What's New in the Dermatology Medicine Cabinet?

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VA Portland Health Care System

Skin, Bones, Hearts & Private Parts

Disclosures

- I am not representing the Veterans Health Administration
- Speakers' Bureaus/Consultant/Advisory Board:
  - AbbVie
  - Lilly
  - Celgene
  - Sanofi Genzyme
  - Regeneron
  - UBC

- Most images are kindly provided by VisualDx

Objectives

- The learner will be able to identify 3 biologic therapeutic targets and agents for the treatment of psoriasis.
- The learner will be able to identify 2 novel therapeutic agents for the treatment of atopic dermatitis.
- The learner will be able to identify 3 key patient teaching pearls in order to improve adherence to dermatologic therapies.
- The learner will be able to identify 5 key parameters to assess efficacy for the treatment of common dermatologic conditions.

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- AbbVie
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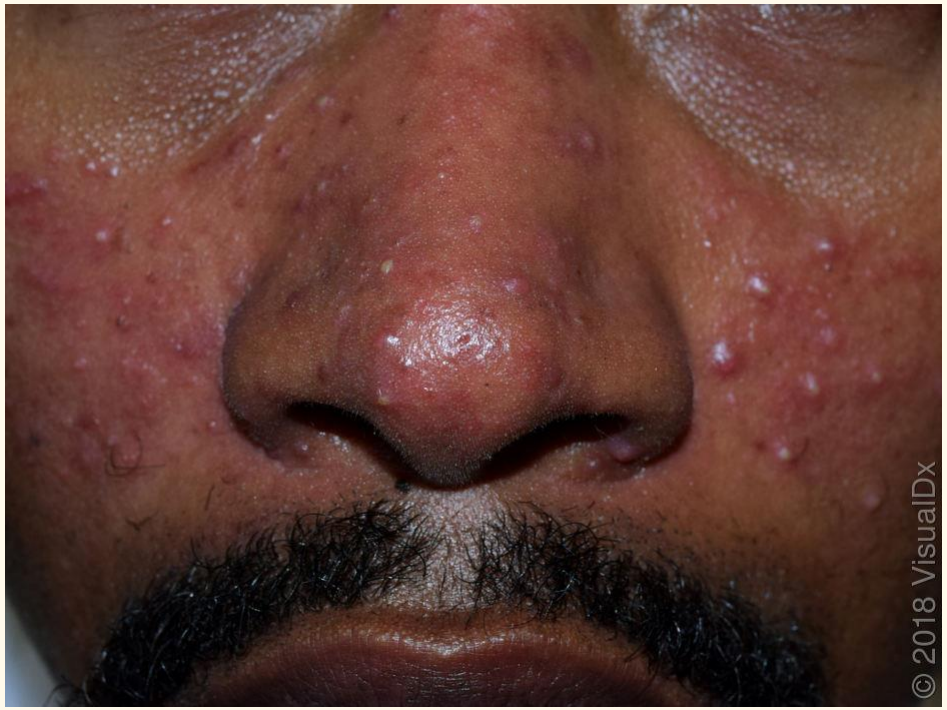
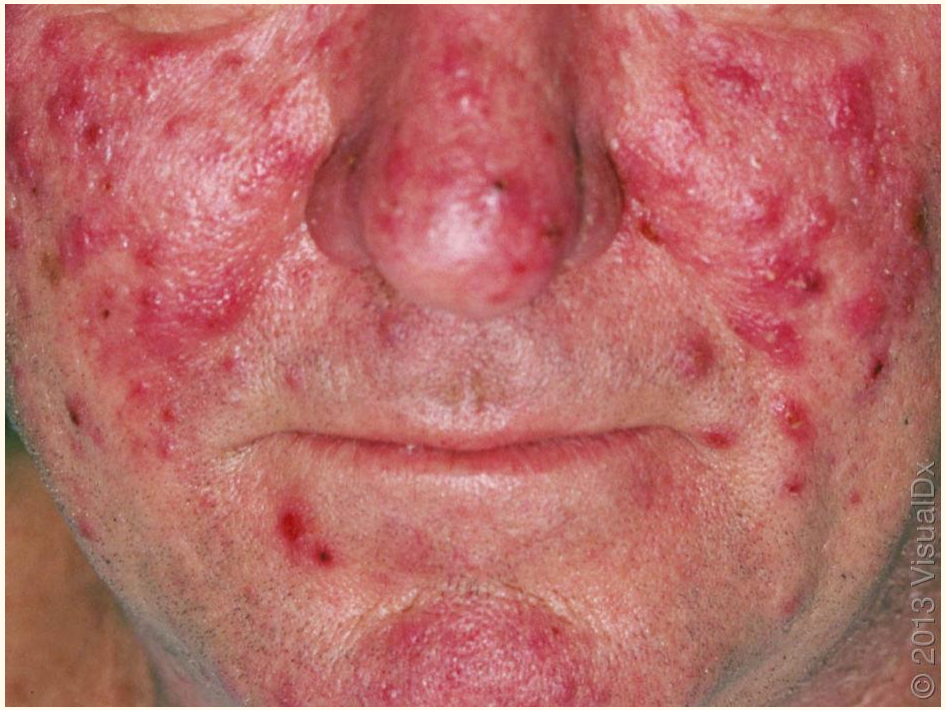
- Regeneron
- Sun Pharma

Images courtesy of VisualDx.

- Not speaking on behalf of the VA or the United States Government or the President.

Case 1





Rosacea

New Guidelines published JAAD 2/6/2020

Rosacea criteria simplified

- New standard management options for rosacea were recently published in the *Journal of the American Academy of Dermatology*.[1]
- Review panel of 27 rosacea experts worldwide
- Phenotypes and diagnostic criteria based on:
  - persistent facial erythema
  - phymatous changes

Guidelines review:

- topical and oral therapies and light devices
- appropriate skin care and lifestyle management
- avoid factors that may aggravate the condition
- combination therapy to target the specific features is often necessary for effective treatment
- Free copy: https://www.rosacea.org/pdf/Standard_Management_Options_for_Rosacea.pdf

Minocycline foam (Zilxi)

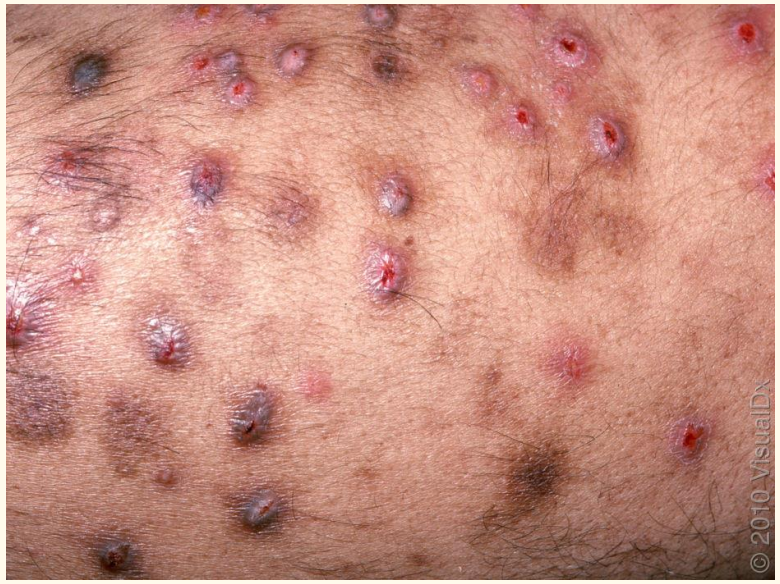
- 1.5% minocycline foam (Menlo Therapeutics)
- Approved: May 2020 for the treatment of inflammatory lesions of rosacea in adult patients.
- Previously, a 4% topical minocycline foam (Amzeeq) approved for treatment of inflammatory lesions of non-nodular mod-sev acne vulgaris in pediatric and adults in 2019
- 2 trials N:1,522 >18yrs old, with rosacea-related papules and pustules
- Zilxi met all co-primary endpoints in both trials
  - Absolute mean change inflammatory lesions counts from baseline at week 12
  - Pts achieving IGA score of 0,1 or minimum of a two-grade decrease from baseline at W12
  - Superiority over vehicle and statically significant decrease in inflammatory lesion count and IGA success
  - Erythema was investigated during the trials, with 40.9% and 48.3% of pts being clear or almost clear of erythema W12.
- Available Q4 2020

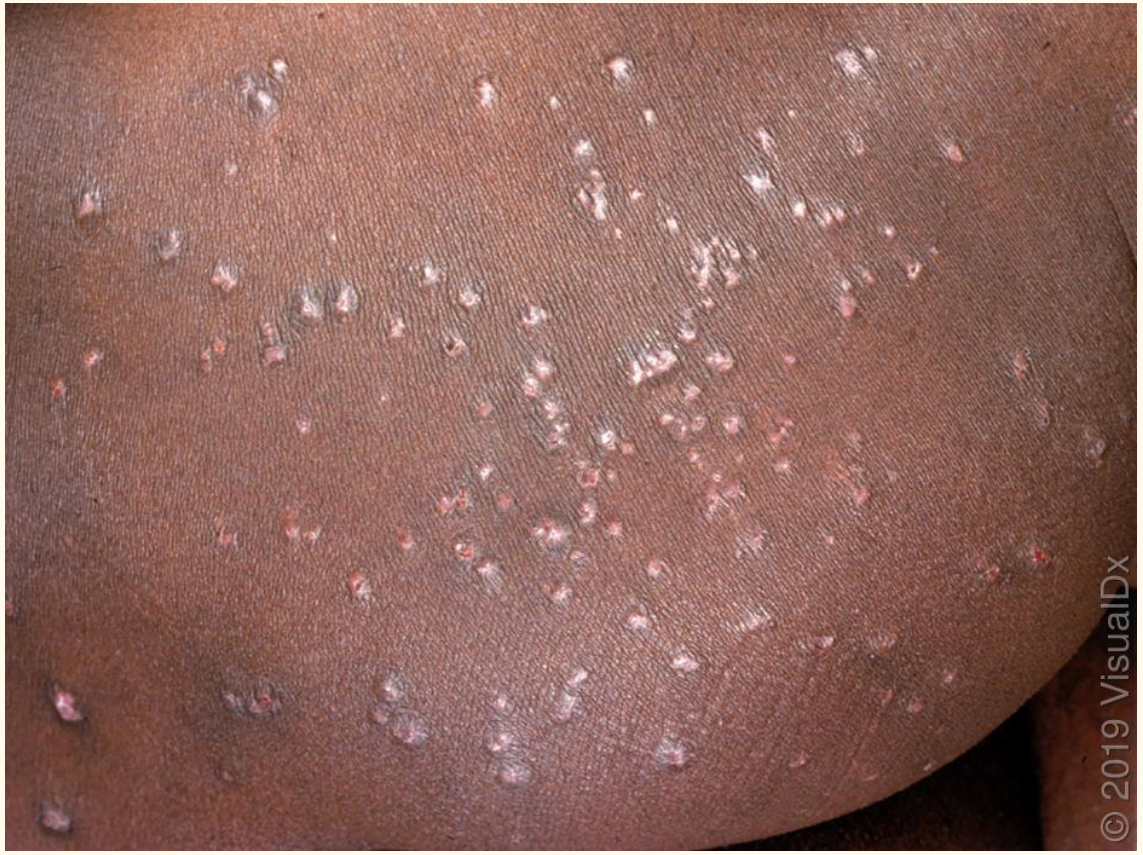
Rosacea and coffee consumption

- Rosacea pts are counseled that coffee and other hot beverages may exacerbate their disease
- Analysis of data from over 80,000 women in the Nurses' Health Study II: compared with women with the lowest consumption of caffeinated coffee, *women with the highest consumption were less likely to develop rosacea*
- Inverse relationship between increased caffeine intake and risk of incident rosacea
- No association between risk for rosacea and consumption of decaffeinated coffee
- Restriction of coffee consumption is not necessary for patients with rosacea.

Reference: Li S, Chen ML, Drucker AM, et al. Association of Caffeine Intake and Caffeinated Coffee Consumption With Risk of Incident Rosacea in Women. JAMA Dermatol 2018; 154:1394.

Case 2





Prurigo nodularis and dupilumab

- Dupilumab —IL-4 receptor inhibitor: reduced pruritus and resolved lesions in patients with recalcitrant PN
- 4 pts with chronic, treatment-resistant PN, treated with dupilumab 600 mg followed by 300 mg every other week
- At 12 weeks, all 4 pts reported a numeric rating scale of itch of 0
- In9 adult pts with AD manifesting as generalized PN, dupilumab at the standard dosing regimen: marked clinical improvement in skin lesions, pruritus, and life quality in all pts
- French, multicentric cohort of 16 adult pts with chronic PN refractory to multimodal treatment regimens:
  - dupilumab induced a complete or partial response of skin lesions and pruritus in 15 pts and no response in 1 patient at 3m

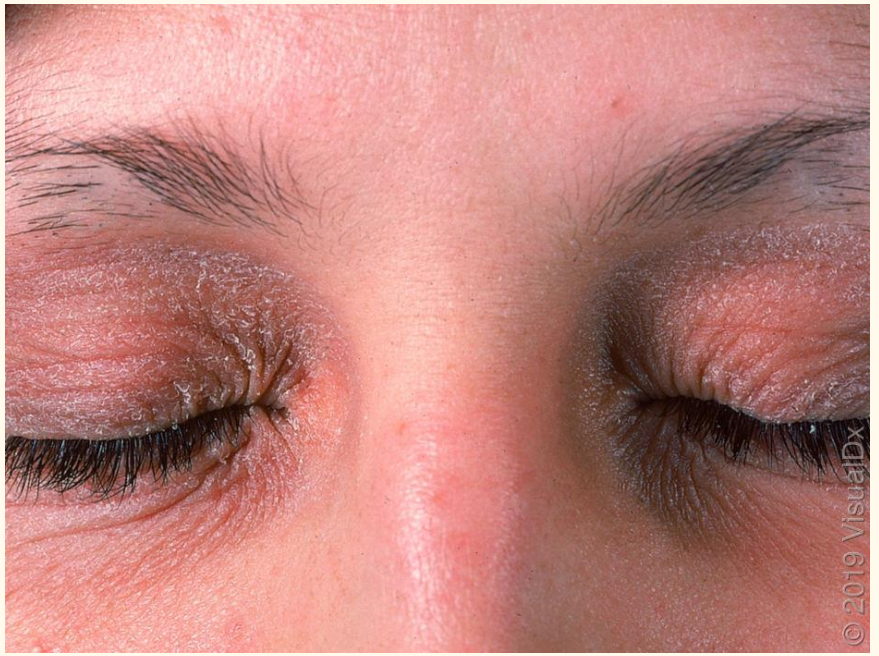
Prurigo nodularis and nemolizumab

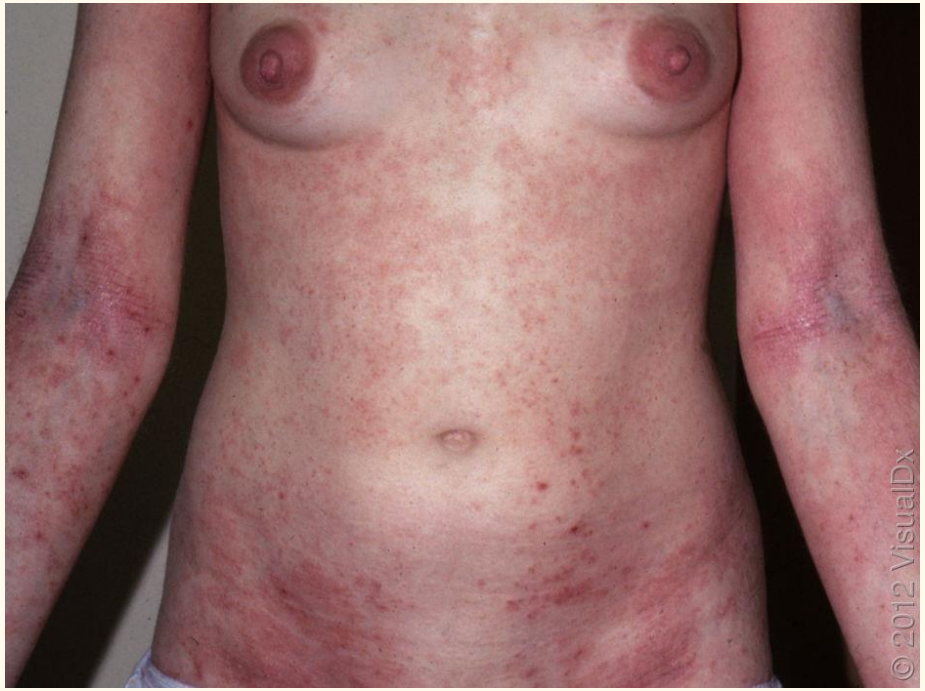
- Nemolizumab, an investigational anti-interleukin (IL) 31 monoclonal antibody
- Phase II, randomized trial of 70 pt with mod/severe PN
- subcutaneous nemolizumab 0.5 mg/kg or placebo at baseline, week 4, and week 8
- more effective than placebo in reducing pruritus at Wk4 and the number of skin lesions at W12
- Adverse events: abdominal pain, diarrhea, and musculoskeletal pain.
- Larger and longer-duration studies are needed to confirm the long-term efficacy and safety of nemolizumab for recalcitrant PN.

