Microbiome and Human Health

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Edited by

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The Book is Dedicated to

Professor Dr. Farzana Mahdi and

Professor Dr. Abbas Ali Mahdi

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PREFACE

The human body is the most complex one but a beautifully designed machine, pretested and delivered on earth by the omnipresent invisible forces of Nature. Many of us do not realize that humans are born and blessed with several innate defence, repair and regulatory mechanisms. Thus, if the human body is treated well and maintained on a regular basis without indulging in extremes, it would not only last long but remain almost free from any possible trouble (disease). However, one cannot guarantee to remain healthy forever. This is because accidental temptations are always there to lure a person to become irresponsible. Nonetheless, with concerted efforts and due awareness, one can enjoy good health, longevity and bountiful blessings of Nature. But then, we do not live on our own. This is because we have a massive support system that comes in the form of Microbiomes. These microbes have tremendous potential to impact our physiology, both in health and diseased conditions.

There are more than 10,000 different species of Microbiomes identified thus far that are present in the human body. The Microbiomes actually provides more genes (~8 million of microbial genes vs. ~22,000 human ones) that contribute to human survival than the human genome itself. Microbiomes protect the human body against pathogens, educate, encourage and regulate the immune systems and affect directly or indirectly most of our physiological and metabolic functions. Microbiomes are responsible for the maintenance of homeostasis. Thus, the humans need bacteria and other microbes and their genes for achieving a fine-tuned homeostasis to live a healthy life. These Microbiomes, though related to human health, may vary amongst different individuals. In addition, good health and longevity require some cautions, precautions, corrective measures, sacrifice, nutritious food, smart living and healthy interaction with fellow beings. More than that, one has to have a positive and healthy attitude towards life sustaining the influx of happiness all the time. Above all, positive and healthy attitudes and strong will powers are of epistemological importance. Choice of mating partners, food and food habitats, beverages, overall healthy lifestyle, moderation in routines and remaining close to Nature are some of the tried and tested mantra of good health. "***Early to bed, early to rise makes a person; healthy, wealthy and***

wise". This is not only an old adage but also a life mantra that ensures good health and longevity. Alcohol, tobacco and other such substances warrant sacrifice. This is because our bodies have been designed to process food items and not chemicals. However, this is not practiced all the time by everyone. If we obey the law of Nature and keep an eye on it, the genotype and phenotype would remain in harmony. While we have no control on sporadic mutations, we can at least avoid those factors that are known to cause or speed up the process of mutations. Mutational landscapes in our lives are affected by a number of environmental factors including the profession we opt for and the habitat we live in. Choice of healthy mating partners with robust genotype akin to Artificial Selection is also favoured by Natural Selection. This is because as **Darwin** says, ***"Nature favours the fittest genome for survival".*** There are some set rules of genetics that are evoked parallel for evolution of species. A larger gene pool coupled with a heterogeneous population having healthy individuals, all living in a serene and clean environment with accessibility to clean water, air, and food would ensure a healthy population. On the other hand, a small, homogenous (consanguineous) population confined in an unhealthy environment, away from the bounties of nature with poor or wrong profession will continue to acquire deleterious mutations. People who are exposed to natural background radiation or working in nuclear facilities or hazardous chemical factories are more likely to face the mutational brunt. Similarly, night shift workers by and large have messed up their circadian rhythm which is a known health hazard. Noise pollution adversely affects the lives of millions of people. Studies have shown that there are direct links between noise pollution and health. Problems related to noise include stress related illnesses, high blood pressure, speech interference, hearing loss, sleep disruption, and loss of productivity. Similarly, lack of 8 hour regular sleep (largely neglected) also affects human health. Further, abuse of substances and alcohols not only damage the body organs but also cause undue addiction jeopardizing the overall wellbeing of a person. Unfortunately, there is no safe limit of alcohol consumption as there is no such thing like a small fire. These nuances though not noticed often, individually or collectively affect human health curtailing longevity. It may be noted that each of these factors tend to affect our Microbiomes which under extreme conditions causes dysbiosis.

Present book on Microbiomes and Human Health is an offshoot of an earlier publication on Precision Medicine and Human Health edited by Farzana Mahdi and Abbas Ali Mahdi, two noted Academic luminaries of Era University, Lucknow, UP, India.

In the present book on Microbiomes and Human Health, we have attempted to collect data from across the spectrum of humans living in varying conditions, with different food habits, lifestyles and genetic background. Even within the individuals, different organs in the body show variation in the Microbiomes. We are acutely aware of the fact that many of our assumptions and hypotheses may not withstand the rigours of scientific scrutiny. Nonetheless, our modest attempt would set the ball rolling and impel researchers to think along the line and prove or disprove our assumption or lend support to it. Clearly, more research data is needed from across the spectrum of the society before one draws an unequivocal conclusion on the overall significance of Microbiomes and Human Health. Notwithstanding enormous uncertainties of the types of the Microbiomes across different sections of the society, we are certain to reach somewhere along the path to understand the heterogeneity of the Microbiomes and its correlation with human health. Detailed data on this line is envisaged to streamline the concept of precision medicine bridging the gap amongst nature, nurture, mutation, environment, disease, ethnicity, lifestyle, genetics and human health.

