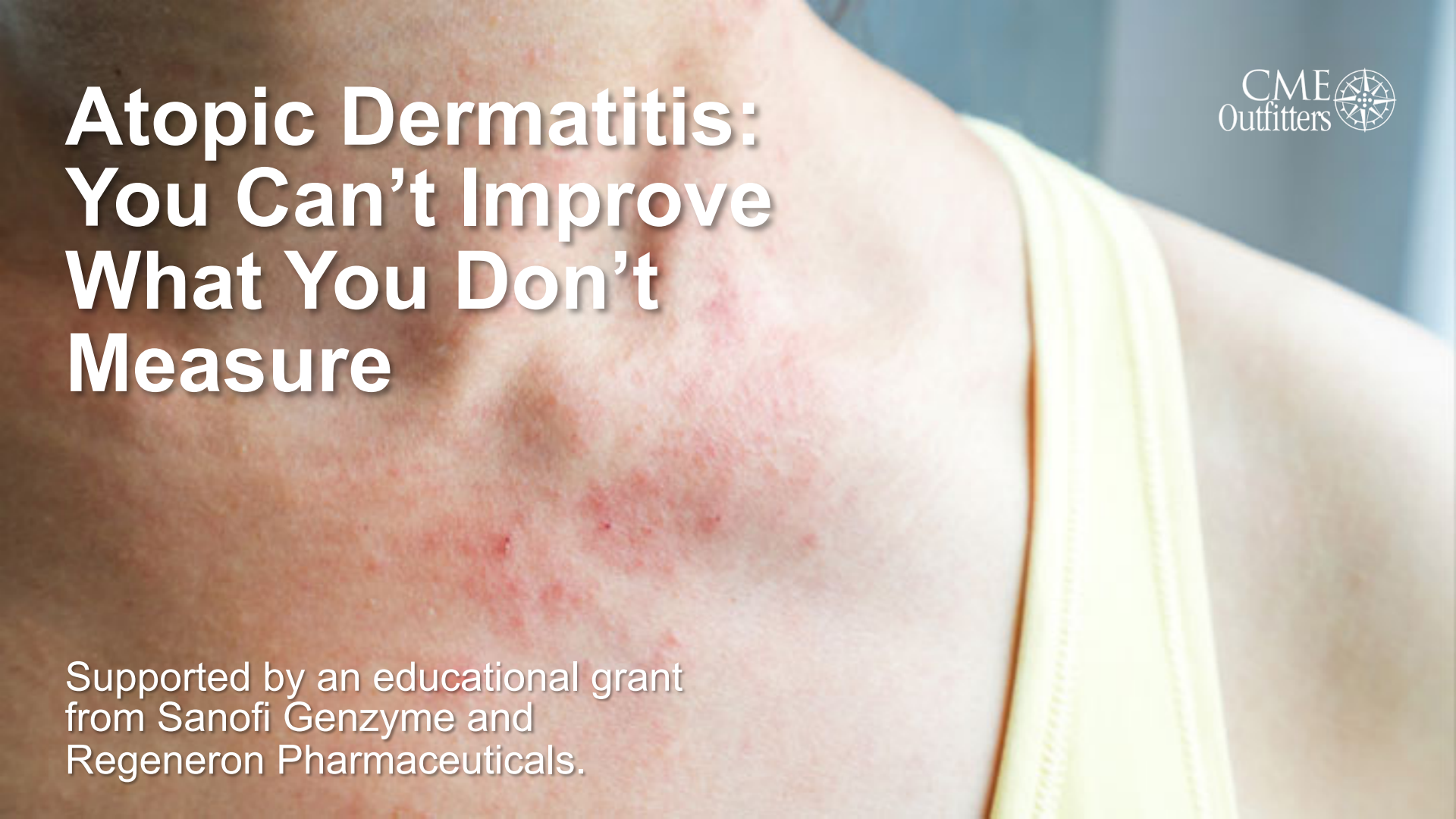
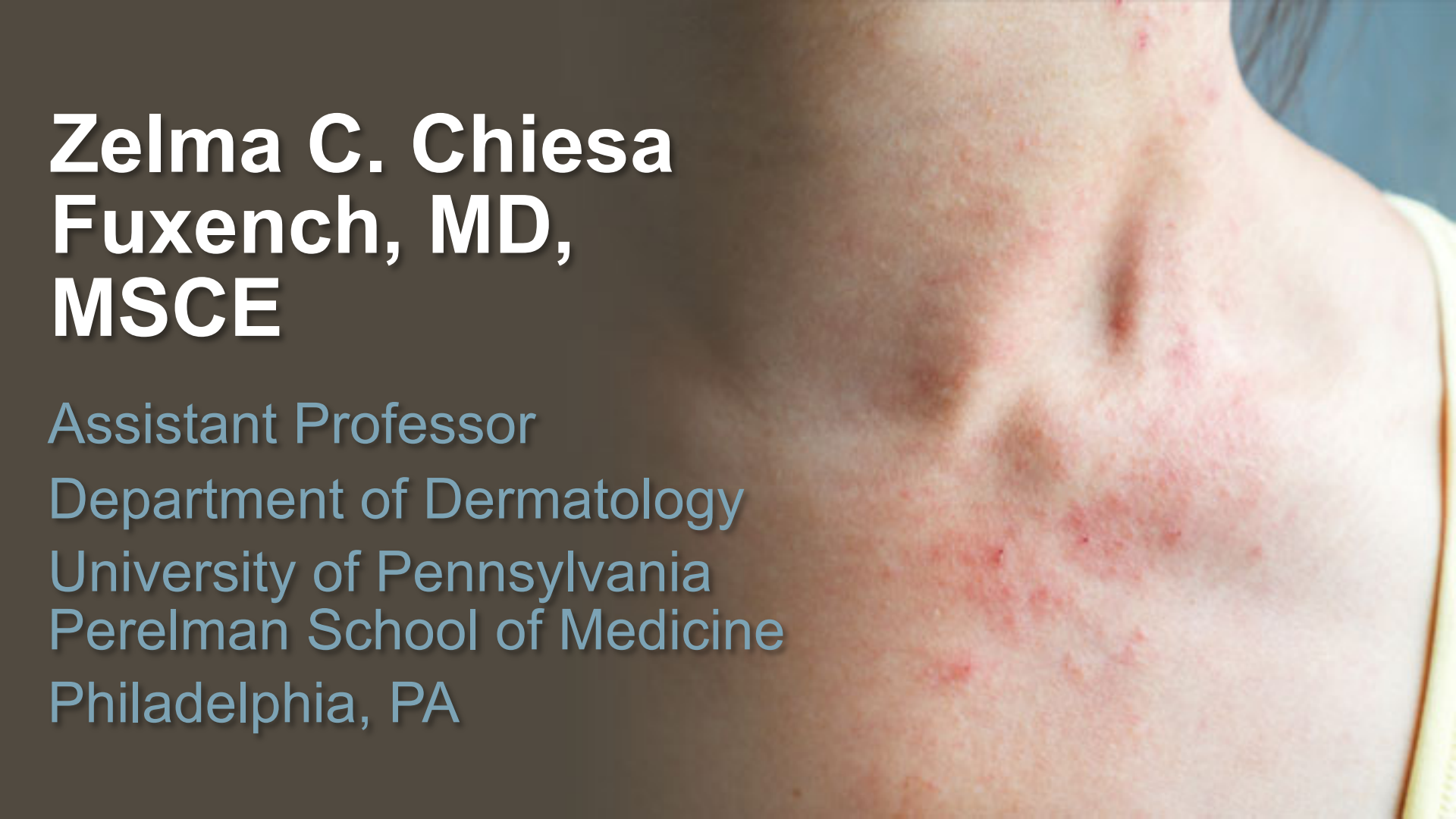


Atopic Dermatitis: You Can't Improve What You Don't Measure

CME Outfitters

Supported by an educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals.



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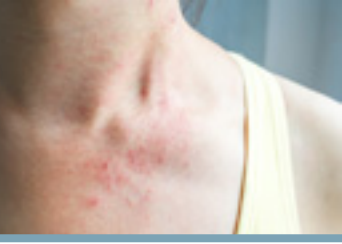
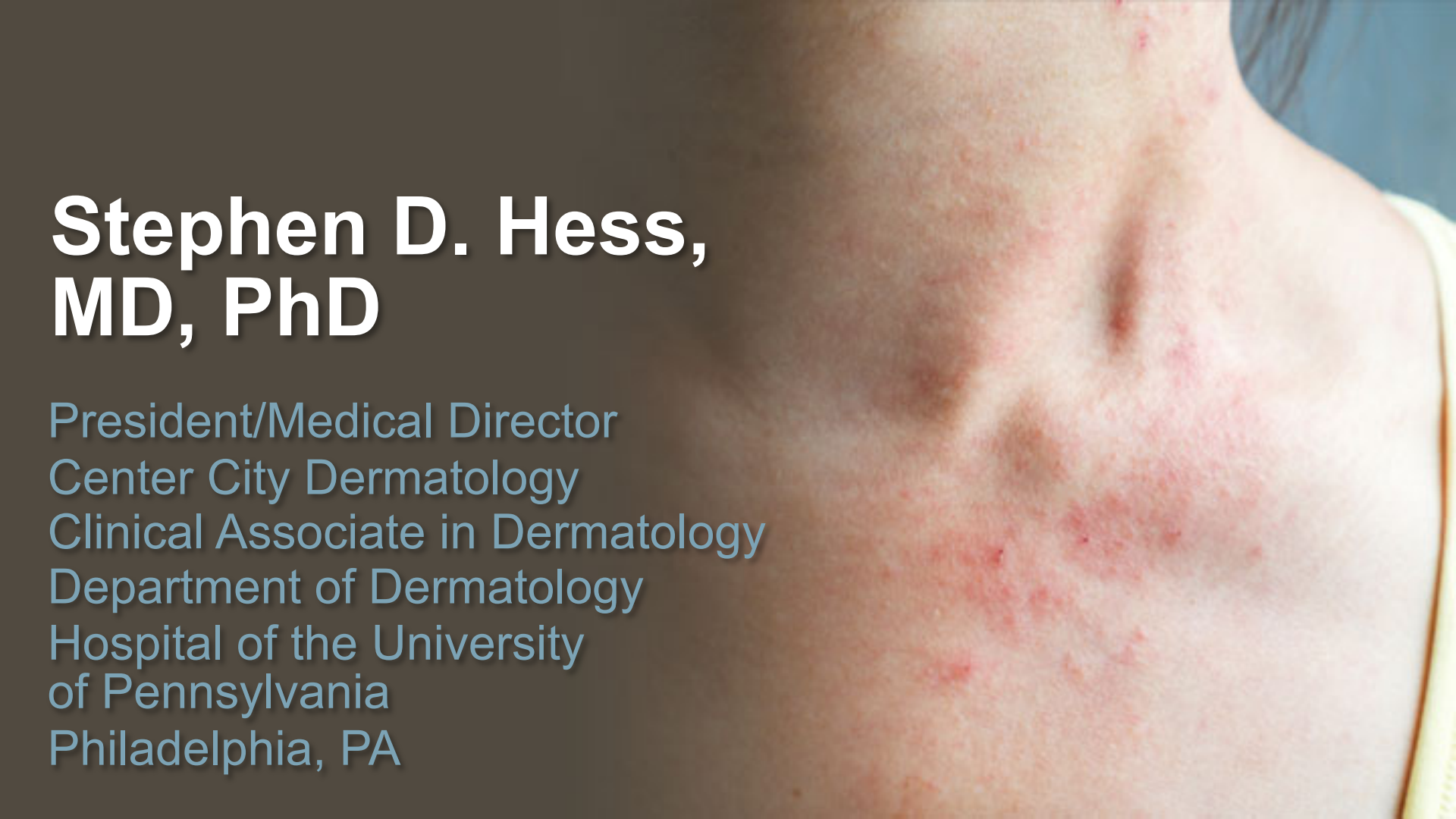
Disclosures



- ***Research Support:*** Sanofi Genzyme/Regeneron Pharmaceuticals; Tioga Pharmaceuticals; Vanda Pharmaceuticals
- ***Consultant:*** Asthma and Allergy Foundation of America; National Eczema Association



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Stephen D. Hess, MD, PhD

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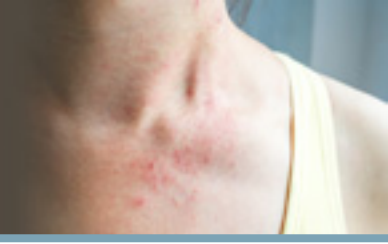
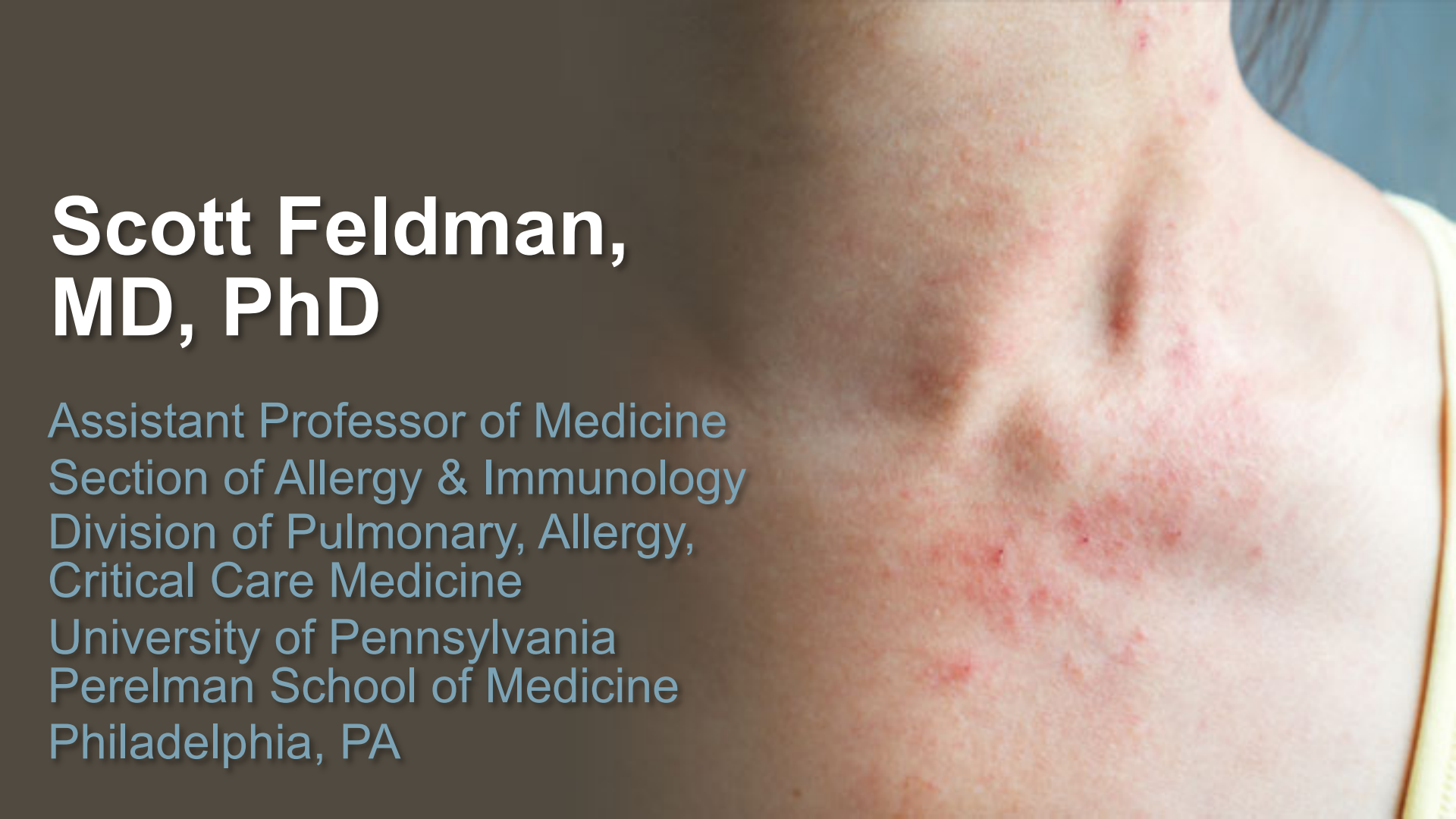


