Journal of Health and Rehabilitation Research 2791-156X JHRR

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Review Article

From Microbes to Immunity: A Comprehensive Review of Microbiome Modulation

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Conflict of Interest: None.

Shahid A., et al. (2023). 3(2): DOI: https://doi.org/10.61919/jhrr.v3i2.238

ABSTRACT

The host environment and the native microbial population, or microbiota, make up the microbiome, which is changing how medical professionals see pathogens in connection to human disease and health. The discovery that the majority of bacteria in human bodies perform ecosystem-critical tasks that benefit the entire microbial host system is perhaps the most fundamental development. The microbiome is the broad term for the diverse and abundant population of bacteria found in the gastrointestinal system. This ecosystem contains billions of microbial cells, the majority of which are essential to the preservation of human health. Nutrient consumption, immunology, digestion, and metabolism have all been related to the microbiome. Scientific research has recently established a correlation between alterations in the microbiome and the development of cancer, obesity, inflammatory pulmonary disease, and cardiovascular complications. Epithelial-intestinal microbiome modifications have a substantial impact on the development of diseases and human health. Numerous factors contribute to these changes, such as underlying medical issues and lifestyle decisions. Depending on where in the body it occurs, dysbiosis increases an organism's susceptibility to various threats. Due to the inherent diversity of the human microbiota, these bacteria carry out specific metabolic tasks and play unique roles in each anatomical location. It follows that knowledge of the microbial makeup and activities of the human microbiome in connection to health and disease is essential.

Keywords: Micro-biome, Bioactive Microbes, Host-Microbe Symbiosis, Immunomodulation, Microbiota Therapeutics.

INTRODUCTION

Researchers belongs to different fields are interested in learning more about the human microbiome, an intricate ecology of microbes that live in different niches within and on the human body. The dynamic interaction between these microbial populations and the immune system of humans is an emerging field that provides significant insights into health, illness, and treatment strategies. The objective of this thorough study is to offer a thorough examination of the complex interplay between immunological regulation and the microbiome, illuminating the processes underlying this dynamic interplay and its consequences for human health.

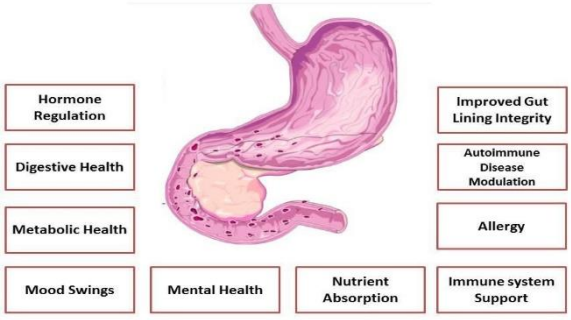

Figure 1 Multifaceted Benefits of a Balanced Gut Microbiome

MICROBIOME COMPOSITION

The human microbiome is made up of an astonishing variety of microorganisms, such as fungus, viruses, bacteria, and archaea. These microorganisms work together to produce a complex ecosystem that mimics the coexistence of microbes and humans throughout evolution. With the gut microbiome having a major impact on host physiology, research on the microbiome has focused on its diversity and richness, as demonstrated by recent advancements in high-throughput sequencing methods. Actinobacteria, Proteobacteria, Bacteroidetes, Firmicutes, and other phyla make up the majority of the gut microbiome, an active community of

Journal of Health and Rehabilitation Research 2791-156X JHRR

microorganisms. These microbes actively participate in activities including immunological regulation, energy extraction, and nutrient metabolism, all of which contribute to the complex equilibrium that exists within the ecosystem. A symbiotic relationship between the microbiome and its human host has been shaped via coevolutionary processes, which are reflected in the microbial variety found in the gut. These processes also demonstrate the adaptability and durability of these communities (1).

