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THE IMPORTANCE OF NORMAL MICROFLORA FOR HUMAN HEALTH AND THE RELEVANCE OF ITS STABILIZATION

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ABSTRACT

The microorganisms normally present in healthy individuals are known as the normal microbiota. These microorganisms, which can be pathogenic (able to cause disease) but are not now doing so, are found throughout the body. Some of the usual microbiota are thought to be indigenous since they are always present. Others are temporary, appearing in some healthy individuals for a brief period of time without producing illness before being removed. Since its discovery, several studies have emphasized the importance of microbiota in health and illness. Microbiota can be divided into four categories based on the localized areas: gastrointestinal, mouth, respiratory, and skin. Together with the host, the microbial populations maintain homeostasis and control immunological response. On the other hand, dysbiosis of the microbiota can result in diseases such as cancer, respiratory disorders, cardiovascular diseases (CVDs) and dysregulation of body systems. We go over what is currently known about the relationship between microbiota and pathogenesis or host health in this review. The study on microbiota in healthy conditions, including immune regulation, colonization resistance and the gut-brain axis, is first

summarized. Next, we discuss the pathophysiology of microbiota dysbiosis in the onset and progression of disease, which is mainly linked to the generation of chronic inflammation, host immune response modulation, and dysregulation of community composition. Lastly, we present clinical strategies that use microbiota to treat diseases, including fecal microbial transplantation and microbiota regulation.

Introduction. In healthy individuals, the bacteria are known as the normal microbiota. These microorganisms can be pathogenic, meaning they have the ability to cause disease, but they are not currently doing so. They are found throughout the body. It is thought that some of the regular microbiota are indigenous since they are always present. Others are transitory, appearing briefly in healthy individuals without causing illness before being removed. Numerous microbiome species are regarded as opportunistic pathogens. These microorganisms typically do not cause illness in healthy individuals, but they can do so in a compromised host (one that lacks a fully functional immune system because of immunosuppressive medication, a genetic defect in one or more immune system components, or an infection with agents that target immune system cells). When opportunistic infections are introduced to an exposed place, they can also infect an immunocompetent host and cause illness. *Staphylococcus epidermidis*, for instance, is a common bacteria found on the skin's surface [1,2,3,4]. However, bacteria can cause infection if they penetrate deeper tissues or even the bloodstream through a skin break. It is possible for certain pathogens to exist in a host without producing obvious signs of illness. Sometimes a pathogen infection occurs, but the symptoms are not yet clinical. The germs can spread to other people since they are reproducing and can shed. Carriage is the definition of this. Since there is no commensal interaction, this is not the same as typical microbiota. Even though the patient is unaware of it, the infection has probably caused damage. Female genital infections caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* are a well-known example. The normal microbiome does not include either of these. Cervical infections or even infections that spread to the fallopian tubes, however, could not show any signs. Over 50% of women infected with these viruses experience this. Despite not being aware that they are afflicted, these ladies are capable of spreading the infection to others [5,6,7,8]. Each geographic region has a different distribution and variety of glands and hair follicles in the human skin. Different skin regions have different microbiota compositions due to their physical and chemical variations. In general, *Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes* and *Proteobacteria* make up the skin microbiota. Numerous studies conducted in the last few decades have brought attention to the connection between bacteria and illnesses like cancer, diabetes, and neurological conditions. Furthermore, modifying the human body's microbiome may be essential for treating illnesses. Here, we provide an overview and discussion of the current understanding of the role of the human microbiota in disease

formation, health condition mediation, and possible therapeutic applications in disease treatment [9,10,11,12].

The main purpose of the presented peer-reviewed manuscript is to conduct a brief analysis of the importance of normal microflora for human health and the relevance of its stabilization.

