MASTERS OF PEDIATRIC DERMATOLOGY

CELEBRATING 30 YEARS
of Advanced Pediatric Dermatology Education

Inflammatory Skin Disorders: AD and Psoriasis

Latanya Benjamin, MD, FAAD, FAAP

Associate Professor of Pediatric Dermatology

Learning Objectives

Demonstrate how common inflammatory skin disorders show diversity in clinical presentation

Recognize the ways in which pediatric AD and psoriasis patients with SOC are affected in terms of managing their condition

Review current and emerging AD and psoriasis treatments for pediatric patients

Atopic Dermatitis

Atopic Dermatitis

A chronic, relapsing, inflammatory condition

18 million Americans

9.6 million children (~15% of children in USA)

AD: Psychosocial Impact

AD can negatively impact QoL of both the child and family

Sleep disruption (47-60%), poor mood

Low self esteem

Parental self-blame and guilt

Increased reports of suicidal ideation among adolescents with AD

Atopic Dermatitis

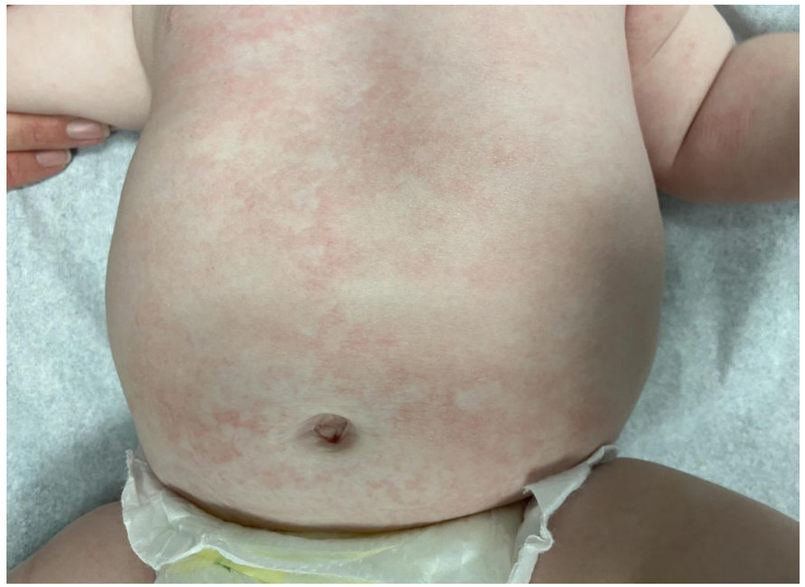
AD disproportionally affects Black children

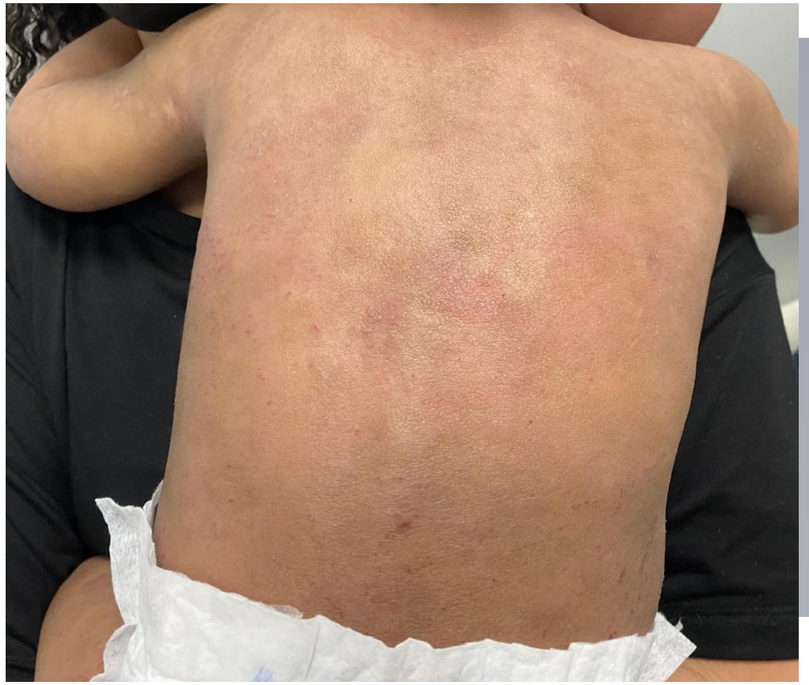
Among US children, more likely to suffer from AD and more likely to seek medical care for AD

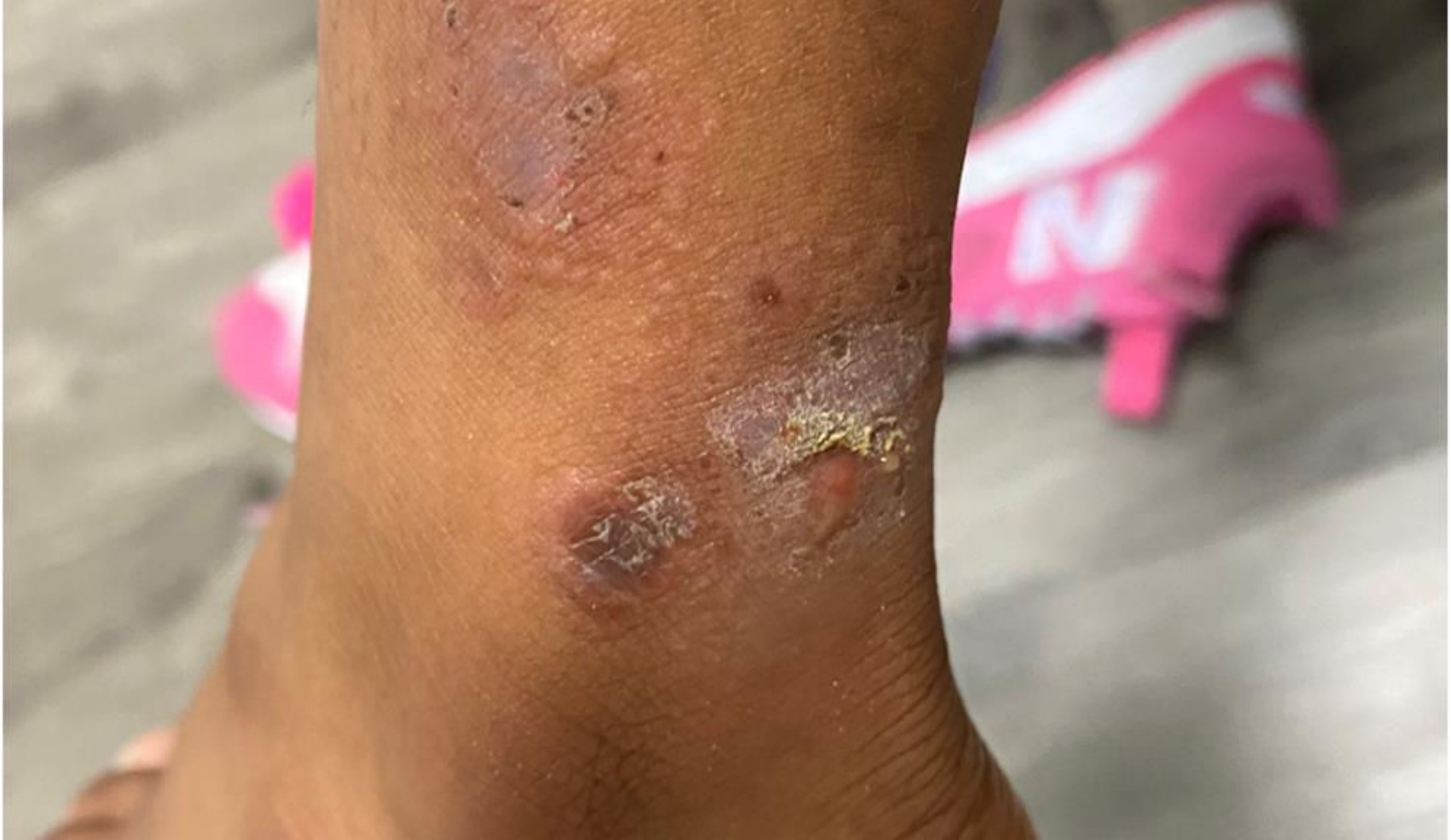
More disfiguring in SOC patients (hypo/hyper-pigmentation)

