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# The wheel of microbiome rises, and it falls- the role and results of microbiome transplantation and the recent reports

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## Abstract

**Intoduction:** The gut microbiome plays a significant role in maintaining gastrointestinal health. Microbiota therapies involving fecal product transplantation from healthy donors, for

patients with mild to moderate forms have shown significant potential to induce improvement and remission in patients suffering from inflammatory bowel disease and *Clostridioides difficile*infection. There is growing interest in modulating the gut microbiome with probiotics, prebiotics and microbiota products. The undergoing rapid development over the past decade, while it is encountering some regulations related to the safety use of this method. The following paper describes and analyzes the conclusions that can be drawn from research on microbiota therapies.

**Methods:** The review was based on the analysis of materials collected in the "Pubmed", "Google Scholar", "ResearchGate", using the mentioned below keywords.

**State of knowledge:** Disorders of the intestinal microflora, have serious consequences in the functioning of the gastrointestinal tract and the intestinal barrier, which in turn can lead to metabolic disorders, autoimmune or neurological diseases. Therefore, from the point of view of physicians, it is crucial to learn new methods of identifying the intestinal microflora in each person and to learn techniques for its restoration.

**Summary:** Therefore, from the point of view of physicians of various specialties, it is so important to learn new methods of identifying the intestinal microflora in each person and to learn techniques for its restoration, which can be the basis for treatment or support of the main therapy of many diseases. For many patients who do not respond sufficiently to the therapies used so far, they are the hope for improving therapeutic options, used combination with immunomodulatory drugs to raise the ceiling of their efficacy or as complementary treatment.

**Keywords:** intestinal microbiota, eubiosis, dysbiosis, immune-stimulating bacteria, faecal microbiota transportation, immune-mediated disease

CDI- Clostridium difficile infection,
TMJ- Gut microbiota transfer,
SCFAs- Short-chain fatty acids

**Pathophysiology**

The gut microbiota is referred to as everyone's specific collection of microorganisms colonizing different sections of the gastrointestinal tract. Microorganisms also colonize the skin, respiratory system and genitourinary tract, with the largest population of bacteria, but also viruses, fungi and archaea [1]. In addition, commensal microorganisms collectively contain more than 100 times more genes than the human genome [2]. The main representatives of the gastrointestinal microflora are *Firmicutes* and Bacteroidetes, to a lesser extent *Proteobacteria, Actinobacteria* and *Fusobacteria* [3]. The upper gastrointestinal tract is characterized by rapid transport of food content, so the development of microorganisms here is relatively low. The low pH of the stomach and duodenum also has an inhibitory effect on the occurrence of many bacterial species, except for *Helicobacter pylori*, *Lactobacillus, Streptococcus* and the yeast *Candida albicans*. On the course of the intestine, the abundance gradually increases. *Bacteroides, Lactobacillus* and *Streptococcus* predominate in the jejunum, ranging from 105 cfu/g to 108 cfu/g in the ileum, where *Bacteroides, Clostridium, enterococcus, Lactobacillus, Weillonella, Enterobacteriaceae* predominate. However, the microbial complex is most numerous in the large intestine section, where the total weight of bacteria can reach 1.5-2 kg. Bacteria found in the large intestine belong to four genera: *Firmicutes, Bacteroidetes, Proteobacteria* and *Actinobacteria.* Publications suggest that the abundance of bacteria in a gram of colonic contents is up to 1012 cells, and the total number of species reaches 800-900 bacteria and archaeons [4], [5], [6]. The large intestine has been found to be the home of tǫ:

- mainly completely anaerobic bacteria: *Bacteroides, Clostridium, Ruminococcus, Fusobacterium, Butyrivibrio, Peptostreptococcus*, *Eubacterium* and *Bifidobacterium*;
- Aerobic and relatively anaerobic bacteria: Gram-negative bacilli belonging to the *Enterobacteriaceae* family, Gram-positive *Lactobacillus bacilli*, *Enterococcus* and *Streptococcus granulomas;*
- small amounts of *Candida spp.* ($10^2$–$10^4$ cells in 1 gram of feces).

