What's New in Medicine Kennewick, WA

## Common Dermatologic Problems in Kids

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#### **Disclosure Statement**

Consultant: Leo (Tralokinumab), Lilly (Lebrikizumab) Speaker: Beiersdorf (Aquaphor)

I will discuss off label use of medication I see exclusively pediatric patients, most of whom are on Medicaid

#### Outline

- 1. What are the most common things I see?
- 2. What's New?
- 3. What are the most common questions parents ask?
- 4. What are the most common questions asked by providers?

#### Atopic Dermatitis (aka eczema)

#### Case 1

• 8 month old boy with itchy rash on face, trunk extremities. Parents are frustrated.



#### What is New In Atopic Dermatitis?

- A lot!
- New comorbidities
- 4 novel FDA-approved treatments in the past year

#### Is associated

#### Is probably associated May be associated Is uncertain May not

#### <sup>d</sup> Table III AD Comorbidity Statements

Atopic	Immune	Mental Health	ADHD and Autism spectrum	Cardio Vascular	Metabolic	Bone	Infection
<mark>Asthma</mark>	Alopecia areata	Depression	ADHD	<mark>HTN</mark>	<mark>Obesity</mark>	Osteoporosis	Skin infection
Food allergy	Urticaria	Anxiety	<mark>Autism</mark>	Coronary artery disease	Dyslipidemia	Fractures	
Allergic rhinitis		<mark>Suicide</mark>		Myocardial infarction	<mark>Diabetes</mark>		
Eosinophilic esophagitis		<mark>Alcohol</mark> abuse		<mark>Stroke</mark>			

Davis DM et al, JAAD, 2022

AAD Guidelines: Comorbidities takeaway • No surprise: food allergy, asthma

 Newer associations: ADHD, depression, anxiety, cardiovascular conditions, metabolic syndrome, substance abuse, osteoporosis and fractures

• Actionable: \*

- Situational (eg child not focused in school);
- Tween or teen (screen for depression);
- Adult (consider with other CV risk factors)
- Consider earlier, more aggressive treatment of inflammation to mitigate extracutaneous outcomes? A la psoriasis
- Infections- HSV; Vaccines; COVID

## What is New Therapeutically?



## What's New?

- Crisabarole
  - Topical phosphodiesterase inhibitor for mild to moderate AD
  - Non-steroidal, approved down to 3 months of age
  - No boxed warning
  - Stings many
- Dupilumab
  - Injectable biologic for <u>moderate to severe AD</u>
  - Approved down to 6 months of age
  - Life altering for some
  - 5-10% develop inflammatory conjunctivitis

• Nguyen HL et al. New and emerging therapies for pediatric atopic dermatitis. Pediatric Drugs 2019 Aug;21(4):239-260

Mechanism	Agent	Indication	Route	Phase
Anti II 12 m Ab	Lebrikizumab	Moderate to severe	SC	3
Anti–IL-13 mAb	Tralokinumab	Severe	SC	3
Anti–IL-31 mAb	Nemolizumab	Moderate to severe	SC	3
JAK1/2 inhibitor	Baricitinib	Moderate to severe	Oral	3
	<mark>Ruxolitinib</mark>	Mild to moderate	Topical	3
JAK 1 inhibitor	<mark>Abrocitinib</mark>	Moderate to severe	Oral	3
JAK 1 inhibitor	<mark>Upadacitinib</mark>	Moderate to severe	Oral	3

#### Parental Questions

- Is bathing good or bad?
- What causes it?
- When will my child grow out of it?
- Is it due to a food allergy? What harm could there be in just eliminating foods to see if that helps?

## Role of bathing



## Is Moisturizing Good for Atopic Dermatitis?

#### Is Bathing Good for Atopic Dermatitis?

#### Is bathing regularly good or bad for atopic dermatitis?

#### • YES!

#### **BATHING DRIES**

#### THE SKIN -- TRUE:

Wetting followed by evaporation causes stratum corneum contraction and fissures, impairing the epidermal barrier.



# 

#### **BATHING HYDRATES**

THE SKIN -- TRUE, IF:

Moisturizer is applied within 3 minutes to retain hydration, keeping the stratum corneum barrier intact and flexible.



