

2nd Edition

GLOBAL ATLAS OF ASTHMA



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INFECTIONS AND ASTHMA- BACTERIA

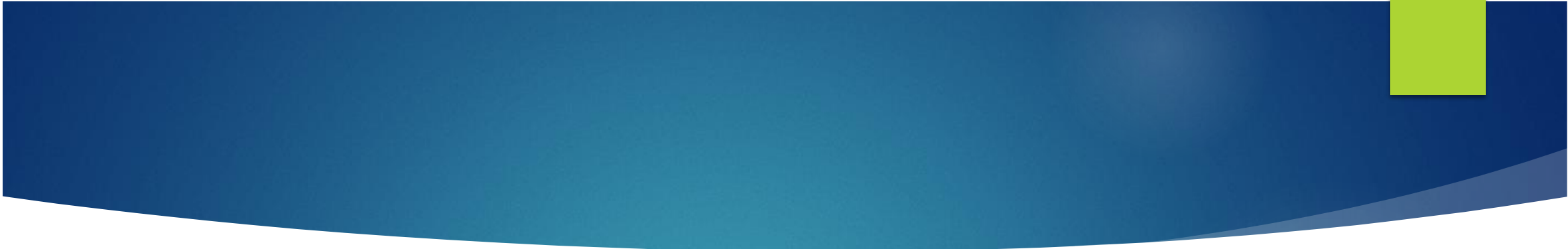
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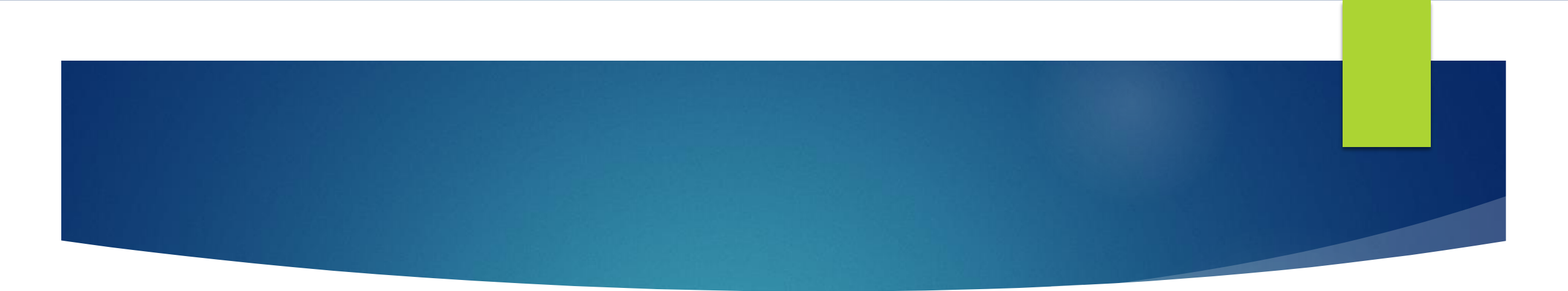
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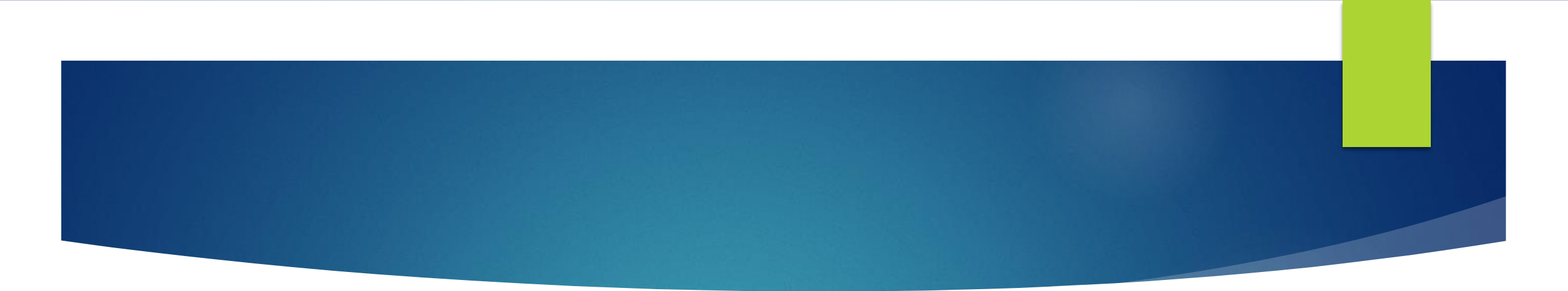


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- ▶ It has been known for many years that **respiratory viruses** are *important determinants of asthma inception and exacerbations*.
 - ▶ However, emerging data from the past decade have also highlighted ***the role of airway bacteria in these processes***.

