Atopic Dermatitis: Update for Pediatricians

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Disclosures

- No relevant conflicts of interest.

Learning Objectives

- Summarize epidemiology and pathophysiology
- Describe clinical features
- Discuss common myths
- Devise a treatment plan
- Review new treatments

Atopic dermatitis

- Immune-mediated, CHRONIC, relapsing skin disorder
  - Pruritus
    - “the itch that rashes”
  - Xerosis
  - Inflammation
  - Lichenification

Atopic Dermatitis

- Often first manifestation of :
  - “atopic triad”
    - Atopic dermatitis
    - Asthma
    - Allergic rhinitis
  - “atopic march”
    - Eczema
    - Food allergy
    - Asthma
    - Allergic rhinitis

Atopic Dermatitis

- Prevalence
  - Children: 15-20%
  - Adults: 6-10%
- Tends to appear early
  - 60% of patients present during 1st year
  - 80 - 90% diagnosed by 5 y/o
- CHRONIC but sometimes “outgrown”
  - Up to 60% of patients w/ early onset disease may have resolution by 12 y/o

Kay J et al. J Am Acad Dermatol 1994;30:35-9.
Yamamura et al. J Clin Med 2022;(11)20:6145
Perkins MR et al. Pediatr Allergy Immunol 2004;15:221-9.
Jackson KD et al. National Center for Health Statistics. 2013.
Silverberg JI et al. Pediatr Allergy Immunol. 2013:24(5):476-86.

Atopic Dermatitis

- Clinical Diagnosis
  - History
  - Morphology
  - Distribution
  - Associated clinical signs
    - pruritus

Distribution

- Infant
  - Scalp
  - Face
  - Extensors
- Child
  - Neck
  - Wrists
  - Ankles/feet
  - Flexures
- Teen/adult
  - Hands>feet
  - Flexures
  - Scattered

Atopic Dermatitis

Atopic Dermatitis

Atopic Dermatitis

Etiology

- Multifactorial
  - Genetic
    - 70% of patients have +FH of atopy
  - Immune mediated
    - TH2-mediated w/ upregulation of chemokines
      - IL-4, IL-10: stimulate IgE synthesis
      - IL-5: activates eosinophils
    - Explosion of info about multiple complex pathways
      - New targeted therapies

Sugarman JL et al. Semin Cutan Med Surg 2008;27:108-14.
Czarnowicki T et al. J Allergy Clin Immunol Pract 2014;2:371-9.
David Boothe W et al. Adv Exp Med Biol 2017;1027:21-37.