This book has a total of 22 chapters encompassing several sub-topics related to Microbiomes. The chapter 1 "Interrelationship, Nutrition, Immunity and Microbiome: A critical Appraisal" deals with these triad focusing on their impact on human health. The microbiome affects immune function and overall health by facilitating complex carbohydrate breakdown, synthesizing vital vitamins, and defending us from pathogens. Recent advances on microbiome research have enhanced our understanding of the intricate interactions between nutrition, the immune system, and the microbiome, offering both opportunities and challenges. This bidirectional relationship, where microbiota and their metabolites drive immune activation while chronic inflammation alters microbial communities, is crucial yet not fully understood. Advances such as shotgun metagenomic sequencing and full-length 16S rRNA sequencing, provide deeper insights into microbial taxonomy and function. However, challenges like their variability and data processing remain unresolved.

The word micro is used to indicate that this ecosystem is not visible to human eyes. With the help of a microscope looking inside of our bodies, we would find trillions of microorganisms (also called micro biota, or microbes) representing different species. This biota represents not only bacteria but also fungi, parasites, and viruses coexisting peacefully in the small and large intestine and throughout the body. It is largely believed that these microorganisms (symbionts) play an important role promoting the seamless daily operations of the human body. Each person has an entirely unique network of microbiota that is originally determined by one's DNA and regulated by the environment. A person is first exposed to microorganisms at the time of birth as an infant, during delivery and subsequently through the mother's breast milk. Exactly which microorganisms the infant is exposed to depends solely on the species found in the mother's body and the mode of parturition. Later on, environmental exposures and diet can change one's microbiome to be either beneficial to health or the disease causing ones. The human microbial metagenome contains the vast majority of common bacterial species. An individual's microbiome is quite stable over time, but varies at the extremes of age across different genomes. Thus, Microbiomes would be different across the spectrum of the organs in human populations in the world. Barring *Clostridium difficile* infection, the role of microbiota in the pathogenesis of disease is uncertain. The variety of food that we partake affects the microbiota. It is largely believed that high quality nutritious food maintains a healthier Microbiome. This chapter provides a comprehensive overview of current research and future directions. This integrated perspective can lead to more effective nutritional and therapeutic interventions, ultimately fostering a healthier society.

The chapter 2 "Gender Nuanced and Human Microbiome" takes into consideration the overall distribution of the microbiome not only in normal male and female but also in the intersex individuals. Fewer reports are there that deal with the biomes of different types of intersex individuals. Clearly, they differ with respect to their food, physiology, lifestyle and social conditions. We have localized Microbiomes on our skin, in our lungs, and within our guts. These Microbiomes have co-evolved alongside with humans, adapting well with our lives. Gut microbiome is important to health as it helps us digest and absorb food and metabolize vitamins, minerals and medicines. In addition, it plays a great role in supporting our immune system. This is because 70% of our immune system is located within the gut and it has to process a large number of environmental antigens. An antigen is the substance that causes our immune system to produce antibodies against it. This could be pollen, chemicals or viruses. In just one day, the gut will have to deal with more antigens than the rest of the immune system dealing during an entire lifetime. Our gut microbiome is responsible for educating our immune systems as we grow and regulate them to function later in life, as we age. It has now become clear that our gut microbiome defines the risk of chronic or noncommunicable diseases, such as diabetes, arthritis, allergies and cancer. Usually, male, female and intersexes have different compositions of Microbiomes in their guts. Females seem to show more variations in their Microbiomes at phyla, genus and species levels. On the other hand, hormones and tissue structure shape the genital microbiome, meaning both hormone therapy and gender-affirming surgeries typically cause microbial changes. Thus, male, female, and intersexes all have varying Microbiomes. In this chapter, we elucidate the profound impact of GIT microbiota on immune system regulation, hormonal interactions, and behavioural outcomes. This exploration sheds light on the emerging concept known as the "microgenderome”.

The chapter 3 deals with intraocular microbiota in the context of eye health. Considering how recently the ocular microbiome was discovered, we still have to learn much about its makeup and function in preserving eye health. The fact that the intraocular microbiota and any potential bacteria that live inside the eye are mysterious adds to the complexity to this topic. A highly vascularized and immunologically dense environment exists inside the eye. An important unanswered question is how intraocular microbiota and the immune environment interact and how these interactions affect inflammatory eye disorders. Because of their very low numbers and anaerobic nature, it is exceedingly difficult to culture them in laboratory settings. Therefore, studying the intraocular microbiota is a huge challenge. The complex interplay among the immune system, the gut microbiota, and eye health has wide-ranging effects on several medical disorders, including ocular ones. To safeguard eye health by manipulating the gut microbiome, further research is essential to gain a profound understanding of the underlying pathways involved.

