Comprehensive Atopic Dermatitis Care:

Enhancing Patient Care through Collaborative Management

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Speakers

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Dr. Lee receives research funding from Pfizer Inc.

Program Goals

1. Review strategies to overcome AD gaps (e.g., identification, prevention, reducing disease burden)
2. Assess pharmacologic/non-pharmacologic options for pediatric AD treatment
3. Discuss strategies for coordination of care with specialists based on evidence-based standards
4. Review the QoL burden of AD (e.g., emotional/psychosocial, sleep disturbance, decreased productivity)

Diagnosis, Epidemiology, and Pathogenesis

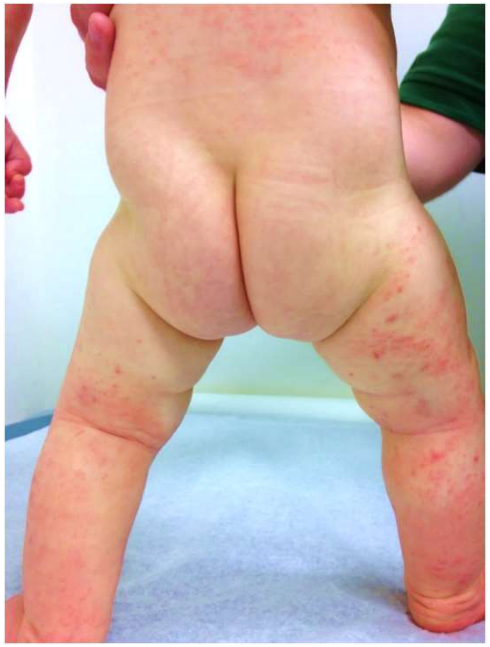
Features

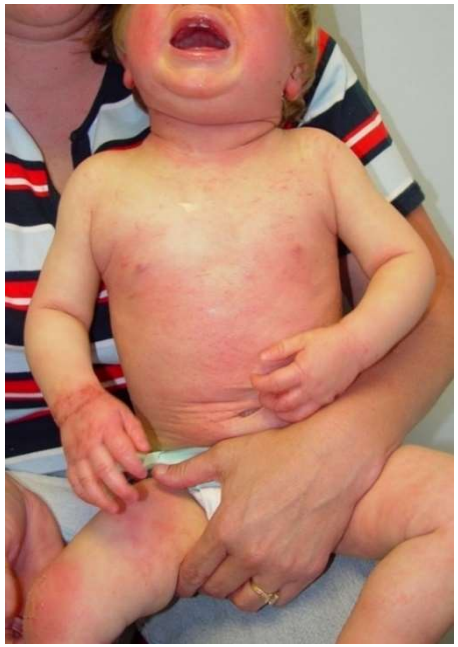
Chronic, pruritic, inflammatory skin disease characterized by

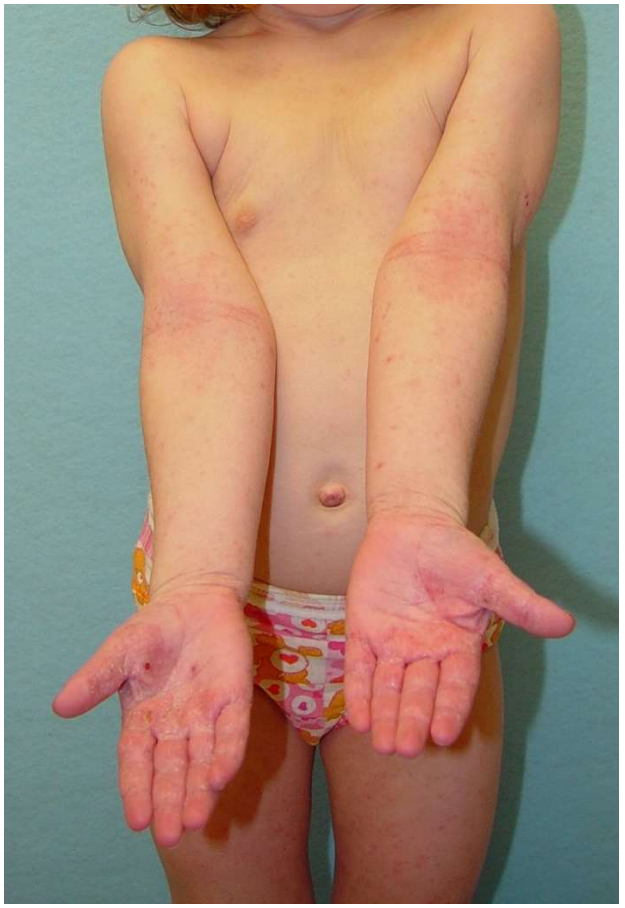
- Onset under age 5
- Acute flares
- Eczematous change
  - erythema
  - induration, papulation
  - excoriation
  - lichenification
- Distribution
- Associated skin conditions (minor diagnostic criteria)
- Associated morbidities
- Familial occurrence

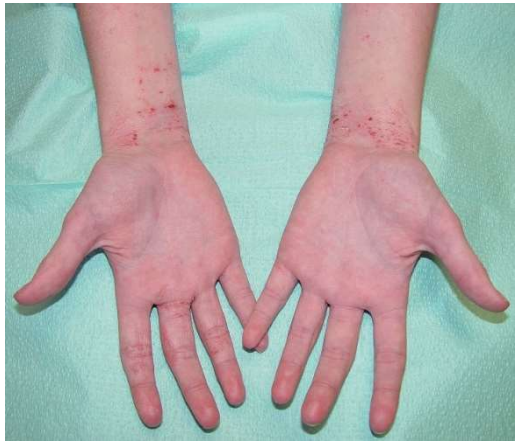
Ring J et al. *J Eur Acad Dermatol Venereol.* 2012;26:1045-1060.

