Microbiome and Human Health: From Dysbiosis to Therapeutic Interventions

13

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Abstract

Human body is a complex system housing multiple biomes such as virome, microbiome, and eukaryome which governs human health. Unicellular archaea, bacteria, virus, and multicellular eukaryotes together regulate the physiological functions along with the internal homeostatic mechanisms. With the next-generation sequencing technology, the composition of the "internal biome" and its role in health and disease has become much clearer. Joshua Lederberg coined the term "microbiome" in 2001, which defines the full complement of microbes (bacteria, viruses, fungi, and protozoa), their genes, and genomes in or on the human body. Human Microbiome Project was launched in 2007 through 2016 by the National Institutes of Health to characterize the genomic makeup of all microbes inhabiting the human body and analyze its role in health and disease. Bacteria outnumber the human cells tenfold and make up about 1–3% of body mass. The composition of the microbiome changes during the lifetime, impacting human physiology in healthy and diseased state by modulating the metabolic and immune functions. The current chapter provides an introduction to the "human

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microbiome" and also compares the bacterial diversity in healthy and diseased state. A comparison of microbiome of Indian and Western population has also been added. Gut bacteria play a regulatory role in the metabolism and have a strong connection with brain, influencing behavior. Some bacterial species are found to be either abnormally abundant or reduced in certain diseases. Dysbiosis or imbalance in microbial flora has been recognized as a cause or consequence. Therefore there is a need to adopt certain therapeutic strategies for restoring the balance of microbiome.

Keywords

Microbiome · Dysbiosis · Gut microbiome · Homeostasis · Therapeutic strategies

13.1 Introduction

Microbes which include unicellular archaea, bacteria, virus, and multicellular eukaryotes are present in virtually every habitat on earth and in every organism. For example, a reference man weighing 70 kg would have approximately 3.8×10^{13} bacteria, which weigh about 0.2 kg and in the body, they work in a coordinated fashion performing various functions in metabolism (Sender et al. 2016). These trillions of microorganisms belong to thousands of different species (Kumar et al. 2022). The robustness in data generation and interpretation has shown the obvious role of these species in health homeostasis (Lynch and Pedersen 2016). Not only this, but also multiple reports suggest that human health is influenced by multiple microbiota interactions throughout their lives (Milani et al. 2017; Collado et al. 2012; Song et al. 2021). The multispecies microbial communities found in human hosts show a wide range of behavior depending on their microenvironment, which can be dynamic, interactive, commensal, or parasitic (Hou et al. 2022). Humans alone represent several ecological niches with different compositions and relative abundances of microbiota, such as the skin microbiome, oral microbiome, gut microbiome, urogenital microbiome (Hou et al. 2022). In order to maintain human health, the human gut microbiota play crucial roles in assisting in the breakdown of food substances and liberating nutrients inaccessible to the host otherwise (Kumar et al. 2020). Additionally, they modulate the immune system by triggering immune cell differentiation, protecting the host from pathogen colonization (Hou et al. 2022; Kumar et al. 2020). Microbes begin colonizing the neonatal gut immediately after birth. Early gut commensals are shown to be shaped by the immediate environment, especially the mother's microbiome (birth canal microbial interactions, followed by nursing) (Milani et al. 2017).

The gastrointestinal microbial composition majorly defines the state of health and disease of an individual through various metabolic processes. The recent scientific interpretations suggest that these microbial populations are not static and keep fluctuating based on environment and lifestyle (Flandroy et al. 2018; Nguyen et al. 2021). Coming on to the roles of microbes in the gut, they perform a vast range of