The chapter 4 “Genetical Tapestry of Miscarriages and their Microbiome Connection” deals with spontaneous abortions. This is a complex and emotionally challenging aspect of reproductive health. Besides genetics, emerging research suggests that the microbiome may also contribute to pregnancy outcomes, including miscarriage. Genetic abnormalities either in the embryo or within the parents can increase the risk of pregnancy loss. This may be caused owing to chromosomal anomalies, gene mutations, or structural abnormalities in the reproductive organs. The microbiota in the reproductive tract, has gained attention for its potential roles in the sustenance of pregnancy or otherwise. Research suggests that an imbalance in the vaginal or uterine microbiome, known as dysbiosis, may increase the risk of miscarriage. Imbalances can lead to inflammation, immune dysregulation, and other factors that could compromise pregnancy. Studies have shown associations between specific types of vaginal microbiota and miscarriage risk. For example, an overgrowth of certain harmful bacteria, such as *Gardnerella vaginalis* or *Atopobium vaginae*, has been linked to increased miscarriage risk. Conversely, a healthy balance of *Lactobacillus* species in the vaginal microbiome is associated with better pregnancy outcomes. Recent research has suggested that the uterus may harbor its own microbiome. Imbalances in the uterine microbiome, similar to those in the vaginal microbiome, may contribute to inflammation and pregnancy complications, including miscarriage. The microbiome plays a crucial role in regulating the immune response, both locally in the reproductive tract and systemically. Dysbiosis can trigger an inappropriate immune response, leading to inflammation and tissue damage, which may increase the risk of miscarriage. Understanding the connection between the microbiome and miscarriage opens avenues for potential therapeutic interventions. These interventions may include probiotics, prebiotics, or antibiotics to restore microbial balance in the reproductive tract and reduce the risk of miscarriage. Genetic testing, combined with microbiome analysis, could help identify individuals at higher risk of miscarriage. This improved diagnostic method would lead to the development of preventive strategies.

Chapter 5 relates to “SARS-CoV-2 Association with Gut Microbiome”. Its importance was realized during Covid-19 pandemic. This pandemic is presumed to be associated with alterations in the composition and diversity of the gut microbiota. Dysbiosis, characterized by an imbalance in microbial communities, may contribute to systemic inflammation affecting the severity of COVID-19 symptoms. The emergence of the COVID-19 pandemic has sparked heightened interest in understanding the intricate relationship between the gut microbiota and viral infections, particularly SARS-CoV-2. This chapter aims to provide a comprehensive overview of the interaction between gut microbiota and COVID-19, shedding light on the potential implications for disease susceptibility, severity, and long-term outcomes. Understanding the complex interplay between gut microbiota and COVID-19 is crucial for targeted therapeutic interventions and development of preventive strategies. The chapter unifies current knowledge, identifies research gaps, and emphasizes the need for interdisciplinary approaches.

The chapter 6 “Role of Gut Microbiota in Osteoarthritis (OA) deals with chronic musculoskeletal condition that leads to the deterioration of cartilage in the joints causing inflammation of the synovial membrane. Studying the pathophysiology of osteoarthritis is crucial for the advancement of innovative preventive and therapeutic strategies. This chapter delves into the notion of a "gut-joint axis," presenting compelling evidence regarding the interplay between gut microbiota and various factors associated with OA, such as age, gender, genetics, metabolism, central nervous system function, and joint traumas. The intricate dynamics of this interaction shed light on the varied symptoms observed in osteoarthritis. Furthermore, the chapter explores the potential for modulating gut microbiota to address OA symptoms, advocating for strategies like physical activity and faecal microbiota transplantation (FMT) as effective interventions. It provides valuable information on how gut microbiota can be used to predict the progression of osteoarthritis and evaluate the effectiveness of treatment interventions. The study concludes by highlighting potential areas for future research, such as the development of stronger therapies, investigations into gene regulation, and the examination of the relationship between certain cell subgroups and gut microbiota in the setting of OA.

The Chapter 7 “Role of Gut Microbiome in Cardiovascular Diseases” is a highly thought provoking area. Cardiovascular disease (CVD) is a major global health concern with risk factors encompassing smoking, hypertension, dyslipidaemia, obesity, inflammation, and diabetes. The gut microbiota produces metabolites like short-chain fatty acids (SCFAs), bile acids, and Trimethylamine N-Oxide TMAO, which are important modulators and have been linked to an increased risk of CVD. As a result, the gut microbiota has become a target for therapeutic approaches. This chapter summarizes current knowledge on the role of the gut microbiome in CVD development, involvement of microbial communities and their metabolic functions. The focus on gut microbiota-derived metabolites, specifically Trimethylamine N-oxide, short-chain fatty acids, and phenylacetylglutamine is warranted because they either promote or prevent the course of cardiovascular disorders. Studies on the microbiome of individuals with CVD across the spectrum of ethnicity may provide information on their susceptibility facilitating diagnosis and better patient care. The dynamic ecology of Microbiomes and their nuances in the context of CVD are highlighted.

