ATOPIC DERMATITIS: A BLUEPRINT FOR SUCCESS

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University of Arizona, College of Medicine
THE PLAN

- Is it atopic dermatitis?
- What is atopic dermatitis?
- Guidelines for treatment
- How to assess for (and treat) complicating factors
- When to refer
INSPECTION: IS IT ATOPIC DERMATITIS?
Atopic dermatitis (AD)

- Chronic, relapsing, noncontagious, pruritic inflammatory skin
disease that has an age-specific morphology and distribution
**Major Features (3 of 4)**

- Pruritus
- Typical morphology and distribution of skin lesions
- Chronic or chronically relapsing dermatitis
- Personal or family history of atopy

**Minor Features (3 of 23)**

- Xerosis
- Ichthyosis/palmar hyperlinearity/keratosis pilaris
- Immediate (type I) skin test reactivity
- Elevated serum IgE
- Early age of onset
- Tendency toward cutaneous infections/impaired cell-mediated immunity
- Tendency toward nonspecific hand or foot dermatitis
- Nipple eczema
- Cheilitis
- Recurrent conjunctivitis
- Dennie–Morgan infraorbital fold
- Keratoconus
- Anterior subcapsular cataract
- Orbital darkening
- Facial pallor/erythema
- Pityriasis alba
- Anterior neck folds
- Pruritus when sweating
- Intolerance to wool and lipid solvents
- Perifollicular accentuation
- Food intolerance
- Course influenced by environmental/emotional factors
- White dermatographism/delayed blanch

Adapted from Hanifin 1984
PRACTICAL DIAGNOSIS

• Essential Features
  • Pruritus
  • Eczematous dermatitis (age specific pattern and morphology)
  • Chronic or relapsing
DISTRIBUTION

Diagram from Atopic Eczema. JAMA. 2014.
INFANTS

Face and scalp
Extensor surfaces and creases
Never in diaper area

Exudative/weepy
SCHOOL AGE

Face and neck
Flexures

Lichenification (rubbing)
Excoriations (scratching)
ADULTS

Neck
Flexures
Hands
FOLLICULAR VARIANT

Found in darker skin types

Follicular based, grouped, dry papules

Often mistaken for keratosis pilaris or ‘dry skin’
PRACTICAL DIAGNOSIS

• Important Features
  • Early age of onset (before age 5; majority before age 2)
  • Atopy (self or family members)
  • Xerosis
PRACTICAL DIAGNOSIS

• Associated Features
  • KP/ichthyosis/hyperlinear palms
  • Perifollicular accentuation or lichenification
  • Atypical vascular response (eg white dermatographism)
• Most importantly, it is a **diagnosis of exclusion!**
BUILDING THE FOUNDATION:
WHAT IS ATOPIC DERMATITIS?
FACTS AND FIGURES

• Estimated to affect 12.5% of children in the United States
• Over 2/3 of cases have mild disease
• The Hygiene Hypothesis
  • Early exposure to infections and pathogens reduces incidence of atopic disorders
PATHOGENESIS

• Atopic March Hypothesis
  • Sequential development of atopic dermatitis, asthma and allergic rhinitis implies causality

Dual-Allergen Exposure Hypothesis

- Impaired skin barrier + exposure to environmental food allergens can lead to induction of sensitization and subsequent food allergies
- Ingestion promotes immune tolerance

Epidemiologic risks for food allergy
PATHOGENESIS

1. Skin barrier impairment
2. Immune dysregulation
3. Pruritus
4. Microbial shifts
5. Genetics
6. Environmental factors

PREVENTION

Maternal Dietary Restrictions

• Maternal avoidance of cow milk, egg and other ‘high antigen’ foods during pregnancy and/or breastfeeding
• Five trials, involving 952 participants
• No protective effect on infant’s development of allergic disease (eczema, allergies, asthma)

Maternal dietary antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child. Cochrane Review. 2012.
PREVENTION

