Atopic Dermatitis: Biologics and Beyond

Keri Holyoak PA-C, MPH

Disclosures

- Arcutis (psoriasis/atopic dermatitis), Organon (psoriasis/atopic dermatitis), Galderma (acne), Incyte (atopic dermatitis), Pfizer (atopic dermatitis), Sanofi/Regeneron (atopic dermatitis).
- All relevant financial relationships have been mitigated.

Objectives

1. Highlight the differences in AD clinical presentation and differential diagnosis
2. Review multiple factors and symptoms that contribute to the assessment of AD disease severity and diagnosis
3. Apply patient, disease, and therapy-specific considerations in treatment decisions for patients with moderate-to-severe atopic dermatitis

“Eczema has been rightly called the keystone of dermatology, and he who fully masters its management is not only skilled in regard to treating one of the most common and distressing of all cutaneous diseases, but has acquired a knowledge of the principles of dermatologic practice which will assist in the treatment of many, if not all, other maladies of the skin.”

-L. Duncan Bulkley

Eczema and Its Management: A Practical Treatise Based on the Study of Three Thousand Cases of the Disease, 1881

Atopic Dermatitis Definition

Barrier dysfunction and immune activation	• Childhood onset: mutations in barrier function and immune genes • Acquired: chronic, ubiquitous environmental exposures driving epigenetic (genetic mutations) changes in keratinocytes and immune cells (air pollution, water hardness, laundry detergent, chemicals in clothing, likely more…)
Pruritus + eczema (spongiotic dermatitis) + a typical pattern that spares groin/axilla	• Cycles of flares and worsening symptoms • Average 7.5 flares per year
Is it childhood-onset or acquired?	• We can assume that 100% of AD in pts under 18 is inherited • Data suggests 50% of AD in adults is acquired • Most adults with AD do not have any atopic comorbidities • Acquired AD is generally not flexural

Air Pollution and Atopic Dermatitis, from Molecular Mechanisms to Population-Level Evidence: A Review

Raj P Fadadu [1,2,3], Katrina Abuabara [1,3], John R Balmes [3,4], Jon M Hanifin [5], Maria L Wei [1,2,*]

Editor: Hui-Tsung Hsu

PMCID: PMC9916398 PMID: 36767891

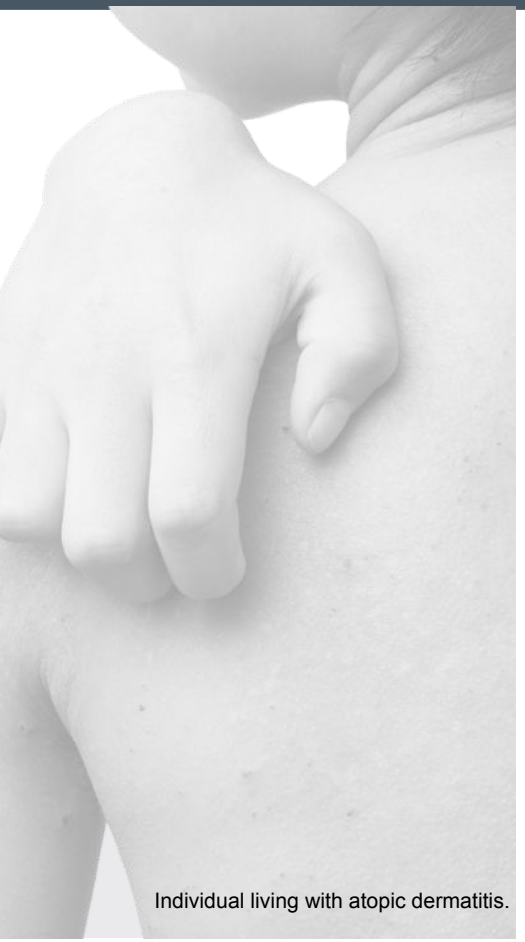
Air pollution?

- In “elderly-onset” AD air pollution was a 2x stronger risk than genetic risk
- Being in areas with bad air quality increase risk of AD by 13x
- Air pollution predicts flares in those on dupilumab
- Toluene Diisocyanate (TDI) in particular
  - Major source of TDI is catalytic converts in cars
    - Became mandatory on call cars in mid 1970”s

Diet?

- Gut microbiome play a big role (more than the skin microbiome)

Many patients with atopic dermatitis are not satisfied with their treatments and the time-intensive regimens involved



Individual living with atopic dermatitis.

Individual living with atopic dermatitis.

