Taming Atopic Dermatitis: An Allergy/Immunology Perspective

Thomas A. Lupoli, D.O.
May 1st, 2016
Disclosures & Conflicts of Interest

• Allergy & Asthma Specialists of North Florida

• President-elect -- Florida Allergy, Asthma & Immunology Society

• Section Chief of Allergy & Immunology -- Baptist Medical center Jacksonville

• No financial conflicts
Objectives

• Discuss recent updates on immunopathology and genetics of AD

• Review key diagnostic features of AD

• Discuss practical strategies to improve QOL and sleep for patient with AD
Atopic March

The Allergic March

Eczema

Food Allergy

Rhinitis

Asthma

Birth, 3 months, 1 year, 2 years, 3 years, 7 years, 15 years

Typical Age of Onset

www.allergyuk.org/
AD

• Most frequently affects children (up to 25%)*
  – can persist into adulthood (3%, 5-7% Asia)**

• Variable clinical presentation
  – Dry skin and severe pruritus
  – Scale, fissuring and oozing
  – Hypertrophic changes
  – Pigment changes

**Thappa, D.M. Indian J Dermatol Venereol Leprol. 2013; 79: 145–147
Atopic dermatitis: Infantile

Confluent erythema, microvesiculation, papules, crust, and scale on the face of an infant.

Flexural atopic dermatitis

Typical appearance of atopic dermatitis in flexural areas of the legs.

Courtesy of James C Shaw, MD.
Atopic dermatitis

Hyperpigmented, slightly scaly patches and lichenified plaques are present in the popliteal fossae of this patient with atopic dermatitis.

Lichenified, hyperpigmented plaque in the elbow flexure of a 35-year-old woman with atopic dermatitis.
Classic Distribution

Infantile Eczema

Childhood Eczema

Typical Sites of Eczema:
- Face
- Neck
- Elbows
- Wrists
- Groin
- Knees
- Ankles
AD: Chicken or the egg?
Epidermal Barrier

• 1st line of defense between the body and the environment
  – irritants, allergens, microbes from entering the body and prevents excessive water loss.

• Primarily located in the stratum corneum
  – vertical stacks of anucleate corneocytes packed with keratin filaments embedded in a matrix of filaggrin breakdown products

• AD= dysfunctional skin barrier
  – Even nonlesional skin in AD harbors defective barrier
Filaggrin (FLG)

- Filament-aggregating protein
- Key protein involved in cornification and hydration
- *Epidermal differentiation complex locus* on chromosome 1q21
  - cluster of more than 60 genes encoding cornified envelope
Loss of Function FLG mutations

• Up to 50% AD cases\(^1\)
  – 9% of non-AD population

• Deficiency →
  – increased pH (altered microbial colonization)
  – impaired skin integrity and hydration
  – impaired protease activity antimicrobial peptide function (altered microbiome)

• Carriers have greatly increased risk of atopic dermatitis, contact allergy, asthma, allergic rhinitis, and peanut allergy\(^2\)

Filaggrin and the Atopy

Healthy skin

Filaggrin-deficient skin

Impaired skin barrier
Increased skin-surface pH
Increased allergen priming
Decreased hydration of stratum corneum
Decreased resistance to staphylococcus

Allergen

Filaggrin mutation

Odds ratio, 5.3
Peanut allergy

Odds ratio, 1.5

Odds ratio, 3.1
Atopic dermatitis

Asthma (overall risk)

Peanuts

Healthy skin

Filaggrin-deficient skin

Asthma (overall risk)

N Engl J Med 365;14 NEJM.org October 6, 2011
Altered Microbiome

• Altered microbiome $\rightarrow$ barrier defects
• AD= altered innate and adaptive immunity
• 90% AD colonized/infected with S. aureus
• Th2 cytokines (IL-4, IL-13) have permissive effect on microbial invasion
  – cell-mediated immunity and antimicrobial peptides

Czarnowicki. The Journal of Allergy and Clinical Immunology: In Practice, Volume 2, Issue 4, 371 - 379
Altered Microbiome

• S. aureus “superantigens” → ↑ IL-31 → ↓ FLG expression and ↑ proinflammatory cytokines
  – S. aureus maintains chronic inflammation in AD

• IL-17 upregulates antimicrobial β-defensins and antiviral capacity
  – Reduced IL-7 in AD skin → ? Skin infections

Czarnowicki. The Journal of Allergy and Clinical Immunology: In Practice, Volume 2, Issue 4, 371 - 379
Altered Microbiome

• Topical emollients and topical anti-inflammatory agents (calineurin inhibitors and topical steroids) reduce bacterial load and improve skin barrier function*

*Czarnowicki. JACI: In Practice, Volume 2, Issue 4, 371 - 379
Skin Hydration

• Moisturizer application after water soaks for 20 minutes:
  – improves barrier function and moisture retention
  – powerful itch relief
  – corticosteroid-sparing effect

• Topical emollients- little comparative data

Lio, Peter A. et al. The Journal of Allergy and Clinical Immunology: In Practice, Volume 2, Issue 4, 361 - 369
Topical Calineurin Inhibitors

• Used when topical steroids may not be appropriate
  – No skin atrophy (face and eyelids)
• Tacrolimus and pimecrolimus inhibit T cells, dendritic cells and mast cells
  – Effect similar to midpotency steroids
• Abundant safety data for AD ages ≥ 2 years
• Local burning affect most common side effect
Safety of Topical Calcineurin Inhibitors

- What about the 2006 FDA black box warning?
  - 2007 case controlled study of 300,000 AD patients on TCI’s found NO increased risk of lymphoma

Lio, Peter A. et al. The Journal of Allergy and Clinical Immunology: In Practice, Volume 2, Issue 4, 361-369
Antihistamines

