



INFANTS GUT MICROBIOME: CURRENT KNOWLEDGE, CHALLENGES AND FUTURE DIRECTIONS

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ABSTRACT

The acquisition and development of the infant microbiome plays a key role in healthy host-microbiome symbiosis. The neonatal and infancy periods are most important stages in the establishment of the intestinal microbial community. There are many maternal factors that play a major role in acquiring the balanced gut microbiota during birth. Moreover, continuous acquisition of nascent microbiome is a relatively dynamic process influenced by breastfeeding practices, weaning to solid food, antibiotics and other practices. Therefore, development of the gut microbiota in infancy occurs during a 'critical window,' and a disturbance in this process may cause many health problems. The current interactions and associations of the early-life exposures on the development and colonization of the gut microbiota in infants and disease conditions requires further researches to determine the causes.

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INTRODUCTION

The first microbiota that colonizes a human gut will pave the way for our future health. The newborn was exposed to first microflora via the mother's view and genitourinary tract immediately after birth. Infants gut microbiomes can shape their metabolic and immune-related health and their lifelong risk for obesity, asthma, allergies, and autoimmune diseases. The gut flora can influence the infants health in three major ways, such as by directly defending against pathogens, fortifying host defence by its role in developing and maintaining the intestinal epithelium and inducing antibody production, and metabolizing indigestible compounds in food. Colonization of the infant gut microorganisms in the first year of life is more crucial for development of a balanced immune response. Early alterations in the gastrointestinal microbiota of neonates have been linked with subsequent development of asthma and atopy, obesity and cognitive development in older children.

Impact of Breast Milk on Infant's Gut Microbiome

However there are various factors such as intrapartum antibiotic prophylaxis, mode of delivery, timing of delivery (premature vs term), hospitalization, and use of probiotics in both the mother and neonate have shown to influence infant gut microbiome. Moreover, breastfeeding and formula feeding also has effects on the neonatal microbiome outcomes. Baby begins to acquire his gut bacteria *in utero* from the mother's digestive system. These bacteria are affected by the maternal

diet and lifestyle and have been linked to have impact on infant's health.

Recently, Koleva *et al* (2015) stated that women with pre-existing conditions like atopy and overweight during pregnancy have altered breast milk composition, which in turn, influences the gut microbial community of the infants. Breast milk, in turn may interact with the infant's host system to modify the effectiveness of administered pre- and probiotics. Pannaraj *et al* (2017) conducted a longitudinal study, in which the infant gut microbial communities were more closely related to an infant's mother's milk and skin compared with a random mother. Infants in first 30 days of life (breast fed more than 75% of daily intake), received 27.7% of the bacteria from breast milk and 10.3% from areolar skin. The proportion of daily breast milk intake in a dose-dependent manner changes the Bacterial diversity and composition even after the introduction of solid foods

In breast-milk, Streptococcus was the most frequently isolated genus and Lactobacillus and Bifidobacterium were also obtained, which might contribute to the initial establishment of the microbiota in the newborn. In 1-day-old newborns, *Enterococcus* and *Streptococcus* were the microorganisms most frequently isolated, from 10 days of age until 3 months *bifidobacteria* become the predominant group. (Solis *et al.*, 2010). After weaning, Bifidus flora is outcompeted by adult-type microorganisms, represented mainly by bacteria in the genera *Bacteroides*, *Prevotella*, *Ruminococcus*, *Clostridium*, and *Veillonella*, which colonize an infant's intestines.

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Eventually, by about three years of age, a typical adult-like gut microbiota is established (Valles et al., 2014).

External Factors

The use of antibiotic in early life has profound effects on the development of the gut microbiota. Yassour *et al* (2016) reported that antibiotic-treated children had less stable and less diverse bacterial communities. Antibiotic resistance genes within the guts of these children peaked after antibiotic treatment but rapidly reduced to baseline. Moreover the delivery mode (vaginal versus cesarean) also had strong long-term effects on microbial diversity. Interestingly, the gut microbiota of a newborn will closely resemble the microbiota that it encountered during birth. In *vaginally* delivery infants, gut microbiotas resemble their mothers' vaginal microbiotas, dominated by *Lactobacillus*, *Prevotella*, or *Sneathia*, whereas the microbiotas of infants born by caesarean section are most similar to skin microbiota, which is dominated by *Staphylococcus*, *Corynebacterium*, and *Propionibacterium* (Dominguez-Bello *et al.*, 2010). In addition, the same studies have shown that infants born by elective caesarean section had particularly low bacterial diversity.

The length of the gestational period may also play an important role in initial infant gut microbial colonization. Colonization in preterm infants has been shown to take place slowly, with low diversity, than full-term infants. Healthy full-term infants are usually colonized by beneficial microbes, such as *Bifidobacterium* and *Lactobacillus*, which are absent or detected in low levels in preterm infants (Valles *et al.*, 2014).

Impact of Gut Microbiome on Infants Development

The healthy gut microbiome has beneficial health impact on infants. Recently, Carlson *et al* (2017) shown that microbial composition of the human gut at 1 year of age predicts cognitive performance at 2 years of age, particularly in the area of communicative behavior. Results may have implications for developmental disorders characterized by cognitive or language delay. Hence, further research, is needed to guide the development of the gut microbiome through targeted interventions, thereby supporting cognitive development.

Methods to Improve the Infants Gut Microbiome

Swabbing of babies with maternal vaginal fluids (pink) can partially restore the ancestral microbiota. In a recent study, infants receiving prebiotic supplemented formula exhibited specific *Bifidobacterium* microbiota composition. This would suggest that early gut *Bifidobacterium* microbiota can be modified by special diets up to the age of 6 months.

Conclusion and Future Challenges

Stable microbial communities in infancy stage are affected by various environmental factors such as the mode of delivery and methods of milk feeding, antibiotic treatment. The effect of long early-life factors on gut microbiota in the childhood period remains limited. However few study confirms the continued development and maturation of the gut microbiota during the initial years of life.

The recent researches suggest that, inherited microbiome can influence the offspring health to a larger extent and it's important to understand the metabolic phenotypes and it's attributed intestinal bacterial communities. Promoting the colonization of the beneficial bacteria in infants is key for the better gut health. Future studies should focus on ways of promoting and or maintaining colonization by the beneficial bacteria in infants and prebiotics and probiotics supplementation on infant gut health. The addition of Pro and prebiotics to the infant formula is safe, however, the evidence for health benefits remains limited and future research has to focus on specificity, safety, dosage, and combinations

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