Pediatric Psoriasis

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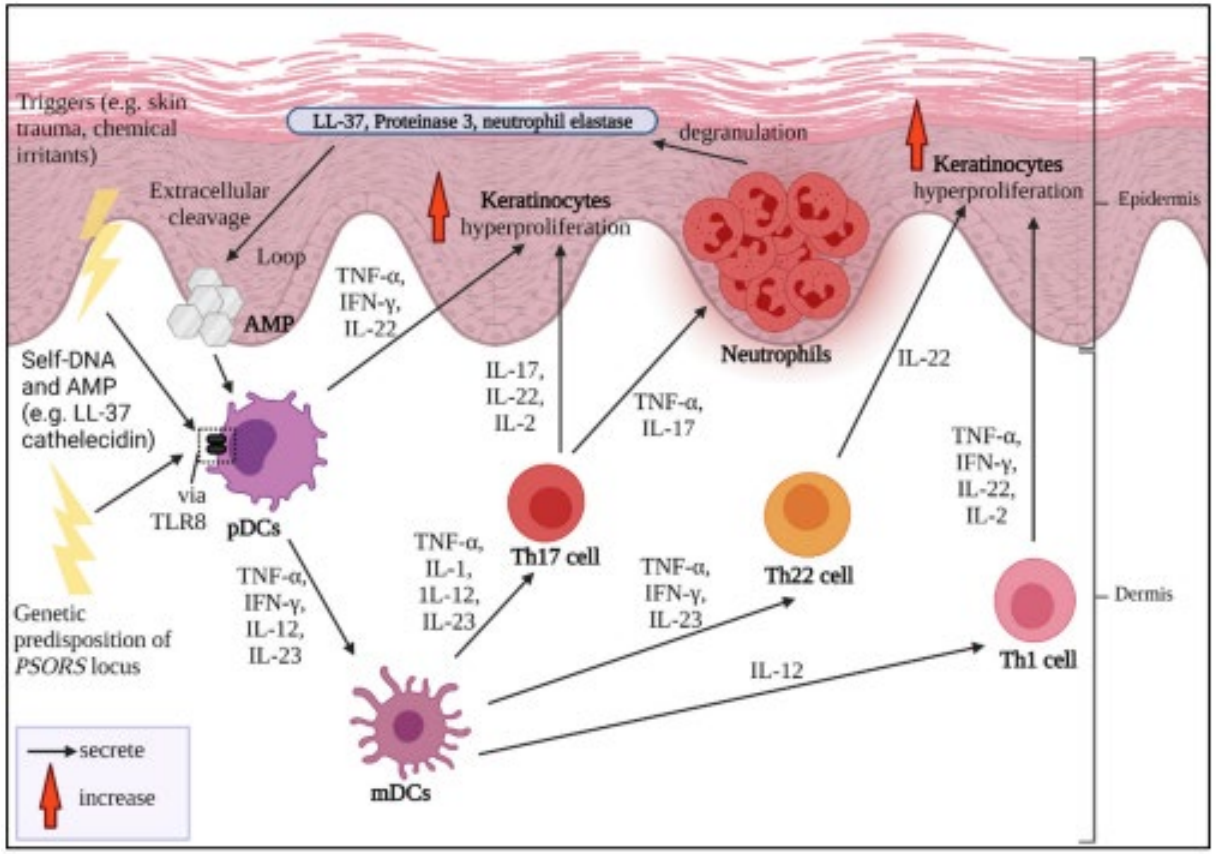
Overview

- 1/3 present before age 20, many in infancy
- Mean age of onset: 2 to 10 yr (varying by psoriasis type and the population studied)
- >70% with + family history
- Incidence: 40.8 per 100,000 (2-fold increase since 1970)
- Prevalence: 2.5%

Eichenfield LF, Paller AS, Tom WL, Sugarman J, Hebert AA, Friedlander SF, Siegfried E, Silverberg N, Cordoro KM. Pediatric psoriasis: Evolving perspectives. Pediatr Dermatol. 2018 Mar;35(2):170-181.

Immunopathophysiology

- Multiple clinically well-recognized triggers
- Evolving understanding of immune mechanisms
  - *HLA-Cw6* (aka PSORS1; psoriasis susceptibility locus 1)
  - Immunologic mediators
    - Th1, Th17, and Th22 lymphocytes
    - Key cytokines TNF-α, INF-γ, IL-17, IL-12, IL-23, IL-36

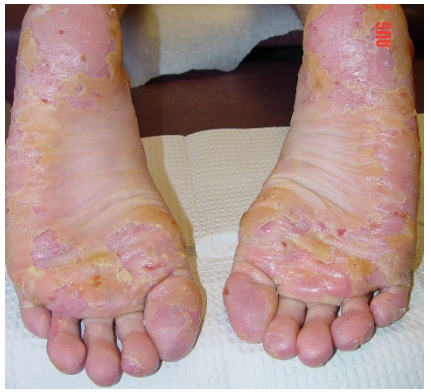


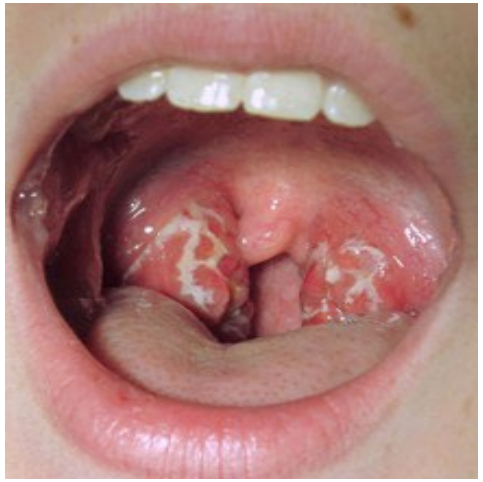
Chen L, Tsai TF. HLA-Cw6 and psoriasis. Br J Dermatol. 2018;178(4):854-862.
Mohd Noor AA, Azlan M, Mohd Redzwan N. Orchestrated Cytokines Mediated by Biologics in Psoriasis and its Mechanisms of Action. Biomedicines. 2022;10(2):498.

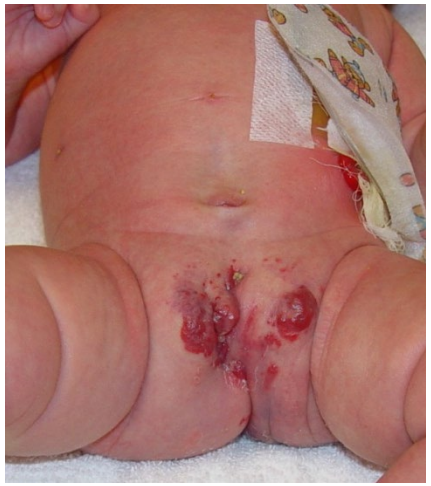
Triggers

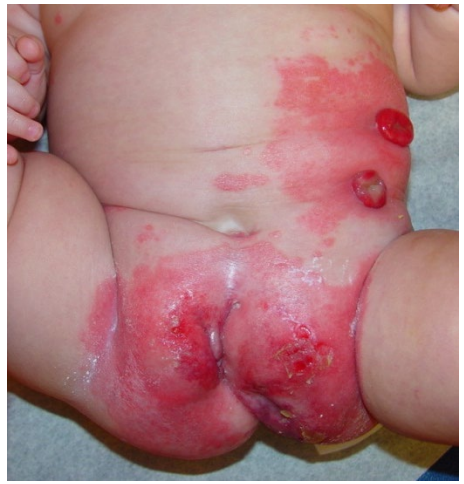
Precipitating factors are more often reported in children than adults

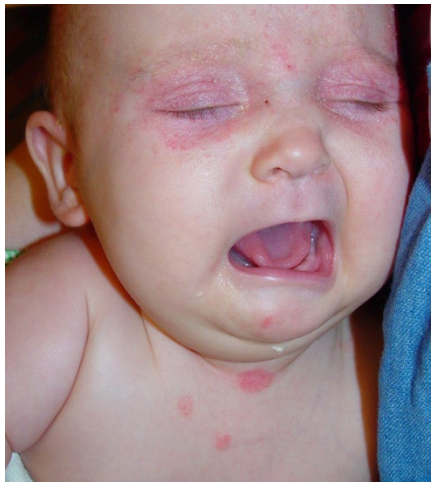
- Microbes (perianal/pharyngeal **Group A Strep**; fungal, viral)
- Cutaneous trauma ("**koebnerization**")
- Stress (home, school)
- Obesity
- Tobacco smoke
- Drugs (corticosteroid withdrawal, antimalarials, anti-TNFα, **beta blockers**)

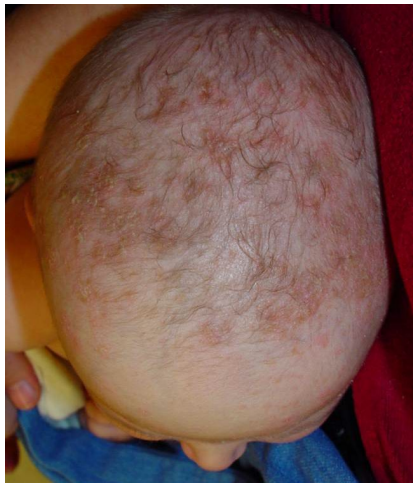












Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. Lancet. 2021;397(10281):1301-1315.

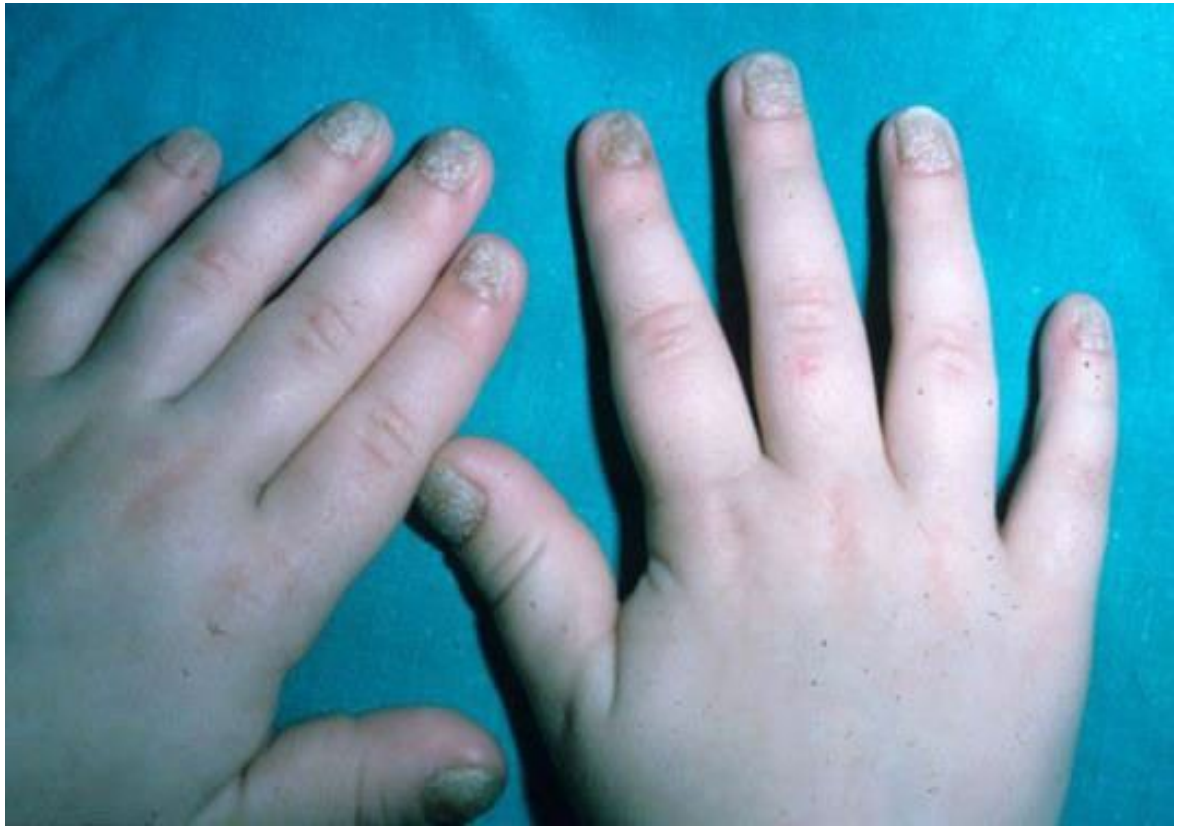
Associated Morbidities

- Arthritis
- Uveitis
- Obesity (likely bidirectional association)
- Other metabolic syndrome-associated conditions (HTN, dyslipidemia, NIDDM, NASH)
- Cardiovascular disease ("psoriatic march")
- Psychiatric disorders (depression, anxiety)
- Impaired quality of life (patients and caregivers)
- Inflammatory bowel disease, especially Crohn's

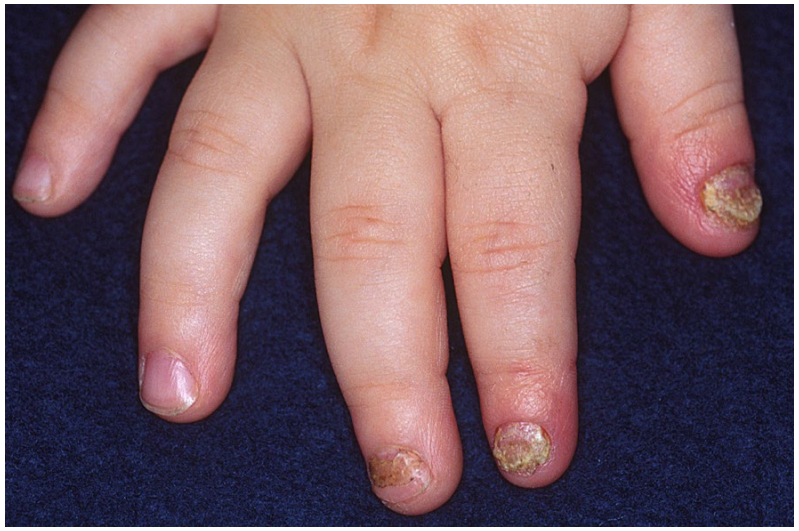
Osier et al. JAMA Derm 2017

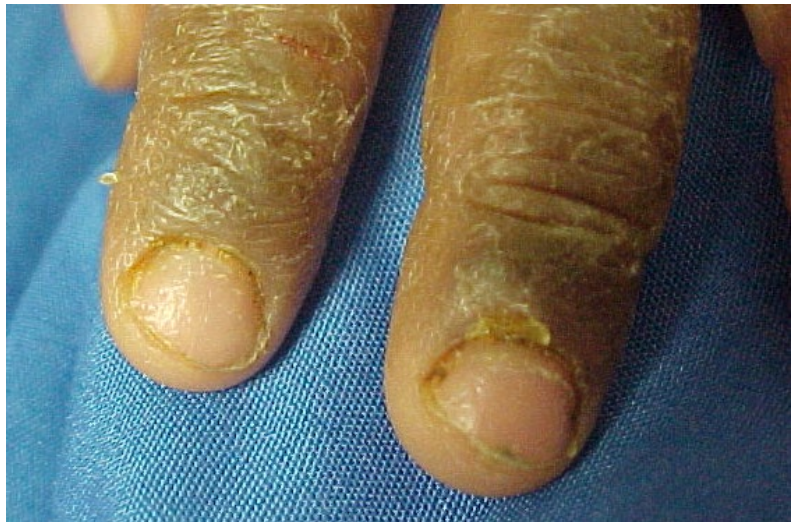
Psoriatic Arthritis

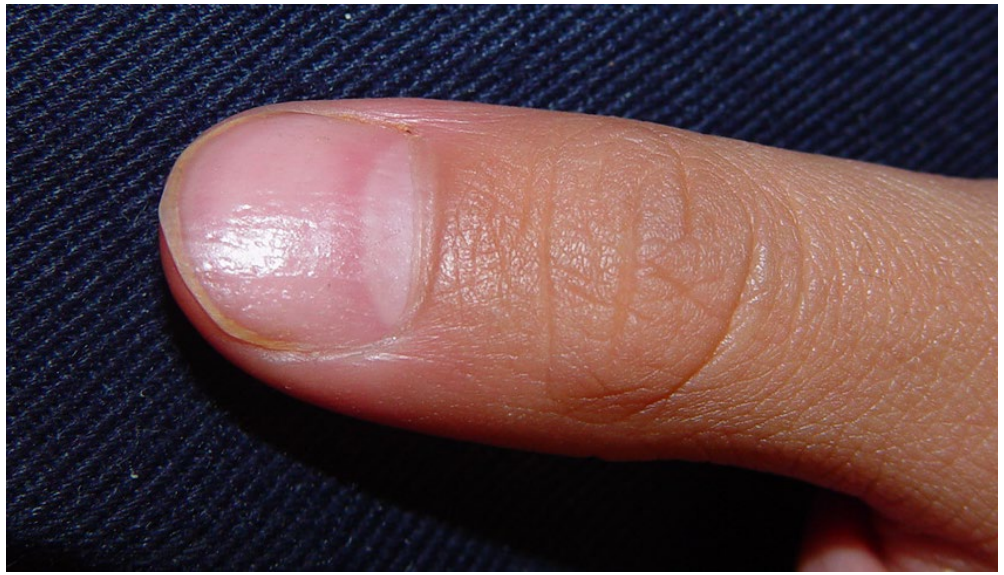
- Peak age of onset in children: 9-12 yr
- Poor correlation with skin disease severity
- Common sites
  - dactylitis - digits
  - enthesitis - tendon/ligament insertion
- Nail dystrophy may mark an increased risk



