



## Review

## Association between the gut microbiota and diet: Fetal life, early childhood, and further life



Daria A. Kashtanova M.D.<sup>a,\*</sup>, Anna S. Popenko Ph.D.<sup>b</sup>,  
Olga N. Tkacheva M.D., Ph.D.<sup>c</sup>, Alexander B. Tyakht Ph.D.<sup>b</sup>,  
Dimitry G. Alexeev Ph.D.<sup>b</sup>, Sergey A. Boytsov M.D., Ph.D.<sup>d</sup>

<sup>a</sup> Research of Age and Age-associated Conditions Department, National Research Centre for Preventive Medicine, Moscow, Russian Federation

<sup>b</sup> Laboratory of Bioinformatics, Scientific Research Institute for Physical-Chemical Medicine, Moscow, Russian Federation

<sup>c</sup> Russian Clinical Research Center for Gerontology, Moscow, Russian Federation

<sup>d</sup> Department of Cardiology and Molecular Genetics, National Research Centre for Preventive Medicine, Moscow, Russian Federation

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## ABSTRACT

Gut microbiota establishment and further microbiota shifts are very important for maintaining host health throughout life. There are some factors, including genetics, the mother's health and diet, delivery mode, breast or formula feeding, that may influence the gut microbiota. By the end of approximately the first 3 y of life, the gut microbiota becomes an adult-like stable system. Once established, 60 to 70% of the microbiota composition remains stable throughout life, but 30 to 40% can be altered by changes in the diet and other factors such as physical activity, lifestyle, bacterial infections, and antibiotic or surgical treatment. Diet-related factors that influence the gut microbiota in people of all ages are of great interest. Nutrition may have therapeutic success in gut microbiota correction. This review describes current evidence concerning the links between gut microbiota composition and dietary patterns throughout life.

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## Introduction

The human gut microbiota has become a widely discussed topic over the past decade. Gut microbiota plays an important role in the normal functioning of the host organism. This is confirmed by a growing number of studies, which reveal more about mechanisms of interaction between the microorganisms and the human body. A host also may affect its gut microbiota by changing lifestyle; naturally diet is a very important factor. One study showed that an increase in caloric intake from 2400 to 3400 kcal/d (with similar nutrient profile that included 24% protein, 16% fat, and 60% carbohydrates) over 3 d increases *Firmicutes* representation and decreases the representation of

*Bacteroidetes* [1]. Inverse changes in the gut microbiota occur while reducing caloric intake [2]. It is difficult to investigate the effects on energy intake. Normal caloric intake differs from person to person and depends on age, habits, metabolism, and so on. For this reason, we have paid more attention to different nutrition compounds.

Dietary habits determine what our bacteria can consume; it is the way we are “feeding” our microbiota. Bacteria metabolic activity is defined mostly by its genome and epigenome. Saccharolytic bacteria are able to metabolize carbohydrates; this bacteria group includes *Bacteroides*, *Bifidobacterium*, *Lactobacillus*, *Eubacterium*, *Propionibacterium*, *Escherichia*, *Enterococcus*, *Peptostreptococcus*, *Fusobacteria*, and others. Proteolytic bacteria derive energy from protein fermentation and are represented by *Streptococcus*, *Staphylococcus*, *Proteus*, *Escherichia*, and some species of *Clostridium*, *Fusobacteria*, *Bacillus*, *Propionibacterium*, and others. Some of them are strictly proteolytic, whereas others have mild saccharolytic activity or are actively engaged in carbohydrate fermentation. Thus, many bacteria are capable of metabolizing both proteins and carbohydrates. The aim of this

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\* Corresponding author. Tel.: +7 916 393 9188; fax: +7 495 790 7172.

E-mail address: [dr.kashtanova@gmail.com](mailto:dr.kashtanova@gmail.com) (D. A. Kashtanova).

review was to provide partial answers to at least some questions about the gut microbiota and diet based on published studies; and to identify important gaps in knowledge where further research should be done.

## Gut microbiota establishment and diet

### Antenatal period and delivery

Gut microbiota colonization begins during the antenatal period [3,4]. Recent studies have proved the presence of bacteria in the amniotic fluid, placenta, cord blood, meconium [5–7]. A mother's diet before and during pregnancy influences the development of the child's gut microbiota [8,9]. For example, excessive maternal intake of trans-fats in rats has been shown to induce a low-grade inflammation in babies, whereas supplementation with Jussara (*Euterpe edulis* Mart.) during pregnancy and lactation reverses the effects of trans-fatty acids and increases *Lactobacillus* spp. in offspring [10]. A maternal gluten-free diet increases the number of *Akkermansia*, *Proteobacteria*, and *TM7* bacteria in the gut microbiota of mice offspring and reduces the incidence of diabetes and low-grade inflammation [11].

It has been shown in humans that an unhealthy mother's diet during pregnancy as well as poor early childhood nutrition can lead to the establishment of a lean defective intestinal microbiota [12]. This results in further dysfunction of the immune system and in a dysregulation of genes involved in a lipid and glucose metabolism [12,13]. Interestingly, a recent study found that even maternal consumption of the oily fish influences the infant gut microbiota composition [14].