#### How Do You Convince Parents?



## **Bleach baths**

\*Gain acceptance, start low, rinse afterwards

- Prevention AND treatment
  - Mechanism: Anti-inflammatory
  - Newer evidence suggests they do not kill staph
- Formula varies
  - ¼ cup per full tub in adult atopic patients
  - Teaspoon per gallon (eg "bleach showers")

#### CLn wash for teens

- Can use more frequently if tolerated
- Huang JT et al. Treatment of staphylococcus aureus colonization in atopic dermatitis decreases disease severity. Pediatrics 2009 May 123(5):e808-14
- Sawada Y et al. Dilute bleach baths used for treatment of atopic dermatitis are not antimicrobial in vitro. J All Clin Immunol 2019;143(5):1946-8

#### Etiological Factors in Atopic Dermatitis

Genetic immunology: TSLP, IL-4, IL-13, TLR-2, IGE/FcεRI

Non-genetic immunology: Allergic sensitization

ATOPIC DERMATITIS Genetic barrier dysfunction: Filaggrin, Spink/LEKTI, Hornerin, CARD14

Non-genetic barrier dysfunction: Dryness, excoriations, microbial, toxins, phototoxicity

Eyerich K, et al. *Allergy*. 2013;68(8):974-982.

Is Atopic Dermatitis an Allergic Disease or a Disease with Allergies?



#### **Food Allergies and Atopic Dermatitis**

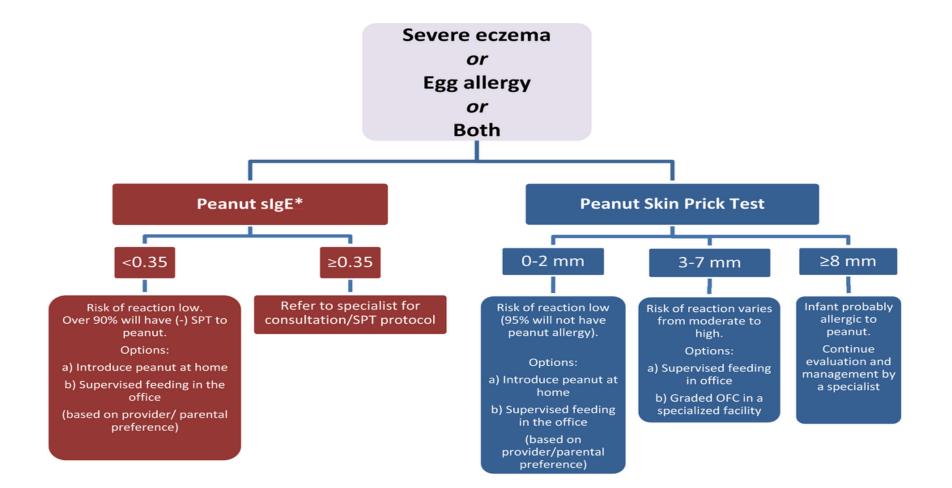
Is it a cause? Is it a trigger? Is it unrelated?
Yes

- Patient history trumps all
  - Infants –egg, milk
  - Older– wheat, soy, peanut

#### History guided testing can be a roadmap; blind testing can be worse than unhelpful

Eapen AA et al. Oral food challenge failures among foods restricted because of atopic dermatitis. Ann All Asthm Immunol 2019

#### Addendum guidelines for the prevention of peanut allergy in the United States



#### **Provider Questions**

- Safe use of topical steroids? Too much? Too strong?
- Are non-steroidal alternatives like tacrolimus or pimecrolimus safe? What about the black box warning?
- Are the new non-steroidal agent crisaborole and dupilumab safe and effective?

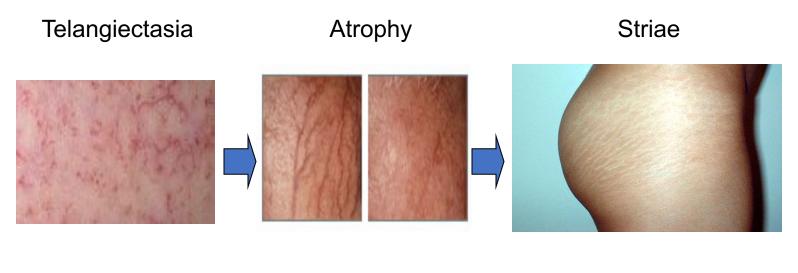
#### Simple Instructions to Increase Comfort Level with Topical Steroids

- Steroid phobia leads to non-adherence
- Describe skin thinning
- Natural history spontaneous resolution\*
- No refills
- Mandatory breaks vs limits
- "Touch test"





### **Describe Thinning of the Skin**



Reversible

Reversible

Scar

#### What Do I write for?



- Face
  - HC 2.5% oint
  - 30 gm
  - 0-2 RF
  - Alternatives: Aclometasone 0.05%; Desonide 0.05%
- Body
  - Same
  - Alternatives: TAC 0.1% oint, Mometasone 0.1% oint
  - 60 gm
  - 0-2 RF