- ***Speakers Bureau:*** Celgene Corporation; Janssen Pharmaceuticals, Inc.; Pfizer Inc.; Sanofi Genzyme/Regeneron Pharmaceuticals; Sun Pharmaceutical Industries Ltd.
- ***Consultant:*** Celgene Corporation; Janssen Pharmaceuticals, Inc.; Verrica Pharmaceuticals
- ***Stock Shareholder (Directly Purchased):*** Aclaris Therapeutics, Inc.; Celgene Corporation; Verrica Pharmaceuticals



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Scott Feldman, MD, PhD

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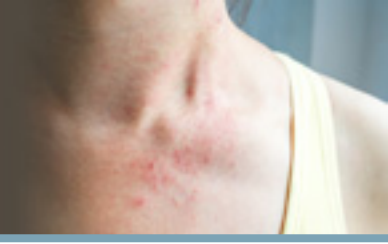
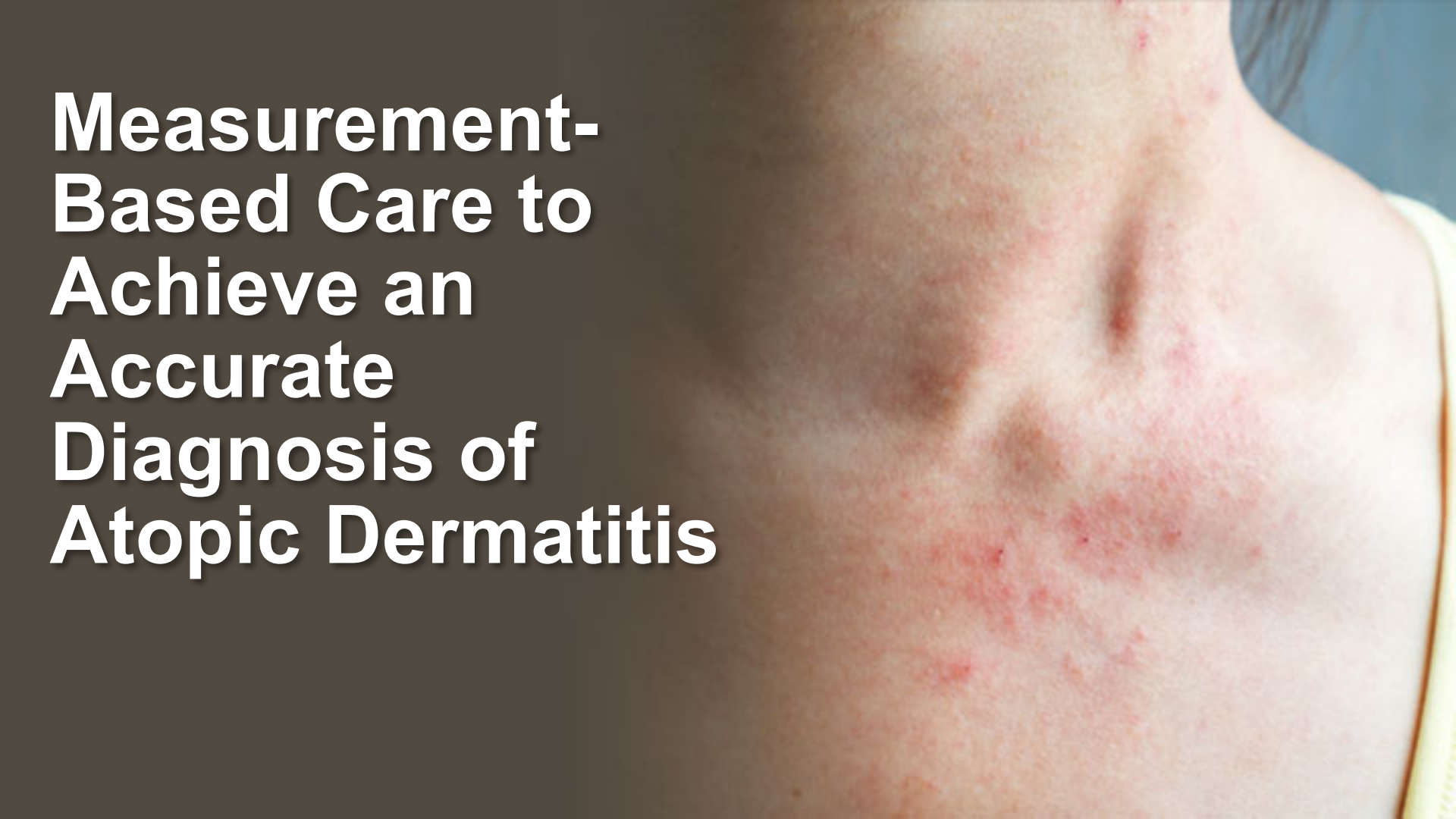
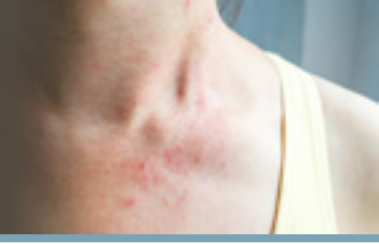


- No relevant financial relationships to disclose

Measurement-Based Care to Achieve an Accurate Diagnosis of Atopic Dermatitis

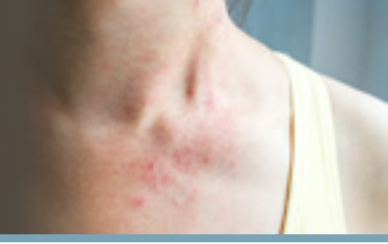


Case Presentation: JC



- JC is a 36 y/o man with an itchy, red rash
- ***Duration:*** Has had intermittent symptoms throughout his entire life. Feels as if these have been getting progressively worse in recent years
- ***Location:*** Rash is primarily located on the neck, arms, legs, and back
- ***Symptoms:*** Extremely itchy, feels as if he cannot stop scratching, results in waking up from sleep almost every night
- Impact on lifestyle and career choices

Medical History



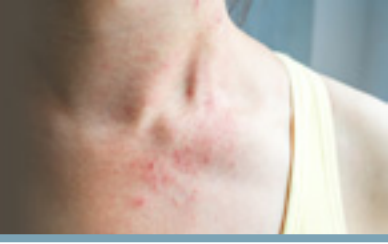
Medical History

- No history of cancer or serious infection
- No known allergies to foods or other medications
- Non-smoker, alcohol intake (4-5 drinks/week)
- ROS: Denied any constitutional symptoms, negative in detail

Physical Examination

- Presence of multiple, somewhat ill-defined, erythematous patches and plaques with evidence of lichenification and excoriation on the scalp, trunk, arms, and legs

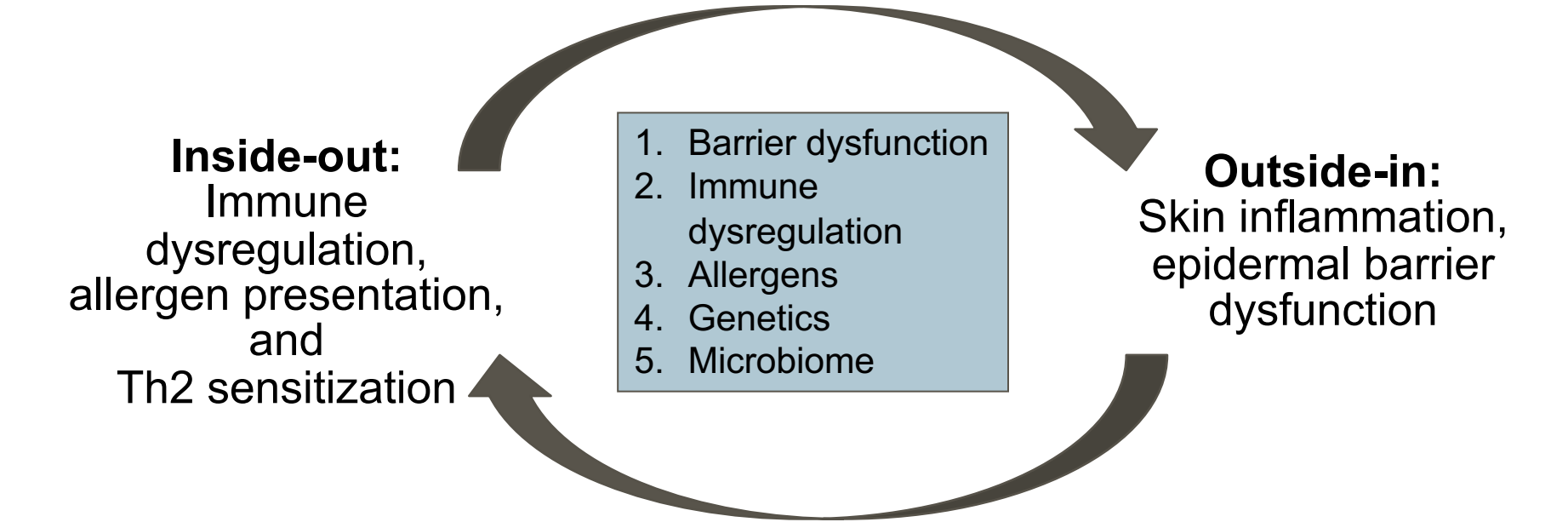
Atopic Dermatitis (AD): Epidemiology[1-5]



- AD is a chronic, pruritic, inflammatory skin disease characterized by periods of acute disease flare
- Prevalence of AD in the United States:
  - Children ~ 20%
  - Adults ~ 3.2% to 10.7% (studies vary)
- Adult-onset AD is considered rarer
  - Occurs more frequently during third decade of life
  - 30% of all cases of AD are in adult population

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.
2. Hanifin JM, et al. *Dermatitis*. 2007;18:82-91.
3. Garmhausen D, et al. *Allergy.* 2013;68:498-506.
4. Silverberg JI, et al. *J Allergy Clin Immunol.* 2013;132:1132-1138.
5. Silverberg JI, et al. *Br J Dermatol*. 2015;173:1400-1404.

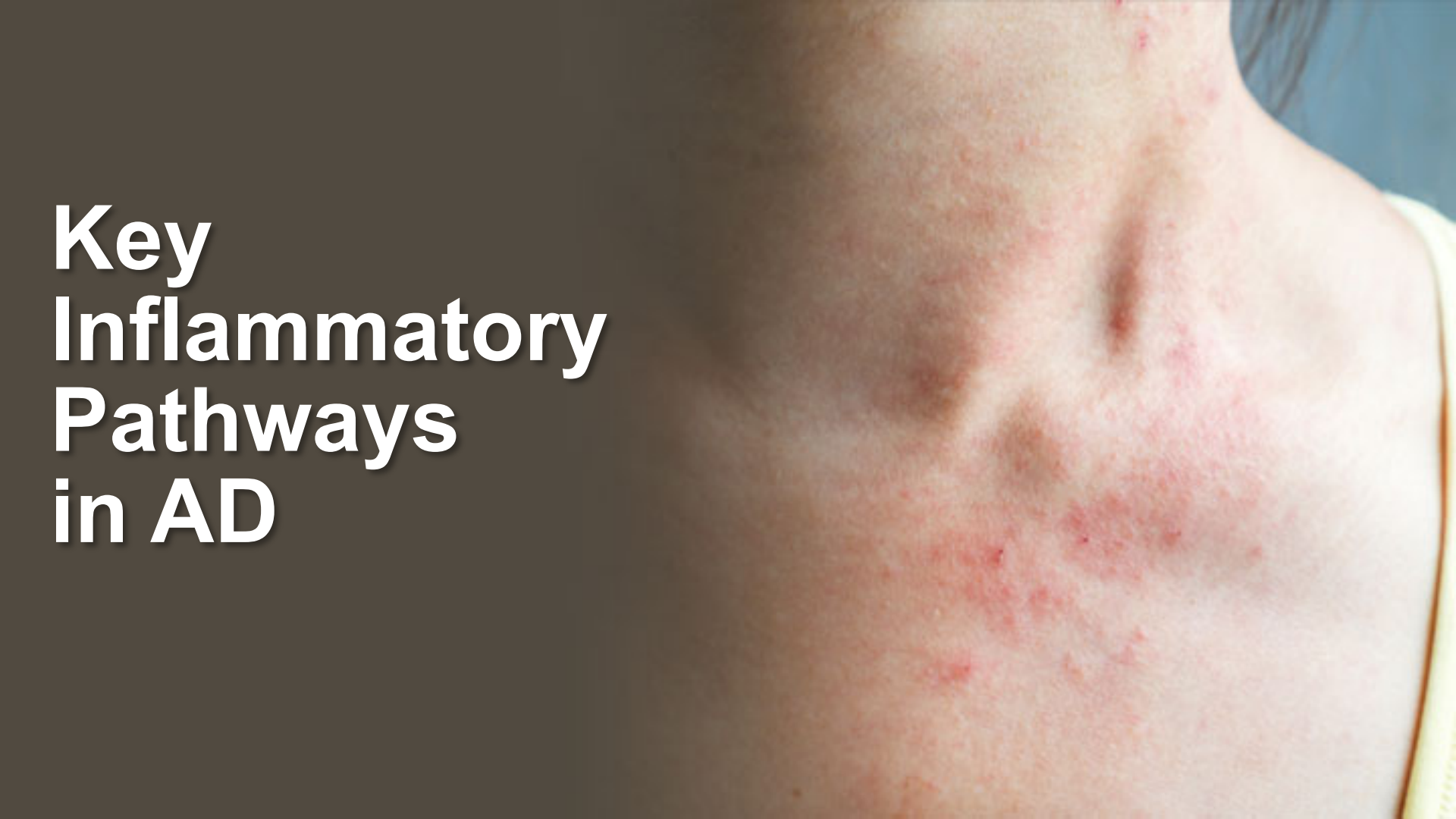
Pathogenesis of AD[1-8]



Th = T helper cell

1. Novak N, et al. *J Allergy Clin Immunol*. 2003;112:252-262. 2. Napolitano M, et al. *G Ital Dermatol Venereol*. 2016;151:403-411. 3. McLean WH. *Br J Dermatol*. 2016;175(suppl 2):4-7. 4. Palmer CN, et al. *Nat Genet*. 2006;38:441-446. 5. Fallon PG, et al. *Nat Genet*. 2009;41:602-608. 6. Paternoster L, et al. *Nat Genet*. 2015;47:1449-1456. 7. Tamari M, et al. *J Dermatol*. 2014;41:213-220. 8. Sasaki T, et al. *J Dermatol Sci*. 2014;76:10-15.