functions such as degradation of undigested carbohydrates, production of vitamin B, antioxidants, protection against pathogens, etc. (Milani et al. 2017; Kumar et al. 2020). During the degradation of undigested carbohydrates in large intestine, these microbes produce the short-chain fatty acids (SCFA) through fermentation (den Besten et al. 2013). The food quantity and type determine the amount and type of SCFA production. Their concentration varies between 50 and 200 mM in the large intestine, mostly contributed by acetate (60%), propionate (25%), and butyrate (15%) (den Besten et al. 2013; McNabney and Henagan 2017). The *Bacteroidetes* phylum mainly produces acetate and propionate, while the butyrate is produced by the phylum *Firmicutes* (Magne et al. 2020). These SCFAs differ in their fate and tissue distribution as butyrate is the most preferred energy source by the gut mucosa, while the propionate mostly contributes to the gluconeogenesis in the liver and acetate is taken up for synthesis of essential molecules such as cholesterol, long-chain fatty acids, glutamine, and glutamate (Magne et al. 2020; Correa-Oliveira et al. 2016). These SCFAs are also known to regulate immune and inflammatory response and thus are considered to benefit health, including protection against colorectal cancer (Correa-Oliveira et al. 2016). Due to the abundance of these microbes in the lower gastrointestinal tract, this microbial mass is a significant contributor of fecal bulk and thus their presence and diversity can easily be detected with a scoop of fecal sample. Till now, there are numerous studies on human microbiome composition and it has been estimated that the collective human microbiota is composed of over 35000 bacterial species and over 10 million nonredundant genes (Jandhyala et al. 2015).

One of the major key players apart from environment and host genetics which defines the microbial relative abundance in a specific population is diet (Singh et al. 2017). The current paradigm shift in research mainly complies with the impact of different nutrients in shaping the gut microbial community. Nonetheless, defining the proper impact of a specific nutrient in a complex microbial niche still remains a challenge. Understanding this will be the main priority of the upcoming research.

13.2 Microbiome in Healthy Individuals and Its Impact

13.2.1 Gut Microbial Composition

The most abundant phyla in a healthy gut comprise *Firmicutes*, *Bacteroidetes*, *Actinobacteria*, and *Proteobacteria (*Xiao et al. 2021*;* Das and Nair 2019*)*. The genus under firmicutes which are most abundant include *Clostridium*, *Lactobacillus*, *Streptococcus*, *Enterococcus*, *Ruminococcus*, *Faecalibacterium*, *Eubacterium*, *Catenibacterium*, *Megamonas*, *Veillonella*, etc. The two most abundant genera which belong to phylum *Bacteroidetes* include *Prevotella* and *Bacteroides*. *Bifidobacterium*, *Olsnella*, *Collinsella*, *Eggerthella* are the other dominant genera which belong to phylum *Actinobacteria*. *Eschericia* and *Shigella* are the abundant genera from phylum *Proteobacteria*. When the gut undergoes dysbiosis, the composition of microbes and their ecology shifts to an extent that it overcomes their

resilience proficiencies. Thus, leading to the onset of variety of diseases namely inflammatory bowel disease (IBD) (Glassner et al. 2020), cardiovascular diseases (Witkowski et al. 2020), rheumatoid arthritis (Zaiss et al. 2021), colon cancer (Garrett 2019), depression (Lach et al. 2018), Parkinson's disease (Sampson et al. 2016), etc.

A healthy human gut microbiota predominantly differs between individuals based of factors such as diet, antibiotics, age, sex, host genetics, immunity (hyperimmunity or immunodeficiency), etc. and it keeps changing throughout the life (Das and Nair 2019). The massive data interpretation in the recent past focused on the microbe centric indicator of different populations. Based on the abundance of different taxa, the enterotypes are broadly divided in three categories: Enterotype 1: The best indicator of this enterotype is *Bacteroides* (a genus of Phylum *Bacteroidetes*); Enterotype 2: This enterotype is driven by genus *Prevotella* (another genus of Phylum *Bacteroidetes*) whose abundance is inversely proportional to *Bacteroides*, Enterotype 3: *Ruminococcus*, a genus of phylum *Firmicutes* distinguishes this enterotype (Costea et al. 2018). Countries like the USA, where people mostly consume animal-based diets and therefore their microbiota is mostly dominated by *Bacteroides*, while countries like India, where people prefer plant-based diets, the genus *Prevotella* dominates, suggesting the role of diet in shaping the microbial community (Costea et al. 2018). The third enterotype is common in European samples as the members of genus *Ruminococcus* are known to degrade mucins and subsequent hydrolysis of complex carbohydrates into simple sugars (Arumugam et al. 2011). The concept of enterotypes lies in the idea that they will be identifiable in the human microbiome of any cohort irrespective of age, gender, body weight, and national division.

