PEDIATRIC DERMATOLOGY

SUMMER 2017

Pivotal dupilumab results for eczema create a sensation

Fight back against psoriasis bullies

Monthly lab testing for isotretinoin? No need

Consider all acne in Latinos inflammatory

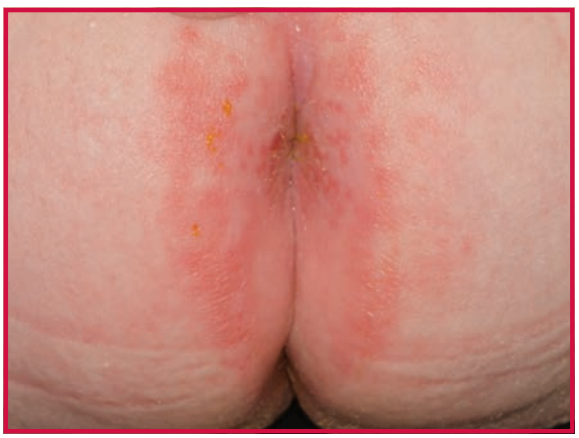
Commentaries by Lawrence F. Eichenfield, MD & Robert Sidbury, MD, MPH

A SUPPLEMENT TO
Pediatric News®
Dermatology News®

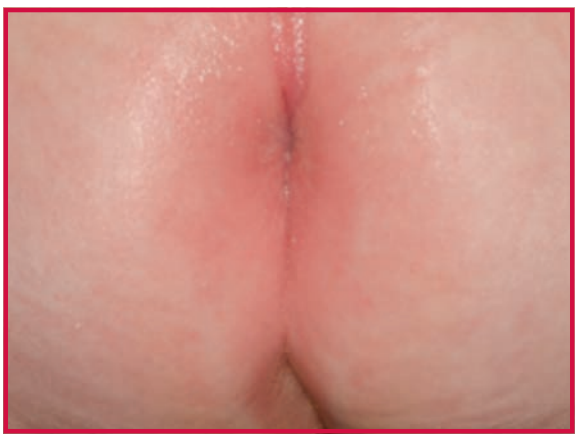
RECOMMEND

Aquaphor® Diaper Rash Cream

3 IN 1: PREVENTS, SOOTHES & TREATS DIAPER RASH



Baseline



1 Week

This was a single-center, Independent Review Board–reviewed clinical trial conducted to assess the efficacy and tolerability of Aquaphor Diaper Rash Cream (zinc oxide diaper rash cream) when used on infants during each diaper change over the course of 1 week. Subjects were assessed at baseline, at 6 hours after a single use, and after 1 week of regular use.[1]

PROVEN TO HELP RELIEVE DIAPER RASH[1]

Formulated with:

- Zinc oxide
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Pediatric dermatology today

Exciting times are here!

BY LAWRENCE F. EICHENFIELD, MD

What an exciting time in the field of pediatric dermatology. There is increasing recognition of the impact of dermatologic diseases on children and adolescents, and evolving knowledge and therapies that can help us to minimize their impact. The articles discussed have a range of topic areas, with some very common diseases, such as acne, and some less common but quite distressing conditions, such as psoriasis, alopecia areata, and hyperhidrosis. Psoriasis now has been tied to a set of associated medical problems that really impact health over a lifetime, and a pediatric approach to screen for risk factors and to try to minimize their development makes intuitive sense.

We have desired better therapies for alopecia areata, and there are some signs of exciting breakthroughs in the field. The questions about how acne is influenced by diet are still being asked, without definitive answers, but with more data to move us beyond the "does chocolate matter" discussion that is common during our patient visits. In addition, issues of postinflammatory pigmentation in patients with skin of color are highlighted in one of our articles. Helping us get to the bottom of some issues in diaper dermatitis are two articles on irritant and allergic contact dermatitis.

In the realm of more specialized aspects of pediatric dermatology, we have some excellent tips on minimizing pain and anxiety during pediatric dermatology procedures in young children, as well as an article on Steven-Johnson Syndrome and toxic epidermal necrolysis, conditions we have to keep an eye out for given the incredible morbidity and rare but distressing mortality they are associated with. In addition, some pointers on management of Rocky Mountain spotted fever and information on teen tanning and sun protection round out a great set of articles and some hopefully useful commentary!

Dr. Eichenfield is in the division of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego, and the University of California, San Diego. Relative to the commentaries, Dr. Eichenfield disclosed he has served as a consultant for Pfizer.

Advances abound in atopic dermatitis therapy

BY ROBERT SIDBURY, MD, MPH

The National Eczema Association has proclaimed this "the decade of eczema" for a reason: New data suggest the concept of primary prevention of atopic dermatitis (AD) may no longer be a "pipe dream" and new therapies are emerging to improve the lives of affected patients.

In the articles discussed herein, there will be data examining the prevention of atopic dermatitis and its pharmacoeconomic implications. Early use of emollients reduces the risk of developing AD and possibly other comorbidities, and investigators have translated these benefits into dollars and cents. Likewise, the role of probiotics as eczema prevention also is discussed, pivoting off of the incredible interest in the skin and gut microbiome.

We also will discuss new topical and systemic medications for AD. A novel topical phosphodiesterase inhibitor will offer a nonsteroidal option unshackled by a boxed warning to children with mild to moderate AD over 2 years of age. For more moderately to severely affected patients, for whom currently available options are truly inadequate, a new biologic medication called dupilumab shows tremendous promise.

If the next decade belongs to eczema, this past one has belonged to hemangiomas – if only because it gave us propranolol. Systemic beta-blockade for infantile hemangiomas has gone from serendipitous discovery in 2008 to standard therapy in 2017. We continue to refine how we use it, and this issue will devote time to these details. Is an ECG necessary before treatment? How safe is propranolol in healthy infants? Do certain locations like the nasal tip get treated more often?

Finally, as a parent and health care provider, I spend more time furrowing my brow over the potentially negative effects of social media on teenagers. We will review a case to the contrary, where social media helped guide a group of teens to better medical care.

Dr. Sidbury is chief of dermatology at Seattle Children's Hospital and professor, department of pediatrics, University of Washington, Seattle. Relative to the commentaries, Dr. Sidbury disclosed he has served as site primary investigator on phase III trials of crisaborole.

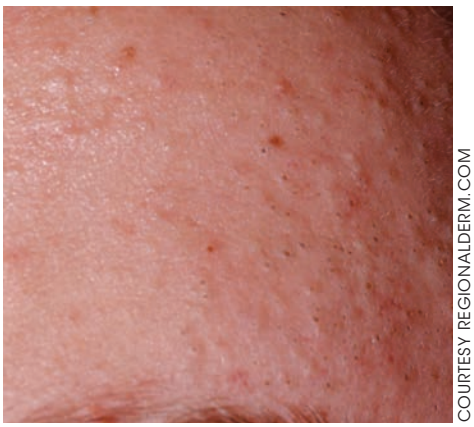
New topical agents for acne rolling out

BY BRUCE JANCIN

Expert Analysis from the SDEF Hawaii Dermatology Seminar

WAILEA, HAWAII – The Food and Drug Administration's approval of adapalene gel 0.1% as an OTC treatment for acne is a potential game changer that could lead to revision of guideline-recommended treatment algorithms, Lawrence F. Eichenfield, MD, predicted at the Hawaii Dermatology Seminar.

In announcing approval of adapalene gel 0.1% as an OTC product, the FDA cited as a major factor in the regulatory decision the opportunity to afford acne patients greater access to retinoid therapy. The drug is now on pharmacy and supermarket shelves, marketed by Galderma Laboratories under the brand name Differin gel 0.1% for once-daily application by patients aged 12 years and older at a cost of $20-$28 for 45 g.



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Newer classes of drugs are diversifying therapeutic options for acne.

"This development could be very interesting from an access standpoint and in terms of how physicians write prescriptions for retinoids, in light of the copays for other agents," said Dr. Eichenfield, professor of dermatology and pediatrics at the University of California, San Diego, and chief of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego.

"We know that with other retinoids, access is an issue. In Southern California, for example, we have strong pharmacy benefits' managers for the insurance companies, and they're very restrictive. It seems like every 3 months, they change the tiering of the different retinoids. It's something we have to work on to get our patients a fair price," Dr. Eichenfield said at the meeting, sponsored by the Global Academy for Medical Education/Skin Disease Research Foundation.

Dapsone 7.5% gel, marketed as Aczone gel, 7.5% by Allergan, is a once-daily reformulation of the older 5% product administered twice daily. It received FDA approval for use in patients aged 12 years and older based on two 12-week, double-blind, placebo-controlled, randomized trials totaling more than 4,300 acne patients. The studies showed the stronger once-daily product was extremely well tolerated, with application site dryness and itching rates similar to placebo. In terms of efficacy, a Global Acne Assessment Score of 0 or 1 with at least a 2-grade improvement was achieved in 30% of patients assigned to dapsone 7.5% gel, compared with 21% of vehicle-treated controls.

Dr. Eichenfield was lead investigator in a recently published positive phase IIb, randomized, vehicle-controlled study of a topical nitric oxide–releasing agent for acne known for now as SB204 (J Drugs Dermatol. 2016 Dec 1;15[12]:1496-502).

The product has both antimicrobial and anti-inflammatory properties, bacteria don't develop resistance to it, and there is no significant systemic absorption.

In its press release, Novan stated that the company believes "its cash on hand is sufficient to fund operations at least through the end of 2017, of which the allocation of capital will be dependent upon further assessment of the SB204 phase III trial results."

DRM01 is a novel topical inhibitor of acetyl coenzyme-A carboxylase, an enzyme involved in synthesis of the fatty acids that are an essential component of sebum.

A phase IIb randomized trial in 420 adult acne patients yielded positive results, according to Dermira, which is developing DRM01. The company plans to begin a pivotal phase III trial in the first half of 2017.

Another investigational topical acne therapy to keep an eye on is cortexolone. This peripherally selective antiandrogenic agent is under development by a company called Cassiopea.

Dr. Eichenfield's financial disclosures included serving as an investigator for Novan, Regeneron, Galderma, and Astellas Pharma US; and as a consultant for Galderma, Genentech, Janssen, Lilly, Otsuka, and TopMD.

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COMMENTARY
BY DR. SIDBURY

▶ Topical retinoids long have been an essential part of acne therapy. Their track record of efficacy, coupled with recognized but manageable side effects like dryness, irritation, and photosensitivity have the hallmarks of an appropriate OTC medication. This has been true for decades, and yet only in the past year has adapalene 0.1% gel been approved for OTC use. Improved access to this class of medications should lead to better outcomes. Newer classes of medications also are diversifying therapeutic options, including topical dapsone gel in children 12 years and older. Aczone 7.5% gel is a stronger iteration than the first generation topical dapsone product (5%), but deceased recommended dosing to once daily appears to result in excellent tolerability. Dr. Eichenfield further describes encouraging but early results from the therapeutic pipeline.

Atopic dermatitis: Pivotal dupilumab results create a sensation

BY BRUCE JANCIN
At the EADV Congress


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Dr. Eric L. Simpson discusses this promising new option for severe atopic dermatitis.