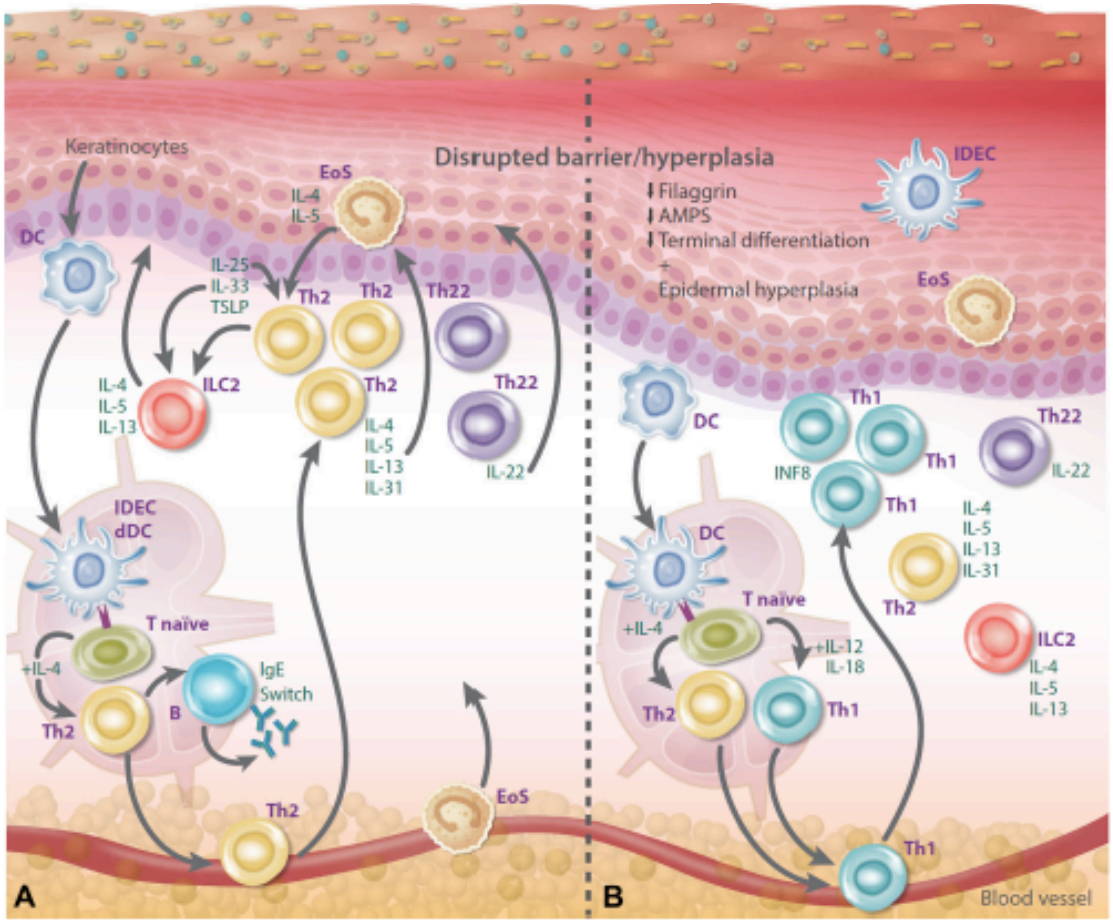
Key Inflammatory Pathways in AD



ACUTE AD

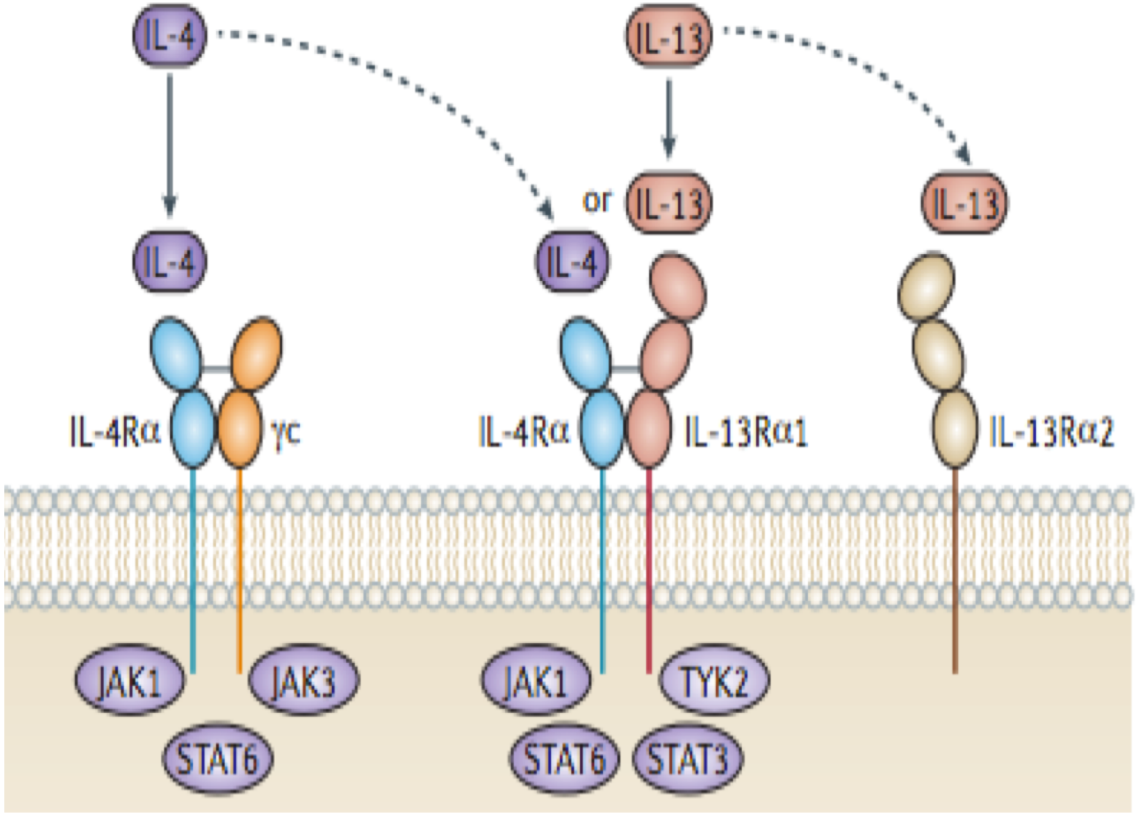
Itch → Scratch → Lichenification

CHRONIC AD



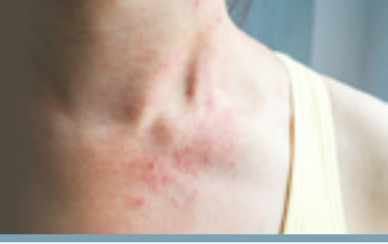
Gooderham MJ, et al. *J Am Acad Dermatol*. 2018;78:S28-S36.

JAK/STAT Pathway



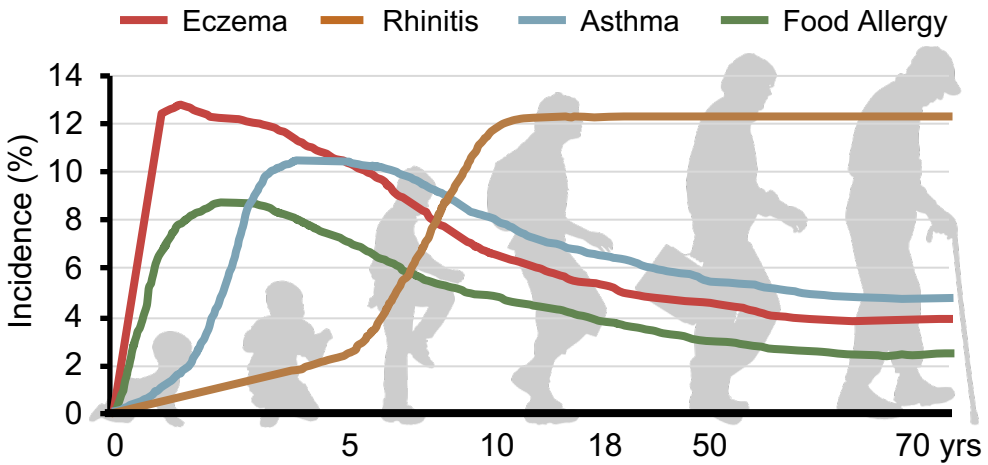
Gandhi NA, et al. *Nat Rev Drug Discov*. 2016;15:35-50.

Comorbidities in Adults With AD



- Higher rate of other atopic diseases:[1,2]
  - Nasal allergies/hay fever
  - Bronchial asthma
- Non-atopic diseases:
  - Higher rates of skin infections[3]
  - Sleep disturbances[4]
  - Neuropsychiatric (anxiety, depression, ADD/ASD)[5-9]
  - Other: cardiovascular disease, cancer (eg, lymphoproliferative malignancies)[10,11]

The Atopic March[1]

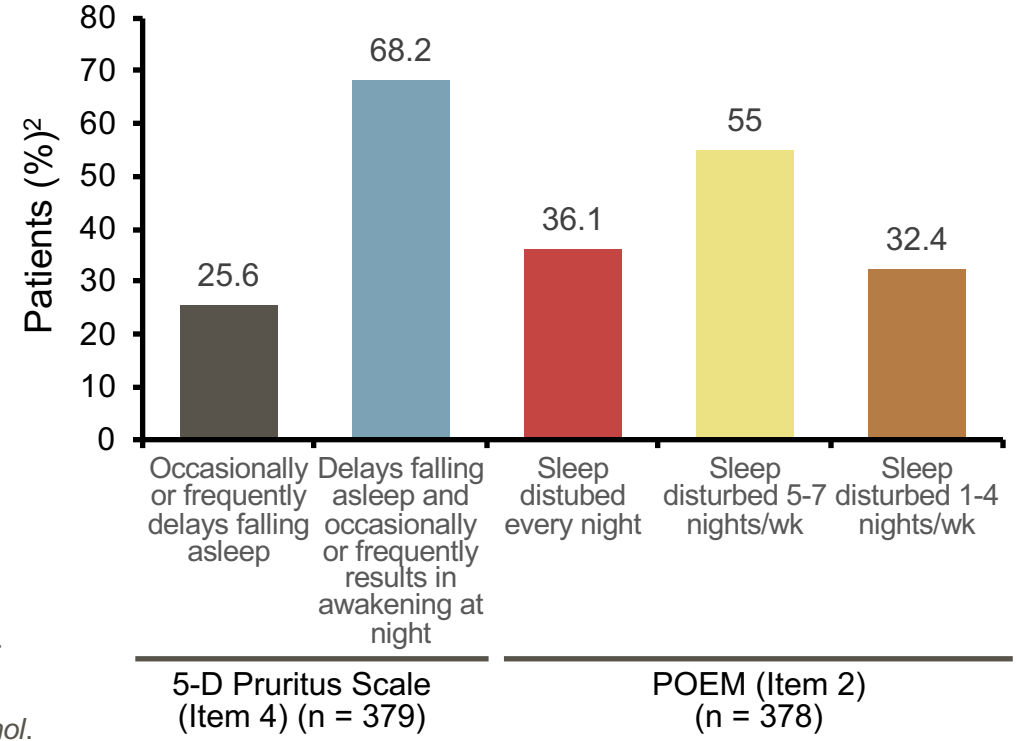


ASD = Autism Spectrum Disorder.

1. Tran M, Sears M. *Ann Allergy Asthma Immunol.* 2018;120:115-119. 2. Silverberg JI, et al. *J Allergy Clin Immunol*. 2013;132:1132-1138. 3. Czarnowicki T, et al. *J Allergy Clin Immunol*. 2017;139:1723-1734. 4. Jeon C, et al. *Dermatol Ther (Heidelb)*. 2017;7:349-364. 5. Sanna L, et al. *J Affect Disord*. 2014;155:261-265. 6. Klokk M, et al. *BMC Dermatol*. 2010;10:3. 7. Dalgard FJ, et al. *J Invest Dermatol*. 2015;135:984-991. 8. Strom MA, et al. *Br J Dermatol.* 2016;175:920-929. 9. Billeci L, et al. *Am J Clin Dermatol.* 2015;16:371-388. 10. Silverwood R, et al. *BMJ.* 2018;361:k1786. 11. Fletcher CL, et al. *Arch Dermatol.* 2004;140:449-454.

AD: Impact on Quality of Life

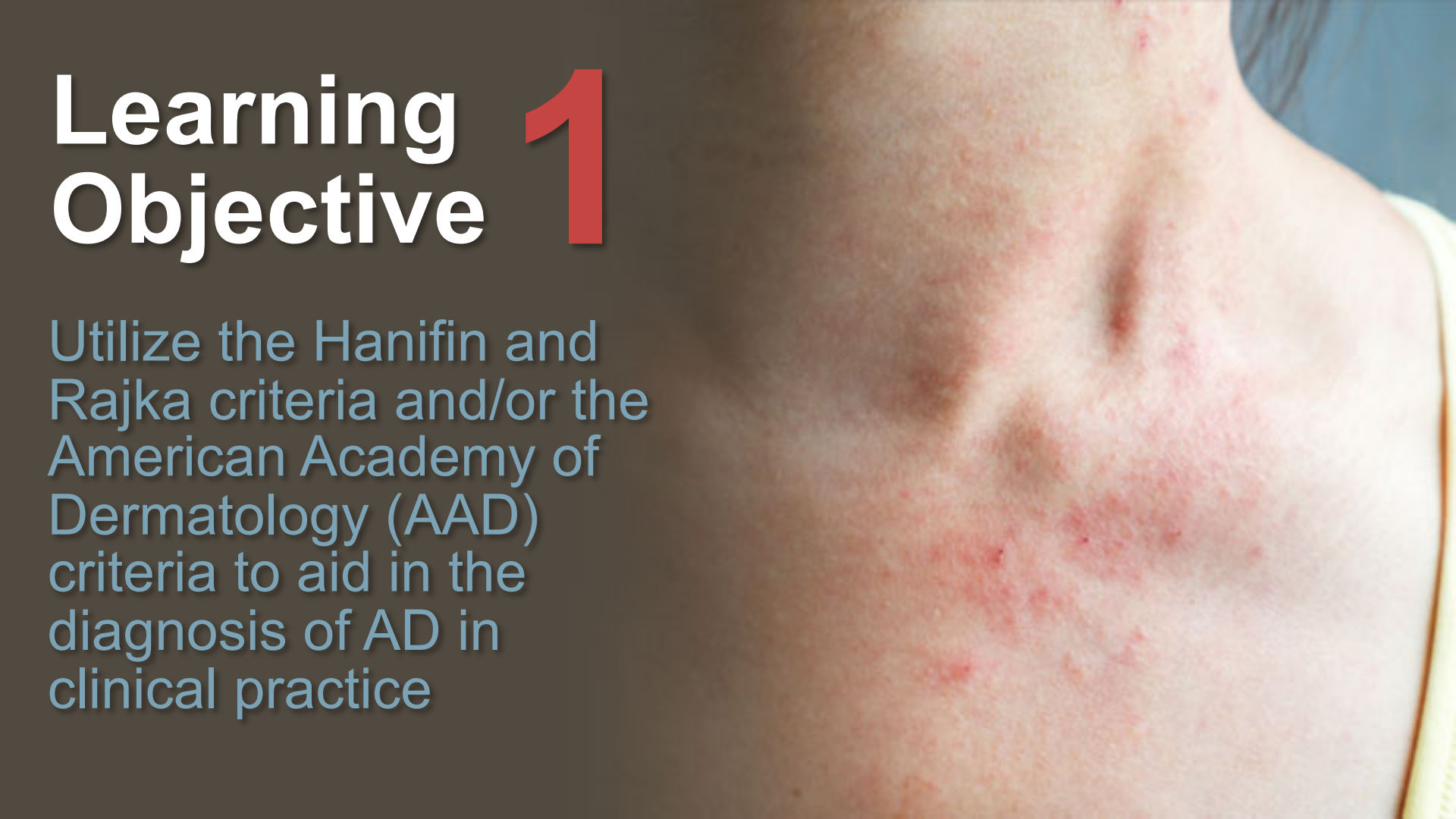
- Adults with moderate-to-severe AD:[1]
  - 49% experience moderate-to-significant sleep disruption
  - ~ 82% underwent lifestyle modifications
  - 55% experience decreased confidence
- 14% of adult patients in the ISOLATE study believed that their career progression had been hindered by AD.[3]



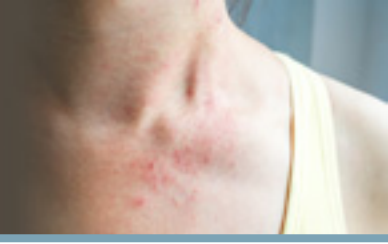
1. https://www.prnewswire.com/news-releases/new-survey-reveals-the-widespread-and-serious-impact-of-moderate-to-severe-atopic-dermatitis-on-people-living-with-the-disease-300339444.html 2. Simpson EL, et al. *J Am Acad Dermatol*. 2016;74:491-498. 3. Zuberbier T, et al. *J Allergy Clin Immunol*. 2006;118:226-232.

