CONVENTIONAL THERAPIES FOR PEDIATRIC AD

Dr. Lawrence Schachner, MD
1. A disease of the whole family

2. No patient should leave the office without an instructional handout with the therapeutic ladder

3. If your stable atopic patient is flaring, think:
   - STAPH
   - STAPH
   - STAPH

4. TCI’s remain a very good approach re: safety and efficacy

5. New therapies
Avoiding treatment pitfalls

• **Printed regimen goes home:** NO HANDOUT, NO COMPLIANCE

• Atopic Dermatitis Made EZ: Easy sliding scale treatment tree
  - 2 minutes of education
  - 2 minutes of treatment explanation

• When in doubt: Dx/Rx infection.

• Give adequate volumes of medication.

• Supply and refills for **ACUTE AND MAINTENANCE** treatment.

• Remember the whole family is the patient: psychosocial intervention when necessary.
Typical flexural AD in a child
Typical facial and extensor AD in an infant
Ad with staph infection
The intact Skin Barrier

Skin barrier disruption is characteristic of ad

### Structural and Functional Differences Between Infant and Adult Skin

<table>
<thead>
<tr>
<th></th>
<th>Infant</th>
<th>Adult</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structural differences</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidermal thickness</td>
<td>Thinner</td>
<td>Thicker</td>
<td>1</td>
</tr>
<tr>
<td>Cell attachments and epidermal cellularity</td>
<td>Less</td>
<td>More</td>
<td>1</td>
</tr>
<tr>
<td>Dermoepidermal junction</td>
<td>Flat</td>
<td>Undulating</td>
<td>1</td>
</tr>
<tr>
<td>Lipids</td>
<td>Less</td>
<td>More</td>
<td>1</td>
</tr>
<tr>
<td><strong>Functional differences</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanin</td>
<td>Less</td>
<td>More</td>
<td>2</td>
</tr>
<tr>
<td>Sweat</td>
<td>Less</td>
<td>More</td>
<td>2</td>
</tr>
<tr>
<td>Water content</td>
<td>Higher</td>
<td>Lower</td>
<td>1,2</td>
</tr>
<tr>
<td>Natural moisturizing factor concentration</td>
<td>Lower</td>
<td>Higher</td>
<td>1-4</td>
</tr>
<tr>
<td>pH</td>
<td>Higher</td>
<td>Lower</td>
<td>3,4</td>
</tr>
</tbody>
</table>

Basic Rules:
- Short nails, short bath (3 minutes), cotton clothing, and cool environment
- Laundry: Hypoallergenic detergent with no bleach or fabric softener.

Bath care:
- If previous Staph infection, use antibacterial soap from the neck down (do not use on face) for three minutes before bath
- If history of Staph infections, ¼ cup of bleach in 1 ft of water; bleach in a bottle
- After bath, **pat dry. Do not rub!**
  - Emollient to ENTIRE body.

• **Morning and evening:**
  - **Emollient to entire body,** even if no inflammation (nothing pink or red).

  AND

  - Medium strength topical steroid and/or Topical Calcineurin Inhibitors (TCI) and/or Phosphodiesterase inhibitors (PDI) to **red** areas on **body**.

  - Hydrocortisone and/or Topical Calcineurin Inhibitors (TCI) and/or PDI to **slightly red or pink** areas on body.

  - Hydrocortisone and/or Topical Calcineurin Inhibitors (TCI) and/or PDI to **pink or red** areas on **face, groin, and armpits.**
Antibiotics
- Oral or Topical

Topical Calcineurin Inhibitors (TCI)
- Tacrolimus (Protopic 0.03%, 0.1%)
- Pimecrolimus (Elidel)

Phosphodiesterase inhibitors

Antihistamines & Bedtime
- Non-sedating in a.m.
- Sedating at bedtime
- Doxepin – the secret weapon
- Additional pearl: use of melatonin in infants and children in AD

Scalp care:
- Shampoo
- Topical Steroid

ATOPIC DERMATITIS: TREATMENT MADE E.Z. SM:
The Simple Sliding Scale
Atopic dermatitis made easy: The Schachner Ladder

Kate E. Oberlin MD | Sonali Nanda MS
Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Miami, Florida

Abstract
The vast majority of atopic dermatitis follows a mild, chronic relapsing course. In this article, we highlight the art and practice of treating atopic dermatitis based upon a foundation of maintenance use and a wider array of therapies that can optimize the management of this disease.

KEYWORDS
Atopic dermatitis, corticosteroid, topical, diagnosis, therapy - topical

1 | DISCUSSION

Atopic dermatitis is a chronic, relapsing skin disease that presents with clinical features of pruritus, inflammation, and excoriation. The lesions present in a characteristic distribution, aligned with the age of the patient, and it often coexists with a family history of atopy, asthma, and allergic rhinitis. Most patients present before 6 months of age, and the typical course is a mild form of disease.