Daily bath, BIW bleach, petrolatum, mupirocin, hydroxyzine\* 1mg/kg qHS \*Exceptions: lichenification; palmoplantar; nummular Other favorite moisturizers: Cerave, Vanicream, Cetaphil creams

#### Warts

#### Case 2

• 14 yo girl with plantar warts. I have "tried everything"



### What's New(ish)---Intralesional Candida

- A form of immunotherapy
- Immune response to candida eliminates wart
- 21 one studies in systematic review of IL immunotherapy
  - Candida, MMR, Tuberculin PPD, BCG
  - Clearance rates from 23.3-95.2%
- Method: Candin HCP; 27 g needle; 0.1 mL directly into wart; frequency variable
- Can repeat in 4-6 weeks

• Fields JR et al. Intralesional immunotherapy for pediatric warts: a review. Pediatr Dermatol 2020 Jan

#### Parental Questions

- Can't you just cut it out?
- What is the best treatment at home?
- How do you know what to stop treatment?

# Warts--- Factors determining treatment choice

- What is not the driving factor: inherent efficacy of the treatment itself
- What is:
  - Age of child
  - Wart number and size
  - Is a big deal? For the child?
  - Co-morbidities
  - Patience/adherence







#### **Treatment Options**

- Excision? No
- OTC regimens
- Liquid nitrogen
- Other
  - Cantharidin
  - Imiquimod
  - Cimetidine 30-40 mg/kg divided BID
  - Squaric acid contact immunotherapy
  - Candida Ag



### OTC Regimen

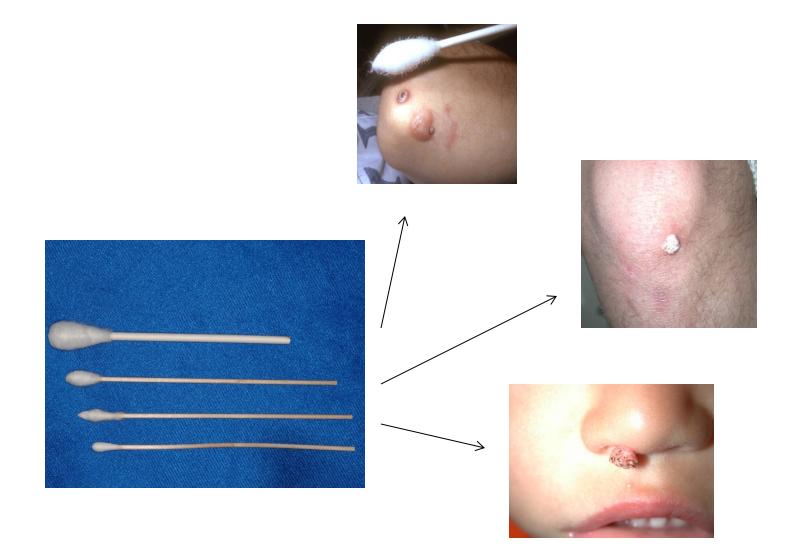
- Soak x 10 minutes
- Apply liquid medicine (pads tend to fall off) Salicylic acid eg. Duofilm
- Cover with an adhesive or something that will stay on overnight. Duct tape OK, simple bandaid OK though apply adhesive rather than bandage portion
- Leave overnight
- In AM file or emery board (dedicated) dead skin
- Repeat nightly
- Look for skin lines before stopping treatment!!!!!



## Liquid nitrogen

- If no response after 4 treatments try a different therapy
- Buff up your q tip
- Freeze adequately
- Caution in darker pigmented individuals, proximal nail fold





#### Freeze Adequately

- Pare first
- 1-6 10 second cycles
- Location, thickness
- 1-2 mm rim of normal skin at base
- Consequence of an inadequate freeze?



#### Ring Wart



This is also why I don't use cantharidin for warts!

#### Molluscum Contagiosum

- Pox virus--- loves hair follicles
- Anywhere but palms and soles



#### What's New---Nitric-Oxide!

- Berdazimer 10.3% gel
- Topical nitric-oxide releasing gel
- Once daily x 12 weeks
- 6 months of age an older

 Browning JC et al. Efficacy and safety of topical nitric oxide-releasing Berdazimer gel in patients with molluscum contagiosum. JAMA Derm 2022; July 13

#### What's Old is New--- Cantharidin

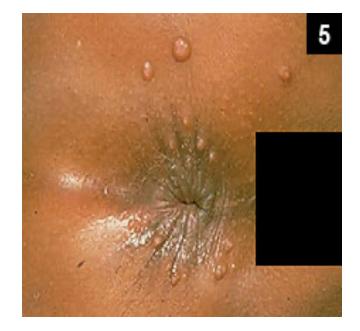
- Verrica product--- VP-102
- Topical single use in office cantharidin 0.7%
- Blistering agent used for years
- Never FDA approved

