Atopic Dermatitis: Management Recommendations for Pediatricians

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FUTURE OF PEDIATRICS
Objectives

- Learn about new medications that are FDA approved for pediatric atopic dermatitis
- Become familiar with criteria to distinguish severe from mild to moderate atopic dermatitis
- Become comfortable with treatment, counseling, and practical aspects of mild to moderate atopic dermatitis management
Atopic dermatitis (AD)

- Affects up to 20% of pediatric population in Western countries
- Associated with comorbidities and serious impact on quality of life
  - Increased risk of depression, attention deficit hyperactivity disorder, learning disabilities
  - Symptoms of itch, pain, insomnia
  - Bacterial and viral superinfections, hospitalizations
  - Association with asthma, food allergies
  - Parental sleep deprivation, decreased parental work productivity
- Etiology involves complex interplay between skin immune system (innate and type 2 immunity), epidermal barrier, and microbiome – genetic and environmental factors
- Traditional treatments more broadly immunosuppressive
- Novel treatments are more targeted to AD pathway
Traditional therapies

**Topical**
- Corticosteroids
  - Mainstay of treatment for mild-moderate AD
  - Safe if used appropriately
- Calcineurin inhibitors
  - Protopic (tacrolimus) 0.03% ointment (2 yrs+)
  - Protopic (tacroimus) 0.1% ointment (16 yrs+)
  - Elidel (pimicrolimus) cream (2 yrs+)
    - Continuous long-term use not recommended
    - Black box warning lymphoma/skin cancer

**Systemic**
- Methotrexate (MTX)
- Cyclosporine (CsA)
- Azathioprine
- Mycophenolate mofetil
- Prednisone/prednisolone
  - Risk of severe rebound, serious adverse effects w/ repeated short courses

**Phototherapy**
- Psoralen plus UVA
- Narrowband UVB
Eucrisa (crisaborole) ointment

• First non-steroid approved in infants
  • Useful as cheeks/face eczema is stubborn in this population
    • Saliva, food, pacifier aggravate this area
    • Some require constant application of low to mid-potency steroids to prevent flares
• FDA approved for patients 3 months of age and older (March 2020) for mild to moderate atopic dermatitis
  • Only non-steroid topical approved under 2 yrs of age
  • No black box warning
• Phosphodiesterase-4 (PDE-4) inhibitor
  • Raises cAMP levels, decreases expression of proinflammatory cytokines
• SE: local reactions, application site burning
  • No limitation on duration of use
Eucrisa (crisabarole) ointment

- Use this in infants for cheeks and other stubborn spots
- Use this for stubborn eczema on eyelids, face, skin folds, other sensitive spots for all patients
- Use topical steroid first for acute flares
  - Eucrisa can burn on flared skin
- Then transition to Eucrisa ointment BID as steroid sparing agent

- Commercial insurance: $10 copay card on manufacturer website
  - Avoid need for prior authorization (PA) and delays in obtaining medication
- Medicaid: documentation is key to successfully obtain PA
  - Failure of steroids
  - Documentation of mild to moderate severity eczema (eg IGA score of 2 or 3)
Dupixent (dupilumab) injections

- First non-immunosuppressive targeted therapy for moderate to severe eczema
  - Many of our patients on immunosuppressives for years
- Dermatology prescribes this for refractory moderate to severe AD
  - Bridge with immunosuppressives (MTX, CsA) as failure is usually required for insurance
- FDA approved in patients 6 months of age and older (March 2021) for moderate to severe atopic dermatitis
  - Phase 3 trials in children 6 mo to 6 years of age
- IL-4Ra blocker:
  - Inhibits downstream signaling of IL-4 and IL-13, critical in TH2 cytokine phenotype

From: Kim et al J Allergy Clin Immunol 2020
Dupixent (dupilumab) injections

- Significant (75%) improvement in eczema severity in 69% of patients at 16 wks, 64% at 52 wks
  - Near-max benefits seen at 4 weeks
- Up to 48% mean itch reduction at 16 wks
- Benefits: targeted therapy, not immunosuppressive, no lab monitoring; approved for mod-severe asthma, adjunct tx
- Downside: injection
- SE: ocular (conjunctivitis, keratitis, blepharitis), injection site reactions, HSV infection; facial dermatitis, inflammatory arthritis/enthesitis

atopic dermatitis, mod-severe

pre-filled syringe form, 6-17 yo, 15-29 kg
Dose: 300 mg SC q4wk; Start: 600 mg SC divided in 2 sites x1

pre-filled syringe form, 6-17 yo, 30-59 kg
Dose: 200 mg SC q2wk; Start: 400 mg SC divided in 2 sites x1

pre-filled syringe form, 6-17 yo, >60 kg
Dose: 300 mg SC q2wk; Start: 600 mg SC divided in 2 sites x1

pen form, 12-17 yo, 15-29 kg
Dose: 300 mg SC q4wk; Start: 600 mg SC divided in 2 sites x1

pen form, 12-17 yo, 30-59 kg
Dose: 200 mg SC q2wk; Start: 400 mg SC divided in 2 sites x1

pen form, 12-17 yo, >60 kg
Dose: 300 mg SC q2wk; Start: 600 mg SC divided in 2 sites x1
Emerging therapies in pediatric atopic dermatitis