IMMUNE SYSTEM INTERACTION

Early in infancy and continuing throughout an individual's lifespan is the dynamic and bidirectional process of interaction between the human immune system and the microbiome. An important center for immune-microbiome interaction is the gastrointestinal tract, which contains the gut-associated lymphoid tissue (GALT). The immune system of the mucosa continuously scans the wide variety of microorganisms in the gut to identify possible pathogens and beneficial commensals. The early years of life are a critical learning period for the growing immune system. The development of immunological tolerance, a critical defense against inappropriate immune reactions to advantageous bacteria and food antigens, is made possible by this training process (2). By keeping defense and tolerance in check, the GALT coordinates immunological responses. T cells and antigen-presenting cells are examples of specialized cells that actively monitor the mucosal environment, reacting to microbial signals and helping to maintain immunological homeostasis. That delicate equilibrium promotes a state of tolerance towards the wide variety of commensal microbes living in the gut while assuring that the immune system stays alert against invasive infections (3).

IMMUNE MODULATION MECHANISMS

There are numerous and intricate ways that the microbiome influences immune responses. Signaling molecules that influence the activity of immune cells are generated through the fermentation of dietary fibers and other substrates into microbial products and metabolites. Butyrate, propionate, and acetate, which are microbial metabolites that are crucial for immune system function; they are called short-chain fatty acids (SCFAs). SCFAs, which inhibit the activation of the proinflammatory immune cells, exhibit anti-inflammatory properties and originate from regulatory T cells (Tregs). By blocking the entry of pathogenic microbes and antigens into the systemic circulation, SCFAs additionally aid in maintaining the integrity of the gastrointestinal barrier. (4). Moreover, the microbiome actively contributes to the maturation and stimulation of different subsets of immune cells. Under the impact of microbial signals, T cells, B cells, and dendritic cells go through stages of differentiation and maturation. As an example, it has been demonstrated that segmented filamentous bacteria (SFB) can stimulate the development of Th17 cells, a subgroup of T cells related to mucosal defense (5). Beyond the mucosal immune system, the gut microbiome affects systemic immune responses by modifying the makeup of immune cell subsets. Research has indicated that affect the ratio of pro- to anti-inflammatory immune cell subsets, which in turn can affect immunological responses in other organs (6).

DYSBIOSIS AND DISEASE

A proper microbiome aids in immunological homeostasis, but dysbiosis, or an imbalance in this delicate balance, has been linked to a number of diseases. Allergies, metabolic issues, inflammatory bowel diseases (IBD), autoimmune disorders, and other conditions might alter the activity and composition of the microbiome. In the presence of autoimmune diseases, dysbiosis has been associated with the occurrence of harmful immune system reactions against self-antigens and the loss of immunological tolerance. For instance, there is evidence to suggest that dysbiosis may contribute to the progression of joint inflammation and autoimmune production by increasing the concentration of Prevotella copri in patients with rheumatoid arthritis (7). Alterations in the relative amount of specific bacterial taxa and reductions in microbial diversity are the root causes of the imbalanced immune systems observed in conditions like colitis with ulcers and Crohn's disease (8). An additional association has been established between dysbiosis and allergic disorders, including atopic dermatitis and asthma. There is a correlation between alterations in the gastrointestinal microbiota during early life and an increased susceptibility to allergic reactions and allergic illnesses (9). Dysbiosis also has an impact on metabolic diseases including type 2 diabetes and obesity. Modifications in the composition of the gut microbiome have been linked to changes in insulin resistance, inflammation, and the consumption of energy from the diet, all of which are factors in the etiology of metabolic disorders (10).

THERAPEUTIC IMPLICATIONS

The understanding of the microbiome's crucial function in immune regulation has opened the door for novel treatment approaches meant to improve health and restore microbial equilibrium. Probiotics are one such treatment option; they are characterized as live micro- organisms , when given in adequate proportions, impart health advantages. The potential of these advantageous

microorganisms, which are frequently membersof genera Lctobacillus and Bifido-bacterium, to improve immunological responses, preserve the integrity of the gut barrier, and reduce inflammation has been investigated (11). Another strategy for modifying the microbiome is the use of prebiotics, which are indigestible materials that act as growth media for beneficial bacteria. Prebiotics aid in the restoration of microbial balance and the improvement of immune function by encouraging the growth of particular bacterial taxa with beneficial properties (12). Fecal microbiota transplantation (FMT) is a more advanced treatment approach that involves transferring fecal material from a healthy donor to a recipient. Microbiome-based therapeutics have shown great promise in managing certain diseases, as seen by the remarkable success of treating persistent infections caused by Clostridium difficile with FMT (13). Because of its potential for therapeutic use, the idea of postbiotics—bioactive substances made by microbes—has drawn interest. Postbiotics are a broad class of compounds that include extracellular vesicles, metabolic products, and components of cell walls that might influence immune responses and improve general health (14). The possibilities for individualized and targeted treatment interventions keep growing as our understanding of immune regulation and the microbiota develops. Precision microbiome-based medicines, customized to each patient's needs, have the potential to treat a broad range of illnesses.