The chapter 8 “Impacts of Human Gut Microbiomes on Type 2 Diabetes Mellitus” deals with the bacterial community that resides in the human stomach and in other parts of the body. Both microbiota and human life are evolutionarily adapted. The beneficial roles of gut microbiota in human health such as regulation of metabolic and immunological responses are well established. Studies have shown that dysbiosis, an imbalance in the gut microbiota, is linked to the onset and progression of a variety of clinical manifestations, including diabetes. When compared to non-diabetics, people with type 2 diabetes have different compositions of gut microbiota. These variations represent a decline in the microbiota's diversity and adaptability affecting the relative abundance of particular bacterial species. Dysbiosis in the human gut has been reported to cause persistent low-grade inflammation and metabolic endotoxemia. Metabolic endotoxemia occurs when bacterial toxins, such as lipopolysaccharides (LPS), escape from the stomach and enter into the bloodstream. Consequently, the gut microbiota can influence insulin sensitivity and glucose metabolism. This chapter provides valuable insights into the potential role of the gut microbiota in influencing various aspects of diabetes, including insulin resistance, glucose metabolism, and inflammation.

The Chapter 9 “Different Shades of Microbiome and Human Health” covers varying populations of microbes in the human body. Studies have shown that these microbes have a significant impact on human health due to their coevolution with the host. The changes in the human microbiome have the potential to initiate and worsen a number of diseases. Attempts have been made to identify putative driver genes and pathways linked to human health, wellbeing, and susceptibility to various diseases. We show potential connections between the microbiome and different types of illnesses, with an emphasis on the skin, digestive, respiratory, urinary, and reproductive systems. It is envisaged that such efforts would enable to develop a repository of tissue/organ specific biomes and their precise involvement in conferring health to humans. Nuances of microbiome and human health are discussed in the light of prevalent lifestyle, food habits and frequent travels.

The Chapter 10 “Interaction of Nanoparticles with Microbiome and their Impact on Human Health” adds a new dimension. This is because Nanoparticles (Nps) have many technological applications, raising concerns about their potential impact on human health. Microbiome is a symbiotic assembly of microorganisms vital for the well-being of the host. Delving into the mechanisms governing Np-microbiome interactions, we show how these encounters shape microbial communities and influence host-microbe dynamics. This chapter addresses the broader consequences on human health, encompassing immune modulation, gut integrity, and its potential use against dysbiosis. An in-depth understanding of the nanoparticle-microbiome nexus is crucial for designing safe and effective strategies ensuring their harmonious integration without compromising the delicate balance of the human microbiome.

The chapter 11 “Advanced Diagnostics and Therapeutics Based on Nano-engineered Microbiome” deals with convergence of nanotechnology and microbiome. It is envisaged that this will be useful for advanced diagnostics and therapeutics offering unprecedented opportunities to revolutionize the human healthcare system. Nanoparticles, nanosensors, and nanocarriers provide highly sensitive and specific platforms to be used as diagnostic biomarkers enabling early disease diagnosis and subsequent monitoring. Furthermore, nanomaterials offer precise delivery of therapeutic agents, minimizing side effects and enhancing treatment efficacy. Concurrently, understanding the Microbiomes role in health and disease allows for the development of microbiome-targeted diagnostics and therapeutics. Optimized treatment by customizing therapies to each patient's unique microbiome profile is possible by nanotechnology. The synergistic utilization of these technologies holds great promise for personalized diagnostics and therapeutics, providing innovative solutions to address complex diseases and improve patient outcomes. However, in the actual case scenario, one must ensure that the nanoparticle used either for diagnosis or therapeutics must be safe and should not have any side effects.

Chapter 12 addresses “Diversity of Cancers, Microbiome and Human Health” highlighting that the human microbiome has the potential to influence the onset and advancement of cancer. In addition, this can facilitate cancer treatment and complement immunotherapy. This is because bacteria, viruses, and fungi have widespread prevalence in cancers. They have potential for manipulation and treatment to metastases. The mechanisms through which Microbiomes influence cancers can provide novel diagnostic and therapeutic options, although much remains to be discovered. While the majority of research has focused on the gut microbiome, other organs such as the skin, vagina, aboral end and lungs also host unique Microbiomes distinct from the gut. Tumour formation has been linked to dysbiosis not only in the gut but also in the tissue where the tumour originally developed. Critically analysing and constructing frameworks for this evidence in the context of modern cancer biology is a crucial undertaking. In this chapter, attempts have been made to delineate the causal and complicit roles of microbes in cancer. We have discussed progress, limitations, challenges, and potential in comprehending the causal impact of the microbiome on cancer and its responsiveness to treatment.