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- ▶ Recent systematic reviews and meta-analyses demonstrate an **association between RSV LRTI** and RWEC, childhood asthma, reduced lung function and increased airway reactivity with a **3-fold** increased risk compared to children without infant viral LRTI.
 - ▶ Interestingly, comparisons between **children with non-RSV, non-rhinovirus LRTI** (e.g. due to human metapneumo virus, parainfluenza, human coronaviruses) and RSV LRTI, did *not find a difference in the risk* of RWEC/asthma development, suggesting that this may be linked with viral LRTI rather than RSV infection specifically.

BACTERIA AND ASTHMA INCEPTION

- ▶ A pioneering report, published more than a decade ago, revealed that **asymptomatic 1-month-old infants** who had upper airway colonization with *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and/or *Haemophilus influenzae* had *higher odds for future asthma*.
- ▶ **Immune cells taken from these children**, who eventually developed asthma, produced *increased levels of type 2 (T2) cytokines*.
- ▶ Hence, it was suggested that **aberrant immune response** predisposes to airway bacterial colonization, which may lead to T2 airway inflammation and asthma.

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- ▶ A more recent study revealed that the **airway microbiome** is *shaped during the first years of life* and is *dominated by limited number of genera*.
 - ▶ **These respiratory clusters differ between periods of respiratory health** (dominance of *Staphylococcus*, *Corynebacterium*, and *Alloiococcus* dominance; viewed as commensal bacteria) **and acute respiratory illnesses** (dominance of *Streptococcus*, *Moraxella*, and *Haemophilus* dominance; viewed as pathogenic bacteria (Figure 1)).

