What’s New in Eczema Management: Practice Pearls for the Family Physician

Lucia Z. Diaz, MD
Assistant Professor, Department of Internal Medicine and Pediatrics
Dell Medical School, University of Texas at Austin
Austin, Texas

Educational Objectives
By completing this educational activity, the participant should be better able to:
1. Recognize the clinical features and characteristic age distribution patterns of Atopic Dermatitis.
2. Describe the role of skin barrier dysfunction, immune dysregulation, and environmental factors in the pathogenesis of Atopic Dermatitis.
3. Individualize Atopic Dermatitis management regimens according to age, location, disease severity, response to treatment, and quality of life concerns.
4. Implement educational strategies to communicate the safe and appropriate use of skin-directed therapies to individuals with mild to moderate Atopic Dermatitis.

Speaker Disclosure
Dr. Diaz has disclosed that she has no actual or potential conflict of interest in relation to this topic.

Supporter Disclosure
This CME activity is supported by an educational grant from Pfizer. It has been planned and produced by the North Carolina Academy of Family Physicians and Spire Learning with TAFP strictly as an accredited continuing medical education activity.
Off-Label Statement

The faculty will discuss non–FDA-approved or investigational agents for the treatment of atopic dermatitis (eczema), including apremilast, anti-IL-31, fezakinumab, lebrikizumab, OPA-154062, roflumilast, SB011, tofacitinib ointment, tralokinumab, and ustekinumab.

Participants should appraise the information presented critically and are encouraged to consult appropriate resources for any product or device mentioned in this activity.

Learning Objectives

At the conclusion of this live activity, family physicians should be better able to:

- Recognize the clinical features and characteristic age distribution patterns of AD
- Describe the role of skin barrier dysfunction, immune dysregulation, and environmental factors in the pathogenesis of AD
- Individualize AD management regimens according to age, location, disease severity, response to treatment, and QoL concerns
- Educate patients and families about the safe and appropriate use of skin-directed therapies for the treatment of AD

AD, atopic dermatitis; QoL, quality of life.

Worldwide Prevalence of AD

> 50 million Americans suffer from allergic diseases1


Lifetime prevalence of AD is 10%-20% in children2-4

1%-3% in adults2

Can persist into adulthood 10%-30%4

First year

Onset typically within 60% Age 5

85% Can persist into adulthood 10%-30%

Burden of Disease

An average of 9 flares per year, each lasting 15 days1

Itching2

87% experience itching daily

Itching lasts ≥ 18 hours in ~42% of patients

Poor quality of sleep

Sleep disturbances 3 or more days a week, affecting the entire family’s sleep8

Children with moderate disease wake up an average of 36 times per night, negatively impacting mental health and growth rates6

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4. Dogra L. Paper presented at: 42nd Annual Society for Pediatric Dermatology Meeting; July 14-17, 2016; Minneapolis, MN.

Mental health comorbidities5-3

- Anxiety
- Depression
- Poor self-image
- Attention-deficit/hyperactivity disorder (ADHD)
- Behavioral or conduct problems

Of note, in the GINI-plus birth cohort study, even children whose eczema appeared to resolve in the first 1-2 years of life were shown to have persistent emotional and behavioral difficulties at 10 years of age4

Diagnostic Features of AD

- Pruritus (itching)
- Chronic or relapsing dermatitis that exhibits:
  - Typical lesion morphology
  - Age-specific distribution
- Other important features:
  - Early age of onset
  - Personal or family history of atopy
  - Xerosis

What Does AD Look Like?