Learning Objective 1

Utilize the Hanifin and Rajka criteria and/or the American Academy of Dermatology (AAD) criteria to aid in the diagnosis of AD in clinical practice



Diagnosis

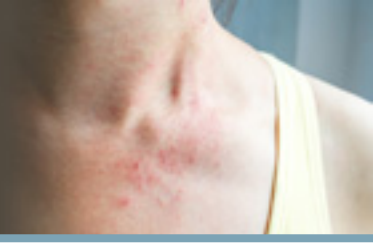


- Clinical diagnostic criteria core sets:
  - Hanifin and Rajka criteria[1]
    - 3 of 4 major criteria and 3 of 23 minor criteria must be met
    - Comprehensive, use limited to clinical trials
  - UK Working Party[2]
    - Core set based on Hanifin and Rajka
    - Primarily used in epidemiologic/population-based studies
  - AAD consensus criteria[3]
    - AAD consensus conference (experts in this field)

1. Rudzki E, et al. *Dermatology*. 1994;189:41-46.
2. Williams HC, et al. *Br J Dermatol.* 1996;135:12-17.
3. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.

Hanifin and Rajka Criteria

Major Criteria

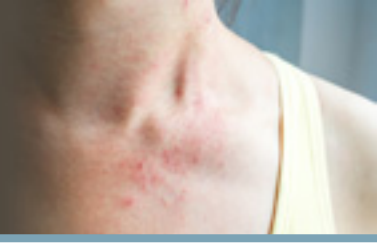


- Major Criteria: Must have ≥3 basic features:
  1. Pruritus
  2. Typical morphology and distribution
     Flexural lichenification in adults
     Facial and extensor eruptions in infants and children
  3. Chronic or chronically relapsing dermatitis
  4. Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

Tada J. *JMAJ.* 2002;45(11):460-465.

Hanifin and Rajka Criteria

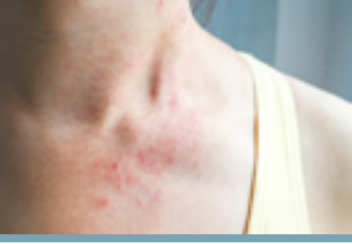
Minor Criteria



- Minor Criteria: Should have ≥3 minor features:
  1. Xerosis
  2. Ichthyosis/palmar hyperlinearity, keratosis pilaris
  3. Immediate (type 1) skin-test reactivity
  4. Raised serum IgE
  5. Early age of onset
  6. Tendency toward cutaneous infections (especially *S aureus* and *herpes simplex*), impaired cell-mediated immunity
  7. Tendency toward non-specific hand or foot dermatitis
  8. Nipple eczema
  9. Cheilitis
  10. Recurrent conjunctivitis
  11. Dennie-Morgan infraorbital fold
  12. Keratoconus
  13. Anterior subcapsular cataracts
  14. Orbital darkening
  15. Facial pallor, facial erythema
  16. Pityriasis alba
  17. Anterior neck folds
  18. Itch when sweating
  19. Intolerance to wool and lipid solvents
  20. Perifollicular accentuation
  21. Food intolerance
  22. Course influenced by environmental or emotional factors
  23. White dermographism, delayed blanch

Tada J. *JMAJ.* 2002;45(11):460-465.

UK Working Party Diagnostic Criteria for Atopic Dermatitis



Must have an itchy skin condition plus 3 or more:
Onset below age 2 (criterion not used in children under 4 years)
History of flexural involvement
History of generally dry skin
Personal history of other atopic diseases (in children aged under 4 years, history of atopic disease in a first degree relative may be included)
Visible flexural dermatitis

Williams HC, et al. *Br J Dermatol*. 1994;131(3):406-416.

AAD Criteria for Diagnosing AD

ESSENTIAL FEATURES—Must be present:
- Pruritus
- Eczema (acute, subacute, chronic)
  - Typical morphology and age-specific patterns*
  - Chronic or relapsing history

Patterns include:

1. *Facial, neck, and extensor involvement in infants and children*
2. *Current or previous flexural lesions in any age group*
3. *Sparing of the groin and axillary regions*

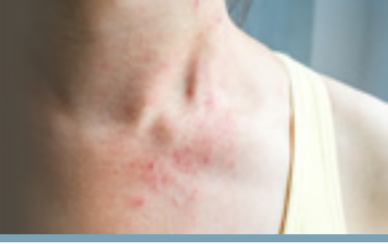
IMPORTANT FEATURES—Seen in most cases, adding support to the diagnosis:
- Early age of onset
- Atopy
  - Personal and/or family history
  - Immunoglobulin E reactivity
- Xerosis

ASSOCIATED FEATURES—These clinical associations help to suggest the diagnosis of atopic dermatitis but are too nonspecific to be used for defining or detecting atopic dermatitis for research and epidemiologic studies:
- Atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)
- Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis
- Ocular/periorbital changes
- Other regional findings (eg, perioral changes/periauricular lesions)
- Perifollicular accentuation/lichenification/prurigo lesions

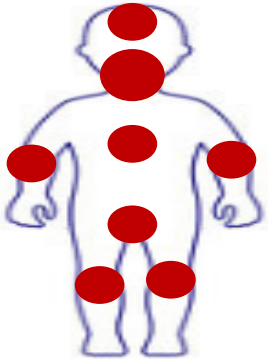
EXCLUSIONARY CONDITIONS—It should be noted that a diagnosis of atopic dermatitis depends on excluding conditions, such as:
- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

Eichenfield LF, et al.
J Am Acad Dermatol.
2014;70:338-351.

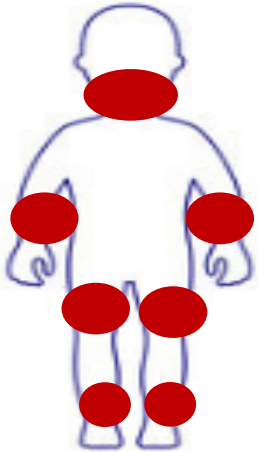
Clinical Manifestations



Infants/early childhood:
face, scalp, trunk, and extensor surfaces



Childhood:
neck, flexors, feet



Adults:
face, neck, hands, feet, trunk (back), eyelids

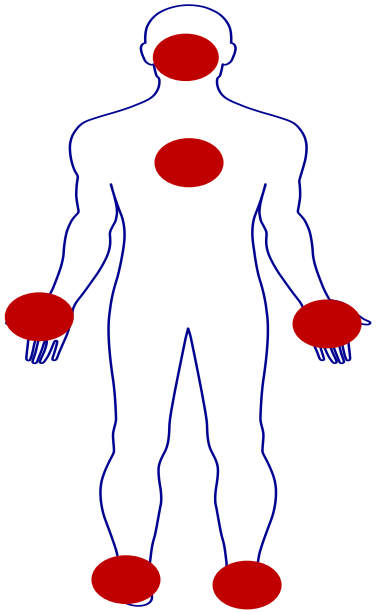
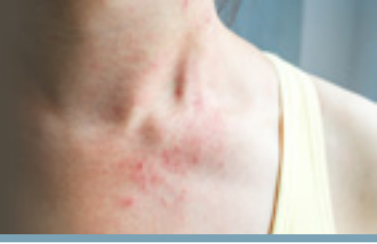


Image courtesy of Dr. Chiesa Fuxench.

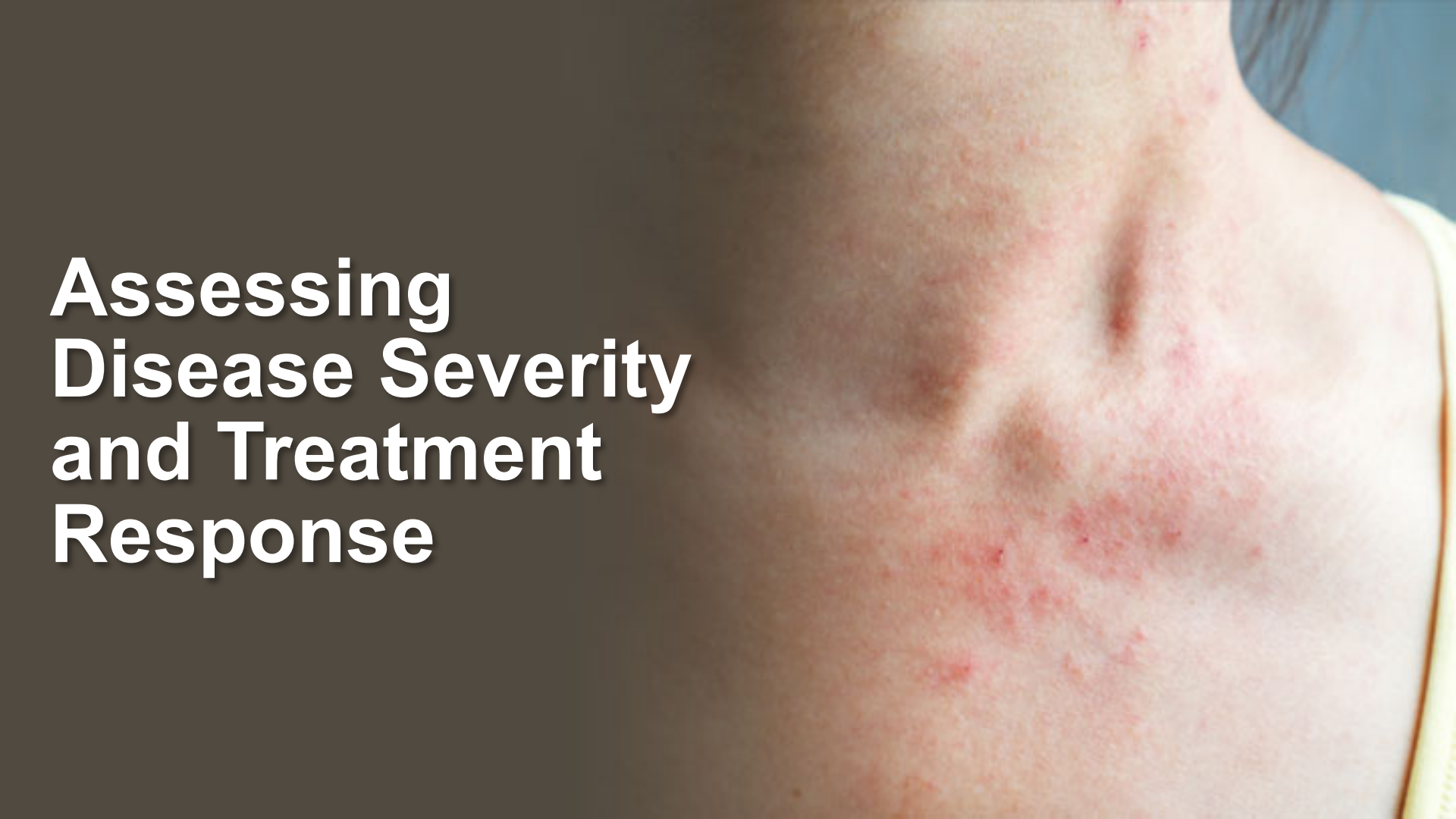
Differential Diagnosis



INFANCY	CHILDHOOD	ADULTHOOD
Seborrheic dermatitis	Scabies	Seborrheic dermatitis
Scabies	Contact dermatitis	Contact dermatitis
Immunodeficiency syndromes: •Wiskott-Aldrich syndrome •Hyper-IgE syndrome •Omenn syndrome •Netherton syndrome	Tinea corporis	Scabies
	Tinea versicolor	Insect bites
	Seborrheic dermatitis	Photoallergic or photoirritant dermatitis
	Psoriasis	HIV-related dermatitis
Langerhans cell histiocytosis	Pityriasis lichenoides/PLEVA/PR	Psoriasis
Acrodermatitis enteropathica	CTCL	CTCL
Metabolic disorders		Drug-induced dermatitis

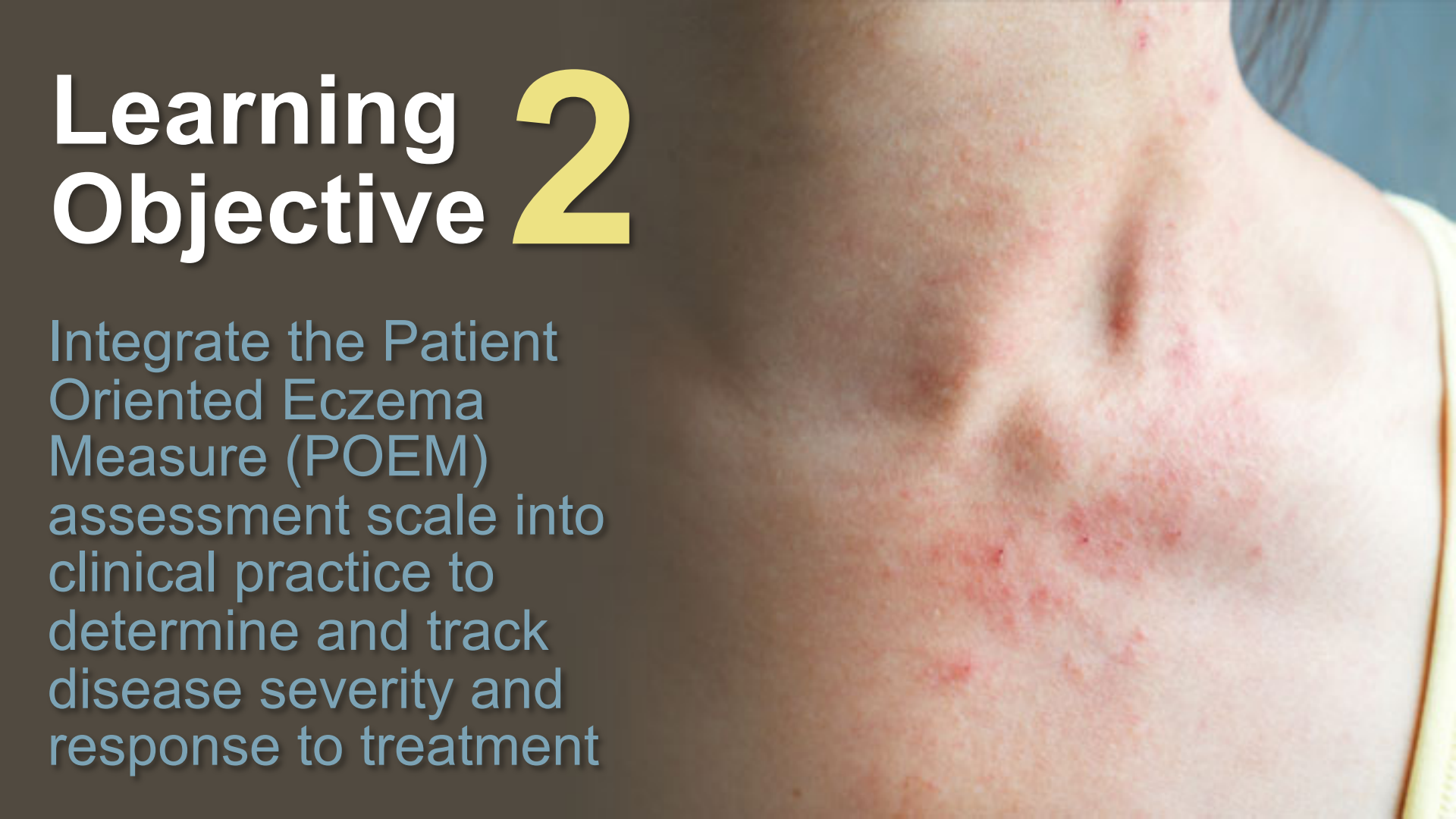
CTCL = cutaneous T-cell lymphoma; PLEVA = pityriasis lichenoides et varioliformis acuta; PR = pityriasis rosea.
Simpson EL, et al. *J Am Acad Dermatol*. 2017;77:623-633.

