

Atopic Dermatitis: Treatment and care

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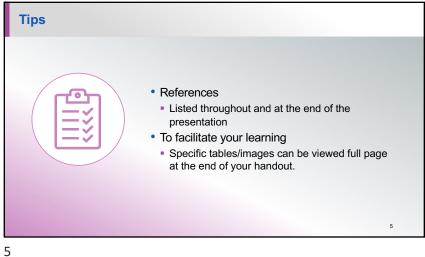
Disclosures

- Speaker's Bureau for Abbvie, Beiersdorf, Eli Lilly, Janssen, Sanofi Genzyme, Sanofi-Aventis/Regeneron[®], and Sun Pharma
- Strategic Advisor and Medical Board Member: Arcutis Biotherapeutics, Incyte Labs, Leo Pharma, and Novartis.
- No experimental or investigational use of drugs or devices will be presented.

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Objectives

- At the end of this presentation, the participant will be able to:
- Recognize symptoms and causes of atopic dermatitis.
- Review the tests and exams necessary for immediate treatment, diagnosis and care.
- 3 Outline and implement follow-up care.
- Demonstrate understanding of recent updates on the latest research, trials, and interventions.







A Brief Introduction to Atopic Dermatitis (AD) One of the most common Affected 7% of children circa chronic skin disorders in 1960, but 25% today America affecting nearly 30% 35 million Americans have of people with past history or active AD, and the incidence current AD. continues to grow. Prevalence of this condition has risen dramatically during the last three decades.





Atopic Dermatitis Notes from the World

- Prevalence of AD is very high world-wide.
- Often associated with asthma, allergic rhinitis and food allergies
- The strongest genetic risk factor for developing AD is in European-descent peoples; but African-Americans tend to have the most serious cases.
- Black children have higher risk for asthma and lower risk of allergic rhinitis and food allergy; while completely opposite for White children.



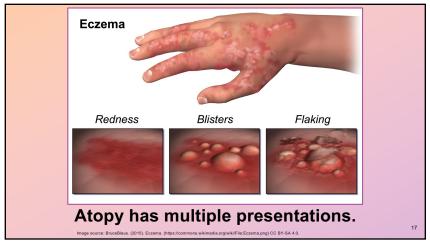




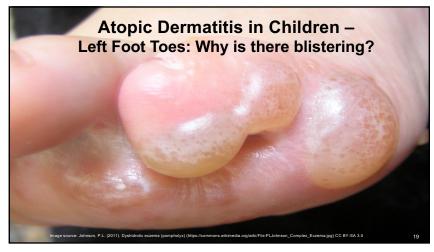


The Official Definition

- A genetically predisposed condition manifesting as exaggerated responses (vasodilation, pruritus, bronchoconstriction, IgE production) to environmental stimuli (irritants, allergens, drugs) predominately in the integument
- In dermatology, we believe that this is "asthma of the skin", or a cutaneous manifestation of deeper, systemic, inflammatory responses either endogenous/exogenous, or a combination of both.







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Careera — Atopic Dermatitis

Greek — Ekzema, from "ekzein," to break out, or boil over

Chronic, pruritic eruption that can appear anywhere on the skin

Associated with scales, fissures, cracking, bleeding and secondary bacterial infections

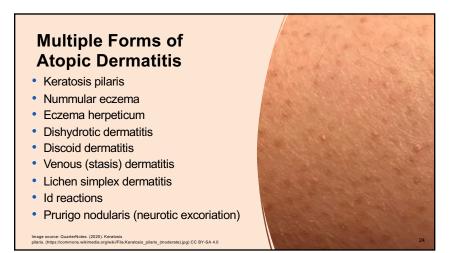


• Intense pruritus
 • Primarily the facial and bilateral involvement of extensors
 • Chronic, relapsing

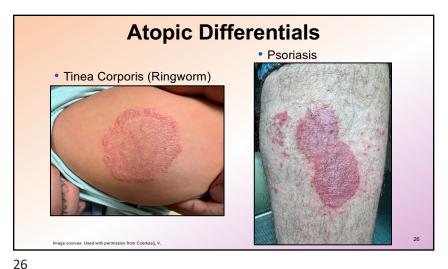
 • Personal and family history
 • Heavy scale, micro blisters, irregular borders
 • Skin texture and color changes

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Differential: Adverse Drug Reaction

- 10-year-old male with sudden outbreak of hives following antibiotic therapy from PCP
- Has a history of atopic dermatitis
- Exaggerated response



Image source: Used with permission from Czerkasij, V

Treatment Paradigms

- Ultimately, a robust discussion between patient and provider is necessary to learn which plan will result in the greatest safety, efficacy, durability, compliance, and access for the patient.
- The options are overwhelming, but generally come in the broad categories of life-style identification: Topical non-steroidal, topical steroidal, systemic steroidal, rarely used immunosuppressants, oral biologics, or injectable biologics.
- Monotherapy or combinations are possible.