VIENNA – The marquee event at this year's annual congress of the European Academy of Dermatology and Venereology – the one everyone was eagerly awaiting – was the first presentation of two large, international, pivotal phase III randomized trials of dupilumab for treatment of inadequately controlled moderate to severe atopic dermatitis in adults.

Attendees at EADV 2016 understood that, if positive, these studies, known as SOLO 1 and SOLO 2, would be transformative. They would herald a new era of highly effective targeted biologic therapy for this common and often debilitating chronic relapsing skin disease, akin to what occurred in psoriasis therapy well over a decade ago.

The results did not disappoint.

"We now have a promising new option for patients whose quality of life was severely diminished by their disease," Eric L. Simpson, MD, declared in presenting the SOLO 1 and 2 results on the last full day of the congress.

"Dual targeting of interleukin-4 and -13 represents a therapeutic option for patients with moderate to severe atopic dermatitis," added Dr. Simpson, professor of dermatology at Oregon Health & Science University, Portland.

These results have implications extending beyond atopic dermatitis. Asthma, chronic sinusitis with nasal polyposis, and eosinophilic esophagitis are other conditions where the type 2 inflammatory cytokines IL-4 and -13 are believed to be important drivers of disease activity. Clinical trials of dupilumab in those diseases are underway.

Dupilumab, a fully human monoclonal antibody that binds specifically to the shared alpha-chain subunit of the IL-4 and -13 receptors, hit all of its primary and secondary outcome measures in SOLO 1 and SOLO 2. Moreover, some of these "secondary" endpoints are consistently reported in patient surveys to be among what they consider to be the most troublesome aspects of atopic dermatitis, including intense itching, disrupted sleep, clinically significant anxiety and/or depression, and generally diminished quality of life.

SOLO 1 and SOLO 2 were identically designed, independent, randomized, double-blind, placebo-controlled clinical trials of 16 weeks' duration. Conducted in North America, Europe, and Asia, they included a total of 1,379 patients, split roughly 50/50 between those with moderate or severe atopic dermatitis. Their average disease duration was 26 years. Participants were randomized to subcutaneous injection of dupilumab at 300 mg once weekly or every 2 weeks or to matching placebo.

The primary endpoint was a score of clear or almost clear – 0 or 1 – on the Investigator's Global Assessment (IGA) at week 16 accompanied by a reduction of at least 2 points from baseline. A key secondary endpoint was at least a 75% improvement in the Eczema Area and Severity Index (EASI-75), considered a coprimary endpoint by regulators in Japan and the European Union.

The use of topical agents for atopic dermatitis was not permitted except as rescue therapy for uncontrolled symptoms. An IGA of 0 or 1 with at least a 2-point drop from baseline was a high bar to reach, given that a median of 50% of participants' body surface area was affected. But in SOLO 1, that target was achieved in 37.9% of subjects on dupilumab every other week, 37.2% with weekly therapy, and just 10.3% of placebo-treated controls. Similarly, in SOLO 2, the rates were 36.1%, 36.4%, and 8.5%, respectively.

Of note, there were essentially no differences in outcomes across the board with weekly versus biweekly dosing of dupilumab.

From a median baseline EASI score

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of 30, an EASI-75 was achieved at 16 weeks in 51.3% of patients on dupilumab every other week, 52.5% on weekly injections, and 14.7% of controls in SOLO 1. In SOLO 2, the corresponding EASI-75 rates were 44.2%, 48.1%, and 11.9%, respectively.

Itch is described by most patients with moderate to severe atopic dermatitis as their No. 1 issue. From a baseline median peak score of 7.7 on a 0-10 numerical rating scale for pruritus, week 16 scores dropped by a median of 51% in patients on dupilumab every 2 weeks, 48.9% with weekly therapy, and 26.1% with placebo in SOLO 1. Results in SOLO 2 mirrored those in SOLO 1.

Particularly noteworthy was the finding that a significant reduction in itch severity was documented by week 2 in both dupilumab treatment arms, Dr. Simpson observed.

Just under half of study participants had a baseline score of 8 or more on the Hospital Anxiety and Depression Scale Anxiety subscale or HADS Depression subscale, considered the cutoff for a clinically significant mood disorder. Among affected patients, a score of less than 8 was achieved at 16 weeks without the use of psychotropic medications in 12.4% of SOLO 1 participants on placebo, 41% on biweekly dupilumab, and 36.3% with weekly dupilumab. In SOLO 2, the rates were 6.1% with placebo, 39.5% with biweekly dupilumab, and 41.2% with once-weekly dupilumab.

The median baseline Dermatology Life Quality Index score was 15 across the two parallel trials. The collective proportion of patients who experienced at least a 4-point improvement, which is considered a clinically meaningful response, was 29.1% in controls, compared with 68.6% in patients dupilumab every other week and 60.2% with weekly dupilumab.

On the Patient-Oriented Eczema Measure, a composite yardstick that emphasizes sleep symptoms, the median baseline score was 22 out of a possible 28. An improvement of 4 points or more, defined as a minimal clinically important difference, was achieved in a collective 25.6% of controls, 69.6% of patients on biweekly dupilumab, and 63.6% on weekly dupilumab.

With regard to safety, no increase in infections was seen with dupilumab. In fact, only two adverse events were more frequent than with placebo. One was injection-site reactions, which were two- to threefold more common than in controls, and all of which were mild to moderate. The other safety issue was conjunctivitis, which occurred in 3 patients in the control arms of SOLO 1 and 2, compared with 36 in the dupilumab arms.

Asked about the mechanism of this conjunctivitis, Dr. Simpson said it remains unknown. There was no signal of an issue in the phase II studies.

"Ongoing studies are attempting to further characterize the affected patients. I would say the comforting thing is that most cases have been mild to moderate and have responded to topical steroids or topical cyclosporine. Only one patient had to discontinue dupilumab," according to the dermatologist.

In any event, 16 weeks of treatment is not sufficient to determine the safety of long-term therapy. Long-term extension studies of SOLO 1 and 2 are well underway, as are earlier stage clinical trials in pediatric patients with moderate to severe atopic dermatitis.

In response to another audience question, Dr. Simpson said he and his coinvestigators plan to drill down into the data to see if patients with severe atopic dermatitis obtained significantly

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COMMENTARY **BY DR. SIDBURY**

▶ Is AD finally catching up with psoriasis? For years, biologic medications have advanced our ability to safely and effectively manage severe psoriasis; at long last we have a similar agent to offer our moderately to severely afflicted AD patients as well. The Food and Drug Administration now has approved dupilumab for the treatment of moderate to severe AD in adults "whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable." Pediatric studies are underway.

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FRONTLINE MEDICAL COMMUNICATIONS

Fighting back against psoriasis bullies

BY RANDY DOTINGA

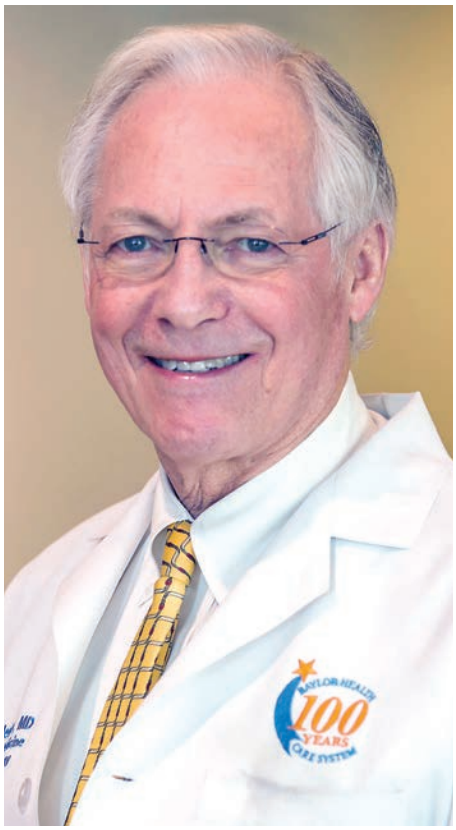
Dallas dermatologist Alan Menter, MD, doesn't boast bullying-prevention superpowers, but what he does have is close enough: an eagerness to get the word out to anyone – parent or principal, psychologist or pediatrician – who can help prevent a child with psoriasis from being bullied.

Over his long career, Dr. Menter has made many calls to adults in positions of influence over children. "I've talked to pediatricians, and I've even called up schools and talked to principals to try get the bullying situation reduced to an extent where the kids can live happy, normal lives without kids taunting them."

Dr. Menter, chief of dermatology at Baylor University in Dallas, has plenty of company. Other dermatologists are paying close attention to their youngest patients with psoriasis as researchers work to get a better handle on the bullying problem.

For this story, Dr. Menter and two other experts talked to this newspaper about the bullying problem and how dermatologists who treat children with psoriasis can make a difference.

"We really want to identify this early on and do whatever is required to turn it around," said Amy S. Paller, MD, professor of dermatology and pediatrics and chair of the department of dermatology at Northwestern University, Chicago. "These visible skin lesions can have a very significant effect on how children feel about themselves and others. When this is going on early in life, during childhood or teen years, there's really a risk for lifelong issues."



Dr. Alan Menter tells you how to make a difference for kids with psoriasis.

Dr. Menter's interest in psoriasis and bullying began during his childhood in South Africa when he watched children bully his brother, who had the condition. "I've always had a great desire to improve the quality of life in psoriasis patients," he said, and that passion grew as he worked in a day care center for children with psoriasis. "I had an opportunity to talk to children and recognize the impact that psoriasis has on them."

Research from across the world reveals that children with psoriasis face an extraordinary burden from bullying. "They're teased incessantly and bullied because they've got such a visible disease," he said.

The introspective and depressed nature of many children with psoriasis makes the situation even more difficult, he noted, since their emotional makeup prevents them from responding easily to taunting.

The extent of the bullying problem, however, isn't fully understood. Research into bullying and skin disorders is "very limited," said Kelly Cordoro, MD, of the departments of dermatology and pediatrics at the University of California, San Francisco. "What little evidence does exist suggests that kids with visible skin disease, including psoriasis, are often bullied, and this can impact them significantly," she said, pointing to a 2013 study that suggested those with acne, psoriasis, and atopic dermatitis are especially vulnerable (Clin Dermatol. 2013;31[1]:66-71).

Dr. Cordoro said her patients have taught her that recurrent themes in bullying are name-calling, teasing, and social exclusion. "Kids with psoriasis

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more benefits from weekly as compared with biweekly therapy, or if treatment every 2 weeks was as good as weekly therapy across the board. It's an important question, but the study finished so recently that the investigators haven't yet had time to conduct the analysis.

The pivotal phase III dupilumab findings met with an enthusiastic reception.

"Biologic therapy for atopic dermatitis is the light at the end of the tunnel," declared session cochair Lajos Kemény, MD, professor and chairman of the department of dermatology and allergology at the University of Szeged (Hungary).

"Seminal work," commented David M. Pariser, MD, professor of dermatology at Eastern Virginia Medical School in Norfolk.

The phase III dupilumab trials were funded by Sanofi and Regeneron Pharmaceuticals. Dr. Simpson reported having received research grants from and serving as a consultant to Regeneron and more than a dozen other pharmaceutical companies.

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may be told they look 'disgusting' and 'gross' and that others are afraid to play with them because they think they are contagious," she said. "Kids are not invited to birthday parties, pool parties, and other group events because of the appearance of their skin."