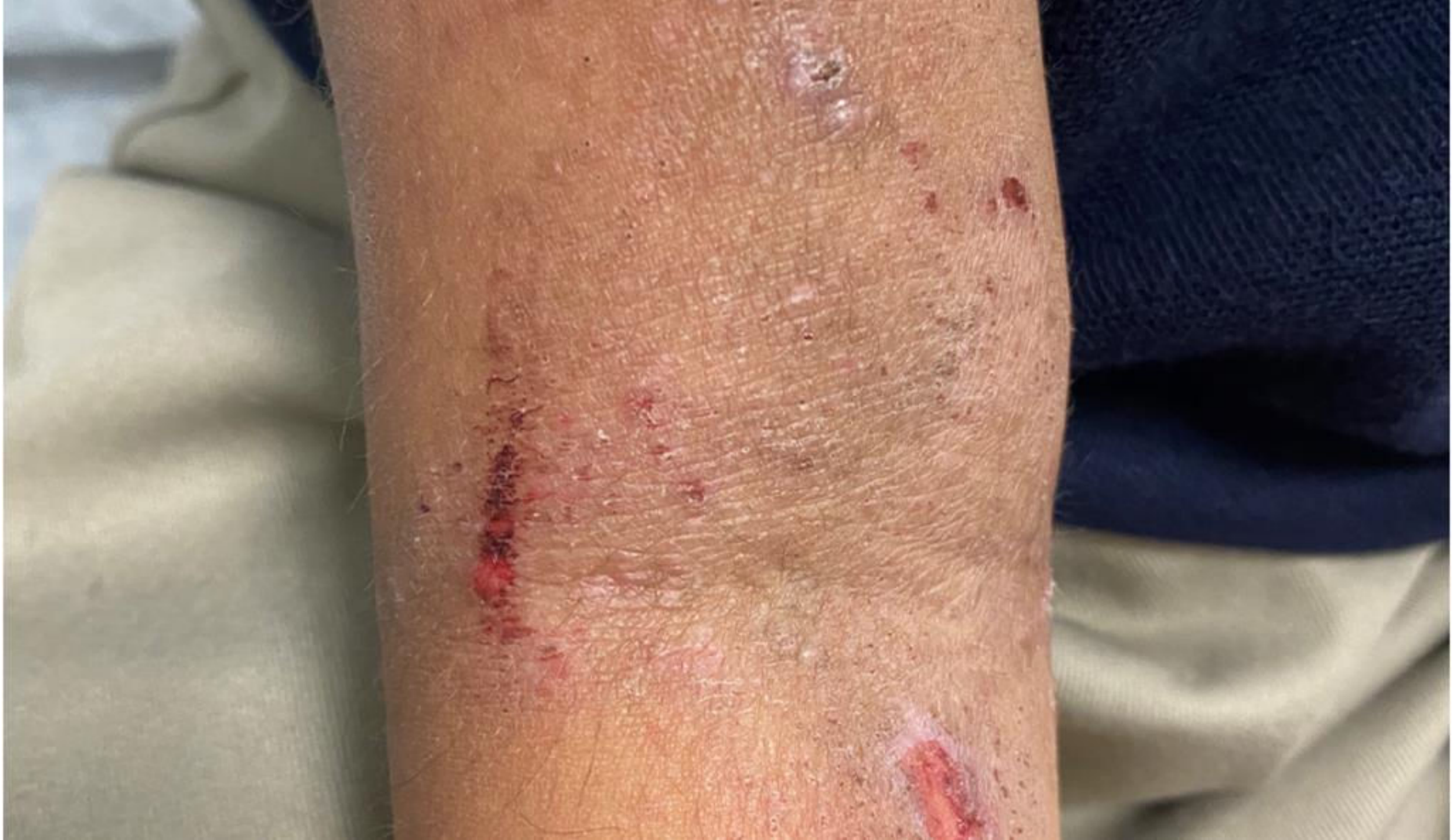
Challenges in diagnosing and treating in pediatric SOC patients

