentation of dietary fibers. These SCFAs play critical roles in gut health and metabolism, linking the microbiome directly to the regulation of appetite and energy balance (Xiao, and Kang, 2020). SCFAs produced by the fermentation of dietary fibers by gut bacteria, play a critical role in immune regulation and gut health (Wu, and Wu, 2011, Zheng et al., 2020). These metabolites can influence inflammation and the development of the immune system (Arpaia et al., 2013).

The functional capacity of the microbiome, determined by the genes present, influences metabolic pathways related to nutrient metabolism, immune modulation, and protection against pathogens (Qin et al., 2010). Research suggests that the infant microbiome may even influence neurological development, gut microbiota has been shown to communicate with the brain via the gut-brain axis, impacting mood and behavior (Dinan and Cryan, 2017).

Microbial Diversity and Health Implications

The diversity of the gut microbiome is closely linked to various health outcomes. A more diverse microbiome is often associated with better immune response and reduced incidence of allergies, obesity, and other metabolic disorders (Zhao et al., 2023). For instance, research has shown that infants with less microbial diversity in their gut are at a higher risk for developing conditions such as asthma and obesity later in childhood (Petraroli et al., 2021, Squillario et al., 2023).

Infant Microbiome in normal and diseased condition:

The infant microbiome has significant implications for long-term health outcomes, influencing various physiological and immunological processes.

The differences between the microbiome in healthy infants and those with diseases are marked by variations in microbial composition, immune interactions, metabolic functions, and long-term health outcomes. Here are some key areas where the infant **microbiome plays a crucial role**:

a. In Healthy Infants: Typically characterized by higher diversity and abundance of beneficial bacteria, particularly Bifidobacteria and Lactobacilli (Arrieta et al., 2014, Sarkar et al., 2021).

1. Immune System Development:

The microbiome plays a key role in the maturation of the immune system, promoting tolerance to non-harmful antigens and enhancing responses to pathogens (Kau et al., 2011). In Healthy Infants: The microbiome is essential for the maturation of the immune system. Early microbial exposure helps train the immune system to differentiate between harmful pathogens and non-harmful antigens, promoting immune tolerance (Kau et al., 2011). Fermentation of dietary fibers by gut bacteria, play a critical role in immune regulation and gut health (Wu, and Wu, 2011, Zheng et al., 2020). These metabolites can influence inflammation and the development of the immune system (Arpaia et al., 2013). presence of Bacteroides in the gut contributes to the maturation of the immune system, helping to establish tolerance and prevent inflammatory responses (Mazmanian et al., 2005, Yatsunenko et al., 2012). By occupying ecological niches and producing antimicrobial substances, Bacteroides can inhibit the growth of pathogenic bacteria, thereby enhancing gut health (Shin et al., 2011). Treg Cell Regulation: The microbiome helps in maturity of the immune system, particularly by promoting the development of regulatory T cells (Tregs), which are crucial for maintaining immune tolerance to non-harmful antigens (Kau et al., 2011). Specific bacteria, such as Bifidobacteria, are known to stimulate the production of regulatory T cells (Tregs), which play a key role in preventing allergic reactions and autoimmune diseases (Arrieta et al., 2014, Sarkar et al., 2021). Cytokine Production: Beneficial microbes can influence the production of cytokines, shaping the immune response towards a balanced state rather than excessive inflammation (Donald, and Finlay, 2023, Wiertsema et al., 2021). Immune Tolerance: A healthy infant microbiome promotes immune tolerance, helping the body differentiate between harmful pathogens and non-harmful antigens. This may reduce the risk of allergies and autoimmune diseases later in life (Kau et al., 2011). Infection Resistance: A well-developed microbiome provides a protective barrier against pathogens, reducing the likelihood of infections that can have long-term health consequences (Aziz et al., 2022, Thänert et al., 2021).

b. Infants with Disease: Often exhibit dysbiosis, characterized by reduced microbial diversity and an imbalance in microbial composition (Shan et al., 2021). Increased presence of pathogenic bacteria and reduced levels of beneficial microbes are common, which can exacerbate health issues. Long-term Disease Risk: A diverse and balanced microbiome in infancy is

associated with a reduced risk of chronic diseases, obesity, including asthma, allergies, and inflammatory bowel diseases (IBD) (Rook, 2010, Rook, 2013, Kapourchali, and Cresci, 2020, Morreale et al., 2023).

1. Dysbiosis: An imbalance in the microbiome, known as dysbiosis, has been associated with various conditions, including allergies, asthma, and gastrointestinal disorders (Shan et al., 2021). Increased presence of pathogenic bacteria and reduced levels of beneficial microbes are common, which can exacerbate health issues. A lack of diversity or an imbalance in microbial populations (dysbiosis) has been linked to increased susceptibility to allergic diseases, such as asthma and eczema (Shan et al., 2021). The use of antibiotics in infancy can disrupt the developing microbiome, leading to long-term health issues, such as increased susceptibility to infections and obesity (Sawicki et al., 2017). Dysbiosis, alterations in the gut microbiome, and low microbial diversity of the preterm neonate significantly correlate with a higher risk and raised rate of complication of necrotizing enterocolitis and, consequently, the development of late-onset sepsis. Low microbiota diversity may provoke pathogenic bacteria overgrowth, a significant risk factor that promotes NEC development (Zhuang et al., 2019). Dobbler et al (2017) found powerful domination of Citrobacter koseri and/or Klebsiella pneumoniae, reduced diversity, less Lactobacillus abundance, and an altered microbial-network structure during the first days of life, correlate with NEC risk in preterm infants.

2. Role in Inflammation: Dysbiosis can lead to increased intestinal permeability and systemic inflammation, which are implicated in conditions like inflammatory bowel disease (IBD) (Sartor, 2008).

3. Autoimmune Conditions: Changes in the microbiome have been implicated in the development of autoimmune diseases, highlighting the importance of early microbial exposure in shaping immune responses (Rook, 2010, Morreale et al., 2023).

4. Protection Against Pathogens

A healthy microbiome acts as a barrier against pathogens, preventing their colonization and reducing the risk of infections such as necrotizing enterocolitis in preterm infants (Aziz et al., 2022, Thänert et al., 2021).

6. Barrier Function:

Intestinal Permeability: A healthy microbiome supports the integrity of the gut barrier. Disruption of this barrier can lead to increased permeability, allowing allergens to enter the bloodstream and triggering allergic reactions (Sartor, 2008).

