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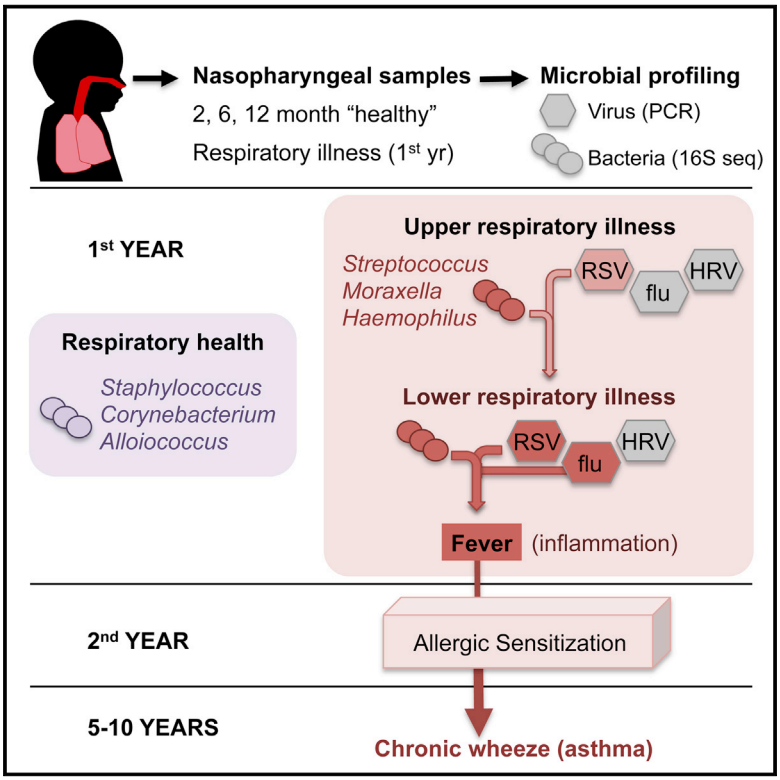
The Infant Nasopharyngeal Microbiome Impacts Severity of Lower Respiratory Infection and Risk of Asthma Development

Graphical Abstract



Highlights

- The nasopharynx microbiome of infants has a simple structure dominated by six genera
- Microbiome composition affects infection severity and pathogen spread to lower airways
- Early asymptomatic colonization with *Streptococcus* increases risk of asthma
- Antibiotic usage disrupts asymptomatic colonization patterns

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In Brief

Teo et al. characterize bacterial and viral communities within the infant nasopharynx during the first year of life, comparing between asymptomatic colonization and episodes of acute respiratory infections. Microbiome composition affects infection severity and spread to lower airways and risk for future asthma development.

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The Infant Nasopharyngeal Microbiome Impacts Severity of Lower Respiratory Infection and Risk of Asthma Development

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SUMMARY

The nasopharynx (NP) is a reservoir for microbes associated with acute respiratory infections (ARIs). Lung inflammation resulting from ARIs during infancy is linked to asthma development. We examined the NP microbiome during the critical first year of life in a prospective cohort of 234 children, capturing both the viral and bacterial communities and documenting all incidents of ARIs. Most infants were initially colonized with *Staphylococcus* or *Corynebacterium* before stable colonization with *Alloiococcus* or *Moraxella*. Transient incursions of *Streptococcus*, *Moraxella*, or *Haemophilus* marked virus-associated ARIs. Our data identify the NP microbiome as a determinant for infection spread to the lower airways, severity of accompanying inflammatory symptoms, and risk for future asthma development. Early asymptomatic colonization with *Streptococcus* was a strong asthma predictor, and antibiotic usage disrupted asymptomatic colonization patterns. In the absence of effective anti-viral therapies, targeting pathogenic bacteria within the NP microbiome could represent a prophylactic approach to asthma.

INTRODUCTION

The human microbiome is now recognized as playing an important role in the etiology and pathogenesis of myriad diseases (Weinstock, 2012). However, elucidation of these complex roles requires targeted characterization of microbial communities present in relevant spatial niche(s) during critical periods of pathogenesis. The focus of this study is the respiratory tract, in particular the nasopharynx (NP), which is an accessible source of airway microbial communities (Hilty et al., 2010) and serves as a conduit for pathogens associated with lower respiratory illnesses (LRIs) that are responsible for substantial morbidity and mortality worldwide.

Of particular interest is asthma, a multi-factorial disease characterized by airway inflammation and associated smooth muscle hyperplasia. It is now recognized that the hallmark persistent wheeze of asthma is consolidated in childhood and, further, may progress to chronic asthma in adulthood (Holt and Sly, 2012; Sly et al., 2008) and potentially chronic obstructive pulmonary disease (Tai et al., 2014). We and others have previously shown that development of persistent atopic (allergic) wheeze in children is linked to the number of virus-associated febrile and/or wheezy LRIs experienced during infancy (Jackson et al., 2008; Kusel et al., 2007, 2012; Oddy et al., 2002). The principal virus type of current interest is human rhinoviruses (HRVs), particularly subtype C (HRV-C) (Bochkov and Gern, 2012); however, respiratory syncytial virus (RSV) is also recognized as a major cause of infant LRI (Wu and Hartert, 2011). The relative contributions of these viral pathogens in asthma initiation remain controversial (Stein and Martinez, 2010). Further complicating the picture, recent studies have also implicated bacterial pathogens as potential independent causal factors in infant LRIs and their long-term sequelae. Notably, culture of *S. pneumoniae*, *M. catarrhalis*, or *H. influenzae* from NP samples taken at 1 month of age has been linked to increased risk for subsequent diagnosis of asthma at 5 years of age (Bisgaard et al., 2007). These findings have fuelled debate around the use of antibiotics and vaccine strategies for respiratory illness in children (Penders et al., 2011; Rollins et al., 2010).

Several studies have investigated airway microbiota in children or adults with chronic respiratory illness, including asthma