Diversity in Clinical Presentation

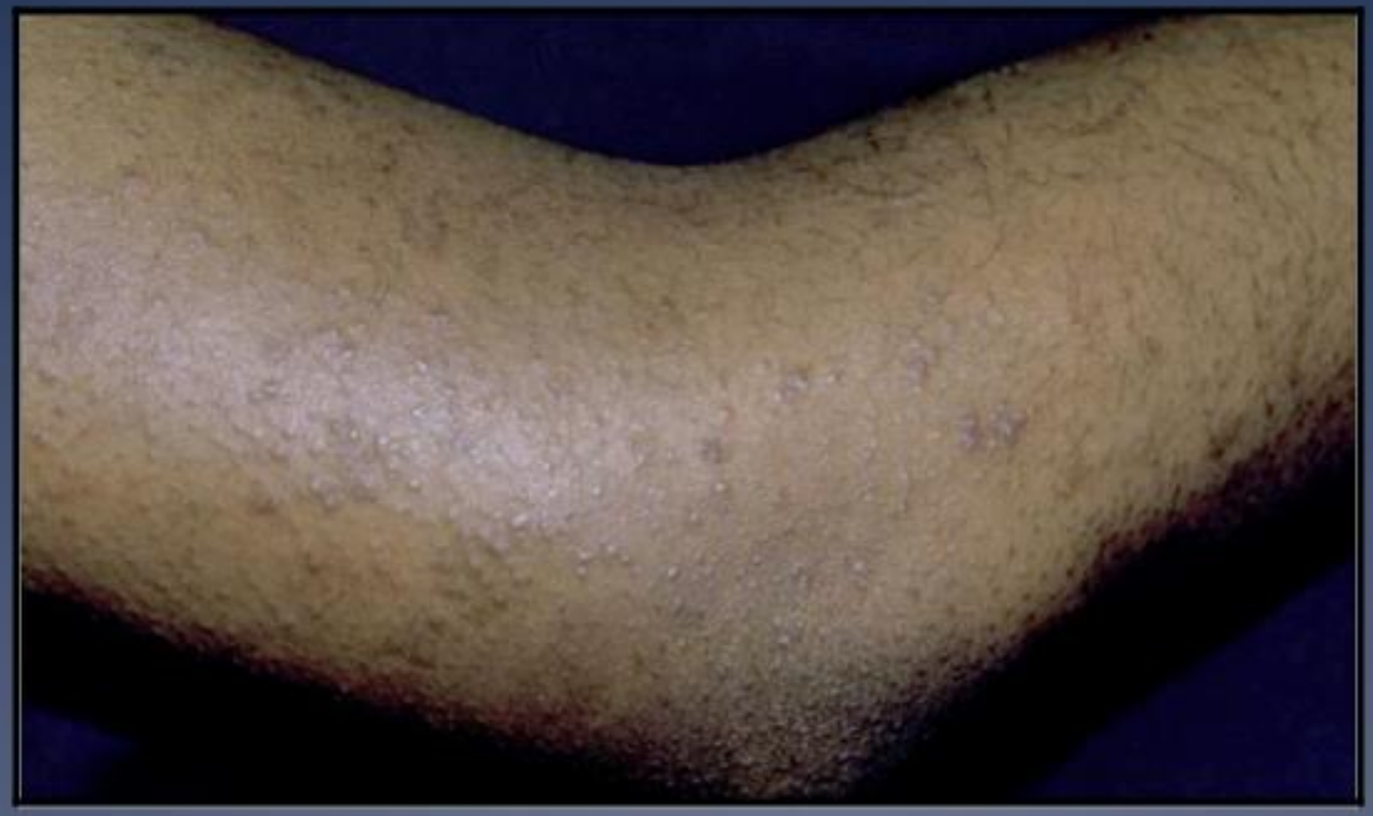




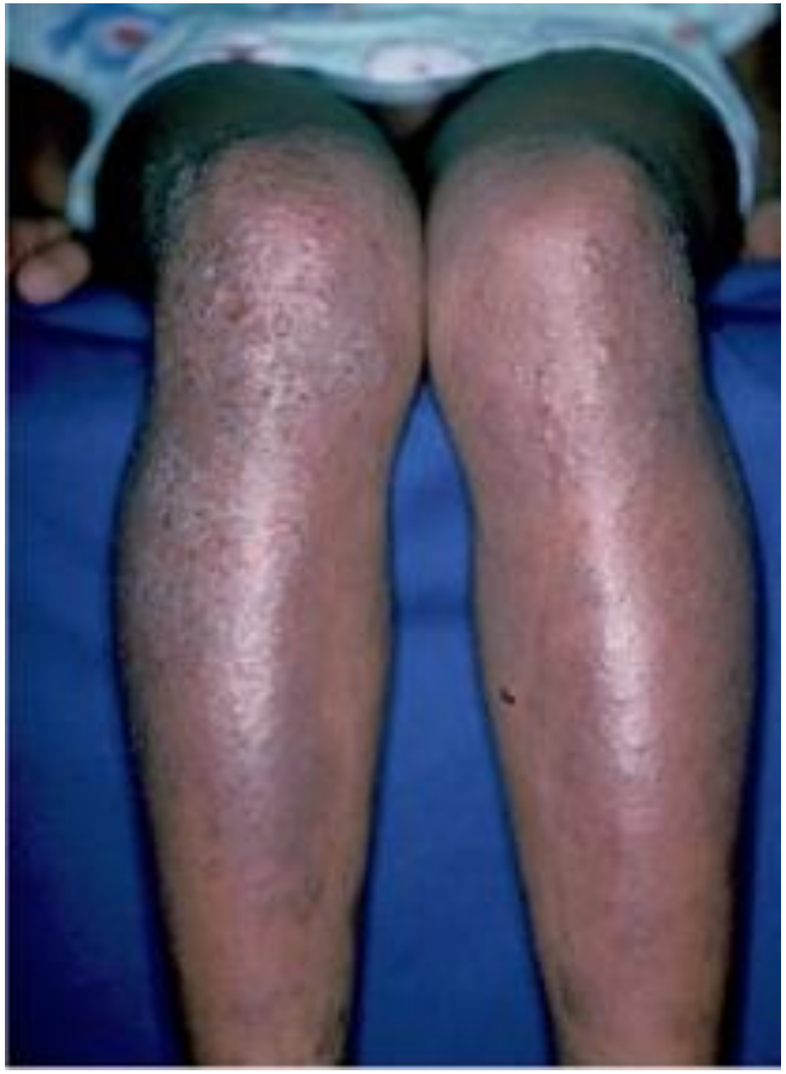




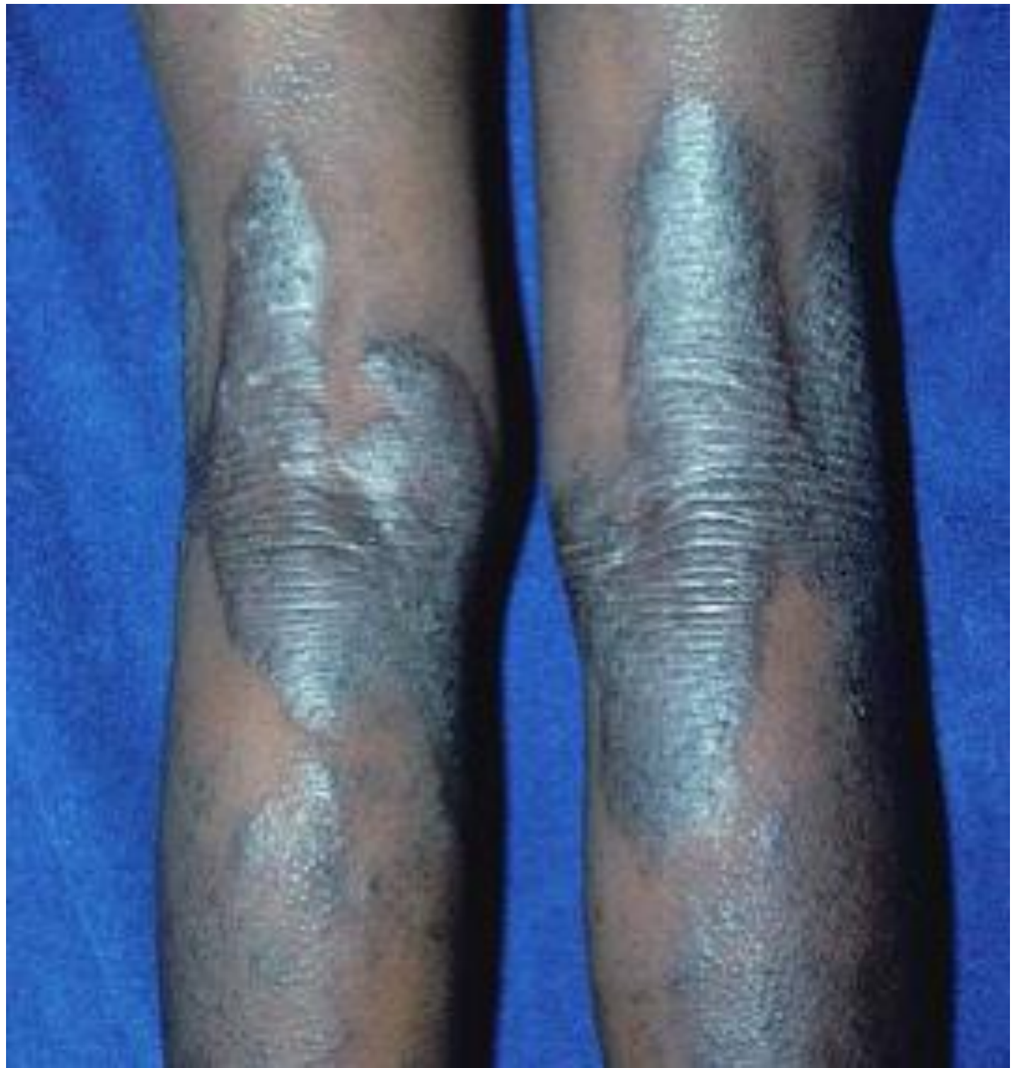
Papular Atopic Dermatitis



AD: Acute Flare



AD: Chronic



AD: Pathogenesis

Complex, multifactorial, poorly understood

Endogenous factors:

- Genetic predisposition
- Defective skin barrier
- Abnormal innate immunity
- Immunologic abnormalities

