ATOPIC DERMATITIS: A BLUEPRINT FOR SUCCESS

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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?

DEFINITION

- Atopic dermatitis (AD)
  - Chronic, relapsing, noncontagious, pruritic inflammatory skin disease that has an age-specific morphology and distribution

DIAGNOSTIC CRITERIA

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)

PRACTICAL DIAGNOSIS

- 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

Translating Atopic Dermatitis Management Guidelines into Practice for Primary Care Providers. Pediatrics. 2015.

PATHOGENESIS

- 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

Novel concepts of prevention and treatment of atopic dermatitis through barrier and immune manipulations with implications for the atopic march. J Allergy Clin Immunol. 2017.

PATHOGENESIS

- 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
J Allergy Clin Immunol. 2008.

PATHOGENESIS

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

An update on the pathophysiology of atopic dermatitis. Dermatologic Clinics. 2017.

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.

PREVENTION

Probiotics

- Meta analysis of 14 RCTs
- Administered during pregnancy, breastfeeding and/or early infancy
- Pooled 20% reduction in incidence of AD

Probiotics supplementation during pregnancy or infancy for the prevention of atopic dermatitis: a meta-analysis. Epidemiology. 2012.

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 frequency recommendations for children with atopic dermatitis: results of three observational pilot surveys. Pediatr Dermatol. 2015.

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

Does bathing frequency matter in pediatric atopic dermatitis? Ann Allergy Asthma Immunol. 2016.

STEP TWO: CHOOSE YOUR TOPICAL THERAPY

Anatomic Site	Mild*	Severe*
Face	Hydrocortisone 2.5% Calcineurin inhibitors	Desonide
Body	Triamcinolone	Fluocinonide
Extremities (esp hands/feet)	Triamcinolone	Fluocinonide Clobetasol
Scalp	Fluocinolone oil	Fluocinonide solution

* Ointment formulation, unless otherwise specified

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Dermatology Referral

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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."

STEP THREE: CHOOSE YOUR METHOD OF APPLICATION

3. Intermittent burst therapy

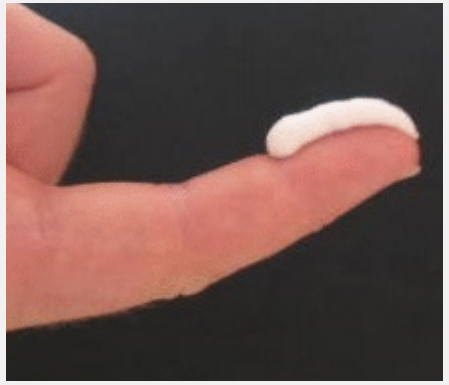
"For a severe flare, apply _____ twice daily to red, scaly, itchy spots on the _____ for up to _____ days at a time then back down to _____ twice daily until rash is smooth. If rash recurs weeks later, restart _____ twice daily until smooth."

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."

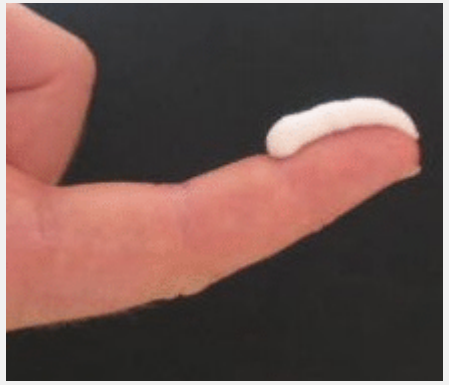
STEP THREE: CHOOSE YOUR METHOD OF APPLICATION



One fingertip unit = 0.5g

= coverage of two adult sized hands

STEP THREE: CHOOSE YOUR METHOD OF APPLICATION



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Age	Face and neck	One upper limb	One lower limb	Trunk	Whole body
3–6 month	1	1	1.5	2.5	8.5
1–2 years	1.5	1.5	2	5	13.5
3–5 years	1.5	2	3	6.5	18
6–10 years	2	2.5	4.5	8.5	24.5
Adult	2.5	4.5	7.6	13.5	40

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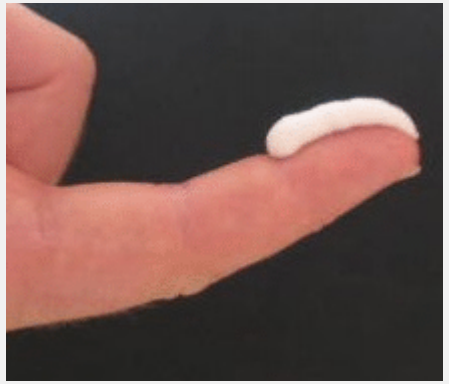

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Adult	2.5	4.5	7.6	13.5	40

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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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

Interventions to increase treatment adherence in pediatric atopic dermatitis. J Clin Med. 2015.

NON-COMPLIANCE

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

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

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- 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)

Topical Corticosteroid Phobia in Atopic Dermatitis.
JAMA Dermatol. July 2017.

STEROID PHOBIA – HPA AXIS SUPPRESSION

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

Topical steroid risk analysis: differentiating between physiologic and pathologic adrenal suppression. J Dermatolog Treat. 2017.

STEROID PHOBIA – HPA AXIS SUPPRESSION

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

Topical steroid risk analysis: differentiating between physiologic and pathologic adrenal suppression. J Dermatolog Treat. 2017.

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

Adverse effects of topical corticosteroids in paediatric eczema: Austra. J Dermatolog Treat. 2017.

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

Evaluation of the atrophogenic potential of topical corticosteroids in pediatric dermatology patients. *Pediatr. Dermatol.* 2011.

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

Adverse effects of topical corticosteroids in paediatric eczema: Austra. J Dermatolog Treat. 2017.

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

Managing sleep disturbance in children with atopic dermatitis. Ped Derm. 2018

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

BEHAVIOR

- Children with atopic disease have 30-50% greater chance of developing ADHD

Association of atopic diseases and attention-deficit/hyperactivity disorder: A systematic review and meta-analyses. Neurosci Biobehav Rev. 2017.

BEHAVIOR

- Children with atopic disease have 30-50% greater chance of developing ADHD
- Hypotheses: pro-inflammatory milieu, sleep impairment, shared genetic factors

Association of atopic diseases and attention-deficit/hyperactivity disorder: A systematic review and meta-analyses. Neurosci Biobehav Rev. 2017.

CONCOMITANT (BUT NOT STRICTLY CAUSAL) CONDITIONS

- Asthma
- Eosinophilic esophagitis
- Seasonal allergies
- Food allergies

FOOD ALLERGIES

- Food allergies (FAs) affect 4-6% of children and 15% of those with atopic dermatitis

An Update on Pediatric Atopic Dermatitis and Food Allergies. The Journal of Pediatrics. 2015.

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%)

Patterns of Clinical Management of Atopic Dermatitis in Infants and Toddlers. Pediatrics. 2014.

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

Dietary exclusions for established atopic eczema. Cochrane Review. 2008.

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

Dietary exclusions for established atopic eczema. Cochrane Review. 2008.

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

DRUG	PRICE*
Crisaborole**	$619
Pimecrolimus**	$541
Tacrolimus 0.03%	$140
Desonide	$69
Hydrocortisone	$17

* 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

QUESTIONS? COMMENTS? CONCERNS?

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