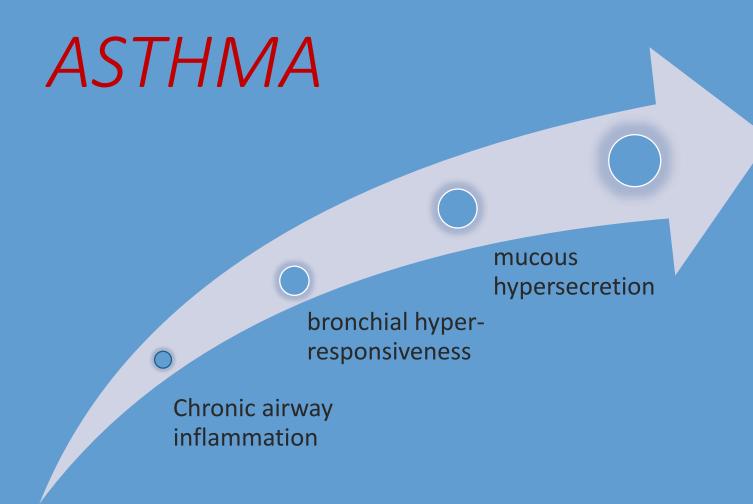
EPIDEMIOLOGY OF INFECTIONS AND

DEVELOPMENT OF ASTHMA

L. Moradi, MD

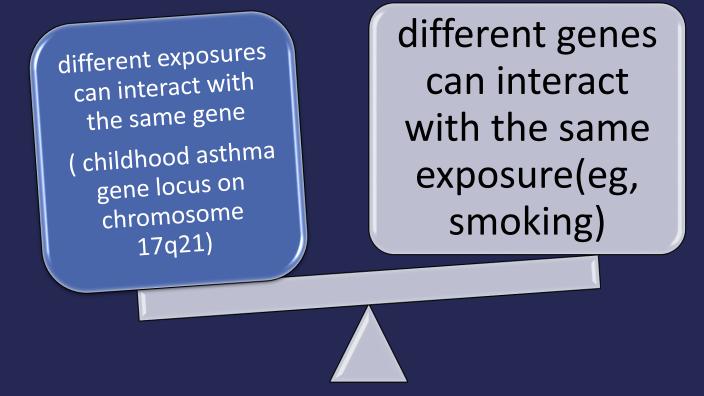
Allergist and clinical immunologist

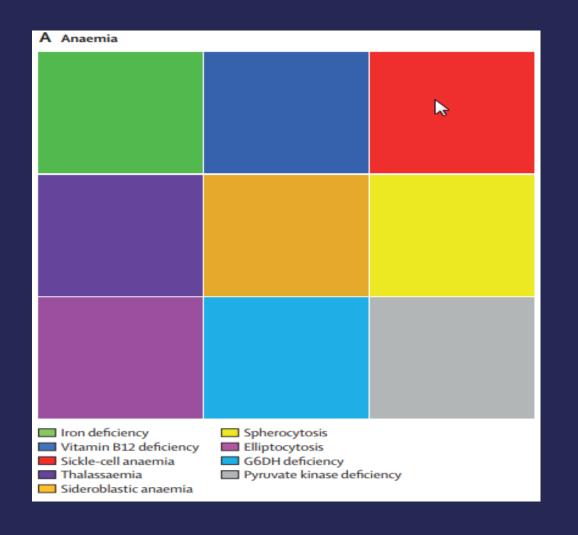


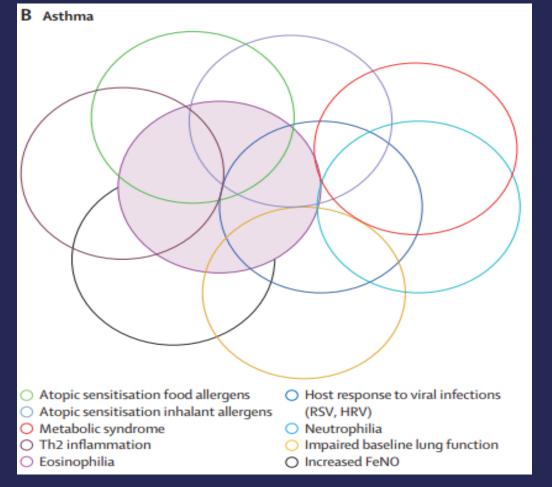
Recurrent, reversible episodes of:

- Wheezing
- shortness of breath
- chest tightness
- coughing

Asthma is determined by many genes interacting with various environmental exposures unequivocally







VIRAL INFECTIONS AND DEVELOPMENT OF ASTHMA

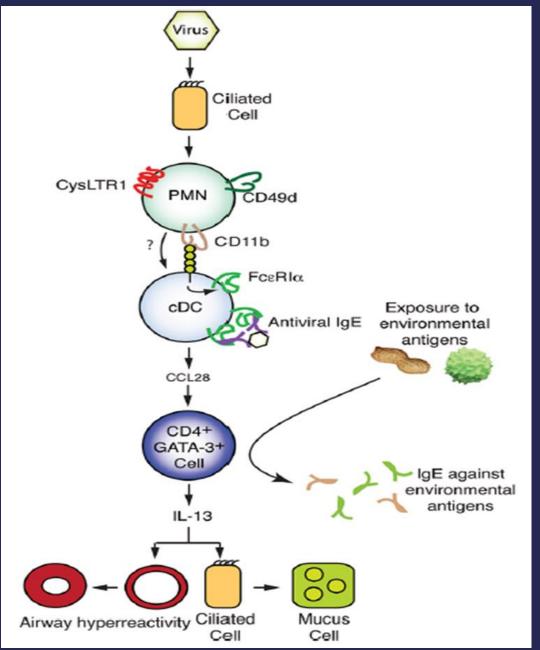
 Infant respiratory viral infection and childhood asthma are the most common acute and chronic diseases of childhood

- 1/3 of all children suffer from infection-induced wheezing during the first 3 years of life
- Up to 50% of all children have acute wheezing at least once before school age amongst these children, 30% to 40% develop recurrent wheezing
- Viral respiratory infections: in up to 80% of wheezing episodes and asthma exacerbations

VIRAL INFECTIONS AND DEVELOPMENT OF ASTHMA

- The role of early-life infections in the development of asthma results from complex interactions between pathogens, genetics, and environmental factors such as tobacco smoke
- viral or bacterial infections: in 70% of adult inpatients with an asthma exacerbation
- asthma onset after an acute respiratory illness is exceedingly common (up to 45% of adult-onset asthma cases)
- Those with asthma are more likely to have clinically significant infections
- Early infections but <u>not smoking</u> history were best indicators for the development of asthma

Mechanistic pathway
translating respiratory viral infection
into atopic disease



Eur. J. Immunol. 2018. DOI: 10.1002/eji.201747052

THE MOST COMMONLY DETECTED VIRUSES IN ASTHMA EXACERBATIONS IN CHILDREN

Respiratory syncytial virus (RSV)

Rhinovirus (RV)

Parainfluenza viruses (parainfluenza virus 1 and 2)

They have been associated as well in the development of the disease - especially with severe infections by these viruses early in life

Wheezing illnesses in infancy and early childhood caused by them strongly correlate with asthma development later in life

OTHER VIRUSES ASSOCIATED WITH ASTHMA EXACERBATIONS (LESS THAN 5%)

- Adenovirus
- Enterovirus (non-RV)
- Influenza
- Metapneumovirus
- Bocavirus
- Coronovirus

~10% of these cases have a co-infection with more than one virus – usually with RV

RSV AND DEVELOPMENT OF ASTHMA

the relevance of severe RSV infections in the development of asthma and asthma symptoms

one of the most common infections in children and infants

Has a causal role in the development of asthma and allergen sensitization

one of the leading causes of severe respiratory infection in infants

ENTEROVIRUSES AND ASTHMA



INFLUENZA AND ASTHMA

Influenza circulates both as a seasonal infection and occasional pandemic

• The seasonal variety:

clearly causes asthma exacerbations

a minor contributor to the overall burden of asthma disease development

DURING THE 2009 INFLUENZA PANDEMIC (PH1N1)

The major differences between the pandemic influenza and seasonal influenza:

pH1N1 was associated with higher incidence of pneumonia and a greater need for ICU

- Asthma was the most common co-morbidity among patients(22-29% of all hospitalized patients)
- Children with asthma: 44% of hospitalized children with influenza
- pH1N1 seemed to cause more disease in older children (median age: 4.8 years old)
- while the median age for seasonal influenza A patients: 1.7 years

