Atopic dermatitis: The Allergist’s Perspective

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Objectives

• To be aware of the role of allergic triggers in atopic dermatitis

• To understand the value of allergy-focused strategies in the management of atopic dermatitis

Robert Rash

• Robert Rash is 13 months old
• His mom says he is fussy and keeps getting rashes all over
• His doctor diagnosed eczema
• He has been sent her to find out his triggers

Differential Diagnosis

• Mom says he gets a lot of skin infections and is often on antibiotics
• He even reacts to the moisturizers
• She is afraid his ‘immune system is weak’ and he has an ‘immune problem’

• Differential diagnoses to rule out?

• How can we explain mom’s concerns with our knowledge of pathophysiology?

Disclosures

I have no actual or potential conflict of interest in relation to this program

Diagnostic approach to patients with s/s of atopic dermatitis: PRACTALL
Eczema and Immunodeficiency

DD to consider:
- Hyper-IgE syndrome
- Wiskott-Aldrich syndrome
- SCID
- IPEX

Hyper- IgE syndrome
- Markedly elevated IgE
- Eczema
- Skin abscesses requiring I/D
- Pulmonary abscesses
- Sinopulmonary infections
- Coarse facies
- Spontaneous fractures
- Delayed shedding of primary teeth

Severe Combined Immunodeficency syndrome
- FTT, interstitial pneumonitis, fungal, opportunistic infections
- Lymphocyte count <1500 at birth is a red flag
- Both T and B cells involved
- Rash due to graft-versus-host disease

Wiskott- Aldrich Syndrome
Triad:
- Recurrent sinopulmonary infections
- Thrombocytopenia with low mean platelet volume
- Eczema

IPEX
- Immune dysregulation
- Polyendocrinopathy
- Enteropathy
- X-linked
- Most common: eczema
- Others: dermatitis, bullae, urticaria, alopecia universalis, and trachyonychia

You have ruled out immunodeficiency on your history and examination.

- What then, is the cause of his recurrent skin infections and need for antibiotics?
Role of *S. Aureus* and other skin colonizers

- Extensive colonization by *S. Aureus*
- Can be cultured even from normal skin
- Decreased secretion of antimicrobial peptides by keratinocytes (defect in innate immunity)
- IgE auto-antibodies trigger further IgE and T cell-mediated responses

Defects in innate immunity

- *S. Aureus* exotoxins act as **SUPER**antigens

Identification of triggers

- Mom saw in the ‘internet’ that “allergies” cause eczema
- What can she do to identify and eliminate triggers?

You tell mom: "You are dead right… Let me explain TH1/TH2 cytokine activation"....

Eczema triggers

- Climactic factors: Temperature, Humidity
- Irritants: detergents, wool, perspiration
- Emotional stress
- Infections
- Allergens: Food allergens, Aeroallergens
- Others...
Relative significance of complicating or exacerbating factors in patients with AD from infancy to adulthood: PRACTALL

Food Allergy and AD

- Children:
  - Moderate - Severe AD (33%) have food allergy
  - Increasing severity of AD ~ increasing risk of food allergy
  - Food-allergy related AD usually starts < 1 year of age

Adults:
  - Low incidence (< 2%)

Foods responsible (~ 90% of cases):
  - Milk, egg, soy, wheat (usually outgrown)
  - Peanut, fish (usually persistent)

Role of Aeroallergens

- Allergen specific IgE antibodies and allergen specific T cells have been demonstrated
- Both respiratory route and direct contact with inhalant allergens may be important in the induction and exacerbation of AD
- Environmental control measures have resulted in clinical improvement of AD

Allergens in AD

- Food allergy more likely in younger kids
- Older ones (> 5 years) likely to have environmental aeroallergen triggers
  - Perennial allergens: dust mites, animal dander, molds
  - Seasonal exacerbations do occur in some patients; less common

Testing for allergies

- Mom wants to know if allergy testing can be done on him
- She has been told he is too small for allergy testing
- What would you like to tell her?
Types of Allergy Tests

• Skin prick test
  – Takes only 15 minutes
  – Can be done at all ages
  – Results can be visualized by patient - "seeing is believing"
  – Cost-effective

• Blood specific IgE identification (ImmunoCAP RAST test)
  – Can be done even if on antihistamines
  – Useful for monitoring levels - 'outgrowing'
  – Needs careful interpretation

Allergy Skin Tests

Types of Allergy Tests

• Skin prick test
  – Takes only 15 minutes
  – Can be done at all ages
  – Results can be visualized by patient - "seeing is believing"
  – Cost-effective

• Blood specific IgE identification (ImmunoCAP RAST test)
  – Can be done even if on antihistamines or dermatographic
  – Single “poke”
  – Needs careful interpretation

Beware the Curse of Dimensionality

• Exponential increase in volume when adding extra dimensions to a mathematical space…

• In other words, the more tests we order, the more confused we will become….😊

=Multiple allergen panels can be misleading and result in incorrect treatment

Pre-test Probability

Any random high-school athlete

Probability of being an NBA draft pick???
Estimated Probability of Competing in Athletics Beyond the High School Interscholastic Level
http://www.ncaa.org/wps/wcm/connect/public/ncaa/issues/recruiting/probability+of+going+pro

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How does this change the Pre-test Probability?

