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The Developing Microbiome: Understanding the Role of Microbial Communities in Pediatric Health and Disease

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ABSTRACT:

The human microbiome refers to the collective assembly of microorganisms such as bacteria, fungi, viruses and their genetic material that naturally inhabit the body's internal and external surfaces. In contrast, the term microbiota specifically pertains to the genetic profile of these microbial populations. These microscopic organisms colonize diverse anatomical regions including the skin, mucous membranes, gastrointestinal tract, respiratory passages, urogenital system, and mammary glands. Their presence is vital for maintaining physiological equilibrium, supporting immune responses, metabolizing potentially harmful dietary substances, and synthesizing essential nutrients like certain vitamins and amino acids. The composition and richness of these microbial communities are dynamic and subject to variation based on host-specific factors such as age, diet, hormonal status, genetic background, and underlying health conditions. An imbalance in microbial populations termed dysbiosis can contribute to the development of various diseases, while illness itself may disrupt microbial structure and function. This current review gives a brief idea about the microbiome present in the major anatomical structures including skin, gut, respiratory tract, urogenital tract and mammary glands.

1. INTRODUCTION

According to the National Institute of Environmental Health Sciences (NIEHS), the term "microbiome" encompasses the entire community of microorganisms, including bacteria, fungi, viruses, and the genetic material they carry, which reside naturally on and within the human body. Similarly, "microbiota" specifically denotes the genetic composition of these microbial populations. These microscopic inhabitants colonize various anatomical sites such as the skin, mucosal surfaces, gastrointestinal (GI) tract, respiratory system, urogenital tract, and mammary glands (Whiteside et al. 2015). The human microbiome is integral to maintaining physiological balance and overall health, and contributes to immune defence by aiding in the breakdown of potentially harmful dietary components, and plays a crucial role in the biosynthesis of essential nutrients, including specific vitamins and amino acids (den Besten et al. 2013). The composition and diversity of these microbial communities are not static; they are influenced by a range of host-related factors such as age, nutritional habits, hormonal fluctuations, genetic predispositions, and existing medical conditions. Disruptions in the normal microbial equilibrium a phenomenon known as dysbiosis can precipitate serious health disorders. Conversely, the onset of disease can itself alter the structure and

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function of the microbiome (Whiteside et al. 2015). Numerous studies have established correlations between microbial diversity and disease states. For example, individuals with obesity or inflammatory bowel disease (IBD) often exhibit reduced gut microbiome diversity, while those with bacterial vaginosis may present with an elevated vaginal microbial load (The Human Microbiome Project Consortium 2012).

Maintaining a stable and diverse microbiota is therefore essential for sustaining homeostasis and preventing disease. This review seeks to explore the ecological dynamics of host-associated microbial communities. To support the current investigation, a comprehensive literature search was conducted using databases such as PubMed, Google Scholar, and NIEHS. Keywords employed included combinations of “human” AND “microbiome” OR “microbiota” OR “microbial ecology” AND “skin” OR “mucosa” OR “gastrointestinal” OR “GI tract” OR “respiratory tract” OR “urogenital tract” OR “mammary gland”. The search was restricted to English-language publications from the year 2000 onward, and additionally, the reference lists of selected articles were examined to identify further relevant sources.

2. MICROBIOME OF SKIN

Human skin hosts a wide variety of bacteria, fungi, and viruses, yet their overall abundance is lower than in other parts of the body. This reduced microbial load is influenced by factors like limited nutrient availability, constant environmental exposure, and the skin’s naturally dry condition (Chen et al. 2023). Research studies on skin microbiome are evolving quickly, and most commonly used method of investigation is culture-based techniques. Additionally, 16S rRNA gene sequencing is frequently employed due to its cost-effectiveness relative to other sequencing techniques and its ability to bypass sequencing of host DNA (Santiago-Rodriguez et al. 2023). The short-read amplicon-based sequencing is rarely used in microbial sequencing of skin, as they are highly influenced by the sampling methods, which are based on the layer of skin sample and the uneven distribution of species in different layers (Bjerre et al. 2019; Chen et al. 2023). Common techniques for sample collection include cotton swabbing, scraping the skin, performing biopsies, tape-based stripping, using adhesive patches, and conducting punch biopsies (Smith et al. 2024).