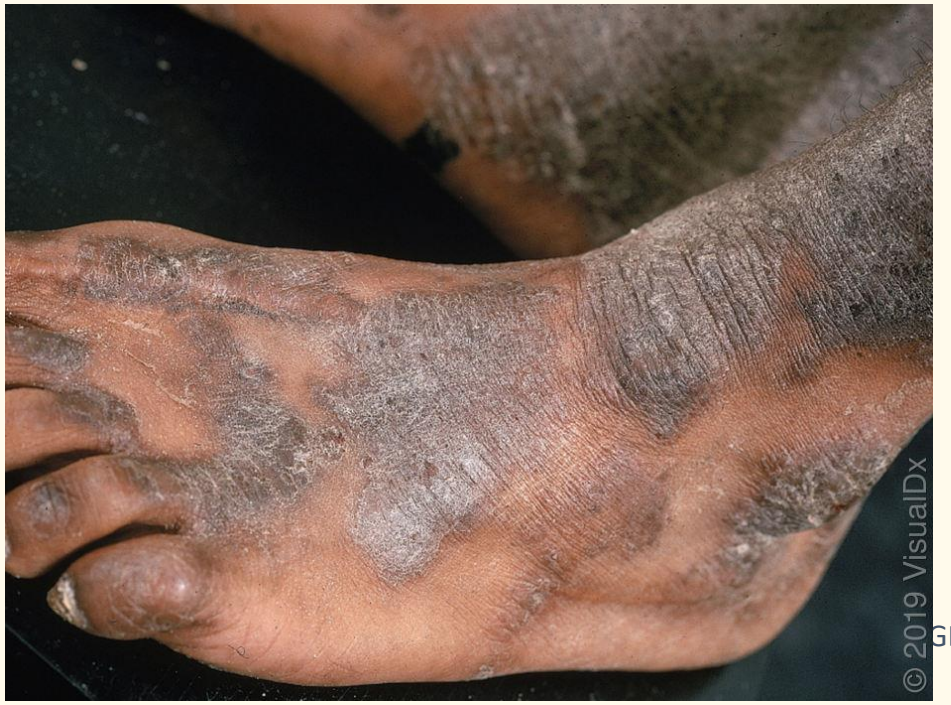
Prurigo nodularis and serlopitant

- Serlopitant is a novel oral neurokinin 1 (NK1) antagonist
- Randomized trial, 128 patients with chronic, treatment-refractory PN
- 5 mg po QD x 8 wks more effective than placebo in reducing the average itch
- Adverse events: nasopharyngitis, diarrhea, and fatigue
- Also being tested for chronic pruritus of unknown origin

Case 3







Probiotics not effective for AD

- Do probiotics given prenatally and/or in early life reduce the risk of developing atopic dermatitis?
- A meta-analysis of 39 randomized trials:
  - Nearly 2600 pts of all ages with mild to severe AD
  - No difference between probiotics (*Lactobacillus* and *Bifidobacteria*) and placebo in improving pt/parent-rated severity of AD, pruritus, sleep loss, or quality of life
- A modest reduction of uncertain clinical significance in the SCORAD score was noted in pts taking probiotics compared with placebo.
- "We do not routinely use probiotics as a complementary treatment for AD, because the clinical benefit is minimal at best".

Reference: Makrgeorgou A, Leonardi-Bee J, Bath-Hextall FJ, et al. Probiotics for treating eczema. Cochrane Database Syst Rev 2018; 11:CD006135.

R. Mucosa NIH study

- Sept. 9 in *Science Translational Medicine.*
- Live *Roseomonas mucosa*—a bacterium naturally present on the skin—originally isolated from healthy volunteers and grown under carefully controlled laboratory conditions
- 10 adults/20 children
- BIW x 3 months and WOD for an additional month
- Sprayed a solution of sugar water containing live *R. mucosa* onto areas of skin with eczema
- Safely reduced diseae severity, improved QOL; persisted for 8 months after tmt
- "A child suffering from eczema, which can be itchy, painful and distracting for the child, also is very difficult for the entire family," said **Anthony S. Fauci, M.D**., director of NIH's National Institute of Allergy and Infectious Diseases (NIAID), which led the study. "These early-stage findings suggest that *R. mucosa* therapy may help relieve some children of both the burden of eczema symptoms and the need for daily treatment."

Montelukast not effective for AD

- Efficacy of montelukast, an oral leukotriene receptor antagonist used as a steroid-sparing agent for asthma and allergic rhinitis, in AD is uncertain.
- Review of 5 randomized trials of montelukast, compared with placebo or usual care, for patients with moderate-to-severe AD found the overall quality of the evidence to be low.
- Montelukast did not decrease disease severity, pruritus, or need for topical corticosteroids, compared with placebo
- One trial found improvement in disease severity with montelukast compared with usual care but another trial did not.
- Because of the limited and low-quality available evidence, the role of leukotriene receptor antagonists in the management of AD remains ?.
- “While waiting for larger and well-designed studies, we do not support the use of this class of agents for atopic dermatitis”.

Reference: Ferguson, L et al. 2018 “Leukotriene receptor antagonists for eczema.” Cochrane Database Syst Rev. 10: CD011224. Epub 2018 Oct 21.

AD and CV risk

- Is there an association between AD and CV disease?
- Past data controversial
- Large UK, 400,000 adult pts with AD and 1.5 million matched controls found that pts with AD, in particular those with severe disease, had an increased risk of CV disease, including MI, unstable angina, a-fib, heart failure, and CV death [4].
- Study could not determine whether AD or treatments for AD confer an increased CV risk
- **Screening for CV disease and known risk factors for CV disease in adults presenting with severe AD may be appropriate.**

Reference: Silverwood RJ, Forbes HJ, Abuabara K, et al. Severe and predominantly active atopic eczema in adulthood and long term risk of cardiovascular disease: population based cohort study. BMJ 2018; 361:k1786.

Dupilumab: Atopic dermatitis

- First FDA-approved biologic for AD
- Target: IL-4 and IL-13 inhibitor
- Expanded to include ≥ 12 years
- Dosing:
  - 60kg or >: 600mg SC in 2 different sites, then 300mg every 2 weeks
  - 60kg or <: 400mg SC in 2 different sites, then 200mg every 2 weeks
- Side effects: conjunctivitis
- No lab monitoring

Reference: https://www.uptodate.com/contents/treatment-of-atopic-dermatitis-eczema?source=see_link&sectionName=Dupilumab&anchor=H556287622#H556287622

Dupilumab: Asthma

- FDA approved for moderate to severe asthma
- 12 years and older
- Dosing: 400mg SQ then 200mg sc every other week
- Don’t stop other treatments unless advised

Reference: https://www.uptodate.com/contents/treatment-of-atopic-dermatitis-eczema?source=see_link&sectionName=Dupilumab&anchor=H556287622#H556287622

Tralokinumab (Leo) fast-tracked: July 2020

- Fully human, immunoglobulin (Ig) G4 MAB: specifically binding to IL-13
  - high affinity, preventing its interaction with subsequent downstream signaling
- 3 pivotal, double-blind, placebo-controlled phase 3 (ECZTRA 1-3) studies
- adults with mod-sev AD (ECZTRA 1 , ECZTRA 2) assessed tralokinumab as monotherapy in 802 and 794 adults, respectively, for 52 weeks.
- ECZTRA 3 assessed tralokinumab in combination with topical corticosteroids in 380 adults for 32 weeks.
- Endpoints:
  - IGA clear (0) or almost clear (1) at week 16
  - 75% or greater change from baseline in EASI score at week 16.
  - Secondary end points: change in Scorad, Pruritus NRS and DLQI
- Results from all 3 studies showed tralokinumab met all primary and secondary end points. Regar
- Safety: overall adverse event rate that was comparable to placebo

Baracitinib: JAK 1/JAK 2 inhibitor for AD

- Phase 2 trials
- 4 mg, achieved EASI-50 than did patients receiving placebo (61% vs 37% [P = .027]) at 16 weeks
- The difference between the proportion of patients receiving baricitinib, 2 or 4 mg, who achieved EASI-50 and the proportion of patients receiving placebo and achieving EASI-50 was significant as early as week 4
- Baricitinib also improved pruritus and sleep loss
- AEs: 24 of the patients receiving placebo (49%), 17 of those receiving 2 mg of baricitinib (46%), and 27 of those receiving 4 mg of baricitinib (71%)

crisaborole (Eucrisa)

- Approved: December 2016
- Indication: atopic dermatitis (2 years of age and older)
- Class: phosphodiesterase 4 inhibitor
- Dosing: Apply a thin layer twice daily to affected areas.
- Side effects: application site pain

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100179/eucrisa-crisaborole-ointment

crisaborole: clinical studies

- 2 multicenter, randomized, double-blind, parallel-group, vehicle-controlled trials (Trials 1 and 2)
- 1,522 subjects 2 to 79 years of age (86.3% of subjects were 2 to 17 years of age) with a 5% to 95% treatable body surface area.
- At baseline, 38.5% of the subjects ISGA score of 2 (mild), and 61.5% had an ISGA score of 3 (moderate): erythema, induration/papulation, and oozing/crusting on a severity scale of 0 to 4.
- In both trials, subjects were randomized 2:1 to receive Eucrisa or vehicle applied twice daily for 28 days.

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100179/eucrisa-crisaborole-ointment

crisaborole: clinical studies

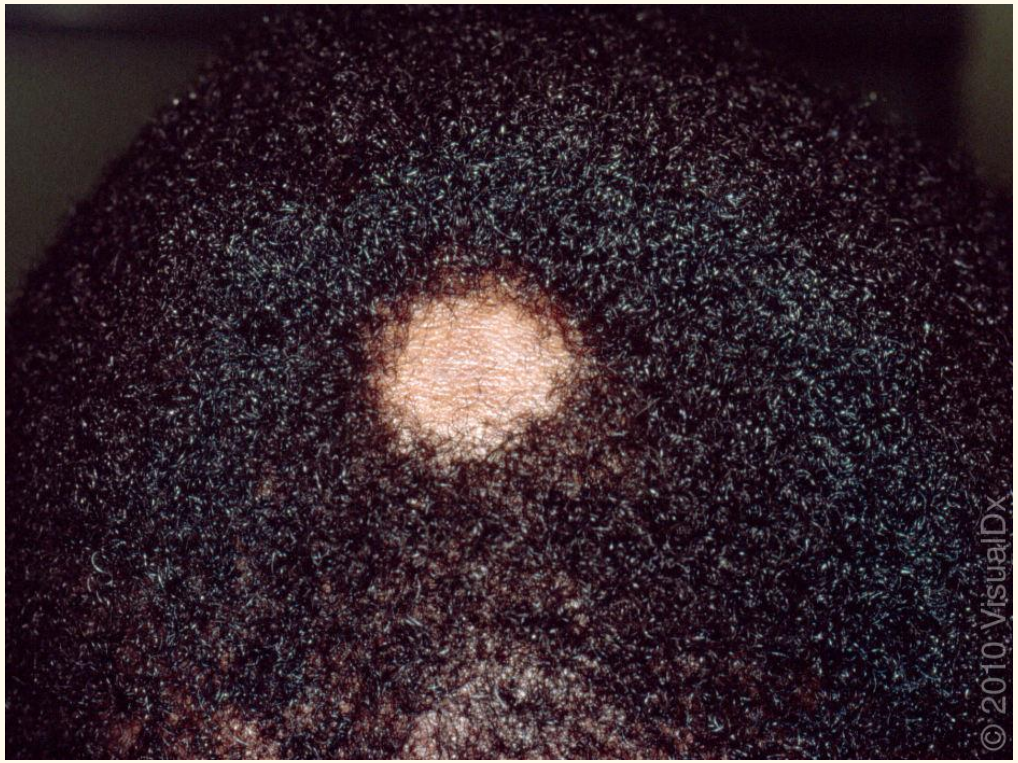
- The primary efficacy endpoint at Day 29 who achieved success, defined as an ISGA grade of Clear Almost Clear (score of 1)
- In Trial 1, 32.8% of subjects achieved the primary endpoint compared to 25.4% in the vehicle group.
- Trial 2, 31.4% of subjects achieved the primary endpoint compared to 18% in the vehicle group.