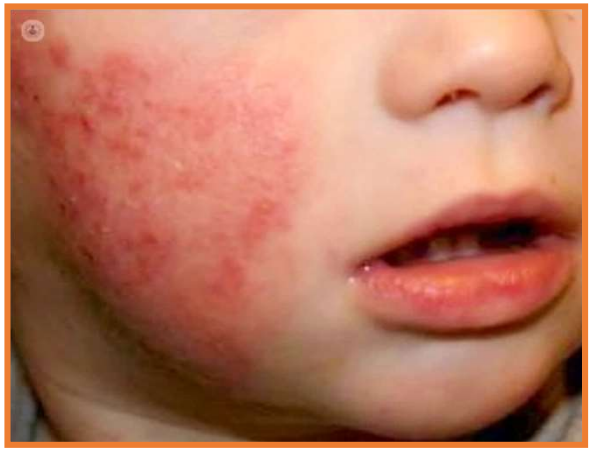
Age-Related Characteristic Distribution



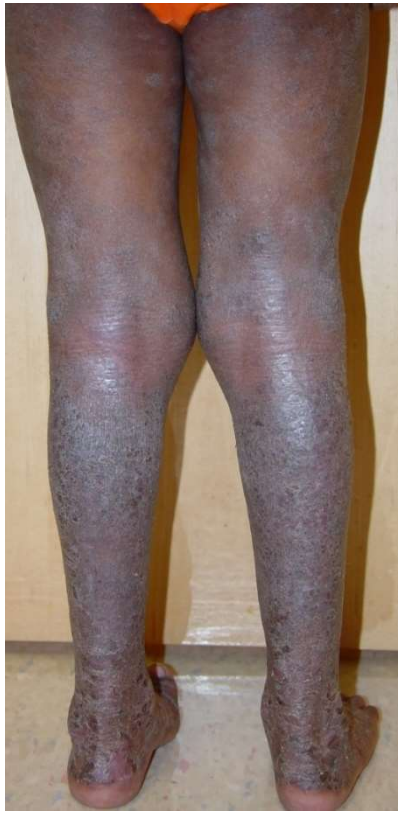


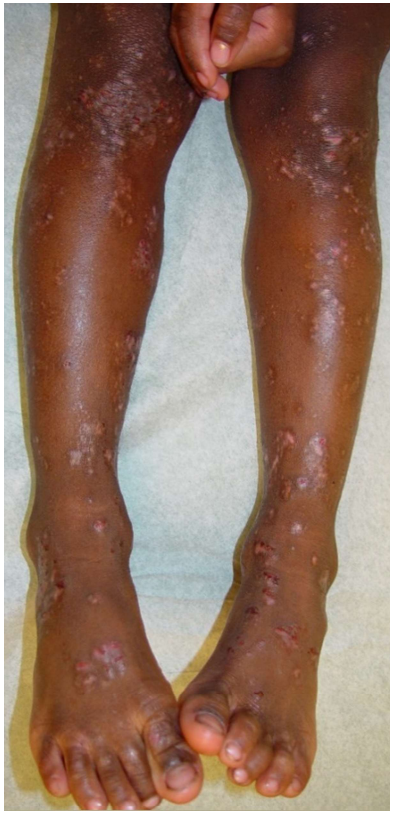


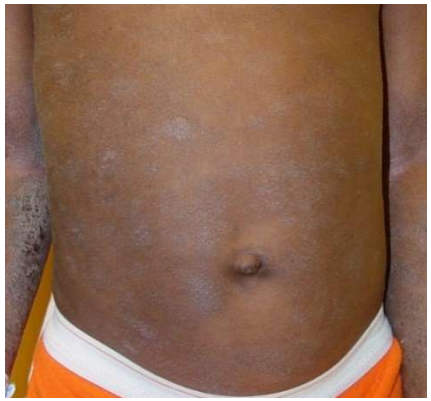




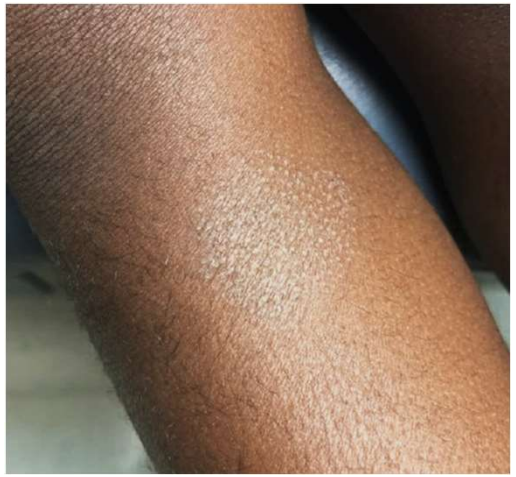
Unique Features in Skin of Color

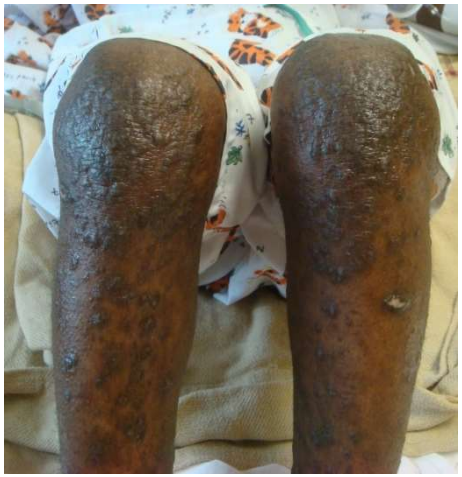






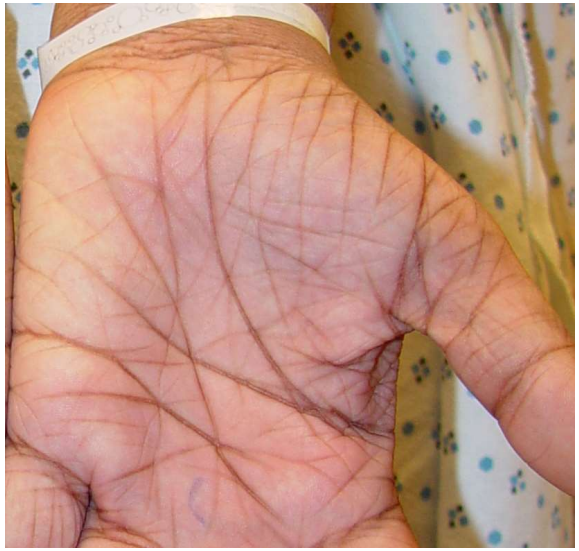
- Follicular/papular & nummular morphology
- Obscured erythema
- Prominent lichenification
- Dyspigmentation

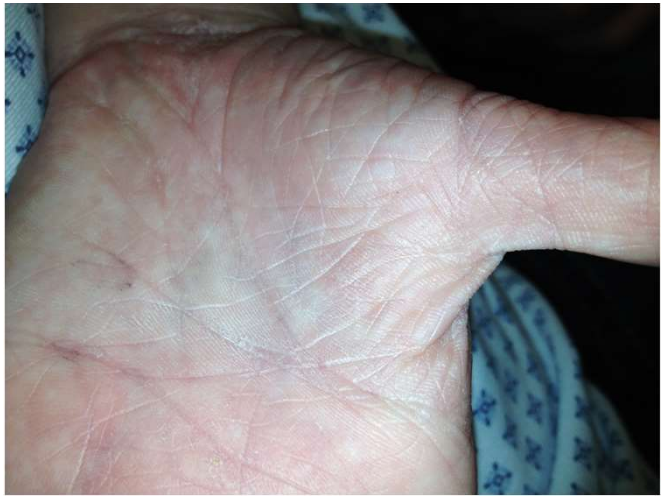


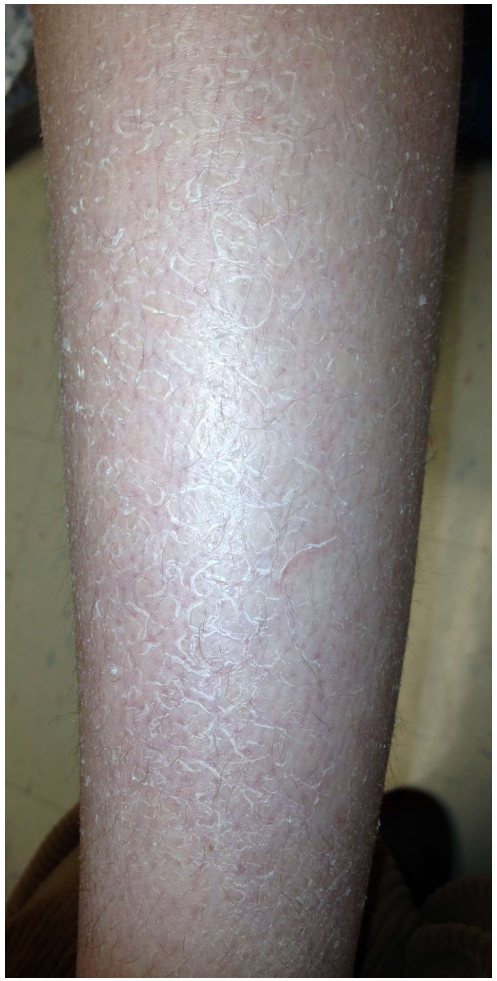


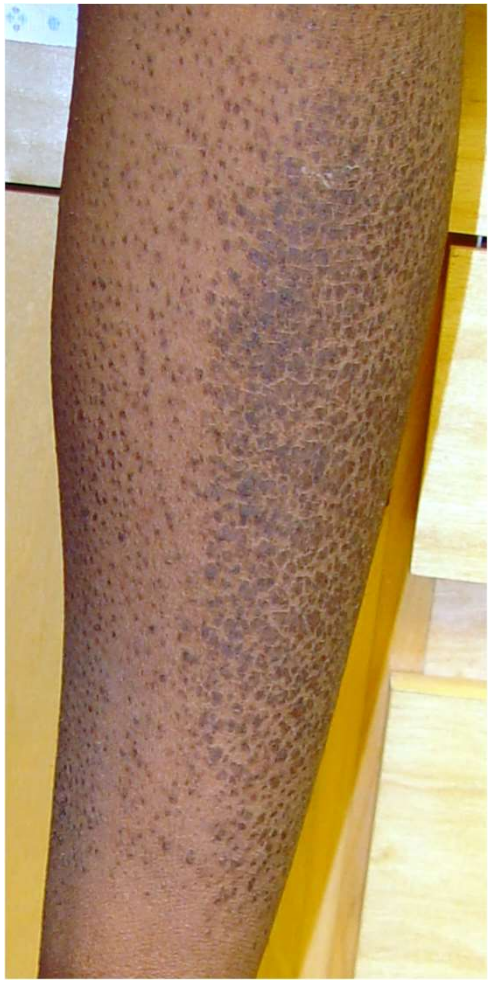
Atopic dermatitis across the lifespan. Available at: https://atopicdermatitis.net/across-lifespan/