The quantitative and qualitative composition of microorganisms, as well as the bidirectional interaction of the intestinal environment and the homeostasis of the whole organism, determines the undisturbed functioning of the host-microbiota system.

In a rich intestinal ecosystem, symbiotic, commensal and pathogenic microorganisms compete for a site of adhesion to the intestinal epithelium and for nutrients. It has been confirmed that administration of probiotic strains to patients can protect them from infections caused by pathogenic bacteria. A well-known example is the prevention of diarrhea associated with antibiotic using *Lactobacillus rhammnosus GG* or *Sacharomyces boulardii* strains, the use of which reduces the risk of post-antibiotic diarrhea by 42 to 56% [7]. Gut dysbiosis has been found in patients with functional gastrointestinal disorders such as diarrhea, bloating, constipation, who simultaneously had irritable bowel syndrome, atopic dermatitis, and psychiatric (despression, schizophrenia) and neurodevelopmental disorders. The association of gut microbiota disorders with civilization diseases of obesity, hypertension, type 2 diabetes and the risk of cardiovascular disorders has been increasingly postulated.

The strongest negative effects on the quantitative and qualitative composition of the intestinal microbiota are medications and stimulants, severe stress, and food. Antibiotics, proton pump inhibitors and non-steroidal anti-inflammatory drugs are particularly frequently abused therapeutic agents. The results of recent studies indicate that PPIs induce dysbiosis by significantly modifying the composition of the intestinal microbiota. This effect is greater the more strongly the secretion of hydrochloric acid in the stomach is inhibited. The acidic environment of the stomach is a natural barrier to bacteria arriving with food and flowing with saliva from the oral cavity, which is a rich reservoir of various microorganisms. PPIs weaken this barrier, resulting in more bacteria from the mouth entering the intestines. The resulting dysbiosis of the gut flora creates conditions that predispose to the growth of *Clostridioides difficile.* Possibly the main agents cited as potential violators of intestinal homeostasis. It is interesting to note that agents with a strong and rapid effect on microbial changes also include dietary regimens. In human studies, it has been observed that modifying a high-fat and low-fiber diet to a low-fat and high-fiber diet causes significant changes in the intestinal microflora in as little as 24 hours. In addition, the diet used also correlates with the enterotype found in the individuals in question. Bacteroides predominate in people who eat a diet rich in animal fats, while those who eat a diet rich in carbohydrates have an enterotype dominated by *Prevotella* [8]. Inhabitation of the gastrointestinal tract by specific microorganisms, is associated with their production of specific metabolites that affect the function of the digestive, nervous and immune systems. In addition to breaking down the remains of undigested food, they provide substrates for biochemical pathways. One of the most important metabolites, include the short-chain fatty acids (SCFAs) formed because of fiber

fermentation, which include butyric acid, acetoacetic acid and propionic acid. SCFAs have been shown to affect the integrity of the intestinal epithelium, which is also crucial in maintaining the intestinal barrier. If, as part of the diet, they are not supplied in adequate amounts of dietary fiber, microorganisms use less favorable sources to produce SCFAs, and as a result, the ferment activity of the microflora and the number of short-chain fatty acids as products are reduced. This, supplementing the diet with dietary fiber, acts to restore the balance in the composition of microorganisms, reduces the concentration of toxic metabolites, and most importantly, increases the number of SCFAs [9]. In addition to fatty acid synthesis, mention should be made of the microbiota's ability to produce amino acids, including glutamic acid (GLU), which is an essential substrate to produce one of the most important neurotransmitters, gamma- aminobutyric acid (GABA). GABA in the gastrointestinal tract is produced by bacteria of the genus *Lactobacillus* and *Bifidobacterium* with particular emphasis on *Latobacillus brevis* [10].