Atopic Dermatitis

2 in 3 patients

LESS THAN VERY SATISFIED

with the disease control achieved on their current topical treatment[1*]

More than half of patients reported spending

>5 hours per week managing their atopic dermatitis[2†]

*Based on data from a 2018 and a 2019 Adelphi AD Disease Specific Programme (DSP™) survey of adult (≥18 years) and pediatric patients (≤17 years) with atopic dermatitis, respectively, receiving topical therapies (n=398; 232 patients had evaluable responses).[1]

†Based on data from the 2019 More Than Skin Deep survey of caregivers and patients of patients with atopic dermatitis (N=1508).[2]

1. Anderson P, et al. *Dermatol Ther (Heidelb)*. 2021;11:1571-1585. **2.** National Eczema Association. More than skin deep: Understanding the lived experience of eczema. Accessed May 25, 2024. http://www.morethanskindeep-eczema.org/uploads/1/2/5/3/125377765/mtsd_report_-_digital_file_1.pdf

Even visibly healed skin needs proactive treatment[1,2]

AD

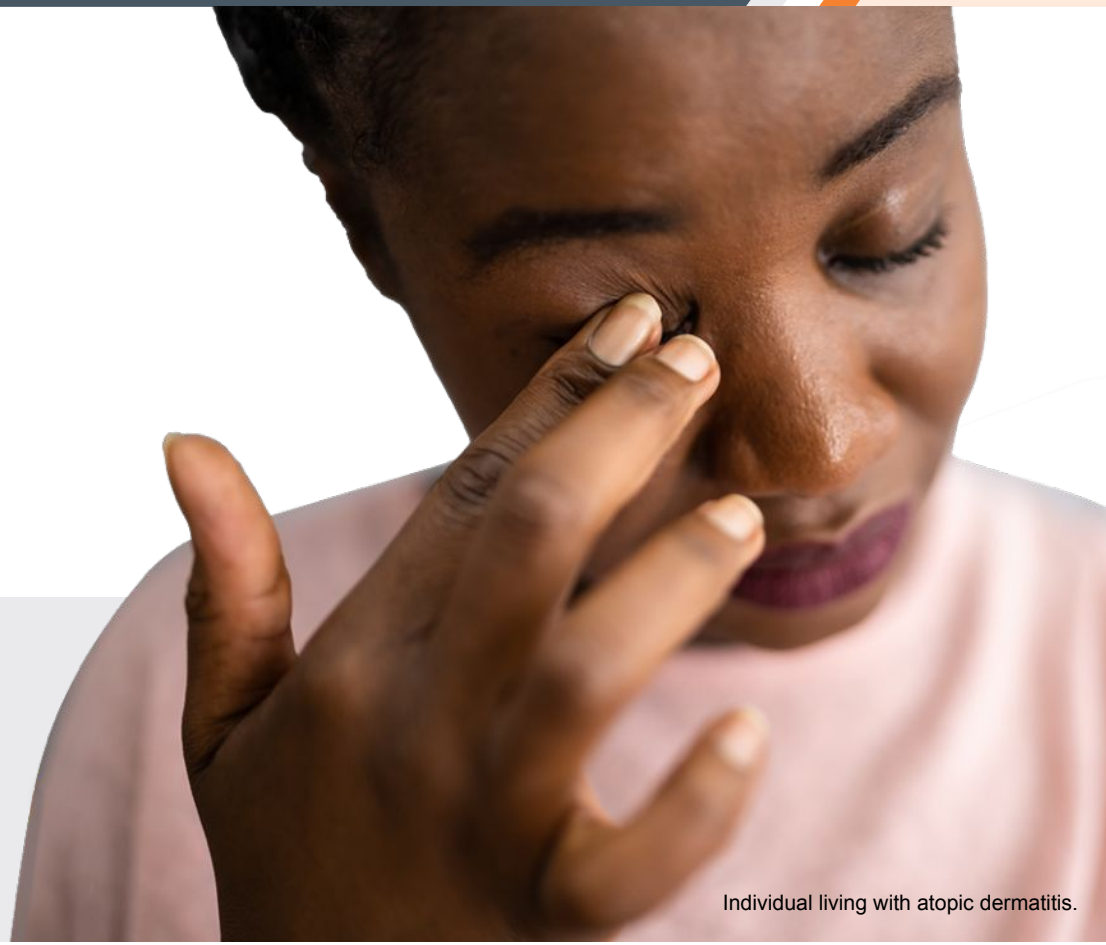
Atopic Dermatitis

Epidermal barrier defects and immune dysregulation

are present in **nonlesional skin**[1,2]

