



THE INTERDEPENDENCE BETWEEN DIET, MICROBIOME, AND HUMAN BODY HEALTH - A SYSTEMIC REVIEW

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ABSTRACT

Recent studies from the literature show more and more the interdependence between diet and intestinal microbiome and the health of the human body and the health of the intestinal microbiome. It has been shown so far that the intestinal microbiome is itself an "organ" that has its metabolic activity influencing the entire metabolism of the body host. In this paper, the main roles of the intestinal microbiome, its composition, and implications in maintaining the health of the organism and the changes in case of existing pathology were pointed out. Our study combines recent in vivo or in vitro tests that have shown a direct link between microbiota imbalances and certain pathologies. Changes in the composition of the microbiome in pathologies such as Alzheimer disease, intestinal or skin pathologies have been described. However, this paper summarizes the main notions and interdependencies between the health of the bacterial intestinal microflora and the health of the human body.

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Introduction

The totality of microorganisms distributed throughout the small intestine forms the intestinal microbiome. It has multiple roles but the most important role is to maintain the normal parameters of the human body. To date, it has been shown in numerous studies that there is a very close link between the health of the gut microbiome and the health of the host organism, and this is influenced by lifestyle [1-3].

Thus, it can be stated that lifestyle changes lead to changes in the bacterial composition of the gut microbiome.

In other words, improving lifestyle and diet will lead to a change in the microbiome (in a positive sense) and improved health, or it may prevent the development of various pathologies [1].

It is therefore very important to know the interaction between food and intestinal bacteria in order to be able to say what is the interaction between them. Many pieces of research prove that a restructuring of the gut microbiome composition can have positive or negative effects on health [4, 5].

Multiple factors such as temperature, pH, presence of bacteriophages, the bioavailability of nutrients, and percentage of anaerobiosis are strongly involved in the type of composition and function of the total intestinal bacterial population, which is directly influenced [6, 7].

The activity of gut microorganisms is so intense and present in the host organism that nowadays the microbiome is considered to function as a "real organ" [8].

The variation of the human intestinal microbiome can reflect the lifestyle and behaviors of the host and it can influence the levels of biomarkers in the blood [9].

Recent findings advance the concept of precise nutrition and they have the potential to present more effective and accurate dietary approaches to disease prevention through changes in the gut microbiome [10].

Therefore, this paper aims to highlight several recent studies on the interrelationship between the health of the microbiome and the health of the human body and to allow an overall assessment of the importance of nutrition in the prevention or treatment of various diseases.

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The Human Colon and Fermentation

The number of bacteria in the colon is impressive, on the order of trillions, and all of them are involved in the processes of digestion, absorption, and metabolism of food, acting in the first phase through the fermentation process [11-13].

Carbohydrates throughout the digestive tract are not fully hydrolyzed by digestive enzymes (especially complex, indigestible ones such as pectin, gums, cellulose, etc.) but through the microbiota they are fermented, this process resulting in energy and production of SCFA (propionate, acetate, and butyrate) and gases [14-17].

Following the fermentation process of carbohydrates and proteins under physiological conditions, in addition to those mentioned above, branched-chain fatty acids (BCFA), lactic acid, amines, etc. are produced, all these reaction products having an important role in maintaining the metabolic balance of the host organism. More recently it has also been shown to play a role in increasing the body's immunity [18, 19].

It is however worth mentioning that protein fermentation occurs only after carbohydrates have been fermented and for this reason, it takes place in the distal colon [20-22].

Protein fermentation can become harmful to the body (considered an important factor in colorectal cancer) but there are also situations in which it is beneficial, namely when it intervenes in regulating the nitrogen balance of the host by releasing ammonia that can be absorbed into cells [23, 24].

The impact of the gut microbiome on lipids is more complex as it generates a variety of fatty acids that in increased amounts can affect the health of the host. For example, the metabolism of linolenic acid has a direct connection with species of *Roseburia* bacteria which play a role in promoting the health of the host organism by forming vaccenic acid (a precursor for conjugated linoleic acid) [18].

