The Allergic Child

Professor Robin J. Green
PhD
Allergy is a hypersensitivity reaction initiated by immunologic mechanisms.
Rhinitis

Allergic rhinitis
Nonallergic rhinitis

IgE-mediated rhinitis
Non-IgE-mediated allergic rhinitis

Intermittent/persistent

Johansson SGO, et al. Allergy 2001:56;813-824
The Hypersensitivity Reactions

- Type I: Immediate
- Type II: Cytotoxic
- Type III: Immune complex
- Type IV: Delayed

Gell & Coombs
Primary Allergic Conditions

- Allergic rhinitis (AR)
  - Seasonal allergic rhinitis (SAR)
  - Perennial allergic rhinitis (PAR)
- Sinusitis
- Chronic idiopathic urticaria (CIU)
- Atopic dermatitis (AD)
- Allergic asthma (AA)
The Origins of Allergy
New thoughts on the origin of allergy 1: Foetal origins

- TH2-like cytokine profile maintains the pregnant state
- *Atopic mothers are more likely to have several children*
- The ‘atopic’ newborn has low levels of IFN-Y for 2 years of life
- Non-atopics: deletion of allergen-reactive T cells by anergy/apoptosis due to high-dose antigen exposure in the gut (oral tolerance) ± IgG anti-IgE mechanism
New thoughts on the origin of allergy 2: Gastrointestinal flora

- Less intensive colonisation with lactobacilli in Swedish neonates (high prevalence of allergy) compared to Estonian children
- Gut flora required for successful oral tolerance as gram-negative products (lipopolysaccharides) stimulate tissue macrophages to produce anti-TH2 cytokines
Pathophysiology of Allergy: Type I Hypersensitivity Reaction

$T_{\text{H}2}$ = Type 2 helper T cell; IL = Interleukin; GM-CSF = Granulocyte-macrophage colony-stimulating factor; IgE = Immunoglobulin E.
Type I Hypersensitivity: IgE Levels in Allergic Conditions

IgE = Immunoglobulin E.
Type I Hypersensitivity: Antigen Re-exposure

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**Broad Allergic Cascade**

**Mediators**

Mast cells/basophils release allergic mediators

- Histamine
- Leukotriene C4
- Prostaglandin D2
- Tryptase

**Acute response (0 - 2 hours)**
- Histaminic response
  - Sneezing, itchy, watery eyes, rhinorrhea, congestion

**Chronic inflammatory response (4 - 24 hours)**
- Allergic inflammatory response
  - Nasal inflammation, nasal obstruction, difficulty breathing, earache, tinnitus

**Cytokines**
- IL-1
- IL-3
- IL-4
- IL-5
- IL-6
- IL-10
- TNF-α

**Chemokines**
- IL-8
- RANTES
- Eotaxin
- MIPs

**Adhesion molecules**
- P-selectins
- VCAM
- ICAM-1

**IL = Interleukin; TNF-α = Tumor necrosis factor-alpha; RANTES = Regulated on activation, normal T cell expressed and secreted; VCAM = Vascular cell adhesion molecule; ICAM-1 = Intercellular adhesion molecule-1.**
Pathophysiology of Eczema

• Allergy
• Abnormal Barrier Function (Skin)
• Neural Disorder of Skin
• Cell Mediated immune Dysfunction
Prevalence of atopic eczema is increasing

Atopic Eczema is a chronic disease that often begins in infancy.
Atopic Eczema

• Chronic, relapsing inflammatory skin disease
• Often familial
• Frequently associated with other atopic disease:
  – food allergy, allergic rhinitis, asthma
• Characterised by intense itching, dry skin & inflammation
• Signs of inflammation:
  – erythema
  – infiltration / papulation
  – lichenification
  – excoriation

Itch is the most bothersome symptom

Ellis C et al, ICCAD II, BJD 2003
The Allergic March

- Food Allergy (0 – 1 year old)
- Eczema (3 months – 2-3 years old)
- Allergic Rhinitis (2 years – adulthood)
- Asthma (3 years – adulthood)