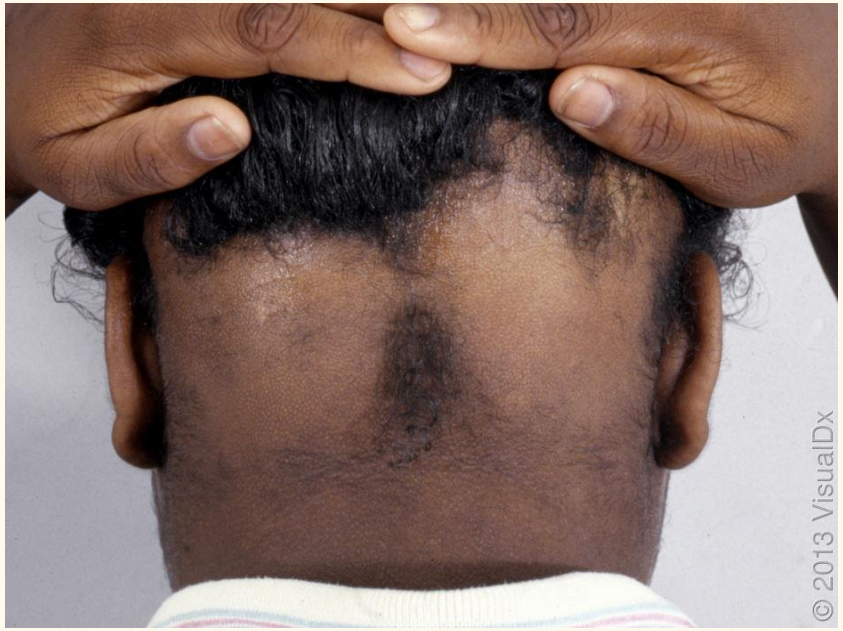
Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100179/eucrisa-crisaborole-ointment

March 2020: Frequency of bathing

- Controversy regarding the frequency of bathing for patients with AD
- ? if bathing or showering is an additional skin irritant for AD pts
- 2W randomized, crossover trial; 42 children with moderate to severe AD
- twice-daily bath for 15 to 20 mins followed by emollient application→greater decrease in the severity score of AD, compared with infrequent bathing (2/WK for 10 mins or less)
- Recommendation is daily bathing
- Rapid application of emollients and/or prescribed topical preparations immediately after ("soak-and-seal") is essential

Case 4





Images kindly provided by Visual Dx

Tofacitinib and alopecia areata (AA)

- Tofacitinib, JAK-inhibitor, is a treatment option for refractory AA
- Limited data for use in children
- First case series to describe oral tofacitinib use in preadolescent children with AA, complete or partial hair regrowth occurred in 3 of 4 children treated for alopecia totalis or universalis
- No adverse events

Reference:
Craiglow BG, King BA. Tofacitinib for the treatment of alopecia areata in preadolescent children. J Am Acad Dermatol 2018.
Putterman E, Castelo-Soccio L. Topical 2% tofacitinib for children with alopecia areata, alopecia totalis, and alopecia universalis. J Am Acad Dermatol 2018; 78:1207.

Tofacitinib and alopecia areata (AA)

- Improvement in children treated with investigational topical tofacitinib is also described in case series

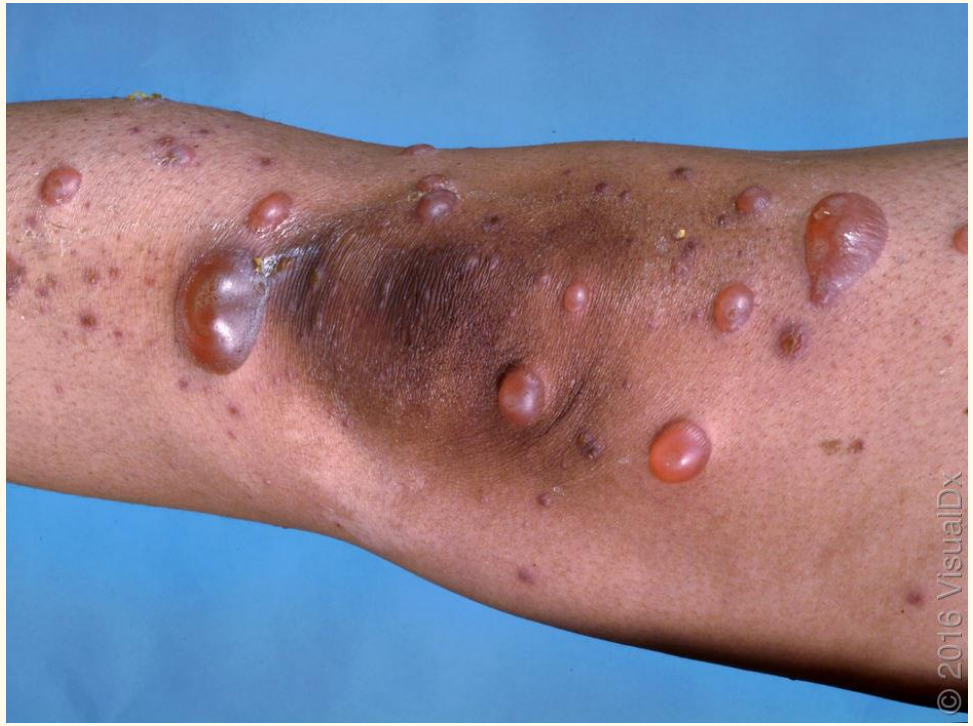
- Further study is needed to confirm efficacy and safety of tofacitinib prior to routine use for pediatric alopecia but promising!

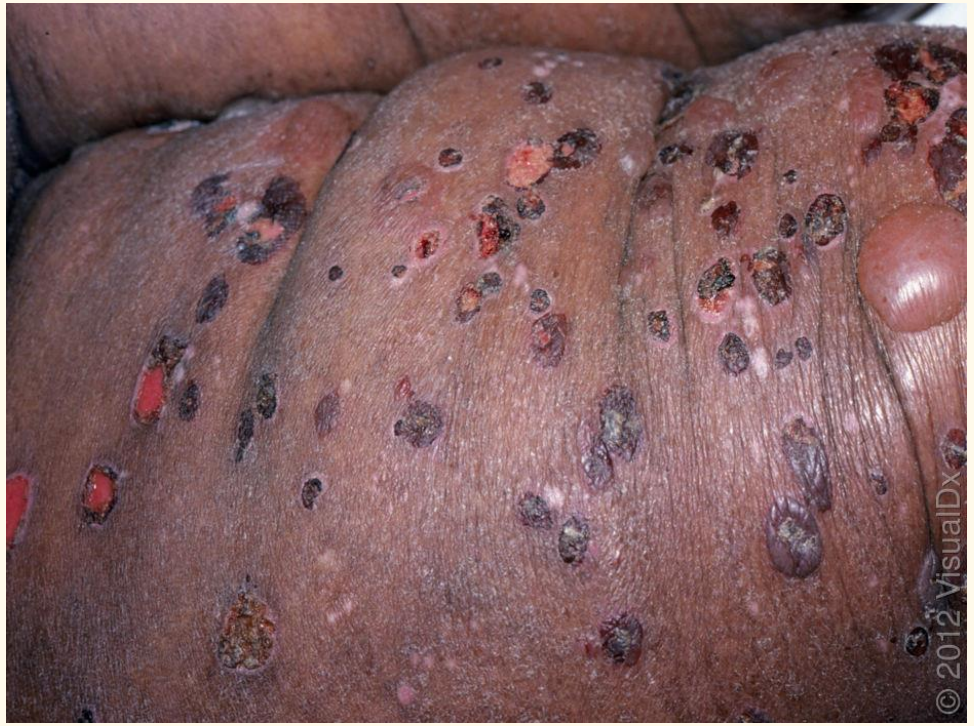
Reference:
Craiglow BG, King BA. Tofacitinib for the treatment of alopecia areata in preadolescent children. J Am Acad Dermatol 2018.
Putterman E, Castelo-Soccio L. Topical 2% tofacitinib for children with alopecia areata, alopecia totalis, and alopecia universalis. J Am Acad Dermatol 2018; 78:1207.

Baricitinib and AA: Fast tracked by FDA 3/2020

- JAK inhibitor, 2 mg orally once daily as monotherapy
- Based on the positive Phase 2 results BRAVE-AA1
  - treatment with baricitinib versus placebo in adult patients with AA
  - BRAVWeek 36, no new safety signals
- The reported treatment-emergent adverse events (TEAEs) were mild or
  - upper respiratory tract infections, nasopharyngitis and acne.
- Phase 3 portion of BRAVE-AA1 and Phase 3 double-blind study (BRAVE-AA2), are currently assessing the efficacy and safety of the 2-mg and 4-mg doses of baricitinib relative to placebo
- Baricitinib is currently approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA
- WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS

Case 5





Images kindly provided by Visual Dx

BP and Dipeptidyl peptidase -4 inhibitors

- Increasing evidence linking bullous pemphigoid (BP) to use of the dipeptidyl peptidase-4 (DPP-4) inhibitors (vildagliptin and linagliptin) in diabetes

- A case-control study of diabetic patients with BP and matched diabetic controls without BP found an association between vildagliptin or linagliptin use and the development of BP

- Pts < 70 y/o and males had strongest link between DPP-4 inhibitor use and BP

Reference: din K, Bergman R. Association of Bullous Pemphigoid With Dipeptidyl-Peptidase 4 Inhibitors in Patients With Diabetes: Estimating the Risk of the New Agents and Characterizing the Patients. JAMA Dermatol 2018; 154:1152.

BP and Dipeptidyl peptidase -4 inhibitors

- Pts who dc'd DPP-4 inhibitors during standard BP therapy had better treatment outcomes than those who continued DPP-4 use

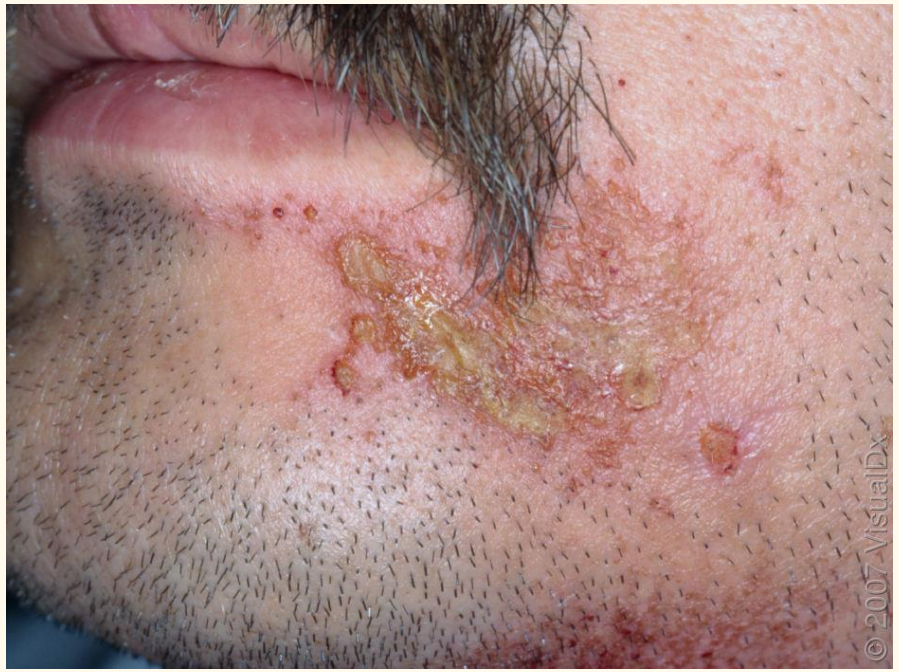
- Findings support a link between vildagliptin or linagliptin use and BP: dc'ing these drugs may benefit some patients with BP

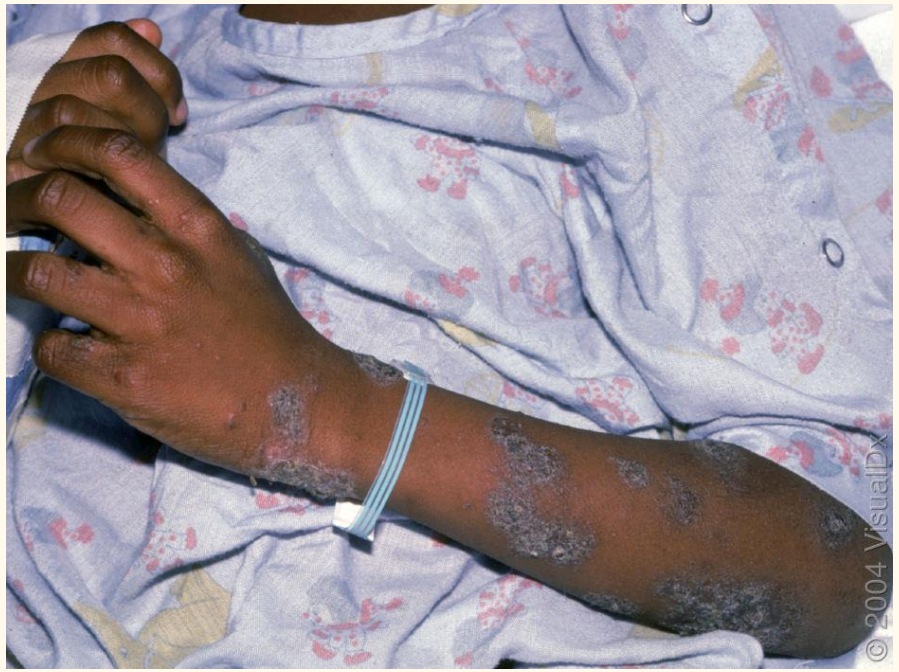
Reference: din K, Bergman R. Association of Bullous Pemphigoid With Dipeptidyl-Peptidase 4 Inhibitors in Patients With Diabetes: Estimating the Risk of the New Agents and Characterizing the Patients. JAMA Dermatol 2018; 154:1152.

Patient pearls: how do you know when a skin condition is getting better?

- Decrease in number of inflammatory lesions
- Decrease in the number of flares
- Decrease in erythema (redness)
- Decrease in pruritus (itch)
- Decrease in pain