Sports are a special area of concern. "They don't want to get into gym shorts, and they don't want to engage in sports because they get hot and itchy," Dr. Paller said. "Or people stay away from them because they think there's something they can catch, so they're not chosen for sports activities."

Indeed, children with psoriasis may be left out of games like tag and contact sports because other children are afraid of touching them, Dr. Cordoro observed. "Other kids do not want to be near them. It is truly heartbreaking and derives largely from ignorance."

What can dermatologists do? Dr. Cordoro recommends that they take time to ask their youngest patients about their lives: "Is your psoriasis affecting your friendships?" "How are things going at school?" "Do kids ask you about your psoriasis? What do you say?"

"We can identify at-risk kids this way and work with parents, schools, coaches, and counselors toward productive interventions like educational programs," Dr. Cordoro said. "Education is the key. As kids, parents, and adults become educated, the psoriatic child is less likely to be teased and excluded. Kids with psoriasis may lack the confidence to defend themselves, and arming them with one-liners and basic educational points about their condition empowers them to address it directly."

DR. CORDORO

'Others are afraid to play with them because they think they are contagious.'

Dr. Paller, who is also director of the Northwestern University Skin Disease Research Center, said it's a good idea to add questions to the usual list of queries about subjects like sleep and itching. In cases when a child is bullied, it may help to reach out to teachers and principals, and to counselors and social workers if needed, she noted.

Parents play an important role, too, Dr. Menter said, although they may be in the dark about bullying. "What I've learned is that kids will seldom come home and tell their parent they've been bullied."

He urges both children and their parents to understand the nature of psoriasis and be open about it. "Don't hide it," he suggested. "Tell people that 'I've got psoriasis, and it's not contagious.'" And then, hopefully, the healing can begin.

Dr. Paller and Dr. Cordoro reported no relevant disclosures. Dr. Menter disclosed relationships with many pharmaceutical companies, including AbbVie, Allergan, Amgen, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, and Pfizer.

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COMMENTARY **BY DR. EICHENFIELD**

▶ Psoriasis is an inflammatory skin disease that may not be as common as atopic dermatitis in children and adolescents but that has tremendous health impact beyond the skin disease itself. Typical psoriasis presents as thickened, sharply demarcated pink-to-red scaly plaques, commonly on the arms and legs as well as the face and scalp. In children and teenagers, the impact on self-image is tremendous, and there is extensive literature displaying the decreased quality of life associated with the disease.

The experts interviewed – Dr. Alan Menter, Dr. Amy S. Paller, and Dr. Kelly Cordoro – all have careers that are entwined with work to improve the therapies and minimize the impact of pediatric psoriasis. The article highlighting Dr. Tanja Todberg of Copenhagen's presentation at the European Academy of Dermatology 2016 meeting fits well with this discussion (see page 38). She presented important data from a large 15-year case-control study from a national registry of more than 4,400 children and adolescents with psoriasis, highlighting psychiatric comorbidities. Pediatric psoriasis patients had higher rates of depression, drug and alcohol abuse, and eating disorders, and of being prescribed benzodiazepines, antidepressants, and antipsychotics.

Other studies have highlighted other health issues associated with psoriasis, including obesity, early myocardial infarction, cholesterol-processing anomalies, and atherosclerosis, as well as psoriatic arthritis and Crohn's disease. Screening guidelines to direct us in management of children and teenagers with psoriasis will be published shortly, thanks to the efforts of the Pediatric Dermatology Research Alliance and the National Psoriasis Foundation. The outward, visible skin disease of psoriasis can set children and adolescents apart from their peers, and these excellent articles point out some of the issues that health care providers may not think about, but should.

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Topical crisaborole boosts quality of life in children and adults with atopic dermatitis

BY BRUCE JANCIN

Expert analysis from the EADV Congress

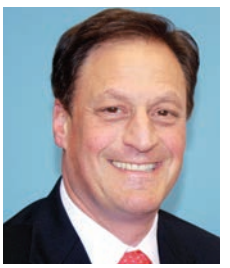
VIENNA – Topical crisaborole 2% ointment administered twice a day was consistently associated with clinically meaningful quality of life improvement scores on multiple measures in the two pivotal phase III, randomized, controlled trials of atopic dermatitis (AD) patients aged 2 years old through adulthood, Amy S. Paller, MD, reported at the annual congress of the European Academy of Dermatology and Venereology.

AD in children and adolescents is infamous for the adverse quality of life impact it imposes upon the patients' parents, family, and caregivers. So the significant improvement seen with crisaborole, compared with its vehicle on the Dermatitis Family Impact (DFI) Questionnaire was particularly gratifying. The DFI questionnaire assesses quality of life in key domains, including family, parent, and caregiver sleep, emotional distress, relationships, family leisure, and ability to do housework or go shopping.

"If approved, crisaborole ... could improve the quality of life for patients with mild to moderate atopic dermatitis and, very importantly, for their families as well," declared Dr. Paller, professor of dermatology and chair of the department of dermatology and professor of pediatrics at Northwestern University, Chicago.

Crisaborole's developer, Anacor Pharmaceuticals, has filed an application for approval for treating mild to moderate AD in patients aged 2 years and older, now under review at the Food and Drug Administration.

In a separate presentation at the EADV congress, Lawrence F. Eichenfield, MD, presented the results of a long-term, open-label crisaborole safety study of 48-52 weeks duration. The long-term study involved 517 participants in the two pivotal phase III trials. There were no serious adverse events and no long-term cutaneous adverse events such as the skin atrophy or telangiectasias that can occur with topical steroids. The safety profile was favorable for long-term treatment of patients 2 years of age or older with mild to moderate AD.



DR. EICHENFIELD

DR. PALLER

"What's nice about this study is that the number of grams of drug used was enough to provide a good picture of safety. Patients used a total of 760 g on average over the course of 11 or 12 months, or about 45-70 g per month of b.i.d. utilization, so they had reasonable exposure to the medication," observed Dr. Eichenfield, professor of dermatology and pediatrics at the University of California, San Diego, and chief of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego.

Crisaborole 2% topical ointment is a novel, boron-based, nonsteroidal inhibitor of phosphodiesterase 4 (PDE-4). AD is marked by overactivity of PDE-4, which results in decreased levels of cyclic AMP and resultant increased release of inflammatory cytokines.

Dr. Paller noted that, in the previously reported efficacy results of the two pivotal, double-blind, 28-day, phase III trials, crisaborole treatment reduced global disease severity and provided early and sustained improvement in itch severity. She presented the prespecified quality of life results for the two identically designed, parallel pivotal trials, which totaled 1,016 patients on crisaborole and 506 on its vehicle. At baseline, 39% of subjects had mild AD, and 61% had moderate AD. The mean body surface area affected was 18%. Participants' mean age

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Quality of life improvements with crisaborole

	Crisaborole (n = 1,016)	Vehicle control (n = 506)
Children's Dermatology Life Quality Index (for children aged 2 to <16 years; 0-30 [most severe] scale)		
Mean score at baseline	9.3	9.0
Improvement at day 28	–4.8	–3.0
Dermatology Life Quality Index (for patients aged 16 years and older; 0-30 scale)		
Mean score at baseline	9.7	9.3
Improvement at day 28	–5.2	–3.5
Dermatitis Family Impact Questionnaire (for family and caregivers of patients aged 2-17; 0-30 scale)		
Mean score at baseline	8.1	7.8
Improvement at day 28	–3.7	–2.7

Note: Based on data from two double-blind, phase III trials.

Source: Dr. Paller

Take hyperhidrosis in teens seriously

BY WHITNEY MCKNIGHT

At AAD 17

ORLANDO – Not quite a fifth of teens experience excessive, uncontrollable sweating, according to the results of an online survey presented during this year's annual American Academy of Dermatology.

Because nearly 70% of teens who reported the condition said it interferes with their activities of daily living, late-breaking research presenter, Adelaide A. Hebert, MD, chief of pediatric dermatology at the University of Texas, Houston, said it was time medical schools paid more attention to it.

"These kids have often seen a number of physicians who really haven't taken this clinical condition to heart," Dr. Hebert said during her presentation. "They don't know what to do, so they tell the kids not to worry. The kids just don't get the answers that will be beneficial to them, so educating physicians is key." Dr. Hebert said that

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COMMENTARY **BY DR. EICHENFIELD**

▶ Hyperhidrosis is actually a fairly common condition in teenage years, as highlighted by Dr. Adelaide Hebert of University of Texas, Houston, in a large online survey study of 1,000 adolescents. It can be remarkably disturbing, with some teens having tremendous quantities of sweat even without provocative stimuli, such as heat and situations causing nervousness. Hyperhidrosis also is variable in regions affected. Some teens have palmar disease, plantar disease, or axillary involvement as isolated conditions, while others can have all permutations of combinations.

Therapies range from topicals to systemic agents, or even neurosurgery. Over-the-counter or prescription-strength antiperspirants often are a first-line therapy, and a useful method is 5-20 minute soaks of involved areas, working up the soak times to clinical responsiveness, versus the more usual "quick swab" of liquid applications. Other options include electrophoresis devices, though a bit unwieldy. Oral anticholinergics (e.g., Robinul) can be very useful in more severe cases, although side effects must be closely monitored. Botulism toxin injections are highly effective, but work only temporarily and are arduous, expensive, and painful. There are some procedural approaches, including infrared treatment of axillae, and neurosurgery approaching the brachial plexus to block autonomic nerve stimuli for sweating. Neurosurgery is used in only the most severely affected patients, as compensatory hyperhidrosis of other areas is a common sequelae.

Be alert to this condition and engage patients to assess if it is affecting their lives, helping to offer therapy or referral to specialists with interest and expertise in the condition.

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was 12.3 years, and 14% were aged 8 years old or older.

All three quality of life instruments featured 10 questions addressing key quality of life domains. The response to each question could be scored from 0 (not at all) to 3 (very much).

The structure of the long-term safety study suggests how crisaborole might be used in clinical practice. During the year-long, open-label study, patients were evaluated every 28 days. If their skin was deemed clear or almost clear on the basis of an Investigator's Static Global Assessment (ISGA) score of 0 or 1, they were taken off crisaborole and could use only emollients for the next 28 days, at which time they would be reevaluated. At that point, if they had an ISGA of 2 or more, they went back on crisaborole twice a day for 28 days until their next evaluation.

Dr. Eichenfield reported that 10.2% of participants in the long-term safety study reported treatment-related adverse events, which were mild to moderate. The most frequently reported of these were mild to moderate flares of AD during a 28-day off-treatment period in 1.3% of patients, application site pain in 2.3%, and application site infection in 1.2%.

Dr. Paller and Dr. Eichenfield reported serving as consultants to Anacor Pharmaceuticals.

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COMMENTARY **BY DR. SIDBURY**

▶ Based upon successful phase III data in over 1,500 children aged 2-18 years, the Food and Drug Administration has now approved another option. Crisaborole, or Eucrisa, is a topical phosphodiesterase inhibitor for mild to moderate AD in children older than 2 years of age. At 1 month, nearly one-third of patients were clear or almost clear using this compound, with application site reactions in about 4%, the only adverse effect noted. This offers a welcome alternative, particularly to those parents frightened by potential adverse effects of currently available options. Additional longer-term, open-label studies have shown both safety and efficacy to be durable, and improvement in itch and rash translate nicely into better quality of life.

