# PEDIATRIC DERMATOLOGY

JUNE 2019

## Atopic dermatitis update: The field continues to evolve

## When treating impetigo, be aware of antibiotic resistance patterns

## Don't sweat axillary hyperhidrosis

## Premature children's skin is different

**Commentaries by Lawrence F. Eichenfield, MD, and Robert Sidbury, MD, MPH**

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Pediatric News®
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**1.** J Drugs Dermatol (2015) 14:478-479.

# 2019 will be an exciting year for pediatric dermatology!

**BY LAWRENCE F. EICHENFIELD, MD**

Children with common and uncommon skin disorders are part of our practices, and the field of pediatric dermatology is evolving.

Atopic dermatitis continues to rapidly evolve as a field as more research gives us insight into the immunologic features of inflammation in the skin, patterns of disease persistence, and the impact of comorbidities; as epidemiologic work reassesses age of onset; and as therapeutic options expand. New topical nonsteroidal medications are being worked into algorithms of care for atopic dermatitis, and new novel topical agents are being developed and studied in children, as highlighted in this issue. Biologic agents and small molecules are being studied for atopic dermatitis, with some medications targeting more than one "atopic" disease state, which opens the way for more effective and apparently safer systemic therapy.

Clinical experience fuels our abilities to diagnose and manage conditions. We see this with our recognition of focal allergic and irritant contact dermatitis from slime! If you don't know about slime or want to know more, read about this and other interesting aspects of pediatric contact rashes in this supplement. Similarly, we learn from our experience that bacterial resistance changes with time and exposure to antibiotics and that resistant impetigo is emerging. Gone are the days where amoxicillin is a good impetigo drug because *Staphylococcus aureus* is so commonly a pathogen and resistance (including mupirocin-resistant staph) has to be considered in our therapeutic decision making.

May you find this supplement useful for your practice and patients.

*Dr. Eichenfield is chief of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego. He is vice chair of dermatology and professor of dermatology and pediatrics at the University of California, San Diego. He has received research support and/or consulting fees from Amgen, Anacor/Pfizer, Dermira, Leo, Lilly, Regeneron/Sanofi, Novan, Novartis, and Valeant. Email him at pdnews@mdedge.com.*

# More than meets the eye

**BY ROBERT SIDBURY, MD, MPH**

A recurring theme in the palette of articles abstracted here is that with pediatric rashes there is often more than meets the eye.

Dr. Sheila Fallon Friedlander highlights a case where detection of the triangular-shaped lunula of the nails helps to identify a genetic condition at considerable risk for end-stage renal failure. Dr. Yvonne E. Chiu and her colleagues remind us that linear morphea on the extremities indicates a risk of musculoskeletal complications, particularly on the left side, while on the face it indicates a risk of neurological morbidity including headaches and seizures.

In the case of pediatric hidradenitis suppurativa, the disease itself may be hidden from view by reticent teens; once diagnosed, providers must remain vigilant for occult associations including precocious puberty and polycystic ovarian syndrome. Finally, Dr. Stanley Vance Jr. reminds us that hidden in plain sight can be the angst and vulnerability felt by many transgender patients, for whom the skin may be only the first layer of concern.

These and other articles help us all remain current in pediatric dermatology.

*Dr. Sidbury is chief of dermatology at Seattle Children's Hospital and professor, department of pediatrics, University of Washington, Seattle. He said he had no relevant disclosures. Email him at pdnews@mdedge.com.*

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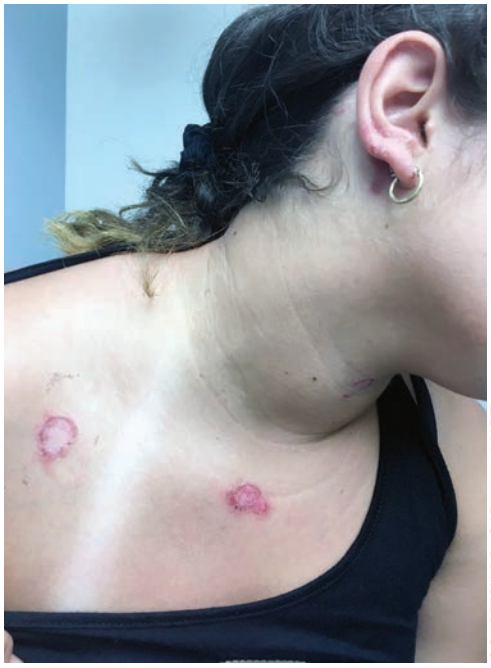
# What's the diagnosis?



COURTESY DR. CATALINA MATIZ

A 12-year-old female with a history of seborrheic dermatitis presents to the pediatric dermatology clinic for evaluation of crusty, somewhat tender lesions on her face, chest, neck, and arms for 5 days. She has been applying hydrocortisone to the lesions without improvement. She reports that about 1 week prior she got a new hamster pet. She denies any other symptoms such as fever, chills, joint pain, hair loss, mouth sores, or sun sensitivity. No other family members are affected. She has no other hobbies and she does not practice any team sports. She takes no oral prescription medications or vitamin supplements. She uses salicylic acid shampoo and fluocinonide oil to treat her seborrheic dermatitis.

On physical exam, the girl is in no acute distress. Her vital signs are stable, and she has no fever.

On skin examination, she has several erythematous, crusted scaly plaques with double ring of scale on the nose, ears, neck, upper chest, and few on the abdomen. On her left abdomen, there is a small blister. Her seborrheic dermatitis is well controlled with mild erythema behind her ears and minimal scale on her scalp.

**What's the diagnosis?**

A. Tinea corporis
B. Allergic contact dermatitis
C. Bullous impetigo
D. Subacute cutaneous lupus
E. Bullous arthropod bite reaction

SEE PAGE 12

# AD update: New insight into pathogenesis, prevention, and treatments

**BY RANDY DOTINGA**
REPORTING FROM SDEF LAS VEGAS DERMATOLOGY SEMINAR

LAS VEGAS – Recent research has provided a rare triple whammy in the world of atopic dermatitis (AD). Over the last few years, studies have provided valuable insight into not just treatments for AD but also its roots and strategies for prevention, Linda F. Stein Gold, MD, said at Skin Disease Education Foundation's annual Las Vegas Dermatology Seminar.

AD affects an estimated 7% of adults in the United States and 13% of children under age 18 years, according to the National Eczema Association. An estimated one-third of the affected children (3.2 million) have moderate to severe disease.

New information about AD includes more information pinpointing the genetic link. Dr. Stein Gold, director of clinical research in the department of dermatology at the Henry Ford Health System, Detroit, pointed out that about 70% of patients with AD have a family history of atopic conditions.

DR. STEIN GOLD

Mutations in filaggrin appear to play a role in the development of AD, but a significant proportion of people with AD do not have evidence of filaggrin mutations, and about 40% of people with defects never develop AD, she noted.

Emollients may be key to preventing AD. To explore the theory that defects on the skin barrier "might be key initiators of atopic dermatitis and possibly allergic sensitization," investigators conducted a randomized controlled study of 124 babies at risk of AD in the United States and United Kingdom; parents of 55 babies applied emollients to their whole bodies from shortly after birth until 6 months while a control group used nothing (J Allergy Clin Immunol. 2014 Oct;134[4]:818-23).

At 6 months, those in the emollient group were half as likely to have developed AD (relative risk, 0.50; $P = .017$).

Bleach baths have received attention on the AD prevention front. Dr. Stein Gold pointed to a 2017 systematic review and meta-analysis of five studies that found both bleach and water baths reduced AD severity. Bleach baths were effective but not more so than water

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baths (Ann Allergy Asthma Immunol. 2017 Nov;119[5]:435-40). Also, there was no difference in skin infections or colonization with *Staphylococcus aureus* between the two.

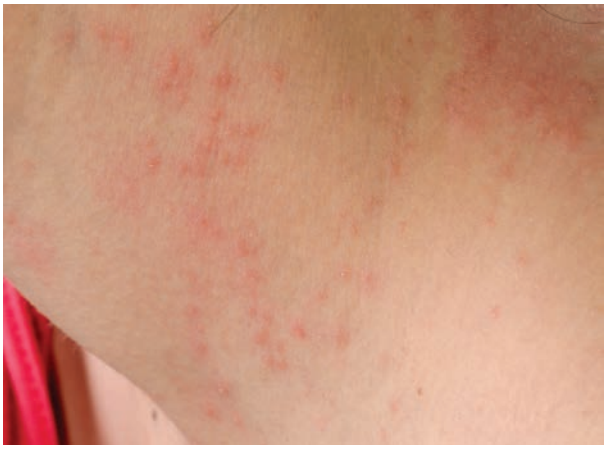
So are water baths just as good as bleach baths? "I'm not 100% sure I buy into this," Dr. Stein Gold said. "I'm still a bleach bath believer."

Topical calcineurin inhibitors (TCIs) can be used as a "proactive," steroid-sparing treatment to prevent relapses in AD, research suggests. For this purpose, the recommended maintenance dosage is two to three applications per week on areas that tend to flare; the TCIs can be used in conjunction with topical corticosteroids (J Am Acad Dermatol. 2014 Jul;71[1]:116-32).

TCIs come with boxed warning because of concerns about such cancers as lymphoma. But recent research has not found a higher risk of lymphoma in patients with AD who are treated with the medication. "We've had these drugs for a long time, and they do appear to be safe," Dr. Stein Gold said.

She referred to a 2015 review of 21 studies of almost 6,000 pediatric patients with AD who were treated with a TCI that concluded that the drugs are safe and efficacious over the long term (Pediatric Allergy Immunol. 2015 Jun;26[4]:306-15).

"Everyone wants to know which ones are better," Dr. Stein Gold said in regard to TCIs. But there aren't head-to-head studies, she said, and it's difficult to compare the available data on response rates between certain topical treatments because the studies are designed differently.



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For example, with crisaborole (Eucrisa), the topical phosphodiesterase-4 (PDE4) inhibitor approved in 2016 for mild to moderate AD in patients aged 2 years and up, clear/almost clear rates are 49%-52%, compared with 30%-40% with placebo, a 10%-20% difference. Rates with OPA-15406, an investigational

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## COMMENTARY **BY DR. EICHENFIELD**

### ATOPIC DERMATITIS: OUR HOT TOPIC IS "ATOPIC"

The world of pediatric atopic dermatitis (AD) is undergoing many changes, with the evolution of understanding of pathogenesis, two relatively newly approved therapies, and many treatments under study. Dr. Stein Gold's talk at the SDEF Las Vegas Dermatology Seminar is an excellent summary of this fast-moving field, but with practitioners' grounding care in the basics of excellent skin care and regular use of moisturizers. There is a push for all practitioners to get on the "long-term disease-control" bandwagon, using anti-inflammatory medications to control disease not just during flares but also in a proactive (vs. reactive) manner.

Dr. Stein Gold highlighted nonsteroidal agents, including crisaborole (Eucrisa), approved for ages 2 years and older. This is the first topical medication that is a phosphodiesterase type 4 (PDE4) inhibitor and has no restriction in duration of use or for region of skin treated; is not a corticosteroid; and is not associated with skin thinning. The TCIs (topical calcineurin inhibitors) also were discussed in regimens to prevent disease recurrence, with application to areas that tend to flare. Using nonsteroids on "hot spots" to prevent recurrence is akin to using an asthma controller therapy.

The first biologic agent for AD has been approved for adults for about 1 year, and there is off-label experience in children and adolescents that has been published (Pediatr Dermatol. 2019 Jan;36[1]:172-6), as well as phase 3 studies for children aged 12-17 years as a basis for expansion of the indication to adolescents. Dupixent is a monoclonal antibody that targets two interleukins (IL-4 and IL-13) – cytokines associated with TH-2 cells – is given as an injection every other week. The same medication already has received approval for ages 12 and older as an add-on maintenance treatment in patients with moderate to severe asthma (with an eosinophilic phenotype or with oral corticosteroid dependence), another TH-2 mediated disease. This medication is the first targeted systemic therapy for AD and can truly change the lives of severely affected individuals.

Dr. Stein Gold mentioned that there is a broad set of therapeutic agents in development for AD, which includes topical and systemic medications (both biologic agents and small molecules). And the timing is good for this because other research has shown the spectrum of associated problems (comorbidities) associated with AD, which includes traditional "atopic" conditions (allergic rhinoconjunctivitis, food allergy, asthma), neurodevelopmental and psychological issues (ADHD, anxiety, depression), infections (bacterial and viral), and others (Am J Clin Dermatol. 2018;19:821-38). The next 5-10 years will be intriguing as we become more conscious of this disease and its impact, given the evolving approaches to management.

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topical selective PDE4 inhibitor, and with the TCI pimecrolimus (Elidel cream 1%) have been about 20% higher than with controls, but studies are designed differently, and the results cannot be compared, according to Dr. Stein Gold.

Dupilumab (Dupixent), a monoclonal antibody that inhibits signaling of both interleukin-4 and interleukin-13, approved in 2017 for adults with moderate to severe AD, has been a "game changer" for this population, Dr. Stein Gold said. "It looks like this drug has a good, durable effect," she added (Lancet (2017 Jun 10;389[10086]:2287-303).

However, she cautioned that up to 10% of patients treated with dupilumab – or more – may develop conjunctivitis. Researchers studying dupilumab in asthma have not seen this side effect, she said, so it may be unique to AD. "It's something that's real," she said, noting that it's not clear if it's viral, allergic, or bacterial. Researchers are exploring the use of the drug in children, she added.

Dr. Stein Gold said there are other drugs in development for AD, but she cautioned that "the field is crowded ... and not all of them are going to make it."

Drugs in development for AD include nemolizumab (a humanized monoclonal antibody that inhibits interleukin-31 signaling), upadacitinib (a JAK1 selective inhibitor), baricitinib (an oral JAK1/2 inhibitor), and topical tapinarof (an agonist of the aryl hydrocarbon receptor).

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Dr. Stein Gold disclosed relationships with Galderma, Valeant, Ranbaxy, Promius, Actavis, Roche, Dermira, Medimetriks, Pfizer, Sanofi/Regeneron, Otsuka, and Taro.

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# Allergy, eczema common after pediatric solid organ transplantation

**BY AMY KARON**
FROM JOURNAL OF PEDIATRICS

A total of 34% of children who underwent solid organ transplantation subsequently developed eczema, food allergy, rhinitis, eosinophilic gastrointestinal disease, or asthma, according to the results of a single-center retrospective cohort study.

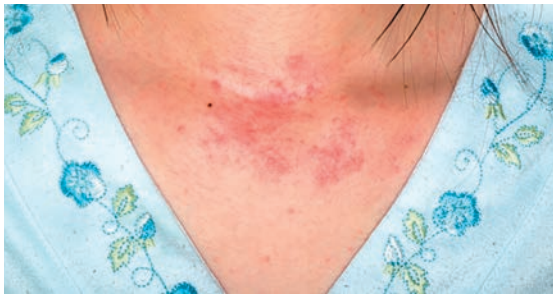
Another 6.6% of patients developed autoimmunity, usually autoimmune cytopenia, inflammatory bowel disease, or vasculitis, said Nufar Marcus, MD, of the University of Toronto and her associates.

Posttransplant allergy, autoimmunity, and immune-mediated disorders (PTAA) likely share a common pathogenesis "and may represent a unique state of post-transplant immune-dysregulation," they wrote. The report was published in the Journal of Pediatrics.

The study included 273 children who underwent solid organ transplantation and were followed for a median 3.6 years (range, 1.7-6.3 years). None had immune-mediated conditions or allergies diagnosed at baseline. Posttransplantation allergies most commonly included eczema (51%), asthma (32%), food allergy (25%, including 5% with associated anaphylaxis), rhinitis (17%), and eosinophilic esophagitis, gastritis, or enteritis (13%).

Median age at transplantation was 2.9 years (range, 0.7-10.3 years), and 59% of patients were male. Procedures usually involved liver (111) or heart (103) transplantation, while 52 patients underwent kidney transplantation and 7 underwent multivisceral transplantation. Heart transplantation patients were significantly more likely to develop asthma and autoimmunity, while liver transplantation patients had a significantly greater incidence of food allergies and eosinophilic gastrointestinal disease. "Recipients of multivisceral transplantation [also] had a high prevalence of autoimmunity [43%]," they wrote.

Although only 31% of patients had information available on family history of allergy, those with a positive family history of allergy had a fivefold greater odds of posttransplantation PTAA, compared with other patients. Other risk factors for PTAA included female sex, young age at transplantation, eosinophilia, and a positive test for Epstein-Barr virus after transplantation, Dr. Marcus and associates said.