Assessing Disease Severity and Treatment Response

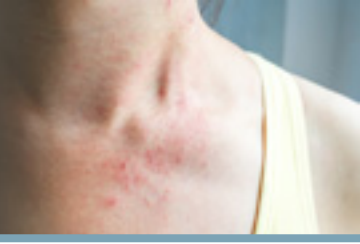


Learning Objective 2

Integrate the Patient Oriented Eczema Measure (POEM) assessment scale into clinical practice to determine and track disease severity and response to treatment



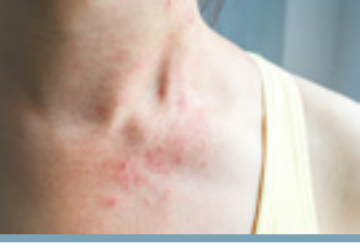
Assessment of Disease Severity and Clinical Outcomes in AD



- Measures of Disease Severity:
  - **SCORAD: SCOR**ing **A**topic **D**ermatitis Index
  - **EASI: E**czema **A**rea and **S**everity **I**ndex
  - **IGA: I**nvestigator's **G**lobal **A**ssessment
  - **SASSAD: S**ix **A**rea, **S**ix **S**ign **A**topic **D**ermatitis severity score
  - **TISS: T**hree-**I**tem **S**everity **S**cale
  - **POEM: P**atient **O**riented **E**czema **M**easure
- Measures of Impact on Quality of Life (QoL):
  - ~ 22 different scales for measuring QoL/psychological outcomes in AD
  - Dermatology Life Quality Index
- Symptom specific:
  - Pruritus Numerical Rating Scale (NRS)

Eichenfield LF, et al. *J Am Acad Dermatol.* 2014;70:338-351.

Assessment of Disease Severity and Clinical Outcomes in AD



- **AAD consensus guidelines for diagnosis of AD:**[1]
  - Pragmatic approach for diagnosis in infants, children, and adults
  - Well-suited for clinical practice
- When practical, scales to consider disease severity: SCORAD, EASI, POEM[2]
  - **POEM:** measure severity from the *patient perspective*

ESSENTIAL FEATURES—Must be present:
- Pruritus
- Eczema (acute, subacute, chronic)
  - Typical morphology and age-specific patterns*
  - Chronic or relapsing history

Patterns include:

1. *Facial, neck, and extensor involvement in infants and children*
2. *Current or previous flexural lesions in any age group*
3. *Sparing of the groin and axillary regions*

IMPORTANT FEATURES—Seen in most cases, adding support to the diagnosis:
- Early age of onset
- Atopy
  - Personal and/or family history
  - Immunoglobulin E reactivity
- Xerosis

ASSOCIATED FEATURES—These clinical associations help to suggest the diagnosis of atopic dermatitis but are too nonspecific to be used for defining or detecting atopic dermatitis for research and epidemiologic studies:
- Atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)
- Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis
- Ocular/periorbital changes
- Other regional findings (eg, perioral changes/periauricular lesions)
- Perifollicular accentuation/lichenification/prurigo lesions

EXCLUSIONARY CONDITIONS—It should be noted that a diagnosis of atopic dermatitis depends on excluding conditions, such as:
- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.
2. Rehal B, et al. *PLoS one*. 2011;6:e17520.

Patient Oriented Eczema Measure (POEM)[1,2]

Please circle one response for each of the seven questions below about your/your child's eczema. If your child is old enough to understand the questions then please fill in the questionnaire together. Please leave blank any questions you feel unable to answer.

1. Over the last week, on how many days has your/your child's skin been itchy because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

2. Over the last week, on how many nights has your/your child's sleep been disturbed because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

3. Over the last week, on how many days has your/your child's skin been bleeding because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

4. Over the last week, on how many days has your/your child's skin been weeping or oozing clear fluid because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

5. Over the last week, on how many days has your/your child's skin been cracked because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

6. Over the last week, on how many days has your/your child's skin been flaking off because of the eczema?

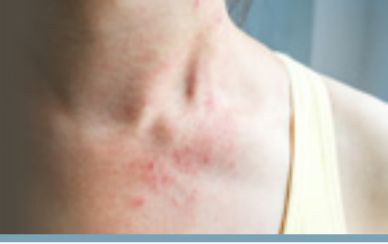
No days | 1-2 days | 3-4 days | 5-6 days | Every day

7. Over the last week, on how many days has your/your child's skin felt dry or rough because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

1. Charman CR, et al. *Br J Dermatol.* 2013;169(6):1326-1332. 2. Charman CR, et al. *Arch Dermatol*. 2004;140:1513-1519.

Patient Oriented Eczema Measure (POEM)[1,2]

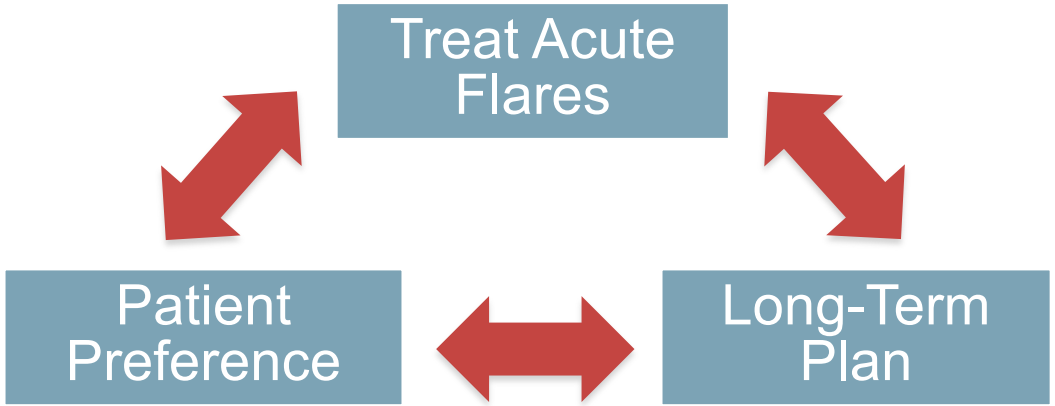


- Scoring POEM (total score max = 28):
  - No days = 0
  - 1-2 days = 1
  - 3-4 days = 2
  - 5-6 days = 3
  - Every day = 4
- What does a POEM score mean?
  - 0-2 = Clear or almost clear
  - 3-7 = Mild eczema
  - 8-16 = Moderate eczema
  - 17-24 = Severe eczema
  - 25-28 = Very severe eczema

1. Charman CR, et al. *Br J Dermatol*. 2013;169(6):1326-1332. 2. Charman CR, et al. *Arch Dermatol*. 2004;140:1513-1519.

Considerations for Treatment

Establishment of an adequate diagnosis and extent of disease severity as well as assessment of the impact of AD on QoL will be critical in determining appropriate treatment plan for our patients.

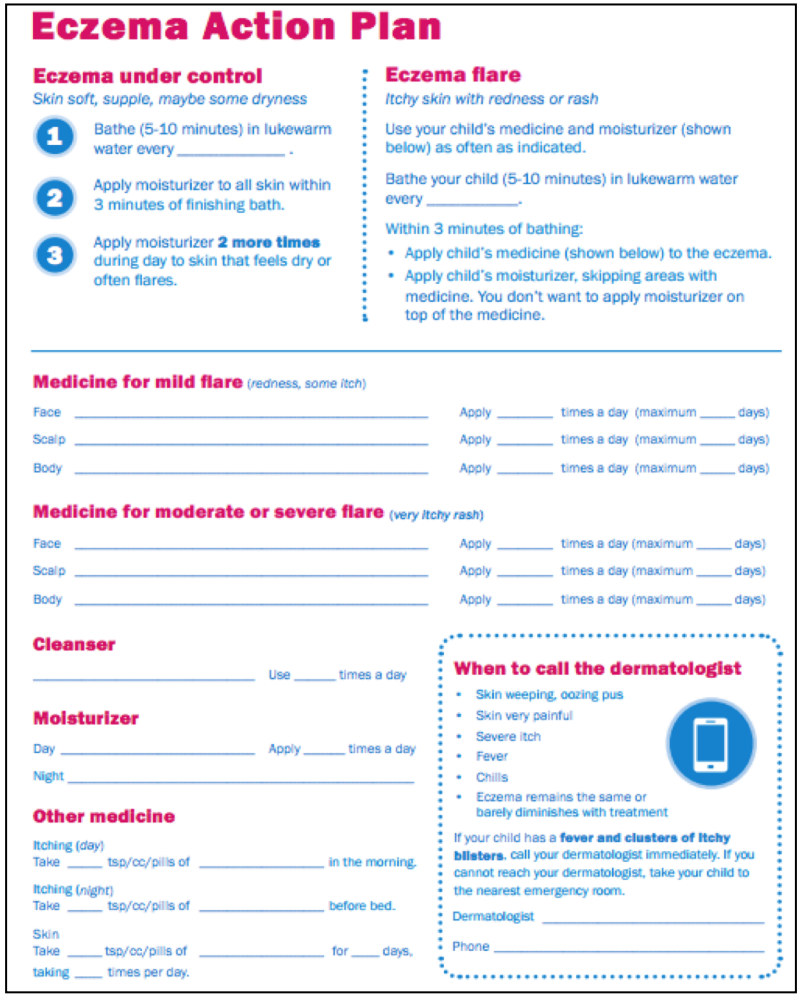


Goals:

- Decrease the rate of acute flares or disease exacerbations
- Maintain a state in which symptoms are mild with minimal to no impact on QoL

Education is KEY![1-4]

- Engage the patient/ provide written instructions
- Skin care **IS** treatment for atopic dermatitis
- Understanding patient preference is **critical**



Eczema Action Plan

Eczema under control
Skin soft, supple, maybe some dryness

1. Bathe (5-10 minutes) in lukewarm water every _____ .
2. Apply moisturizer to all skin within 3 minutes of finishing bath.
3. Apply moisturizer **2 more times** during day to skin that feels dry or often flares.

Eczema flare
Itchy skin with redness or rash

Use your child's medicine and moisturizer (shown below) as often as indicated.

Bathe your child (5-10 minutes) in lukewarm water every _____.

Within 3 minutes of bathing:
- Apply child's medicine (shown below) to the eczema.
- Apply child's moisturizer, skipping areas with medicine. You don't want to apply moisturizer on top of the medicine.

Medicine for mild flare *(redness, some itch)*

Face _____ Apply _____ times a day (maximum ____ days)
Scalp _____ Apply _____ times a day (maximum ____ days)
Body _____ Apply _____ times a day (maximum ____ days)

Medicine for moderate or severe flare *(very itchy rash)*

Face _____ Apply _____ times a day (maximum ____ days)
Scalp _____ Apply _____ times a day (maximum ____ days)
Body _____ Apply _____ times a day (maximum ____ days)

Cleanser

_____ Use _____ times a day

Moisturizer

Day _____ Apply _____ times a day
Night _____

Other medicine

Itching (day)
Take _____ tsp/cc/pills of _____ in the morning.

Itching (night)
Take _____ tsp/cc/pills of _____ before bed.

Skin
Take _____ tsp/cc/pills of _____ for ____ days,
taking ____ times per day.

When to call the dermatologist

- Skin weeping, oozing pus
- Skin very painful
- Severe itch
- Fever
- Chills
- Eczema remains the same or barely diminishes with treatment

If your child has a **fever and clusters of itchy blisters**, call your dermatologist immediately. If you cannot reach your dermatologist, take your child to the nearest emergency room.

Dermatologist _____

Phone _____

1. Bass AM, et al. *J Clin Med.* 2015;4:231-242. 2. Snyder A, et al. *Cutis.* 2015;96:397-401. 3. Ellis RM, et al. *Pediatr Dermatol.* 2011;28:242-244. 4. Smith SD, et al. *Med J Aust.* 2013;199:467-469.

Strength of Recommendation for Use of Topical Therapies in the Treatment of AD

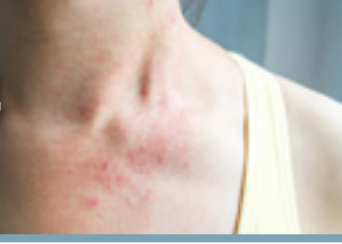
Recommendation	Strength of recommendation	Level of evidence	References
Use of moisturizers	A	I	9-16,18-21,126
Bathing and bathing practices	C	III	23,24,26,28,30
Application of moisturizers after bathing	B	II	24,25
Limited use of nonsoap cleansers	C	III	27-30
Against use of bath additives, acidic spring water	C	III	31,32,127
Wet-wrap therapy	B	II	34-41
Informing patients regarding theoretical risk of cutaneous viral infections with use	C	III	82,98
Awareness of black-box warning of TCI	C	III	98-101
Routine monitoring of TCI blood levels not needed	A	I	102,103
Against routine use of topical antistaphylococcal treatments	A	I	110-112
Bleach baths and intranasal mupirocin for those with moderate to severe AD and clinical infection	B	II	113
Against use of topical antihistamines	B	II	42,115-117

AD, Atopic dermatitis; *TCI*, topical calcineurin inhibitors; *TCS*, topical corticosteroids.

1st line: topical moisturizers, topical corticosteroids +/- prescription topicals, as well as other non-pharmacologic interventions

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.

Role of Proactive Treatment[1-4]



Reactive Approach

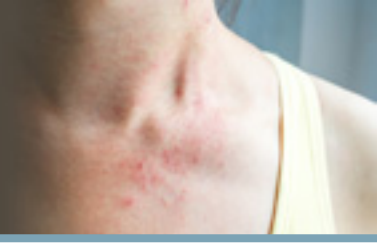
Relies on anti-inflammatory therapies administered to active lesions that are then discontinued once visible skin lesions are cleared

Proactive Approach

A combination of predefined, long-term, low-dose, anti-inflammatory treatments applied to previously affected areas of the skin on a regular schedule, in addition to emollients on the entire body

1. Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747. 2. Torrelo A, et al. *Actas Dermosifiliogr.* 2013;104:409-417. 3. Thaci D, et al. *J Eur Acad Dermatol Venerol.* 2010;24:1040-1046. 4. Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:1218-1233.

Systemic Agents in AD[a]

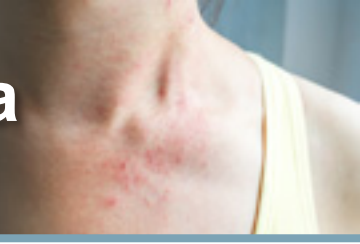


	CsA	AZA	MTX	MPA
Starting dose in adults	5 mg/kg/day	50 mg/day	5 mg/week	MMF 1000-2000 mg/day (EC-MPS 1440 mg/day)
Maintenance dose in adults	2.5–3 mg/kg/day	2–3 mg/kg/day*	Increase to max 25 mg/week	MMF 2000 mg/day† (EC-MPS 1440 mg/day)
Starting dose in children	5 mg/kg/day	50 mg/day	10–15 mg/m^2/week	MMF 20–50 mg/kg/day
Maintenance dose in children	2.5–3 mg/kg/day	2–3 mg/kg/day*	Increase by 2.5–5 mg/week to effective dose, taper by 2.5 mg/week to lowest effective dose	MMF increase daily total dose by 500 mg increments every 2–4 weeks

[a]Off-label. CsA = cyclosporine A; AZA = azathioprine; EC-MPS = enteric-coated mycophenolic sodium; MTX = methotrexate; MMF = mycophenolate mofetil; MPA = mycophenolic acid. *TPMT heterozygote 1–1.5 mg/kg/day. †Children 30–50 mg/kg/day.

Wollenberg A, et al. *J Eur Acad Dermatol Venereol*. 2016;30:729-747.