"MICROBIOME DYNAMICS: SYMBIOSIS TO DYSBIOSIS"

Humans are basically interdependent creatures. Humans are essentially sterile at birth, and as they interact with microbes, they create a microbiota and strengthen their immune systems at the same time. Microorganisms that reside in a particular environment and are present in all multicellular organisms (including plants) constitute a microbiota. This includes all bacteria, archaea, eukaryotes, and viruses. The term "microbiome" is commonly employed to encompass both the discrete environmental niche and the collective genomes of microorganisms that inhabit it. The microbiota not only facilitates metabolic processes, barrier function, and immunological activation but also imparts information to virtually all bodily organs. Through coordination and contact, the intestinal innate and adaptive immunity establish a mutually beneficial relationship with the symbionts that maintain intestinal homeostasis. This is achieved through the maintenance of a pro-inflammatory response toward invasive pathogens by permitting the symbiotic-microbiota to coexist. To maintain general health and well-being, symbiosis must be maintained. Pathogenic intestinal bacteria proliferate more readily when the gut microbiota is disrupted; Decreased growth of beneficial microbial products, such as short-chain fatty acids, and an enhanced pro-inflammatory response of the immune system are observed. The following are several mechanisms through which disruption of the gastrointestinal microbiota can elevate the vulnerability to infection and sepsis (15): Immunological homeostasis will be lost and the risk of inflammatory or immunological illnesses will increase if there is a disruption at the barrier immunity level. To prevent or reduce the hazards, or even for use in microbiome-targeted treatments, it is crucial to comprehend symbiosis and create the means to monitor and modify it. The human body's microbial ecosystem contains 100 trillion microorganisms. Located at the interface between swallowed food and the gut epithelium, the human gut microbiota is in contact with both the body's first immune cell pool and second neural cell pool. Despite this, study on this topic has long been neglected.
It is becoming more widely acknowledged as a real organ that affects both health and illness. Only roughly 30% of the dominant gut microbiota could be evaluated by culture, which is a rather narrow viewpoint (16, 18). Consequently, techniques that are not dependent on culture were created to allow for a thorough assessment of the microbiota. The field of microbiome research has advanced significantly because of shotgun metagenomics. Every human has roughly 23,000 genes, but every microbe has about 600,000 genes. Accordingly, fewer than 4% of the entire hologenome is made up of human material (21, 29). This review aims to provide a current understanding of the human gut microbiome, as well as an explanation of the shift from symbiosis to dysbiosis and how it affects human health.

DISCUSSION

Nowadays, a great deal of information has been provided about the protective bioactivity of several bacterial species, many of which are found in the metagenomic core of the microbiota. Certain bioactive chemicals that are crucial to the host-microbe symbiosis are produced by some of these microorganisms. The immunomodulatory capsular polysaccharide A (PSA) possessed by Bacteroides fragilis is a strong activator of CD4+ T lymphocytes and plays a crucial role in maintaining immunological homeostasis (22). A number of researchers have now initiated phase 1 and 2 clinical studies in which patients are given capsules containing a bioactive microbe in an effort to treat or reduce risks associated with particular medical disorders. The application of F. prausnitzii as a monostrain method in clinical trials for the treatment of IBS is one instance of this. Akkermansia muciniphila serves as an additional example of a bioactive commensal, as it exhibits an inverse correlation with cardiometabolic disorders, obesity, diabetes, and low-grade inflammation (23). An association was established between The presence of A. muciniphila was found to be associated with a decrease in cardiometabolic risk factors and a reduced prevalence of this microbe in mice that had type 2 diabetes and/or obesity (24). Presently under evaluation is the purified, bioactive outer membrane protein (Amuc_1l00) of A. muciniphila, which was the