 Silverberg NB, Sidbury R, Mancini A. Childhood molluscum contagiousum: Experience with cantharidin in 300 patients. J Am Acad Dermatol 2000;43(3):503-7

#### Perianal Molluscum

Easily mistaken for warts

Different implications



#### Molluscum Mimics



Keratosis Pilaris





Molluscum

Lichen niditus

## Molluscum

- Doing nothing fine
- Contagious
  - No school implications
  - Reasonable to cover
  - Spread facilitated by moist skin
- Treatment options
  - Cantharidin
  - Retin A
  - Curettage
  - Liquid nitrogen



## Molluscum---Is this a brewing cellulitis?

- Inflamed molluscum
- May herald clearance
- Do not necessarily require antibiotics



#### Molluscum Contagiousum--- The bump that rashes

Molluscum dermatitis

Localized inflammation--- not a cellulitis

> BOTE sign







Occurs in 5%Heralds involution

Berger et al, Arch Dermatol 2012

Gianotti-Crosti-like reaction

Gianoth-Crosti Like reaction to Mollus >Occurs in 5% >Heralds involution

Berger E J et al. Experience with MC and associated inflammatory reactions in a pediatric dermatology practice: The bump that rashes. Arch Dermatol, 2012

#### Acne

#### Acne– What's New

- Clascoterone cream
- Minocycline foam
- A 4<sup>th</sup> generation tetracycline
- Spironolactone (new-ish)

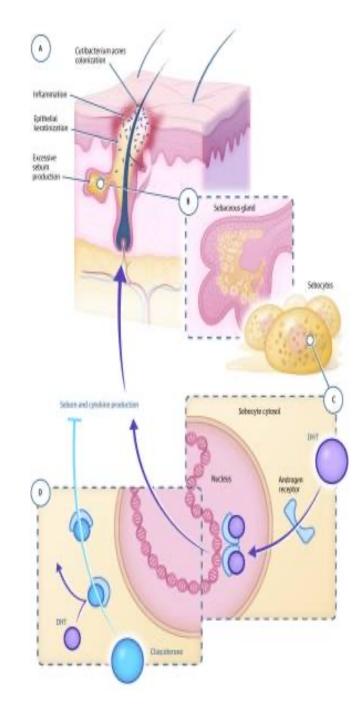
#### Minocycline Foam 4%

- Once daily for moderate to severe non-nodular acne
- FDA approved in 2019 Age 9+
- Low systemic exposure
- Foam is flammable
- Low propensity for C. acnes resistance
- Raoof TJ et al. Efficacy and safety of a novel topical minocycline foam for the treatment of moderate to severe acne vulgaris: A phase 3 study. J Am Acad Dermatol. 2020 Apr;82(4):832-837.
- Paik J Topical Minocycline Foam 4%: A Review in Acne Vulgaris. Am J Clin Dermatol 2020 Jun;21(3):449-456.

#### Clascoterone cream 1%

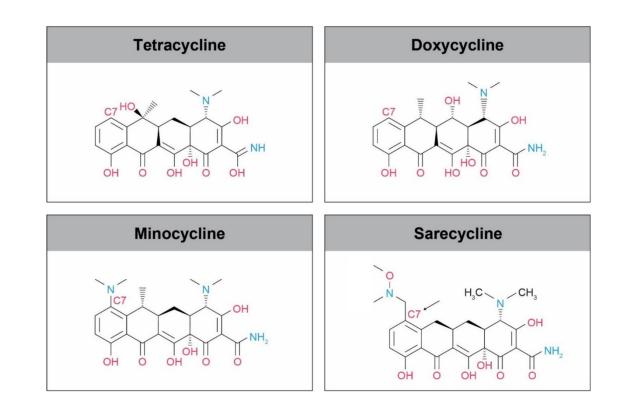
- FDA approved 12 years and older
- Novel topical anti-androgen
- Binds androgen receptor on sebocyte to prevent DHT action
- Avoid larger areas

 Hebert AA et al. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials. JAMA Dermatol 2020 Jun 1;156(6):621-630.



