AtlanticDerm CONFERENCE

ADC 101st Annual Conference

APRIL 19-21, 2024 | HERSHEY LODGE, HERSHEY, PA

Update In Pediatric Dermatology and Camp Discovery

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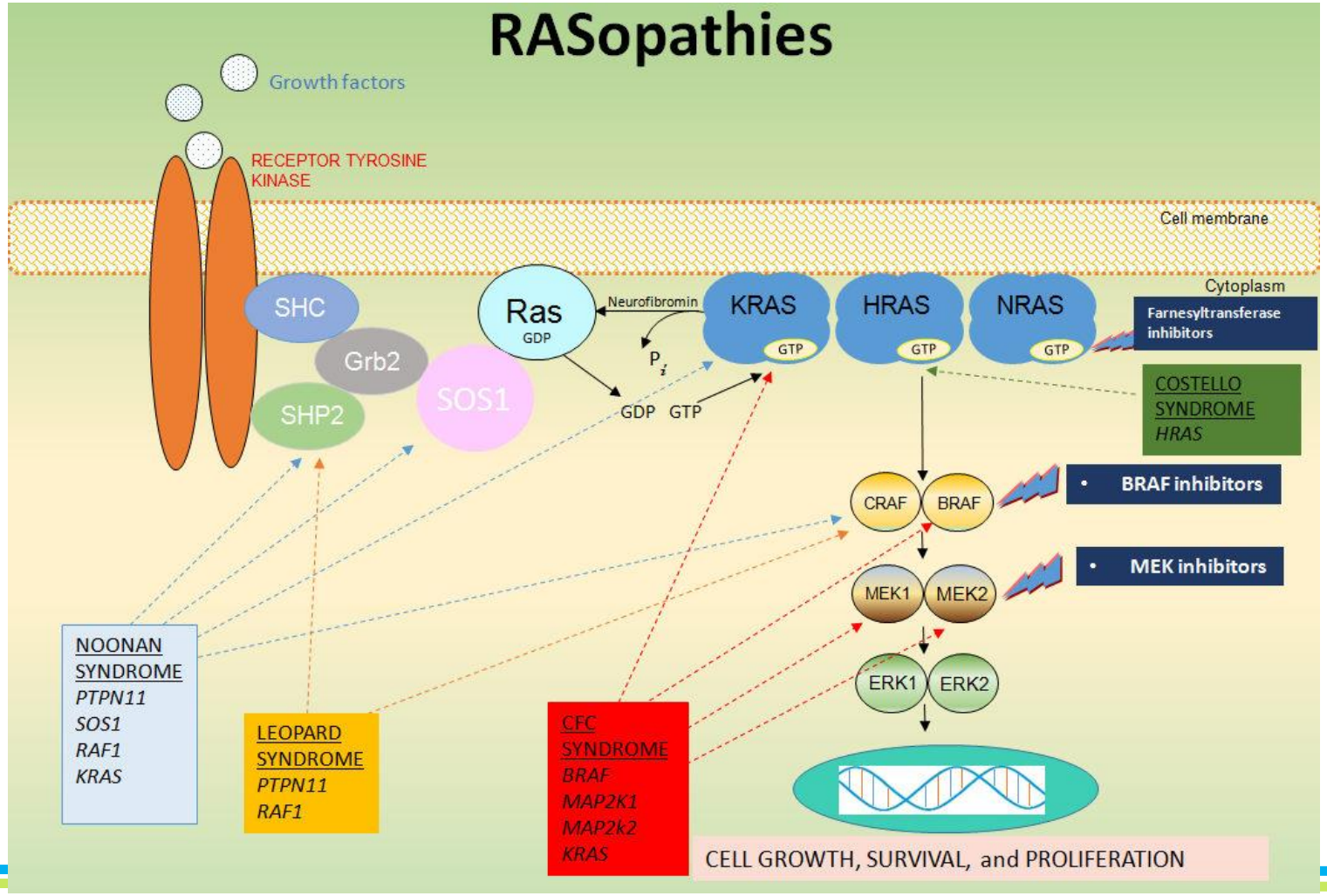
No Disclosures or Conflicts of Interest

Pediatric Dermatology Update Overview

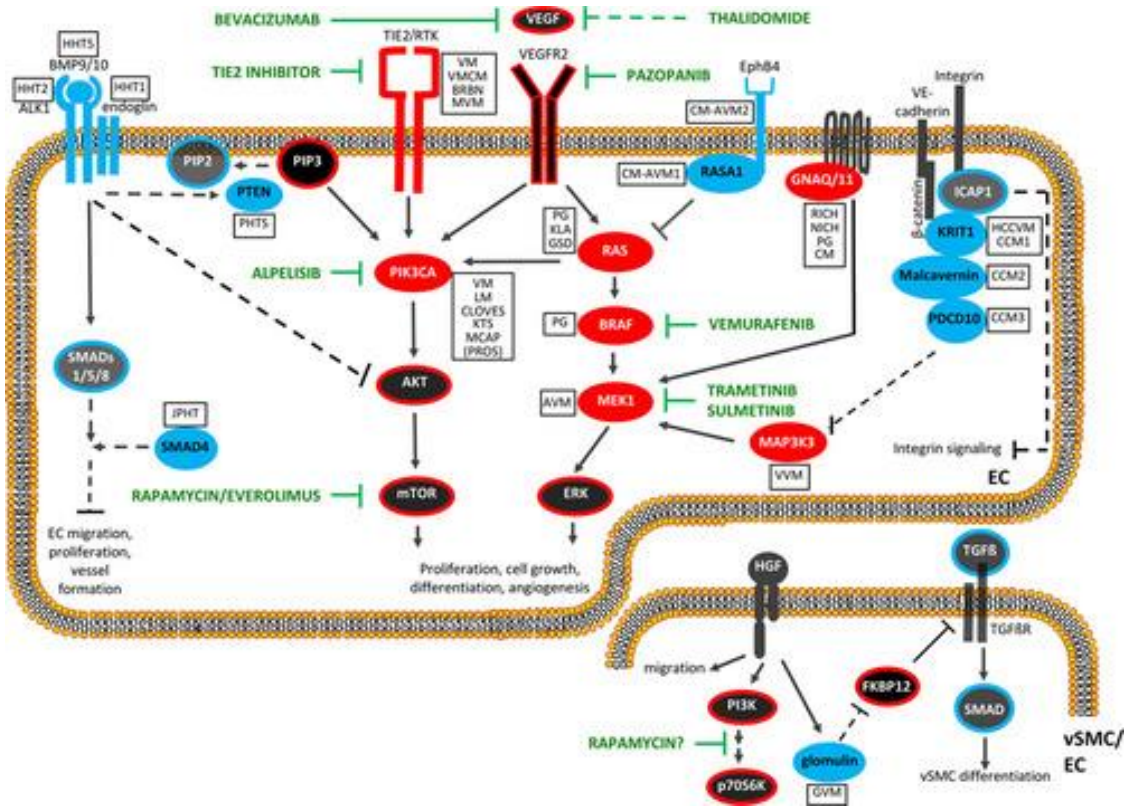
- The vascular overgrowth paradigm and its implications
- Dupilumab- Are immunizations OK? How to taper down?
- Building better mouse traps- New medications
- Woods light for scabies, resistant scabies
- A new resistant *Trichophyton*
- The changing face of coxsackievirus
- Thirty-year anniversaries for Camp Discovery, special guest

The RAS Pathway



JAAD CME Article June 2013

- Paradigm shift towards genetic categories rather than phenotypes
- RAS pathway unified:
  - Noonan Syndrome
  - Costello Syndrome
  - LEOPARD Syndrome
  - Cardiofacial Cutaneous Syndrome
- RASopathies



Angela Queisser. Circulation Research. Genetic Basis and Therapies for Vascular Anomalies, Volume: 129, Issue: 1, Pages: 155-173, DOI: (10.1161/CIRCRESAHA.121.318145)

PIK3CA-Related Overgrowth Spectrum (PROS) An "ATM PROBLEM"

- Asymmetric overgrowth
- Thrombosis tendency
- Malformations- capillary, venous, lymphatic

PRO PIK3CA-Related Overgrowth

- Boney abnormalities- leg length, scoliosis
- Lipomatous growths
- Epidermal nevi
- Megalencephaly

PROS Brings Order to Phenotypic Kaos

- PIK3CA syndromes
  - CLOVES- congenital lipomatous overgrowth, vascular malformation, epidermal nevi, scoliosis and other skeletal
  - Klippel-Trénaunay Syndrome
  - Megalencephaly-Capillary Malformation Syndrome
- But…
  - Similar overgrowth syndrome with PIK3R1 (*Genetic in Medicine* 2021)
  - Port wine stain, Sturge-Webber are *GNAQ*
  - Proteus *AKT1*
  - Parkes-Weber second hit mutation of *RASA1*

Why spend so much time on this…

- Eponyms are going to disappear
- Genotype is not necessarily obvious from phenotype
- Most of the genes involved in vascular overgrowth syndromes are also pathogenic in tumors, so there are emerging chemotherapeutic modalities available for treatment
- They are mosaic disorders resulting from postzygotic mutations, so lesional tissue is needed for genetic analysis


Howard

Medications Making a Difference

Our patient is clear on dupilumab. Now what?