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"The association of blood eosinophilia and PTAA reached statistical significance only when the transplant recipient was at least 6 months of age, demonstrating the nonspecific nature of abnormally high eosinophil counts during the first months of life," they noted. The longer patients had eosinophilia after transplantation, the more likely they were to develop PTAA, which suggests "a potential detrimental effect of prolonged activation of the eosinophilic-associated immune arms."

Ashley's Angels fund provided support. The researchers reported having no conflicts of interest.

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**SOURCE:** Marcus N et al. J Pediatr. 2018;196:154-60.

# Respect is key when treating dermatologic conditions in transgender youth

**BY DOUG BRUNK**
EXPERT ANALYSIS FROM SPD 2018

LAKE TAHOE, CALIF. – The way Stanley Vance Jr., MD, sees it, the No. 1 priority in the care of transgender youth is respecting their gender identity.

"This can really help with rapport and also help them continue to engage with your care," he said at the annual meeting of the Society for Pediatric Dermatology.

One of the first steps is to establish the patient's chosen name and pronouns. "Ask, use, and be consistent," said Dr. Vance, an adolescent medicine specialist at the University of California, San Francisco. "Taking it to another level, you can implement system-level tools to ensure that all of your staff consistently use the chosen name and pronouns. Something we've found helpful is including questions about chosen name and pronouns on patient intake forms and working with the IT department to have a place in our electronic medical record to put the chosen name and preferred pronouns."


DR. VANCE

A study published in the Journal of Adolescent Health showed that the use of chosen names and pronouns was associated with reduced depressive symptoms, suicidal ideation, and suicidal behavior among transgender youth.

Dr. Vance, who also holds a staff position at the UCSF Child and Adolescent Clinic, went on to discuss dermatologic considerations for gender diverse youth. In transgender females, estrogens can reduce the quantity and density of body and facial hair, "but it doesn't necessarily get rid of the hair, so we may refer to dermatology for hair removal or hair reduction. There can also be a decrease in sebum production, which can lead to dry skin for those who are at risk."

Transgender females often seek laser hair removal or electrolysis to aid in "blendability," or how they perceive as being female or feminine. "We know that this can help in psychosocial outcomes for these young people," Dr. Vance said. "Another reason why hair reduction and removal may be important is preoperatively for vaginoplasty."

In transgender males, testosterone increases male pattern hair growth and can increase male pattern hair loss. "Minoxidil does not interact with gender-affirming hormone treatment. If finasteride needs to be considered, it may interfere with the development of secondary sex characteristics." Testosterone also increases sebum production and can increase acne, particularly in the first 6 months to 1 year after initiation, and with increased titration. "Some transmasculine youth may need oral isotretinoin as stopping testosterone can be psychologically damaging," he said.

"Unfortunately, the iPLEDGE program requirements can be perceived as gender nonaffirming because patients must register by the sex assigned to them at birth, they must take pregnancy tests, and there can be provider assumptions about sexuality which does not equate with gender identity."

He recommended having "open and honest" conversations with patients about the requirements and limitations of dispensing oral isotretinoin. "Assure the patient that you will be respectful and affirming of their gender identity while they're in your office."

Dr. Vance had no relevant financial disclosures.

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## COMMENTARY
## BY DR. SIDBURY

### THERAPEUTIC AND PSYCHOSOCIAL DEXTERITY REQUIRED

Caring for transgender patients with acne requires therapeutic and psychosocial dexterity. Stanley Vance Jr., MD, an attending dermatologist in the UCSF Child and Adolescent clinic, touched on several related issues in an address to the Society for Pediatric Dermatology.

Dr. Vance affirmed the profound impact appropriate and consistent use of preferred pronouns can have, reminding providers to correct the record at the system level to assure appropriate encounters across the clinical experience. These efforts are about more than being polite; they can reduce depression and suicide ideation. Iatrogenic hormonal manipulation can have unintended consequences; facility treating unwanted hair, xerosis, and acne will lead to greater patient satisfaction. Responsible advocacy in the face of system barriers, such as the iPledge gender nonaffirming requirements to prevent pregnancy, will establish an important therapeutic foundation for this vulnerable patient population.

Lucia Campos-Munoz, MD, of the Hospital Clinico San Carlos in Madrid and her associates underscored such lessons learned from five patients treated at their institution (Pediatr Dermatol. 2018 Mar 25. doi: 10.1111/pde.13448). The use of isotretinoin is fraught beyond the issue of teratogenicity; this is a patient population at higher risk for depression, and isotretinoin has been associated with affective impacts.

# Treating female-to-male transgender teens with acne presents concerns with depression

**BY IAN LACY**
FROM PEDIATRIC DERMATOLOGY

Special consideration should be given to female-to-male transgender patients because of the dermatologic effects of testosterone, and possibility of accompanying depression, according to the results of a case series.

"Acne is a foreseeable adverse effect of testosterone treatment in transgender adolescents, and it may be advisable that, once such treatment has begun, they be monitored for the appearance of acne," Lucia Campos-Munoz, MD, of the Hospital Clinico San Carlos in Madrid wrote in Pediatric Dermatology. "Even if only mild, treatment should be provided."

Dr. Campos-Munoz and her colleagues examined five female-to-male transgender patients who were admitted to their clinic from 2016-2017. All five patients presented with testosterone-associated acne. Two patients with severe acne were treated with 20 mg/day of isotretinoin. While one patient tolerated this well and discontinued treatment after 4 months, another patient stopped treatment because of a bout of depression at 3 months. The remaining patients received other treatments, including doxycycline, 0.05 topical tretinoin, and 3% benzoyl peroxide.

**ACNE IS A FORESEEABLE ADVERSE EFFECT OF TESTOSTERONE TREATMENT IN TRANSGENDER ADOLESCENTS, AND IT MAY BE ADVISABLE THAT, ONCE SUCH TREATMENT HAS BEGUN, THEY BE MONITORED FOR THE APPEARANCE OF ACNE.**

This case series highlights the unique role that dermatologists and primary care providers play in treating acne in female-to-male transgender patients. Use of the proper pronouns and recognition that physical examinations of the chest and thorax may be especially embarrassing for these patients are important considerations, according to Dr. Campos-Munoz and her colleagues. Also, neither antiandrogenic agents nor contraceptives can be given because "this would conflict with the masculinization sought."

Apart from being aware of the patients' feelings, there are real medical concerns associated with dermatologic treatment of acne in female-to-male transgender patients. One of these risks is depression, which several studies have shown to be associated with severe acne. This is compounded by higher rates of depression and suicidal ideation in transgender adolescents, they said.

An additional concern is the teratogenic effects of isotretinoin in patients with natal female internal genitalia. While these patients may not think they can get pregnant because of testosterone-associated amenorrhea, the potential is still present and pregnancy should be avoided, Dr. Campos-Munoz and her colleagues warned.

No funding or conflicts of interest were disclosed.

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**SOURCE:** Campos-Munoz L et al. Pediatr Dermatol. 2018 Mar 25. doi: 10.1111/pde.13448.

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# Slime is not sublime: It may cause hand dermatitis

**BY IAN LACY**
FROM THE JOURNAL OF PEDIATRICS

Homemade, borax-containing "slime" can contribute to hand dermatitis.

An otherwise healthy 9-year-old girl was evaluated for pruritic hand dermatitis which lasted 5 months after exposure to homemade slime. Physical exam revealed erythematous, scaly plaques on the palmar surfaces of her hands; her fingernails had onychomadesis and longitudinal ridging. Despite frequent emolliation, her dermatitis persisted. She was then treated empirically for scabies and for culture-positive *Staphylococcus aureus* infection, which required a full round of cephalexin and mupirocin ointment. This also did not alleviate the dermatitis. A combination of homemade borax-containing slime avoidance, brief course of high-dose corticosteroids, and frequent bland emollients was prescribed because the dermatitis was assumed to be caused by an irritant.

Many of the components in homemade slime recipes are common household ingredients that are known to cause irritant or allergic contact dermatitis. Irritant contact dermatitis is a response from the innate immune system and is more frequent than the more severe allergic contact dermatitis, a type IV–mediated hypersensitivity reaction.

After review of this case and evaluation of other children with hand dermatitis, Julia K. Gittler, MD, of Columbia University, New York, and her colleagues have made a case that "slime" and new-onset hand dermatitis may be linked.

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**SOURCE:** Gittler JK et al. J Pediatr. 2018 May 3. doi: 10.1016/j.jpeds.2018.03.064 .

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## COMMENTARY **BY DR. EICHENFIELD**

### ITCHY RED HANDS? THINK SLIME

What do slime, jewelry, and potty seats have in common? All have been highlighted in relation to allergic contact dermatitis in children, including the article by Gittler et al. Slime is the most novel, as multiple reports and articles have made it into the literature and helped to improve knowledge about what I have called "SAD," an acronym for slime-associated dermatitis.

Slime, for readers who don't know, is homemade "goo," with various recipes usually containing boric acid (borax) and a variety of household ingredients. Slime is crafted, becoming a semisolid that is more viscous than traditional Play-Doh or Silly Putty. Household ingredients often included in slime include contact lens solution, liquid laundry detergents, shaving creams, and school glue. Slime users can develop hand dermatitis, which can look eczematous with erythema, scaling, vesicles, and – in more chronic cases – lichenification and even can present with nail dystrophy such as onychomadesis. The dermatitis can be both an irritant contact dermatitis or contact allergy to a specific component of the slime.

Chemicals that may be contactants include myristamidopropyl dimethylamine, propylene glycol, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), fragrance, sodium lauryl sulfate, and polyvinyl acetate glue. Articles have pointed out that boric acid is usually more of an irritant, while in one case, contact allergy was proven to be MCI/MI by contact allergy testing and mass spectroscopy showing that the chemical in school glue that was part of the slime concoction. Recognize that hand eczema may be SAD, elicit the history of slime use, and move on to treat with potent topical steroids and slime avoidance!

# Consider potty seats when you see contact dermatitis on toddler bottoms

**BY JILL D. PIVOVAROV**
FROM THE JOURNAL OF PEDIATRIC DERMATOLOGY

Potty-training seats may be to blame in toddlers presenting with pruritic rash on their buttocks and upper thighs. In such cases, be on the alert for contact dermatitis, reported Claire O. Dorfman, DO, of Lehigh Valley Health Network, Allentown, Pa., and her associates at Hershey (Pa.) Medical Center.

A 3-year-old white boy with a 6-month history of a pruritic rash on his buttocks and bilateral posterior thighs was treated without improvement at the pediatric dermatology clinic with low-potency topical corticosteroids, as well as topical antibiotic and antifungal agents.

Although the pattern of the multiple erythematous, scaly symmetrical plaques appeared atypical and not specific, the clinicians suspected contact dermatitis. Their report was published in the Journal of Pediatric Dermatology. Response was initially achieved with triamcinolone 0.025% cream twice daily, but the rash worsened and recurred after treatment concluded. Despite more aggressive treatment with fluocinonide 0.05% ointment twice daily, alternated with tacrolimus 0.03% ointment, and later augmented with betamethasone dipropionate 0.05% ointment twice daily from frequent flares, relief was not achieved.

Only mild improvement was seen once disposable paper toilet seat covers were added to treatment regimen. Following the purchase of a new potty seat through an online retailer, the child's mother discovered a number of consumer product reviews also detailing similar complaints about the manufacturer, Prince Lionheart WeePOD Basix, by more than 30 other consumers. Photos highlighting identical rash presentation in other toddlers confirmed that the toilet seat was responsible for the allergic reaction. A warning had been posted by the manufacturer but this warning was not provided by the online retailer.

Use of the seat was immediately discontinued, and complete resolution of lesions was achieved within 1 month; subsequently, a report to the Consumer Product Safety Commission was made.

Allergic contact dermatitis to toilet seats is becoming increasingly common, the authors noted. Although the source of allergies is varied, wood historically has been identified as the most common material associated with the condition. Polypropylene and polyurethane foam also have been found to cause irritation. However, in the case reported by Dr. Dorfman and her associates, the precise irritant could not be identified because of the atypical pattern of the lesions and their irregular presentation on the buttocks and thighs. They speculated that this irregularity could be attributed to "the small, round shape of the seat and the squirmy behavior of a toddler," because the typical arciform distribution was not present. Relief was not achieved with the paper liners because they did not completely cover the seat.


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Because the rash resolved when the seat was replaced, parents declined patch testing. As a result, it was not possible to identify the specific allergenic component of the polyurethane. The polyurethanes used to make the seats are synthetic polymers that contain isocyanates, and frequently diaminodiphenylmethane, a curing agent. Possible allergy to the dyes used during manufacture also was considered but the presenting rash was reported in all four of the available colors made.

Although it was speculated that exposure to cleansers could be to blame for possible irritant dermatitis given reports of cracking of the potty seat, the mother and several online reviews indicated only soap and water were used, not harsh cleaning agents.

The clinicians had no relevant financial disclosures.

pdnews@mdedge.com

**SOURCE:** Dorfman CO et al. Pediatr Dermatol. 2018 May 29. doi: 10.1111/pde.13534.

## COMMENTARY
## BY DR. EICHENFIELD

**BOTTOM LINE: CONTACT DERMATITIS**

When seeing buttock rashes in toddlers, think potty seats, as pointed out by Dorfman et al. in their paper in Pediatric Dermatology. Peculiar annular-shaped persistent dermatitis should prompt this consideration because allergic contact dermatitis to toilet seats now is clearly a phenomenon. A variety of contactants can be present in toilet seats and covers, and cleansers can be culprits in some cases as well. The usual approach to contact dermatitis should be followed – consider the culprit, treat the dermatitis, and avoid repeat exposure.

# Pediatric Dermatology Consult
# Bullous impetigo

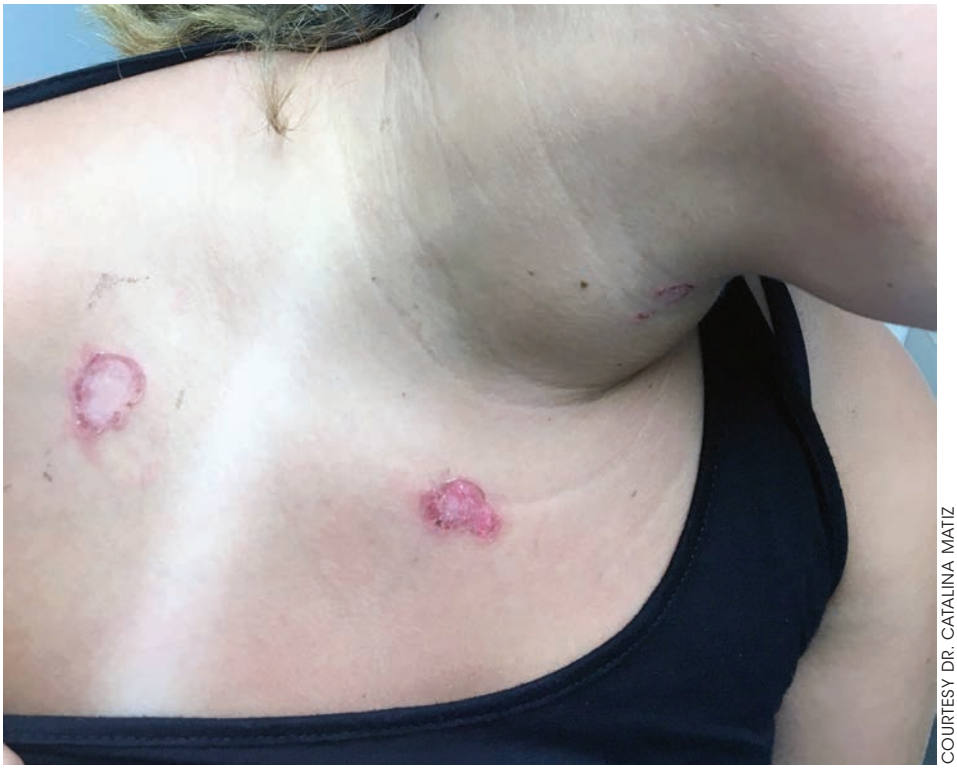
**BY CATALINA MATIZ, MD**

At the visit, the girl's skin scrapings were analyzed under the microscope with potassium hydroxide (KOH), and no fungal elements were seen. A culture from one of the lesions was positive for methicillin-sensitive *Staphylococcus aureus*.

She was diagnosed with bullous impetigo (BI).

Impetigo is the most common superficial skin infection and can present as a nonbullous (most common) and bullous (least common) form.[1] Nonbullous impetigo is usually caused the *Staphylococcus aureus* or *Streptococcus pyogenes* and tends to occur at sites of prior trauma like insect bites, scratches, atopic dermatitis, or varicella. On the other hand, bullous impetigo is caused by the local production of exfoliative toxins (ETA or ETB) by phage group II of *Staphylococcus aureus*. The exfoliative toxin binds to desmoglin-1, one of the desmosomal proteins of the skin, causing acantholysis at the level of the granular layer and blister formation. Different from nonbullous impetigo, bullous impetigo tends to occur in normal, undamaged skin. Lesions are more common in neonates and young infants, but children also can be affected.