Preliminary analysis of the skin specimen revealed a predominance of microbial genera including *Staphylococcus*, *Cutibacterium* (previously known as *Propionibacterium*), *Corynebacterium*, along with fungal species like *Malassezia* (De Pessemier et al. 2021; Chen et al. 2023). The analysis of 160 samples from three different skin sites belonging to 6 healthy children aged 3 to 9 years demonstrated that the within-participant alpha (α) diversity of the cubital fossa and cheek had higher diversity than the axilla. The Chao 1, which is the measure of richness, also indicated that the cubital fossa and cheek had higher richness with a beta of 85.80 (57.82-113.78) and 68.47 (40.49, 96.45) when compared to axillary samples. The cubital fossa demonstrated a higher *Cutibacterium modestum* and *Staphylococcus hominis* with a coefficient and q value of 2.75 (qvalue: 1.57E-05) and 2.30 (qvalue: 2.48E-05), respectively. The cheek sample had an increased abundance of *Streptococcus mitis* [qvalue: 7.41E-07; coeff 1.51] and a decreased value of *Staphylococcus hominis* [qvalue 1.38E-05; coeff −2.98] (Smith et al. 2024).

In skin, the genus *Staphylococcus* is cultivated more effortlessly compared to *Propionibacterium* spp. or *Corynebacterium* spp. Among adults, the physiology of the site of study for skin microbiome is a major factor and its relative abundance in microenvironments such as moist, dry, and sebaceous. The fungal composition of the skin was similar across the different body sites, unlike the bacterial species, which are dependent on physiology. Regarding viruses, colonization by eukaryotic DNA viruses was specific to a particular anatomical site. In newborns, the initial colonization is dependent on various factors, including the delivery mode, and the microbial population ecology is reconstructed during puberty (Byrd et al. 2018). The major microorganism present in different skin sites is shown in Table 1. The factors such as site of the study, exposure to chemicals, gender, geographical location, ethnicity, depth of epidermis, usage of antibiotics, history of vaccination, cosmetic use, age, and presence of any disease condition can significantly alter the skin microbiome. The review by Cundell

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(2016) and Byrd *et al*. (2018) gives a detailed review of the skin microbiome (Byrd et al. 2018; Cundell 2018).

Table 1: The major microorganism reported in different sites of skin samples.

Skin Sample Site	Microorganism
Sebaceous skin site	*Propionibacterium acnes* *Staphylococcus epidermidis* *Corynebacterium tuberculostearicum* *Staphylococcus capitis* *Corynebacterium simulans* *Corynebacterium aurimucosum* *Corynebacterium kroppenstedtii* *Corynebacterium amycolatum* *Streptococcus mitis* *Staphylococcus hominis* *Malassezia* spp. *Beta-Proteobacteria* spp. Unclassified *Actinomycetales* *Flavobacteriales* spp. *Lactobacillales* spp. *Clostridiales* spp. *Gamma-Proteobacteria* spp. *Alpha-Proteobacteria* spp. *Bacteroidales* spp.
Humid skin site	*Propionibacterium acnes* *Staphylococcus epidermidis* *Corynebacterium tuberculostearicum* *Staphylococcus capitis* *Corynebacterium fastidiosum* *Corynebacterium afermentans* *Corynebacterium simulans* *Staphylococcus hominis* *Micrococcus luteus* *Enhydrobacter aerosaccus* *Malassezia* spp. *Beta-Proteobacteria* spp. *Flavobacteriales* spp. *Gamma-Proteobacteria* spp. *Lactobacillales* spp. *Clostridiales* spp. *Alpha-Proteobacteria* Unclassified *Actinomycetales* spp. *Bacteroidales* spp.
Dry skin site	*Propionibacterium acnes* *Corynebacterium tuberculostearicum* *Streptococcus mitis* *Streptococcus oralis* *Streptococcus pseudopneumoniae* *Streptococcus sanguinis* *Staphylococcus epidermidis* *Staphylococcus capitis* *Micrococcus luteus* *Veillonella parvula* *Beta-Proteobacteria* spp. *Flavobacteriales* spp. *Gamma-Proteobacteria* spp. *Lactobacillales* spp. *Clostridiales* spp. *Alpha-Proteobacteria* spp. *Bacteroidales* spp. Unclassified *Actinomycetales* spp.
Core body and arm site	*Malassezia* spp.
Foot site	*Corynebacterium tuberculostearicum* *Staphylococcus hominis* *Staphylococcus warneri* *Staphylococcus epidermidis* *Staphylococcus capitis* *Staphylococcus haemolyticus* *Micrococcus luteus* *Corynebacterium afermentans* *Corynebacterium simulans* *Corynebacterium resistens* *Malassezia* spp. *Aspergillus* spp. *Cryptococcus* spp. *Rhodotorula* spp. *Epicoccum* spp.
Cubitol fossa sample	*Cutibacterium modestum* *Staphylococcus hominis*
Cheek sample	*Streptococcus mitis* *Staphylococcus hominis*
Skin across body sites	*Propionibacterium acnes* *Staphylococcus epidermidis*