The Chapter 13 “Conundrum of Microbiome and Amelioration of Human Diseases” largely focuses on the human diseases and their possible treatment exploiting the knowledge of microbiome. As mentioned earlier, our body hosts a hidden kingdom of Microbiomes containing bacteria, viruses, fungi and continues to be influenced by these organisms, affecting overall health. Microbiome can cause potential diseases because of dysbiosis. Study on Microbiome’s composition is envisaged to uncover regulatory nuances of health and diseases. Microbiome may be modulated, adjusted and realigned using external means and can be optimized. For example, probiotics can be used to enhance the microbiota for modulation or adjustment. Delving into probiotic research, revealing strain impacts on lipid profiles, body weight, and segregating microbial superheroes for combating diseases like inflammatory bowel disease (IBD) are the attractive propositions. A comprehensive examination of probiotic treatment offers insights into their impact on obesity by revealing changes in body mass, lipid profiles, and microbiome diversity. The discourse extends to the application of prebiotics, unravelling their health benefits and nuanced roles in specific medical conditions. The Bacteriophages, natural predators that are placed in appropriate locations to eradicate particular microbiome components are introduced. The constantly changing field of microbiome research highlights the need to create microbiome commensals for targeted therapeutic interventions, overcoming challenges, and using alternative approaches. This chapter describes the interplay amongst environment, genetics, and diet that shapes the microbiome. Identification of Microbiomes specific for a disease condition would open up the door to the development of specialized treatment plans for a variety of human illnesses.

The Chapter 14 “deals with the association of microbiome with kidney diseases”. Gut dysbiosis is typically distinguished by a reduction in the variety and relative abundance of specific microbial groups. Pathological characteristics of gut dysbiosis include increased endotoxin release, increased permeability to gut-derived molecules, and an increased proinflammatory signalling, which allows them to enter the systemic circulation. Kidney diseases are often associated with metabolic abnormalities and gut dysbiosis, which contribute to the development and progression of the disease. Recent research indicates that the primary mechanism of gut dysbiosis in kidney disorders is caused by microbial changes. This results in the creation of toxic metabolites like uremic toxins and reduction in the short chain fatty acids. Kidney disorders can also arise as a result of immune response activation and mitochondrial dysfunction caused by gut dysbiosis. Probiotics, prebiotics, synbiotics and faecal microbiota transfer can modify gut dysbiosis. In this chapter, we discuss the possible roles of the gut, blood, and urine Microbiomes in CKD, AKI, and IgA nephropathy in the pathogenesis of kidney diseases. Thus, by focusing on gut dysbiosis, we may refine possible therapeutic approaches for treating renal diseases.

The Chapter 15 “Microbiome Diversity and Human Health” focuses on the Microbiomes which represent a diverse group of microorganisms residing on and inside the human body playing a critical role in preserving human health. Perusal of literature indicates the significance of a balanced microbiome in preventing inflammatory bowel disease, diabetes, and obesity. Therefore, comprehending the intricate interconnection between the microbiome and human health is crucial for developing targeted interventions that support a healthy microbiome. We examine the elements that control the organisation of the microbiome; such as food, lifestyle, and environmental exposures. We also look at the ways the microbiome influences human health, including how it alters the immune system and produces bioactive compounds. Furthermore, we highlight the possible applications of microbiome research in clinical practices as these could be a promising biomarker for many diseases. The use of probiotics, prebiotics, and faecal implantation has been shown to improve gut function ameliorating disease conditions. We have tried to identify microbial genes in the biome to establish their interlinkage with the human host. This network information is intended to explain how interactions contribute to the maintenance of cellular homeostasis or become the cause of dysbiosis.

The Chapter 16 deals with the interaction of Microbiota and Tuberculosis with the emerging role of Artificial intelligence in the diagnosis of TB and its comorbidities. The interrelationship of comorbidity, Microbiomes, and artificial intelligence (AI) represents a rapidly evolving field with significant implications for healthcare and personalised medicine. Comorbidities, defined as the co-occurrence of multiple diseases, can complicate diagnosis and treatment, particularly with chronic ones. The gut microbiota collaborates with human physiological processes and immune responses, potentially modulating the onset of diseases and the effectiveness of treatments. By examining health patterns, it is possible to identify malfunctioning microbiota in human bodies using AI at an early stage through collective pre-data analysis. AI abilities go beyond single diagnosis and multiple facets because it has the capability to analyse multiple parameters at a glance such as population data, risk factors and comparative data. Accordingly, AI can forecast outbreaks prior to their occurrence based on enormous global data resources it uses. Artificial intelligence, particularly machine learning (ML) and explainable AI (XAI), offer powerful tools for analysing microbiome data, enabling the detection of microbes associated with specific health conditions. By integrating microbiome genomic profiles with demographic and clinical data coupled with other health related variables, AI can enhance predictive models of disease risk and treatment efficacy. Present study explicates the evolving impact of AI on the prior detection of microbiological diseases, explores cutting-edge research advancements in AI-driven diagnosis, and creates innovative strategies to tackle infectious diseases. Thus, AI is going to stay with us as a sincere healthcare partner.