Emollients
• Three RCTs + larger studies underway
• Regular application of emollients to at-risk infants reduces rate of AD by 50%

The skin as a target for prevention of the atopic march. Annals of Allergy, Immunology and Asthma. 2018.
Probiotics

• Meta analysis of 14 RCTs
• Administered during pregnancy, breastfeeding and/or early infancy
• Pooled 20% reduction in incidence of AD
CONSTRUCTION: GUIDELINES FOR TREATMENT
STEP ONE: “SENSITIVE SKIN CARE”

- **Daily bath** or shower (less than 15 minutes, lukewarm water, minimal soap; pH balanced bar soap better than liquid)
- Immediate application of thick cream or ointment based emollient head to toe
- **Simple products** are best
- **Avoidance of irritants** (perfumes, fragrances, dryer sheets, wool)
BATHING

• More than 50% of PCPs recommend infrequent bathing, whereas more than 50% of specialists (dermatology and allergy) recommend daily bathing

BATHING

- Conflicting evidence
- Difficult to control for other factors (water temperature, duration, soaps, emollients)
- Authors nonetheless recommend daily bathing with ‘soak and smear’ approach
  - Benefits: mechanical decontamination, restore skin barrier

## STEP TWO: CHOOSE YOUR TOPICAL THERAPY

<table>
<thead>
<tr>
<th>Anatomic Site</th>
<th>Mild*</th>
<th>Severe*</th>
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<tbody>
<tr>
<td>Face</td>
<td>Hydrocortisone 2.5% Calcineurin inhibitors</td>
<td>Desonide</td>
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<tr>
<td>Body</td>
<td>Triamcinolone</td>
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<td>Triamcinolone</td>
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* Ointment formulation, unless otherwise specified
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STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

1. “Hot spot” treatment

“Apply ______ twice daily to red, scaly, itchy spots on the ______ until smooth and itch free, then stop. Restart when areas of rash return.”
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

1. “Hot spot” treatment

“Apply triamcinolone twice daily to red, scaly, itchy spots on the trunk until smooth and itch free, then stop. Restart when areas of rash return.”
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

2. Intermittent maintenance therapy

“Apply ______ twice daily to red, scaly, itchy spots on the ______ until smooth and itch free, then stop. Then apply ______ three times weekly to trouble spots as maintenance therapy. If rash flares, may switch back to topical steroid until flare resolves.”
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

2. Intermittent maintenance therapy

“Apply desonide twice daily to red, scaly, itchy spots on the face until smooth and itch free, then stop. Then apply tacrolimus three times weekly to trouble spots as maintenance therapy. If rash flares, may switch back to topical steroid until flare resolves.”
3. Intermittent burst therapy

“For a severe flare, apply ______ twice daily to red, scaly, itchy spots on the ______ for up to ____ days at a time then back down to ______ twice daily until rash is smooth. If rash recurs weeks later, restart ______ twice daily until smooth.”
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

3. Intermittent burst therapy

“For a severe flare, apply fluocinonide twice daily to red, scaly, itchy spots on the hands/feet for up to 5 days at a time then back-down to triamcinolone twice daily until rash is smooth. If rash recurs weeks later, restart triamcinolone twice daily until smooth.”
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

One fingertip unit = 0.5g

= coverage of two adult sized hands
**STEP THREE: CHOOSE YOUR METHOD OF APPLICATION**

One fingertip unit = 0.5g

<table>
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<th>Age</th>
<th>Face and neck</th>
<th>One upper limb</th>
<th>One lower limb</th>
<th>Trunk</th>
<th>Whole body</th>
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<td>3–6 month</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>2.5</td>
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<td>5</td>
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<td>4.5</td>
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<td>24.5</td>
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5 yo with atopic dermatitis, flaring on arms/legs requires 10 fingertip units BID, which is equal to **10 grams/day**. A one week supply is therefore **70 grams**.
STEP FOUR: REPETITION, REASSURANCE AND INTERVAL FOLLOW-UP