#### Sarecycline

- 4<sup>th</sup> generation tetracycline
- Approved for 9 years and older
- Weight based daily dosing at 1.5 mg/kg/day
  - < 54 kg then 60 mg PO q day
  - 55-84 kg then 100 mg PO q day
  - 85+ kg then 150 mg PO q day
- Decreased risk of C Acnes resistance
- Adverse effects: GI, yeast infection
- Haidari W et al. Sarecycline: A review. Ann Pharmacother. 2020 Feb;54(2):164-170



#### Spironolactone

- Aldosterone receptor antagonist
- AAP, AAD Guidelines
- 50-200 mg daily
- Issues: Slow onset of action, diuresis (29%), menstrual irregularties(22%)breast tenderness(17%), K+, pregnancy category C, boxed warning, long term safety
- Zaenglein A et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016; 74(5)945-73
- Mackenzie IS et al. Spironolactone and risk of incident breast cancer in women older than 55 years: a matched cohort study. BMJ 2012;345:e4447

#### Spironolactone—long term safety

- Retrospective case series of 403 adult women at an academic center between 2008-19
- Most common initial dosage: 100 mg/d
- Most on combination therapy (retinoid vs COC)
- Time to peak effect: 4-6 months
- Acne documented by CASS (Comprehensive Acne Severity Scale)
  - Face 76% clear
  - Chest– 84% clear
  - Back- 80% clear
- 23% discontinued due to adverse effects
- Mean duration before first discontinuation: 470 days
- Garg V et al. Long term use of spironolactone for acne in women: a case series of 403 women. J Am Acad Dermatol 2021;84:1348-55

#### Spironolactone Long Term

- Minimal impact on BP
  - Systolic BP decreased 3.5 mm Hg
- Safe and effective for extended use
- May reduce use of oral antibiotics in female patients

- 15 yo girl with acne on the face, chest, and back. "I hate it!"
- What are the best OTC options?
- Are there options other than antibiotics and Accutane?



#### Patient and Parent Questions

- Will it scar?
- Is it due to food? She eats a lot of sugar!
- Is Accutane safe?

#### Will It Scar?

No







#### Ask: do lesions sometimes hurt?

#### Is It Caused By Food?

• Ask: Does she smear pizza on her face? If not, no

• Soft literature around dairy and sugar

#### Is Accutane (aka isotretinoin) safe?

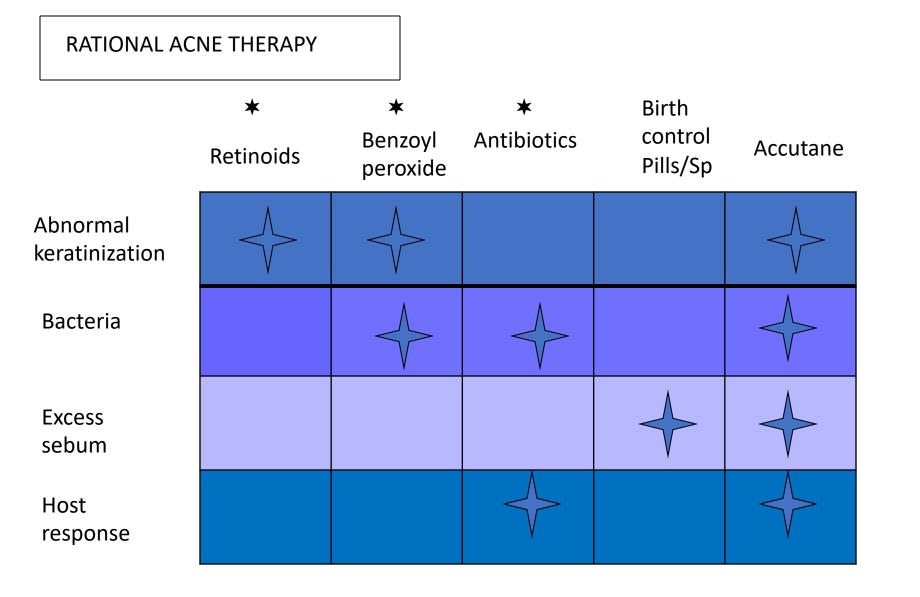
#### • Yes

- Does it have side effects? Yes
  - Real: teratogen, dry lips, back pain, hypertriglyceridemia
  - Rare if real: mood changes
  - Almost certainly coincidental: Inflammatory bowel disease
- The only potential "cure" other than time
  - If scarring potential—worth considering
  - Must balance against safety and efficacy of other treatments