Associated Skin Conditions: Ichthyosis Vulgaris

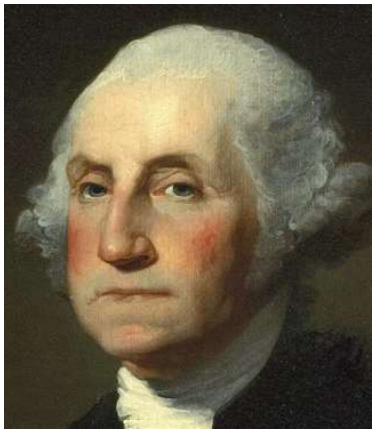
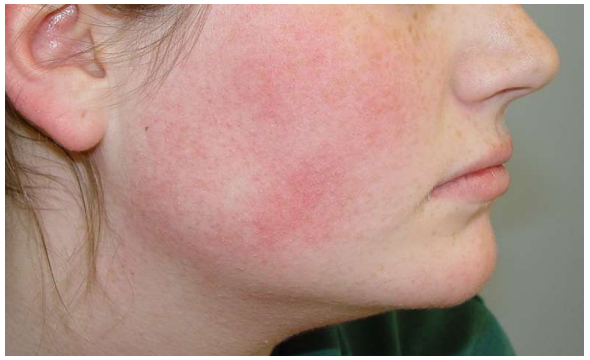
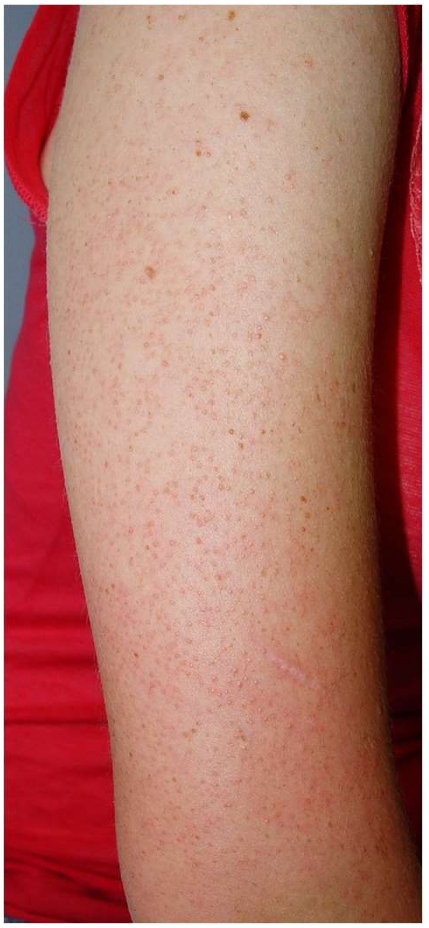


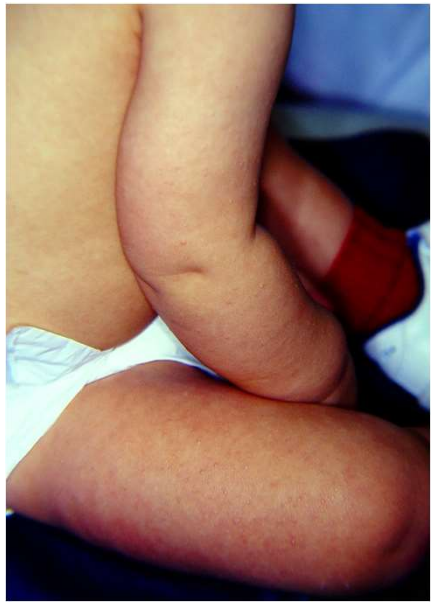




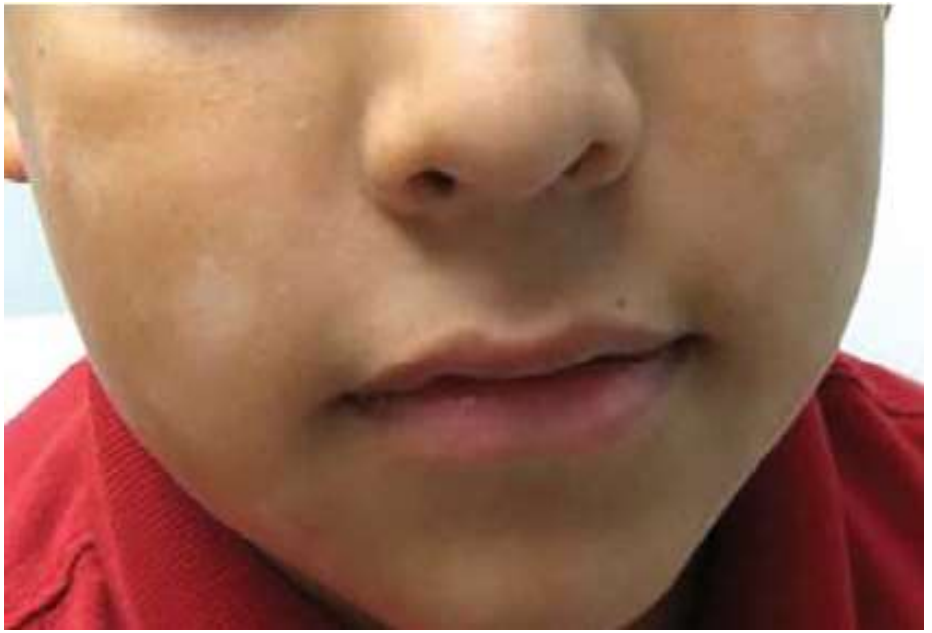


Associated Skin Conditions: Keratosis Pilaris Vulgaris

Associated Skin Conditions: Pityriasis Alba



Impact: Epidemiology

- Onset <5 yrs of age in 90%
- ~1/4 of adults with AD report adult-onset of disease
- Increasing prevalence: 13% in the US
  - 10-20% of US school children
  - Adult-onset in 2-8%
- Increasing costs: ~$5.3 billion/yr
- Greater impact on quality of life than type I DM

Arkwright P, et al. *J Allergy Clin Immunol.* 2013;1:142-51. Lee HH, et al. *JAAD*. 2019;80(6):1526-32.e7. USDHHS/Maternal and Child Health Bureau. *National Survey of Children's Health*. 2007. Drucker AM, et al. *J Invest Dermatol*. 2017;137:26-30.

Multifactorial Pathogenesis

Multiple conceptual models have been developed

- Skin-barrier dysfunction
- Immune dysregulation
- Dysbiosis
- Environmental triggers
- Genetics

Napolitano M et al. *G Ital Dermatol Venereol.* 2016;151:403-411. McLean WH. *Br J Dermatol.* 2016;175(suppl 2):4-7. Paternoster L, et al. *Nat Genet.* 2015;47:1449-1456. Tamari M, Hirota T. *J Dermatol.* 2014;41:213-220. Sasaki T, et al. *J Dermatol Sci.* 2014;76:10-15.

Management

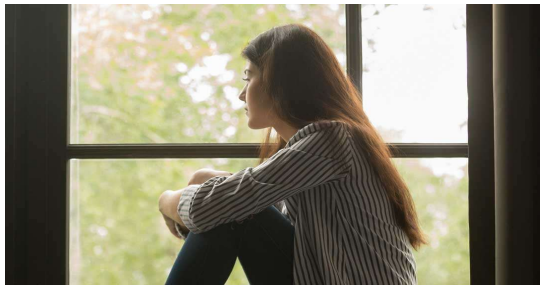
Impact: Patient-Reported Symptoms

Itch Frequency	**86% reported itch occurring every day**
Itch Severity	**61% reported “severe” or “unbearable” itch**
Itch Duration	**42% reported itch lasting ≥18 hours/day**
Sleep Disturbances	**55% reported sleep disturbances ≥5 nights/week**
Pain/Discomfort	**77% reported “moderate” or “extreme” pain or discomfort**

N=380 adults with atopic dermatitis, nearly all of whom were treated with topical therapies during the past 3 months; half of the patients were also treated with systemic therapies during the past year.

Simpson EL, et al. *J Am Acad Dermatol*. 2016;74(3):491-498.

Impact: Psychosocial Impact



50%

of adults AD report negative effect on sexual relationships

40%

of adults with AD report negative effect on social relationships

39%

of children are teased or bullied due to their AD

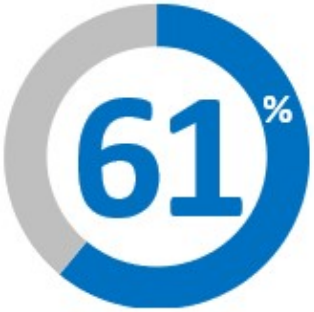
- **83% of teens with AD avoid at least 1 everyday activity**
- **46% of teens with AD report negative effects on school performance**

Zuberbier T, et al. *J Allergy Clin Immunol.* 2006;118(1):226-232. Davis D, et al. *Semin Cutan Med Surg.* 2017;36(3):1-5.

Impact: Sleep

Parents reported child's sleep was disturbed by AD

Children cosleeping with parents



Parents reported their sleep was disturbed by AD

Parents reported being bothered by cosleeping

Sleep disturbance, sleep quality, and cosleeping are directly associated with severity of AD.

N=270 parents of children 0-6 years with atopic dermatitis, responding to a phone survey.
Chamlin SL, et at. *Arch Pediatr Adolesc Med*. 2005;159(8):745-750. Ramirez FD, et al. *JAMA Pediatr*. 2019;173(5):e190025.