**Topical**
- Janus kinase (JAK) inhibitors
- PDE4 inhibitors
- Aryl hydrocarbon receptor agonist
- Bacteriotherapy

**Systemic**
- Biologics targeting IL-13, IL-31 receptor, and IL-5 receptor
  - Pro: Targeted, good safety profile, no need for lab monitoring
  - Con: Injections
- Oral JAK inhibitors
  - Pro: Oral administration, rapid onset of action
  - Con: More broadly immunosuppressive, safety concerns esp in long term use
Severity of AD

- Mild, moderate, severe
- Somewhat subjective
- Various severity scores used in clinical trials
  - Can be time consuming and not readily incorporated into clinical use
- Take into account:
  - Erythema, papulation, lichenification, excoriations, oozing
  - Surface area involved
    - Clinical practice: focal (1 discrete area eg. cheeks or hand eczema), multifocal (2-4 discrete areas), generalized (5+ discrete areas or diffuse)
  - Symptoms of itching and burning
  - Affect on sleep, attention in school, family
**Eczema Area and Severity Index (EASI)**

**Body regions**
- Head/neck
- Upper limbs
- Trunk
- Lower limbs

**Scoring of areas of involvement in each anatomical region (Area)**

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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</thead>
<tbody>
<tr>
<td>No eruption</td>
<td>&lt;10%</td>
<td>10%-29%</td>
<td>30-49%</td>
<td>50-69%</td>
<td>70-89%</td>
<td>90-100%</td>
<td></td>
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</tbody>
</table>

**Calculation of Intensity**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema (E)</td>
<td>None</td>
<td>Faintly detectable erythema, very light pink</td>
<td>Dull red, clearly distinguishable</td>
<td>Deep, dark red</td>
</tr>
<tr>
<td>Infiltration/Papulation (I)</td>
<td>None</td>
<td>Barely perceptible elevation</td>
<td>Clearly perceptible elevation</td>
<td>Extensive elevation</td>
</tr>
<tr>
<td>Excioration (Ex)</td>
<td>None</td>
<td>Scant evidence of excioration No erosion or crust</td>
<td>Several linear mark, some erosion or crust</td>
<td>Many erosive and/or crusty lesions</td>
</tr>
<tr>
<td>Lichenification (L)</td>
<td>None</td>
<td>Light thickening of skin discernable only by touch</td>
<td>Definite thickening of skin with exaggerated markings and markings and visible criss-cross pattern</td>
<td>Thickened Indurated skin and visible exaggerated criss-cross pattern</td>
</tr>
</tbody>
</table>

**Calculations**

<table>
<thead>
<tr>
<th>Area</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head/Neck</td>
<td>(E + I + Ex + L) x Area x 0.1 (In children 0-7 years (E + I + Ex + L) x Area x 0.2)</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>(E + I + Ex + L) x Area x 0.2</td>
</tr>
<tr>
<td>Trunk</td>
<td>(E + I + Ex + L) x Area x 0.3</td>
</tr>
<tr>
<td>Lower limbs</td>
<td>(E + I + Ex + L) x Area x 0.4 (In children 0-7 years (E + I + Ex + L) x Area x 0.3)</td>
</tr>
<tr>
<td>EASI</td>
<td>Sum of the above four body areas</td>
</tr>
</tbody>
</table>
Intensity of redness

Moderate redness. Score=2

Mild redness. Score=1

No redness. Score=0

Severe redness. Score=3
Intensity of lichenification/prurigo

No lichenification. Score=0

Mild lichenification. Score=1

Moderate lichenification. Score=2

Severe lichenification. Score=3

https://dermnetnz.org/topics/easi-score/
AD in infants

- Cheeks are stubborn area: exacerbated by irritant contact dermatitis from saliva
  - Protective layer of emollient prior to feeds/naps
- Extensor predominance
- Glossy erythema in flexural surfaces is often seb derm, not atopic derm
- Generalized distribution is not uncommon
  - Usually spares diaper area but may have concomitant irritant or allergic contact dermatitis
    - Ask about wet wipe use on face/body
- Don’t forget the scalp
  - Itch, erythema, non-greasy scale help distinguish scalp eczema from cradle crap
  - Itch can manifest as wiggling, rubbing of scalp, often a/w alopecia
  - Avoid ketoconazole and OTC dandruff shampoos as they irritate eczema
  - Do use topical steroid ointment on baby scalps
AD in infants