The gut microbiome that is "healthy". The balance of intestinal microbes has a direct bearing on human health and illness. About 100 trillion bacteria are found in the human gastrointestinal (GI) tract, which has a more numerous microbial ecology than other parts of the body. Numerous investigations have been conducted to demonstrate the significant connection between the gut microbiota and fundamental biological functions in humans. Recent research, for instance, has demonstrated the intimate relationship between the human microbiota and immunity, metabolism, and nutritional extraction. Microbiota can influence biological processes in a number of ways. Because of the diverse metabolic genes that produce separate, distinct enzymes and biochemical pathways, the microbiota is essential for the extraction of energy and nutrients from food. Furthermore, the gut microbiota plays a critical role in the creation of bioactive substances such vitamins, amino acids, and lipids [1-5]. In terms of the immune system, the human microbiota plays a vital role in the development of the intestinal mucosa and immune system in addition to creating antimicrobial compounds that shield the host from external infections (figure 1).

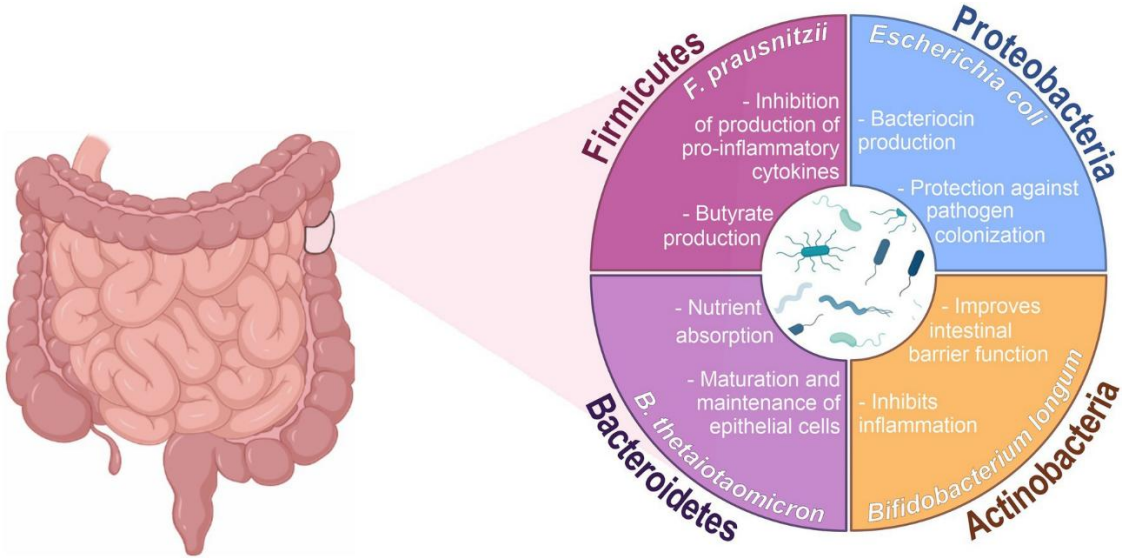

Figure 1. The primary phyla and roles of the gut microbiota [18].

The gut microbiota is stable, resilient, and interacts symbiotically with the host when things are healthy. The concept of a "healthy" gut microbiota and its relationship to host physiological processes are the subject of extensive investigation. Viruses, yeasts, and bacteria make up the gut microbiome. High taxonomic diversity, high microbial gene richness, and stable core microbiota are frequently observed in a healthy microbiome community. It is important to remember that each person has a different relative distribution of microbes, and even within the same person, this distribution might change. Age and environmental factors, such as medication use, can affect a person's gut microbiota. Furthermore, the gut microbiota differs in the GI tract's various anatomical

sections. For instance, the small intestine contains protobacteria like *Enterobacteriaceae*, while the colon does not. Rather, the colon is frequently home to bacteriodetes such *Rikenellaceae, Prevotellaceae* and *Bacteroidaceae*. The various contexts are primarily to blame for these variances [6-11].

