MINI REVIEW

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

The Nasal Microbiome Profile of Healthy Subjects

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Abstract

The nasal passages' microbial communities are vital to human health and can significantly influence infection processes. A remarkable diversity in the nasal passages' microbiota was observed. The taxonomy in the healthy nasal microbiome recognized four major phyla, including *Actinobacteria*, *Firmicutes*, *Proteobacteria*, and *Bacteroidetes*, with little variation in abundance. *Corynebacterium* and *Dolosigranulum*, the most predominant genera, showed the highest relative abundance. It is hypothesized that environmental factors such as delivery routes and milk feeding method may change the nasal microbiome, consequently disrupting its community structure. These findings highlight the potential clinical and public health consequences of nasal microbiome particularly in healthy people.

Keywords: Metagenomics sequencing, nasal passages microbiome, shotgun.

1. Introduction

The microbiota has important roles in the health of their hosts, involving roles in immune system development, nutrition, and resistance to infection (Bomar et al., 2018). Research on the human body's microbiota shows that changes in bacterial communities can either increase or decrease pathogenicity. Furthermore, dysbiosis—a change in the microbial biome—can result in disorder (Littman and Pamer, 2011). Human nasal passageways extend from the nose opening, nostrils, or anterior nares to the nasopharynx, which is located near the back of the throat (Brugger et al., 2016). Clinically relevant pathobionts, or commensal bacteria that can infect healthy hosts, such as Moraxella catarrhalis, Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus, are found in the nasal passages. Furthermore, the nasal passages are thought to be a significant site for viral infections. Children and elderly adults have the highest rates of morbidity and mortality from these microbes (de Steenhuijsen Piters et al., 2015).

Numerous research about the human microbiome and its connection to disease incidence have surfaced recently. According to recent study, opportunistic infections in the nasal cavity can cause diseases such otitis media, asthma, pneumonia, allergic rhinitis, and chronic rhinosinusitis. This occurs because opportunistic infections are primarily found in the nasal cavity, where they can spread to other parts of the respiratory system and cause illness **(Dimitri-Pinheiro et al., 2020)**. Until recently, the features of the human microbiota were mostly a black box because the cultivation method may not be concerned to several of the populated microbes **(Berg et al., 2020)**. Our knowledge of the relationship between disease and the human microbiome is rapidly growing. Our understanding of the structure and

function of the microbiome in both healthy and pathological states has significantly improved due to advancements in the throughput of DNA and protein sequencing of the microbial communities. However, there are still several obstacles to overcome **(Gilbert et al., 2018)**.

Human nasal microbiota

A unique habitat that supports the survival of a variety of bacteria is the nasal cavity. Beginning at birth, microbial communities colonize the human body and continue to exist throughout life in a variety of bodily habitats as commensals or opportunistic pathogens. Due to their ability to prevent pathogen invasion and support immune modulation, these bacteria are essential for preserving a healthy microenvironment **(Thangaleela et al., 2022)**.

By altering the composition of the human nasal microbiota to exclude pathobionts, infections caused by them may be considerably reduced. About 25% of humans are colonized with *Staphylococcus aureus*, one of the prominent nasal pathobionts, along with *Streptococcus pneumoniae*. Furthermore, it increases the danger of infections in far-flung body parts like skin, soft tissues, heart valves, and bones **(Lemon, 2020)**.

The Core Airway Microbiome

Even with advances in molecular technology, it was difficult to identify bacteria from airway samples **(Flanagan et al., 2007)**. In the past, traditional culturing techniques were believed to be sterile in the healthy human lower respiratory tract **(Cardenas and Cookson, 2015)**. However, developments in high-throughput sequencing and culture-independent techniques have shown that distinct microbiome configurations are linked to the onset of disease and that bacterial populations do, in fact, permanently occupy the lower airways **(Beck et al., 2012)**.

The type and richness of the bacterial microbiome in the airways vary along its anatomical trajectory. There are multiple overlapping bacterial niches in the airways, including the nasopharynx, oropharynx, lower (thoracic) airways (seen with a bronchoscope), bronchioles, and alveoli (observable with a bronchoalveolar lavage) (Figure1) **(Hilty et al., 2010)**.

According to the representation, the nasopharyngeal microbiome is composed of seven common genera: *Neisseria*, *Haemophilus*, *Veillonella*, *Staphylococcus*, *Streptococcus*, *Prevotella*, and *Corynebacterium*.