- Adult patients in both studies
- Twelve months of good disease control
- Patients offered a trial of dose reduction of 3- or 4-week intervals “per patient-centered discussion”

Jendoubi F, et al. Longer dupilumab dosing intervals in adults with atopic dermatitis: experience from a French multicentre retrospective cohort study. *Br J Dermatol* 2022;187:602-3

Ardern-Jones, MR, et al. Successful dose reduction of dupilumab in atopic dermatitis. *Br J Dermatol* 2023;188:678-9

Our patient is clear on dupilumab. Now what?

- Assessment at about 12 months after dose reduction
- Proportion obtaining EASI 75 and EASI 90 was slightly **higher** after dose reduction (86% vs 70% and 57% vs 50%)
- IGA slightly worse (1.42 vs 1.00)
- Only 17 patients in the study
- Unknown whether pediatric patients are more or less likely to be tapered on their dose

Ardern-Jones, MR, et al. Successful dose reduction of dupilumab in atopic dermatitis. *Br J Dermatol* 2023;188:678-9

Live Attenuated Vaccination on Dupilumab

- Study protocols in young children prohibited live attenuated vaccine administration within 4 weeks of baseline visit and during treatment.
- Dupilumab should be discontinued for 12 weeks prior to LAV
- Nine children with deviations in dupilumab clinical trials
- No adverse events, seroprotection unknown
- Unrelated study in adults showed seroprotection to yellow fever after immunization while on dupilumab
- IL-4, IL-13 not thought to have a primary role in viral infection

Siegfried EC, et al. A case series of live attenuated vaccine administration in dupilumab-treated children with atopic dermatitis. *Pediatr Dermatol* 2024;41:204-9

Treatment of Alopecia Areata

- Review of published studies using pulsed steroids
- Oral administration of monthly dexamethasone or prednisolone monthly, 5 mg/kg prednisolone or equivalent, 6-8 cycles
- 50-56% response of 75% regrowth
- Most tend to relapse
- Best in those whose hair loss was acute

Gallaga, et al. Pediatric pulse dose corticosteroid therapy dosing and administration in the treatment of alopecia areata: a literature review. *Pediatr Dermatol* 2023;40:276-81

Treatment of Alopecia Areata
Oral JAK Inhibitors

- Dizzying number of articles published
- Topical does not seem to work
- Oral therapy is significantly better than placebo
- Ritlecitinib approved in those 12-years and older

King BA, Craiglow BG. Janus kinase inhibitors for alopecia areata. *J Am Acad Dermatol* 2023;89:S29-32

Liu M, et al. Janus kinase inhibitors for alopecia areata; a systemic review and meta-analysis. *JAMA Network Open* 2023;6:e2320351

Treatment of Alopecia Areata
Oral JAK Inhibitors

- Severity of Alopecia Tool (SALT)
  - SALT20 = 20% or less hair loss
- Baricitinib- 39% (4 mg) and 23% (2 mg) achieved SATL20 after 36 weeks and most achieved SALT10, the proportion increased with an additional 16 weeks of treatment
- Ritlecitinib- 23% achieved SALT20 after 24 weeks, 40% after a total 48 weeks
- Cost (to somebody) in the 10's of thousands per year

Topical Vitiligo Treatment

- FDA-approved ruxolitinib cream, 12 years of age and older
- Vitiligo improvement score (VASI) 50 in 58%, 75 in 52%, 90 in 33% after 52 weeks of bid application
- Intermittent topical steroid, calcineurin inhibitor, ultraviolet light have evidence-based backing as first line therapies

Renert-Yuval Y, et al. Expert recommendations on the use of topical therapeutics for vitiligo in pediatric, adolescent, and young adult patients. *JAMA Dermatol* 2024; Published on-line March 2024

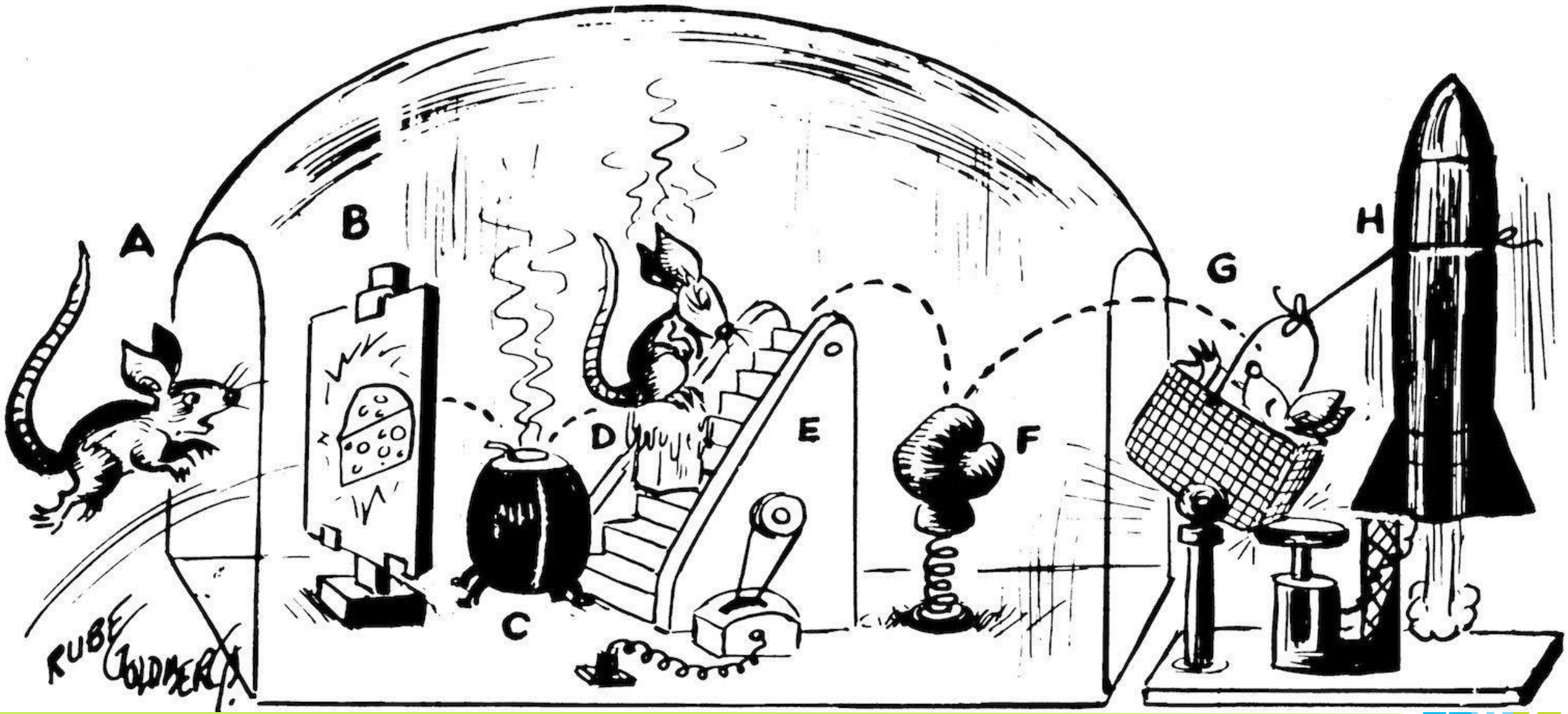
Hwang JR, Driscoll MS. Review of ruxolitinib for treatment of non-segmental vitiligo. *Ann Pharmacotherapy* 2023;57:948-55

Ruxolitinib for Mild-Moderate Atopic Dermatitis

- Twice daily application of 1.5% cream for mild-to-moderate AD
- TRuE-AD1 and 2 clinical trials
  - IGA 0 or 1 in 53.8% and 51.3% versus 24.6% and 14.4% for placebo
  - EISI-75 in 62.1% and 61.8% versus 24.6% and 14.4% for placebo
- Many others in the pipeline
- Expensive
- How much help do we need with mild-to-moderate AD?

Sideris N, et al. New and upcoming topical treatments for atopic dermatitis; a review of the literature. *J Cl Med* 2022;11:doi:10.3390/jcm11174974

How to Get Rid of a Mouse



Mollusca: Does Treatment Help?