Research on human microbiome using rodent models. In recent decades, there has been an increasing amount of research on the human microbiota. However, for pragmatic or moral reasons, local microbiota research necessitates intrusive sample techniques. Studies of the pathogenic and therapeutic potential of microbiota with various diseases have also been conducted using animal models, including mouse and rat models. The germ-free (GF) mouse model has gained popularity because of its translatability, as the majority of microbiota research focuses on gut microbiota. It should be mentioned that the similarities and variances in their microbiome profiles must be taken into account when extrapolating such knowledge from rodents to humans. More than 85% of the genomic sequences between humans and mice are conserved, according to the genome data, with the primary sequence of regulatory elements showing the biggest variance. According to Cheng et al., half of the transcription factor binding sites in the mouse genome might not have human genome orthologous sequences [11-15]. Furthermore, the immune system and how it is regulated in other species differ significantly, according to genetic studies. The gut microbiota plays a significant role in the host's innate and adaptive immune responses, hence it is important to thoroughly evaluate results from rodents before extrapolating them to humans. Although 90% of the phyla and genera in the human and mouse gut microbiota overlap, there are significant differences in the makeup and number of microorganisms. The *Firmicutes/Bacteroidetes* ratio, for example, is much larger in humans than in mice, indicating a considerable difference. Particularly, human *Bacteroidetes* is predominantly composed of *Prevotellaceae* and *Bacteroidaceae*, while mouse *Bacteroidetes* are primarily composed. The main phylum of *Firmicutes* found in humans is *Ruminococcaceae*, while the main phylum found in mice is *Clostridiales. Additionally*, certain genera are present in both humans and mice, including *Mucispirillum* in mice and *Faecalibacterium, Megasphera, Asteroleplasma, Succinivibrio* and *Paraprevotella* in humans [16,17,18].

Disease can be caused by the native microbiota and they are in a very good position to do so. Keep in mind that the resident bacteria are found throughout the body and may be pathogenic, meaning they have the ability to cause disease, but they are not currently doing so. The normal microbiota can serve as a reservoir for infection since a normal resident of one bodily place can cause illness when transferred into another. For immunocompromised people, who are particularly vulnerable to opportunistic infections, this is a major concern. As was previously said, the host may profit from the diverse metabolic capacities of the normal microbiota, but we may also be harmed by the byproducts of their metabolism. Choline, an essential vitamin, for instance, is turned by gut microorganisms into trimethylamine, which is then transformed into trimethylamine oxide (TMAO) in the liver. TMAO has been connected to cardiovascular disease [3-7]. Additionally, resident microbiota may change medications we take for particular purposes and impact how our systems process them, which could impact the effectiveness

of those medications. When attempting to identify the causative agent of an infectious disease, it is crucial to understand which organisms are part of the normal microbiota at a particular site. For instance, the gut microbe metabolite p-cresol can inhibit the liver's ability to metabolize acetaminophen. Other harmful xenobiotics include cyclohexamine, nitrosamines, and deoxycholate. Sometimes a site's bacterial sample will have so many commensals that you won't see the pathogen if it's present. What is considered "normal" at one location may be harmful at another. What one person considers "normal" may be harmful to another. When trying to identify an infectious disease, all of these factors need to be taken into account. Geographical environment, nutrition, age, hormonal state, and physiological variations can all significantly affect an individual's microbiota composition. A person's microbial community will evolve over the course of their lifespan [9-14].

Disease is shifted by microbiota. An individual's overall health is often influenced by their microbial community, or microbiota. Community health is determined by the balance and composition of the community, not necessarily by the presence of a single microbial species. Disease can result from any disturbance in the equilibrium. When the balance of organisms in the microbiota is upset or altered, the condition is commonly referred to as dysbiosis. *Bacterial vaginosis* (BV) is a well-known example of a microbiota shift illness. Actually, a decrease in lactobacilli in the vaginal tract and a matching rise in other microbiota members are diagnostic criteria for bacterial vaginosis. Many bacteria in the gastrointestinal tract may be killed by antibiotics, but not all of them, which can lead to the overgrowth of other bacteria and illness. *Clostridium difficile*, sometimes known as *C. diff,* is the most prevalent gut microbiota member linked to antibiotic-associated diarrhea. Small amounts of *C. difficile* are frequently seen in healthy people's GI tracts without causing any issues. However, *C. difficile* can cause a severe, frequently bloody diarrhea that can progress to pseudomembranous colitis if it is allowed to proliferate to bigger numbers, as may happen when antibiotics are used orally [11-18].