An *in vivo* study shows that the metabolism of unsaturated fatty acids is also influenced by the presence of bacteria such as *Lactobacillus* sp. Reaction intermediates (especially hydroxylated compounds) were monitored and it was shown that depending on the composition of the microbial flora, their level is different. In other words, the lipid profile of the host can be modified depending on the health of the intestinal microbial flora [18, 25, 26].

The bacteria most often involved in fermentation processes are of the genera *Bifidobacterium*, *Ruminococcus*, *Lactobacillus*, and *Clostridium*. Also of major importance are *Eubacterium rectale*, *Roseburia* spp., and *Faecalibacterium prausnitzii* [8, 20, 27, 28].

The Interrelationship of the Microbiome and the Appearance of Multiple Diseases

To date, numerous studies have been performed on the influence of the microbiome on the health of the body and the direct connection with various pathologies. An overview of the intestinal bacterial genera and species commonly affected by diet is presented in **Table 1**.

Table 1. Overview of intestinal bacterial genera and species commonly affected by diet.

Bacteria	Characteristics	Associated physiological changes	Associated disease states	Ref.
<i>Bifidobacterium</i> spp.	<ul style="list-style-type: none"> ○ gram-positive ○ branched-chain anaerobic; 	<ul style="list-style-type: none"> ○ low SCFA production; ○ improve the intestinal mucosa barrier; ○ lower intestinal LPS levels 	<ul style="list-style-type: none"> ○ low amount of obesity 	[29, 30]
<i>Lactobacillus</i> spp.	<ul style="list-style-type: none"> ○ optional anaerobic ○ rod-shaped ○ gram-positive 	<ul style="list-style-type: none"> ○ regulates SCFA production; ○ anti-inflammatory activity ○ anti-cancer activity 	<ul style="list-style-type: none"> ○ low amount in IBD 	[31]
<i>Alistipes</i> spp.	<ul style="list-style-type: none"> ○ gram-negative ○ rod-shaped anaerobic ○ resistant to bile acids and pigments 	-	<ul style="list-style-type: none"> ○ Reported in the tissues of acute appendicitis and perirectal and cerebral abscesses 	[32]
<i>Bilophila</i> spp.	<ul style="list-style-type: none"> ○ gram-negative ○ anaerobic ○ resistant to bile acids and pigments 	<ul style="list-style-type: none"> ○ Promotes TH1 pro-inflammatory immunity 	<ul style="list-style-type: none"> ○ observed in colitis, perforated appendicitis and gangrene, liver and soft tissue abscesses, cholecystitis 	[33, 34]
<i>Eubacterium</i> spp.	<ul style="list-style-type: none"> ○ gram-positive ○ rod-shaped aerobic 	<ul style="list-style-type: none"> ○ involved in SCFA production ○ forms beneficial phenolic acids 	<ul style="list-style-type: none"> ○ low amount in IBD 	[35, 36]

<i>Escherichia coli</i>	<ul style="list-style-type: none"> ○ gram-negative ○ rod-shaped anaerobic 	-	<ul style="list-style-type: none"> ○ increased in gastroenteritis, IBD, and meningitis 	[37, 38]
<i>Akkermansia muciniphila</i>	<ul style="list-style-type: none"> ○ gram-negative ○ anaerobic ○ oval shape 	<ul style="list-style-type: none"> ○ Anti-inflammatory effects 	<ul style="list-style-type: none"> ○ Low amount of IBD, obesity, and psoriasis 	[39]

Alzheimer Disease

Alzheimer's disease (AD) is a progressive neurodegenerative disorder for which there is currently no treatment to stop or cannot be prevented [40]. Theoretically, AD is characterized by extracellular accumulations of peptides and intracellular deposits of hyperphosphorylated proteins [41, 42].

It has recently been shown that there is a close link between the intestinal microbiome and the maintenance of cognitive health, with an imaginary bowel-brain axis that is due to immune, endocrine, and neural signaling pathways.

Thus, in patients with mild cognitive impairment and dementia, there is an imbalance in the intestinal flora that has been shown to be responsible for the accumulation of a pro-inflammatory lipopolysaccharide at the neuronal level [43-46].