- Retrospective review of 170 children at Johns Hopkins, 2008-2011
- Significantly higher number in atopics
- Thirty-six treated with tretinoin, imiquimod, cantharidin, cryo, or curettage

Basdag H, Rainer BM, Cohen BA. Molluscum contagiosum: to treat or not to treat? Experience with 170 children in an outpatient clinic setting in the Northeastern United States. *Pediatr Dermatol* 2015;32:353-57

Mollusca: Does Treatment Help?

- Complete resolution after 12 months
  - Treated 45.6%
  - Untreated 48.4%
- Complete resolution after 18 months
  - Treated 69.5%
  - Untreated 72.6%
- Number of locations, number of lesions, history of atopy did NOT predict outcome

New Treatments for Mollusca Contagiosa

- Berdazimer gel, a novel antiviral, nitric oxide-releasing topical medication
- Applied daily to each lesion for 12 weeks
- Complete clearance of 30% in treatment group versus 20% in placebo group, $P < .001$
- Warren Hayman commentary- “I welcome the opportunity to prescribe a new medication expressly indicated for MC if approved. From the data, I suspect my treatment paradigm will fundamentally remain the same.”

Sugarman JL. Berdazimer gel for molluscum contagiosum: an integrated analysis of 3 randomized controlled trials. *J Am Acad Dermatol* 2024;90:299-308

New Treatments for Mollusca Contagiosa Cantharidin in FDA approved applicator

- Single use applicator of 0.7% cantharidin
- Patients two yeas of age or older
- Applied by health care provider, not for parental use
- Applied to each wart at 21-day intervals, washed off in 24 hours, maximum of four treatments
- Complete clearance at day 84 was 46% and 54% with treatment group versus 18% and 13% in placebo group in two trials

Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two randomized phase III trials evaluating VP-102, a drug-device combination product containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Am J Clin Dermatol* 2021;22:257-265

New Treatments for Mollusca Contagiosa Cantharidin in FDA approved applicator

- What I like:
  - The solution is colored, so it is easy to see which lesions have been treated
  - FDA-approved
  - There is detailed patient information, including help with pronunciation

Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two randomized phase III trials evaluating VP-102, a drug-device combination product containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Am J Clin Dermatol* 2021;22:257-265

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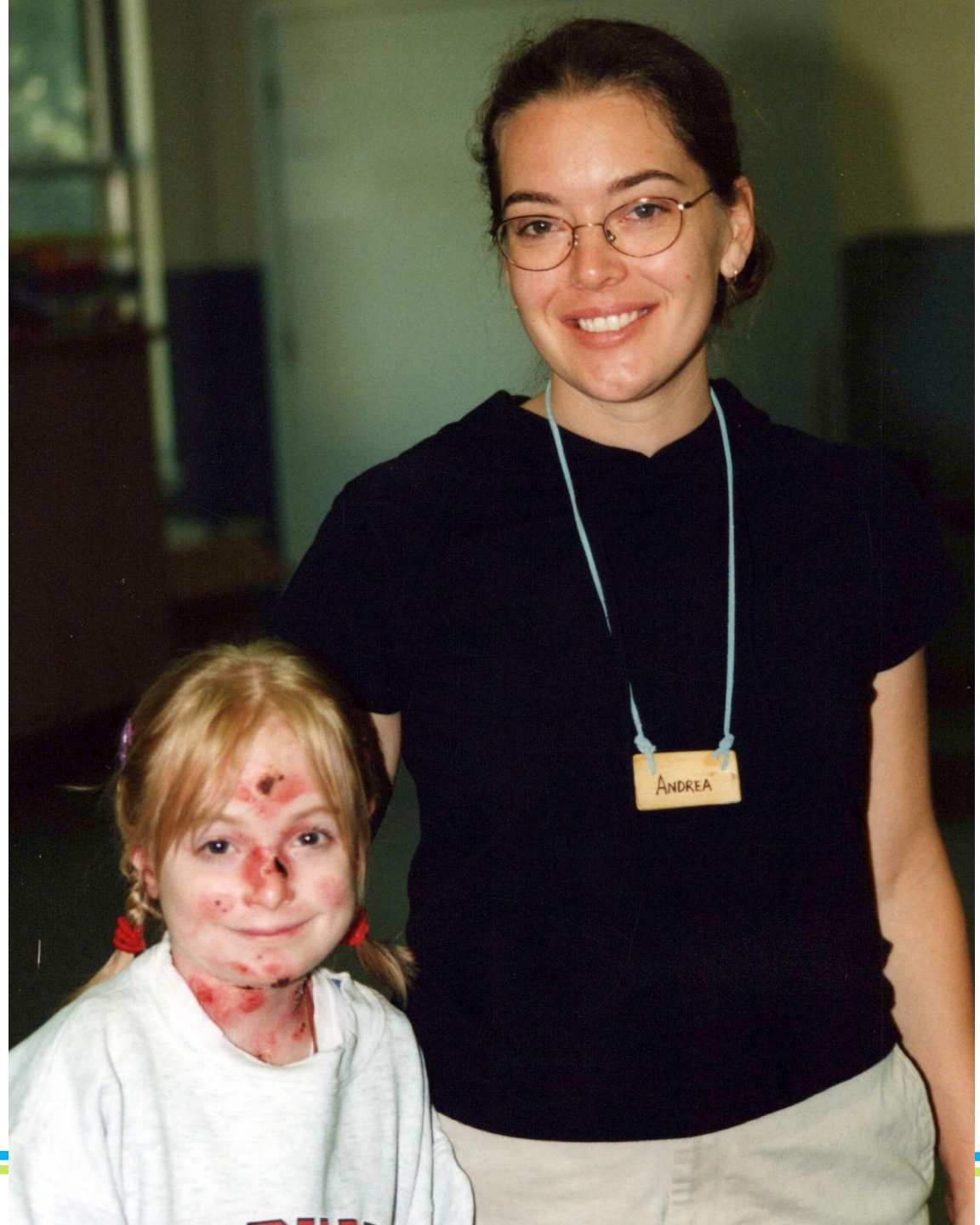
New Treatments for Mollusca Contagiosa My Worries

- Mollusca are going to become villains in the media.
- Years (decades) of educating parents and primary care providers will go down the drain.
- Treatment (? Expensive) will become the norm, whereas watchful waiting has served us well to this point
- Old treatments will be demonized, for instance OTC salicylic acid in collodion 1-2 times per week, $7