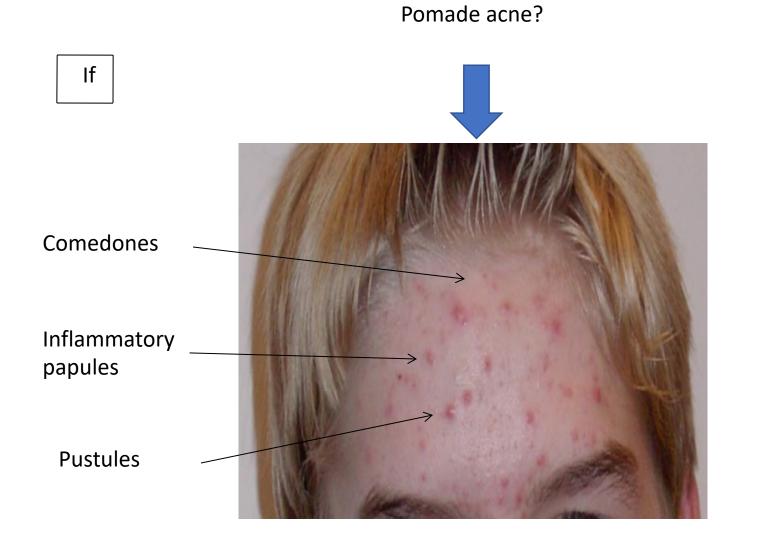
#### **Provider Questions**

• What's next in therapy?

• Other options besides antibiotics and Accutane?



★ OK in infants



Retinoids and/or BP

Then

BP and/or antibiotics

BP and/or antibiotics

## Hormonal Therapy in Female Patients

- Hormonally driven acne betrayed by history and physical
- Consider Stein-Leventhal (PCOS) in appropriate patients
- Oral Contraceptive Pills (OCP) block ovarian androgen production
  - FDA Approved 14+ yo: Ortho-Tri-Cyclen, Estrostep, Yaz
  - Clotting risk (eg Yaz)
    - relative vs absolute risk
    - Risk stratify
  - Bone accrual- wait until 1 year after menstruation
- Spironolactone 25-50 mg/d titrate up to 200mg/d– block androgen effects on sebaceous gland
  - Menstrual irregularity, breast tenderness, hyperkalemia, fatigue
- Response may take months

#### Pediatric Treatment Recommendations for Mild Acne

Mild Acne=Comedonal or Inflammatory/Mixed Lesions

> Mild Comedonal Acne (central face common in preteens and early teens)



#### More Extensive Comedonal Acne

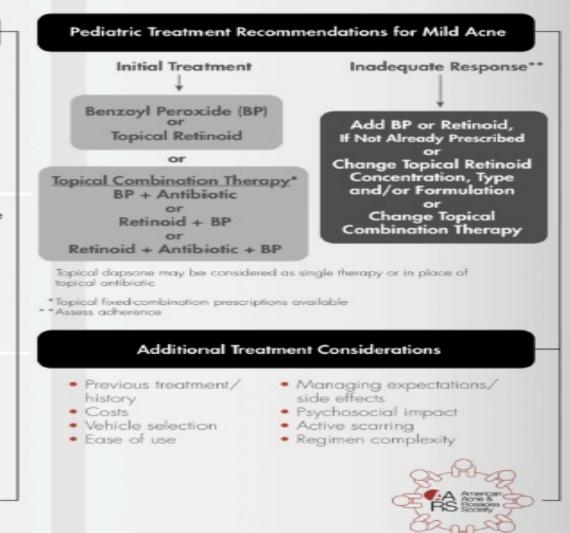
[forehead involvement common in preteens and early teens; often with no or a few scattered superficial inflammatory lesions]



Mild Inflammatory Acne (scattered superficial inflammatory popules/pustules + some comediones)



C American Acre & Rosacea Society, 2011.



Photos courtery of Lawrence F. Eichenfield, MD James G. Del Rosso, DO and Diane Thiboutott, MD

Eichenfield L et al. Pediatrics 2013



# Ideal regimen for moderate to severely affected patient

- Differin 0.1% gel qHS
- BenzaClin gel qAM
- Doxycycline 100 mg PO QD-BID
- Neutrogena facial cleanser QD-BID
- Issues—dryness with topicals, photosensitivity with systemic
- Insurance coverage

#### Case 4

- A 3 month old with a small, dime-sized hemangioma on the upper eyelid
- Does this need treatment?



#### Hemangiomas--when to treat?

• Is the lesion endangering or deforming?

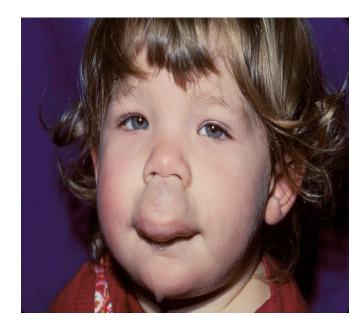


#### Is the hemangioma ENDANGERING?





#### Is the hemangioma DEFORMING?







Large lesions in sensitive locations

Exophytic

Bulky lesions---fibrofatty scarring

## What if you don't treat—who will scar?

- Multi-center, retrospective, cohort study of 187 untreated hemangiomas with photographic follow up
- Average age of complete involution = 3.5 years
- Types of scarring: Telangiectasia, fibrofatty
- Risk factors for scarring:
  - Mixed > superficial > deep
  - Step off border
  - Cobblestone > smooth





