The human microbiome: A critical player in health and disease

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ABSTRACT

Keywords: The human microbiome, ecosystem, gut microbiome, skin microbiome, oral microbiome, dysbiosis.

INTRODUCTION: The human microbiome is a complicated ecology made up of billions of bacteria that live in various regions of the human body, and its importance in supporting human health cannot be understated. The gut microbiome, in particular, has been widely studied and determined to have an important role in immune system regulation, digestion and absorption of nutrients, and the creation of numerous metabolites. Gut microbiome dysbiosis has been related to a variety of conditions and diseases, including metabolic disorders and inflammatory bowel disease. However, the encouraging outcomes of microbiome-based therapeutics like fecal microbiota transplantation and probiotics have given fresh hope for the treatment and prevention of many disorders. Similarly, the skin microbiome and oral microbiome have been discovered to play significant roles in pathogen protection, inflammatory regulation, and general health. Skin and mouth microbiome dysbiosis have been linked to a variety of dermatological and dental, respectively. Microbiome-based treatments, such as topical probiotics, oral probiotics, and prebiotics, have shown success in the treatment and prevention of various disorders. The human microbiome is an intriguing and promising field of research that might lead to new ways of preserving and improving human health. We can create novel ways for preventing and treating a variety of illnesses and diseases by better understanding the intricate connections between the microbiome and the host. It is imperative to continue investigating the microbiome to discover novel and effective therapeutics to battle the increase in chronic illnesses and enhance the general health of our communities.

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seems to be nearly complete. Analysis of waste samples has dominated much of the work done so far in the field of gut microbiome research because they are relatively simple to acquire. Due to the difficulty of collecting samples, the small intestine microbiota has remained an understudied “wilderness”. A minor intestinal enteropathy with an uncertain etiology is term as environmental enteric dysfunction (EED). Undernutrition in children is a symptom of the generational effects of social injustice and poverty. Among the various causes, evidence is mounting for the importance of microbial communities passed down from mothers to their children as well as the disturbed growth of this microbial “organ” during the crucial first two years of life. Although how the various microbial communities in the gut contribute to the growth and metabolism of the host are still unknown (Barratt et al., 2022).

**Functions of the gut microbiome:** The extensive groups of microorganisms residing in the human digestive system, plays a crucial role in digestion and nutrition absorption, in immune system, moreover intestinal barrier maintenance. However, the importance of the gut microbiome in metabolic disorders has become increasingly clear in recent years. For example, studies have shown that gut microbiome changes can cause the body to process food differently, which can lead to obesity. Additionally, type two diabetes has been linked to imbalances in the gut microbiota, which has an impact on over 400 million people globally. Similarly, bowel inflammation, which encompasses inflammatory bowel disease (IBD) and ulcerative colitis is also strongly influenced by disruptions to the gut microbiome (Zhao et al., 2022) (Figure 1).

**Dysbiosis and gut microbiome-based therapies:** There is mounting evidence that the development of both intestinal and extra-intestinal illnesses is influenced by gut microbiota dysbiosis, but environmental factors like nutrition (high sugar low fiber), xenobiotics (antibiotics, medications, food additives), and cleanliness play a more significant role (Hrncir, 2022). Coeliac disease, irritable bowel syndrome (IBS), and inflammatory bowel disease are intestinal disorders. In this respect, intestinal bacteria are becoming important regulators of human health and illness. The important function of the microbiome in the gut is attested to by the fact that a person receives a variety of essential services from it. These include converting indigestible food components into absorbable metabolites, synthesizing essential vitamins, removing harmful substances, competing with pathogens, and fortifying the intestinal wall.

**Gut Microbiome and metabolic disorders:** Trillions of microbes residing in the human gut make up the gut microbiota or gut microbiome. Recent research has shown that the gut microbiome plays a crucial part in maintaining overall well-being and good health. Various factors influence the makeup of the gut microbiome. Diet, environment, genetics, etc. are some of these factors. Gut microbiome disruptions can cause various metabolic disorders, which may include obesity, type two diabetes, and bowel inflammation. Additionally, the importance of the gut microbiome in metabolic disorders has become increasingly clear in recent years. For example, studies have shown that gut microbiome changes can cause the body to process food differently, which can lead to obesity. Additionally, type two diabetes has been linked to imbalances in the gut microbiota, which has an impact on over 400 million people globally.