Etiology

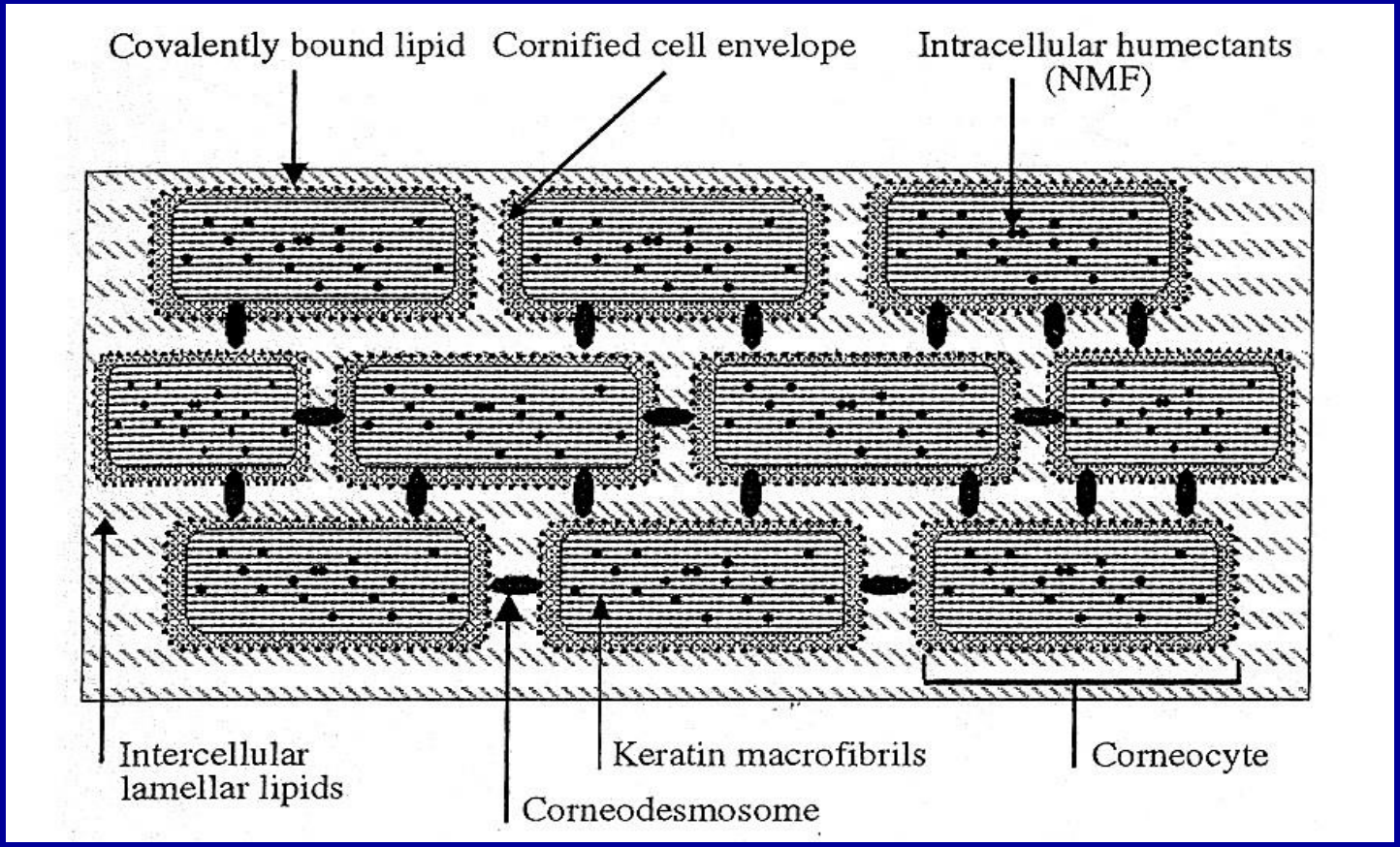
- Multifactorial
  - Neuroendocrine
    - “scratch-itch cycle”
    - stress-associated flares
  - Abnormal barrier function

Abnormal Barrier Function

- Decreased filaggrin, ceramides, other lipids
- Increased trans-epidermal water loss
  - dryness
- Increased allergen/irritant absorption
  - Inflammation, pruritus

Scharschmidt TC, et al. J Allergy Clin Immunol 2009 Sep;124(3):496-506.
Di Nardo A et al. Acta Derm Venereol 1998;78: 27-30.

“Bricks and Mortar”



Elias P et al. J Invest Dermatol 2005; 125:183-200.

Daily Skin Care Regimen

- Gentle cleansing
- Aggressive moisturizing
- Topical medications as indicated

- Details matter!

Bathing

- **No evidence that daily bathing worsens atopic dermatitis!**
  - **Removes bacteria**
  - **Removes scale and crusts**
  - **Removes irritants/allergens**
  - **Provides moisture**
  - **Enhances absorption of topicals**
  - **Especially important in hot weather.**
    - **Sweat!**
    - **Allergens**

Krakowski et al. Pediatrics 2008; 122:812-824.