- Erythematous papules and plaques
- Excoriations
- Xerosis
- Erosions/crusting
- Lichenification
- Dyspigmentation
- Generally spares axillae and groin

Clinical Features in Darker Skin Types

- Erythema may be difficult to see
- Follicular accentuation
- Hypo- or hyperpigmentation
- Grayish-white skin discoloration (“ashy skin”)

Lesion Distribution Varies With Age

Differential Diagnoses (All Ages)

- Seborrheic dermatitis
- Contact dermatitis (allergic and irritant)
- Scabies
- Psoriasis
- Ichthyosis vulgaris
- Tinea corporis
- Keratosis pilaris
- Nutritional deficiencies in young children
- Immune disorders/immunodeficiency

Differential Diagnoses: Considerations in Adolescents and Adults

- Cutaneous T-cell lymphoma (mycosis fungoides or Sézary syndrome)
- HIV-associated dermatoses
- Dermatomyositis
- Graft-versus-host disease
- Lupus erythematosus
- Pemphigus foliaceus
- Drug eruptions
Seborrheic Dermatitis (Infant)

Photos courtesy of Anthony J. Mancini, MD

Differential Dx

Scabies

Photos courtesy of Anthony J. Mancini, MD

Differential Dx

Psoriasis

Photos courtesy of Anthony J. Mancini, MD

Differential Dx

Ichthyosis Vulgaris

Photos courtesy of Anthony J. Mancini, MD

Differential Dx

Tinea Corporis

Photos courtesy of Anthony J. Mancini, MD

Differential Dx

Keratosis Pilaris

Photos courtesy of Anthony J. Mancini, MD

Differential Dx
Impetigo

Differential Dx

AD Pathogenesis Basics

Epidermal Barrier Dysfunction
- Filaggrin gene mutation (in a subset)
- ↑ Skin pH
- ↓ Ceramides
- ↑ TEWL
- ↑ S. aureus colonization
- ↑ Allergen sensitization

Immune Dysregulation
- Decreased filaggrin protein levels
- Th2 cell activation
- ↑ IL-4, IL-5, IL-13 (also IL-17, IL-22, IL-31, others)
- ↑ Serum IgE
- ↑ PDE-4 activation
- ↑ Allergen sensitization

Aggravating Factors
- Sweat
- Heat
- Seasonal change
- Infection
- Stress
- Harsh soaps, detergents, wool
- Allergens

Immune Dysregulation

Stepwise Management of AD

Treatment Goals

Water: Irritant or Therapeutic?

Water irritates skin IF:
- Skin is frequently wet, without immediate application of effective moisturizer
- Moisture evaporates, causing skin barrier to become dry, irritated

Water hydrates skin IF:
- Effective moisturizer is applied and hydration is retained, keeping skin barrier intact and flexible
Skin Barrier Dysfunction Is Predictive of Future AD

- Cork Babies After Scope Study1,2
  - 1903 infants
  - TEWL measured at day 2, 2/6 months
  - AD scored at 6/12 months
  - Day 2 TEWL, highly predictive of AD at 12 months
  - 2-month TEWL – highly predictive of AD

- Infants in the Babies After Scope Study1,3
  - Day 2 TEWL predictive of food allergy at 2 years


Is Early Emolliation Effective?

<table>
<thead>
<tr>
<th>RCT</th>
<th>Simpson EL, et al1</th>
<th>Horimukai K, et al2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of neonates, high AD risk</td>
<td>124</td>
<td>150</td>
</tr>
<tr>
<td>Intervention</td>
<td>Full-body emollient daily (starting 3 weeks of age) vs no emollient</td>
<td>Moisturizer applied daily for first 32 weeks of life in 68 neonates</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Cumulative AD incidence at 6 months</td>
<td>Cumulative AD/eczema incidence at week 32</td>
</tr>
<tr>
<td>Results</td>
<td>50% relative risk reduction in AD (emollient arm)</td>
<td>No effect on allergic sensitization</td>
</tr>
<tr>
<td></td>
<td>32% fewer neonates with AD in emollient arm</td>
<td></td>
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</tbody>
</table>

Address barrier dysfunction in AD with good dry skin care:

- Bathe daily (short bath or shower)
- Apply emollient/barrier repair product immediately after bathing
- Apply emollient after topical medications
- May play a role in prevention as well