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Many atopic dermatitis cases require attention to detail and only OTC care.

Cooler, quicker showers

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- Moisturizing cleansers and soaps
- Use OTC lotions, creams, and ointments within 3 minutes after a shower to trap residual moisture.
- Look up the "3-minute rule" and other great resources at the National Eczema Association website: https://nationaleczema.org

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Many atopic dermatitis cases require attention to detail and only OTC care. (continued)

 To prevent eczema flares, the Barrier Enhancement for Eczema Prevention (BEEP) trial did not show that use of OTC moisturizers or bathing prevented the development of eczema in infants, but patients did not worsen when compared to those who avoided moisturizers and bathing.

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Classic Irritants Alcohol-based hand gels Repeated washing of hands Strong soaps, detergents, disinfectants and home remedies Occupational settings Residual laundry detergents Nickel Neomycin topical ointment

Many atopic dermatitis cases require attention to detail and

Products that are dye-free,

PABA-free, paraben-free,

lifestyle changes first.

well-tolerated.

fragrance-free, and are labelled

as hypo-allergenic are generally

Patients sometimes appreciate

only OTC care. (continued)

Look for products that contain

ceramides, oatmeal, filaggrin,

dimethicone, petrolatum,

glycerin, and humectants.



The Bleach Bath Controversy

- On the "pro" side, ¼ cup to forty gallons (59.1 mL-151.4 L) seem to seriously lessen MRSA infections and result in clearer skin.
- On the "con" side, limited studies, can cause serious irritation to some, and odor is repulsive.
- The American Academy of Dermatology no longer recommends.
- The opinion is that some individuals may have low-level staph colonization on their skin excreting irritating toxins, and the diluted bleach may destroy this bacteria.

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Wet Wrap Therapy

- Generally effective approach of wrapping a person's body in cool, wet towels to relieve itching, burning, and inflammation
- Facilitates removal of scale
- Increases penetration of topical medication in stratum corneum: "soak and seal"
- Best reserved for acute episodes
- Inexpensive, safe, and absolutely organic
- Time-consuming and inconvenient

Wet-Wrap Therapy

- Details from a spa in Hot Springs Arkansas
- The wooden object over the tub is to help handicapped or obese people to enter the bathtub.
- Also known as a "Hubbard" tub

Image source: Beckers, W. (2006). Hydrotherapy. (https://en.wikipedia.org/wiki/Hydrotherapy) GNU Free Documentation License v 1.2



Phototherapy

- Controversial in studies –
 While sunlight is somewhat
 beneficial, heat and humidity
 trigger exacerbations for
 many patients.
- Erythema, skin pain, pruritus and irregular pigmentation results
- Very difficult to find this therapy
- Insurance usually does not reimburse.
- Different wavelength from psoriasis treatment

Irritant Management

- Swimming hydrates skin.
- Chlorinated pools have been observed as helpful as bleach baths.
- Consider whole house humidifiers: Optimal setting at 40–60% humidity
- Where possible, swimming until the skin has lightly "pruned," or wrinkled, is evidence of maximum water absorption.
- "I went to Florida, and my eczema disappeared!"

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Sleep quality disturbance in children with atopic dermatitis affects quality of life for all.

Foods as AD Trigger

- Aeroallergens (i.e., dust mites, animal danders, molds and pollens) are classic AD exacerbators.
- Foods as AD exacerbators undergoing intense studies, particularly dairy and sugar.

Image source: NIAID. (2017). Milk. (https://commons.wikimedia.org/wiki/File:Glass_of_Milk_(33657535532).jpg) CC BY 2.0



Foods as AD Trigger (continued)

Milk, egg, peanut, soy, wheat, fish and chocolate account for 90% of allergens thought to exacerbate AD.





Sugar – The Less, the Better

 Sugar is an enormous culprit responsible for inflammatory processes throughout the body.

 See reference: Intakes and sources of dietary sugars and their association with metabolic and inflammatory markers. Clin Nutr. 2018;37(4):1313-1322.



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Topical Non-Corticosteroidal Agents for Atopic Dermatitis

- Referred to as "medical device creams," approved by FDA for treatment of atopic dermatitis
- Medical device designation means that there is no active drug in the formulation.
- Non-corticosteroidal, lipid-rich, fragrance-free emulsion (Eletone[®])
- 70% oil dispersed in 30% water, and provides an ointment's occlusion yet feels like a cream

(continued)

Topical Non-Corticosteroidal Agents for Atopic Dermatitis

- Topical non-corticosteroidal skin cream (Mimyx®)
- Contains palmitamide MEA, lipid improver
- These products require prescription.
- They do not have generic name designations.