Antibiotic resistance in infant biota:

Antibiotic resistance in the microbiota of infants presents a complex challenge with significant consequences. The premature administration of antibiotics can disturb the natural microbiome, promoting the development and retention of resistance genes (Samarra et al., 2023). Excessive antibiotic use is linked to immature microbiota, which may result in metabolic disorders, malnutrition, infections, and an increased risk of colon cancer (Langdon et al., 2016). Furthermore, antibiotic treatments can enhance the prevalence of microbes harboring antibiotic resistance genes (ARGs), which may facilitate the transfer of these genes to pathogenic bacteria, complicating infection management (Ferreiro et al., 2018). Resistance genes can be exchanged among bacteria through horizontal gene transfer. The infant microbiome may serve as a reservoir for antibiotic resistance, potentially undermining the efficacy of antibiotics for treating infections in later life (Bernabeu et al., 2024). Instances of resistance genes, including those that provide resistance to β -lactams, aminoglycosides, and macrolides, have been identified in the microbiota of infants (Samarra et al., 2023). A study

involving 662 stool samples from one-year-old children utilized shotgun metagenomics, revealing 409 distinct types of ARGs associated with 34 different drug classes. Notably, 167 out of these 409 types (40.8%) were identified as conferring multidrug resistance (Li et al., 2021). Every child in the study exhibited at least one type of multidrug resistance ARG in their gut, with a median count of 43 ± 18 . In the gut resistomes, antimicrobial resistance genes were categorized into three levels: important, highly important, and critically important (WHO, 2018; Li et al., 2021). Infants delivered by cesarean section exhibited a tendency towards a higher likelihood of possessing unique antimicrobial resistance genes (ARGs) [relative risk = 1.12 (95% CI: 0.97–1.29)], as well as an elevated risk for overall ARG relative abundance [relative risk = 1.43 (95% CI: 1.12–1.84)] at one year of age compared to those born vaginally. Additionally, ARGs have been detected in the first stools of infants shortly after birth, even before any direct exposure to antibiotics (Yassour et al., 2018). Research indicates that the prevalence of ARGs in the infant gut tends to decline with age (Moore et al., 2015). Furthermore, ARGs can be transferred horizontally among bacteria via mobile genetic elements or vertically within the infant gut (Pärnänen et al., 2018).

Microbiome interventions strategies to promote health and reduce disease risk:

Research is actively exploring various microbiome interventions for infants, focusing on probiotics, dietary strategies, and novel therapeutic approaches. These interventions aim to optimize the infant microbiome for better health outcomes through:

1. Probiotics and Prebiotics:

Probiotic Research is currently investigating the role of specific probiotic strains in infants to mitigate issues such as allergies, colic, and gastrointestinal disorders. For instance, certain *Lactobacillus* and *Bifidobacterium* strains are being studied for their ability to alleviate atopic dermatitis (Kalliomäki et al., 2001). Probiotic supplementation can enhance the metabolic functions of the intestinal microbiota and alter their composition by suppressing the growth of harmful bacteria, breaking down their antigens, producing antimicrobial agents, and boosting mucosal IgA levels. Additionally, probiotics contribute to the enhancement of mucosal barrier function and the maintenance of its integrity by reinforcing epithelial junctions and stabilizing intestinal permeability. They also influence the immune responses of intestinal epithelial and mucosal cells, promoting T-cell apoptosis. As a result, probiotics play a role in regulating immune responses and reducing the production of pro-inflammatory factors (Salminen et al., 2006; Morais and Jacob, 2006). The use of probiotics in treating inflammatory bowel diseases (IBDs) remains a topic of debate; however, the administration of *Saccharomyces boulardii* has shown promise in maintaining remission and improving intestinal permeability and bowel sealing in patients with Crohn's disease (Vilela et al., 2008). *E. coli* Nissle1917, *B. breve*, *B. bifidum*, and *L. acidophilus* had a promising effect on in maintaining the remission phase in patients with ulcerative colitis as effective as the standard mesalazine therapy but with high safety and tolerability profiles (Kato et al,2004, Kruis et al,2004).

Prebiotic Formulations: Research is evaluating prebiotics, such as oligosaccharides found in breast milk, to enhance beneficial gut bacteria and improve immune responses (Arrieta et al., 2014, Sarkar et al., 2021).

2. Dietary Interventions:

Early Introduction of Allergenic Foods: Trials are assessing the timing and types of solid foods introduced to infants, particularly allergenic foods like

peanuts and eggs, to determine their role in allergy prevention (Du Toit et al., 2015, Trogen et al., 2022).

Diverse Diets: Studies are investigating how introducing a variety of foods can influence microbiome diversity and overall health outcomes (Morreale et al., 2023).

3. Birth Mode and Microbiome Restoration:

Cesarean Delivery: Research is being conducted on interventions for infants born via cesarean section, who may have altered microbiome development. Some studies are exploring the potential benefits of "microbiome restoration" techniques, such as administering maternal vaginal fluids to cesarean-born infants (Dominguez-Bello et al., 2016).

4. Fecal Microbiota Transplantation (FMT):

FMT in Infants: While still experimental, some studies are examining the safety and efficacy of fecal microbiota transplantation in infants with severe dysbiosis or conditions like *Clostridium difficile* infection (Hourigan, 2016, Korpela et al.,2020).

5. Longitudinal Studies:

Microbiome Development: Long-term studies are being conducted to track the changes in the infant microbiome over time and how these changes correlate with health outcomes, including allergies, obesity, and autoimmune diseases (Kapourchali, and Cresci, 2020).

Promoting a beneficial microbiome in infants:

Promoting a beneficial microbiome in infants involves several strategies that focus on early life practices and environmental exposures. Effective ways parents can encourage a healthy microbiome including:

1. Breast feeding:

Exclusive Breastfeeding: For the first six months, exclusive breastfeeding provides essential nutrients and prebiotics that promote the growth of beneficial bacteria (Schack-Nielsen et al., 2005, Krol, and Grossmann, 2018). **Longer Duration:** Continued breastfeeding beyond six months, alongside appropriate complementary foods, can further support microbiome diversity (Arrieta et al., 2014, Sarkar et al., 2021).

2. Introduction of Solid Foods:

Diverse Diet: Introduce a variety of solid foods around six months, focusing on fruits, vegetables, whole grains, and proteins to enhance microbial diversity (Morreale et al., 2023).

Early Allergenic Foods: Introducing allergenic foods (e.g., peanuts, eggs) early can help reduce the risk of allergies and support a balanced microbiome (Du Toit et al., 2015, Trogen, et al., 2022).

3. Avoiding Unnecessary Antibiotics: Only use antibiotics when prescribed by a healthcare professional. Avoid unnecessary antibiotic prescriptions, as these can disrupt the microbiome. If antibiotics are necessary, discuss strategies for microbiome recovery with a healthcare provider (Sawicki et al., 2017).

4. Promoting a Healthy Environment:

Natural Exposure: Allowing infants to explore different environments (e.g., outdoor play, contact with pets) can enhance microbial diversity and resilience (Rook, 2010, Rook, 2013).

Hygiene Practices: While hygiene is important, overly sterile environments may limit microbial exposure. Balance cleanliness with opportunities for microbial interaction.

5. Probiotics and Prebiotics:

Consider Probiotics: Consult with a healthcare provider about the use of specific probiotic supplements that may benefit infants, particularly for those with gastrointestinal issues (Kalliomäki et al., 2001).

Here are some of the most effective probiotic strains in promoting gut health and overall well-being in infants, *L. rhamnosus* GG can prevent and manage gastrointestinal infections and reduce the incidence of diarrhea in infants (Kalliomäki et al., 2001). *B. bifidum* is well Known for enhancing immune function and improving gut health, *B. bifidum* is one of the predominant bacteria in healthy infant guts (Arrieta et al., 2014, Sarkar et al., 2021). *B. lactis* usually supports overall gut health and has been linked to improvements in digestive issues and colic in infants (Koukou et al., 2023). *B. breve* is beneficial for infants, particularly in breastfeeding, as it helps digest human milk oligosaccharides and supports immune health (Morreale et al., 2023). *L. reuteri* has been shown to reduce crying time in infants with colic and to improve gastrointestinal health (Savino et al., 2010). *L. casei* can help in modulating the immune response and improving gut microbiota composition, contributing to overall health (Koukou et al., 2023).

6. Prebiotic Foods: Incorporate prebiotic-rich foods (e.g., bananas, onions) into the infant's diet as they can support beneficial gut bacteria.