The species diversity of the nasopharyngeal microbiome is lower than that of the oropharynx **(Huse et al., 2012)**. *Actinobacteria* (especially *Corynebacterium* and *Propionibacterium* species), *Firmicutes* (mostly *Staphylococcus* species), and *Proteobacteria* (represented by *Enterobacter* species) make up the majority of the nasal microbiome **(Lemon et al., 2010)**.

In contrast to the oropharynx, where Gram-positive bacteria make up over 80% of the community, the nasopharyngeal microbiome is composed of more than 50% Gram-negative bacteria **(Bogaert et al., 2011)**. The composition of the nose and nasopharynx microbiome is comparable to that of the skin microbiome, with a significant concentration of Staphylococcus species **(Costello et al., 2009)**.

The upper respiratory tract microbiome of infants

Six major genera— *Haemophilus, Dolosigranulum, Streptococcus, Staphylococcus, Moraxella, and Corynebacterium* —usually make up an infant's nasopharyngeal microbiome, with one or two genera frequently displaying dominance **(Shilts et al., 2016)**. Beginning at birth, the nasopharyngeal bacterial colonization mimics the mother's skin or vaginal microbiota **(de Steenhuijsen Piters et al., 2015)** (Figure 2).

Breastfeeding maintains the makeup of this early microbiome by the time the child is 1.5 months old, fostering stable profiles of *Dolosigranulum*/*Corynebacterium*. On the other hand, babies who are fed formula typically have higher levels of Staphylococcus aureus. Notably, breastfed infants' microbiome seems to offer protection against respiratory infections. **(Biesbroek et al., 2014a)** (Figure 2). At 1.5 months of age, the nares and nasopharynx are characterized by the predominance of signatures from *Dolosigranulum, Corynebacterium, Streptococcus, Moraxella, and/or Staphylococcus* **(Biesbroek et al., 2014b)**.

Except for *Moraxella catarrhalis*, that has been associated to wheezing in newborns as early as one month of age when present with *H. influenzae* and *Streptococcus pneumoniae*, children with profiles dominated by *Moraxella* spp. have decreased susceptibility to upper respiratory tract infections (URTI). However, in children who are nearly two months old, Nasopharyngeal *Streptococcus* has been found to be a major predictor of asthma. **(Teo et al., 2015)**.

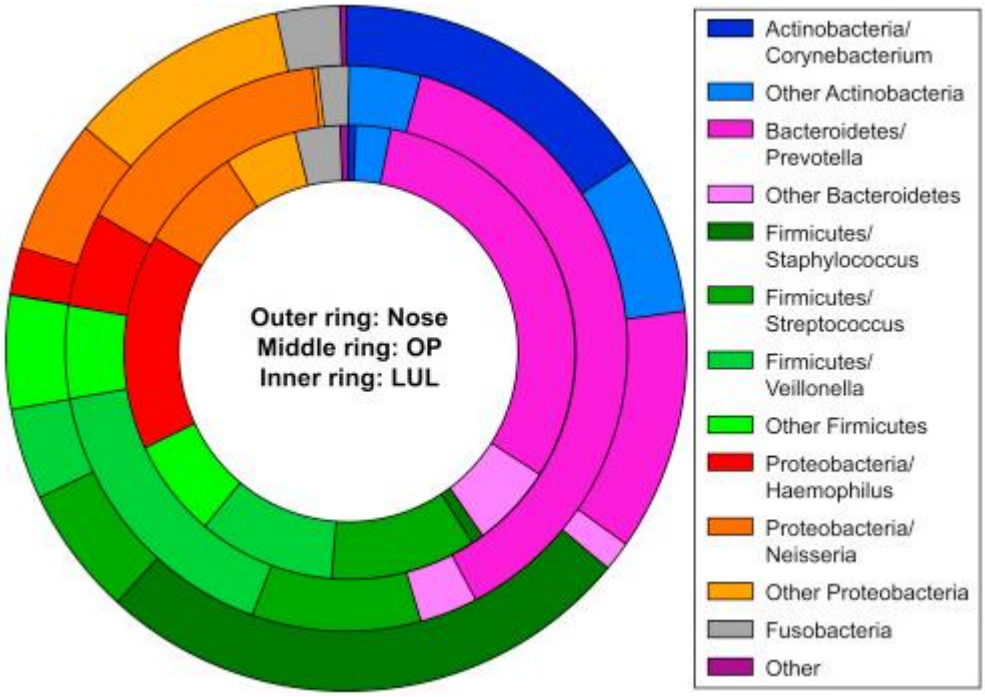

Figure 1: Common phylum and genera shown by percentage distribution at various airway levels: nose; left upper lobe (LUL); oropharynx (OP) **(Hilty et al., 2010)**.