The united airway
Systemic Model for Allergic Disease

• Systemic allergic inflammation conveys the concept that allergy is a systemic immunologic dysfunction with local manifestations rather than a set of discrete, autonomous symptoms
Allergic Rhinitis and Asthma: Two Related Conditions Linked by One Common Airway
Allergic Rhinitis and Asthma Have Similar Prevalence Patterns


Allergic rhinitis increased the risk of asthma ~3-fold

23-year follow-up of college freshmen undergoing allergy testing; data based on 738 individuals (69% male) with average age of 40 years.

Most Patients with Asthma Have Allergic Rhinitis

• Approximately **80%** of asthmatics have allergic rhinitis

Allergic Rhinitis and Asthma Have Similar Early- and Late-Phase Responses

Aspiration of inflammatory secretions from the upper airway into the lower airway

Shift from nasal to mouth breathing

Nasobronchial reflex

Systemic mediation of nasal and lower-airway inflammation

Adapted from Togias A Allergy 1999;54(suppl 57):94-105.
Clinical Links Between Allergic Rhinitis and Asthma
Treatment of Seasonal Allergy with Nasal Steroids Reduced

Asthma Symptoms

Randomized clinical trial to compare nasal steroids given from July to September (ragweed season) in patients 12 to 50 years of age with ragweed seasonal rhinitis.

**Nasal steroids are not indicated for the treatment of asthma.**

BDP = beclomethasone dipropionate

*Chest tightness and wheezing

Clinical Links Between Allergic Rhinitis and Asthma
Antileukotriene Therapy Improves Endpoints in Allergic Rhinitis and Asthma

Multicenter, 12-week double-blind, randomized trial in patients 15 to 81 years with seasonal allergic rhinitis.
Multicenter, randomized, 12-week double-blind trial of montelukast vs. placebo in patients 15 years and older with asthma
*p<0.001 montelukast vs. placebo

Allergic Rhinitis
Definition

Rhinitis = Inflammation of the lining of the nose ... characterised by:

sneezing/rhinorrhoea
Definition

itching

nasal congestion

Allergy = Hypersensitivity response to allergens mediated by IgE antibodies
Complications

Otitis media with effusion

Infected sinusitis

Long face syndrome

Impaired quality of life
Clinical diagnosis of Atopic Eczema: (Four criteria are sufficient)

• Early onset and typical localization of skin lesions according to age
• Pruritis
• Stigmata of atopy
• Personal or family history of atopy
• IgE mediated sensitization
Stigmata of Atopy

- Sebostatis, xerosis
- Hyperlinearity of palms and soles
- Linear grooves of fingertips
- Dennie-Morgan fold (atopy fold, doubled intraorbicular fold)
- Hertoghe’s sign (hypodense lateral eyebrows)
- Short distance of scalp hair growth to eyebrows
- Periorbital shadow
- White dermatographism
- Delayed blanching after intracutaneous injection of acetylcholine
- Hypersensitivity to wool fabric
Atopic eczema may be *acute* with erythema, scaling and vesicles.
Chronic Eczema with:

- thickening,
- altered pigmentation and
- increased markings (lichenification).
Distribution of the rash typically varies with age.

- In infancy (3 months to 2 years) the cheeks, wrists and extensor aspects of the arms and legs are usually involved.
- The entire body may be affected but the nappy area is usually spared.
In young children (2 years to 12 years) flexor surfaces, the neck, wrists and ankles are generally involved.
In teenagers and young adults flexural surfaces, the face (especially periorbital region), hands and feet are frequently affected.
Asthma
HISTORY

It is characterised by symptoms of:

– cough
– wheeze
– dyspnoea

Can have only 1, 2 or all 3
ASTHMA SYMPTOMS

These symptoms may occur in diseases other than asthma

In asthma, they are classically episodic or variable (can come & go)

