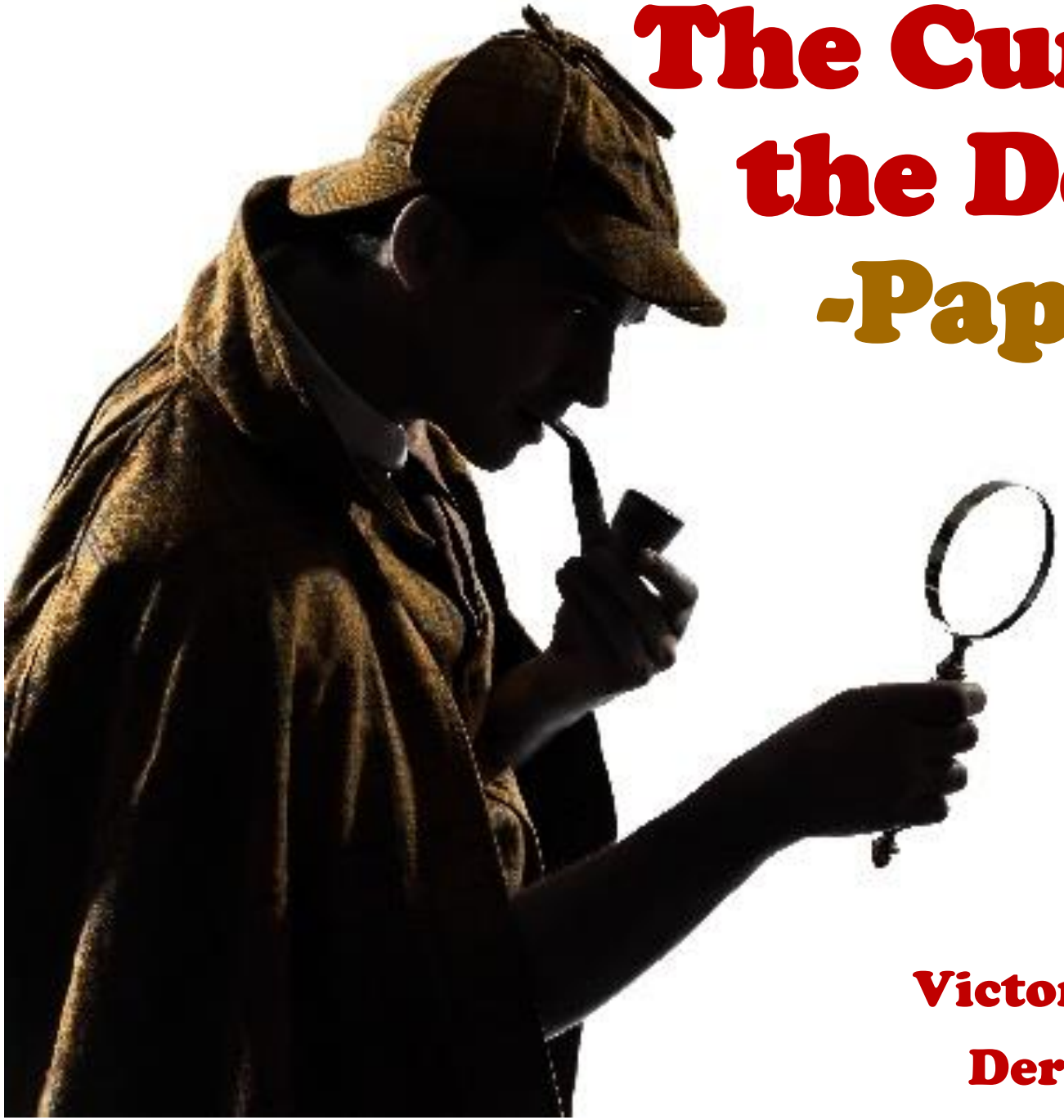


The Curious Incident of the Dog in the Night -Papulosquamous Diseases

Victoria Lazareth MA, MSN, NP-C, DCNP
Dermatology Nurse Practitioner, MA

- Organon (Dermavant) announced that the U.S. Food and Drug Administration (FDA) approved VTAMA® (tapinarof) cream, 1%, an aryl hydrocarbon receptor agonist, on Dec. 16, 2024 for an additional indication of the topical treatment of atopic dermatitis (AD) in adults and pediatric patients 2 years of age and older. The FDA approved VTAMA® (tapinarof) cream, 1% for the treatment of plaque psoriasis in adults in May 2022.
- In the ADORING pivotal studies, VTAMA cream, 1% demonstrated, in moderate to severe patients as young as 2 years old with AD, a statistically significant difference versus vehicle in the proportion of patients achieving a score of clear (0) or almost clear (1) and a minimum 2-grade improvement from baseline at Week 8 on the Validated Investigator Global Assessment for AD (vIGA-AD) 45.4% versus 13.9% of patients in ADORING 1 and 46.4% versus 18.0% in ADORING 2 (both $P < 0.0001$).
- The most common adverse reactions (incidence ≥1%) were upper respiratory tract infection (12%), red raised bumps around the hair pores (folliculitis) (9%), lower respiratory tract infection (5%), headache (4%), asthma (2%), vomiting (2%), ear infection (2%), pain in extremity (2%), and stomach-area (abdominal) pain (1%).
- In ADORING 3, patients (N=728) were followed for up to 48 weeks, with safety and efficacy endpoints that included the achievement of complete disease clearance (vIGA-AD=0), and the achievement of clear or almost clear skin (vIGA-AD=0 or 1). The safety profile with long term use was generally consistent with the safety profile observed at Week 8.
- “VTAMA cream approval in AD is important because it can be prescribed for children as young as 2 years old. VTAMA cream has the potential to bring much needed relief to a significant number of children suffering from this disease,” said Adelaide A. Hebert, MD, Professor and Chief of Pediatric Dermatology at McGovern Medical School at UTHealth Houston and Children’s Memorial Hermann Hospital and lead investigator for the ADORING program. “Moreover, because the prevalence of itch makes this condition extremely burdensome to patients and their families, the itch data from the ADORING program demonstrates reduction of one of the condition’s most prevalent symptoms with use of VTAMA cream.” https://www.biospace.com/press-releases/fda-approves-vtama-tapinarof-cream-1-for-the-treatment-of-atopic-dermatitis-in-adults-and-children-2-years-of-age-and-older

Photo Courtesy V.Lazareth,NP

nemolizumab

- Galderma today announced that the United States (U.S.) Food and Drug Administration (FDA) has approved Nemluvio® (nemolizumab) on December 13, 2024 for the treatment of patients 12 years and older with moderate-to-severe atopic dermatitis, in combination with topical corticosteroids (TCS) and/or calcineurin inhibitors (TCI) when the disease is not adequately controlled with topical prescription therapies. This follows the recent U.S. FDA approval of Nemluvio for subcutaneous injection for the treatment of adults with prurigo nodularis in August 2024.
- Nemluvio is the first approved monoclonal antibody that specifically targets IL-31 receptor alpha, inhibiting the signaling of IL-31.8 IL-31 is a neuroimmune cytokine that drives itch and is involved in inflammation and epidermal dysregulation in atopic dermatitis.2,9-11
- This approval is based on positive results from the phase III ARCADIA clinical trial program which evaluated the efficacy and safety of Nemluvio in combination with background TCS, with or without TCI, versus placebo in combination with TCS, with or without TCI, in 1,728 patients aged 12 years or older with moderate-to-severe atopic dermatitis.20
- Results demonstrated that patients treated with Nemluvio, administered subcutaneously every four weeks in combination with TCS, with or without TCI, showed statistically significant improvements on skin clearance in both co-primary endpoints. These were clearance (0) or almost-clearance (1) of skin lesions when assessed using the investigator's global assessment (IGA) score, and achieving a 75% reduction in the Eczema Area and Severity Index (EASI) - when compared to placebo in combination with TCS, with or without TCI, after 16 weeks of treatment.20
- The trials also met all key secondary endpoints confirming significant responses on itch as early as Week 1, and statistically significant improvements in sleep disturbance with Nemluvio in combination with TCS, with or without TCI, when compared to placebo in combination with TCS, with or without TCI.20 Overall, Nemluvio was well tolerated, and the safety profile was generally consistent between Nemluvio and placebo groups.20

https://www.galderma.com/news/galderma-receives-us-fda-approval-nemluvior-nemolizumab-patients-moderate-severe-atopic

nemolizumab

Nemolizumab (Nemluvio) IL-31 inhibitor

- **December 13, 2024** –FDA has approved Nemluvio® (nemolizumab) for pts ≥12 years with moderate-to-severe atopic dermatitis, in combination with topical corticosteroids (TCS) and/or calcineurin inhibitors (TCI) when the disease is not adequately controlled with topical prescription therapies.
- This follows the recent U.S. FDA approval of Nemluvio for subcutaneous injection for the treatment of adults with prurigo nodularis in August 2024.[12]
- Nemluvio is the first approved monoclonal antibody that specifically targets IL-31 receptor alpha, inhibiting the signaling of IL-31.[8] IL-31 is a neuroimmune cytokine that drives itch and is involved in inflammation and epidermal dysregulation in atopic dermatitis.[2,9-11]
- Nemolizumab showed significant efficacy for pruritus in patients with AD. However, its efficacy for AD signs was not strong. Therefore, other biologics or Jak inhibitors should be considered for patients with AD with severe AD signs. Other biologics and Jak inhibitors are efficacious for both pruritus and AD signs. In Japan, nemolizumab has been approved for patients with AD with an EASI score of 10 or above who suffer from severe pruritus, whereas other biologics and Jak inhibitors can be prescribed to patients with AD with an EASI score of 16 or above. Patients with AD have heterogeneous clinical phenotypes, including different combinations of itch and lesional severity (Chovatiya et al., 2021). Some patients suffer from severe pruritus with mild-to-moderate AD signs. Nemolizumab can be considered for those patients, for instance, patients with an EASI score of 10–16 and severe pruritus (Figure 2). EASI scores in some patients with prurigo nodularis–like phenotype in AD are low because of small areas of affected lesions. These patients are also candidates for nemolizumab.

Disclosures

Information presented is current as of 12/1/2024

Advisory Board

- Bristol Myers Squibb -Psoriasis
- Incite -Vitiligo
- JDNPPA -Dermatology
- UCB -Psoriasis

Speaker Panel

- American Association of Nurse Practitioners -Dermatology
- Dermatology Nurses' Association -Dermatology
- MauiDerm NP+PA -Dermatology
- Nurse Practitioner Association for Continuing Education -Dermatology

Photo Courtesy V.Lazareth,NP

Objectives

Upon completion of this activity the participant will

- Design treatment plans with patients which incorporate current guidelines for the management of Atopic Dermatitis; The Itch that Rashes
- Evaluate Psoriasis patients for potential comorbidities and formulate management plans to help them gain control over this complex disease
- Construct a differential diagnosis, analytics and treatment modalities for patients with Contact Dermatoses
- Recognize Cutaneous Manifestations of underlying Systemic Disease

Photo Courtesy V.Lazareth,NP

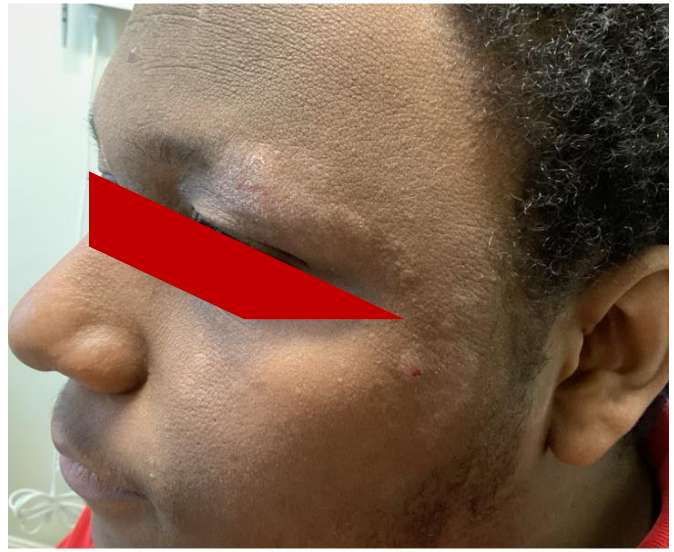
Atopic Dermatitis

Photo Courtesy V.Lazareth,NP

Case Study

- 29 yr old male complains of extremely itchy areas of skin at his arms and legs which have spread to his face and neck.
- He has had eczema since childhood which waxes and wanes but never resolves. He has used multiple TCS, TCI and prednisone.
- He presents with depigmented macules and patches, large hyperkeratotic plaques and a loss of eyebrows. His neck is hyperpigmented and lichenified.
- PMH: exercise-induced asthma

- What treatment would you consider next?



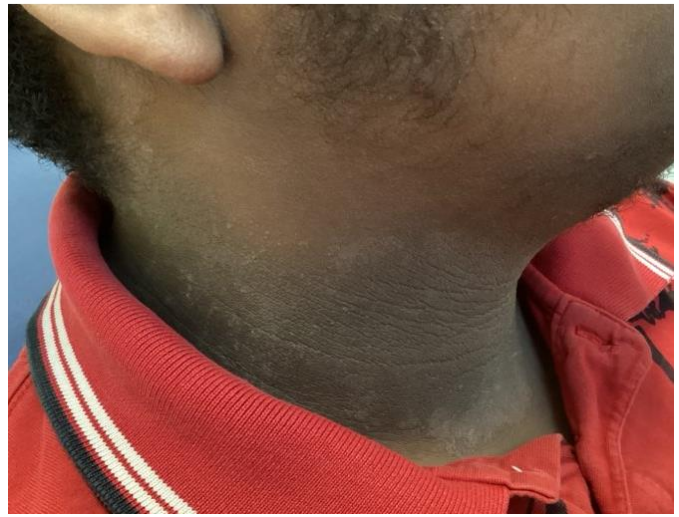


Photo Courtesy V.Lazareth,NP

Atopic Dermatitis (AD)

- most common type of eczema
- onset usually age 3-6 months
- 60% in the first year of life
- 90% of childhood onset AD occurs before age 5
- 90% have mild to moderate disease
- family history ~70%
- up to 66% have concomitant allergic rhinitis and/or asthma
- “Allergic March” – progression from AD to allergic rhinitis to asthma

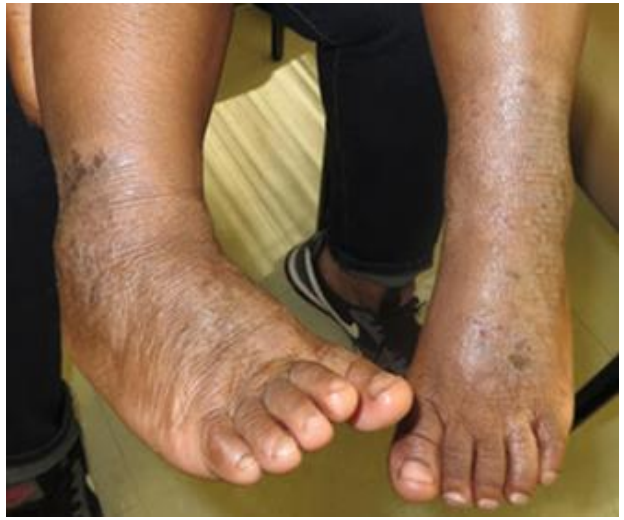
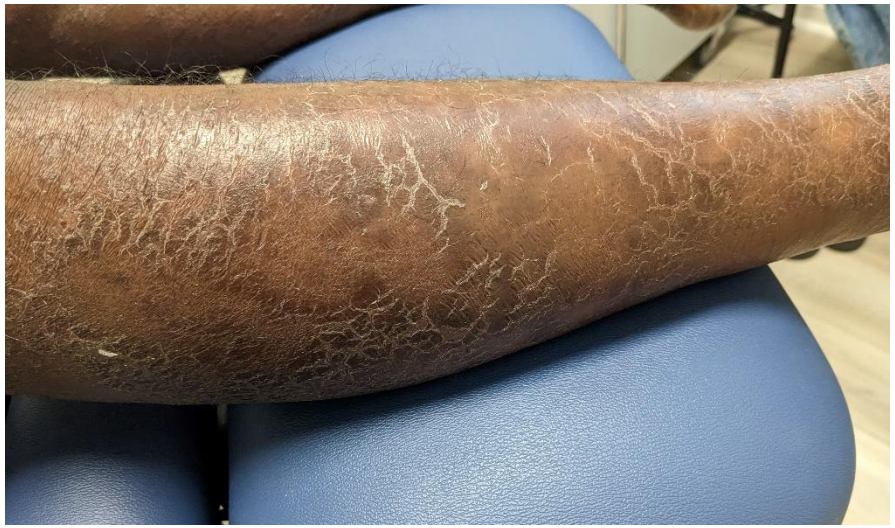


Photo Courtesy V.Lazareth,NP

AD: incidence

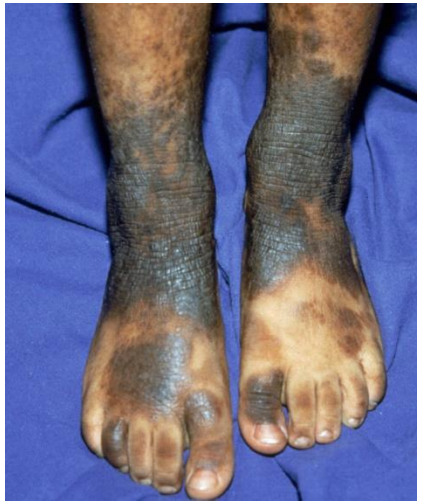
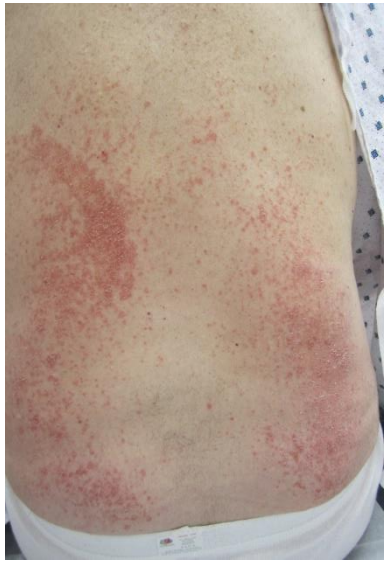
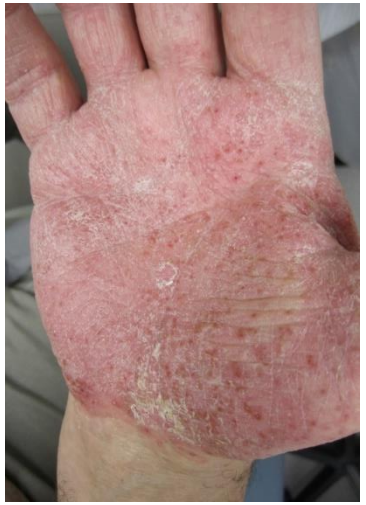
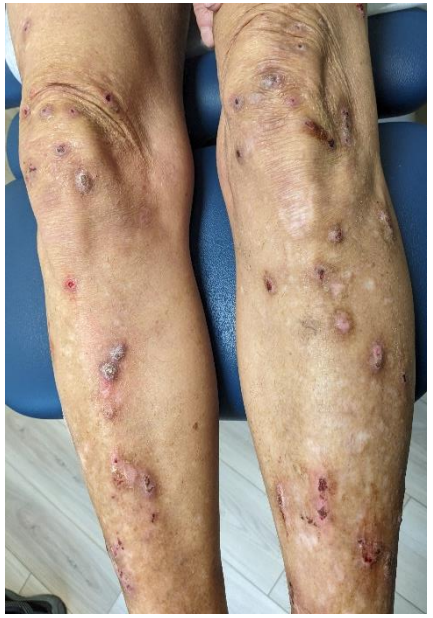
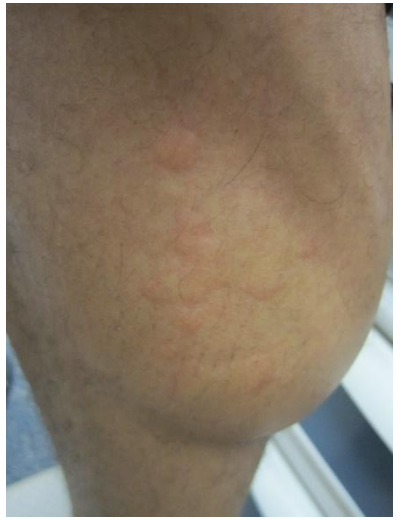
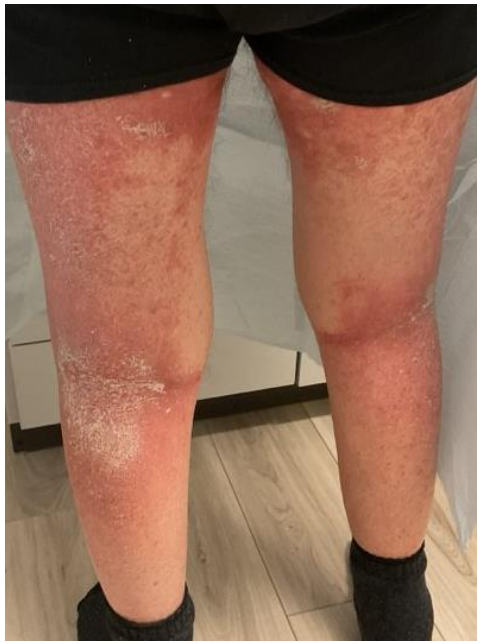
- 20% of children and 10% of adults
- 10-30% persisting into adulthood
- risk factors for persistence
  - later onset
  - number of years of persistence
  - severity
- ~25% of adults with AD have “adult onset” without a history of AD in childhood
- up to 76% of adult patients with AD suffer from at least one other atopic comorbidity (allergic rhinitis, asthma, allergic conjunctivitis, other allergies)



Silverberg NB and Duran-McKinster C Deratol Clin 2017;35:351-63

Photo Courtesy V.Lazareth,NP

AD: clinical presentations

childhood, classic, hand dermatitis, prurigo nodularis, urticarial, erythroderma

Photo Courtesy V.Lazareth,NP

AD: pathophysiology

- chronic pruritus: disease-defining symptom causing significant sleep disturbances, impaired quality of life, increased anxiety, depression, suicidal behavior
- genetic predisposition, immune dysfunction and environmental factors (irritants, allergens, microbiome), and their interactions play significant roles in AD
- IL-4 and IL-13 disturb skin barrier and function by downregulating barrier proteins, fueling atopic inflammation and pruritus
- IL-31, “itch-cytokine” induces itch and sensitizing nerves to further pruritic stimuli playing a critical role in the so-called “itch-scratch-cycle”
- improved understanding of AD pathophysiology has prompted new treatments targeting specific cytokines, receptors, or their intracellular signaling

Legat FJ. Itch in Atopic Dermatitis - What Is New? Front Med (Lausanne). 2021 May 7;8:644760.