Video: Tina and Lydia

The AD Circle of Comprehensive Care: "Integrated 5 I's"

bleach baths, avoid topical allergens, topical corticosteroids/calcineurin inhibitors/crisaborole, systemic anti-inflammatory medication

ointment emollient, wet wraps, ambient humidity

Impaired Skin Barrier

Inflammation

Itch

Integrated Care

Psychosocial assessment tools, referrals, letters

Infection Risk, Infection

intervention; non-sedating antihistamines for urticarial itch

bleach baths, surveillance testing, appropriate antimicrobial medication

Impacted Sleep

short-term sedating antihistamines, sleep hygiene

5 I's concept courtesy of Lisa Shen MD.

Diagnosis

Audience Response Question

Which of the following is true of AD in skin of color as compared to AD in fair skin?

1. More frequent extensor involvement on extremities
2. Greater likelihood of follicular/papular eczema
3. Increased nummular and more severely lichenified lesions
4. More difficult to appreciate erythema
5. All of the above

Audience Response Question

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AD: Classic Distribution Changes with Age

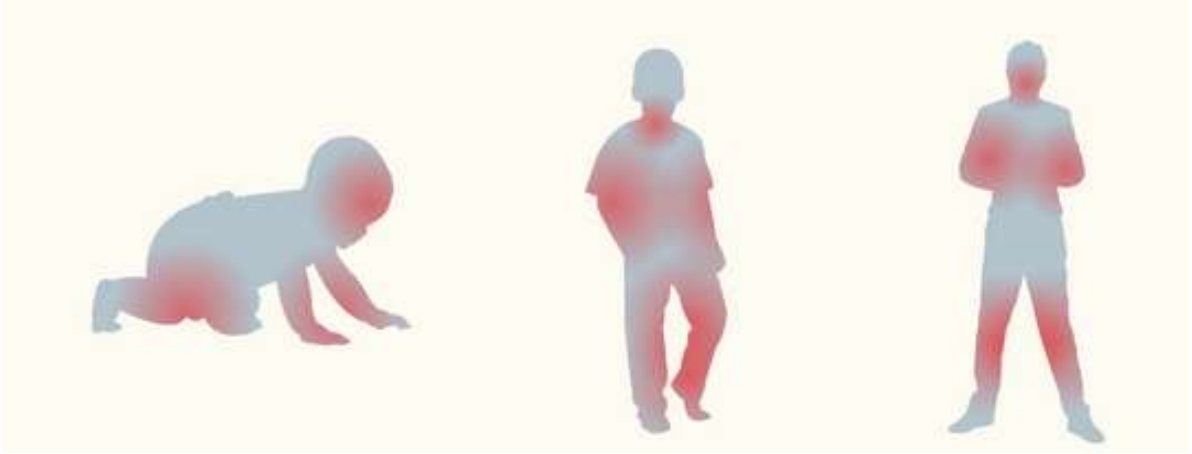
Skin of Color

Clinical diagnosis

- Historical features
- Distribution and morphology of skin lesions
- Associated clinical signs

Infants	Children	Adults
Usually facial; extensor extremities	Flexural folds of extremities; wrists; ankles	Hands; feet; head; neck

Greater extensor involvement of extremities along with flexural; more follicular/papular eczema; increased nummular and more severely lichenified lesions



Atopic dermatitis across the lifespan. Available at: https://atopicdermatitis.net/across-lifespan/

AAD Simplified AD Diagnostic Criteria

"Essential"

- Pruritus
- Eczema (acute, subacute, chronic)
  - Typical morphology and age specific patterns
  - Chronic or relapsing history

"Important"

- Early age of onset
- Atopy
  - Personal and/or family history
  - Immunoglobulin E reactivity
- Xerosis

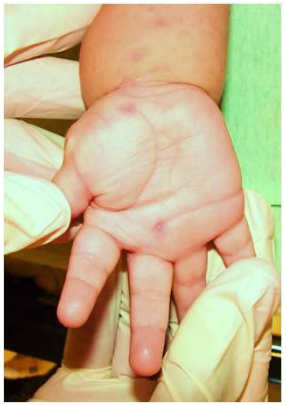
"Associated Features"

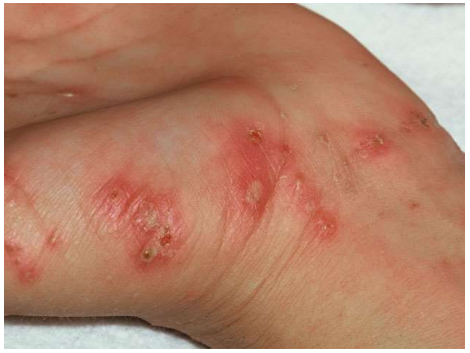
- Atypical vascular responses (e.g., facial pallor, white dermographism, delayed blanch response)
- Keratosis pilaris/ pityriasis alba/ hyperlinear palms/ ichthyosis
- Ocular/periorbital changes
- Perifollicular accentuation/ lichenification/ prurigo lesions

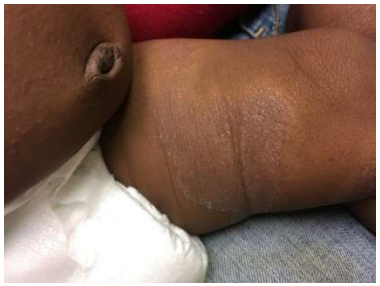
AAD. Atopic Dermatitis: Diagnostic Recommendations. Available at: https://www.aad.org/practicecenter/quality/clinical-guidelines/atopic-dermatitis/diagnosis-and-assessment

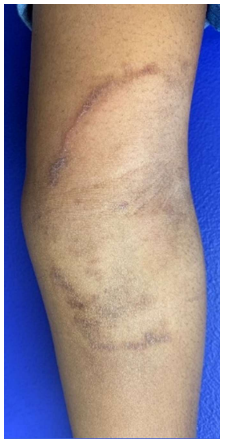
Other Common Misdiagnoses

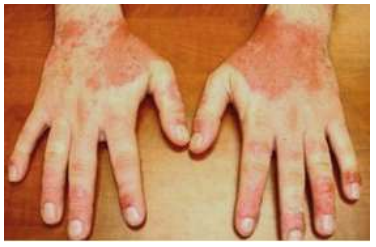
Scabies	Burrows; palm/sole involvement
Tinea Incognito	Border accentuation, hair thinning
Non-Atopic Eczema	Occupational exposures, winter eczema

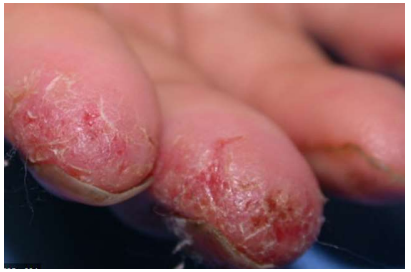












Treatment

Treatment Should Consider Patient Preferences & Capabilities

AD is chronic, and characterized by episodic flares

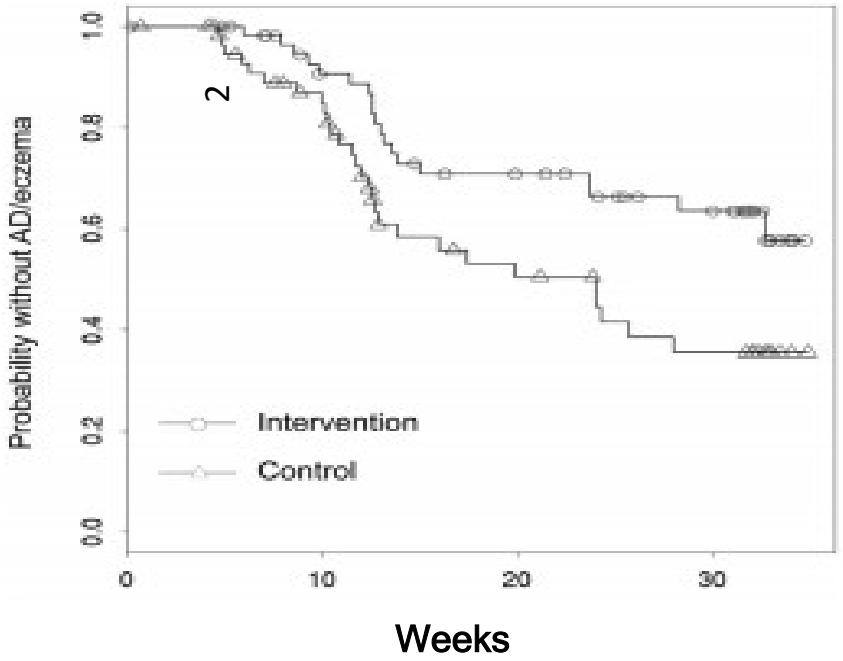
- Consider benefits and risks of each option
- Consider patient preference and adherence
- Treat flares
- Address disease chronicity

Goals of Treatment

- Mild or absent symptoms
- Undisturbed activities of daily living
- Decrease acute flares

Wang D, Beck LA. *Am J Clin Dermatol.* 2016;17:425-443. Saeki H et al. *J Dermatol.* 2016;43:1117-1145. Ring J et al. *J Eur Acad Dermatol Venereol.* 2012;26:1045-1060.
Ring J et al. *J Eur Acad Dermatol Venereol.* 2012;26:1176-1193.