**Figure 1:** Representative description of the metabolic diseases, gastrointestinal disorders, neuromusculoskeletal conditions, endocrine pathologies, neurodegenerative, and cardiovascular diseases associated with gut dysbiosis (Baptista et al., 2020). The statistics and facts surrounding gut microbiome and metabolic disorders are jaw-dropping; the condition may have a major effect on life expectancy and quality of life. The gut microbiome is involved in digestion and nutrition absorption, the regulation of the immune system, moreover intestinal barrier maintenance. However, disturbances to the gut microbiome can lead to various gastrointestinal disorders, including bowel inflammation. Bowel inflammation, which includes Crohn’s disease and ulcerative colitis, is a chronic inflammatory illness of the gastrointestinal tract [20]. In this condition, there is inflammation in the intestinal lining, which might bring on signs like tummy pain, diarrhea, and bleeding from the rectum. The exact causes of inflammatory bowel disease (IBD) are not fully understood, but research suggests that disruptions to the gut microbiome can have an impact on the onset and spread of the disease (Candidi et al., 2021).

**Gut Microbiome and inflammatory bowel disease:** The gut microbiome, which comprises trillions of microorganisms that reside in the human digestive system, plays a crucial role in maintaining human health. The gut microbiome is involved in digestion and nutrition absorption, the regulation of the immune system, moreover intestinal barrier maintenance. However, disturbances to the gut microbiome can lead to various gastrointestinal disorders, including bowel inflammation. Bowel inflammation, which includes Crohn’s disease and ulcerative colitis, is a chronic inflammatory illness of the gastrointestinal tract [20]. In this condition, there is inflammation in the intestinal lining, which might bring on signs like tummy pain, diarrhea, and bleeding from the rectum. The exact causes of inflammatory bowel disease (IBD) are not fully understood, but research suggests that disruptions to the gut microbiome can have an impact on the onset and spread of the disease (Candidi et al., 2021). Furthermore, the statistics and facts surrounding IBD highlight the significant impact that this condition has on individuals and communities worldwide. According to the World prevalence of approximately 0.3% in North America and Europe. The condition may have a major effect on life quality, with studies showing that individuals with IBD experience lower levels of employment, education, and social participation compared to the general population. Additionally, the healthcare
costs associated with IBD are substantial, with estimates suggesting that the annual cost of IBD in the United States alone is over $6 billion (Sýkora et al., 2018). Finally, the impact of IBD on communities is multifaceted, affecting individuals, families, and healthcare systems. The chronic nature of the disease requires ongoing medical care, including medications and regular monitoring, which can be burdensome for individuals and families.

Additionally, IBD can lead to long-term complications, such as intestinal strictures and cancer, which can further impact the well-being of individuals and place additional strain on healthcare systems. The gut microbiome’s evolving role in IBD highlights the need for further research and development of new treatments that target the gut microbiome, with the potential to improve outcomes and reduce the burden of this condition on individuals and communities (Candelli et al., 2021).

Gut microbiome: The human skin is an important element of pathogen protection. Throughout the organism changes in its characteristics affect the microbial makeup. The skin microbiome comprises fewer taxa in comparison to the most varied body regions because of its textural properties, including oil, water, sebaceous glands, and hair. The skin microbiome differs in terms of density and content, there are bacteria as well as fungi, viruses, archaea, and mites. The microbiome of the skin is made up of all of these different species (Grice et al., 2009). The significance of skin homeostasis is highlighted by the consequences for wound healing and defense against possible pathogens or environmental factors (Boxberger et al., 2021).

Skin microbiome composition and functions: The human skin microbiome is made up of bacteria, fungi, archaea, viruses, and mites (Demodex) (Boxberger et al., 2021). The physiology of the skin site was revealed to be the primary determinant of the makeup of microbial communities, with variations in the relative numbers of bacterial taxa that are associated with moist, dry, and sebaceous microenvironments (Byrd et al., 2018). Staphylococcus, Propionibacterium, Corynebacterium, and Streptococcus are the four most prevalent genera in the skin. Additionally, skin microbiome species dominate oilier environments (lipophilic), whereas Staphylococcus and Corynebacterium species flourish in humid niches. The microbiome includes fungi as a significant component. Malassezia, for instance, is a common lipophilic yeast found all over the body. Whereas some fungi such as Aspergillus species, Cryptococcus species, and Rotorua species are site-specific and only inhabit certain regions of the body (McLean et al., 2018).