Case 6





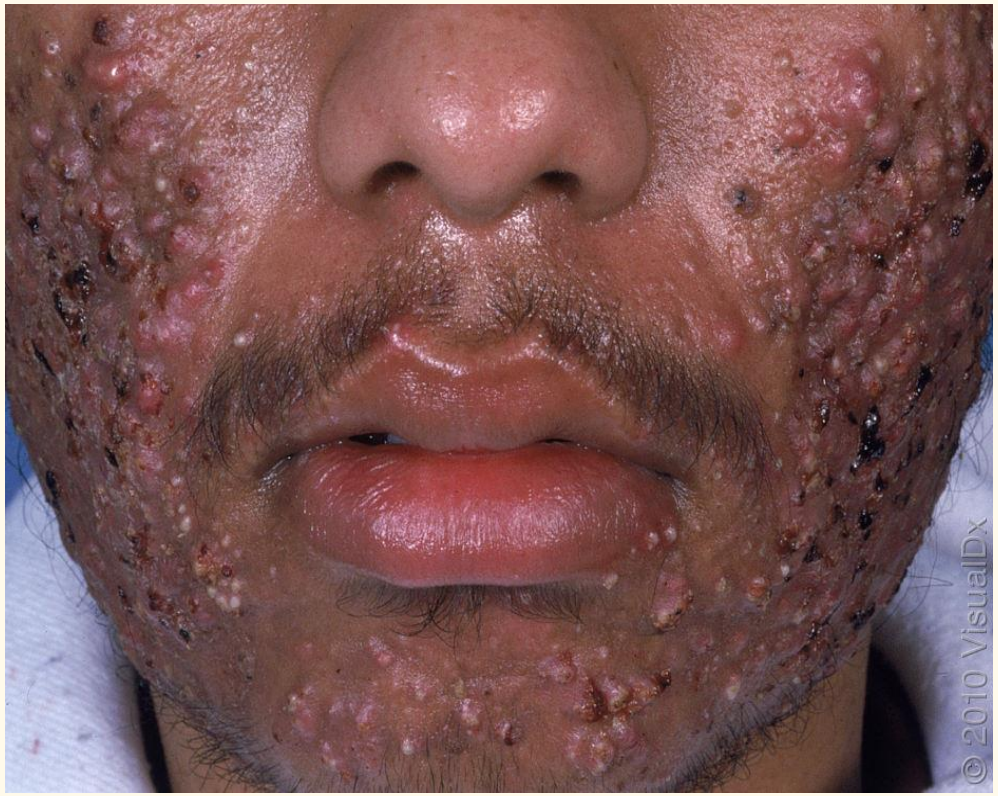
Images kindly provided by Visual Dx

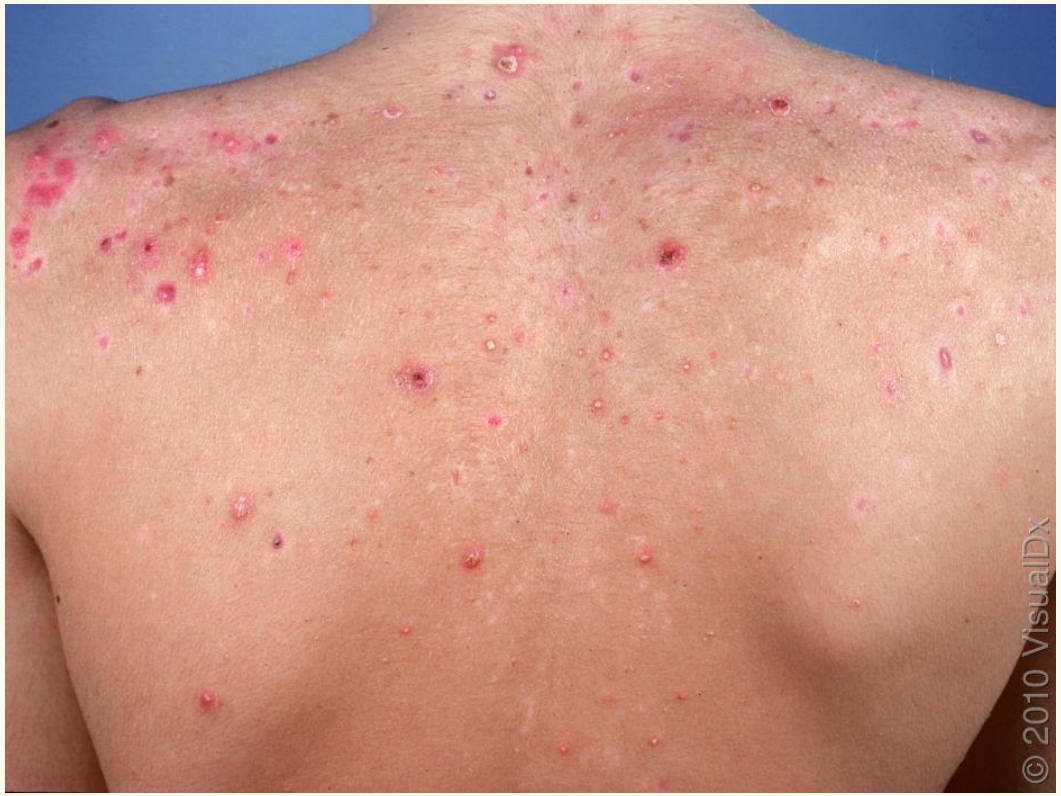
Ozenoxacin and impetigo

- Growing resistance to standard topical therapies for impetigo
- A phase 3 study found ozenoxacin 1% cream, a topical quinolone antibiotic, effective and well tolerated in adults and children
- No serious adverse events noted
- Further study is necessary to determine appropriate use of ozenoxacin in the treatment algorithm for impetigo
- Ozenoxacin not yet commercially available

Reference: Rosen T, Albareda N, Rosenberg N, et al. Efficacy and Safety of Ozenoxacin Cream for Treatment of Adult and Pediatric Patients With Impetigo: A Randomized Clinical Trial. JAMA Dermatol 2018; 154:806.

Case 7





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- Baricitinib is currently approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA
- WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS

Trifarotene (Aklief)

- Topical retinoid selectively targets retinoic acid receptor gamma (the most common RAR found in the skin)
  - Exact MOA unknown
- 9 yrs and older
- Thin film once daily in the evening
- 2 Phase 3 trials, 2420 pts
  - Sig reduced inflammatory lesions as early as Week 2 on the face, and Week 4 on trunk
- Tolerated well
- Most common SEs: irritation, pruritus, sunburn
- Approved 20-1-2019 (Galderma)
- 45gm tube of .0005% $548.00

Topical clascoterone (Winlevi)

- 1% cream, an investigational topical androgen receptor inhibitor
- Approval: 8/25/2020
- Indication: 12 years and older with acne
- Systemic hormonal therapy effective for acne; typically limited to females; associated risk for systemic AEs
- 2 Phase III randomized; ~1400 males and females (> 8yrs) with acne vulgaris: more effective than a vehicle cream for reducing acne severity: 18.4% and 20.3% vs 9.0% and 6.5% with vehicle
- Dosing: thin layer BID
- Clascoterone exhibited a safety profile similar to the vehicle cream.
- AEs: erythema/reddening, pruritus and scaling/dryness; edema, stinging, and burning

AMZEEQ® (minocycline) topical foam, 4%

- Approval: Oct 2019 (Menlo Therapeutics)
- Indication: inflammatory lesions of non-nodular moderate to severe acne vulgaris in adults and pediatric patients
- Significantly reduced acne lesion counts using IGA compared with placebo
- AEs:
  - Headache
  - mild erythema
  - Hyperpigmentation
  - mild dryness

Sarecycline (Seysara)

- Approved: October 2018
- FDA Use: Mod-severe acne in patients ≤ 9
- MOA: narrow-spectrum TCN-derived antbx with anti-inflame props
- Dosing: once daily with/without food; enc increase fluids
  - 33 to 54 kg 60 mg tablet
  - 55 to 84 kg 100 mg tablet
  - 85 to 136 kg 150 mg tablet

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100263/seysara-sarecycline-

Sarecycline (Seysara)

- Two identically-designed, large, multicenter, randomized, double-blind, placebo-controlled, Phase III studies:
- 2,002 subjects 9 years of age and older with moderate to severe facial acne vulgaris
- Once-daily sarecycline 1.5 mg/kg significantly improved acne severity based on IGA success
- Significantly reduced inflammatory lesion count versus placebo at week 12.
  - **Study 1:** IGA Success: 21.9% versus 10.5% and Mean absolute reduction in inflammatory lesions: 15.3 versus 10.2.
  - **Study 2:** IGA Success 22.6% versus 15.3% and Mean absolute reduction in inflammatory lesions: 15.5 versus 11.1.

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100263/seysara-sarecycline-

Age and hyperkalemia risk for women on spironolactone

- Controversial whether to monitor potassium levels in young women on spironolactone for acne
- Retrospective study shows 0.01% among 112 women 18-45 y/o vs 17% in 12 women 46-65 y/o.
- Recommendation:
  - Periodic monitoring of serum potassium in women > 45 y/o who have risk factors for hyperkalemia
  - No need to check in others.

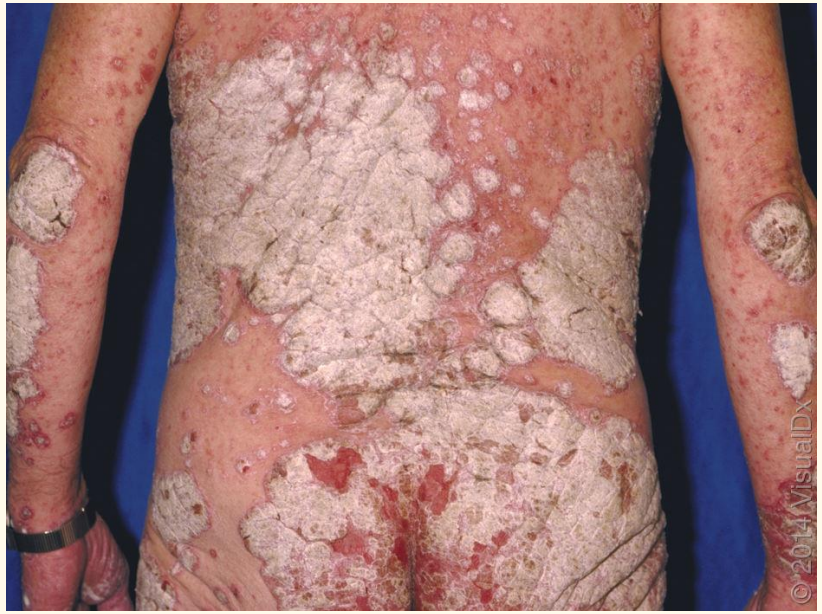
Reference: Thiede RM, Rastogi S, Nardone B, et al. Hyperkalemia in women with acne exposed to oral spironolactone: A retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. *Int J Womens Dermatol*. 2019;5(3):155–157. Published 2019 Apr 25. doi:10.1016/j.ijwd.2019.04.024

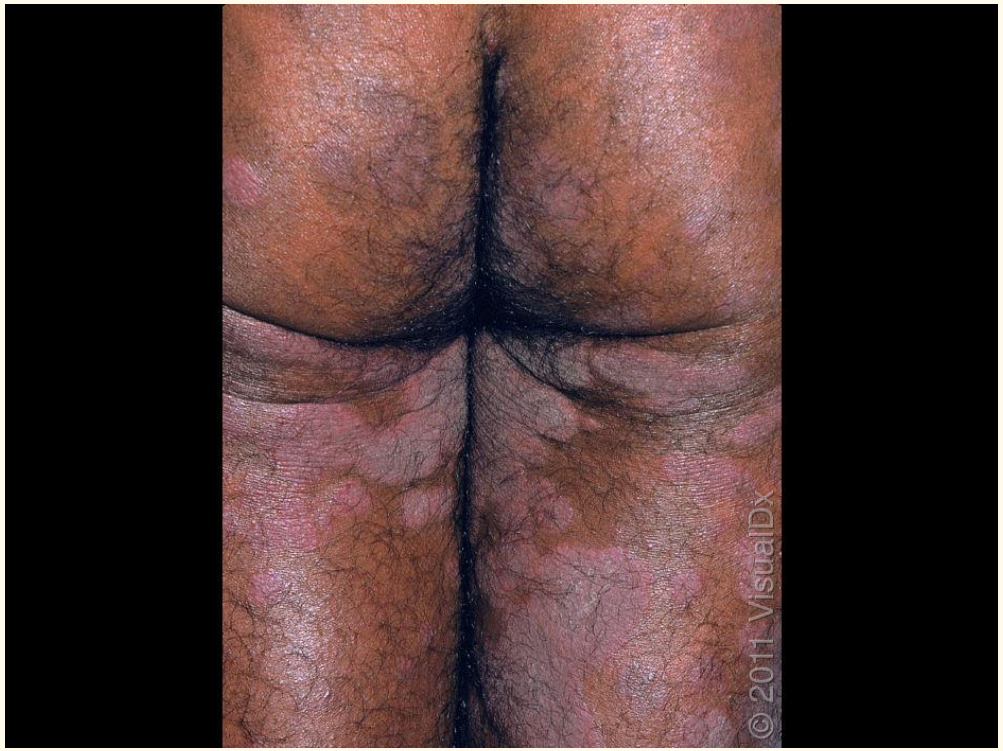
Acne and diet: NEW NEWS!!!

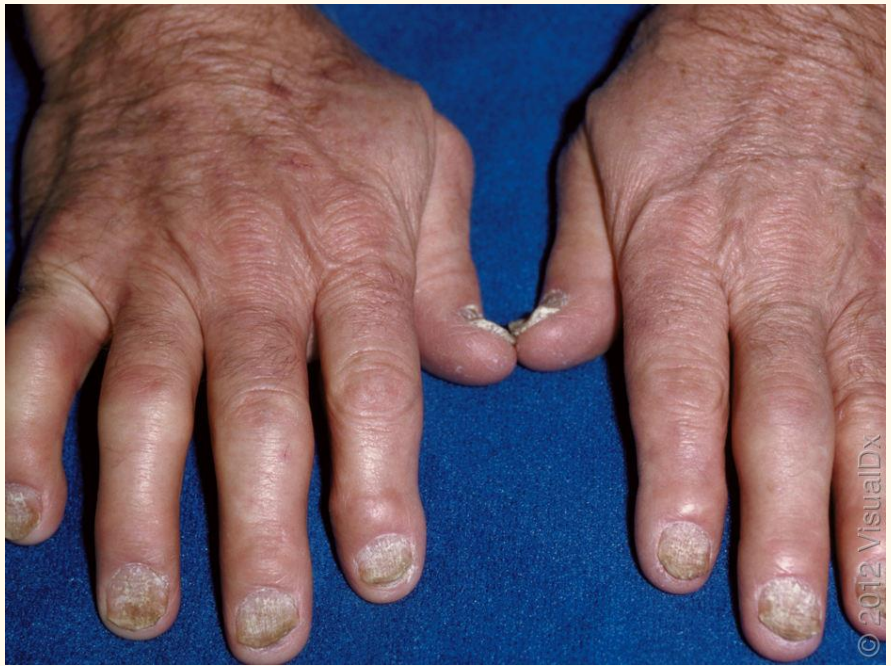
- No conclusive data in the past to link a specific diet with increased risk of acne
- Some recent studies show link between high glycemic diets can exacerbate acne
- Milk and skim milk may also exacerbate acne
- Recommendation: no specific dietary changes are recommended

Reference: Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-73.e33.

Case 8







Images kindly provided by Visual Dx

Trifarotene (Aklief)

- Topical retinoid selectively targets retinoic acid receptor gamma (the most common RAR found in the skin)
  - Exact MOA unknown
- 9 yrs and older
- Thin film once daily in the evening
- 2 Phase 3 trials, 2420 pts
  - Sig reduced inflammatory lesions as early as Week 2 on the face, and Week 4 on trunk
- Tolerated well
- Most common SEs: irritation, pruritus, sunburn
- Approved 20-1-2019 (Galderma)
- 45gm tube of .0005% $548.00

Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients

- NPF guidelines
- J AM Acad Dermatol. 2020; 82 6) 1445. Epub 2020
- Tofacitinib, apremilast, fumaric acid esters

Halobetasol/tazarotene (Duobril)

- New topical combination for adults with plaque psoriasis
- Steroid and retinoid
- 0.01/0.045% thin later of lotion to affected areas QD
- Efficacy: Clear to near clear: 36-45% Duobril vs 7-13% placebo
- Side effects:
  - contact derm
  - application site pain
  - Folliculitis
- Price: $ 800
- Approved: 2019

Calcipotriene/betamethasone (Wynzora)

- MC2 Therapeutics and EPI Health
- calcipotriene and betamethasone dipropionate, w/w 0.005%/0.064%
- Approved: July 2020 July for the treatment of plaque psoriasis in adults ages 18 years and older.
- Patented technology:
  - remain stable in an aqueous formulation
  - quickly absorbs into the skin without feeling greasy
- Phase3 study: Wynzora versus Taclonex and placebo
  - PGA clear/almost clear 14.6% (95% CI; 7.6%, 21.6%), with results in favor of Wynzora, respectively.
  - Itch reduction 4 point improvement in the 11-point peak pruritic NRS
  - Baseline to W4: larger proportion of patients reached reduction of pruritus in the Wynzora arm (60.3%) versus vehicle (21.4%)

New indications

- Ixekizumab
  - Approved for ≥ 6 years
  - Trial: 171 pts 6-17 yrs of age with mod-severe psO;
  - 89% achieved PASI-75 at W12 vs 25% on placebo

Psoriasis and new(er) therapies

- Lots of new trials of novel targets in psoriasis
- 2 phase 3 trials found risankizumab, an IL-23, p19 subunit inhibitor was superior to both ustekinumab and placebo for moderate to severe plaque psoriasis
- Guselkumab and tildrakizumab are also IL-23 inhibitors and very effective
- In addition, a phase 2 trial found the investigational tyrosine kinase 2 (TYK2) inhibitor BMS-986165 effective for improving moderate to severe plaque psoriasis
- Additional study is needed to clarify the long-term efficacy and safety of TYK2 inhibition in patients with psoriasis; psA trials ongoing

Reference:
Gordon KB, Strober B, Lebwohl M, et al. Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomized, placebo-controlled and ustekinumab-controlled phase 3 trials. Lancet 2018; 392:650.
Papp K, Gordon K, Thaçi D, et al. Phase 2 Trial of Selective Tyrosine Kinase 2 Inhibition in Psoriasis. N Engl J Med 2018; 379:1313.