Teen indoor tanning drops significantly

BY HEIDI SPLETE
From AAD 2017

Indoor tanning among adolescents in the United States has dropped significantly, but fewer than half of schools in the United States reported sun safety practices to help minimize students' UV exposure in the school setting, based on data from two studies presented at the annual meeting of the American Academy of Dermatology and published simultaneously in JAMA Dermatology.

To characterize sun safety practices at schools, Sherry Everett Jones, PhD, MPH, and Gery P. Guy Jr., PhD, MPH, of the Centers for Disease Control and Prevention, reviewed data from the 2014 School Health Policies and Practices Study Healthy and Safe School Environment questionnaire including 577 elementary, middle, and high schools (JAMA Dermatol. 2017. doi: 10.1001/jamadermatol.2016.6274).

Overall, 48% of schools reported that teachers allowed students time to apply sunscreen at school (the most frequent sun safety practice). However, only 13% made sunscreen available, 16% asked parents to ensure sunscreen application before school, and 15% made an effort to avoid scheduling outdoor activities during times of peak sun intensity. High schools were less likely than elementary or middle schools to follow sun safety practices.

"Interventions driven by the public health and medical community educating school leadership and policy makers about the importance of sun safety are needed regardless of level, location, size, and poverty concentration of the school. These efforts could be instrumental in increasing the adoption of sun safety practices among schools," Dr. Jones and Dr. Guy emphasized.

However, data from another study showed a significant reduction in the prevalence of indoor tanning among adolescents. CDC researchers led by Dr. Guy pooled data from the 2009, 2011, 2013, and 2015 national Youth Risk Behavior Surveillance System Surveys (JAMA Dermatol. 2017. doi: 10.1001/jamadermatol.2016.6273). Overall, the prevalence of indoor tanning among U.S. high school students decreased from 16% in 2009 to 7% in 2015.

"Public health efforts could help address the misconception that indoor tanning protects against sunburn. The medical community also can play a key role in counseling adolescents and young adults in accordance with the U.S. Preventive Services Task Force guidelines."

None of the researchers on either study had relevant financial conflicts.

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COMMENTARY **BY DR. EICHENFIELD**

▶ Thumbs up for new data showing a drop in indoor tanning amongst adolescents. Years of advocacy – including public education campaigns – are paying off!

Early intense UV exposure is associated with higher risks of melanoma, and indoor tanning not only does direct damage to the skin but also is associated with teens getting more sunburns.

As we head into our spring and summer months, it is good to remember that messaging about sun protection should be reasonable but consistent. I like to stress that we should consider avoiding exposure during peak sun intensity, using clothing and hats, seeking shade, and applying sunscreen for the areas that will be exposed. The messaging needs to be broader than just suggesting sunscreen use.

It sounds like in Portugal sun safety messages worked when printed on sugar packets. I'm not sure if that would work in the United States, and bringing attention to sugar might annoy our colleagues working to decrease the obesity epidemic! Perhaps a smartphone home screen message?

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global medical education devotes virtually no time to the study of hyperhidrosis in adolescents.

For the study, Dr. Hebert and her colleagues online-surveyed 1,000 adolescents between 12 and 17 years who meet the accepted diagnostic criteria for primary focal hyperhidrosis. An analysis of the 981 surveys that were complete showed that 17.1% of respondents experienced excessive, uncontrollable sweating and that 68.6% of these reported the sweating was moderate or major, impairing their normal functioning.


DR. HEBERT

The average age of onset for the condition was 11 years, although more than a quarter of respondents said their sweating began at age 10 years. Nearly all those surveyed said they sweat from at least two focal areas, with five areas being the average number of focal areas.

Adolescence is when hyperhidrosis begins for many adults with the condition, yet few if any data exist regarding the condition in this age group, according to Dr. Hebert. "We have to figure out what is going on so maybe we can make a difference later."

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Monthly lab testing for isotretinoin? No need

BY BRUCE JANCIN

Expert Analysis from SDEF Hawaii Dermatology Seminar

WAILEA, HAWAII – Many physicians perform laboratory monitoring monthly when prescribing isotretinoin for severe acne, but recent evidence indicates that's excessive, according to Julie C. Harper, MD, president-elect of the American Acne and Rosacea Society.

She pointed to a meta-analysis of isotretinoin studies, which she called "a game changer" in her own dermatology practice in Birmingham, Ala.

"I used to check labs monthly, too, but I've changed my practice as a result of this study. I perform a lipid and hepatic panel at baseline and after 2 months of isotretinoin therapy, and if those numbers are okay I don't check them again," she said at the Hawaii Dermatology Seminar provided by the Global Academy for Medical Education/Skin Disease Education Foundation.

The investigators published a meta-analysis of 26 studies including 1,574 isotretinoin-treated acne patients with serial laboratory values available (JAMA Dermatol. 2016 Jan;152[1]:35-44).

The meta-analysis demonstrated that triglyceride levels rose by a mean of 45.3 mg/dL after 8 weeks on isotretinoin. Notably, however, the mean difference in triglycerides between baseline and 20 weeks was essentially the same at 45.6 mg/dL.

"Therefore, if you're going to have a change in triglycerides, you're going to have it early. If it's good at week 8, it should be good at week 20. And if it's not good at week 8, you probably ought to keep checking," she said.

Similarly, there was no substantial late effect of isotretinoin on total cholesterol. The investigators determined that they had insufficient data to draw conclusions regarding late changes in liver function tests. For guidance on that score, Dr. Harper turned to an earlier study of nearly 14,000 isotretinoin-treated patients led by Lee T. Zane, MD, a dermatologist at University of California, San Francisco.

They found that 1.5% of patients experienced a moderate elevation in transaminase levels, and no one experienced high-risk or grade 2 elevations in transaminases, triglycerides, or total cholesterol. They also concluded that monitoring white blood cells, platelets, and hemoglobin was meritless (Arch Dermatol. 2006 Aug;142[8]:1016-22).

"I'm not checking white blood cells, platelets, or hemoglobin. I check only triglycerides, total cholesterol, and hepatic function – and a pregnancy test, of course," Dr. Harper said. "I've practiced for 17 years. And I would agree with [Dr.] Zane – we don't see elevated liver function tests very often with this drug, and when we do there's often another explanation for why they're high."

In her own practice, when a patient on isotretinoin develops a high triglyceride approaching 300 mg/dL, the first thing she does is recheck it and make sure the patient is fasting. If it's a true elevation, she pulls the dose back because this is a dose-related side effect. She also recommends that the patient begin taking fish oil supplements at a starting dose of 2 g/day. In a handful of refractory patients, she prescribes fenofibrate. The exceptions she makes to her policy of no further lab testing if the first 2 months are problem free are patients with polycystic ovary syndrome, central obesity, or outright metabolic syndrome, since they are probably already at increased risk for developing lab abnormalities.

She reported serving on speakers' bureaus for Allergan, Bayer, Galderma, LaRoche-Posay, Promius, and Valeant.

SDEF and this news organization are owned by the same parent company.

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COMMENTARY **BY DR. EICHENFIELD**

▶ Isotretinoin is widely used in teenagers and young adults, as well as some preteens, for severe, refractory acne vulgaris. Traditionally, laboratory monitoring is done monthly, including liver function tests, triglyceride and cholesterol levels, CBCs, and pregnancy testing for women of childbearing years, mandated by the iPLEDGE program. Recent articles have looked critically at "automatic" monthly laboratory work. A meta-analysis found that rises in triglycerides tend to occur early, arguing for following these over 2 or 3 months but not necessarily beyond that. This same article stated there were insufficient data to draw conclusions on late changes in liver function, although some experts state that late changes are unlikely.

The question is do we liberalize lab follow-up? It's still a tricky issue, as one of the purposes of following the labs, such as liver function tests, is to see if there are individuals with high-grade transaminase elevations. Are we certain that if we do only 2 months of lab monitoring that we won't get rises? What happens with intercurrent infections, such as mononucleosis, not uncommon in the age group? Also, many physicians start with low dosing of isotretinoin, increasing over several months.

So, what do we do in our pediatric dermatology practice? Our general policy is that, after a few months of stable labs at stable dosing, we may forgo further testing, although, of course, continuing monthly pregnancy tests. If we raise doses, we recheck the laboratory work. As more data come out, and a stronger consensus on less testing, we will be happy to save money and "save the sticks" that go along with such frequent monitoring.

Consider all acne in Latinos inflammatory

BY MICHELE G. SULLIVAN
Expert Analysis from AAD 17

ORLANDO – Postinflammatory hyperpigmentation is a common consequence of acne in Latino skin, and aggressive medical treatments or procedures can aggravate the problem, said Mercedes Florez-White, MD.

"Most of the time, the postinflammatory hyperpigmentation [PIH] has much more impact on the patient's quality of life even than the disease itself, so you need to be very careful when treating these patients," said Dr. Florez-White of Florida International University, Miami.

Every Fitzpatrick phototype can be observed in the Latino population, but one feature seems to link them: inflammation linked with all types of acne, even comedonal, she said at the annual meeting of the American Academy of Dermatology.

Overview and diagnosis

Nodulocystic acne is the most common type in this population, followed by comedonal acne. Although the comedonal type is not generally considered inflammatory acne, it should be in Latino patients, given their sensitivity to skin inflammation and its outcome. "There is inflammation there from the beginning – treat it as an inflammatory disease for the best results." A thorough history – including a rundown of hair and skin products the patient is using – is critical. "You never know when something you think is acne is really something else," like an allergic reaction, she said.

Treatment

There are no AAD-generated treatment guidelines for acne in Latino patients. She manages her patients according to a treatment algorithm published by the Ibero-Latin American College of Dermatology and a paper published in the Journal of Dermatologic Treatment (2010 May;21[3]:206-11), as well as her own 35 years of clinical experience.

Topical therapy

- Start topical retinoids at a lower concentration, two to three times a week, and gradually increase the dose and frequency until the desired effect is reached. Also, start benzoyl peroxide at lower doses.
- For a patient with very proinflammatory cystic acne, initiate a short course of corticosteroids to decrease inflammation – this will reduce the risk of PIH.
- Add azelaic acid in a 20% cream or 15% gel. "It's an anti-inflammatory and antibacterial, and it really does help reduce the chance of PIH. This is used all over Latin American and Asia, but it is an off-label use in the U.S." she said.
- For adult women, consider 5% dapsone gel, but not in combination with benzoyl peroxide.

Oral therapy

- Doxycycline is first-line treatment for moderate to severe papulopustular or nodulocystic acne. Other primary agents could be minocycline or tetracycline. Second-line antibiotic choices include erythromycin, azithromycin, and sulfamethoxazole/trimethoprim. Antibiotics should be given with benzoyl peroxide to reduce the chance of bacterial resistance.
- For nonresponsive cases, use oral isotretinoin, started at half the recommended dose. Increase gradually to treatment response.
- For women with hormonally mediated acne, give a trial of oral contraceptives with antiandrogen properties, or spironolactone. "I like to combine oral contraceptive pills with isotretinoin. You can give this because the absorption of isotretinoin is very superficial. You won't have any problems with that," she noted.

Skin care

Good skin care will help promote healing and generally increase patient compliance with medication, Dr. Florez-White said.