Functions of skin microbiome: Human skin microbiomes are assumed to be distinct based on lifestyle and genetic susceptibility (Bay et al., 2020). Comparable to those found in the gut, the skin microbiome plays important functions in the breakdown of natural products, immune system development, and defense against pathogen invasion. The skin microbiome can promote both innate and adaptive immune responses (Shen et al., 2014). Skin’s microbiome helps in maintaining skin homeostasis and its ability to act as a barrier. The desquamation process as well as stratum corneum renewal are aided by the production of protease enzymes by the skin microbiome. The production of sebum and free fatty acids also help in maintaining the skin’s pH regulation (Meihan et al., 2020). Lipase enzyme secretion is involved in the breakdown of the lipidic film surface. In addition to these functions, the microbiome also makes biofilm, produces bacteriocins, and sensed quorums (Baldwin et al., 2017).

Skin microbiome and dermatological disorders: Different disease states can develop as a result of genetic or environmental changes in the normal microbiome (Grice et al., 2017). However, there is a chance that human skin’s microbiome could be pathogenic, which closely corresponds to host homeostasis (Chen et al., 2018). Pathogens are associated with some skin conditions including chronic wounds, psoriasis, atopic dermatitis, and acne vulgaris (Yang et al., 2022) (Figure 2).

Role of the skin microbiome in acne: Teenagers frequently suffer from the chronic inflammatory skin condition acne vulgaris (Bhat and Williams, 2013). Acne is characterized by symptoms including nodular cystic lesions, pimples, and pustules that are brought on by bacteria that penetrate hair follicles (Kurokawa et al., 2009). P. acnes, follicular keratinocytes, and the sebaceous glands are thought to be the three main contributors to the formation of acne (Tom and Barrio, 2008). Antibiotics are being used to prevent the growth of acne; it is crucial to comprehend the skin microbiome related to acne and find alternative acne treatment methods because bacterial resistance is an increasing issue in clinical practices (Xu and Li, 2019).

Psoriasis: The relationships between innate and adaptive immune cells and keratinocytes which are facilitated by cytokines in addition to signaling molecules are hypothesized to be the pathophysiology of psoriasis (Martins et al., 2020). The psoriasis-affecting skin and skin adjacent to it had similar microbiomes. Particularly, it was found that skin with psoriasis lesions had higher levels of firmicutes, Bacteroidetes, and streptococcus and lower levels of actinobacteria and Propionibacterium (Yan et al., 2017; Langan et al., 2019). Xanthomonadacea, a proteobacterium known to be keratolytic, was linked to clinical improvement following to 3-week halotherapy treatment. Probiotics taken orally have a favorable effect on the course of psoriasis (Oleinikzak-Stanich et al., 2021).

Atopic dermatitis (AD): Atopic dermatitis often known as eczema, is a persistent allergic skin disease characterized by an erythematous, dry, and severely pruritic rash with a characteristic distribution (Avena-Woods, 2017). Atopic dermatitis is recognized as multifactorial, with both hereditary and epigenetic factors playing a role (Avena-Woods, 2017). Generally, the skin microbiome of AD patients is low in diversity with S. aureus predominating (Tom and Barrio, 2008). In certain cases, S. aureus overgrowth precedes the formation of AD (Grice et al., 2009). However, studies investigating the effect of systemic antibiotics alone did not show lasting improvements in AD skin lesions and only revealed a short-
term decrease in the cutaneous *S. aureus* burden (Boguniewicz et al., 2001).

**Rosacea**: Rosacea is a severe inflammatory disorder of the facial skin (Tan and Berg, 2013). *Demodex folliculorum*, a mite that exists within the sebaceous glands of normal skin, is a pathogen that is frequently linked with rosacea (Jarmuda et al., 2012). *Bacillus Oleronius* is a pro-inflammatory, gram-negative bacterium that is thought to be carried by *Demodex* mites. This bacterium is susceptible to many antibiotics typically prescribed for eating rosacea, including doxycycline (Lacey et al., 2007) (Table 1).