Psoriatic arthritis and IL-23

- Guselkumab, (IL-23 monoclonal antibody) is approved for mod to severe psoriasis
- 150 patients with active psoriatic arthritis (PsA) and plaque psoriasis, guselkumab was more effective for PsA than placebo at 24 weeks [12].
- Well tolerated and rates of adverse events were same in both groups
- Further data are needed to determine how guselkumab compares with other biologic agents for PsA.

Reference: Deodhar A, Gottlieb AB, Boehncke WH, et al. Efficacy and safety of guselkumab in patients with active psoriatic arthritis: a randomized, double-blind, placebo-controlled, phase 2 study. Lancet 2018; 391:2213.

Psoriasis and diet

- Diet and psoriasis: is there an association?
- Based upon the findings of a systematic review, the NPF Medical Board issued dietary recommendations for adults with psoriasis or psoriatic arthritis
- Key recommendations:
  - weight reduction with a hypocaloric diet for overweight or obese adults
  - gluten-free diets for patients with celiac disease or positive serologic markers for gluten sensitivity
- The recommendations provide useful guidance for counseling patients with psoriasis or psoriatic arthritis.

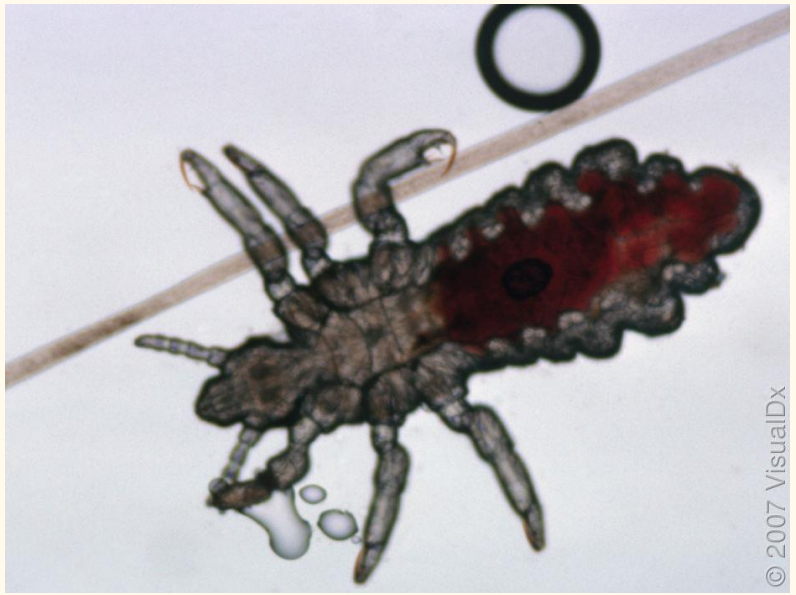
Reference: Ford AR, Siegel M, Bagel J, et al. Dietary Recommendations for Adults With Psoriasis or Psoriatic Arthritis From the Medical Board of the National Psoriasis Foundation: A Systematic Review. JAMA Dermatol 2018; 154:934.

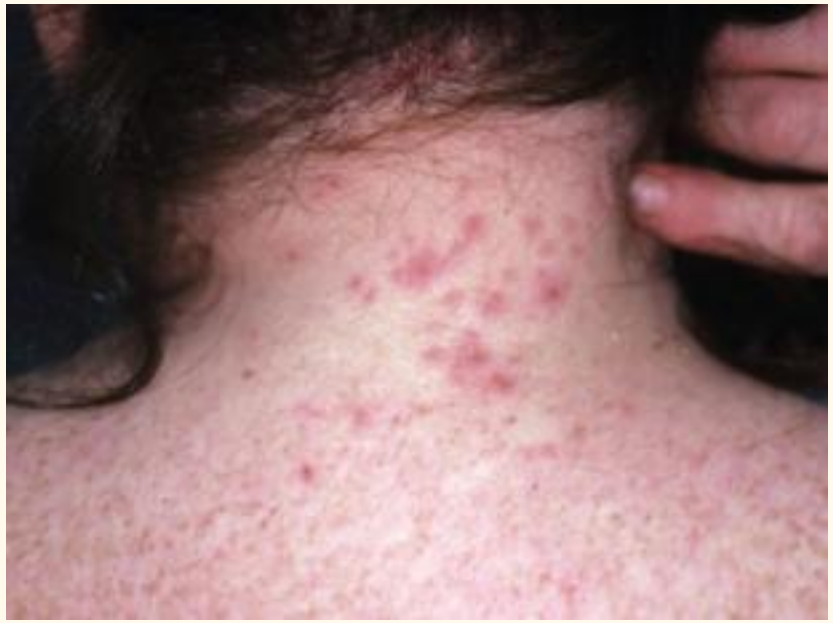
Psoriasis and certolizumab

- Certolizumab pegol (pegylated humanized TNF-alpha blocker) approved for psA
- Approved for psO: CIMPASI-1 and CIMPASI-2 trials
  - adults with mod to severe chronic plaque PsO
  - two dosing regimens of certolizumab (200 or 400 mg every two weeks) or placebo
- Certolizumab pegol improved response rates at 16 weeks that were maintained through 48 weeks
- Efficacy not compared with other psoriasis treatments
- Certolizumab pegol is also a good option in pregnancy

Reference: Gottlieb AB, Blauvelt A, Thaçi D, et al. Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). J Am Acad Dermatol 2018; 79:302.

Case 9





Images kindly provided by Visual Dx

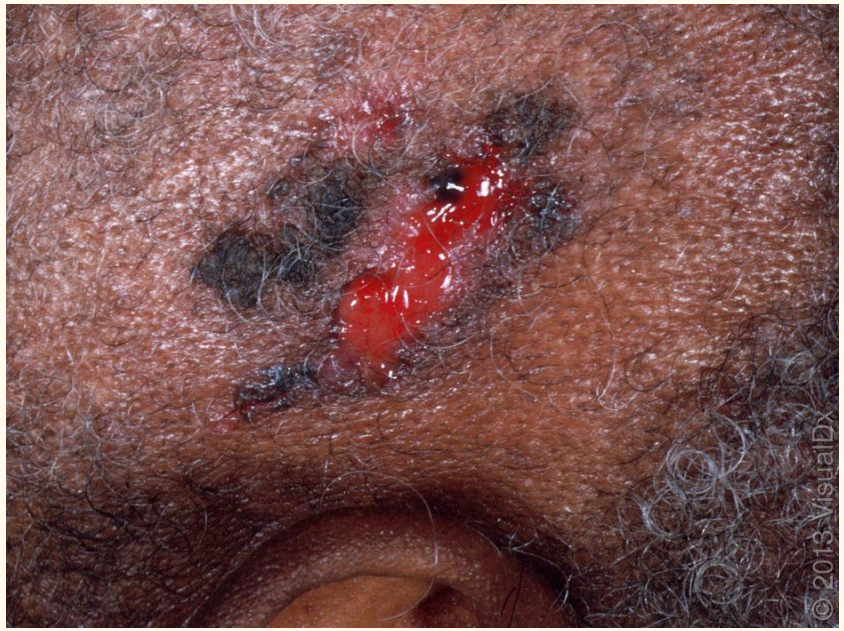
Xeglyze (abametapir) 0.74% lotion

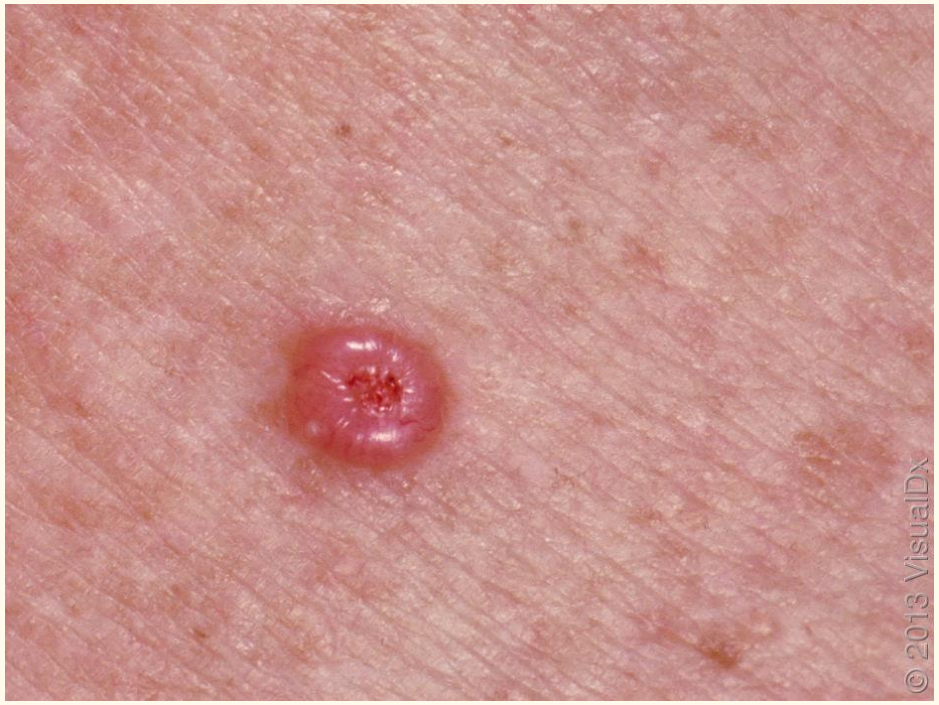
- Approval: 7/24/2020 by Dr. Reddy's Laboratories, Inc. (metalloproteinase inhibitor developed to target metalloproteinases critical to the development of adult lice and eggs)
- Indication: pediculicide indicated for the topical treatment of head lice in patients 6 months of age and older
- 2 randomized, double-blind, multicenter, vehicle-controlled studies : abametapir lotion versus vehicle control for eliminating head louse infestations without nit combing.
- Abametapir lotion was applied to dry hair for 10 minutes on day 0 and then rinsed with water.
- Checked for live lice on days 1, 7, and 14

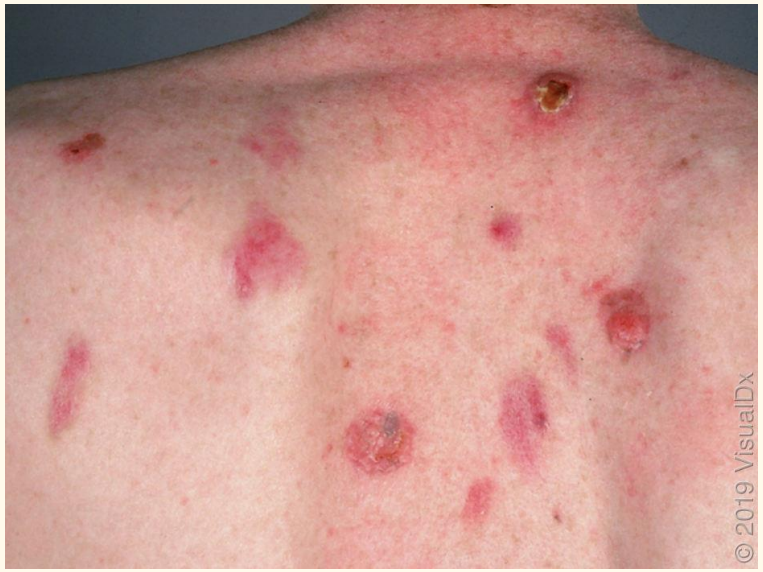
Xeglyze (abametapir) 0.74% lotion

- Primary endpoint was the proportion of index subjects (youngest household member with ≥ 3 live lice at screening) in the in ITTpopulation who were louse free at all follow-up visits through day 14. Older household members with one or more live lice at screening were designated as nonindex subjects and treated as per the index subject within their household.
- Results:
  - Index N = 216), 81.5% of subjects treated with abametapir lotion were louse free through day 14 after a single treatment, versus 49.1% with vehicle ($P < 0.001$).
  - For the combined index and nonindex population (N = 704), 85.9% were louse free through day 14 in the abametapir group, versus 61.3% in the vehicle group ($P < 0.001$).
- Adverse events: erythema, rash, skin burning sensation, contact dermatitis, vomiting, eye irritation, pruritus, and hair color change
- Conclusion:
  - Effective at clearing active head louse infestations through day 14 in subjects aged 6 months and older.
  - All adverse events (including one serious but unrelated to study drug) resolved uneventfully

Case 10







Images kindly provided by Visual Dx

NMSCs and methotrexate

- Link between low dose methotrexate (MTX) use in rheumatic disease pts and increased risk of multiple myeloma and nonmelanoma skin cancers: small number of cases

- Recent trial of MTX versus placebo for CV prevention
  - 5000 adults with elevated CV risk

- Incidence of non-basal-cell skin cancers was approximately 3x higher in the MTX group with a median follow-up of 2.3 years

- Primary endpoint of the trial showed no benefit of MTX on CV outcomes.

Reference: Ridker PM, Everett BM, Pradhan A, et al. Low-Dose Methotrexate for the Prevention of Atherosclerotic Events. N Engl J Med 2018.