Mixed Clinical Evidence on the Impact of Bland Skin Care in AD Prevention

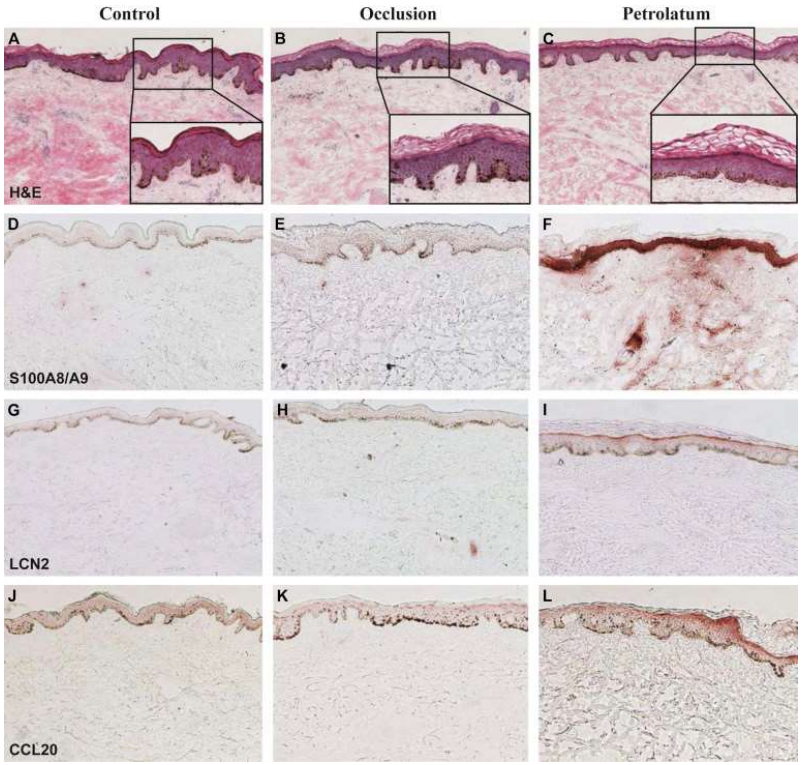


- Cochrane review of 77 studies: most moisturizers showed “some beneficial effects” (e.g., reduced flares/time to flare) with no single agent better than another[2]
- Recent abstracts of large-scale studies in unselected patients report no protective effect[3,4]

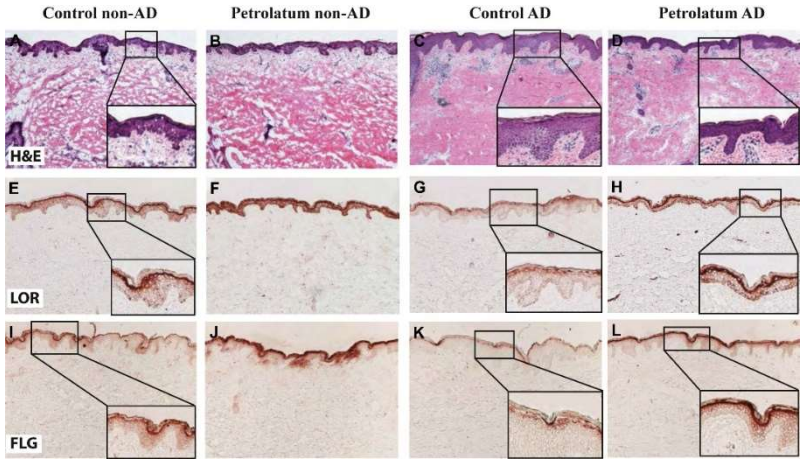
1: Horimukai K et al. *J Allergy Clin Immunol* 2014;134:824-30. 2: van Zuuren et al. Cochrane Database Rev. 2017;2017(2):CD012119. 3: Chalmers JR, et al. *Lancet* 2020;395(10228):962-72. 4: Skjerven H, et al. *Lancet* 2020;395(10228):951-61.

Petrolatum Increases Antimicrobial & Structural Skin Peptides

Increased AMP expression and SC integrity



Increased LOR/FLG expression

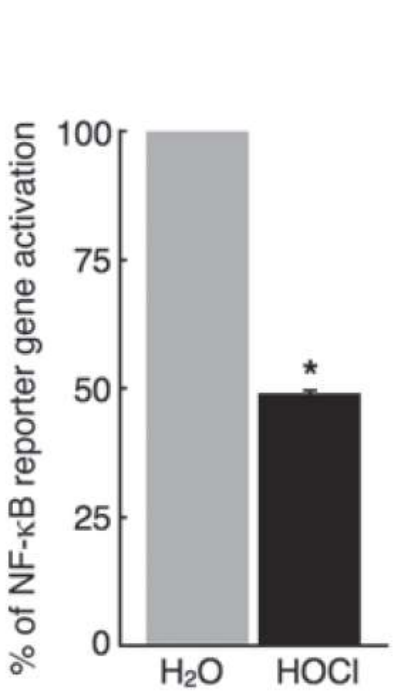


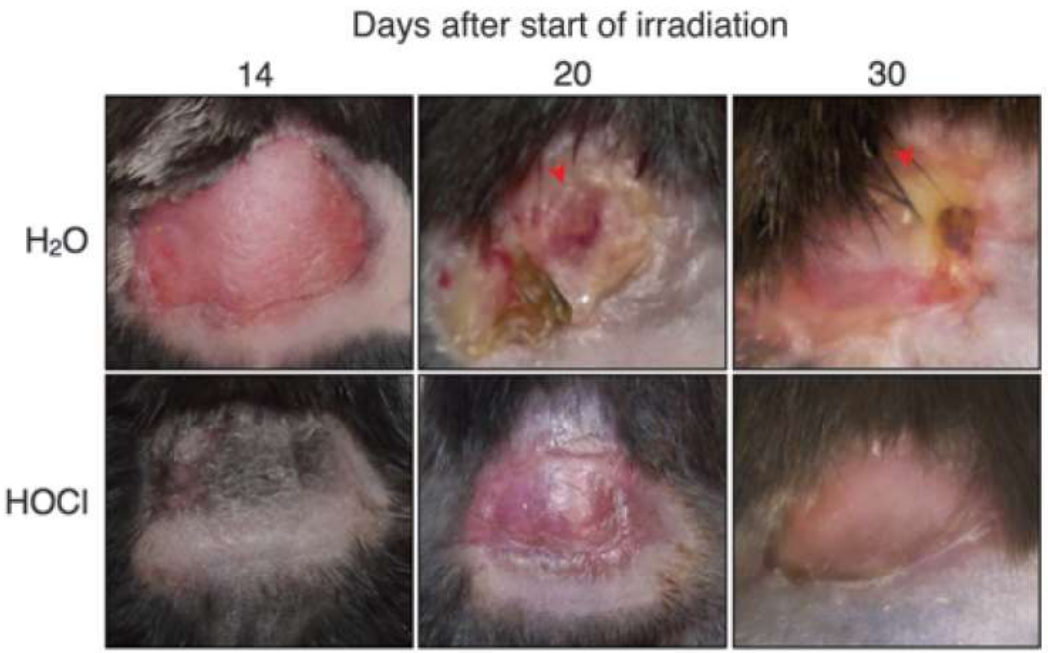
- Cost-effective
- Doesn't burn or sting
- Non-allergenic

- Tactile aversion
- Beware added fragrance
- Risk of rubbing

Czarnowicki T, et al. *J Allergy Clin Immunol*, 2016;137(4):1091-102.

Dilute Bleach Soaks are Anti-inflammatory





Mice pretreated with 0.005% bleach x 30 min before 6 Gy irradiation daily X 10d had less inflammation and ulceration.