Systemic Agents in AD, cont.[a]

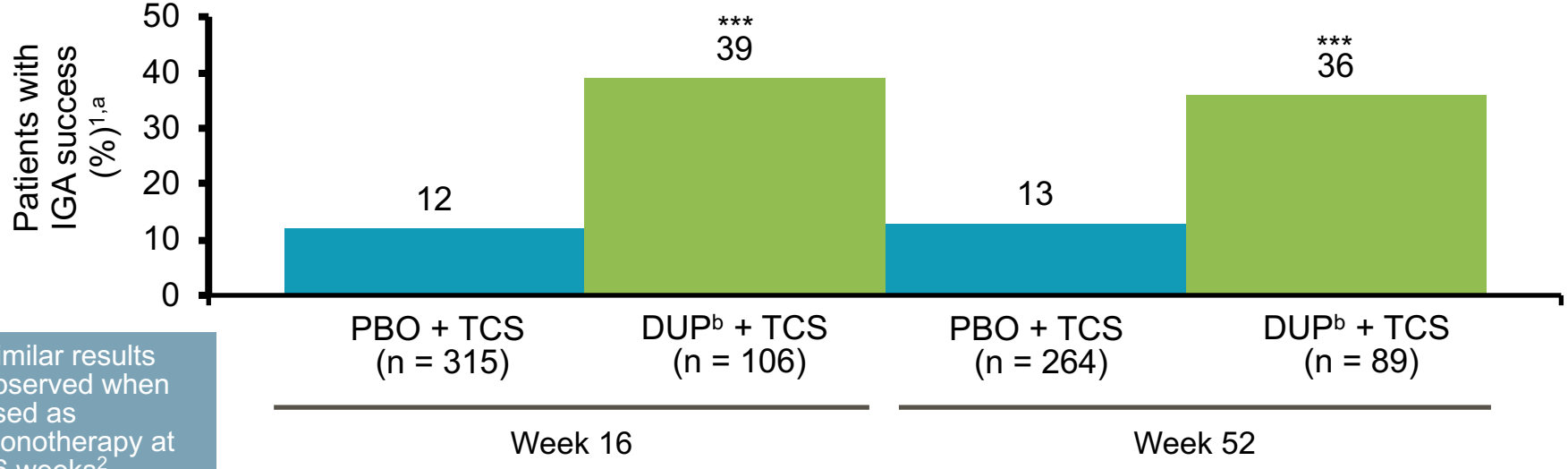


	CsA	AZA	MTX	MPA
Decrease in clinical score (%)	54–95	26–39	42–52	55–68
Treatment period in trials (wks)	Max 52	Max 24	Max 24	Max 30
Time to respond (wks)	2	8–12	8–12	8–12
Time to relapse (wks)	< 2	>12	> 12	> 12
Most important side effects	Serum creatinine ↑ Blood pressure ↑	Hematological Liver enzymes↑ Gastrointestinal	Hematological Liver enzymes↑ Gastrointestinal	Hematological Skin infections Gastrointestinal
Pregnancy	Possible	Conflicting data, possible with strict indication	Teratogenic, absolutely contraindicated	Conflicting data, better not to use
Fathering	Possible	Little information, possible with strict indication	Little information, conflicting data, contraindicated	Little information, better not to use

[a]Off-label. Wollenberg A, et al. *J Eur Acad Dermatol Venereol*. 2016;30:729-747.

New Therapeutic Targets: Dupilumab

- First FDA-approved systemic therapy for adult patients ≥18 y/o age or older with moderate-to-severe atopic dermatitis

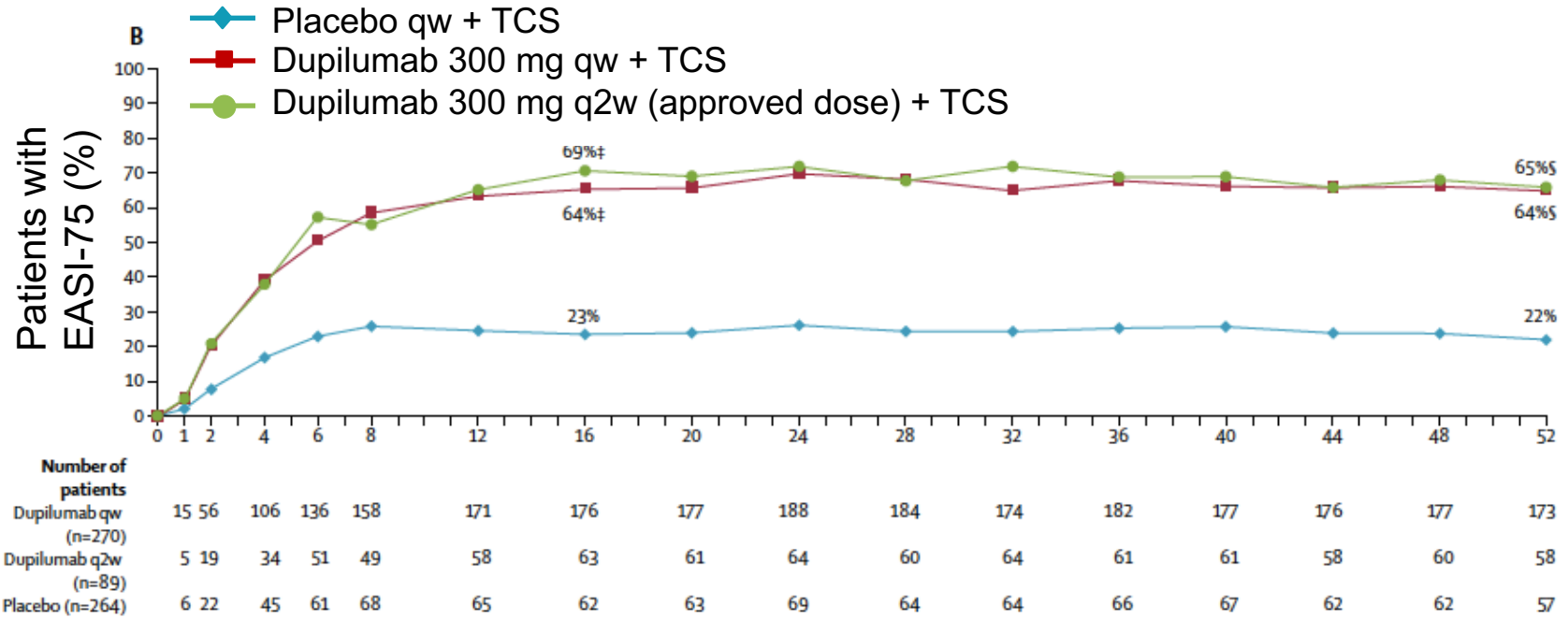


Similar results observed when used as monotherapy at 16 weeks[2]

TCS = topical corticosteroids. [a]Score of 0 or 1 and ≥2-pt improvement from baseline. [b]300 mg q2w (approved dose). ***$p < .0001$ vs. placebo.

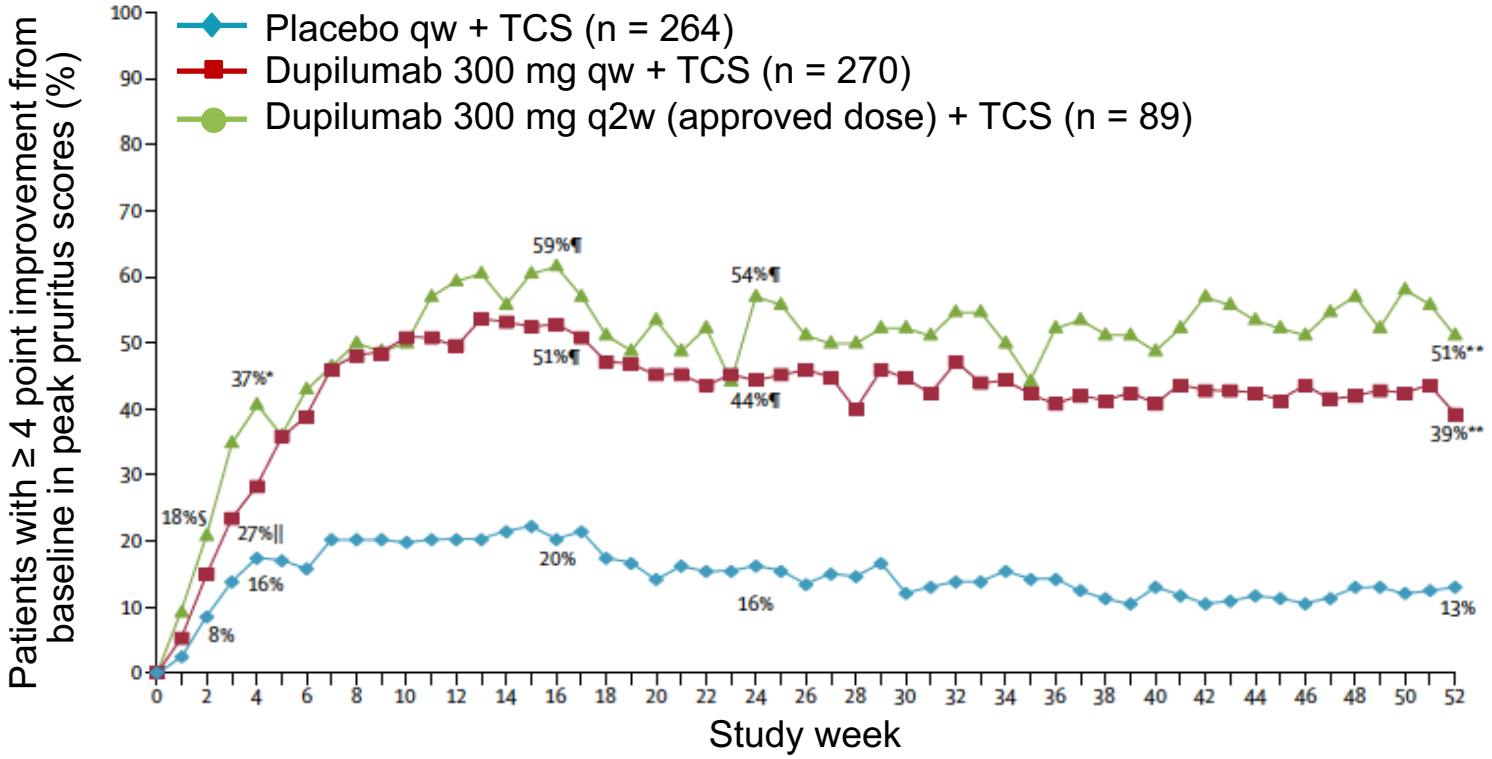
1. Blauvelt A, et al. *Lancet*. 2017;389:2287-2303. 2. Simpson E, et al. *N Engl J Med.* 2016;375:2335-2348.

Dupilumab + TCS: Impact on EASI-75



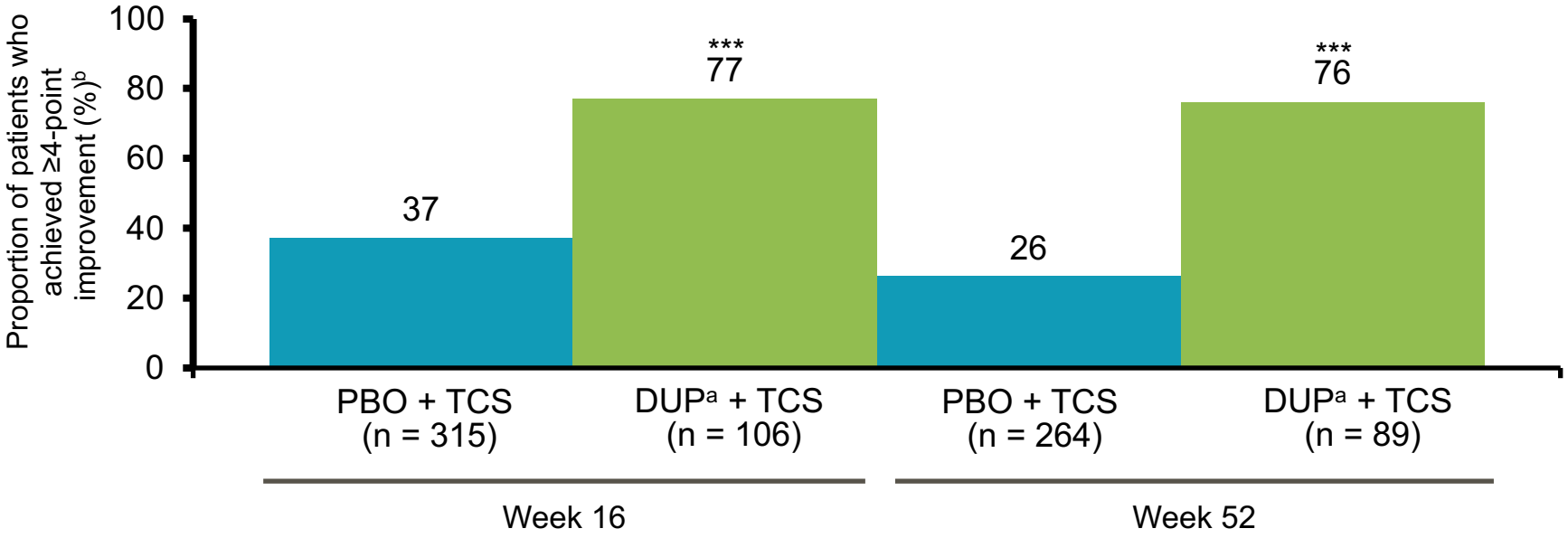
‡$p < .0001$ vs. PBO + TCS (FAS). §$p < .0001$ vs. PBO + TCS (FAS-52).
Blauvelt A, et al. *Lancet*. 2017;389:2287-2303.

Dupilumab + TCS Improves Pruritus



*p<.0001, DUP q2w + TCS vs. PBO + TCS. §p=.0062, DUP q2w + TCS vs. PBO + TCS. ¶p<.0001, DUP q2w + TCS and DUP qw + TCS vs. PBO + TCS. ‖p=.0021, DUP qw + TCS vs. PBO + TCS. **p<.0001, DUP q2w + TCS vs. PBO + TCS and DUP qw + TCS vs. PBO + TCS. Blauvelt A, et al. *Lancet*. 2017;389:2287-2303.

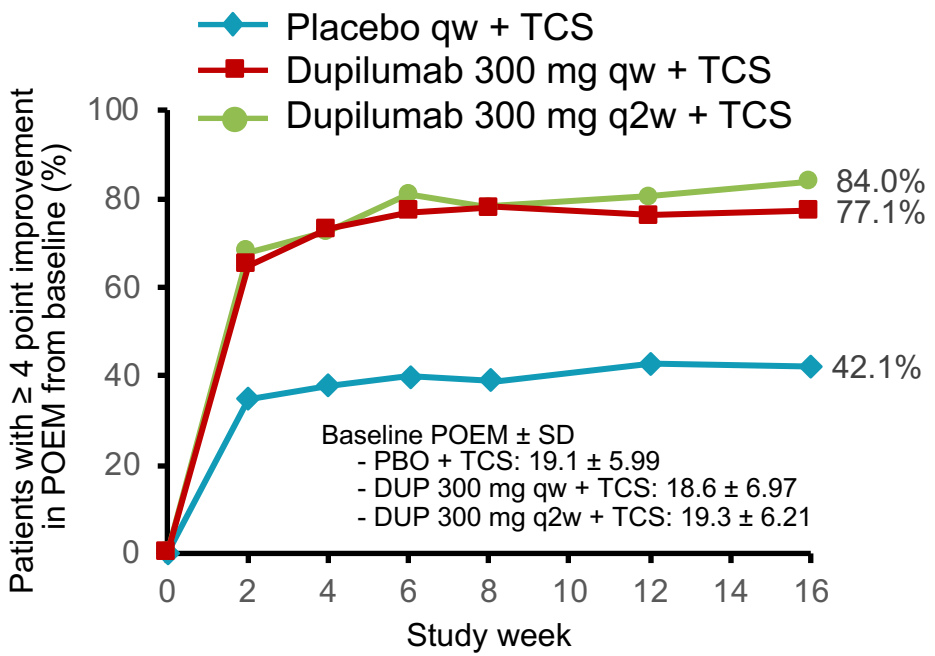
Dupilumab + TCS Improves POEM Scores



[a]300 mg q2w (approved dose). [b]MCID. ***$p < .0001$ vs. placebo.

Blauvelt A, et al. *Lancet*. 2017;389:2287-2303.