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Topical JAK Inhibitor Non-Steroidal Cream

- Ruxolitinib cream 1.5% is indicated for topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older.
- Labelling states that this product is not to be used with other Janus kinase (JAK) inhibitors or immunosuppressants.
- JAK inhibitors may cause serious infections, respiratory tract infections and not recommended in patients with active hepatitis B or hepatitis C.

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The Challenge of Location Treatment



Image source: Used with permission from Czerkasii V

- What would be your strategy when atopic dermatitis is present where skin is naturally thin, and absorption is to be avoided?
- What do you anticipate your patient's questions would be?

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Topical JAK Inhibitor Non-Steroidal Cream (continued)

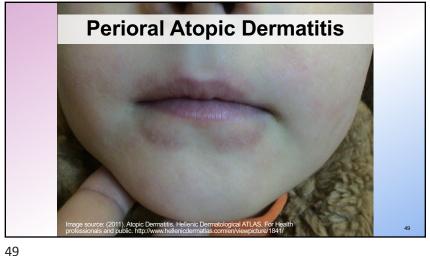
- May be used anywhere on the body every day for up to one-month
- This product is very helpful for periorbital, perioral, axilla, under breasts, groin and inguinal folds, where steroids would not be appropriate.

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Topical Non-Steroidal Ointment: Crisaborole

- Prescription non-corticosteroidal topical ointment for mild-tomoderate atopic dermatitis
- PDE4 anti-inflammatory action
- Approved age two years or older
- Apply twice a day for up to one-month.
- Most common adverse effect burning, itching, swelling at application site.
- Often best to refrigerate the product to use as a cooling agent on sensitive skin.

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Topical Non-Corticosteroidal Agents: Topical Calcineurin Inhibitors (TCIs)

- Original non-corticosteroidal milestone
- Tacrolimus ointment 0.03%
- Pimecrolimus cream 1%
- Strong safety profile for current length and difficult skin areas
- Boxed warning for lack of long-term (4+ years) safety data

Topical Non-Corticosteroidal Agents: Topical Calcineurin Inhibitors (TCIs) (continued)

- Back in 2006, TCIs had been given a "boxed" warning of possible malignancies occurring if used regularly over four
- No published study has proven the validity of this warning.
- Carefully weigh theoretical risks against benefits.

History of Corticosteroids Along with antibiotics and the revelation of DNA, one of the 20th centuries greatest medical discoveries

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Topical Corticosteroids

- · Important tool to gain control of AD
- 30 g covers entire skin of adult once
- · Seven potency classes based on vasoconstrictor assay.
- The lower the number, the longer the use allowed.
- Creams and ointments preferred as gels have drying glycol base.
- Good clinical skills required to balance potency and adverse effects.

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Topical Corticosteroids (continued)

- Corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.
- The complete mechanism of activity of topical corticosteroids is unclear.
- Thought to act by inducing increase of lipocortins to lessen inflammation

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Topical Corticosteroids (continued)

- · Adverse effects are both local and systemic.
- Atrophy and adrenal suppression
- · Studies do include children as young as age three months.
- Good example of a low potency corticosteroid include hydrocortisone 1% and desonide 0.05% creams.
- Midpotency is triamcinolone 0.1%.
- Super potent is clobetasol 0.05% or betamethasone 0.1%.

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Cutaneous absorption of topical corticosteroids is determined by many factors, especially the integrity of the epidermal barrier.

Image source: Cruz Roja, (2014). Topical medication. (https://en.wikipedia.org/wki/Topical.medication/Cream) CC BY 3.0

When Corticosteroids Attack: Interesting Observations from the Front Line

- Paradoxically, some patients will suffer from inflammatory episodes caused directly from topical corticosteroids.
- Multiple supporting studies find that midpotency clocortolone pivalate 0.1% has lowest potential to cause allergic reaction.

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Generalized Atophy

A Curious Comment from the NEA on Honey

- Medical-grade honey processed by gamma irradiation and filtration in a lab-setting and filtered from impurities or contaminants, is recommended if used topically for eczema.
- Available OTC

 Manuka honey, found in Australia and New Zealand from the nectar of the Manuka tree, has unique antimicrobial properties.

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A Sweet Option for Atopic Dermatitis

- Do not use raw honey from the beehive for topical use.
- Recognized for sealing in moisture, well-tolerated
- Excellent wound healing product for cracks and fissures.