subject of the initial proof-of-concept study involving Akkermansia in humans, which was supported by an abundance of evidence (23, 25). However, some research indicates that A. muciniphila could be harmful, especially in instances of graft-versus-host disease following allo- HSCT (26) or intestinal inflammation induced by Salmonella enterica Typhimurium (27). Patients who have compromised immune systems are particularly vulnerable to Bacteroides fragilis, a notorious opportunistic pathogen (28, 29). All things considered, this begs the question of whether bacterial therapy could be harmful, depending on the pathology and host environment. As next-generation probiotics, several additional bioactive commensals, like Roseburia intestinalis and Blautia hydrogeno trophica, are now being produced. Similarly, commensal Hafnia alvei strain appears as a new promising probiotic for appetite and body weight management and decreases food intake and fat accumulation in obese rats (30).

Secretory IgA has always been an explosive chemical. A minority of immunologists argue that IgA insufficiency is not significant because of its modest phenotype, while others argue that it is because of its abundance and evolutionary history. Furthermore, opinions on the relative roles of "natural" and T cell-independent IgA vs affinity-matured, T cell-dependent IgA in microbiota and infection control are widely held but are becoming less so. Good evidence backs up differing viewpoints, as it does in any well-argued argument. Here, we review some long-standing issues related to IgA biochemistry. The topic of intestinal IgA antigen specificity and important definitions of IgA induction, specificity, and function are where we begin the debate. Next, these criteria need to be woven together with the molecular and cellular processes that influence IgA responses as well as the mechanisms that underpin IgA action. We suggest that IgA could play a role in the formation and upkeep of advantageous relationships with the microbiota based on findings (31).

Microbial cells make up 1%–3% of our total body mass and are found in the human body in 10- fold higher concentrations than human cells. As our understanding of this symbiotic relationship deepens, it seems that almost every portion of the body engages in this intricate interaction— even the parts that were once thought to be sterile. The role of the microbiome in human reproduction has been studied for both the upper and lower reproductive tracts, and interactions have been found all the way up to gametogenesis. Even before bacteria were given names, we have been aware of their significance for more than 150 years, which makes them all the more fascinating. As a result of an exciting technological revolution that has advanced our knowledge of the microbiome, we now seem to be at the frontier of understanding microorganisms, the biofilms they form, and how health and illness are impacted by them in human reproduction (32).

The medium via which we mediate relationships with our surroundings throughout our lives is our skin. Normal cutaneous microbial colonization, immunological development, and disease prevention depend on the skin's epidermis, adnexal structures, and barrier function developing at early stages. Skin health can be uniquely and permanently impacted by microbiological exposures from early childhood. The identification of skin microorganisms in neonates and the environment in which they are initially encountered—that is, through a weakened skin barrier or in association with cutaneous inflammation—can have implications for both short- and long-term health. The main characteristics of baby skin and the internal and external variables that influence how it interacts with the cutaneous microbiota during early life are covered here, with an emphasis on the practical applications (33).

Children who are undernourished in low-income nations frequently react poorly to oral vaccinations. Undernutrition is associated with disrupted microbiome development, but it's unclear if and how these alterations impact vaccination response. Here, we demonstrate that the mucosal IgA responses to oral vaccination with cholera toxin (CT) differed depending on the microbiota in gnotobiotic mice colonized with microbiota from malnourished Bangladeshi children and given a Bangladeshi diet. A nutraceutical supplement containing vitamins, spirulina, amaranth, and flaxseed increased the synthesis of CT-IgA. After being colonized with bacteria from cagemates with a more "responsive" microbiota, mice whose original microbiota was linked to poor CT responses showed increased immunogenicity. A group of five cultivated bacterial invaders also gave to mice given the enriched food and colonized with the "hypo- responsive" community increased CT-IgA responses. Preclinical evidence is presented by these findings supporting the notion that microbiota and diet affect mucosal immune responses to CT immunization and suggest a potential synbiotic formulation (34).