Bathing

- Basic method
  - Short (5-10 minutes)
    - Warm (not hot)
  - Gentle cleanser
  - Pat dry
  - Apply medication to affected areas
  - Apply emollient all over

Cleansers

- Gentle, moisturizing, dye- & fragrance-free*
- Examples
  - Dove® for sensitive skin (bar)
  - CeraVe® hydrating cleanser (bar or liquid)
  - Cetaphil® gentle cleanser (liquid)
  - Aveeno® Cleansing Therapy wash (liquid)
  - Vanicream® Cleansing Bar

*unscented ≠ fragrance free

Emollients

- **Ointments and creams** are preferred
  - more lipids
  - fewer ingredients
  - ceramide-rich creams
    - CeraVe®, Aveeno® Advanced Care
  - Dye-free, fragrance-free
  - Applied at least twice daily (more if severe)
  - Applied after medication

Loden M et al. Am J Clin Dermatol 2003: 4(11): 771-788.
Lebwohl M et al. Cutis 2005 Dec; 76(6 Suppl): 7-12.
Chamlin SL et al. J Am Acad Dermatol 2002 Aug; 47(2): 198-208.

Emollients

- Examples
  - Aquaphor® ointment*
  - Vaseline® ointment
  - Vanicream®
  - Cetaphil® cream
  - CeraVe® cream
  - Aveeno® Eczema Therapy cream
  - Eucerin® cream*

* Contain lanolin

Topical Steroids (TCS)

- Ointment preparations generally work best.
  - Occlusive vehicle aids penetration.
  - Less likely to burn and sting on open skin.
  - Fewer ingredients/preservatives.

Krakowski et al. Pediatrics 2008; 122:812-824.

GENERIC NAME	EXAMPLES OF BRANDED PRODUCTS
CLASS 1—SUPER POTENT	
0.05% clobetasol propionate	Clobex® Lotion/Spray/Shampoo, Olux®E Foam, Temovate E® Emollient/ Cream/Ointment Gel/Scalp
0.05% halobetasol propionate	Ultravate® Cream
0.1% fluocinonide	Vanos® Cream
CLASS 2—POTENT	
0.05% diflorasone diacetate	ApexiCon® E Cream
0.1% mometasone furoate	Elocon® Ointment
0.1% halcinonide	Halog® Ointment
0.25% desoximetasone	Topicort® Cream/Ointment
CLASS 3—UPPER MID-STRENGTH	
0.05% fluocinonide	Lidex-E® Cream
0.05% desoximetasone	Topicort® LP Cream
CLASS 4—MID-STRENGTH	
0.1% clocortolone pivalate	Cloderm® Cream
0.1% mometasone furoate	Elocon® Cream
0.1% triamcinolone acetonide	Aristocort® A Cream, Kenalog® Ointment
0.1% betamethasone valerate	Valisone Ointment
0.025% fluocinolone acetonide	Synalar® Ointment
CLASS 5—LOWER MID-STRENGTH	
0.05% fluticasone propionate	Cutivate® Cream/Cutivate Lotion
0.1% prednicarbate	Dermatop® Cream
0.1% hydrocortisone probutate	Pandel® Cream
0.1% triamcinolone acetonide	Aristocort® A Cream, Kenalog® Lotion
0.025% fluocinolone acetonide	Synalar® Cream
CLASS 6—MILD	
0.05% alclometasone dipropionate	Aclovate® Cream/Ointment
0.05% desonide	Verdeso™ Foam, Desonate Gel™
0.025% triamcinolone acetonide	Aristocort A Cream, Kenalog Lotion
0.1% hydrocortisone butyrate	Locoid Cream/Ointment
0.01% fluocinolone acetonide	Derma-Smoothe/FS® Scalp Oil, Synalar® Topical Solution
CLASS 7—LEAST POTENT	
2%/2.5% hydrocortisone	Nutracort® Lotion, Synacort® Cream
0.5- 1% hydrocortisone	Cortaid® Cream/Spray/Ointment and many other over-the-counter products

Corticophobia

- Prevalence of 21-84%
  - Nonadherence
- Top concerns
  - Skin “thinning”
    - Unusual when used as directed
      - Inappropriate use!
    - Sometimes reversible

Chopra R et al. Ann Allergy Asthma Immunol. 2017 Nov;119(5):435-440.
Hong E et al. Pediatr Dermatol. 2011;28:393-6.

