



REVIEW ARTICLE

Microbiota and Aging. A Review and Commentary

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Although there is a consensus that the dominant species that make up the adult microbiota remains unchanged in elderly people, it has been reported that there are significant alterations in the proportion and composition of the different taxa, leading to reduced microbiota diversity, as well as an increase of enteropathogens that may lead to chronic inflammation. The ageing of mucosal immune and motor systems also contributes to these changes. As the individual ages, there is a loss in the number of Peyer's patches, an altered local capacity of T and B cell functions as well as chronic macrophage activation. Also, environment, diet, place of residence and biogeography are regulatory factors of the microbiota. Communication in the gut-brain-axis is regulated by many intermediaries including diverse metabolites of the microbiota. Microbial changes have been observed in several geriatric diseases, like Parkinson's and Alzheimer's. In addition, evidence has shown that individuals with high frailty scores had a significant reduction on *lactobacilli* species when compared to non-frail individuals. Oral microbiota may be also especially important because of the opportunities for access to the brain through the olfactory nerve at the roof of the nose or through the abundant innervations of the oral cavity by the trigeminal and other cranial nerves. Also, there are an increasing number of reports that have suggested potential mechanisms by which the microbiota promote human health span and aging. The study of the microbiota represents an important advance in the understanding of the aging process. © 2017 IMSS. Published by Elsevier Inc.

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Introduction

The human microbiota can be defined as a highly variable and compartmentalized ecosystem of commensal, symbiotic and pathogenic microorganisms that lives in our body. These populations consist of bacteria, fungi, parasites and archaea, which coevolved with our ancestors over millions of years. Numerous reports show an immense diversity in the human microbiota, depending on body localization, health and disease status, as well as age. In contrast with the genomic variation between humans, which reaches minimal differences, microbiome achieves 80–90% variation between regions of the same person (1,2). Specialized populations are a

product of their coevolutionary interactions, which contributes significantly to our physiology, facilitating the provision of nutrients and protection against pathogens (3). In this context, researchers have demonstrated that changes in the composition of the microbiota contribute to the development of diseases and the aging process (4,5).

Despite the high inter-individual variability, determined by height, sex, age, or place of residence, it has been determined that three specific microbial enterotypes (Bacteroides, Prevotella or Ruminococcus) are constants (6). These enterotypes are linked with dietetic pattern (7). In the case of gut microbiota it has been reported that there are around 1500 bacterial species, 10% of which could be present per person (8). In healthy adults approximately 80% of the total gut microbiota is integrated by the phyla Firmicutes and Bacteroidetes (9).

Taking into account the potential of the gut microbiota to affect the health status of individuals, particularly of elderly

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people, the understanding of this field has fundamental relevance and must likely will become one of the most significant current research areas because of its relation with healthy aging, longevity, chronic diseases, and neurodegeneration, among others. Therefore, the aim of this review is to present and analyze the relevant literature regarding the topic, to discuss gaps in knowledge and consider the future of microbiota research in aging.

Microbiota During Life Course

The gut microbiota evolution is determined by the individual's aging process. Despite extensive interpersonal variation as well as its fluctuations over time, several studies have found similar patterns of microbiome's modification associated with both host and environmental factors. Host factors such as genetics, gut senescence and immunosenescence have been involved in the composition of the microbiome (10–12). Gut microbiota may also be influenced by genetic factors through diverse mechanisms, such as biliary secretion, dietary patterns, digestive enzymes, mucosal barrier composition, intestinal immunity and intestinal motility, among others (13). Changes in gut microbiota have also been associated with age related conditions such as chronic inflammation present in frailty and other neurological conditions like Parkinson's and Alzheimer's (14,15).

The gut microbiota development starts at the birth, showing instability and reduced diversity. Environmental factors include the mother's intrauterine microbiota (16) and birth type. In this sense, the infant's microbiota will be more or less diverse depending on the birth method, inducing quick changes. This finding are supported by

many studies comparing gut microbiota of babies born by caesarean section or vaginal delivery, showing that the first have less diversity of bacteria, specifically, less *Bifidobacteria* (17,18). As soon as the baby starts feeding, the food source (formula or breast) will also determine the gut microbiota (19). Some argue that microbiota from formula fed babies is characterized by having more pro-inflammatory taxa as well as higher bacterial loads (20). Gut microbiota will remain unstable until the infant is 2–3 years old, and will highly depend on environmental factors such as introduction of solid food, place of residence, antibiotic exposure and genetic host factors (10,21,22). The child's microbiota matures at around three years old when it reaches a more stable composition, as reported in adulthood (9,23) (Figure 1).

The microbiota remains relatively stable throughout adulthood (under healthy conditions). However the ageing process deeply affects the composition of the microbiota, losing diversity, reducing the proportion of beneficial bacteria and changing the dominant species (23). In this sense a direct correlation between bacterial diversity and healthy status of microbiota has been recognized (24,25). Therefore, age-related changes in microbiota induce physiological alterations able to modify immune system homeostasis and inflammatory state that contribute to increased risk of disease and frailty (26–28).

Aged-related Changes in Microbiota

As previously discussed, several studies have focused on the determination of the standard composition of the microbiota in adulthood, however the findings in elderly people has been inconsistent. These results could be explained

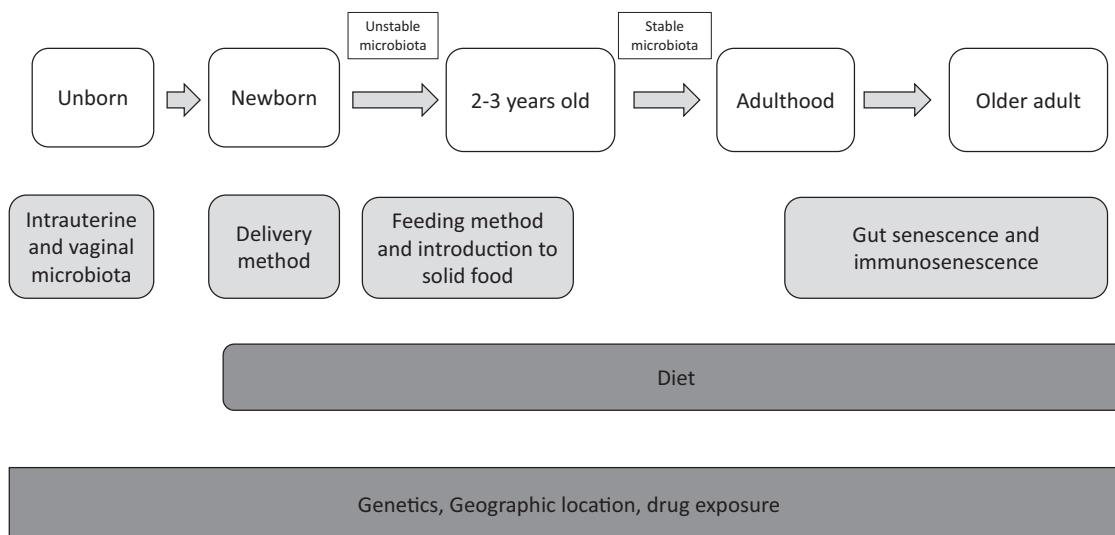


Figure 1. Gut microbiota development.

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