



ELSEVIER

**BIAA**  
British Infection Association

www.elsevierhealth.com/journals/jinf

# The respiratory microbiome and respiratory infections

Stefan A. Unger<sup>a</sup>, Debby Bogaert<sup>b,\*</sup>

<sup>a</sup> Department of Child Life and Health, University of Edinburgh, Edinburgh EH9 1UW, UK

<sup>b</sup> The University of Edinburgh/MRC Centre for Inflammation Research, The Queen's Medical Research Institute, Edinburgh EH16 4TJ, UK

Available online 23 June 2017

## KEYWORDS

Microbiome;  
Caesarean section;  
Vaginal delivery;  
Breast feeding;  
Acute respiratory illness;  
Viral lower respiratory illness;  
Asthma;  
Wheeze

**Summary** Despite advances over the past ten years lower respiratory tract infections still comprise around a fifth of all deaths worldwide in children under five years of age with the majority in low- and middle-income countries. Known risk factors for severe respiratory infections and poor chronic respiratory health do not fully explain why some children become sick and others do not. The respiratory tract hosts bacteria that can cause respiratory infections but also normal commensal bacteria. Together, this microbial population is called the microbiome. The composition of the respiratory microbiome in the first few months of life is likely influenced by external factors such as environment, mode of delivery and infant feeding practices, which are also associated with susceptibility to respiratory infections and wheezing illness/asthma. Recently, multiple studies have shown that respiratory microbiota profiles early in life are associated with an increased risk and frequency of subsequent respiratory infections, disease severity and occurrence of wheeze in later childhood. Early interactions between infectious agents such as viruses and the respiratory microbiome have shown to modulate host immune responses potentially affecting the course of the disease and future respiratory health. Deeper understanding of these interactions will help the development of new therapeutic agents or preventive measures that may modify respiratory health outcomes and help us to stratify at risk populations to better target our current interventional approaches.

© 2017 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

## Introduction

Lower respiratory tract infections (LRTI) are related to approximately a fifth of all causes of childhood deaths

worldwide.<sup>1</sup> Equally the burden of respiratory morbidity is substantial with up to 40% of paediatric presentations in primary health care being respiratory in nature.<sup>2–5</sup> Severe LRTI in infancy, particularly with respiratory syncytial virus

\* Corresponding author. The University of Edinburgh/MRC Centre for Inflammation Research, The Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, UK. Tel.: +44 (0)131 242 6352.

E-mail addresses: sunger@exseed.ed.ac.uk (S.A. Unger), D.Bogaert@ed.ac.uk (D. Bogaert).

(RSV) is not only an important cause of hospitalization, but also associated with higher risk of subsequent preschool wheeze and asthma.<sup>6,7</sup> It has become clear that the bacteria and perhaps also viruses, which cause respiratory infections are part of the normal commensal flora of young children, and are found frequently in asymptomatic children.<sup>8-10</sup> Nasal carriage of bacteria such as *M. catarrhalis* and *Streptococcus pneumoniae* can be asymptomatic but may also lead to infections such as otitis media and pneumonia via mucosal transfer or sepsis and meningitis as part of a systemic infection.<sup>9,11</sup> Why some children are more likely to develop severe disease is not exactly known but appears multifactorial.<sup>12</sup> It has been hypothesised that health is dependent on the interplay between changes in the microbiome and infection on the background of human genetic make up and environmental factors.<sup>12</sup>

## The respiratory microbiome

Advances in molecular techniques, particularly metagenomics, have allowed us to gain an insight into the symbiosis between humans and their resident microbes, termed the human microbiota. This complex microbial ecosystem in and on our bodies seems to play an important role in health by stimulation of the immune system, contributing to the development of mucosal and/or epithelial barriers and containment of pathogens.<sup>12</sup>

The microbiome within the various niches in the respiratory tract (including oropharynx and nasopharynx), differ significantly, possibly impacted by environmental influences, anatomical factors and epithelial characteristics.<sup>9</sup> However there is also considerable overlap in the microbial composition between these niches.