**Factors influencing gut microbiota composition in human**

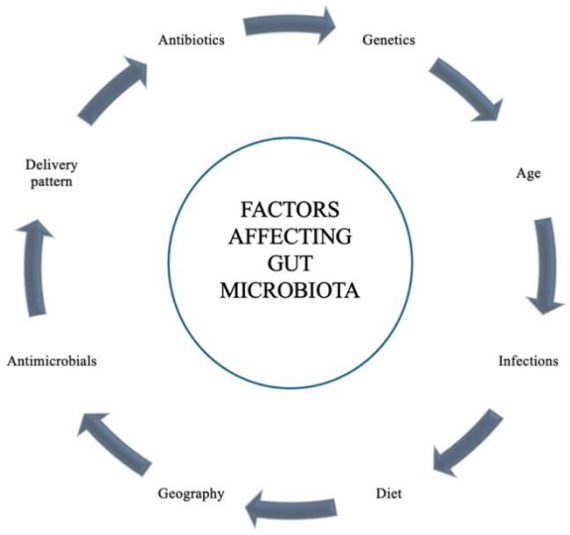


Fig.1. Factors affecting gut microbiota

The intestinal microbiota forms a complex and active system that supports immunity and ensures the maintenance of homeostasis in the human body. It stimulates the maintenance of an efficient intestinal barrier and improves the absorption of nutrients. However, certain bacteria are sensitive to factors that can disrupt their quantitative and qualitative composition.

Among the most disruptive factors to the composition of the intestinal microflora are diet, antibiotics, and environmental pollution. There are. Also, some non-modifiable factors like the route of delivery, age or genetic predisposition.

**Establishment and evolution of the microbiota throughout life**

The intestinal microbiota is an integral part of the body, affecting the homeostasis of the system, taking part in the production of specific metabolites that regulate and support the gastrointestinal tract. Changes in the intestinal microbiota reflect pathological processes going on in the human body. At the same time, the microbiota is sensitive to environmental changes, dietary modifications, stress or medications used. Therefore, qualitative and quantitative changes in the microbiota can often be an early symptom of disease, or a component of the cause of the condition. There are also scientific reports showing that a pregnant woman's gut microbiome, her dietary habits and health status have a direct impact on the child's later gut bacteria profile [11]. One of the most key elements determining the colonization of the gastrointestinal tract by the microbiota is delivery and the route of delivery. In a study by Dominguez-Bello et al. showed that the microbiota of newborns born physiologically was similar the vaginal microbiota with a high proportion of lactobacilli, in contrast to newborns born by cesarean section, whose microbiota contained more cutaneous bacteria, for example, Streptococcus, Staphylococcus [12]. There are also reports that unequivocally link intestinal dysbiosis to cesarean section births, which in turn increases the risk of allergies, atopy, bronchial asthma, type 1 diabetes and obesity [13], [14], [15]. An additional issue is the so-called nutritional programming, where the choice of feeding form remains integral. Breast milk is the "gold standard", which, despite the thriving development of available formula mixes, still fails to match its bioactivity. Considering studies, there are reports that in children fed with breast milk, *Bificobacterium* and *Lactobacillus* or protective bacteria predominate, with much smaller amounts of *Clostridium* and *Escherichia bacteria* [16].

**The role of selected representatives of the intestinal microbiota**

The most abundant bacteria in the large intestine are the bacteria that perform protective functions of *Bifidobacterium ssp., Bacterioides ssp.* and *Lactobacillus spp.* They play a significant role in biochemical mechanisms, participating in the breakdown of carbohydrates, proteins (endogenous and exogenous) and lipids. The slightly acidic pH

environment maintained in the intestines has a protective effect, inhibiting the growth of pathogenic bacteria and is maintained through the synthesis of lactic acid by fermentation involving protective bacteria. In addition, *Lactobacillus spp*. Synthesizes hydrogen peroxide with unique properties that inhibit the growth of pathogenic bacteria [17]. The fermentation process also produces fatty acids (SCFAs). Important for maintaining intestinal health is the unstable butyric acid, which is converted into butyrate. It has anti-inflammatory, nourishing and regenerative effects on the intestinal epithelium, and improves intestinal motility, thus ensuring the smooth functioning of the intestinal barrier. Surprisingly, butyric acid has been proven to inhibit the growth and induce apoptosis of colon cancer cells. Among the most significant producers of butyrate are: *Faecalibacterium prausnitzii* and representatives of the genera *Clostridium* and *Butyrivibrio* [18].