Photo Courtesy V.Lazareth,NP

AD -pathogenesis

adapted from Sayaseng et al. Pathophysiology and Management of Mild to Moderate Pediatric Atopic Dermatitis. https://www.jpedhc.org/article/S0891-5245(17)30357-7/fulltext

Epidermal Barrier Dysfunction

filaggrin gene impairment

↓ ceramides, hydration

↑ skin pH, S. aureus resistance, allergen susceptibility

Immunologic Abnormalities

↑ IL-4, IL-13 production (↑ inflammation, ↓ barrier function)

↑ PDE-4 activation

↑ calcineurin-mediated Th2 cell activation

↑ serum IgE

↑ allergen susceptibility

↑ trans-epidermal water loss

Aggravating Factors

- dry skin, harsh soaps,
- seasonal changes, heat,
- sweating, infections, stress,
- food allergies

Photo Courtesy V.Lazareth,NP

AD: 2023 Treatment Guidelines

moisturizers with ceramides

- relieve dry, cracked skin, decrease inflammation
- reduce the severity of, and increase the time between, flare-ups

topical corticosteroids

- 1st line treatment in all skin regions to reduce inflammation, itch and infection

topical calcineurin inhibitors

- pimecrolimus, tacrolimus
- steroid-sparing treatments to reduce inflammation and itch, and decrease flare-ups

Photo Courtesy V.Lazareth,NP

AD: Topical Steroids

- Use a low-potency topical steroid (class 6-7) on thinner skin and on the face hydrocortisone 1%, hydrocortisone 2.5%, desonide, alclometasone BID
- Use a mid-potency topical steroid (class 3-4) until inflammation subsides (<1 week) triamcinolone, mometasone, fluocinolone BID
- Transition the patient to a lower-potency agent once inflammation begins to abate.
- Corticosteroid ointments are preferable to creams and lotions, as they contain fewer preservatives and patients are therefore less likely to develop sensitization
- Use high-potency topical steroids (class 1-2) infrequently for severe cases clobetasol, halobetasol, betamethasone dipropionate, fluocinonide, desoximetasone BID
- Potent corticosteroids should not be used on intertriginous areas due to skin atrophy and striae formation. Use for a maximum of 2 weeks

Photo Courtesy V.Lazareth,NP

AD: Adverse Effects of Topical Steroids

Tachyphylaxis

- loss of efficacy when agent is used for prolonged periods; creates a “tolerance”
  - * use higher potency meds for flares, lower potency for maintenance
  - * use pulse dose regimens (every other day or weekends only)

Local AEs

- skin atrophy, striae, acniform eruptions, tinea incognito, hypersensitivity reactions, purpura, hypopigmentation, excess facial hair growth, delayed wound healing
  - *use the lowest effective potency TCS for the shortest period of time

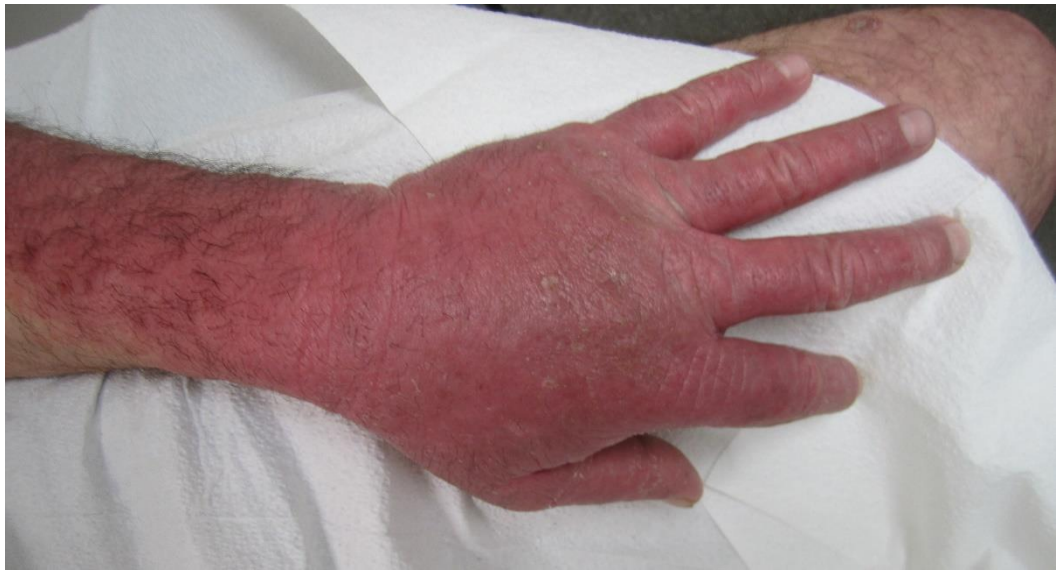
Systemic AEs

- hypothalamic-pituitary-adrenal axis suppression especially in infants
  - *avoid *systemic* steroids for eczema, psoriasis due to likely rebound phenomenon

Photo Courtesy V.Lazareth,NP

AD: Topical Steroid Withdrawal

- adverse reaction presenting *after stopping* prolonged, inappropriate, or frequent use of topical corticosteroids
- erythema, edema, papular eruption, burning, stinging, itch, desquamation
- rash days to weeks of discontinuing TCS
- develops only where the TCS was applied (though it may spread)
- flare may be worse than original rash



* more *burning* than itch, *confluent* rather than patchy erythema
* resembles atopic dermatitis but involves *unusual* sites
* *hx* of prolonged, continuous use of mid- or high-potency TCS

Photo Courtesy V.Lazareth,NP

AD: Topical Calcineurin Inhibitors

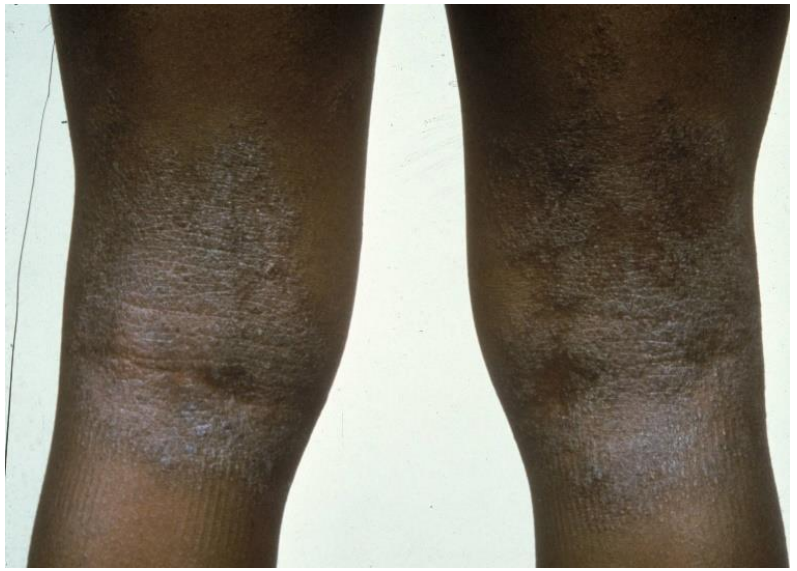
- steroid sparing agents which reduce symptoms of atopic dermatitis
- helpful to avoid topical steroids at the face, intertriginous sites

tacrolimus 0.1% and 0.03% ointment daily

- initial burning, itching, sensitivity, folliculitis flu-like symptoms

pimecrolimus 1% cream BID

- AE: less irritating & greasy than tacrolimus



"Black Box Warning" due to the extrapolated risk of lymphoma and SCC from systemic tacrolimus.
A 2022 Review found no difference of absolute risk of any cancer between TCI vs controls.
No incidence of higher sensitivity among pediatric pts.

Photo Courtesy V.Lazareth,NP

AD: 2023 Treatment Guidelines

topical Phosphodiesterase-4 (PDE4) inhibitors

- crisaborole 1% ointment once to twice daily in patients ≥ 3 months
- reduce proinflammatory mediators and increase anti-inflammatory mediators
- roflumilast 0.15% cream once daily in patients ≥ 6 years
- designed to be a long-term treatment option for disease control

topical Janus kinase inhibitor

- ruxolitinib 1.5% cream, JAK1-JAK2 inhibitor, twice daily, up to 20% BSA
- short term treatment in mild to moderate atopic dermatitis in patients ≥ 12 yr

aryl carbon receptor agonist

- tapinarof 1% cream once daily in patients ≥ 2 years
- not yet FDA approved as of 11/2024

Photo Courtesy V.Lazareth,NP

AD: topical JAK inhibitor

- ruxolitinib (Opzelura) 1.5% cream -JAK1 + JAK2 inhibitor
- mild to moderate atopic dermatitis
- topical short-term and non-continuous chronic treatment
  - in immunocompetent pts >12 yr
  - whose disease is not adequately controlled with topical Rx therapies (TCS, TCI)
  - apply BID up to 20% BSA
  - TRuE-AD1 & 2: 52% clear/near clear & itch reduction
  - AEs: nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, rhinorrhea

Photo Courtesy V.Lazareth,NP

AD: Guidelines

AD Treatment Failure

- pts with mild AD: majority can expect clinical improvement and disease control with emollients and conventional topical therapies (TCS, TCI, PDE4)
- pts with moderate to severe (>10% BSA) or difficult-to-control disease: may need systemic therapy

AD Biologic Therapy

- Interleukin-4 (IL-4) and Interleukin-13 (IL-13) are produced by immune cells and contribute to inflammatory processes, skin barrier disruption and lipid abnormalities
- Biologic drugs block IL-4 and IL-13 from binding to cell surface receptors

Sidbury R, Alikhan A, Bercovitch L, Cohen DE, Darr JM, Drucker AM, Eichenfield LF, Frazer-Green L, Paller AS, Schwarzenberger K, Silverberg JI, Singh AM, Wu PA, Davis DMR, Guidelines of care for the management of atopic dermatitis in adults with topical therapies, Journal of the American Academy of Dermatology (2023), doi: https://doi.org/10.1016/j.jaad.2022.12.029.

Photo Courtesy V.Lazareth,NP

AD: 2023 Guidelines

updated recommendations for pts who do not respond to topical therapies:

strongly recommend

- dupilumab, tralokinumab (biologics)
- baricitinib, abrocitinib, upadacitinib (JAK inhibitors)

conditionally recommend

- Phototherapy
- cyclosporine, methotrexate, azathioprine, mycophenolate

do not recommend

- systemic corticosteroids

Davis D, Drucker A, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023. doi.org/10.1016/j.jaad.2023.08.102.

Photo Courtesy V.Lazareth,NP

AD: 2023 strong recommendation

Monoclonal Antibodies

- dupilumab ≥6 m and tralokinumab ≥12 yr: FDA-approved biologics for AD with overall strong efficacy and safety data. Conjunctivitis is common

JAK Inhibitors

- upadacitinib ≥12 yr and abrocitinib FDA-approved JAKs for moderate-severe AD pts who have failed other systemic treatments including biologics
- both JAKs demonstrate high efficacy. higher doses show the highest efficacy in a network meta-analysis and were superior to dupilumab in head-to-head clinical trials
- baricitinib approved in Europe, but not yet FDA-approved for AD (11/2024)

Davis D, Drucker A, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023. doi.org/10.1016/j.jaad.2023.08.102.

AD: Biologics

Interleukin-4 (IL-4) and Interleukin-13 (IL-13)

- proteins produced by immune cells
- contribute to inflammatory processes
- skin barrier disruption and lipid abnormalities

Biologic drugs

- block IL-4 and IL-13 from binding to cell surface receptors
- dupilumab ≥6 mo
- tralokinumab ≥12 yr
- nemolizumab ≥12 yr

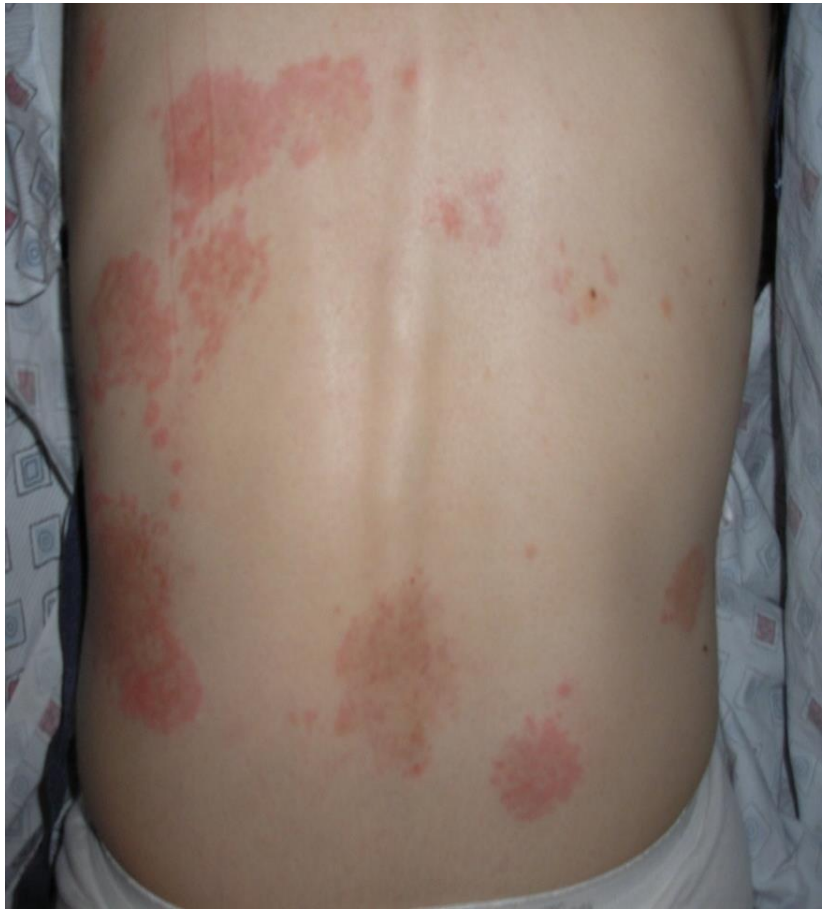


Photo Courtesy V.Lazareth,NP

AD: Biologics

dupilumab IL-4, IL-13 Inhibitor

- I: moderate-severe Atopic Dermatitis >6 mo
- Dosage: 600 mg SC, then 300 mg SC q 2 wks (modified dosing for children)
- AEs: conjunctivitis, keratitis, blepharitis, eye pruritis, HSV, injection site reaction
- LIBERTY AD SOLO 1-2: ~38% clear/almost-clear; reduction in itch, improved sleep & QOL
- Monitoring: none required

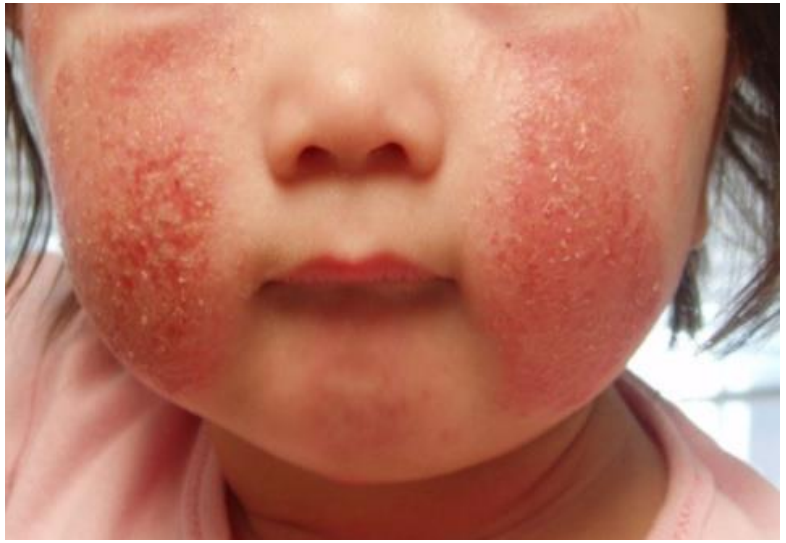


Photo Courtesy V.Lazareth,NP

AD: Biologics

tralokinumab IL-13 inhibitor

- moderate-severe AD in patients ≥ 12 yr
- Dosing: initial 600 mg SC then 300mg SC every other wk
- AEs: URIs, conjunctivitis, keratitis, injection site reactions, eosinophilia
- ECZTRA 1-2: ~22% clear/almost clear; reduction in itch, improved sleep & QOL

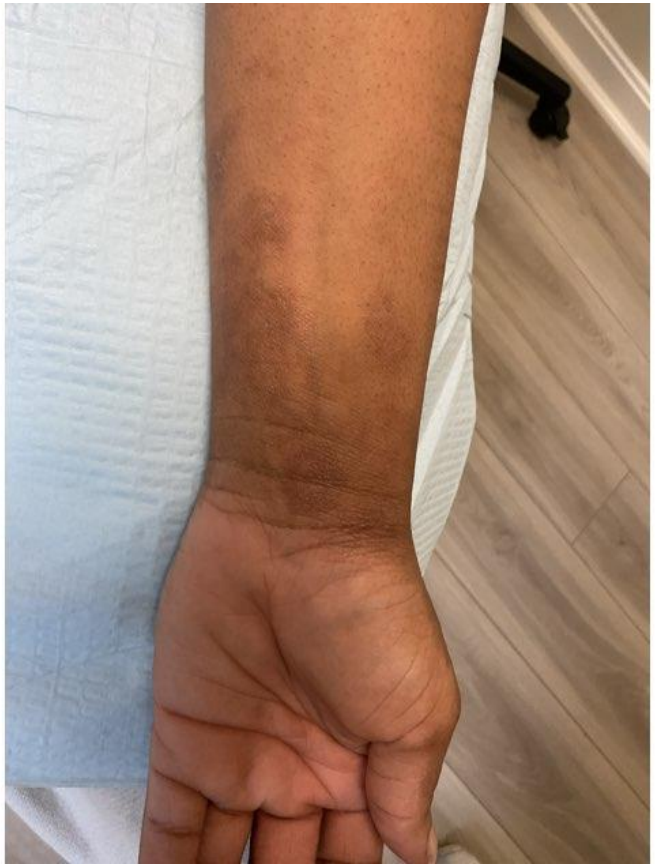


Photo Courtesy V.Lazareth,NP

AD: Biologics

- nemolizumab IL-31 inhibitor
- inhibits IL-31 signaling, a key cytokine involved in causing itch
- moderate to severe atopic dermatitis ≥12 yr (88 lbs / 40 kg)
- Dosing: 250 mg SC every 4 weeks
- AE: eye and eyelid inflammation (redness, swelling, itching), injection site reactions, shingles (herpes zoster)
- ADvocate 1 and 2, 38% achieved clear or almost-clear skin at 16 weeks; 77% maintained those results at 1 yr

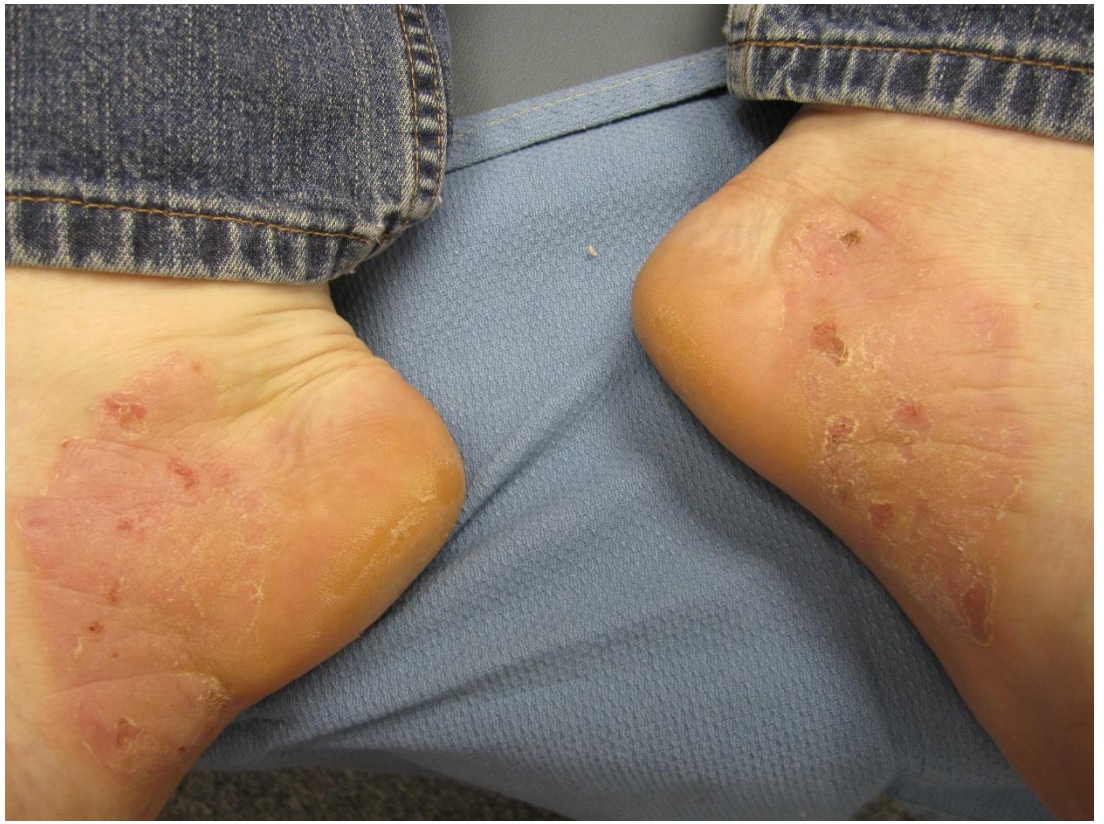


Photo Courtesy V.Lazareth,NP

AD: Janus Kinase Inhibition

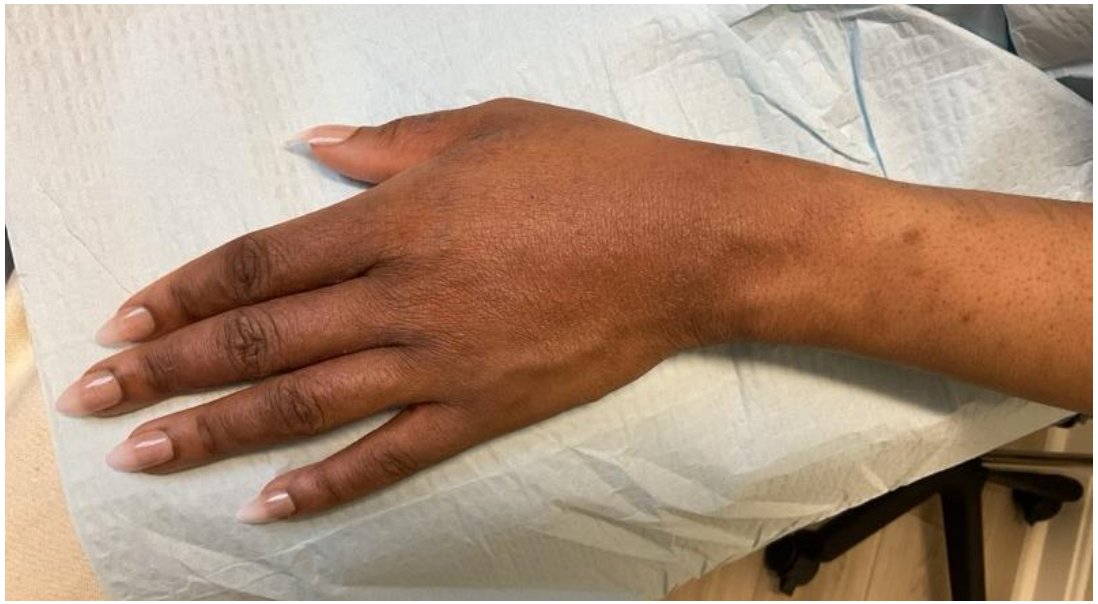
- Janus kinases are key drivers of cytokine signaling and inflammatory response
- JAK inhibitors (JAK1, JAK2, JAK3, TYK2)
  - small molecules that inhibit cytokine blocking the inflammatory response
  - JAK-STAT pathway mediates signaling of IL-4, IL-5, IL-13, IL-31 in *acute* AD; mediates T helper (Th1, Th17, Th22) cytokines in *chronic* AD
  - JAK1, JAK2 and TYK2 impact IL-13 (itch)
- FDA approved JAK inhibitors to treat AD
  - ruxolitinib cream (JAK1, JAK2)
  - abrocitinib (JAK1) 100-200 mg po daily >12 yr
  - upadacitinib (JAK1) 15-30 mg po daily >12 yr

