The role of diet on gut microbiota composition

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Abstract. – Gut microbiota is characterized by an inter-individual variability due to genetic and environmental factors. Among the environmental ones, dietary habits play a key role in the modulation of gut microbiota composition. There are main differences between the intestinal microbiota of subjects fed with prevalent Western diet and that of subjects with a diet rich in fibers. Specific changes in the composition of gut microbiota have been demonstrated among subjects according to a different dietary intake. A particular diet may promote the growth of specific bacterial strains, driving hosts to a consequent alteration of fermentative metabolism, with a direct effect on intestinal pH, which can be responsible for the development of a pathogenic flora. Moreover, a high-fat diet can promote the development of a pro-inflammatory gut microbiota, with a consequent increase of intestinal permeability and, consequently, of circulating levels of lipopolysaccharides.

In this review, we discuss the direct role of the diet in the composition of gut microbiota and about the possible clinical consequences.

Key Words:
- Gut microbiota, Diet, Inflammation, Lipopolysaccharide, Fiber, High-fat.

Introduction

Our organism is colonized by an enormous number of micro-organisms, both on its surface and inside. They amount for more than 1 kg of weight, and outnumber human eukaryotic cells at least ten times. The majority of them live in our gut, constituting the so-called gut microbiota. As gut microbiota and human beings are in a symbiotic relationship, the idea of a combined “super-organism” has been recently developed.

In health, gut microbiota plays a relevant role within our body, mainly being involved in the development and growth of immunity and in the regulation of several fundamental metabolic pathways.

Quantitative and/or qualitative alterations of gut microbiota bring to the impairment of this homeostasis, leading to the development of several gut microbiota-related diseases, such as functional gastrointestinal diseases, intestinal infectious diseases, inflammatory bowel disease, liver diseases, gastrointestinal malignancies, obesity and metabolic syndrome, diabetes mellitus, allergic diseases, autism, and others.

Since a large part of microorganisms, in particular, anaerobes, is not cultivable through conventional microbiology techniques, our understanding of gut microbiota is substantially limited. However, the development of culture-independent tools, based on metagenomics technologies, has led us to take a step forward in the assessment of gut microbiota composition.

Currently, four major microbial phyla are known to represent over 90% of the bacterial component of gut microbiota: Firmicutes, Bacteroides, Proteobacteria and Actinobacteria. The majority of “good” bacteria harbouring the human gut microbiota are represented by Firmicutes and Cytophaga-Flavobacterium-Bacteroides (CFB). Firmicutes are sub-grouped in Clostridium cocoides (Clostridium cluster XIVa) and Clostridium leptum (Clostridium cluster IV); whereas CFB group is represented mainly by Bacteroides phyla with a great number of Prevotella and Porphyromonas.

Moreover, our gut microbiota includes viruses, especially phages, Eukarya, as Fungi, Blastocystis, Amoeboza, and Archaea.
Gut microbiota has been classified into three main enterotypes, each one owning specific metabolic features. Each enterotype is characterized by the relative abundance of one of the following genera: *Bacteroides* (more represented in enterotype 1), *Prevotella* (more abundant in enterotype 2), *Ruminococcus* (prevalent in enterotype 3). Prevalence of a specific enterotype can depend on long-term dietary habits, indeed high-fat and protein diet enhances the growth of enterotypes 1 and 3, while a diet rich in carbohydrates supports the raise of enterotype 2. Recent findings suggest that gut microbiota composition is influenced also by short-term dietary changes.

Both genetic and environmental factors are involved in influencing the inter-individual diversity of gut microbiota. Among environmental ones, the interest of the scientific community in dietary factors has progressively increased, and the role of diet on the composition of gut microbiota has been particularly emphasized over the last years.

**Relationship Between Diet and Gut Microbiota**

Diet is known to have a strong influence on the composition of intestinal microbiota. To confirm this hypothesis, some researchers sequenced oral microbiota from skeleton teeth of people who lived over the various eras. They showed that the most significant changes in human gut microbiota had occurred during two socio-dietary breakthroughs over the human history: the passage from the hunter-gatherer Paleolithic era to the farming Neolithic era (10000 years ago), with a diet rich in carbohydrates, and the beginning of the industrialized period, characterized by processed flour and sugar diet (about two centuries ago).

Further studies identified also differences in gut microbiota composition among different populations of our planet, probably due to variability in both diet and genetics of each population.

De Filippo et al. have compared the gut microbiota of children from rural Africa (Burkina Faso) with that of Italian children living in urban areas showing that these two populations have radically different diets; in particular, open children have a lower dietary intake of fibers. The bacterial profiles of the two groups of children clustered separately: microbiota of the African children is dominated by Bacteroidetes, whereas among European children there is a prevalence of *Enterobacteriaceae* and a decrease in *Bacteroides*.

