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THE RELEVANCE OF IMPROVING MICROFLORA IN CASE OF WEAKENED IMMUNITY AND STABILIZATION MEASURES

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ABSTRACT

A complex ecosystem made up of many cells far more numerous than the total number of cells in the human body is comprised of the microbial communities that inhabit it. Given its complexity, relationship to health, and involvement in a number of clinical disorders, it is well acknowledged that the human gut microbiota is a subject of study interest. The demand for more research is fueled by the desire to thoroughly clarify and record hitherto unidentified facets of the gut microbiota and its connections to health. Additionally, it has served as a catalyst for doing the current examination of the research sources that have been submitted thus far. Because of competition and natural selection throughout life, the human intestine is a natural ecosystem containing a complex of diverse and dynamic microorganisms. These intestinal microbes, known as microbiota, interact with the host and are consequently in contact with the organs of the different systems. They are also involved in a number of the organism's functions. But they also have an impact on the host's behavior and are essential for preserving homeostasis. Therefore, microbes carry out a number of biological tasks that are crucial to human health. In addition to giving the microorganisms their surroundings and nourishment, the host also reaps numerous advantages from them, including their support of trophic, metabolic, immunological, and other processes. Because of these factors, it has been claimed that both its quantitative and qualitative makeup might either positively or negatively impact the host's health. As a result, a

dysbiosis may result in a cluster of adverse conditions that cause the physiological processes of homeostasis to become dysregulated. The pathophysiology of autoimmune illnesses, diabetes mellitus, obesity, atherosclerosis, neurological disorders (such as autism, neurological diseases, etc.), colorectal cancer, and other conditions has therefore been observed to be influenced by the gut microbiota.

Introduction. The human organism is colonized by trillions of microbes. The microbiome refers to all the genes of microbes found in various locations in an individual's body. Instead for microbiota we mean the total of microorganisms quantitatively and qualitatively present. The human host and the microbiota have co-evolved for the benefit of both parties especially the intestinal one. In fact, on the one hand, the host provides space, suitable conditions, and food for the growth of the intestinal microbiota and this in turn generally participates in obtaining useful substances and induces resistance to various infections. The relationship between the human gut microbiota and the host is symbiotic, in which both the host and the microorganisms are mutually beneficial. For its part, the host offers a place of growth and nourishment to the symbiotic intestinal bacteria, which in turn favors the function of the host on the one hand by inducing resistance to infections and on the other hand by facilitating the absorption of digested food. The host provides the symbiotic intestinal bacteria with a location to live and feed, which benefits the host's function by promoting infection resistance and, on the other side, making it easier for the bacteria to absorb food that has been digested [1-5]. Therefore, it would seem that symbiotic bacteria and eukaryotic hosts have "co-evolved" through interactions based on mutually beneficial nutrition. Diseases like mild chronic intestinal inflammation or metabolic abnormalities can develop when this equilibrium is upset (dysbiosis) for a variety of causes, including excessive and improper use of antibiotics or alcohol misuse. Particularly interesting are the interactions between (symbiotic) microbes. Members of the phylum *Bacteroidota*, including the *Prevotellaceae spp.,* have been found to negatively correlate with one another in the intestine; this could be a result of different "metabolic specializations." Therefore, the gut microbiota is especially crucial for preserving human health. Since many biological processes are necessary for maintaining homeostasis and cannot be carried out independently, they are actually dependent on the microbiota. The term "superorganism" often refers to the beneficial and reciprocal interaction between the intestinal microbiota and the host organism. Additionally, the microbiota has a trophic and protective role that influences a number of the host organism's homeostatic functions, including tissue trophism, immunological balance, metabolic activity, neuro-endocrine function, etc. The most prevalent community in the entire organism is the intestinal microbiota. Actually, there are roughly 103–104 bacteria per gram of tissue in the stomach, 105–106 in the duodenum, and 108–109 in the terminal ileum [6-11]. The large intestinal one, which has about 1012–14 bacteria per gram of tissue, is the most crowded. From birth, a complex