• Review of 16 controlled studies found little effectiveness of oral antihistamines for AD itch
  – histamine only one of several mediators that can induce itch

• May helpd in controlling trigger events in those with demonstrated environmental allergies

• Beneficial role of sedation

Vitamin D

• AD often worse in winter months lead to trial of Vit-D supplementation in winter
  – Significant improvement in children supplemented with daily Vit-D (80% with improvement vs 17% of control group)

• Beneficial effect of winter-time supplementation seems to greatly outweigh negligible risks

Treatment of Infections

• Staph aureus - significant role in AD
  – Colonizer $\rightarrow$ drives inflammation $\rightarrow$ infection

• Common anti-staphylococcal antibiotics (oral/topical) not helpful in non-infected AD$^1$
  – Poor study quality, small sample size

Treatment of infections

- Oral abx are appropriate for frank infection
Use of Disinfectants

- Dilute sodium hypochlorite bath soaks significantly decrease AD severity, may reduce need for systemic abx
  - \( \frac{1}{4} - \frac{1}{2} \text{ cup household bleach per full bathtub (40 gallon)} \times 10 \text{ min twice or more per week} \)

“Wet Wraps”

• For severe, difficult to control cases
• Extremely powerful therapy
• Soaking skin, applying topical steroid to affected lesions, covered by dampened layer of gauze/clothing, covered by dry layer
DYI Wet Wraps
Commercially Available
“Wet Wraps”

• Benefits:
  – Skin barrier recovery
  – Increases effectiveness of topical steroids
  – Protects skin from scratching
  – May allow for more rapid healing
  – Safe up to 14 days

• (maceration possible w/ prolonged use

Trigger Elimination

• Irritants
  – Soaps, chemicals, certain fabric

• Environmental allergens
  – Dust mites’ proteolytic activity damages skin barrier * (independent of allergy)

• Foods
  – 1/3 AD patients have allergic sensitization to foods
  – Improved control with restriction of foods with positive IgE but no benefit unless has + IgE

Food Allergy Testing

- Recommended for children <5 years old with persistent AD despite optimal treatment or hx of immediate reaction to a food.

Improving QOL

• **Sleep Disruption**
  – Daytime somnolence, lack of concentration, behavioral/mood problems

• Improved with:
  – effective anti-inflammatory tx
    • Wet wraps at bedtime
  – Sleep hygiene
    • Consistent, relaxing bedtime routine

  – Sedating H1 may be helpful on short-term basis*

Kelsay. JACI, 2006; 118:198-201
Pruritis and Scratching

- **Breaking the itch-scratch cycle**
  - Non-blaming approach
    - Focus on what pts can do when itchy (soaks, moisturizers)
  - Optimize topical emollient plan
  - Cover skin at night
    - long pajamas, cotton gloves
  - Distraction
    - handheld electronics, knitting
  - Competing sensory sensations
  - Managing stress
    - cognitive-behavior therapy
ECZEMA ACTION PLAN

NAME: ___________________________ Date: ___ / ___ / ___

<table>
<thead>
<tr>
<th>When SEVERE (itchy, red, oozing)</th>
<th>When BETTER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AM</strong></td>
<td><strong>AM</strong></td>
</tr>
<tr>
<td>1. Apply topical medication to eczema areas</td>
<td>1. Apply moisturizer liberally</td>
</tr>
<tr>
<td>2. Apply moisturizer liberally</td>
<td>2. Take Vitamin D supplement (1,000 IU/day)</td>
</tr>
<tr>
<td>3. Apply antibiotic ointment to open sores</td>
<td>4. Take Vitamin D supplement (1,000 IU/day)</td>
</tr>
<tr>
<td>4. Take Vitamin D supplement (1,000 IU/day)</td>
<td></td>
</tr>
<tr>
<td><strong>DURING THE DAY</strong></td>
<td><strong>DURING THE DAY</strong></td>
</tr>
<tr>
<td>1. Apply moisturizer liberally</td>
<td>1. Apply moisturizer liberally</td>
</tr>
<tr>
<td>2. Apply antibiotic ointment to open sores</td>
<td></td>
</tr>
<tr>
<td><strong>PM</strong></td>
<td><strong>PM</strong></td>
</tr>
<tr>
<td>1. Soak in dilute bleach bath for 10 minutes (1/4-1/2 cup of bleach per bathtub FULL of water)</td>
<td>1. Soak in dilute bleach bath for 10 minutes twice weekly (1/4-1/2 cup of bleach per bathtub FULL of water)</td>
</tr>
<tr>
<td>2. Pat dry but while still damp do the next steps</td>
<td>2. Pat dry but while still damp, apply moisturizers liberally.</td>
</tr>
<tr>
<td>3. Apply topical medication to eczema areas</td>
<td>3. <strong>OPTIONAL</strong>: apply low dose topical steroid to eczema prone areas twice weekly to maintain control.</td>
</tr>
<tr>
<td>4. Apply moisturizer liberally</td>
<td>5.</td>
</tr>
<tr>
<td><em>Repeat steps 1-4 for several nights until better</em></td>
<td>6. Wet wraps to affected areas (see below)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Moisturizer(s):** ☐ Vanicream cream (great any time of day) ☐ Petroleum Jelly (best used after bathing)

Other: ___________________________

2. **Topical Medication(s):** __________________________________________

3. **Topical Antibiotic ointment:** ☐ Mupirocin ointment ☐ Other: ___________________________

4. **Wet wrap instructions:** Apply topical medication followed by moisturizer to eczema areas, then cover with a dampened cotton garment (gauze, clean sock or t-shirt). The dampened garment is then covered with a dry garment. You may use these dressings overnight or change them every eight hours during the day.

Additional notes: __________________________________________

__________________________________________
Questions?