7. Regular Pediatric Check-ups:

Regular check-ups by monitor growth and development can help ensure the infant is developing healthily and can address any microbiome-related concerns early on. Research indicates that routine pediatric visits facilitate the monitoring of growth parameters, such as weight and height, which are essential indicators of overall health (American Academy of Pediatrics, 2019). These visits also allow healthcare providers to discuss dietary practices, vaccination schedules, and developmental milestones, thereby addressing any concerns that may arise. Moreover, the infant microbiome plays a significant role in health, influencing immune function and metabolic processes (Bäckhed et al., 2015). Regular check-ups can help identify microbiome-related issues, such as gastrointestinal disturbances or allergies, allowing for early intervention and management strategies to support a healthy microbiome.

Studying the infant microbiome:

Studying the infant microbiome involves various methods that allow researchers to analyze microbial composition, diversity, and function. Here are some methods used in this field:

1. Sampling Techniques:

Stool Samples: The most common method for studying the gut microbiome is through stool samples, which provide a non-invasive way to assess microbial composition (Kapourchali, and Cresci, 2020).

Swabs: Oral and skin swabs can also be used to study the microbiome of different body sites, offering insights into the microbial communities present in infants (Dominguez-Bello et al., 2010).

2. DNA Sequencing:

16S rRNA Gene Sequencing: This method targets the 16S ribosomal RNA gene, which is present in all bacteria. It allows for the identification and comparison of microbial taxa in samples (Caporaso et al., 2011).

Metagenomic Sequencing: This approach sequences all genetic material in a sample, providing a comprehensive view of microbial diversity, including bacteria, fungi, and viruses (Qin et al., 2010). This method can reveal functional capabilities of the microbiome.

3. Bioinformatics Analysis:

Data Processing: Sophisticated bioinformatics tools are employed to analyze sequencing data, allowing researchers to identify microbial species, assess diversity, and explore functional characteristics (Belkaid, and Hand, 2014).

Statistical Analyses: Various statistical methods are used to evaluate differences in microbial communities across populations, dietary conditions, or health statuses (Mallick et al., 2017, 2021).

4. Culture Techniques:

While less common due to the complexity of the microbiome, traditional culture methods can be used to isolate and study specific bacterial strains in the lab (Joynt et al., 2006). This approach is useful for understanding the metabolic activities of individual species.

5. Functional Studies:

Metabolomic Analysis: This involves studying metabolites produced by the microbiome, such as short-chain fatty acids, to understand their role in health and disease (Salzman, 2014).

Animal Models: Researchers often use germ-free or gnotobiotic animal models to investigate the effects of specific microbial populations on health outcomes (Round and Mazmanian, 2009).

6. Longitudinal Studies:

Cohort Studies: Longitudinal studies track the microbiome over time in the same individuals, providing insights into how it changes with diet, environment, and development (Morreale et al., 2023).

Conclusion:

The exploration of the infant microbiome from birth to early growth reveals its critical role in shaping health and development.

The development of infant gut microbiota is a dynamic process influenced by various factors, including mode of delivery, feeding practices, environmental exposures, and antibiotic use. Promoting a healthy microbiome from infancy is essential for long-term health. The infant microbiome is established through a combination of genetic, environmental, and dietary factors. The infant microbiome significantly influences long-term health outcomes by shaping immune function, metabolism, neurological development, and susceptibility to chronic diseases. Understanding these relationships underscores the importance of promoting a healthy microbiome from infancy. Highlighting the importance of understanding these processes to promote better health outcomes. Probiotics strains like *L. rhamnosus* GG, *B. bifidum*, and *L. reuteri* are the most effective in infants.

Understanding how various factors influence microbial colonization can inform strategies for promoting healthy microbiome development, potentially mitigating health risks associated with microbial imbalances. Continued research in this area will be essential for unveiling the complexities of the microbiome and its impact on lifelong health.

Acknowledgments

Not applicable.

Funding statement

This review didn't receive any funding support.

Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

Ethical of approval

Not applicable

Authors' contributions:

All authors M M.A and A. M. A, are sharing the collected data, writing and revising the original draft. The authors approved the final manuscript.

References:

1. American Academy of Pediatrics. (2019). Pediatric Primary Care. 5th ed. Elk Grove Village, IL: American Academy of Pediatrics.
2. Bäckhed, F., Roswall, J., Frisen, L., et al. (2015). Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host & Microbe*, 17(5), 853-864.
3. Aagaard, K., Ma, J., Antony, K. M., Ganu, R., and Petrosino, J. F. (2014). The human microbiome during pregnancy. *Nature Medicine*, 20(2), 202-210.
4. Aburto MR, Cryan JF. (2024). Gastrointestinal and brain barriers: unlocking gates of communication across the microbiota-gut-brain axis. *Nat Rev Gastroenterol Hepatol*.
5. Addiss, D.G., Shaffer, N., Fowler, B.S. and Tauxe, R.V., 1990. The epidemiology of appendicitis and appendectomy in the United States. *American journal of epidemiology*, 132(5), pp.910-925.
6. Aggarwala, V., Liang, G. and Bushman, F. D. (2017). Viral communities of the human gut: metagenomic analysis of composition and dynamics. *Mob. DNA* 8, 12.
7. Arpaia, N., Campbell, C., Fan, X., Dikiy, S., DeRoos, P., et al. (2013). Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature*, 504(7480), 451-455.
8. Arrieta, M., Stiemsma, L. T., Amenyogbe, N., Brown, E. M., and Finlay, B. (2014). The Intestinal Microbiome in Early Life: Health and Disease. *Frontiers in Immunology*, 5, 105813.
9. Arumugam M., Raes J., Pelletier E., Le Paslier D., Yamada T., et al. (2011). Enterotypes of the human gut microbiome. *Nature*, 473:174–180.
10. Aziz, M., Prince, J. M., and Wang, P. (2022). Gut microbiome and necrotizing enterocolitis: Understanding the connection to find a cure. *Cell Host and Microbe*, 30(5), 612-616.
11. Bäckhed, F., Roswall, J., Peng, Y., et al. (2015). Dynamics and stabilization of the human gut microbiome during the first year of life. *Nature*, 478(7368), 204-209.
12. Belkaid, Y., and Hand, T. (2014). Role of the Microbiota in Immunity and inflammation. *Cell*, 157(1), 121.
13. Benavides-Ward A, Vasquez-Achaya F, Silva-Caso W, Aguilar-Luis MA, Mazulis F, et al. (2018). *Helicobacter pylori* and its relationship with variations of gut microbiota in asymptomatic children between 6 and 12 years. *BMC Res Notes*, 11: 468.
14. Benler, S. et al. (2011). Thousands of previously unknown phages discovered in whole-community human gut metagenomes. *Microbiome* 9, 78.
15. Bernabeu, M., Cabello-Yeves, E., Flores, E., Samarra, A., Kimberley Summers, J., et al. (2024). Role of vertical and horizontal microbial transmission of antimicrobial resistance genes in early life: Insights from maternal-infant dyads. *Current Opinion in Microbiology*, 77, 102424.
16. Bernheim, A. and Sorek, R. (2020). The pan-immune system of bacteria: antiviral defence as a community resource. *Nat. Rev. Microbiol.* 18, 113–119.
17. Bode, L. (2012). Human milk oligosaccharides: The role of the mother's milk in the infant gut microbiota. *Advances in Nutrition*, 3(3), 466S-475S.
18. Breitbart, M. et al. Viral diversity and dynamics in an infant gut. *Res. Microbiol.* 159, 367–373 (2008).
19. Brunse, A. et al. (2022). Fecal filtrate transplantation protects against necrotizing enterocolitis. *ISME J* 16, 686–694.
20. Caporaso, J. G., Lauber, C. L., Walters, W. A., Lozupone, C. A., Turnbaugh, P. J., et al. (2011). Global patterns of 16S rRNA diversity at a depth of millions of sequences per sample. *Proceedings of the National Academy of Sciences*, 108(supplement_1), 4516-4522.
21. Chen J., Cai W., Feng Y. (2007). Development of intestinal bifidobacteria and lactobacilli in breast-fed neonates. *Clin. Nutr.*, 26:559–566.
22. Chichlowski M, De Lartigue G, German JB, et al. (2012). Bifidobacteria Isolated From Infants and Cultured on Human Milk Oligosaccharides Affect Intestinal Epithelial Function. *J Pediatr Gastroenterol Nutr.*, 55(3):321–327.
23. Chichlowski, M., Shah, N., Wampler, J. L., Wu, S. S., and Vanderhoof, J. A. (2020). Bifidobacterium longum Subspecies infantis (B. Infantis) in Pediatric Nutrition: Current State of Knowledge. *Nutrients*, 12(6).
24. Christopher R. and Moir, M.D. (1996). Abdominal Pain in Infants and Children. Concise review for primary-care physicians, 71 (10): 984-989.
25. Clemente J.C., Ursell L.K., Parfrey L.W., Knight R. (2012). The impact of the gut microbiota on human health: An integrative view. *Cell*, 148:1258–1270.
26. Cryan, J. F., M. Cowan, C. S., Sandhu, K. V., S. Bastiaanssen, T. F., Boehme, M., et al. (2019). The Microbiota-Gut-Brain Axis. *Physiological Reviews*.
27. Depoorter, L., and Vandenplas, Y. (2021). Probiotics in Pediatrics. A Review and Practical Guide. *Nutrients*, 13(7).
28. Dinan, T. G., and Cryan, J. F. (2017). The Microbiome-Gut-Brain Axis in Health and Disease. *Gastroenterology Clinics of North America*, 46(1), 77-89.
29. Dobbler PT, Procianny RS, Mai V, Silveira RC, Corso AL, et al. (2017). Low Microbial Diversity and Abnormal Microbial Succession Is Associated with Necrotizing Enterocolitis in Preterm Infants. *Front Microbiol.*, 8: 2243.
30. Dominguez-Bello MG, De Jesus-Laboy KM, Shen N, Cox LM, Amir A. et al. (2016). Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer. *Nature Medicine*, 22(3), 250-253.

