Section A-Research paper

Brief overview about Nasal Microbiota

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Abstract

Background: Many unicellular and multicellular microbial populations, including bacteria, viruses, fungus, and parasites, are hosts for all humans and other animals. Both the environment and the human body are home to a wide variety of microbes. The term "microbiota" was developed in 2020 by a group of international specialists composed of more than 100 members. They came to the conclusion that the microbiota is made up of prokaryotes and eukaryotes and that is active in a variety of microbial structures, metabolites, and moveable genetic elements. Numerous distinct (micro-)niches for microbial communities are provided by the topography of the upper respiratory tract and its various epithelial linings and circumstances. The microbial community structures in other locations in the nasal cavity and down the nasopharynx are distinct, especially in adults. While the anterior naris (the passage between the skin and the nasal cavity) harbours commensals and opportunistic pathogens such as Staphylococcus aureus, S.epidermidis, Propionibacterium (now: Cutibacterium) acnes, Dolosigranulumpigrum, Finegoldiamagna, Corynebacterium spp., Moraxella spp., Peptoniphilus spp.,and Anaerococcus spp., Even though the URT microbiome is mostly individual, alterations in inter-individual bacterial community profiles throughout various ages and seasons (winter vs. summer) can nevertheless be seen.

Keywords: Nasal Microbiota

Introduction

Many unicellular and multicellular microbial populations, including bacteria, viruses, fungus, and parasites, are hosts for all humans and other animals. Both the environment and the human body are home to a wide variety of microbes **(1).**

The term "microbiota" was developed in 2020 by a group of international specialists composed of more than 100 members. They came to the conclusion that the microbiota is made up of prokaryotes and eukaryotes and that is active in a variety of microbial structures, metabolites, and moveable genetic elements **(2).**

The term "microbiome" was initially introduced in 1988 by Whipps and colleagues. Comparatively speaking, microbiome covers a greater spectrum than microbiota. Phages, viruses, plasmids, free DNA, and a number of others such as prions and viroids are not considered to be members of the microbiota, but are included in the microbiome **(3).**

Human health and disease are significantly influenced by the more than 100 trillion symbiotic microbes that reside on and within humans. It has even been said that the human microbiota, particularly the gut microbiota, is a "essential organ" because it contains 150 times more genes than the human genome. The gut microbiota is engaged in fundamental human biological processes, such as regulating epithelial formation, modifying metabolic phenotype, and affecting innate immunity, according to significant research **(1).**

The human microbiota in disease:

The human microbiome has been linked to chronic conditions such as obesity, inflammatory bowel disease (IBD), diabetes mellitus, metabolic syndrome, atherosclerosis, alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD), cirrhosis, and hepatocellular carcinoma **(4).**

- **The human microbiota and infectious diseases:**

One of the most widespread disorders brought on by a dysbiosis of the microbiota (i.e a change in the composition of the healthy microbiota) is infection. The fate of an infectious disease in the human host is crucially influenced by the human microbiota, which is critically affected by infectious disease and its treatment. The colonization of the intestinal mucosa by the offending pathogens causes a significant inflammatory response, which is followed by the translocation of the intestinal bacteria **(5).**

- **The microbiota and allergic diseases:**

The abnormalities in the microbiota and their consequent impact on the immune system have received a lot of attention. Numerous studies show that the commensal microbiome controls the susceptibility to allergic disorders. The absence of commensal bacteria increases basophil proliferation, the overall number of infiltrating lymphocytes and eosinophils, exacerbates Th2 cell responses and allergic inflammation, and decreases the amount of RORγt+ regulatory T cells (Tregs) and TH17 cells **(6).**

The onset and progression of allergic asthma are strongly tied to rhinovirus, one of the most prevalent viruses in the human respiratory system, and it is essential for the propagation of the type 2 immune response. Human respiratory epithelial cells activated by the rhinovirus release IL-25 and IL-33, which in turn cause the production of IL-5 and IL-13 by binding to receptors on Th2 cells and basophils **(7).**

An early-life, antibiotic-driven low diversity in the gut microbiota increases sensitization to allergic asthma, and may also have an impact on how asthma develops in children following a long period of follow-up. Of course, the method, location, and newborn feeding also impact the GI microbiota composition and, consequently, the risk of atopic symptoms **(7).**