Large variations in gut microbiota among Americans, Europeans and Africans have also been documented in other studies. Gut microbiome of Africans clustered with that of South American people, correlating with large consumption of plant-based polysaccharides, but were different from North Americans (which have mainly a low-fiber diet). Carbohydrates intake from the diet could, therefore, contribute to the large variation observed in gut microbiota composition. Indeed, a high-fiber diet seems to be positively correlated with bacterial richness. Therefore, permanent changes in gut microbiota composition might be achieved through dietary modifications.

While Western diet, typically constituted by high consumption of red meat, animal fat, high sugar and low fiber food, was therefore associated with an increased number of *Bacteroides* phyla (mainly mucin-degrading bacteria) and also *Ruminococcus*.

Specific changes in the gut microbiota have been associated with long-term or short-term dietary modifications. Wu and colleagues found that the microbiota composition is strongly associated with long-term dietary habits. Prevalence of *Bacteroides* and *Actinobacteria* is positively associated with high-fat diet, but is negatively associated with fiber intake, whereas *Firmicutes* and *Proteobacteria* show the opposite association. Bacteroidetes-predominant enterotype is strictly associated with animal protein and saturated fats, suggesting its prevalence in Western countries. In contrast, *Prevotella*-prevailing enterotype is associated with high consumption of carbohydrates and simple sugars, indicating a correlation with a carbohydrate-based diet more typical of agrarian societies and vegetarians.

Also, a short-term dietary alterations can modify the microbial communities of our body. An animal-based diet increased the abundance of bile-tolerant microorganisms (such as *Alistipes*, *Bilophila* and *Bacteroides*) and decreased the levels of *Firmicutes* metabolizing dietary plant polysaccharides (*Roseburia, Eubacterium rectale* and *Ruminococcus bromii*). Such data confirm the existing differences between gut microbiota of vegetarians and mainly carnivorous subjects, that are fundamental respectively for carbohydrate and protein fermentation.

**High-fiber diet and gut microbiota**

Dietary fibers are divided into complex carbohydrates (digestible and non-digestible) and oligosaccharides. They exert a strong influence on the gut microbiota, promoting the growth of beneficial bacteria such as *Bifidobacterium* and *Eubacterium*, while inhibiting the growth of pathogenic bacteria such as *Clostridium*. The consumption of dietary fibers is associated with a decrease in body weight and a decrease in the risk of developing chronic diseases such as type 2 diabetes and colorectal cancer.
on the composition of the gut microbiota and consequently on the gut fermentative metabolism.

**Complex carbohydrates**

A fraction of normal human dietary intake remains undigested in the small intestine and passes through to the large intestine to be eliminated. Non-digestible components include plant cell wall polysaccharides (such as cellulose and pectin) and certain storage polysaccharides (such as inulin and oligosaccharides). Dietary starch incorporates a resistant component that is not fully digested in the small intestine\(^a\). There are four types of resistant starch (RS1 to RS4) consumed with diet\(^b\). Resistance features of dietary starch are respectively the protection from plant cell wall polymers (type 1), granular structure (type 2), retrogradation resulting from heating and cooling (type 3) or chemical cross-linking (type 4)\(^c\).

Several studies have analyzed the role of different types of resistant starch in gut microbiota regulation. Leitch et al\(^d\) showed that subjects fed with resistant starch type 2 (RS2) from high amylose maize showed an increased abundance of *Ruminococcus* spp. and *Eubacterium rectale*, while consumption of RS 3 promoted the growth of *Eubacterium rectale*, *Roseburia* spp. and *Ruminococcus bromii*\(^e\).

Additionally, RS2 have been shown to promote an enrichment of *Bifidobacterium adolescentis*, *Eubacterium rectale*, and *Ruminococcus bromii*. These last two species are increased during RS3 consumption. Moreover, RS4 is positively correlated with *Parabacteroides distasonis* abundance and negatively correlated with *Eubacterium rectale* and *Ruminococcus bromii* prevalence. Strikingly, RS4 also leads to phylum level alterations, decreasing the proportion of *Firmicutes* while increasing *Bacteroides* and *Actinobacteria*\(^f\). Walker et al\(^g\) confirmed that *Firmicutes* bacteria related to *Ruminococcus bromii* and *Eubacterium rectale* are commonly stimulated by the RS diet.