- A noncomedogenic broad-spectrum sunscreen should be used daily. Consider one with mineral oxides, especially iron oxide, as only these preparations scatter both visible light and infrared radiation, which both increase the risk of PIH.
- Cleanse with a synthetic detergent or lipid-free cleanser.
- Recommend daily use of a salicylic, lactic, or glycolic acid.

Camouflage is very important for some patients, especially teens. "I always recommend a noncomedogenic fluid makeup," she said.

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COMMENTARY
BY DR. EICHENFIELD

▶ Our preteens and teens with skin of color and acne can have profound hyperpigmentation. This aspect of acne in Latino patients was stressed by Dr. Mercedes Florez-White. Postinflammatory hyperpigmentation can occur from whiteheads and blackheads, which have an inflammatory component and aren't only from inflammatory papules and pustules. I often point out that these "leftover lesions," or blemishes, are distinct from active noninflammatory papules, pustules, and cysts, and may take weeks to months longer to resolve with therapy. Topical retinoids are a mainstay of therapy, and include tretinoin, adapalene, and tazarotene. Of note, adapalene 0.1% gel (Differin Gel, Galderma) is the first topical retinoid approved over the counter. Dr. Florez-White's article lists some other medications and recommendations on skin care that may help control active lesions, minimize development of hyperpigmentation, and help resolve the "blemishes."

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crisaborole ointment 2%

BIG NEWS IN ATOPIC DERMATITIS!

Now Approved

EUCRISA™ – the first and only nonsteroidal, topical PDE4 inhibitor; a monotherapy for mild-to-moderate atopic dermatitis in patients 2 years of age and older.[1]

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.

Visit **www.EucrisaHCP.com** for more information

Reference: **1.** EUCRISA™ (crisaborole) Prescribing Information. December 2016.

Please see Brief Summary of Full Prescribing Information on adjacent page.

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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 5 and 3 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 (5 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 (18 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 (3 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 (18 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 (2 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 (18 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, issued December 2016.

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How social media solved a skin outbreak

BY RANDY DOTINGA

Several teens who came home from a trip abroad with ugly ulcerated skin lesions in 2014 got vague and unhelpful diagnoses: Physicians thought they had bug bites. True, but that was only part of the story. It took an alert dermatologist and Facebook to identify the true cause, spread the word, and stop the outbreak.

"Social media facilitated communication between patients, crowd sourcing a diagnosis," said Kanokporn Mongkolrattanothai, MD, who treated three of the teens at Children's Hospital Los Angeles.

What did the kids have? Read on and see if you can make the diagnosis yourself.

The story begins in the early summer of 2014 when about 50 teens were on an adventure trip to Israel. Among other things, they camped outdoors in the Southern part of Israel's Negev Desert.

Upon their return, pruritic red papules appeared on a 16-year-old girl's ankle and thigh. They transformed into ulcers with raised edges and a central crater, according to a report that published online in Pediatric Dermatology (2016 Sep;33[5]:e276-7. doi: 10.1111/pde.12910). At least 12 teens from the trip had similar ulcerated lesions, mostly in exposed areas like arms and legs, said Dr. Mongkolrattanothai, an infectious disease specialist at Children's Hospital Los Angeles and a coauthor of the report.

DR. KRAKOWSKI

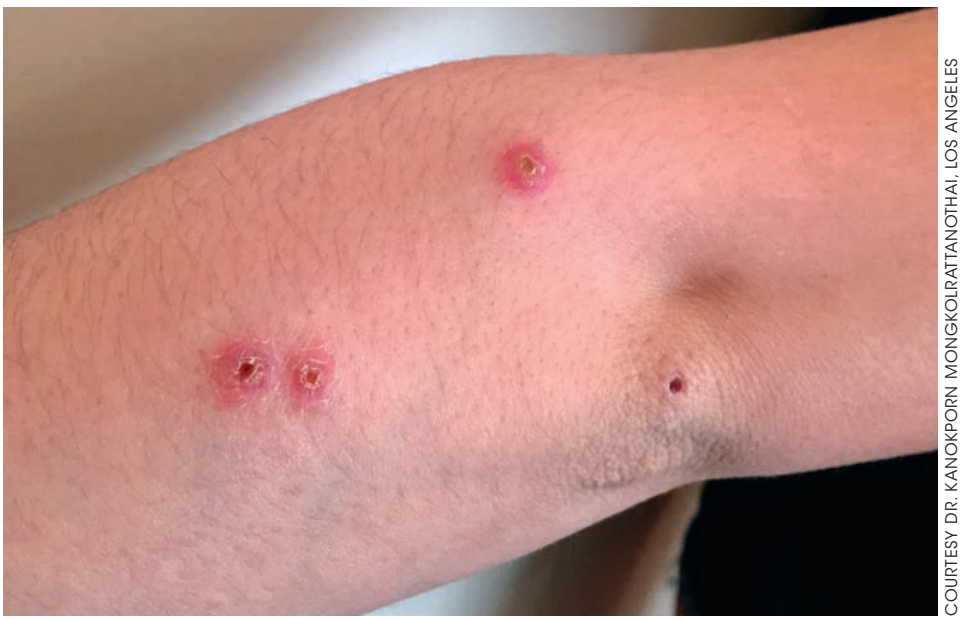
Six patients received a diagnosis of insect bites, and one was diagnosed with a bacterial skin infection, noted Dr. Mongkolrattanothai of the University of Southern California, Los Angeles. But these diagnoses were incorrect.

Andrew Krakowski, MD, a pediatric dermatologist in West Conshohocken, Pa., solved the mystery after examining the 16-year-old: The teens had been infected with cutaneous leishmaniasis, caused by protozoan parasites that are transmitted by the bites of female sand flies.

"The light bulb really came on when she mentioned that the lesions were still present several months after the trip to Israel," said Dr. Krakowski, who was at Rady Children's Hospital–San Diego at the time. "On physical exam, the lesions were ulcerated and eroded and did not look to be typical bug bite reactions." The Centers for Disease Control and Prevention confirmed the diagnosis.

On Facebook, the teenager posted a picture of a T-shirt with the words "I went to Israel, and all I got was leishmaniasis." At the same time, another traveler on the same trip posted pictures of lesions. This set off a wave of awareness that sent affected teens to seek care at Children's Hospital Los Angeles, Mattel Children's Hospital UCLA, Cedars-Sinai Medical Center, Kaiser Permanente Woodland Hills Medical Center, and Rady Children's Hospital–San Diego.

"It is likely that our patients became infected with leishmaniasis while camping in the Negev Desert, sleeping on sand dunes at night without use of mosquito netting or tents," Dr. Mongkolrattanothai said in an interview. "Most of the affected teens did not take precautions against insect bites, which would have included appropriate clothing to minimize areas of exposed skin and the use of repellent products. This placed them at risk for sand fly bites, as sand flies are most active in twilight, evening, and nighttime hours."



COURTESY DR. KANOKPORN MONGKOLRATTANOTHAI, LOS ANGELES

A skin lesion is shown in one of the teenagers with cutaneous leishmaniasis, treated by Dr. Kanokporn Mongkolrattanothai at Children's Hospital Los Angeles.

As for treatment, 12 patients were treated with topical paromomycin therapy with the addition of gentamicin to a petroleum base, and one was observed without treatment, she added. "All patients are recovering well with no recrudescence of disease and

CONTINUED ON FOLLOWING PAGE

Prescribing the landmark hemangioma drug: The challenges and the benefits

BY RANDY DOTINGA

For Beth Drolet, MD, a pediatric dermatologist in Wisconsin, the tremendous impact oral propranolol has had on the treatment of severe infantile hemangioma is written on the faces of children diagnosed with the condition in recent years.

"You can tell which drugs the kids were on by their age," said Dr. Drolet, professor of dermatology and pediatrics at the Medical College of Wisconsin, Milwaukee. "If they were born before 2008, before we used this medication, those kids have had multiple surgeries and are still not looking that good. But we rarely see that in the kids born after."

Because of this landmark treatment, "thousands of kids won't have to grow up disfigured," she said in an interview. But for individual dermatologists, even those who routinely work with children, treatment with oral propranolol poses unique challenges. In many cases, they refer appropriate patients to pediatricians and pediatric cardiologists.

Still, it is possible for dermatologists to successfully treat their smallest patients with oral propranolol, according to Dr. Drolet and Ilona J. Frieden, MD, professor of dermatology and pediatrics at the University of California, San Francisco.

In interviews, the two pediatric dermatologists spoke about the challenges and benefits of treating hemangioma patients with oral propranolol solution, which was approved by the Food and Drug Administration in 2014 for "proliferating infantile hemangioma requiring systemic therapy."

"It's more complicated than many conditions we see, but most dermatologists should be able to use [propranolol] comfortably," Dr. Frieden said. "The tricky part is understanding which hemangiomas need treatment with propranolol and which ones can be left to resolve spontaneously. That requires judgment and understanding that a time frame is involved. There is a window of opportunity for making more of a difference."

The oral form of the drug was used off label to treat patients with hemangi-

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no appearance of new lesions."

Cutaneous leishmaniasis can lead to permanent scarring, and another form, visceral leishmaniasis, can be fatal.

What helped Dr. Krakowski crack the case? "Training at the University of California at San Diego, in such close proximity to the Navy's Balboa Medical Center, we are taught from day 1 to think outside of the box because 'there are zebras in Africa,'" he said. "With so much international travel in and out of the region, including to locations where leishmaniasis is endemic, it is warranted to consider that specific diagnosis on the differential. Normally, I do not have to biopsy 'bug bites,' but considering the patient's entire presentation, you almost have to do a biopsy to make sure the lesions were not leishmaniasis."

DR. MONGKOLRATTANOTHAI

Dr. Krakowski praised the CDC. "They have a tremendous amount of resources dedicated to helping investigators work through diagnostic dilemmas such as this, and they helped us – free of charge – to confirm the diagnosis, type the leishmaniasis, and plot a treatment course to resolution," he said. "They also were instrumental in helping us identify and educate other potentially exposed patients from the camping trip."

In November, the Infectious Diseases Society of America and the American Society of Tropical Medicine and Hygiene published new guidelines about leishmaniasis in Clinical Infectious Diseases (doi: 10.1093/cid/ciw670). The societies warn that leishmaniasis is becoming more common in the United States, in part because of ecotourists infected in Central and South America and returning soldiers infected in Afghanistan and Iraq.

Dr. Mongkolrattanothai and Dr. Krakowski reported no relevant financial disclosures.

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COMMENTARY **BY DR. SIDBURY**

▶ When I think of social media and teenagers my first thought is not "useful dissemination of medical information." Yet that is precisely what happened when a group of teens went on an adventure to the Israeli desert and came back with mystifying ulcerative skin lesions. The relatively obscure diagnosis escaped identification until an astute dermatologist in San Diego recognized it in one of the affected teens. This patient took to social media and as quickly as a tweet her entire peer group was aware of the proper diagnosis, hastening proper care and minimizing morbidity. Now that deserves a "like."

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oma after a French dermatologist discovered in 2007 that it could effectively treat the condition. A topical form of propranolol is also used for hemangiomas that do not require systemic treatment.