**Application of gut microbiota transplantation**

The results of gut microbiota studies offer important information for clinical practice. They make it possible to demonstrate a causal relationship between the gut microbiome and various somatic conditions, such as inflammatory bowel diseases, diabetes, obesity, cancer, cardiovascular diseases, as well as psychiatric diseases - depression, anxiety disorders. Fecal microbiota transplantation is commonly used therapeutically for antibiotic-induced dysbiosis, inflammatory bowel disease or recurrent *Clostridioides difficile* infections, but the context of other diseases microbiota transplantation represents a promising starting point for innovative therapies [19]. Fecal microbiota transplants, which have already been introduced into clinical practice, and the observed phenotypic changes are widely studied to demonstrate the association between specific conditions. Clinical trials in these areas are ongoing. However, there is some controversy regarding the risk-benefit ratio for the use of microflora transplants for indications other than those currently registered by the FDA. There are three forms of administration of the suspension, which is dosed:

-via oral suspension in capsule form, using a naso-duodenal/gastric probe,

-through the gastroscope,

-during a colonoscopy (most common and effective in *Clostridium difficile* infection),

For the treatment of metabolic disorders, the material is administered duodenally.

Donor selection is also important. Thorough donor screening is performed to exclude the risk of transmitting infectious diseases. The history should include the presence of autoimmune, metabolic and cancerous diseases in the donor and among his closest relatives. Adverse effects are observed relatively rarely. The most common were diarrhea on the day of transplantation, abdominal pain and constipation. In another study in 317 patients with CDI [20]. Severe adverse effects were observed in 3 of 317 patients (upper gastrointestinal bleeding, peritonitis or enteritis). In subsequent observations, colonoscopic TMJ did not cause aný adverse effects [21]. However, it is important to note that there are insufficient data on the potential risks between the use of TMJ and the possibility of infections, inflammatory lesions and gastrointestinal cancers [22]. In addition, most patients do not accept this method for cultural and aesthetic reasons. The trials conducted seem to indicatę the great potential of modifying the intestinal microflora in the treatment of various diseases.

## Intestinal microbiota transplantation as the gold standard for Clostrium difficile infection

Fecal microbiota transplant (FMT) is a method where feces from a healthy donor is placed in the recipient's digestive tract to normalize the pathologically altered gut microbiome. The gold standard is the accepted and internationally recognized treatment for recurrent Clostridium difficile infections. The disease is caused by toxins A and B produced by C. difficile, which excessively multiplies in the intestine because of an imbalance in the bacterial flora caused most often by the use (for various reasons) of broad-spectrum antibiotics. The risk of developing infection is greatest during antibiotic therapy and gradually decreases from 1 to 3 months after the end of antibiotic therapy (most patients develop symptoms in the 1st week of antibiotic therapy). The most important tests to confirm Clostridioides difficile infection are stool tests for the presence of these bacteria and their toxins (substances produced by the bacteria that damage the large intestine). This etiology is the most common cause of infectious diarrhea and is a major health care problem worldwide. The course of Clostridium difficile infection can be moderate to severe; with the co-occurrence of watery odorous diarrhea, abdominal pain, increased C-reactive protein (CRP), hypoalbuminemia, peripheral leukocytosis, and acute renal failure. Very severe CDI can lead to dangerous complications such as toxic megacolon or spontaneous colon perforation. Clinically, the