Nail Dystrophy





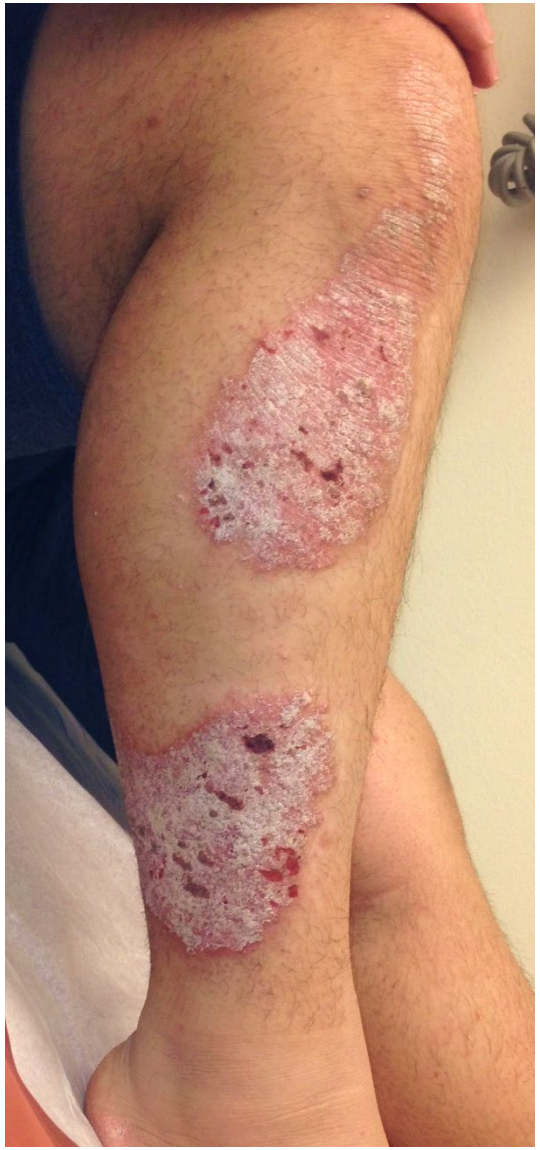


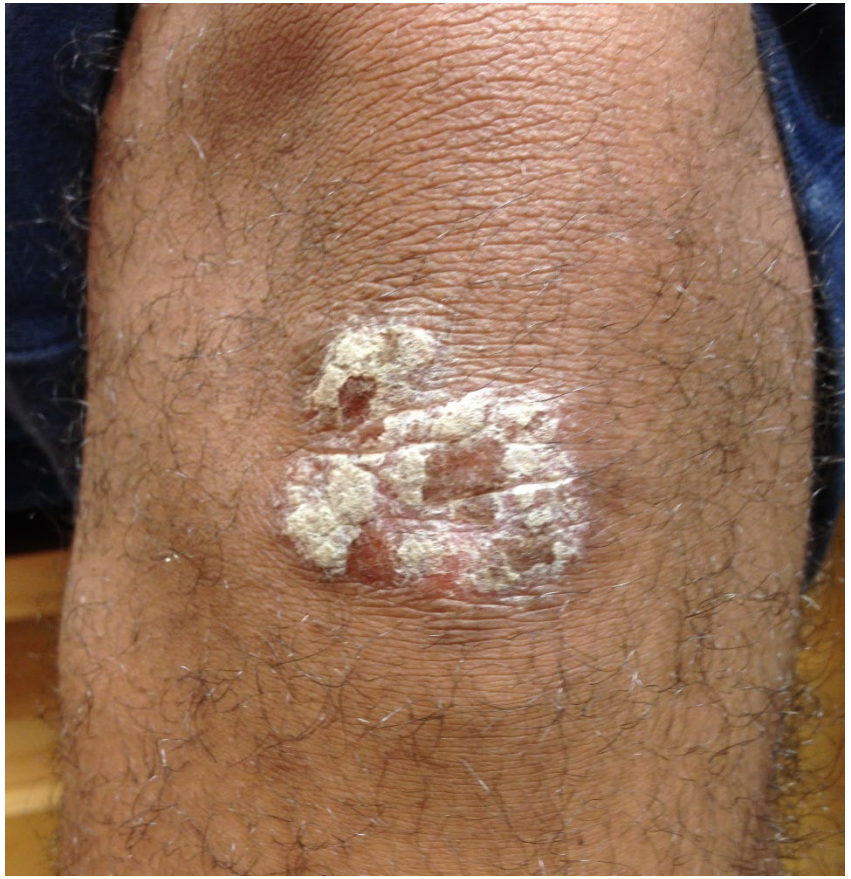
Clinical Spectrum

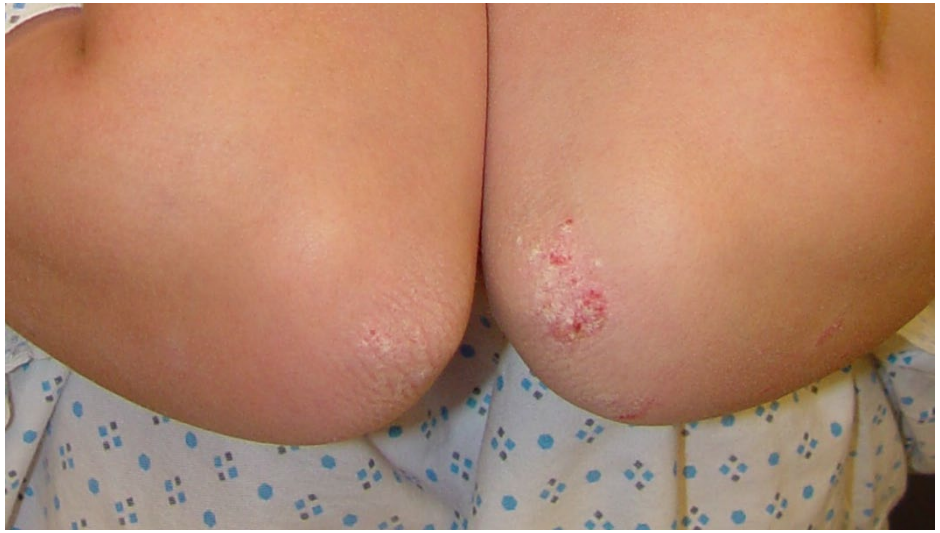
- Plaque - most common (~90%)
  - Palmoplantar
  - Annular
  - Linear
  - Petaloid
  - Overlap
- Guttate
- Inverse
- Nail
- Paradoxical
- Pustular - localized or generalized
- Erythrodermic

Eichenfield LF, et al. Pediatric psoriasis: Evolving perspectives. Pediatr Dermatol. 2018;35(2):170-181.