Itch

is experienced by 65% of patients **even on clear skin**[3*]

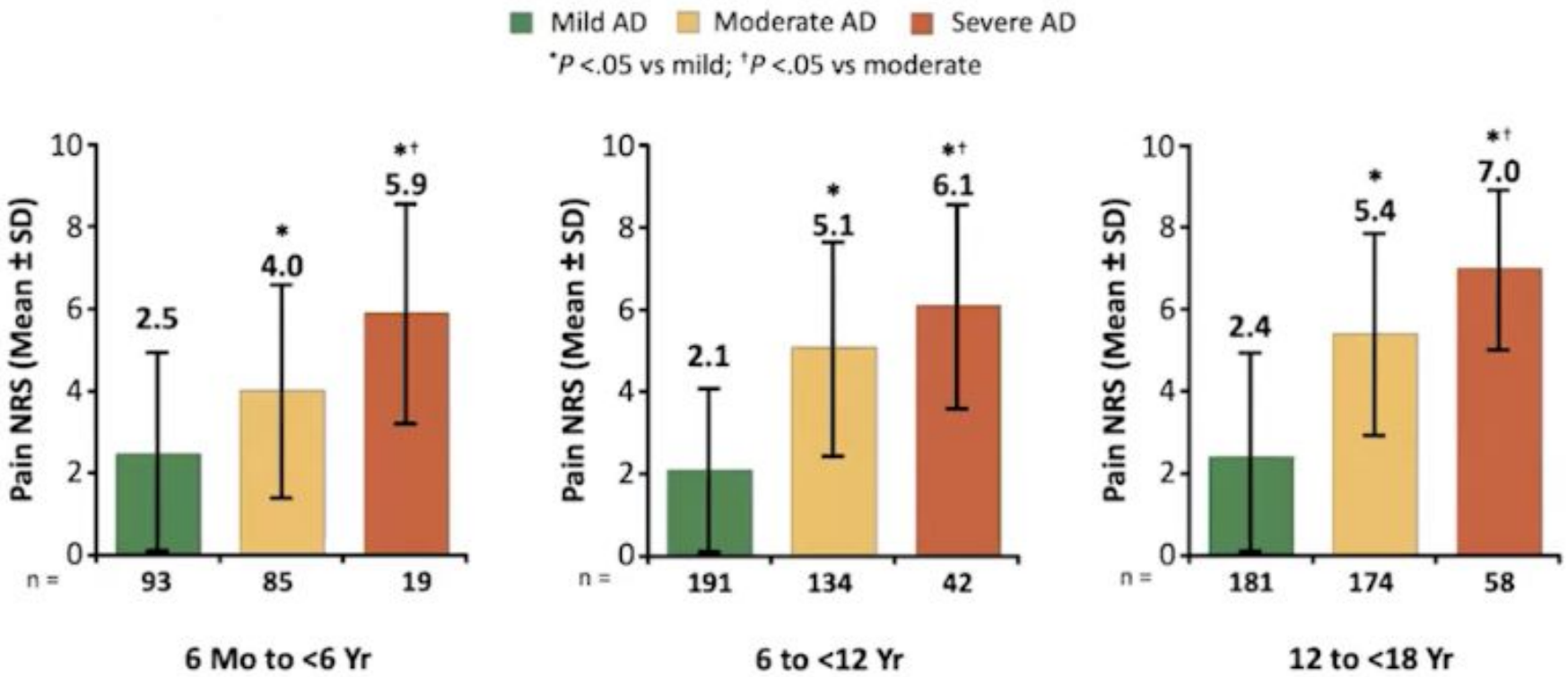


Individual living with atopic dermatitis.

*Based on data from a 2021 burden of disease and unmet needs in atopic dermatitis (BANDAD) internet-based survey of patients with atopic dermatitis (N=2005).[3]

