



Allergic Asthma More Than A Runny Nose

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Learning Objectives


- Identify the differences between allergic and non-allergic asthma
- Understand the role of allergens in inducing Th-2 inflammation in allergic asthma
- Understand how allergic targeted therapies can improve asthma patient outcomes.

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How did we get here?



Charles Harrison Blackley



Clemens von Pirquet

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Almost there...

- *One very curious circumstance in connection with hay fever is that the persons who are most subjected to the action of pollen belong to a class which furnishes the fewest cases of the disorder, namely, the farming class. This remarkable fact may be accounted for in two different ways: it may, on the one hand, be due to the absence of the predisposition which mental culture generates; or, on the other hand, it may be that in this disease there is a possibility of a patient being rendered unsusceptible to the action of pollens by continued exposure to its influence.*
 - Charles Harrison Blackley
 - Experimental researches on the causes and nature of catarrhus aestivus, 1873

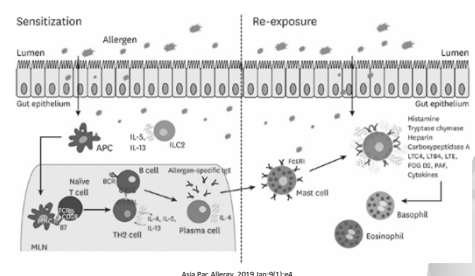
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Allergy at last

- 1903 – von Pirquet noticed incubation period similar amongst infections
- Correctly assumed must be from the immune system, not the organism
- Described serum sickness in 1905, but needed a term
- “allos” meaning other or different, “ergia” meaning energy or action

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So what is allergy?



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Th1 vs Th2

Th1 – Intracellular

- Produce IFN- γ , TNF, IL-1
- Macrophages
- IgG
- Defense against intracellular pathogens
- Protective

Th2 – Extracellular

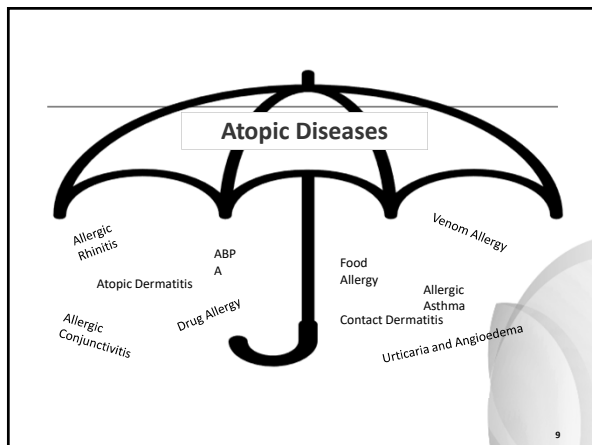
- Produce IL-4, 5 and 13
- Eosinophils, mast cells, basophils
- IgE
- Defense against parasites
- Allergy!

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But what is allergy?

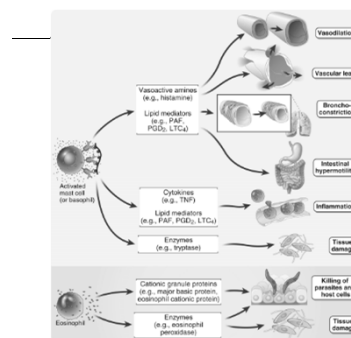
- Positive skin or blood testing?
- Runny nose, congestion and sneezing every spring?
- Wheezing, coughing, and chest tightness around cats?

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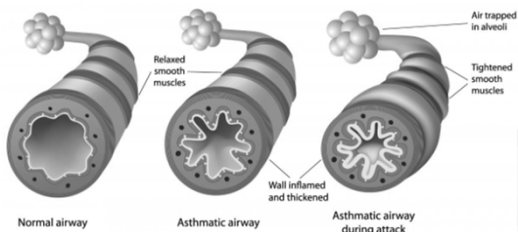
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Location Location Location



Abbas et al. Cellular and Molecular Immunology, 9th Edition, Pg 446.

Asthma



About asthma. (n.d.). Retrieved March 5, 2021, from <https://www.asthmafriendly.ca/home/about-asthma>

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Asthma

Allergic (Extrinsic)

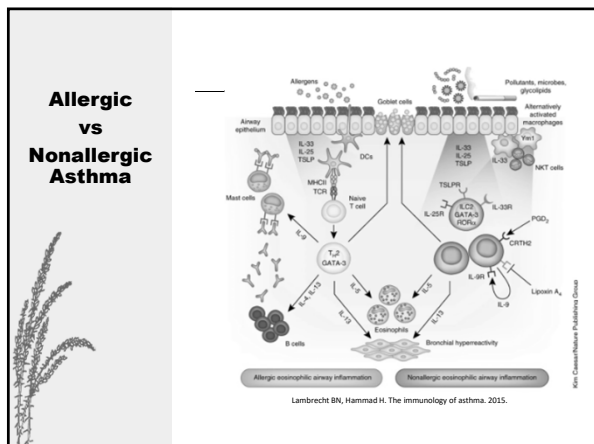
- Earlier onset (mean 15.8yrs)
- Atopic
- Eosinophils, mast cells, Th2
- Typically milder course
- Responsive to ICS