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3. MICROBIOME OF THE GASTROINTESTINAL TRACT OR GUT

The analysis of the gut microbiome is based on the samples collected from feces, mucosal biopsy, and intestinal fluid, etc. Currently, the different types of samples include feces, biopsy, luminal brush, laser capture microdissection, catheter aspiration, intelligent capsules, surgery, in vivo model, while the in vivo model is limited to patients who underwent ileostomy (Tang et al. 2020). The gut microbiome is subjected to modification during infancy and early childhood, but despite these changes, certain characteristics or strains of bacteria were found to be persistent (Tamburini et al. 2016). Feeding practices significantly influence bacterial diversity, richness, and gut colonization, with breastfed infants exhibiting distinct microbial profiles compared to those fed with formula (Bokulich et al. 2016). Several key elements—including genetic makeup, age, daily habits, hygiene practices, exposure to allergens, dietary choices, intake of probiotics or prebiotics, and infections—can profoundly influence the composition and dynamics of the gut microbiota (Sommer and Bäckhed 2013).

The gut contains 10^1 bacteria per gram with colon (10^{12} bacteria/g), ileum (10^7 bacteria/g), jejunum (10^4 bacteria/g), and duodenum (10^3 bacteria/g) having diverse bacterial diversities (Sekirov et al. 2010). The gut microbiome is predominantly dominated by anaerobic bacteria. Distinct microbial compositions have been observed between the gut lumen and the epithelial surface, where goblet cells serve as the primary producers of glycosylated proteins like mucins (Sommer and Bäckhed 2013). The gut microbiome was found to be significantly altered in individuals with disorders or diseases, including diabetes mellitus (DM), arterial stiffness, GI disorder, obesity, and arthritis. In addition to the microbes, the metabolic products of these microbes, such as short-chain fatty acids (SCFA), gases, and metabolites such as trimethylamine and indolepropionic acid, can be measured. SCFAs such as acetate, propionate, and butyrate are commonly synthesized by the gut microbial community. Smoking has been associated with gut microbiomes, with smokers demonstrating lower diversity of gut microbiomes (Valdes et al. 2018). The ratio between Firmicutes and Bacteroidetes—currently referred to as the Bacillota/Bacteroidota ratio—has emerged as a widely acknowledged indicator of health status within gut microbiota research (Khachatryan et al. 2008). Hence, functional resilience, metabolic outputs, ecological balance, host compatibility, and environmental adaptability play a vital role in defining a healthy gut microbiome.

Table 2: The microbial composition of the gut microbiome

Gut Site	Microbes
Small Intestine	*Lactobacillaceae*
	Enterobacteriaceae
Colon	*Prevotellaceae*
	Bacteroidaceae
	Rikenellaceae
	Ruminococcaceae
	Lachnospiraceae
Gut	*Bacteroidetes* spp.
	Firmicutes spp.
	Bacteroidota
	Actinobacteriota
	Verrucomicrobiota
	Proteobacteria spp.
	Actinobacteria spp.
	Verrumicrobia spp.
	Acidobacteria spp.
	Fusobacteria spp.
	Lactobacillus spp.
	Veillonella spp.
	Helicobacter spp.
	Aspergillus spp.
	Candida spp.
	Cryptococcus spp.
	Penicillium spp.
	Bifidobacterium spp.
	Lactobacillus spp.
	Akkermansia muciniphila
Duodenum, jejunum or ilenum	*Bacilli* spp.
	Streptococcaceae spp.
	Actinomycinaeae spp.
	*Corynebacteriaceae*spp.
Colon	*Lachnospiraceae* spp.
	Bacteroidetes spp.
Epithelial cells	*Clostridium*
	Lactobacillus
	Enterococcus

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4. MICROBIOME OF THE RESPIRATORY TRACT