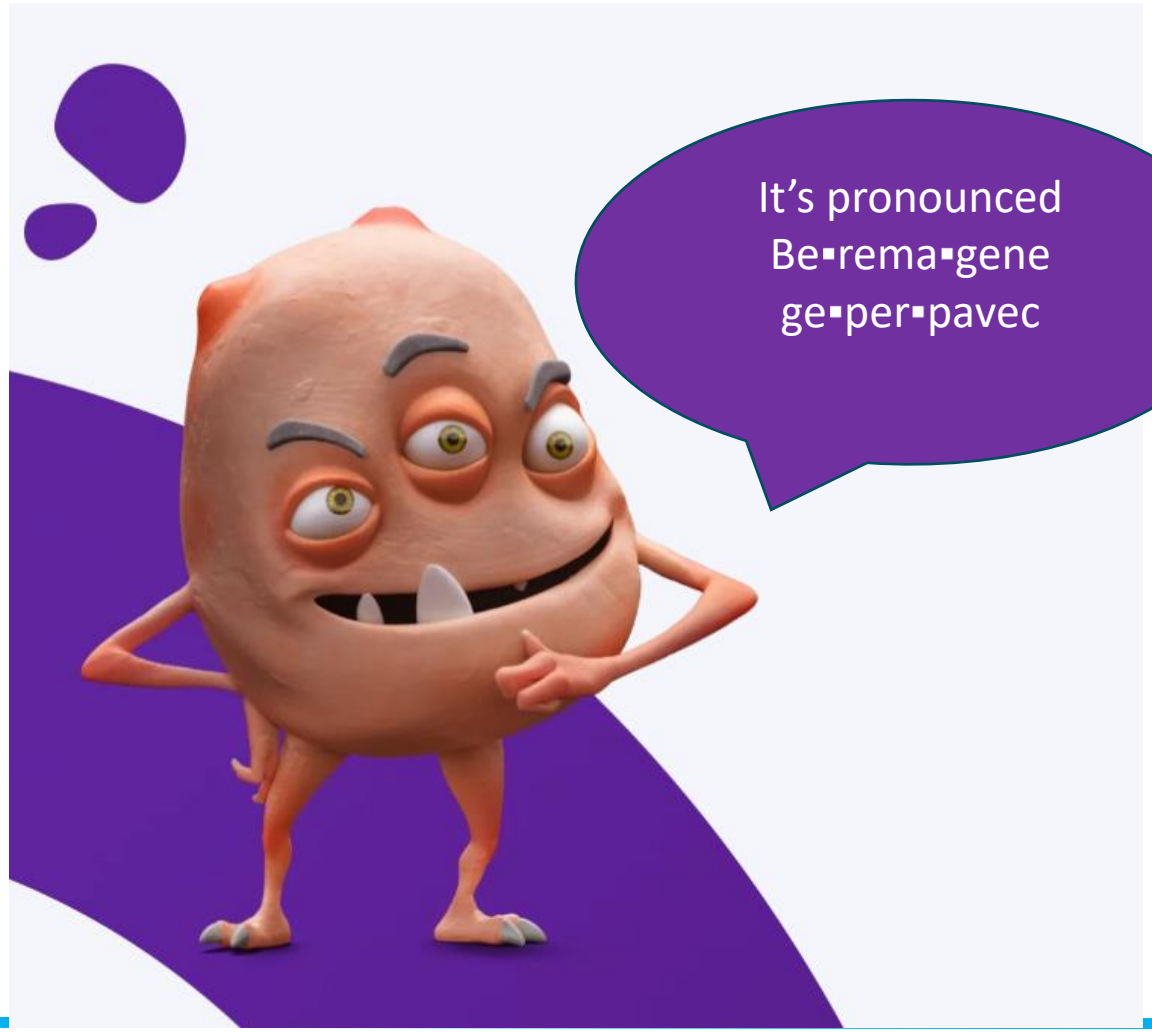

ANDREA

Topical Treatment for Patients with Dystrophic Epidermolysis Bullosa

- Beremagene geperpavec aka Vyjuvek aka B-VEC
- Non-replicating herpes simplex virus used to deliver the missing collagen 7 gene
- Wound pairs in 31 patients with dystrophic EB treated with B-VEC or placebo
- Complete healing after six months of weekly treatment in 67% of B-VEC versus 22% of placebo
- Is this a model that could be used for other autosomal recessive skin conditions (ARCI) or other respiratory or GI genetic conditions?

Guide SV, et al. Trial of Beremagen Geperpavec (B-VEC) for dystrophic epidermolysis bullosa. *N Engl J Med* 2022;387:2211-19

Topical Treatment for Patients with Dystrophic Epidermolysis Bullosa



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Topical Treatment for Patients with Dystrophic Epidermolysis Bullosa

Hello All,
Brie (CC'd on this email) is reviewing Vyjuvek (beremagene geperpavec-svdt) at a quickly approaching GHP P&T meeting (materials due 11/13/23). Vyjuvek is a herpes-simplex virus type 1 vector-based gene therapy and is indicated to treat dystrophic epidermolysis bullosa (DEB) with mutations in the COL7A1 gene in patients 6 months of age and older. Unfortunately, Vyjuvek **carries a price tag of roughly $1,513,200.00 per patient per year** (for a patient requiring year-round treatment).

In short…

- We have many diseases in pediatric dermatology that are physically and emotionally devastating.
- I am extremely thankful for the many new treatment options and optimistic about the future of new developments.
- I am unsure of when and how the American health system will implode with a cost burden that is unsustainable.

Revisiting Petroleum Jelly

- "What is the best emollient?"
  - Chemical-free
  - Very thick
  - Cheap
- Petroleum jelly is noncarcinogenic, nonallergenic, noncomedogenic, safe in preterm neonates, nonflammable
- Thirty-eight cents per ounce on Amazon

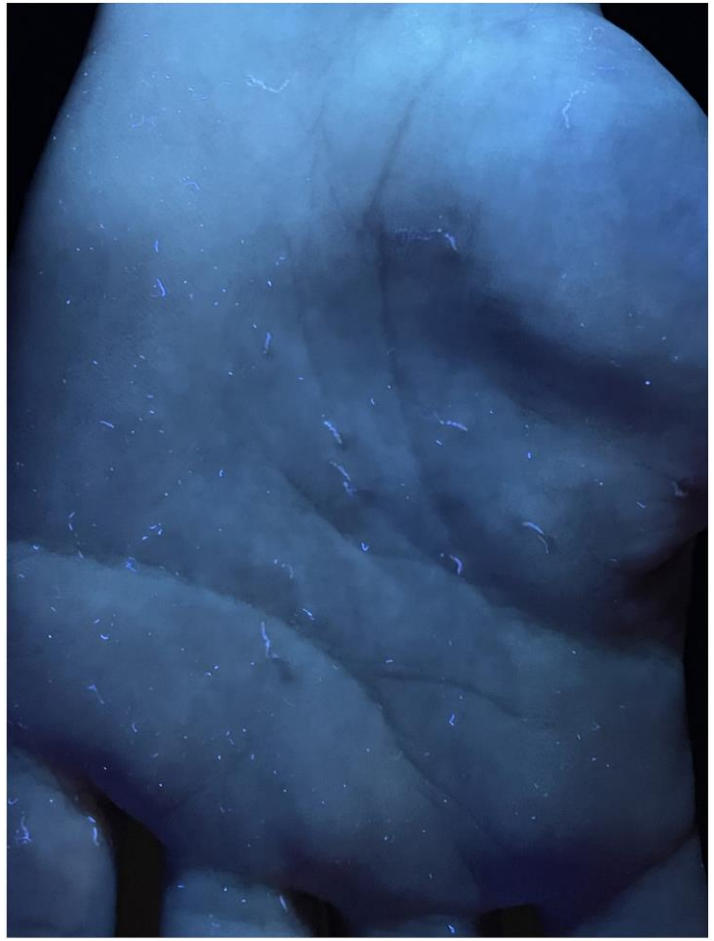
Kamrani P, Hedrick J, Marks, JG, Zaenglein AL. Petroleum jelly: a comprehensive review of its history, uses, and safety. *J Am Acad Dermatol* 2024;90:807-13

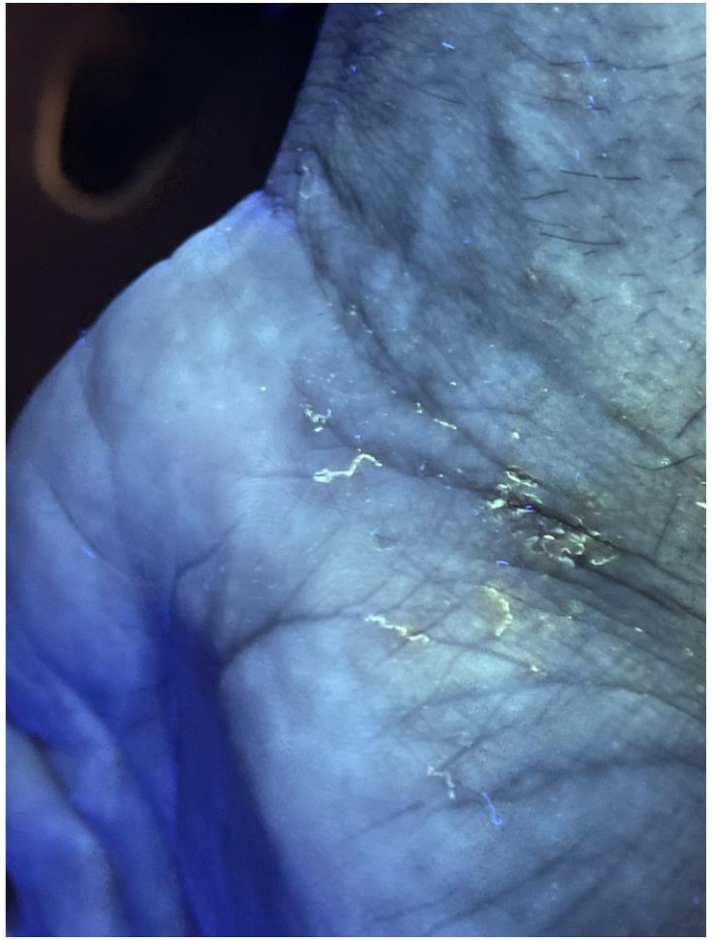
Woods Light For Diagnosing Scabies

- I prefer entering the treatment of scabies with a firm diagnosis, preferably with a positive KOH
- Scalpel blades and squirming children are a bad combination
- Dermoscopy
- “Scabies Sign” using Wood’s light
- Bright reflex of tunnels

Yürekli A, Can I, Oğuz M. Using ultraviolet light in diagnosing scabies; scabies’ sign via Wood’s lamp. *J Am Acad Dermatol* 2023;89:e195-6