collection of bacteria forms in the colon, a section of the gastrointestinal tract. Compared to the human microbiota of the small intestine, the microbiota of the large intestine is denser and more varied. *Bacteroidota* and *Lachnospiracae* are more prevalent in colonic samples, whereas *Bacillota* and *Actinomycetota* are richer in intestinal tissue. The intestinal microbiota is thought to consist of 400–500 distinct genera of microorganisms, with 90% of these species being primarily anaerobic. The majority of them are members of the *Bacteroidota* and *Bacillota genera. Pseudomonadota, Actinomycetota, Fusobacteria* and *Verrucomicrobia* comprise the remaining bacterial communities. Bacteria that cannot be cultivated using standard microbiological methods make up an estimated 70% of these microbial ecosystems [12,13,14]. The microbial populations in the intestinal lumen and intestinal mucosa have been discovered to be different. The majority of microbial cells, which differ in species from person to person and are arranged in discrete microbial communities throughout its course, are found in the large intestine. Last but not least, probiotics are the "good" bacteria that are present in the gut microbiota but are also given to certain diets or fermented foods. Probiotics support the body by boosting immunity and improving gastrointestinal health, particularly in cases of irritable bowel syndrome (IBS). Fuller enumerated the therapeutic uses and positive effects of probiotic bacteria in 1989. Probiotics can be found in a variety of foods, including pickled vegetables and dairy products like aged cheeses and yogurt. By encouraging the growth of beneficial microorganisms, probiotics help the body fight off potentially dangerous germs and fortify its defenses. Studies employing cultures of *Lactobacillus acidophilus, Bifidobacterium, Streptococcus thermophilus* and *Lactobacillus delbrueckii subsp*. bulgaricus are cited in a number of scientific publications discussing these findings. The human body can benefit greatly from consuming probiotic supplements in several ways. Probiotics' antimicrobial qualities allow them to combat intestinal and other illnesses, help with infections (including those caused by the coronavirus disease 2019 and others), lower serum cholesterol, boost immunity, lessen allergy symptoms, help with lactose intolerance, prevent osteoporosis and hypercholesterolemia, and more [15-19].

The main purpose of this brief review is to analyze the relevance of improving the microflora in case of weakened immunity and stabilization measures based on reputable scientific literature.

The primary factors influencing the inheritance of intestinal microbiota. There is still more to learn about the mechanisms underlying host-bacteria interactions. The interaction between the gut bacteria and the host genotype is poorly understood. It does, however, appear to have an impact on intestinal populations. The makeup of gut microbes can alter as a result of simple genetic mutations. To identify the methods by which this happens, more research is required. Studies comparing the intestinal microbiota of family members are scarce. The gut microbiota of monozygotic and dizygotic twins was found to be more comparable than that of dizygotic siblings, highlighting the significance of genetic background. Additionally, in an animal model, it was found that, despite a shared environmental effect, the gut microbiota of the same strain of mice was more similar than that of mice of a different species. Uncertainty

surrounds the impact of parental genetic influence on intestinal microbial colonization [5-10].

Immunological responses and defense against pathogen colonization. Both the gut microbiota and environmental pathogenic microorganisms are encountered by the host's organism. Prior research on the immune system has concentrated on the ways in which it can protect itself from harmful microorganisms. Furthermore, the gut microbiota's microbes generate antimicrobial compounds like hydrogen peroxide and bacteriocins that stop the growth of other dangerous species. The immune system has changed throughout time to be able to support increasingly complex symbiotic bacterial communities while still being able to combat harmful germs. The innate and acquired immune systems' growth and operation are regulated by the microbiome. The intestinal microbiota continuously stimulates the immune system, even when the host is in good health. An efficient initial line of defense against harmful microorganisms is the "low physiological inflammation" that results from this condition. Additionally, the microbiota plays a protective role by metabolizing resources required for the pathogens' survival and generating chemicals that prevent their growth since resident and pathogenic microorganisms fight for accessible locations and nutrients [12-15]. Indeed, it has been demonstrated that the introduction of specific compounds made by *Eubacterium rectale* and *Bacteroides thetaiotamicron* can cause the development of particular mucosal glycans. These two bacterial species are the only ones that can digest them; pathogens cannot, which stops them from growing. As a result, nutrition seems to play a major part in changes in the microbial composition. The immune system functions through learning, meaning that while it has the required elements (cells, internal cellular mediators, etc.) at birth, it lacks environmental information that it gains during the first few years of life through interactions with other humans and the environment. The immune system's regulatory systems may not function properly if these early childhood data are not acceptable. As a result, the immune system targets innocent objects like pollen, household dust, and food antigens in addition to harmful germs, which causes allergic disorders to develop. As demonstrated experimentally by the restoration of systemic T-cell deficiency and Th1/Th2 imbalance of sterile muscle microbes following a single colonization of the muscle gut with the bacterium Bacteroides fragilis, recolonization of these muscles with muscle-specific bacteria can reverse some of these perturbations. Together, these findings demonstrate how crucial the gut microbiota is to the healthy growth of the peripheral immune system in immunocompetent hosts [3-12].