31. Dominguez-Bello, M. G., Costello, E. K., Contreras, M., et al. (2010). Delivery mode alters gut microbiota and metabolic profiles of newborns. *Proceedings of the National Academy of Sciences*, 107(26), 11971-11975.
32. Dominguez-Bello, M. G., Godoy-Vitorino, F., Knight, R., et al. (2010). Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proceedings of the National Academy of Sciences*, 107(26), 11971-11975.
33. Donald, K., and Finlay, B. B. (2023). Early-life interactions between the microbiota and immune system: Impact on immune system development and atopic disease. *Nature Reviews Immunology*, 23(11), 735-748.
34. Du Toit, G., Foong, R. M., and Lack, G. (2016). Prevention of food allergy – Early dietary interventions. *Allergy International*, 65(4), 370-377.
35. Dufour, N., Delattre, R., Chevallereau, A., Ricard, J.-D. and Debarbieux, L. (2019). Phage therapy of pneumonia is not associated with an overstimulation of the inflammatory response compared to antibiotic treatment in mice. *Antimicrob. Agents Chemother.* 63, e00379–319.
36. Duranti S., Lugli G.A., Mancabelli L., Armanini F., Turrone F., et al. (2017). Maternal inheritance of bifidobacterial communities and bifidophages in infants through vertical transmission. *Microbiome*, 5:66.
37. Emara MH, Mohamed SY, Abdel-Aziz HR. (2014). Lactobacillus reuteri in management of Helicobacter pylori infection in dyspeptic patients: a double-blind placebo-controlled randomized clinical trial. *Therap Adv Gastroenterol.*, 7: 4-13.
38. Faith, J. J., Guruge, J. L., Charbonneau, M., Subramanian, S., Seedorf, H., et al. (2013). The long-term stability of the human gut microbiota. *Nature*, 499(7456), 465-470.
39. Favier, C. F., de Vos, W. M., and Akkermans, A. D. L. (2002). Molecular monitoring of the human intestinal microbiota. *Nature Reviews Microbiology*, 1(3), 228-234.
40. Ferreira, A., Crook, N., Gasparini, A.J. and Dantas, G. (2018). Multiscale evolutionary dynamics of host-associated microbiomes. *Cell*, 172(6), pp.1216-1227.
41. Fluckiger, A. et al. (2020). Cross-reactivity between tumor MHC class I-restricted antigens and an enterococcal bacteriophage. *Science* 369, 936–942.
42. Fouhy, F., et al. (2012). The gut microbiota of healthy infants and its association with the mode of delivery. *BMC Microbiology*, 12, 118.
43. Frerichs, N. M., and Niemarkt, H. J. (2024). Microbiome and its impact on fetal and neonatal brain development: Current opinion in pediatrics. *Current Opinion in Clinical Nutrition and Metabolic Care*, 27(3), 297-303.
44. Garcia Vilela E, De Lourdes De Abreu Ferrari M, Oswaldo Da Gama Torres H, Guerra Pinto A, Carolina Carneiro Aguirre A, et al. (2008). Influence of Saccharomyces boulardii on the intestinal permeability of patients with Crohn's disease in remission. *Scand J Gastroenterol.*, 43: 842-848.
45. Górski, A. et al. (2018). Perspectives of phage therapy in non-bacterial infections. *Front. Microbiol.* 9, 3306.
46. Grönlund M.M., Lehtonen O.P., Eerola E., Kero P. (1999). Fecal microflora in healthy infants born by different methods of delivery: Permanent changes in intestinal flora after cesarean delivery. *J. Pediatr. Gastroenterol. Nutr.*, 28:19–25.
47. Han, D. H., Shin, M., An, S., Kim, J. S., Kim, Y., et al. (2019). Long-term Breastfeeding in the Prevention of Allergic Rhinitis: Allergic Rhinitis Cohort Study for Kids (ARCO-Kids Study). *Clinical and Experimental Otorhinolaryngology*, 12(3), 301-307.
48. Harama, D., Hamaguchi, S., Fukuie, T., and Ohya, Y. (2023). Feasibility and Safety of the Early Introduction of Allergenic Foods in Asian Infants with Eczema. *Nutrients*, 16(11), 1578.
49. Henrick B.M., Hutton A.A., Palumbo M.C., Casaburi G., Mitchell R.D., et al. (2018). Elevated fecal pH indicates a profound change in the breastfed infant gut microbiome due to reduction of Bifidobacterium over the past century. *mSphere*, 3
50. Hobbs, Z. and Abedon, S. T. Diversity of phage infection types and associated terminology: the problem with 'Lytic or lysogenic'. *FEMS Microbiol. Lett.*
51. Hourigan, S. K. (2016). Fecal microbiota transplantation in children: A brief review. *Pediatric Research*, 80(1), 2-6.
52. Korpela, K., Helve, O., Kolho, K., Saisto, T., Skogberg, K., et al. (2020). Maternal Fecal Microbiota Transplantation in Cesarean-Born Infants Rapidly Restores Normal Gut Microbial Development: A Proof-of-Concept Study. *Cell*, 183(2), 324-334.e5.
53. Huda M.N., Lewis Z., Kalanetra K.M., Rashid M., Ahmad S.M., et al. (2014). Stool microbiota and vaccine responses of infants. *Pediatrics*, 134: e362–e372.
54. Huycke, M. M., and Moore, D. R. (2002). "Bacterial endocarditis." **Journal of Clinical Microbiology**, 40(9), 3133-3137.
55. Jernberg, C., Lofmark, S., Edlund, C., Jansson, J.K. (2010). Long-term impacts of antibiotic exposure on the human gut microbiota. *Microbiology*, 156(11), 3216-3223.
56. Joynt, J., Bischoff, M., Turco, R., Konopka, A. and Nakatsu, C.H., (2006). Microbial community analysis of soils contaminated with lead, chromium and petroleum hydrocarbons. *Microbial Ecology*, 51, pp.209-219.
57. Kalach N, Bontems P, Raymond J. (2017). Helicobacter pylori infection in children. *Helicobacter*, 22 Suppl 1,
58. Kalliomäki, M., Salminen, S., Arvilommi, H., Kero, P., Koskinen, P., et al. (2001). Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. *The Lancet*, 357 (9262): 1076 - 1079.
59. Kaper, J. B., Nataro, J. P., and Mobley, H. L. T. (2004). Pathogenic Escherichia coli. *Nature Reviews Microbiology*, 2(2), 123-140.
60. Kapourchali, F. R., and M. Cresci, G. A. (2020). Early-Life Gut Microbiome—The Importance of Maternal and Infant Factors in Its Establishment. *Nutrition in Clinical Practice*, 35(3), 386-405.
61. Kato K, Mizuno S, Umesaki Y, Ishii Y, Sugitani M, et al. (2004). Randomized placebo-controlled trial assessing the effect of bifidobacteria-fermented milk on active ulcerative colitis. *Aliment Pharmacol Ther*, 20: 1133-1141.
62. Kau, A. L., Ahern, P. P., Griffin, N. W., Goodman, A. L., and Gordon, J. I. Human nutrition, the gut microbiome, and immune system: Envisioning the future. *Nature*, 474(7351), 327.