Several studies have shown that microbial diversity in the form of a microbiome in the human body is extremely important for maintaining human health (Jandhyala et al. 2015; Das and Nair 2019; Clapp et al. 2017). As explained, dysbiosis of the microbiome has been linked to a large number of diseases (Glassner et al. 2020; Garrett 2019; El-Salhy et al. 2021; Horn et al. 2022). Therefore, it becomes extremely important to study what constitutes a healthy microbiome and what functions these microbes are performing. However, understanding what constitutes a healthy microbiome is challenging as the microbiome is affected by personal hygiene, genetics, gender, diet, lifestyle, and geography of stay for different individuals. Several populations' specific studies from all around the world have documented the diversity of microbes associated with different surfaces of the human body (Potbhare et al. 2022; Mahajan et al. 2022; Moffatt and Cookson 2017). Healthy individuals from different countries have been shown to have major differences in microbiome composition. In addition to this, the microbiome is reported to shift with the progression of the age of the individuals as well. Another limitation in deciphering what constitutes a healthy microbe is the presence of microbial dark matter, i.e., uncharacterized microbes.

The most widely studied microbiome from the human body is from the skin, gut, vagina, nasal cavity, oral cavity, conjunctiva, lung, urethra, bladder, uterus, placenta, and biliary tract (Table 13.1).

Table 13.1 The comparison of microbial diversity in Western and Indian populations

Microbiome	Western population	Indian population	References
Skin	Gram-positive genera: *Staphylococcus* spp., *Corynebacterium* spp., *Enhydrobacter* spp., *Micrococcus* spp., *Cutibacterium* spp., and *Veillonella* spp Gram-negative bacteria (GNB): *Roseomonas mucosa*, *Pseudomonas* spp., *Acinetobacter* spp., *Pantoea septica*, and *Moraxella osloensis* as commensal residents	*Staphylococcus*, *Bacillus*, *Corynebacterium*, and *Anaerococcus*, *Pseudomonas*, *Arthrobacter*, *Anaerococcus*, *Oceanobacillus*, *Cutibacterium*, *Acinetobacter*, *Salmonella*, *Moraxella*, *Pantoea*, *Enterobacter*, *Exiguobacterium*	Potbhare et al. (2022), Skowron et al. (2021)
Gut	*Lactobacillus*, *Bacillus*, *Clostridium*, *Enterococcus*, *Ruminicoccus*, *Bacteroides,* and *Prevotella*	*Prevotella*, *Dialister*, *Bacteroides*, *Megamonas*, and *Succinivibrio*	Rinninella et al. (2019), Chaudhari et al. (2020)
Vagina	*Lactobacillus* species such as *L. crispatus*, *L. gasseri,* and *L, jensenii*	In North East Indian Women: in addition to *Lactobacillus*, *Staphylococcus,* and rarely by *Propionibacterium avidum*, *Bacillus subtilis*, *Escherchia coli*, *Janthinobacterium lividum,* and *Kocuria kristinae*	Mahajan et al. (2022), Das Purkayastha et al. (2019)
Nasal cavity	*Firmicutes*, *Bacteroidetes*, *Proteobacteria*, *Actinobacteria*, *Cyanobacteria*, *and Fusobacteria*	No study	Chen et al. (2022)
Oral cavity	774 oral bacterial species identified and recorded in human oral microbiome database	*Neisseria*, *Streptococcus*, *Prevotella*, *Porphyromonas*, and *Haemophilus*	https://www.homd.org/ Chaudhari et al. (2020)
Conjunctiva	*Corynebacterium*, *Pseudomonas*, *Staphylococcus*, *Acinetobacter*, *Streptococcus*, *Millisia*, *Anaerococcus*, *Finegoldia*, *Simonsiella*, and *Veillonella*	Only fungal microbiome deciphered *Ascomycota*, *Basidiomycota*, *Zygomycota*	Huang et al. (2016), Prashanthi et al. (2019)
Lung	*Firmicutes*, *Bacteriodetes*, *Proteobacteria*, *Fusobacteria*, and *Actinobacteria* Genera*: Prevotella*, *Veillonella*, and *Streptococcus* spp	No study	Moffatt and Cookson (2017)