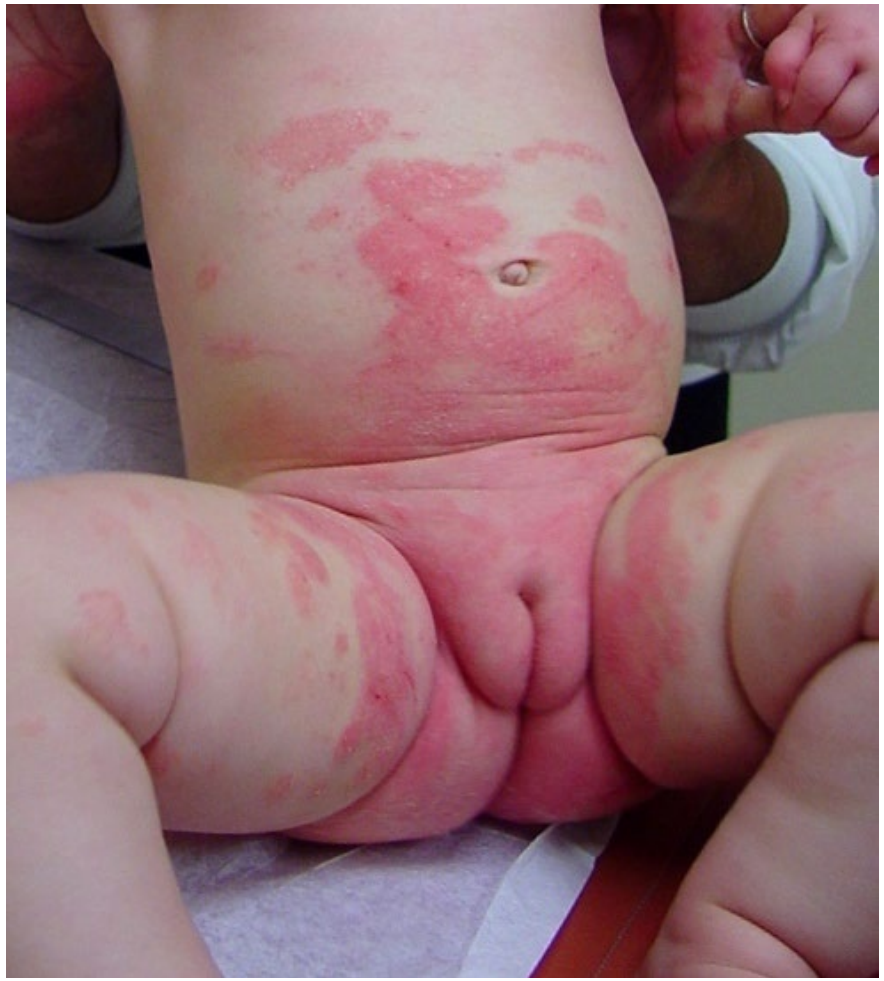
Classic Plaque Psoriasis

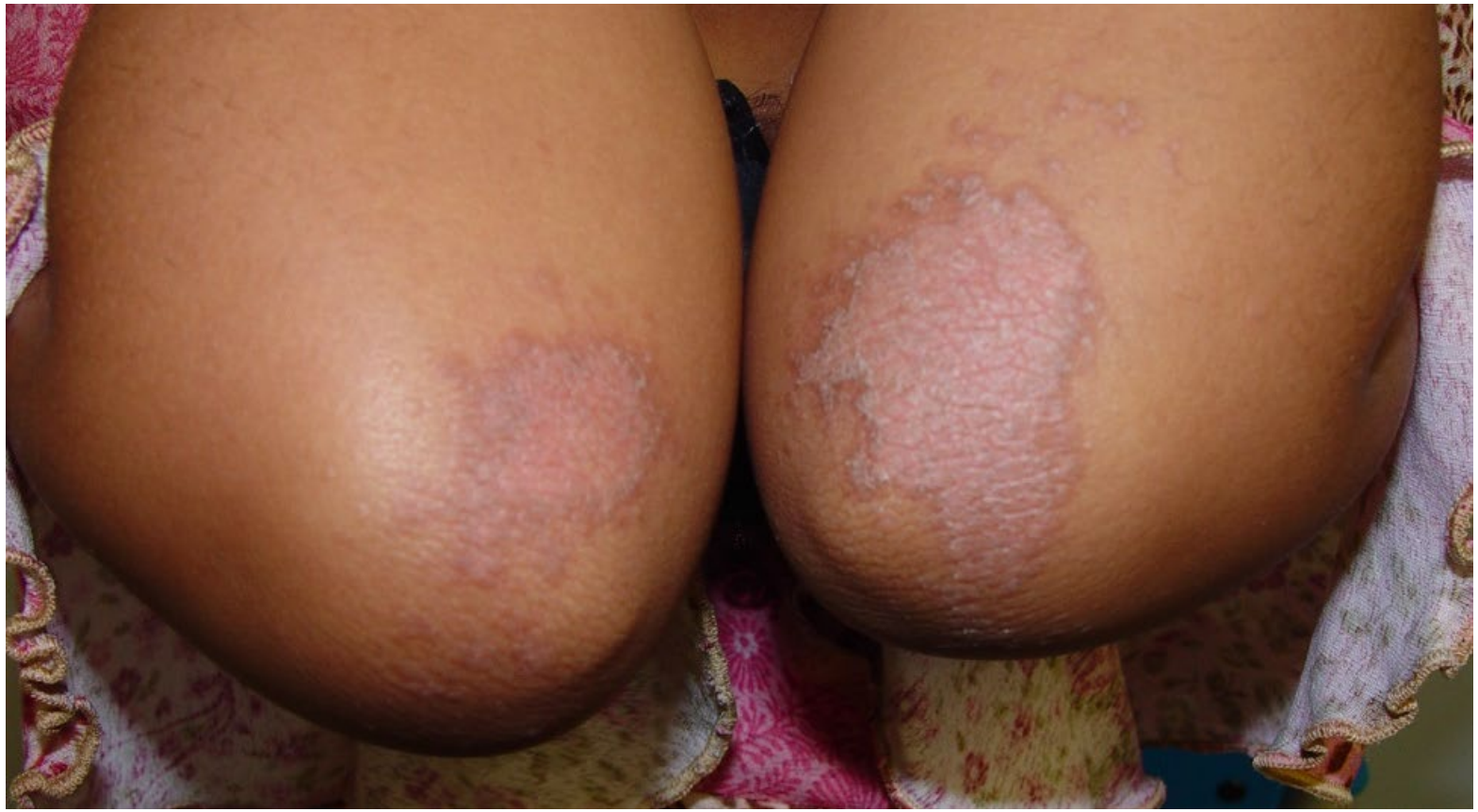




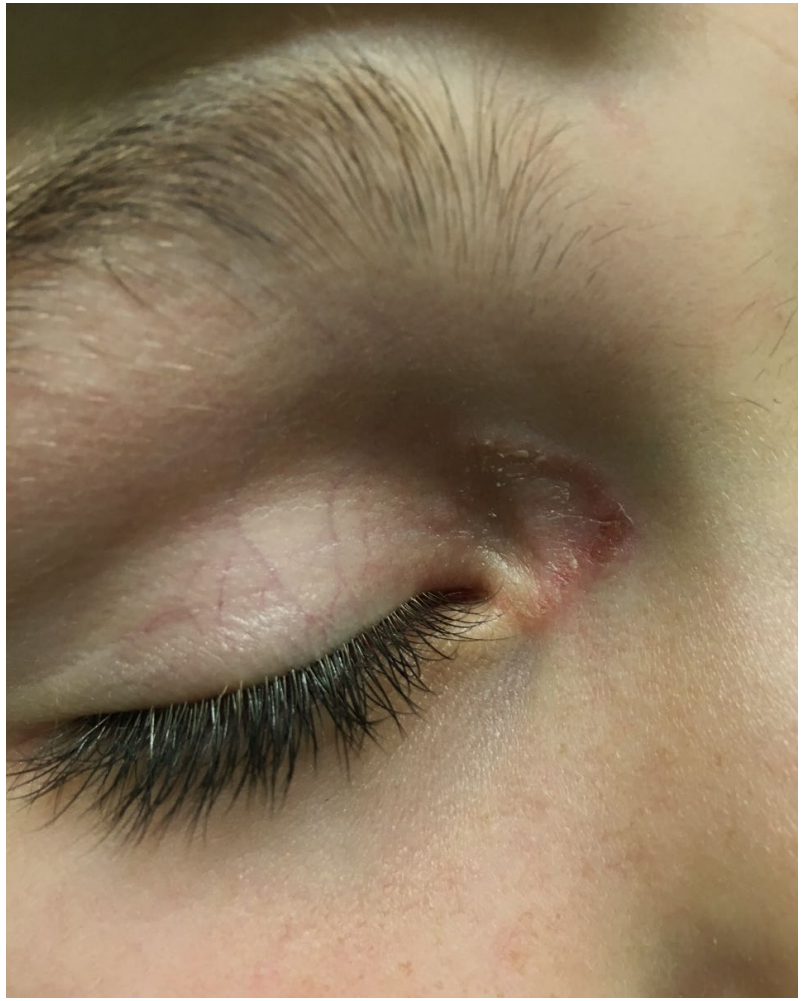


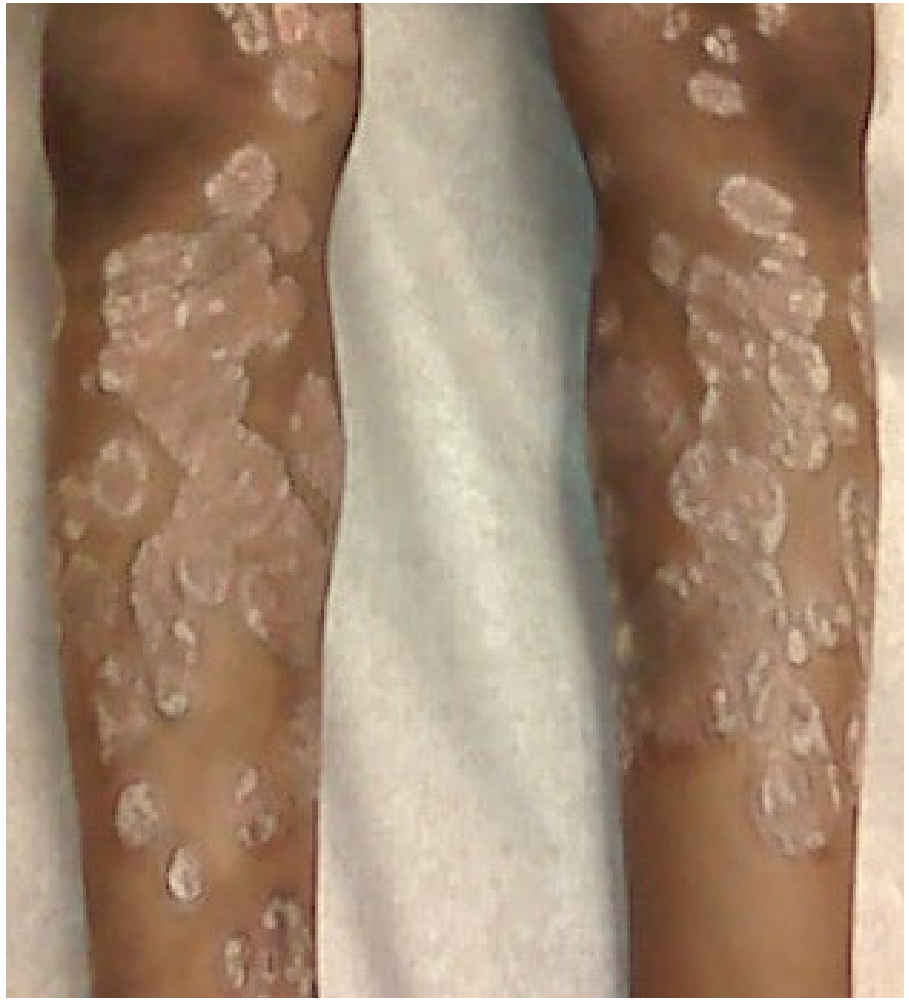
Scale is often less prominent in children.