The next step in the microbiota establishment is a delivery. Method of the delivery is of great importance for microbiota colonization. For instance, cesarean delivery is accompanied by lower microbiota diversity and postponed *Bacteroidetes* colonization [15]. In contrast, vaginal delivery is accompanied by an extensive colonization of child's microbiota by vaginal bacteria, mainly represented by *Lactobacillus*. Thus, vaginally delivered infants acquired the microbiota similar to their mother's vaginal microbiota, represented by *Lactobacillus* and *Prevotella*, and babies born by cesarean delivery acquired the microbiota similar to the mother's skin microbiota, dominated by *Staphylococcus*, *Corynebacterium*, and *Propionibacterium* [16].

### Early childhood: breast and formula and complementary feeding

The neonatal and early childhood periods are critical for the formation of a healthy intestinal microbiota in children. Following birth, child's gut microbiota is characterized by a low diversity until 2 to 3 y old [13,17]. It is assumed that initial colonization of the gut microbiota with facultative anaerobes, such as *Staphylococcus*, *Streptococcus*, *E. coli*, and *Enterobacterium*, make further obligate anaerobe colonization possible [18,19].

Later, during the breast feeding period, the digestive tract is colonized with *Actinobacteria* and *Firmicutes* [20]. *Actinobacteria* in breast-fed children are represented mainly by *Bifidobacterium* (*B.*), *B. breve*, *B. longum*, *B. dentium*, *B. infantis*, *B. pseudocatenulatum* [21]. With regard to *Firmicutes* phylum, it is at most represented by *Lactobacillus*, *Enterococcus*, and *Clostridium* [17,20]. Breast feeding is considered to be the perfect nutrition for children. Healthy mothers' breast milk contains 10<sup>9</sup> microorganisms/L [22], and a healthy maternal diet is crucial for the child's normal milk composition and proper gut microbiota establishment [23].

The gut microbiota in formula-fed children differs from that of breast-fed infants. Formula-fed infants' microbiota contains more *Bacteroides*, *Enterobacteriaceae*, including *Klebsiella*, *Atopobium*, and *Clostridia* [21,24] and lower levels of *Bifidobacterium* [25]. Although, according to some studies, the total number of *Bifidobacterium* but not levels of *Bifidobacterium cantenulatum* and *Bifidobacterium adolescentis* are relatively similar in breast-fed infants and in those fed with formula supplemented with galactooligosaccharides and fructooligosaccharides [22,26].

The composition of the gut microbiota also differs among breast-fed infants. In many respects, it is determined by the maternal nutrition [27]. Findings from one study demonstrated that high-fat maternal diet results in microbiota dysbiosis in primate offspring [28]. Certainly, new studies are required for further development and practical application of this hypothesis.

An adult-like microbiota is established approximately between 2 and 3 y of age, after cessation of breast feeding. Its composition largely depends on the type of complementary feeding [17,24]. For instance, the more polysaccharides a diet contains, the more bacteria in the gut are able to ferment it (e.g., *Prevotella*) [29]. Research conducted in 2014 in Denmark with 330 healthy infants aged up to 3 y found that significant changes in the gut microbiota occurred after weaning. The number of *Bifidobacterium*, *Lactobacillus*, and *Enterobacteriaceae* decreased, whereas *Bacteroidetes* phylum members were observed to increase. Regardless of the age of weaning, the number of butyrate-producing bacteria such as *C. leptum*, *Eubacterium Hallii*, and *Roseburia* is growing along with microbiota diversity [17,30].

By 36 mo after birth the baby's gut microbiota undergoes last shifts it becomes a stable system mainly represented by *Bacteroidetes*, *Firmicutes*, and smaller rates of *Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia* [17,29–31]. "Proper" microbiota establishment is crucial because about 60% to 70% of microbiota bacteria remain unchanged throughout life. Notably, *Bacteroidetes* and *Actinobacteria* rates are much more stable than *Firmicutes* and *Proteobacteria* [32,33].

## Nutrients in a diet affecting gut microbiota

We still cannot say what comprises "healthy" microbiota; its composition varies greatly according to the lifestyle, diet, and many other factors [34]. Scientists are attempting to identify major features of the gut microbiota in healthy people to set up a conception of normal gut flora. However, to our knowledge, there are no precise conclusions to date, and microbiota appears to be similar in people living in the same area and having contact with each other [18,35].

In 2011, three enterotypes with a predominance of *Bacteroides*, *Prevotella*, or *Ruminococcus* were described. *Bacteroides* enterotype is common in people following a Western diet that is rich in fat and protein. *Prevotella* enterotype is common in people who consume a lot of fiber [31]. Protein- and fat-degrading bacteria are more abundantly present in the gut of people who eat more fat and protein (e.g., such a pattern was observed in the US population). In turn, microbiota of Malawi (East Africa) residents contains more polysaccharide-degrading microorganisms [35]. A high-fat diet is associated with high levels of *Bacteroidetes* and *Actinobacteria* in the gut. The same bacteria are in inverse proportion to the plant fiber consumption. *Firmicutes* and *Proteobacteria* have an opposite association with these macronutrients [36]. Although, the relevancy of enterotypes or "fecotypes" is disputed, 30% to 40% of adults' gut microbiota can

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