The Allergic March and How to Stop it

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NMIMR
Atopy

- The genetic propensity to develop IgE antibodies in response to exposure to allergens.
- Generally agreed that atopy is an important risk factor for allergic diseases such as asthma, rhinitis, and eczema.
“Atopic diseases”

- allergic asthma,
- allergic rhinoconjunctivitis,
- atopic eczema/dermatitis,
- immediate food allergy
The Atopic March”

- Natural history of allergic or atopic manifestations characterised by a typical sequence of clinical symptoms and conditions appearing during a certain age period and persisting over a number of years (Weinberg 2005)

The progressive appearance of new allergies and allergic diseases over time. This begins with food sensitivities and atopic dermatitis in infancy, and progresses to include persistent inhalant allergies with allergic rhinoconjunctivitis and allergic asthma in older childhood.

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Characteristics of the Allergic March

- Food allergies and atopic dermatitis precede and predict asthma and allergic rhinitis.
- Eczema and some food allergies (milk, egg, soy) tend to be outgrown or improve with age.
- Allergic rhinitis and other food allergies (nuts, seafood) tend to persist.
- Allergy-associated asthma persists but can improve; “asthma” without allergy tends to be outgrown or improve.
- Disease severity predicts persistence and progression.
How do one stop the march?

- Research to understand mechanisms and risk factors involved
- Improved and early diagnosis
- Education and awareness creation
- Prevention and treatment
What do we know?
The allergic reaction

Ragweed pollen

B cell

IgE

Plasma cell

These IgE molecules attach themselves to mast cells.

Mast cell

The second time that person has a brush with ragweed,

the IgE primed mast cells release granules and powerful chemical mediators, such as histamine and cytokines, into the environment.

Symptoms

These chemical mediators cause the characteristic symptoms of allergy.

The first time an allergy prone person runs across an allergen such as ragweed

he or she makes large amounts of ragweed IgE antibody.
- Lower prevalence of asthma and allergies in developing countries where Th2 driven helminth infections are endemic

- Increase of the overall prevalence of Th1-mediate autoimmune diseases accompanies increase in prevalence of atopic diseases
Regulatory T cells (Tregs) secrete downmodulatory cytokines (IL-10 and TGFβ).

- Control both Th1 and Th2 response
- Anti-inflammatory network may be central to hygiene hypothesis
The information that has been published has resulted in many more questions. A lot still needs to be done:

“"The dozen or so genes involved in asthma are only just beginning to be understood"” – Prof. Dale Umetsu
Where do we stand with diagnosis?

- SPT
- Specific IgE detection and quantification
- Medical history
- Clinical diagnosis
- Food challenges
What does the public know?
Information to the public

- Feel in control and not overwhelmed!
- Ensure that children are properly diagnosed
- Let children be involved in their treatment
Wheezing Infants

Intervention Measures

Adapted from Ricardo Sorensen
Preventive measures

- Primary preventions try to optimize development of early immunity so children can overcome other aspects of risk.
- Secondary preventions intervene in young at-risk children prior to the development of chronic lung processes.
Food Allergy Treatment

- Avoidance
  - Attention to Labels
  - Education on sources of “hidden foods”
- Extensive hydrolysate formulas
- Amino acid formulas
Preventing Pediatric Allergy

- Allergy, particularly atopic dermatitis, is a significant health issue
  - High incidence in developed countries
  - Increasing incidence and prevalence
  - High costs of treatment
  - Impact on quality of life
  - Allergy March may greatly magnify the problem

Primary Prevention is a Priority

Adapted from Ricardo Sorensen
Recommendations applicable to all children

- Breast feeding 4-12 months
- If supplements needed then hydrolysate with proven efficacy
- No solids before 4 years of age
- No contact with tobacco smoke
Treatments

Early interventions attempt to normalize conditions for lung growth and development.
Treatments

- **Anti-histamines for atopic eczema**

- **Asthma controller therapies** (e.g., inhaled corticosteroids (ICS), leukotriene antagonists) in young children with recurrent wheezing who are at risk for developing persistent asthma.

- **Immunotherapy**
Treatment

- **History of immunotherapy**
  - In investigating his own hay fever, Dr. Charles Blakely performs the first skin test by applying pollen through a small break in his skin. He introduces concept that pollen causes hay fever.

- **In 1910, St Mary’s Hospital in London**
  - Tests with subcutaneous injections of pollen extracts.
  - Administered at increasing doses of crudely prepared whole allergen extracts to sensitised patients until symptoms were ameliorated.
    - Experiments represented the beginnings of the development of ‘de-sensitising immunotherapy’.

1911 - Noon and Freeman make sterile extracts of pollens and demonstrate that repeated injections improve clinical tolerance to allergen exposure, establishing the basis for allergen extract immunotherapy.
Introduction – immunotherapy

- There are few paediatric studies.
- Previous paediatric trials suffer from being too small, non-randomised, enrolling inappropriate subjects or using insufficient allergen.
- There is also concern about the potential for adverse effects in asthmatic children.

[Abramson M et al. Allergy 1999; 54:1022-1041]
Allergen specific immunotherapy

- The vast majority of randomized, double-blind, placebo-controlled trials have been performed since the 1960s
- Standardized allergen vaccines have only been available for the past 25 years
SIT seems to be even more effective in children than in adults.

SIT decreases symptoms and medication usage in childhood asthma and rhinitis.

SIT modifies the natural history of allergic disease and has long term benefits.

SIT prevents the development of asthma in children with hayfever.
Pollen immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis (The PAT-study)

Moller et al., 2002 J Allergy Clin Immunol;109:251-6
Immunotherapy with a standardized *Dermatophagoides pteronyssinus* extract: Specific Immunotherapy prevents the onset of new sensitizations in children

A. Des Roches, Bousquet et al., *J Allergy Clin Immunol* 1997; Vol 99, no 4, pp 450-453
ANTI-IgE TREATMENT FOR ALLERGY

- **IgE<sub>R</sub>**
- Circulating IgE
- Allergen cross-bridging
- Histamine
- Secretory granule
- Anchored IgE
- Anti-IgE
Conclusions

- Proper diagnosis, public education and early interventions may offer a way to shape and optimize immune development to lead to better outcomes in atopic children.

- As we know more we can design better studies to answer the current questions.