The respiratory system comprises both the upper (URT) and lower (LRT) segments, and the composition of its microbiome (RTM) is influenced by structural and functional variations across these regions (Pagano and Márquez 2022). During the initial stage of life, the mother's vaginal and skin microbiome and breastfeeding significantly affect the RTM and RTM attain maturation and diversity over time. The mechanism of maturation and diversity of RTM needs to be elucidated (Perdijk et al. 2024). Unlike other sites, RTM was found to harbor prominent eukaryotic viruses, such as *Anelloviridea*, and *Redondoviridea*, as well as bacteriophages, including *Inoviridae*, *Myoviridae*, *Podoviridae*, and *Siphoviridae* (de Córdoba-Ansón et al. 2025). The RTM was demonstrated to have the presence of anaerobic microniches in RT, such as adenoids, tonsils, and the pharynx (Brook 2012). Microbial communities residing in both the URT and LRT are recognized for their significant contribution to modulating immune responses (Di Simone et al. 2023). The influence of RTM on the airway immune system has been discussed widely and in detail by Natalini et al. (2022) and Di Simone et al. (2023) (Di Simone et al. 2023; Natalini et al. 2023). The presence of RTM is associated with improved lung infection outcomes, protection mechanism against infections, innate immune priming, rapid pathogen clearance, and improved survival. The microbial intermediates and products such as lipoproteins, secreted by *P. melaninogenica,* can activate a signalling cascade leading to improved protective immunity. Likewise, experimental research using cell cultures and animal models has shown that *Corynebacterium accolens*, residing in the nasal passages and nasopharynx, can effectively suppress *Streptococcus pneumoniae* at the mucosal surface (Bomar et al. 2016; Drigot and Clark 2024). Under homeostatic conditions, the prevention of the outgrowth of pathogenic microbes by RTM is referred to as the "colonization resistance". The mechanism behind the colonization resistance needs to be studied further (Perdijk et al. 2024). The RTM is widely dependent on the environment, including social interaction, season, air pollution, and other factors such as the microbiome intrinsic factor, host intrinsic, and host extrinsic factor. Apart from these, the primary source of RTM is principally associated with the oral and nasal microbiome. The Gut-lung axis has been directly associated with microbial signals and indirectly stimulates the innate immune response. Oral bacteria and the nasal microbiome are vital for immune health and prevent the colonization of harmful microbes (de Córdoba-Ansón et al. 2025). Hence, the RTM is widely dependent on various factors and is vital for the innate immune response. The presence of microbes in RTM has been described in Table 3.

Table 3: The microbial composition of respiratory tract

Respiratory Tract Site	Microbes
Respiratory tract	*Firmicutes*
	Actinobacteria
	Bacteroidetes
	Proteobacteria
	Candida
	Saccharomyces
	Pencillium
	Cladosporium
	Fusarium
	Methanobrevibacter
	Streptococcus
	Veillonella
	Prevotella
	Neisseria
	Cladosporium cladosporioides
	Eremothecium sinecaudum
	Staphylococcus
Oral	*Actinomyces*
	Corynbacterium
	Veillonella
	Streptococcus oralis
	Streptococcus mitis
	Streptococcus peroris
Nasal	*Corynbacterium*
	Propionibacterium
	Haemophillus
	Moraxella
	Neisseria
	Dolosigranulum
	Sthaphylococcus
	Streptococcus

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5. MICROBIOME OF THE UROGENITAL TRACT

The urethra, bladder, and urine contain resident microbiome in both males and females. The suprapubic aspiration (SPA) and transurethral catheterization (TUC) are the commonly used methods to collect the urine sample for microbiome analysis (Saenz et al. 2024). The identification of the potential pathogens in the urinary samples needs more advanced culture techniques, including metagenomic analysis, 16s rRNA amplicon sequencing, etc (Čeprnja et al. 2023; Saenz et al. 2024).

In female reproductive structures, the vagina contains bacteria and other microbes, but the uterus and the fallopian tubes are sterile, with the cervix being a major barrier. The 16s rRNA gene amplicon sequencing studies of vaginal microbiota demonstrated *Lactobacillus* as the major microbes (Ding and Schloss 2014). The lactic acid production associated with the *Lactobacillus* is vital in maintaining a lower pH of 3.5-4.5, and alterations in the vaginal microbiome are seen in diseased conditions such as bacterial vaginosis, sexually transmitted diseases, urinary infection, and preterm birth (Hyman et al. 2014). The pH is crucial for maintaining homeostasis and reducing the risk of disease development. It has been noted that the vaginal microbiome was modified drastically during pregnancy due to the presence of female hormones, with estrogen playing a vital role. During pregnancy, the concentration of *G. vaginalis*, *A. vaginae*, and *P. bivia* was found to be increased, and after delivery, the vaginal microbiome was found to return to normal (Zhu et al. 2022). The studies of the microbiome present in the male reproductive tract are limited due to the invasive nature of sample collection. Microbial colonization in the upper genital tract has been linked to ongoing infections within the reproductive system or the urinary tract. The presence of microbes in the testes are limited and further extended studies are needed to confirm the microbiome present in male reproductive tract (Zuber et al. 2023). The commonly found microbiome in the urinary tract and reproductive tract is shown in Table 4.