13.2.2 Brain-Gut-Microbiome (BGM)

The term "gut-microbiota-brain axis" describes the web of connections involving various biological systems that permit bidirectional communication between gut bacteria and the brain and is essential for preserving the homeostasis of the gastrointestinal, nervous, and microbial systems of animals (Morais et al. 2021).

Thus, a model of two-way communication between the gut, its microbiome, and the central nervous system (CNS), known as the BGM system, is being supported by new research. The three hubs in the wider BGM network are the microbiome, the gut connectome, and the brain connectome (Horn et al. 2022). The brain and gut microbiome thus communicate largely through the neuronal, endocrine, and immunoregulatory pathways (Osadchiy et al. 2019; Slyepchenko et al. 2017). Some of the molecules derived from microorganisms are ingested and travel to the brain via the vagus nerve and/or systemic circulation. Similar to this, the brain can also modify the microbiome indirectly through changes to the gut microbial environment or directly through the influence of neuroactive molecules released into the gut lumen, affecting gene expression and the behavior of microbes.

In continuation, tryptophan, an important amino acid, serves as a precursor for several neuroactive signaling molecules, such as serotonin, kynurenine, and indoles (Gao et al. 2020). Conversely, the synthesis of indoles is solely dependent on the metabolism of gut microbes, unlike the production of serotonin and kynurenine, which microorganisms just modulate (Yano et al. 2015; Tolhurst et al. 2012). The brain needs a variety of compounds to remain healthy and operate properly, and indoles are the precursor molecules for many of these neurotransmitters. In the GI tract, brain, and systemic circulation, these have been identified (Agus et al. 2018). Indole is further metabolized by the liver, and one of these by-products, indoxyl sulfate, is thought to have an impact on ASD, AD, and depression, among other brain illnesses (Osadchiy et al. 2019).

13.3 Disease, Dysbiosis, and Microbiome

Human microbiome has a great impact on health and diseases; however, to understand its role, it is important to know the microbial load as well as the diversity inhabiting different regions of the body (Das and Nair 2019). In diseases, the balance of diverse microorganisms is disturbed leading to a condition, termed dysbiosis (Jandhyala et al. 2015; Das and Nair 2019). In a healthy individual, the cross regulation and cross talk among microbes present in different parts of the body maintain the homeostasis balance. However, when the balance between the "beneficial" and "pathogenic" microbes is altered, the body shifts from an equilibrium state to a state of chaos, disturbing the underlying regulatory mechanisms of the healthy state. Dysbiosis can arise as a result in change of composition of microbial flora either by the loss of beneficial microbes or increase in pathogenic species, thus altering the entire microbial diversity of a homeostatic body (Glassner et al. 2020; Garrett 2019; El-Salhy et al. 2021; Horn et al. 2022; Chen et al. 2022).

Amongst all the systems of the human body, the gut is recognized as the most diverse region followed by skin and mouth. Gut microbiota is highly diverse probably due to different food habits of individuals and it varies from individual to individual (Li et al. 2012). Further, microbial communities in gut are mainly anaerobes outnumbering facultative anaerobes and aerobes. Human gut is found to harbor more than 50 bacterial genera to date but the dominant gut colonizers majorly belong to Bacteroidetes, Firmicutes, Proteobacteria, and Actinobacteria (Bull and Plummer 2014). It is reported that changes in the gut community structure have implications on human health, diseases, and treatment. Past studies were mainly focused to ascertain the gut microbiota changes between healthy individuals; however, with newer sequencing technologies, and improved computational tools, the exploration of normal healthy gut microbiota versus altered microbiome in diseased individuals has been an area of extensive research. There is a complex interplay between gut microbiome and neurodegenerative diseases and gastric inflammatory diseases (Table 13.2). Neurodegenerative diseases are regulated by the gut-brain axis that involves cross talk between gut microbiota and nervous system. Broadly they interact via three pathways, i.e., chemical signaling; neural pathways; and immune system (Fig. 13.1). There are a number of dysbiosis-related diseases which are mentioned in the Table 13.2 (Chen et al. 2021).