The Chapter 17 “Nuances of Microbiome and Human Health” address the issues in the context of debilitating diseases and their possible remedies. Microorganisms inhabit almost all parts of our body including skin. These microbes in a balanced state play a vital role in maintaining our well-being by supporting the immune system and other bodily functions. However, when this delicate balance is disturbed, it can lead to various health problems. For example, an imbalance in gut microbiota has been linked to cardiovascular diseases (CVDs), certain types of cancers, and respiratory ailments. This disruption, known as dysbiosis, can occur due to factors like diet, stress, medications, or infections. Understanding the role of microbiota in both health and disease is a topic of extensive research. These microbes are not just passive inhabitants; they actively communicate with the host (our body) and influence our immune responses. This interaction forms the basis of gut-brain axis, where gut microbiota can affect brain function. In addition to immune modulation, microbiota also provides resistance, which means they can prevent harmful pathogens from taking over thus protecting us from infections. When the microbiota's balance is disrupted, this protection weakens, leading to an increased susceptibility to infections and chronic inflammation. Despite the potential risks posed by microbiota dysbiosis, researchers and clinicians are exploring innovative ways to utilize microbiota for therapeutic purposes. One such approach is microbiota modulation, where interventions like probiotics, prebiotics, or dietary changes are used to restore a healthy microbial balance. Another method gaining attention is faecal microbial transplantation (FMT), where beneficial microbes from a healthy donor are transferred to a patient to treat certain conditions.

The Chapter 18 focuses on “Processed Food, Microbiome and Human Health”. Microbiology is essential for the production, processing, preservation, and storage of safe food since bacteria are heavily involved during all these phases. Microorganisms like bacteria, moulds, and yeasts are used to produce food and ingredients, including dairy products, wine, beer, and baked items. However, harmful bacteria can cause food contamination, its spoilage and loss. Technology can prevent and delay microbial growth and contamination of food but deterioration and pathogenic activity of microorganisms still persist. Food loss from spoilage or contamination has an impact on consumers and the food industry. This results in financial losses and higher expenses on hospitalization. Food that is prevented from deterioration will eventually reach a larger population. Processed foods can range from minimally processed items like bagged salads or frozen vegetables to highly processed products like sugary snacks, packaged meals, and fast food. While some processed foods can be part of a balanced diet, consuming too many highly processed foods can have negative health effects. They often contain high levels of added sugars, salt, unhealthy fats, and artificial additives, while being low in essential nutrients like fibre, vitamins, and minerals. Overconsumption of processed foods has been linked to an increased risk of obesity, heart disease, type 2 diabetes and other health problems. Thus, it's important for individuals to be mindful of their intake of processed foods and strive to incorporate more whole, unprocessed foods like fruits, vegetables, whole grains, lean proteins, and healthy fats into their diets for optimal health. Since food and bacteria are friends and foe simultaneously, it is important to know the microbiome and their diverse nature to uncover their effects on food. This includes their diversity, balance, functions and interactions offering a rich tapestry to understand gastrointestinal disorders (e.g., irritable bowel syndrome, inflammatory bowel disease and menstrual cramp). Promoting human health requires a holistic approach that addresses the interconnectedness of physical, mental, and social well-being, as well as the broader environmental and socioeconomic determinants of health. This involves not only individual efforts to adopt healthy behaviours but also collective action to create supportive environments, policies, and systems that prioritize health equity and well-being for all. This chapter provides critical appraisal on different food processing methods and microorganisms involved in the process at industrial scale. It is envisaged that this chapter will enhance the awareness of the nuances related to the food industry in general and food safety in particular. The potential of processed food is acknowledged in a number of sectors, including defence, aviation, tourism, and academic institutions.

The Chapter 19 “Involvement of Microbiome in Cancer and its Management” highlights the collection of microscopic organisms in our bodies’ playing a pivotal role in the development of cancer. The chapter addresses the potential link between dysbiosis, or abnormalities in the microbiome, and inflammatory illnesses and different types of cancer. Viruses like HPV, Epstein-Barr virus and pathogens like *Helicobacter pylori* play their own roles in the development of cancer. Our emphasis is placed on the role played by the gut microbiome, particularly bacteria like *Fusobacterium*, in *esophageal* and colorectal malignancies. Microbiome affects immunotherapy, chemotherapy, and radiotherapy, besides other cancer treatments. Pharmacological reactions, side effect incidence, and treatment efficacy can all be influenced by the microbiota. In conclusion, this chapter highlights the importance of the microbiome and its ability to either cause or treat cancer.

The Chapter 20 deals with microbiome in diabetic patients and their management. The human microbiome is a highly diverse micro ecosystem and compartmentalized one, often known as the “second genome”. The gut microbiome composition may be altered by various factors including antibiotic treatment, lifestyle, environment, diet, health conditions, genetics, sleep disorder, lack of physical exercise, sedentary life and use of wrong medicine. These alterations often lead to different metabolic and autoimmune disorders including type 1 (T1DM) and type 2 diabetes mellitus (T2DM). Gut microbiome may cause diabetes either by dysbiosis, “leaky gut” or molecular mimicry. Furthermore, an increase in short-chain fatty acids (SCFAs) enhances metformin efficacy. Similarly, increased *Firmicutes* and *Bacteroidetes* improve dipeptidyl peptidase 4 (DPP4) inhibitor efficacies. Consequently, the microbiome offers great potential for diabetes management, and likely to ameliorate patient care. However, there is limited knowledge regarding the precise mechanisms through which the microbiome causes disturbances in glucose homeostasis triggering autoimmunity against β-cells, and determining drug response.