Woods Light For Diagnosing Scabies





Resistant Scabies

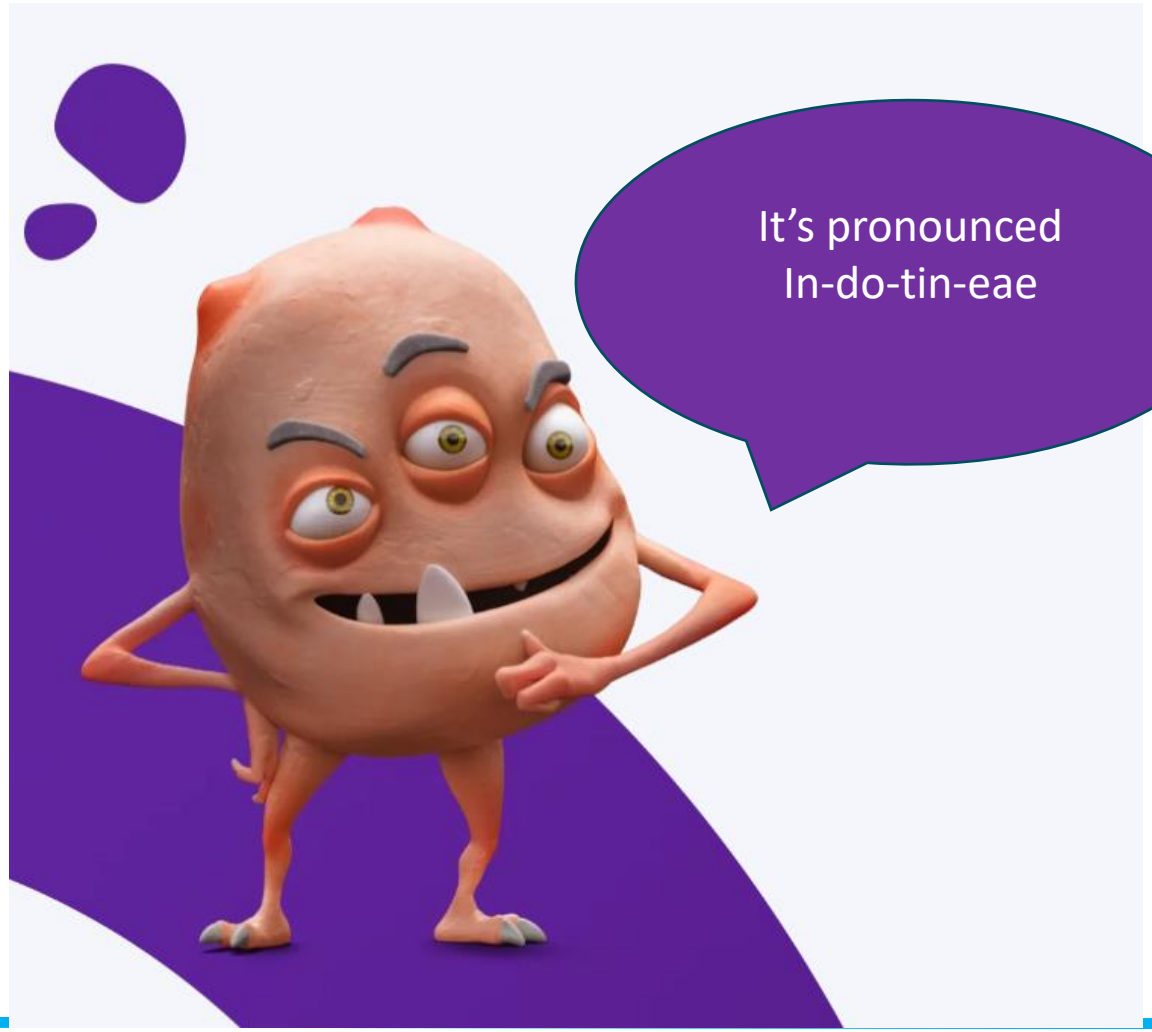
- Study out of Austria
- Fifty-two patients treated with permethrin 5% cream, fifty-four with benzyl benzoate 25%
- Applied three consecutive days
- Cure in **27% with permethrin**, 87% with benzyl benzoate

Meyersburg D, et al. Comparison of topical permethrin 5% vs. benzyl benzoate 25% treatment in scabies: a double-blinded randomized controlled trial. *Br J Dermatol* 2023;190:486-91

A New Fungus On The Loose *Trichophyton indotineae*

- Reports of resistant *Trichophyton mentagrophytes* emerged from India in the 2000's
- Later given a unique species name of *Trichophyton indotineae*
- Increasing reports outside of India, some without travel history
- February 2023 two cases in NYC, one with NO travel

Gupta AK, et al. Antifungal resistance, susceptibility testing and treatment of recalcitrant dermatophytosis caused by Trichophyton indotineae: a North American perspective on management. *Am J Cl Dermatol* 2023;24:927-38


It’s pronounced
In-do-tin-eae

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A New Fungus On The Loose *Trichophyton indotineae*

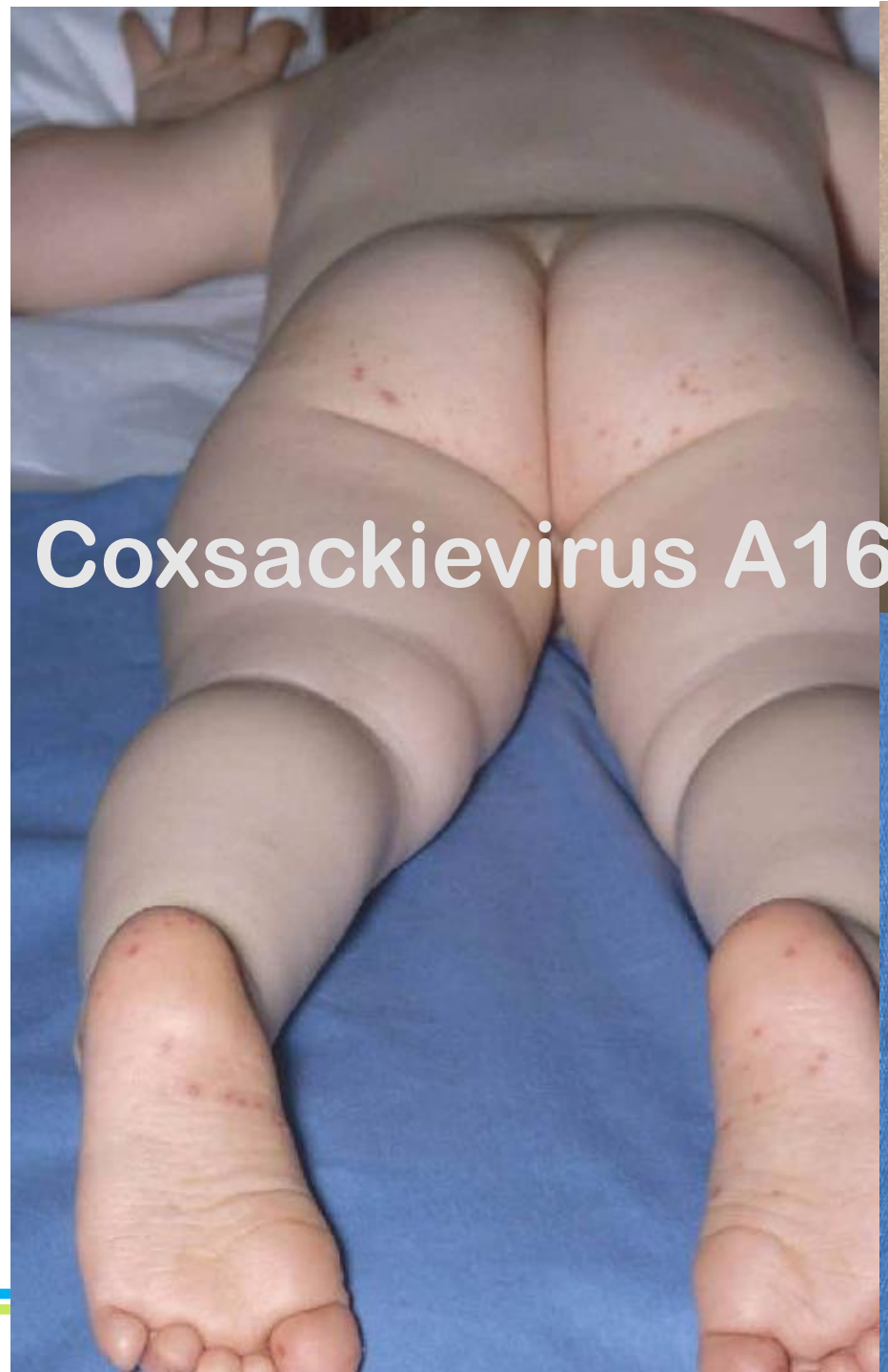
- Hard to identify by morphology so most labs will report as *Trichophyton species*
- Need to request PCR for correct identification and susceptibility testing to determine the best antifungal agent
- Generally resistant to terbinafine and griseofulvin
- Sensitive to itraconazole, limited efficacy of fluconazole and ketoconazole

