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The Role of Diet in Shaping Gut Microbiota Across the Lifespan

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Abstract

The gut microbiome is essential for human health throughout life, with dietary choices affecting its composition and function at various stages. Dietary influences shape microbial diversity, metabolism, immune response, and cognitive function from early development to adulthood. This article examines how dietary exposures from fetal development to adulthood affect the gut microbiome and, consequently, impact health, disease susceptibility, and overall well-being. By investigating the connection between diet and microbial diversity, this communication seeks to emphasize potential dietary interventions for personalized health approaches, disease prevention and improvement of life quality throughout the lifespan.

Keywords: Gut microbiome; Healthspan; Diets; Personalized health; Longevity

Introduction

The reciprocal relationship between nutrition and gut bacteria has led researchers to emphasize the microbiome's significant role in overall health [1-3]. It is essential to comprehend how our dietary habits impact the gut microbiome at various stages of life, as this affects metabolism, immune response, and cognitive function, all of which play a role in healthspan [4-6]. While detailing how the microbiome evolves has been beneficial, there is considerably less knowledge regarding how dietary influences from fetal development through early childhood, adolescence, and into adulthood shape microbial composition and functionality [7-9]. Gaining insight into this ongoing interaction will ultimately be necessary to assess their impact on long-term health, vulnerability to disease, and lifespan.

Fetal beginnings: Shaping the gut microbiome for life

The formation of the gut microbiome may start before birth, influenced by the mother's diet, lifestyle, and microbial exposures that shape the microbial community in the fetus [10,11]. While there is ongoing debate about its significance, the presence of bacterial DNA in the fetal gut prior to birth indicates the potential for prenatal transmission of microbes [12,13]. Throughout pregnancy, changes in the maternal gut microbiota can affect the placenta, with dietary factors playing a role in its microbial makeup and the metabolites it produces [14,15]. Microbial metabolites, including short-chain fatty acids (SCFAs), can pass through the placenta and affect fetal growth, immune system development and the establishment of the gut microbiome [16-18].

The maternal microbiota undergoes changes in distinct phases throughout pregnancy, each with different effects on fetal development. In the first trimester, the gut microbiome remains relatively stable, resembling that of a woman who is not pregnant [14]. During the second trimester, microbial diversity increases, with beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* playing a role in supporting metabolism and immune response [19,20]. By the third trimester, there is a notable transition towards a pro-

inflammatory environment, marked by a rise in Proteobacteria and a reduction in overall microbial diversity [21,22]. This transition during pregnancy is thought to prepare the maternal immune system for childbirth, possibly affecting the microbial and metabolic makeup of the amniotic fluid, which may influence how the fetal gut becomes colonized [23,24]. Changes in the microbiome can alter the production of metabolites that control immune responses and metabolic functions, thus impacting fetal development and shaping the microbial communities after birth [25,26].

Additionally, maternal nutrition plays a crucial role in altering microbial communities and is vital for the health of both the mother and the child. A diet rich in fiber, prebiotics, and polyphenols promotes the growth of beneficial bacteria and enhances the production of SCFAs, resulting in a more diverse and resilient microbiome for the offspring [27-29]. An unhealthy maternal gut, caused by poor nutrition, stress, gestational diabetes, or antibiotic use, increases the likelihood of health issues for the child in the future [30,31]. It highlights a critical period during pregnancy for implementing dietary and microbiome adjustments to enhance health and ensure the well-being of both the mother and child, ultimately leading to improved resistance to diseases in the long term [32,33].

Early childhood: Laying the groundwork for microbial diversity

The early years of life are vital for the development and maturation of the gut microbiome, and early microbial exposures have a lasting impact on health [34,35]. Newborns primarily obtain their gut microbiota from their mothers and the method of delivery significantly influences the microbial composition [36,37]. During vaginal birth, the mother exposes the infant to Lactobacilli, Bacteroides, and other microorganisms from her vagina and feces [38,39]. In contrast, cesarean-born infants experience a delay in the colonization of skin bacteria, which affects their immune responses [40,41]. Breastfeeding supports initial microbial colonization by supplying beneficial bacteria, human milk oligosaccharides (HMOs), and substances that encourage the growth of bifidobacteria and other microbes, thus enhancing gut and immune health [42,43]. Infants who are fed formula tend to have lower levels of Bifidobacterium and a less varied microbiome, which increases their susceptibility to inflammatory and metabolic diseases [44,45]. The introduction of solid foods in the first year encourages the growth and diversity of the gut microbiota [46,47]. In particular, incorporating fiber and complex carbohydrates promotes the growth of Bifidobacteria and Firmicutes [48,49]. Foods high in fiber enhances metabolic health and diversification of the microbiome by strengthening immune function and safeguarding the gut barrier [50,51].