• Baselga E et al. Risk factors for degree and type of sequelae after involution of untreated hemangiomas. JAMA Dermatol 2016 152(11):1239-43

# Sequelae After Involution of Untreated IH

A. <u>Deep</u> hemangioma that regressed without sequelae

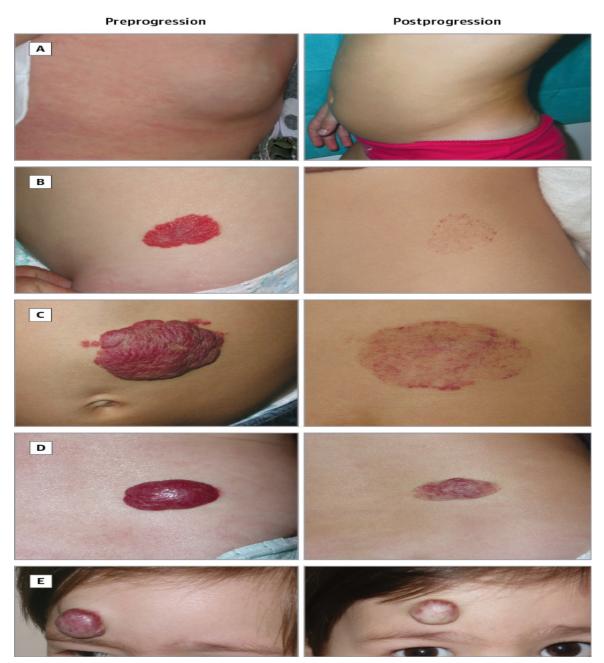
B. <u>Superficial</u> hemangioma that left only telangiectasia

C. Mixed hemangioma that left anetodermic skin

D. Mixed hemangioma that left redundant skin

E. Mixed hemangioma that left fibrofatty tissue.

Baselga et al. JAMA Dermatol. 2016;152(11):1239-1243.

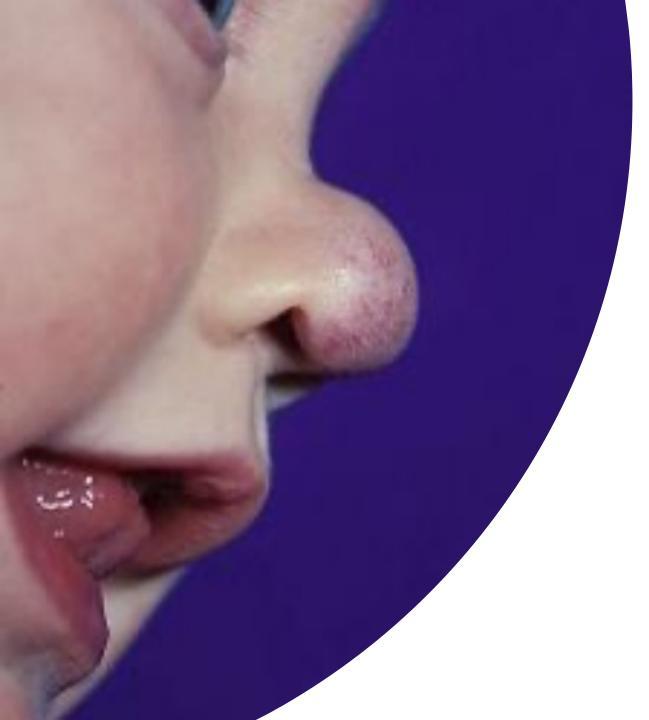


#### Slide courtesy of H. Brandling-Bennett

#### Two scenarios where size belies significance...



# Nasal tip hemangiomas



Nasal tip hemangiomas---Cyrano deformity

# Which One Represents a Dermatologic Emergency?





Α.

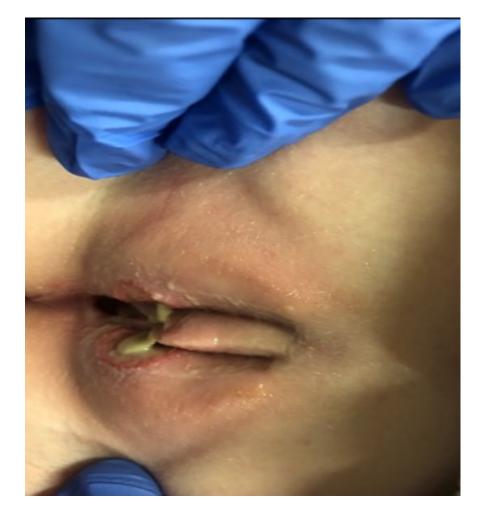


# Upper Eyelid

#### Do We Have Time for a few more Cases????

CASE 5: 12 yo girl with acute onset of painful genital ulcerations in the wake of a cough and low grade fever





### Lipschutz ulcer

- Post infectious (classically EBV)
  - Recent case post COVID vax
- Pre-adolescent females
- Very painful
- Once infectious causes ruled out, prednisone is miraculous

• Sidbury R. Lipschutz ulcers. UpToDate.