ROLE OF INNATE LYMPHOID CELLS (ILCS) TRANSLATING RSV INFECTION INTO ASTHMA AND ATOPIC DISEASE

- ILCs:
- ILC1
- ILC2
- ILC3

largely emulate the adaptive CD4+Th1,Th2,Th17 produce high levels of interleukin 5 (IL-5) interleukin 13 (IL-13)

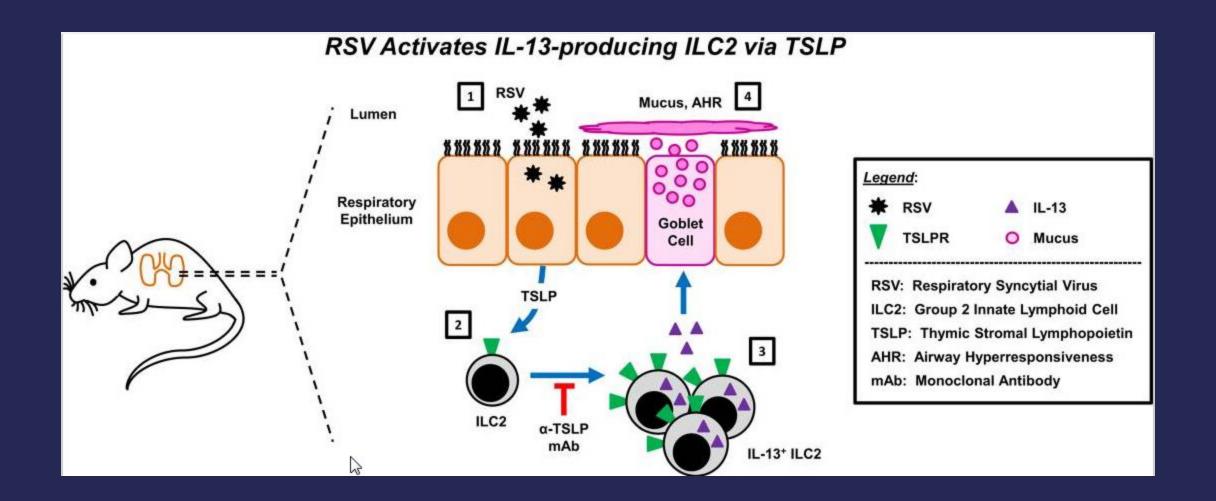
• ILC2s

• **IL-5**: eosinophil development

IL-13:

IgE synthesis
Mucus hypersecretion
Airway hyperresponsiveness
Fibrosis

RSV induces robust IL-13 production from ILC2 during the early phase of the infection via TSLP



ATYPICAL BACTERIAL INFECTION AND DEVELOPMENT OF ASTHMA

Chlamydophila pneumoniae (CP)

Mycoplasma pneumoniae (MP)

fungi like Aspergillosis

Streptococcus, Moraxella, and Haemophilus genera

CHLAMYDOPHILA PNEUMONIAE

anti-chsp60 IgA anti-CP IgE

- MP has been associated with recurrent wheeze
- may be present as a co-infection with respiratory viruses
- Children with asthma were more likely to have MP-specific IgM than those without asthma (39% vs 0%) suggesting increased exposure/colonization of MP in those with asthma

Early infection with CP or MP:

 a higher risk for asthma through induction of type 2 airway inflammation, mucus cell metaplasia, and airway hyperreactivity

CP infection:

- induce a Th2 immune response
- airway eosinophilia and neutrophilia
- leading to permanent alteration of lung structure and function

Hypopharyngeal colonization with S. pneumoniae, H. influenza, or M. catarrhalis in neonates was reported to increase the risk for recurrent wheeze and asthma early in life

B. Pertussis has not been associated with development of asthma, but may infect asthma patients more frequently

In subjects under 40 years of age, **H. pylori infection** (as documented by IgG against H. pylori in the peripheral blood) appears to protect against asthma (OR 0.503), but not other allergic diseases

If CP and MP do cause asthma, then treatment with macrolide antibiotics (for which CP and MP are sensitive) should prevent or ameliorate asthma

In fact, treatment with a macrolide antibiotic in vitro, did block CP induced mucin production in cultured human airway cells

A larger clinical study found macrolide treatment reduced the severity of respiratory tract infections, but had no impact on the symptom scores or the use of albuterol

Therefore, it remains unclear how important atypical bacterial infections are to the pathogenesis of asthma