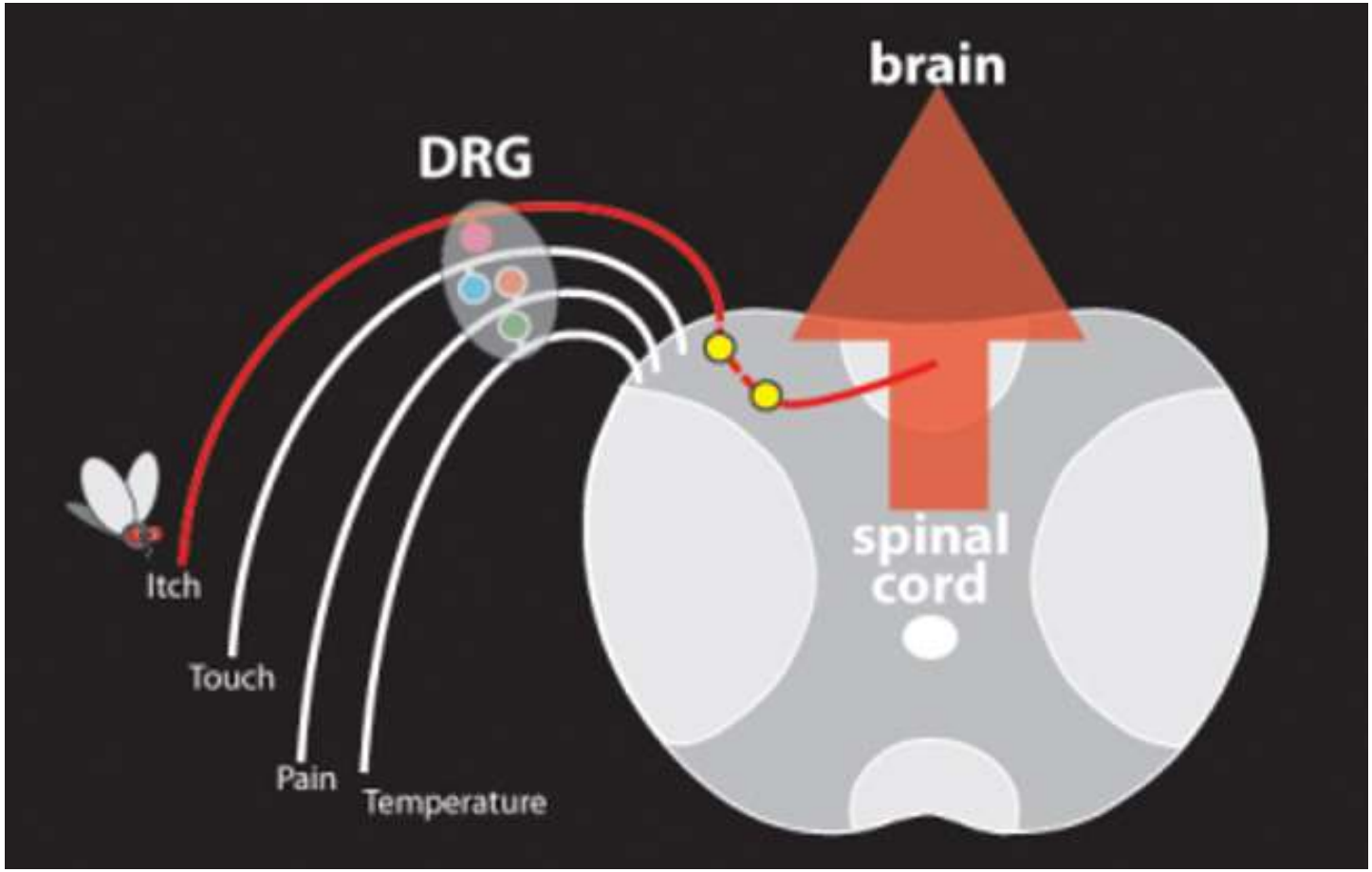
Leung T, et al. *J Clin Invest.* 2013;123(12):5361-5370.

Mixed Clinical Evidence on the Efficacy of Bleach Baths in Treating AD

- Improved disease in patients with bacterial infections[1,2]
- No more effective than plain water bathing[3,4]

1. Maarouf M, et al. *Dermatitis*. 2018;29(3):120-6.
2. Wong SM, et al. *J Dermatol*. 2013;40(11):874-880
3. Hon KL, et al. *J Dermatolog Treat*. 2016;27(2):156-162
4. Chopra R, et al. *Ann Allergy Asthma Immunol*. 2017;119(5):435-440

Itch Intervention with Cooling
Itch and Cold Perception Compete



Mishra S, et al. *Science*. 2013;340(6135):968-71. https://directorsblog.nih.gov

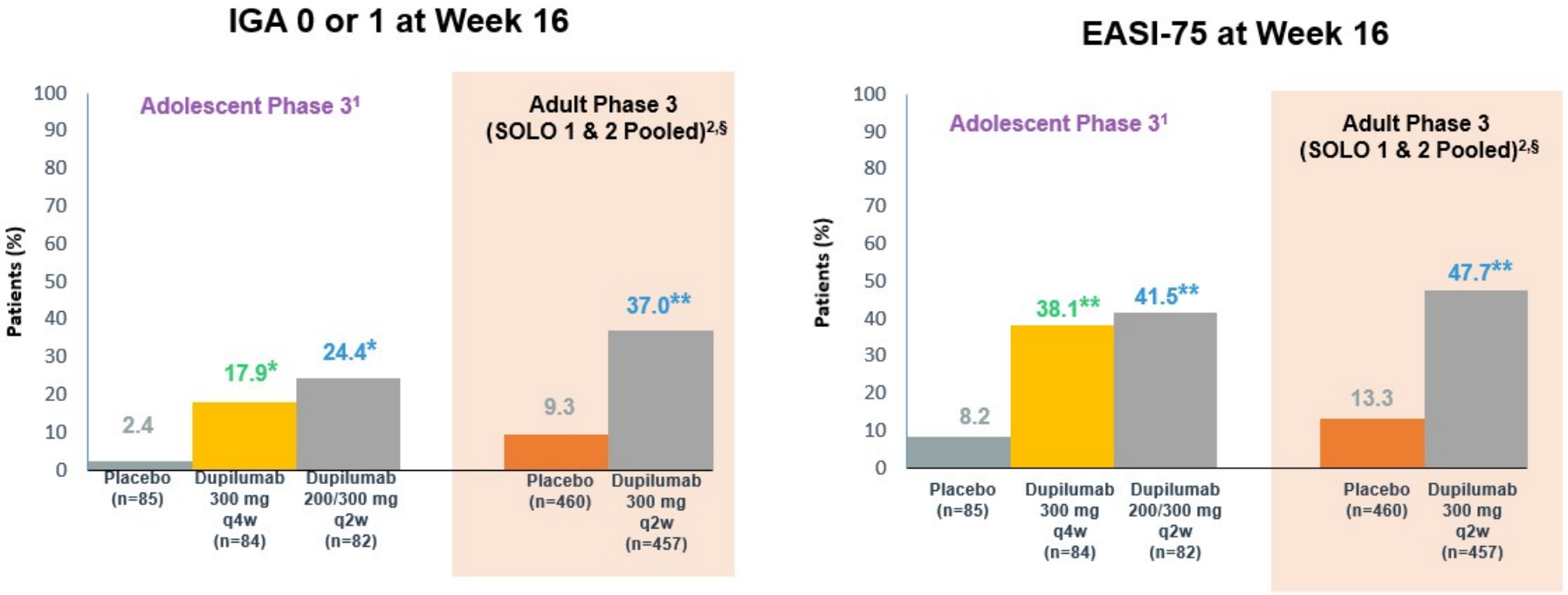
AD Severity Informs *Customized* Stepped Therapy

	MILD	MODERATE	SEVERE
Maintenance	**Skin Care** Daily bath (bleach optional) Liberal, frequent moisturizer use **Trigger avoidance** Irritants, potential topical allergens, low ambient humidity **Consider comorbidities**	**Consider specialist referral** **Add bleach baths, wet wraps** **Maintenance TCI or crisaborole** • Up to twice daily • Monitor quantities **Intermittent TCS** • Medium potency • 15 days per month • Monitor quantities	**Specialist referral** **Consider comorbidities** **Short-term aggressive treatment** • Wet wraps • Hospitalization **Phototherapy** **Systemic Immunosuppressants** • Cyclosporine A • Methotrexate • Mycophenolate mofetil • Azathioprine **Dupilumab**
Flare	**TCS** • Low-to-medium potency • PRN up to 15 days per month • Monitor quantities	**TCS** • Medium-to-high potency • Consider complicating factors	**Other considerations** • Non-adherence • Infection • Misdiagnosis • Contact allergy

TCS, topical corticosteroid; TCI, topical calcineurin inhibitor

Adapted from Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120(1):10-22.