Immune dysregulation (autoimmunity and allergies). A mature gut microbiota requires the systemic and local mucosa to have their immunity effectively aroused. Failure to do so may result in dysregulation, which may cause allergic reactions or an asthmatic phenotype from a young age. Asthma and other allergy illnesses have been found to be less common in underdeveloped nations than in developed ones. Thus, the "hygiene hypothesis" was created, which states that this disease can be brought on by a lack of exposure to pathogenic bacteria or products of non-pathogenic bacteria by having a detrimental effect on the immune system's development. The "microbiota hypothesis" was then created, which postulates that dietary modifications and the greater use of

antibiotics in modern countries result in a less diversified gut microbiota in terms of its microbial components. According to its definition, this "immature" gut microbiota changes how the immune system develops, preventing the appropriate progression of events that lead to the formation of immunological tolerance and raising the risk of allergic hypersensitivity. More precisely, during the first few months of life, levels of enterococci and Bifidobacterium seemed to be linked to allergy symptoms [2-7]. Children with atopy symptoms had a higher *Bacteroidota/Bifidobacterium* ratio in their second year of life. Children who later developed allergies had lower rates of colonization with *Lactobacillaceae phyla, Bifidobacterium* and *Clostridium difficile* strains in their second month of life. An immune-mediated assault on the body's own organs is a common etiology among autoimmune illnesses, including rheumatoid arthritis and others. A wide range of traits and symptoms are typically present in autoimmune disorders. The most prevalent of these traits might be, for instance, increased vessel and epithelial permeability (including intestinal permeability), mitochondrial dysfunction, chronic infections and progressive inflammation, hypothalamic-pituitary-adrenal (HPA) axis imbalance, and microbiota dysbiosis. Finally, the intestinal microbiota seems to play a fundamental role in the development and course of celiac disease. There is an unfavourable qualitative and quantitative composition of the intestinal microbiota characterized by a greater presence of the genus *Bacteroides* and *Escherichia coli* and a minor presence of *Bifidobacterium spp.* (e.g., B. longum compared to healthy controls). Furthermore, this condition does not seem to change even after a gluten-free diet. Finally, it has been noted that children born by caesarean section have a higher risk to develop the disease [8-13].

Modulation of the immune system. Commensal bacteria are essential for immunological homeostasis education and maintenance. In industrialized nations, the prevalence of autoimmune disorders including type 1 diabetes (T1D) and allergic diseases such food allergies, atopic dermatitis, and asthma has significantly increased in recent decades. It's interesting to note that people who migrate before a particular age from nations with low incidence rates of these disorders to those with greater rates typically take on the disease prevalence of their new country. For example, studies show that children who relocate to nations with higher rates of allergic asthma before the age of five are more likely to catch the disease at rates comparable to those of the host nation's population [1-4]. It is acknowledged that crucial developmental stages are involved in an individual's immune system development. Early exposure to a wide variety of microorganisms is crucial for the immune system's healthy development because it activates immune regulatory pathways, especially those that include Toll-like receptors (TLRs), which promote a balanced immunological response. It is believed that this mechanism encourages the production of regulatory T cells (Treg), which reduce overactive immune responses and may lower the risk of developing autoimmune and allergy illnesses by producing anti-inflammatory cytokines including TGF-β and IL-10. It has also been proposed that commensals' beneficial benefits include antigenic competition and the regulation of inflammatory responses, potentially via processes like TLR desensitization [12-15].