“Pathogenesis-Based Therapy” With Emollients/Barrier Repair Agents

- Add to the skin “what is missing”
- Restore the barrier, maintain hydration
  - Ceramide-based products:
    - Aveeno® Eczema Therapy
    - CeraVe® cream or lotion
    - EpiCeram® (prescription only)
    - Mario Badescu® A.H.A & Ceramide Moisturizer
  - Filaggrin-based products:
    - AFAs™ Moisturizer
    - Cetaphil® RestoraDerm
    - Dr.G Filagrin™ Barrier cream or balm
    - pH Drop Filaggrin product line

Topical Corticosteroids (TCSs): Benefits and Limitations

- Benefits:
  - Highly effective at treating inflammation
  - Rapid onset of action
  - Multiple potency and delivery vehicles
  - Varying potency frequently required per patient

- Limitations:
  - Product-specific age limits (although often used off-label)
  - Potential for local and systemic side effects (but rare when used appropriately):
    - Local: Striae, telangiectasias, skin atrophy, dyspigmentation, periorificial dermatitis, acne rosacea
    - Systemic: HPA axis suppression
    - Periorbital administration: Cataracts, glaucoma

HPA, hypothalamic-pituitary-adrenal.

Best Practices When Using TCSs

- Examples of location-appropriate corticosteroids:
  - Face/fold areas: Low potency (e.g., hydrocortisone 2.5%, desonide, alclometasone)
  - Transepidermal: Mid potency (e.g., flucinolone, triamcinolone)
  - Severe flares (trunk/extremities): High potency (e.g., mometasone, triamcinolone)
- Apply twice daily to actively inflamed areas
- Oral corticosteroids (e.g., prednisone) rarely indicated in the treatment of AD; risks of rebound, side effects

Topical Calcineurin Inhibitors (TCIs) – Benefits

- Extensive clinical trials experience
- Nonsteroid alternative
- Good efficacy for mild, moderate, and severe AD
- Used for acute AD and maintenance therapy
- Little systemic absorption
- Can be applied to face, fold areas, periorbital region, genitals


C, cream; F, foam; G, gel; L, lotion; Oi, oil; O, ointment; S, solution.
**TCIs: Limitations and Potential AEs**

- Second-line agents\(^1,2\)
- Not approved for use in children < 2 years of age\(^1,2\)
- Limited range of vehicles available vs TCS
- Stinging and burning in a subset of patients\(^1,2\)
- FDA-mandated boxed warning and medication guide

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**Available TCIs**

<table>
<thead>
<tr>
<th>TCI</th>
<th>Vehicle</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pimecrolimus</td>
<td>Cream</td>
<td>Approved for mild to moderate AD (2 years and older)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Ointment</td>
<td>Approved for moderate to severe AD (0.03%: 2 years and older; 0.1%: 15 years and older)</td>
</tr>
</tbody>
</table>

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**Crisaborole 2% Ointment**

- A nonsteroidal, boron-based PDE-4 inhibitor\(^1,2\)
- Indicated for mild to moderate AD in adults and children ≥ 2 years\(^3\)
- Benefits\(^3,4\)
  - Reduces inflammation and itching
  - Maintains skin barrier
  - Low molecular weight enhances skin penetration
  - Limited systemic exposure
  - Favorable safety profile over 48-week study\(^3\)
- Limitations
  - Stinging and burning at application site

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**Dupilumab**

- Human monoclonal IgG antibody targets IL-4Rα; blocks IL-4 and IL-13 signaling\(^1\)
- Indicated for patients ≥ 12 years with moderate-to-severe AD; subQ injection every 2 weeks\(^1\)
- Phase III trials: > 33% of patients achieved significant improvement in AD severity\(^2\)
- Topical therapies can be combined with dupilumab for additional benefit in adults with refractory AD\(^3\)
- Associated with potentially serious side effects, requires close monitoring\(^1,4\)
  - Conjunctivitis
  - Injection-site reactions

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**Emerging Treatments for AD**