The characteristic lesions in bullous impetigo are small blisters that enlarge to 1-cm to 5-cm bullae that easily rupture, which leaves an erythematous plaque with a collarette of scale or "double ring scale," with minimal crust and mild erythema. They commonly occur on the face, trunk, buttocks, and intertriginous areas. The lesions heal within 4-6 weeks, leaving no scarring. Associated systemic symptoms are rare, but some patients can present with weakness, fever, and diarrhea. The toxin can disseminate and cause staphylococcal scalded skin syndrome in neonates or older patients with renal failure or immunodeficiency.



COURTESY DR. CATALINA MATIZ

**IMPETIGO IS THE MOST COMMON SUPERFICIAL SKIN INFECTION AND CAN PRESENT AS A NONBULLOUS (MOST COMMON) AND BULLOUS (LEAST COMMON) FORM.**

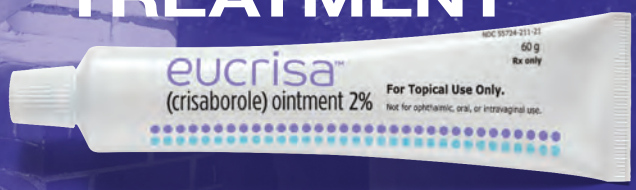
The transmission of *Staphylococcus aureus* can occur from colonized or infected family members, from engagment in contact sports, and from contact with animals such as dogs, cattle, and poultry.[2] Transmission from a pet rabbit also has been reported. In our patient, transmission from her pet hamster could have occurred as the areas on the body where there were lesions were areas where she was holding and cuddling her new pet.

The differential diagnosis of the type of lesions our patient presented with includes tinea corporis and bullous tinea, which also can be transmitted by animals such as kittens. A KOH analysis ruled out this diagnosis. Tinea skin lesions tend to be more scaly than bullous impetigo lesions, which are more inflamed and crusted. Bullous arthropod reactions should be considered in the differential diagnosis as well. Bullous bite reaction lesions present with tense bullae as they are subepidermal in nature and are pruritic. Subacute cutaneous lupus lesions present as annular

Pages 12a—12b ▸

For the treatment of mild-to-moderate atopic dermatitis in patients 2 and older


# MANY BODY PARTS SAME TREATMENT




**Steroid-free EUCRISA provides efficacy and can be used in a long-term treatment plan[1-4]***

**In 28-day pivotal trials (see Study Design below):**
**Significantly more EUCRISA patients achieved success in ISGA† at Day 29[1-3]**
- **EUCRISA (n=503) 32.8%, vehicle (n=256) 25.4%; *P*=0.038 in Trial 1**
- **EUCRISA (n=513) 31.4%, vehicle (n=250) 18.0%; *P*<0.001 in Trial 2**

For topical use only.
Not for ophthalmic, oral, or intravaginal use.

**Studied in pivotal trials for 28 days and in a long-term, open-label safety extension study for up to 48 weeks**

*Should be applied twice daily to affected areas.
†Success in ISGA, a stringent metric, is defined as Clear (0) or Almost Clear (1) **AND** at least a 2-grade improvement from baseline.[1]
ISGA=Investigator's Static Global Assessment.

## STUDY DESIGN[1-4]

Two multicenter, randomized, double-blind, vehicle-controlled trials (Trial 1 and Trial 2) treating 1522 patients (1016 EUCRISA; 506 vehicle), 2 to 79 years of age, with mild-to-moderate atopic dermatitis. Patients were instructed to apply EUCRISA or vehicle twice daily for 28 days. Efficacy and safety endpoints were evaluated at Days 1 (baseline), 8, 15, 22, and 29. The primary efficacy endpoint was success in ISGA at Day 29.

Eligible patients from pivotal trials were enrolled in the open-label safety extension study for up to 48 weeks. Patients were evaluated every 28 days, and entered an on-treatment or off-treatment cycle, based on disease severity. 517 patients were analyzed, of which 396 were followed for 6 months and 271 were followed for 12 months. Treatment-related adverse events occurring in ≥1% of EUCRISA patients were application site pain (2%; n=12); application site infection (1%; n=6); and atopic dermatitis (3%; n=16). **The open-label safety extension study did not evaluate the efficacy of EUCRISA.**

## INDICATION

EUCRISA is indicated for topical treatment of mild-to-moderate atopic dermatitis in patients 2 years of age and older.

## IMPORTANT SAFETY INFORMATION

### Contraindications

EUCRISA is contraindicated in patients with known hypersensitivity to crisaborole or any component of the formulation.

### Warnings and Precautions

Hypersensitivity reactions, including contact urticaria, have occurred in patients treated with EUCRISA and should be suspected in the event of severe pruritus, swelling and erythema at the application site or at a distant site. Discontinue EUCRISA immediately and initiate appropriate therapy if signs and symptoms of hypersensitivity occur.

### Adverse Reactions

The most common adverse reaction occurring in ≥1% of subjects in clinical trials was application site pain, such as burning or stinging.

***Please see brief summary of Full Prescribing Information on reverse page.***

eucrisa®
crisaborole ointment 2%

**Learn more at www.EucrisaHCP.com**

**References: 1.** EUCRISA® (crisaborole) Full Prescribing Information. December 2018. **2.** Paller AS, Tom WL, Lebwohl MG, et al. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. *J Am Acad Dermatol.* 2016;75(3):494-503.e4. **3.** Data on file. Pfizer Inc, New York, NY. **4.** Eichenfield LF, Call RS, Forsha DW, et al. Long-term safety of crisaborole ointment 2% in children and adults with mild to moderate atopic dermatitis. *J Am Acad Dermatol.* 2017;77(4):641-649.e5.

PP-CRI-USA-1700

Printed in USA/February 2019
Pfizer

**EUCRISA™ (crisaborole) ointment, 2%**
**Brief Summary of Prescribing Information**

## INDICATIONS AND USAGE

EUCRISA is indicated for topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.

## DOSAGE AND ADMINISTRATION

Apply a thin layer of EUCRISA twice daily to affected areas. EUCRISA is for topical use only and not for ophthalmic, oral, or intravaginal use.

## DOSAGE FORMS AND STRENGTHS

Ointment: 20 mg of crisaborole per gram (2%) of white to off-white ointment.

## CONTRAINDICATIONS

EUCRISA is contraindicated in patients with known hypersensitivity to crisaborole or any component of the formulation. [*see Warnings and Precautions*]

## WARNINGS AND PRECAUTIONS

**Hypersensitivity Reactions** Hypersensitivity reactions, including contact urticaria, have occurred in patients treated with EUCRISA. Hypersensitivity should be suspected in the event of severe pruritus, swelling and erythema at the application site or at a distant site. If signs and symptoms of hypersensitivity occur, discontinue EUCRISA immediately and initiate appropriate therapy.

## ADVERSE REACTIONS

**Clinical Trials Experience** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In two double-blind, vehicle-controlled clinical trials (Trial 1 and Trial 2), 1012 subjects 2 to 79 years of age with mild to moderate atopic dermatitis were treated with EUCRISA twice daily for 4 weeks. The adverse reaction reported by ≥1% of EUCRISA-treated subjects is listed in Table 1.

**Table 1: Adverse Reaction Occurring in ≥1% of Subjects in Atopic Dermatitis Trials through Week 4**

| Adverse Reaction | EUCRISA N=1012 n (%) | Vehicle N=499 n (%) |
|---|---|---|
| Application site pain[a] | 45 (4) | 6 (1) |

[a] Refers to skin sensations such as burning or stinging.

Less common (<1%) adverse reactions in subjects treated with EUCRISA included contact urticaria [*see Warnings and Precautions*].

## USE IN SPECIFIC POPULATIONS

**Pregnancy** Risk Summary There is no available data with EUCRISA in pregnant women to inform the drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there were no adverse developmental effects observed with oral administration of crisaborole in pregnant rats and rabbits during organogenesis at doses up to 3 and 2 times, respectively, the maximum recommended human dose (MRHD) [*see Data*]. The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies carry some risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects in the U.S. general population is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies. Data *Animal Data* Rat and rabbit embryo-fetal development was assessed after oral administration of crisaborole. Crisaborole did not cause adverse effects to the fetus at oral doses up to 300 mg/kg/day in pregnant rats during the period of organogenesis (3 times the MRHD on an AUC comparison basis). No treatment-related fetal malformations were noted after oral treatment with crisaborole in pregnant rats at doses up to 600 mg/kg/day (13 times the MRHD on an AUC comparison basis) during the period of organogenesis. Maternal toxicity was produced at the high dose of 600 mg/kg/day in pregnant rats and was associated with findings of decreased fetal body weight and delayed skeletal ossification. Crisaborole did not cause adverse effects to the fetus at oral doses up to the highest dose tested of 100 mg/kg/day in pregnant rabbits during the period of organogenesis (2 times the MRHD on an AUC comparison basis). In a prenatal/postnatal development study, pregnant rats were treated with crisaborole at doses of 150, 300, and 600 mg/kg/day by oral gavage during gestation and lactation (from gestation day 7 through day 20 of lactation). Crisaborole did not have any adverse effects on fetal development at doses up to 600 mg/kg/day (13 times the MRHD on an AUC comparison basis). Maternal toxicity was produced at the high dose of 600 mg/kg/day in pregnant rats and was associated with findings of stillbirths, pup mortality, and reduced pup weights.

**Lactation** Risk Summary There is no information available on the presence of EUCRISA in human milk, the effects of the drug on the breastfed infant or the effects of the drug on milk production after topical application of EUCRISA to women who are breastfeeding. EUCRISA is systemically absorbed. The lack of clinical data during lactation precludes a clear determination of the risk of EUCRISA to a breastfed infant. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EUCRISA and any potential adverse effects on the breastfed infant from EUCRISA or from the underlying maternal condition.

**Pediatric Use** The safety and effectiveness of EUCRISA have been established in pediatric patients age 2 years and older for topical treatment of mild to moderate atopic dermatitis. Use of EUCRISA in this age group is supported by evidence from two multicenter, randomized, double-blind, parallel-group, vehicle-controlled 28-day trials which included 1,313 pediatric subjects 2 years and older [*see Adverse Reactions and Clinical Studies in Full Prescribing Information*]. The safety and effectiveness of EUCRISA in pediatric patients below the age of 2 years have not been established.

**Geriatric Use** Clinical studies of EUCRISA did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects.

## NONCLINICAL TOXICOLOGY

**Carcinogenesis, Mutagenesis, Impairment of Fertility** In an oral carcinogenicity study in Sprague-Dawley rats, oral doses of 30, 100, and 300 mg/kg/day crisaborole were administered to rats once daily. A drug-related increased incidence of benign granular cell tumors in the uterus with cervix or vagina (combined) was noted in 300 mg/kg/day crisaborole treated female rats (2 times the MRHD on an AUC comparison basis). The clinical relevance of this finding is unknown. In a dermal carcinogenicity study in CD-1 mice, topical doses of 2%, 5% and 7% crisaborole ointment were administered once daily. No drug-related neoplastic findings were noted at topical doses up to 7% crisaborole ointment (1 times the MRHD on an AUC comparison basis). Crisaborole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and human lymphocyte chromosomal aberration assay) and one in vivo genotoxicity test (rat micronucleus assay). No effects on fertility were observed in male or female rats that were administered oral doses up to 600 mg/kg/day crisaborole (13 times the MRHD on an AUC comparison basis) prior to and during early pregnancy.

## PATIENT COUNSELING INFORMATION

Advise the patient or caregivers to read the FDA-approved patient labeling (Patient Information). Hypersensitivity Reactions: Advise patients to discontinue EUCRISA and seek medical attention immediately if signs or symptoms of hypersensitivity occur [*see Warnings and Precautions*]. Administration Instructions: Advise patients or caregivers that EUCRISA is for external use only and is not for ophthalmic, oral, or intravaginal use.

**Rx only** This Brief Summary is based on EUCRISA Prescribing Information LAB-0916-3.0, issued December 2018.

scaly plaques with an erythematous border and central clearing usually in sun exposed areas similar to the distribution of our patient. Severe contact dermatitis reactions also can blister and form lesions similar to those seen in our patient but with the difference that our patient didn't complain of pruritus, which is a characteristic feature of allergic contact dermatitis. In neonates or young infants with bullous lesions, other conditions such as herpes simplex infection, epidermolysis bullosa, bullous pemphigoid, linear IgA bullous dermatosis, bullous mastocytosis, and bullous erythema multiforme should be considered in the differential diagnosis.

First-line treatment for impetigo consists of the use of topical application of mupirocin (Bactroban) 2% ointment, retapamulin (Altabax) 1% ointment, or fusidic acid 2% cream. A Cochrane review compared systemic versus topical treatment for impetigo, concluding that topical treatment with either mupirocin or retapamulin is equally if not more effective than oral antibiotics.[3] Ozenoxacin (Xepi), a new nonfluorinated topical quinolone, has recently been approved by the Food and Drug Administration for the treatment of localized impetigo in patients 2 months of age and older.[4] When there is treatment failure with topical antibiotics, widespread disease, or systemic symptoms, oral antimicrobials should be consider, such as beta-lactamase–resistant penicillin, first-generation cephalosporins, or clindamycin. The use of bleach baths and general hygiene measures for 4 months can reduce the risks of recurrence in 20% of the patients, as noted by a study by Kaplan et al.[5]

Our patient was treated with oral cephalexin for 7 days as well as topical mupirocin with fast resolution of the lesions. Sadly, the parents gave her hamster pet away.

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## COMMENTARY **BY DR. EICHENFIELD**

**IMPETIGO: BE AWARE OF RESISTANCE PATTERNS AND A NEW TOPICAL AGENT**

Bacterial resistance is a major health care issue, reflecting the evolution of nature and adaptation to antibiotics. Antibiotics can be miraculously effective, but resistant strains can emerge, which changes the epidemiology of even common infections. Such is the case with impetigo and other soft-tissue infections, which have evolved over the years and decades. Impetigo is associated with staph and strep infections, but regional variations in staph sensitivity should affect the approach to antibiotic selection. For instance, with broader use of clindamycin in pediatrics, presumably as a response to community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), we have seen many children in our practice with "garden variety impetigo that is clindamycin resistant, also seen in staphylococcal scalded skin patients in our and other centers" (Pediatr Dermatol. 2014 May-Jun;31[3]:305-8).

And while topical therapy is appropriate for localized impetigo, as discussed by Catalina Matiz, MD, in her teaching case, mupirocin resistance is more common (Antimicrob Agents Chemother. 2015;59[6]:3350-6). Be aware of regional patterns of bacterial sensitivity, and consider culturing impetigo and other soft-tissue infections, especially if there is poor clinical response to initial therapy. Dr. Matiz pointed out the new nonfluorinated topical quinolone, ozenoxacin (Xepi), which is approved for localized impetigo for 2 months of age and older and apparently has excellent coverage for mupirocin-resistant *S. aureus*.

**IN OUR PATIENT, TRANSMISSION FROM HER PET HAMSTER COULD HAVE OCCURRED AS THE AREAS ON THE BODY WHERE THERE WERE LESIONS WERE AREAS WHERE SHE WAS HOLDING AND CUDDLING HER NEW PET.**

# Site of morphea lesions predicts the risk of extracutaneous manifestations

**BY DOUG BRUNK**
REPORTING FROM SPD 2018

LAKE TAHOE, CALIF. – Morphea lesions on the extensor extremities, face, and superior head are associated with higher rates of extracutaneous involvement, results from a multicenter, retrospective study showed.

**JOINT CONTRACTURES SHOWED THE GREATEST DISCREPANCY BETWEEN LEFT AND RIGHT EXTREMITY. SO PERHAPS IF YOU'RE USING THAT ONE SIDE MORE, YOU'RE LESS LIKELY TO HAVE A JOINT CONTRACTURE.**

"We know that risk is highest with linear morphea," lead study author Yvonne E. Chiu, MD, said at the annual meeting of the Society for Pediatric Dermatology. "Specifically, linear morphea on the head and neck is associated with neurologic issues, and linear morphea on a limb is associated with musculoskeletal issues. However, risk stratification within each of those sites has never really been studied before."