Dupilumab + TCS Improves POEM Scores in Patients With Inadequate Response or Intolerance to Cyclosporine



	PBO + TCS (n = 108)	DUP qw + TCS (n = 110)	DUP q2w + TCS (n = 107)
POEM LS mean change from baseline at week 16 ± SE	-4.3 ± .62	-11.4 ± .59***	-11.9 ± .60***

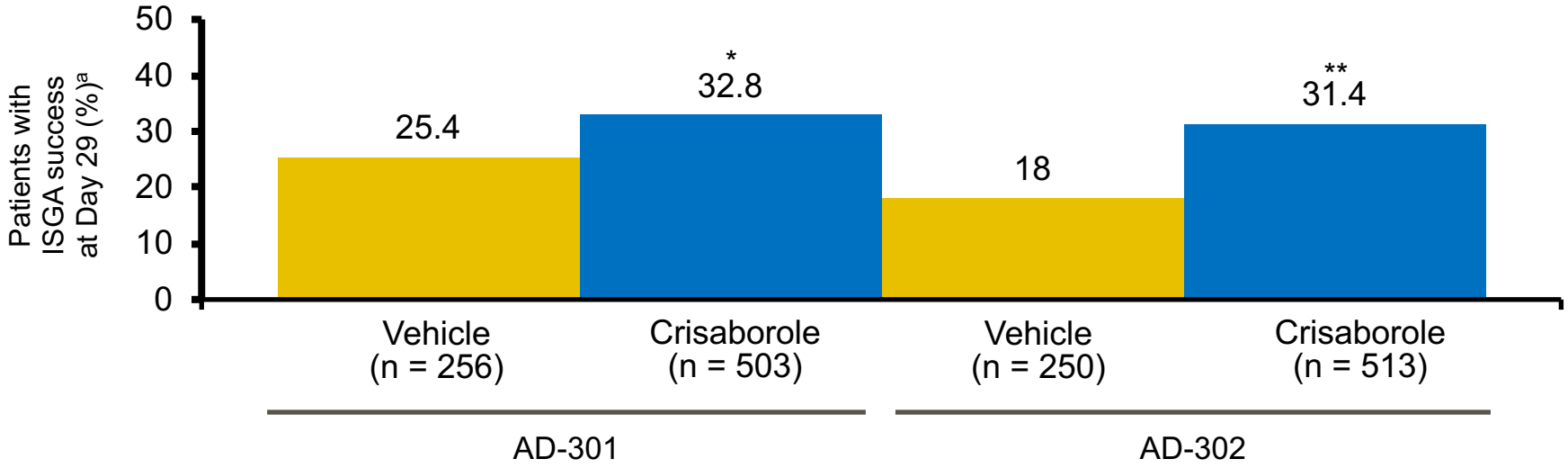
Patients with 4-point improvement in POEM from baseline (%):

- >70% of patients by week 4 achieve this improvement

***p < .001 vs. PBO + TCS. de Bruin-Weller M, et al. *Br J Dermatol*. 2018;178(5):1083-1101.

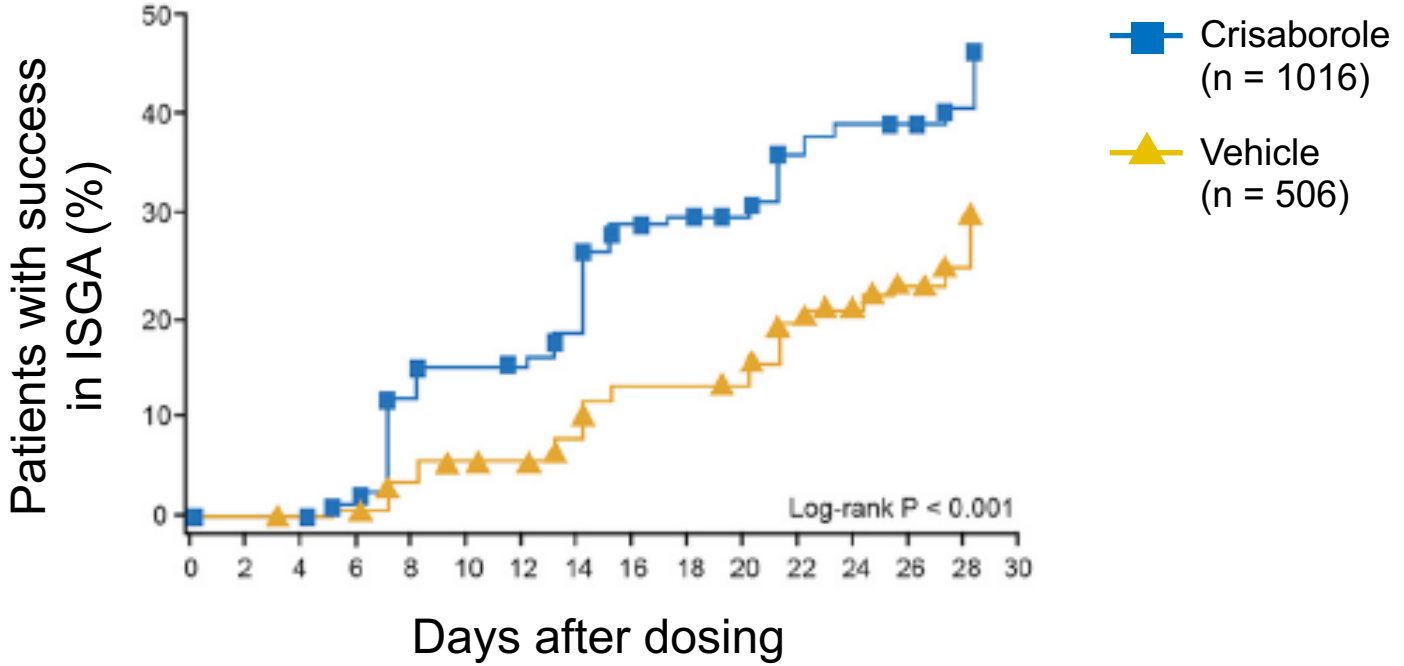
New Therapeutic Targets: Crisaborole

- Topical PDE4 inhibitor approved for treatment of mild to moderate atopic dermatitis in patients 2 years of age and older



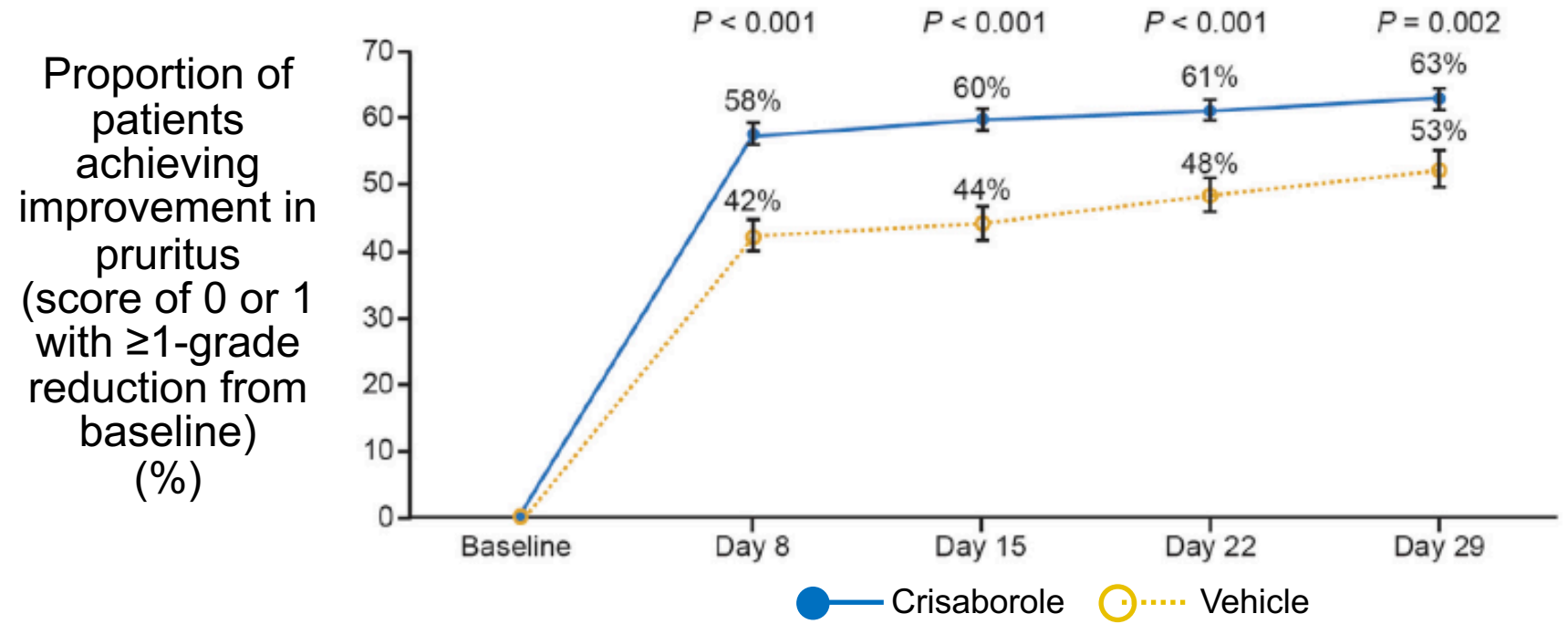
[a]Score of 0 or 1 with ≥2-grade improvement. *$p < .038$ vs. vehicle. **$p < .001$ vs. vehicle.
Paller A, et al. *J Am Acad Dermatol.* 2016;75:494-503.

Crisaborole Effects on ISGA: Pooled Data From AD-301 and AD-302



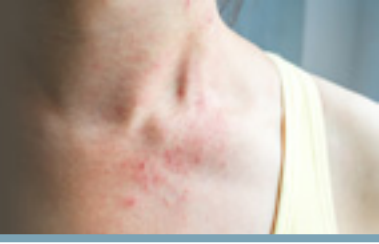
Paller A, et al. *J Am Acad Dermatol*. 2016;75:494-503.

Crisaborole Effects on Pruritus: Pooled Data From AD-301 and AD-302



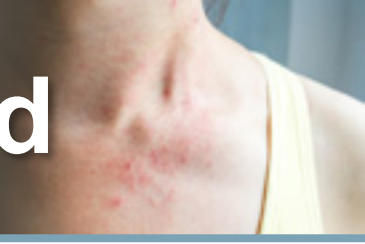
Paller A, et al. *J Am Acad Dermatol*. 2016;75:494-503.

Case Presentation: JC Revisited



- JC is a 36 y/o man with an itchy, red rash
- ***Duration:*** Has had intermittent symptoms throughout his entire life. Feels as if these have been getting progressively worse in recent years
- ***Location:*** Rash is primarily located on the neck, arms, legs, and back
- ***Symptoms:*** Extremely itchy, feels as if he cannot stop scratching, results in waking up from sleep almost every night.
- Impact on lifestyle and career choices

JC's Medical History Revisited



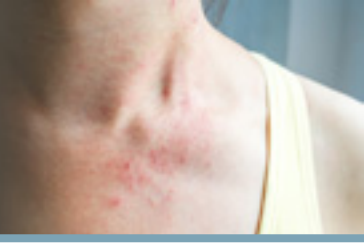
Medical History

- No history of cancer or serious infection
- No known allergies to foods or other medications
- Non-smoker, alcohol intake (4-5 drinks/week)
- ROS: Denied any constitutional symptoms, negative in detail

Physical Examination

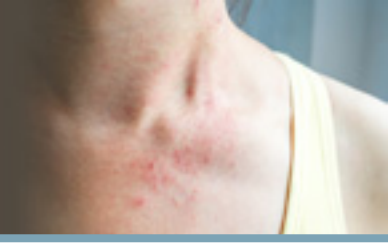
- Presence of multiple, somewhat ill-defined, erythematous patches and plaques with evidence of lichenification and excoriation on the scalp, trunk, arms, and legs

Case Presentation: Assessment of JC's Disease Severity

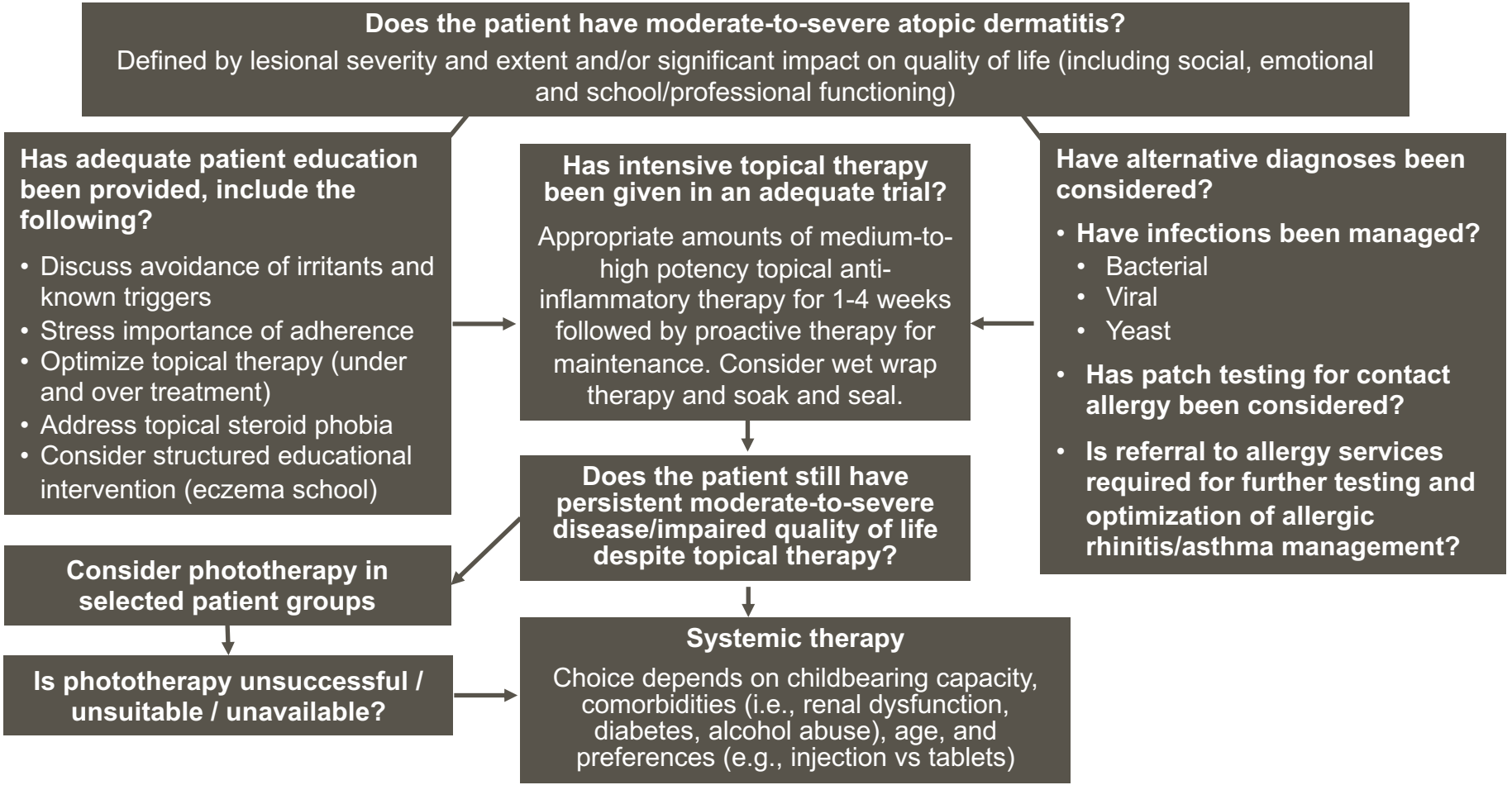


- EASI Score: 25
- IGA: 4
- SCORAD: 30
- Pruritus NRS: >4
- POEM: 20

Case Presentation: JC's Current Treatments



- Multiple topical corticosteroids, oral/IM steroid injections
- Oral antihistamines
- Bathes daily, uses a mild soap and white petrolatum as an emollient



Simpson EL, et al. *J Am Acad Dermatol.* 2017;77(4):623-633.