Dupilumab: Targeted Biologic Therapy; FDA-approved age ≥6



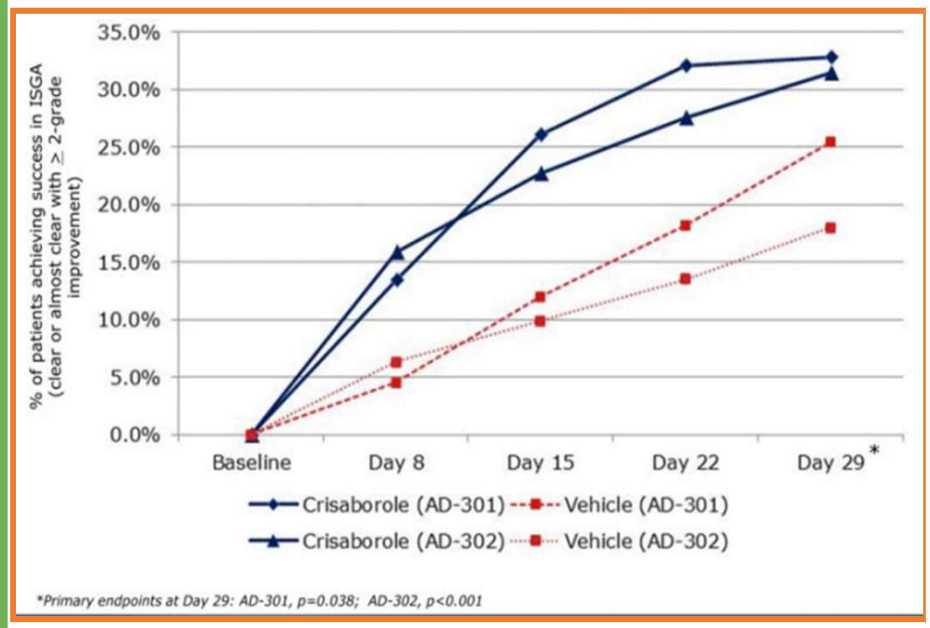
*P<0.001 vs placebo, **P<0.0001 vs placebo.

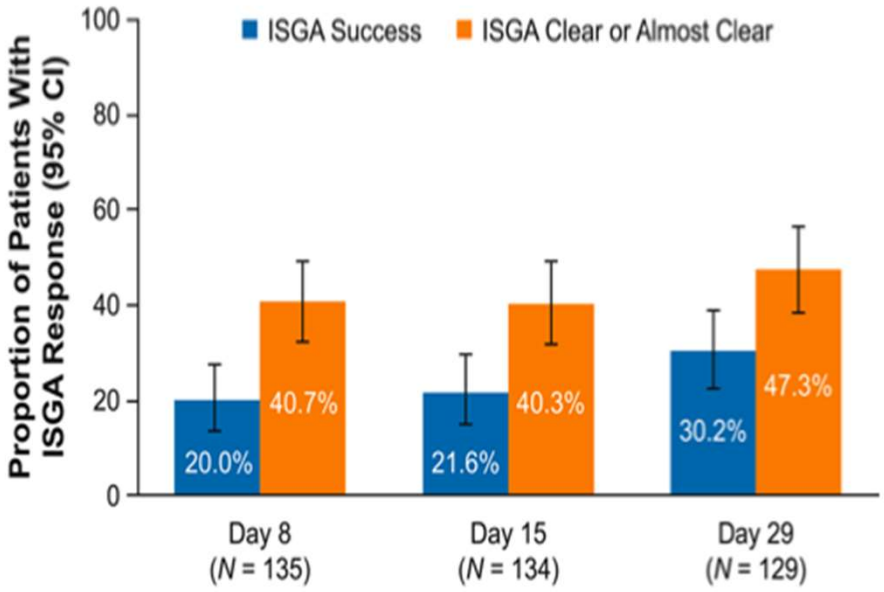
- Most common AEs: injection site reaction, conjunctivitis

†Patient considered non-responder after rescue treatment use. ‡EASI-75 at week 16 was a coprimary endpoint outside of the US. §The primary endpoint in the SOLO 1 & 2 trials was IGA score 0 or 1 and ≥2-point improvement from baseline at week 16. EASI-75, reduction of EASI (Eczema Area and Severity Index) score by at least 75% from baseline; IGA, Investigator's Global Assessment; q2w, every 2 weeks; q4w, every 4 weeks.

1. Simpson et al. Oral presentation D3T01.1L, EADV 2018. 2. Ferrándiz et al. Oral presentation FC07.09, EADV 2018.

Crisaborole: Topical PDF-4 Inhibitor FDA-approved Age ≥ 3 months





Most common AE: application-site pain/discomfort/erythema

Jarnagin K et al. *J Drugs Dermatol.* 2016;15:390-396. http://leaddiscovery.blogspot.com/2015/07/anacor-reports-positive-phase-3-data-on.html.
Schlessinger J, Shepard JS, Gower R, et al. Safety, Effectiveness, and Pharmacokinetics of Crisaborole in Infants Aged 3 to < 24 Months with Mild-to-Moderate Atopic Dermatitis: A Phase IV Open-Label Study (CrisADe CARE 1). *Am J Clin Dermatol.* 2020;21(2):275-284.

Investigational Therapies for Moderate-to-Severe AD

	Agent	Class	Phase
Monoclonal Antibodies	Tezepelumab	Anti-TSLP	2
	Fezakinumab	Anti-IL-22	2
	ISB-830	Anti-OX40	2
	Nemolizumab	Anti-IL-31Rα	3
	Lebrikizumab	Anti-IL-13	3
	Tralokinumab	Anti-IL-13	3
Small Molecules	Upadacitinib	JAK 1 inhibitor	3
	Abrocitinib	JAK 1 inhibitor	3
	Baricitinib	JAK 1/2 inhibitor	3
	Adriforant	H4R antagonist	2

Optimizing Care Strategies

Recommendations are Often Conflicting and Confusing

1: To bathe or not to bathe?

2: Soap or no soap?

3: How strong a steroid can be used on face and folds?

4: Cream vs. ointment Rx?

5: Dietary restrictions/formula changes/IgE testing (and when?)

6: When to refer to dermatologist/allergist?

List courtesy of Margaret Lee, MD, PhD. Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120(1):10-22.

Video: Lisa

Practice Shared Decision-Making

- Spend time listening to the patient and/or caregiver
- Understand the patient's goals and expectations
- Clarify current medications and which ones are succeeding or failing
- Consider socioeconomic level and ability to adhere to treatment
- Explain the nature and severity of the disease
- Give treatment options, explaining the risks and benefits of each
- Work to find the right treatment plan
- Provide patient education materials and other support measures

Brar KK, et al. *J Allergy Clin Immunol Pract*. 2019;7:1-16.

Individualize Management

COMPLAINT	STRATEGY
Inconsistent recommendations	Clarify controversies
Confusing, unclear plan	Concise, written instructions (daily maintenance, intermittent flare control)
Medication phobia	Discuss relative risks of uncontrolled AD; emphasize skin care/trigger avoidance
Impact on family QOL	Better prevention; fast-acting flare plan
Impact on school performance	504 and other collaborative plans
Out-of-pocket expenses	Simple, safe, affordable products

Audience Response Question

True or false:

If a young infant develops chronic eczema, restrict dairy, peanut, egg, soy, seafood and wheat from a breastfeeding mother's diet and from early introduction of the infant's solid foods.

1. True
2. False

Audience Response Question

True or false:

If a young infant develops chronic eczema, restrict dairy, peanut, egg, soy, seafood and wheat from a breastfeeding mother's diet and from early introduction of the infant's solid foods.

1. True
2. False

Effective Topical Therapy Allays Food Allergy Concerns

Parents of children with AD often believe their child has a food allergy and the food causes AD.

- 95% of parents believed their child had food allergy that exacerbated AD
- 70% had positive food allergy tests; only 30% had history of immediate IgE reactions to food
- The level of concern about food reactions significantly decreased (from 7.7 to 4.0 on a 10 point scale; $P < 0.001$)
- Parental estimates of the number of food reactions pre- vs posttreatment declined 80% ($P = 0.001$) during effective topical therapy
  - Encouraged parents to refocus on direct skin care

N=23 children 3 to 11 years of age with chronic moderate to severe AD enrolled in a long-term study of topical tacrolimus, and their parents retrospectively assessed by questionnaire pretreatment and posttreatment about their AD and food allergy parameters.
Thompson MM, Hanifin JM. *J Amer Acad Dermatol*. 2005;53(2):S214-S219. Roerdink EM, et al. *Ann Allergy Asthma Immunol.* 2016;116(4):334-8. Manam S, et al. *Curr Opin Allergy Clin Immunol*. 2014;14(5):423-9.