Interaction with exogenous factors

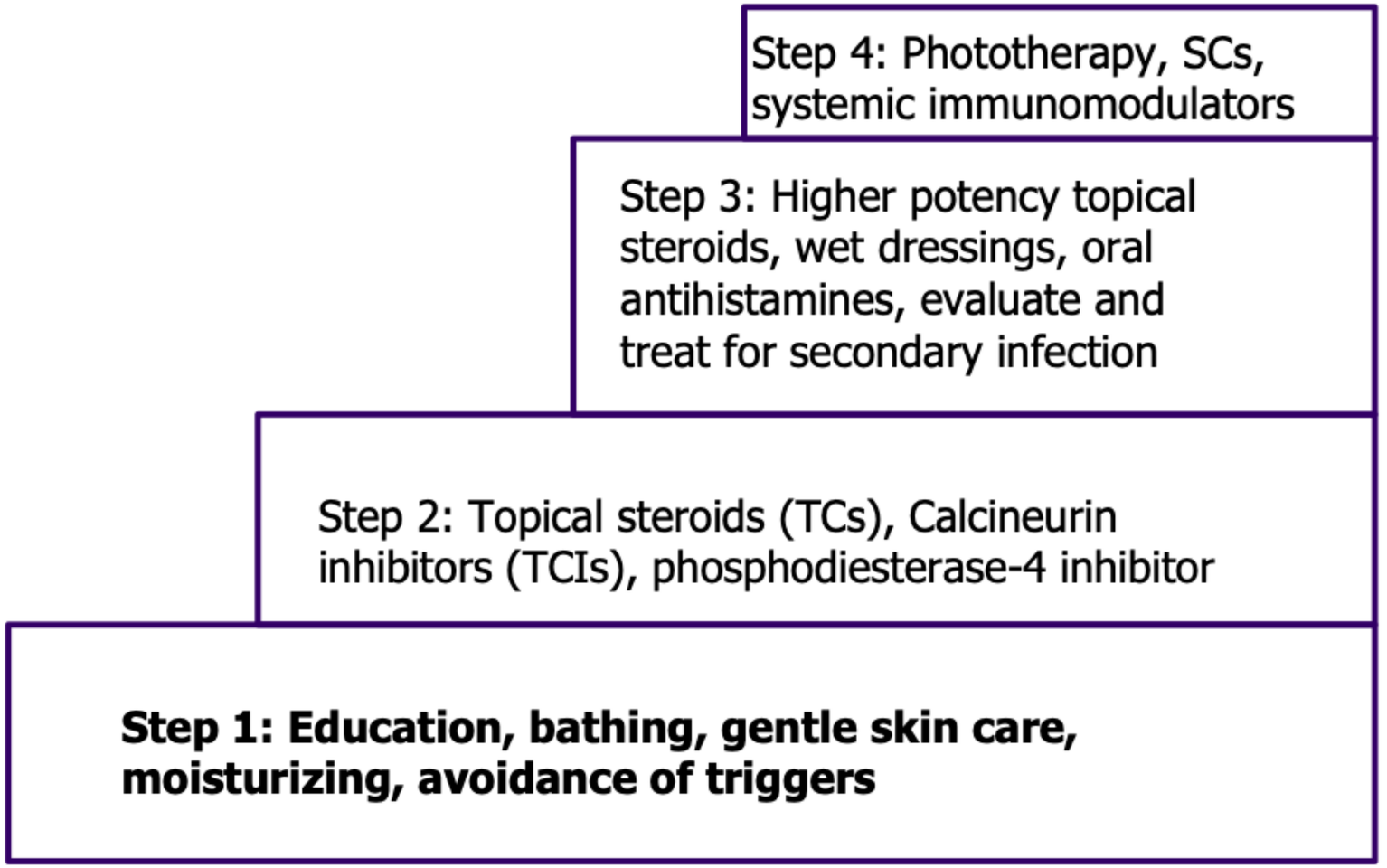
Immune Response

Acute AD characterized by Th2 immune response

IL-4, IL-13

Drives IgE synthesis

Atopic Dermatitis
Treatment Overview



Therapies for recalcitrant AD

Phototherapy

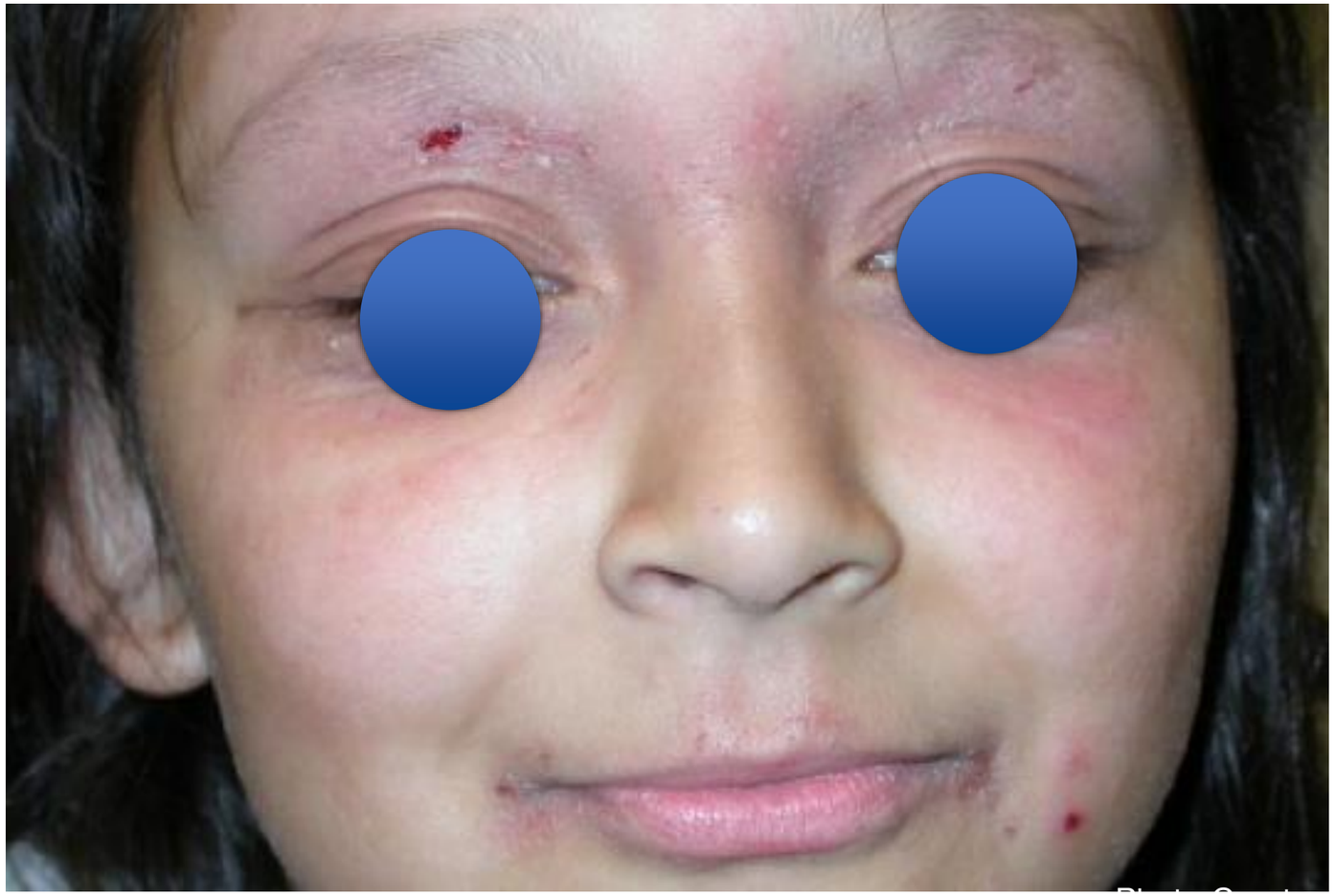
Cyclosporin

Azathioprine

Mycophenolate mofetil

Methotrexate

Facial/ Periocular Involvement



Topical Calcineurin Inhibitors (TCIs)