The most widely used probiotic bacteria to prevent and treat allergies and respiratory conditions are those from the Lactobacillus and Bifidobacterium genera, as many of them have the ability to colonize stably in the intestinal tract, modify the composition of the gut flora, increase levels of microbial metabolites, particularly short-chain fatty acids (SCFAs), and regulate host immunity **(8).**

Nasal Microbiota:

1) Classification:

Related to site and age:

Numerous distinct (micro-)niches for microbial communities are provided by the topography of the upper respiratory tract and its various epithelial linings and circumstances. The microbial community structures in other locations in the nasal cavity and down the nasopharynx are distinct, especially in adults. While the anterior naris (the passage between the skin and the nasal cavity) harbours commensals and opportunistic pathogens such as Staphylococcus aureus, S.epidermidis, Propionibacterium (now: Cutibacterium) acnes, Dolosigranulumpigrum, Finegoldiamagna, Corynebacterium spp., Moraxella spp., Peptoniphilus spp.,and Anaerococcus spp., Even though the URT microbiome is mostly individual, alterations in inter-individual bacterial community profiles throughout various ages and seasons (winter vs. summer) can nevertheless be seen. Several studies have recently pointed towards an increased occurrence and prevalence of several taxa of the lactic acid bacteria (LAB) in the microbiota of the upper respiratory tract (URT) under healthy conditions versus disease **(9).**

In infants:

The six most prevalent genera are Moraxella, Staphylococcus, Streptococcus, Haemophilus, Dolosigranulum, and Corynebacterium, and one or two of them typically predominate in the nares and nasopharyngeal microbiome of babies**.** The infant's nasopharyngeal microbiome matches the mother's vaginal or skin microbiome as the first nasopharyngeal bacterial assemblage occurs after birth **(10).**

In adults:

Basic concepts on the bacterial microbiome composition of the nasal cavity of healthy adults are presented in the table (I). It is formed by 3 main types: Actinobacteria, Firmicutes and Proteobacteria. A number of researchers also assign a certain role to the type Bacteroidetes **(11).**

Table (I): The main types and genera of bacteria in the microbiome of the nasal cavity of healthy adults **(11).**

Type	Genus	Pathogenicity
Actinobacteria	• Corynebacterium	Commensal / pathogen
	• Cutibacterium/Propionibacterium	Commensal
Firmicutes	• Lactobacillus	Commensal
	• Staphylococcus	Commensal / pathogen
	• Streptococcus	Commensal / pathogen
	• Dolosigranulum	Commensal
Proteobacteria	• Haemophilus	Commensal / pathogen
	• Moraxella	Commensal / pathogen
	• Acinetobacter	Commensal
	• Neisseria	Commensal
	• Helicobacter	Commensal
	• Burkholderia	Commensal
	• Pseudomonas	Pathogen
Bacteroidetes	• Prevotella	Commensal
	• Bacteroides	Commensal / pathogen

Comparing the microbial community compositions of different nasal cavity sample sites revealed that the anterior nares exhibited much lower microbial community diversity than the middle meatus (MM) and sphenoethmoidal recess (SR). Additionally, compared to MM and SR, the anterior nares have a higher proportion of Firmicutes and Actinobacteria and a smaller proportion of Proteobacteria**.** The microbial communities in the anterior nares of adults (18–40 years) are noticeably different from those of other URT sampling locations (nasopharynx, tongue, buccal mucosa, oropharynx), although these apparent differences eventually disappear as people age. In contrast to the microbial population in the URT, the nasal microbiota is distinct and stable throughout maturity. Adults in their middle years may begin to see changes in their nasal microbiota. Staphylococcus, Streptococcus, Veillonella, Cutibacterium, and Corynebacterium species entirely dominate the nasal microbiota of healthy adults between the ages of 40 and 65 **(4).**