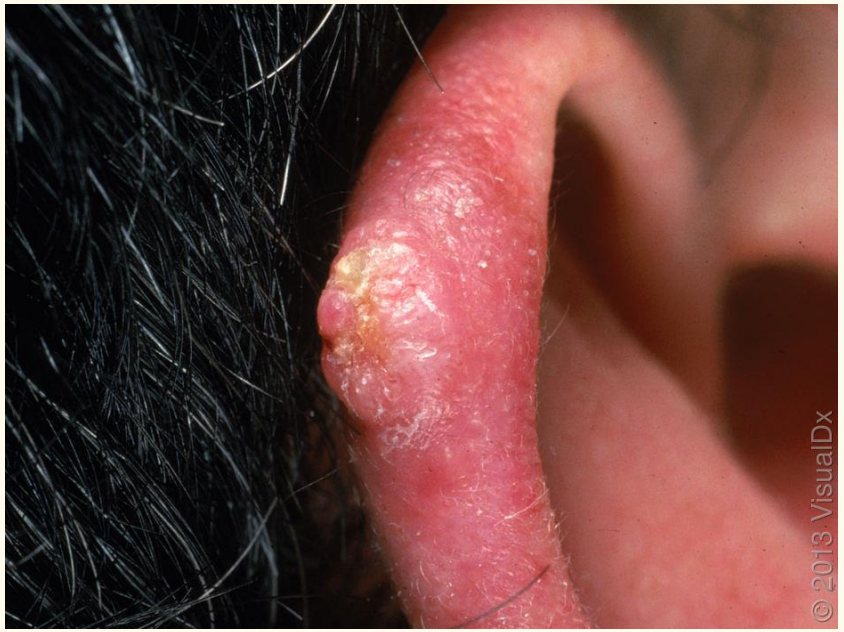
NMSCs and methotrexate

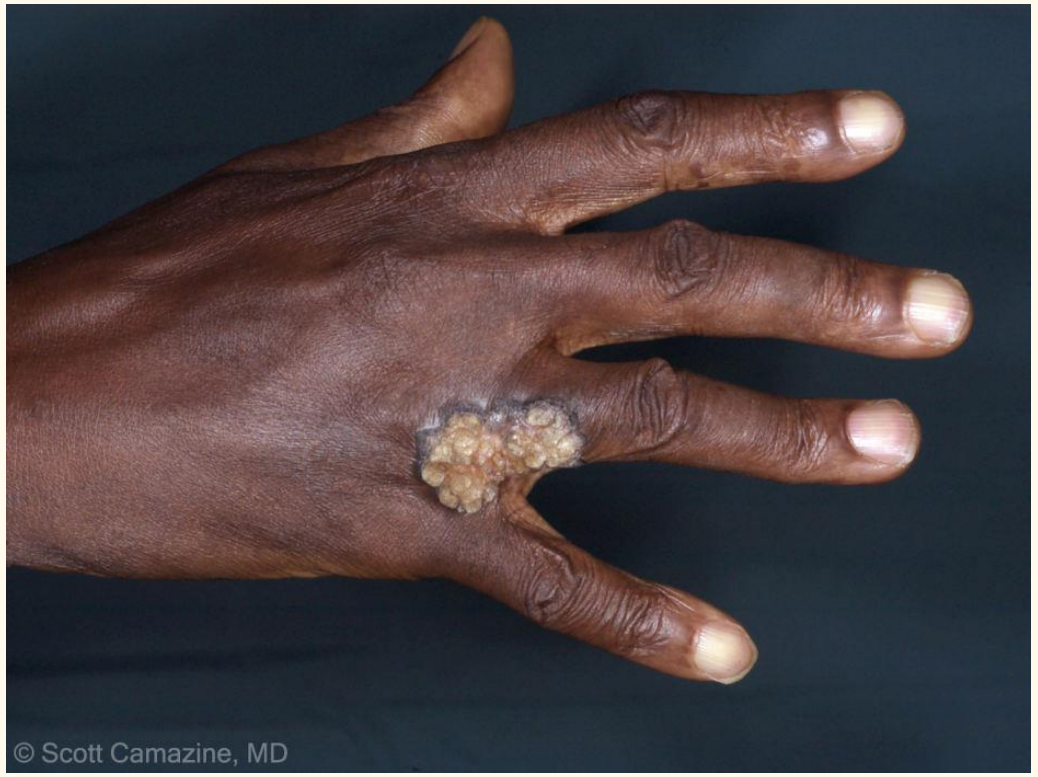
- Further study of this association is warranted in patients treated with chronic low-dose MTX for rheumatic disease and ? psoriatic disease

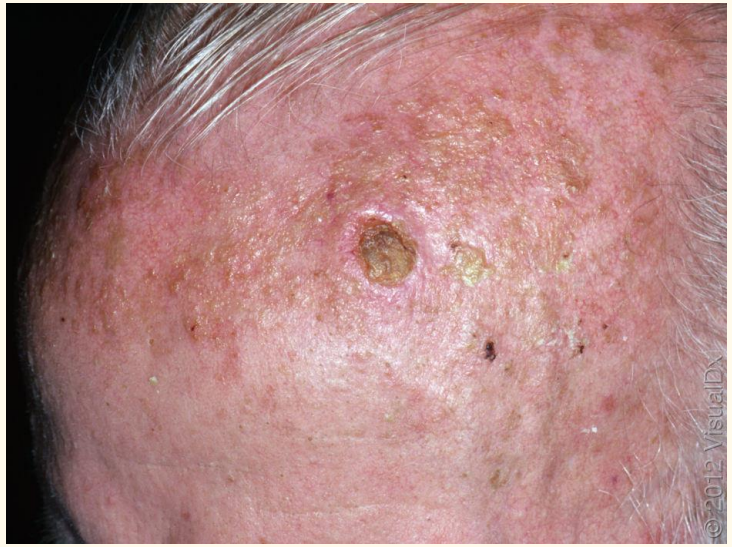
- Be cautious of long-term mtx in patients with pre-existing NMSCs and/or higher risk of CVD.

Reference: Ridker PM, Everett BM, Pradhan A, et al. Low-Dose Methotrexate for the Prevention of Atherosclerotic Events. N Engl J Med 2018.

Case 11







Images kindly provided by Visual Dx

Cemiplimab-rwlc (Libtayo)

- Approved Sept 2018: metastatic cutaneous scca/locally advanced
- Programmed death receptor-1 (PD-1) blocking antibody
- Dosing: 350 mg IV administered over 30 minutes every 3 weeks until disease progression or unacceptable toxicity
- 2 open-label trials: 108 pts (75 with mets and 33 with locally advanced disease
  - Objective response rate, partial shrinkage or complete disappearance after tmt
  - 8.9 months:
    - reduced tumor volume in 47%---61% lasting > 6 months
    - Mets: 47%, including 5% with complete responses
    - Local/inoperable: 49%
- Side effects: fatigue, rash, diarrhea

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100281/libtayo-cemiplimab-rwlc

SCCs and thiazide diuretics

- Is there a link between SCC among patients using photosensitizing medications, specifically, thiazide diuretics?

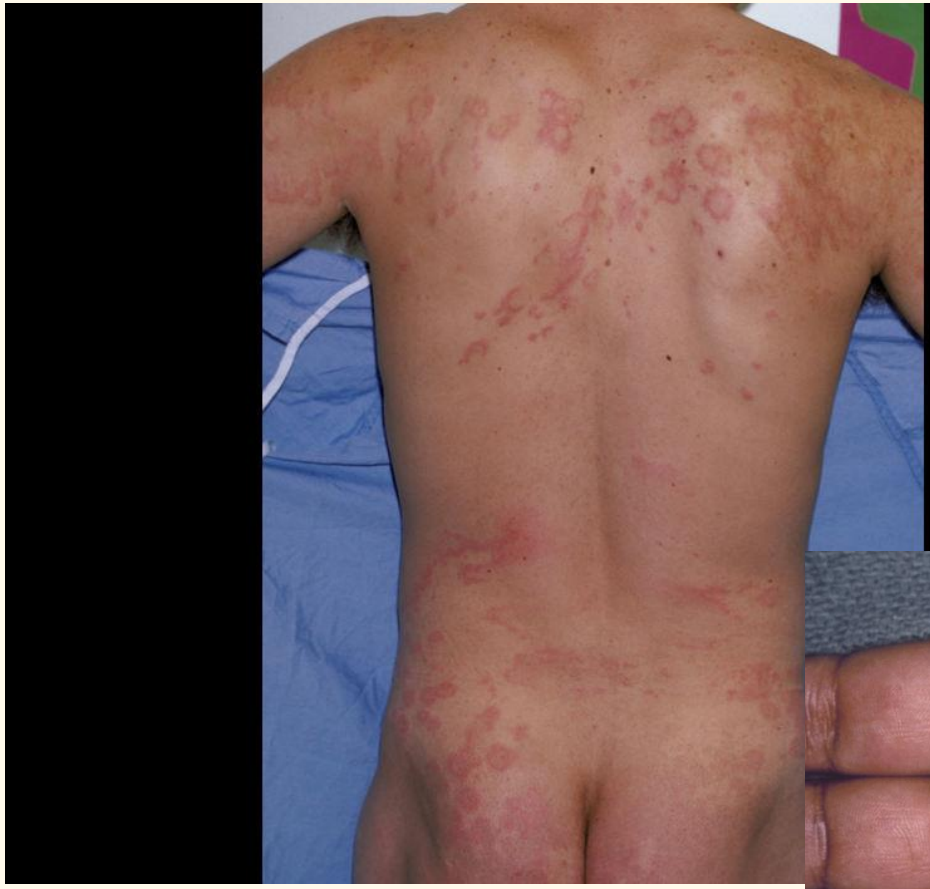
- Danish case-control study
  - 8000 patients with SCC and 172,000 controls

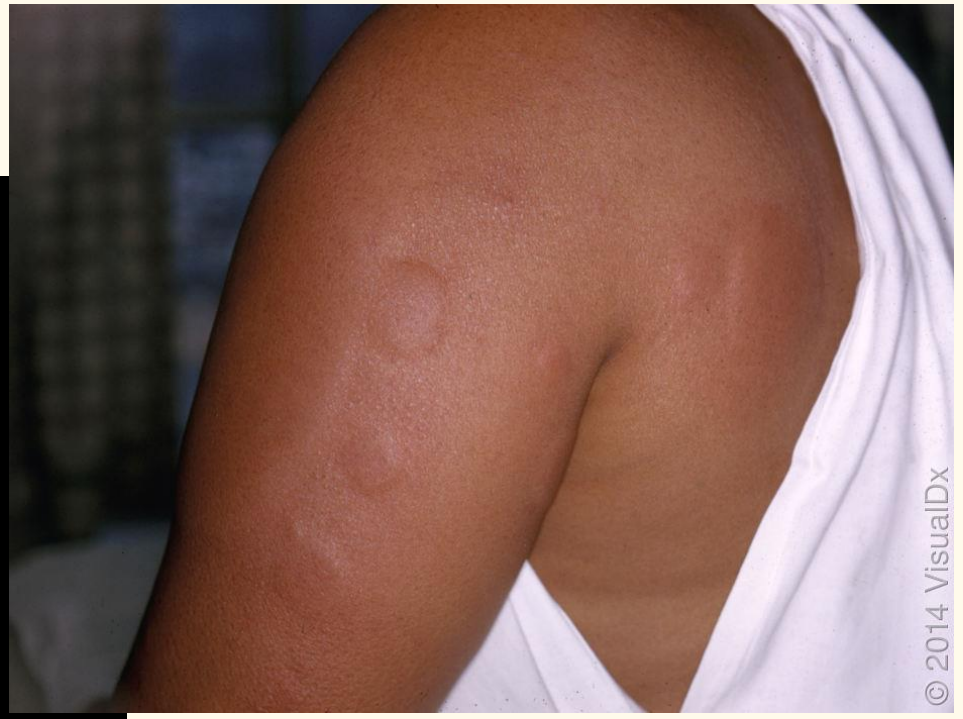
- High users of hydrochlorothiazide had a 2-7X increased risk of cutaneous SCC, with a clear dose-response effect

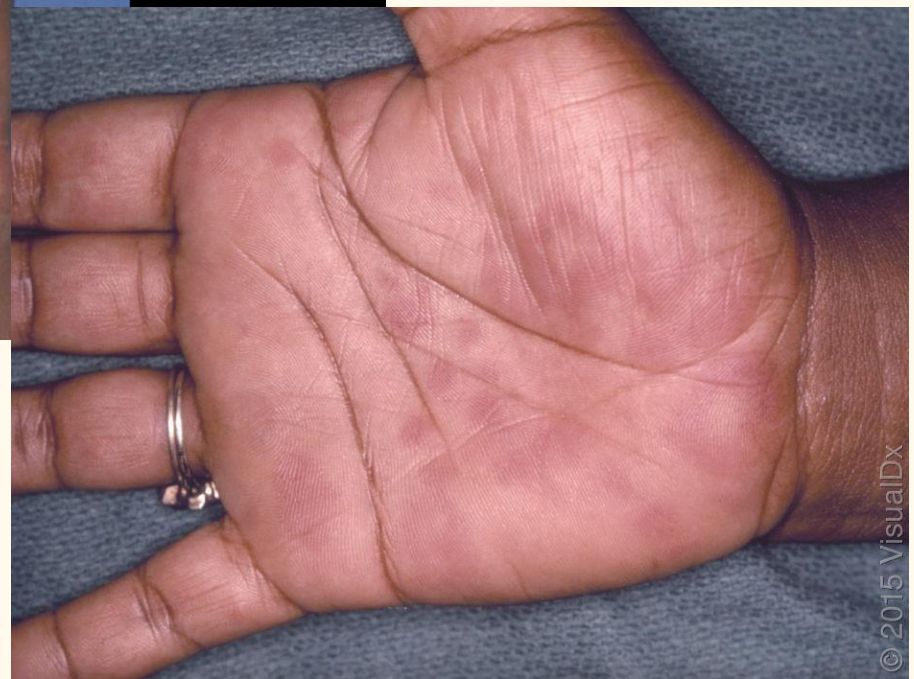
- "Although additional studies controlling for known risk factors for SCC (eg, sun exposure, phototype, smoking) are still needed, education on sun avoidance and sun protection may be appropriate for patients taking thiazide diuretics".

Reference: Pedersen SA, Gaist D, Schmidt SAJ, et al. Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol 2018; 78:673.

Case 12







Images kindly provided by Visual Dx

International guidelines for urticaria: omalizumab

- New guideline for the diagnosis and management of urticaria
  - 42 national and international dermatology and allergy societies

- Notable differences from previous American practice guidelines for chronic spontaneous urticaria refractory to high doses of a nonsedating antihistamine

Reference: Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy 2018; 73:1393.

International guidelines for urticaria: omalizumab

- New guidelines suggest proceeding directly to omalizumab (monoclonal antibody approved for asthma)

- SubQ: 150 or 300 mg every 4 weeks
  - Dosing is not dependent on serum IgE (free or total) level or body weight
  - Approved for “chronic idiopathic urticaria in adults and adolescents 12 years and older who remain symptomatic despite H_1 antihistamine treatment”

Reference: Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy 2018; 73:1393.

Case 13

Reference:https://www.google.com/search?biw=1376&bih=749&tbs=sur%3Af&tbm=isch&sa=1&ei=W_kkXO-7A4ic_QbVwJSADg&q=hyperhydrosis&oq=hyperhydrosis&gs_l=img.3..0i10l10.83279.86402..86584...2.0..0.292.2938.0j9j6.....0....1..gws-wiz-img.....0j0i67j0i24j0i10i24.-yMt384ZA-8#imgrc=VpLLWakQHMYpHM:&spf=1545927090968

Topical glycopyrronium for axillary hyperhidrosis

- Systemic anticholinergic drugs effective for hyperhidrosis
- Side effects often lead to discontinuation
- Two identical 4-week randomized trials in patients with axillary hyperhidrosis (ATMOS 1 and ATMOS 2): topical glycopyrronium tosylate, an anticholinergic drug, to vehicle
- Glycopyrronium tosylate improved diary ratings of sweating severity
  - one of the trials showed sig decrease in sweat production
- Side effects with glycopyrronium tosylate were transient, mild to moderate
- Topical glycopyrronium, expected to become commercially available in 2018, will be a treatment option for axillary hyperhidrosis not responding to antiperspirants.