Photo Courtesy V.Lazareth,NP

AD: JAKs

abrocitinib JAK 1 inhibitor

- 100-200 mg po daily
- I: pts ≥12 yr with refractory, moderate-severe AD whose disease is not adequately controlled with other systemic drugs, including biologics
- CI: antiplatelet therapies (except low-dose ASA) during first 3 mo of treatment
- AEs: nasopharyngitis, nausea, headache
- JADE MONO 1-2: ~60% achieved EASI-75, significant improvement in itch



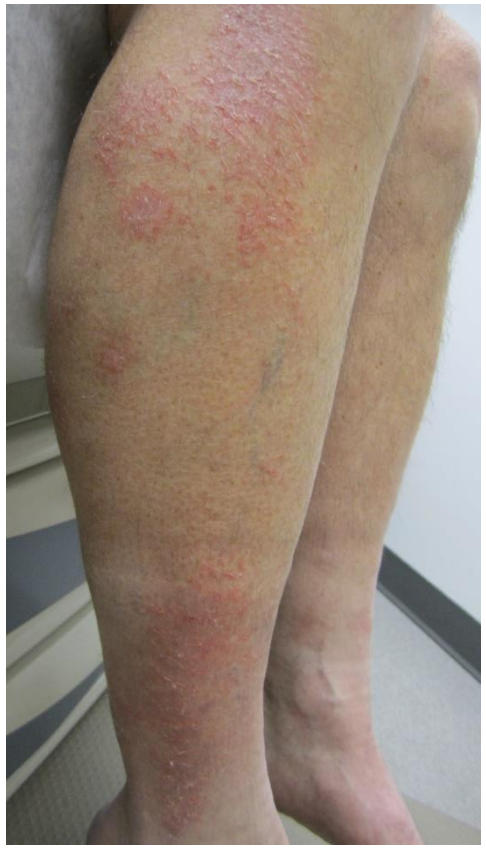
https://cibinqo.pfizerpro.com/

Photo Courtesy V.Lazareth,NP

AD: JAKs

upadacitinib JAK1 Inhibitor

- 15-30 mg po daily
- I: pts ≥12 yr with refractory, moderate-severe AD whose disease is not adequately controlled with other systemic drugs, including biologics
- AEs: nausea, cough, fever, acne, headache
- MeasureUp 1-2:≥65% achieved EASI-75, significant improvement in itch



https://www.hmpgloballearningnetwork.com/site/thederm/advances/upadacitinib-approved-adults-and-children-aged-12-years-and-older-refractory?hmpid=dmljdG9yaWEubGF6YXJldGg4M0BnbWFpbC5jb20=&utm_medium=email&utm_source=enewsletter&utm_content=1574829797

Photo Courtesy V.Lazareth,NP

AD: 2023 conditional recommendation

Narrowband UVB (NB-UVB)

- is the most widely used form of phototherapy
- is effective for AD for adults with moderate to severe AD
- is not suitable for infants and young children

Antimetabolites and Immunosuppressants

- cyclosporine, methotrexate, azathioprine, and mycophenolate were conditionally recommended by the AAD guidelines based on low or very low certainty evidence
- all require baseline and ongoing laboratory monitoring for AEs
  - cyclosporine: renal impairment, HTN
  - methotrexate: liver damage
  - azathioprine and mycophenolate: cytopenias

Davis D, Drucker A, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023. doi.org/10.1016/j.jaad.2023.08.102.

AD -2023 Guidelines: insufficient data

Systemic corticosteroids

- commonly prescribed for pts with moderate-to-severe AD; very effective in the short term and easy to prescribe,
- however, guidelines conditionally recommend against systemic corticosteroids for use in AD

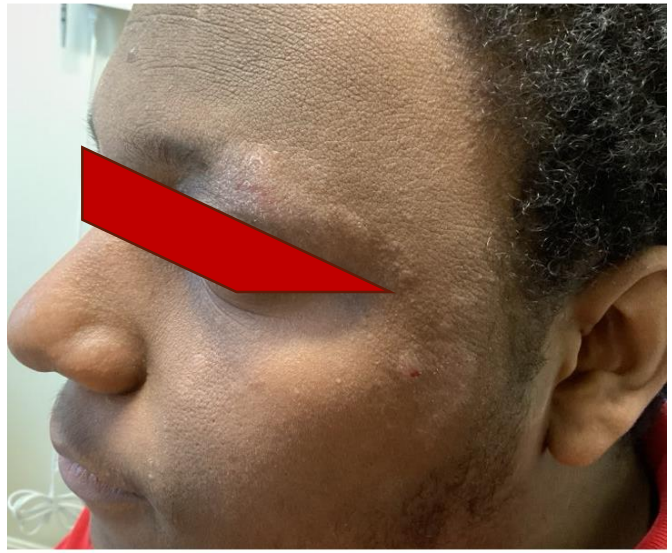
Insufficient data

- PUVA phototherapy, systemic antibiotics, oral antihistamines, montelukast, apremilast, ustekinumab, intravenous immunoglobulin, interferon gamma, omalizumab, tumor necrosis-alpha inhibitors, systemic calcineurin inhibitors (other than cyclosporine), or mepolizumab for the treatment of AD

Davis D, Drucker A, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023. doi.org/10.1016/j.jaad.2023.08.102.

Case Study: Answer

- 29 yr old male complains of extremely itchy areas of skin at his arms and legs which have spread to his face and neck.
- He has had eczema since childhood which waxes and wanes but never resolves. He has used multiple TCS, TCI and prednisone.



Which treatments would you consider next?

crisaborole ointment topical PDE-4 inhibitor: apply BID

ruxolitinib cream topical JAK 1-2 inhibitor: apply BID up to 20% BSA

dupilumab sc IL-4, IL-13 inhibitor: no monitoring

tralokinumab sc IL-13 inhibitor: no monitoring

abrocitinib po systemic JAK1 inhibitor: requires some monitoring

upadacitinib po systemic JAK1 inhibitor: requires some monitoring

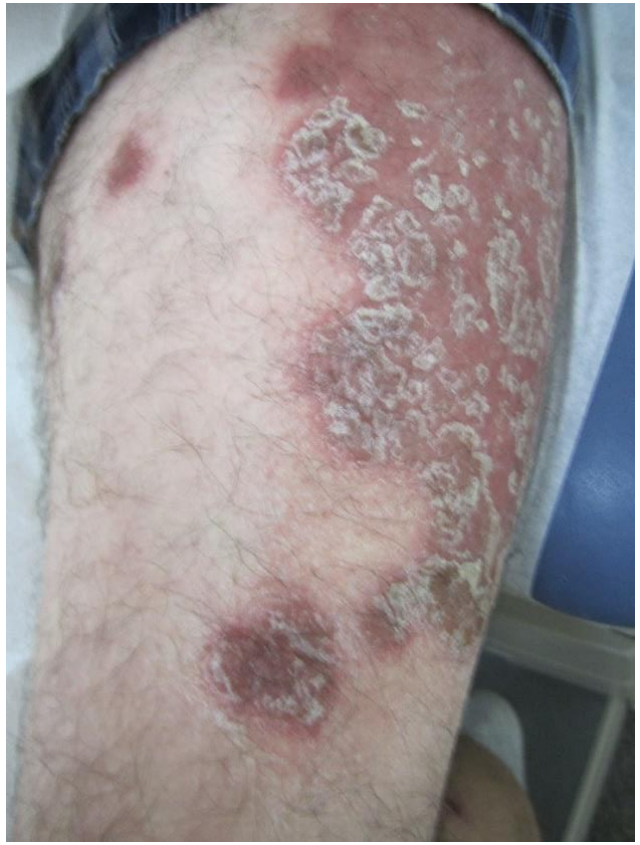
Photo Courtesy V.Lazareth,NP

Psoriasis

Photo Courtesy V.Lazareth,NP

Psoriasis

- chronic, genetic, immune-mediated, inflammatory disease
- a dysregulation of the T-cells of the innate immune system
  - triggers cytokine release (TNF-α, IL-17, IL-23)
  - which causes chronic inflammation
  - triggers rapid accumulation of epidermal cells
  - which leads to raised, scaly cutaneous plaques

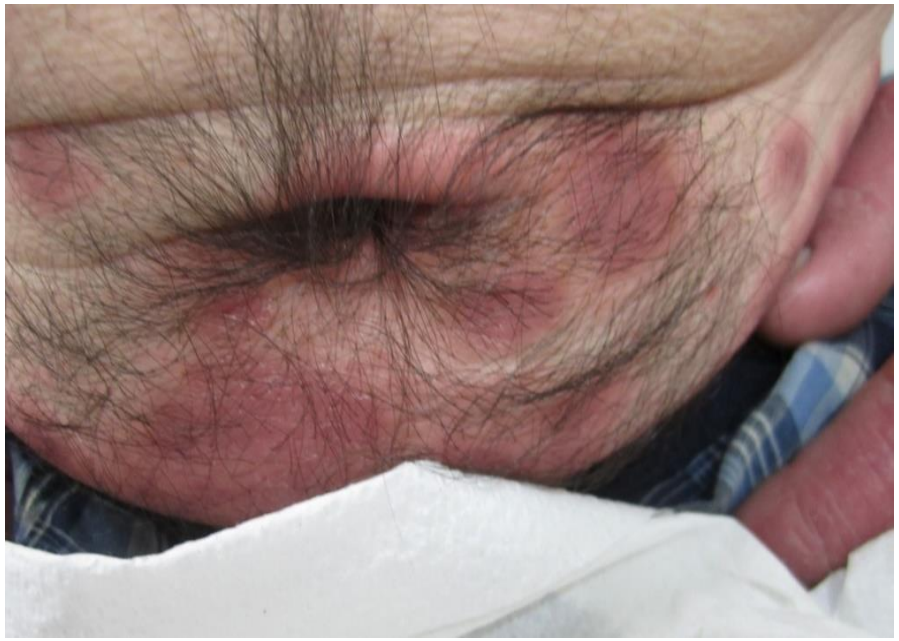


https://www.psoriasis.org/understanding-psoriatic-disease/

Orsmond A, Bereza-Malcolm L, Lynch T, March L, Xue M. Skin Barrier Dysregulation in Psoriasis. Int J Mol Sci. 2021 Oct 7;22(19):10841. doi: 10.3390/ijms221910841. PMID: 34639182; PMCID: PMC8509518.

Photo Courtesy V.Lazareth,NP

Psoriasis



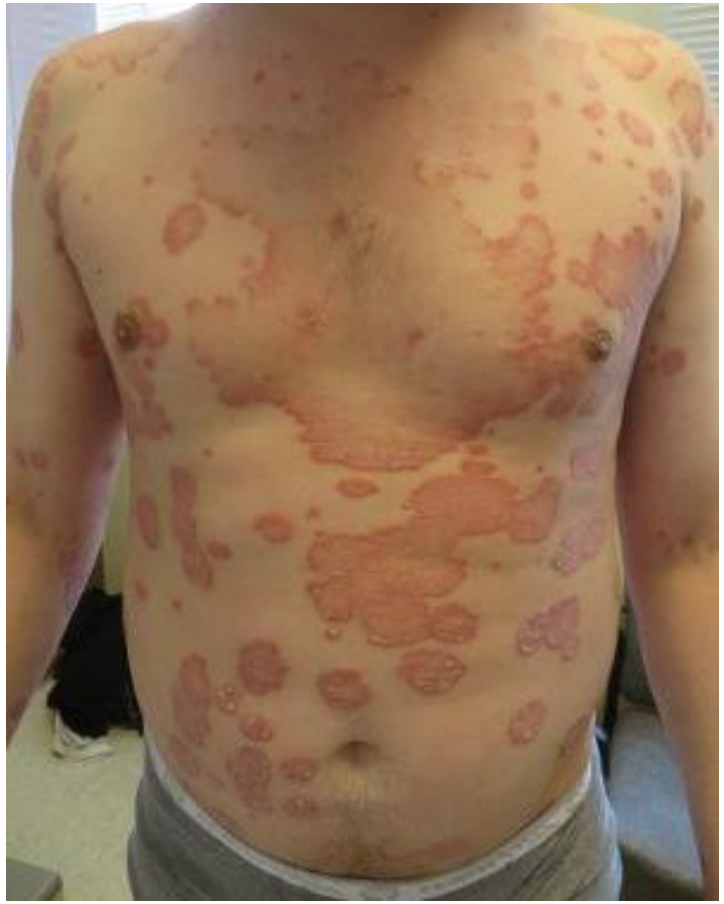
- itching, bleeding, burning, stinging, pain
  flares are triggered by physical or emotional stress
- association between psoriasis and
  - psoriatic arthritis, depression, substance abuse
  - obesity, diabetes, heart disease, stroke
- young psoriatic pts have increased mortality risk
  - systemic inflammation generates elevation of C-reactive protein, homocysteine, inflammatory cytokines (TNF-a, IL-6, IL-17, IL-20, IL-22, IL-23)
  - may contribute to morbidity and mortality in these pts
- associated with psychological disability
  - poor body image, depression, substance abuse

Farley E, Menter A. Psoriasis: comorbidities and associations. Giornale Italiano di Dermatologia e Venereologia : Organo Ufficiale, Societa Italiana di Dermatologia e Sifilografia. 2011 Feb;146(1):9-15. PMID: 21317853.

Photo Courtesy V.Lazareth,NP

Psoriasis: comorbidities

- Obesity
- Dyslipidemia
- Diabetes
- Inflammatory bowel disease
- Cardiovascular disease
- Metabolic syndrome
- Uveitis
- Malignancy
- Mood disorders
- Alcohol and addictive behaviors



Abuaara K, et al. *Br J Dermatol*. 2010;163(3):586-592; Armstrong AW, et al. *J Hypertens*. 2013;31:433-442; discussion 442-443; Azfar RS, et al. *Arch Dermatol*. 2012;148(9):995-1000; Gelfand JM, et al. *JAMA*. 2006;296(14):17351-741; Gelfand JM, et al. *J Invest Dermatol*. 2006;126(10):2194-2201; Kurd SK, et al. *Arch Derm*. 2010;146:891-895; Langan SM, et al. *J Invest Derm*. 2012;132(3 Pt 1):556-562; Li W, et al. *Am J Epidemiol*. 2012;175(5):402-413; Ma C, et al. *Br J Dermatol*. 2013;168(3):486-495; Mehta NN, et al. *Eur Heart J*. 2010;31(8):1000-1006; Najarian DJ, et al. *J Am Acad Dermatol*. 2003;48(6):805-821; Yeung H, et al. *JAMA Derm*. 2013;149(10):1173-1179.

Photo Courtesy V.Lazareth,NP

Plaque Psoriasis (vulgaris)

- most common type
- well demarcated plaques or papules characterized by white adherent micaceous scale on an erythematous base
- assoc. signs incl. pustules, maceration, dystrophic nails
- anywhere, favoring *extensor* aspects, umbilicus, genitals and post-auricular sulcus
- *Auspitz sign:* pinpoint bleeding that occurs when adherent scale is removed from the skin
- *Koebnerization:* development of new plaques over an area of trauma

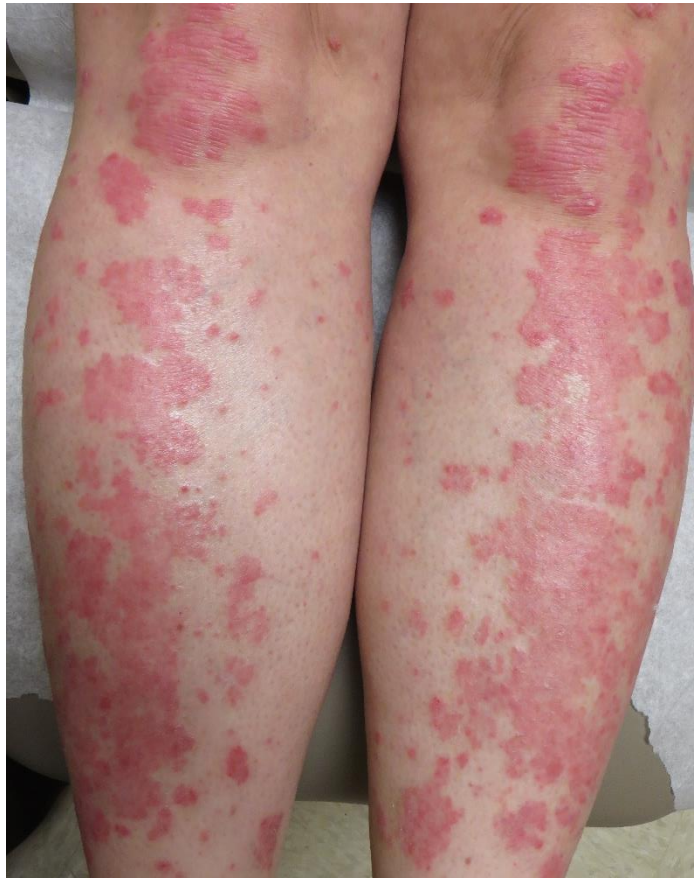
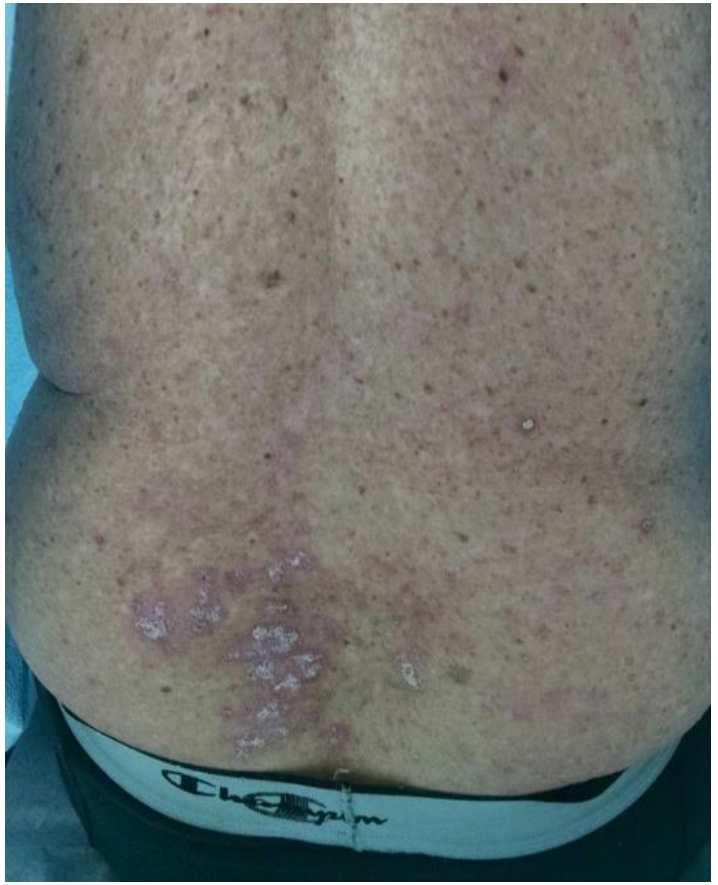


Photo Courtesy V.Lazareth,NP

Psoriasis in SOC

- inflammation: redness on lighter skin but more violaceous, dark brown, reddish-brown gray or just darker than the pt's normal skin color in SOC
- less erythema but thicker plaques, more scale, hyperpigmentation, induration than in lighter skin
- plaques in Latinos may be salmon-colored with silvery or white scales
- Asian pts tend to have the largest BSA affected
- scalp PS is common in SOC pts, especially Asians

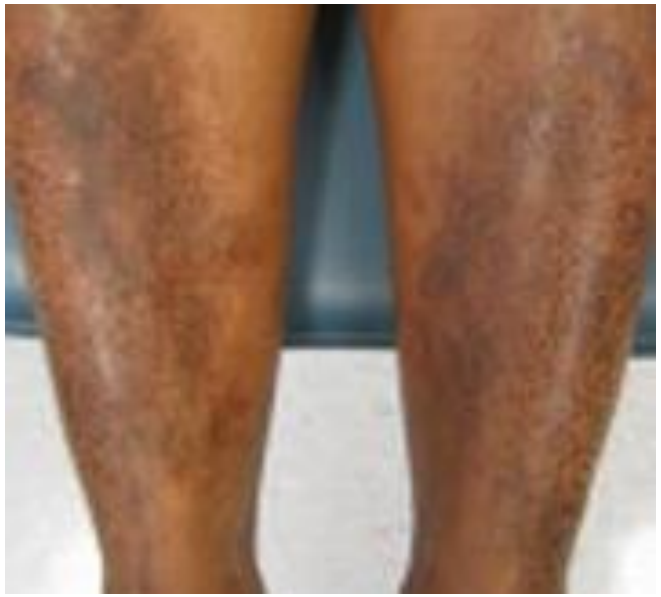


McKinley-Grant L. Recognizing psoriasis in skin of color. *The Dermatologist.* Sept 2020: 24-29.

