

RESPIRATORY INFECTIONS  
AND  
ASTHMA

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NO DISCLOSURES  
NO FINANCIAL INTEREST

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INFORMATION OBTAINED  
JACI  
AJRCCM

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HISTORY

2 year old male  
 -Daycare since 9 months of age  
 -Recurrent symptoms since 10 months of age:  
 1. Rhinorrhea  
 2. Colored drainage off and on  
 3. Cough and wheezing with exacerbation  
 4. Increased in winter (early spring, late fall)  
 -Symptoms increasing in frequency and severity  
 -In doctors office every 4 to 6 weeks  
 -Symptoms respond partially to antibiotic treatment and bronchodilator  
 -No history of asthma and allergies in parents  
 -No atopic dermatitis  
 -No GERD symptoms  
 -Parents missing lot of work  
 -No O.S.A symptoms  
 -Few ear infections  
 -No pneumonias  
 -Prior history at 10 months of age of RSV bronchiolitis

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HISTORY CONT'D

- I. Investigations**
- i. Nasal smear shows polys, bacteria, and many eosinophils
  - ii. Skin test to dust/animal/mold – negative  
     IgE is normal or mildly elevated (25)
  - iii. CBC, diff shows no eosinophilia
  - iv. CxR shows perihilar changes and normal lung parenchyma
- II. Diagnosis**
- i. Recurrent upper and lower respiratory infections likely from contact with children in daycare.
  - ii. Associated with Reactive Airway Disease

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HISTORY CONT'D

- III. Treatment**
- i. Out of daycare
  - ii. Intent ==> give time for respiratory mucosa to recover, repair, and regenerate
  - iii. Nasal saline washes
  - iv. Complete the course of antibiotic and steroids this patient was on at the time of appointment
  - v. If no improvements, further studies such as immune studies etc.

Mother was not agreeable

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HISTORY CONT'D

- I. ENT referral
- II. Trial of anti reflux medication
- III. Surgery
  - adenoidectomy
  - functional endoscopic sinus surgery
  - evaluation of trachea with ciliary studies (Inadequate sample)
  - culture (Negative)

\*Patient still required antibiotic treatment until mom took him out of daycare, as she was pregnant with her second child.

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VIRUSES  
AND  
ASTHMA

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EVIDENCE LINKING RSV AND RV LOWER RESPIRATORY TRACT INFECTION(LRTI) WITH ASTHMA INCEPTION

	<u>Evidence</u>	<u>RSV LRTI Data</u>	<u>RV LRTI Evidence</u>
<u>Association with asthma</u>	+	Among infants with RSV LRTI, the estimated risk of later developing asthma from OR 2.07 to 12.7	+
<u>Precedes asthma onset</u>	+	Longitudinal studies demonstrate that RSV LRTI precedes atopic sensitization and asthma onset	+/-

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EVIDENCE LINKING RSV AND RV CONT'D			
	RSV LRTI		RV LRTI
	Evidence	Data	Evidence
<u>Dose-response relationship demonstrated</u>	+	-RSV LRTI severity is associated in a dose-dependent fashion with both increasing asthma risk and increasing asthma severity -A dose-response relationship with no infection, mild infection, and infection with wheezing has been demonstrated for RSV.	0/+
<u>Contributes to a substantial proportion of asthma</u>	+	-A majority of infant LRTIs are attributable to RSV infection. -Infant RSV LRTIs therefore contribute to a higher proportion of asthma in the population.	+

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EVIDENCE LINKING RSV AND RV CONT'D			
	RSV LRTI		RV LRTI
	Evidence	Data	Evidence
<u>Defined risk groups</u>	+	-Family history of asthma -Premature birth -Male sex -Seasonality of birth -Genetic polymorphisms commonly in immune response genes	+
<u>Host genetic and viral genetic determinants of disease risk and severity</u>	+	-Host: Several genes are associated with both RSV infection and asthma, suggesting a genetic susceptibility to both -Virus: RSV strain differences have been shown in mouse and human studies to affect the pathogenicity, which await demonstration as to whether they are associated with asthma risk after infant infection	+