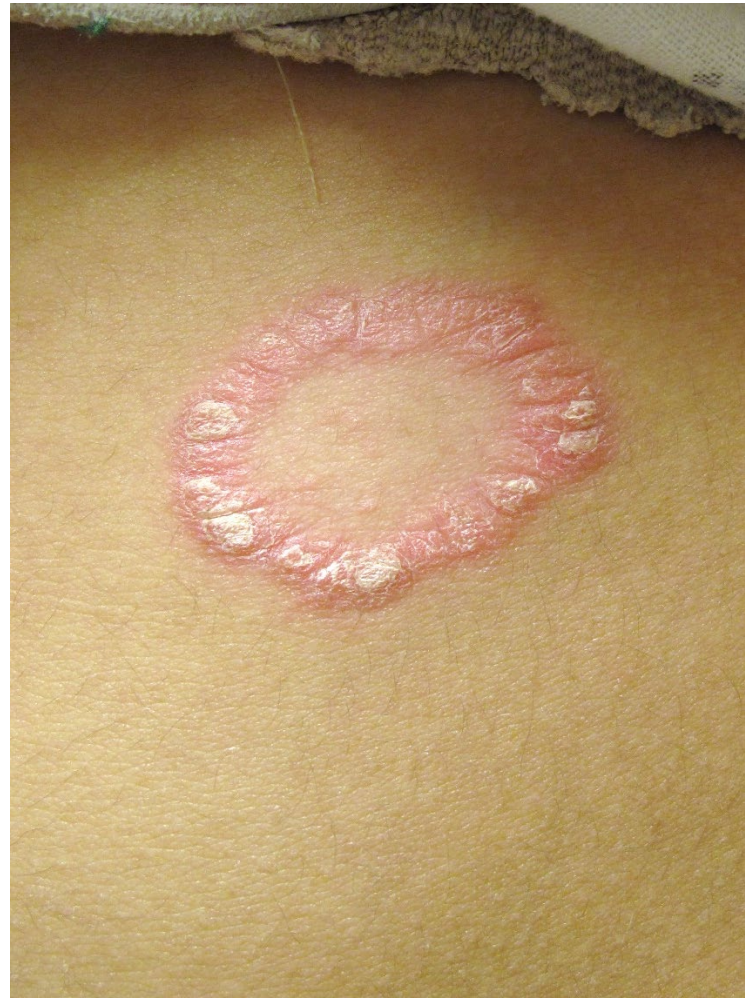




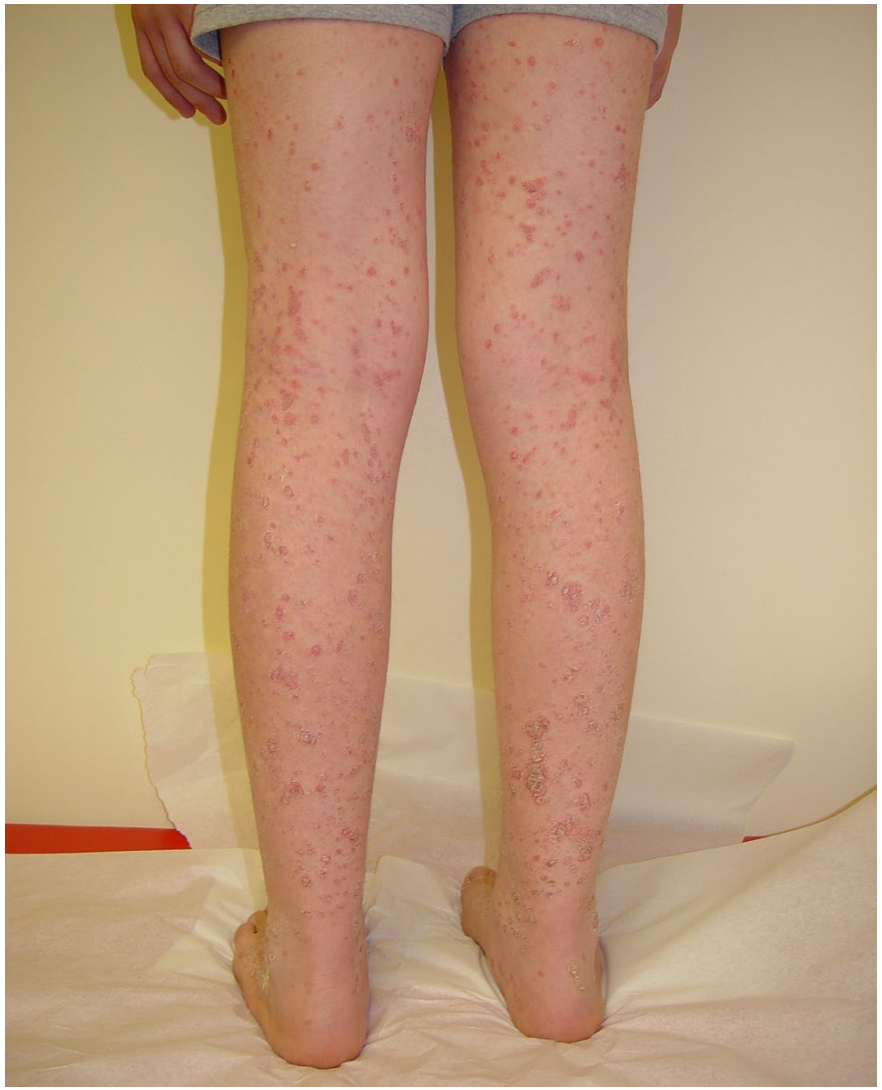
Annular Psoriasis

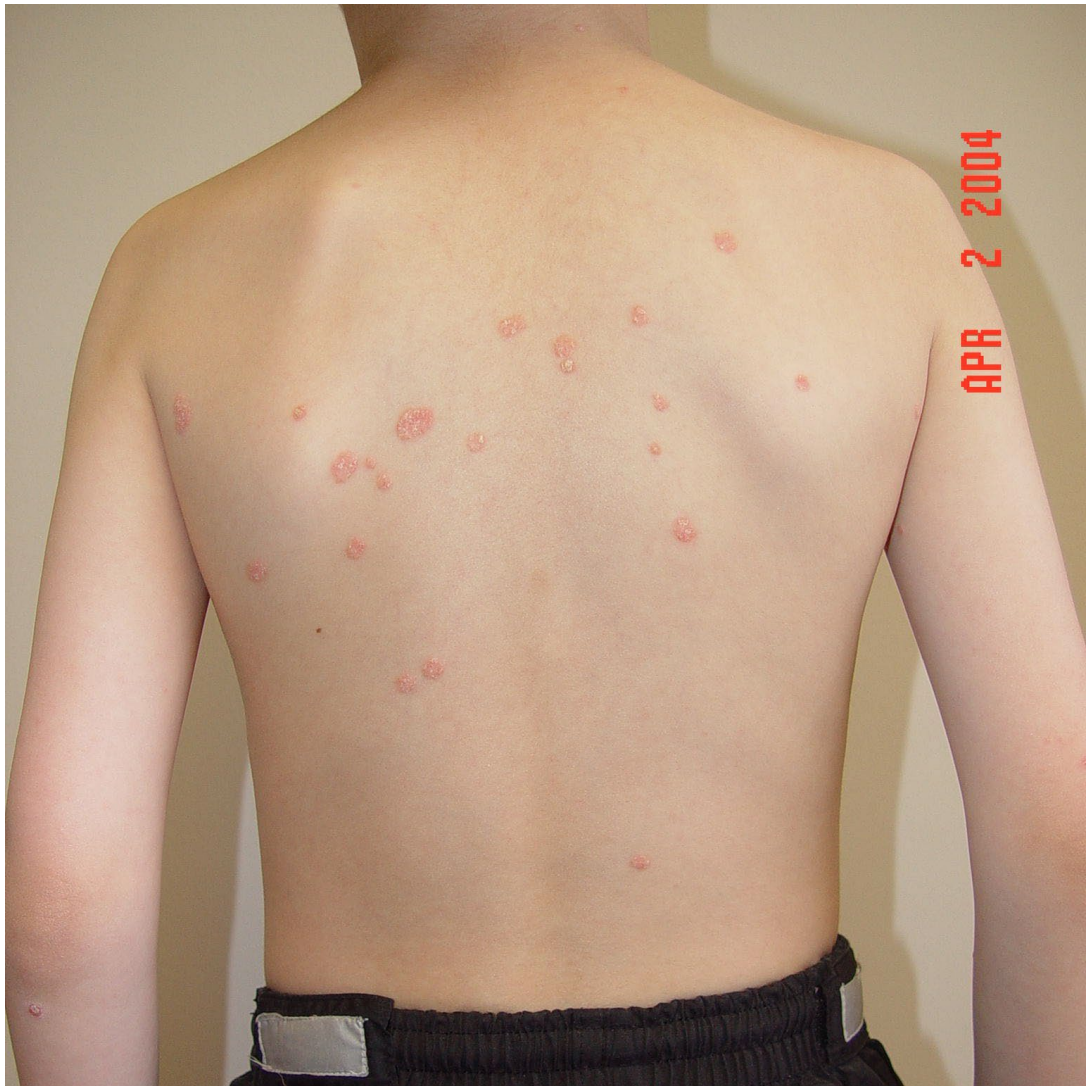




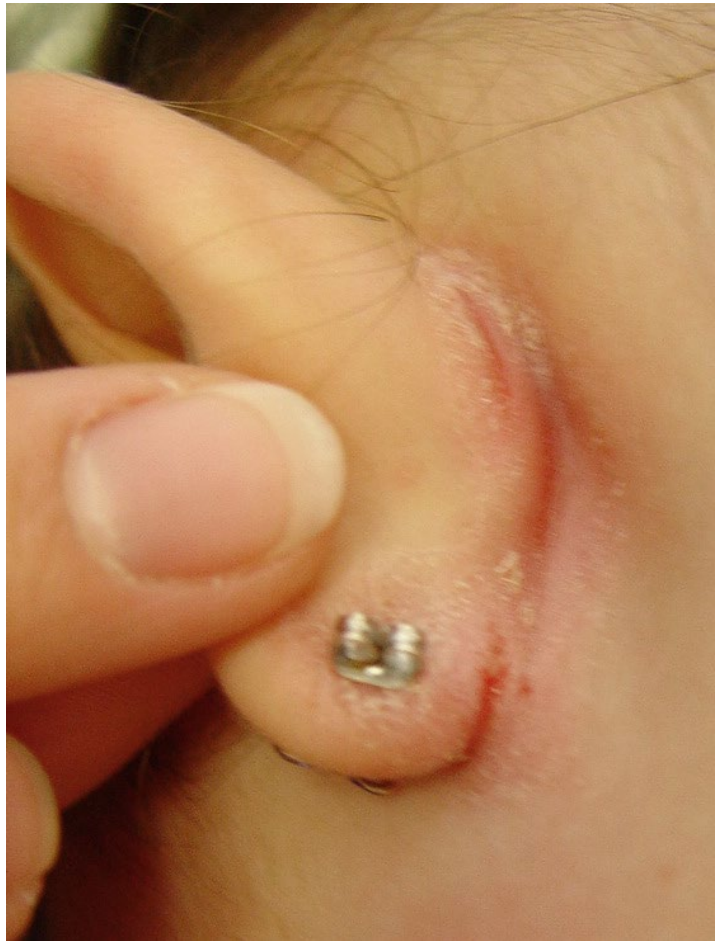


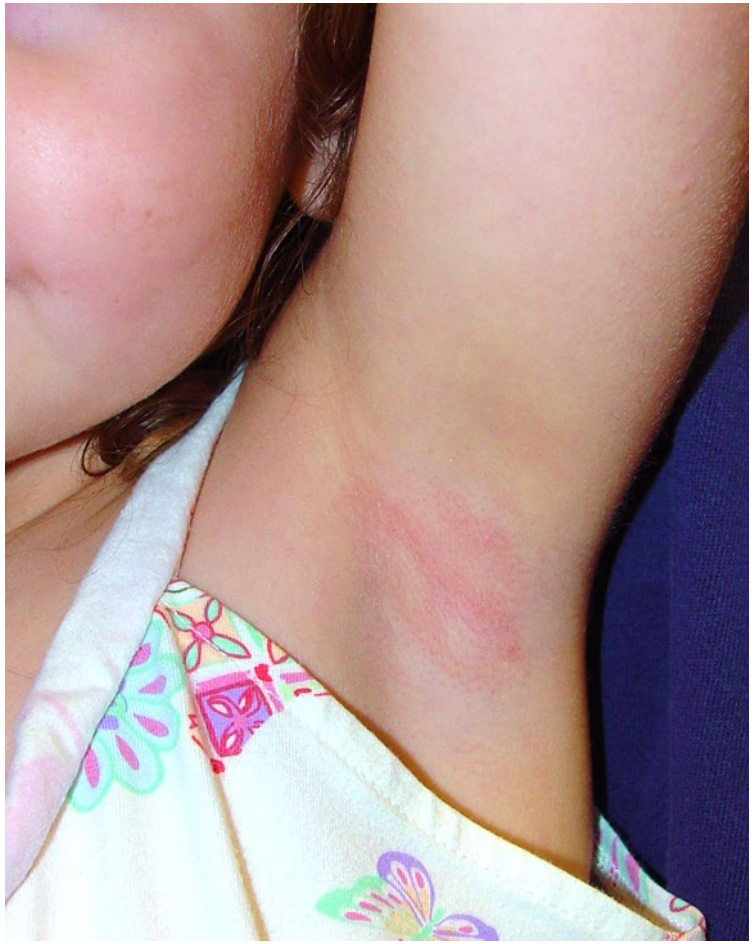
Guttate Psoriasis

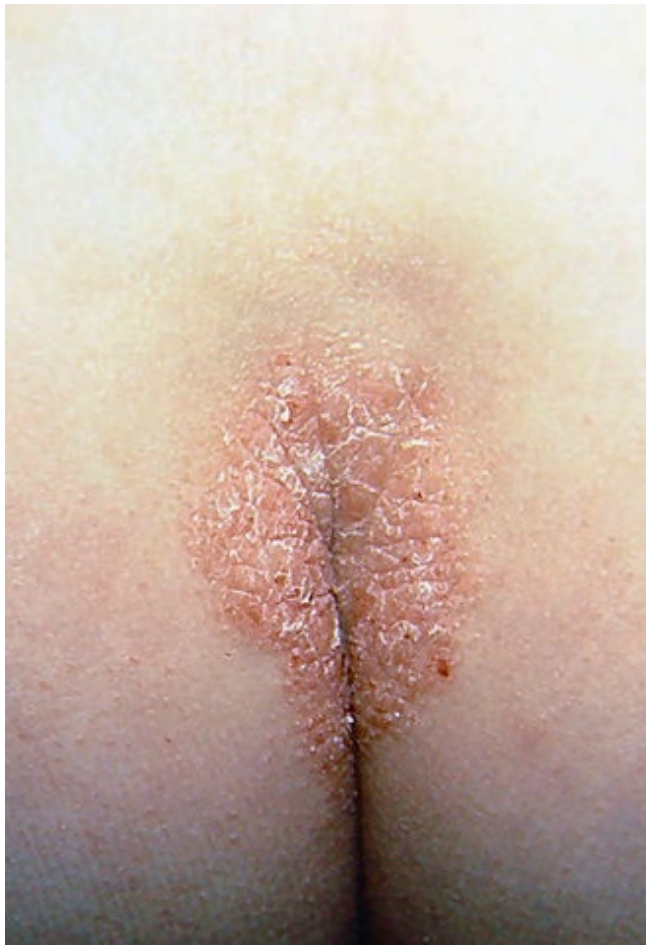




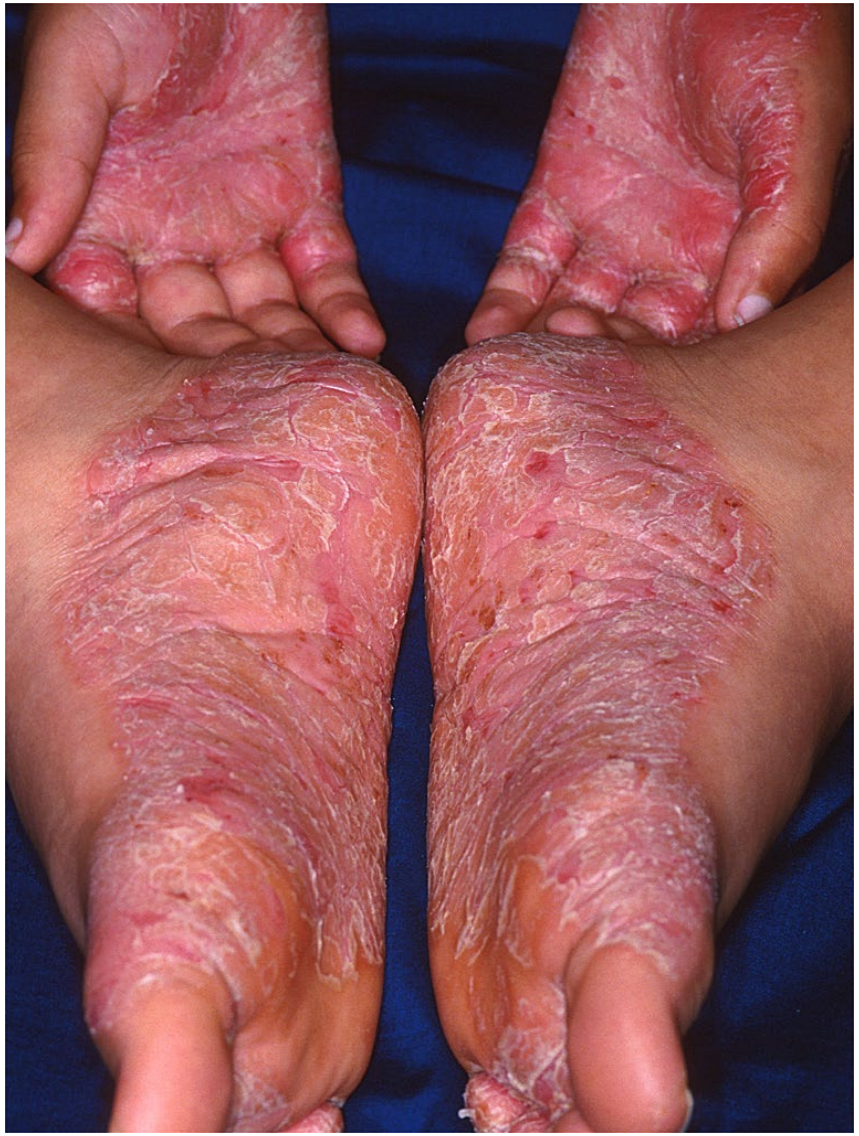
Inverse Psoriasis

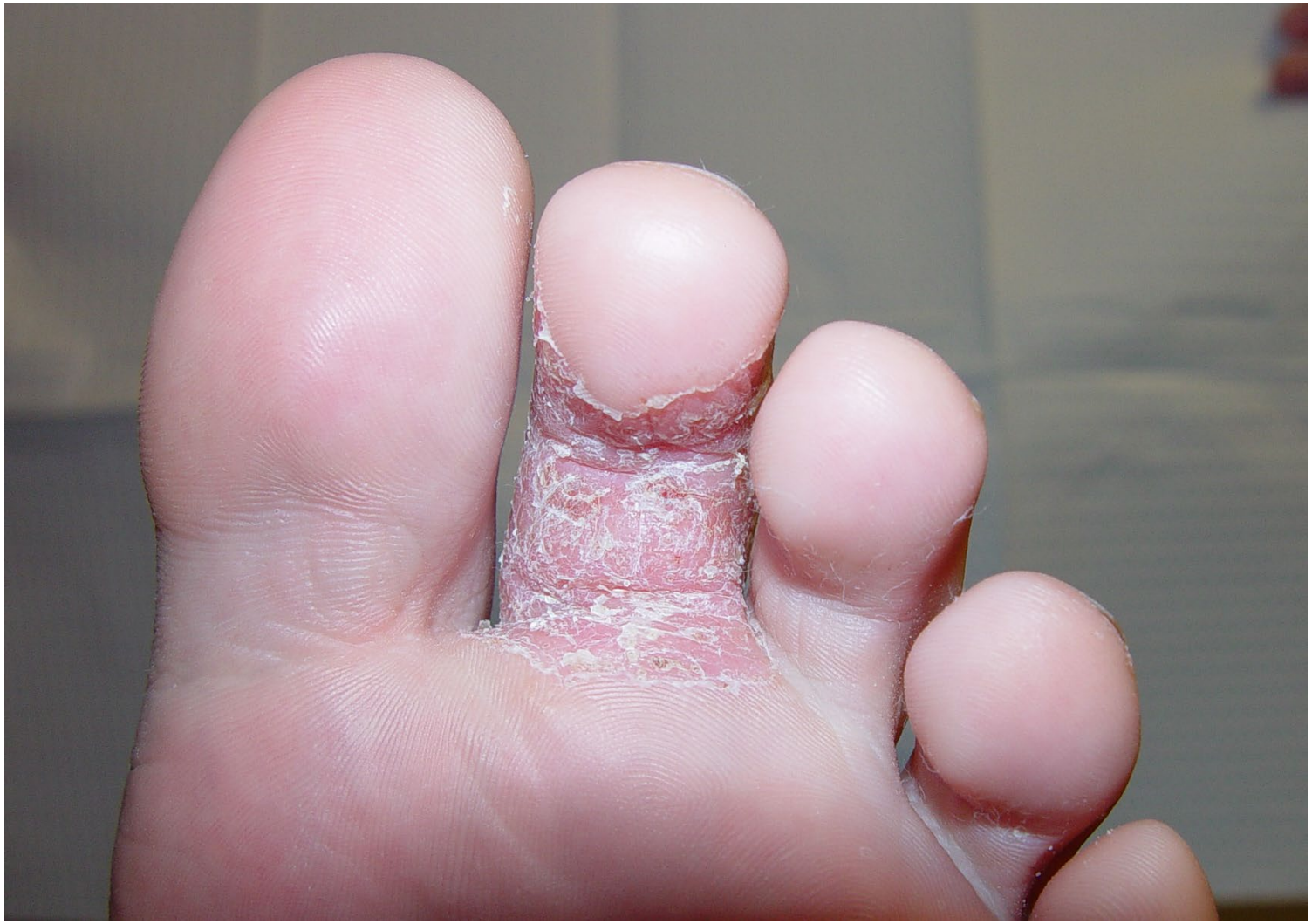




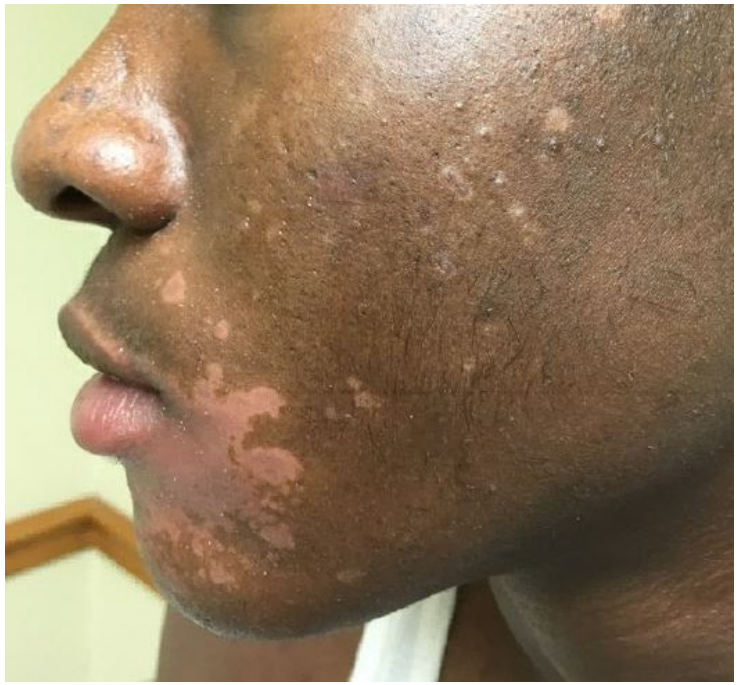


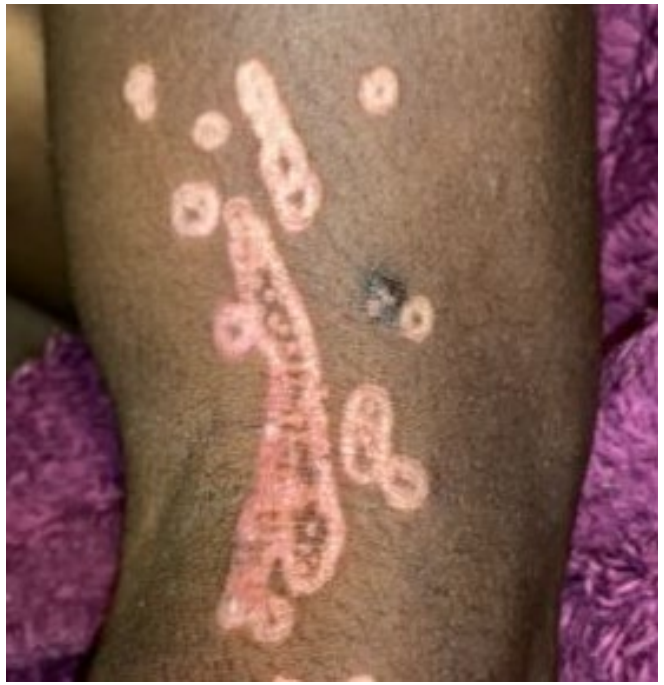
Palmoplantar Psoriasis

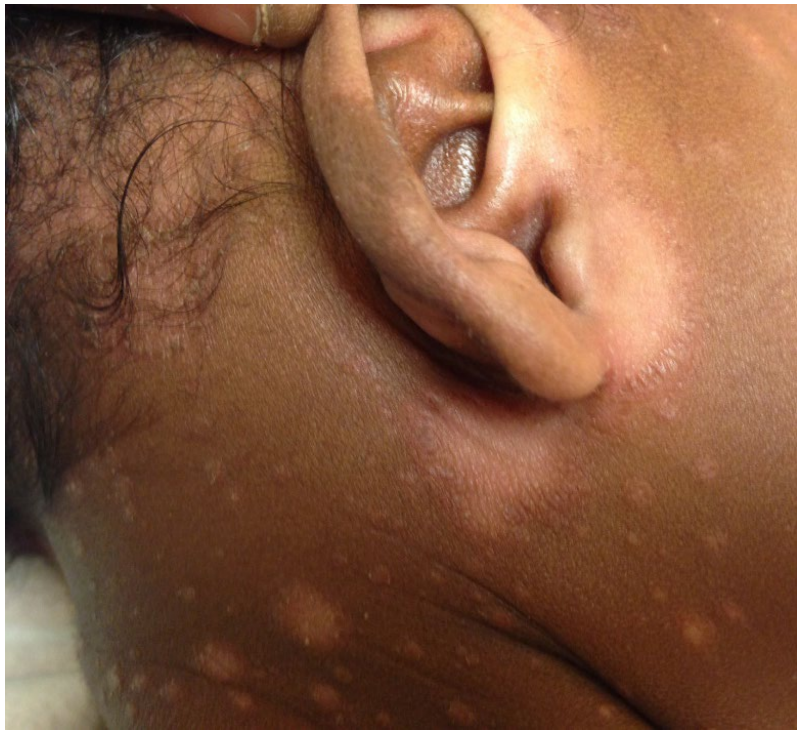


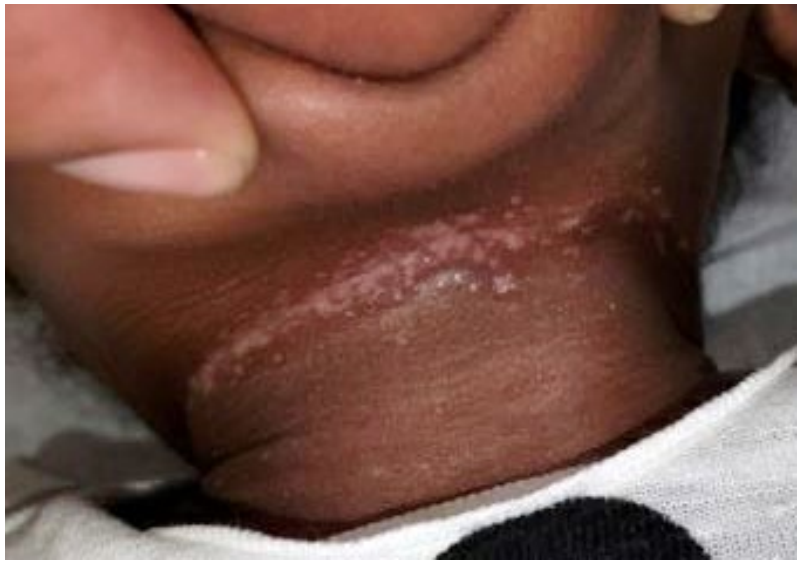


Petaloid Sebopsoriasis
Most Prominent in Skin of Color



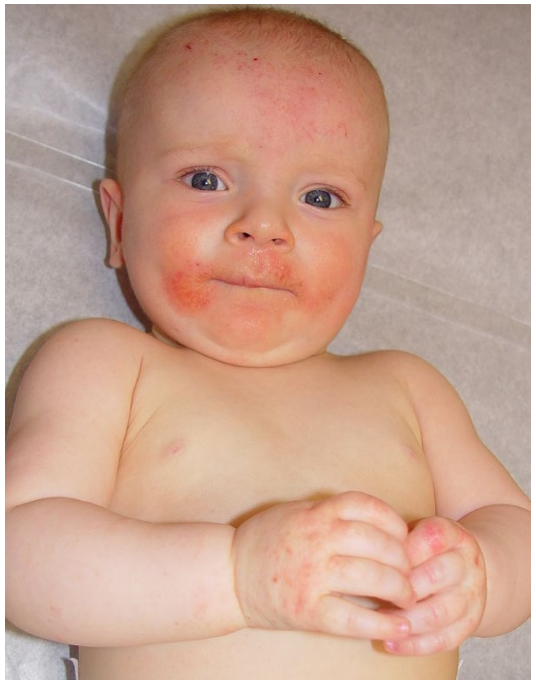


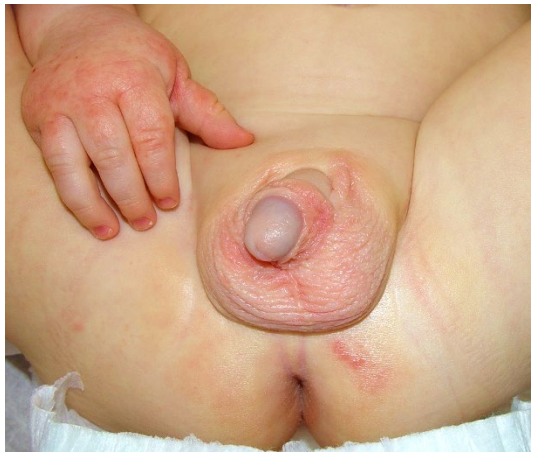


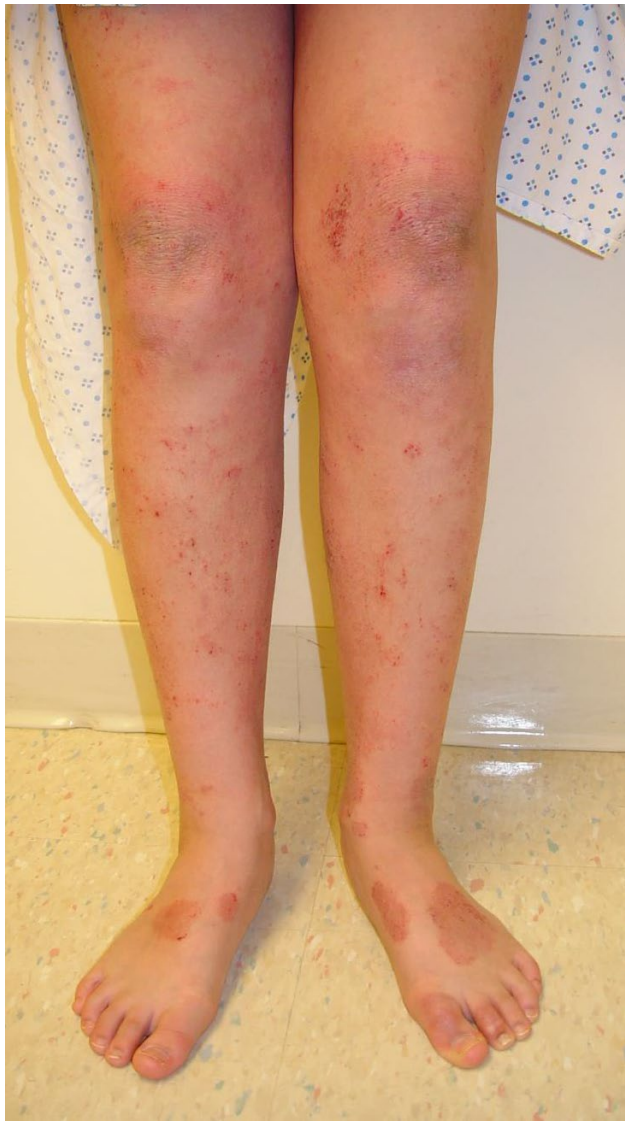


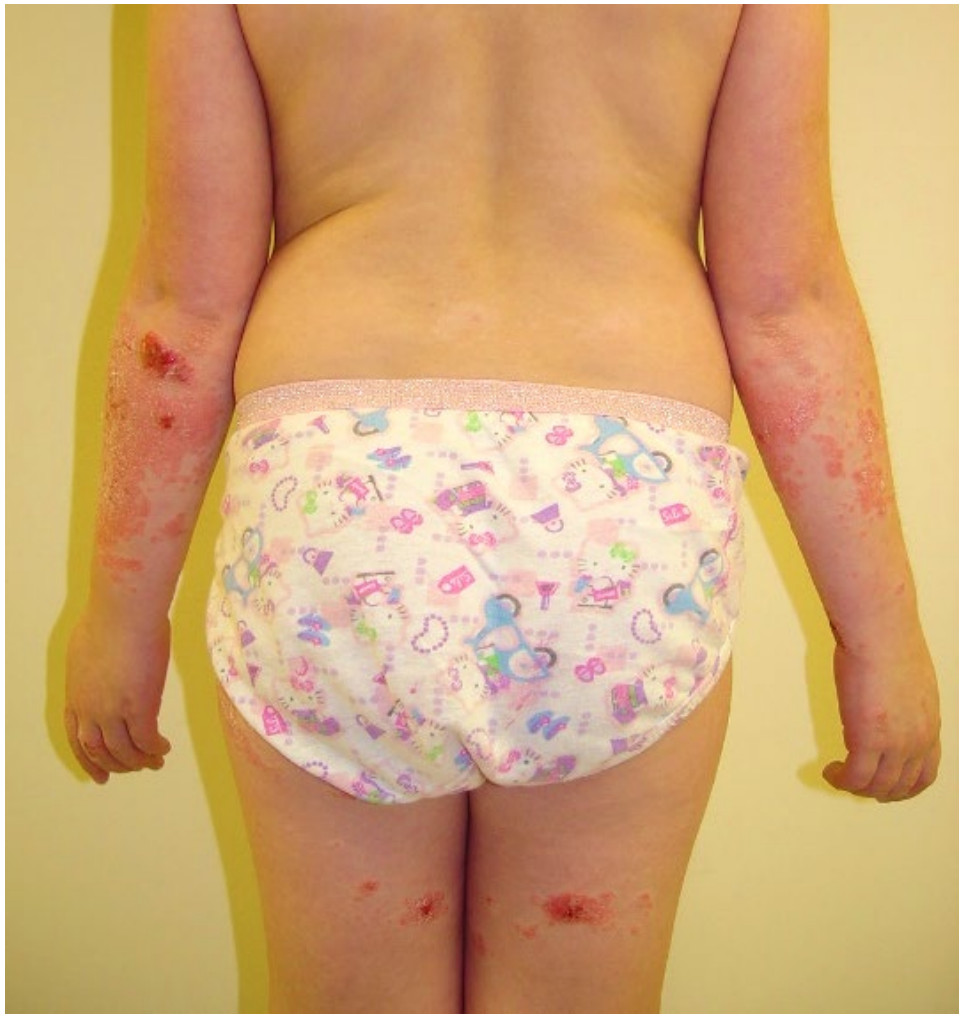