Photo Courtesy V.Lazareth,NP

Psoriasis in SOC

- under-diagnosed as it is more difficult to identify in darker skin
- Ddx: eczema, lichen planus, sarcoidosis, cutaneous T cell lymphoma, discoid lupus
- disproportionately higher risk: comorbidities (diabetes, heart disease, stroke, fatty liver disease)
- inadequate health insurance
- less access to dermatology providers



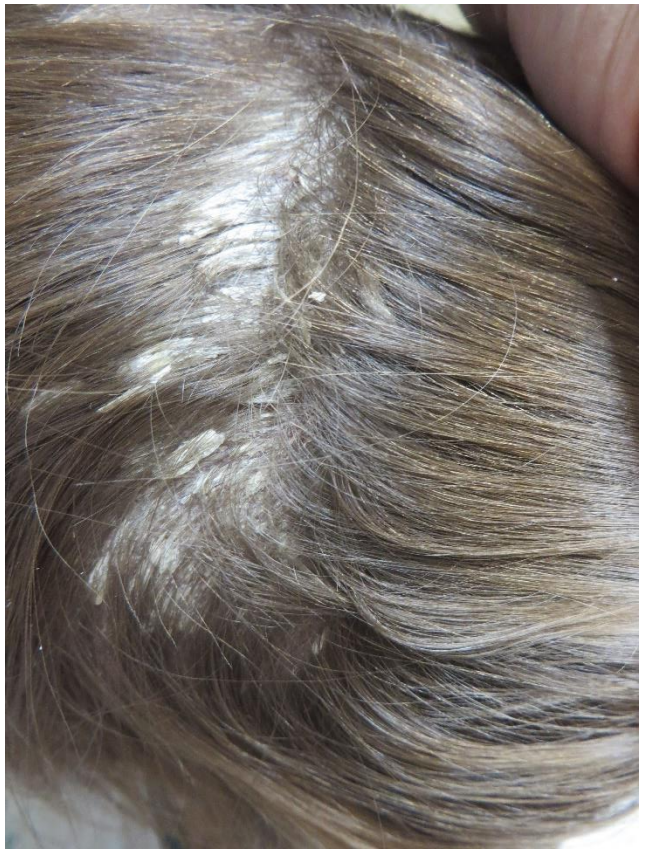
https://www.psoriasis.org/advance/psoriasis-misdiagnosed-in-skin-of-color/

https://www.mdedge.com/dermatology/article/259775/diversity-medicine/consider-gaps-access-and-knowledge-diagnosis-and/page/0/1?channel=171%3Fecd%3DWNL_DERM_221209_mdedge

Photo Courtesy V.Lazareth,NP

Scalp Psoriasis

- wide variation of presentation and usually complaints of severe itching
- scale can be mild to thick, plaques that cover some or all of the scalp
- posterior sulcus of the ears can be symptomatic



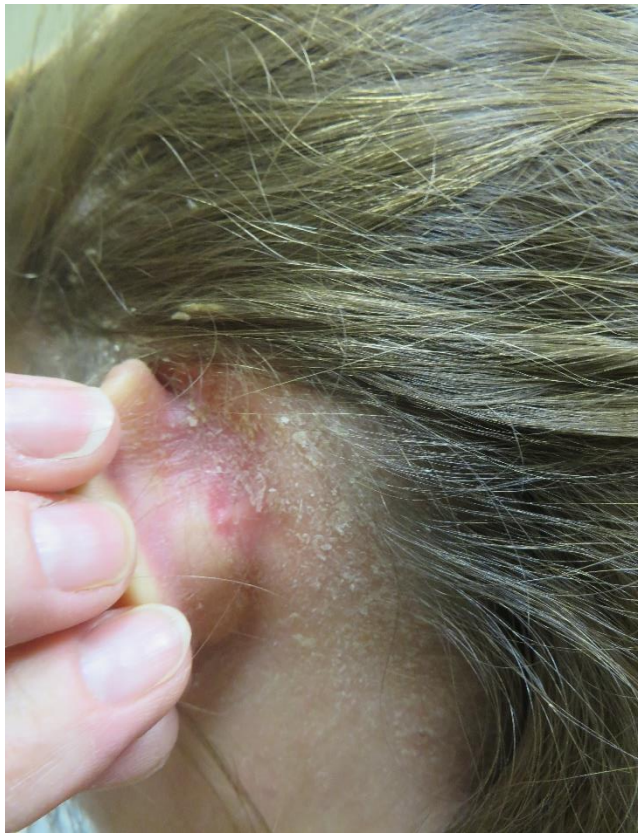
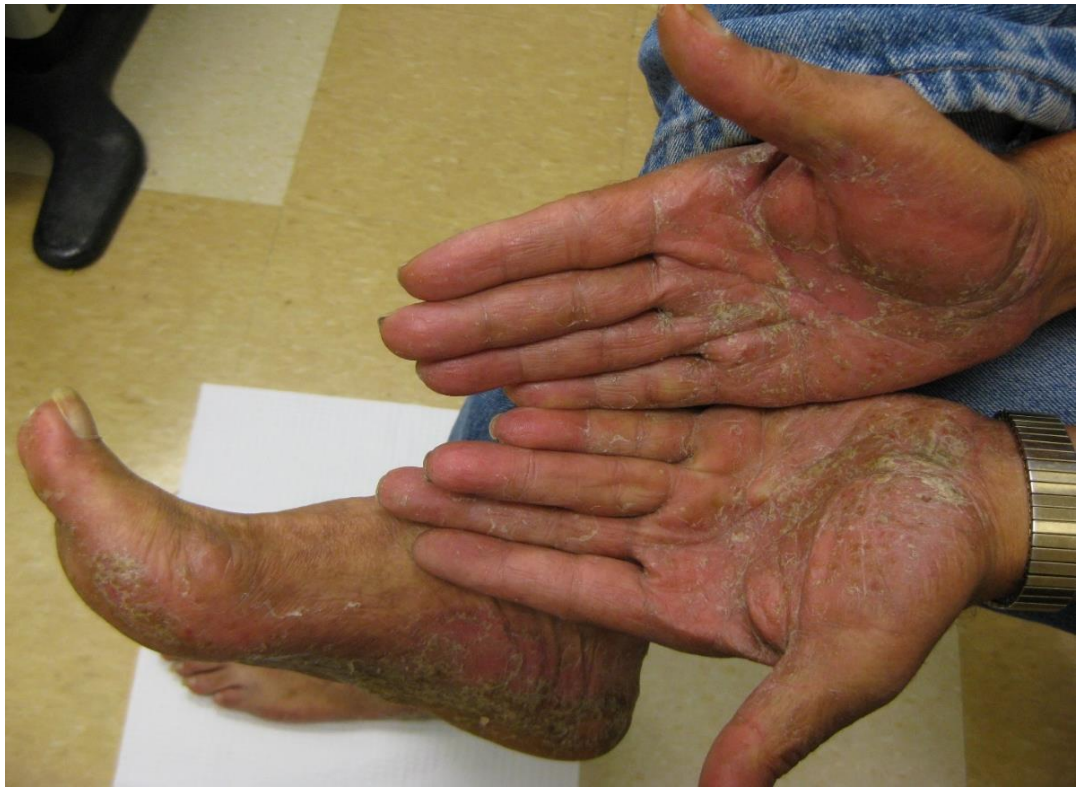


Photo Courtesy V.Lazareth,NP

Palmoplantar Psoriasis



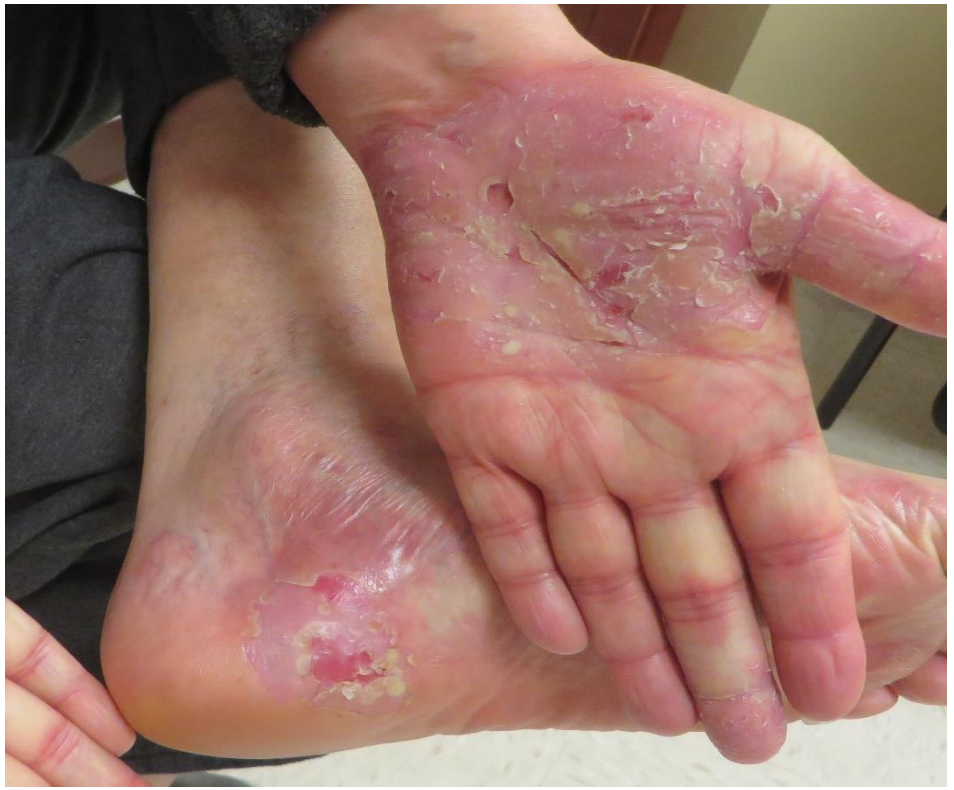


Photo Courtesy V.Lazareth,NP

Inverse Psoriasis

- Intertriginous areas of the skin including inguinal, inframammary, axillary or abdominal folds
- not scaly, usually smooth, erythematous plaques that are often macerated

Genital Psoriasis

- Involves the genitals including labia, vulva, penis, scrotum, and perianal area
- may not include intertriginous areas

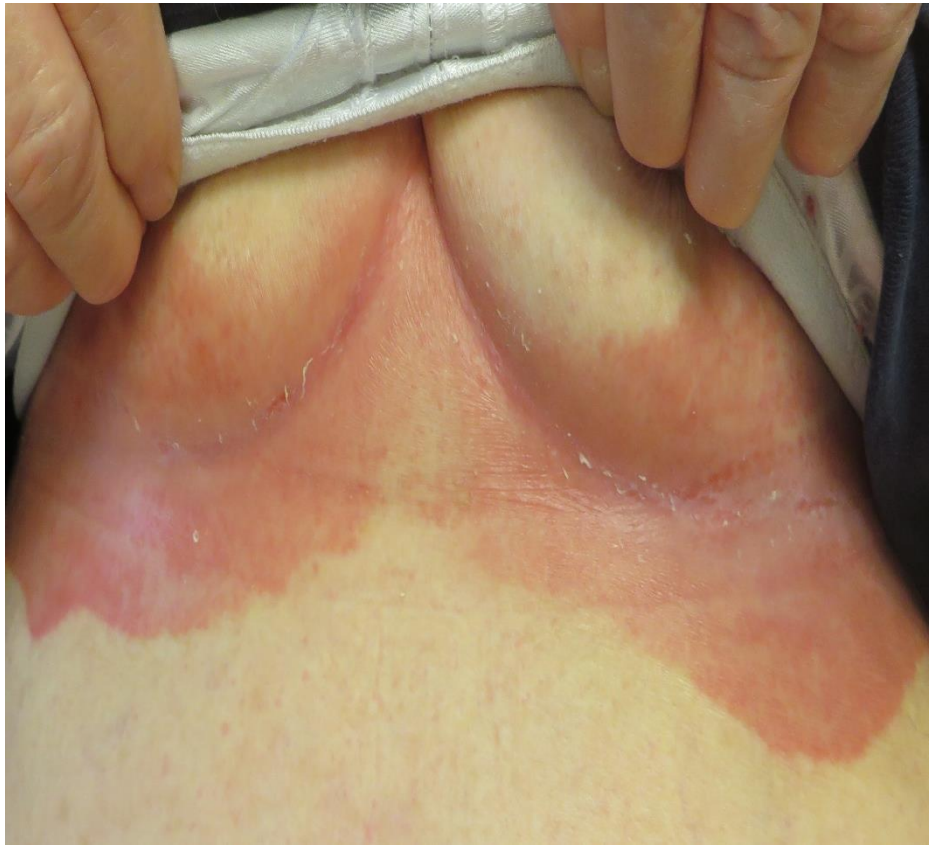


Photo Courtesy V.Lazareth,NP

Guttate Psoriasis

- small or “rain-drop” like scaly papules/plaques
- can be triggered many pathogens, most often tonsillar infections with *S. pyogenes*
- psoriasis can resolve after tx of infection
- usually, children and young adults

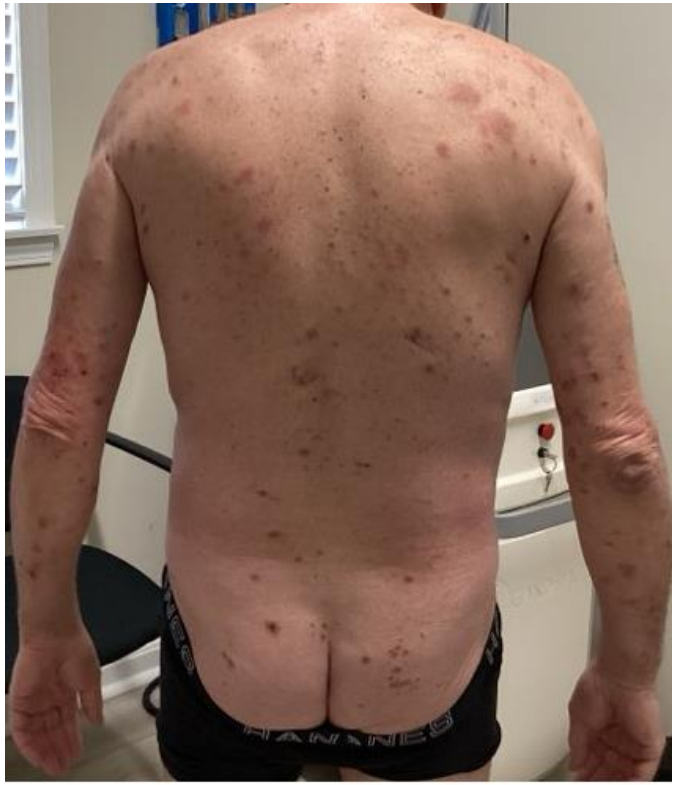


Photo Courtesy V.Lazareth,NP

Erythrodermic Psoriasis

- may be considered a dermatologic emergency
- rare and severe subset of psoriasis
- gradual or explosive
- erythema affecting >75% BSA
- fever, chills, headache, and general discomfort
- possible dehydration, fatigue, staphylococcal infection, insomnia, electrolyte abnormalities
- frequent cause is the sudden withdrawal of psoriasis treatment, often requires multidisciplinary supportive measures

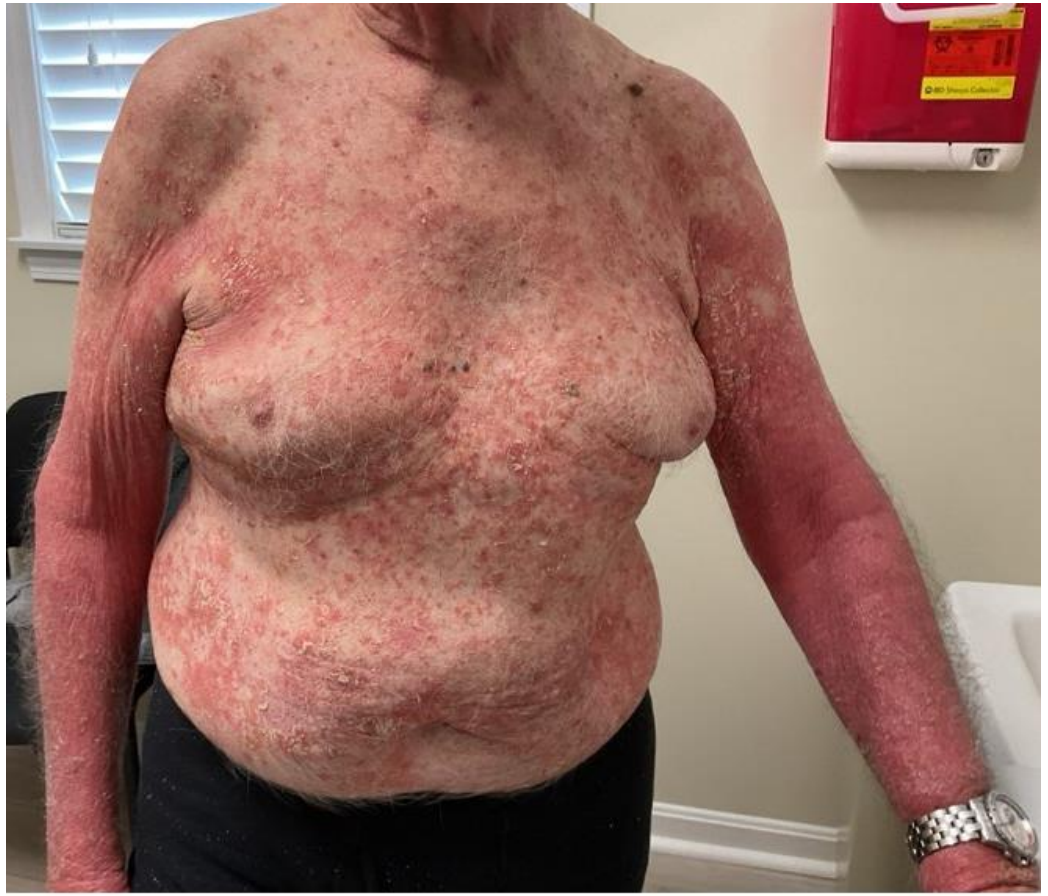


Photo Courtesy V.Lazareth,NP

Pustular Psoriasis

- rare variant of psoriasis
- tender yellowish pustules on an erythematous base
- widespread or localized sterile neutrophilic infiltrate
- Subtypes of pustular psoriasis include:
  - Generalized: von Zumbusch subtype

    Diffuse generalized pustular eruption with systemic symptoms (fevers, arthralgias, etc.)
  - Localized: Acrodermatitis continua of Hallopeau:

    fingers, toes, nail beds.
  - other: Annular, Exanthematic, Impetigo herpetiformis, Palmoplantar

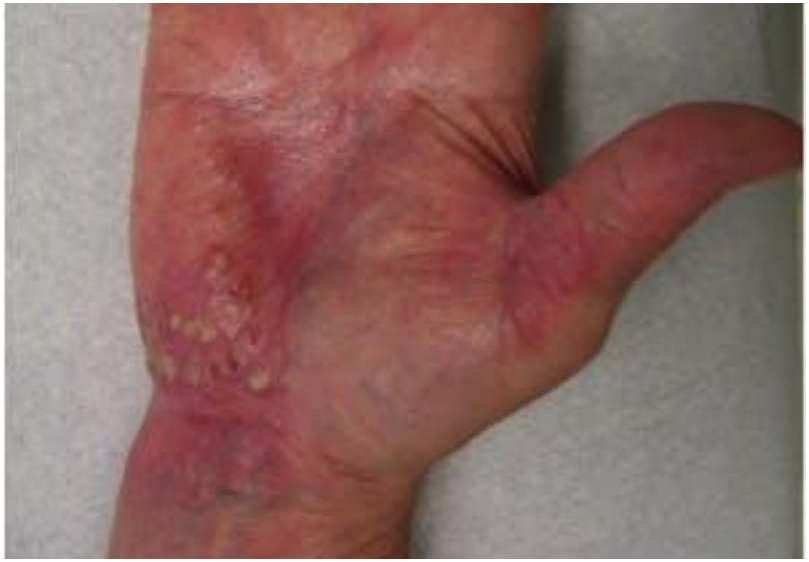


Photo Courtesy V.Lazareth,NP

Nail Psoriasis

- Nail pitting and oil spots
- Dystrophic nails crumbling, separation of nail plate (onycholysis), yellowing, and/or thickening
- Often misdiagnosed as fungal nail infection (but can occur concomitantly)

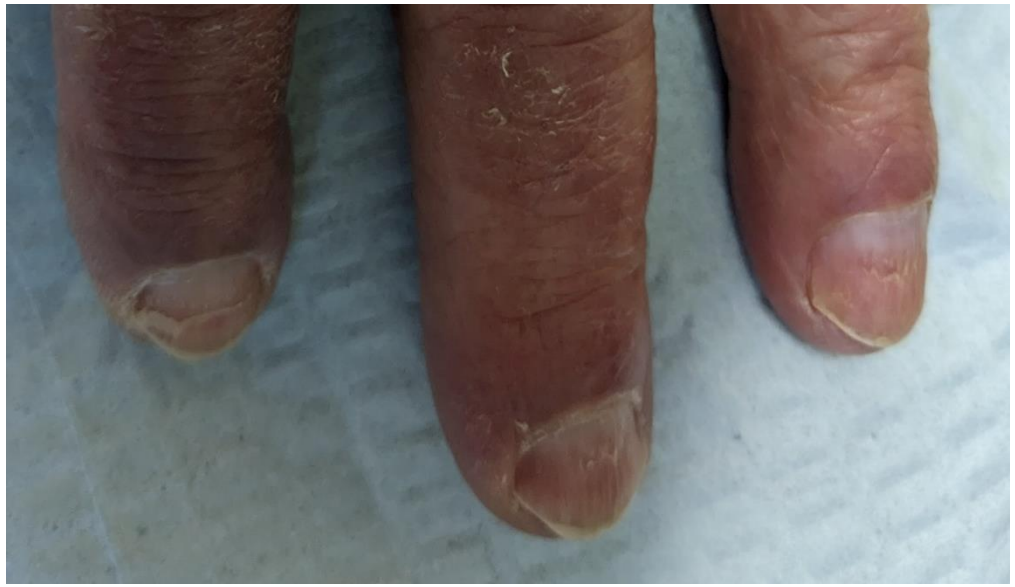


Photo Courtesy V.Lazareth,NP

Psoriatic Arthritis (PsA)