It has been proposed that internal and external drivers affect the development of the respiratory microbiome, particularly during the first year of life. These include genetic predisposition, mode of delivery, infant feeding, exposure to antibiotics, vaccination, dentition, geographical variations and seasonal differences.<sup>12</sup>

Birth is regarded by many as the starting point of development of the infant's microbiome including the population of respiratory mucosal surfaces.<sup>13</sup> In a recent birth cohort study of 102 healthy, unselected infants the impact of mode of delivery on nasopharyngeal microbiota development was studied from birth to 6 months of life.<sup>14</sup> Bacterial DNA of nasopharyngeal samples was isolated followed by amplification of the hypervariable V4 region of the 16S rRNA gene and sequencing by Illumina MiSeq. Samples taken directly after birth contained a mixture of bacteria, most likely from faecal, vaginal, skin and/or environmental origin. However, within a day, first *Viridans streptococcus* emerged rapidly followed at one week of age by outgrowth of *Staphylococcus aureus*. Over the time period of two weeks to six months, predominance of *S. aureus* gradually declined and others emerged, such as *Moraxella catarrhalis*, *Corynebacterium* spp. and *Dolosigranulum* spp. Bacterial colonisation with *Streptococcus pneumoniae* and *Haemophilus influenzae* also started to emerge over the first 6 months of life.

Using co-occurrence spectral clustering algorithms to define clusters of samples with similar bacterial co-occurrence patterns, elicited further insight into microbial

succession patterns over time.<sup>14</sup> For the identified 11 distinct clusters or profiles, again strong age-related dynamics were observed over time. In the first weeks of life domination of a single profile, i.e. first a *Streptococcus*-dominated, followed by a *S. aureus*-dominated profile was observed in most infants. These were gradually replaced by profiles dominated by *Moraxella*, *Corynebacterium*, *Dolosigranulum*, and/or *Haemophilus* species. In general, the shifts in microbial composition were most dramatic over the first two months of life, where certain microbiota profiles were associated with more change, therefore less ecological stability over time.

## The respiratory microbiome and mode of delivery

It had previously been shown that directly after birth bacterial inhabitants in the respiratory tract differ between those born vaginally and those born by Caesarean section.<sup>15</sup> In vaginally delivered babies, the first bacteria detected in the respiratory tract resemble the maternal vaginal environment (*Lactobacillus*, *Prevotella*, or *Sneathia* spp.). In contrast skin-type bacteria (*Staphylococcus*, *Corynebacterium*, and *Propionibacterium* spp.) dominate the microbiota in those born by Caesarean section. Using co-regularized spectral clustering and permutation tests to look at the differences between modes of delivery in the cohort study described above, a delay in switch over from a *S. aureus* dominated to a *Moraxella*- or *Corynebacterium*/*Dolosigranulum*-dominated profile was observed for those children born by Caesarean section when compared to vaginally born children, even after correction for mode of feeding.<sup>14</sup>

## Respiratory microbiome and infant feeding

Infant feeding certainly has shown to affect composition of the intestinal microbiota regarding the abundance of genera such as *Bifidobacterium* and *Lactobacillus*.<sup>16</sup> However, infant feeding is suggested to also impact other microbial environments, including the respiratory tract.<sup>17</sup> In a study among 202 infants, breastfed children had higher abundances of the Gram-positive commensals *Corynebacterium* and *Dolosigranulum* and decreased abundance of *Staphylococcus* spp. in their nasopharynx compared to formula fed infants at six weeks of life.<sup>17</sup> These particular microbial patterns were also associated with decreased susceptibility to (mild) respiratory infections and wheeze in infancy and beyond.

## Respiratory microbiome and respiratory health in childhood

Respiratory microbiota composition early in infancy seems to determine the shape and stability of the microbiome later on in life: in a retrospectively analysed study of 60 infants the microbiota composition at six weeks of life was strongly associated with both microbial (in)stability as well as with parental-reported symptoms of respiratory infections during follow-up.<sup>18</sup> Eight distinct microbiota profiles in the upper respiratory tract were identified. More stable patterns and lower rates of respiratory infections were observed in those with early presence and high abundance of *Corynebacterium*/

Download English Version:

<https://daneshyari.com/en/article/5668788>

Download Persian Version:

<https://daneshyari.com/article/5668788>

[Daneshyari.com](https://daneshyari.com)