Topical immunosuppressive agents that inhibit T cells

Pimecrolimus cream1%

Tacrolimus ointment 0.03% and 0.1%

Approved for treatment of AD in patients at least 2 years of age

Phosphodiesterase-4 Inhibitor

FDA approved December 2016

Non-steroidal

Crisaborole ointment 2%

Approved for treatment of mild-moderate AD in patients 3 months of age and older

Side Effects

Common side effects: burning, stinging

Does NOT cause: atrophy, telangiectasia, hypopigmentation

Dupilumab

FDA approved March 2017* / May 2020 (children)

Targets IL-4 and IL-13

Dupilumab injection 200mg and 300mg

First biologic approved for children aged 6 months and older with uncontrolled moderate to severe AD

Ruxolitinib

FDA approved September 2021

Janus kinase (JAK1/ JAK2) inhibitor

Ruxolitinib cream 1.5%

Approved for short-term and non-continuous chronic treatment of mild-moderate AD in non-immunocompromised adults and children 12 years of age and older whose disease is not well controlled with topical prescription therapies or when those therapies are not advisable

Upadacitinib

FDA approved January 2022

Janus kinase (JAK1) inhibitor

Extended-release tablets 15 mg and 30 mg

Approved for adult and adolescents 12 years and older with refractory, moderate to severe AD

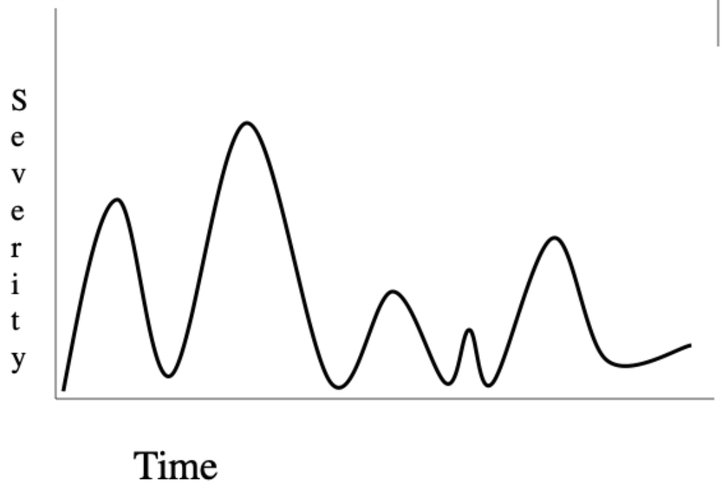
Other FDA approvals for Adults with Moderate to Severe AD

Tralokinumab - IL-13 inhibitor approved Dec 2021

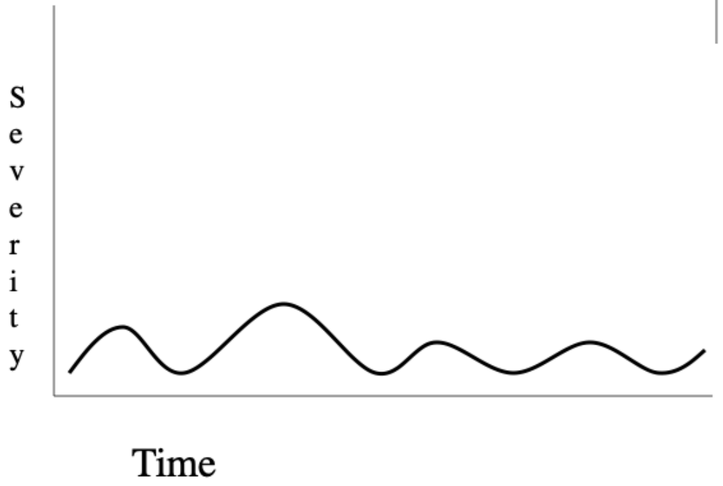
- Abrocitinib - JAK 1 inhibitor approved Jan 2022

Baricitinib - JAK 1/ JAK 2 inhibitor (approved in Europe)

Untreated AD



Treated AD



Psoriasis

Psoriasis

Chronic, mutisystem, inflammatory disease

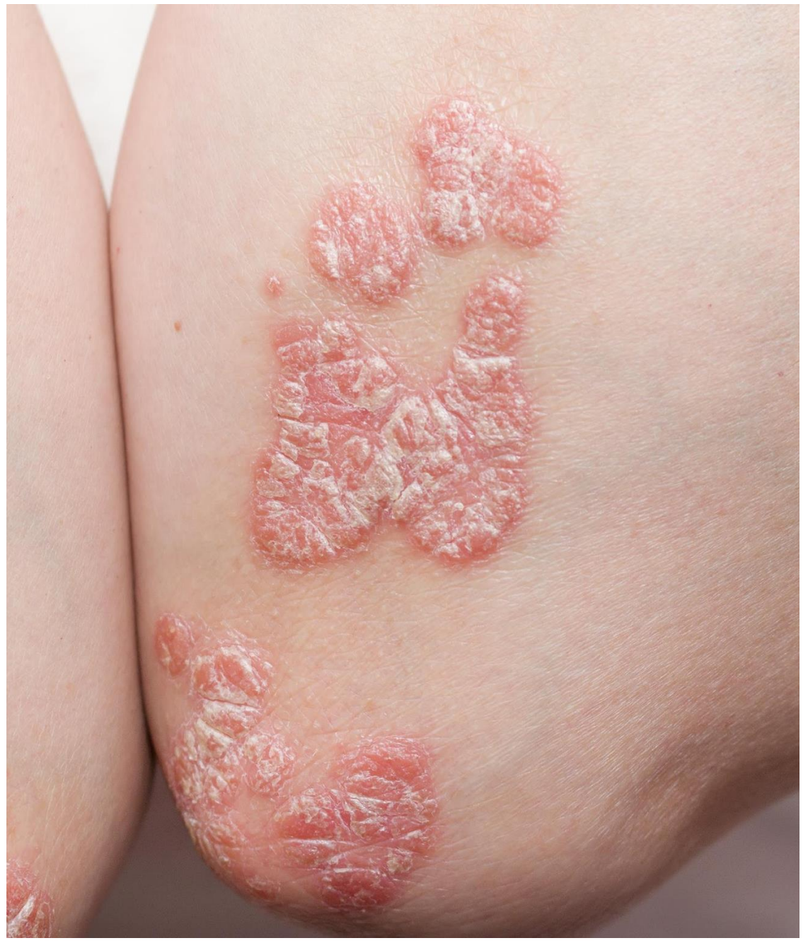
Occurs in 2-4% of the general population

Affects approx 1% of children

Characterized by bright red, plaques with silvery scales

Wide spectrum of clinical manifestations (scalp, nails, joints, palmoplantar)