Hypopigmentation

- Post inflammatory!
- From Eczema!
- Intralesional steroids
- Inappropriate use
  - High potency
  - Prolonged

Corticophobia

- Systemic Absorption
  - Impact on growth/development
  - Suppression of HPA axis
    - Overuse
    - Prolonged exposure
    - High potency
    - Occlusion

Ellison JA et al. Pediatrics. 2000;105:794-9.

Topical Calcineurin Inhibitors (TCI's)

- Tacrolimus (12/00)
  - Moderate to severe
    - Protopic® ointment 0.03%

      2-15 yr
    - Protopic ® ointment 0.1%

      >15 yr
- Pimecrolimus (12/01)
  - Mild to moderate
    - Elidel® cream 1%

      2 yrs and older

Safety of TCI's

- Safety and efficacy demonstrated in multiple clinical trials
- Do not lead to tachyphylaxis
- Do not cause side effects of topical steroids

Czarnecka-Operacz et al. J of German Soc of Derm 2012; 10: 167-172.

Black Box

- Jan 2006
- Theoretical risk of malignancy
- Little to no systemic absorption
- Prevalence of malignancy is less than or similar to that in general pediatric population

Siegfried EC et al. am J Clin Dermatol 2013;14:163-78.

Cancer Risk for TCI's

- Systematic review and meta-analysis
  - 52 RCT's and 69 non-randomized studies
    - 86 included children (18 with infants)
    - 3.4 million patients
    - Followed for up to 10 yrs (mean of 11 months)
  - No increased risk of cancer
    - Infants, children, adults

Devasenapathy et al. Lancet Jan 2023;17:13-21.

Efficacy of TCI's

- Mild to moderate
- Maintenance/prevention
- Delicate areas
  - Eyelids
  - Groin/genitalia
- Cons
  - $$$
  - Insurance coverage

Eucrisa™

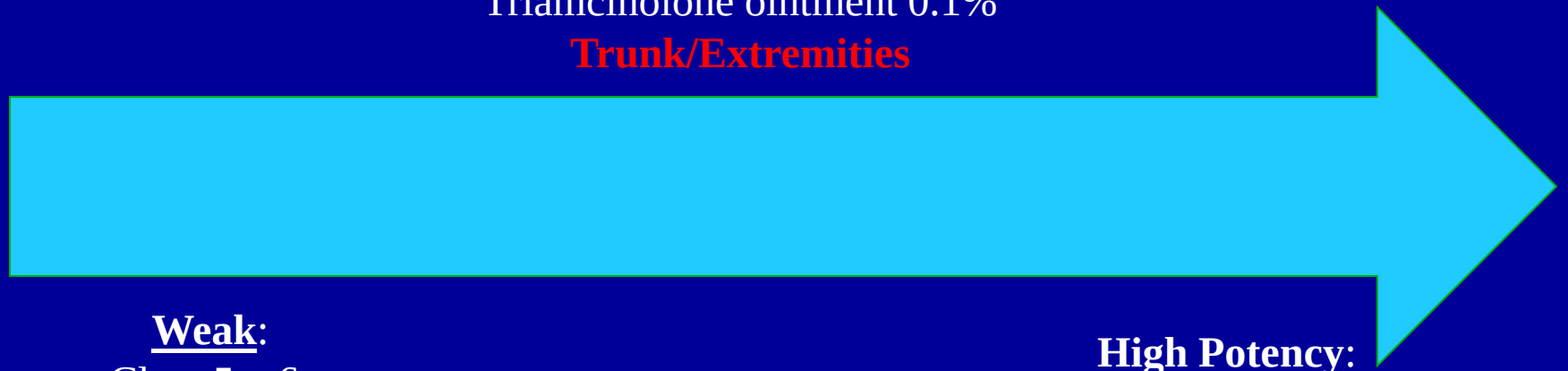
- Crisaborole ointment 2%
- FDA approved 12/2016
  - Mild to mod AD in 2 yr +
  - ≥ 3 months in 3/2020
- MOA
  - Inhibits PDE4
    - Suppresses pro-inflammatory cytokines
      - Decreases inflammation