- inflammatory arthritis in 30% of psoriasis pts
- higher risk in pts with nail, scalp, inverse PS
- 15% develop PsA before skin disease
- tender, painful, swollen joints
- possible erythema, effusion, and warmth
- Dactylitis: inflammation and swelling of entire digit resembling a "sausage"
- Enthesitis: tender inflammation at tendinous insertion into bone; Achilles tendon

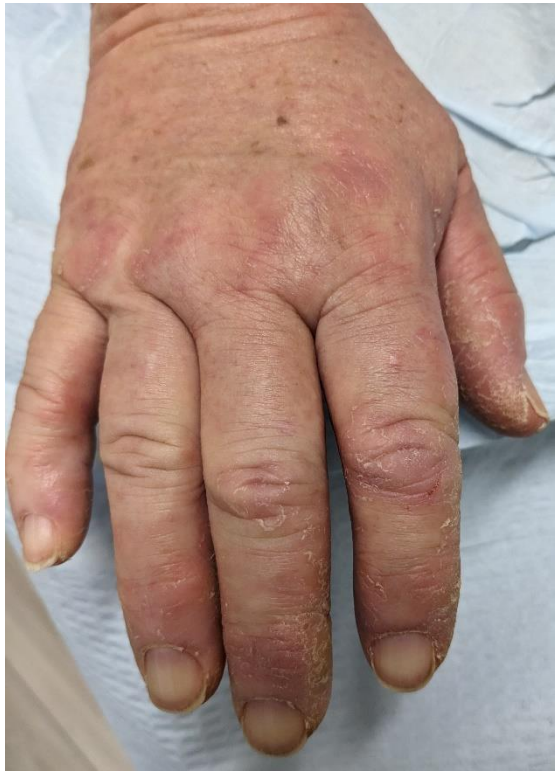


Photo Courtesy V.Lazareth,NP

Psoriasis: therapeutic approach

- Clinicians should consider:
  - ✓BSA
  - ✓Areas of involvement
  - ✓Quality of life
  - ✓Presence/severity of PsA
- Individualized treatment
- Behavior health/modifications

Shared-Decision Making

- Goals for disease
- Comorbidities
- Preferences (rapidity of onset, dosing frequency, route of administration, convenience)
- Cost
- Requirements for labs & monitoring

Photo Courtesy V.Lazareth,NP

Psoriasis: therapeutic approach

Therapeutic approach based on severity of disease and pt preference

- Topical therapies (limited by adherence)
  - mild and localized skin disease & NO signs of PsA
  - may use monotherapy or combination agents
  - may be used as *adjunctive tx* in moderate to severe disease
- Phototherapy
  - consider NB-UVB or Excimer laser
  - not suitable for infants/younger children
- Systemic Agents
  - moderate or severe skin disease
  - PsA

Photo Courtesy V.Lazareth,NP

Psoriasis: disease severity

- to determine the extent of psoriasis
- use the size of the *pt's* palm
    - Mild <5% BSA
    - Moderate 5-10%
    - Severe >10%

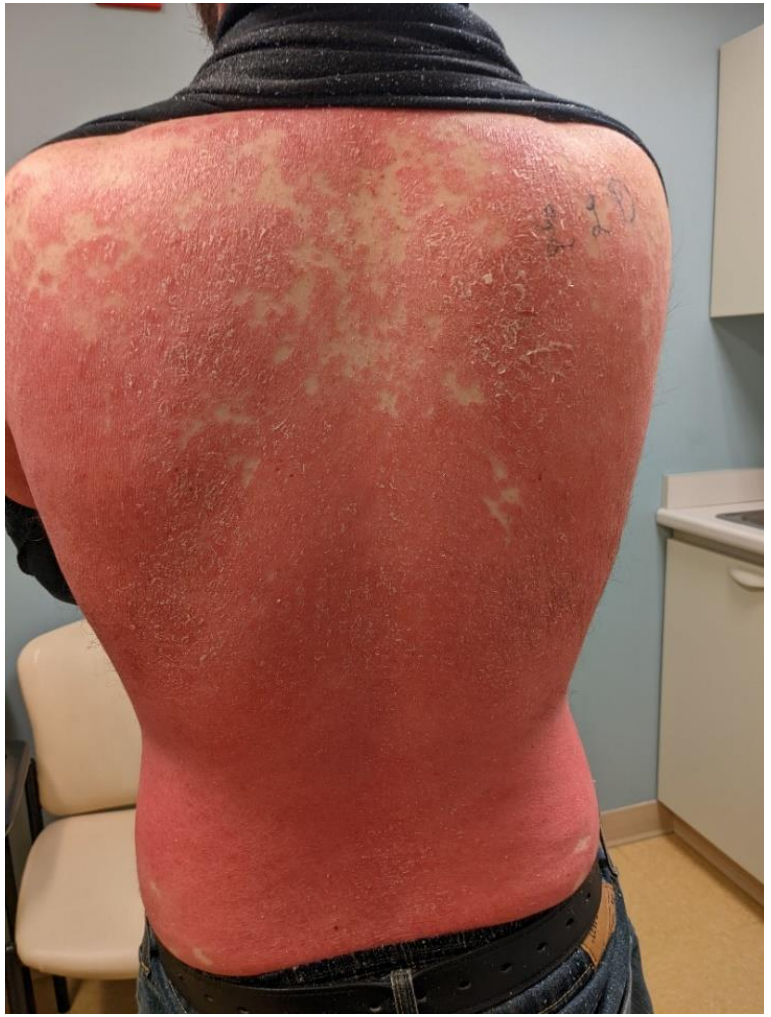


Photo Courtesy V.Lazareth,NP

Psoriasis: disease severity

- BSA alone does not always reflect the severity of disease
- certain sites can also reflect severe disease due to pain or disability i.e.,
  - palms
  - soles
  - genitalia
  - nails

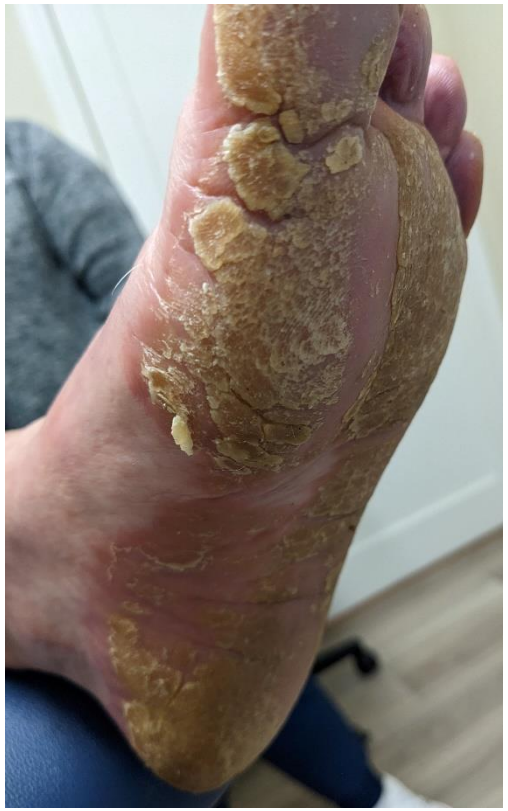


Photo Courtesy V.Lazareth,NP

OTC TOPICAL ADJUNCTIVE THERAPIES

Emollients	Helps to hydrate or seal moisture into the skin and should be used right after showering or bathing. Softens scale and reduces irritation. Thick ointments and creams are preferred.
Anti-itch topicals	Many use camphor, diphenhydramine hydrochloride, menthol, benzocaine which provide some relief from itch but may cause irritation and dryness.
Pyrithione	Pyrithione zinc preparation acts an antimicrobial that reduces yeast, anti-inflammatory, and dandruff. Available as a shampoo used 2-3 times a week or topical bar or spray for scalp irritation.
Salicylic acid	Keratolytic soften and exfoliate the outer skin layer. It can be found in shampoos, lotions, creams and gels. Shampoos: apply to scalp, wait 5-10 mins then rinse. Apply creams/lotions daily to plaques. It may cause irritation. Sal acid is systemically absorbed so strong preparations or large amounts may cause nausea. Can weaken hair shaft and contribute to hair loss as well as cause thinning of healthy skin. SA can thin thick plaques and removes scale in psoriasis and seb dermatitis. Enhances penetration of other topicals. Caution, salicylic acid inactivates vitamin D3 analogs, so should not be used together.
Coal tar	Unknown MOA but slows proliferation and decreases inflammation. Message into scalp and leave on for 5-10 minutes, then rinse. Can cause irritation and stain clothing, bathtubs or skin. Often used as adjunctive therapy. Helpful for pruritus especially of the scalp. Irritation and photosensitivity for up 24 hours after application.

Photo Courtesy V.Lazareth,NP

Psoriasis: mild disease Rx

Topical Corticosteroids (TCS): 1st line

- MOA: vasoconstriction; suppress release of pro-inflammatory cytokines; slow proliferation of keratinocytes; reduce inflammation
- apply thin film directly to lesions once or twice daily for 2 to 4 weeks
- limit / avoid mid-higher potency TCS in pregnancy and on thin skin (neck, face, folds)
- adverse/side effects:
  - hypothalamic-pituitary-adrenal axis suppression; adrenal insufficiency
  - children higher BSA-to-weight ratio → higher degree of absorption; growth delay
  - striae
  - cataracts and glaucoma
  - osteoporosis

Stein Gold LF. *Semin Cutan Med Surg*. 2016;35(2 Suppl 2):S36-S44. Koyama G, et al. *Int J Pharm Compd*. 2015;19(5):357-365.

Mild to Moderate Disease Rx

Vitamin D^3 analogues

Calcitriol - natural, *causes irritation* esp. to face and genitals

- Can lower Vitamin D levels (especially in children) and possible elevation of serum calcium level

Calcipotriene - synthetic and does *not* cause irritation

- Safe for use on face and intertriginous areas. may cause itching
- Apply thin layer QD - BID for up to 8 weeks

Calcipotriene & betamethasone - combination therapy

- Combination therapy applied QD
- More efficacious, less irritation, more expensive

Vitamin A analogue

Tazarotene gel - FDA approved indication. Pregnancy category X

- Decreases the rapid cell proliferation. SEs including irritation
- optimal efficacy when used as combination rather than monotherapy

Anthralin

- Helps to reduce rapid cell proliferation, skin irritation, can stain skin and clothing

Photo Courtesy V.Lazareth,NP

Psoriasis: treatment goals

Psoriasis

- (skin) reduce itch, pain, bleeding
- (psychosocial) reduce depression, social withdrawal, substance abuse
- (general health) reduce systemic inflammation -obesity, CHD, DM, HTN, HLD

Psoriatic Arthritis

- (joints) reduce pain, limit arthritic progression and deformity
  - 60% Asymmetric oligoarticular PsA: stiffness, swelling, erosion (knees, elbows, ankles)
  - 32% Spondylitis PsA: pain and stiffness of the vertebrae
  - Enthesitis: swelling and tenderness in the Achilles Tendon
  - Dactylitis: diffuse swelling of a finger or toe

Feldman SR, Zhao Y, Shi L, Tran MH. Economic and comorbidity burden among patients with moderate-to-severe psoriasis. *J Manag Care Spec Pharm.* 2015;21(10):874-888.

BF Mandell, JM Sobell. The Role of TNF Inhibitors in Psoriatic Disease. Seminars in Cutaneous Medicine and Surgery, Vol. 33, No. 4S, June 2014. https://www.healthline.com/health/psoriatic-arthritis/asymmetric-oligoarticular-psoriatic-arthritis#types-of-ps-a

Photo Courtesy V.Lazareth,NP

Psoriasis: phototherapy

- controlled doses of UVB light from an artificial light source can treat single patches or widespread psoriasis
- NB-UVB decreases the production of inflammatory cytokines and T-cells in the Th1 pathway reducing keratinocyte proliferation
- NB-UVB is a 1st line treatment for stable, moderate-to-severe plaque PS affecting >10% BSA in children and adults
- also used as adjuvant therapy

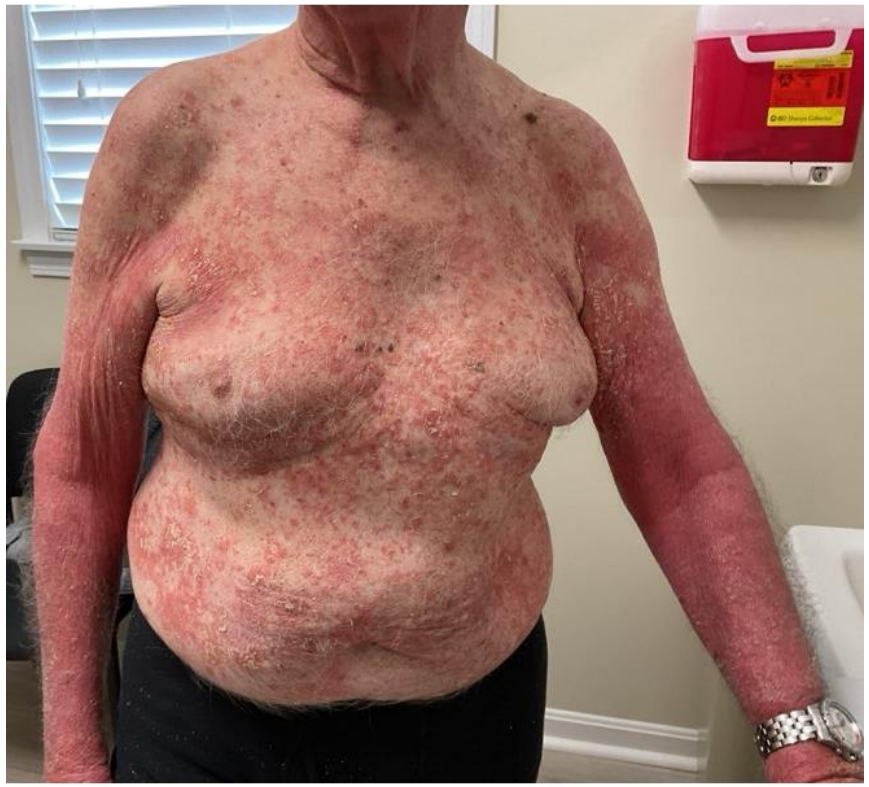


Photo Courtesy V.Lazareth,NP

Psoriasis: immunosuppressants

methotrexate tabs (variable dosing)

- I: chemotherapy (breast, lung), immunosuppressant (autoimmune)
- CI: women of childbearing potential, concomitant alcohol, NSAIDs, AIDS, blood-bone marrow disorders, immunodeficiency, liver disease, decreased renal function
- AEs: teratogenic, liver-renal toxicity, lymphoma, cirrhosis, rash, fatigue, confusion, fever, chills, SOB, cough, palpitations, bruising, MTX pneumonitis, NMSC

cyclosporin tabs

- I: to quell psoriatic flare but must not be used for >6 mo
- CI: pregnancy, HTN
- AEs: HTN, renal dysfunction, headache, hyperlipidemia. infections, nausea, diarrhea, paresthesia, tremor, hypertricosis, gingeval hyperplasia, hyperkalemia, hypomagnesemia, hyper-uricemia -lipidemia. myalgias, dyspnea, bronchospasm

Photo Courtesy V.Lazareth,NP

Psoriasis: oral systemic agents

- apremilast phosphodiesterase-4 (PDE-4) inhibitor; reduces cytokine activation and inflammation: 33% clearer skin, 46% reduction in itch
- I: plaque, scalp, palmoplantar PS and PsA ≥6 years old
- CI: pregnancy, lactation. depression, Crohn's, IBD
- AE: diarrhea, nausea, URI, HA, wt loss, mood changes, depression, suicidal ideation

- deucravacitinib TYK2 inhibitor; blocks IL-23: 55% clear/ almost clear
- once-daily 6 mg oral treatment for moderate-severe PsO
- CI: pregnancy, lactation, concomitant immunosuppressants
- AEs: nasopharyngitis, URI, headache, diarrhea, nausea, HSV-HZV reactivation
- Monitoring: vaccines. Q Gold, Hepatitis B+C, Lipids. Routine annual labs

Psoriasis: TNF-*a* Inhibitors

etanercept

PsO >4 yr, PsA. safe and effective for children and elders

adalimumab

PsO, PsA (adults), HS >12 yr. CI: infection, demyelinating disease, live vaccines

certolizumab

- PsO, PsA. Pregnancy: negligible placental transfer

TNF-*a* inhibitors

- increased risk of serious infections (TB). Lymphoma has been reported in children and adolescents. BCC, SCC and hepatitis B reactivation

1. https://www.enbrelpro.com/clinical-data/efficacy-plaque-psoriasis 2. https://www.ucb.com/stories-media/Press-Releases/article/Final-CIMZIA-certolizumab-pegol-Phase-3-Trial-Meets-Primary-Efficacy-Endpoint-in-Patients-with-Moderate-to-Severe-Chronic-Plaque-Psoriasis#:~:text=CIMZIA%20demonstrated%20statistically%20significant%20improvements%20in%20the%20primary%20endpoint.,every%20two%20weeks%20and%2061.3.

Psoriasis: IL-12/23

ustekinumab IL-12/23 inhibitor

- I: PsO >6 yr, PsA >6 yr. wt-based dosing SC q 12 wks
- CI: active infection, live vaccines, concomitant methotrexate - prednisone
- AEs: nasopharyngitis, URI, HA, fatigue, itch, nausea, vomiting, diarrhea, injection site reactions, vaginal yeast infections, arthralgias
- rare: rapid onset of SCCs, reversible posterior leukoencephalopathy syndrome
- Monitoring: baseline: TB, HIV, Hep B, Hep C, CBC, CMP, LFT
  q 6-12 mo: CBC, CMP, LFT. annual: TB
- Efficacy: 61% (45 mg) - 72% (90 mg) maintained PASI-75 after 5 yrs

Photo Courtesy V.Lazareth,NP

Psoriasis: IL-17

ixekizumab IL-17 Inhibitor

- I: PsO >6 yr, PsO (plaque, nail, inverse, genital) & PsA adults

secukinumab IL-17 Inhibitor

- I: PsO >6 yrs, PsO (scalp, nails, palms-soles, pustular) & H.S. -adults, PsA >2 yrs

bimekizumab IL-17A + IL-17F inhibitor

- I: PsO -adults, high efficacy for PsA -adults

Recent Studies

- ixekizumab and secukinumab (IL-17 blockers)
  - equal to adalimumab (TNF-a blocker) to inhibit radiographic joint progression
- ixekizumab and secukinumab (IL-17 blockers)
  - work better in the skin than TNF-a blockers
- bimekizumab (IL-17A + IL-17F blocker)
  - beat secukinumab (IL-17A blocker) in psoriasis clearing
  - beat adalimumab (TNF-a blocker) in inhibiting radiographic progression PsA

https://thedermdigest.com/new-treatments-for-psoriasis-2/

Photo Courtesy V Lazareth MD

Psoriasis: IL-23

tildrakizumab (Ilumya)

- I: PS (not PsA). Dose: 100 mg SC wks 0 & 4 then q 12 wks

guselkumab (Tremfya)

- I: PsO, PsA. Dose: 100 mg wk 0 & 4, then q 8 wks

risankizumab (Skyrizi®) IL-23 inhibitor

- I: PsO, PsA, Nail psoriasis, Pustular psoriasis, Erythroderma
- Dose: 150 mg SC wk 0 & wk 4, then q 12 wks
- 64% achieved PASI-100 at 5 yr / 87% achieved PASI-90 at 5 yr

https://www.hmpgloballearningnetwork.com/site/thederm/advances/tildrakizumab-presented-consistent-reduction-detectable-psoriasis-through-5?hmpid=dmljdG9yaWEubGF6YXJldGg4M0BnbWFpbC5jb20=&utm_medium=email&utm_source=enewsletter&utm_content=1596823478

https://www.skyrizihcp.com/dermatology/psoriasis-efficacy

Photo Courtesy V.Lazareth,NP

Contact Dermatitis

Photo Courtesy V.Lazareth,NP

Irritant Contact Dermatitis

- Immediate reaction caused by direct physical or chemical injury to the epidermis
- damaged barrier keratinocytes → activation of inflammatory cytokines
- innate immunity; not immune mediated!
- the inflammation manifests as erythema, edema, and scaling
- initial burning or stinging progresses to pruritus

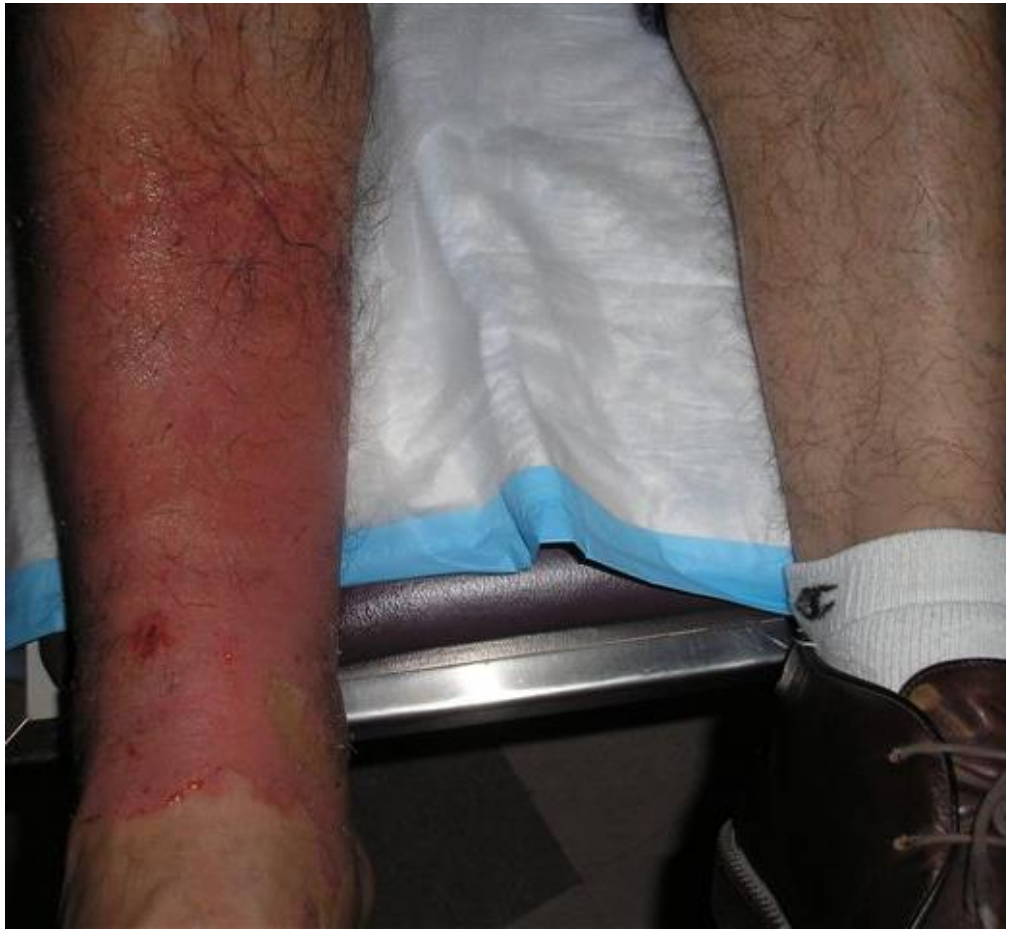


Photo Courtesy V.Lazareth,NP

Irritant Contact Dermatitis

- Acute: patches and plaques with a sharp geometric border corresponding to the areas of chemical exposure
- Severe: vesicles, bullae, and erosions
- Fingertip ICD: desquamation, fissures, and scaling
- Chronic: secondary lichenification of the skin due to repetitive rubbing