- Topical therapies
  - PDE-4 inhibitors (e.g., roflumilast,\(^1\) OPA-154062)
  - Janus kinase inhibitors: tofacitinib ointment\(^3\)
- Systemic therapies
  - Apremilast: an oral PDE-4 inhibitor\(^5\)
  - Anti-IL-31\(^6\)
  - Ustekinumab, lebrikizumab, tralokinumab, fezakinumab (IL inhibitors)\(^7\)
- Numerous other potential targets in development\(^7\)

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**Dupilumab: Pediatric Studies Underway...**

**ClinicalTrials.gov**

- [U.S. National Library of Medicine](https://clinicaltrials.gov)
- [ClinicalTrials.gov](https://clinicaltrials.gov)
**Wet Wraps**

- Wet wraps prevent scratching and promote moisture retention
- Use with emollients or a TCS
- Taper from TCS to Vaseline
- Sporadically or frequently (during acute flares)
- Extensive or localized
- Absorption toxicity risk is minimal


**Colonization With Staphylococcus aureus**

- Carriage common in nares/subungual areas
- Worsens disease status
- Renders disease harder to control
- Patients do not have to be infected to be adversely impacted by *S. aureus*
- Skin that is colonized: A trigger for disease flares


**Bleach Therapy**

- Sodium hypochlorite has disinfectant and antimicrobial properties
- Bleach baths/intranasal mupirocin shown to:
  - Improve disease severity in patients with moderate to severe AD
  - Minimize antibiotic use
- When is bleach therapy indicated?
  - Moderate to severe AD
  - Frequent infection/antibiotic use


**Bleach Therapy Delivery Options**

- Clorox bleach – 6% sodium hypochlorite (newer formulas 8.25%)
  - 1/8-1/2 cup bleach in full tub; soak 10-15 min, TIW
- CLn wash – OTC cleanser with sodium hypochlorite (0.006%); good option for older kids and teens (www.clnwash.com)
- Levicyn – Rx antipruritic gel and spray gel with hypochlorous acid/water
  - Broad antimicrobial activity
  - Indicated for burning and itching of dermatoses, pain of burns

Rx, prescription; TIW, three times a week.

**Oral Antihistamines in AD**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Vehicle</th>
<th>Properties</th>
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<tbody>
<tr>
<td>Diphenhydramine*</td>
<td>Oral</td>
<td>Sedating antihistamine</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>Oral</td>
<td>Sedating antihistamine</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Oral</td>
<td>Sedating antihistamine</td>
</tr>
<tr>
<td>Cetirizine*</td>
<td>Oral</td>
<td>Nonsedating antihistamine</td>
</tr>
</tbody>
</table>

- Some controversy, but many use them, especially for sleep
- Hydroxyzine most commonly used sedating antihistamine at bedtime

*Available over-the-counter.

**Maintenance Therapies for AD**

- Liberal and frequent application of moisturizers to reduce dryness and itching, prevent flares
- Warm baths/showers (< 5 min) using non-soap cleansers or mild soaps
- Antiseptic measures
  - Dilute bleach baths, if indicated
  - Trigger avoidance, when feasible
- Intermittent application of TCSs or TCIs to prevent flares ("hot zones")

Customizing Patient Treatment Plans

- Written treatment plan increases likelihood of adherence
- Tailor treatment plan based on:
  - Age
  - Locations of disease
  - Previous treatment success/failures
  - Patient/caregiver preferences
- Identify/eliminate triggers, if possible
- Address quality-of-life issues (e.g., sleep disruption, co-sleeping)
- Provide basic skin care instructions (e.g., bathing, emollients)
  - Moisturize frequently throughout the day
  - Topical medications do not take the place of moisturizers
  - Continue maintenance therapies, even if skin “appears” healthy

When to Test for Food Allergies

- Food allergy testing should be considered when:
  - Moderate to severe AD is persistent despite optimal management
  - Reliable history of anaphylaxis or immediate reaction after ingestion of a specific food

Specialist Referral

- Early referral in the case of severe, persistent disease
- Otherwise, refer if the patient is not responding to conservative measures and standard treatment modalities

Case Presentation

- 5-month-old female who developed an eczematous rash on her cheeks at about 3 months of age, and more recently has had involvement of her neck and outer aspects of upper extremities. She has not had any open or weeping lesions.
- Her pediatrician prescribed hydrocortisone 2.5% cream, but her parents are concerned about using a topical steroid. They are wondering about allergic triggers.