NIAID Says Don't Change Maternal/Child Diet Without Proven Food Allergy

- In children <5 yo with moderate-to-severe AD, consider food allergy evaluation for milk, egg, peanuts, wheat, and soy if ≥1 of the following applies
  - — Child has persistent AD despite optimized management and topical therapy
  - — Child has a reliable history of an immediate reaction after ingestion of a specific food

- In patients without documented food allergy, it is **not** recommended to avoid allergenic foods to manage AD, asthma, or eosinophilic esophagitis

NIAID, National Institute of Allergy and Infectious Diseases. Boyce JA, et al. *J Allergy Clin Immunol*. 2010;126(6): 1105-1118. Greer FR, et al. *Pediatrics*. 2019;143(4):e20190281.

The AD Action Plan: As Clear & Comprehensive As Possible

- Plan summarizes all parts of skin care
- Baseline care never changes (or minor seasonal modifications)
- Flare vs maintenance therapy
- Most rapid improvement is seen when all aspects of skin care plan are done:
  - Consistently
  - At the same time

The AD Circle of Comprehensive Care: "Integrated 5 I's"

bleach baths, avoid topical allergens, topical corticosteroids/calcineurin inhibitors/crisaborole, systemic anti-inflammatory medication

ointment emollient, wet wraps, ambient humidity

Impaired Skin Barrier

Inflammation

Itch

Integrated Care

Psychosocial assessment tools, referrals, letters

Infection Risk, Infection

intervention; non-sedating antihistamines for urticarial itch

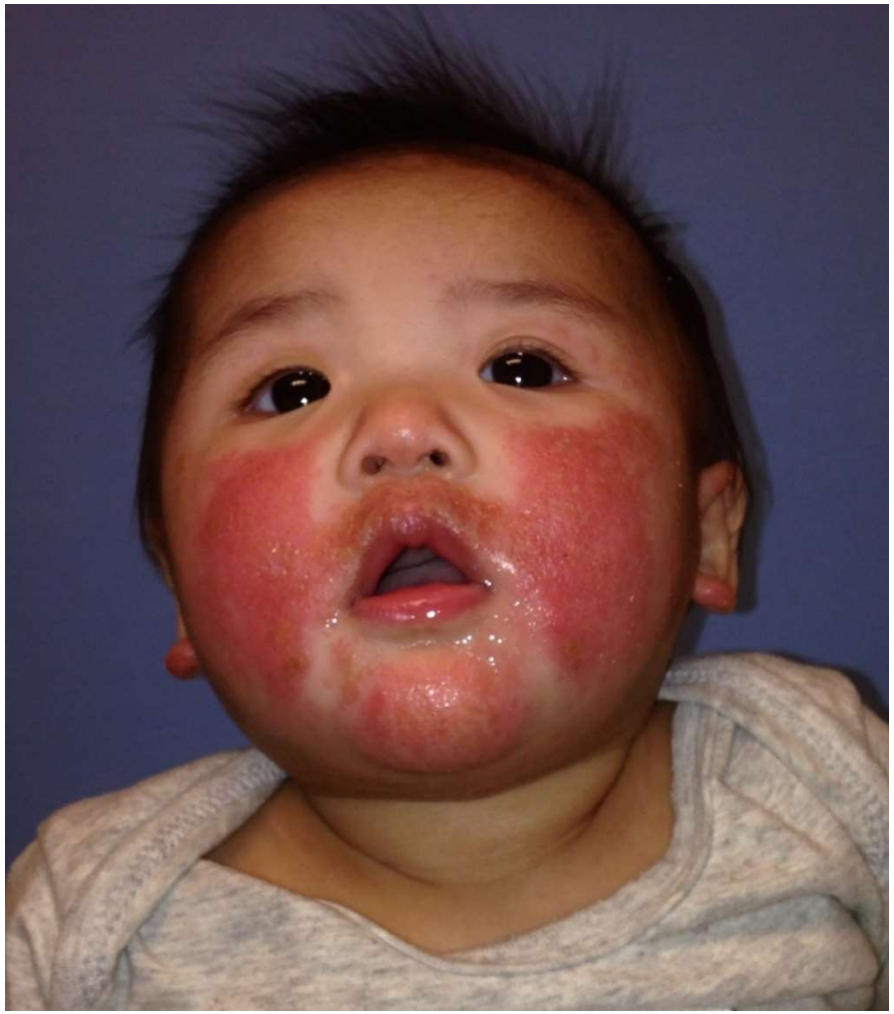
bleach baths, surveillance testing, appropriate antimicrobial medication

Impacted Sleep

short-term sedating antihistamines, sleep hygiene

5 I's concept courtesy of Lisa Shen MD.

First Step: Put Out the Fire



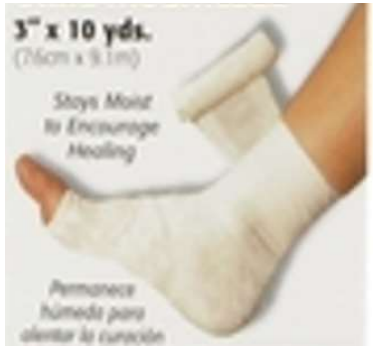
Putting Out the Fire

1) Aggressive skin care
   - Frequent bathing
   - Bland emollients
   - Higher potency topical medications
   - Wet wraps
2) Consider infection
3) Antihistamines for allergy triggers
4) Promote restful sleep
5) Itch intervention

Wraps

www.adrescuewear.com

http://www.flyintheface.com/plastic%20mulch.html

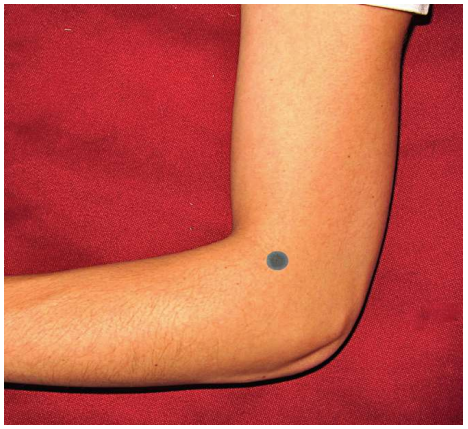


Itch Intervention
"Stop Scratching!" Doesn't Work

Avoid Triggers
- Sweat
- Friction
- Microbes
- Low humidity

Skin Care Strategies
- Rinse/shower/bath
- Moisturizer
- Cold pack/cool compress
- Corticosteroid
- Wraps
- Squeeze or pat

Distraction Strategies
- Fun
- Relaxation
- Delay scratching
- Acupressure



LeBovidge JS, et al. *Clin Rev Allergy Immunol*. 2016;138(2);325-34. Lee KC, et al. *Acupunct Med*. 2012 Mar;30(1):8-11. Kapur S, et al. *Allergy Asthma Clin Immunol*. 2018;14(suppl 2):52.

Second Step: Long-Term Control

Proactive

- daily maintenance skin care
- recognize and avoid triggers

Reactive

- intermittent, insufficient medication use

Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747.
Torrelo A, et al. *Actas Dermosifiliogr.* 2013;104:409-417.
Thaci D, et al. *J Eur Acad Dermatol Venerol.* 2010;24:1040-1046.
Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:1218-1233.

Sample Plan for "Fire Prevention"
AD Maintenance

1) Steroid maintenance plan if needed
2) Continue bland emollients
3) Continue wraps over emollient alone (optional)
4) Behavioral replacement for itch
5) Multidisciplinary team involvement

Optimizing Specialist-PCP Communication Helps Optimize Care

Diagnosis: The Critical Questions

- Are complaints/symptoms consistent with AD diagnostic guidelines?
- Is lesion location/presentation consistent with AD for the patient's age?
- What treatments have been effective/not effective to date?
- Skin biopsy or lab tests to rule out other causes?

Best Practices: Suggestions for Improving Communication/Collaboration

- Follow up w/ severe pts in 2-4 weeks to assess efficacy; reinforce compliance
- Telemedicine: improves access to patients and specialist input/triage
- Consider increasing quality of life assessments (disturbed sleep, school, work)
- Develop referral protocols with local dermatologists for truly urgent issues

Summary

- AD is chronic and challenging to treat, and often results in significant impairments in patient's quality of life.
- Diagnosis is based primarily on clinical findings, rather than genetics or biomarkers.
- Directions in the treatment AD:
  - Increased understanding of pathogenesis
  - Implementing the "Circle of Complete Care"
  - Proactive vs. reactive care
  - Expansion in treatment choices
- Treatment choices must take into account individual patient characteristics and patient preference.

Useful Resources

Society for Pediatric Dermatology: Educational Videos
https://pedsderm.net/for-patients-families/patient-education-videos/

American Academy of Dermatology: Learning Modules
https://www.aad.org/education/basic-derm-curriculum/suggested-order-of-modules/atopic-dermatitis

National Eczema Association:

- Educational Videos: https://nationaleczema.org/videos/
- Tools for School: https://nationaleczema.org/tools-for-school/

Thank You!

Questions/Answers