treatment of CDI is hampered by the increasing prevalence of antibiotic resistance and frequent relapses. The only way to break this circulus vitiosus seems to be to restore the gut microbiota with fecal microbiota transplantation (FMT). FMT is a new therapy for CDI that offers the possibility of quickly and permanently eliminating infection by restoring a healthy microbiota. FMT is the process of transferring feces from one or more healthy donors into the intestine of a patient [23]. The success rate of using gut microflora transplantation is 90%, while the success rates of antimicrobial therapy are much lower at 20-30% [24], [25], [26]. The effectiveness of FMT in patients with CDI provides important evidence that dysbiotic gut microflora can be restored by transplanting microbiota from a healthy donor. Results of microbiota transplantation in inflammatory bowel diseases

There are also scientific reports where success rates have been reported for inflammatory bowel diseases (IBD) including Crohn's disease and ulcerative colitis. The pathogenesis of IBD involves a dysregulated autoimmune response to intestinal dysbiosis, which in turn is triggered by exposure to various environmental factors. The bacterium Faecalibacterium prausnitzii accounts for 2 to 15% of the total intestinal microbiota, and reduced abundance of this species and butyrate is observed in patients with inflammatory bowel disease [27].

Fecal microbiota transplantation has been widely used to treat patients suffering from but can also causes IBD flares [28]. It needs to be noted that cases of IBD activation after FMT have been reported. A systemic review published in 2021 collected data on the success of microbiota transplantation treatment in ulcerative colitis, Crohn's disease, where remission rates of 36% and 50.5% were achieved [29], [30]. However, the use of FMT is not an entirely safe procedure, as many cases of people who developed disease exacerbations after the therapy have been reported [31]. Studies have shown that the rate of exacerbation development is about 15-25%, with a higher rate in those who underwent transplantation by the lower administration route than by the oral method [32], [33]. Thus, this therapy remains available only as a clinical trial.

**The role of the microbiota in neurological disorders**

Based on preliminary studies in humans, changes in the microbiome are being pointed to as a potential marker of a developing neurological condition to determine the onset, phenotypic variability and activity of a neurological disease. In addition, the possibility of

using knowledge of the characteristics of microbiome changes to obtain well-defined benefits for the patient seems promising. One area of this research is Parkinson's disease, a neurodegenerative disorder with atrophy of dopaminergic neurons and accumulation of alpha-synuclein in areas of the central nervous system [34]. Accompanying typical motor symptoms, changes in the composition of the intestinal microflora result in an impaired intestinal barrier and increased permeability, which affects cells in the gastrointestinal tract, the immune system and the enteric nervous system. The interplay between the brain and gut and microbiota determines the formation of an anti-inflammatory response, which, in the face of the altered functional composition of the microflora, predisposes to motor and non-motor symptoms of the disease [35]. Recent studies indicate a dependence of the course of Parkinson's Disease on quantitative and qualitative changes in the intestinal microflora. The presentation of postural and gait abnormalities in patients showed a correlation with an increased abundance of Enterobacteriaceae, compared to patients in whom tremor was prevalent. In contrast, a reduction in the Bifidobacterium population may disposition to the onset of manufacturing symptoms [36], [37]. Subjecting to the analysis of the important influence of intestinal microorganisms in the development of Parkinson's disease symptoms, attempts are being made to restore intestinal balance and alleviate disease symptoms using probiotics. Probiotics have been found to reduce anxiety and depression by decreasing GABA Aa2 mRNA expression in the prefrontal cortex and amygdala, but increasing GABA Aa2 in the hippocampus [38]. Learning about the detailed relationship between altered microbiota and specific symptoms of the disease, as well as the search for new therapeutic approaches based on knowledge of the changes taking place within the gut microbiota, offers hope for the effectiveness of future therapies, as well as early diagnosis.