Can have an immense impact of QOL



Clinical Manifestations of Pediatric Psoriasis

Plaque

Inverse

Guttate

Pustular

Erythrodermic

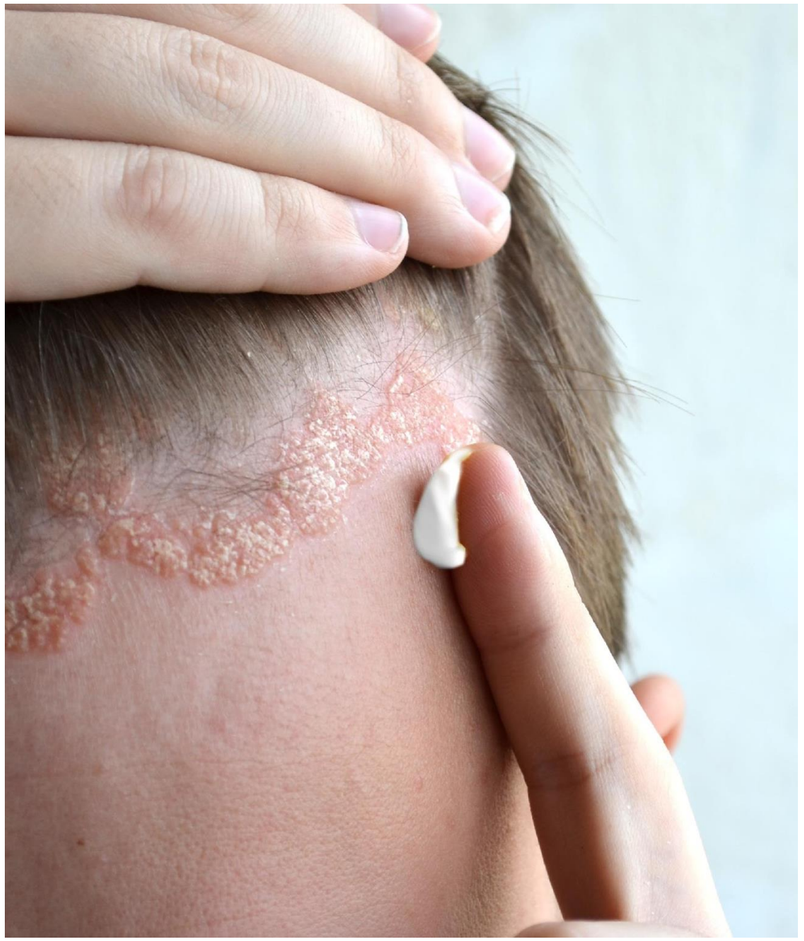
Scalp

Diaper area

Palmoplantar

Nail

Extracutaneous involvement



Psoriasis- Pathogenesis

Chronic activation of T-helper cells (Th17)

Secretion of pro inflammatory cytokines (IL-17) & (IL-23)

TNF-α alpha

Psoriasis - Comorbidities

Cardiovascular disease

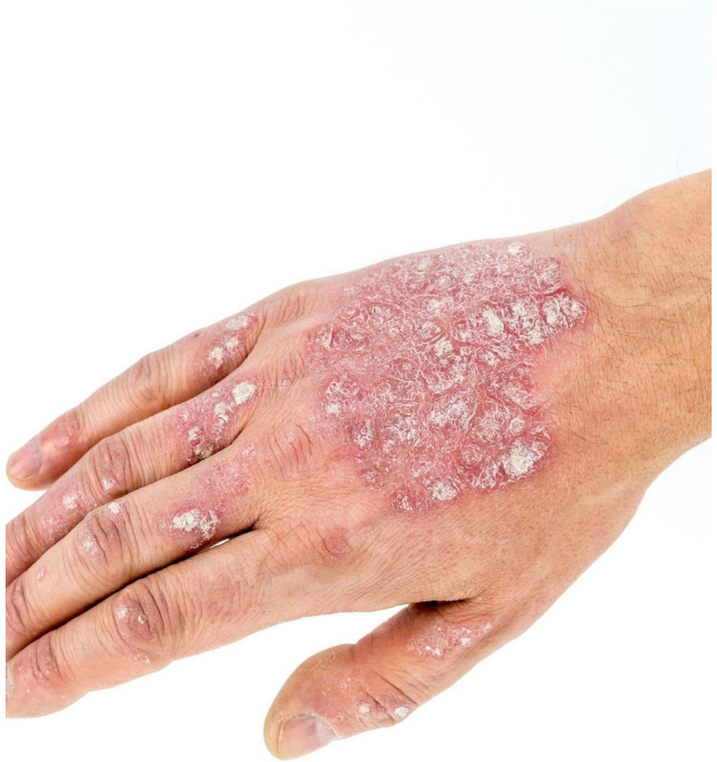
Insulin resistance/ Diabetes

Metabolic syndrome

Psoriatic arthritis

IBD

Mental health *



* Evidence shows that Black, Asian and Hispanic patients with psoriasis report greater QOL impact, regardless of disease severity

National Psoriasis Foundation Study

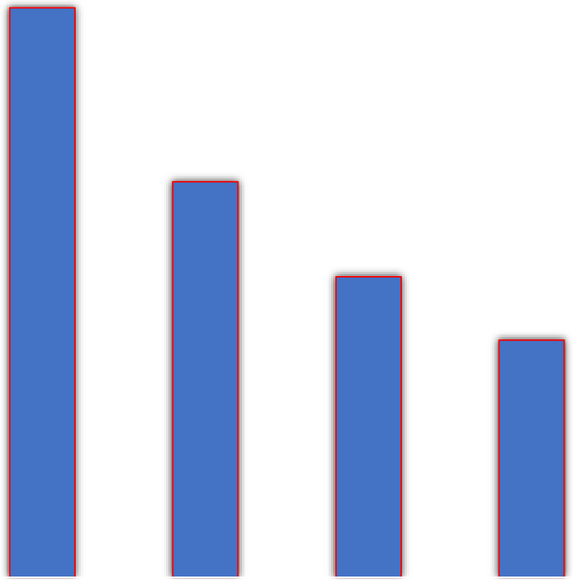
Found 72% of minorities reported an impact on their QOL due to psoriasis (54% in Caucasians)

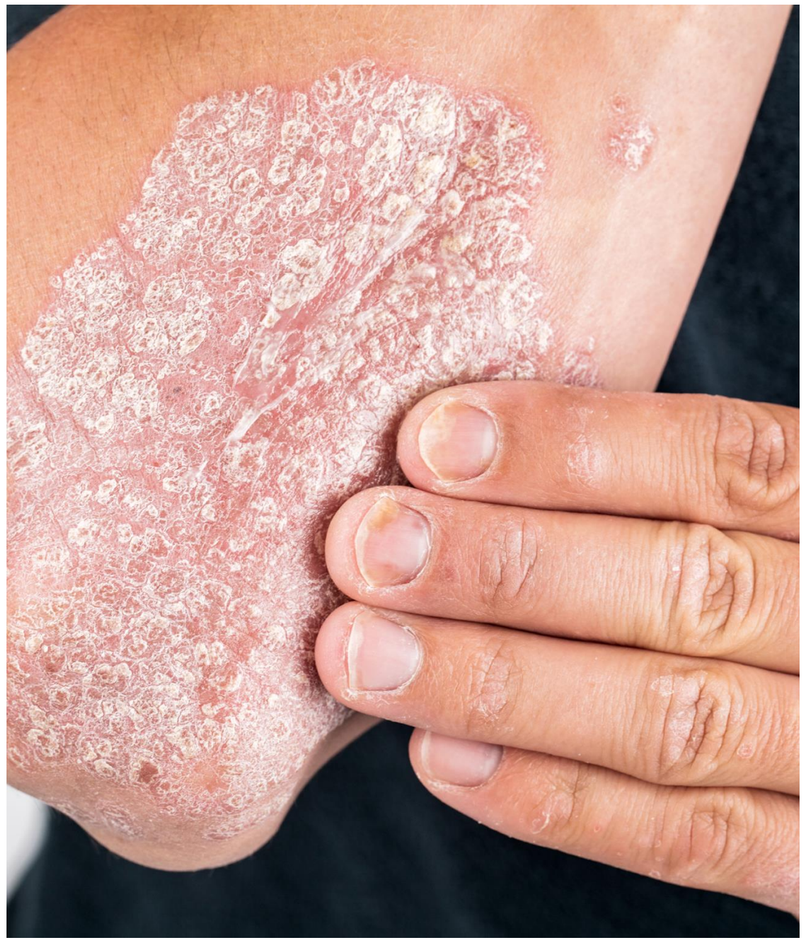
A higher percentage of African Americans (23%) reported having very severe psoriasis compared to Caucasian patients (8%)

Alexis AF, Blackcloud P. *J Clin Aesthet Dermatol*. 2014;7(11):16-24

Psoriasis- Race & Ethnicity

In a 2021 study, the percentages of adults 20 years and older who'd been diagnosed with psoriasis





Psoriasis- Question 1
Racial Differences in Presentation

Compared to White patients, which ethnoracial group is more likely to present with erythrodermic psoriasis?