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EVIDENCE LINKING RSV AND RV CONT'D			
	RSV LRTI		RV LRTI
	Evidence	Data	Evidence
<u>Biologic mechanisms through which these viruses may cause asthma</u>	+	-Pathology: RSV in animal models causes acute and chronic lung changes similar to asthma -Physiology: RSV infection is associated with prolonged airway hyper-responsiveness -Immune Development: In animal models RSV infection results in long-term immunomodulatory changes and impairs regulatory T-cells	+
<u>Currently available interventions</u>	+	-Avoidance -Birth timing -RSV immunoprophylaxis -Ribavirin	0

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**EVIDENCE LINKING RSV AND RV CONT'D**

	<u>Evidence</u>	<u>RSV LRTI Data</u>	<u>RV LRTI Evidence</u>
<u>Acceptable interventions in pregnant women and children</u>	+	Most would consider both birth timing and the currently available RSV immunoprophylaxis as acceptable interventions	0
<u>Proof of concept studies available by challenging, preventing, or removing</u>	+	Randomized controlled trial of RSV immunoprophylaxis among premature infants demonstrated reduced risk of wheezing at 1 yr Observational studies of infants treated with ribavirin or RSV immunoprophylaxis demonstrated significantly lower incidence of asthma or recurrent wheezing	0

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**INFANCY WHEEZING**

50% Wheeze



40% Asthma

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**EPIDEMIOLOGIC DATA**

- I. Never wheezers – 51%**
- II. Early Transient Wheezers – 20%**  
(Onset < 3 years, resolution 6 years)
- III. Persistent wheezers – 14%**  
(Onset < 3 years, Sustained at 6 years)
  - i. Non atopic
    - first episode at one year
    - less wheezing in adolescence
    - most outgrown
    - low lung functions
    - increase in BHR
  - ii. IgE associated/atopic
    - wheezing starts at 2 years
    - persists into adolescence
    - parental asthma
    - male sex
    - atopic dermatitis
    - eosinophilia
    - food and aero allergy
- IV. Late Onset Wheezers – 14%**  
(Onset between 3 and 6 years)

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### MELBOURNE STUDY 7-35 YEARS

<ol style="list-style-type: none"> <li>1. Atopic condition in childhood</li> <li>2. Severe asthma in childhood</li> <li>3. Severe asthma in early life</li> </ol>		<p>Increased risk of severe asthma later</p> <p>Increased risk of atopic eczema or allergic rhinitis</p> <p>Increased risk for persistent and severe asthma</p>
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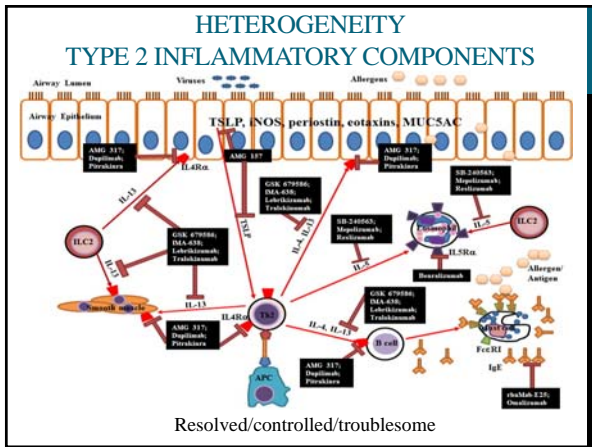
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### GUIDELINE-DIRECTED CARE VS GUIDELINE-DIRECTED CARE PLUS OMALIZUMAB

IgE dependent factors are risk factors for viral infections  
Reducing IgE levels attenuates exacerbations due to respiratory viral infections

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**MICROBIOTA AND ASTHMA**

1. Healthy bronchial tree contains 2,000 bacterial genomes/sq cm – mostly bacteroides
2. Asthmatics have higher population of proteo bacteria
3. Altered airway microbiota is a feature of asthma

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**MICROBIOTA AND ASTHMA**

1. Gut and respiratory mucosal bacteria interacts with immune system and pre critical for proper immune development
2. Feeding preterm infants with probiotic prevents illness from rhinovirus infection
3. Antibiotics and proton inhibitor treated infants appear to be at higher risk for atopy and asthma