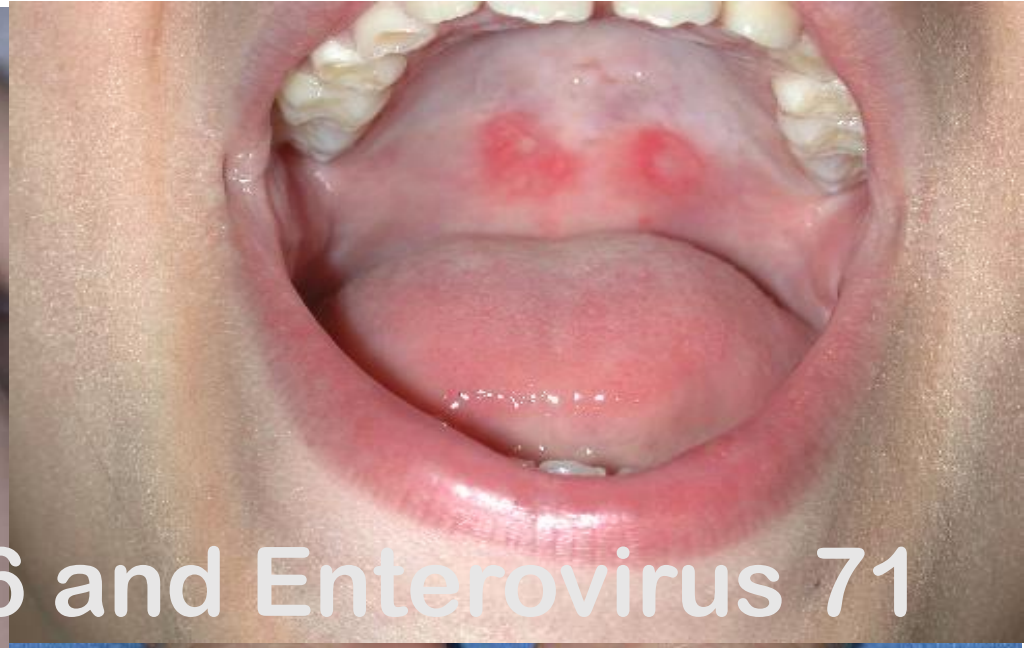
Gupta AK, et al. Antifungal resistance, susceptibility testing and treatment of recalcitrant dermatophytosis caused by *Trichophyton indotineae*: a North American perspective on management. *Am J Cl Dermatol* 2023;24:927-38

A New Fungus On The Loose *Trichophyton indotineae*

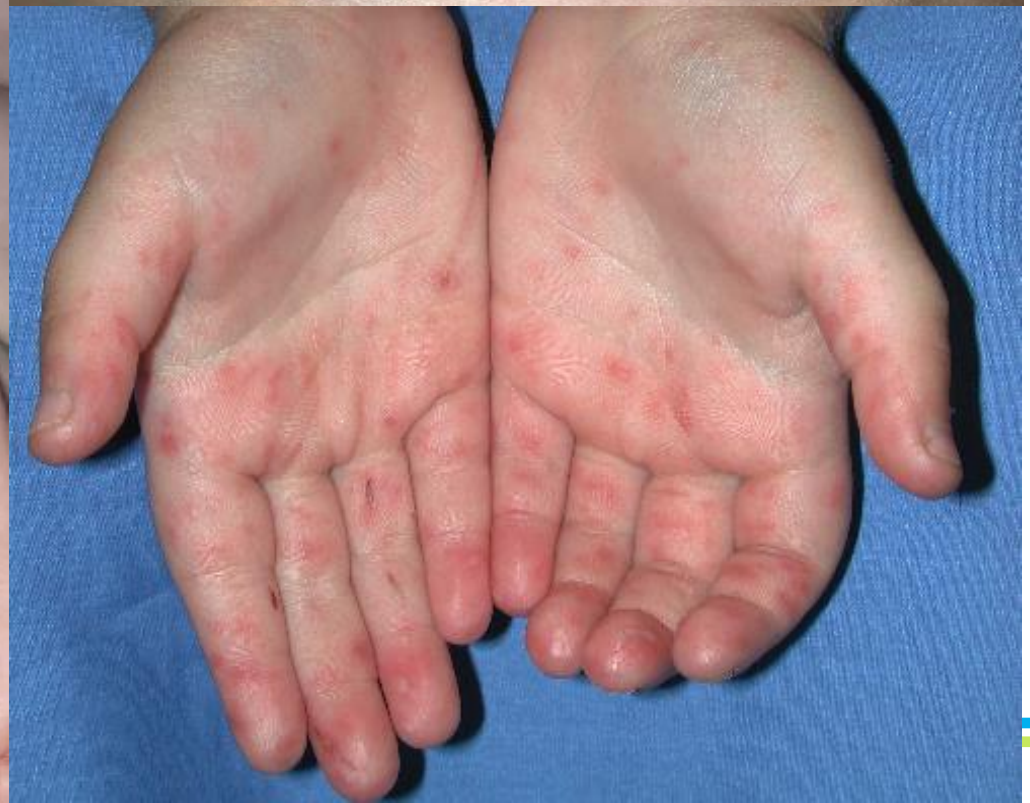
- Fourteen cases reported in China
- Multiple sites, “unbearable itching”
- All resistant to terbinafine, griseofulvin, fluconazole
- **Nine resistant to itraconazole**
- All susceptible to voriconazole, GoodRx price of $74 for 60 pills

Xie W, et al. Rapid emergence of recalcitrant dermatophytosis caused by a cluster of multidrug-resistant *Trichophyton indotineae* in China. *Br J Dermatol* 2024;190:585-7





Coxsackievirus A16 and Enterovirus 71



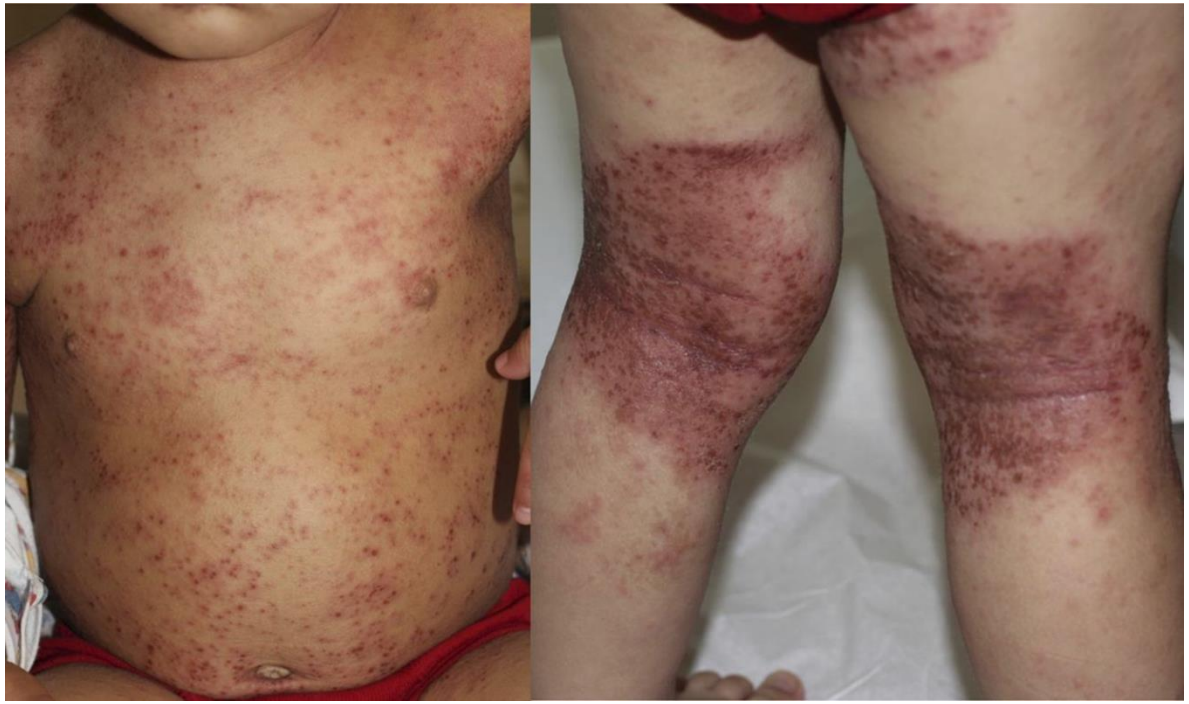
Atypical Coxsackievirus

- Emergence of Coxsackievirus A6 around 2008
- Literature review, 85 studies, 1359 patients
- Males 61%
- Mean age 2.4 years
- Vesicles (53%), papules (49%), bullae (36%), macules (20%), eczema coxsackium (19%)
- Hands and feet (61%), arms/legs (47%), **face (45%), perioral (22%),** oral mucosa (31%), buttocks (28%), groin (15%)

Starkey SY, et al. Atypical cutaneous findings of hand-foot-mouth disease in children: a systemic review. *Pediatr Dermatol* 2024;41:23-7