13.4 Therapeutic Strategies to Restore the Microbiome Balance

The recent microbiome research is expanding at a great pace. So far, this research has generated multiple strategies that are known to restore the microbial diversity within and help to control the various pathological conditions. Some are personalized dietary modulation, inclusion of probiotics, prebiotics, symbiotic, phage therapy, fecal transplantation, etc. which are discussed below.

13.4.1 Diet and Microbiome

The majority of the microbes in the gut are symbiotic (beneficial to both the human body and the microbiota), while a tiny number are harmful (promoting disease) as well. Pathogenic and symbiotic bacteria can coexist together in a healthy body. As mentioned earlier, the diet significantly influences the types of bacteria that exist in the colon, in addition to environmental factors, medication use, and genetics from the family (Flandroy et al. 2018; Singh et al. 2017; Chaudhari et al. 2020; Slyepchenko et al. 2017). Each individual's microbiome is distinct due to these characteristics. The diversity of bacteria in the gut can be influenced by dietary choices and certain foods. The addition of fruits and fiber-rich diets may elevate the production of SCFA, while in return helps in maintaining healthy gut (den Besten et al. 2013). In addition to having a substantial impact on the gut flora, diet can alter the anatomy and function of the brain (Horn et al. 2022). It is also well established that changes in the gut microbiota's composition or activity affect both health and

Table 13.2 Association of microbiomes with various diseases (↑ increased, ↓ decreased)

S. No.	Disease	Role of gut microbiome (GM)	References
1	Parkinson disease	*Bifidobacterium*, *Pasteurella*, and *Enterococcus*↑ *Brautella*, *Prevotella*, and *Faecoccus*↓	Hill-Burns et al. (2017), Hopfner et al. (2017), Peng et al. (2018), Scheperjans et al. (2015), Bedarf et al. (2017), Heintz-Buschart et al. (2018))
2	Alzheimer disease	Similar to Parkinson disease along with ↑ in proinflammatory bacteria *Escherichia* and *Shigella*	Hill-Burns et al. (2017), Hopfner et al. (2017), Peng et al. (2018), Scheperjans et al. (2015), Bedarf et al. (2017), Heintz-Buschart et al. (2018), Minter et al. (2017)
3	Cardiovascular diseases (CVD) like hypertension; atherosclerosis	Different metabolic products of GM like trimethylamine oxide (TMAO); SCFAs; bile acids interact and influence occurrence of CVD	Yan et al. (2017), Yang et al. (2015)
4	Obesity	*Fermicutes*↑ *Bacteroides*, *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*↓	Turnbaugh et al. (2006), Vallianou et al. (2019)
5	Type I diabetes	*Clostridium*, *Prevotella*↓	Zhou et al. (2020)
6	Type II diabetes	*Dallella*↑ *Bifidobacteria*, *Akkermansia*↓	Li et al. (2020)
7	Gestational diabetes	*Desulfovibrio*, *Enterobacter*, *Prevotella*, *Ruminococcus*, *Bacteroides*↑ *Bifidobacterium*, *Fischeri*↓	Crusell et al. (2018)
8	Nonalcoholic fatty liver disease	*Lactobacillus*, *Streptococcus*, *Dorea*↑ *Prevotella*, *Ruminococcus*, *Flavobacterium*↓	Da Silva et al. (2018), Raman et al. (2013), Jiang et al. (2015)
9	Inflammatory bowel disease	*Enterobacter and Proteobacteria*↑ *Firmicutes*↓	Caruso et al. (2020), Li et al. (2014)
10	Colorectal cancers	*Escherichia coli*, *Bacteroides fragilis*, and *Fusobacterium nucleatum*↑ *Bifidobacteria*, *Lactobacillus*, and *Bacteroides*↓	Si et al. (2021), Tsoi et al. (2017)
11	Asthma and allergic rhinitis	*Rothia*, *Bacteriodes*, *Propionibacterium*, and *Corynebacterium*↑ *Sphingomonas*, *Halomonas*, and *Streptococcus* sp.↓	Chen et al. (2022), Sokolowska et al. (2018)
12	Anxiety and depression	*Actinomycineae*, *Coriobacterineae*,	Barandouzi et al. (2020)