Table 4: Microbiome of Urogenital tract

Urogenital Tract Site	Microbes
Urinary	*Lactobacillus crispatus*
	Lactobacillus gasseri
	Lactobacillus jensenii
	Lactobacillus johnsonii
	Streptococcus
	Bifidobacterium
	Staphylococcus
	Enterococcus
Vagina (Female reproductive tract)	*Lactobacillus iners*
	Lactobacillus crispatus
	Lactobacillus gasseri
	Lactobacillus jensenii
	Gardnerella vaginalis
	BVAB1
	Atopobium vaginae
	Prevetolla cluster
	Sneathia amnii
Male reproductive tract	
Penis	*Prevotella*
	Porphyromonas
	Corynebacterium
	Anaerococcus
	Finegoldia
	Peptoniphilus
	Staphylococcus
Semen	*Staphylococcus*
	Lactobacillus
	Corynebacterium
	Prevotella
	Streptococcus
Urethra	*Corynebacterium*
	Prevotella
	Streptococcus
Prostate	*Propionibacterium*
	Staphylococcus
	Escherichia
	Streptococcus

6. MICROBIOME OF MAMMARY GLANDS

Human milk is vital for the growth and development of infants, and human milk contains

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dynamic and complex site-specific microbes. The microbes present in clostrum and human milk are responsible for the gut microbiome in infants. Dysbiosis of human milk microbiome has been associated with alterations in infant colonization, metabolism, immune and neuroendocrine development in infants(Fernández et al. 2020). More than 200 different bacterial, archaeal, and fungal microbes were identified in breast milk (Fernández et al. 2013). Human milk has been found to contain a diverse array of bacterial species, encompassing coagulase-negative strains as well as both gram-positive and gram-negative types. Under normal physiological conditions, the bacterial load in milk typically ranges from less than 1 to 4 $\log_{10}$ colony-forming units per milliliter (Fernández et al. 2013).

Table 5: Microbiome of human mammary gland

Mammary gland site	Microbes
Human Milk	*Lactomassilus* *Lactimicrobium* *Anaerolactibacter* *Galactobacillus* *Acidipropionibacterium* *Staphylococcus epidermidis* *Streptococcus salivarius* *Streptococcus mitis* *Corynebacterium* *Cutibacterium* *Lactococcus* *Enterococcus* *Lactobacillus* *Leuconostoc* *Weissella* *Lactobacillus salivarius* *Lactobacillus reuteri* *Lactobacillus gasseri* *Lactobacillus fermentum*

Therefore, the microbiome is integral to maintaining physiological health, and its imbalance—known as dysbiosis—can serve as a key marker for various disease conditions. Several factors can affect the microbiome, as shown in Figure 1. Further detailed studies in different ethnicities and under different physiological conditions are needed to better understand the metabolic role, gene expression, and host interaction of the microbes. The usage of novel third-generation sequencing methods is required to detect rare species of the microbiome. The Gut-Brain axis is currently widely studied; however, the studies focusing on gut-skin or gut-urogenital tract are limited.

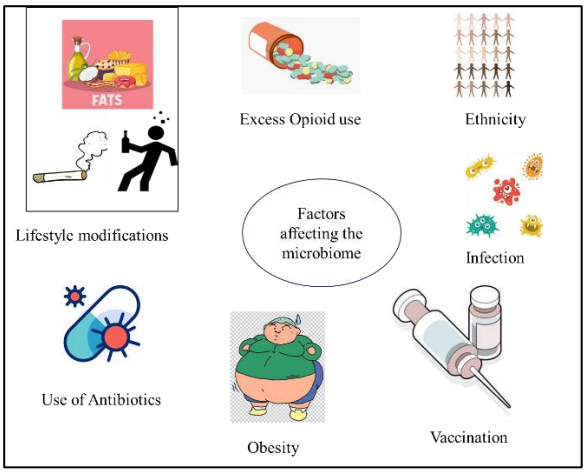

Figure 1: The Several factors affecting the microbiome

7. CONCLUSION

The microbiome plays a major role in human homeostasis, and dysbiosis of the microbiome has been associated with the development of diseases. However, further studies focusing on factors affecting the microbiome, microbiome interaction across different anatomical sites, interaction of the microbiome with other genetic and environmental factors needs to be studied.

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