Dr. Chiu, who is a pediatric dermatologist at the Medical College of Wisconsin and Children's Hospital of Wisconsin in Milwaukee, and her associates carried out a 14-site retrospective study in an effort to characterize morphea lesional distribution and to determine which sites had the highest risk for extracutaneous manifestations. They limited the analysis to patients with pediatric-onset morphea before the age of 18 and adequate lesional photographs in their clinical record. Patients with extragenital lichen sclerosis and atrophoderma were included in the analysis, but those with pansclerotic morphea and eosinophilic fasciitis were excluded. The researchers used custom, Web-based software to map the morphea lesions, and linked those data to a REDCap database where demographic and clinical information was stored. From this, the researchers tracked neurologic symptoms such as seizures, migraine headaches, other headaches, or any other neurologic signs or symptoms; neurologic testing results from those who underwent MRI, CT, and EEG; musculoskeletal symptoms such as arthritis, arthralgias, joint contracture, leg length discrepancy, and other musculoskeletal issues, as well as ophthalmologic manifestations including uveitis and other ophthalmologic symptoms. Logistic regression was used to analyze association of body sites with extracutaneous involvement.

Dr. Chiu, who also directs the dermatology residency program at the Medical College of Wisconsin, reported findings from 826 patients with 2,467 skin lesions of morphea, or an average of about 1.92 lesions per patient. Consistent with prior reports, most patients were female (73%), and the most prevalent subtype was linear morphea (56%), followed by plaque (29%), generalized (8%), and mixed (7%).

The trunk was the single most commonly affected body site, seen in 36% of cases. "However, if you lumped all body sites together, the extremities were the most commonly affected site (44%), while 16% of lesions involved the head and 4% involved the neck," Dr. Chiu said. Patients with linear morphea had the highest rate of extracutaneous involvement. Specifically,

## COMMENTARY **BY DR. SIDBURY**

**STRATIFYING EXTRACUTANEOUS MANIFESTATIONS WITH LINEAR MORPHEA**

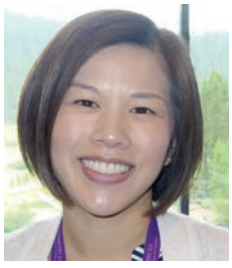
Linear morphea has been associated with musculoskeletal and neurologic morbidity. Chiu et al. in the Pediatric Dermatology Research Alliance (PeDRA) conducted a multicenter, retrospective study to drill down on these associations.

While other types of morphea rarely have extracutaneous manifestations, the linear subtype had the highest incidence: 34% had musculoskeletal involvement, 24% neurologic, and 10% ophthalmologic. A fascinating and novel finding was the strong predilection for left extremity musculoskeletal morbidity, particularly contracture. Although handedness was not captured, a plausible explanation may be that increased utilization of an affected extremity may decrease morbidity. Similarly, anterior head involvement was more likely (odds ratio, 2.56) associated with neurologic sequelae, although reasons for this remain unclear.

All patients diagnosed with linear morphea should be screened for musculoskeletal, neurologic, and ophthalmologic morbidity, but Dr. Chiu's work will help pediatricians risk stratify.

34% had musculoskeletal involvement, 24% had neurologic involvement, and 10% had ophthalmologic involvement. There were small rates of extracutaneous manifestations in the other types of morphea as well.

The most common musculoskeletal complications among patients with linear morphea were arthralgias (20%) and joint contractures (17%), followed by other musculoskeletal complications (15%), leg length discrepancy (5%), and arthritis (2%). Contrary to previously published reports, nonmigraine headaches were more common than seizures among patients with linear morphea (17% vs. 4%, respectively), while 4% of subjects had migraine headaches. Of the 134 subjects who underwent neuroimaging, 19% had abnormal results. Ophthalmologic complications were rare among patients overall, with the exception of those who had linear morphea. Of these cases, 1% had uveitis, and 9% had some other ophthalmologic condition.



DR. CHIU

Among all patients, the researchers found that left-extremity and extensor-extremity lesions had a stronger association with musculoskeletal involvement (odds ratios of 1.26 and 1.94, respectively). "The reasons for this are unclear," Dr. Chiu said. "We didn't assess handedness in our study, but that perhaps could explain it; 90% of the general population is right-hand dominant, so perhaps there's some sort of protective effect if you're using an extremity more. Joint contractures showed the greatest discrepancy between left and right extremity. So perhaps if you're using that one side more, you're less likely to have a joint contracture."

When the researchers limited the analysis to head lesions, they observed no significant difference in the lesions between the left and right head (OR, 0.72), but anterior head lesions had a stronger association with neurologic signs or symptoms, compared with posterior head lesions (OR, 2.56), as did superior head lesions, compared with inferior head lesions (OR, 2.23). The association between head lesion location and ophthalmologic involvement was not significant.

"The odds of extracutaneous manifestations vary by site of morphea lesions, with higher odds seen on the left extremity, extensor extremity, the anterior head, and the superior head," Dr. Chiu concluded. "Further research can be done to perhaps help us decide whether this necessitates difference in management or screening."

The project was funded by the Pediatric Dermatology Research Alliance and the SPD. Dr. Chiu reported having no relevant financial disclosures.

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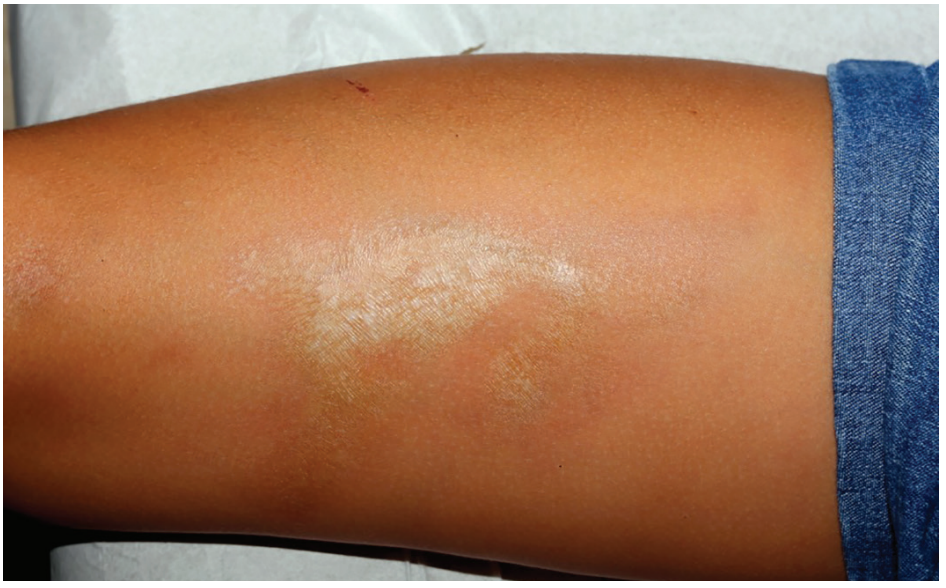
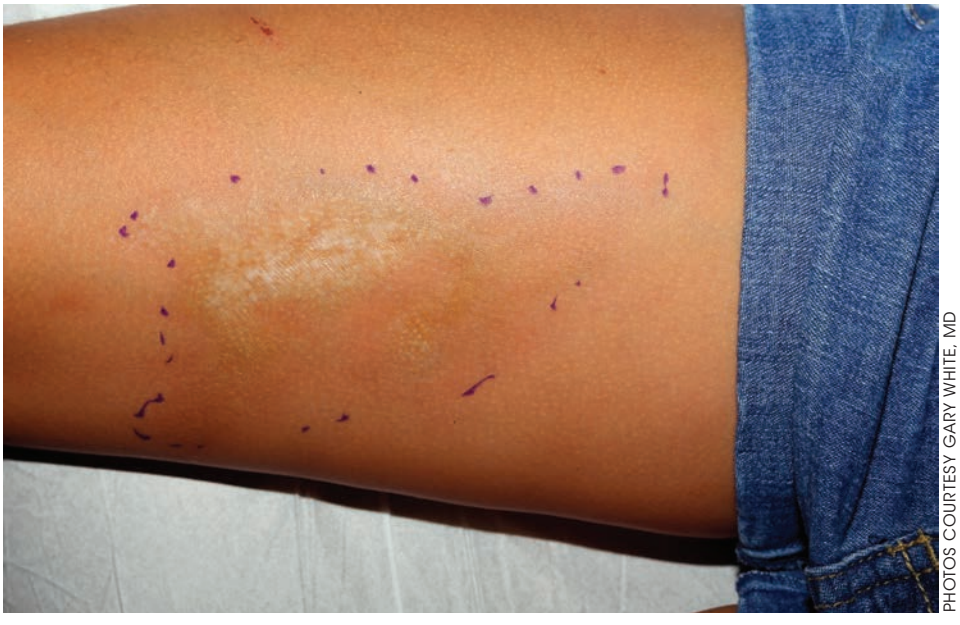


*A morphea lesion is evident on the thigh of this child.*



PHOTOS COURTESY GARY WHITE, MD

*A morphea lesion is seen on the thigh of this child, with purple marks indicating the extent of the lesion.*

# Guidelines-based intervention improves pediatrician management of acne

**BY BIANCA NOGRADY**
FROM THE JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

A guidelines-based educational program on treating acne in teenagers has led to significant improvements in pediatricians' management of the condition and decreased referrals to dermatologists, new research suggests.

A research letter published online May in the Journal of the American Academy of Dermatology described the results of a study involving 116 pediatricians, who participated in an educational program, including brief live sessions, on how to manage acne in teenagers.

The participants also used an EHR ordering tool that allowed for prescriptions based on the severity of the acne and delivered customized care plans and educational materials.

After 4 months, researchers saw that acne-coded visits to pediatricians increased by 18% ($P$ less than .001), but this did not translate to more work for the physicians involved; instead, three-quarters of those involved said the treatment process involved "minimal to no work."

At the same time, the intervention was associated with a 26% decrease in the percentage of acne referrals to dermatologists, reported Jenna Borok of the Rady Children's Hospital in San Diego, and her coauthors.

The researchers saw a fivefold increase in the likelihood of pediatricians prescribing retinoids ($P = .003$), after controlling for confounding factors such as sex and insurance status, and significantly less topical clindamycin being prescribed.

The study was initiated to address what the authors described as a "practice gap" between pediatricians treating acne, compared with dermatologists treating acne, which included significantly lower prescribing rates of topical retinoids among pediatricians.

Ms. Borok and her coauthors wrote that their educational program and prescribing tool aimed to address this practice gap without increasing the workload for pediatricians or dermatologists. "Adherence to guidelines by pediatricians has the potential to improve treatment provided in the primary care setting, better patient satisfaction, and allow greater access to dermatologists and pediatric dermatologists for patients with more severe acne and other conditions."

Acknowledging that the study took place over a relatively short period of time, the authors said future research would examine the impact of the educational program and ordering tool on patient acne outcomes.

No funding or conflicts of interest were declared.

*pdnews@mdedge.com*

RAWPIXEL/THINKSTOCK

**SOURCE:** Borok J et al. J Am Acad Dermatol. 2018 May 9. doi: 10.1016/j.jaad.2018.04.055.

## COMMENTARY **BY DR. SIDBURY**

### OPTIMIZING ACNE CARE BY PEDIATRICIANS

In 2013, the American Academy of Pediatrics sanctioned acne treatment guidelines for the first time (Pediatrics. 2013 May;131[Suppl 3]:S163-86). A combination of factors including earlier age at presentation of both puberty and acne, the lack of Food and Drug Administration–approved treatment options for younger children, and a documented discrepancy between prescribing patterns of dermatologists and primary care doctors highlighted an important treatment gap.

Borok et al. now have shown that application of these guidelines by pediatricians can lead to improved outcomes. During the relatively brief 4-month study window, acne-related visits to pediatricians increased, while related referrals to dermatologists decreased by 26%. Prescriptions for topical retinoids, a first-line topical agent, increased fivefold. With access to pediatric dermatologists challenging, optimizing acne care at the primary care level will improve patient and provider satisfaction.

# AAP infantile hemangioma guideline should empower primary care clinicians

**BY JILL D. PIVOVAROV**
FROM PEDIATRICS

The American Academy of Pediatrics has issued its first clinical practice guideline on infantile hemangiomas (IHs), given the dramatic increase in information available over the past decade.

The aim in providing an evidence-based approach to evaluating, triaging, and managing IH cases is to arm primary care providers with the confidence needed to successfully treat high-risk cases, reported Daniel P. Krowchuk, MD, of the department of pediatrics and dermatology, Wake Forest University, Winston-Salem, N.C., and his associates who are members of the AAP subcommittee on the management of IHs.

With an occurrence rate of 4%-5%, IHs are the most common benign tumor presenting in childhood, especially occurring in girls, twins, preterm or low-birth-weight infants, and white neonates.

The AAP's guideline "provides a framework for clinical decision-making" – it should not be considered a sole source of guidance. It also should not be used to replace clinical judgment or as a protocol for managing all patients with IHs, explained Dr. Krowchuk and his associates.

Clinicians are especially encouraged to consult promptly with a hemangioma specialist if they are not experienced in managing IHs.

According to one study cited by the authors, the mean age of examination by a dermatologist is 5 months, when most growth has already been completed. Lesions are first noticed, on average, at 2 weeks; 4 weeks has been recommended as the ideal time for professional consultation. It is important for clinicians to recognize the difficulty families are likely to face in obtaining an appointment, which makes caregiver and clinician advocacy on behalf of infants affected critical, urged Dr. Krowchuk and

**'PROMPT EVALUATION, EITHER IN-PERSON OR VIA PHOTOGRAPHS, IS WARRANTED FOR ANY INFANT REPORTED BY PARENTS TO HAVE A CHANGING BIRTHMARK DURING THE FIRST 2 MONTHS OF LIFE.'**

## COMMENTARY **BY DR. EICHENFIELD**

### HEMANGIOMAS: SETTING A NEW STANDARD BEYOND 'WATCHFUL WAITING'

Infantile hemangiomas (IH), now the preferred term for these proliferative vascular lesions, are quite common, with an occurrence rate of 4%-5% in infants. The approach to hemangiomas is remarkably different than decades ago, as we have learned about PHACE syndrome with facial hemangiomas, systemic propranolol for functionally significant and deforming hemangiomas, timolol for early superficial lesions, and that the timing for intervention to minimize their impact is very early in life.

The American Academy of Pediatrics clinical practice guideline published in January 2019 is a landmark paper that should establish new standards of practice for IH management. My takeaway: Every practitioner taking care of infants should read it!

Early evaluation is critical, and as first author Daniel Krowchuk has stated, "prompt evaluation" is warranted for "a changing birthmark during the first 2 months of life." Pediatric practitioners should evaluate early and carefully, and refer and/or initiate aggressive management as appropriate. Dermatologists and especially pediatric dermatologists should set up pathways to allow infants to be seen without significant delays that may allow the hemangioma to proliferate in a way that may leave permanent sequelae that could be avoided. Let's not "let the horse out of the barn" or the "cow out of the pasture."

The management of more high-risk IH with oral propranolol can be tremendously successful, as highlighted in the paper by Baselga et al. Dr. Baselga has expanded the literature, as previous studies of propranolol did not include high-risk patients, and this study shows great efficacy with higher doses (3 mg/kg), often treated to 1 year of age or sometimes beyond in the face of rebound on withdrawal. It is good to know that multiple studies, including the highlighted one by Lund et al., have supported that pretreatment ECGs are unnecessary prior to initiating propranolol, unless certain risk factors exist that would warrant it, so it is one less activity that might delay initiation of propranolol for IH when appropriate.

his colleagues. In cases or locations where hemangioma specialists are in short supply, telemedicine triage or photographic consultation is especially helpful.

Dr. Krowchuk and his associates noted several possible challenges in implementing this clinical practice guideline (CPG) published in Pediatrics. The growth of individual IHs is difficult to predict, especially in young infants, and there are no markers or imaging studies to correct this challenge. For this reason, they advised: "Prompt evaluation, either in-person or via photographs, is warranted for any infant reported by parents to have a changing birthmark during the first 2 months of life."

Wide heterogeneity in terms of size, location, patterns, of distribution, and depth, when coupled with unpredictable growth, makes management of IHs unpredictable. Thus, there can be no one-size-fits-all treatment approach.