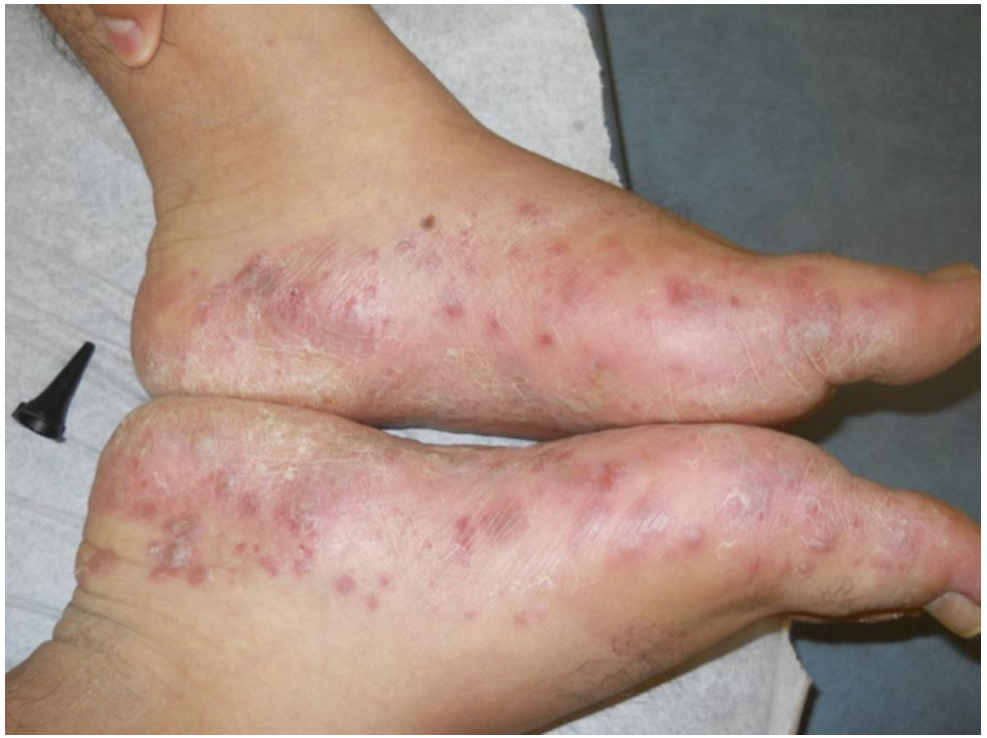
Coxsackievirus A6

- Eczema Coxsackium: Monomorphous erosions and vesicles in areas affected by atopic dermatitis (5



Coxsackievirus A6

- Hemorrhagic or purpuric lesions, usually older children



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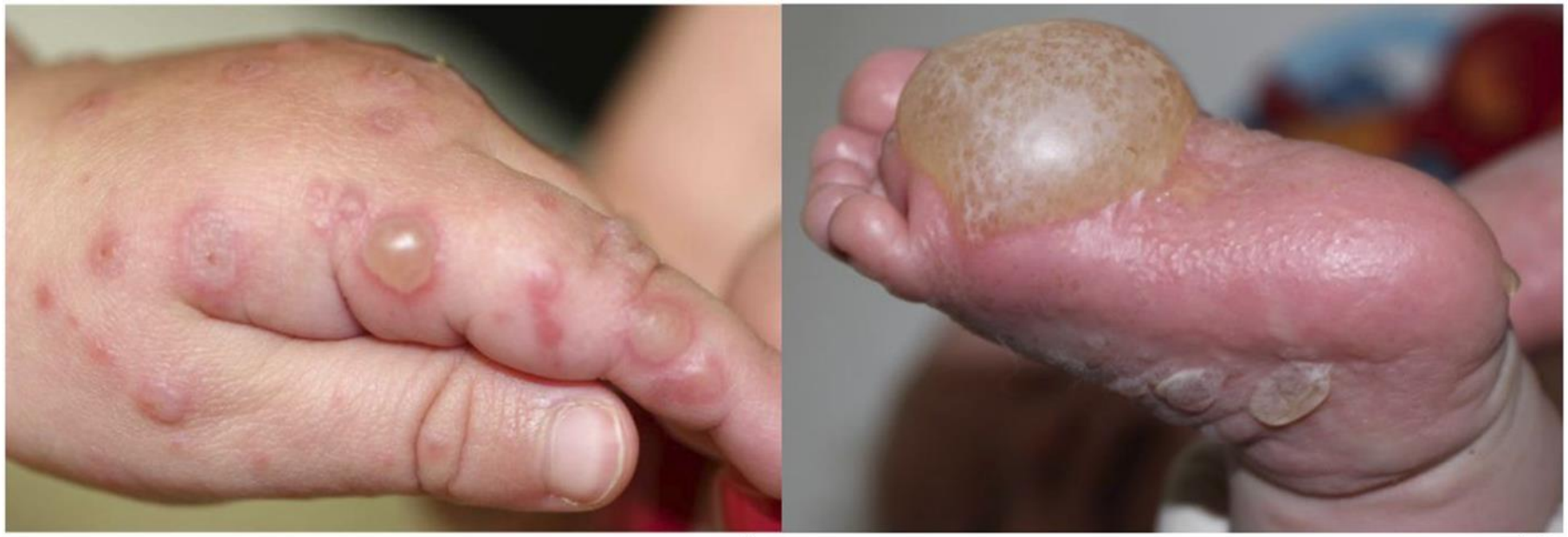
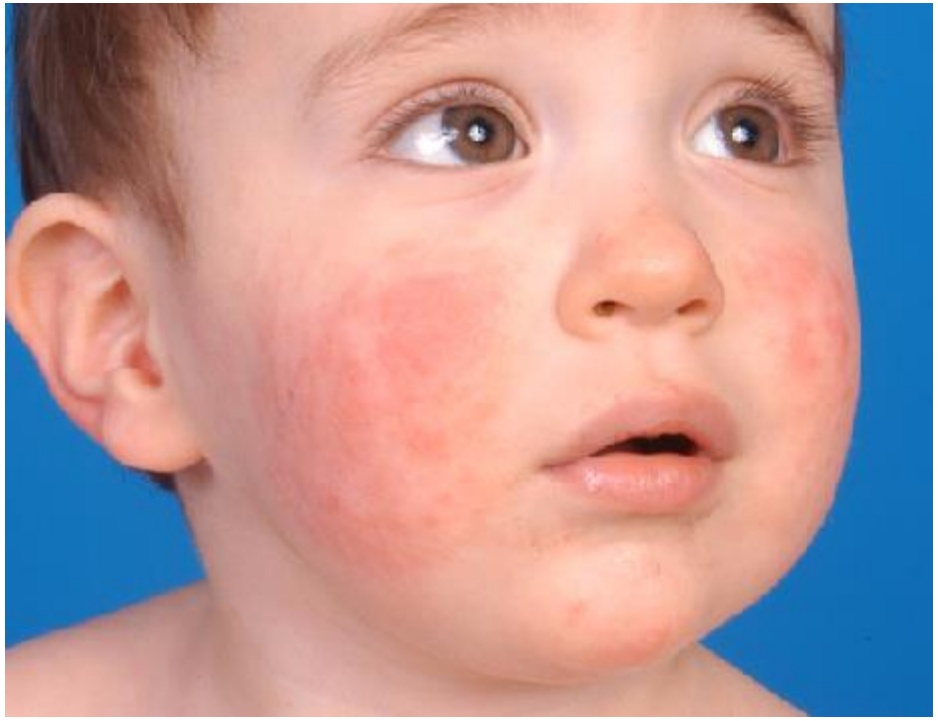


A B

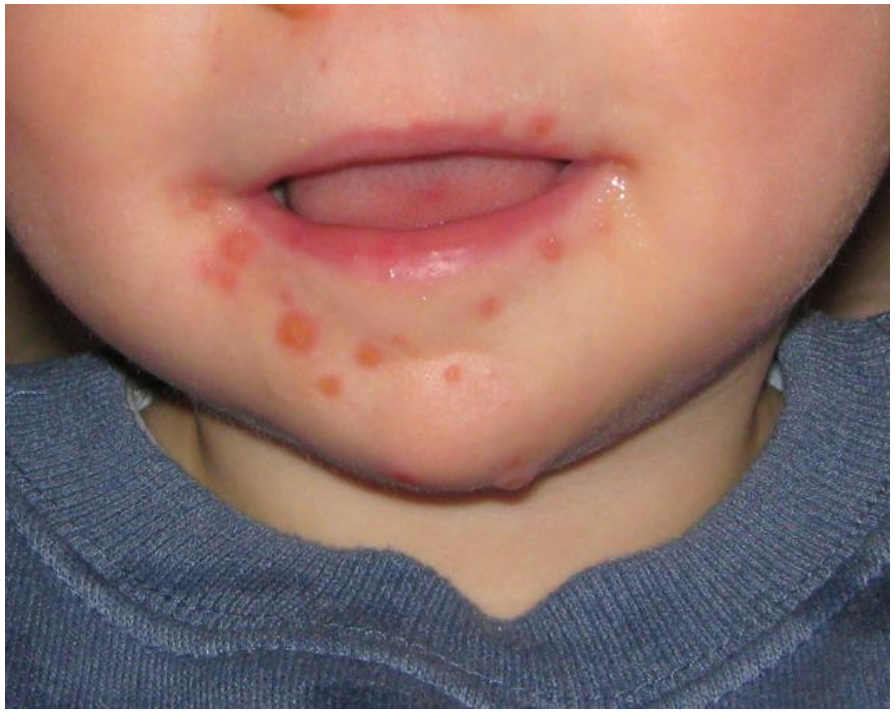
Coxsackievirus A6

- Gianotti-Crosti-like eruptions (37%)