**Indications for gut microbiota transplantation in metabolic diseases**

Transplantation of the gut microbiota (TMJ) increases the diversity of the gut microbiota, which is extremely beneficial. Visceral obesity is one of the leading causes of metabolic syndrome. In recent years, a large role has been attributed to the importance of the gut microbiota, which may be involved in the pathogenesis of obesity, insulin resistance, type 2 diabetes or lipid disorders. So far, promising results from studies involving pro- and prebiotics, used to modify the microbiome, have been very proficient, so researchers are attempting to use gut microflora transplantation from lean individuals for obese people as an

innovative treatment. A study of obese couples and lean twins found that obesity is associated with reduced gut bacterial diversity [39]. These changes involve an increase in Firmicutes and a decrease in Bacteroidetes, but an abnormal quantitative ratio of bacterial types alone cannot be considered a marker of metabolic disorders [40]. Then there is the component of a damaged intestinal barrier, leading to bacterial ingress and generalized endotoxemia, which can translate into chronic inflammation, lipid disorders and consequent obesity [41]. A pilot study was conducted to evaluate the effect of transplanting gut microflora from lean donors on insulin resistance and metabolic syndrome in recipients struggling with these conditions. This method has been shown to improve insulin sensitivity, where the main role is attributed to an increase in the amount of butyric acid produced by gut bacteria during the fermentation process [42]. The effectiveness of gut microflora transplantation in the treatment of diabetes and insulin resistance has been validated by randomized clinical trials. Dysbiosis, obesity, insulin resistance and the development of type 2 diabetes are associated with chronic systemic inflammation involving adipose tissue. Gram-negative bacteria contain LPS and peptidoglycans with pro-inflammatory properties. Fat-rich diet contributes to increased serum LPS levels in humans. A stable microbiota regulates insulin secretion - it is its abnormal composition that may be the reason why some diabetic patients do not respond to drugs with proven beneficial therapeutic effects.

**Clinical practice**

A test that can demonstrate a supportive impact in the practice of family physicians and other specialties associated with conditions that are associated with intestinal dysbiosis is the evaluation of the intestinal microbiota. This analysis includes genetic aspects of non-culturable bacteria and detailed microbiological cultures. There are KyberKompakt Pro microbiota tests on the market. They consist of non-invasive fecal examination- qualitative and quantitative analysis of protective autochthonous microorganisms (anaerobic bacteria of the genus *Bacteroides* and *Bifidobacterium*, *Lactobacilli* of the genus *Lactobacillus,* also producing hydrogen peroxide), immunostimulating bacteria (*Enterococcus* and bacilli of the species E. coli), feeding on the intestinal epithelium (*Faecalibacterium prausnitzii* and *Akkermansia* muciniphila), and proteolytic bacteria (*Clostridium, family Enterobacteriaceae* including *Klebsiella spp*. *Enterobacter spp., Citrobacter spp., Proteus spp.*) and *Pseudomonas*, as well as the total number of bacteria. Many intestinal ailments can run with abnormalities in

the composition of the bacterial intestinal microflora. Symptoms that could indicate this and that should prompt the patient to evaluate the condition of his or her intestines include:
food intolerances, frequent intestinal infections, chronic diarrhea or constipation, frequent abdominal pain, bloating and gas, irritable bowel syndrome. The use of the test can allow the selection of targeted probiotic therapy and individualized treatment according to therapeutic needs. Diet and probiotics, containing clinically tested bacterial strains (most commonly *Lactobacillus* and *Bifidobacterium*, can significantly support the intestinal microflora in this situation [43].