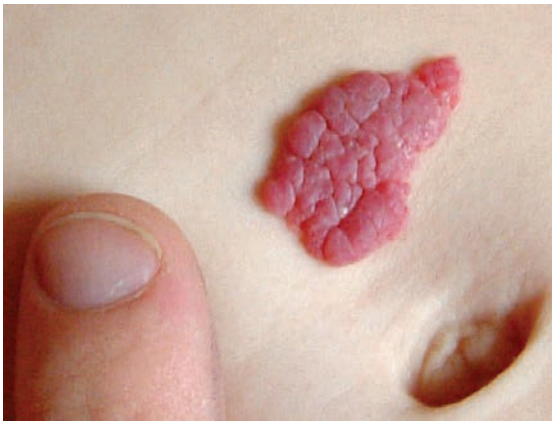
Further complicating implementation of the CPG is the long-held myth that IHs are benign and resolve spontaneously. While this may accurately describe the vast majority of outcomes, "ample evidence" demonstrates what can happen when family and/or caregivers yield to such "false reassurance." According to Dr. Krowchuk and his associates, hemangioma specialists have seen their share of "examples of lost opportunities to intervene and prevent poor outcomes because of lack of or delayed referral."

The paucity of data on high-risk cases in primary care and referral care settings should be the subject of future research, the authors noted. Scorings systems, such as the Hemangioma Severity Score, are growing in popularity as a triage tool, but more research is needed to demonstrate that primary care physicians are accurately interpreting findings and that high-risk cases are accurately identified to avoid overreferral to specialists.

Dr. Krowchuk and his colleagues did call attention to important evidence gaps that may be answered by research currently underway, or that may require further research in the future by asking the following questions: How safe is treatment with topical timolol in early infancy, and what proportion of patients can be observed without referral? For healthy infants 5 weeks or older, to what extent, if any, is cardiovascular monitoring for propranolol necessary? How should pediatricians be involved in beta-blocker management of infants and when should specialty reevaluation be made? What is the accuracy of primary care identification of high-risk IH cases using many of the parameters offered within this CPG? Are pediatric trainees being sufficiently trained in stratifying and managing IH risk?

One noteworthy barrier to improved management and outcomes noted by the authors is the "imprecision of current diagnostic codes." At present, the existing coding in the International Classification of Diseases, 10th Revision does not include specific reference to IH but rather describes "hemangioma of the skin and subcutaneous tissues" and can include congenital as well as verrucous hemangioma. The codes also do not address the details characteristic of IHs or the higher risk aspects of IH, such as location or multifocality. Advocacy, in this instance, would be appropriate, advised Dr. Krowchuk and his associates.

In an interview, Dr. Krowchuk provided additional insight into what sets the AAP's CPG apart from consensus statements published previously by European and Australasian expert groups. Although these might appear to be similar documents with analogous content at first glance, there are important differences, he said.



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The consensus statements were based on expert opinion, while "the academy's CPG was founded on an extensive review of the medical literature (1982-2017) regarding the potential benefits and harms of diagnostic modalities and pharmacologic and surgical treatments," Dr. Krowchuk explained. The information that came out of this extensive review is what members of the subcommittee used to develop key action statements that pediatricians can use to evaluate and manage infants with IHs.

**DR. KROWCHUK PROVIDED ADDITIONAL INSIGHT INTO WHAT SETS THE AAP'S CPG APART FROM CONSENSUS STATEMENTS PUBLISHED PREVIOUSLY BY EUROPEAN AND AUSTRALASIAN EXPERT GROUPS.**

"The scope of the consensus statements was more limited, focusing primarily on the treatment of IH with propranolol. While the benefits of propranolol, its use and dosing, and potential adverse effects were addressed in depth in the academy's CPG, the document went well beyond this," he clarified.

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The AAP also previously published a clinical report that provides a comprehensive evaluation of the pathogenesis, clinical features, and treatment of IH (Pediatrics. 2015 Oct. doi: 10.1542/peds.2015-2485).

There was no external funding for the CPG, and the authors said there were no potential conflicts of interest. Ilona J. Frieden, MD, is a member of the data monitoring safety board for Pfizer and the scientific advisory board for Venthera/Bridge Bio; Anthony J. Mancini, MD, said he has advisory board relationships with Verrica, Valeant, and Pfizer.

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**SOURCE:** Krowchuk DP et al. Pediatrics 2019;143(1):e20183475.

# Summary of the clinical practice guideline's key action statements

| Indication | | Definition/implication | Evidence quality | Strength of recommendation |
|---|---|---|---|---|
| Risk stratification | IA | IHs should be classified as high risk if there is evidence or potential for life-threatening complications, functional impairment or ulceration, structural anomalies, or permanent disfigurement. | X | Strong |
| | IB | Once identified as high-risk, IHs should be evaluated as soon as possible by a hemangioma specialist. | X | Strong |
| Imaging | 2A | Imaging should not be performed unless IH diagnosis is uncertain, five or more cutaneous IHs are present, or anatomic abnormalities are suspected. | B | Moderate |
| | 2B | Ultrasonography should be the first choice in imaging when IH diagnosis is uncertain. | C | Weak |
| | 2C | MRI is recommended when there are concerns about structural abnormalities. | B | Moderate |
| Pharmacotherapy | 3A | Oral propranolol should be the first-line agent in cases of IH that require systemic treatment. | A | Strong |
| | 3B | In the absence of comorbidities or adverse effects such as sleep disturbance, propranolol should be dosed between 2 and 3 mg/kg per day. | A | Moderate |
| | 3C | Treatment providers are advised to recommend administration of propranolol during or after feeding and suspension of treatment when there is "diminished oral intake or vomiting to reduce the risk of hypoglycemia." | X | Strong |
| | 3D | Patients should be evaluated and caregivers educated concerning the potential adverse effects of propranolol, such as sleep disturbances, bronchial irritation, and "clinically symptomatic bradycardia and hypotension." | X | Strong |
| | 3E | Oral prednisolone or prednisone may be prescribed to treat IHs in the presence of contraindications or inadequate response to oral propranolol. | B | Moderate |
| | 3F | Intralesional injection of triamcinolone and/or betamethasone may be recommended for "bulky IHs during proliferation or in certain critical anatomical locations," such as the lip. | B | Moderate |
| | 3G | Topical timolol maleate may be prescribed as therapy for IHs that are thin and/or superficial. | B | Moderate |
| Surgical management | 4 | Surgery and laser therapy may be recommended as options for treating select cases of IHs. | C | Moderate |
| Parent education | 5 | Treatment providers are advised to educate parents about the "expected natural history of IH and its potential for causing complications or disfigurement." | X | Strong |

Source: Pediatrics 2019;143(1):e20183475

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**2.** Balazs EA, Band P. Hyaluronic acid: its structure and use. *FDC Rep Drugs Cosmet.* 1984;99:65-72.



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# Extended propranolol use boosts success in high-risk infantile hemangioma

**BY MADHU RAJARAMAN**
FROM PEDIATRICS

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Extending oral propranolol treatment up to 12 months of age increased the success rate for high-risk infantile hemangioma, according to results published in Pediatrics.

Previous studies of oral propranol for infantile hemangiomas (IH) have revealed its efficacy, although there is no consensus on the optimal treatment duration. Nonetheless, treatment up to 12 months of age has been proposed if patients don't respond after 6 months. Infants with high-risk hemangiomas, however, have been excluded from previous studies, authors of the current study explained.

In an open-label study of patients aged 35-150 days the success rate of oral propranolol was 47% after 6 months of treatment. The rate increased to 76% after the initial treatment period, reported Eulalia Baselga, MD, of the department of dermatology at Hospital de la Santa Creu i Sant Pau in Barcelona, and coauthors.

**TREATMENT SUCCESS WAS ACHIEVED BY 21 (47%) PATIENTS AFTER 6 MONTHS AND BY 34 (76%) PATIENTS BY THE END OF THE ITP.**

Investigators studied 45 patients from 10 hospitals in Spain and Poland between June 2015 and February 2017. The patients had high-risk IH in the proliferative phase. High-risk hemangiomas were defined as those that were life threatening, at risk for functional impact, disfiguring, or ulcerated nonresponsive to standard wound care measures.

Oral propranolol was administered twice daily at a dosage of 3 mg/kg per day. During the initial treatment period (ITP), patients received propranolol for a minimum of 6 months, and if treatment was not successful, it continued until success or up to 12 months of age.

Patients who achieved success in the initial phase were managed for 3 months with no treatment, and if there was rebound growth, treatment was restarted for up to 6 months at the provider's discretion.

Treatment was considered a success if the target hemangioma resolved and there was no functional impact. The IH was considered resolved if it disappeared, even if there were minimal telangiectasias, erythema, skin thickening, soft tissue swelling, or the presence of sequelae.

Treatment success was achieved by 21 (47%) patients after 6 months and by 34 (76%) patients by the end of the ITP. Functional impact was determined using the Hemangioma Severity and Hemangioma Dynamic Complication scales. Adverse events, reported by 80% of patients, were resolved by the end of the study and included respiratory syncytial virus bronchiolitis, ulcerated hemangioma, pneumonia and respiratory failure, inguinal hernia, upper respiratory tract infection, dehydration, bronchitis, choking, and thermal burn. Although no patients experienced adverse events that resulted in discontinuation of treatment, 35 events led to temporary discontinuation, primarily because of respiratory events, the authors reported.

The results indicate that "oral propranolol is effective in treating high-risk IH with a favorable safety profile," the authors concluded.

The study was funded by the Institut de Recherche Pierre Fabre Several authors were employed by or had other relationships with Pierre Fabre. The other authors had no conflicts of interest.

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**SOURCE:** Baselga E et al. Pediatrics. 2018. doi: 10.1542/peds.2017-3866.

# Orodental issues often associated with facial port-wine stains

**BY DOUG BRUNK**
REPORTING FROM SPD 2018

LAKE TAHOE, CALIF. – Several years ago, David H. Darrow, MD, DDS, began to notice a pattern in the conversation threads on websites dedicated to support for parents of children with facial port-wine stains (PWS).

Parents were reporting that dental problems arose earlier on their child's side of face with the PWS, and that the alveolar ridge was lower on the side of the face that harbored the lesion. "Most importantly, parents were concerned that dentists were not touching their children because they were concerned about bleeding," Dr. Darrow said at the annual meeting of the Society for Pediatric Dermatology. A search in the medical literature for port-wine stains and oral cavity changes, did not turn up much except for a few articles on bleeding. "One said that port-wine stains or capillary malformations rarely present major problems for the oral and maxillofacial surgeon. The other said that periodontal probing should not be done, as even gentle probing can result in uncontrolled bleeding," he noted.

**'THE GOALS OF THERAPY ARE PREVENTION OF PERIODONTAL DISEASE WITH METICULOUS ORAL HYGIENE.'**

This prompted Dr. Darrow, who directs the Center for Hemangiomas and Vascular Birthmarks at the Eastern Virginia Medical School, Norfolk, and coinvestigators, Megan B. Dowling, MD, and Yueqin Zhao, PhD, to characterize manifestations of PWS in the oral cavity via an anonymous paired survey of volunteers with facial PWS and their dentists who were recruited from birthmarks.com and 10 collaborating physician practices (J Am Acad Dermatol. 2012;67:687-93). Volunteers ranged in age from 1 to 62 years; mean age was 29 years. A total of 30 patients participated, and most (67%) were female.

The five most common oral manifestations reported by the patients were lip hyperplasia (53%), stained gingiva (47%), malocclusion (30%), bleeding gingiva (27%), and spacing between teeth (23%). Only 3% reported bleeding from dental procedures. When the researchers evaluated the orodental findings in the paired patient-physician responses, "most of the time there was good agreement between the patient and the dentist," Dr. Darrow said. "The only one that fell out of agreement was lip hyperplasia. That's probably because most dentists look right past the lips and into the oral cavity."

When the researchers examined patients who had stained gingiva versus those who did not, they found that early-stage lesions demonstrated a reddish blush of the oral mucosa and gingiva, while late-stage lesions demonstrated increased blush of the oral tissues, as well as hyperplasia of the soft tissue or bone in the affected area. "Based on our review of the literature, bleeding of gums is rarely prolonged and dental procedures are safe," Dr. Darrow said.

The findings are important, he continued, because capillary malformations of the oral cavity may result in periodontal disease associated with gingival overgrowth. The depth of the gingival pocket should be no more than 2-3 mm. "When you have areas of inflammation and deep-pocket formation, plaque and bacteria slowly erode the connection between the tooth and the soft tissue," he explained. "At some point, that pocket becomes so deep that it reaches down into the bone in which the tooth is anchored. As that bone is eroded, the teeth loosen and begin to fall out. The goals of therapy are prevention of periodontal disease with meticulous oral hygiene."

Soft tissue hyperplasia may be exacerbated by medications such as calcium channel blockers, cyclosporine, and phenytoin and phenobarbital, which are sometimes used by patients with Sturge-Weber syndrome, he said.

Dr. Darrow reported having no financial disclosures.

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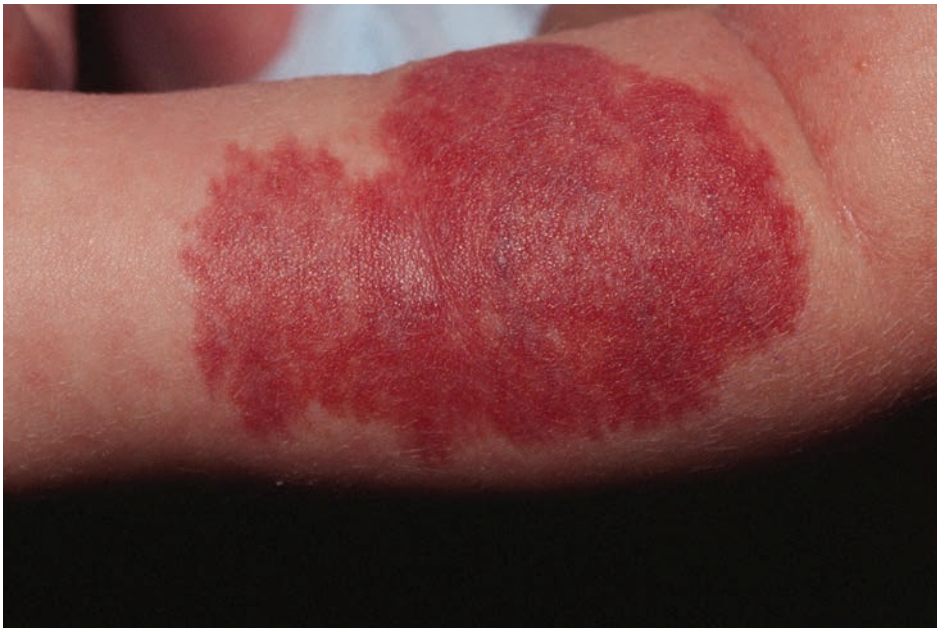
## COMMENTARY
## BY DR. EICHENFIELD

**OTHER RED LESIONS? PORT-WINE STAINS MAY BE ASSOCIATED WITH DENTAL AND OTHER ORAL PROBLEMS**

Dr. David H. Darrow is a pediatric otorhinolaryngologist who is also a dentist, and an expert in vascular tumors and hemangiomas based in Norfolk, Va. He and his colleagues have reported myriad dental and orofacial problems associated with facial port-wine stains in children. Gingival hyperplasia, staining, bleeding, lip hyperplasia, malocclusion, and abnormal spacing between teeth were the most common associations. Patients should be encouraged to have good oral care to prevent periodontal disease. While patients with port-wine stains should be made aware of orodental associations, it appears that dangerous bleeding is rare, presumably seen with more complex vascular anomalies.

# Pretreatment ECG unwarranted for most infantile hemangioma patients on propranolol

**BY JILL D. PIVOVAROV**
FROM PEDIATRIC DERMATOLOGY



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Pretreatment ECG screening is unnecessary for most infants with infantile hemangioma who are prescribed propranolol therapy, reported Emily B. Lund, MD, of the University of Chicago, and her associates.

This finding supports previously published studies that pretreatment ECG is not necessary, despite consensus guidelines published in 2013 that recommend ECG screening of high-risk infants presenting with below-normal heart rate, arrhythmia, or family history of either arrhythmia or congenital heart disease.

Dr. Lund and her associates conducted a retrospective chart review of 272 patients with infantile hemangioma seen in the Lurie Children's Dermatology Clinic in Chicago between Jan. 1, 2010, and Jan. 1, 2015. Of the patients evaluated, 71% were female and 75% had been carried to term.

Among the 6% of patients included in the study who had a positive personal cardiac history, congenital heart disease was most common; coronary artery disease was most prevalent among the 41% with a positive family cardiac history. Baseline vital signs revealed no hypotension or bradycardia.

All patients prescribed propranolol were routinely screened with ECG prior to therapy during the study period. Baseline heart rate and blood pressure were observed for abnormalities; patients also were observed during follow-up for possible propranolol side effects.

A total of 43% of ECG screenings performed were found to be abnormal; left ventricular hypertrophy was the most common abnormality. Despite further cardiac evaluation of all but one patient with abnormal ECG, no contraindications to treatment were identified, Dr. Lund and her colleagues reported in Pediatric Dermatology.