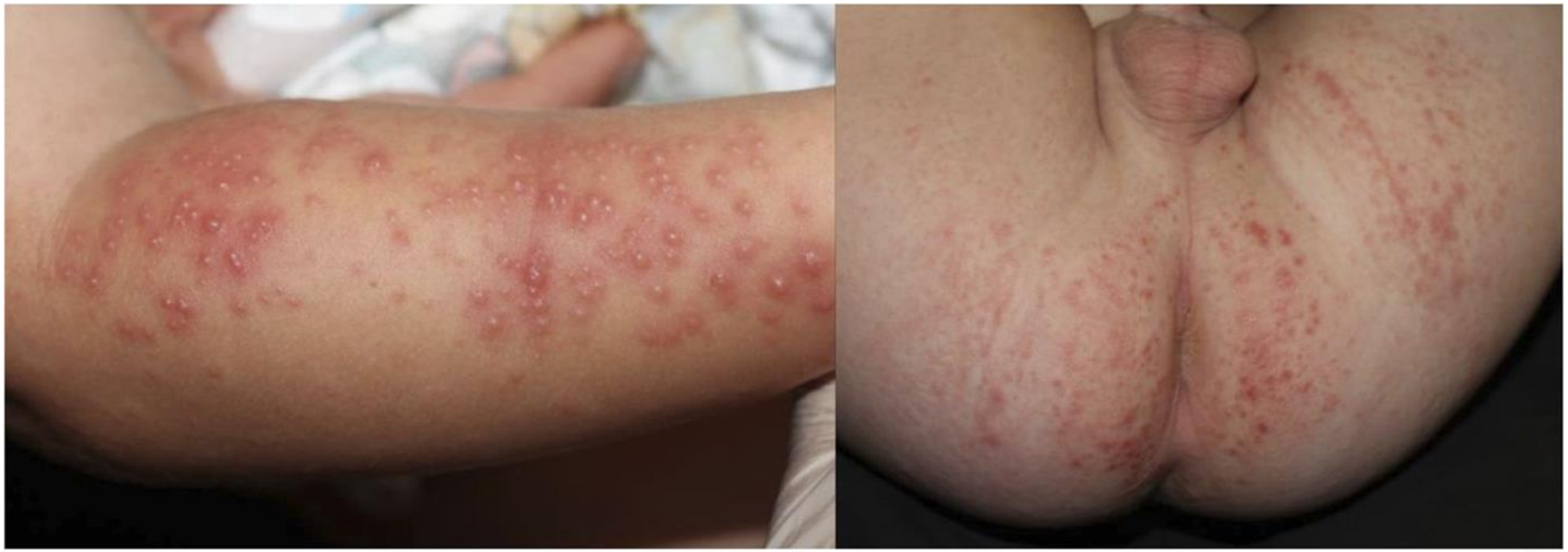
Coxsackievirus A6

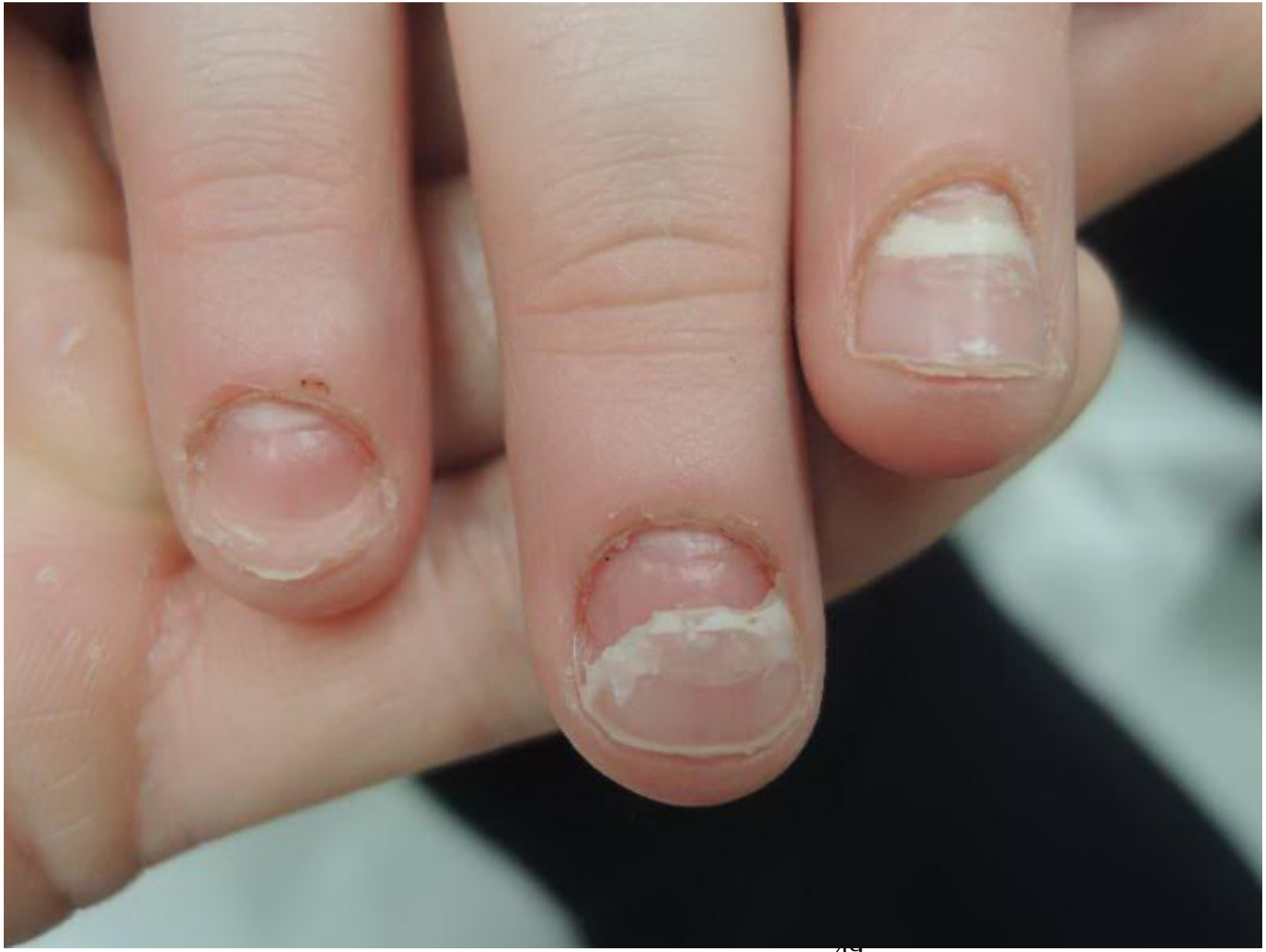
- Perioral lesions



Coxsackievirus A6

- Lesions in areas of previous trauma- sunburn, irritant dermatitis, thumb-sucking, diaper rash





Coxsackievirus A6

- Systemic symptoms
  - Fever 74%
  - Sore throat/mouth 18%
  - Less frequently cough (16%), vomiting, diarrhea, headache
  - No serious complications, no neurologic problems
- Duration 3-70 days, mean 10 days
- Hospitalization in 40%, reporting bias


Camp
Horizon
STAFF


Jan


CAMP HORIZON
1996

Camp Discovery 2024

- Week-long camps in Minnesota, Pennsylvania, Massachusetts (Connecticut), and Texas
- New camp starting in Southern California
- Creation of AAD Reimagining Camp Discovery Committee 2022
  - Securing economic stability
  - Strong push toward resident participation
  - Creation of new and varied camps- weekend, parents and siblings, non-summer

Camp Discovery 2024

- Refer campers:
  - With severe atopic dermatitis, psoriasis, alopecia areata
  - With genetic skin conditions such as epidermolysis bullosa, ichthyosis, ectodermal dysplasia, many others
  - With significant quality of life impairment due to their skin condition
- Google “AAD Camp Discovery referral form”
- E-mail Janine Mueller at the AAD office, jmueller@aad.org


adidas