The gut-brain axis and microbiome Over the last ten years, it has become more evident in autoimmune neuron inflammation that the gut and its resident microbiota are important factors in a number of disorders, including multiple sclerosis. About the same number of diverse microorganisms as human cells, mostly bacteria, are found in the gut in trillions (35). It is believed that gut colonization starts at birth in humans and other mammals (36). The two predominant phylotypes of the adult microbiome are Firmicutes and Bacteroidetes (37). Several investigations have determined the basic functions of the gut microbiota, including defense against invading pathogens and conversion of nutrients into bioactive compounds including fatty acids, vitamins, and neurotransmitters (38). A complex network of communication between the gut and the central nervous system (CNS) is known as the "gut-brain axis" or "microbiome gut-brain axis," and it includes the microbiota, which is crucial for activating the host's immune system. The hypothalamus pituitary adrenal axis, the vagus nerve, the enteric nervous system, and the autonomic nervous system

are other components of this two-way communication system (39). Multiple pathways connect the gastrointestinal microbiome to the central nervous system (CNS). Vagus nerve direct activation can induce the secretion of acetylcholine or catecholamines (40), in addition to the production of various neuropeptides, gastrointestinal hormones, neurotransmitters, and microbial-associated molecular patterns (MAMPs). The gut microbiota also produces immunostimulatory signals that have the potential to trigger both innate and adaptive immune reactions. It has been demonstrated that the intestinal microbiome's diversity and composition are regulated by the adaptive immune system, and vice versa.(41) As a result, the immune system is crucial to the dynamic balance that exists between the intestines and the brain and all other main organs (42). Thus, it is not unexpected that several autoimmune illnesses, including MS, have been linked to changes in the composition of the commensal gut microbiota (43, 44). A dysbiotic gut microbiota, characterized by a decrease in species belonging to the Clostridia XIV and IV clusters, has been found in MS patients, according to recently published studies (45). The use of probiotics and fecal transplants, the use of antibiotics to eradicate the microbiota, and germ-free animals have all been aspects of experimental research examining the role of the gut microbiome in CNS autoimmunity. The intestinal microbiota has been shown to exist in mice to be crucial in promoting CNS inflammatory processes. When myelin peptide is administered actively, For example, germ-free mice—mice raised and housed in a sterile environment—have significantly lower EAE severity. Furthermore, the incidence of spontaneous EAE was identified to be significantly reduced in T-cell receptor transgenic rodents housed in germ-free environments (46, 47). Oral antibiotic therapy eliminated a substantial quantity of bacteria while consistently impeding the growth of EAE in wild-type rodents. This defense mechanism was associated with an upregulation of pro-inflammatory cytokines and a downregulation of IL-10 and IL-13 production (47). Numerous studies, nevertheless, have identified the benefits of the intestinal microbiome and underscored its criticality for maintaining optimal immunity.

CONCLUSION

A paradigm shift is taking place in the dynamic field of microbiota research, with a growing emphasis on the medicinal potential of bioactive bacteria and their complex functions in host- microbe symbiosis. Bacterial species that contain capsule polysaccharide A (PSA), an immunomodulatory compound, serve as an illustration of the intricate interplay among microbial activity and immunological homeostasis. This has prompted clinical trials investigating the use of bioactive bacteria such as Akkermansia muciniphila and F. prausnitzii, which suggest a potentially fruitful avenue for microbiome-targeted therapies. But in some therapeutic situations, the possibility of negative consequences from dual-natured bioactive commensals like A. muciniphila reduces this optimism. This highlights the importance of a complex understanding specific to the illness and host context and raises important considerations about careful application of bacterial therapy. The identification of the human microbiome as a legitimate organ, particularly in human reproduction, represents a paradigm change in our understanding of the influence of bacteria on health and illness across multiple bodily regions, extending beyond the gut. The role of various IgA types in positive interactions with the microbiota is still a topic of debate in the field of IgA science. Still, it's clear that IgA contributes significantly to the development and upkeep of a beneficial relationship with the microbiota. Remarkably, vaccine response is also influenced by the microbiome, as observed in children who are malnourished. Improving the effectiveness of oral vaccines may be possible through the modification of mucosal IgA responses by diet and microbiota management. A thorough study of the gut microbiota's impact on numerous physiological processes and its association with autoimmune illnesses such as MS is necessary, as it plays a critical role in autoimmune neuron inflammation within the microbiome gut-brain axis. The microbiome's implications for human health and disease highlight the need for ongoing research and innovation in this rapidly developing subject, which holds forth the promise of revolutionary possibilities as we negotiate this complicated area.

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Journal of Health and Rehabilitation Research 2791-156X JHRR

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