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease-Associated Skin Microbiota</th>
<th>Further Insight</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne vulgaris</td>
<td>Particular strains of <em>Propionibacterium</em></td>
<td>Probiotic bacteria administration may provide a protective benefit.</td>
<td>(Lomholt &amp; Kilian, 2010)</td>
</tr>
<tr>
<td>Atopic Dermatitis</td>
<td>Decreased bacterial diversity. Increased abundance of <em>S. aureus</em>.</td>
<td>AD skin is susceptible to viral infections, including <em>Herpes simplex</em> and <em>coccidioides</em> viruses.</td>
<td>(Callaway et al., 2020; Chng et al., 2012; Kong et al., 2012; Sli et al., 2015)</td>
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<td>Psoriasis</td>
<td>Higher abundance of <em>Staphylococcus</em> and <em>Streptococcus</em>. Skin microorganism changes can occur as a result of psoriasis therapy.</td>
<td>(Aleksyenko et al., 2013; Chang et al., 2012; Statnikov et al., 2013; Takenotu et al., 2015)</td>
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<tr>
<td>Rosacea</td>
<td><em>Demodex folliculorum</em> (mites)</td>
<td>Rosacea is associated with alterations in skin microbiota composition, including decreased <em>C. acnes</em>, increased levels of <em>Sphingogranella Alvi</em>, <em>Geobacillus</em>, and <em>Gordonia</em>.</td>
<td>(Fortun &amp; Sey, 1993; Woo et al., 2016)</td>
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Table 1: Skin disorders and their associated microbiota.

**Strategies for skin disease treatment**: Skin illness can be brought on by an unbalanced microbiome or by specific strains of microbes. Skin health is believed to be linked with lifestyle choices. To maintain healthy skin might benefit from exercise (Yeh et al., 2022). Regular exercise can help to protect the skin from free radicals, but intense or prolonged training as well as inactivity may cause oxidative stress and contribute to the development of skin cancer (Kruk and Durnik, 2014). Living in an environment that is polluted may decrease skin hydration speed up sebum production and exacerbate the signs of chronic inflammatory skin conditions (Frank et al., 2012). Vigorous exercise, especially calisthenics and aerobic exercise has been independently associated with a lower chance of developing psoriasis. Therefore, in addition to other commonly used treatment methods, a proper diet, cleaning, exercise, and moisturizing should be used (Yang et al., 2022).

**Dysbiosis and skin microbiome-based therapies**: When healthy and harmful bacteria in the gut are out of balance, it is called Dysbiosis. It can hurt our health. This might occur as a result of factors like taking excessive amounts of antibiotics, eating unhealthily, being very stressed, or having specific medical conditions. We can treat it by altering our food, taking probiotics, and using other treatments to balance the healthy bacteria in our gut (Petersen and Round, 2014). Clinically managing AD may benefit by reducing the number of harmful bacteria and re-establishing the skin’s normal microbial balance (Huang et al., 2009). Probiotics have been found to be beneficial and the addition of probiotics to the diet helps to increase the number of beneficial bacteria and can decrease the number of harmful bacteria. The use of probiotics has been associated with improvements in skin health and reduced symptoms of dermatitis (Deo and Deshmukh, 2019).

**Oral microbiome**: The microbiome found in the human oral cavity are often called the oral microbiome, oral microbiota, or oral microbiomes. Dutch scientist Antony van Leeuwenhoek was the one who initially recognized the oral microbiota. After the gut, it is the second biggest microbial population in humans. The human microbiome has a core microbiome and a variable microbiome. All people contribute the same core microbiome, yet have different variable microbiomes based on their way of living and physiological makeup. The hard and soft tissues of teeth and the oral mucosa, are two places in the mouth where microorganisms can colonize. The bacterial biofilm is a great layer of bacteria that shields the whole oral cavity (Deo and Deshmukh, 2019).

**Oral microbiome development**: Usually, the womb of the fetus is free of microbiota. As the mouth begins its development, microbiota first colonize the mouth at birth. Bacterial colonization later in life in the mouth occurs in as much as 70% of pregnant women, according to new studies. The baby is exposed to the microbiome of the mother’s womb and vagina during delivery, and after birth, the baby is exposed to the bacteria in the environment. A newborn’s mouth cavity is frequently sterile despite the considerable risk of contamination. The mouth obtains regular microbiological inoculations starting with the first meal, encouraging growth of the unique oral microbiota. The cultivable bacteria *Faecalibacterium prausnitzii* has been identified to be the most prevalent. Any surface gains the residing microbiota by frequently transferring microbes to the location suitable for colonization. Although passive transfer from a mother and microbes found in milk, water, and the environment is also a way of transmission, salivum is the main method. Colonization starts at or soon after birth. Settler species, like *Streptococcus salivarius* are the first to colonize the mouth. To first colonize the mouth, the first year, aerobes, such as *Streptococcus*, *Lactobacillus*, *Actinomyces*, *S. neisseria*, and *Veillonella*, are the main invaders of the oral cavity. These microorganisms can colonize nonshedding surfaces after tooth eruption starts. Following the emergence of all the teeth, more surfaces are created for colonization. To allow periodontal microorganisms to colonize, gingival fissures develop. As new teeth erupt and the mouth cavity is formed, the oral flora is visible at various places on the tooth, such as smooth edges and pits, and fissures. This process leads to the development of significant diversity of species and microbial subsequence. When all the teeth are lost with aging, the flora resembles that of a child just before tooth emergence (Deo and Deshmukh, 2019).