• Frame the disease appropriately from the onset
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• Frame the disease appropriately from the onset
• Education, education, education
STEP FOUR: REPETITION, REASSURANCE AND INTERVAL FOLLOW-UP

• Frame the disease appropriately from the onset
• Education, education, education
• Set appropriate follow-ups
TAKE THESE OUT OF YOUR TOOLBOX

- Infrequent bathing
- Non-sedating antihistamines
- Topical antibiotics
- Topical diphenhydramine
- Oral corticosteroids
- Food elimination diets in unselected populations
SETBACKS AND DELAYS: ASSESSING FOR COMPLICATIONS
INFECTION

- Crusts, erosions, fissures
INFECTION

- MSSA
- Strep
- MRSA
INFECTION

- Bacterial culture swab followed by empiric oral antibiotics (if indicated)
- Bleach baths TIW
- Pulsed monthly intranasal mupirocin (especially with MRSA)
BLEACH BATHS
OTHER INFECTIONS

• HSV
• Coxsackie virus
• Tinea
• HPV
• Molluscum contagiosum
ECZEMA COXSACKIUM
NON-COMPLIANCE

• One third of dermatology patients never pick up their prescriptions
• Mean adherence rate in atopics of 40% for 5 days after the appointment and down to 30% by 8 weeks
• Nurse or doctor-lead education modules, eczema action plans, and close interval follow-up improve adherence
NON-COMPLIANCE

• Nurse or doctor-lead education modules, eczema action plans, and close interval follow-up improve adherence

• Inquire about and address the easy fixes at each follow-up (e.g. stinging sensations, greasiness, cost, inadequate tube sizes, time constraints)
NON-COMPLIANCE

• Nurse or doctor-lead education modules, eczema action plans, and close interval follow-up improve adherence

• Inquire about and address the easy fixes at each follow-up (e.g. stinging sensations, greasiness, cost, inadequate tube sizes, time constraints)

• Close interval follow-up
STEROID PHOBIA

- Prevalence of 21 to 83%
- Higher rate of nonadherence
- Physicians and health care workers are in top 3 sources of information about topical corticosteroids (TCS)
STEROID PHOBIA – HPA AXIS SUPPRESSION

• Adults
  • *Physiologic* suppression with potent TCS for prolonged periods of time (e.g., desoximetasone 70g/week x 22 weeks)
  • *Pathologic* suppression in several patients with prolonged and excessive use of superpotent TCS (e.g., clobetasol 100g/week for 3-18 months)

STEROID PHOBIA – HPA AXIS SUPPRESSION

• Pediatric
  • Few case reports of adrenal suppression with use of potent/superpotent TCS in diaper area

STEROID PHOBIA – CUTANEOUS ATROPHY

- Survey of 276 Australian pharmacists
  - 46% state atrophy is most common SE of TCS
  - 67% advise patients to use no longer than 2 weeks
STEROID PHOBIA – CUTANEOUS ATROPHY

• Initial reports were low quality studies from the 1960s-1980s

• 70 pediatric patients with AD treated with standard topical therapy based on severity (potent → mid potency → low potency)

• No cases of atrophy at 280 studied anatomic sites

STEROID PHOBIA – CUTANEOUS ATROPHY

- The safety profile of TCS remains robust when it is used appropriately.
- Appropriate use is defined as 1–2 generous applications per day to all the inflamed skin until the active eczema is controlled.