The ketogenic and low-calorie diet is considered to be beneficial in this category of patients because it has a neuroprotective effect and does not allow the accumulation of extracellular peptides at the neuronal level. also, this type of diet modulates positively and balances the important bacterial species in the intestine [17, 47].

Inflammatory Bowel Disease

Genetic factors and lifestyle are some of the factors that can have an important contribution to the occurrence of intestinal pathology such as inflammatory bowel disease (IBD) [48]. The unbalanced microbiome seems to have an extremely high contribution to these pathologies because the imbalance of the microbial population produces by fermentation proinflammatory components that will become precursors of this pathological sphere which includes Crohn's disease and ulcerative colitis [38, 49].

Crohn's disease (CD) affects the mucous and submucosal tissues, leading to regional ileitis. It is shown that the microbial changes that occur in this condition are characterized by an increase in the abundance of the bacterial species *Enterobacteriaceae*, including *Escherichia coli*, *Fusobacterium*, *Serratia marcescens* and *Candida tropicalis*, something not found in patients without this condition [50]. The impact of this imbalance is major, modifying the host's metabolism and thus causing oxidative stress. The basal metabolic rate decreases in these patients a lot, which also leads to a decrease in the production of intermediates that benefit the human body, such as short-chain fatty acids, which are easily absorbed [51-53].

The imbalance of the intestinal bacterial flora in the sense of the increase of the population of *Enterobacteriaceae sp.* and *Bacteroides fragilis* is the main feature of ulcerative colitis pathology [3, 54, 55].

Inflammatory Skin Diseases

Atopic dermatitis (AD) affects 15% -20% of children and 1% -3% of adults worldwide [56]. As for the balance of the intestinal microbiome in this condition, it is disturbed, and unbalanced. However, studies are showing that the use of probiotics leads to the remission of inflammatory dermatological conditions, thus confirming the existence of the intestinal-skin axis. For this reason, future treatments for these conditions will consider rebalancing the microbial flora and then topical treatment [56-60].

Type 2 Diabetes and Obesity

Increased consumption of high-fat and high-sugar diets has been shown to alter the microbial flora, which leads up to the idea that gut microbiota may function as an "environmental" factor that results in increased energy production and obesity [61, 62].

Obesity pathology is conceded to be associated with changes in the diversity and composition of the intestinal microbiota. There is an increased concentration of *Firmicutes* and a decreased one of *Bacteroids*, which are the 2 dominant types of intestinal microbiota. *In vivo*, it has been illustrated that a high-fat diet is associated with a decreased level of bacteria associated with *Firmicutes* (*Eubacterium rectale* and *Blautia coccoides*), bifidobacteria, and intestinal bacteria [17, 63]. The pathology of obesity and type 2 diabetes is associated with changes in the abundance of the main bacteria and the increase of the *Firmicutes* / *Bacteroidetes* ratio [30, 64-66].

In humans, the abundance of *Bifidobacterium* appears to be lower in overweight, obese, or type 2 diabetic patients than in healthy subjects.

Another species with a low concentration in type 2 diabetes is *Faecalibacterium prausnitzii*. *Bifidobacterium* and *Faecalibacterium prausnitzii* are associated with anti-inflammatory effects. Furthermore, another study indicated that the microbial composition during childhood may predict overweight [30].

In other studies, was identified a higher level of *Staphylococcus aureus* and a lower level of bifidobacteria in the faecal samples of children who became overweight. In a recent study, intestinal microbiota infusion from a healthy donor has been shown to temporarily improve insulin sensitivity in people with metabolic syndrome [2, 67, 68].

Conclusion

Based on clinical, epidemiological, and immunological evidence, changes in the gut microbiota may be a key factor in the incidence of many inflammatory disorders. The recent identification of symbiotic bacteria with strong anti-inflammatory properties and their correlative absence during the disease suggests that certain aspects of human health may depend on the condition of the microbiota. The medical and social reconsideration of microbial flora can generate profound consequences for the health of our future generations. Therefore, it is important to understand the complexity of gut microbial flora and how colonization patterns based on potential disorders can have both immediate and long-term consequences.

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