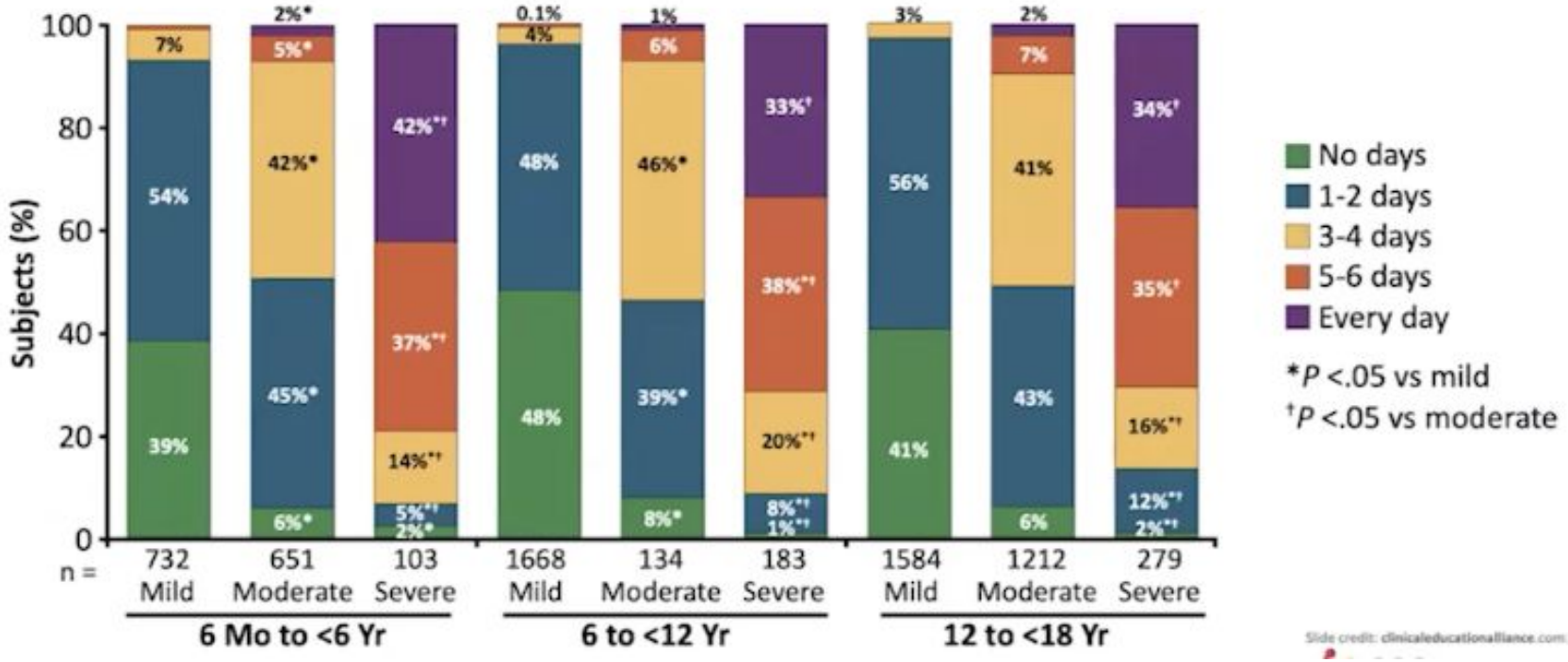
1. Migayron L, et al. *J Allergy Clin Immunol.* 2024;153:606-614. **2.** Pavel AB, et al. *Allergy*. 2021;76:314-325. **3.** Silverberg JI, et al. *Dermatitis*. 2023;34(2):135-144.

Patient Burden Pain



Patient Burden: Sleep

- Higher AD severity is associated with more frequent sleep disturbance for patients



Slide credit: clinicaleducationalliance.com

Available Topical Therapies

Class/Agent	Guideline Recommendations	Considerations
Corticosteroids	First line with nonresponse to skin care routines and emollients*	▪ Apply 1-2x/day ▪ Address steroid phobia and assess adherence
Calcineurin inhibitors ▪ Tacrolimus ointment ▪ Pimecrolimus cream	Second line, short term, noncontinuous	▪ Approved for patients ≥2 yr of age ▪ May cause burning or stinging ▪ Risk of secondary infections and rare cases of malignancy
PDE-4 inhibitor ▪ Crisaborole ▪ Roflumilast	Safe and effective option for mild to moderate AD	▪ Crisaborole approved for patients ≥3 mo of age ▪ Roflumilast approved for patients ≥6 yr of age
JAK inhibitor ▪ Ruxolitinib	Approved for adolescents ≥12 yr of age; reserved for patients who do not respond to other treatments	▪ Approved for short-term and noncontinuous treatment in nonimmunocompromised patients ▪ Applied 2x/day, not exceeding 20% BSA or 60 g/wk or 100 g/2 wk
AhR-modulating agent ▪ Tapinarof cream	Approved for patients ≥2 yr of age	▪ Most common ADRs included URTI, folliculitis, headache, asthma, vomiting, pain in extremities

*Dosing based on vasoconstrictive properties; use the lowest dose possible for the shortest duration possible.