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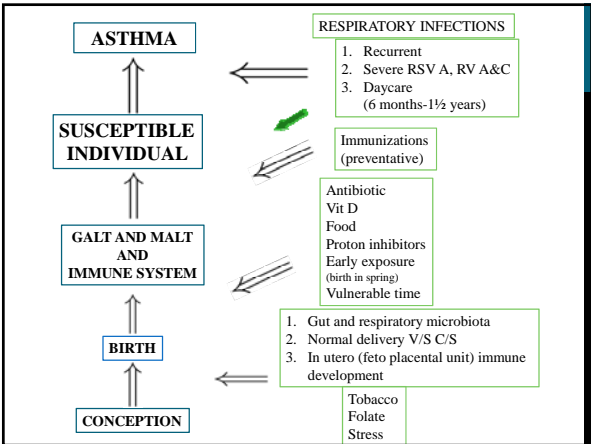
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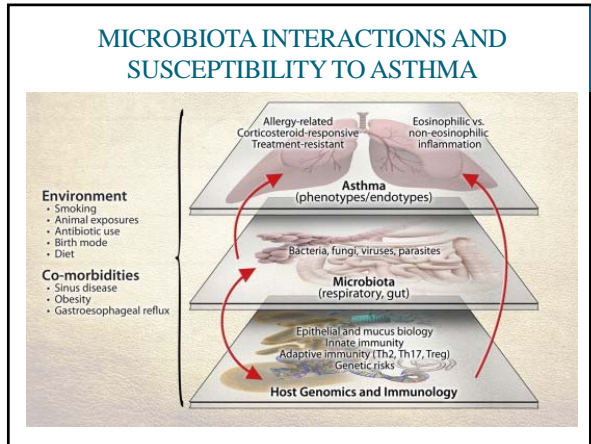
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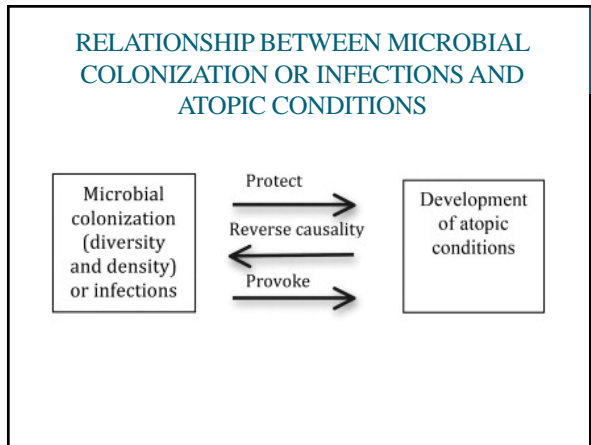
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- ### INCREASED RISK OF INFECTIONS IN ASTHMA AND ATOPIC DISEASES
1. Invasive Pneumococcal disease and pneumonia (ACIP recommends PPV23 vaccine)
  2. URI - Streptococcus Pyogenes
  3. Staph Aureus colonization in nose and skin
  4. Bordetella Pertussis infection
  5. Community acquired E.Coli blood stream infection
  6. Mycoplasma Pneumoniae infection
  7. H1N1 Influenza infection
  8. Reactivation or latent viral infection

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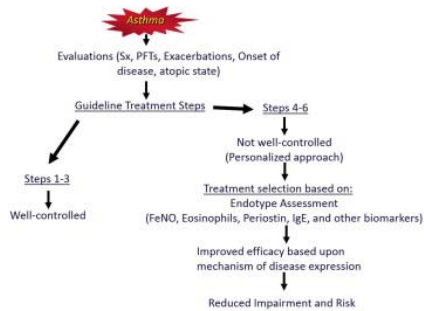
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## INDIVIDUALIZED MANAGEMENT OF ASTHMA



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## SUMMARY

1. Asthma is a very heterogenous disease
2. Recurrent viral respiratory infections are associated with development of asthma
3. Gut and respiratory microbiota play a role in development of immune system and determines susceptibility to asthma
4. Small changes in the ecosystem of microbiota results in profound effect on atopic inflammation
5. Treatment of asthma in the future may be dependent on phenotypes
6. Pneumococcal vaccine for asthmatics

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