Allergy testing for Foods

- Food diary helpful in identification
- Extremely helpful in RULING OUT food allergy (if negative > 95% correct)
- High FALSE positive rate- > 50%
- Gold standard is double blind placebo controlled food challenge

Skin tests for food allergy

Skin prick wheal > 8 mm for milk, egg and peanut are >95% predictive of clinical reactivity

Clinical Utility of Food specific IgE: “Different strokes for different folks” 😊

- Peanut
  - IgE > 14: 95% PPV
  - IgE > 57: 100% PPV
- Cow’s milk
  - IgE > 15: 95% PPV (age 4; atopic)
  - IgE > 5: 95% PPV (infants)
- Egg
  - IgE > 7: 95% PPV (age 4; atopic)
  - IgE > 2: 95% PPV (infants)

Natural history of food allergies

- Majority of milk, wheat, egg and soy allergy resolve by school age
  (85% of milk and soy allergy and 66% of egg allergy)
- Peanut allergy- 20% of children outgrow
- 9% tree nuts allergy
Management of triggers

- Robert had allergies to dust mites and egg on testing
- What are your recommendations on elimination and avoidance of triggers?

Management of aeroallergens

Pollens
- Oak
- Mulberry
- Birch
- Ragweed
- Tree pollen= spring
- Grass pollen=summer
- Weed pollen= fall

Avoidance (Pollen)
Indoors:
- Air-conditioning (central) during seasons
- Filtered Air (HEPA filter)
- Caution-Attic Fan
Outdoors:
- Wear mask when working in garden, cutting grass, raking leaves
- Careful of vectors, (e.g. pets outdoor to indoors, drying laundry outdoors)
- Contact urticaria with grass etc- wear long cool protective clothing
- Shower and change clothes after coming indoors / before bedtime

Avoidance (Pets)
- Avoidance of pet (? get rid of pet)
- Keep in kennel (outside home)
- Bathe/wash regularly
- Pick non-sensitive, non-furry pet
- Air filtration
- Treat reservoir (e.g. carpeting, furniture, bedding)

Avoidance (Mites)
- Low humidity <50% (ideally 30-50%)
- Low temperature
- Dust mite-proof covers
- Wash bedding weekly in hot water
- Remove carpet in bedroom
- Vacuum (HEPA Filter Type)
Avoidance (mold)
- Dehumidifier (keep moisture content <50%; ideally 30-50%)
- Dry up damp areas—cellar/basement
- Fix leaks, if any
- Use antifungal solution
- Caution regarding reservoirs (e.g. humidifiers)
- Avoid warm, dark, humid places
- Organic matter breeds mold

Avoidance (Roach)
- Perennial symptoms
- Abatement procedures
- Exterminator
- Take trash out
- Keep water sources covered

Management of food allergies
- Food diary, elimination, look for improvement, reintroduction and look for worsening
- Avoidance, avoidance.... strict avoidance!
- Reading food labels; beware of cross-contamination
- Referral to Food Allergy and Anaphylaxis Network
  www.foodallergy.org
- Food emergency plan if indicated (benadryl for minor reactions and epinephrine for major reactions)
- F/u with allergist to determine 'outgrowing'

Atopic diathesis and complications
- Mom wants to know if he is at increased risk for ‘allergies and asthma’
- What would you tell her?

Relationship to Atopy: Atopic March
- 50% of patients with AD develop asthma
- 50-75% develop allergic rhinitis

Primary and Secondary prevention
- Before leaving, mom asked how she could prevent eczema and allergies in her next child
- What would you like to tell her?
Food Allergy Prevention: AAP 2008

• No E/o protective effect of dietary maternal restrictions during pregnancy/lactation
• For infants at high risk of atopy, exclusive breast-feeding for at least 4 months decreases cumulative incidence of AD in first 2 years
• Exclusive breast-feeding for at least 3 months protects against wheezing in early life but not beyond 6 years

Pediatrics 2008; 121; 183-191

Food Allergy Prevention: AAP 2008

• In high risk infants, extensively hydrolyzed formula protects against development of AD in early childhood
• No convincing E/o for the use of soy formula in allergy prevention
• No E/o that delayed introduction of solid food beyond 4-6 months has protective effect
• For infants older than 4-6 months, there is insufficient data to support a protective effect of dietary intervention

Pediatrics 2008; 121; 183-191

Summary

Natural history has 3 phases:
1) Non-atopic form in early infancy; sensitization has not occurred
2) 60-80% pts-genetic factors induce IgE sensitization to foods or aeroallergens
3) Scratching damages skin cells; releases autoantigens inducing IgE autoantibodies and perpetuating cycle of inflammation
4) The Allergist can help with identification and management of allergic triggers, and contribute to the evaluation when the diagnosis is in doubt

Thank you for your attention! 😊

Genetic and risk factors for AD

• Mom recalls that dad has very dry skin on his hands which crack and peel in the winter
• She wants to know if it could run in families
• What would you like to tell her?

Genetic and risk factors for AD

• Parental atopy, in particular AD, is significantly associated with the manifestation and severity of AD in kids
• Higher in monzygotic twins (77%) than dzygotic (15%)
• Some genes have been implicated [3q21 (European study of 200 families); 6 other regions: 1q21, 17q25, 20p, 16q, 3p26, 5q31 (=regulation of IgE synthesis); Highest linkage: 1q21-epidermal differentiation complex]
• Filaggrin gene (FLG) on 1q21, key protein in epidermal differentiation, (also in ichthyosis vulgaris), Japanese patients and 30% in European patients, occur in early-onset atopic dermatitis and indicate propensity towards asthma
Decreased Filagrin expression in the epidermis
TH2 cytokines can modulate levels of Filagrin
Found only in few people

Non-genetic risk factors for AD

- Breast-feeding for 4 months reduces infantile AD but effect is probably transient and disappears by 3 yrs
- Passive tobacco exposure inconclusive
- Sensitivity to cow’s milk and hen’s egg
- Aeroallergen sensitization
- Increased risk in migrant populations in developed countries, in smaller families and among higher social class