63. Kelley, S. T., et al. (2016). Dietary induced changes in the gut microbiota of infants. *Frontiers in Microbiology*, 7, 64.
64. Kijner, S., Kolodny, O., and Yassour, M. (2022). Human milk oligosaccharides and the infant gut microbiome from an evolutionary perspective. *Current Opinion in Microbiology*, 68, 102156.
65. Koonin, E. V. et al. Global organization and proposed megataxonomy of the virus world. *Microbiol. Mol. Biol. Rev.* 84, e00061–19 (2020).
66. Koren, O., Konnikova, L., Brodin, P., Mysorekar, I. U., and Collado, M. C. (2024). The maternal gut microbiome in pregnancy: implications for the developing immune system. *Nature Reviews Gastroenterology and Hepatology*, 21(1), 35–45.
67. Korpela, K. (2021). Impact of Delivery Mode on Infant Gut Microbiota. *Ann Nutr Metab* 77 (Suppl. 3): 11–19.
68. Koukou, Z., Papadopoulou, E., Panteris, E., Papadopoulou, S., Skordou, A., et al. (2023). The Effect of Breastfeeding on Food Allergies in Newborns and Infants. *Children*, 10(6), 1046.
69. Krol, K. M., and Grossmann, T. (2018). Psychological effects of breastfeeding on children and mothers. *Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz*, 61(8), 977–985.
70. Kruis W, Fric P, Pokrotnieks J, Lukás M, Fixa B, K, et al. (2004). Maintaining remission of ulcerative colitis with the probiotic *Escherichia coli* Nissle 1917 is as effective as with standard mesalazine. *Gut*, 53: 1617–1623
71. Kunz, C., et al. (2017). Human Milk Oligosaccharides: A Key to the Future of Infant Nutrition. *Food and Function*, 8(8), 2823–2835.
72. Langdon, A., Crook, N. and Dantas, G., (2016). The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. *Genome medicine*, 8, pp.1–1.
73. Laterza L., Rizzatti G., Gaetani E., Chiusolo P., Gasbarrini A. (2016). The gut microbiota and immune system relationship in human graft-versus-host disease. *Mediterr. J. Hematol. Infect. Dis.*, 8: e2016025.
74. Laursen, M. F., Bahl, M. I., Michaelsen, K. F., and Licht, T. R. (2017). First foods and gut microbes. *Front. Microbiol.* 8, 356.
75. Lax, S., Smith, D. P., Hampton-Marcell, J., Owens, S. M., Handley, K. M., et al. (2014). Longitudinal analysis of microbial interaction between humans and the indoor environment. *Science (New York, N.Y.)*, 345(6200), 1048.
76. Lebreton, F., Willems, R. J., and Gilmore, M. S. (2014). *Enterococcus* diversity, origins in nature, and gut colonization. *Enterococci: From Commensals to Leading Causes of Drug Resistant Infection*, 1.
77. Leclercq, R. (2001). *Enterococcus*: a multifaceted pathogen. *Clinical Microbiology and Infection*, 7(1), 1–5.
78. Levin, A. M., Sitarik, A. R., Havstad, S. L., Fujimura, K. E., Wegienka, G., et al. (2016). Joint effects of pregnancy, sociocultural, and environmental factors on early life gut microbiome structure and diversity. *Sci. Rep.* 6, 31775.
79. Li Y, Toothaker JM, Ben-Simon S, Ozeri L, Schweitzer R, McCourt BT, McCourt CC, Werner L, Snapper SB, Shouval DS, Khatib S, Koren O, Agnihorti S, Tseng G, Konnikova L. (2020). In utero human intestine harbors unique metabolome, including bacterial metabolites. *JCI Insight*;5(21): e138751.
80. Li, X., Stokholm, J., Brejnrod, A., Vestergaard, G. A., Russel, J., Trivedi, U., et al. (2021). The infant gut resistome associates with *E. Coli*, environmental exposures, gut microbiome maturity, and asthma-associated bacterial composition. *Cell Host and Microbe*, 29(6), 975–987.e4.
81. Ling X., Linglong P., Weixia D., Hong W. (2016). Protective effects of bifidobacterium on intestinal barrier function in LPS-induced enterocyte barrier injury of caco-2 monolayers and in a rat NEC model. *PLoS ONE*, 11: e0161635.
82. Lloyd-Price, J., Mahurkar, A., Rahnavard, G., Crabtree, J., Orvis, J., et al. (2016). Strains, functions and dynamics in the expanded Human Microbiome Project. *Nature* 550, 61–66 (2017).
83. Ly N.P., Litonjua A., Gold D.R., Celedón J.C. Gut microbiota, probiotics, and vitamin D: (2011). Interrelated exposures influencing allergy, asthma, and obesity? *J. Allergy Clin. Immunol.*, 127:1087–1094.
84. Ma, J., Li, Z., Zhang, W., Zhang, C., Zhang, Y., Mei, H., Zhuo, N., Wang, H., and Wu, D. (2022). Comparison of the Gut Microbiota in Healthy Infants with Different Delivery Modes and Feeding Types: A Cohort Study. *Frontiers in Microbiology*, 13.
85. Maggie C. (2022) An interpretative research study focusing on the nature and impact of conversations between health visitors and parents relating to infant weight, in the delivery of the Healthy Child Programme (DH, DSCF 2009). Doctoral thesis, Northumbria University
86. Mahurkar, A., Rahnavard, G., Crabtree, J., Orvis, J., Hall, A. B., et al. (2017). Strains, functions and dynamics in the expanded Human Microbiome Project. *Nature*, 550(7674), 61–66.
87. Makino H., Kushiro A., Ishikawa E., Muylert D., Kubota H., et al. (2011). Transmission of intestinal *Bifidobacterium longum* subsp. *longum* strains from mother to infant, determined by multilocus sequencing typing and amplified fragment length polymorphism. *Appl. Environ. Microbiol.*, 77:6788–6793.
88. Makino H., Martin R., Ishikawa E., Gawad A., Kubota H., et al. (2015) Multilocus sequence typing of bifidobacterial strains from infant's faeces and human milk: Are bifidobacteria being sustainably shared during breastfeeding? *Benef. Microbes*, 6: 563–572.
89. Mallick H, Rahnavard A, McIver LJ, Ma S, Zhang Y, et al. (2021) Multivariable association discovery in population-scale meta-omics studies. *PLoS Comput Biol* 17(11): e1009442.
90. Mallick, H., Ma, S., Franzosa, E. A., Vatanen, T., Morgan, X. C., et al. (2017). Experimental design and quantitative analysis of microbial community multiomics. *Genome Biology*, 18.
91. Martens, E. C., et al. (2011). How the gut microbiota affects the metabolism of dietary fiber. *Nature Reviews Microbiology*, 9(9), 619–628.
92. Martinelli, M., Banderali, G., Bobbio, M., Civardi, E., Chiara, A., et al. (2020). Probiotics' efficacy in paediatric diseases: Which is the evidence? A critical review on behalf of the Italian Society of Pediatrics. *Italian Journal of Pediatrics*, 46.
93. Martinez, I., Lattimer, J. M., Hubach, J. R., et al. (2016). Gut microbiome composition is linked to diet quality in healthy adults. *Nutrition Research*, 36(12), 1378–1384.