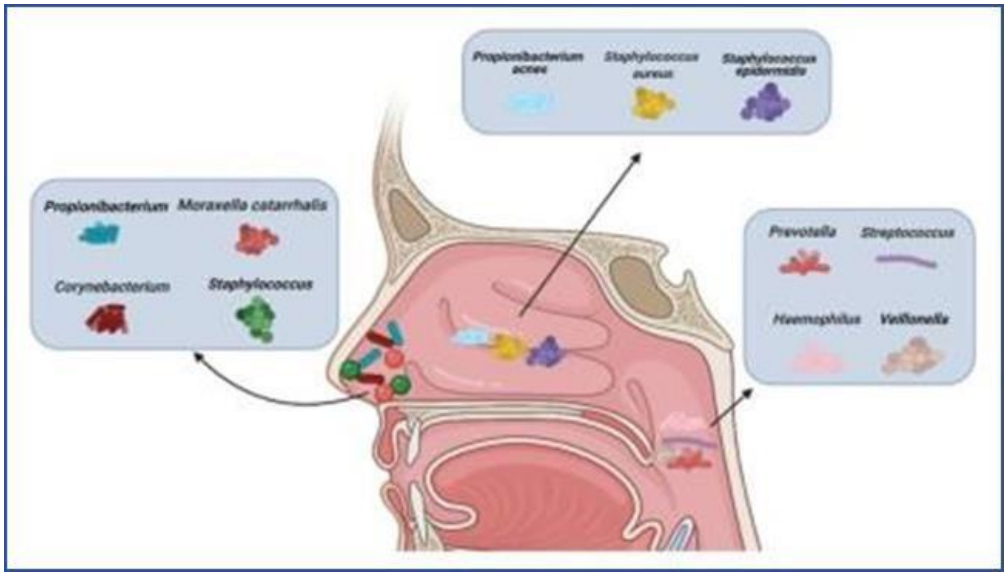

Figure (1): Types of microbiota in normal nasal mucosa and other parts of the upper airway **(3).**

In elderly:

As people age, the composition of their nasal and oropharyngeal microbiota changes and resembles that of their oropharyngeal region. The diversity of the nasal microbiome in elderly subjects living in nursing homes and independent residences was studied by several authors. These studies found that the nasal passages of the elderly individuals contained an abundance of Streptococcus and a relative abundance of other species, including Lactobacillus reuteri, Staphylococcus epidermidis, and Rothia mucilaginosa **(3).**

2) Role of nasal microbiota in immune defense mechanism:

Numerous bacteria live in the nasal cavity. Epithelial cells with cilia line the respiratory system. The epithelial layer of the nasal cavity serves as a barrier that recognizes, filters, and aids in the removal of the inhaled germs, dust, or undesirable particles, preventing infection of the host system or pathogens from reaching the LRT **(3).**

The microbiota, or the communities of microorganisms that colonize all of the surfaces of the human body exposed to the external environment, is believed to affect the barrier function of the nasal mucosa as well as the regulation of the local and distal immune response. The microbiome may influence host physiological and pathological processes locally or distantly**.** The nasal cavity, like other mucosal regions on the body, is home to a colony of commensal microorganisms that probably play a significant role in mucosal homeostasis and protection against infection **(12).**

It is thought that commensal bacteria in the nasal cavity defend against opportunistic pathogens by competing for resources and space as well as by creating toxic molecules **(13)**.

Additionally, it has recently been demonstrated that Staphylococcus epidermidis, which rises throughout human nasal microbiome development, stimulates the nasal epithelium's synthesis of antimicrobial peptides, which effectively lower pathogen colonization**.** Additionally, S. epidermidis can encourage healthy nasal epithelial cells to produce interferon λ-dependent innate immunity to defend against the influenza virus **(14).**