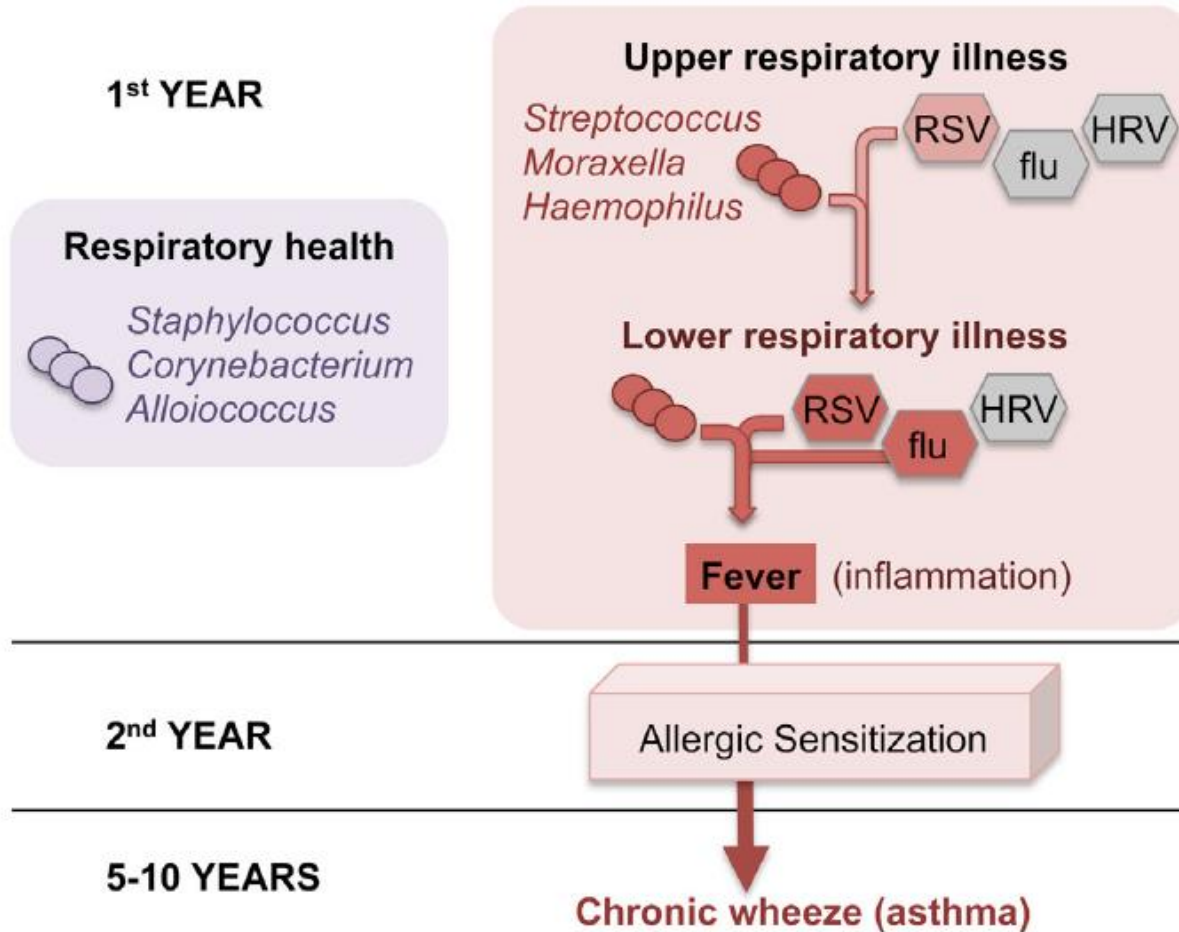
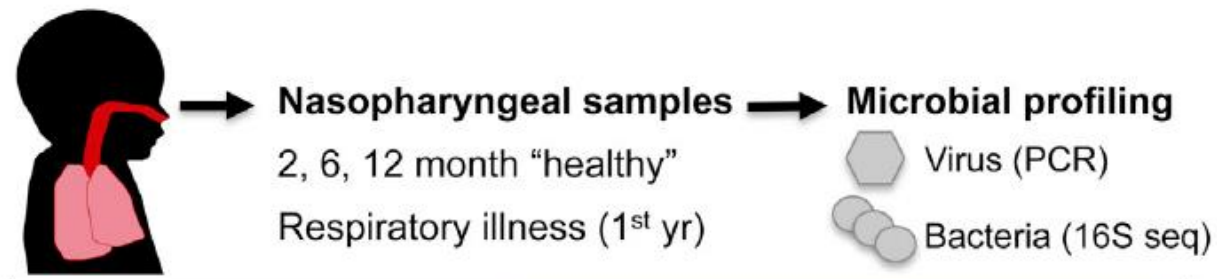
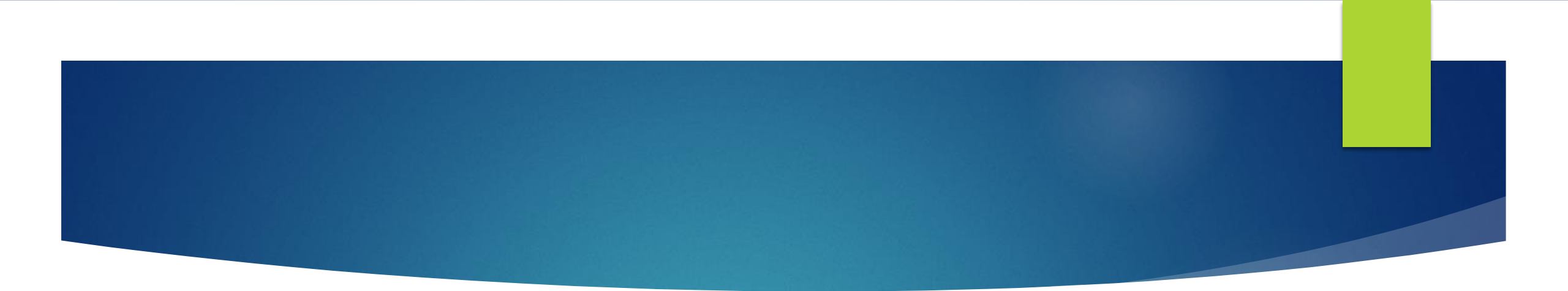


Figure 1 The airway microbiome is shaped during the first years of life.

(Reproduced from Teo SM, Mok D, Pham K, et al. The infant nasopharyngeal microbiome impacts severity of lower respiratory infection and risk of asthma development. *Cell Host Microbe*. 2015;17:704-15)

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- ▶ **The airway microbiome composition** is dynamic with changes into pathogenic bacteria clusters preceding respiratory infections and predicting future wheezing episodes.
 - ▶ **Early life sensitisation to aeroallergens**, in combination with airway microbiome dysbiosis, *predicted development of the persistent wheeze phenotype*; while the **dysbiosis**, but without allergic sensitization, *predicted development of the transient wheeze phenotype*.
 - ▶ These associations highlight the **importance of bacteria and immune system interactions in asthma inception**.