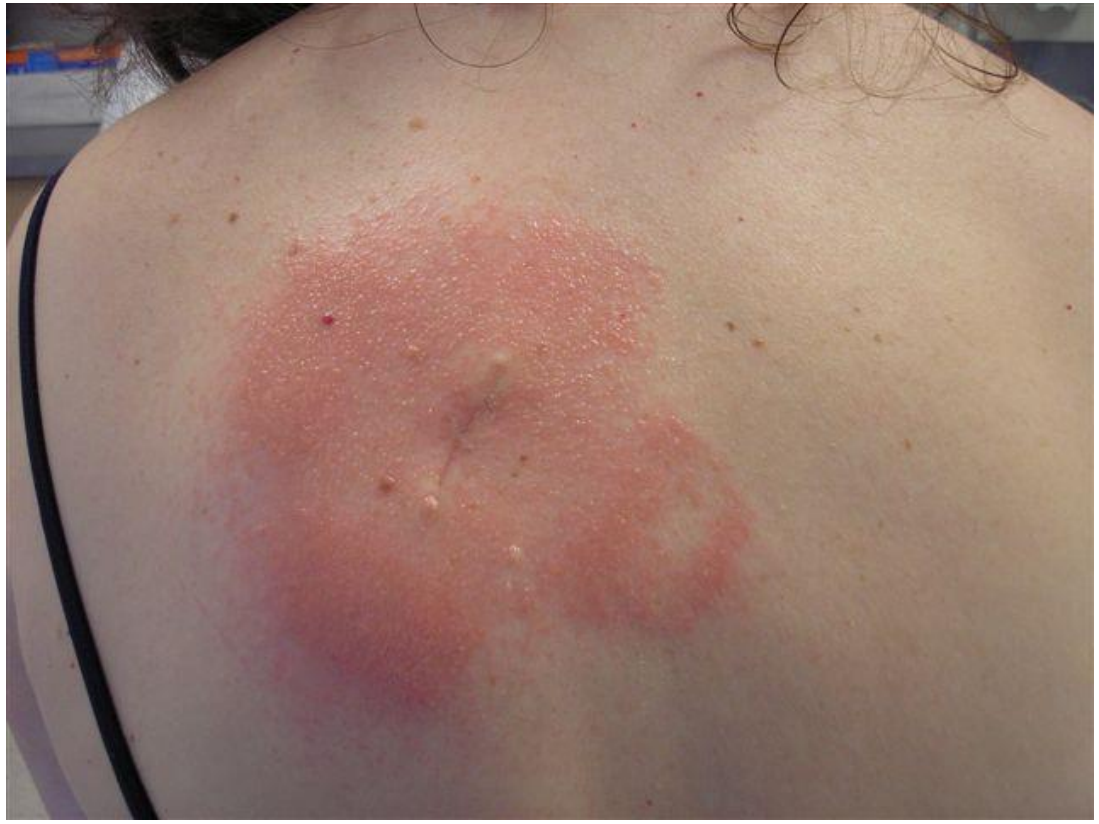


Photo Courtesy V.Lazareth,NP

Irritant Contact Dermatitis

- most common on the hands
- 80% of occupational contact dermatitis cases are localized to area of exposure
- other common locations: genitals and eyelids due to very thin skin and the unwitting transmission of irritant substances by the hands
- atopic dermatitis pts are predisposed to ICD
- environmental factors: repeated exposure to water, frequent hand washing, soaps, solvents, fiberglass, mild acids, alkalis, dry air
- high-risk jobs: cleaning, health care, food preparation, hairdressing. any age. F>M

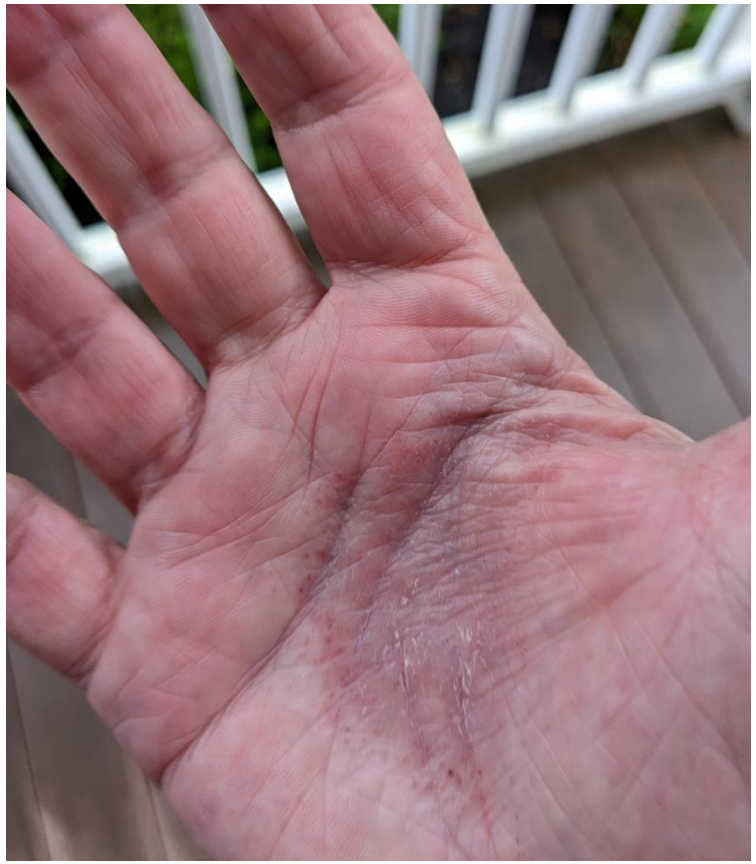


Photo Courtesy V.Lazareth,NP

ICD: approach

- clinical diagnosis and a diagnosis of exclusion
- no laboratory studies exist to confirm the definitive diagnosis
- detailed hx: occupational, recreational, home exposures (diary)
- if scaling present, consider a KOH prep to rule out a dermatophyte infection
- Patch testing to r/o true allergic contact dermatitis
- Risk factors for poor medical and economic prognosis
  - chronic dermatitis
  - hx of AD, asthma
  - inability to change occupations

Photo Courtesy V.Lazareth,NP

Allergic Contact Dermatitis

- delayed-type (type IV) hypersensitivity reaction that occurs when allergens activate antigen-specific T cells in a sensitized individual.
- Immune mediated!
- ACD allergens are small molecules that trigger memory T cells to mount an immune response, resulting in an eczematous rash on exposed skin
- requires repeat exposures before an allergic response is noted
- occurs 48-72 hours after exposure to the offending agent
- pruritus

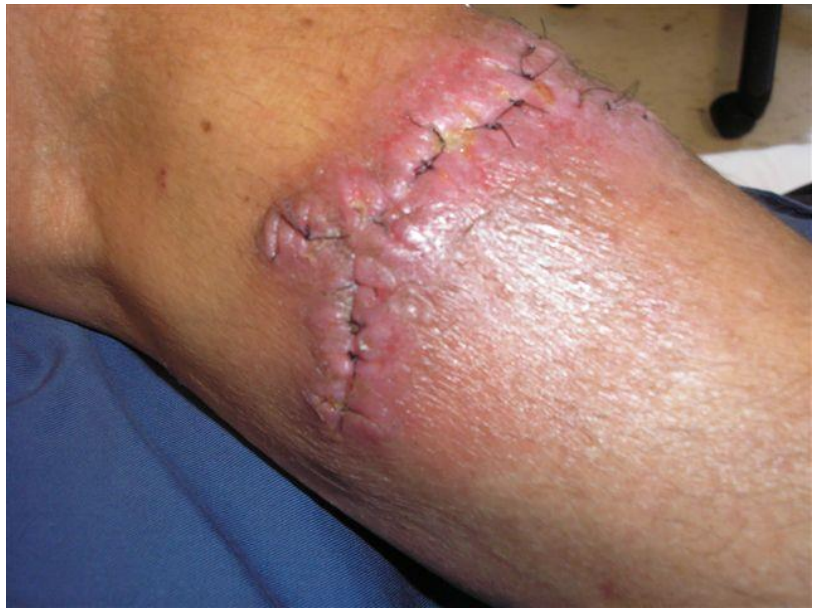


Photo Courtesy V.Lazareth,NP

Allergic Contact Dermatitis

- acute ACD: erythema, vesicles, bullae, oozing, crusting. Geometric shapes with well-demarcated borders
- subacute ACD: scaly plaques, round erosions, crusts
- chronic ACD: scaling, lichenification, fissures, cracks
- ACD can occur in reaction to topical agents, ingested agents, implanted biomedical devices, and airborne materials
- The distribution and geometry of lesions are important clues
- Airborne contact dermatitis: face (upper eyelids), the neck, the upper chest, the forearms, and the hands (palmar)
- Systemic: widespread lesions when ingested or implanted device

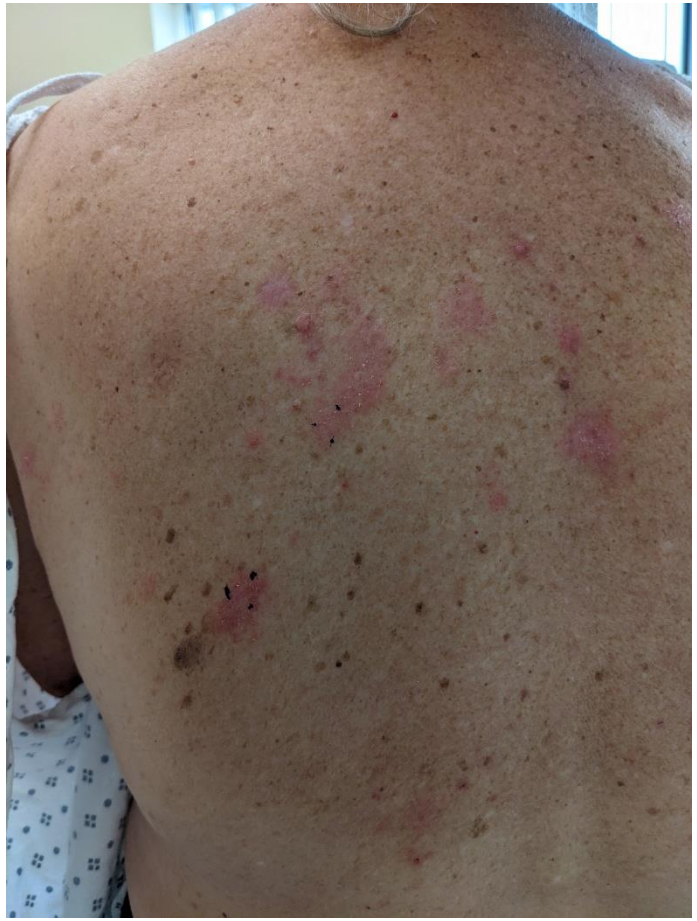


Photo Courtesy V.Lazareth,NP

Allergic Contact Dermatitis

the most common contact allergens

- urishiol (poison ivy, oak, sumac), nickel, fragrance, cobalt, chromates (leather products), neomycin, thimerosal (ophthalmic preparations and vaccines), adhesives, and oxybenzone (sunscreens). Formaldehyde preservatives in surgical masks

American Contact Dermatitis Society Allergens of the Year

- 2020: Isobornyl acrylate, an adhesive in medical devices (insulin pumps, acrylic nails)
- 2021: Acetophenone azine, foams used for cushioning (shin pads, footwear)
- 2022: Aluminum (vaccines, allergen-specific immunotherapies, antiperspirants)
- 2023: Lanolin (emollients, Aquaphor) children and older adults
- 2024: Sulfites (preservatives and antioxidants in food, drinks, pharmaceuticals, and personal care products)

Photo Courtesy V.Lazareth,NP

Allergic Contact Dermatitis

Agents frequently implicated

- Latex
- PPE
- Resins
- Acrylics
- Soaps/Cleansers
- Fragrances
- Preservatives
- Hair Care Chemicals
- Glues/Plastics/Rubbers

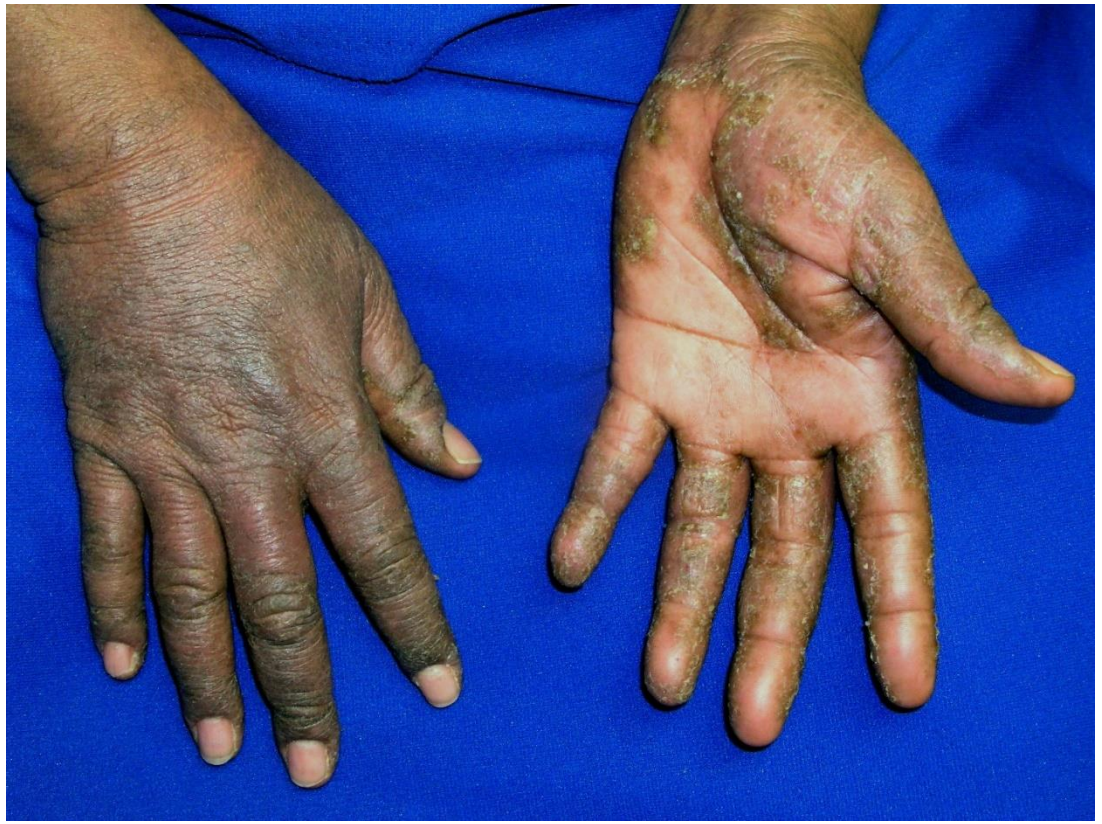


Photo courtesy of M. Zirwas MD

Allergic Contact Dermatitis

Major Risk Factors

- Age
- History of AD
- Occupation
  - health care workers
  - beauticians
  - construction workers
  - chemical industry
  - machinists

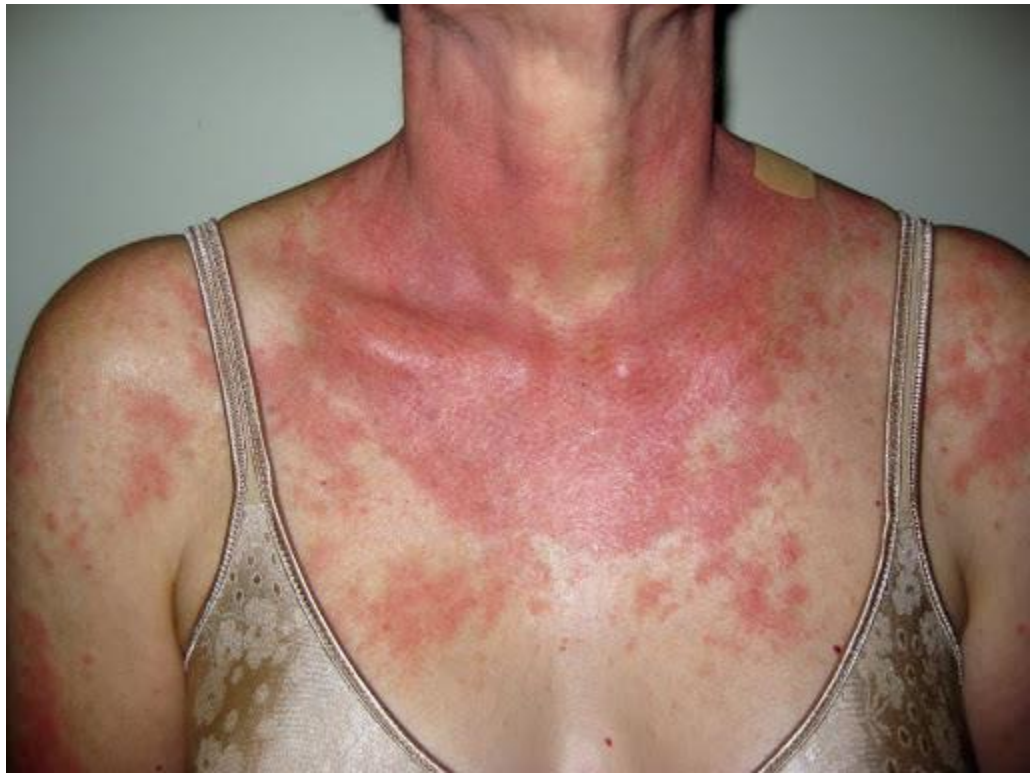


Photo courtesy of L.A.Pansch NP

Allergic Contact Dermatitis

Pt History

- Consider allergy to formaldehyde in permanent press resins if antecubital or popliteal fossae are involved.
- Consider allergy to adhesive, wound dressings, and/or antimicrobial treatments in patients with chronic wounds including stomas (mupirocin and Stomahesive paste)
- Consider allergy to implanted biomedical devices (pacemakers, orthopedic implants, and endovascular stents) which can present as a rash at a previous site or a symmetric intertriginous and flexural rash

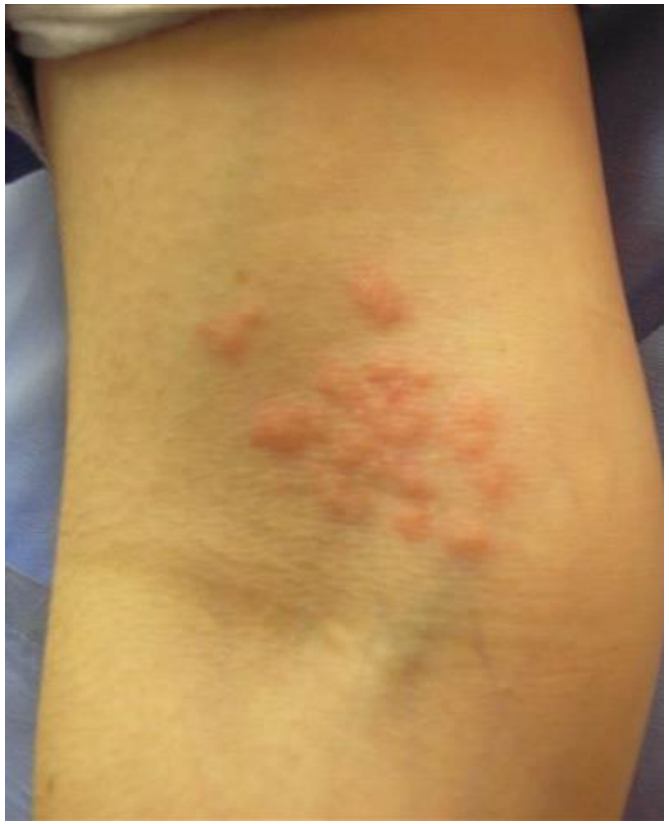


Photo Courtesy V.Lazareth,NP

Allergic Contact Dermatitis: Rx

- Patch testing can be performed using the TRUE test (Thin-layer Rapid Use Epicutaneous Test), which contains 36 antigens commonly implicated in ACD. However, some important antigens may be missed by the TRUE test so customized patch testing can also be considered.
- Treatment of ACD involves avoidance of potential offending agents
- Once offending agents are identified, databases that provide lists of "safe" products that are free of identified allergens, such as the American Contact Dermatitis Society's Contact Allergen Management Program (CAMP) and SkinSAFE can be provided to the pt
- short term topical steroids are the mainstay of therapy for ACD and have well-documented efficacy
- Phototherapy can be considered for patients who have refractory ACD unresponsive to topical or oral steroids and those who cannot avoid all potential culprit agents. Both oral psoralen photochemotherapy (PUVA) and shortwave ultraviolet light (UVB) have been utilized
- Topical tacrolimus and pimecrolimus have both been studied to treat ACD. ACD reactions to topical tacrolimus have been reported
- Antihistamines may be used for treatment of itch.