The Chapter 21 deals with Microplastics, gut Microbiome Interaction and human health. Microbiome represents the complex community of microorganisms residing in the gastrointestinal tract. Microplastics, ingested through various sources, can alter the composition and function of gut microbiota, potentially leading to dysbiosis, compromised gut barrier integrity, and inflammatory responses. Dysbiosis may interfere with the host immune system and trigger the onset of chronic diseases, promote pathogenic infections, and alter the gene capacity and expression of gut microbiota. Microplastics can act as vectors for harmful chemicals and pathogens, influencing gut microbiota homeostasis and metabolic activities. Moreover, the presence of Microplastics in the environment exacerbates their bioaccumulation in marine and terrestrial food chains, raising concerns about indirect effects on human health through dietary exposure. Understanding the mechanisms by which Microplastics affect the gut microbiome is therefore crucial for assessing their broader implications for environment and human health. It is envisaged that this chapter would be of interest to researchers, clinicians, environmentalists and perhaps politicians because of its health related relevance.

The Chapter 22 takes up the issues related to complexities of Gut microbiome in diabetic patients. Almost all the key aspects related to diabetes have been carefully examined and highlighted in the light of current research and global understanding.

Diabetes mellitus, a chronic metabolic disorder marked by persistent hyperglycemia, is often complicated by severe conditions such as cardiovascular disease, neuropathy, nephropathy, and retinopathy. Emerging research underscores the significant role of the gut microbiome which represents a complex bio-ecosystem in the gastrointestinal tract involved in progression of diabetes-related complications. Dysbiosis, or an imbalance in the gut microbiome, has been closely linked to heightened cardiovascular risk in diabetic individuals. Key microbial players, such as *Firmicutes* and *Bacteroidetes*, glaringly impact systemic inflammation and lipid metabolism. Certain gut microbes produce Trimethylamine-N-oxide (TMAO) from dietary choline and carnitine, a metabolite strongly associated with atherosclerosis and cardiovascular disease. In the realm of diabetic neuropathy, bacteria like *Lactobacillus* and *Bifidobacterium* contribute to the production of short-chain fatty acids (SCFAs), which influence nerve health and inflammation. SCFAs can modulate Neuroinflammation and neuronal repair processes, potentially exacerbating peripheral nerve damage. In diabetic nephropathy, dysbiosis is characterized by an increased abundance of Enterobacteriaceae and a reduced presence of *Akkermansia muciniphila*. These microbial changes affect renal inflammation and fibrosis, partly through the production of uremic toxins such as indoxyl sulfate. Similarly, diabetic retinopathy, a leading cause of vision loss in diabetes, is influenced by gut microbiome health. Specific gut bacteria, including *Prevotella* and *Roseburia*, play critical roles in modulating systemic inflammation and oxidative stress, both of which are crucial to the development of retinopathy. This chapter not only explores how gut dysbiosis contributes to diabetes-related complications but also reviews current and emerging therapeutic strategies aimed at modulating the gut microbiome to alleviate these health issues. It is envisaged that this book will be useful both for researchers and clinicians alike providing a much broader perspective on the bugs, body, brain, gut and human health.

Editors
Sher Ali and **Anam Farooqui**

FOREWORD

The vast universe is full of a lot of mysteries and unknowns, so is the functioning of the human body with a bustling community of microbes. Tiny, yet mighty organisms, that collectively form the microbiome. The intricate micro-ecosystem, residing primarily in our gut and in various other niches throughout our body, plays a profound role in shaping our health and well-being.

The study of Microbiomes has emerged as a frontier in modern science, captivating researchers and healthcare professionals alike with its promise of unlocking the secrets of human health and disease. With each discovery, we gain deeper insight into the intricate saltation between these microbial inhabitants and our own physiological processes. We learn of their influence on everything from digestion and metabolism to immune function, mental health and reproduction.

As we navigate the complexities of microbiome research, we are continually reminded of the profound interconnectedness of all life forms. The symbiotic relationship between humans and their microbial companions strengthens the fundamental truth that we are not solitary entities, but rather an ecosystem unto ourselves. Our health is intricately intertwined with the health of these microbial communities. Understanding this relationship, therefore, is of paramount importance in promoting wellness and prevention of disease.

This volume, "Microbiome and Human Health," represents a compendium of knowledge amassed by experts at the forefront of microbiome research. Within its pages, readers will find a treasure trove of insights into the myriad ways in which the microbiome impacts human health, as well as the innovative strategies being developed to harness its therapeutic potential.

From the exploration of the gut-brain axis to the elucidation of microbial contributions to chronic disease, each chapter offers a glimpse into the fascinating world of the microbiome and its implications on human health. As we embark on this journey of discovery, let us not only marvel at the complexity of the microbiome but also recognize the immense responsibility we bear in stewarding its delicate balance.

I commend the contributors of the Chapters and the Editors, Sher Ali and Anam Farooqui, of this volume for their dedication and indulgence to advance our understanding of Microbiome and its implications for Human Health.