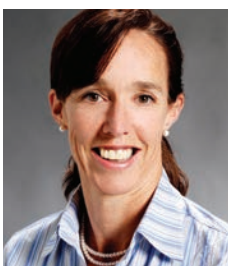
In general, infantile hemangiomas "have a natural course of gradually involuting even without treatment," Dr. Frieden noted. But the most severe cases can produce functional impairment, scarring, and anatomic distortion.

Dr. Drolet said she considers treatment if hemangioma threatens a vital function (hearing, sight, breathing) or can lead to pain, infection, or scarring.

One challenge for dermatologists is that standard of care treatment with oral propranolol requires in-office cardiac monitoring, especially as the dose is increased over the first week or two.

"I don't think most dermatologists are comfortable taking a heart rate and blood pressure in an infant," said Dr. Drolet, who is director of the birthmarks and vascular anomalies section at Children's Hospital of Wisconsin, Milwaukee. Instead, they tend to refer patients to a pediatrician or pediatric cardiologist. Her clinic hired a cardiac nurse to train the staff in how to take heart rate and blood pressure in babies. "Partnering with cardiology was really important for us. We worked really closely with our pediatric cardiology team to gain that expertise for our staff to assess that. You have to be pretty comfortable with it. If you're not, you're going to have to find someone else."

DR. FRIEDEN



DR. DROLET

Another option for dermatologists, Dr. Frieden said, is to focus on heart rate alone since blood pressure in infants is difficult to measure. "It's not FDA sanctioned, but many people seem to do that and it's OK," she said.

Dr. Frieden and Dr. Drolet provided the following recommendations about treating babies with oral propranolol:

COMMENTARY **BY DR. SIDBURY**

▶ Dr. Ilona J. Frieden, and Dr. Beth Drolet, two experienced hemangioma investigators, address several critical questions, such as whom to treat and how to monitor if planning to use propranolol to treat hemangiomas. If hemangiomas threaten vision or other vital function; are complicated by ulceration, bleeding, pain, or infection; or have significant scarring potential; then intervention is indicated. If obtaining a blood pressure is challenging, as it can be in infants, this should not dissuade a provider from utilizing this medication, as heart rate can serve as a reasonable marker of beta-blockade. Dr. Frieden also reminds us that, while cardiac concerns such as bradycardia and hypotension are real, they are incredibly uncommon in an appropriately selected population. Hypoglycemia and bronchospasm in infants using a beta-agonist inhaler are potentially more dangerous adverse effects. Dr. Drolet's parting advice is to consider the development of an educational program with videos or written materials in order to optimize the chance of successful outcomes.

• Caution parents about side effects. Cardiac side effects have been "extraordinarily rare," Dr. Drolet said. "We have seen problems with wheezing and, very rarely, severe hypoglycemia," which can be prevented by educating the family. While it's uncommon for the medication alone to produce wheezing, this may occur when a respiratory infection and propranolol combine to stress the body, she noted.

In some cases, physicians prescribe albuterol for wheezing without realizing that it will interact with propranolol, she added. "One is a beta-blocker, and the other is a beta-antagonist. They completely cancel each other out."

To prevent hypoglycemia, Dr. Frieden said she recommends that children be fed every 6 hours if they're under 6 months old or every 8 hours if they're over 6 months of age. And Dr. Drolet said she advises parents to stop propranolol when their infants are sick.

A major focus of an educational video provided by Dr. Drolet's clinic is advising parents "to stop the medication if the infant is not eating regularly, vomiting, or has diarrhea. It interferes with how you respond to low blood sugar if you're not eating," she said. "That surprised us. Now that we've been teaching parents about when to call us, that's been pretty preventable."

Minor side effects include cold hands and feet and sleep disturbances such as sleepiness and apparent nightmares, Dr. Frieden pointed out.

• Monitor guidelines regarding safety and protocols. "Over time, we're getting more and more expertise," Dr. Drolet said. For example, her clinic no longer performs ECGs on babies who take the medication because research has suggested they are not needed.

• Spend time developing an education program for parents. Dr. Drolet's clinic provides the educational video to teach parents about how oral propranolol is used. "We haven't done that for any other drugs," she said. "But we want to make sure we aren't overdosing it. We've been very careful about our parent education to prevent that."

Dr. Frieden has consulted for Pierre Fabre Dermatologie, the manufacturer of the oral propranolol product, marketed as Hemangeol. Dr. Drolet has received an investigator-initiated grant from the company.

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Lab values poor surrogate for detecting pediatric Rocky Mountain spotted fever

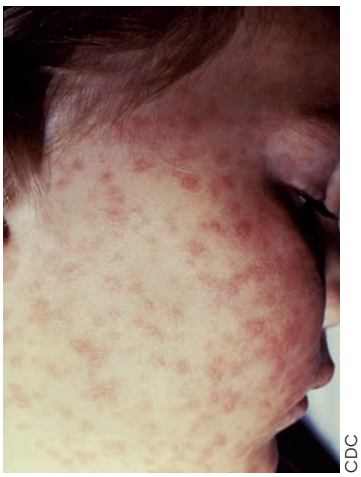
BY WHITNEY MCKNIGHT
From Pediatric Dermatology

The three fatalities observed in a retrospective analysis of six cases of Rocky Mountain spotted fever (RMSF) in children were associated with either a delayed diagnosis pending laboratory findings or delayed antirickettsia treatment.

"The fact that all fatal cases died before the convalescent period emphasizes that diagnosis should be based on clinical findings instead of RMSF serologic and histologic testing," wrote the authors (Pediatr Derm. 2016 Dec 19. doi: 10.1111/pde.13053).

Rechelle Tull of Wake Forest University, Winston-Salem, N.C., and her colleagues conducted a retrospective review of 3,912 inpatient dermatology consultations over a period of 10 years at a tertiary care center, and identified 6 patients aged 22 months to 2 years (mean, 5.1 years) diagnosed with RMSF. The patients were evaluated in the months of April, May, and June, and three of the six patients infected with the vector-borne obligate intracellular bacterium, *Rickettsia rickettsii*, had died within 4 days of hospitalization.

Two of the fatal cases involved delayed antirickettsial therapy after the patients were misdiagnosed with group A streptococcus. None of the six children were initially evaluated for *R. rickettsii;* they averaged three encounters with their clinician before being admitted for acute inpatient care where they received IV doxycycline after nearly a week of symptoms.



CDC

This image depicts the characteristic rash that had been caused by Rocky Mountain spotted fever.

"All fatal cases were complicated by neurologic manifestations, including seizures, obtundation, and uncal herniation," a finding that is consistent with the literature, the authors said.

Although the high fatality rate might be the result of the small study size, Ms. Tull and her coinvestigators concluded that the disease should be considered in all differential diagnoses for children who present with a fever and rash during the summer months in endemic areas, particularly since pediatric cases of the disease are associated with poorer outcomes than in adult cases.

Given that RMSF often remains subclinical in its early stages, and typically presents with nonspecific symptoms of fever, rash, headache, and abdominal pain when it does emerge, physicians might be tempted to defer treatment until after serologic and histologic results are in, as is the standard method. Concerns over doxycycline's tendency to stain teeth and cause enamel hypoplasia are also common. However, empirical administration could mean the difference between life and death, since treatment within the first 5 days following infection is associated with better outcomes – an algorithm complicated by the fact that symptoms caused by *R. rickettsii* have been known to take as long as 21 days to appear.

Ms. Tull and her colleagues found that the average time between exposure to the tick and the onset of symptoms was 6.6 days (range, 1-21 days).

Currently, there are no diagnostic tests "that reliably diagnose RMSF during the first 7 days of illness," and most patients "do not develop detectable antibodies until the second week of illness," the investigators reported. Even then, sensitivity of indirect fluorescent antibody serum testing after the second week of illness is only between 86% and 94%, they noted. Further, the sensitivity of immunohistochemical (IHC) tissue staining has been reported at 70%, and false-negative IHC results are common in acute disease when antibody response is harder to detect.

Ms. Tull and her colleagues found that five of the six patients in their study had negative IHC testing; two of the six had positive serum antibody titers. For this reason, they concluded that RMSF diagnosis should be based on "clinical history, examination, and laboratory abnormalities" rather than laboratory testing, and urged that "prompt treatment should be instituted empirically." The authors did not have any relevant financial disclosures.

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COMMENTARY
BY DR. EICHENFIELD

▶ RMSF still can be fatal, as shown in the article by Tull et al. The fact that there were three fatalities out of six cases, all who died within 4 days of hospitalization, and that they had several encounters with clinicians before being admitted for inpatient care, shows that we should remember this in our differential diagnosis of fever and rash during the summer months. The article highlights that the diagnostic tests that rely on antibodies are not helpful in the crucial early stages of disease presentation and that negative tests may contribute to slow reactions to possible cases.

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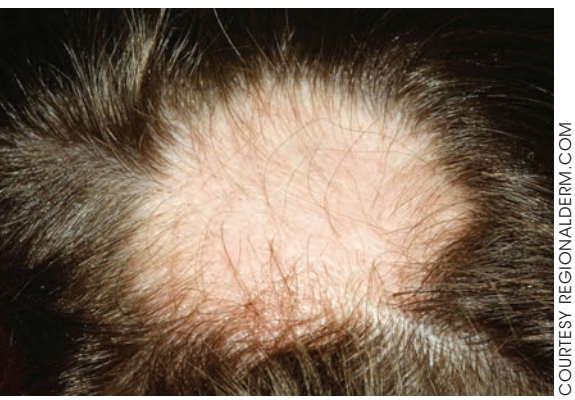
Tofacitinib clears pediatric alopecia areata

BY KARI OAKES
At the SPD Annual Meeting

MINNEAPOLIS – The first study to evaluate tofacitinib's effectiveness at treating severe alopecia areata in the pediatric population found that the Janus kinase inhibitor was effective for more than half of the patients, and well tolerated by all.

Of a case series of 13 pediatric patients who had alopecia areata (AA) and were treated with tofacitinib, 9 (68%) experienced "clinically significant" regrowth of hair, with mean improvement in the Severity of Alopecia Tool (SALT) score of 88% for these responders. The nonresponding group, all of whom had alopecia universalis or totalis, had a 1% reduction in SALT score.



COURTESY REGIONALDERM.COM

Alopecia has an unpredictable course.

Lucy Y. Liu, a medical student at Yale University, New Haven, Conn., presented the findings at the annual meeting of the Society for Pediatric Dermatology. Ms. Liu and her coinvestigators reported that all of the patients had severe AA by SALT scoring, with an overall mean pretreatment SALT score of 74. Eight of the patients (62%) had alopecia universalis, and two (15%) had alopecia totalis.

The patients ranged in age from 12 to 17 years, with a median age of 15. All but three were male, and patients were an average 9 years old at onset of AA. For patients with alopecia totalis or universalis, the duration of the current episode was a median 1.75 years.

Five patients (38%) had atopic dermatitis, while one (8%) had thyroid disease. Three patients (23%) had family members with AA; all but one patient, however, had a family history of autoimmune disease of some sort.

Patients were given tofacitinib 5 mg orally twice daily for 5 months. One patient developed new patches of alopecia during treatment, so the dosing for that patient was increased to 10 mg/5 mg daily. Adverse events for participants included headaches, upper respiratory infections, and "mild, transient increases in transaminases," they said. No serious adverse events were reported.