Photo Courtesy V.Lazareth,NP

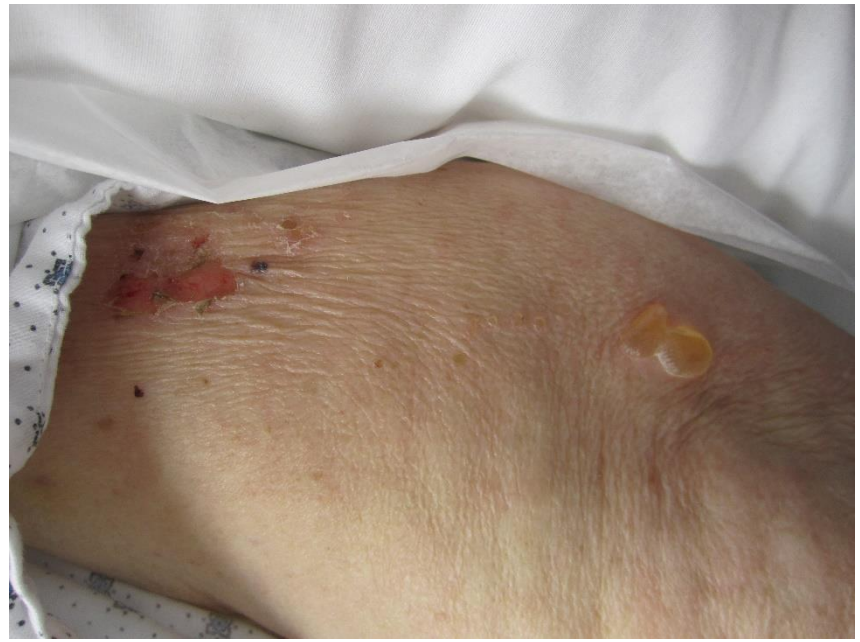
Cutaneous Manifestations of Systemic Disease

Photo Courtesy V.Lazareth,NP

Cutaneous Manifestations of Systemic Disease

Skin signs of Systemic Disease which can indicate an internal disorder

- are common
- can help to establish the correct systemic diagnosis
- can serve as the initial sign of a systemic disorder



➢*Bullous Pemphigoid*
may signal an internal malignancy

Photo Courtesy V.Lazareth,NP

Cardiovascular:
Stasis Dermatitis

- affects the lower extremities of pts with compromised vein function:
- obesity, venous hypertension from prolonged standing, CHF, DVT, hx of a leg fx, prior surgery in the LEs or pelvic area
- pruritus, aching, throbbing
- scaly papules and plaques. erosion, crust, weeping and chronic eczema features (lichenification, hyper- hypopigmentation)
- complications: ulceration, infection, woody induration from chronic ischemia

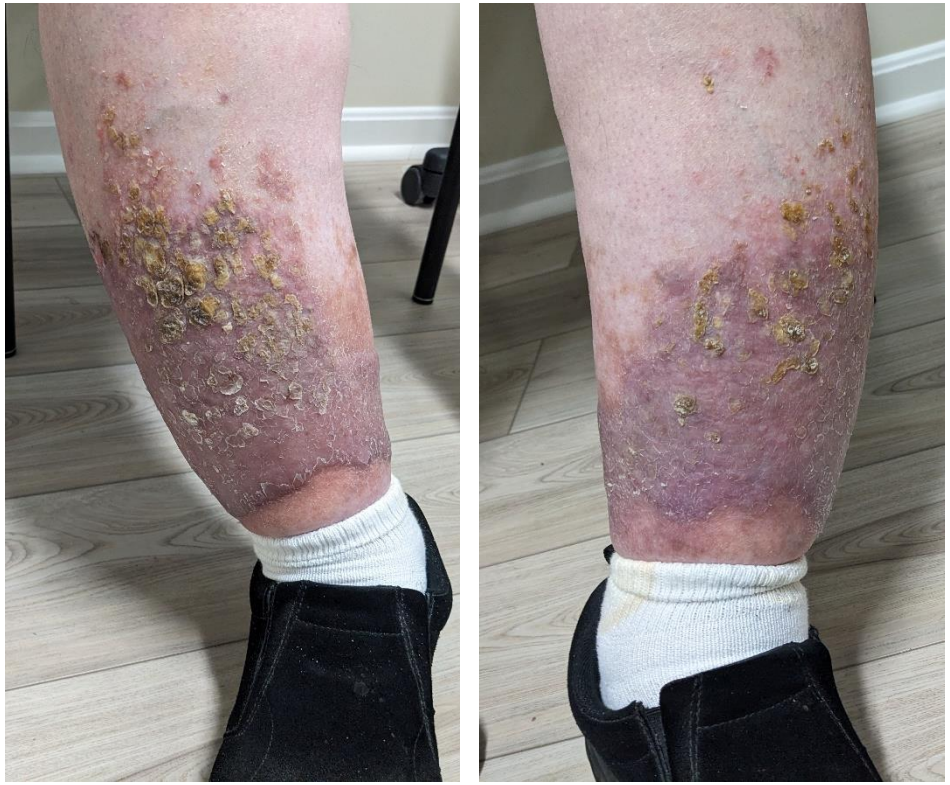


Photo Courtesy V.Lazareth,NP

Cardiovascular:
Kawasaki disease

- acute febrile multisystem disease in children <5 yrs
- most common cause of acquired heart disease in US children
- >5 d unexplained, high spiking fever + 4 of the following:
  - conjunctival injection
  - lip fissures
  - oropharyngeal hyperemia “strawberry tongue”
  - cervical lymphadenopathy
  - morbilliform exanthem
  - peripheral extremity erythema, edema, desquamation

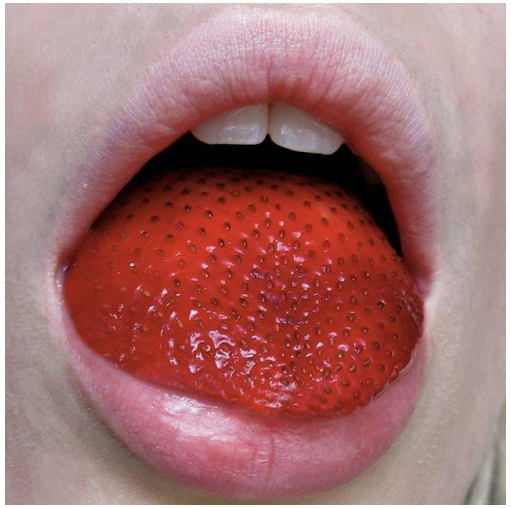
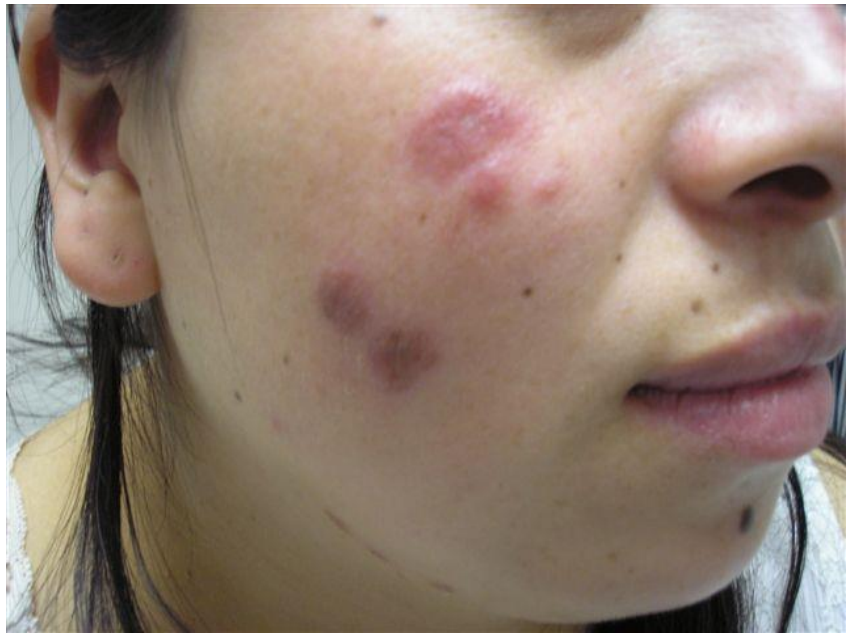


Photo Courtesy V.Lazareth,NP

Rheumatology:
Lupus Erythematosus

- “butterfly” facial eruption may indicate Systemic Lupus; multisystem disorder
- interaction between genetic and environmental factors (*UVR, medications, smoking, viruses*) trigger complex inflammatory cascade
- cytokine, chemokine, inflammatory cell responses from cells residing *within* the skin, as well as cells recruited *to* the skin
- risk factors: F 6 : M 1.
  African-American 4 : Caucasian 1



Discoid Lupus Erythematosus

Photo Courtesy V.Lazareth,NP

Rheumatology:
Subacute Cutaneous Lupus Erythematosus

- photosensitivity eruption
- sides of the face, upper trunk, extensor UEs
- *mid-facial skin usually spared*
- red annular plaques with central clearing
  or chronic psoriasiform or eczematous appearance

Rx

- sun protection, TCS, ILK, topical calcineurin inhibitors, topical retinoids
- hydroxychloroquine to decrease flares & risk of thromboembolic events

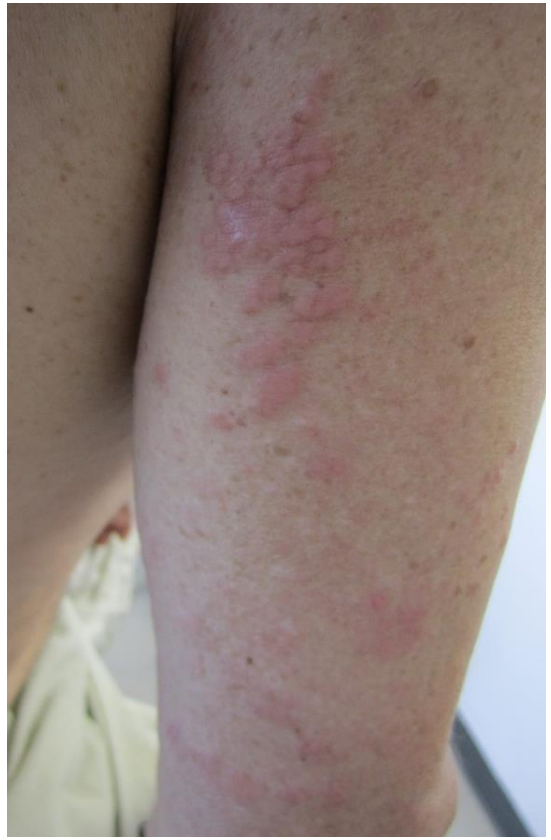


Photo Courtesy V.Lazareth,NP

Drug-Induced SCLE

Common

- Anti-epileptics (carbamazepine)
- Calcium channel blockers (diltiazem)
- PPIs (pantoprazole, omeprazole)
- Taxanes (docetaxel, paclitaxel)
- Terbinafine
- Thiazide diuretics (HCTZ)
- Thrombocyte inhibitors (ticlopidine)
- TNF-α inhibitors

Less common

- ACE inhibitors (enalapril, lisinopril)
- β-blockers
- Doxorubicin
- Interferon-α and -β
- Leflunomide
- Ranitidine
- Statins (HMG-CoA reductase inhibitors)

Photo Courtesy V.Lazareth,NP

Metabolic:
Graft-versus-Host-Disease (GvHD)

- high dose chemotherapy can destroy cancer cells but also stem cells in bone marrow that produce blood cells
- affected pts may receive stem cells or bone marrow from a donor ("donor or allogeneic txp") to resume production of blood cells
- in GvHD, the graft (donated T cells) identify the host (txp recipient) cells as foreign and attack them
- results in a multi-organ disorder with destruction of target tissues (skin, liver, GI tract) by cytotoxic T lymphocytes, natural killer cells, cytokines

Cromvik J, Varkey J, Herlenius G, et al. Graft-versus-host Disease After Intestinal or Multivisceral Transplantation: A Scandinavian Single-center Experience. *Transplant Proc.* 2016;48(1):185–190. Moody MN, Kazakevich N, Smith JR, et al. Sweat the small stuff: the importance of clinical-pathologic correlation in cutaneous GVHD following orthotopic liver transplant. *Arch Dermatol.* 2011;147(11):1345–1346. Jeanmonod P, Hubbuch M, Grünhage F, et al. Graft-versus-host disease or toxic epidermal necrolysis: diagnostic dilemma after liver transplantation. *Transpl Infect Dis.* 2012;14(4):422–426.

Photo Courtesy V.Lazareth,NP

Metabolic:
Graft-versus-Host-Disease (GvHD)

- also occurs following transfusion of non-irradiated blood products (to immunocompromised hosts, maternal–fetal transmission, SOTR)
- Acute GVHD (<100 days after transplantation)
  - acral – upper trunk morbilliform rash, diarrhea, transaminitis, hyperbilirubinemia
  - significant morbidity and mortality
- Chronic GVHD (>100 days after transplantation)
  - lichenoid or sclerodermoid appearance

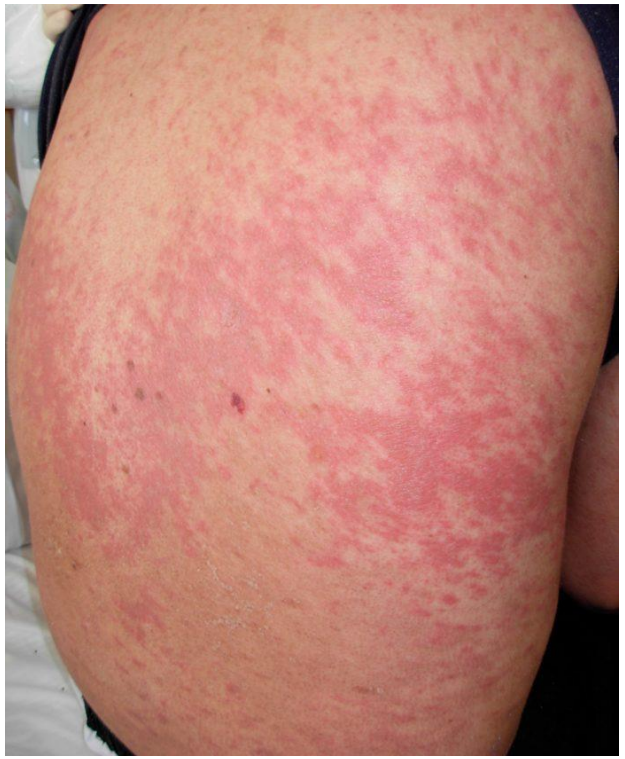


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Photo Courtesy V.Lazareth,NP

Endocrine:
Acanthosis Nigricans

- velvety hyperpigmentation of intertriginous sites
- large symmetrical area of hyperpigmentation evolves into hyperkeratotic plaques, acronchordons
- obesity, insulin resistance, diabetes: adults & children
- associated with malignancy with abrupt onset >40 yr
- tumors of GI tract, lung, kidney, bladder, ovaries, pancreas, mycosis fungiodes (cutaneous T-cell lymphoma)
- skin signs appear *before* the tumor in 20% of pts, *after* cancer diagnosis in 20%, *simultaneously* in 60%

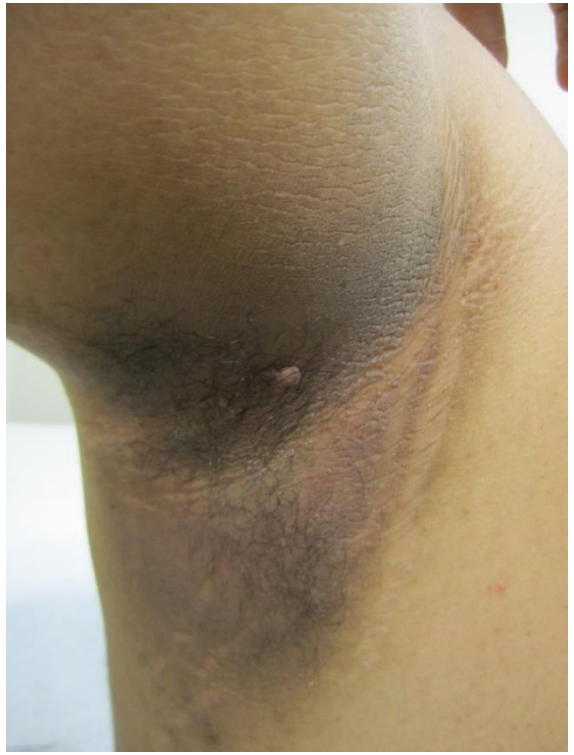
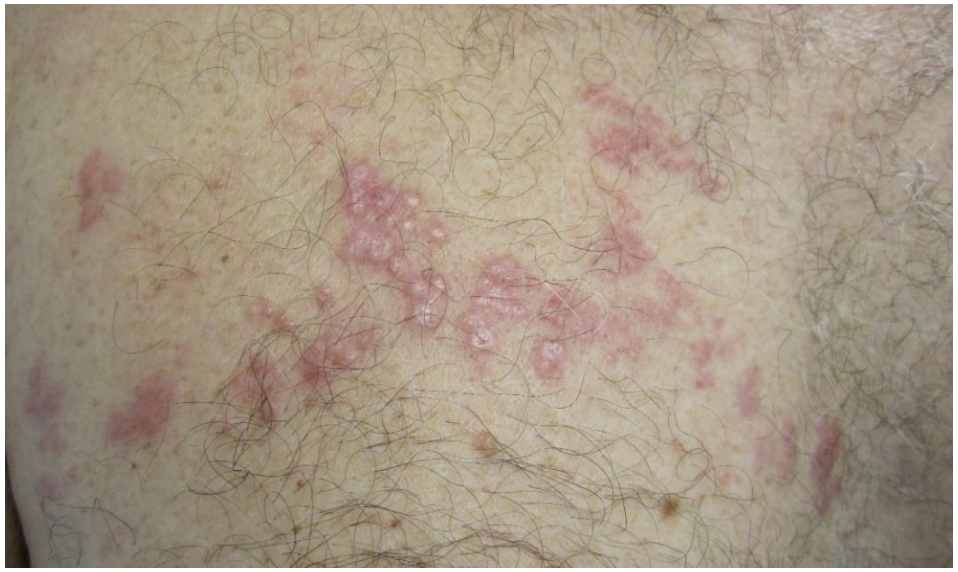
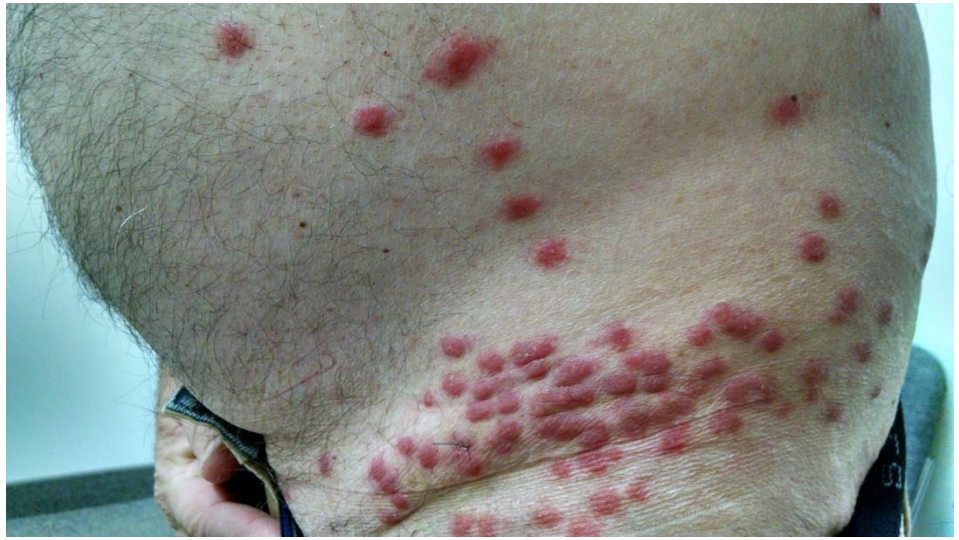


Photo Courtesy V.Lazareth,NP

Hepatic: Lichen Planus

- inflammatory cutaneous and mucosal reaction pattern
- associated with liver disease (Hep C)
- characteristic morphology and distribution
  - pruritic
  - planar (flat topped)
  - polyangular (angulated border)
  - purple
  - papules
- lacy, reticular pattern of crisscrossed white lines (Wickham Striae)





Lichenoid Drug Eruption

Photo Courtesy V.Lazareth,NP

Renal:
Erythema Nodosum

- F>M, 2nd-5th decades of life
- acute, tender, erythematous, SC pretibial nodules
- arthritis, arthralgia, fever, malaise
- flare of IBD (Crohns > UC) or Sarcoidosis
- delayed hypersensitivity response to:
- Infection: strep or viral URI, bacterial gastroenteritis
- Drugs: estrogens, OCP, sulfonamides, PCN, bromides, iodides, TNF inhibitors, BRAF inhibitors

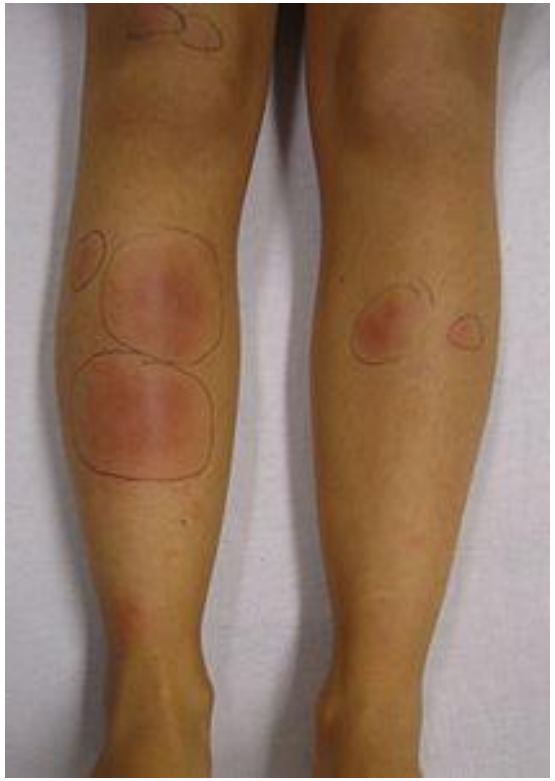
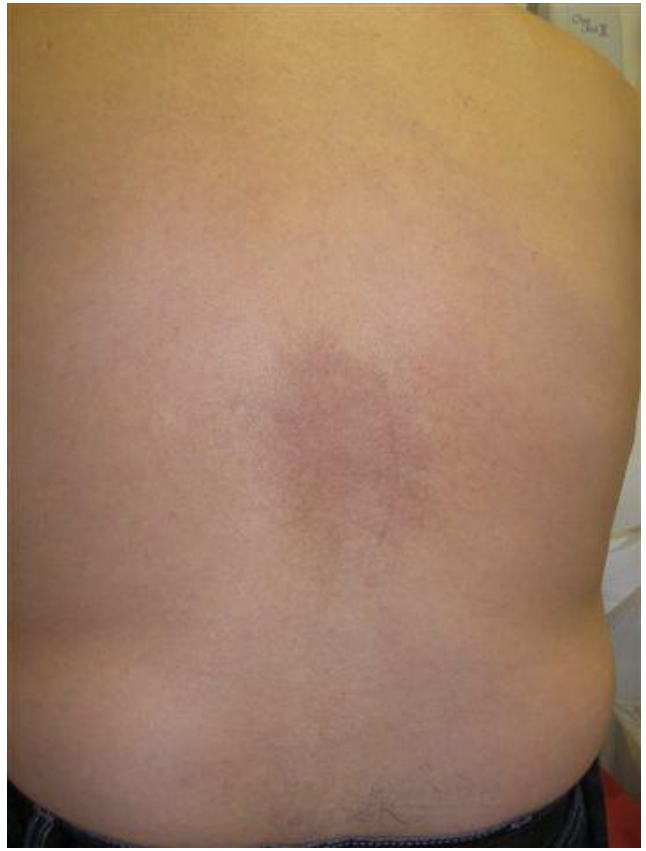