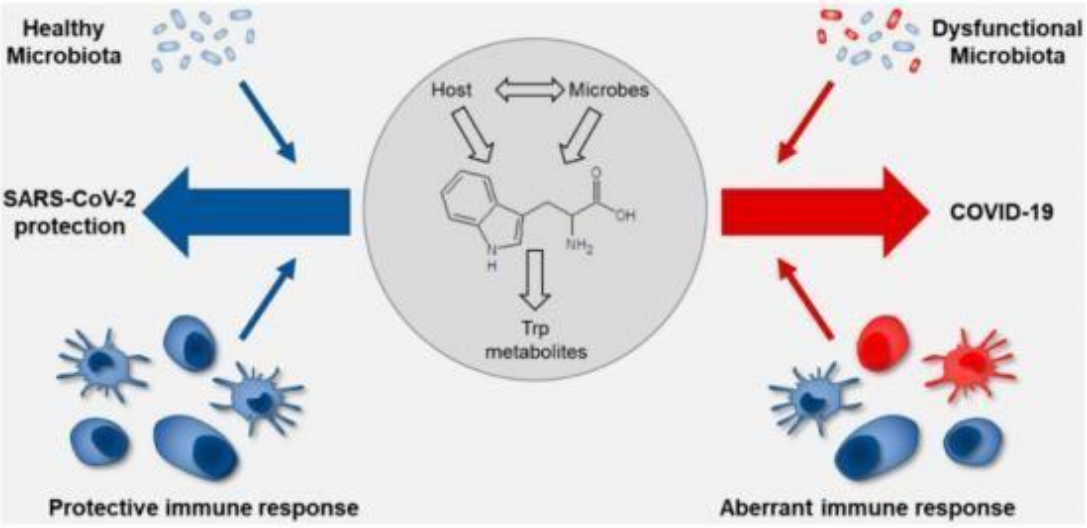

Figure (2): The cross-talk between the commensal microorganisms and the immune system plays a crucial role in mucosal homeostasis, including the interaction with pathogens and the outcome of infection **(12).**

The immune system is given instructions by the microbiota to be accepting to commensal microbes while preparing an aggressive response in the event of pathogen invasion. This type of mucosal tolerance is essential for balancing the immune system's exposure to a variety of microbial stimuli and for fine-tuning the immune response based on the actual risk of infection. The complex regulatory processes that occur in mucosal membranes are subject to changes that could lead to pathological disorders, such as those that follow microbial dysbiosis, disturbance of the integrity of the epithelial barrier, or loss of the immune system's discriminatory function. The nasal mucosa, which is constantly exposed to microbial or non-microbial environmental antigens inhaled from the outside and interacting with the stable communities of microorganisms that populate the nasal cavities and the immune cells residing within the nasal-associated lymphoid tissue, is most likely subject to these general mechanisms described in mucous membranes, such as the intestine and the lung. So protecting against various assaults, such as pathogen invasion, by re-establishing mucosal homeostasis may be a useful method **(12).**

The development of the olfactory epithelium normally depends on the microbiota. Numerous writers investigated how the nasal microbiome and olfactory function interact **(15).**

In the olfactory area's microbiome of healthy, normosmic volunteers, Koskinen et al. discovered 23 bacterial phyla and four archaeal phyla, including Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes predominating. The most prevalent genus-level signatures were found to be those of Corynebacterium, Staphylococcus, and Dolosigranulum. They discovered that the community composition and diversity of the microbiome of hyposmic participants were considerably different from those of normosmic subjects (**16).**

The health condition and functionality are reflected by the nasal microbial community, which can be used as an evaluation tool for disease diagnosis **(16).**

3) Dysbiosis of nasal microbiome:

A change in the composition of the healthy microbiota, known as microbial dysbiosis, results in pathological disorders that have a negative impact on one's health. Various factors, such as drugs, surrounding environmental microorganisms, habitat, nutritional availability, and host factors, such as host hygiene, immunity, and genetics, and physical factors, such as oxygen, pH, moisture, and other microbial interactions, all affect how diverse the microbiota is. The microbiota can be both transient and resident **(16).**

Numerous investigations shown that the lower airway mucosal immunity is impacted by changes in microbiota. The changes in the composition of the airway microbiota are associated with eosinophilic inflammation, TH17 gene expression, neutrophilic inflammation, and the indicators of allergic inflammation **(5).**

Due to the host immune system's low reactivity in the upper respiratory tract immune system, microbiota are tolerated, and diseases of the upper respiratory tract result from microbiome dysbiosis, just like they do in other parts of the human body **(17).**

Nasal inflammatory illnesses may be brought on by a dysbiosis of the nasal microbiota because it has been shown that nasal microbiota are involved in immune function regulation. Chronic rhinosinusitis (CRS), one of the common inflammatory disorders of the URT, is connected to inflammation in the sinus and nasal mucosal layers, and symptoms of CRS include stuffy nose, sinus pain, headaches, attention problems, and depression. Inflammation and a chronic immunological response are brought on by secondary bacterial overgrowth, immune system injury, mucosal epithelial inflammation, and dysbiosis of microbiota **(18).**

Respiratory tract infection:

The human nasal mucosa is the initial site of contact for irritants from the environment that are inhaled. Microbiota in nasal mucosa are anticipated to play a significant role in mucosal immunity, just as gut microbiota that can protect the intestinal mucosa through immunological modulation **(1).**