POOR SLEEP

- Disturbed sleep in 47-60% of children with AD
- Correlates with more severe disease, poor school performance, lower quality of life and impacts family dynamics
POOR SLEEP

- No consensus statement on management
- Therapeutic options
  - Sedating antihistamine
  - Melatonin
  - Behavioral modification strategies
  - Antidepressants (doxepin)

Managing sleep disturbance in children with atopic dermatitis. Ped Derm. 2018
• Children with atopic disease have 30-50% greater chance of developing ADHD
BEHAVIOR

- Children with atopic disease have 30-50% greater chance of developing ADHD
- Hypotheses: pro-inflammatory milieu, sleep impairment, shared genetic factors
CONCOMITANT (BUT NOT STRICTLY CAUSAL) CONDITIONS

• Asthma
• Eosinophilic esophagitis
• Seasonal allergies
• Food allergies
Food allergies (FAs) affect 4-6% of children and 15% of those with atopic dermatitis.
FOOD ALLERGIES

• Survey of pediatricians, dermatologists and allergists (150 respondents)

• Pediatricians (59%) and allergists (62%) report treating some patients with dietary management alone; as compared to dermatologists (27%)
FOOD ALLERGIES

• Nine RCTs (of which 6 were limited to exclusion of egg and milk)
• Little evidence supports the use of various exclusion diets in unselected people with atopic eczema

FOOD ALLERGIES

• There may be some benefit in using an egg-free diet in infants with suspected egg allergy who have positive specific IgE to eggs

EXPERT CONSULTATION: WHEN TO REFER
IT’S NOT ECZEMA

Seborrheic Dermatitis
IT’S NOT ECZEMA

Psoriasis
IT’S NOT ECZEMA

Scabies
IT’S NOT ECZEMA

Langerhan’s Cell Histiocytosis
IT’S NOT ECZEMA

Tinea
IT’S NOT ECZEMA

Discoid Lupus
IT’S NOT ECZEMA

Papular Urticaria
IT’S MORE THAN “JUST” ECZEMA
SEVERE OR STUBBORN DISEASE
DERMATOLOGIST’S (T)RUSTY OLD TOOLBOX

• Wet wraps
• Narrowband UVB (light therapy)
• Methotrexate
• Mycophenolate
• Azathioprine
• Cyclosporine
DERMATOLOGIST’S SHINY NEW TOOLBOX

- Crisaborole
- Dupilumab
CRISABOROLE

- FDA approved December 2016 for mild to moderate AD in patients 2 years and older
- Twice daily application of a cream
- Phosphodiesterase 4 inhibitor (involved in pro-inflammatory cytokine cascade)
CRISABOROLE

- Statistically significant reduction in eczema severity scores (non-inferiority) – earlier reduction of pruritus and redness as compared to vehicle
- Side effects: stinging sensation
- Future directions: head-to-head comparisons with TCSs and TCIs, special site considerations
## COST COMPARISON

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PRICE*</th>
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<tbody>
<tr>
<td>Crisaborole**</td>
<td>$619</td>
</tr>
<tr>
<td>Pimecrolimus**</td>
<td>$541</td>
</tr>
<tr>
<td>Tacrolimus 0.03%</td>
<td>$140</td>
</tr>
<tr>
<td>Desonide</td>
<td>$69</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>$17</td>
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* Cash price for a 60 gram tube via goodrx.com on 3/12/18
** Brand name only available
DUPILUMAB

• FDA approved March 2017 for adults with moderate to severe AD
• Biweekly SQ injection
• Antagonist of shared receptor subunit of IL-4 and IL-13 (normally amplify a Th2 immune response)
DUPILUMAB

• Majority (86%) of patient experience 50% reduction of symptoms on eczema severity scale
• Sustained response
• Side effects: conjunctivitis, injection site reactions
• Future directions: pediatric studies, long term safety data
THE PIPELINE

- Other PDE-4 inhibitors
- Other IL-13 inhibitors
- IL-31 inhibitors (thought to mediate sensation of itch)
- JAK inhibitors (currently used to treat multiple hematologic and inflammatory diseases)
- Transient receptor potential ion channel antagonists (mediators of itch, barrier function)
- Also T-cell inhibitors, antimicrobial peptides, topical anti-inflammatories, skin specific antihistamines, opioid receptor agonists
FINISHING TOUCHES
TAKE HOME POINTS