Nonallergic (Intrinsic)

- Late onset (mean 32.2yrs)
- Less atopy
- More mixed (neutrophils)
- Can be more refractory
- Less responsive to ICS

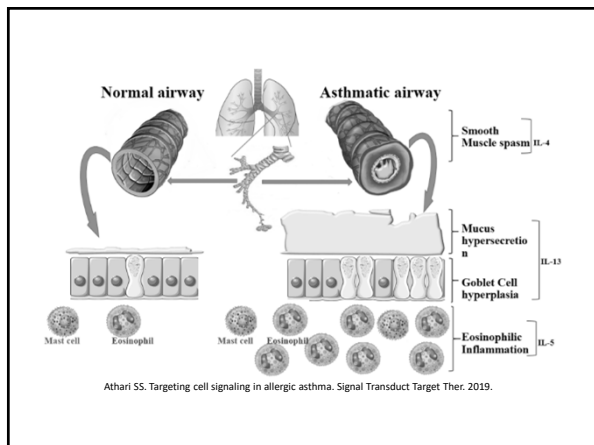
- Can be more severe in children

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Allergic Asthma

- Sensitization to aeroallergens
- Correlation between exposure and asthma symptoms
- Fraction of Exhaled Nitric Oxide (FENO) typically elevated
- 80% of school aged children with asthma are sensitized to at least 1 allergen
 - Number of positives correlates with symptoms

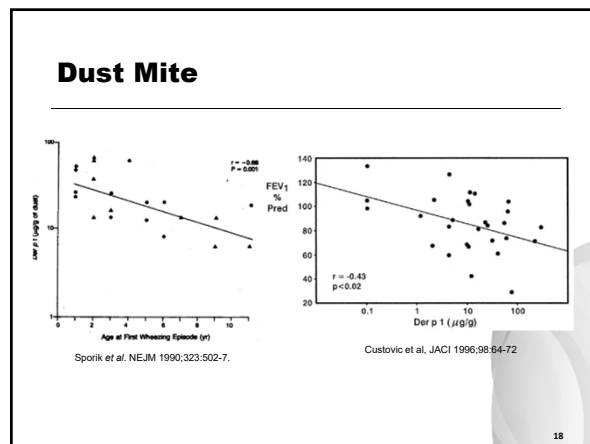


Dust Mite

- Live in furniture, stuffed animals, bedding
- Need humidity above 50% to survive
- Allergen is a large particle, stays airborne for 20-30min after disturbed
- Typically does not cause acute worsening
 - Chronic exposure

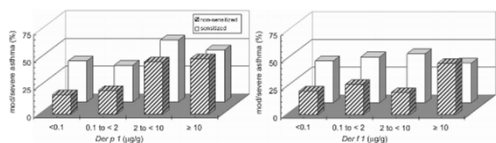
Dust Mite

- 80% of children with asthma are dust mite sensitive
 - 30% of control population
- Average dust mite levels:
 - 2.4µg/g in living room
 - 4.3µg/g in bedroom
 - 18.4µg/g in mattress
- RR of asthma 4.8x if exposed to > 10µg/g in infancy



Dust Mite

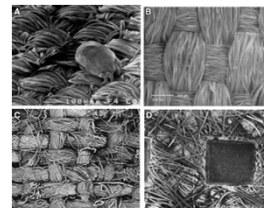
- 450 children with asthma
- Retrospective look comparing severity to exposure
- 2x more likely to have moderate-severe asthma regardless of atopy



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Dust Mite Precautions

- Mattress and pillow covers
- Wash sheets and blankets every 1-2 weeks
- Remove carpet and drapes
- Vacuum twice weekly
 - Disturbs dust at the same time
- HEPA filters
- Decrease humidity to under 45%



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Cat and Dog

- Smaller particles than dust mite
- Passively transferred on clothing
- Present in public buildings and homes without pets
 - 100x higher in homes with pets than without



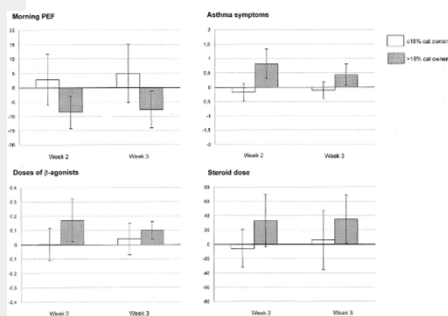
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Cat Study

- 90 children with asthma, cat allergy, and no direct exposure
- Peak flows measure before school and after school
- Divided classroom into high and low cat ownership (18% cutoff)
- 5-fold increase in Fel d 1 in high cat class

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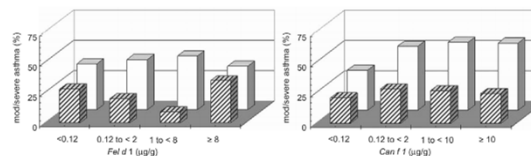
9-fold increased risk of asthma worsening



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Yale Study

- If sensitized, detectable pet allergen can worsen asthma



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So what do we do with that?