(continued)

Table 13.2 (continued)

S. No.	Disease	Role of gut microbiome (GM)	References
		Bifidobacteriaceae, *Clostridiales incertae sedis XI*, *Porphyromonadaceae*, *Clostridiaceae*, *Lactobacillaceae*, *Streptococcaceae*, *Eubacteriaceae*, *Thermoanaerobacteriaceae*, *Fusobacteriaceae*, *Nocardiaceae*, *Streptomycetaceae*↑ *Veillonellaceae*, *Prevotellaceae*, *Bacteroidaceae*, *Sutterellaceae*, *Oscillospiraceae*, *Marniabilaceae*, and *Chitinophagaceae*↓	
13	Atopic dermatitis	*Staphylococcus aureus*, *Streptococcus*, *Gemella*, and *Haemophilus*↑ *Dermacoccus*↓	Kim and Kim (2019)
14	Psoriasis	*Firmicutes*, *Staphylococcus*↑ Actinobacteria, *Corynebacterium*↓	Chen et al. (2020)

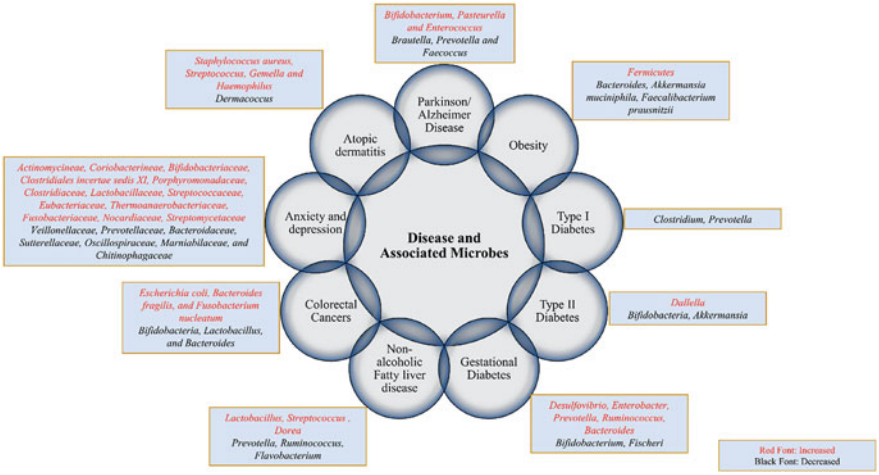

Fig. 13.1 Microbial dysbiosis and their association with disease (family/genus)

disease. The host bacterial species that are already present undergo predictable modifications as a result of the consumption of a particular diet (Singh et al. 2017), although these interactions are complex and might vary depending on the individual (Asnicar et al. 2021).

13.4.2 The Role of Probiotics as Therapeutic Agent

One of the earliest examples of use of probiotics for improving human health was in the early nineteenth century (Wieërs et al. 2020). Diarrhea and constipation among children is treated with *Bifidobacteria*. Incidentally *Bifidobacterium* is among the first bacterial species which colonize the intestine in newborns during the birth. Probiotics have been extensively used for diseases of the gut and skin (Kumar et al. 2020; Wieërs et al. 2020).

Probiotics help to replace the pathogenic bacteria and restore the eubiosis of the gut microbiome. These are defined as live microorganisms which when administered in adequate amounts can confer health benefits on the host. After prolonged antibiotic treatment, chronic diseases, and general health, dysbiosis can be reversed or prevented by the use of probiotics in the diet. Mostly *Lactobacilli*, *Bifidobacteria*, *Enterococci*, *Propionibacteria*, *Staphylococcus*, and some other species are used as probiotics (Kumar et al. 2020; Wieërs et al. 2020). These strains are regarded as safe for consumption as they form normal components of the gut microbiome. Probiotics provide both immunological and nonimmunological benefits including activation of local macrophages, modulation of cytokine profiles, production of immunoglobulins (Wieërs et al. 2020).