Prospects for the future. The worldwide burden study, which was just released, emphasizes the enormous obstacles we face in a number of public health emergencies, such as cancer, cardiovascular disease, gastrointestinal problems, diabetes, obesity and malnutrition, and antibiotic resistance. We have also been forced to consider how we may improve our prevention and treatment methods for possible future infectious disease outbreaks as a result of the novel coronavirus outbreak. The human adative genome, or microbiome, offers a possible path toward future advancements in this field. Despite advancements, the mysteries surrounding the interaction between germs and humans remain to be fully revealed. Future studies are required to get a better idea of what's underneath the surface. Among the instructions include, but are not restricted to, the following: Potential tactics that rely on interdisciplinary and global cooperation include preserving the diversity of human and environmental microbiomes, preventing the progressive loss of adaptive genetic components, and creating and maintaining microbiome banks. These preventative steps have the potential to significantly benefit a variety of organisms, such as increasing crop yields, strengthening plant resilience to climate change, and maybe saving endangered animal species. It is crucial to continue figuring out how the microbiome interacts with different organs and tissues [5-13]. Research on microbiota is now being conducted on the following: Equity is a crucial issue in the field of microbiome research. Compared to studies conducted in rich countries, those conducted in developing or impoverished countries are underrepresented and at a major disadvantage. In this sense, policy preferences for underrepresented regions or research should be taken into account by worldwide professional associations, pertinent governmental and social research funding authorities, and scholarly journals. The success of citizen science techniques used by Belgium and the latest African Equitable Scheme proposed by Ovokeraye H. Oduaran and colleagues are commendable in regions or nations where conducting large-scale population surveys is difficult. We are currently on the path to understanding natural occurrences, unraveling complex mechanisms, and utilizing germs to maximize human health. Ultimately, concentrating just on our inherent genome and neglecting our adaptive genome may result in broader health problems if human colonization of other planets is indeed feasible. Therefore, considering an interplanetary microbiome initiative becomes an unavoidable requirement in all possible scenarios [14-20].

Discussion. The induction, training, and operation of the host immune system are all significantly influenced by the microbiota. In exchange, the immune system has mostly developed as a mechanism to preserve the host's symbiotic relationship with these incredibly varied and dynamic microorganisms. When functioning at its best, the immune system-microbiota partnership enables the activation of defense mechanisms against pathogens and the preservation of regulatory pathways that contribute to tolerance to harmless antigens. But in high-income nations, the overuse of antibiotics, dietary modifications, and the eradication of essential partners like worms have led to the selection of a microbiota that lacks the diversity and resilience needed to create balanced immune responses. In regions of the world where our symbiotic interaction with the microbiota has been most impacted, this phenomenon is thought to partially explain the

sharp increase in autoimmune and inflammatory illnesses [7,11,13]. The immune system is made up of an intricate web of both innate and adaptive parts that have the remarkable ability to adjust and react to a wide range of situations. In the face of microbial and environmental interactions, this cellular network functions as a powerful regulator of host homeostasis, enabling the maintenance and restoration of tissue function. The acquisition of a complex microbiota has coincided with the development of distinct immune system arms, particularly those linked to adaptive immunity. This supports the idea that a significant portion of this machinery has evolved as a way to maintain symbiotic relationships with these incredibly diverse microbial communities. Despite the fact that microbiota members are frequently called commensals, the term "symbiosis" refers to the ongoing interaction between the microbiota and its mammalian host, which can take many different forms, such as mutualistic, parasitic, or commensal relationships. However, the way certain microbiota members interact with their host can vary greatly depending on the host's genetic makeup, co-infection, or nutrition. A single bacterium may develop as a parasite or mutualist. The last ten years have seen a re-discovery of a more comprehensive understanding of host physiology as a result of the investigation of both optimum and dysregulated relationships between the microbiota and its mammalian host [6-12]. The microbiota then supports and balances every component of the immune system. In fact, the idea that microbial partners can improve human health is not new; it was first put forth in Döderlein's (1892) groundbreaking work, which included his comprehension of the function of lactobacilli as guardians of the vaginal ecosystem and Metchnikoff's observation that fermented milk products have a longer lifespan. Our knowledge of the microbiome and how differences in these populations can contribute to disease states has changed as a result of recent attempts to sequence the human meta-genome. In this review, we will go over some of the key ideas that have come out of the recent discussions among immunologists, geneticists, microbiologists, and clinicians that emphasize the intricate relationship between the immune system and the microbiota in both health and illness [13-17].

Conclusions. The so-called microbiota is a vast community of microorganisms of different composition that progressively invade the human body both internally and outside. The intestine one is the most populous and significant. The host's health is crucial to the gut microbiota because it provides a stable and nutrient-rich environment for them to flourish. The host gains from this since they not only stop infections from colonizing, but they also have a constant and dynamic impact on the homeostasis of their host. As a result, this symbiosis establishes the host/gut microbiota axis that affects a person's health over the course of their lifetime.

In actuality, a disruption of the gut microbiota has been linked to a variety of illnesses, including mental and psychic issues as well as neurological conditions, diabetes, obesity, and asthma. More research is necessary to determine the makeup of the microbiota that causes or results in a disease, though, as not all correlation mechanisms are yet fully understood. This study focuses on the human microbiota and its composition in order to correlate physiological and pathological issues throughout life. In actuality,

the scientific community is still working to comprehend it and connect its evolution and transformation to a number of human medical disorders.

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