Sher Ali (MSc. Gold Medalist, PhD, FNA, FASC, FNASc, FSASc and JCBNF) is working at the Era University as Distinguished Professor, Dean, Research and Development and Senior Administrator. He has availed Alexander Von Humboldt Foundation Fellowship, Germany, Fulbright Fellowship, USA, and has worked at the Max Planck Institute for Immunology, Freiburg, Germany, University of Bochum, Bochum Germany, University of Utah, Salt Lake City, Utah, USA, Georgetown University Medical Center, Washington DC, USA, Leicester University, Leicester, England, UK and Australian National University, Canberra, Australia. Professor Ali has more than four decades of National and International Research Experiences in the area of Molecular Genetics, Genomics, Gene Expression, Regulation and Manipulation. He encouraged Anam to delve into this fascinating aspect that relates to Microbiome and Human Health. Dr. Anam Farooqui is working as a Project Scientist-I at the "ICMR-National Institute for Research in Reproductive and Child Health", Parel, Mumbai - 400012. Her work delves into the intricate realm of Functional Genomics, large scale Data Management and Systems Biology. She holds a M.Sc. degree in Biosciences, an M. Phil in Computational Biology, and a Ph.D. degree in Bioinformatics from Jamia Millia Islamia, New Delhi (India). With a relentless passion for unravelling the mysteries of life at its molecular core, her research endeavours have garnered acclaim through many publications in esteemed journals. Her dedication to advancing the boundaries of scientific inquiry, coupled with her expertise in computational biology, mark her as an emerging young researcher in her field.

I feel assured that this book will evoke interest in those who are associated with human health-care system and wish to remain updated with its nuances. I am delighted to see the outcome of a combined experience of a seasoned and the young researcher, Sher Ali and Anam Farooqui, in editing this book, which is the need of the hour.

Rameshwar N. K. Bamezai

CHAPTER 1

INTERRELATIONSHIP AMONGST NUTRITION, IMMUNITY AND MICROBIOTA: A CRITICAL APPRAISAL

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Abstract

Human health is largely influenced by the critical triad of nutrition, the immune system, and microbiota. Adequate nutrition supports immune cell proliferation and activity, enhancing the body's ability to respond effectively to infections. The microbiome significantly affects immune function and overall health by facilitating complex carbohydrate breakdown, synthesizing vital vitamins, and defending against pathogens. Recent advances in microbiome research have significantly enhanced our understanding of the intricate interactions between nutrition, the immune system, and the microbiome, revealing both opportunities and challenges. Mechanistic studies demonstrate that the commensal microbiome profoundly influences immune function in health and disease. This bidirectional relationship, where microbiota and their metabolites drive immune activation while chronic inflammation alters microbial communities, is crucial yet not fully understood. Integrating multi-omics data—including metagenomics, single-cell transcriptomics, epigenomics, proteomics, and metabolomics—will be key to deciphering the cross-regulation between the gut microbiome and the immune system. Advances in sequencing technologies, such as shotgun metagenomic sequencing and full-length 16S rRNA sequencing, provide deeper insights into microbial taxonomy and function, though challenges like variability and data processing remain unresolved. Understanding the interplay among diet, the immune system, and the microbiota is imperative for developing strategies to boost immunity, prevent diseases, and promote health. This chapter covers these topics in depth, providing a comprehensive overview of current research and future directions. This integrated perspective can lead to more effective nutritional and therapeutic interventions, ultimately fostering a healthier society.

Keywords: Dysbiosis, Microbiome, Immune System**,** Homeostasis, Nutrition and Human Health.

Abbreviations: Acquired Immunodeficiency Syndrome (AIDS), Gastrointestinal (GI), Germ-free (GF), Fecal Microbiota Transplantation (FMT), Inflammatory Bowel Disease (IBD), Type 1 Diabetes (T1D), Colorectal Cancer (CRC), Dendritic Cell (DC), Antimicrobial Peptides (AMPs), Pattern Recognition Receptors (PRRs), Toll-like Receptors (TLRs), Nucleotide-Binding Oligomerization Domain (NOD), Trimethylamine N-oxide (TMAO), Innate Lymphoid Cells (ILCs), Regulatory T cells (Tregs), Polymeric Ig Receptor (PIgR), Aryl Hydrocarbon Receptor (AhR), Socioeconomic Status (SES), Crohn's Disease (CD), Rheumatoid Arthritis (RA), Trimethylamine-N-Oxide (TMAO), Non-Alcoholic Fatty Liver Disease (NAFLD), Short-Chain Fatty Acids (SCFAs), Monounsaturated Fats (MUFAs), American Heart Association (AHA), Systemic Lupus Erythematosus (SLE), Low-Density Lipoprotein (LDL), Gut Microbiome (GMB), Galactooligosaccharides (GOS), Fructooligosaccharides (FOS), Microbiota Accessible Carbohydrates (MACs), Gut-associated Lymphoid Tissue (GALT), Alpha-Linolenic Acid (ALA), Whole-Genome Sequencing (WGS)