**A TOTAL OF 43% OF ECG SCREENINGS PERFORMED WERE FOUND TO BE ABNORMAL; LEFT VENTRICULAR HYPERTROPHY WAS THE MOST COMMON ABNORMALITY. DESPITE FURTHER CARDIAC EVALUATION OF ALL BUT ONE PATIENT WITH ABNORMAL ECG, NO CONTRAINDICATIONS TO TREATMENT WERE IDENTIFIED.**

Ultimately, 96% of patients observed started treatment with propranolol; of the remaining 4% who did not, the authors cited parental preference and lack of follow-up as the primary reasons for nontreatment.

The researchers found no association between reported side effects and abnormal ECG, a positive personal history of cardiac problems, or a positive family history of cardiac problems.

Dr. Lund and her associates suggested that future revision of the guidelines should emphasize the absence of significant positive predictive value of ECG abnormalities for treatment-related side effects.

The researchers reported no relevant financial disclosures.

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**SOURCE:** Lund EB et al. Pediatr Dermatol. 2018. doi: 10.1111/pde.13508.

# Consider examining nails in cases of relapsing scabies

**BY JILL D. PIVOVAROV**
FROM THE JOURNAL OF PEDIATRICS

Nails should not be overlooked in treating common scabies, cautioned Marie Chinazzo, MD, of Centre Hospitalier Régional et Universitaire Tours, France, and her associates.

Nails can harbor mites, representing a potential source for relapse, not only in children, but also in adults.

Few studies have addressed scabies on the nails, which is typically observed in immunocompromised adults with crusted scabies, but also rarely in healthy adults and children.

## COMMENTARY
## BY DR. EICHENFIELD

### NAILING THE TREATMENT OF SCABIES: REMEMBER THE NAILS

Scabies remains a common condition that can be straightforward to diagnose, or rather tricky, as presentations can mimic eczematous dermatitis, drug reactions, contact allergy, and more serious systemic conditions. The article by Chinazzo et al. emphasizes that nails can harbor scabies mites. While this is more common in adults with crusted scabies and immunocompromise, 47 children were reported with mites on their thumbnails and toenails, with almost half of patients under 2 years of age! The treatments used on these patients varied from traditional permethrin application to oral ivermectin. After reading this article, I will make sure to counsel families to include nails when applying topical permethrin for treatment of scabies, and consider nails as a possible area for "hiding mites" in cases that appear to not respond to topical therapy.

In an observational, multicenter, prospective study conducted between June 2015 and January 2017, 47 pediatric patients with common scabies, including 3 children under 2 years of age, presented with mites on the first toenail/thumbnail; 2 of them had already completed treatment and were experiencing relapse. All children with dermatologic diagnosis that was confirmed by visual inspection of "the delta sign" (presence of the mite seen as a triangle representing the head) using dermoscopy or by microscopic identification of *Sarcoptes scabiei* were included in the study. Dermatologists were required to complete a standardized questionnaire for each participant. Full body inspections and nail samplings also were done.

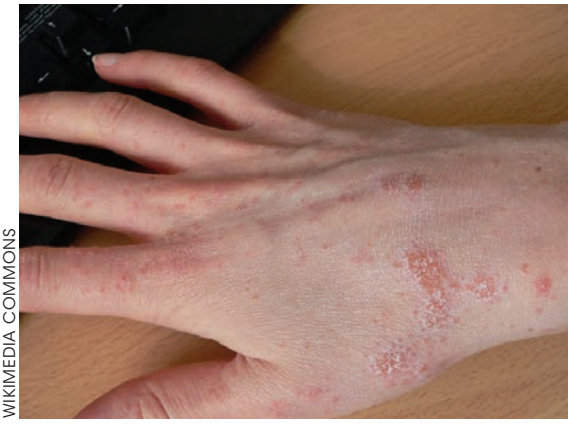
Clinical nail damage, consisting of hyperkeratosis, onycholysis, onychoschizia, and pachyonychia, appeared in 5 of the 47 patients (11%). No other cause of nail damage was determined in four of the cases, for which mites were not directly visualized, the researchers noted. The report was published in the Journal of Pediatrics.

Of the 47 confirmed cases, 26 were female; 23 were under 2 years of age; 20 were 2-12 years; and 4 were older than 12. Ten cases presented with significant medical history; none were classified as immunocompromised.

Fully 42 of the 47 children (89%) reported pruritus, and of these, 64% also had pruritus present in the family home; 60% of siblings and 45% of parents were affected.

None were diagnosed with crusted scabies. The mean delay from disease onset to diagnosis was 55 days. In 38% of cases, previous treatment for scabies had been rendered.

Treatments varied based on presentation. Ivermectin, esdepallethrin, and



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40% urea were repeated after 10 days in at least one case. In another case, an entire family was treated once with topical 5% permethrin; once the child experienced relapse, oral ivermectin was employed. In the case of an 18-month-old girl with pruritus and skin lesions, topical corticosteroid was used for 10 days until such time that dermatoscopy revealed the "delta sign" and 5% topical permethrin was added.

The authors observed that nail scabies in the medical literature is more commonly seen in immunocompromised patients with crusted scabies and higher concentrations of parasites. They were able to locate only three other reports, all in adults, of nail scabies occurring with common scabies.

"Treatment of nail scabies is difficult and is not highly evidence based," cautioned Dr. Chinazzo and her associates. The primary study limitations were the small patient population and that nail sampling was taken only from the first fingers and toes, which could mean that the number of mites present is actually underestimated, they added.

The authors had no relevant financial disclosures.

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**SOURCE:** Chinazzo M et al. J Pediatr. 2018. doi: 10.1016/j.jpeds.2018.01.038.

# Nickel allergy common in children, significantly higher in girls

**BY JILL D. PIVOVAROV**
FROM THE JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

Nickel sensitivity appears to be common in children, and more frequent in girls than boys, said Erin M. Warshaw, MD, MS, of the University of Minnesota, Minneapolis, and her associates.

"Although nickel sensitivity is reported to be problematic in children, the pediatric population is often underrepresented in large-scale epidemiologic studies," they added.

In this retrospective, cross-sectional study of 1,894 children aged 18 years or younger tested by the North American Contact Dermatitis Group (NACDG) between 1994 and 2014, 23.7% of those patch tested were found to be sensitive to nickel. This included 6.5% who were 5 years or younger, 34.2% who were 6-12 years, and 59.4% who were 13-18 years.

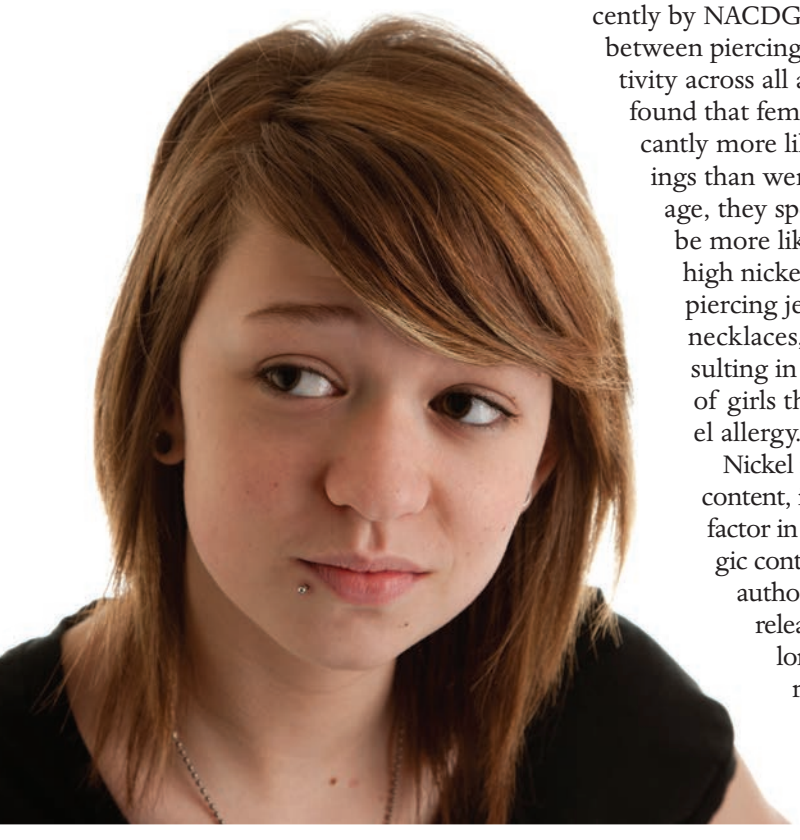
Among all three patient groups, jewelry was the most common source of nickel sensitivity (36.4%), and this sensitivity was found to increase with age (5 years and younger, 20.7%; 6-12 years, 28.3%; and 13-18 years, 42.9%; $P = .0006$).

More than two-thirds of positive patch test reactions to nickel were found to be extreme or strong, Dr. Warshaw and her colleagues reported in the Journal of the American Academy of Dermatology.

Notably, girls were significantly more likely to exhibit nickel sensitivity than boys, a result the authors credit to "trends and social norms."

Citing a separate study conducted recently by NACDG on the correlation between piercing and nickel sensitivity across all ages, researchers found that females were significantly more likely to have piercings than were males, and with age, they speculated, "girls may be more likely to encounter high nickel release through piercing jewelry, bracelets, necklaces, hair clips, etc., resulting in higher proportions of girls than boys with nickel allergy."

Nickel release, not nickel content, is an important factor in cases of nickel allergic contact dermatitis, the authors added. For nickel release to occur, prolonged skin contact is required. According to the European Chemicals Agency, prolonged exposure is defined as more than 10 minutes over three or more occasions within a 2-week period or more than 30 minutes over one or more occasion within the same 2 weeks.



## COMMENTARY
## BY DR. EICHENFIELD

### WATCH OUT FOR THE JEWELRY

Jewelry wearing in children, particularly piercing jewelry, is presumably contributing to nickel exposure and rates of nickel allergy in this population, as is shown in the study by Warshaw et al. High rates of nickel sensitivity were found in more than 20% of the children aged 5 years and younger, increasing to 23% in those aged 13-18 years! Erin M. Warshaw, MD, pointed out that most of the positive patch tests used to diagnose nickel sensitivity were strong and were more common in girls. We should be alert for allergic contact dermatitis from earrings and jewelry, which in practice most commonly is seen with silver jewelry. While in Europe, there has been regulation to minimize nickel release, this isn't the case in the United States, so that nickel used in earrings and other jewelry may be more allergenic.

The research was funded by the Minneapolis Veterans Affairs Medical Center, and in part, by the Nickel Producers Environmental Research Association. Three of the researchers have ties to various pharmaceutical companies and other organizations. Dr. Warshaw and the remaining researchers had no relevant financial disclosures.

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**SOURCE:** Warshaw EM et al. J Am Acad Dermatol. 2018 Apr 14. doi: 10.1016/j.jaad.2018.02.071.

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# So it's pediatric onychomycosis. Now what?

**BY KARI OAKES**
EXPERT ANALYSIS FROM
SUMMER AAD 2018

CHICAGO – Though research shows that nail fungus occurs in just 0.3% of pediatric patients in the United States, that's not what Sheila Friedlander, MD, is seeing in her southern California practice, where it's not uncommon to see children whose nails, toe nails in particular, have fungal involvement.

"I know I started out telling you fungus isn't that common in children. … but you do need to think about it," said Dr. Friedlander during a nail-focused session at the annual summer meeting of the American Academy of Dermatology. Dr. Friedlander, professor of dermatology and pediatrics at the University of California San Diego and Rady Children's Hospital, said that she suspects that more participation in organized sports at a young age may be contributing to the increase, with occlusive sports footwear replacing bare feet or sandals for more hours of the day, presenting more opportunities for toenail trauma in sports such as soccer.

When making the clinical call about a nail problem, bear in mind that the younger the child, the less likely a nail problem is fungal, Dr. Friedlander noted. "Little children are much less likely than older children to have nail fungus. Pediatric nails are thinner, and they are faster growing, with better blood supply to the matrix."

And if frank onychomadesis is observed, think about the time of year, and ask about recent fevers and rashes, because coxsackievirus may be the culprit. "Be not afraid, and look everywhere if the nail is confusing to you," she said. In all ages, the diagnosis is primarily clinical, "but I culture them, I 'PAS' [periodic acid-Schiff stain] them, too. If you do both, you'll increase your yield," Dr. Friedlander said, adding, "the beauty of PAS is you can use it to give your families an answer very soon."

Once you've established that fungus is to blame for a nail problem, there's a conundrum: There are no Food and Drug Administration–approved therapies, either topical or systemic, for pediatric onychomycosis, Dr. Friedlander said. She, along with coauthors and first author Aditya Gupta, MD, of Mediprobe Research, London, Ont., recently published an article reviewing the safety and efficacy of antifungal agents in this age group (Pediatr Dermatol. 2018 Jun 26. doi: 10.1111/pde.13561).

Reviewing information available in the United States and Canada, Dr. Friedlander and her coauthors came up with three topical and four oral options for children, along with recommendations for dosage and duration.

In response to an audience question about the use of topical antifungal treatment for nail involvement, Dr. Friedlander responded, "I think topicals would be great for kids, but it's for kids where there is no nail matrix in-

**'I KNOW I STARTED OUT TELLING YOU FUNGUS ISN'T THAT COMMON IN CHILDREN. … BUT YOU DO NEED TO THINK ABOUT IT.'**

## COMMENTARY **BY DR. SIDBURY**

### PEDIATRIC DYSTROPHIC NAILS

There is a large disconnect between what children with dystrophic nails are referred for and their ultimate diagnosis. Onychomycosis, a common adult malady, is not a common cause of pediatric onychodystrophy, so providers should cast a broader diagnostic net, according to Dr. Sheila Friedlander.

Dr. Friedlander emphasizes the importance of history because congenital onychodystrophy raises unique considerations. Hair, teeth, skin, and bones should be scrutinized to help identify the appropriate diagnosis. She highlights this point by describing a patient with nail-patella syndrome: The distinctive triangular lunula and abnormal elbows and knees instantly raise the specter of a diagnosis that can have significant medical morbidity.

Dr. Friedlander also makes clear that, while uncommon, pediatric onychomycosis can occur and may raise unique issues. She notes that younger age is inversely correlated with onychomycosis, whereas sports participation increases likelihood. Barriers to treatment can include the lack of Food and Drug Administration approval, cost, and adherence – particularly with systemic agents. While topical agents such as ciclopirox 8%, efinaconazole 10%, and tavaborole 5% are very appealing from both a safety and convenience perspective, she advises against their use if any nail matrix involvement is noted.

Dr. Friedlander highlights four potential systemic agents: griseofulvin, terbinafine, itraconazole, and fluconazole. While pediatricians and pediatric dermatologists have ample familiarity and comfort using griseofulvin, prolonged courses and significant recurrence risk lessen its role in onychomycosis therapy.

volvement. Also, cost is a problem. Nobody will cover it. But some families are willing to do this to avoid systemic therapy," and if the family budget can accommodate a topical choice, it's a logical option, she said, noting that partial reimbursement via a coupon system is available from some pharmaceutical companies.

Where appropriate, ciclopirox 8%, efinaconazole 10%, and tavaborole 5% can each be considered. Dr. Friedlander cited one study she coauthored, which reported that 70% of pediatric participants with nonmatrix onychomycosis saw effective treatment, with a 71% mycological cure rate ($P = .03$), after 32 weeks of treatment with ciclopirox lacquer versus vehicle (Pediatr Dermatol. 2013 May-Jun;30[3]:316-22).

Systemic therapies – which, when studied, have been given at tinea capitis doses – could include griseofulvin, terbinafine, itraconazole, and fluconazole.

In terms of oral options, Dr. Friedlander said, griseofulvin has some practical limitations. While prolonged treatment is required in any case, terbinafine may produce results in about 3 months, whereas griseofulvin may require up to 9 months of therapy. "I always try to use terbinafine … griseofulvin takes a year and a day," she said.

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She also shared some tips to improve pediatric adherence with oral antifungals: "You can tell parents to crush terbinafine tablets and mix in peanut butter or applesauce to improve adherence. Griseofulvin can be flavored by the pharmacy, but volumes are big with griseofulvin, so it's a challenge to get kids to take it all," she said.

Dr. Friedlander reported that she had no relevant financial disclosures.

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# When fingernails are the clue to a bigger problem

**BY KARI OAKES**

REPORTING FROM SUMMER AAD 2018

CHICAGO – When a child or adolescent comes to the dermatologist's office with a concern about fingernails or toenails, physician antennae may go up. "The world is different in the world of pediatrics – and even in the world of adolescents," said Sheila Fallon Friedlander, MD.