Reference: https://www.uptodate.com/contents/whats-new-in-dermatology

Topical glycopyrronium for axillary hyperhidrosis

Glycopyrronium tosylate (Qbrexza)

- 9 years and older
- Apply once daily using a single cloth to clean dry skin on the underarm areas, wiping across the entire underarm once
- Do not use more frequently than once every 24 hours
- Use the same cloth for each arm
- Contraindicated: conditions that can be exacerbated by the anticholinergic effect (eg, glaucoma, paralytic ileus, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis, Sjogren syndrome

Reference: Micromedex: glycopyrronium tosylate

Glycopyrronium tosylate (Qbrexza)

Common Adverse Effects:

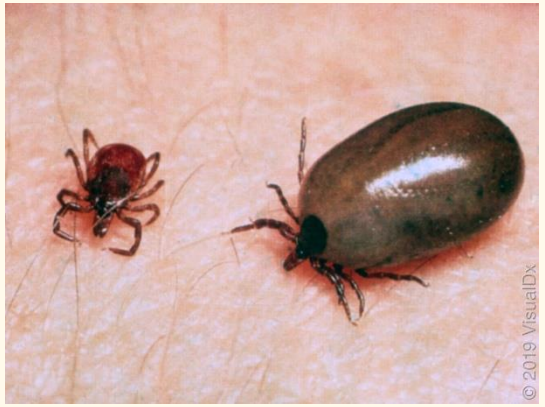
- **Dermatologic:** Burning sensation, Dry skin (2.2%), Erythema (2.4% to 17%), Pruritus (3.8% to 8.1%), Stinging of skin
- **Gastrointestinal:** Constipation (2%), Pain in throat (5.7%), Pharyngeal dryness (2.6%), Xerostomia (16.9% to 24.2%)
- **Neurologic:** Headache (5%)
- **Ophthalmic:** Dry eyes (2.4% to 2.9%), Mydriasis (5.3% to 6.8%)
- **Renal:** Delay when starting to pass urine (3.5% to 4.2%)
- **Respiratory:** Nasal mucosa dry (2.6% to 3.6%)

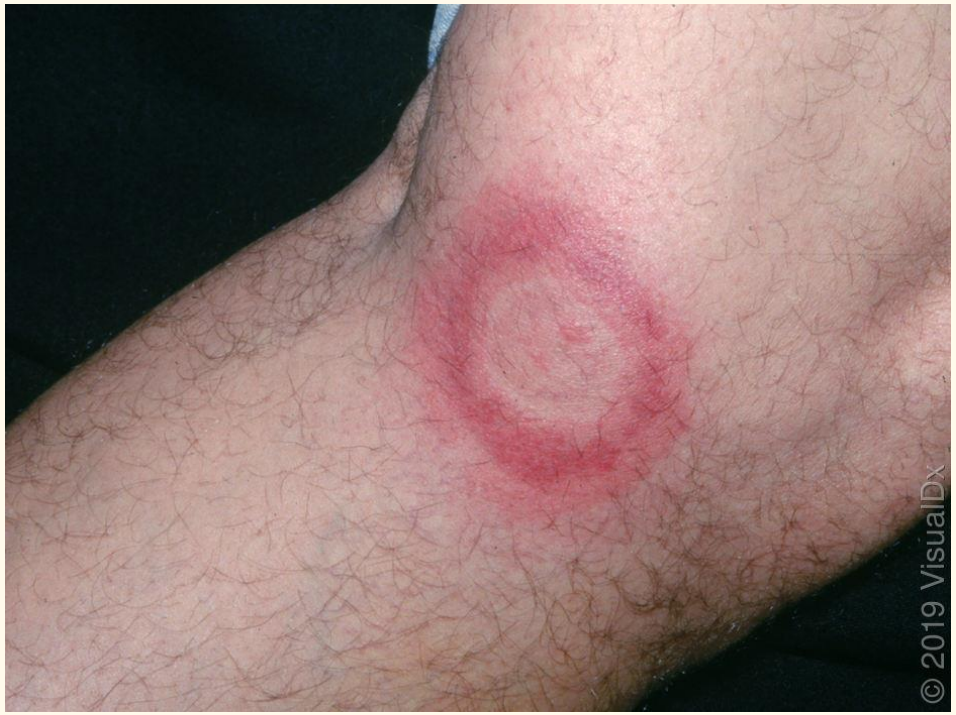
Serious:

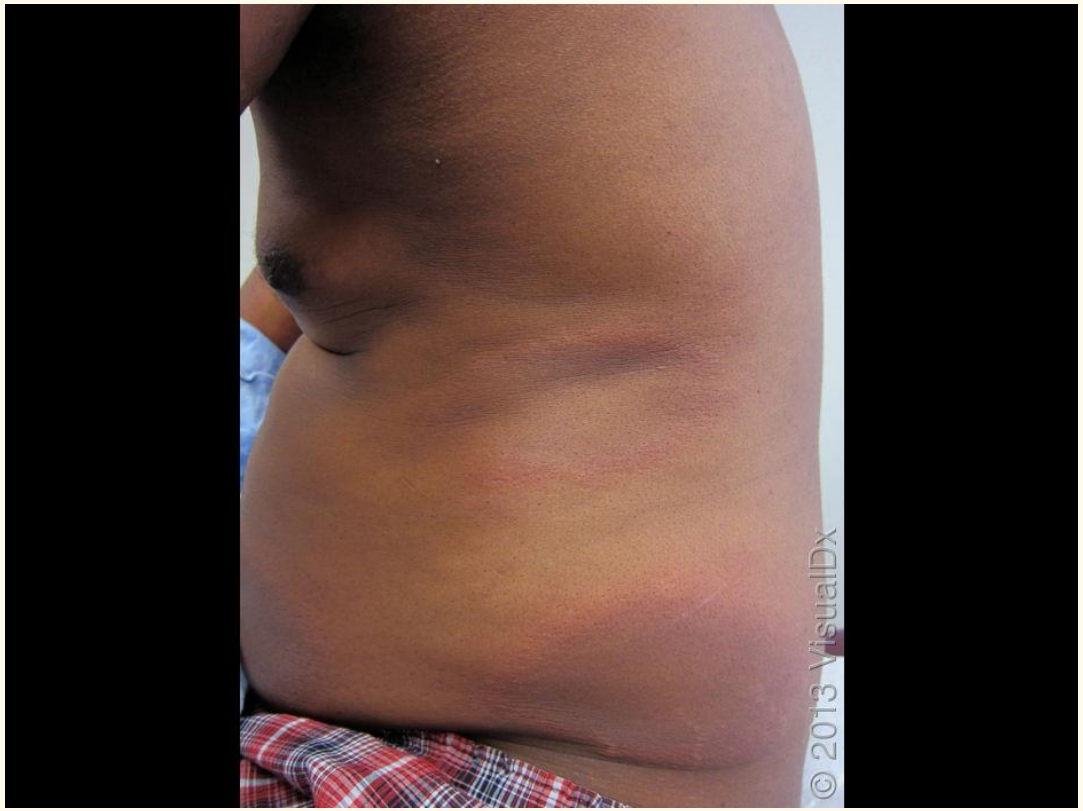
- **Dermatologic:** Heat illness
- **Ophthalmic:** Blurred vision (3.5% to 6.7%)
- **Renal:** Urinary retention

Reference: Micromedex: glycopyrronium tosylate

Case 14







Images kindly provided by Visual Dx

Doxycycline in children

- Tetracycline antibiotics: avoid in children <8 years d/t risk of permanent tooth discoloration associated with repeated use
- Doxycycline binds less readily to calcium than other tetracyclines
- Risk of dental staining with short courses of doxycycline is minimal
- Updated recommendations from the American Academy of Pediatrics: doxycycline for ≤21 days in children of all ages
- Children who use doxycycline should avoid excess sun exposure given the photosensitivity associated with doxy

Reference: American Academy of Pediatrics. Tetracyclines. In: Red Book: 2018 Report of the Committee on Infectious Diseases, 31st ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics, Itasca, IL 2018. p.905.

Doxycycline in children

- Increase fluid intake to prevent esophageal irritation/ulcers
- Extended release should not be used in children of any age

Lyme disease:

- (8 years or older) 4 mg/kg ORALLY in 2 divided doses for 14 days (range, 10 to 21 days) in early localized or early disseminated Lyme disease associated with erythema migrans;
  - for 14 days (range, 14 to 21 days) in Lyme carditis to complete a course of therapy or to treat ambulatory patients
  - for 14 days (range, 14 to 21 days) for seventh-cranial-nerve palsy with no CNS involvement
  - for 28 days for Lyme arthritis without neurological involvement
  - for 14 days (range, 10 to 21 days) for borrelial lymphocytoma
  - for 21 days for acrodermatitis chronica atrophicans; maximum daily dose, 200 mg
- (8 years or older, intolerant of beta-lactam agents) 4 to 8 mg/kg/day ORALLY in 2 divided doses for 14 days (range, 10 to 28 days) for Lyme meningitis or seventh-cranial-nerve palsy with CNS involvement
  - for 14 days (range, 14 to 21 days) for Lyme carditis for the initial treatment of hospitalized patients; maximum daily dose, 200 to 400 mg

Reference: Micromedex: Doxycycline

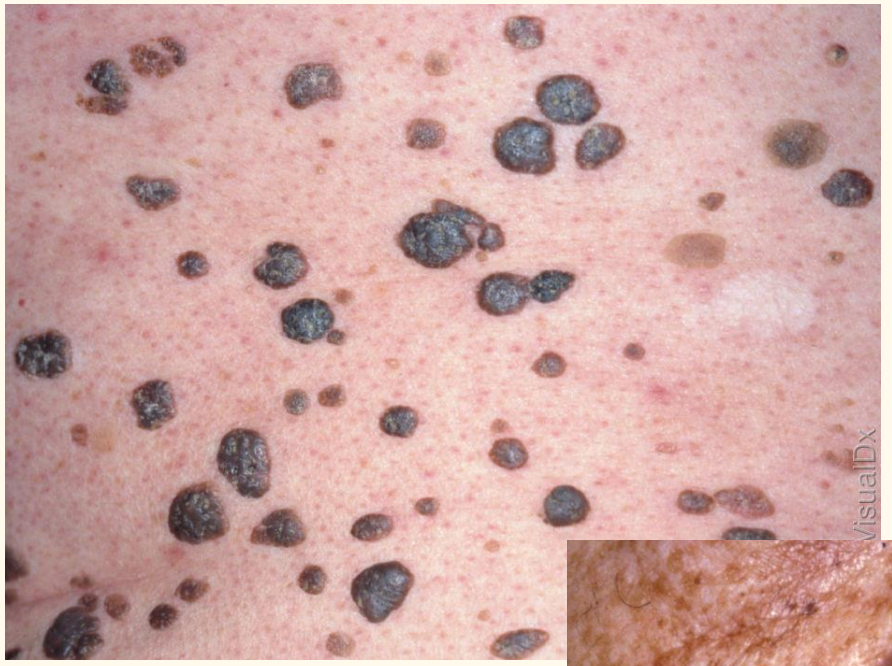
Doxycycline in children

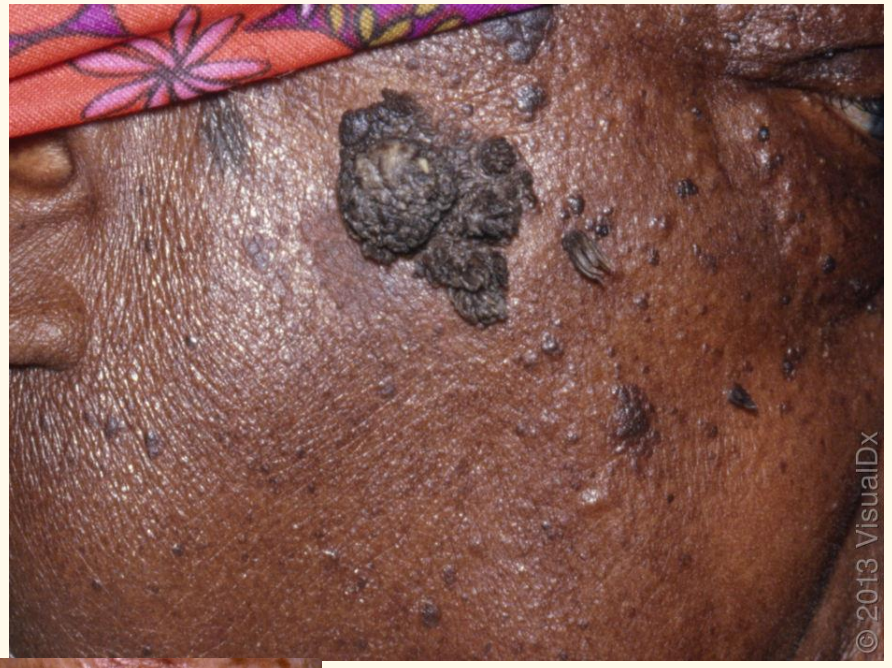
Acne:

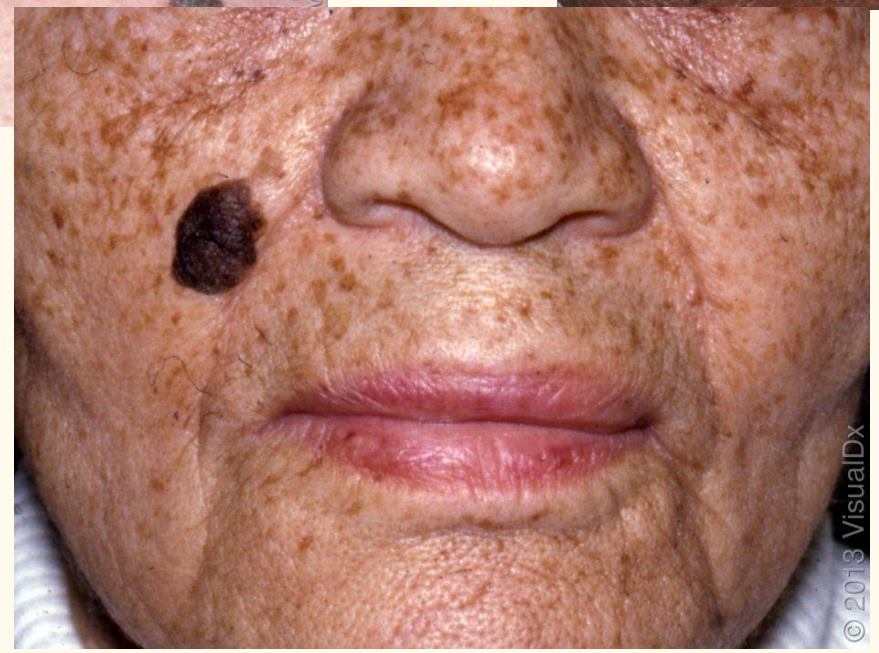
- (older than 8 years, under 45 kg) 4.4 mg/kg ORALLY in 1 to 2 divided doses on day 1, then 2.2 to 4.4 mg/kg/day ORALLY in 1 to 2 divided doses
- (older than 8 years, over 45 kg) 100 mg ORALLY every 12 hours on day 1, then 100 mg/day ORALLY in 1 to 2 divided doses or severe infections, 100 mg ORALLY every 12 hours if severe infection

Reference: Micromedex: Doxycycline

Case 15







Images kindly provided by Visual Dx

Hydrogen peroxide (Eskata)

- Approved December 2017
- High concentration (40%) hydrogen peroxide-based topical solution
- Indicated for treatment of raised seborrheic keratosis
- Single, in-office treatment session: applies to SKs 4 times, 1 minute apart
- If not cleared after 3 weeks, may repeat
- Side effects: erythema, stinging, edema, scaling, crusting, pruritus

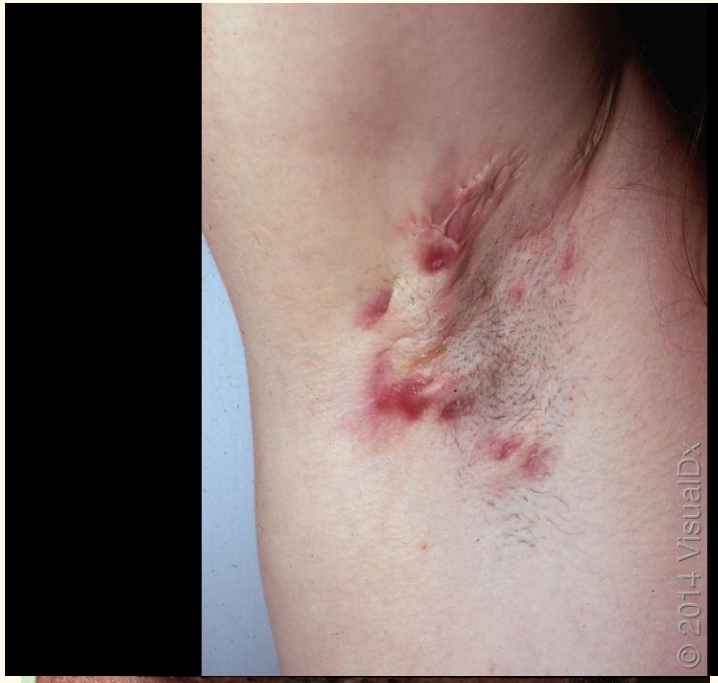
Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100242/eskata-hydrogen-peroxide