In a study comparing the nasal microbiome of healthy controls and CRS patients, it discovered that various genera of the Lactobacillaceae, such as Lactiplantibacillus, Lactilactobacillus, and Lacticaseibacillus, were more common and numerous in healthy controls than in CRS patients **(9).**

Olfactory dysfunction:

It is believed that a compromised nasal airflow indirectly affects the URT microbiota by altering regional variables (such as humidity, temperature, oxygenation). The organization of the microbial community may be affected by such influenced airflow, which can also lead to a decline in olfactory function. The conditions affecting the airflow include rhinosinusitis, allergic rhinitis, congenital causes, head trauma, nasal surgery, and congenital sinusitis **(19).**

COVID-19:

The pathogen entrance point and the host's response have an impact on the course of the disease. The nasal barrier and URT contribute significantly to infection prevention. Despite the fact that human nasal mucosa gives rise to a variety of microbial communities, the URT served as the primary entrance point for the coronavirus disease 2019 (COVID-19) pathogenicity. The nasal or respiratory tract microbiota may be related to the pathogenesis of COVID-19 **(18).**

Numerous authors noted that the phyla Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, and Fusobacteria, which were discovered in both severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infected and uninfected participants, were not altered in the nasopharynx of COVID-19 patients. The nasopharynxes of COVID-19 patients included high concentrations of bacteria from the phyla Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria, as well as the genera Streptococcus, Prevotella, Veillonella, Haemophilus, and Moraxella **(20).**

AR and Microbiota:

The interactions between the host system and local microbiota have a strong influence on the prevalence of allergic disorders. According to some studies, symbiotic microbiota regulate the susceptibility allergic diseases, and their absence can increase basophil proliferation, boost the number of infiltrating lymphocytes and eosinophils, exacerbate allergic inflammation and Th2 cell reactions, and decrease the number of regulatory T (Treg) and Th17 cells **(21).**

The incidence of inflammatory nasal mucosal illnesses, such as AR, is rising each year. The precise etiology of many these disorders is still unknown, despite significant advancements in their pathogenic mechanism. The function of the human microbiome in health and disease has emerged as a hot topic of research due to recent developments in culture-independent technologies **(22).**

It is reasonable to predict that the local microbiome could affect immunological homeostasis through host-to-microbe and microbe-to-microbe interactions since the upper airways are exposed to the external environment and because mucosal surfaces are heavily populated with bacteria. It is generally recognized that genetic and environmental variables interact to generate a complicated disease as AR **(7).**

Six phyla, including Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Cyanobacteria, and Fusobacteria, dominated the nasal microbiome in samples from healthy controls **(23).**

The inferior turbinate mucosal microbiota of normal controls and patients with AR was described and compared using 454 pyrosequencing based on the 16S rRNA gene in the study of 20 patients with AR and 12 normal controls. The researchers found that the inferior turbinate microbiota imbalance in patients with AR was related to the total IgE level; their findings highlighted the relationship between inferior turbinate microbiota imbalance and the onset of AR **(2).**

According to the findings of numerous studies, microbiota play a significant role in triggering type 2 immune responses in the upper respiratory tract. After binding with the toll-like receptor (TLR), S. aureus triggers the production of type 2 cytokines, like IL-5 and IL-13, via IL-33 released by human airway epithelial cells **(21).**

The type 2 immune response is actively mediated by these produced type 2 cytokines. IL-5 is associated with the formation and activation of eosinophils and takes role in their recruitment. IgE class conversion is encouraged by IL-13, which also increases class II production in B cells. IgE then attaches to mast cell receptors **(2).**

Children who have both a viral and Mycoplasma pneumoniae infection are more likely to have severe airway inflammation than children who just have a virus infection. These findings imply that a host's ability to defend itself may be diminished to variable degrees following simultaneous infection with a number of viruses or bacteria. It is crucial to comprehend the microbiota's role in allergic illnesses and how the immune system changes following infection **(3).**

The microbiome colonizes the nasal mucus, where interaction with allergens or infections that are inhaled occurs, and may interact functionally with the nasal epithelium, particularly in relation to the control of immunological processes in the upper airway. Hence, analyzing compositional changes in the microbiome and identifying dominating microbial species in nasal mucus may be crucial for understanding the precise pathophysiologic mechanism of upper airway illnesses, including AR **(14).**

Conflicts of Interest: The authors declare no conflict of interest.

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