Eucrisa™

- Efficacy
  - 2 DB RCT's (n=1522)
    - Approx 30% achieved "clear" or "almost clear"
    - Vehicle alone: 25.4% and 18%
  - Safety
    - Burning
      - 4% (?)
      - Vehicle: 1%
- Cost
  - 60 gm is > $600

Paller AS et al. J Am Acad Dermatol 2016;75:494-503.

Mid-Potency:
Class 4:
Triamcinolone ointment 0.1%
Trunk/Extremities



Weak:
Class 5 – 6:
Hydrocortisone ointment 2.5%
Desonide ointment

High Potency:
Class 2:
Mometasone ointment 0.1%
Nummular eczema

Super High Potency:
Class 1:
Clobetasol ointment 0.05%

Pimecrolimus
Tacrolimus 0.03%, 0.1%
Face, skin folds

Topical Regimen

- Practical Approach
  - Appropriate strengths/amounts
  - Realistic time frame
  - Written instructions/action plan


043895H

Bleach Baths?

- Background
  - higher *S. aureus* colonization
    - >70% vs 10-20%
  - AD severity correlates with *S. aureus* density
  - Staph infections and overgrowth can trigger flares
    - Pro inflammatory cytokines

Totte JE et al. Br J Dermatol. 2016;175:687-695.

Bleach Baths

- Method
  - 1/4 cup bleach to 1/2 tub water
  - 1 tsp per gallon
- Conflicting evidence
  - Cochrane review
    - no significant improvement if not clinically infected
  - RCT twice weekly bleach baths and intranasal mupirocin 5 times per month
    - significant improvement over placebo

Bath-Hextall FJ et al. Br J Dermatol 2010; 163:12-26.
Huang JT et al. Pediatrics 2009; 123:e808-e814.
Chopra R et al. Ann Allergy Asthma Immunol. 2017 Nov;119(5):435-440.

Wet Wraps

- For flares and recalcitrant disease
- Enhance penetration
- Decrease water loss
- Prevent scratching
- Studies show topical steroid + wet wraps superior to emollient + wet wraps

Schnopp C et al. Dermatology 2002;204:56-9.

Wet Wraps

- Bathe as usual
- Pat dry
- Apply topical steroid
- Apply Vaseline
- Apply warm, damp clothing
- Apply dry clothing

Oral Steroids?

- Avoid!
- Lasting remissions rare
- Rebound/relapse is common
- Multiple side effects
- Exceptions:
  - Severe diffuse flares
  - During initiation of other systemic therapy
  - Needed for co-morbid condition (eg, asthma)

Sidbury R et al. J am Acad Dermatol. 2014;71:327.

Eczema and Food Allergy

- Controversial
- Confusing for parents
  - >90% reported their child had food-induced AD
  - 75% had tried changes in diet
- Associated
  - May coexist
    - Prevalence of food allergy in children with AD = 15 – 40%
- Generally not causal (trigger)
- Younger age, more severe disease

Boyce et al. J Am Acad Dermatol. 64(1): 176 – 192.
Lio. Cutis. Nov 2022;110(5):264-266.

Eczema and Food Allergy

- When should patients be referred for allergy testing?
  - If child ≤ 5 y/o with moderate – severe AD
    - Persistent dz despite optimized topical management
  - If reliable h/o immediate allergic rxn after ingestion of a specific food

Dupixent™

- Dupilumab
- Monoclonal antibody
  - Inhibits IL-4 and IL-13
- SQ qother week or qmonth

Fishbein AB et al. J Allergy Clin Immunol Pract 2019; Article in Press.