Prebiotics on the other hand, are the nonstarch polysaccharides and oligosaccharides in the diet which stimulate the growth and metabolic activity of beneficial bacteria in the gut (Kumar et al. 2020). Prebiotics include fructooligosaccharide supplements (FOS), galactooligosaccharides, inulin (also able to increase calcium absorption), lactulose (a synthetic disaccharide used as a drug for the treatment of constipation and hepatic encephalopathy), and breast milk oligosaccharides (Kumar et al. 2020). These nondigestible carbohydrates are a source of energy for intestinal bacteria (den Besten et al. 2013). Nowadays, common formulations of prebiotics and probiotics are available which are referred as synbiotics (Kumar et al. 2020).

13.4.3 Personalized Responses to Dietary Composition

Diet affects the microbiome and microbiota in turn affects disease risk. In order to predict a person's metabolic response to foods based on personal characteristics, the Personalized Responses to DIetary Composition Trial (PREDICT) used both standardized "test" meals and collected "free-living" nonstandardized food consumption (Berry et al. 2020). In this study, more than 1098 people were investigated by the researchers, and deep metagenomic sequencing was performed on 1203 of

these gut microbiomes. In order to assess the dietary patterns of the participants, the researchers gathered comprehensive, long-term data on dietary intake from each of these individuals. This study found that the panel of intestinal species linked with good cardiometabolic and postprandial indicators overlapped with those related with healthy eating practices. The panel of intestinal species linked to good cardiometabolic and postprandial indicators coincided with those linked to healthy eating habits (Asnicar et al. 2021).

This study acquired the data on a wide range of factors, including pre- and postmeal assessments of blood sugar (glucose), cholesterol, and inflammation, which are known to affect metabolism and disease risk. Additionally, measurements were made of the study participants' age, weight, body fat, body mass index (BMI), and blood pressure (Asnicar et al. 2021). *Prevotella copri* and *Blastocystis* spp. were detected, indicating that postprandial glucose metabolism was favorable. These microorganisms were also connected with a wide range of cardiometabolic blood indicators, such as fasting and postprandial glycemic, lipemic, and inflammatory indices (Asnicar et al. 2021). Loss of keystone species, such *Faecalibacterium prausnitzii* (Banerjee et al. 2018), which control microbiome form and function, is unmistakably linked to a range of disease conditions.

Dietary habits that are less nutritious (such as dairy desserts, fatty meats, and processed foods) were seen to promote gut species that correlate with high blood sugar, cholesterol, and inflammatory conditions, all of which are strongly linked to a higher risk of cardiac events, strokes, and type 2 diabetes. On the contrary, a more varied gut microbiota was seen to be associated with good eating habits (high-fiber foods like spinach and broccoli, almonds, and healthy animal meals like fish and eggs), and polyunsaturated fats (fish, walnuts, flax and chia seeds, sunflower, etc.). All of which in turn correlated well with the metrics associated with a reduced risk of developing several chronic diseases (Asnicar et al. 2021). The gut microbiome can thus, flourish when minimally processed plant meals are chosen, it helps protect from and lowers the risk of chronic diseases like heart disease, diabetes, metabolic disease, and obesity (Asnicar et al. 2021).

Nevertheless, distinguishing correlation from causation is one of the most difficult tasks in microbiome research.

13.4.4 Precision Nutrition in Cancer

Dietary habits are also predicted in raising the risk of developing cancer (Zhu et al. 2013). Separately, many malignancies are influenced by microbial factors. More research is required, though, to fully comprehend how nutrition and the microbiome interact to affect how well cancer treatments work (Greathouse et al. 2022). Higher intakes of fiber, calcium, omega-3 fatty acids, and milk are specifically linked to a decreased risk of death from colorectal cancer (CRC), whereas whole-grain consumption is linked to a lower risk of death from CRC specifically (Song et al. 2017, 2018; Yang et al. 2019). On the other hand, a CRC diet high in processed meat is linked to a worse rate of disease-free survival (Zhu et al. 2013).