• often worse at night or early morning
• may be seasonal
• vary from day to day
• have specific triggers
**HISTORY**

- Past / Family History of atopy (allergy) esp. rhinitis (hay fever), conjunctivitis, eczema or urticaria may point to asthma

- History of childhood asthma important
  (but not all asthma begins in childhood - some present for the first time in adult life and these patients tend not to be allergic)
Allergy Diagnosis

• History and Examination
• Identification of the Atopic Patient
• Identification of the Causative Allergen
• Evaluation of the Patient’s Environment
• Monitoring Allergic Inflammation
Total IgE

Useful for Screening:

• Small children < 3 years old
• Parasite infestation not common
• Allergic Broncho-pulmonary Aspergillosis
• Non Aero-allergen Allergy – Food/Occupational
• Suspected Allergy but Negative Specific Allergy Tests
Identification of Causative Allergen

• Skin Prick Test
• Cap RAST – Individual / Mixed
A Plan to Address the Management of Allergic Conditions
Corticosteroids

• *Topical steroid therapy* remains the mainstay of treatment in atopic eczema.
• In general, use the least potent steroid that controls the patient's symptoms in order to minimise side effects.
• Used correctly, topical steroids will usually suffice for lesions on the trunk and limbs, and 1% hydrocortisone for the face. 
• In small children only 1% hydrocortisone or dilute strengths (e.g. 10%) of the mid-potency steroids should be used.
• Occasionally, more potent steroids are required to suppress acute exacerbations and for treatment of lichenified lesions.
Corticosteroids

• Strong steroids should be used for short periods only, but never on the face or delicate flexures because of the risk of side effects (e.g. skin atrophy, striae and steroid rosacea, hypothalamic-pituitary adrenal suppression and Cushing's syndrome due to systemic absorption).

• The choice of cream or ointment is also important. Cream bases are more acceptable to certain patients, e.g. in warm, humid conditions, though they tend to dry the skin; ointment bases, which are greasy, are more suitable as they lubricate dry skin.

• In general, oral corticosteroids should be avoided when treating atopic eczema because it is difficult to wean patients off these drugs and tolerance may develop.
Start treatment at any step depending on the level of severity.

**ALL CATEGORIES**
- Short-acting $\beta_2$ agonist as needed (reliever)
- Environmental control
- Education / self management

**Step 1: Intermittent**
- No daily preventer or controller medication needed

**Daily medication**
- Low-dose* inhaled corticosteroid
- Secondary options:
  - Cromoglicate/nedocromil
  - Sustained release theophylline
  - Leukotriene receptor antagonist

**Step 2: Mild persistent**

**Daily medication**
- Medium-dose* inhaled corticosteroid
- And if needed:
  - Long-acting inhaled $\beta_2$ agonist or sustained release theophylline
  - Consider adding leukotriene receptor antagonist

**Step 3: Moderate persistent**

**Daily medication**
- High-dose* inhaled corticosteroid
- And if needed:
  - Long-acting inhaled $\beta_2$ agonist or sustained release theophylline
  - Consider adding leukotriene receptor antagonist
- If still not controlled
- Add:
  - Prednisone long-term (preferably alternate days) – reduce to lowest dose that controls symptoms

**Step 4: Severe persistent**

**Increase treatment**
- If control is not achieved, consider step up. First review medication technique, adherence, environmental control.
- A short course of oral steroids may be required to achieve control (prednisone 1 - 2 mg/kg/day for 7 - 14 days).

**Reduce treatment**
- Review treatment every 3 - 6 months. If control is sustained, reduce treatment.
- Reduce or stop controllers before reducing dosage of inhaled steroids.
Principles of Management

Drug Delivery System

- Spacer devices (with MDI)
  - birth to 5 years
- Powder devices
  - over 5 years
- Metered dose inhaler (MDI)
  - over 8 years