Discussion. The term "microbiota" has its roots in the early 1900s. Numerous microorganisms, such as bacteria, yeasts, and viruses, have been discovered to dwell in different parts of the human body, such as the stomach, skin, lungs, and oral cavity. Furthermore, the human microbiota—also referred to as "the hidden organ"—contributes more than 150 times as much genetic material as the human genome as a whole. Despite their frequent interchangeability, the terms "microbiota" and "microbiome" have some distinctions. The term "microbiota" refers to the live microorganisms, such as gut and oral microbiota, that are present in a certain environment. The term "microbiome" describes the collection of genomes from all of the microorganisms found in the environment, which encompasses the microbial population as well as the metabolites, structural components, and environmental factors. In this sense, the microbiome is more diverse than the microbiota [1,2,3]. We primarily address the role of bacteria in human health and illness in this review. Each site has a different microbial composition. The gut microbiota is thought to be the most important one for preserving human health. In addition to fermenting food, the gut bacteria also fight against infections, boost the immune system, and produce vitamins. In general, the phyla *Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria* and

Verrucomicrobia make up the gut microbiota, with Firmicutes and Bacteroidetes being the most common forms. The most researched fungus (gut mycobiota) are *Cladosporium, Saccharomyces*, *Candida* and *Malassezia.* The human gut microbiota includes not only bacteria and fungus but also viruses, phages, and archaea, primarily *M. smithii.* Although less well-established than in the gut, microbiota can also be found in the skin, lung, vagina, and oral cavity [11,14,15]. The human oral microbiota is thought to be the second-largest microbial population. Saliva, tongue, tooth surfaces, gums, buccal mucosa, palate, and subgingival/supragingival plaque are among the various microbiota habitats that make up the oral cavity. These habitats may undergo significant and quick changes in composition and activity due to things like pH fluctuations, bacterial interactions, and gene mutations. Although there are minor variations, the microbial makeup of all seven sites is generally comparable. *Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria* and *Fusobacteria* are the main types of bacteria found in the oral microbiota. Numerous investigations have shown that microbiota is present in lung tissues, despite the long-held belief that healthy human lungs are sterile. *Firmicutes, Proteobacteria, Bacteroidetes* and *Actinobacteria* comprised the core lung microbiota. Three main factors influence the composition of the lung microbiota: 1) microbial immigration, 2) microbial removal, and 3) microbial reproduction rates. Each geographic region has a different distribution and variety of glands and hair follicles in the human skin [7,8,9,10]. Different skin regions have different microbiota compositions due to their physical and chemical variations. In general, *Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes* and *Proteobacteria* make up the skin microbiota. Numerous studies conducted in the last few decades have brought attention to the connection between bacteria and illnesses like cancer, diabetes, and neurological conditions. Furthermore, modifying the human body's microbiome may be essential for treating illnesses. Here, we provide an overview and discussion of the current understanding of the role of the human microbiota in disease formation, health condition mediation, and possible therapeutic applications in disease treatment [4,5,6,7].

Conclusions. We have gradually discovered a new role for bacteria in health and illness after decades of investigation. It has now been established that the microbiota can impact nearly every element of the host, and that a wide range of illnesses are linked to its dysbiosis. We can now closely examine how bacteria contribute to pathogenesis and preserve human health because of new research technologies. However, the majority of research on microbiota focuses on the bacterial component; it is yet unclear how fungi, viruses, and other microorganisms affect health and illness. Furthermore, whereas microbial dysbiosis is frequently seen in disease states, the microbiota's causal function has not yet been determined.

As a result, this discipline still has many unanswered questions. The development of microbiota-based therapies like FMT and bacterial modulation has been made possible by a better knowledge of the host-microbiota interaction. In the treatment of inflammatory bowel disease, diabetes, C. difficile infection, and other conditions, these approaches are well on their way to producing the best possible therapeutic outcome. In conclusion, by manipulating the microbial symbionts, we are now better equipped to cure illnesses and promote health.

As a result, it might cause the gut microbial ecology to undergo substantial alterations, which could have an impact on how immune responses are modulated and how inflammatory reactions arise. To determine whether dysbiosis is the cause or an effect of the pathologies examined here and additional illnesses with an inflammatory foundation, more research is necessary. attempting to identify which alterations in the metabolites or gut microbiota affect the range of human cytokine responses in immunological disorders.

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