Simple preventative measures, such as daily topicals, emollients, and bathing and skin barrier therapy, can decrease the incidence of atopic dermatitis at 4 months to upwards of 80%. In addition, novel developments have provided enhanced therapeutic options for atopic dermatitis. Dupilumab, a novel biologic agent that targets the IL-4 receptor, was approved for moderate to severe atopic dermatitis. Omalizumab, a unique topical phosphodiesterase 4 inhibitor, has been approved for mild-to-moderate atopic dermatitis. However, as we are fortunate to have these additional medications, a valid foundation of care for the patient must still be implemented. Basic sensitive skin care and a consistent topical regimen is the framework for treatment. Treatment escalation or deceleration

TABLE 1 The Schachner Ladder for (A) mild-to-moderate disease starting therapy, (B) moderate-to-severe disease starting therapy with the most potent corticosteroid and tapering down. Therapy is in addition to twice daily emollient use always.

<table>
<thead>
<tr>
<th></th>
<th>Medication</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>If moderate</td>
<td>Triamcinolone (medium potency CS) + TCI or PDI</td>
<td>Twice daily for 3-5 d</td>
</tr>
<tr>
<td>If mild</td>
<td>Alclometasone (low potency CS) + TCI or PDI</td>
<td>Twice daily for 3-5 d</td>
</tr>
<tr>
<td>Controlled</td>
<td>TCI or PDI to areas of predilection</td>
<td>Twice daily for 2 wks</td>
</tr>
<tr>
<td>Maintenance</td>
<td>TCI or PDI to areas of predilection</td>
<td>Twice weekly</td>
</tr>
</tbody>
</table>

| If severe                | Clobetasol (high potency CS) + TCI or PDI       | Twice daily for 3-5 d |
| If moderate              | Triamcinolone (medium potency CS) + TCI or PDI  | Twice daily for 3-5 d |
| If mild                  | Alclometasone (low potency CS) + TCI or PDI     | Twice daily for 3-5 d |
| Controlled               | TCI or PDI to areas of predilection              | Twice daily for 2 wks |
| Maintenance              | TCI or PDI to areas of predilection              | Twice weekly       |

Abbreviations: CS, Corticosteroid; PDI, Phosphodiesterase 4 inhibitor; TCI, Topical calcineurin inhibitor
**Severity** | **Topical Treatment** | **Schedule**
--- | --- | ---
If Severe: | Clobetasol (high potency CS) + TCI or PDI + emollients | Twice daily for 3-5 days
If Moderate: | Triamcinolone (medium potency CS) + TCI or PDI + emollients | Twice daily for 3-5 days
If Mild: | Alclometasone (low potency CS) + TCI or PDI + emollients | Twice daily for 3-5 days
Controlled: | TCI or PDI or TS + emollients | Twice daily for 2 weeks
Maintenance (to areas of predilection): | TCI or PDI or TS + emollients | Twice weekly for 6 months
Long-term Maintenance & Prevention: | Emollients | Twice daily

* Abbreviations: CS: Corticosteroid. PDI: Phosphodiesterase inhibitor. TCI: Topical Calcineurin Inhibitor

* Antihistamines as needed
* Antibiotics as needed
Algorithm For The Treatment Of Moderate To Severe Atopic Dermatitis

If successful:
- Titrate down
- TCI’s 2x a week or role for PDI or topical steroid
- Emollients only

If unsuccessful:
1. Patch testing
2. **DUPILUMAB**
3. UVA, UVB, narrowband UVB
4. Tar
5. Prednisone
6. IVPS
7. Cytotoxic and Biologic agents: cyclosporine, cellcept, cyclophosphamide, azathioprine, methotrexate
8. INF α or γ subcutaneously
9. IVIG
10. Alternative therapies: Relaxation / Massage therapy / Behavioral / Probiotics
Benefits of moisturizing

- Decreases steroid use
- Reduces pruritus
- Reduces SCORAD, EASI, and IGA
- Improves quality of life index scores
- Reduces the number of flares
- Increases the time to flare
- Plays a role in preventing AD in atopic prone newborns
- Plays a role in reducing contact dermatitis

What should the ideal moisturizer have?

- Safe
- Effective
- Inexpensive
- Additive free
- Fragrance free
- Sensitizing agent free
- Pleasant to use
- Should optimize lipid and water content of the SC
Results:

- Three studies showed that UVA1 is both faster and more efficacious for treating acute AD.
- Two trials used medium dose (50J/cm²) UVA1 for treating acute AD with success.
- Two trials revealed that combined UVAB was superior to UVA alone in the management of AD.
- Two studies demonstrated the narrow-band UVB is more effective than either broadband UVA or UVA1 for managing chronic AD.
e.g. – 20 kg child with severe atopic dermatitis

- $1\text{mg/kg/day} \times 4 \text{ days} = 20 \text{ mg/day}$
- $0.75 \text{mg/kg/day} \times 4 \text{ days} = 15 \text{ mg/day}$
- $0.50 \text{mg/kg/day} \times 4 \text{ days} = 10 \text{ mg/day}$
- $0.25 \text{mg/kg/day} \times 4 \text{ days} = 5 \text{ mg/day}$
Nine studies used higher cyclosporine doses (4-5mg/kg) and 4 studies used 2.5-3mg/kg.