Dupixent™

- FDA approved for mod to severe AD
  - 18 yr+ in 3/2017
  - 12 to 17 yr in 3/2019
  - 6 to 11 yr in 5/2020
  - 6 months to 5 yr in 6/2022
- Multiple studies supporting efficacy and safety
  - AE's: injection site reactions, conjunctivitis

Adbry™

- Tralokinumab
- MOA: IL-13 antagonist
- FDA approved 12/2023
- 12-17 yr old
- Moderate to severe AD
- SQ qother week

Adbry™

- Adverse Events
  - Hypersensitivity reaction
  - Conjunctivitis/keratitis
  - Parasitic infection
- Efficacy
  - RCT 192 patients 12-17 yr
    - Week 16: 21% clear/almost clear vs. 4% in placebo

JAK Inhibitors

- JAK/STAT Pathway
  - Janus Kinase/Signal Transducers and Activators of Transcription
- Mediates cellular responses to cytokines and growth factors
- Essential role in the dysregulation of immune responses in AD
  - exaggeration of Th2 cell response
  - the activation of eosinophils
  - suppression of regulatory T cells

Opzelura ™

- Ruxolitinib cream 1.5%
- FDA approved 9/2021
  - Short-term non-continuous
  - Mild to moderate
  - Non-immunocompromised patients
  - ≥ 12 yr old
  - Up to 8 weeks
  - 3-20% TBSA and/or 60 gm/week

Opzelura ™

- MOA
  - JAK 1/2 inhibitor
- AE:
  - Most common
    - Nasopharyngitis
  - Serious
    - Primarily oral JAKi’s
- Cost: 60 gm > $2,000

Rinvoq ™

- Upadacitinib (oral)
- FDA approved 1/2022
  - Moderate to severe
  - Refractory
  - ≥ 12 yr old (40 kg)
- MOA: JAK1 inhibitor

Rinvoq ™

- Adverse Events:
  - Common: URI, acne
  - Black Box (based on data for adult RA pts on tofacitinib)
    - Serious infections (most on other IS drug)
    - All cause mortality
    - Malignancy
      - Lymphoma, lung
    - MACE (≥ 50 yr, at least one CV risk factor)
      - MI, stroke
    - Thrombosis

Rinvoq ™

- Other
  - GI perforation
  - Lab abn’s
    - Neutropenia
    - Lymphopenia
    - Anemia
    - Elevated lipids
    - Elevated LFT’s

Rinvoq ™

- Efficacy
  - 3 randomized clinical trials
    - 552 adolescents
  - “effective treatment for adolescents with moderate-to-severe atopic dermatitis, with an acceptable safety profile”

Paller et al. JAMA Dermatol. 2023;159(5):526-535.
doi:10.1001/jamadermatol.2023.0391

Cibinqo ™

- Abrocitinib (oral)
- FDA approved 1/2022 (adults only)
  - 2/2023 for ≥ 12 yr old
  - Moderate to severe
  - Refractory
  - MOA: JAK1 inhibitor

Cibinqo ™

- Adverse Events
  - Common: nasopharyngitis, nausea, headache
  - Black Box Warning: same as Rinvoq
- Other
  - Retinal detachment
  - Lab abn’s
    - Thrombocytopenia
    - Lymphopenia
    - Elevated lipids
    - Elevated CPK

Cibinqo ™

- Efficacy
  - RCT 284 patients 12-17 yr old
    - 60-70% saw 75% improvement within 3 months

Eichenfield et al. JAMA Dermatol. 2021;157(10):1165-1173. doi:10.1001/jamadermatol.2021.2830

Stay Tuned

- Topical and systemic therapies:
  - Calcineurin inhibitors
  - PDE4 inhibitors
  - Janus Kinase (JAK) inhibitors
  - IL inhibitors
  - Microbial interventions
  - Other?

Mandlik DS et al. Immunopharm and Immunotox 2021, 43(2):105-125.

Thank you!

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