94. Martín-Rodríguez, A., Bustamante-Sánchez, Á., Martínez-Guardado, I., Navarro-Jiménez, E., Plata-SanJuan, E., et al. (2022). Infancy Dietary Patterns, Development, and Health: An Extensive Narrative Review. *Children*, 9(7).
95. Matharu, D., Ponsero, A. J., Dikareva, E., Korpela, K., Kolho, K., (2022). Bacteroides abundance drives birth mode dependent infant gut microbiota developmental trajectories. *Frontiers in Microbiology*, 13, 953475.
96. Matsuki T., Yahagi K., Mori H., Matsumoto H., Hara T., et al. (2016). A key genetic factor for fucosyllactose utilization affects infant gut microbiota development. *Nat. Commun*, 7:11939.
97. Matsumiya Y., Kato N., Watanabe K., Kato H. (2002). Molecular epidemiological study of vertical transmission of vaginal Lactobacillus species from mothers to newborn infants in Japanese, by arbitrarily primed polymerase chain reaction. *J. Infect. Chemother*, 8:43–49.
98. Mazmanian, S. K., et al. (2005). "An immunomodulatory molecule of symbiotic bacteria directs maturation of the host immune system." *Cell*, 122(1), 107–118.
99. McCann, A. et al. (2018). Viromes of one year old infants reveal the impact of birth mode on microbiome diversity. *PeerJ* 6, e4694.
100. McGuire, M. K., and McGuire, M. A. (2017). Got bacteria? The astounding, yet notso- surprising, microbiome of human milk. *Curr. Opin. Biotechnol.* 44, 63–68.
101. Milani C., Mancabelli L., Lugli G.A., Duranti S., Turrone F., et al. (2015). Exploring vertical transmission of bifidobacteria from mother to child. *Appl. Environ. Microbiol.*, 81:7078–7087.
102. Mitsuoka T. (2014). Development of Functional Foods. *Biosci. Microbiota Food Health*, 33:117–128.
103. Moore AM, Ahmadi S, Patel S, Gibson MK, Wang B, et al. (2015). Gut resistome development in healthy twin pairs in the first year of life. *Microbiome [Internet]*; 3:1–10.
104. Morais MB, Jacob CM. (2006). The role of probiotics and prebiotics in pediatric practice. *J Pediatr (Rio J)*; 82: S189-S197.
105. Morreale, C., Giaroni, C., Baj, A., Folgori, L., Barcellini, L., et al. (2023). Effects of Perinatal Antibiotic Exposure and Neonatal Gut Microbiota. *Antibiotics*, 12(2).
106. Morrison, D. J., and Preston, T. (2016). Formation of short chain fatty acids by the gut microbiota and their role in intestinal health. *Current Opinion in Gastroenterology*, 32(2), 128-133.
107. Moubareck, C. A. (2021). Human Milk Microbiota and Oligosaccharides: A Glimpse into Benefits, Diversity, and Correlations. *Nutrients*, 13(4).
108. Nataro, J. P., and Kaper, J. B. (1998). Diarrheagenic Escherichia coli. *Clinical Microbiology Reviews*, 11(1), 142-201.
109. Newburg DS, Walker WA. (2007). Protection of the neonate by the innate immune system of developing gut and of human milk. *Pediatr Res.*, 61(1):2–8.
110. Nowrouzian, F. L., Clermont, O., Edin, M., Östblom, A., Denamur, E., et al. (2019). Escherichia coli B2 Phylogenetic Subgroups in the Infant Gut Microbiota: Predominance of Uropathogenic Lineages in Swedish Infants and Enteropathogenic Lineages in Pakistani Infants. *Applied and Environmental Microbiology*, 85(24).
111. O'Brien, K. L., et al. (2015). Invasive disease due to Enterococcus spp. in infants: a population-based study. *Pediatric Infectious Disease Journal*, 34(4), 421-426.
112. O'Hara, A. M., and Shanahan, F. (2006). "The gut flora as a forgotten organ." *EMBO Reports*, 7(7), 688-693. doi: 10.1038/sj.embor.7400748
113. Onigbanjo MT, Feigelman S. The first year. In: Kliegman RM, St. Geme JW, Blum NJ, Shah SS, Tasker RC, Wilson KM, (2020). eds. Nelson Textbook of Pediatrics. 21st ed. Philadelphia, PA: Elsevier; chap 22 020):
114. O'Sullivan, A., et al. (2016). The infant gut microbiome: a key player in the development of allergies and asthma. *Allergy*, 71(8), 1130-1137.
115. Ott, S. J. et al. (2007). Efficacy of sterile fecal filtrate transfer for treating patients with Clostridioides difficile infection. *Gastroenterology* 152, 799–811.e7.
116. Palmer C., Bik E.M., DiGiulio D.B., Relman D.A., Brown P.O. (2007). Development of the Human Infant Intestinal Microbiota. *PLoS Biol.*, 5:1556–1573.
117. Pannaraj, P. S., Li, F., Cerini, C., Bender, J. M., Yang, S., Rollie, A., et al. (2017). Association between Breast Milk Bacterial Communities and Establishment and Development of the Infant GutMicrobiome. *JAMA. Pediatr.* 171, 647–654.
118. Pärnänen K, Karkman A, Hultman J, Lyra C, Bengtsson-palme J, et al. (2018). Maternal gut and breast milk microbiota affect infant gut antibiotic resistome and mobile genetic elements. *Nat Commun [Internet]*, 9:1–11.
119. Patel RM, Underwood MA. (2018). Probiotics and necrotizing enterocolitis. *Semin Pediatr Surg*; 27: 39-46
120. Penders, J., et al. (2013). The role of antibiotics in the development of the gut microbiota in infants. *Current Opinion in Gastroenterology*, 29(1), 1-6.
121. Penders, J., Thijs, C., Vink, C., et al. (2006). Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics*, 118(2), 511-521.
122. Petraroli, M., Castellone, E., Patianna, V., and Esposito, S. (2021). Gut Microbiota and Obesity in Adults and Children: The State of the Art. *Frontiers in Pediatrics*, 9.
123. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, et al. (2010). A human gut microbial gene catalogue established by metagenomic sequencing. *Nature*, 464(7285), 59-65.
124. Rahman, M. M., Islam, F., Harun, M., Mamun, A. A., Rahaman, M. S., Islam, M. M., Meem, A. F., Sutradhar, P. R., Mitra, S., Mimi, A. A., Emran, T. B., Idroes, R., Tallei, T. E., et al. (2022). The Gut Microbiota (Microbiome) in cardiovascular disease and Its Therapeutic Regulation. *Frontiers in Cellular and Infection Microbiology*, 12, 903570.
125. Rasmussen, T. S. et al. (2020). Faecal virome transplantation decreases symptoms of type 2 diabetes and obesity in a murine model. *Gut* 69, 2122–2130.
126. Rautava, S., et al. (2012). "The influence of the environment on the development of the gut microbiome in infants." *Nature Reviews Gastroenterology and Hepatology*, 9(5), 277-284.
127. Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Donato Miggiano, G. A., et al. (2018). What is the Healthy Gut

- Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. *Microorganisms*, 7(1).
128. Romaní-Pérez, M., Bullich-Vilarrubias, C., López-Almela, I., Liébana-García, R., Olivares, M., and Sanz, Y. (2021). The Microbiota and the Gut–Brain Axis in Controlling Food Intake and Energy Homeostasis. *International Journal of Molecular Sciences*, 22(11).
 129. Rook, G. A. (2010). 99th Dahlem Conference on Infection, Inflammation and Chronic Inflammatory Disorders: Darwinian medicine and the ‘hygiene’ or ‘old friends’ hypothesis. *Clinical and Experimental Immunology*, 160(1), 70–79.
 130. Rook, G. A. (2013). Regulation of the immune system by biodiversity from the natural environment: An ecosystem service perspective. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 368(1624), 20120129.
 131. Round, J. L., and Mazmanian, S. K. (2009). The gut microbiota shapes intestinal immune responses during health and disease. *Nature Reviews Immunology*, 9(5),
 132. Rutayisire, E., Huang, K., Liu, Y., and Tao, F. (2016). The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review. *BMC Gastroenterol* 16, 86.
 133. Saeed, N. K., Al-Beltagi, M., Bediwy, A. S., El-Sawaf, Y., and Toema, O. (2022). Gut microbiota in various childhood disorders: Implication and indications. *World Journal of Gastroenterology*, 28(18), 1875–1901.
 134. Salminen S, Benno Y, de Vos W. (2006). Intestinal colonisation, microbiota and future probiotics? *Asia Pac J Clin Nutr*, 15: 558–562.
 135. Salzman, N. H. (2014). The role of the microbiome in immune cell development. *Annals of Allergy, Asthma and Immunology*, 113(6), 593–598.
 136. Samarra A, Esteban-Torres M, Cabrera-Rubio R, Bernabeu M, Arbolea S, et al. (2023). Maternal-infant antibiotic resistance genes transference: what do we know? *Gut Microbes*;15(1):2194797.
 137. Sarkar, A., Yoo, J. Y., Ozorio Dutra, S. V., Morgan, K. H., and Groer, M. (2021). The Association between Early-Life Gut Microbiota and Long-Term Health and Diseases. *Journal of Clinical Medicine*, 10(3).
 138. Sartor, R. B. (2008). Microbial influences in inflammatory bowel diseases. *Gastroenterology*.
 139. Savino, F., et al. (2010). Lactobacillus reuteri and colic in infants: a randomized trial. *Pediatrics*.
 140. Sawicki, C. M., Livingston, K. A., Obin, M., Roberts, S. B., Chung, M., et al. (2017). Dietary Fiber and the Human Gut Microbiota: Application of Evidence Mapping Methodology. *Nutrients*, 9(2).
 141. Schack-Nielsen, L., Larnkjær, A., Michaelsen, K.F. (2005). Long Term Effects of Breastfeeding on the Infant and Mother. In: Koletzko, B., Dodds, P., Akerblom, H., Ashwell, M. (eds) *Early Nutrition and its Later Consequences: New Opportunities. Advances in Experimental Medicine and Biology*, vol 569. Springer, Dordrecht.
 142. Segers, M.E., Lebeer, S. (2014). Towards a better understanding of Lactobacillus rhamnosus GG - host interactions. *Microb Cell Fact* 13 (Suppl 1), S7.
 143. Sela, D. A., et al. (2011). The Role of Human Milk Oligosaccharides in the Development of the Infant Gut Microbiota. *Nature Reviews Gastroenterology and Hepatology*, 8(9), 619–628.
 144. Selma-Royo, M., Calatayud Arroyo, M., García-Mantrana, I. et al. (2020). Perinatal environment shapes microbiota colonization and infant growth: impact on host response and intestinal function. *Microbiome* 8, 167.
 145. Shah, S. A., Deng, L., Thorsen, J., Pedersen, A. G., Dion, M. B., L., et al. (2023). Expanding known viral diversity in the healthy infant gut. *Nature Microbiology*, 8(5), 986–998.
 146. Shan, Y., Lee, M., and Chang, E. B. (2021). The Gut Microbiome and Inflammatory Bowel Diseases. *Annual Review of Medicine*, 73, 455.
 147. Shao, Y., Forster, S. C., Tsaliki, E., Vervier, K., Strang, A., et al. (2019). Stunted microbiota and opportunistic pathogen colonization in caesareansection birth. *Nature* 574, 117–121.
 148. Sharma N, Bhatia S, Chunduri V, Kaur S, Sharma S, et al. (2020). Pathogenesis of Celiac Disease and Other Gluten Related Disorders in Wheat and Strategies for Mitigating Them. *Front Nutr*, 7: 6
 149. Shin, N. R., et al. (2011). "The role of Bacteroides in the protection of the gut from pathogenic bacteria." *Microbial Ecology*, 61(1), 1–12.
 150. Shkoporov, A. N. and Hill, C. (2019). Bacteriophages of the human gut: the ‘known unknown’ of the microbiome. *Cell Host Microbe* 25, 195–209.
 151. Slavin, J. (2013). Fiber and Prebiotics: Mechanisms and Health Benefits. *Nutrients*, 5(4), 1417–1435.
 152. Sorek, R., Kunin, V. and Hugenholtz, P. (2008). CRISPR a widespread system that provides acquired resistance against phages in bacteria and archaea. *Nat. Rev. Microbiol.* 6, 181–186 (2008).
 153. Squillario, M., Bonaretti, C., La Valle, A., Di Marco, E., Piccolo, G., et al. (2023). Gut-microbiota in children and adolescents with obesity: Inferred functional analysis and machine-learning algorithms to classify microorganisms. *Scientific Reports*, 13(1), 1–16.
 154. Stewart, C. J., Ajami, N. J., O'Brien, J. L., Hutchinson, D. S., Smith, D. P., et al. (2018). Temporal development of the gut microbiome in early childhood from the TEDDY study. *Nature*. 562, 583–588.
 155. Tannock, G. W. (2002). Bifidobacterium: a key genus in the gut microbiota of infants. *Journal of Clinical Microbiology*, 40(9), 3477–3480.
 156. Taylor R, Keane D, Borrego P, Arcaro K. (2023). Effect of Maternal Diet on Maternal Milk and Breastfed Infant Gut Microbiomes: A Scoping Review. *Nutrients*;15(6):1420.
 157. Thäner, R., Keen, E. C., Dantas, G., Warner, B. B., and Tarr, P. I. (2021). Necrotizing Enterocolitis and the Microbiome: Current Status and Future Directions. *The Journal of Infectious Diseases*, 223(Suppl 3), S257.
 158. Thum, C., et al. (2018). The Role of Human Milk Oligosaccharides in the Development of the Gut Microbiome and Immune System. *Frontiers in Pediatrics*, 6, 229.
 159. Trogen, B., Jacobs, S., and Nowak-Węgrzyn, A. (2022). Early Introduction of Allergenic Foods and the Prevention of Food Allergy. *Nutrients*, 14(13).