The dietary habits formed during infancy have lasting effects on the composition and functionality of the microbiome [52,53]. Introducing fiber-rich foods such as fruits, vegetables, and whole grains within the first year helps foster a healthy and stable microbiome, which in turn supports long-term metabolic and immune health [54,55]. On the other hand, factors like an unhealthy

diet, the use of antibiotics, or high levels of stress can interfere with microbiome development and heighten the likelihood of immune-related disorders such as asthma, allergies, and obesity [56,57]. These insights highlight the significance of considering both food and microbial exposure to establish a healthy gut microbiome in children and reduce the risk of chronic diseases in the future.

Teen years: The microbiome in flux under dietary influence

Adolescence is a critical time marked by physical and metabolic changes, along with major shifts in the gut microbiome [58,59]. Throughout this period, the microbiome remains dynamic and has not yet reached its established adult form. There is a reduction in the number of aerobes and facultative anaerobes, while the levels of obligate anaerobes rise [60,61]. These changes in microbial composition are shaped by a mix of internal factors, including hormonal and metabolic changes, as well as environmental influences, especially dietary patterns. Crucially, evaluating microbial biodiversity via α - and β -diversity is essential for forecasting the stability and resilience of the microbiome across various life stages [62-64]. α -diversity assesses both the quantity and distribution of species within the microbiome, reflecting its level of maturity and potential [65,66]. β -diversity looks at how the composition of the microbiome changes over time due to environmental factors [67,68]. Adolescence is especially important for microbiome development, causing significant changes in these diversity measures [69,70].

Diet plays a crucial role in determining the variety of microorganisms present during adolescence. Consuming a diet rich in fiber and plant-based foods enhances the levels of Bifidobacterium and Akkermansia, which contribute positively to gut health, metabolism, and immune function [71,72]. Conversely, a diet typical of Western lifestyles, laden with processed items, fats, and sugars, diminishes microbial diversity and promotes an increase in pro-inflammatory bacteria such as Proteobacteria [73,74]. This dietary pattern results in a disruption of gut balance, elevating the chances of developing metabolic syndrome, obesity, and immune-related problems. It is important to highlight that during adolescence, the microbiome exhibits the greatest adaptability, meaning dietary modifications can yield long-term impacts. Indeed, research indicates that teenagers adhering to a Mediterranean diet, which is abundant in fiber from fruits, vegetables, and whole grains, display distinct microbial characteristics compared to those following a Western diet [75,76]. The Mediterranean diet enhances the growth of bacteria that digest polysaccharides and generate SCFAs, thereby promoting gut health and metabolic function [77,78]. On the other hand, the Western diet fosters bacteria that metabolize protein and carbohydrates while diminishing beneficial microbes, which can lead to inflammatory conditions [79]. A more recent study suggests that besides diet, the gut-brain axis may play a role in adolescent health [80,81]. There is evidence of a relationship between the neuroendocrine system and the microbiome. Probiotic supplements, particularly those containing Lactobacillus, are shown to reduce cortisol levels linked to stress

and lower anxiety [82,83]. Research indicates a bidirectional relationship between the gut microbiome and the brain, implying that treatments centered on the microbiome may enhance mental health in adolescents [84,85]. Modifying diet by incorporating more fiber, reducing ultra-processed foods, and introducing probiotics could positively influence the teenage microbiome and lower the likelihood of chronic illnesses in the future [86]. It is essential to enhance teenagers' nutrition to cultivate a robust and varied gut microbiome that promotes lasting metabolic, immune and cognitive well-being.

Adulthood: Nurturing the microbiome to counter age-related shifts

Diet, lifestyle and environmental factors influence the gut microbiome, which is established in adulthood yet remains flexible. As people get older, their microbiome composition deteriorates, shifting from a low-diversity profile to one that often contains potentially harmful microbes [87,88]. This alteration is thought to be associated with age-related health issues, including metabolic disorders, cardiovascular diseases, immune system problems, and neurodegenerative conditions. Interestingly, some research indicates that microbiome diversity may be vital for healthy aging in older adults [89,90]. Investigations into nonagenarians and centenarians have uncovered a consistent trend: they typically possess a more varied gut microbiota than their younger counterparts [91]. Certain bacterial groups that generate SCFAs, such as *Clostridium* cluster XIVa, are more prevalent in those who live longer [92]. SCFAs contribute to reducing inflammation, bolstering gut health, and enhancing metabolism, which may all assist in promoting longevity [93,94].

Additionally, an adult's nutrition plays a crucial role in shaping the gut microbiome's composition, stability, and functionality. A diet abundant in fiber, prebiotics, polyphenols and fermented foods can nourish and support the diverse array of microorganisms that make up the gut microbiome [95,96]. Fiber, especially non-digestible polysaccharides found in fruits, vegetables, and whole grains, serves as a vital prebiotic that promotes the growth of beneficial microbes such as *Bifidobacterium* and *Lactobacillus* [97]. These microorganisms ferment fiber into SCFAs like acetate, propionate, and butyrate, which are essential for maintaining the integrity of the gut barrier, managing inflammation, and influencing the metabolism of the host [98,99].