Study limitations included the small sample size and the relatively short duration of follow-up, an important consideration because relapse has been observed after tofacitinib treatment in AA. Still, "Tofacitinib is a promising therapy for the treatment of severe AA in adolescents," wrote Ms. Liu and her colleagues, recommending randomized clinical trials for further exploration of efficacy and safety in the pediatric population.

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COMMENTARY **BY DR. EICHENFIELD**

▶ Alopecia areata is a common inflammatory skin disease manifesting as acquired, localized alopecia, presenting as singular or multifocal annular, smooth, hairless areas of the scalp. Alopecia areata has an unpredictable course, with regrowth common with limited, patchy hair loss, but with a subset of patients having loss of all scalp hair (alopecia totatalis) and body hair (alopecia universalis). The alopecia is nonscarring, and associated with T cell–mediated inflammation that disrupts the normal hair cycle. Genetic factors mediate the development of cytotoxic T cells, and it's been found that the Janus kinase (JAK) pathways may be important in the immunology of the hair loss.

This is a tough condition for children and teenagers, as more severe disease is so noticeable, and given that the therapeutic armamentarium for effective and relatively safe therapies is limited. Local disease can be observed for spontaneous improvement, or treated with topical or intralesional corticosteroids. Topical immunotherapy or anthralin have been used, essentially trying to get an inflammatory response in the scalp that alters the local immune environment, but these therapies have lots of issues with side effects and potential toxic effects. Oral agents, including corticosteroids, have a poor track record for efficacy, with significant side effects.

The article highlighting tofacitinib, a JAK inhibitor, as systemic therapy for alopecia areata highlights an exciting area in pediatric dermatology! The Yale department of dermatology has been at the forefront of the study of JAK inhibitors for alopecia areata (and other inflammatory skin diseases). This work is still in the early phase, and the article points out that only a subset of patients responded to the tofacitinib, and that some had adverse events, albeit not serious ones. There are several JAK inhibitors utilized for other diseases, and others under development, and it is expected that both systemic and topical agents might be studied over the next several years. This is exciting news for patients and families with alopecia areata who would love to have effective therapy to "fill in the missing" therapeutic gaps (and alopecia)!

When AD is really contact dermatitis

BY DOUG BRUNK

Expert Analysis at the 2017 AAAAI Annual Meeting

DOUG BRUNK/FRONTLINE MEDICAL NEWS

Dr. Luz Fonacier offered tips for reading skin patch tests at the AAAAI meeting.

ATLANTA – When patients present with atopic dermatitis that worsens, changes distribution, fails to improve, or immediately rebounds, think contact dermatitis, Luz Fonacier, MD, advised at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

Clinical signs of contact dermatitis include lesions with an atypical distribution/pattern, such as head, eyelid, or cheilitis/perioral predominance, or lesions on the hand or foot. Also elevate your suspicion in patients with therapy-resistant hand eczema, adult- or childhood-onset atopic dermatitis without childhood eczema, as well as in cases of severe or widespread dermatitis prior to initiating a systemic immunosuppressant. The list of potential allergens to consider includes metal (especially nickel, cobalt, and potassium dichromate), fragrances such as formaldehyde and balsam of Peru, and preservatives, as well as topical emollients, corticosteroids, antibiotics, and antiseptics.

If you choose to perform patch testing, the hypothetical detection rate of the Thin-Layer Rapid Use Epicutaneous Patch (T.R.U.E. test) (TT), compared with the North American Contact Dermatitis Group screening series is 69.7%-75.1%. Antigens on the TT but not on the NACDG series include thimerosal, gold, and quinoline mix. The TT also has a higher false-positive rate to neomycin, thiuram mix, balsam of Peru, fragrance mix, cobalt, and lanolin.

Dr. Fonacier, professor of medicine at the State University of New York at Stony Brook and section head of allergy at Winthrop University Hospital, Mineola, N.Y., recommends loading acrylates, fragrances, and allergens in an aqueous vehicle immediately before application. She noted that delayed patch test readings are common to metals, topical antibiotics, and topical corticosteroids, and that positive reactions to gold are often not clinically relevant. "The patch test positivity of gold can be as high as 30% in adults and a little bit less in children, but results from two large studies show clinical relevance in only 10%-15% of cases," she said. A trial of gold avoidance may be warranted in patients with suspected jewelry allergy, facial or eyelid dermatitis, or exposure through gold dental restorations.

She went on to share tips for reading skin patch tests. The first reading should be done after 48 hours, while the second should be done 3, 4, or 7 days after application. "The second reading helps distinguish irritant from allergic responses," she said. "Thirty percent of negative tests at 48 hours may be positive on delayed readings." Most true allergic reactions occur between 72 and 96 hours. Allergens that may peak early include thiuram mix, carba mix, and balsam of Peru. Those that disappear after 5 days include balsam of Peru, benzoic acid, disperse blue #124, fragrance mix, mercury, methyldibromo glutaronitrile, phenoxyethanol, and octyl gallate. Delayed patch test reactions after 5 days include metals (gold potassium dichromate, nickel, and cobalt), topical antibiotics (neomycin and bacitracin), and topic corticosteroids.

Dr. Fonacier disclosed that she has received research and educational grants from Baxter and Genentech. She is also a consultant to Church and Dwight and Regeneron.

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COMMENTARY
BY DR. SIDBURY

▶ Is it eczema or allergic contact dermatitis? Yes! It is instructive to remember that allergic contact dermatitis is a type of eczema, and just looking at the morphologic or even histologic features of a rash cannot necessarily distinguish one from the other. Dr. Luz Fonacier instead points to abrupt flares, changes in pattern or distribution, or an immediate rebound after treatment as clues to a potential contact trigger. She details a number of potential allergens that can be in myriad OTC and prescription products, many used putatively to help the rash. This is a set-up for missed diagnosis and ever-escalating therapeutic intensity. In cases of refractory dermatitis, particularly if systemic therapy is considered, Dr. Fonacier recommends patch testing to rule out a delayed type IV hypersensitivity reaction; although logistically cumbersome, it can be quite rewarding when a culprit allergen is identified.

Daily moisturizing to stop AD cost effective

BY MARY ANN MOON
From JAMA Pediatrics

Daily full-body moisturizing of babies from birth to 6 months of age was cost effective and may prove to be a simple preventive strategy to reduce the burden of atopic dermatitis (AD), according to a report.

The annual cost of AD in the United States is estimated at $364 million to $3.8 billion. Preliminary studies have suggested that applying moisturizers every day for the first several months of life to babies at high risk of developing AD reduces the cumulative incidence of the disorder by approximately 50%, said Shuai Xu, MD, of the department of dermatology, Northwestern University, Chicago, and his associates.

To assess the cost-effectiveness of this preventive strategy, the investigators calculated the body surface area of hypothetical babies from birth to 6 months and obtained the average price of seven common moisturizers available at four online retailers to determine the cost per full-body application. They then calculated the quality-adjusted life-years (QALY) for AD using reported prevalences of mild, moderate, and severe disease, then calculated the cost-effectiveness of moisturizing using the previously reported relative

MAXRIESGO/THINKSTOCK

risk reduction of 50%. Their mathematical model assumed that all the moisturizers had equivalent efficacy (JAMA Ped. 2016 Dec 5. doi: 10.1001/jamapediatrics.2016.3909).

The average amount of moisturizer needed was 3.6 g/day at birth, increasing to 6.6 g/day at age 6 months. The cost for these amounts ranged from $0.13 per ounce to $2.96 per ounce for the seven moisturizers. Petroleum jelly was the most affordable product, costing just $7.30 for a 6-month supply, and Vaniply ointment was the most expensive, costing $173.39 for a 6-month supply. The costs of Aveeno Eczema Therapy moisturizing cream, Cetaphil moisturizing cream, CeraVe moisturizing cream, Aquaphor Baby Healing ointment, and sunflower-seed oil fell between the costs of these two products.

For preventing AD, petroleum jelly was the most cost-effective product at $353 per QALY and Vaniply ointment was the least cost effective at $8,386 per QALY. All the moisturizers easily met the widely accepted threshold for cost-effectiveness of $38,000 per QALY, Dr. Xu and his associates said.

"Beyond the direct cost savings in preventing atopic dermatitis, preserving the skin barrier early in life for high-risk individuals may theoretically reduce the risk of developing other atopic diseases. For instance, neonatal skin barrier dysfunction is associated with food allergies at 2 years of age," they noted.

"Furthermore, prophylactic moisturization may mitigate the risk of the occurrence of a growing list of atopic dermatitis comorbidities, which include sleep disturbances, obesity, anemia, and attention-deficit/hyperactivity disorder."

This study was limited in that it did not include any human participants and did not measure the actual development of AD throughout childhood, but instead relied on mathematical estimates and predictions. "Larger-scale studies with longer follow-up will determine whether prophylactic moisturization simply delays the onset of atopic dermatitis or alters the actual disease course," Dr. Xu and his associates wrote.

No sponsor was cited for this study. Dr. Xu reported being the founder and an equity owner of a website providing safe product recommendations for patients with AD, which has no financial relationships with makers of any skin products. He also reported receiving a one-time travel award from Aquaphor manufacturer Beiersdorf to present research at a medical conference. One of his coauthors reported being a consultant and/or adviser for Anacor/Pfizer, Exeltis, Galderma, Johnson & Johnson, Pierre Fabre, Regeneron, Sanofi, Theraplex, and Valeant.

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COMMENTARY **BY DR. SIDBURY**

▶ As complex and vexing as atopic dermatitis is, could it possibly be prevented for a dollar a month? Emerging data from several studies have shown that regular application of a moisturizer in high-risk infants can reduce their risk of developing AD by as much as 50%. These investigators, knowing that AD cost estimates run to $4 billion/year in the United States, have shown just how cost effective this solution could be. Vaseline, at just over $7/6 month supply was the most effective, based upon their model, but even more expensive emollients generated nearly unheard-of cost-effectiveness. As it seems increasingly likely that improving the skin barrier has other benefits not even captured here (for example, fewer skin infections) and could possibly even prevent other atopic comorbidities (such as asthma and food allergies), the cost-effectiveness of early emolliation will look only better.

Common allergic dermatitis culprits are hiding in plain sight

BY KARI OAKES

Expert Analysis from The SPD Annual Meeting

MINNEAPOLIS – When it comes to allergic contact dermatitis in children, the answer is sometimes hiding in plain sight. Cleansers, moisturizers, shampoos, detergents – all can contain ingredients that provoke significant reactions, yet many of these ingredients are not on the most common testing panels.

Erin Warshaw, MD, professor of dermatology at the University of Minnesota, Minneapolis, reviewed common but often unsuspected causes of allergic dermatitis in the pediatric population at the annual meeting of the Society for Pediatric Dermatology.

DR. WARSHAW

Even some hypoallergenic and frequently recommended products can contain preservatives and other ingredients that provoke allergic reactions, according to Dr. Warshaw. A chief culprit is methylisothiazolinone (MI), a preservative that came into common use as formaldehyde has been gradually phased out.

"If there's anything I could emphasize from this talk, it's MI, MI, MI. This is the major epidemic of our time in the contact dermatitis world," Dr. Warshaw said. Upcoming publications, she added, will place MI in the top five most common contact allergens. "MI is in everything, including things you would think would be hypoallergenic," she said. She recommended looking at ingredient labels with a keen eye when making testing decisions.