Photo Courtesy V.Lazareth,NP

Nervous: Neuropathic

- Notalgia paresthetica:
  focal, intense pruritus with focal hyperpigmentation from chronic rubbing of the upper back (T2–T6)

- Brachioradial pruritus:
  pruritus or burning pain on dorsolateral forearms and elbows in pts with degenerative spinal osteoarthritis



Notalgia Paresthetica

Photo Courtesy V.Lazareth,NP

Pulmonary: Sarcoidosis

- granulomatous disease; potential for multi-organ involvement (~90% lung disease)
- African and Scandinavian Americans
- lesions at trunk & extremities or sites of trauma turn the golden color of “apple jelly” with blanching (pressure)
- *Lupus pernio:*
  - scaly, violaceous, bead-like papules at nose and cheeks
  - associated with chronic sarcoidosis of the respiratory tract

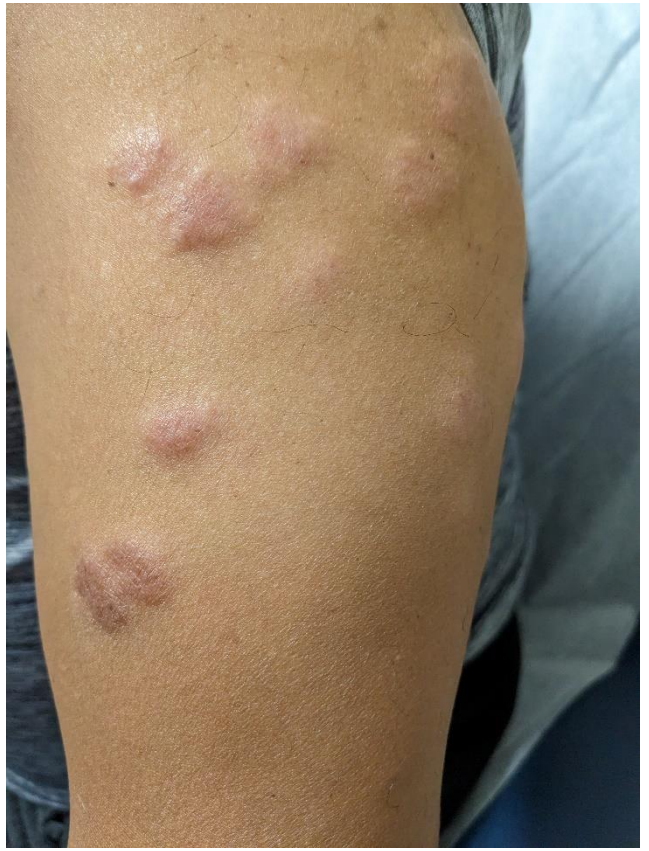


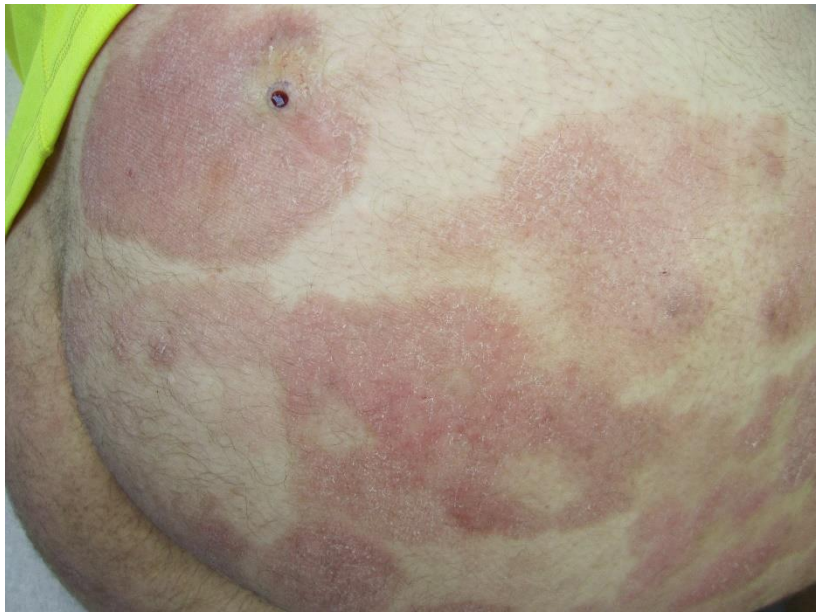
Photo Courtesy V.Lazareth,NP

Paraneoplastic:
Cutaneous T-cell lymphoma

heterogeneous group of cutaneous lymphomas of T cells

<u>Mycosis fungoides</u>

- most common type (50%)
- 4-6 yrs nonspecific eczematous or psoriasiform skin lesions and non-diagnostic biopsies often precede diagnosis
- classic MF progresses from patch to plaque to tumor stage disease over years or decades



<u>Sézary Syndrome</u>

- <5% of all CTCL; erythroderma; intensely pruritic
- poor prognosis, 25% 5-year survival (opportunistic infections)

Photo Courtesy V.Lazareth,NP

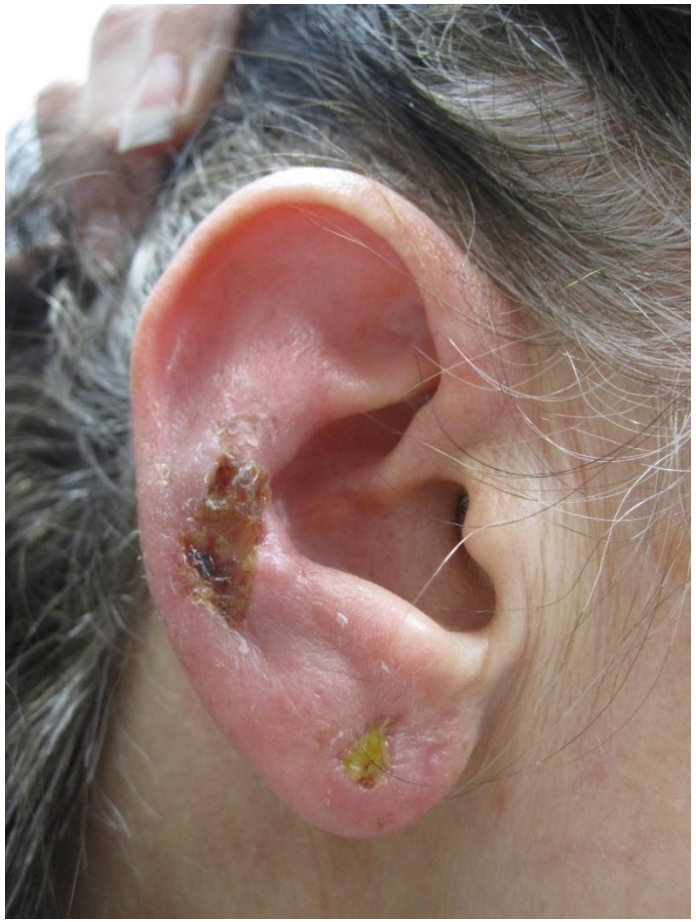
Psychological:
Psycho Dermatoses

Delusions of Parasitosis

- pts typically have long hx of alleged “parasites”
- “matchbox sign” bits of skin, lint, etc. that pt believes represent “parasites”
- c/o crawling, biting, stinging
- self-induced excoriations, lichenification, prurigo nodularis, ulcerations resulting from pt’s efforts to dig out “parasites”

Morgellons disease

- pts claim to observe “fibers” exuding from their skin



Dermatitis Artefacta

Photo Courtesy V.Lazareth,NP

Pruritus

Itch is a manifestation of systemic disease in up to 25% of cases

- Drug Reaction:
  - virtually any drug
  - morbilliform or urticarial eruptions
  - pruritus may be the predominant manifestation
- Xerosis: pruritus aggravated by cold, dry climates resulting in impaired barrier function of the stratum corneum
- Age: dry skin, age-related changes in nerve and pain fibers decreased skin surface lipids; diminished barrier repair
- Aquagenic pruritus: 2ndary to polycythemia vera, urticaria
- Fiberglass exposure: manufacturing or construction

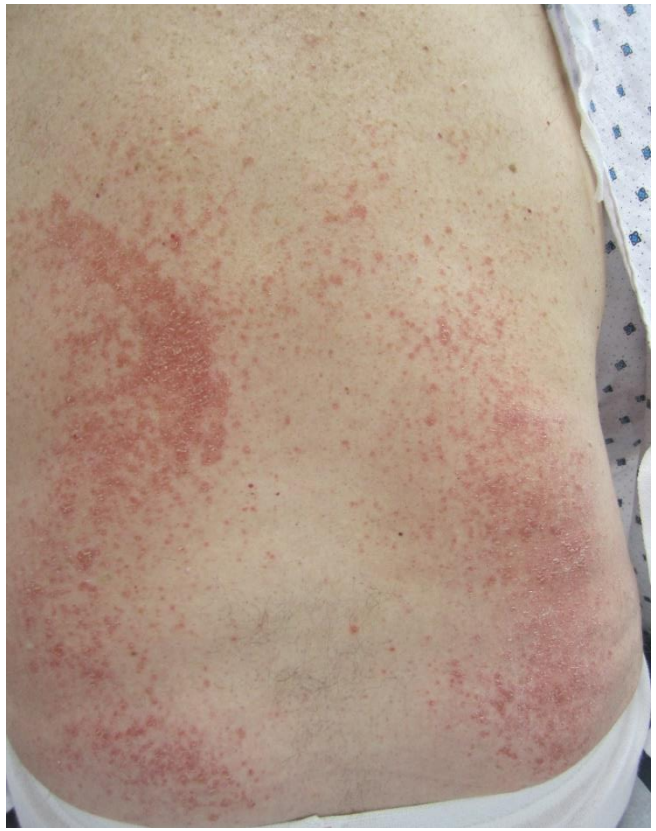


Photo Courtesy V.Lazareth,NP

Pruritus

- Hematologic Pruritus:
  - iron deficiency (perianal or vulvar pruritus)
- Cholestatic Pruritus:
  - in nearly any liver disease
- Renal Pruritus:
  - frequent in advanced chronic kidney disease
- Paraneoplastic itch:
  - any malignancy; early or advanced disease
  - polycythemia vera, Hodgkin and non-Hodgkin lymphoma; CLL

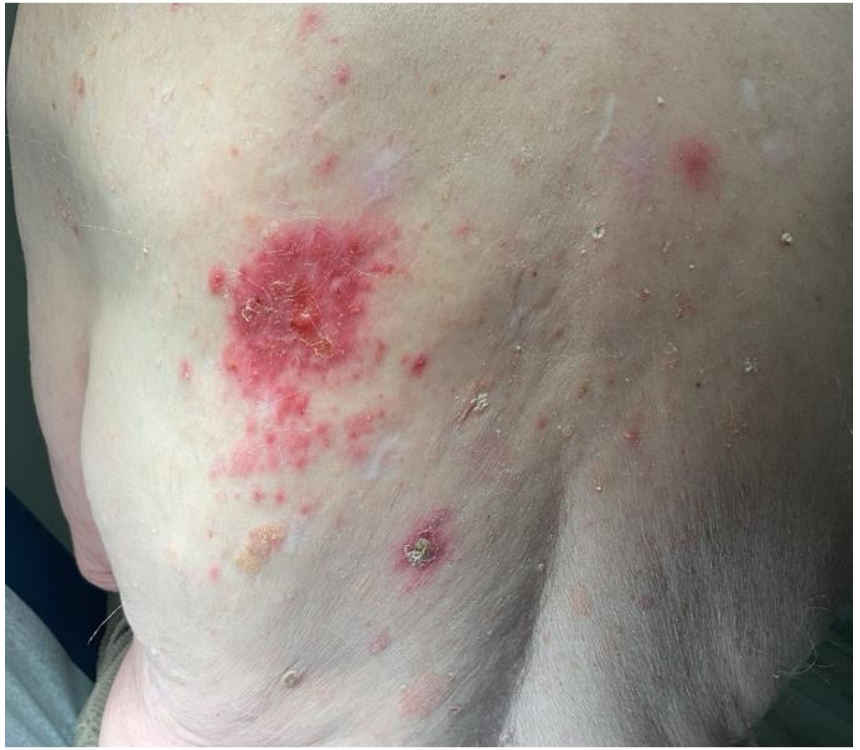
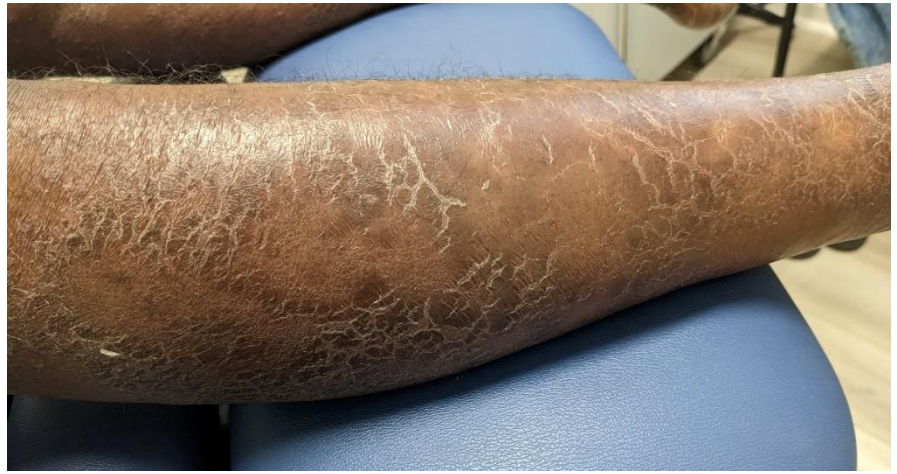


Photo Courtesy V.Lazareth,NP

Pruritus



Inflammatory dermatoses

Atopic Dermatitis

- 100% of pts; multiple triggers

Psoriasis

- 85% of pts; exacerbated by stress, heat, xerosis, heat

Contact Dermatitis

- Type III & Type IV sensitivity reaction to drugs, metals, chemicals, medical implants, plants, foods, beverages, aromatic substances

Urticaria

- inflammatory response characterized by hives, angioedema or both caused by release of histamine, vasoactive substances from mast cells

Photo Courtesy V.Lazareth,NP

Pruritus

Infectious Disease / Infestations

- Bacterial, Viral, Fungal Infections
- Folliculitis
- Scabies, Pediculosis Infestations
- HIV: severe, treatment-resistant pruritus from pruritic dermatoses

Pregnancy

- Polymorphic eruption of pregnancy,
- Pemphigoid gestationis,
- Prurigo gestationis

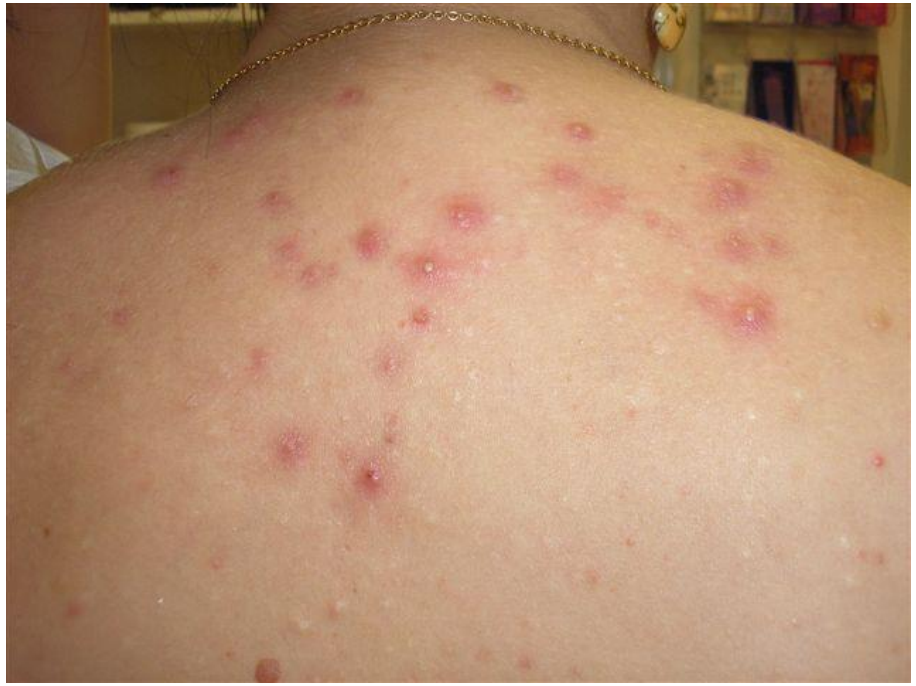


Photo Courtesy V.Lazareth,NP

Pruritus

Chronic secondary scratch-induced lesions

- Prurigo nodularis
- Lichen simplex chronicus

Autoimmune Disorders

- Bullous pemphigoid
- Dermatitis herpetiformis
- Dermatomyositis
- Lupus erythematosus

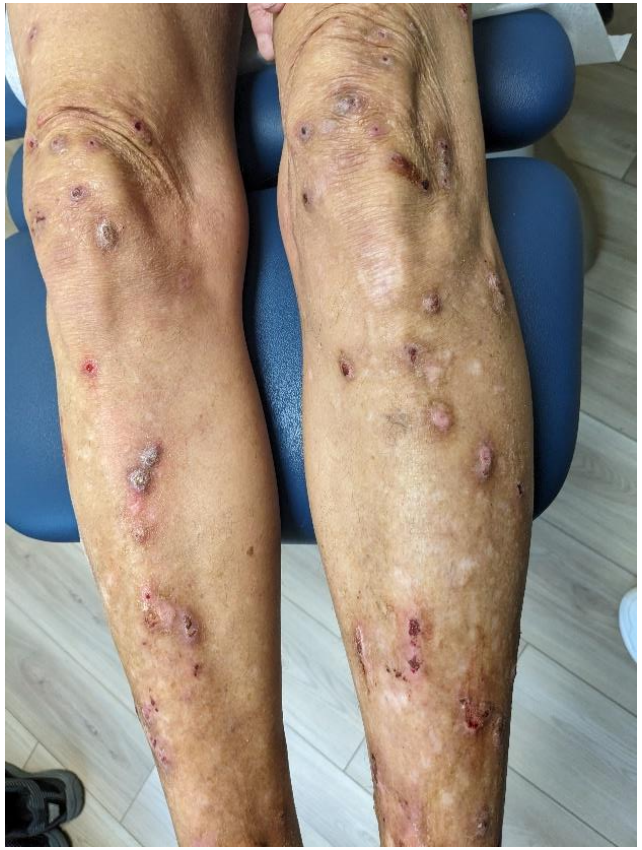


Photo Courtesy V.Lazareth,NP

Pruritus

Genodermatoses

Darier's disease

Hailey–Hailey disease -*autosomal dominant*

Tuberous Sclerosis -*autosomal dominant*

Ichthyoses -*autosomal recessive*

Keratoderma

Neurofibromatosis

Malignancy

- Cutaneous T-cell lymphoma
- Cutaneous B-cell lymphoma
- Leukemia

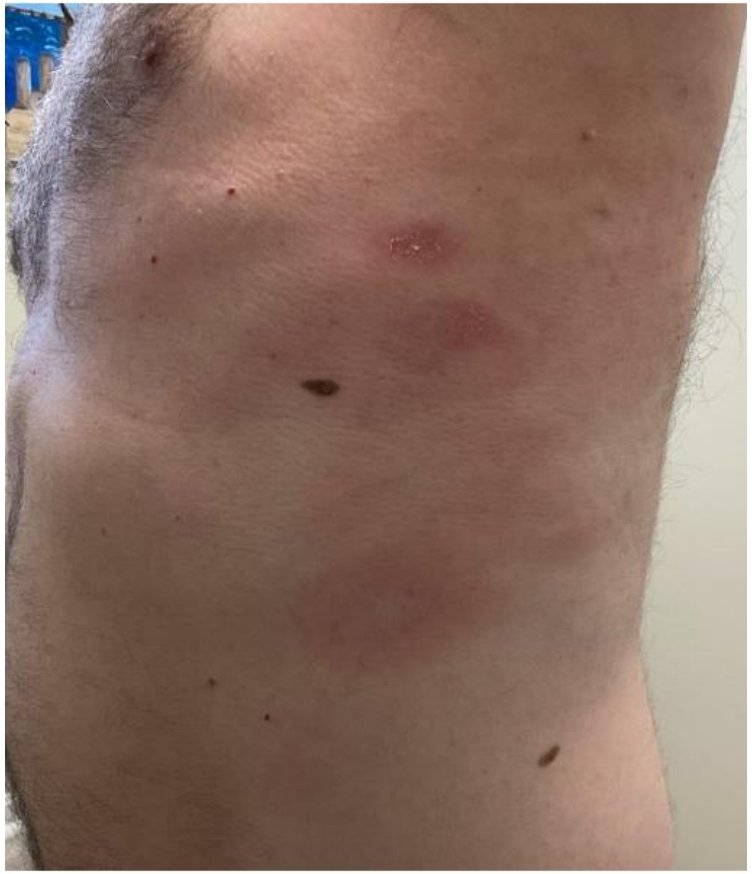


Photo Courtesy V.Lazareth,NP

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