Together, polyphenols found in foods such as berries, tea, coffee, and dark chocolate contribute to a healthy gut microbiome. While they are not efficiently absorbed in the small intestine, gut bacteria metabolize them into compounds that have antioxidant, anti-inflammatory, and neuroprotective properties. Foods that undergo fermentation, like yogurt, kefir, kimchi, and sauerkraut, contain live probiotic strains that promote microbial diversity and strengthen the gut mucosal barrier [100,101]. Dietary changes are considered one of the most effective methods for restoring microbial balance, boosting gut resilience, and reducing the risk of illness in adulthood given the microbiome's vital role in metabolic, immune and neurological health.

Future Directions

Significant advancements have been achieved in understanding the intricate relationship between diet and gut microbiota at different stages of life, aiming to enhance dietary interventions throughout one's lifetime. Nevertheless, there is still much to uncover regarding the long-term, transgenerational impacts of dietary behaviors on microbiome composition and the health of the host [102,103]. To fill these knowledge gaps, it will be essential for researchers to carry out extensive studies investigating the influence of nutrition on the microbiota from prenatal development through adulthood. Utilizing multi-omics techniques, such as metagenomics, metabolomics, and transcriptomics, can yield important insights into the reciprocal relationships among nutrition, the microbiota, and metabolic pathways that govern host physiology.

Initial dietary experiences significantly influence the metabolic structure and induce epigenetic memories in humans [104,105]. Suboptimal dietary decisions during this developmental stage can lead to permanent epigenetic changes, potentially heightening the risk of chronic illnesses in later years [106,103]. These ramifications may continue to affect individuals even if they make healthier dietary choices in adulthood. This indicates that nutritional interventions in early life could foster the development of healthy, varied microbiomes in children, thereby decreasing their likelihood of developing metabolic disorders and providing enduring health advantages that should be prioritized in public health initiatives. Future studies should aim to explore how dietary selections might counteract deleterious epigenetic modifications and encourage health benefits related to the microbiome throughout an individual's life. Early dietary interventions are likely to yield the most substantial and enduring effects, as changes in epigenetics due to diet may last into adult life. Achieving a thorough understanding of the interactions among food, microbiome composition, and host physiology will set the stage for tailored, evidence-based dietary guidelines that not only prolong life but also enhance healthspan and improve overall quality of life. Considering the new evidence regarding the influence of the microbiome on DNA damage and telomere length, maintaining a healthy gut microbiome throughout all life stages may enhance healthspan, reduce age-related diseases, and increase longevity [107,108].

Looking ahead, gaining a deeper understanding of maternal and early-life factors that affect chronic health via the gut microbiome will be crucial. Since diet, lifestyle, and environmental conditions significantly influence the gut microbiome, particular focus should be given to microbial diversity. Profiles with low microbial diversity often show a predominance of potentially harmful bacteria, especially gram-negative species that generate lipopolysaccharides (LPS)-pro-inflammatory endotoxins linked to metabolic disorders, cardiovascular disease, immune dysfunction, and neurodegeneration [109-111]. For instance, LPS is involved in the pathophysiology of AD. The extended exposure to bacterial LPS, a component found in the outer cell wall of Gram-negative bacteria, replicates numerous degenerative and inflammatory traits observed in the brains of patients with AD. Diets that are high in fat and low in fiber can worsen microbial imbalance. Assessing LPS

levels in maternal and fetal plasma could serve as an early indicator of dysbiosis, and future dietary interventions during conception and early life aimed at decreasing the prevalence of gram-negative bacteria represent a practical preventive approach, fostering healthier outcomes from pregnancy through fetal development and into adulthood.

Finally, emerging nutritional strategies hold promise for enhancing health and preventing disease throughout different stages of life, and a significant advancement would be to incorporate insights from microbiome research into public health nutrition policies, clinical practices, and precision medicine. Applying microbiome research to practical scenarios will contribute to creating personalized dietary guidelines that support microbiome stability and metabolic well-being, furthering the role of precision nutrition as a vital aspect of preventive healthcare.

Conclusion

The composition of the diet greatly influences the gut microbiome from the stages of fetal growth through adulthood, impacting metabolism, immune function, and overall well-being. Gaining insight into this intricate relationship provides crucial information for preventing diseases and promoting health. Tailored, research-backed nutritional strategies based on microbiome studies should enhance healthspan and alleviate the impact of chronic illnesses. Future investigations should emphasize prolonged studies and applicable outcomes to create focused approaches for improving gut microbiome health throughout different life phases. Applying this understanding in health practices and public policies could transform preventative healthcare, improving both life quality and longevity.

Conflict of Interest

The authors do not have anything to declare.

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Author Contribution

Conceptualization and supervision: S. K. C.; Formal analysis: S. K. C.; Original draft preparation: S. K. C.; Writing-review and editing: S. K. C. and D. C.; Project administration: S. K. C.; Funding acquisition: S. K. C.

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