In adults, the most common cause of nail dystrophy is tinea, but for younger pediatric patients, less than 1% of nail problems are attributable to fungus, so dermatologists may need to look further.

"It's so important in kids to do a good history and physical exam," said Dr. Friedlander, professor of dermatology and pediatrics at the University of California, San Diego. History-taking should include determining whether the condition has been present since birth and how nail appearance has changed over time.

DR. FRIEDLANDER

For Dr. Friedlander, the approach to nail abnormalities includes a full head and skin exam. "I always look at the teeth, the hair, the skin," she said; underlying bony anomalies also may surface. A complete exam often will turn up important clues if a syndrome underpins the nail abnormalities, she said, speaking at the American Academy of Dermatology summer meeting.

Her exemplar patient, she said, is a 19-year-old male who comes in with a parent because he's bothered by his fingernails, which are dystrophic and small. A head-to-toe exam shows micronychia of both toes and fingers, with lunulae that are triangularly shaped. The hair, skin, and teeth of the patient all are normal in appearance. However, "The knees and elbows were odd," Dr. Friedlander said.

This patient has nail-patella syn-

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drome. "Even though it's rare, I want you to think about it," Dr. Friedlander said. The autosomal dominant condition is seen in about 1 in 50,000 patients. It's thought to be caused by heterozygous loss-of-function mutations in gene LMX1B, she said, that codes for a LIM homeobox transcription factor 1 beta.

Though the small nails and triangular lunulae may be what brings the patient to the dermatologist's office, a careful exam and one radiograph can pick up a tetrad of anomalies, Dr. Friedlander said. Abnormalities can be seen in both the knees and elbows; the patellae are often small, and may even be absent. In addition, a hip radiograph will show characteristic "horns" on the posterior iliac crests.

Coming back to the dermatologic exam, Dr. Friedlander said nails may be absent, hypoplastic, and dystrophic – but those are features that can be shared with other nail disorders, inherited and acquired. The pathognomonic finding for nail-patella syndrome is the presence of the triangular lunula, she said.

Now that the diagnosis has been made, Dr. Friedlander asked about this young man: "Where will you refer him?" Knowing the diagnosis means that there are a lot of calls for your staff to make, she said.

The patient with nail-patella syndrome should be referred to an orthopedist to assess knees and elbows; radial head subluxation also is common in these patients, she said.

An ophthalmologic referral is important as well; hyperpigmentation of the pupillary margin – a "Lester iris" – can be seen, and increased rates of cataracts and glaucoma also are associated with nail-patella syndrome.

"The message I want you to leave with is that these kids need to be seen by a nephrologist," Dr. Friedlander said. Up to half of nail-patella syndrome patients will have kidney involvement that initially presents with hematuria and proteinuria. Because the LMX1B mutation impairs how podocytes and glomerular filtration slits develop and function, up to 10% can develop end-stage renal failure, she said.

Parents also should be on the lookout for associated behavioral issues: "The other thing that's interesting is that these kids have an increased risk of [attention-deficit/hyperactivity disorder] and major depression," Dr. Friedlander said.

Dr. Friedlander reported that she had no relevant conflicts of interest.

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**SOURCE:** Friedlander, S. Summer AAD 2018. Session F004.

# Pediatric data on novel axillary hyperhidrosis treatment reported

**BY BRUCE JANCIN**

REPORTING FROM THE EADV CONGRESS

PARIS – Two compelling reasons exist to take excessive sweating in children and adolescents more seriously, Lawrence J. Green, MD, asserted at the annual congress of the European Academy of Dermatology and Venereology.

One is that this is a surprisingly common and embarrassing medical condition that can have a profound adverse developmental impact in young people at a time when they are engaged in forming their self-image.

The other reason to get serious about addressing primary axillary hyperhidrosis in pediatric patients is the recent approval of glycopyrronium tosylate as a topical therapy, Dr. Green, a dermatologist at George Washington University, Washington. The treatment, glycopyrronium pads (Qbrexza), was approved by the Food and Drug Administration for the topical treatment of primary axillary hyperhidrosis in patients aged 9 years and older in June 2018.

He presented new data from a 44-week, open-label extension of two pivotal 4-week, phase 3, randomized, double-blind, placebo-controlled trials known as ATMOS-1 and ATMOS-2. The new post hoc analysis from the extension study, known as the ARIDO study, provides reassurance that the product remains both safe and durably effective with long-term use.

Dr. Green's analysis focused on the 44 pediatric participants aged 9-16 years. That's because even though primary axillary hyperhidrosis affects people of all ages, with an estimated 4.8% prevalence in the U.S. population – 5.3 million people – it is more common in children and adolescents than adults. And it hits them particularly hard.

"Hyperhidrosis is largely underdiagnosed and undertreated, particularly among pediatric patients," he said. "The impact on quality of life is comparable to or greater than acne, psoriasis, or eczema."

The glycopyrronium pad is self-applied as a once-daily wipe. Glycopyrronium is an anticholinergic agent that blocks sweat production by inhibiting the receptors that activate sweat glands.

Dr. Green noted several key findings from the 44-week ARIDO analysis, presented for the first time at the EADV congress.

The median absolute decrease in sweat production in pediatric patients at 44 weeks as measured gravimetrically was 50.3 mg/5 min from a baseline of

150 mg/5 min is comparable with the mean 75-mg reduction from a baseline of 175 mg in the 507-patient older cohort. However, Dr. Green advised not to make too much of this endpoint, as sweat production is notoriously difficult to measure accurately. In addition, an individual's sweat rate can vary widely depending upon a multitude of factors, including ambient temperature and even what a patient is thinking about. The FDA recognizes this and therefore elevated several validated patient-reported outcomes to the status of co-primary endpoints in the clinical trials.

A positive result on one such patient-reported outcome, the Hyperhidrosis Severity Scale, was achieved in 57% of pediatric patients and 64% of adults at week 44 of open-label therapy. This required at least a 2-grade improvement from baseline, when roughly 60% of youths had a score of 3 and the remainder scored 4 on the 1-4 point scale.

From a mean baseline score of 9.2 on the Children's Dermatology Life Quality Index, the pediatric group averaged a mean 6.2-point improvement at week 44, while adults experienced a mean 8.7-point improvement on the Dermatology Life Quality Index from a baseline of 11.25.

There was no diminution in treatment efficacy through 44 weeks, Dr. Green noted. Treatment-emergent adverse events consisted largely of transient mild to moderate anticholinergic effects, which seldom led to study discontinuation.

BRUCE JANCIN/MDEDGE NEWS

*Dr. Lawrence J. Green said, "Hyperhidrosis is largely underdiagnosed and undertreated, particularly among pediatric patients."*

Dilated pupils and blurred vision were more common in children than adults (7.9% and 10.5% vs. 5.1% and 6.4%, respectively). "Why that is I can only speculate. Kids do tend to touch their eyes more often than adults. Pretty much everything else was the same. The adverse events can be worked around by educating people to use the pads appropriately. We saw the anticholinergic side effects more often in the first 4 weeks of the double-blind trials than in the long-term extension because once patients learned how to use the pad and not touch themselves afterwards, the adverse events came down," he said.

The studies were sponsored by Dermira. Dr. Green has received research funding from and been a consultant to the company.

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## COMMENTARY **BY DR. EICHENFIELD**

### DON'T SWEAT AXILLARY HYPERHIDROSIS: NEW FDA-APPROVED MEDICATION

Hyperhidrosis is underappreciated, but not so uncommon in pediatric patients, especially in adolescents. Axillae, palms, and soles can manifest significant sweating that caused tremendous distress to affected patients and their families.

It is exciting that there is a new topical medication that has been approved for axillary hyperhidrosis, and that the studies included patients as young as 9 years of age. Glycopyrronium tosylate works as a topical anticholinergic agent, and showed efficacy and reasonable safety in studies discussed by Lawrence Green, MD, at the European Academy of Dermatology and Venereology Congress in Paris, and recently published by Hebert et al. (Pediatr Dermatol. 2019 Jan;36[1]:89-99). The medication is administered as a daily wipe, with the glycopyrronium applied to the axillae once a day. The pediatric patients in this study had significant hyperhidrosis, with high baseline sweat production rates (150 mg/5-min baseline) and high axillary daily diary scores, with significant reductions with medication during the 4-week study period. Patients who are prescribed this medication should be instructed to wash their hands compulsively after application, as dilated pupils (often unilateral) and blurred vision were side effects, often seen early in the study, presumably less with time as patients learned to used the medication carefully. Our experience is that patients with this condition are very self-conscious and tremendously affected, so we are pleased to have a medication studied and FDA approved!

# Warmth and moisture help keep preterm neonates' skin healthy

**BY MICHELE G. SULLIVAN**
FROM PEDIATRIC DERMATOLOGY

Tub bathing, emollients, and even plastic dressings can protect the fragile skin of preterm infants during the first few crucial weeks of extrauterine life.

The skin of premature infants is very fragile and can take up to 4 weeks to become cornified. Until then, it's apt to rapidly lose water and heat, putting babies at risk of hypothermia, dehydration, and electrolyte imbalances, Ayan Kusari and his colleagues wrote in Pediatric Dermatology.

The team examined evidence-based skin care in these tiny patients, extracting recommendations from a meta-analysis of 68 studies.

"There are a number of unifying features that distinguish preterm skin from term skin," wrote Mr. Kusari, a clinical research associate at the Rady Children's Hospital–San Diego, and his associates. "Preterm skin is thinner, making preterm neonates more susceptible to skin infections and caustic agents. The vernix caseosa is typically thicker in preterm neonates [though thinner in extremely preterm neonates]. Accordingly, there are a number of general principles that can guide skin care for most preterm neonates."

## Bathing

The team identified eight studies of bathing preterm neonates and concluded that a daily bath isn't necessary.


MR. KUSARI

"Colonization by pathogenic bacterial strains, size of the total bacterial population, and incidence of skin infection do not vary between preterm infants bathed every 2 days and preterm infants bathed every 4 days in all studies," the authors wrote.

These less frequent baths appear to decrease the risk of temperature variability, and tub baths are preferable to sponge baths. "In sponge bathing, wet skin is more exposed to ambient air, which is typically colder than body temperature. Physiological and behavioral parameters in preterm infants are often disrupted during sponge bathing. In contrast, tub bathing results in less variability in body temperature and warmer temperatures after bathing," Mr. Kusari and his associates found.

However, premoistened baby wipes appeared beneficial, lowering skin pH, which might help "facilitate acid mantle development, infection control, and barrier repair," they wrote.

## Emollients

Seven studies and one meta-analysis examined the use of emollients in preterm infants; there was agreement that emollients do improve skin condition. Plant-based emollients appeared superior to petrolatum-based products.

"In developing countries where oil massage of infants and children is traditional, there appears to be a clear benefit to massage with some oils. In developed countries, research has emphasized petrolatum-based creams and ointments, whose benefits are tempered by the increased risk of serious infections with some products," Mr. Kusari and his colleagues wrote.

Sunflower seed oil was particularly beneficial in studies carried out in developing countries. A mixture of 70% lanolin and 30% olive oil proved better than olive oil alone. Coconut oil also displayed positive impact on skin condition.

"In contrast, multiple studies show an increased risk of sepsis with the application of petrolatum ointment to preterm neonates," they noted.

In one study, following the adoption of a new skin care protocol involving regular application of petrolatum-based ointments for extremely low-

## COMMENTARY **BY DR. SIDBURY**

### PREMATURE CHILDREN'S SKIN IS DIFFERENT

An old pediatric adage states that children are not little adults. From a skin standpoint, this can be further modified to: Premature infants are not little children. In the first weeks of life, premature skin may lack a cornified layer, and it certainly lacks full homeostatic competence. Kusari et al. have derived helpful guidance from 68 studies in the present meta-analysis. Less-frequent bathing decreased infection risk and lessened the chance of temperature instability that can attend a bath. Plant-based emollients were deemed superior to petroleum products; they were sufficiently hydrating and may not pose an equivalent infection risk. Kusari also cautions that there is no consensus regarding preprocedure skin sterilization with common products such as chlorhexidine gluconate 0.5% or povidone iodine, as each can have risks (for example, irritation, thyroid suppression). More definitive is the recommendation for air drying the cord as opposed to antiseptic cleansing, which can delay separation. Guidelines for the care of premature skin, with attention to resource-limited populations, are needed.

birth-weight neonates, researchers in Texas observed a significant, 200% increase in the incidence of systemic candidiasis. A study in Saudi Arabia replicated this finding. The largest study of a petrolatum-based ointment on premature babies was conducted in Vermont and found a statistically significant increase in infection with coagulase-negative staphylococcus (CoNS). "This ... study appears to be the driving force in a Cochrane Database meta-analysis, which concludes that topical emollients are associated with increased CoNS infection in preterm neonates," the authors wrote.

## Temperature regulation

It's notoriously tough to maintain core temperature in preterm newborns. Six studies in the meta-analysis tackled this issue using impermeable plastic wraps or garments after birth and semipermeable barriers in the weeks after.

"Plastic wraps or bags can help neonates to retain their body heat, and greater skin coverage with plastic devices appears to be associated with a better outcome. In infants less than 28 weeks' gestational age, the use of polyethylene occlusive wraps prevents heat loss after delivery and results in higher NICU admission temperatures and a lower incidence of hypothermia," Mr Kusari and his associates wrote.

Semipermeable wraps can be used for an extended period after birth to reduce transepidermal water loss. Seven studies examined this technique, using both adhesive and nonadhesive polyurethane dressings.

"These studies show that semipermeable adhesive membranes decrease water loss, reduce skin breakdown, and decrease erythema while applied, but may strip superficial skin layers when they are removed, leading to a transient post-removal increase in transepidermal water loss. Furthermore, due to their semipermeable design, application of these adhesive membranes does not appear to decrease fluid requirement or affect electrolyte status in preterm neonates; however, skin barrier function is disrupted following removal of plastic tape, with increased transepidermal water loss at sites of tape removal," the investigators wrote.

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Pectin-based dressings and those containing hydrocolloid or acrylate can damage preterm neonatal skin by inflicting medical adhesive-related skin injury, the team wrote; this can involve epidermal stripping, tension injury, shearing, maceration, folliculitis, or contact dermatitis.

## Skin sterilization

There's little consensus when it comes to sterilization choices for preterm neonatal skin about to undergo a venipuncture or other procedure. Popular methods are povidone-iodine and chlorhexidine, with gestational age affecting choice. Iodine-based antiseptics have been associated with thyroid disruption and chlorhexidine with chemical burns.

"Some studies suggest 0.2% chlorhexidine gluconate may be an attractive alternative to povidone-iodine for the very and extremely preterm," the authors wrote. One study they examined compared chlorhexidine gluconate 0.2% and 0.5% in extremely preterm infants, showing a significant decrease in skin irritation in the lower-concentration group.

But a randomized trial following this finding, which compared 0.2% chlorhexidine gluconate with 10% aqueous povidone-iodine, found no differences in any infection outcome or skin irritation, but there was more thyroid suppression in the povidone-iodine group.

More research is needed, the team concluded.

## Cord care

Tincture of time may be the best alternative here.

The investigators examined a meta-analysis of 21 umbilical cord care studies and found that cleaning the cord with antiseptic prolonged the time to cord separation, compared with simple air drying.

"Interestingly, one study does suggest that one-time cleansing with chlorhexidine reduces neonatal mortality when compared to dry cord care; however, most of the existing evidence suggests that antiseptic treatment does not offer a benefit over dry cord care," they wrote.

"Further studies, particularly in the very preterm and extremely preterm neonates, with an emphasis placed on subclassifying the preterm patient population based on gestational age, are needed to further examine and validate the real-world utility of these interventions," Mr. Kusari and his associates concluded. "In the meantime, it may be useful to establish practice guidelines based on the evidence we have presented here."

The authors reported no relevant financial disclosures.

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**SOURCE:** Kusari A et al. Pediatr Dermatol. 2018 Dec 12. doi: 10.1111/pde.13725.

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# Topical treatment with retinoid/benzoyl peroxide combination reduced acne scars

**BY BRUCE JANCIN**
REPORTING FROM THE EADV CONGRESS

PARIS – Treatment with the fixed combination adapalene 0.3%/benzoyl peroxide 2.5% gel not only reduced facial acne lesions, it also decreased the atrophic acne scar count in a multicenter, randomized trial, Brigitte Dreno, MD, reported at the annual congress of the European Academy of Dermatology and Venereology.

"To my knowledge, this is the first time that we have seen a topical therapy showing a reduction in atrophic acne scars," said Dr. Dreno, professor and chair of the department of dermatology at Nantes (France) University Hospital.