**Perspectives**

Research findings raise high hopes for the high therapeutic potential of treatment with gut microbiota transfer. However, this guess remains the subject of much research, and the available results of randomized clinical trials confirming the efficacy of gut microbiota treatment apply only to the treatment of Clostridium difficile infections, type 1 diabetes and type 2 diabetes/insulin resistance. The effectiveness of TMJ therapy in other conditions induced by intestinal dysbiosis (multiple sclerosis, chronic fatigue syndrome, spontaneous thrombocytopenia, ulcerative colitis, Crohn's disease, irritable bowel syndrome) remains, for now, confirmed only by the results of observational studies [44]. The convention of using intestinal microflora transplantation has long been known. The first descriptions of such a procedure date back to the 4th century in China, where Ge Hong described the use of TMJ in various clinical conditions [45]. Subsequently, there were reports in the literature of Bedouins treating diarrhea by consuming warm camel stool [46]. And in modern medicine, the method was described in 1958 by Eisman et al, who successfully used stool transplantation to treat pseudomembranous enteritis [47]. Despite this long history of application, the validity of further research and clinical trials is postulated. Previously, it was claimed that gut bacteria from healthy donors would replace bacteria in patients. However, Kellermayer's study examined this issue, concluding that TMJ does not result in the repopulation of the recipient with new microorganisms, but acts as shock therapy on the host microflora and has a stimulating effect on its activity [48]. There is no reliable evidence straddling which of these postulates is more plausible. Microbiota transfer methods are currently devoid of the unpleasant sensations associated with the smell or taste of the therapeutic method, as freeze-dried preparations in enteral capsules are used. Alternative methods to the use of TMJ remain

the administration of pre- and probiotics with clinically proven efficacy of the bacterial strains in question. These are also interventions with a superior safety profile against most patient groups. Single-strain formulations containing Lactobacillus plantarum 299v or bifidobacterium infantis 35624 are available, as well as multi-strain probiotics combined with prebiotics.

**Latest findings**

Studies are now linking certain microbiota such as *Butyricimonas, Akkermansia* and *Odoribacter* to healthy aging. Moreover, clinical and preclinical studies have shown, promising mechanisms for restoring quality microbiota through diet, physical activity interventions. Based on senior patients comorbidities, an individualized approach is needed to achieve optimal microbiome functional outcomes. It is highly likely that there are certain features of the microbiome that confer longevity. For example, bacterial strains that are often reduced in the elderly, such as *Christensenella* and *Bifidobacterium*, are increased in semi-supersenior citizens (i.e., 105-109 years old), suggesting their beneficial effects. Additionally, the highly studied taxon *Akkermansia*, which is abundant in healthy aging, is even more dramatically increased in extreme aging [49]. An excellent example of aging mechanisms related to the gut microbiome I axis is illustrated by a study by Parker et al. A study by Parker et. al demonstrated that transfer of an "aged" microbiome from elderly mice to younger mice caused several age-associated phenotypes including advanced central nervous system deterioration and vision deficits. Importantly, in a set of correlating experiments, age-related changes improved in elderly mice after microbiome transplantation with stool of younger mice [50]. Although, we know that microbiome compositions shift throughout the aging process, the exact mechanisms for this are unclear. Below, we explore some common life changes and medical conditions among the elderly in which intestinal microbiomes are altered. Medicine is moving toward a individualized field. With innovations in genetics and biomarker capabilities, the microbiome profile must be considered in diagnosis and treatment. A common theme of many of the studies available to date is the role of individualized care, with therapies based on prior analysis of the patient's microbiome. Nevertheless, early research suggests that there is potential to reverse the aging microbiome with interventions such as microbiota transplantation, dietary modifications and physical activity.

## Conclusion

The involvement of the microflora in the onset, development and maintenance of inflammation, in the course of many diseases and clinical conditions, is currently not in doubt. However, it remains an object of research whether differences in the composition and function of the intestinal microflora, are in the given diseases the primary factor and direct cause of the clinical condition, or whether it is a consequence of reactions and changes as a secondary consequence. Scientists have yet to identify one specific healthy microbiome, and it is generally agreed upon that there is no singular "normal" composition. It is always depending on factors that influence the microbiome, including diet, genetics, environmental conditions. When commensalism between host and microbes is disrupted, many human diseases can result, and the microbiome transfer method in the face of this disruption remains extremely promising. The hope remains to bring nagging ailments under control and, in the long run, to achieve permanent remissions using gut microbiota transfer.

All authors have read and agreed with the published version of the manuscript.
The authors report no conflict of interest.

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