13.4.5 Antimicrobial Therapy

In sepsis patients, antimicrobial therapy with appropriate dosage and duration helps to provide protection against toxins and antigens of the harmful microflora (Niederman et al. 2021). During the sepsis disease, there is a dysregulation in the host response to infection. Bacteroidetes abundance in contrast to *Firmicutes* in stool samples of the deceased patients has been confirmed in case of sepsis death (Ojima et al. 2016). Surviving patients had higher ratios of *Pseudomonas aeruginosa*, *Bifidobacteria,* and other *Actinobacteria*. Antimicrobial therapy is provided to ill patients with β-lactamase inhibitor combination, cephalosporins, carbapenems, and fluoroquinolones (Bhalodi et al. 2019). Targeted antimicrobial therapy can be one of the ways to restore the original gut microbiota in the sepsis patients. However, there is a need for research to understand the effects of the dosage so that unnecessary exposure can be avoided.

13.4.6 Lifestyle Modifications

Overindulgence and consumption of processed food, fats, sweeteners, smoking, drinking, drugs, etc. has changed the normal microbiota with which a person is born. The gut dysbiosis is disturbed by an unbalanced diet, sleep deprivation, emotional stress or even genetics (Redondo-Useros et al. 2020). By changing sedentary lifestyle and including a high-fiber diet with water and high protein, a person can restore the balance of intestinal microflora. Exercise combined with a nourishing diet can help to improve cardiovascular health, weight loss, and improved insulin sensitivity.

13.4.7 Fecal Microbiota Transplantation

FMT is a method that involves administering the patient (i.e., the recipient) specially prepared stool material from healthy donors in an effort to treat certain medical disorders by reestablishing the balance of the gut microbial population (Ser et al. 2021). Currently, FMT is focused primarily on transferring bacteria from the donor to the recipient and these microbes are being isolated and purified to understand their precise roles (Aggarwala et al. 2021). However, evidence is pointing increasingly toward the possibility that bacteriophages are also contributing to FMT's efficacy in treating recurrent *Clostridium difficile* infections (Hanssen et al. 2021). Altogether, the microbiome alone can significantly modify human physiology (de Groot et al. 2017). The ability of FMT from lean donors to reorient host glucose metabolism is influenced by the recipient's initial microbial composition (Ser et al. 2021). This may be partially explained by the fact that following FMT, species from both donors and recipients continued to exist in the gut, illustrating the difficulties in effectively altering the microbiome's composition (Li et al. 2016). In spite of limited safety data

and major safety concerns, the FMT seems to be very effective in the real world (Kelly et al. 2021).

13.4.8 The Challenges in Personalized Dietary Modulation of the Gut Microbiota

Whether it is chronic illnesses such as diabetes, inflammation, or disorders of the brain, the management of disease may depend on individualized dietary manipulation of the gut microbiota. But there is still a lack of comprehensive information about using diet as a tool. Because it is difficult to correctly manipulate the human microbiome, there is currently little proof of causation in people (Mendez-Garcia et al. 2018; Leeming et al. 2021).

New studies should consider improved dietary data collection, further characterization of metabolic interactions, and an increased focus on omic technologies like metabolomics in order to describe the bacterial and metabolic activity of food breakdown as well as its cross talk with the host. Furthermore, clinical evidence with regard to health outcomes is needed before therapeutic food plans for microbial rehabilitation may be developed.

13.5 Conclusions

The impact of microbes on human health is now universally recognized. This chapter discusses diversity-driven microbial composition, diet-driven modulation, and the consequences of microbial dysbiosis. We attempted to elucidate the healthy gut microbiota and its role in maintaining gut homeostasis. A detailed profile of microbial shifts in diseases such as neurodegenerative disease, cardiovascular disease, asthma, colorectal cancer, etc., has also been discussed along with the gut-microbiota-brain axis. Further, we have also emphasized the currently available/needed therapeutic strategies for restoring the microbial dysbiosis.

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