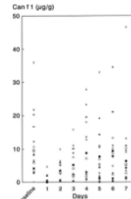
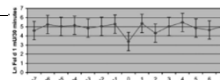
- Remove the pets!
- 20 adults with pets and allergy. 10 removed, 10 kept
- After 1 year
 - 5/10 in removal group on ICS initially, 0/10 after 1 year
 - 6/10 in kept group on ICS initially, 9/10 after 1 year
 - 5.9 fold increase in methacholine dose required in removal group
 - 2.3 fold increase in kept group



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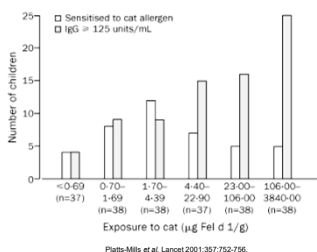
Any other options?

- Air filters?
 - Controversy
- Wash them more frequently?
 - Not sustainable
 - Would need multiple times/week



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Desensitize?



Platts-Mills et al. Lancet 2001;357:752-756.

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Pollen

POLLEN FORECAST



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Prevention?

- Childhood Asthma Prevention Study (Australia)
 - Large cohort of children with family history of asthma
 - Cat or dog prior to age 5 had decreased sensitivity to these
 - No affect on wheeze, eczema or FEV1 at 5 years
- Canadian Healthy Infant Longitudinal Development study
 - Infants had changes in their microbiome that decrease asthma risk
- More siblings and pets may decrease asthma risk
 - Bias?

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Prevention?

- Inhaled Corticosteroids**
 - The Prevention of Early Asthma in Kids study (PEAK) – Arizona
 - 285 children ages 2-3yo with positive predictive asthma scores
 - Fluticasone vs placebo for 2 years followed by 1 year of observation
 - No difference in asthma symptoms during observation year
- Oral Antihistamines**
 - Early Treatment of the Atopic Child study – Germany
 - Infants with atopic dermatitis treated with 18 months of cetirizine vs placebo
 - No difference in asthma prevalence
 - Similar study with levocetirizine

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What about shots?

- Preventative Allergy Treatment study (Germany)
- 183 grass/birch allergic children 6-14yo did 3yrs of SCIT
- Compared to controls treated with medications
- Significantly less asthma 5 and 7 years later
 - Odds ratio of 4.6 for no asthma in AIT group compared to controls

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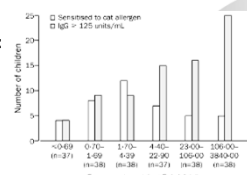
Drops?

- 60 children with dust mite allergy randomized
 - 35 to SLIT, 25 to medications
- Decreased asthma frequency in SLIT group at 4-5 years
- Other studies with similar results
 - Graax Asthma Prevention trial – OR of 0.66 for asthma in SLIT group
- Both SCIT and SLIT need to be done for 3+ years to have benefit

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How?

- Reduces polysensitization
- Dendritic cells initiate change from Th2 to Th1
- Decreases allergic inflammation
- Promotes Treg development



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Treatment

- SCIT and SLIT have been shown to decrease asthma symptoms
 - Some studies showing SCIT more effective than SLIT
- Both also decrease medication usage
 - Both for asthma and rhinitis
 - SCIT > SLIT
- So why not do shots?
 - Higher risk – mortality from shots typically happens in severe asthmatics
 - No mortalities in SLIT

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Who should get this? API

- More than 3 (or 4) episodes of wheezing per year during the first 3 years of life and...

Major Criteria (Need 1)

- Asthma in parent
- Eczema in the child

Minor Criteria (Need 2)

- Allergic rhinitis in child (or sensitization to an aeroallergen)
- Wheezing apart from colds
- Peripheral eosinophilia \geq 4%

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Treatment

- SCIT and SLIT reduce exacerbations and therefore steroid usage
- Can help with asthma therapy stepdown
 - Most helpful in moderate (Step 3/4), less in mild
 - Can reduce ICS doses and medication usage
- Systemic reaction risk of 0.1-0.2% with standard build-up protocols

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Why does it work?

- **Decrease sensitization to allergic triggers**
- **Improves airway remodeling**
 - Study with SLIT for dust mite
 - Decrease FENO and peripheral eosinophilia
 - Increase airway caliber with decreased wall thickness
 - Decreases Th2 cytokines and eosinophil infiltration
- **Improves symptoms**
 - Better FEV1 and improved symptom scores

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What if too uncontrolled to do shots?

- **Omalizumab – monoclonal antibody against IgE**
- **Approved for allergic mod-severe asthma in ages 6+ with**
 - **IgE between 30 and 700**
 - **Sensitivity to perennial allergen**
 - **Weight based dosing**
 - **0.1-0.2% anaphylaxis risk**
- **Can be used as an adjunct to immunotherapy build up**

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Summary

- **Allergic asthma is aeroallergen sensitization with correlating symptoms**
- **Dust mite and pet sensitivity are risk factors for asthma**
- **Uncontrolled allergies can make asthma worse**
- **Lifestyle modifications and allergy immunotherapy can reduce asthma risk and symptoms**

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Questions?



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