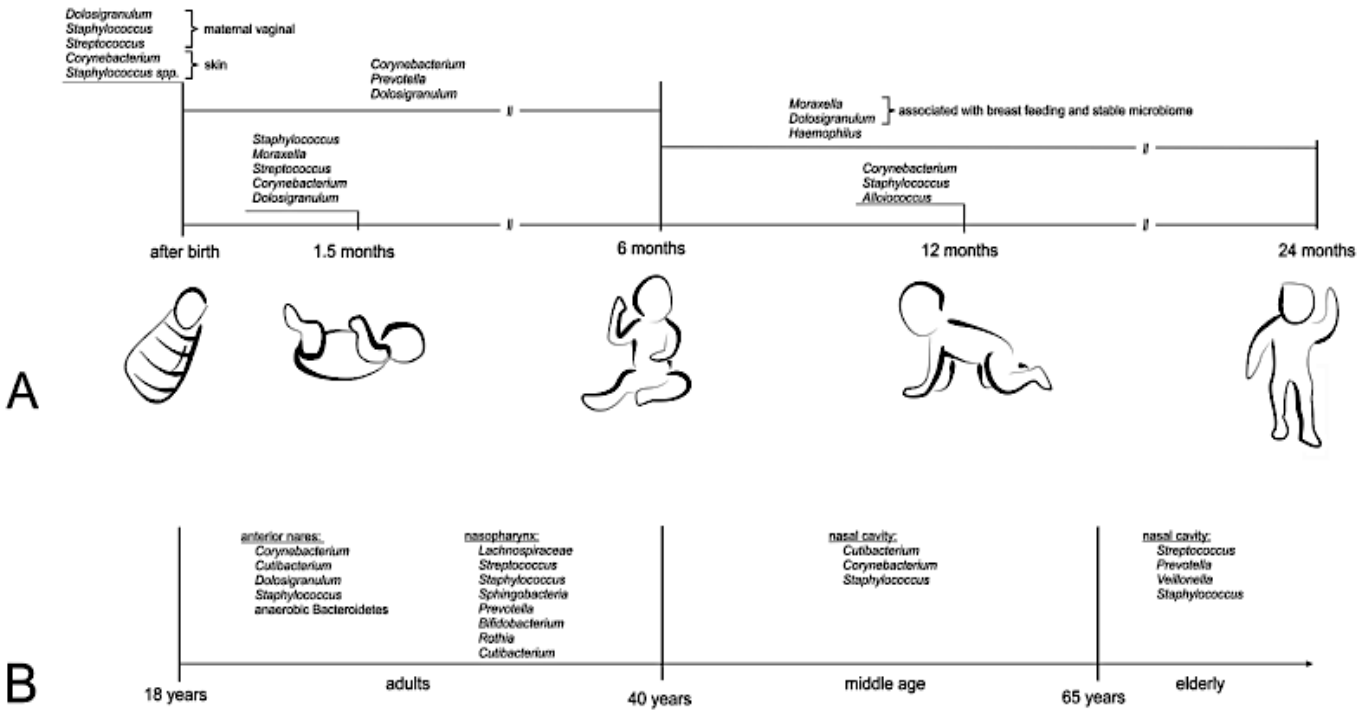

Figure 2: Nasal microbiota in infants and children of various ages **(Kumpitsch et al., 2019).**

By the age of 1.5 months, groups of co-occurring microbes dominated by *Haemophilus* appeared, leading to the disappearance of *Staphylococcus*-dominated profiles and the replacement of *Corynebacterium*/*Dolosigranulum* patterns with groups of *Moraxella/*Dolosigranulum in the upper respiratory tract of neonates **(Biesbroek et al., 2014b)** (Figure 2).

In contrast to *Haemophilus* and *Streptococcus*-dominant profiles, *Corynebacterium*, *Moraxella*, and *Dolosigranulum* appear to make up a more stable microbiome, according on overall observations of children during their first two years of life. **(Prevaes et al., 2016)**. The latter characteristics were connected to respiratory tract viruses and a higher risk of early infantile bronchiolitis, especially those that included *Streptococcus pneumoniae* and *H. influenzae* **(Luna et al., 2018)**.

The upper respiratory tract microbiome of adults

Adults and babies have quite different upper respiratory tract (URT) microbiomes, even though they have similar niche characteristics. Compared to babies, children's nasal microbiomes are frequently denser (having a higher bacterial load) but less diversified **(Stearns et al., 2015)**. Adults' anterior nares are mostly home to *Firmicutes*, *Actinobacteria*, and, to a lesser degree, anaerobic *Bacteroidetes* **(Koskinen et al., 2018)** (Figure 2).