Furthermore, the consumption of high quantities of soluble diet leads to increase in *Bacteroides* spp., *Clostridium leptum* group bacteria, and *Eubacterium rectale* group\(^h\). Soluble fibers are indeed associated with an increased proportion of butyrate-producing bacteria, that mainly belong to the *Clostridium leptum* and *Eubacterium rectale* groups\(^i\). Moreover, complex carbohydrates also increase levels of beneficial bacteria, in particular, *Bifidobacteria* spp., such as *B. longum*, *B. breve* and *B. theta-taomicron*\(^j\). Finally, *Prevotella* spp. are the most represented bacteria in vegetarian subjects\(^k\).

On the other hand, a decrease in total carbohydrate dietary content leads to a significant decrease in the proportion of the *Roseburia/E. rectale* group (Table I)\(^l\).

**Oligosaccharides**

Not only complex carbohydrates, but also oligosaccharides (such as fructans, inulin, fructo-oligosaccharides (FOSs), Galacto-oligosaccharides (GOS) and Arabinoxylan-oligosaccharides) have shown a role in modifying gut microbiota. Inulin and FOSs promote the growth of *Bifidobacterium spp* and *Lactobacillus spp.*, whereas fructan supplementation decreases levels of *Bacteroides spp* and *Clostridium spp.*\(^m\). Furthermore, fructans can promote the growth of beneficial butyrate-producing bacteria, such as *Faecalibacterium prausnitzii*\(^n\).

Galacto-oligosaccharides (GOS) supplementation can stimulate the growth of *Bifidobacteria spp* (especially *B. adolescentis* and *B. catenulatum*) and also increase the *Faecalibacterium prausnitzii* population, but with inter-individual variability\(^o\). Arabinoxylan-oligosaccharides display a similar behavior, and additionally increase total bacterial population (Table II)\(^p\).

**High-fat diet and gut microbiota**

The role of fatty acids in the regulation of gut microbiota has been extensively assessed. Dietary fatty acids are grouped into three main categories: satura-

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Table I. Effect of carbohydrates on gut microbiota composition.

<table>
<thead>
<tr>
<th>Carbohydrates</th>
<th>Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant starch 2</td>
<td><em>Ruminococcus spp</em>, <em>Eubacterium rectale</em>, <em>Bifidobacterium adolescentis</em></td>
</tr>
<tr>
<td>Resistant starch 3</td>
<td><em>Eubacterium rectale</em>, <em>Roseburia spp</em>, <em>Ruminococcus bromii</em></td>
</tr>
<tr>
<td>Resistant starch 4</td>
<td><em>Parabacteroides distasonis</em></td>
</tr>
<tr>
<td>High soluble fiber diet</td>
<td><em>Eubacterium rectale</em>, <em>Ruminococcus bromii</em></td>
</tr>
<tr>
<td>Complex carbohydrates</td>
<td><em>Bacteroides spp.</em>, <em>C. leptum group</em>, and <em>E. rectale</em></td>
</tr>
<tr>
<td>Low fiber diet</td>
<td><em>Bifidobacteria spp</em>, <em>Prevotella spp</em></td>
</tr>
<tr>
<td></td>
<td><em>Roseburia spp</em>, <em>Eubacterium rectale</em></td>
</tr>
</tbody>
</table>
Diet and gut microbiota

**Table II. Effect of oligosaccharides on gut microbiota composition.**

<table>
<thead>
<tr>
<th>Oligosaccharide</th>
<th>Bifidobacterium spp, Lactobacillus spp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructo-oligosaccharides</td>
<td></td>
</tr>
<tr>
<td>Inulin</td>
<td></td>
</tr>
<tr>
<td>Fructans</td>
<td></td>
</tr>
<tr>
<td>Galacto-oligosaccharides</td>
<td></td>
</tr>
<tr>
<td>Arabinoxylan-oligosaccharides</td>
<td></td>
</tr>
</tbody>
</table>

**Table III. Effect of high-fat diet on gut microbiota composition.**

<table>
<thead>
<tr>
<th>Diet</th>
<th>Microbiota Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safflower oil (ω-6 PUFA)</td>
<td>↑ Firmicutes, Actinobacteria, Proteabacteria</td>
</tr>
<tr>
<td>PUFA</td>
<td>↓ Bacteroides</td>
</tr>
<tr>
<td>ω-6 PUFA</td>
<td>↓ Lactobacillus spp</td>
</tr>
<tr>
<td>1PUFA</td>
<td>↓ Bifidobacteria</td>
</tr>
<tr>
<td>MUFA</td>
<td>↓ L. casei Shirota</td>
</tr>
<tr>
<td>High-fat diet</td>
<td>↑ delta-proteabacteria ssp, Bilophila wadsworthia</td>
</tr>
</tbody>
</table>

Metabolic effects

The effect of dietary induced changes of gut microbiota on local and systemic inflammation has also been extensively investigated. Intestinal barrier plays an important role in the regulation of the immune system, in particular through gut microbiota. Gut microbiota can alter the function and feedbacks of intestinal immune cells, by regulating systemic and mucosal immunity. For this reason, there is a growing interest for factors, such as diet, that can modulate gut microbiota itself.