Elgash M, Dlova N, Ogunleye T, Taylor SC. Seborrheic Dermatitis in Skin of Color: Clinical Considerations. J Drugs Dermatol. 2019;18(1):24.

Psoriasis Eczema Overlap (L30.9)









Additional Features

Koebnerized sites of predilection are influenced by age and gender

- "thumb sign"
- "shin guard sign"
- tinea-triggered
- face/diaper area involvement in infants
- nail involvement in boys
- scalp involvement in girls
- eyelids
- peristomal

Hypopigmentation

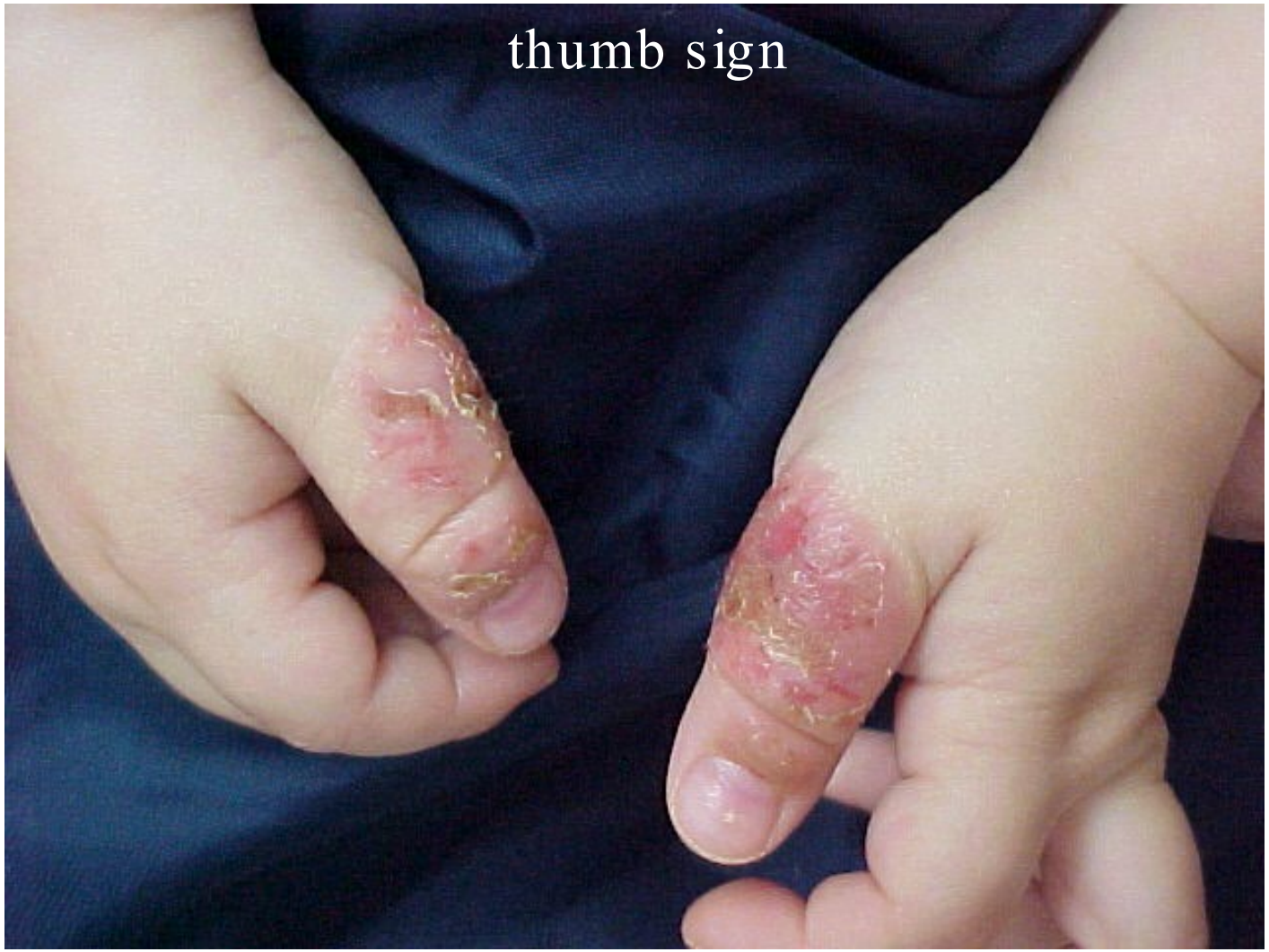
Underappreciated manifestations

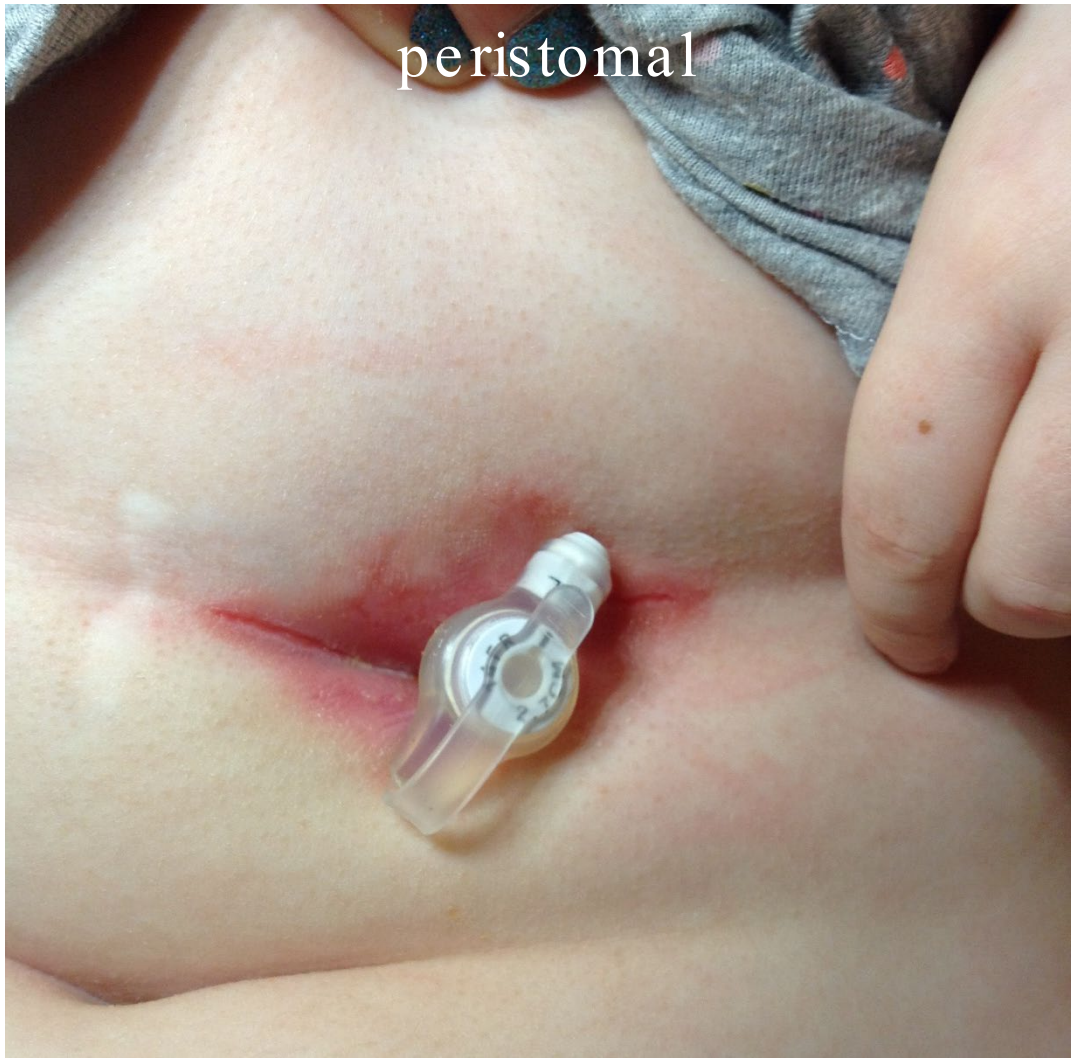
- glossitis
- otitis externa

Paradoxical

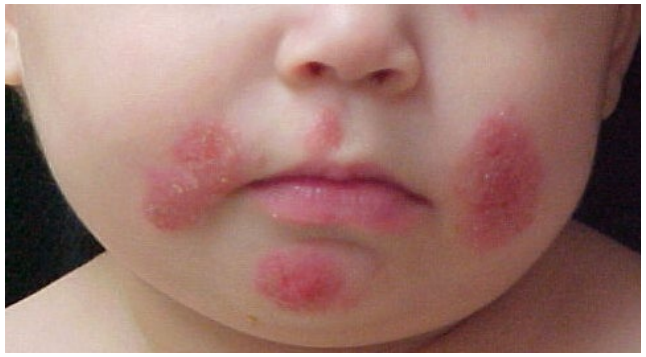
Hebert A, Browning J, Kwong P, Duarte AM, Price H, Siegfried E. Managing Pediatric Psoriasis: Update on Treatments and Challenges—A Review. Journal of Dermatological Treatment, accepted for publication Mar 2022