Comparative evaluations of several nasal cavity specimen locations reveal that the microbial community compositions of the sphenoethmoidal recess (SR) and middle meatus (MM) are almost identical, while the anterior nares exhibit significantly less variety. Additionally, the anterior nares have a higher proportion of *Actinobacteria* and *Firmicutes* but a lower amount of *Proteobacteria* than SR and MM **(Yan et al., 2013)**.

The greater diversity seen in nasal mucosal specimens may be explained by the nasal mucosa's principal function, which is the removal of breathed air **(Yan et al., 2013)**. At the phylum level, the adult nasopharynx microbiome is similar to that of the anterior nares; however, the lower taxa that have been found have site-dependent traits **(Stearns et al., 2015)**.

Factors affecting the microbiota of the respiratory tract

Delivery mode

The colonization and spread of lung bacteria are influenced by the lung's structural characteristics, respiratory function, evacuation capacity, and environmental factors, such as ambient air quality. Shared illnesses between the intestine and lung microbiota systems demonstrate the interdependence of these two systems **(Martín et al., 2016)**.

The immune system's growth and effectiveness in the upper and lower respiratory tracts are greatly influenced by environmental variables, especially in the early postnatal period when exposure to certain microorganisms occurs. During this crucial time, exposure to particular bacteria can provide protection against asthma and other allergy illnesses **(Ballini et al., 2019)**.

The impact of nursing and delivery mode on the colonization of helpful microbes, such as *Dolosigranulum* and *Corynebacterium*, in newborns has been highlighted in a study. While breastfeeding is linked to increased levels of these beneficial species, infants born via caesarean section show decreased colonization by these bacteria, which may be crucial in supporting the immune system. **(Arrieta and Finlay, 2014)**.

Type of milk feeding

Numerous studies have repeatedly shown that certain rural settings, like farms, where breastfeeding and the consumption of unpasteurized milk are prevalent, along with exposure to animals and endotoxins, offer substantial protection against allergenic sensitivity and adult asthma **(Schuijs et al., 2015)**.

By changing the makeup of the intestinal microbiota, breast milk, which is high in fatty acids and oligosaccharides, protects against the beginning of allergies and asthma. Together with the activation of T-regulatory cells, this modification promotes the proliferation of advantageous bacteria like Lactobacilli and Bifidobacteria, which support a balanced Th1/Th2 immunological reaction **(Loss et al., 2015)**. Additionally, it has been showed that a diet high in fiber can alter the gut microbiota's makeup, increasing *Actinobacteria* and *Bacteroides* while decreasing *Proteobacteria* and *Firmicutes* ***(*Trompette et al., 2014*)***.

Because of this qualitative and quantitative shift in gut

microbiota, the lungs' immune response is regulated by a greater generation of short-chain fatty acids (propionate, acetate and butyrate), which lowers Th-2 cell activity and eosinophil levels **(Trompette et al., 2014).**

Use of antibiotics and specific diets

Antibiotic administration has been linked to a higher risk of Moraxella, H. influenzae, and Streptococcus colonization. Compared to their non-colonized peers, children who are colonized by these viruses during the first month of life are more likely to experience wheezing **(Abrahamsson et al., 2014)**. Furthermore, dysbiosis, which is defined by a lack of vital microorganisms necessary for immune system growth and maintenance, may be caused by inadequate or changed microbial colonization **(Santacroce et al., 2020)**.

Therefore, interventions such as specific dietary regimens, particular living environments, and probiotic supplementation may serve as protective factors against the onset and progression of respiratory ailments **(Santacroce et al., 2019)**.

Conclusion

Microbial populations in the nasal passages have a significant impact on human health and illness. The nasal microbiome can be changed by environmental factors such the style of delivery, the kind of milk feeding, the use of antibiotics, and particular diets, which can disrupt the organization of the microbiome community. Therefore, it is essential to identify nasal microbiota and the relationships between community members to prevent and cure a variety of respiratory illnesses. According to general findings of infants throughout the first two years of life, *Corynebacterium*, *Moraxella*, and *Dolosigranulum* form a more reliable microbiome than profiles that are dominated by *Haemophilus* and *Streptococcus*. The nasal microbiomes of children are less diversified but denser (have a larger bacterial load). The major microorganisms in healthy adults' anterior nares are *Firmicutes*, *Actinobacteria*, and, to a lesser degree, anaerobic *Bacteroidetes*.

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