High fiber diet alters fermentative metabolites and intestinal pH. Colonic microbiota is able to metabolize complex carbohydrates and sugars into short-chain fatty acids (SCFAs), such as acetate, butyrate and propionate. Such metabolites play a role in regulating intestinal pH.

For instance, in vegetarian subjects, the high amounts of fiber result in an increase of SCFAs production by microbes, which lower the local pH. Little variation of acid concentrations may exert important consequences. A one-unit decrease in pH (from 6.5 to 5.5) has been shown to have a profound selective effect on the colonic microbial population, with a prevalent decrease of Bacteroides spp. and a growth of butyrate-producing gram-positive bacteria.

The decrease of pH caused by high concentration of SCFAs prevents the growth of potentially pathogenic bacteria, such as *E. coli* and other members of the *Enterobacteriaceae*. Moreover, SCFAs...
production can be a potential modulator of intestinal flora. Several gut bacteria, such as some *Firmicutes* spp, especially those belonging to *Clostridium cluster XIVa*, are tolerant of lower, while *Bacteroides* spp. and *Bifidobacterium* spp. are not.

Western diet was considered responsible of the intestinal dysbiosis that triggers local inflammation, causing an increase of intestinal permeability. It is known that certain types of intestinal flora may promote inflammation. The exact mechanism is, however, not completely understood. Besides, metabolic adaptation to high-fat diet is associated to a change in gut microbiota composition.

It was observed that high fat diet induces the proliferation of certain gram-negative bacteria, such as *Enterobacteriaceae*, which can ultimately result in increased intestinal lipopolysaccharide (LPS). To confirm this, Pendyala et al. reported that only 1 month of western diet is responsible of an important increase of LPS plasma levels.

Furthermore, increased gut permeability is associated with a decrease in *Bifidobacteria* spp, bacteria that are known to reduce LPS levels and also improve gut barrier function. Interestingly, prebiotic treatment with non-digestible carbohydrates increases *Bifidobacteria*, reduces intestinal permeability, LPS concentrations, and metabolic endotoxaemia.

In a mouse model, consumption of a high-fat diet increased the incidence of colonic inflammation; this effect seems to be induced by the secretion of bile acid, in particular taurine, promoted by fat food. Such phenomenon stimulates the growth of sulphite-reducing pathobionts such as *Bilophila wadsworthia*, whose production of H₂S is thought to inflame intestinal mucosa. *Bilophila wadsworthia* is promoted by a high-fat diet also in human beings. Moreover, high-fat diet causes low-grade inflammation in the gut, leading to increased levels of plasma markers of inflammation, and higher levels of circulating LPS.

A decreased numbers of *Bifidobacteria* was associated with the higher ω-6 PUFA intake. Interestingly, high ω-6 PUFA intake decreases certain immune functions, such as Th1 and Th2 responses, adhesion moleule expression and proinflammatory cytokines. Moreover, high-protein diet stimulates the activity of bacterial enzymes such as B-glucorinidase, azoreductase and nitroreductase, which produce toxic metabolites that trigger inflammatory response.

Consequently, the Western diet can therefore create the favorable conditions for chronic endotoxemia, defined as an excess of circulating bacterial wall LPS, through the impairment in gastrointestinal barrier function and the changes of the microbiota. Endotoxemia is associated with systemic inflammation and with the metabolic syndrome.

**Conclusions**

In this review, we analyzed how dietary factors can modify the gut microbiota. Recent discoveries have allowed us to set aside the idea that only individual genetics play a role in determining the composition of the intestinal flora. It is evident how the food choice of every individual, both because of survival needs and taste preference, causes a substantial and significant variability in gut microbiota. As increasing evidence is showing us, diet can be definitely included, as it is for antibiotics, among the microbiota modulators, with a two-faced behavior toward gastrointestinal disorders.

We have briefly discussed how a diet rich in fats may favor an “inflammatory” flora. Diet rich in fats and low in fibers, typical of Western Countries, is rapidly spreading around the world. Similarly, inflammatory diseases are increasing in prevalence even in areas where were less common until a few years ago. Between these two observations maybe there is a link, which could be represented by the diet. It is still too early to comprise whether this is only a suggestion or if behind this observation there is a precise pathophysiological mechanism. For this reason, further studies are needed to understand the role of the intestinal barrier, and in particular of gut microbiota, in the development of systemic and local immune response. Full understanding of this issue will provide the medical community with new therapeutic targets for gastrointestinal and extraintestinal disorders.

**Conflicts of interest**

The authors declare no conflicts of interest.

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