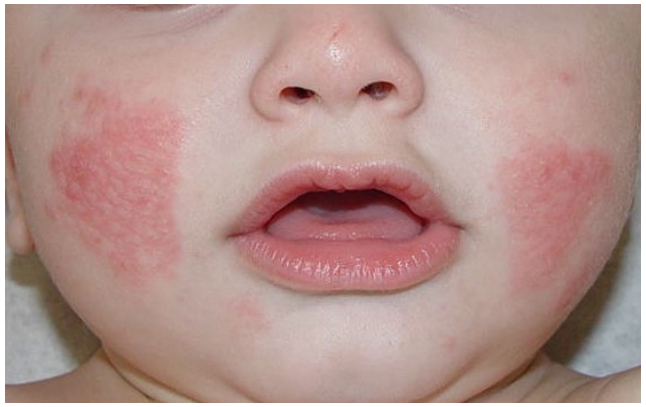
Koebner Distribution

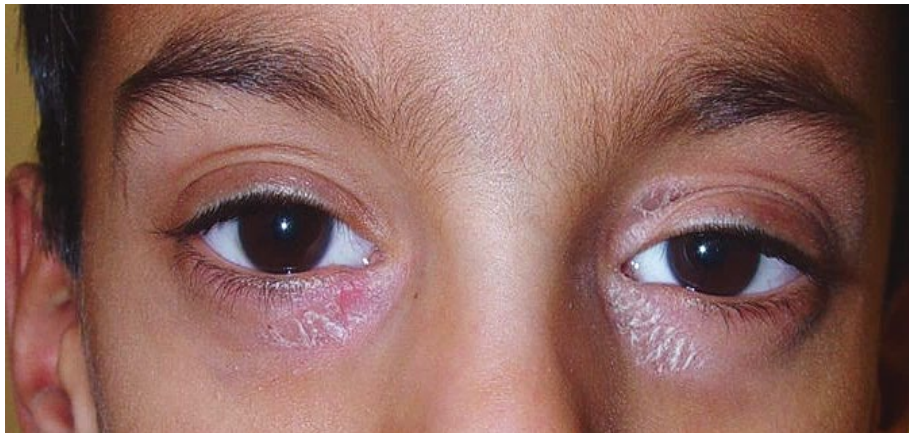


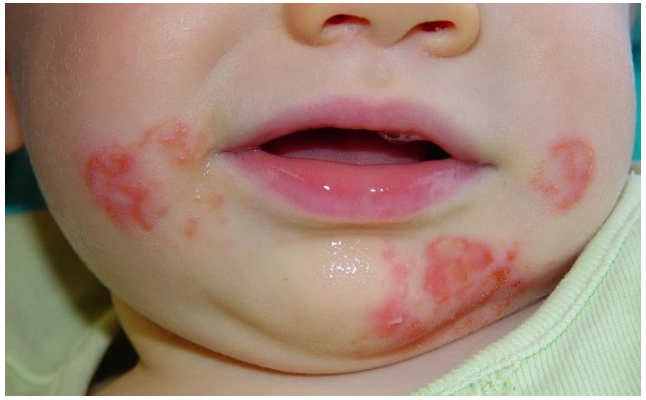


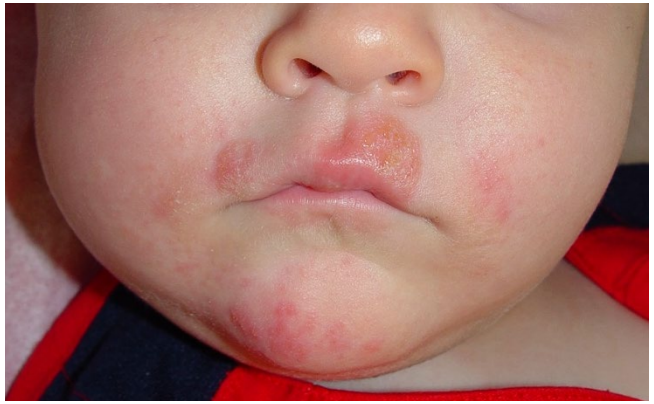
Face and Eyelid Involvement

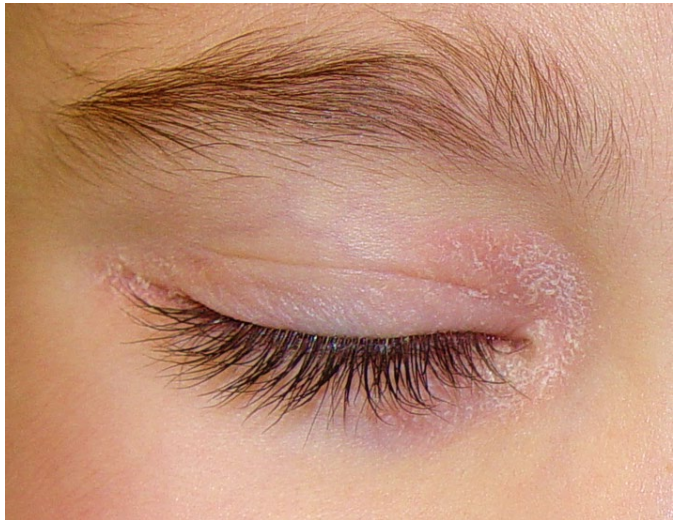




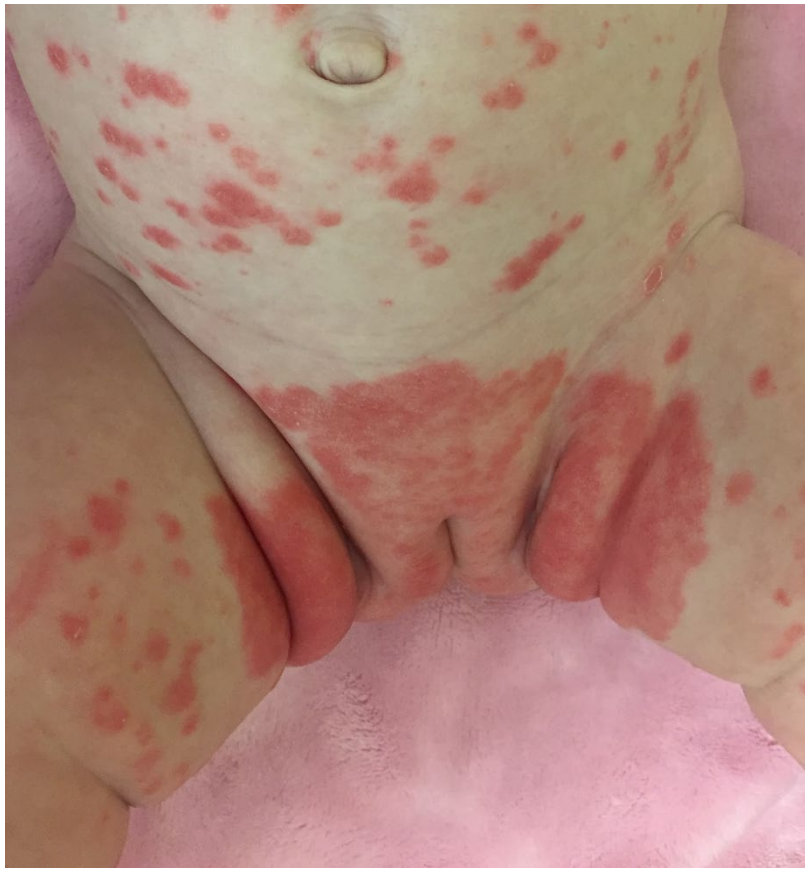


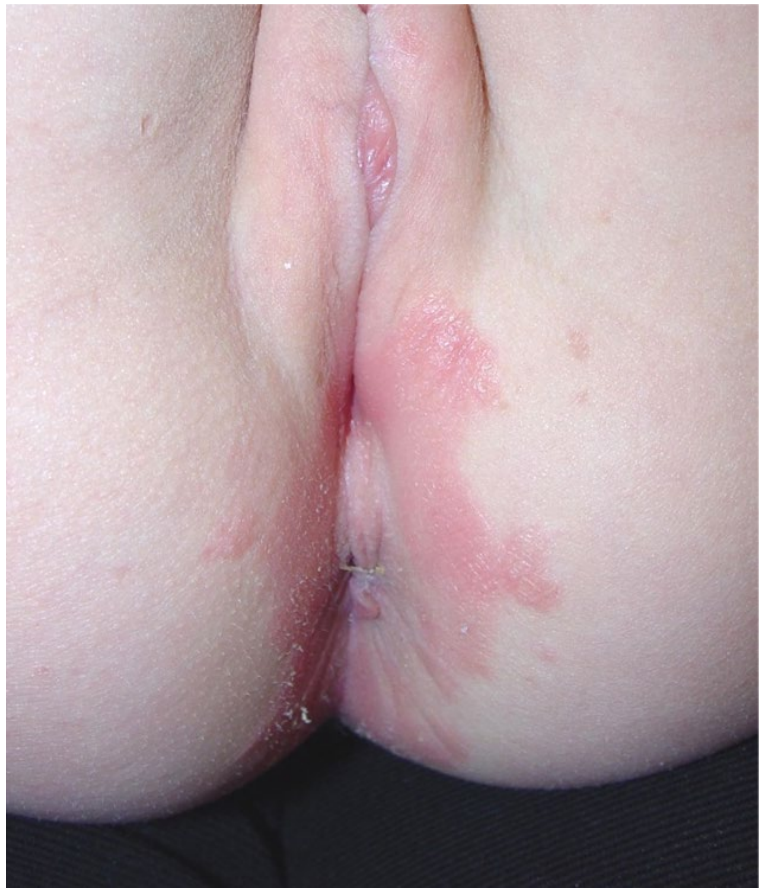


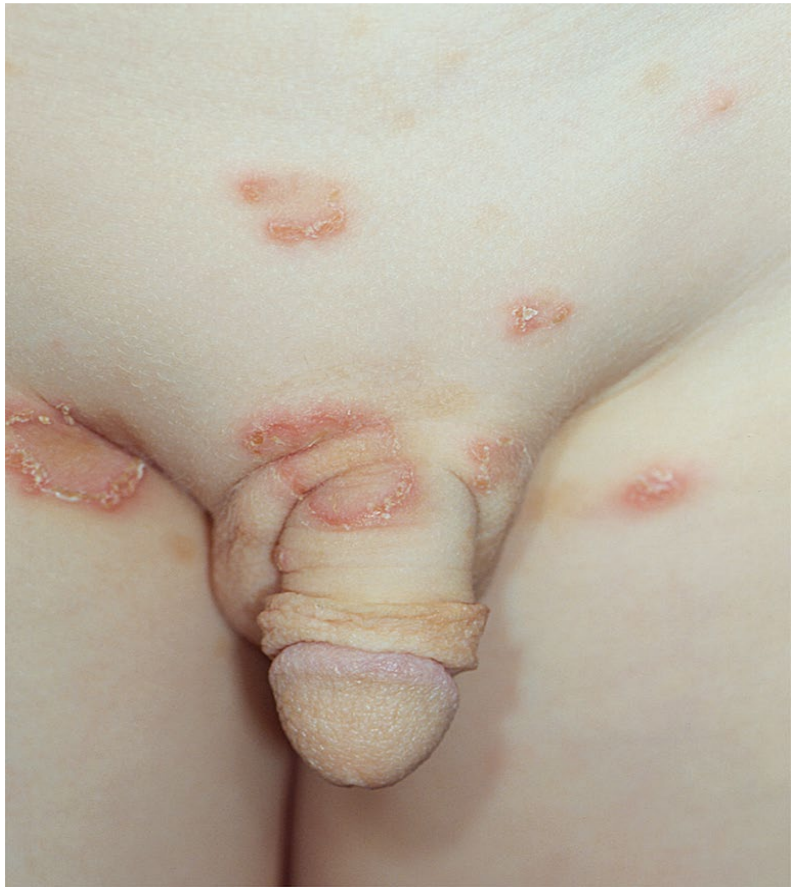




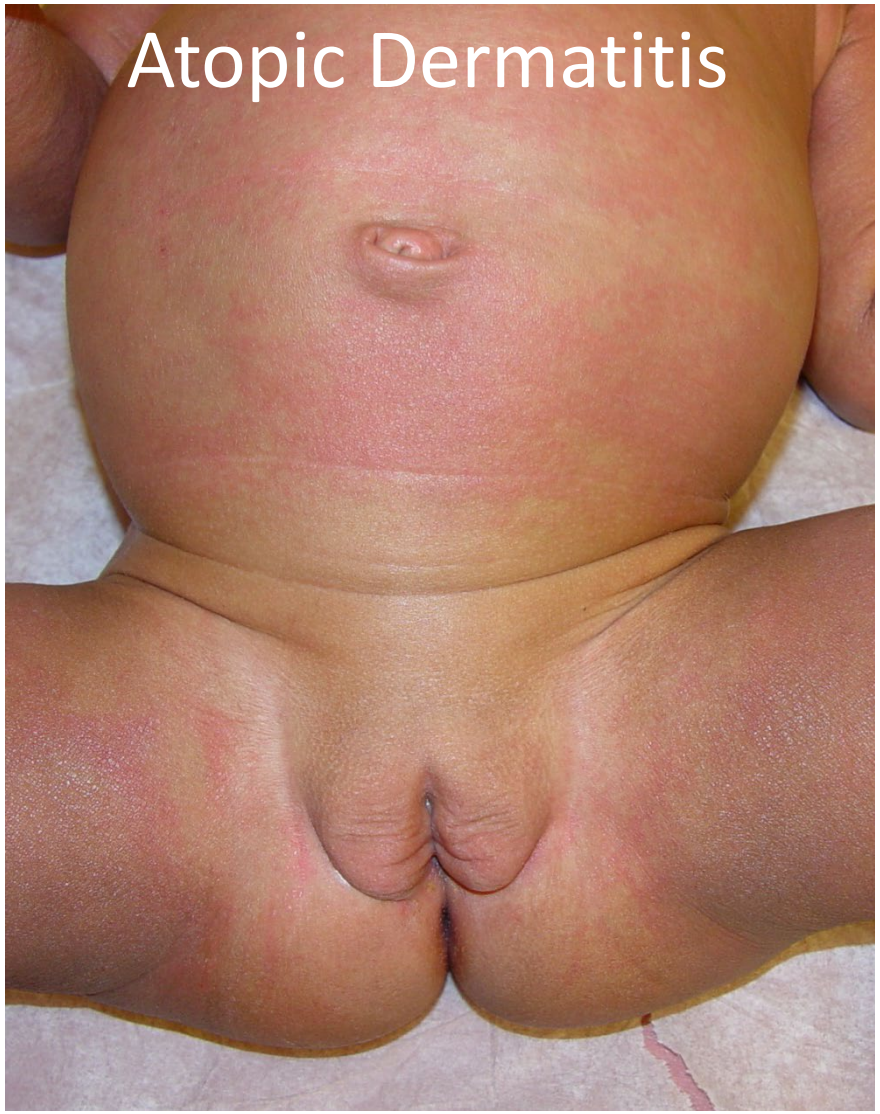
Diaper Area Involvement

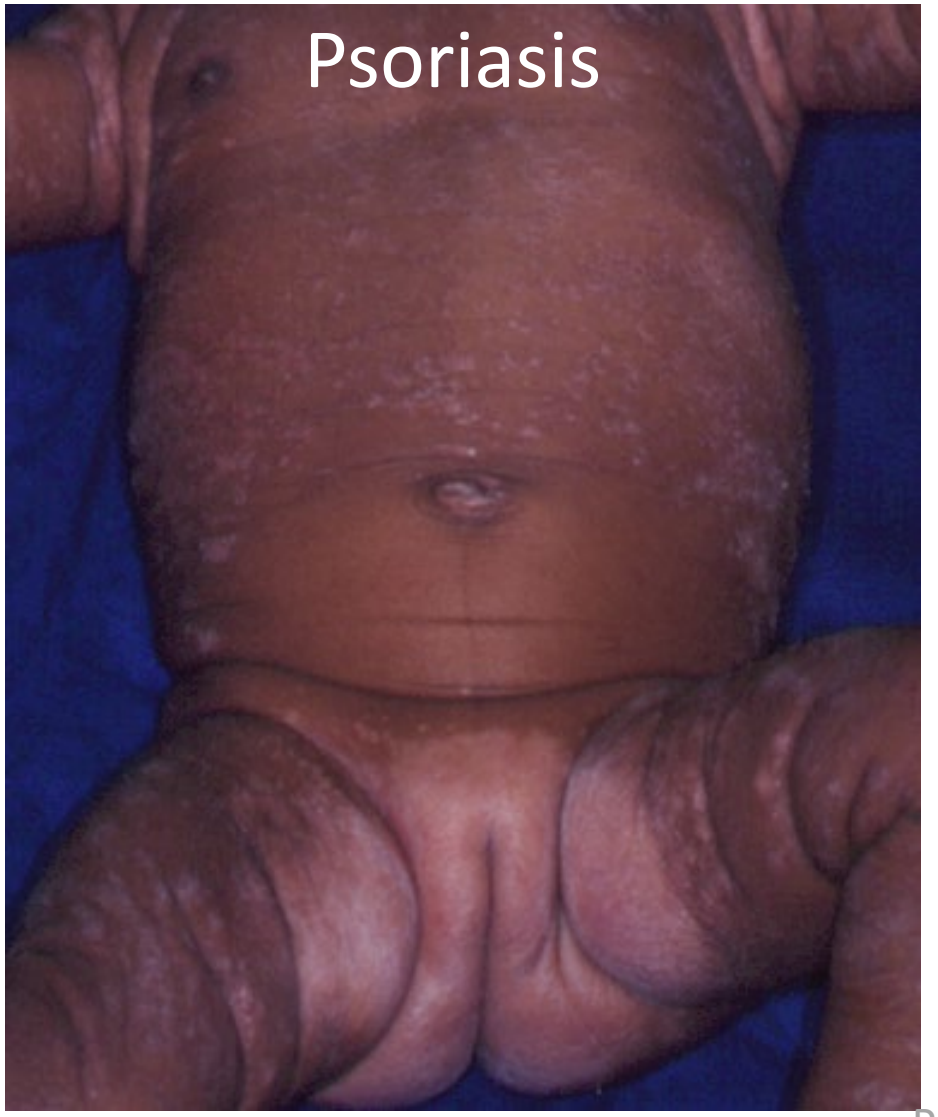




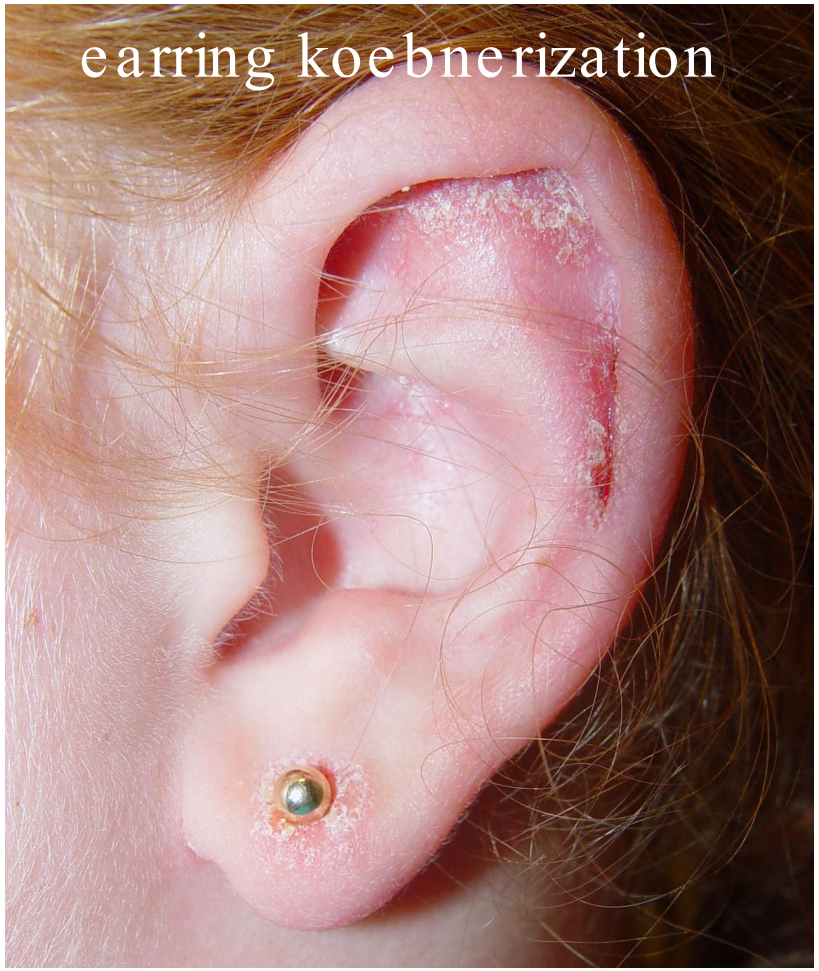


Diaper Area Involvement, Pigment Change

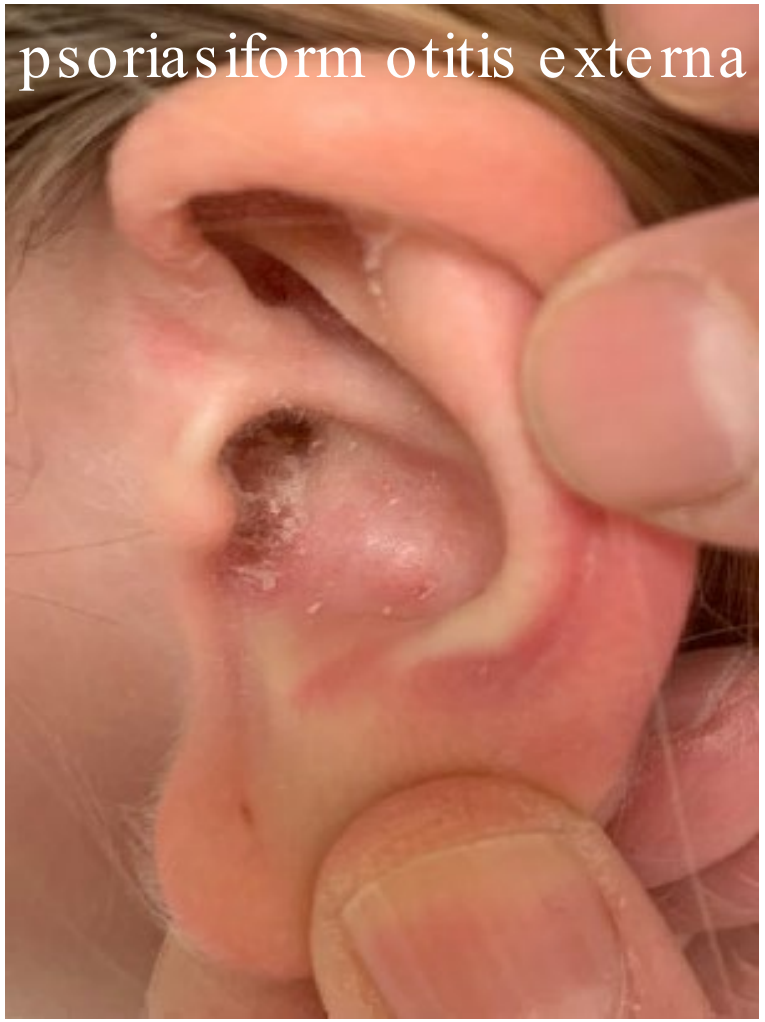




Ear Psoriasis

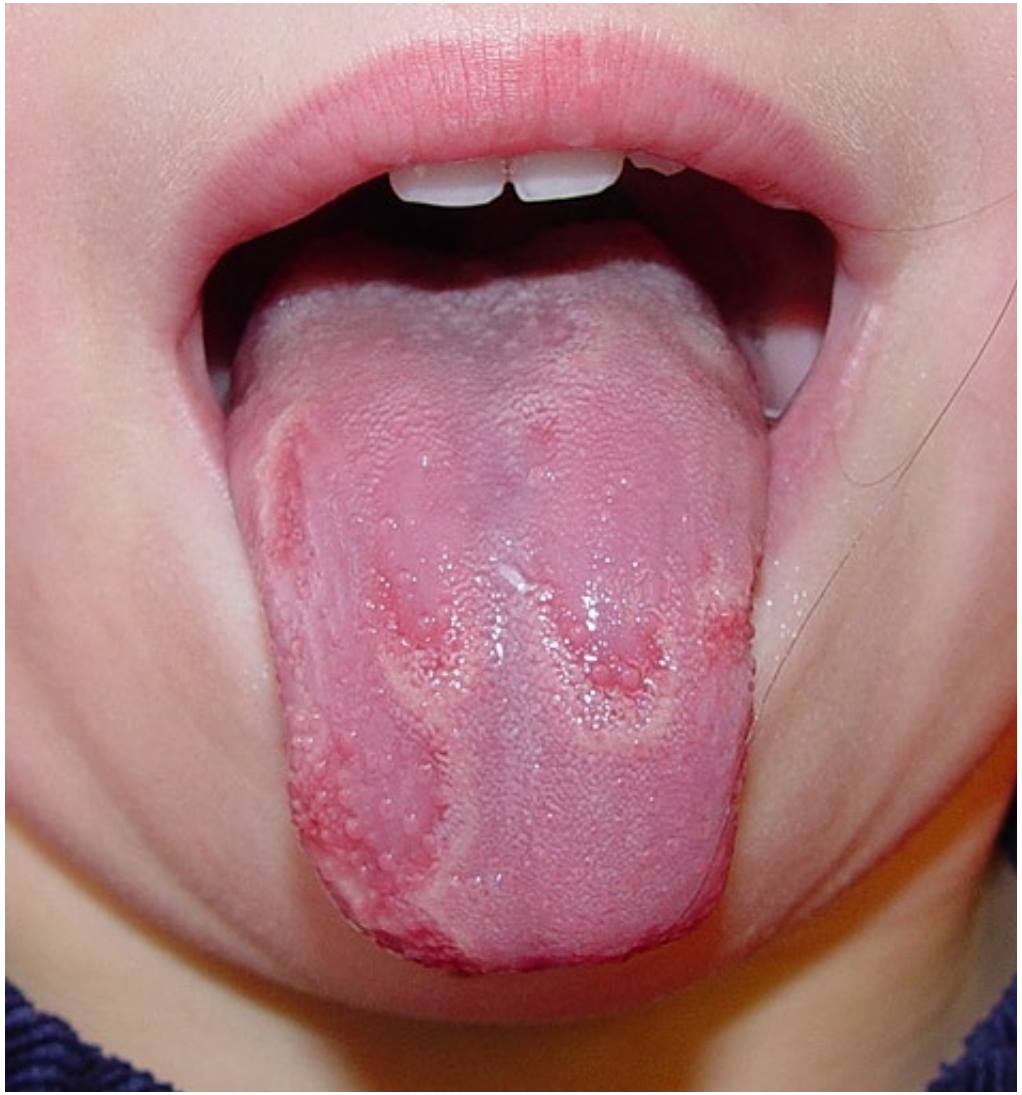


not nickel dermatitis



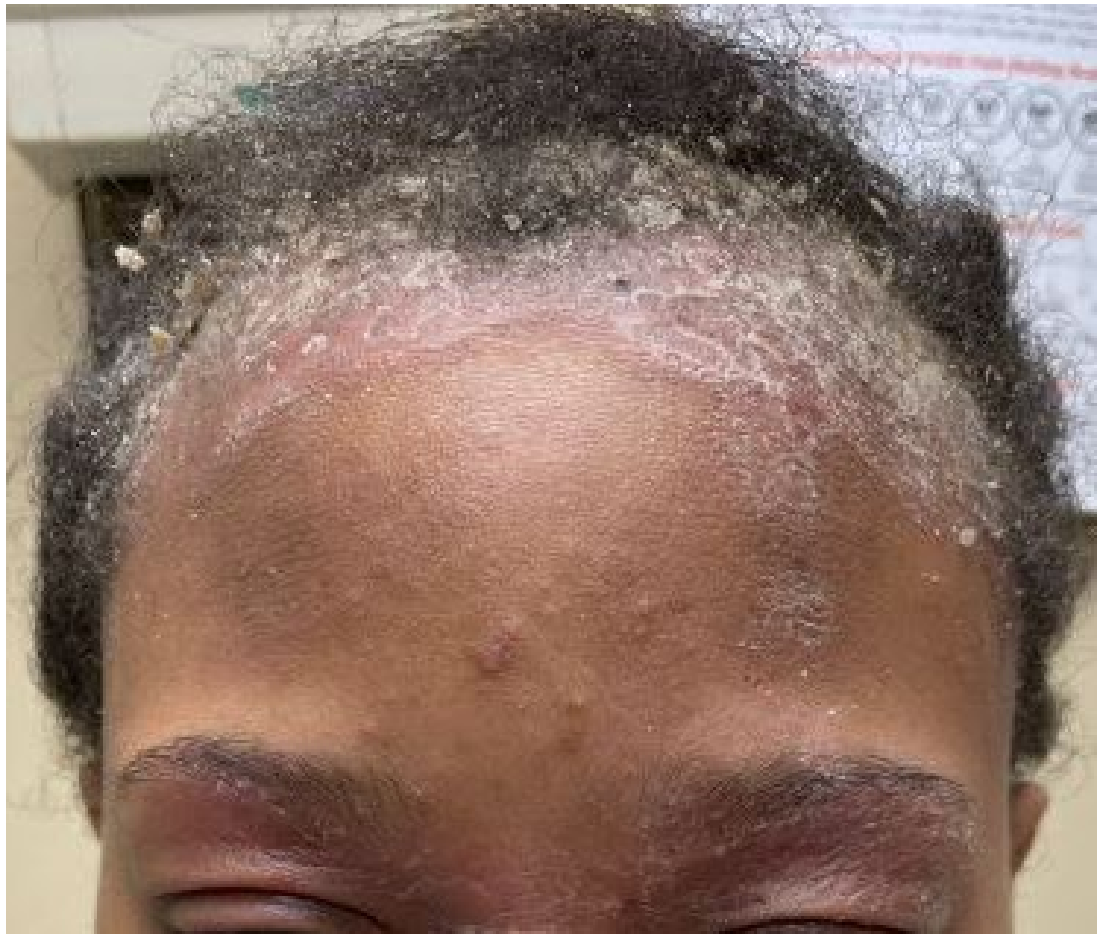
not impacted cerumen

Mucosal Psoriasis



Paradoxical Psoriasis

- <5% of children treated with TNF-α inhibitors for IBD, JIA, CRMO
- Infliximab > adalimumab >> etanercept
- Onset typically after >1 yr treatment
- Possibly linked to IL-23R polymorphisms
- Most respond to added topical treatment with continued anti-TNF therapy
- >80% clearance after change to an alternate biologic
- My approach: add low-dose methotrexate



Cyrenne BM, Parpia AS, Sibbald C. Paradoxical psoriasis in pediatric patients: A systematic review. Pediatr Dermatol. 2021;38(5):1086-1093.

Bucalo A, et al. Paradoxical Psoriasis Induced by Anti-TNFα Treatment: Evaluation of Disease-Specific Clinical and Genetic Markers. Int J Mol Sci. 2020, 23;21(21):7873.