Asian

Black

Hispanic

Psoriasis- Question 1
Racial Differences in Presentation

Compared to White patients, which ethnoracial group is more likely to present with erythrodermic psoriasis?

A. Asian

Black

Hispanic

Nicholas MN et al. *Cutis*. 2020;106(2S):7-E10

Psoriasis- Question 2
Racial Differences in Presentation

Compared to White patients, which ethnoracial group (s) are more likely to present with pustular psoriasis?

Asian

Black

Hispanic

Psoriasis- Question 2
Racial Differences in Presentation

Compared to White patients, which ethnoracial group (s) are more likely to present with pustular psoriasis?

A. Asian

Black

C. Hispanic

Yan D et al. *Dermatol Online J*. 2018;24(7)

Psoriasis- Question 3
Racial Differences in Presentation

Compared to White patients, which ethnoracial group is less likely to present with inverse psoriasis?

Asian

Black

Hispanic

Psoriasis- Question 3
Racial Differences in Presentation

Compared to White patients, which ethnoracial group is less likely to present with inverse psoriasis?

A. Asian

Black

Hispanic

Nicholas MN et al. *Cutis*. 2020;106(2S):7-E10

Psoriasis- Question 4
Racial Differences in Presentation

Compared to White patients, which ethnoracial group has been reported to have lower frequencies of PsA?

Asian

Black

Hispanic

Psoriasis- Question 4
Racial Differences in Presentation

Compared to White patients, which ethnoracial group has been reported to have lower frequencies of PsA?

Asian

B. Black

Hispanic

Kerr GS et al. *Clin Rheumatol*. 2015;34:1753-1759

Psoriasis- Question 5
Racial Differences in Presentation

Compared to White patients, which ethnoracial group has been reported to have higher PASI scores?

Asian

Black

Hispanic

Psoriasis- Question 5
Racial Differences in Presentation

Compared to White patients, which ethnoracial group has been reported to have higher PASI scores?

A. Asian

B. Black

C. Hispanic

Kerr GS et al. *Clin Rheumatol*. 2015;34:1753-1759

Psoriasis-
Racial Differences in Presentation

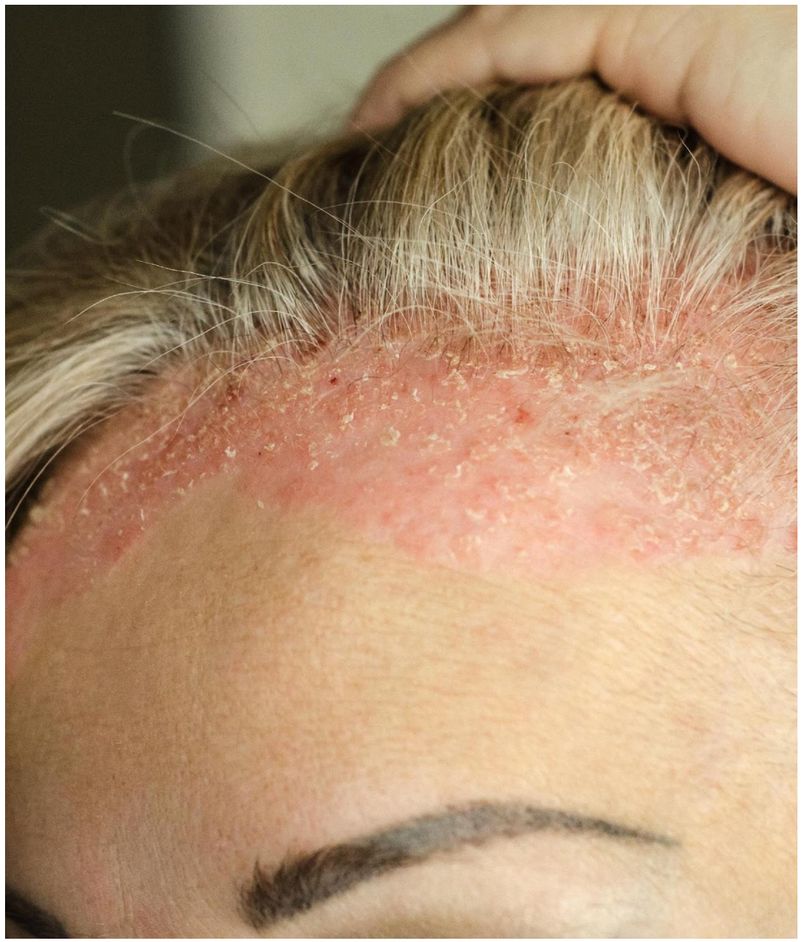
As compared to White patients, Black patients may experience:

- More extensive disease involvement/BSA at initial presentation
- Less conspicuous erythema (usually appears violaceous)
- More hypo- or hyperpigmentation

Scalp Psoriasis

Minority groups are less likely to see a dermatologist for their psoriasis in the US

Scalp psoriasis in AA have used traditional/cultural therapies before seeking dermatologic consultation



Fischer AH, Shin DB, Gelfand JM, Takeshita J. Health care utilization for psoriasis in the United States differs by race: an analysis of the 2001-2013 Medical Expenditure Panel Surveys. *J Am Acad Dermatol.* 2018;78(1):200-203

Treatment Gaps

In the United States, Black patients are less likely to receive biologic treatment for psoriasis compared to White patients

In a 2015 study, the odds of receiving a biologic therapy to treat psoriasis was 69% lower in Black patients than in White patients

Biologic-naive participants were more likely to be receiving phototherapy or topical therapy only