She reported on 67 adolescents and adults with mainly moderate facial acne randomized to treat half their face with adapalene 0.3%/benzoyl peroxide 2.5% gel (Epiduo Forte) and the other half with the product's vehicle daily for 6 months. Investigators were blinded as to which side was which. At baseline, patients averaged 40 acne lesions and 12 scars per half face.

The primary efficacy endpoint was the atrophic acne scar count per half face at week 24. At that point, the mean total was 9.5 scars on the active treatment side, compared with 13.3 on the control side. This translated to a statistically significant and clinically meaningful 15.5% decrease in scars with active treatment versus a 14.4% increase with vehicle. The between-side difference achieved statistical significance at week 1 and remained so at all follow-up visits through week 24.


DR. DRENO

By Scar Global Assessment at week 24, 32.9% of half faces treated with the combination product were rated clear or almost clear, compared with 16.4% with vehicle.

At 24 weeks, 24.1% of participants reported having moderately or very visible holes or indents on the active treatment side of their face, compared with 51.8% on the control side. The number of inflammatory acne lesions fell by 86.7% with the active treatment and 57.9% with vehicle over the course of 24 weeks. Again, the difference became statistically significant starting at week 1. By the Investigator's Global Assessment at week 24, 64.2% of adapalene/benzoyl peroxide gel–treated faces were rated clear or almost clear, as were 19.4% with vehicle. In addition, 32% of patients reported a marked improvement in skin texture on their active treatment side at 24 weeks, as did 14% on the control side.

The salutary effect on acne scars documented with a topical therapy in this study represents a real advance in clinical care.

"Facial acne scars are a very important and difficult problem for our patients and also for dermatologists," Dr. Dreno observed, adding that the evidence base for procedural interventions for acne scars, such as dermabrasion and laser resurfacing, is not top quality.

Not surprisingly with a topical retinoid, skin irritation was the most common treatment-emergent adverse event, reported by 14.9% of patients on their active treatment side and 6% with vehicle. This side effect was typically mild and resolved within the first 2-3 weeks.

The improvement in preexisting acne scars documented in this trial was probably caused by drug-induced remodeling of the dermal matrix, according to Dr. Dreno.

The study was funded by Galderma. Dr. Dreno reported receiving research grants from and/or serving as a consultant to Galderma, Bioderma, Pierre Fabre, and La Roche–Posay.

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## COMMENTARY **BY DR. SIDBURY**

### POSSIBLY A MORE ACCESSIBLE ACNE SCAR TREATMENT

The two workhorses of topical acne care are retinoids and benzoyl peroxide. Alone or in combination they have proven effective against active acne. Conversely, once scarring has occurred, most dermatologists advocate a tincture of time or cosmetic intervention with tools such as dermabrasion or laser.

Dreno et al. have shown that, as early as 1 week, patients using a combination adapalene/benzoyl peroxide product showed not only less active acne, but a smoother facial texture and fewer scars. This statistically significant difference persisted throughout the 29-week study, with only expected transient skin irritation noted. Topical tretinoin has been used for several years to treat wrinkles in older adults, so a "scar effect" is consistent with the known retinoid mechanism.

Further study will be needed to confirm this finding, but if true, topical adapalene/benzoyl peroxide would represent a considerably more accessible and sustainable intervention for acne scarring. The blinded study design notwithstanding, author conflicts should be noted.

# Low incidence of HS in children does not diminish importance of early diagnosis

**BY JILL D. PIVOVAROV**
FROM THE JOURNAL OF INVESTIGATIVE DERMATOLOGY

Hidradenitis suppurativa, which occurs in only 28 per 100,000 U.S. children and teens, is most common in African American and biracial girls aged 15-17 years, investigators have found.

"The relatively low disease burden must not overshadow the extreme quality of life impact this disease has on those afflicted with it," noted Amit Garg, MD, and associates at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hyde Park, N.Y.

The cross-sectional gender- and age-adjusted population analysis established an overall standardized point prevalence of 0.028%, occurring in 1,240 U.S. patients aged 0-17 years with hidradenitis suppurativa (HS) in a population of 4,578,790 for whom gender and age was known; the standardized prevalence was 28 per 100,000. Patients were classified into one of three age groups (0-9 years, 10-14 years, and 15-17 years) and one of five racial classifications (white alone, African American alone, biracial [white and African American], other, and unknown).

The clinical term "hidradenitis' was used to locate pediatric patients within a multi-institutional database of 55 million patients participating in 27 integrated health care organizations whose records were active in the database between March 2014 and March 2017.

The standardized prevalence of HS among girls was 3.75 times greater than in boys (*P* less than .0001), and the condition was most common in those aged 15-17 years (72%) across each racial group. "HS disproportionately affects African American children and adolescents, who have a 3.5-fold greater standardized prevalence than do Caucasians," the authors wrote. The report was published in the Journal of Investigative Dermatology. Specifically, the highest prevalence by race was found in females aged 15-17 years who were African American (525 per 100,000) and biracial (253 per 100,000).

The authors acknowledged the availability of limited existing HS pediatric data from case reports and small series, none of which provided descriptions of subgroups by gender, age, or race.

In their review of the existing literature, Dr. Garg and his associates noted several key observations that may further aid in clinical diagnosis of pediatric patients at greater risk of developing HS:

- HS appears most likely to be a postadrenarche disease; children with the disease more frequently present with a hormonal imbalance, compared with adults. In fact, HS in children may be a marker of precocious puberty, as noted in those presenting with adrenal hyperplasia and premature adrenarche.
- A separate population-based analysis revealed an association between HS and polycystic ovary syndrome.
- Pediatric patients diagnosed with HS are more likely to present with a family history of the condition, and those experiencing early onset appear likely to develop more widespread HS.
- A fivefold likelihood of HS in pediatric Down syndrome patients is also attributed to genetic mutations.

The higher incidence of HS among adults (0.1%) is likely attributable to largely postpubertal disease onset, the authors speculated. They acknowledged that delays in diagnosing adolescent HS could account for the difference in prevalence between pediatric and adult populations. According to one study cited by Dr. Garg and his colleagues, adults with HS may have symptoms as many as 7 years prior to receiving a diagnosis.

The research was funded by an unrestricted educational grant from AbbVie. Dr. Garg has served as an adviser for and received honoraria from AbbVie; the remaining researchers had no relevant financial disclosures.

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**SOURCE:** Garg A et al. J Investig Dermatol. 2018 Apr 2. doi: 10.1016/j.jid.2018.04.001.

## COMMENTARY **BY DR. SIDBURY**

### IDENTIFY CHILDREN AT HIGH RISK OF HS

The diagnosis of hidradenitis suppurativa frequently is delayed, sometimes by years. This is unfortunate in a disease state that causes such physical and psychological morbidity.

Dr. Garg and associates have helped identify at-risk populations to heighten awareness of this potentially "hidden" scourge. Utilizing a 55-million–person database across multiple integrated health care organizations, these authors found that African American and biracial teenage girls were at greatest risk. Pediatricians must be mindful that HS can affect any race or gender; however, awareness of susceptible groups can improve chances of identifying HS, especially in reluctant teens.

The investigators also note that HS can be a marker for precocious puberty and polycystic ovary syndrome, further emphasizing the importance of early diagnosis.

# Twin study highlights environmental factors that may aggravate acne

**BY RANDY DOTINGA**
FROM THE JOURNAL OF DRUGS IN DERMATOLOGY

A survey conducted at the world's largest twin celebration provides more evidence that twins share a genetic propensity toward acne, and provides information about several aggravating factors.

The study "further supports that there may be a genetic phenotypic link, though social and environmental factors may also have an influence in the disease process," the authors wrote.

The study, led by Amanda Suggs, MD, of University Hospitals Cleveland Medical Center, appears in the April issue of the Journal of Drugs in Dermatology.

Previous twin research has linked genetic factors to 80% of acne variance, with environmental factors, such as stress and low intake of produce, believed to account for the rest of the risk (J Invest Dermat. 2002;119[6]:1317-22). For the new study, researchers surveyed twins at the 2016 Twins Day Festival in Twinsburg, Ohio. Thousand of twins – and triplets and quadruplets – from around the world attend the annual event.

After incomplete surveys were discarded, the survey population included 202 identical twins (101 pairs) and 53 fraternal twins or triplets. (A set of triplets was included in addition to 25 pairs of twins.) The majority of participants were female: 23% of identical twins and 17% of the fraternal twins and triplets were male. The mean age was 29 years among the identical twins and 21 years among fraternal twins.

Identical twins were more likely to both have acne (64%) than fraternal twins (49%), which supports the results of previous studies that suggest "acne is largely attributable to genetics," the authors observed. Among identical twins, those with acne were more likely to have polycystic ovarian syndrome ($P = .045$), anxiety ($P = .014$), and asthma ($P = .026$).

"Identical twin pairs with acne had a higher BMI [body mass index] and exercised less than those without," the researchers added. These two associations were statistically significant, both for higher BMI ($P = .020$) and for less exercise ($P = .001$). "This suggests that a higher BMI and lack of exercise may contribute [along with genetics of course] to acne development. Thus, regular exercise and lower BMI may keep acne at bay," they noted.

They also analyzed 56 pairs of identical twins with acne, who reported different severities, and found that the twin with more severe acne was more likely to report that sun exposure ($P = .048$), cosmetic product use ($P = .002$), and sugar intake ($P = .048$) aggravated their acne. Refined carbohydrates, as an aggravating factor, approached statistical significance, they said.

A separate analysis of 45 pairs of female identical twins with different degrees of acne severity produced similar findings. There were no significant differences between acne severity groups in terms of menstruation flare frequency or with oral contraceptive use. The twin with more severe acne, however, "was more likely to report aggravation of acne with sun exposure," cosmetic use, and sugar intake, all associations which reached statistical significance. They were also more likely to report that refined carbohydrates and intake of fried foods aggravated their acne, associations that approached statistical significance.

"This twin study provides further support for reducing intake of sugar and refined carbohydrates to decrease acne severity in susceptible individuals," the authors wrote. "For females, reducing intake of fried foods may also help."

There's a twist to their results: The finding that those with more severe acne reported worsening symptoms with sun exposure "conflicts with prior research, which has found that acne improves with sun," the authors wrote, adding that "perhaps the data was confounded by comedogenic sunscreen use."

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**SOURCE:** Suggs A et al. J Drugs Dermatol. 2018 Apr;17(4):380-2.

## COMMENTARY **BY DR. SIDBURY**

### ACNE TIPS

The pathogenesis of acne is multifactorial. Investigators (and parents) have long parsed the relative contribution of genetic and environmental factors.

Suggs et al. surveyed 101 pairs of identical twins and 53 sets of fraternal twins or triplets attending the 2016 Twins Day Festival to learn more. Identical twins were more likely to both have acne than fraternal twins (64% vs. 49%), supporting a genetic role. Investigators likewise noted worse acne with higher BMI, greater refined carbohydrate intake, and less exercise.

Contrary to many prior studies, and my own anecdotal experience, acne seemed to be worse with sun exposure. Though hardly settled science, this study will offer ammunition for parents who want to leverage their child's acne toward better health behaviors: Eat less sugar; exercise more; and moderate sun exposure. If only the investigators had found that texting worsened acne; parents might have nominated them for the Nobel Prize by acclimation!

# Sunscreen use in grade schoolers: Wide racial, ethnic disparities seen

**BY KARI OAKES**
FROM PEDIATRIC DERMATOLOGY

In a study of more than 5,000 fifth graders, fewer than a quarter of participants almost always used sunscreen, and the figures were much lower for non-Hispanic black children.

The odds of sunscreen adherence across the group were higher if a child also performed other preventive health behaviors; those who flossed regularly, for example, had an odds ratio of 2.41 for regular sunscreen use (95% confidence interval, 1.86-3.13, *P* less than .001).

Just 23% of fifth graders almost always used sunscreen, according to data drawn from the Healthy Passages study, which surveyed the parents or caregivers of 5,119 fifth graders. That figure was similar in the 1,802 Hispanic respondents, but fell to just 6% of the 1,748 non-Hispanic black respondents.

Some other factors that were associated with less chance of adherence to sunscreen use included being male and having lower socioeconomic status, wrote Christina M. Correnti, MD, and her study coauthors. The report was published in in Pediatric Dermatology. Perhaps surprisingly, they said, "School-based sun-safety education and involvement in team sports were not significant factors."

Healthy Passages is a prospective multisite cohort study of child and adolescent health. Dr. Correnti, a dermatology resident at the University of Maryland, Baltimore, and her colleagues used baseline Healthy Passages data collected from the period of 2004-2006. Children enrolled in fifth grade at public schools in Birmingham, Ala., Houston, and Los Angeles, together with their caregivers, participated in the survey. Deidentified demographic data were collected, and participants were asked about four preventive health behaviors in addition to sunscreen use and flossing teeth: brushing teeth, helmet use, seatbelt use, and well-child examinations.

Dr. Correnti and her colleagues used multivariable analysis to calculate odds ratios for the association between the various demographic factors and other preventive behaviors and sunscreen use. They found that sunscreen adherence was correlated with all other preventive behaviors (*P* less than .001), but that the interrelationship with helmet use was confounded by racial and ethnic variables. Seatbelt use was not significantly correlated with sunscreen use for non-Hispanic black or Hispanic respondents.

"Children from more-educated and affluent households were more likely to use sun protection. Perhaps they had greater parental awareness and practice of sun safe habits," wrote Dr. Correnti and her colleagues, noting that other work has shown that even low-income parents generally don't see the cost of sunscreen as a barrier to use.

Although overall use of sunscreen among non-Hispanic black children was low, both non-Hispanic black and Hispanic children were more likely to use sunscreen if they had three or

**'CHILDREN FROM MORE-EDUCATED AND AFFLUENT HOUSEHOLDS WERE MORE LIKELY TO USE SUN PROTECTION. PERHAPS THEY HAD GREATER PARENTAL AWARENESS AND PRACTICE OF SUN SAFE HABITS.'**

## COMMENTARY **BY DR. SIDBURY**

### IMPROVING SUNSCREEN USE

Preventative health behaviors are most durable when ingrained early in life. A survey of parents or caregivers of more than 5,000 fifth graders in three U.S. cities suggests there is considerable room for improvement when it comes to sunscreen use, particularly among certain groups.

Only 23% of respondents reported "almost always" using sunscreen; that figure dropped to 6% for non-Hispanic black individuals. Other factors negatively correlating with sunscreen use included male sex, and lower socioeconomic status. Kids who engaged in other preventative health behaviors, such as flossing, were more likely to use sunscreen.

Correnti et al. acknowledge barriers to use including cost and limited primary care time available for proper education, but their work and others' have not clearly linked these factors. They advocate for school-based education to decompress busy well-child care visits, with attention to age-appropriate messaging. For better or worse, teens are likely moved more by a risk of wrinkles and age spots than skin cancer.

more sunburns within the prior 12 months. "Although darker skin tones may afford some sun protection, melanoma incidence is growing in Hispanic populations," the researchers wrote.

To address these overall low rates of sunscreen use, the investigators discussed the utility of a variety of education options. The well-child visit affords an opportunity to reinforce the importance of preventive behaviors, but physicians may run into a time crunch and forgo thorough sun safety education, they said. Written materials can be a useful adjunct for clinicians in this setting.

"Health care practitioners may use absence of other preventive behaviors as potential markers for inadequate sunscreen use, prompting a point-of-care sun-safety intervention," they suggested.

A school-based public health approach offers another route for education. "School sun-safety programs may alleviate the primary care burden," wrote Dr. Correnti and her coinvestigators. The opportunity to deliver repeated, age-tailored messages as children progress through school may be effective in promoting healthy sun behaviors. Messaging that focuses on the negative effects of sun exposure on appearance such as age spots and wrinkles have been more effective than those warning of the risk of skin cancer for teens; investigating appearance-based content for this age group might be a good idea, the authors said.

The fact that the survey sites were in southern cities may mean that national rates of consistent sunscreen use for elementary schoolers may be even lower, said Dr. Correnti and her coauthors. Many other real-world factors, such as frequency and amount of sunscreen applied and the use of sun-protective clothing, couldn't be captured by the survey, they acknowledged.

"Even in the most adherent group, non-Hispanic whites, only 44.8% always used sunscreen," the researchers wrote. The study's findings leave plenty of room for implementation of broad-based programs, especially in low-resource communities.

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**SOURCE:** Correnti CM et al. Pediatr Dermatol. 2018. doi: 10.1111/pde.13550.

**'HEALTH CARE PRACTITIONERS MAY USE ABSENCE OF OTHER PREVENTIVE BEHAVIORS AS POTENTIAL MARKERS FOR INADEQUATE SUNSCREEN USE, PROMPTING A POINT-OF-CARE SUN-SAFETY INTERVENTION.'**

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