- Use hydrocortisone 2.5% ointment on face daily for 1-2 weeks
- Use triamcinolone 0.1% ointment daily on body/scalp for 2 weeks if moderate or recalcitrant to hydrocortisone 2.5% ointment
  - Avoid in diaper area – systemic absorption
  - If severe, use on face for short periods (3-5 days)
  - If triamcinolone 0.1% ointment fails: refer to derm
  - Triamcinolone 0.025% ointment is comparable to HCT 2.5% ointment
- Don’t forget the scalp - treat it like the body
- Use twice weekly for maintenance or transition to Eucrisa ointment BID if consistently flares after steroid course
- As eczema clears, post inflammatory hypopigmentation becomes visible
  - DDx steroid overuse
  - Less likely to be steroid overuse in short-term (weeks)
  - Counsel on this as parents attribute to medication and then stop using it
  - Reassure that will re-pigment normally when eczema controlled
Skin of color

- Erythema may be more subtle
- Hyperpigmentation can indicate active disease (not just post-inflammatory changes)
  - Violaceous hue in medium skin tones
- Papular morphology
- Follicular prominence
- Pityriasis alba on the cheeks
  - Treat w/ moisturizer, sunscreen
  - Eucrisa ointment
- Post inflammatory hypopigmentation very common in babies
Mainstays of AD management

- Counsel families that this is a chronic disorder
  - Flares expected; liberal emollient use, avoiding irritants and allergens, use medications PRN flares
- Moisturizers/emollients
  - Plain Vaseline ointment is adequate and affordable
  - Aquaphor more elegant but risk of allergic contact dermatitis (ACD) to lanolin and more pricey
    - Empirically eliminate if generalized/severe including in infants
  - Ceramide containing creams (not lotions) (Cerave body, Eucerin eczema relief, Aveeno eczema therapy)
  - Natural options
    - Virgin (cold-pressed) sunflower seed oil + coconut oil are anti-inflammatory and antimicrobial, respectively
    - Olive oil increases transepidermal water loss – avoid
    - Essential oils carry risk of ACD – avoid
- Bathe daily or every other day; mild gel cleanser or Dove Sensitive Skin bar (avoid soaps with sodium lauryl sulfate)
- Free and clear laundry detergents
- Evidence in allergy literature that early food introduction via gut helps prevent food allergies; contact through eczema skin may lead to sensitization
Adjuvant treatments

Bleach baths
- Plain non-concentrated bleach
- One tsp/gallon of water or ¼ cup in ½ tub water
  - Soak for up to 20 min 2-3x/wk, rinse well, apply moisturizer
  - 2-3 times per week
- Anti inflammatory, anti-itch, +/- antimicrobial
- Can sting if eroded so consider avoiding during acute flares
- Compare to swimming pool if parents hesitant

Oatmeal baths
- Anti-itch, anti-inflammatory, pre-biotic, normalize skin pH
  - Commercially available in packets
  - DIY: grind whole, uncooked oats into fine powder, 1 cup into sprinkled in bath water under running water
- Can alternate with bleach baths or recommend to families hesitant to use bleach baths

Oclusion
- Wet pajamas: +/- medication, then Vaseline, then damp pjs (dunk in warm water, wring out), then dry pjs
- Saran wrap: +/- medication, then Vaseline, then saran wrap
  - Helpful for focal stubborn thickened areas (lichen simplex chronicus)
  - Caution w/ high potency topicals – limit to 1 week

Oral medications:
- Sedating histamines PRN HS trouble sleeping due to itch
- Antihistamines do not help directly with atopic itch
- Non sedating antihistamines usually not indicated
  - Role for facial eczema worsened by seasonal allergies
- Melatonin 1-3 mg gummy 20 min before bedtime
Topical steroids

- Ointments >>> creams: more potent, less stinging, fewer irritants/allergens in vehicles
  - For face/skin folds/genitals: hydrocortisone 2.5% ointment
  - For mild-moderate areas on body: triamcinolone 0.1% ointment
  - For moderate-severe areas and palms/soles: mometasone ointment (med-high) or clobetasol ointment (Clobex, Temovate) (high potency)
  - For scalp: same as body.
    - If long/thick hair, fluocinolone liquid (medium) or clobetasol liquid (high potency)
    - If eroded, use ointment first as liquids burn – also can dry textured hair
  - Prescribe necessary quantity - 454 gm tub of triamcinolone and apply to AA on “upper and lower ext, abdomen, chest, back”

- Use daily for 1-2 weeks on face, 2 weeks on body, 2-3 weeks on thick/acral surfaces; resume as needed for flares
  - If use too sparingly, will never control the eczema
  - If use too often without breaks, will get side effects (atrophy, striae, erythema, telangiectasias, dyspigmentation)

- Can switch to 2 days on, 5 days off or non steroid for maintenance

- Steroid phobia:
  - Emphasize risks of untreated eczema: quality of life, infection risk, hospitalization
  - Reframe: short term more intensive use to “shut down” flare + bridge to non-steroid options (which sting on flared skin)
  - Safe when they are used properly
Referral to Dermatology

- In infants, refractory to hydrocortisone 2.5% ointment, desonide ointment, Eucrisa ointment, +/- triamcinolone 0.1% ointment on body
- In children/adolescents, refractory to triamcinolone 0.1% ointment in more generalized distribution or higher potency topicals in focal distribution
- Extensive to the point that continued application of topicals is impractical
- Patient/family are suffering despite first line treatments
References