Photo courtesy of Anthony J. Mancini, MD

Case Presentation

- 12-year-old female with onset of eczema in early childhood. Over the years, it has involved her head and neck, trunk, and flexural aspects of her upper and lower extremities. She has had infrequent superficial skin infections.
- On exam: Moderate patches of eczema involving face (including eyelids), neck, and flexural aspects of all 4 extremities with lichenification. Several areas with crusting.
- Parents want to discuss TCI options

Photo courtesy of Anthony J. Mancini, MD

Mild Atopic Dermatitis

- Basic skin care (hydration and moisturizer)
- Avoid irritants (and known allergens)
- TCSs
  - Use lower strength in thin-skin areas (face, axillae, genital areas) and for mild eczema anywhere on the body
  - Caution with TCSs in periorbital locations
- TCIs
  - Pimecrolimus indicated for ages 2 years and older for mild to moderate AD
  - Tacrolimus ointment indicated for ages 2 years and older for moderate to severe AD (0.03% for ages 2-15 years; 0.1% for > 15 years)
- Discuss potential indications (especially around eyes), boxed warning
- Crisaborole ointment indicated for mild to moderate AD in ages 2 years and older
- Sedating antihistamine may help with itch and sleep disruption
- Nonsedating antihistamine may help in patients with allergic triggers, better for daytime (school)
- Dilute bleach baths
  - 1/8-1/2 cup of bleach in a full bathtub (about 40 gallons) of water
  - Soak 5 to 10 minutes 2-3 times weekly
- Oral antibiotic for bacterial infection (usually MRSA; consider MSSA if history or suggestive clinical findings)

Moderate Atopic Dermatitis

- Basic skin care (hydration and moisturizer)
- Avoid irritants (and known allergens)
- TCSs
  - Use lower strength in thin-skin areas (face, axillae, genital areas)
  - Use mid-potency for trunk and extremities
  - Caution with TCSs in periorbital locations
- TCIs
  - Pimecrolimus indicated for ages 2 years and older for mild to moderate AD
  - Tacrolimus ointment indicated for ages 2 years and older for moderate to severe AD (0.03% for ages 2-15 years; 0.1% for > 15 years)
- Discourage in periorbital locations
- Crisaborole ointment indicated for mild to moderate AD in ages 2 years and older
- Sedating antihistamine for sleep disruption/ocular pruritus
- Non-sedating antihistamine may help in patients with allergic triggers, better for daytime (school)
- Dilute bleach baths
  - 1/8-1/2 cup of bleach in a full bathtub (about 40 gallons) of water
  - Soak 5-10 minutes 2-3 times weekly
- Oral antibiotic for bacterial infection (usually MSSA; consider MRSA if history or suggestive clinical findings)

MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus.
Patient/Parent Education

- Chronic disease, prone to flares and remissions
- Importance of dry skin care and maintenance use of emollients/barrier-repair agents
- Treat acute flares aggressively
- Recognize/treat infection, and attempt to prevent (bleach) when indicated
- Optimize sleep, consider antihistamines for this and control of pruritus
- Escalate therapy if response suboptimal (and good adherence)

Take-Home Messages

- Most patients with mild to moderate AD can be managed by the primary care physician
- AD impacts the entire family’s QoL, not just the patient’s
- Need to educate patients and caregivers about the disease, provide a written action plan, and review/modify PRN at follow-up
- Address itch-scratch cycle, sleep disturbance, behavioral associations
- Underlying skin inflammation is always present, even when the skin appears normal – treat with the appropriate agents and consider maintenance anti-inflammatory therapy
- Patient adherence is critical to AD management
- Consistent skin care can reduce flare-ups

Questions?

Thank You

Please complete the post-assessment and evaluation located in your meeting handout.