In the higher cyclosporine dosage (4-5mg/kg) groups, there was an average of 40% change in mean disease severity after 2 weeks compared to an average of 20% change in disease severity in the studies using lower dose 2.5 - 3mg/kg.
• First topical Phosphodiesterase 4 inhibitor (PDE-4)

• U.S. FDA approved in December 2016 for mild-moderate atopic dermatitis in patients 2 years of age and older

• Mechanism of action: by inhibition PDE-4, results in increase intracellular cAMP levels which is suppression the release of pro-inflammatory cytokines

• EUCRISA™ (Crisaborole) ointment 2% apply twice daily supplies in 60 g and 100 g tube.
• Now FDA-approved (March 2020) for children with mild to moderate atopic dermatitis as young as **3 months and up**

• An open-label multicenter study by Eichenfield *et al.* confirmed long-term safety of Crisaborole use in children 2 years and up*

• Adverse events (AEs) were mostly mild and unrelated to treatment (93.1% of cases)

• Of those treatment-related AEs, atopic dermatitis (3.1%) was most frequently seen followed by application-site pain (2.3%), & application-site infection (1.2%)

---

• Dupilumab is the only currently available biologic treatment of a **moderate to severe** Atopic Dermatitis (AD)

• It is a fully human monoclonal antibody that is directed against the shared alpha subunit of the IL-4 receptor resulting in signaling blockade of IL-4 and IL-13, which are key drivers of Th2-mediated inflammation of AD

• Suppresses the expression of genes related to the activation of Th2 cells and related inflammatory pathways, a major driver in AD clinical disease

• **Now FDA approved for 6-year-olds and up !!!**
### DIPILUMAB (Dupixent) Dosages for Pediatric Age Groups 6 to 17 years of Age

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Dose</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 Kg</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every other wk</td>
</tr>
<tr>
<td>30 to &lt; 60 Kg</td>
<td>400 mg (two 200 mg injections)</td>
<td>200 mg every other wk</td>
</tr>
<tr>
<td>15 to &lt; 30 Kg</td>
<td>600 mg (two 300 mg injections)</td>
<td>300 mg every 4 wks</td>
</tr>
</tbody>
</table>
What are emerging therapies in ad?

- Monoclonal antibodies against IL-4, IL-13 and 31RA
  - Available and/or in phase 3 studies

- JAK inhibitors
  - Phase 1, 2, 3

- Phosphodiesterase 4 inhibitors
  - Phase 2, 3, 4

- Transient receptor potential (TRPV1) antagonist
  - Phase 2, 3

- T-cell inhibitors
  - Phase 2

- Prostaglandin/leukotriene inhibitors
  - Phase 1, 2
Two prospective, randomized controlled trials demonstrated that the daily use of a moisturizer prevented AD in 32% of Japanese and 50% of Anglo-American high-risk newborns (Horimukai et al. J Allergy Clin Immunol., 2014; Simpson et al. J Allergy Clin Immunol., 2014)

Daily use of emollients in high risk neonates may serve as a novel and simple approach to primary prevention of AD
Randomized, double blind, placebo-controlled crossover study in a Taiwan tertiary hospital

- 48 patients, 1 to 18 years old (Mean 7 yo)
- **Melatonin 3mg/day** for 4 weeks, followed by 2 weeks wash out, crossover to alternate treatment for 4 weeks
- **SCORAD reduced by 9.1** (p<0.001) versus placebo from a mean of 49.1
- **Sleep latency reduced by 21 minutes** (p = 0.02) versus placebo from a mean of 44 minutes
- No adverse events were reported

Chang YS, Lin MH et al. Melatonin supplementation for children with atopic dermatitis and sleep disturbance: A RCT. JAMA Pediatr Nov 2015 online first
Atopic Dermatitis Symptoms Decreased In Children Following Massage Therapy

Schachner LA, Field T, Hernandez-Reif M, Duarte A, Krasnegor J
**Review on ladder therapy**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Topical Treatment</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>If Severe:</td>
<td>Clobetasol (high potency CS) + TCI or PDI + emollients</td>
<td>Twice daily for 3-5 days</td>
</tr>
<tr>
<td>If Moderate:</td>
<td>Triamcinolone (medium potency CS) + TCI or PDI + emollients</td>
<td>Twice daily for 3-5 days</td>
</tr>
<tr>
<td>If Mild:</td>
<td>Alclometasone (low potency CS) + TCI or PDI + emollients</td>
<td>Twice daily for 3-5 days</td>
</tr>
<tr>
<td>Controlled:</td>
<td>TCI or PDI or TS + emollients</td>
<td>Twice daily for 2 weeks</td>
</tr>
<tr>
<td>Maintenance (to areas of predilection):</td>
<td>TCI or PDI or TS + emollients</td>
<td>Twice weekly for 6 months</td>
</tr>
<tr>
<td>Long-term Maintenance &amp; Prevention:</td>
<td>Emollients</td>
<td>Twice daily</td>
</tr>
</tbody>
</table>

*Antihistamines as needed  
Antibiotics as needed

*Abbreviations: CS: Corticosteroid. PDI: Phosphodiesterase inhibitor. TCI: Topical Calcineurin Inhibitor*