**Functions of the oral microbiome**: At both the Micron and host level, the oral microbiota contribute to the functions of the host. Microorganisms can help the immune system to distinguish between harmful and non-harmful pathogens and can influence the development of oral cavity disease (Deo and Deshmukh, 2019).

**Oral microbial disease**: A healthy condition (in symbiotic), or a disease-related state (in dysbiosis) is maintained by the intricate balancing between species that live in the oral cavity. When the variety and average number of species or taxonomy within the oral community are disrupted, the microbiome is said to be dysbiosis. While the diversity of microbial communities in the healthy mouth is extremely stable (after its microbiome developed in childhood), the interaction between the microbiome of the mouth and its host is dynamic, and biological alterations in an individual’s life can affect the equilibrium of the species within those communities. These include changes in the body like aging or hormonal ones like those associated with puberty and pregnancy, which healthy people can typically adapt without harming their oral health. Other times, the delicate environment in the mouth can be upset, resulting in a dysbiotic shift, a loss of social balance or harmony. Dysbiosis can be caused by a number of species, and an elevated risk of disease. Salivary gland dysfuction, or modifications to saliva flow and composition, poor oral hygiene, gum inflammation, and lifestyle decisions including...
smoking and eating habits are all modifiable causes of oral dysbiosis.

Listed below is a summary of the dysbiosis-causing factors (Kilian et al., 2016) (figure 3).

**Figure 3: Causes of dysbiosis, diseases like diabetes (Graves et al., 2019), genetic differences (Rosier et al., 2010), activity of salivary proteins (Marsh et al., 2015), salivary flow rates (Lyne Pedersen & Belstrøm, 2019), innate/adaptive immune factors (Desai & Landay, 2018), oral hygiene (Kilian et al., 2016), diet (Gasmì Benahmed et al., 2021), smoking (Huang & Shi, 2019), and antibiotics/antimicrobial agents (Marsh, 2018).**

It is now widely understood that the bacteria formerly thought of as oral pathogens can be found in small amounts in healthy areas and that oral disease results from a harmful alteration of the microbiota’s natural equilibrium rather than from a foreign infection.

**Oral microbiome-based therapies: Oral microbiome and periodontitis: Orals and systemic disorders may be brought on by disruptions in the symbiotic relationship between the human body and the oral microbiota. Through the breathing or circulatory systems, as well as the digestive tract, microorganisms from biofilm in the mouth can spread to other regions of the body. Periodontitis (PD) is a bacterially induced chronic periodontal inflammation that causes alveolar bone resorption, tooth loss, and progressive irreversible breakdown of the connective dental attachment. The most prevalent types of PD are linked to anaerobic, Gram-negative bacteria, including *Porphyromonas gingivalis* or *Prevotella intermedia* (Sela, 2001).**

**Figure 4: Insights into Oral Microbiome model of dysbiosis (Kilian et al., 2016).**

In addition, PD or linked to systemic illnesses. These illnesses include cardiovascular, neurological, respiratory or autoimmune disorders, osteoporosis, diabetes, cancer, or premature birth. Improvements in systemic disorders may coincide with improvements in periodontal health, and vice versa; PD may be lessened by the therapy of these illnesses. Early detection and management of PD may be crucial in the treatment of systemic diseases.

**Oral microbiome and Diabetes mellitus: Diabetes mellitus and oral flora change both influence the development and course of the disease, whereas high glycaemic levels change the composition of the microbiome. Treatments for periodontal disease may enhance metabolic regulation and blood glucose levels.**

**CONCLUSION:** To summarize, the human microbiome is a complicated and varied ecology of microbes that live in many regions of the human body, such as the stomach, skin, and oral cavity. These microbiomes conduct critical tasks that benefit human health, including digestion, immune system modulation, and pathogen defense. Dysbiosis, or a microbiome imbalance, can be linked to a variety of ailments and diseases. Probiotics and fecal microbiota transplantation, for example, show promise in the treatment and prevention of various disorders. However, much remains to be discovered about the human microbiome, including the intricate interactions between the microbiome and the host as well as the impact of environmental variables on changing the microbiome. Future research on this subject will be critical for generating new products.

**CONFLICT OF INTEREST:** Authors have no conflict of interest.


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