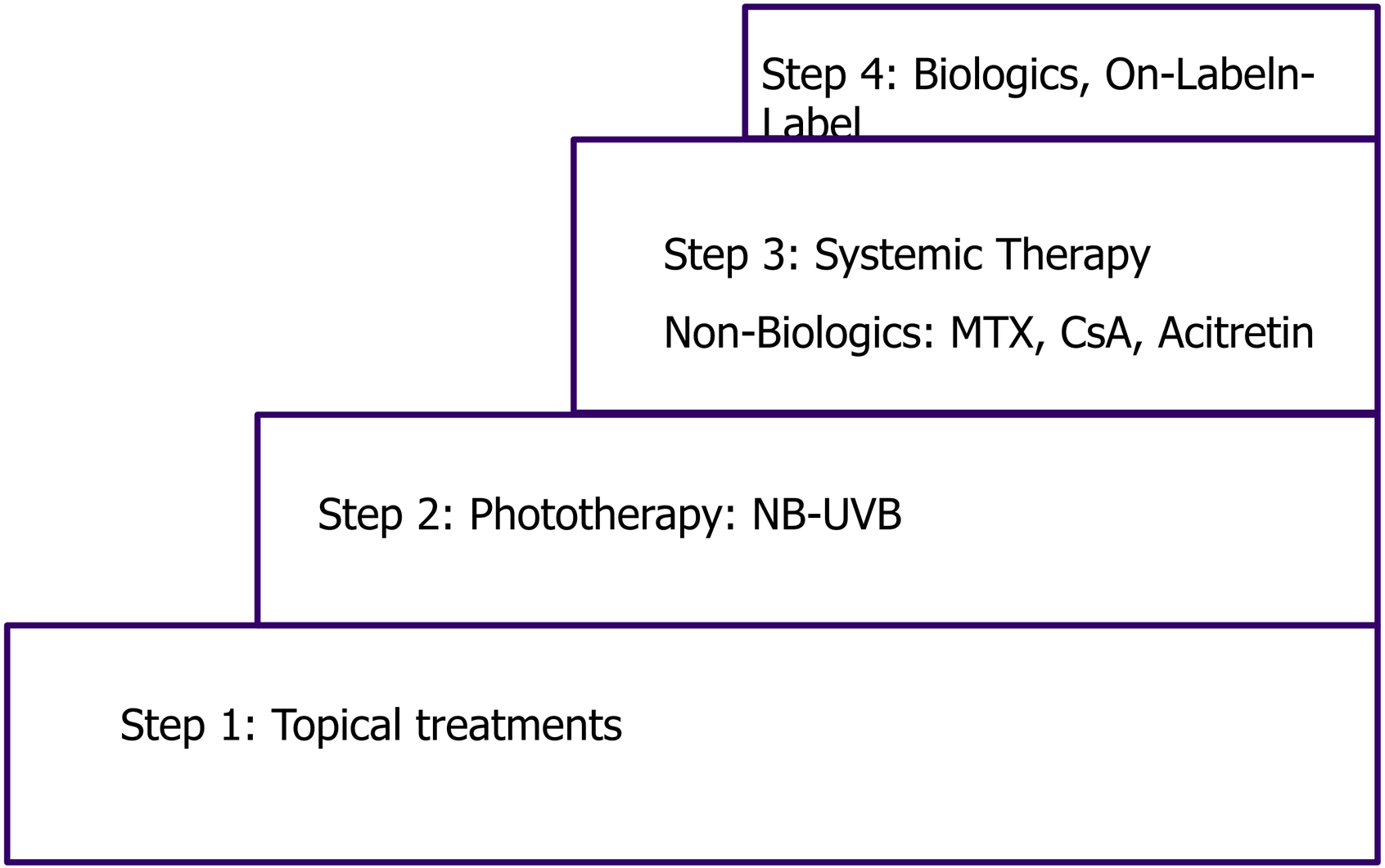
They were also less likely to have received oral systemic therapy in the past

Takeshita J et al. *J Invest Dermatol*. 2019;139(8):1672-1679.

Takeshita J, Gelfand JM, Li P, et al. Psoriasis in the U.S. Medicare population: prevalence, treatment, and factors associated with biologic use.

J Invest Dermatol. 2015;135(12):2955-2963

Pharmacologic Strategies



TNF-α inhibitors
Approved for pediatric psoriasis

Etanercept *(*1st biologic to be investigated in pediatric psoriasis)*

Ages 4-17 years (US & Canada)

Ages 6-17 years (Europe)

Has the longest followup data among biologics for pediatric psoriasis (no serious or opportunistic infections or malignancies were observed up to 264 weeks)

Adalimumab

Ages 4 or > years (Europe)

No serious or opportunistic infections or malignancies reported

IL-12/-23 inhibitor
Approved for pediatric psoriasis

- Ustekinumab

  Ages 12-17 years (US, Canada & Europe)

  Most common AE nasopharyngitis (2.5% ustekinumab….27% placebo)

  No serious or opportunistic infections or malignancies observed over 60 weeks of follow-up

- Current

  Now approved in ages 6-11 years (2020)

  Long-term safety data (aged 12-17) underway for up to 10 years

IL-17A inhibitor
Approved for pediatric psoriasis

- Secukinumab

  Ages 6 years and older (US, Canada & Europe)

  Most common AE nasopharyngitis, diarrhea, and upper respiratory tract infections

  Favorable safety profile for over 5 years of treatment across multiple indications

- Ixekizumab

  Ages 6 years and older

  Most common AE injection site reactions, upper respiratory tract infections, nausea, tinea

  Conjunctivitis, influenza and urticaria also seen in pediatric psoriasis

Biologics- by Pediatric Age Groups

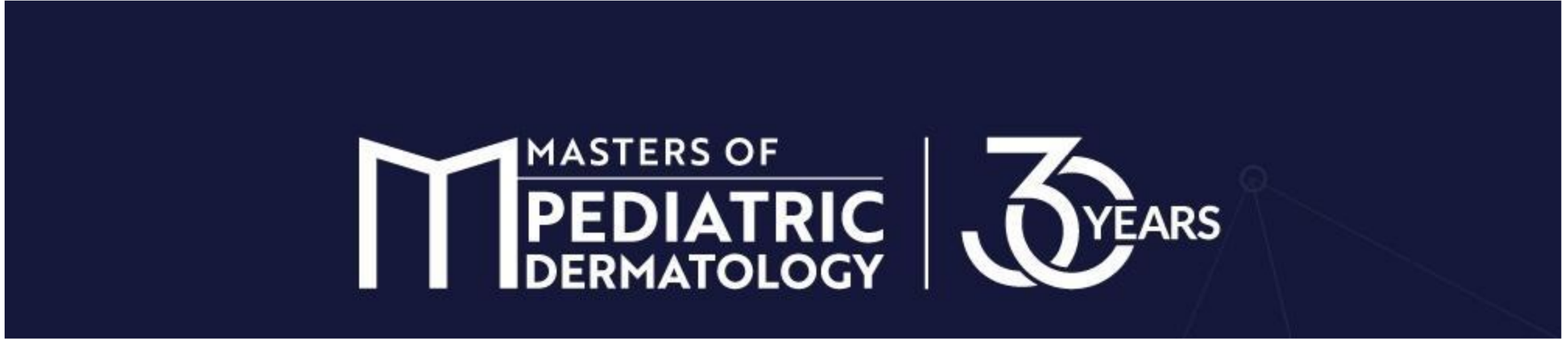
- Children - Etanercept, Ixekizumab, Secukinumab
- Preteens - Etanercept, Ustekinumab, Ixekizumab, Secukinumab
- Teens - Etanercept, Ustekinumab, Ixekizumab, Secukinumab

Biologics- Pediatric Dosing

- Etanercept 0.8 mg/kg (*max* 50mg/dose) once weekly
- Adalimumab 0.8 mg/kg (*max* 40mg/dose) Week 0 & 1 followed by every other week
- Ustekinumab 0.75 mg/kg (<=60 kg); 45mg (>60-100 kg); 90mg (>100 kg) Week 0 & 4, followed by every 12 weeks
- Secukinumab 75 mg (<50 kg); 150 mg (>=50 kg) Week 0-4 and then every 4 weeks
- Ixekizumab Week 0 = 40mg (<25 kg); 80mg (25-50 kg); 160mg (>50 kg), followed by half dose every 4 weeks

Consider Biologics for Pediatric Psoriasis

- Efficacy & Safety demonstrated in well-designed studies
- Reports of real-world use have been reassuring
- AE's overall have been consistent with findings in RCT
- No new safety signals have been observed



Thank you!

lbenjamin@health.fau.edu