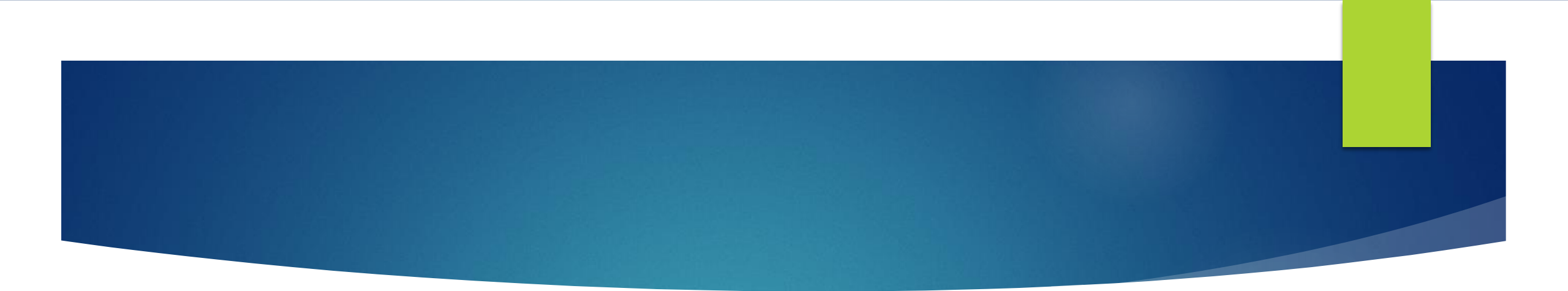
VIRAL AND BACTERIAL INTERACTIONS

- ▶ **The interactions between airway bacteria and viruses** are important in asthma inception.
- ▶ This concept may be illustrated by the development of **recurrent wheezing and asthma** following severe respiratory syncytial virus (RSV) bronchiolitis.
- ▶ Although this is a common sequel, **not all children with severe RSV bronchiolitis develop these outcomes**; hence it may be that the **composition of airway microbiome during the RSV infection** contributes to the development of post-RSV recurrent wheezing.

- ▶ Indeed, **high abundance of airway *Moraxella* or *Haemophilus*** was found to be related to the development of post-RSV wheeze.
- ▶ Furthermore, a small proof-of-concept study (Table 1) revealed that **azithromycin therapy during the acute RSV infection**, reduced airway *Moraxella* abundance, which in turn was related to *lower likelihood to develop post-RSV recurrent wheeze*.
- ▶ However, **some airway bacteria may be beneficial** as higher abundance of airway *Lactobacillus* during RSV illness was associated with a reduced risk of future wheezing.

AIRWAY BACTERIA AND ASTHMA EXACERBATIONS

- ▶ Although **exacerbations of acute episodic wheeze in preschool children** were traditionally related to viral infections, dominance of airway bacteria was noted during many of these episodes.
- ▶ Furthermore, two clinical trials in this age group, have shown **beneficial effects of azithromycin therapy** for the prevention and the treatment of these episodes (Table 1) suggesting a potential mechanistic role of bacteria in these exacerbations.
- ▶ However, it should be noted that other mechanisms (e.g., **anti-inflammatory effects**) may have mediated these beneficial effects.

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- ▶ On the other hand, **some bacteria** may actually promote respiratory health.
 - ▶ A study among school-age asthmatic children revealed that **children whose respiratory microbiome was dominated by the more commensal bacteria *Corynebacterium+Dolosigranulum*** were less likely to experience loss of asthma control.
 - ▶ Finally, **although airway bacteria have roles in asthma pathogenesis**, their roles should be viewed in the broader context of the ***complex interaction between airway bacteria and the gut microbiome***, which has the capacity to shape airway immune response.

KEY MESSAGES

- Airway bacteria are important determinants of asthma inception and exacerbations
- The airway microbiome evolves in early life and usually comprises of limited number of dominant bacterial clusters
- The early life airway microbiome composition is dynamic: changes in bacterial respiratory clusters may precede respiratory infections and may predict future wheezing episodes
- Interactions between airway bacteria and other factors such as respiratory viruses, the gut microbiome, and the immune system are important drivers of asthma pathogenesis
- The airway microbiome is a potential target for future primary, secondary and tertiary asthma prevention strategies