The Importance and Integration of Documentation Processes in AD

Learning Objective 3

Document the use of tools and results of clinical assessments in patients' charts

Integration of Clinical Tools in Clinical Practice:
Diagnosis and Assessment of Disease Severity in AD

- AAD guidelines, disease severity and QoL measurement scales are not recommended for routine use → not designed for this purpose[1]
- Ask open-ended questions: itch, sleep loss[2]

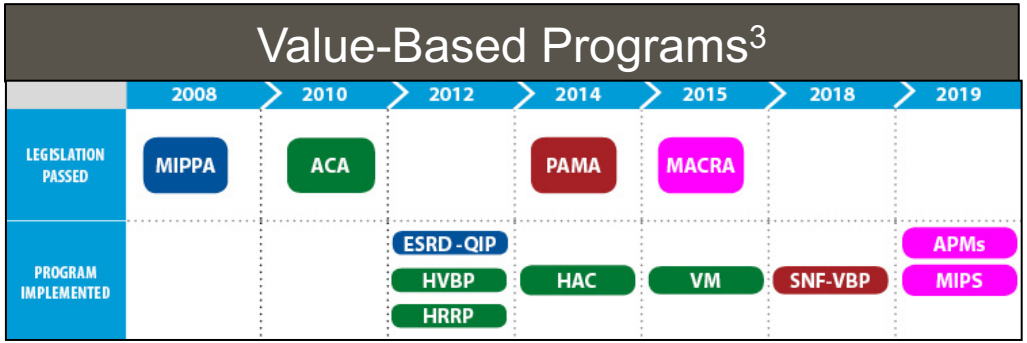
Why integrate these measures?

How to integrate measures to improve diagnosis and assessment of disease severity in daily clinical practice?

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351. 2. Rehal B, et al. *PLOS One*. 2011;6:e17520.

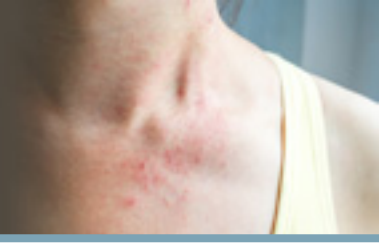
Value-Based Healthcare

- Programs designed to reward health care providers with incentive payments for the quality of care provided[1]
- "Value" is derived from measuring health outcomes against the cost of delivering these outcomes[2]



1. Bodenheimer T, et al. *Ann Fam Med*. 2014;12:573-576. 2. https://catalyst.nejm.org/what-is-value-based-healthcare/
3. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/Value-Based-Programs.html.

Value-Based Healthcare[1-3]



- Triple Aim:
  - Enhancing patient experience
  - Improving population health
  - Reducing cost

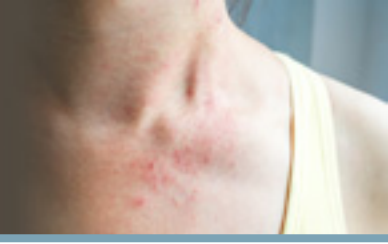
- Quadruple Aim:
  - Enhancing patient experience
  - Improving population health
  - Reducing cost
  - Improving work-life of healthcare providers

Chronic Illnesses: difficult to treat and represent a major cost in the U.S. health care system

Emerging treatment options are expensive

1. Bodenheimer T, et al. *Ann Fam Med*. 2014;1573-576. 2. Block J. *Value in Health*. 2018;21:380-385.
3. https://catalyst.nejm.org/what-is-value-based-healthcare/.

Economic Burden of Atopic Dermatitis[1,2]



- Estimated annual cost in US: ~$5 billion

DIRECT COSTS →
- Healthcare visits
- Prescription costs
- Hospital stays
- Transportation

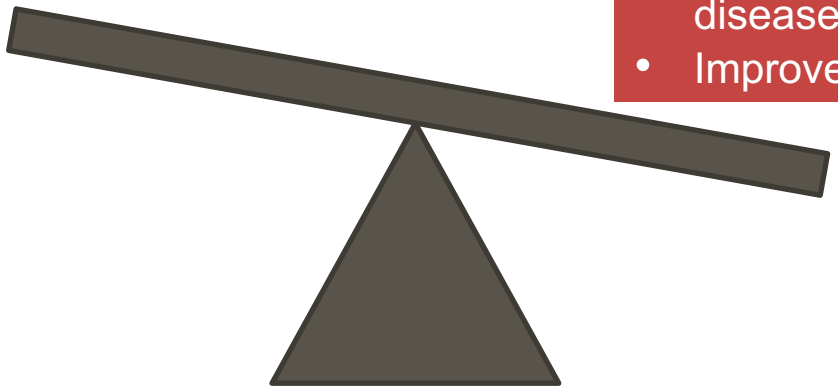
INDIRECT COSTS →
- Missed days
- Loss of productivity
- Career changes
- Impact on QoL

1. Adamson AS. *Adv Exp Med Biol*. 20171027:79-92.
2. Drucker AM, et al. *J Invest Dermatol*. 2017;137:26-30.

Cost-Effectiveness of Biologics for AD

- Importance of demonstrating value of health care interventions

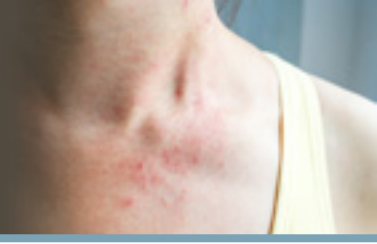
- Chronic disease
- Challenging to treat
- High impact on QoL



- Benefits of long-term disease control
- Improvements on QoL

Kuznik A, et al. *Dermatol Ther (Heidelb)*. 2017;7:493-505.

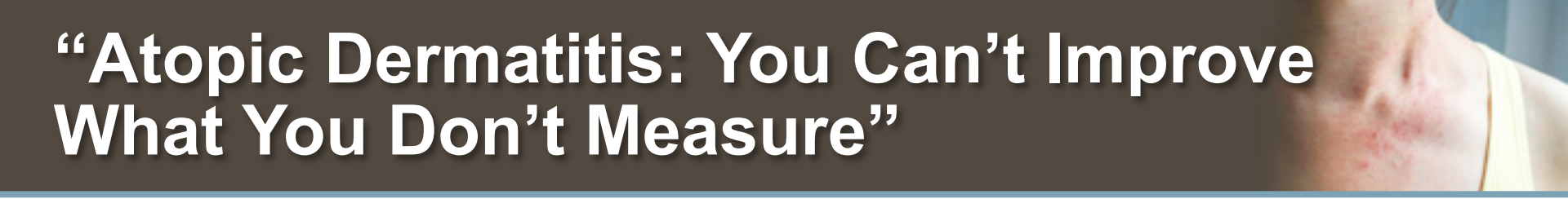
Cost-Effectiveness of Biologics for AD



- Biologics for AD: high price tag (~$37,000/year)[1]
- Dupilumab was cost-effective for the treatment of moderate-to-severe AD with a better cost-effectiveness ratio for patients with more severe disease compared to those with moderate disease.[1,2]
- Shown to be an intervention of high value as compared to secukinumab for psoriasis[3]
  - Related to drug efficacy, cost of the intervention, unmet need, and PROs

1. Kuznik A, et al. *Dermatol Ther*. 2017;7:493-505.
2. Zimmerman M, et al. *J Drugs Dermatol*. 2018;17:750-756.
3. Zozaya N, et al. *BioDrugs*. 2018;32:281-291.

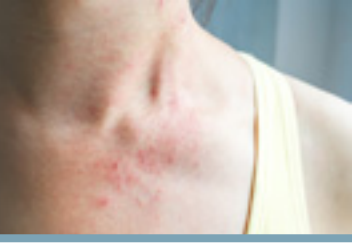
"Atopic Dermatitis: You Can't Improve What You Don't Measure"



Strategies for improving diagnosis and management in adult patients with AD

- Integration of the AAD consensus guidelines in the diagnosis of AD in clinical practice
- Integration of the Patient Oriented Eczema Measure (POEM) in clinical practice: determining disease severity and response to treatment

Assessment of Disease Severity and Clinical Outcomes in AD



- **AAD consensus guidelines for diagnosis of AD:**[1]
  - Pragmatic approach for diagnosis in infants, children, and adults
  - Well-suited for clinical practice
- When practical, scales to consider disease severity: SCORAD, EASI, POEM[2]
  - **POEM:** measure severity from the *patient perspective*

ESSENTIAL FEATURES—Must be present:
- Pruritus
- Eczema (acute, subacute, chronic)
  - Typical morphology and age-specific patterns*
  - Chronic or relapsing history

Patterns include:

1. *Facial, neck, and extensor involvement in infants and children*
2. *Current or previous flexural lesions in any age group*
3. *Sparing of the groin and axillary regions*

IMPORTANT FEATURES—Seen in most cases, adding support to the diagnosis:
- Early age of onset
- Atopy
  - Personal and/or family history
  - Immunoglobulin E reactivity
- Xerosis

ASSOCIATED FEATURES—These clinical associations help to suggest the diagnosis of atopic dermatitis but are too nonspecific to be used for defining or detecting atopic dermatitis for research and epidemiologic studies:
- Atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)
- Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis
- Ocular/periorbital changes
- Other regional findings (eg, perioral changes/periauricular lesions)
- Perifollicular accentuation/lichenification/prurigo lesions

EXCLUSIONARY CONDITIONS—It should be noted that a diagnosis of atopic dermatitis depends on excluding conditions, such as:
- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.
2. Rehal B, et al. *PloS one*. 2011;6:e17520.

Patient Oriented Eczema Measure (POEM)[1,2]

Please circle one response for each of the seven questions below about your/your child's eczema. If your child is old enough to understand the questions then please fill in the questionnaire together. Please leave blank any questions you feel unable to answer.

1. Over the last week, on how many days has your/your child's skin been itchy because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

2. Over the last week, on how many nights has your/your child's sleep been disturbed because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

3. Over the last week, on how many days has your/your child's skin been bleeding because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

4. Over the last week, on how many days has your/your child's skin been weeping or oozing clear fluid because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

5. Over the last week, on how many days has your/your child's skin been cracked because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

6. Over the last week, on how many days has your/your child's skin been flaking off because of the eczema?

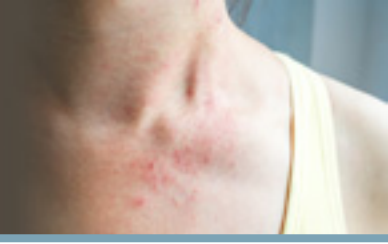
No days | 1-2 days | 3-4 days | 5-6 days | Every day

7. Over the last week, on how many days has your/your child's skin felt dry or rough because of the eczema?

No days | 1-2 days | 3-4 days | 5-6 days | Every day

1. Charman CR, et al. *Br J Dermatol.* 2013;169(6):1326-1332. 2. Charman CR, et al. *Arch Dermatol*. 2004;140:1513-1519.

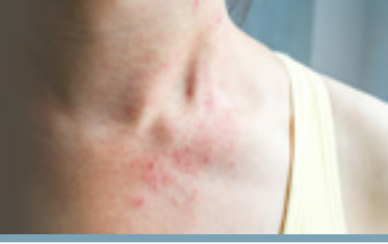
Patient Oriented Eczema Measure (POEM)[1,2]



- Scoring POEM (total score max = 28):
  - No days = 0
  - 1-2 days = 1
  - 3-4 days = 2
  - 5-6 days = 3
  - Every day = 4
- What does a POEM score mean?
  - 0-2 = Clear or almost clear
  - 3-7 = Mild eczema
  - 8-16 = Moderate eczema
  - 17-24 = Severe eczema
  - 25-28 = Very severe eczema

1. Charman CR, et al. *Br J Dermatol*. 2013;169(6):1326-1332. 2. Charman CR, et al. *Arch Dermatol*. 2004;140:1513-1519.

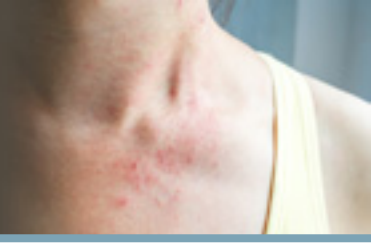
Case Presentation: Next Steps for JC



- Due to cost and time constraints, phototherapy was not an option
- JC was a candidate for systemic therapy based on disease severity and inadequate response to topical steroids
- Dupilumab was added based on risk-benefit analysis
- Other off-label systemic therapies were options, but they are associated with side effects and contraindications

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Atopic Dermatitis is a **chronic** disease, challenging to treat, and often results in **significant** impairments in patient's quality of life
- Treatment strategies:
  - Balance of clinical efficacy and safety with individual patient characteristics and preferences
  - Expansion in treatment alternatives → new interventions with improved efficacy and safety
- Integration of patient outcome measures such as POEM is critical to demonstrate the value of high-cost interventions

Questions & Answers

Get Your Credit

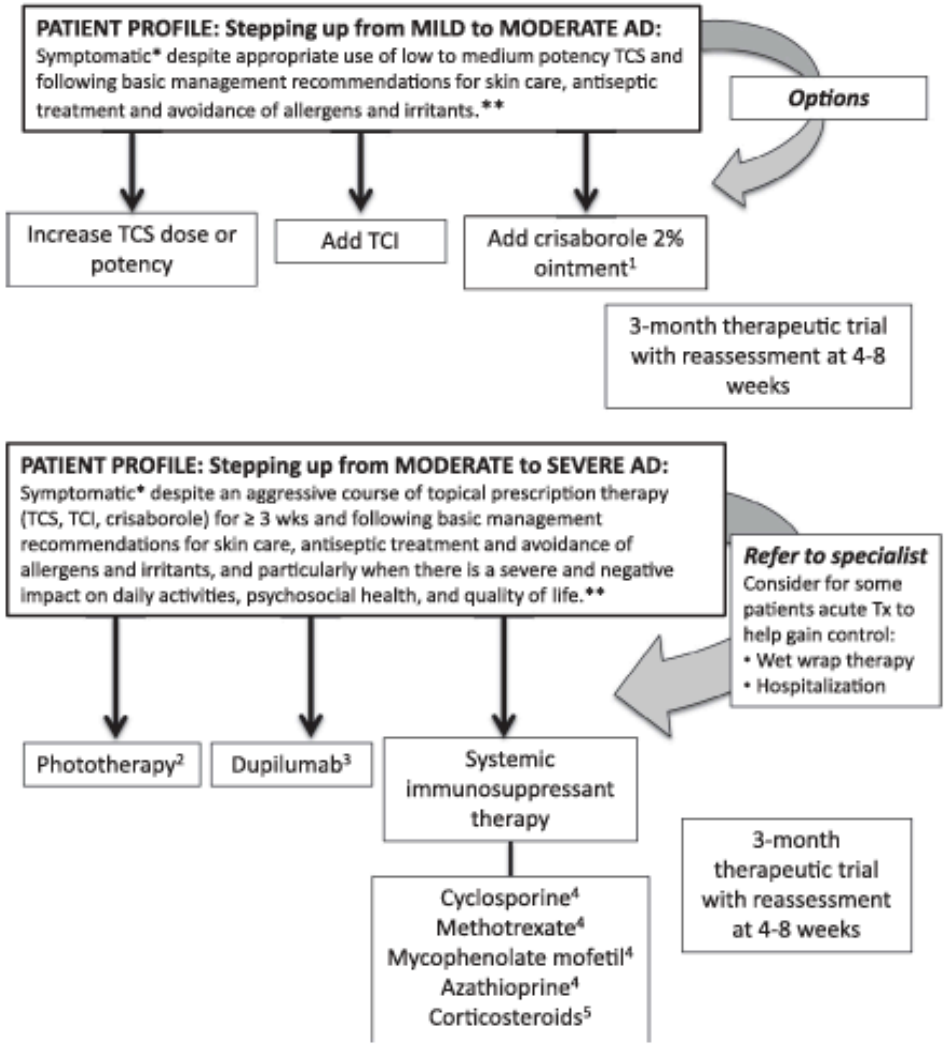
Don’t forget to turn in your forms so you can collect your credit.

Downloadable Resources

Available for your convenience at

www.cmeoutfitters.com/
/ADupdateResources

Example of Treatment Algorithm for Atopic Dermatitis: AD Yardstick



*Poorly or inadequately controlled signs and symptoms of AD.
**Before stepping up therapy, the patient should be assessed for nonadherence, potential comorbidities, and other factors that might negatively affect response to therapy. [1]Indicated for patients at least 2 years old with mild to moderate AD. [2]The patient should be willing and able to commit to phototherapy in terms of cost, convenience, and access. [3]Indicated for patients at least 18 years old with moderate to severe AD. It is the authors' expert opinion that dupilumab has a safety and efficacy profile that is better than that of immunosuppressive agents or phototherapy; cost and coverage are extremely important considerations.[4]Not approved. [5]Approved to treat AD but not recommended for long-term maintenance.
Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120:10-22.