#### Back to back ED consults-How do you tell the difference? Case 6 Case 7





14 mo girl with eczema and new rash

7 mo boy with eczema and new rash

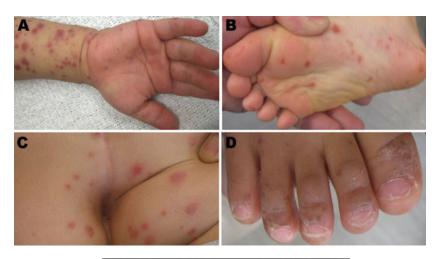
CASE 6: Eczema "Coxsackium" 14 mo old with eczema and progressive vesicular eruption



#### Coxsackievirus A6 HFM disease

HFM usually caused by A16

- Fever, irritability, pain
- Impressive rash
  - Eczema herpeticum-like
  - "Eczema coxsackium"
    - Accentuated in areas of AD
    - Looks like EH
- Onychomadesis
- Can diagnosis with aspirate of blister fluid and PCR
- Usual enteroviral panels do not have A6
- Add to clinical differential of eczema herpeticum
- <u>MMWR Morb Mortal Wkly Rep.</u> 2012 Mar 30;61(12):213-4.
- Mathes E et al. Eczema coxsackium and unusual cutaneous findings in an enterovirus outbreak. Pediatrics 2013;132(1):e149-157
- Lynch MD et al. Disseminated CVA6 affecting children with AD. Clin Exp Dermatol 2015; Jul 40(5):525-8





#### Case 7: Eczema Herpeticum



## **Eczema Herpeticum**

- This case quite extensive and symmetrical which raised possibility of CVA6
- Spread from single source (neck) more suggestive of HSV
- Admit: < 1 yo; male; febrile</p>
- Treat:
  - Acyclovir 10-20 mg/kg/d IV tid
  - Topical steroids OK
- D/C home: no new lesions for 24-48 hours, afebrile



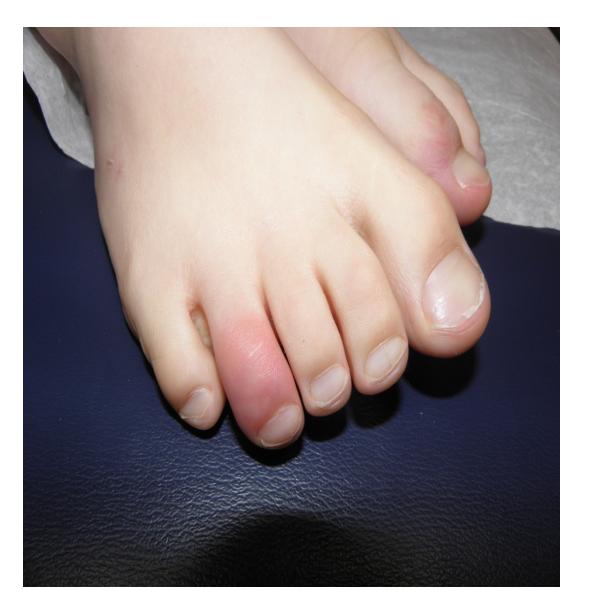
- Luca NJC et al. Eczema herpeticum in children: Clinical features and factors predictive of hospitalization. J Pediatr 2012;161:671-5
- Aronson P et al. Topical corticosteroids and hospital length of stay in children with eczema herpeticum. Pediatr Dermatol 2012; Oct 5

Connective Tissue Disease or ADHD?

Asymptomatic erythema progressing to blue discoloration No triggers (eg cold) Adderall XR begun 6 months earlier

## Perniosis due to stimulants

Aboud AA, Abrams M, Mancini AJ. Blue toes after stimulant therapy for pediatric attention deficit hyperactivity disorder. J Am Acad Dermatol 2011;64(6):1218



#### COVID toes

Pernio-like lesions

Pediatric population

Convalescent finding

Other cutaneous manifestations of COVID > KD like > morbilliform > papulosquamous > EM-like >...

"Any drug, any rash..."

"COVID, any rash..."



#### Summary

- Skin care first for eczema, then allergy care, caution with food elimination
- Individualize wart therapy
- Rational therapy for acne
- Caution with upper eyelid hemangiomas

## Thank you