Safety Concerns with Prolonged Topical Corticosteroids

TCS-related ARDS are rare, generally associated with high potency and long treatment duration (telangiectasia, striae, hypopigmentation, acne, rosacea, and skin thinning)

Long-term and excessive use of TCS can lead to systemic absorption and ocular adverse effects

Systemic effects include adrenal insufficiency, diabetes mellitus/hyperglycemia, and mineral corticoid effects (edema, hypocalcemia, hypokalemia, hypertension)

Ocular adverse effects include posterior subcapsular cataracts and glaucoma

There is an increased risk of rebound eruptions as the skin becomes dependent on the TCS and exhibits signs of withdrawal or addiction once they are discontinued.

Roflumilast (Zoryve)

- Selective PDE-4 inhibition → increases intracellular cAMP
- Downregulates inflammatory cytokines (Th2/Th17 pathways)Reduces itch, erythema, and inflammation
- Very good for face, eyelids, and intertriginous areas
- Often preferred over crisaborole due to less stinging and better adherence
- Can be layered with moisturizers (many patients apply moisturizer shortly after)
- Works well as baseline maintenance therapy or step-down from steroids/JAKs

Ruxolitinib (Opzelura)

- Inhibits JAK1/JAK2 → reduces cytokine signaling involved in inflammation and itch (IL-4, IL-13, etc.)
- Rapid itch reduction (often within days)
- Works well for itch-dominant AD, especially face/hands
- Can be combined with emollients and topical steroids (on different areas or step-down strategy)
- Expensive—often requires prior authorization
- Good “bridge” therapy while waiting for biologics like dupilumab or tralokinumab to work

Tapinarof (VTAMA)

- Activates Aryl Hydrocarbon receptor
- Improved skin barrier function + reduces oxidative stress
- Steroid-sparing (no skin atrophy, no tachyphylaxis)
- Can be used for longer continuous courses than many topicalsGood option for maintenance therapy after biologics or in mild–moderate disease
- Works on both inflammation and itch-scratch cycle
- Common side effects:
    - Folliculitis (most characteristic)

Non-FDA Approved Options

- If need fast relief:
  - Cyclosporin (4 mg/kg) then cross taper onto something else
- Long term options
  - Oral roflumilast ($5/month- no labs, no immunosuppression)
    - 500 mcg q hs for 6 weeks
    - GI side effects (diarrhea, nausea, abdominal pain) lowered if taken with food
  - Low dose (<15 mg/wk) methotrexate
    - A good option, but does require labs and has a long term risk of toxicity
  - Mycophenolate mofetil
    - No labs but definite long term immunosuppression risk

Important questions to ask

- Any atopic co-morbidities
- History of staph infections, herpes infections, zoster
- Do you have warts or molluscum or cancer or chronic infection
- Any auto-immune diseases
- Any history of arthritis, psoriasis, seborrheic dermatitis
- Concern over pain with injections
- Ratio of itch to rash
- How likely to become pregnant

Dupilimab (Dupixent)

- Favors
  - If they have atopic co-morbidities
  - If they have warts, molluscum, active or history of cancer, chronic infection
  - History of Staph infections
- Against
  - History of arthritis, psoriasis, seborrheic derm
  - Significant facial involvement
  - History of ocular disease

Tralokinumab (Adbry) or Lebrikizumab (Ebglyss)

- Favors
  - No atopic co-morbidities
  - History of staph infections
  - History of arthritis
- Against
  - Ocular disease

Nemolizumab (Nemluvio)

- Favors
  - Itch out of proportion to rash
  - Hesitant about injections
  - No atopic co-morbidities
- Against
  - Highly concerned about appearance of their AD

Abrocitinib (Cibinqo) /Upadacitinib (Rinvoq)

- Favors
  - Hesitant/fearful of injections
  - Wants the highest short-term efficacy
  - Has auto-immune disease of any type
- Against
  - History of cancer, Hep B, Hep C, HIV, chronic infections, molluscum, warts, HSV, VZV
  - History of blood clots, high cardiovascular risk

If none of the above apply

- Dupixent has the longest safety track record but the highest risk of annoying side effects
- Tralokinumab or Lebrikizumab have similar MOA to Dupixent so unexpected new side effect unlikely, lower risk of annoying side effects
- Nemolizumab fastest biologic for itch least painful injections, fewest annoying side effects, but gets rash better slower
- Abrocitinib/Upadacitinib fastest for itch, no injections but do slightly weaken the immune system