160. Underwood M.A., German J.B., Lebrilla C.B., Mills D.A. (2015). *Bifidobacterium longum* subspecies *infantis*: Champion colonizer of the infant gut. *Pediatr. Res.*,77:229–235.
161. Underwood, M. A., et al. (2013). Human milk oligosaccharides promote the growth of *Bacteroides* in a neonatal rat model. *Gut Microbes*, 4(3), 129-136.
162. Ursell LK, Metcalf JL, Parfrey LW, Knight R. Defining the human microbiome. *Nutr Rev* 2012; 70 Suppl 1: S38-S44.
163. Vallès Y., Artacho A., Pascual-García A., Ferrús M.L., Gosalbes M.J., et al. (2014). Microbial Succession in the Gut: Directional Trends of Taxonomic and Functional Change in a Birth Cohort of Spanish Infants. *PLoS Genet*, 10: e1004406.
164. Voreades N., Kozil A., Weir T.L. (2014). Diet and the development of the human intestinal microbiome. *Front. Microbiol*;5
165. Wampach L., Heintz-Buschart A., Hogan A., Muller E.E.L., Narayanasamy S., (2017). et al. Colonization and succession within the human gut microbiome by archaea, bacteria, and microeukaryotes during the first year of life. *Front. Microbiol.*; 8:738.
166. Weinstein, M. P., et al. (1997). The significance of *Enterococcus* in human disease. *Clinical Infectious Diseases*, 24(6), 1127-1139.
167. WHO, 2009. Infant and Young Child Feeding: Model Chapter for Textbooks for Medical Students and Allied Health Professionals. Geneva: World Health Organization; 2009. SESSION 3, *Complementary feeding*.
168. (2018). WHO (2018)? Critically Important Antimicrobials for Human Medicine 6th Revision,
169. Wibowo, M. C., Yang, Z., Borry, M., Hübner, A., Huang, K. D., (2021). Reconstruction of ancient microbial genomes from the human gut. *Nature*, 594(7862), 234-239.
170. Wiertsema, S. P., Garssen, J., and J. Knippels, L. M. (2021). The Interplay between the Gut Microbiome and the Immune System in the Context of Infectious Diseases throughout Life and the Role of Nutrition in Optimizing Treatment Strategies. *Nutrients*, 13(3).
171. Witkin, S. S., and Linhares, I. M. (2017). Why do lactobacilli dominate the human vaginal microbiota. *Br. J. Obstetr. Gynaecol.* 124, 606–611.
172. Wu, J., and Wu, E. (2011). The role of gut microbiota in immune homeostasis and autoimmunity. *Gut Microbes*, 3(1), 4-14.
173. Xiao, H., and Kang, S. (2020). The Role of the Gut Microbiome in Energy Balance With a Focus on the Gut-Adipose Tissue Axis. *Frontiers in Genetics*, 11, 499030.
174. Xiao, W., Su, J., Gao, X., Yang, H., Weng, R., et al. (2022). The microbiota-gut-brain axis participates in chronic cerebral hypoperfusion by disrupting the metabolism of short-chain fatty acids. *Microbiome* 10, 62.
175. Yang, I., Corwin, E. J., Brennan, P. A., Jordan, S., Murphy, J. R. (2016). The Infant Microbiome: Implications for Infant Health and Neurocognitive Development. *Nursing Research*, 65(1), 76.
176. Yassour M, Jason E, Hogstrom LJ, Arthur TD, Tripathi S, et al. (2018). Strain-level analysis of mother-to-child bacterial transmission during the first few months of life short article strain-level analysis of mother-to-child bacterial transmission during the first few months of life. *Cell Host Microbe [Internet]*; 24:146–154.
177. Yatsunencko T., Rey F.E., Manary M.J., Trehan I., Dominguez-Bello M.G., et al. (2012). Human gut microbiome viewed across age and geography. *Nature*.;486:222–227.
178. York, A. (2018). Delivery of the gut microbiome. *Nat. Rev. Microbiol.* 16, 520–521.
179. Yu Z, Chen C, Kling DE, et al. (2013). The principal fucosylated oligosaccharides of human milk exhibit prebiotic properties on cultured infant microbiota. *Glycobiol.*;23(2):169–77.
180. Yutin, N. et al. (2021). Analysis of metagenome-assembled viral genomes from the human gut reveals diverse putative CrAss-like phages with unique genomic features. *Nat. Commun.* 12, 1044.
181. Yutin, N. et al. (2018). Discovery of an expansive bacteriophage family that includes the most abundant viruses from the human gut. *Nat. Microbiol.* 3, 38–46.
182. Zhang, X., Mushajiang, S., Luo, B., Tian, F., Ni, Y., et al. (2020). The Composition and Concordance of *Lactobacillus* Populations of Infant Gut and the Corresponding Breast-Milk and Maternal Gut. *Frontiers in Microbiology*, 11.
183. Zhao, X., Hu, M., Zhou, H., Yang, Y., Shen, S., et al. (2023). The role of gut microbiome in the complex relationship between respiratory tract infection and asthma. *Frontiers in Microbiology*, 14, 1219942.
184. Zheng, D., Liwinski, T., and Elinav, E. (2020). Interaction between microbiota and immunity in health and disease. *Cell Research*, 30(6), 492-506.
185. Zhuang L, Chen H, Zhang S, Zhuang J, Li Q, et al. (2019). Intestinal Microbiota in Early Life and Its Implications on Childhood Health. *Genomics Proteomics Bioinformatics*; 17: 13-25
186. Zimmermann P, Curtis N. (2020). Effect of intrapartum antibiotics on the intestinal microbiota of infants: a systematic review. *Archives of Disease in Childhood - Fetal and Neonatal Edition*; 105:201-208.

Ready to submit your research? Choose ClinicSearch and benefit from:

- fast, convenient online submission
- rigorous peer review by experienced research in your field
- rapid publication on acceptance
- authors retain copyrights
- unique DOI for all articles
- immediate, unrestricted online access

At ClinicSearch, research is always in progress.

Learn more <http://clinicsearchonline.org/journals/clinical-trials-and-clinical-research>



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.