Image source: Chiswick Chap. (2013). Long-tongued Amegilla bee on long tube of Acanthus ilicifolius flower. (https://en.wikipedia.org/wiki/Bee) CC BY-SA 4.0



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The Treatment Landscape: New Non-steroidal Oral Options – Upadacitinib

- 15 mg or 30 mg tablet 1 by mouth every day
- Treatment for patients ages 12 years and older with moderate to severe atopic dermatitis.
- JAK inhibitor that requires CBC, CMP, lipid and TB screening prior to initiation and again three months later and then annually.
- Fast-acting on itching in trials, with results in one day.
- Significant safety panel includes increased infections, blood clots, stroke, and cardiovascular events.

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The Treatment Landscape: New Non-steroidal Oral Options – Abrocitinib

- 100–200 mg tablet one by mouth every day
- Treatment for patients ages 18 years and older with moderate to severe atopic dermatitis.
- AK inhibitor that requires CBC, CMP, lipid, Hep B and C and TB screening prior to initiation and then annually or after dose increase.
- Effective medication in trials for scale and itching
- Significant safety panel includes increased infections, mortality, malignancies, blood clots, and cardiovascular events.

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The Treatment Landscape: Injectable Non-steroidal -**Dupilumab Targets IL-4 and IL-13**

- Dupilumab An FDA approved biologic for atopic dermatitis age ≥6 months.
- Most common adverse effects include allergic reactions, cold sores, and inflammation of the cornea.

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- Does not require prior labs or testing, nor does it interact with any known disease or medication.
- Initial subg injection for adults 18 years of age and older is 300 mg × 2, followed by 300 mg every other week for maintenance.

The Treatment Landscape: Injectable Non-steroidal -**Dupilumab Targets IL-4 and IL-13 (continued)**

- Pediatric and adolescent dosing is determined by age and weight.
- Can be used concurrently with corticosteroids if warranted
- Highly effective on pruritus

The Treatment Landscape: Injectable Non-steroidal -**Tralokinumab Targets IL-13**

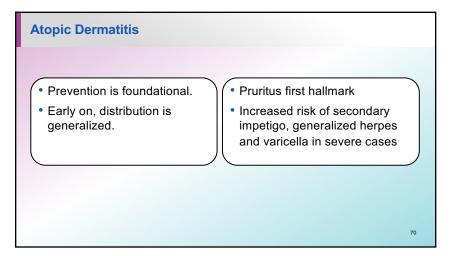
- Most common adverse effects include allergic reactions, cold sores, and inflammation of the cornea.
- testing, nor does it interact with any known disease or medication.

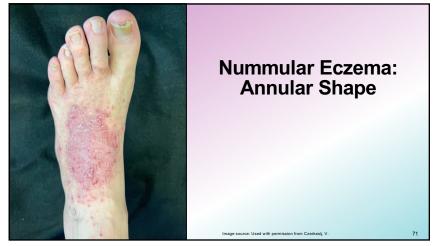
Does not require prior labs or

The Treatment Landscape: Injectable Non-steroidal -**Tralokinumab Targets IL-13 (continued)**

- Initial subq injection for adults 18 years of age and older is 150 mg × 4, followed by 150 mg × 2 every other week for maintenance
- Flexible dosing of q2w and q4w on patients less than 220 lb (100 kg)
- Can be used concurrently with corticosteroids if warranted
- Highly effective on pruritus









Is it really atopic dermatitis?

- A few classic differentials: Psoriasis, seborrheic dermatitis, allergic urticaria, adverse drug reaction, discoid lupus erythematosus, scabies infestation, or subclinical fungal infection
- Always ask for a robust patient history of condition and treatment.
- Don't be shy to biopsy the site.
- Always be aware of what the condition is not.
- Don't accept what the patient tells you they have: YOU are the professional.

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Lichen Simplex Chronicus



- Unusual case of 14-year-old Hispanic male who had an enlarging left areola over one year.
- Stated that it had slight itching, treated with anti-fungal by PCP.
- Punch biopsy revealed severe atopic dermatitis with components of lichen simplex chronicus.
- Class one steroid BID × 2 weeks completely resolved it.

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Common Keratosis Pilaris: Cooler Showers, Moisturizing Soap and OTC Daily Lotion





• Microbiome modulation: Exploring the *Staphylococcus* aureus theory of colonization on the skin and combining a topical bacterial "cocktail"

On the Horizon: Novel Treatments for AD Still in Trials

- Difelikefalin (DFK): A novel selective kappa-opioid receptor (KOR) agonist, on itching and lesional severity
- Oral tablet
- Novel, oral, selective sphingosine 1-phosphate receptor modulator of etrasimod, once daily 1 mg or 2 mg tablet

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End of Presentation Thank you for your time and attention.

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Topical Corticosteroids Potency Chart

- National Psoriasis Foundation® Potency Chart, available at https://www.psoriasis.org/sublearn03 mild potency
- The Dermatologist, available at https://www.hmpgloballearningnetwork.com/site/thederm

These are continuously updated to reflect generic and brand names.

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