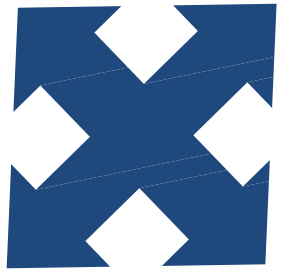
Management

- Review Triggers
  - Trauma
  - Infections
  - Drugs
  - Psychogenic stress
- Evaluate severity
- Screen for comorbidities

Multimodal Approach

Topical therapy

Lifestyle Modification/ Education & Support (NPF)



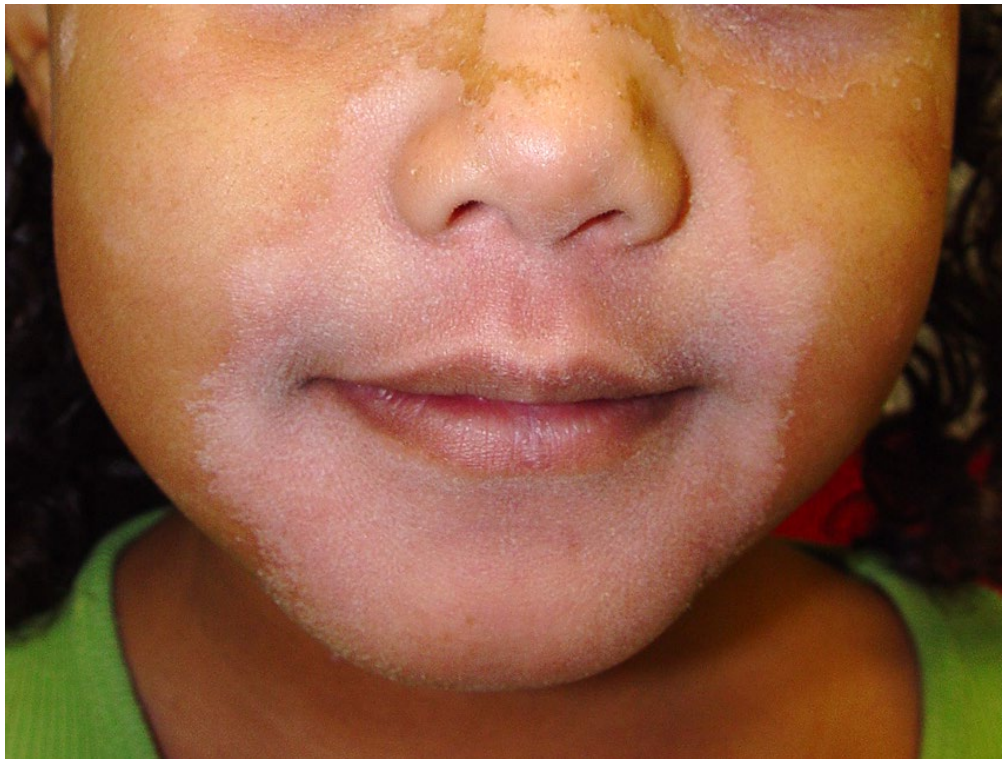
Trigger Avoidance

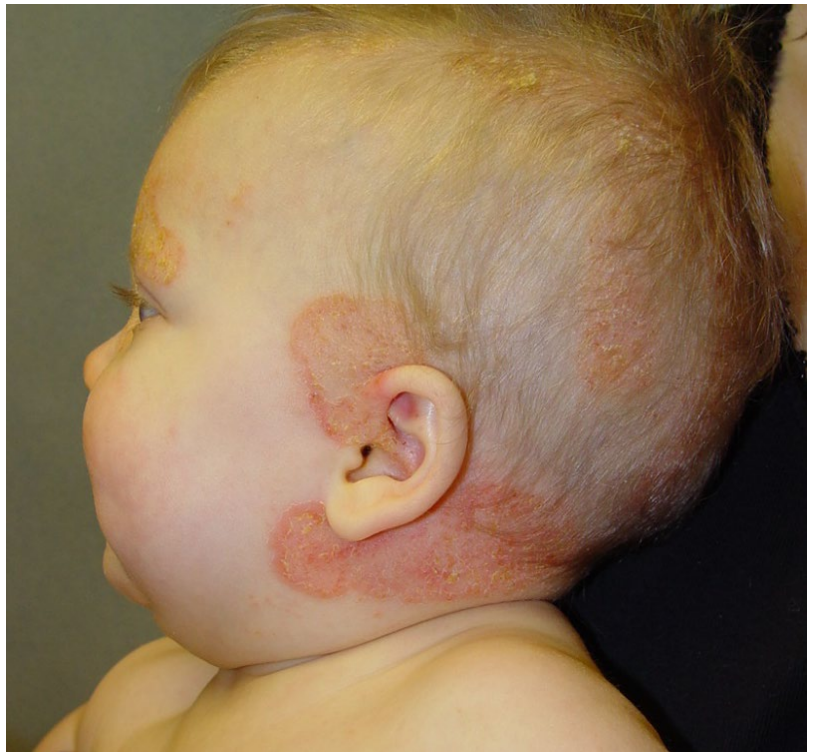
Systemic therapy/ Phototherapy/ Biologics

First-line treatment for mild psoriasis and eczema is similar; second-line treatment diverges

Topical Therapy Considerations

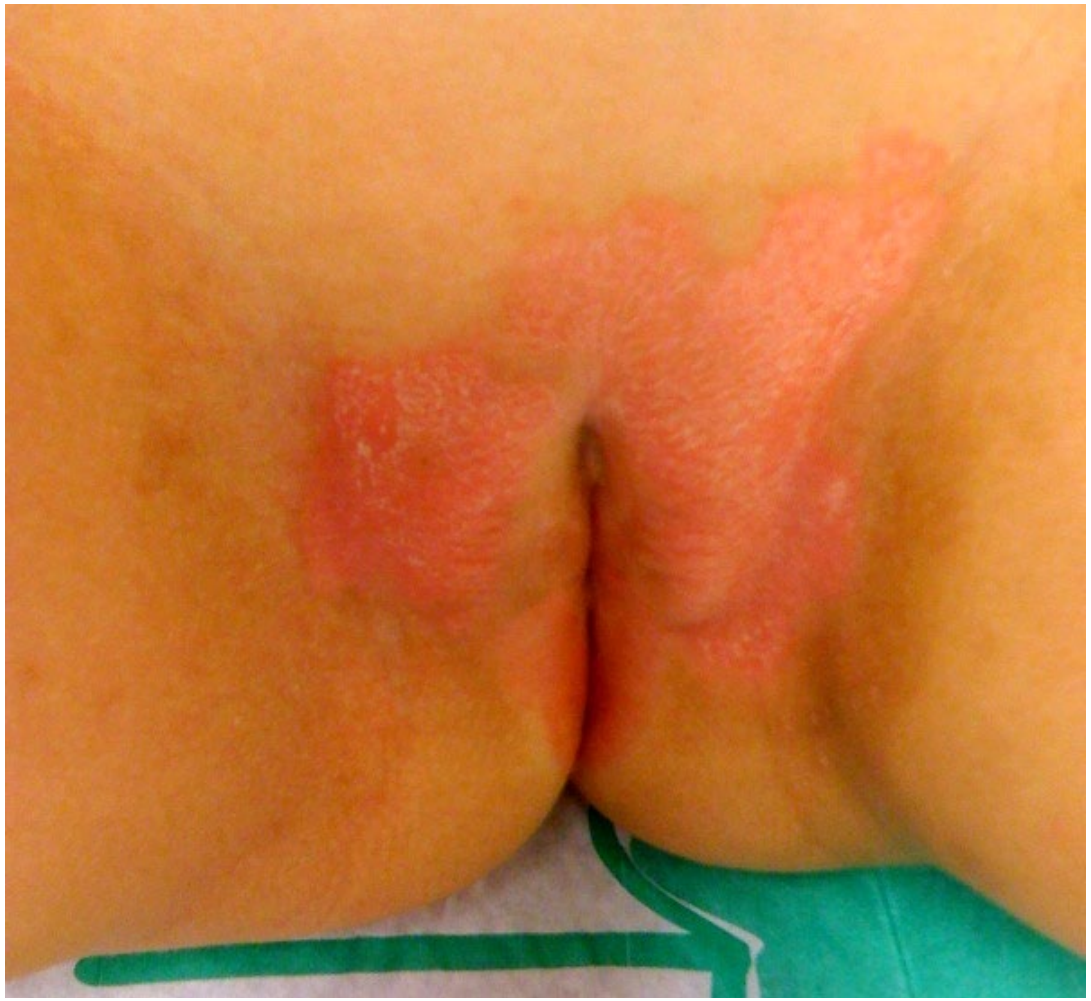
- Corticosteroid monotherapy is less effective/associated with rebound
- Beware increased pediatric risk of percutaneous absorption
- Reported HPA-axis suppression lower is lower for combination calcipotriene products
- Site-specific considerations: scalp, face/folds, BSA
- Vehicle-specific issues: acceptance, potency, irritation, allergenicity





Off-Label Diaper Area Treatment

- Screen for secondary *Candida*
- Zinc oxide barrier protection
- Avoid complex topicals
- Products with infant safety data
  - low potency TCS
  - pimecrolimus
  - crisaborole



Topical Corticosteroid Alternatives

	Brand Names	Boxed Warning	Labelled Indications	Avg Retail Price (60g)
Emollients	Vaseline		OTC	$ 2 (Equate)
Coal tar/LCD	Cutar		OTC	$ 26 (180g)
Salicylic acid	CVS Scalp Relief		OTC	$ 10
Vit D analogs calcipotriene calcitriol	 Dovonex, Sorilux Vectical		 ≥4 yr ≥2 yr	 $ 100 (generic) $ 500
TCIs tacrolimus pimecrolimus	 Protopic Elidel	✓	≥2 yr	$ 47 (generic) $ 160 (generic)
Combination TCS/Vit D	Taclonex Enstilar		≥3 mo ≥12 yr	$ 200 $ 1300
PDE4 inhibitors Crisaborole Roflumilast	 Eucrisa Zoryve		 ≥3 mo; AD ≥12 yr; psoriasis	 $ 750 $ 850
Tapinarof (AhR agonist)	Vtama		≥18 yr; psoriasis	$ 1400
Ruxolitinib	Opzelura	✓	≥12 yr; vitiligo, AD	$ 2000

Systemic Therapy

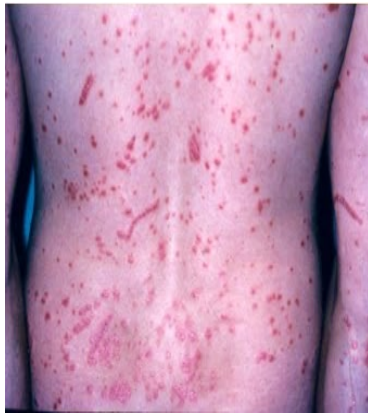
Candidates

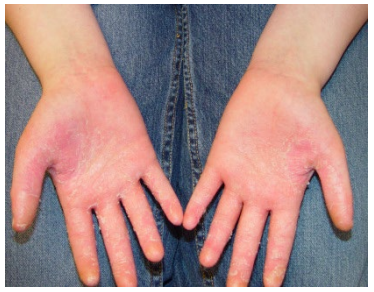
- Moderate-severe
- >10% BSA
- Higher-risk/topically difficult-to-treat sites (scalp, folds, palms/soles, nails)
- Co-morbidities (arthritis, IBD, autoinflammatory variants)
- QoL impact (Children's Dermatology Life Quality Index)

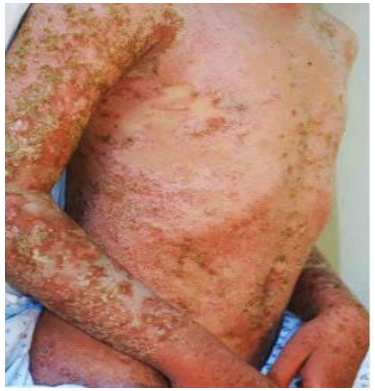
Consider all choices

Menter A et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients . J Am Acad Dermatol 2020; 82(1): 161-201.

Consider Immunologic Impact, Carcinogenicity







Non-Immunosuppressive

- Anti-Strep (Strep trigger antibiotic challenge)
- Phototherapy
- Oral retinoids

Immunomodulating

- Methotrexate
- Apremilast
- Biologics

Immunosuppressive

- Cyclosporine
- Biologics
- JAK inhibitors

Customizing Therapeutic Choices

- Primary psoriasis morphology
- Speed of disease progression
- Age and gender
- Comorbidities
- Level of disability (physical, psychological)
- Family/patient preference
- Risk:benefit
- Access, cost
- Genetic variants

Time-honored Systemic Therapy Pearls

- Avoid oral corticosteroids.
- Phototherapy is an “entry point” option for children without arthritis.
- Methotrexate is effective and readily available for all types and sites of psoriasis, especially plaque.
- Cyclosporine and JAK inhibitors are rescue drugs to treat the acute phase and control flares.
- Potential adverse effects require clinical and laboratory monitoring.

Systemic Retinoid Pearls

- Acitretin is non-immunosuppressive choice for severe generalized and palmoplantar psoriasis.
- Avoid in patients with pregnancy potential within 3 years
- Isotretinoin is a more widely used, but possibly less effective option
  - Bone toxicity rare with low dose/short duration
  - Teratogenicity is a relative contraindication in girls
- Combination NB-UVB and acitretin are synergistic.

2023 Labelled Biologic Options for Pediatric Psoriasis

2007: 7 year FDA moratorium on pediatric development

Biologic	USFDA		EMA	
	Pediatric Indication	Approval	Pediatric Indication	Approval
Etanercept	≥4 years	2016	≥6 years	2009 (age 8); 2011
Adalimumab	*	*	≥4 years	2015
Ustekinumab	≥12 years	2017	≥4 years	2015
Ixekizumab	≥6 years	2020	≥6 years	2020
Secukinumab	≥6 years	2021	≥6 years	2021

*USFDA-approved for JIA+uveitis ≥2 yr IBD ≥6 yr & HS ≥12 yr; biosimilar available

Hebert AA, Browning J, Kwong PC, Duarte AM, Price HN, Siegfried E. Managing pediatric psoriasis: update on treatments and challenges-a review. J Dermatolog Treat. 2022;33(5):2433-2442.

Available Off-Label Systemic Options for Pediatric Psoriasis

- Ongoing trials for pediatric psoriasis, with enrollment challenges
  - Biologics: guselkumab, tildrakizumab, brodalumab, rizankizumab, certolizumab
  - Small molecules: apremilast, methotrexate (comparator)
  - Comparator: risankizumab or brodalumab/ustekinumab; ixekizumab or tildrakizumab/etanercept
- No pediatric trials in process:
  infliximab, abatacept, cyclosporine, JAK inhibitors
- Age is the most common reason for payor denial, an illegal form of age discrimination. (ACA Section 1557)

Hebert A, Browning J, Kwong P, Duarte AM, Price H, Siegfried E. Managing Pediatric Psoriasis: Update on Treatments and Challenges—A Review. Journal of Dermatological Treatment, accepted for publication Mar 2022
https://clinicaltrials.gov/ct2/results?cond=Psoriasis&term=&cntry=&state=&city=&dist=&Search=Search&type=Intr&age=0

Systemic Biologic Therapy Pearls

- Role of biologics for children is rapidly evolving.
- The pipeline is robust.
- Access is often limited.
- Consider for severe, recalcitrant or pustular psoriasis, and arthritis+psoriasis
- TNF-inhibitors are considered 1st line.
- IL17-inhibitors may be most effective.
- Dosing frequency range: Qwk (etanercept) – Q3mo (IL12/23s)
- Goal for skin disease is to achieve clinical clearance, then discontinue if possible.
- Taper/discontinuation regimens are not well-defined.

Specific Treatment Choice Considerations

- Needle phobia: PO or Q3mo biologics
- Obesity: anti-TNFs may cause weight gain
- Inflammatory bowel disease: avoid ant- IL-17s; ustekinumab is effective, methotrexate may be used
- SLE: ustekinumab is not effective
- Hypertension: avoid cyclosporine
- Renal/hepatic dysfunction: avoid methotrexate & cyclosporine

Final Message

- Psoriasis is a clinical phenotype with a variety of presentations and associated morbidities.
- Many factors impact optimal management.
- The therapeutic pipeline is robust.
- Optimal decision-making is shared (patient/provider/payer).