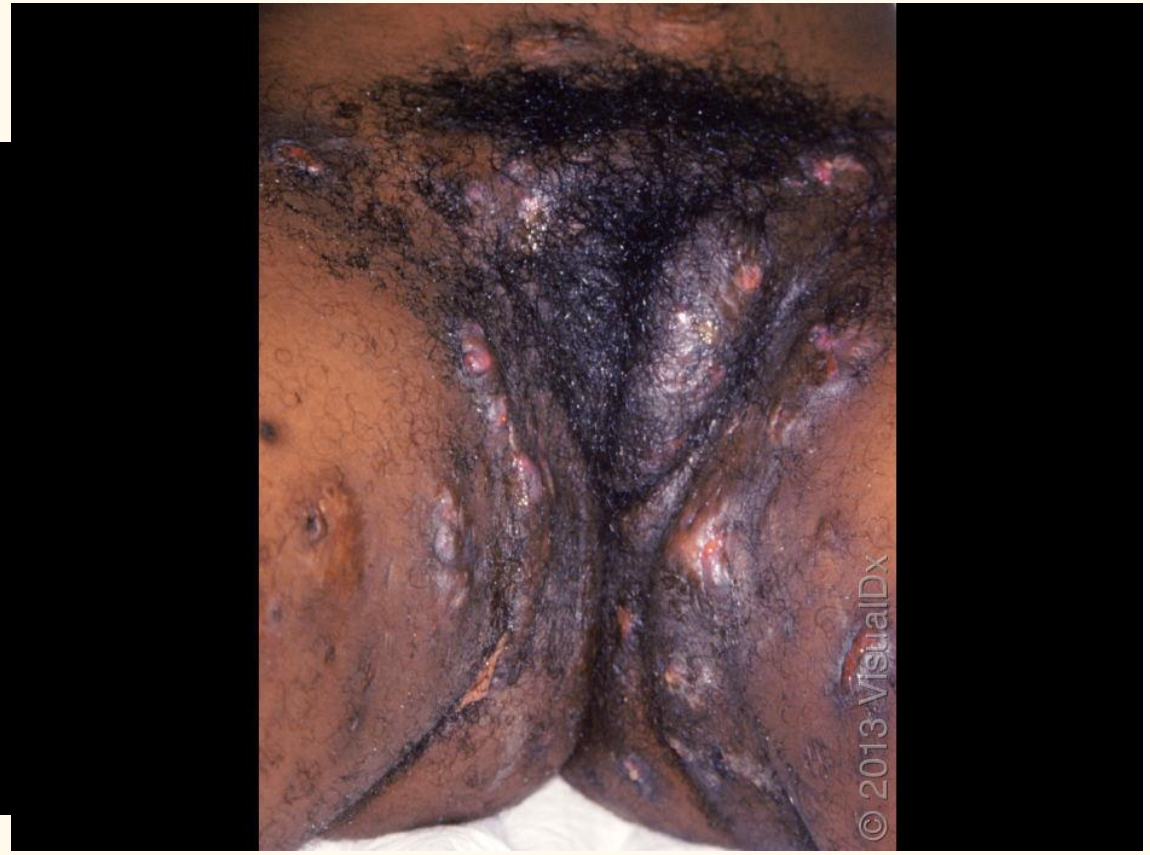
Hydrogen peroxide (Eskata)

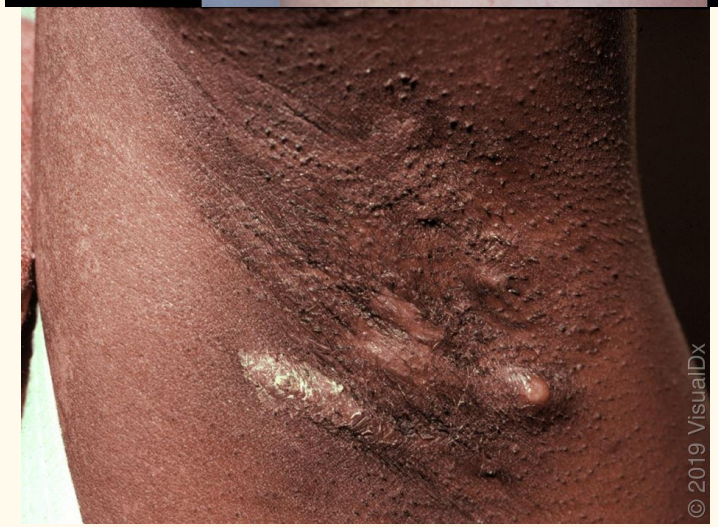
- 2 phase 3 trials (SEBK-301, SEBK-302)
- 937 patients
- 51.3% of lesions treated with Eskata were assessed as clear or near clear versus 7.3% of lesions in the placebo group
- The primary endpoint of both trials was the percentage of patients treated with Eskata who achieved clearance (PLA=0) of all four target SK lesions.
- In the SEBK-301 trial, 4.0% of patients treated with Eskata achieved clearance of all 4 target SK lesions ($p<0.002$
- SEBK-302 trial, 7.8% of treated patients achieved clearance of all four target SK lesions ($p<0.0001$).
- None of the patients administered placebo achieved clearance of all four target SK lesions in either trial.
- SEBK-301 trial, 13.5% of patients treated with Eskata achieved clearance of at least three of the four target SK lesions ($p<0.0001$);
- SEBK-302 trial, 23.0% of treated patients achieved clearance of at least three of the four target SK lesions ($p<0.0001$).

Reference: https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/100242/eskata-hydrogen-peroxide

Case 16







Images kingly provided by Visual Dx

Hidradenitis suppurativa

- New North American clinical management guidelines for HS (July 2019)
- Prevalence is 0.1-2%, > in 3rd and 4th decades of life
- Significant QOL issues
- Zinc: 90mg daily and topical triclosan 2% x 3 months
- Vit D: get to normal levels (63% achieved 20% decrease in inflammatory nodules)
- I & D large lesions

Reference: Albrecht, J and Bigby, M. (2019)*Rifampin and Clindamycin are safe long term Response to North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations Part II: Topical, intralesional, and systemic medical management*.Journal of the American Academy of Dermatology. https://doi.org/10.1016/j.jaad.2019.02.067

Adalimumab in HS

- Only FDA-approved agent for moderate to severe HS
- Dosing is 160mg SC day 1, then 80mg day 8, then 40mg every 7 days thereafter
- Can add doxycycline 50-100mg BID
- Benzoyl peroxide is a good topical astringent; can bleach clothing

IL-17s in HS

- Small French study with N=18, long-standing HS
- 4/18 patients met the Hidradenitis Suppurativa Clinical Response (HiSCR) criteria after W24
- Overall, study population had a statistically significant decrease in the Sartorius Scale
  - disease activity
  - QOL
- High levels of these cytokines in HS skin/blood:
  - TNF-a
  - IL-1b
  - IL-17
  - IL-23
  - several other types of interleukins

Now some fun facts…..

False eyelashes and extensions

- Cyanoacrylate glues can cause dermatitis
- Sleeping in false eyelashes can break or pull out natural lashes
- Expensive

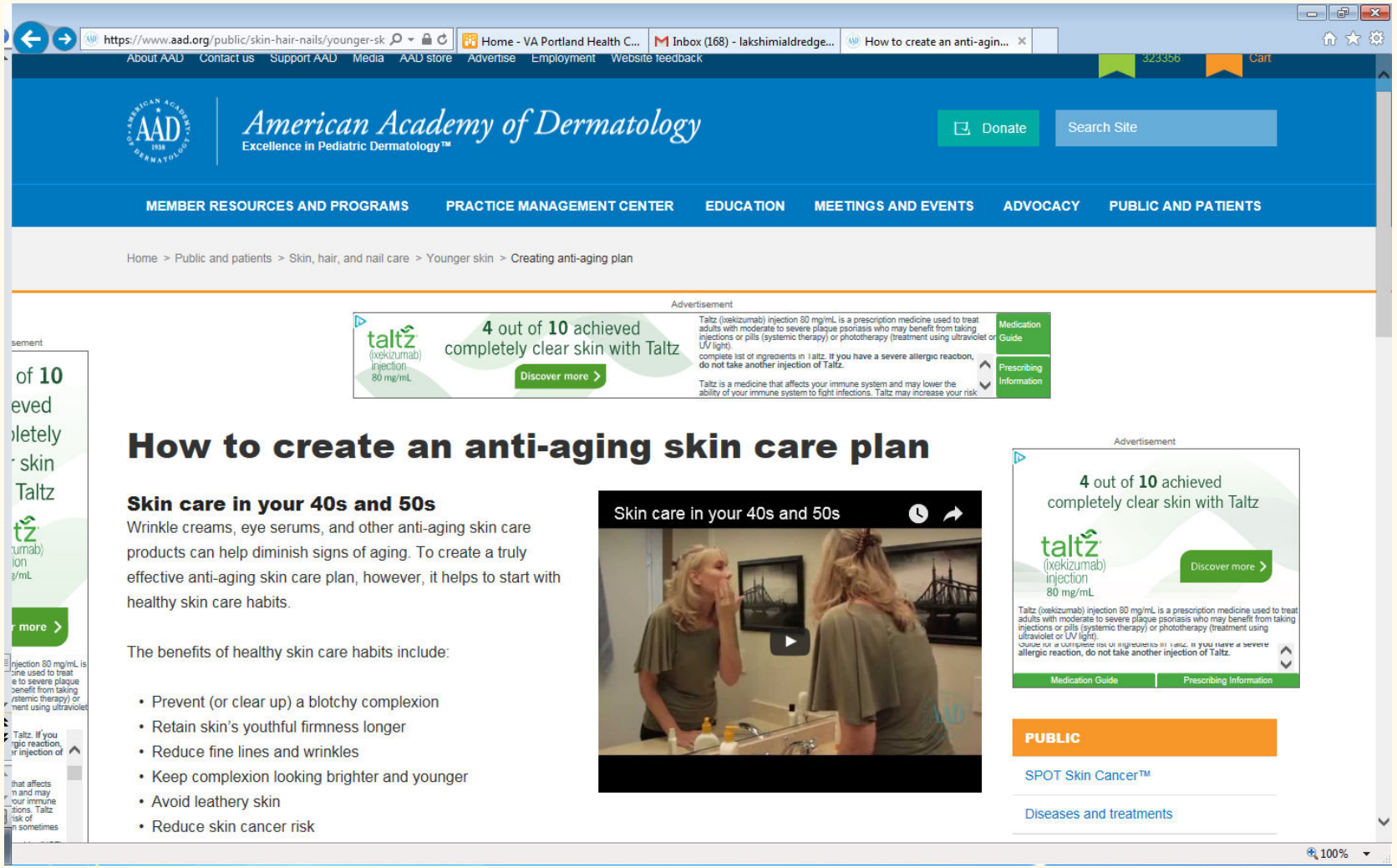
Micellar water

- Contains micelles (tiny balls of hydrophobic molecules surrounded by a hydrophilic layer) and mild detergent
- Good cleanser for both waterproof and water-removal cosmetics
- Useful for patients with eyelid dermatitis, eczema, atopic derm, and “mature” skin
- Cost: 5-10$ (small bottle of diluted baby shampoo)

But what about my *wrinkles*?

https://commons.wikimedia.org/wiki/File:Zmarszczki.jpg

Refer to the AAD



Reference: AAD. "How to create an anti-aging skin care plan". At https://www.aad.org/public/skin-hair-nails/younger-skin/creating-anti-aging-plan

AAD Anti-aging skin care tips

- **Protect your skin from the sun:** Sun protection forms the foundation of every anti-aging skin-care plan. The sun's rays make our skin age more quickly. We have so much evidence that the sun prematurely ages our skin that there is actually a word to describe this effect. This word is "photo aging." To help patients protect their skin from the sun and other harmful UV rays, dermatologists offer these tips:
  - **Seek shade:** Be sure to seek shade between 10 a.m. and 2 p.m. and whenever your shadow looks shorter than you are.
  - **Cover up in style:** Whenever possible, wear a wide-brimmed hat, pants, and long sleeves. Gloves help to minimize common signs of aging on our hands such as age spots. Sunglasses help reduce fine lines around our eyes.
  - **Slather on the sunscreen every day before going outdoors:** To protect your skin, apply sunscreen to all skin that clothing will not cover. You want to use a sunscreen that offers broad-spectrum protection, SPF 30 (or higher), and water resistance.

Reference: AAD. "How to create an anti-aging skin care plan". At https://www.aad.org/public/skin-hair-nails/younger-skin/creating-anti-aging-plan

AAD Anti-aging skin care tips

- **Apply moisturizer every day:** As we age, skin becomes drier. Fine lines and wrinkles appear. Moisturizer traps water in our skin, giving it a more youthful appearance. For best results, use a facial moisturizer, body moisturizer, and lip balm.
- **Wash away dirt and grime twice a day:** How you wash your face can affect your appearance. For best results, you want to wash with warm water and a mild cleanser rather than soap. You also should avoid scrubbing your skin clean.
- **Stop smoking:** Tobacco smoke contains toxins that can lead to smoker's face. Signs of smoker's face include dull and dry complexion, loss of skin's firmness, premature lines and wrinkles, and leathery skin.
- **Eat healthy foods:** A healthy diet promotes healthy skin. Make sure you eat plenty of fruits and vegetables, lean proteins, and healthy fats.
- **Get enough sleep:** It's called beauty rest for a reason. Sleep gives your body time to refresh and renew itself.

Reference: AAD. "How to create an anti-aging skin care plan". At https://www.aad.org/public/skin-hair-nails/younger-skin/creating-anti-aging-plan

AAD: “Dermatologists share their insider tips”

- Start with sunscreen and moisturizer
- Treat your #1 aging-skin concern: wrinkles, dark spots
- Buy a product formulated for your skin type
- Read product labels and select a product that offers all of the following
- Have realistic expectations
- Select a product within your price range
- Maximize the results you see

Reference: AAD. “How to select anti-aging skin care products”. At https://www.aad.org/public/skin-hair-nails/younger-skin/selecting-anti-aging-products.

Educational pearls for patients

- Obtain the proper diagnosis
- Avoid Dr. Google and blogs
- Seek reputable sources for treatment options
- Know your budget/insurance plan
- Set realistic expectations
- Be cautious of “fast cures”
- Use treatments as recommended
- Give it time to work
- Avoid multiple treatments at the same time
- Keep follow up appointments

Objectives: revisited

- The learner will be able to identify 3 biologic therapeutic targets and agents for the treatment of psoriasis (IL-23, TNF-alpha, IL-17)
- The learner will be able to identify 2 novel therapeutic agents for the treatment of atopic dermatitis. (PDE4, IL 4-13)
- The learner will be able to identify 3 key patient teaching pearls in order to improve adherence to dermatologic therapies. (avoid multiple tmts at once, give it time, set realistic expectations)
- The learner will be able to identify 5 key parameters to assess efficacy for the treatment of common dermatologic conditions. (reduction in inflammatory lesions, decrease in erythema, decrease in pain, decrease in itch, decrease in flares)

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Thank you!

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