Despite MI's status as a frequent culprit, it's not an allergen that appears on common test kits, Dr. Warshaw pointed out. For example, it's absent from one of the most commonly used test kits, the Thin-Layer Rapid Use Epicutaneous Patch (T.R.U.E. test).

The T.R.U.E. test, said Dr. Warshaw, has reasonable sensitivity – it can detect 71% of relevant positive patch tests (RPPTs) in children. However, she added, a recent study showed that about 23% of children reacted to a supplemental allergen. "That's significant. One-quarter of these individuals only reacted to a preservative … or a sunscreen, or an acrylate. These aren't on the T.R.U.E. test."

Decyl glucoside is another frequent culprit that is not included in commercial patch test kits. "It's really an important emerging allergen," said Dr. Warshaw, noting that it commonly cross-reacts with coco and lauryl glucoside, frequently found in fragrance-free products. "It's always humbling when we find the allergen in the product we've recommended to our patients." Other important allergens not on the T.R.U.E. test include propolis, tocopherol, oxybenzone, and many surfactants and botanicals.

In order to avoid a confounding reaction to aluminum, Dr. Warshaw recommends testing using plastic-backed test chambers, such as IQ chambers, rather than Finn chambers, which are aluminum backed.

When working with families to track down allergens in the pediatric population, Dr. Warshaw adjusts her approach from what she would use for adults.

"What do I do differently in kids? First of all, I set expectations for children and parents," she said. Some of the most frequent parental questions deal with food allergies, so she allots time to explain the rationale for not testing for food allergens when allergic contact dermatitis is suspected.

CONTINUED ON FOLLOWING PAGE

COMMENTARY
BY DR. EICHENFIELD

▶ Pairing two intersecting articles, diaper dermatitis can sometimes be predominantly irritant contact dermatitis, and other times from allergic contact dermatitis. The study by Harfmann et al. highlights severe diaper dermatitis that was noted in cloth diaper–using toddlers. The impressive rashes appeared consistent with severe irritant dermatitis, presumably because the cloth diapers did a less successful job of wicking moisture from the skin and allowing more prolonged contact of urine and stool on the skin. The change to absorbable diapers and traditional barrier creams fixed the rashes.

Allergic contact dermatitis also can be a cause of rashes in the inguinal/diaper region. Dr. Erin Warshaw, a specialist in allergic contact dermatitis at the University of Minnesota, Minneapolis, highlights the epidemic of allergy to methylisothiazolinone (MI), a preservative that was commonly used in diaper wipes. MI had been used in combination with methylchloroisothiazolinone, another agent known to cause allergic contact dermatitis, but in the last few years, MI alone had been used as a wet wipes preservative. While MI has a low rate of contact allergy, its use in a great many products has moved it into "the Top Five" for most common contact allergies. In unusual or persistent diaper rashes, consider contact allergies to wet wipes; families should be instructed to check the ingredient labels on their wipes.

Testing for contact allergy can be tremendously useful but must be done carefully in children because the testing itself can expose children to allergens.

Possible downside to cloth diapers is bullous diaper dermatitis

BY KARI OAKES
At the SPD Annual Meeting

MINNEAPOLIS – A small study of cloth diaper–wearing toddlers with unusual vesiculobullous and erosive lesions found that the rashes fully resolved with aggressive barrier cream application and a switch to disposable diapers.

The four patients had previously received aggressive work-ups, including biopsy in some cases; all had received systemic antibiotics. Katya L. Harfmann, MD, a pediatric dermatologist at Nationwide Children's Hospital in Columbus, Ohio, was the lead author in a poster presentation at the annual meeting of the Society for Pediatric Dermatology.

The toddlers, aged 17 months to 2 years, had diaper dermatitis of several weeks' to several months' duration, with a presentation of vesicles, bullae, and erosions. All of the children had been placed in cloth diapers since birth.

The patients, three of them male, had undergone work-ups that included bacterial culture for three patients, herpes simplex virus (HSV) polymerase chain reaction testing for three patients, and blood work for two patients. HSV cultures and viral cultures were each performed on one patient. With the exception of one bacterial culture returning methicillin-sensitive *Staphylococcus aureus* (MSSA), all results were negative.

Two patients underwent biopsies. One biopsy was reported as "spongiform dermatitis," while the other was read as a "nonspecific ulcer."

A variety of treatments had been tried for the children. All of the children had received systemic antibiotics; two received systemic antivirals as well. Two patients each received topical steroids and topical antibacterials, and one patient also received topical dapsone. Many treatments were given "in repetitive courses, without improvement in the lesions," they wrote.

The families were advised to switch to exclusive use of disposable diapers and to begin frequent use of a zinc oxide–based thick diaper paste. For all patients, the diaper dermatitis completely resolved within as little as 2 weeks.

The medical literature documents an increased risk of diaper dermatitis with cloth diaper use. "Despite this knowledge in the medical community, nearly half of cloth diaper–using parents select cloth diapers with the assumption that diaper rash is less frequent with their usage," the researchers noted.

They pointed out that bullae in the diaper region are often thought to be associated with such infectious conditions as impetigo and herpes simplex infection, and can also be associated with immunobullous disorders. Diaper changes are less frequent in older children, though, giving the opportunity for prolonged contact with the irritating chemicals in feces and urine. This prolonged contact, exacerbated by the moister environment of a cloth diaper, may account for the unusual, severe presentation seen in these cases.

Also, the three boys had vesicular lesions on their testicles and penis. "It is possible that the thinner skin in these areas has a lower irritation threshold or that the redundancy of skin often seen on the penile shaft leads to trapping of irritants with extended diaper use," they wrote.

"An empiric trial of disposable diapers exclusively with aggressive barrier cream application for several weeks may eliminate the need for more invasive procedures and laboratory tests," wrote Dr. Harfmann and her coauthor.

They reported no conflicts of interest.

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For many patients, "I try and frame that there is probably baseline eczema, and our goal is to try to figure out if there is an allergy in addition to that that is contributing to the flares," she said. She makes sure to convey that "all it takes is one exposure every 3 weeks; that will keep this reaction going."

However, she's judicious in interpreting equivocal results. "I feel a responsibility not to label children with an allergy" if results are unclear. Finally, providing enough time is key, said Dr. Warshaw, who allots an hour for reviewing final testing results.

The take-home points? It's worthwhile to patch test children, since over half of children will have at least one RPPT. Also, contact dermatitis can be an overlay on preexisting allergic dermatitis, so patch testing can still be helpful for these children. Supplemental allergens are important in patch testing, "especially in children with a negative test to a screening series," Dr. Warshaw said.

She recommended accessing the Contact Allergen Management Program (CAMP) database, found on the American Contact Dermatitis Society website. The list is a searchable database that generates a list of "safe" products that don't contain a given allergen. This resource is available for society members, but a member's access code can be shared among faculty members at academic institutions, she said. Patients can also be given unique codes that will give them access for life, so they can use the CAMP database on a computer or via a smartphone app.

Dr. Warshaw reported no relevant financial disclosures.

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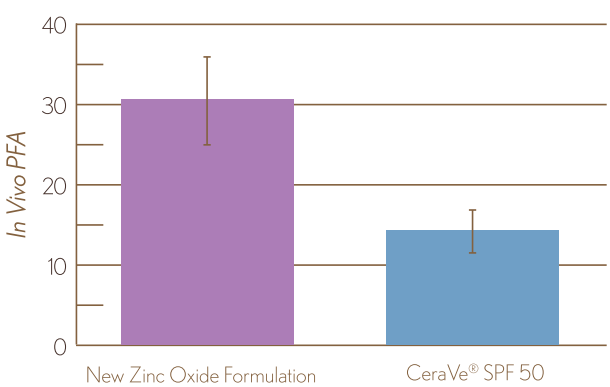

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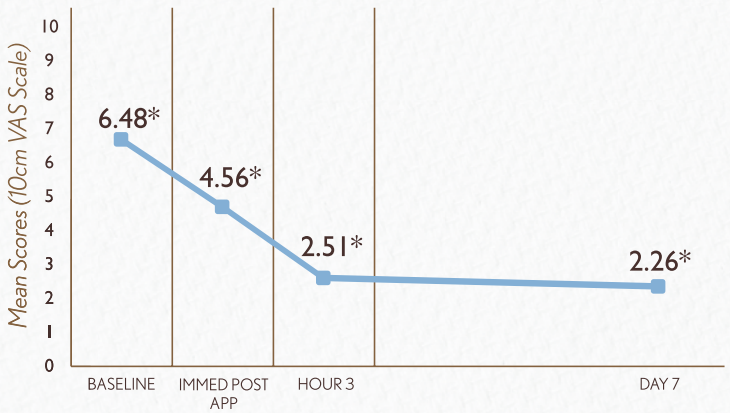

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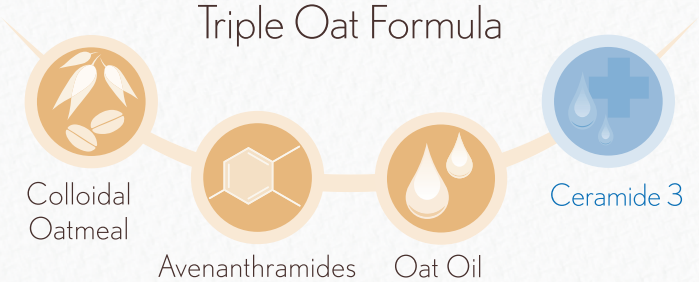

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Milk: Friend to bones, foe to faces?

BY MICHELE G. SULLIVAN

Expert analysis from AAD 17

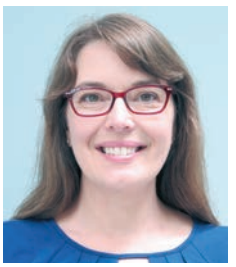
ORLANDO – A greasy hamburger and fries and a chocolate milkshake may all earn the finger of blame when teens fret over acne. But which of these foods is the real culprit?

A growing body of data suggests it may be the milk – especially if it's fat-free milk, according to Andrea Zaenglein, MD, who spoke at the annual meeting of the American Academy of Dermatology. Skim milk has been at the center of a long-simmering acne controversy, said Dr. Zaenglein, professor of dermatology and pediatric dermatology at Pennsylvania State University, Hershey.

A 2005 Nurses Health Study II analysis, comprising 47,355 women, refocused attention on the issue. The women all had physician-diagnosed severe acne as teenagers in 1989. In 1998, they filled out food frequency questionnaires, recalling, among other things, how much milk they drank as teens and the type of milk they drank. After controlling for a number of variables, the study found that whole milk intake increased the risk of acne by 16% and skim milk by 44% (J Am Acad Dermatol. 2005 Feb;52[2]:207-14).

The same association was seen in a subsequent study of 4,273 teen boys, published in 2008. There was a 10% increased risk for acne associated with intake of whole or 2% milk, a 17% increased risk for 1% milk, and a 19% increased risk for skim milk (J Am Acad Dermatol. 2008 May;58[5]: 787-93).

These and other data prompted Dr. Zaenglein and her colleagues at Penn State to conduct their own study, a case-control study of 225 teenagers aged 14-19 years, with moderate or no acne. "We took teens with acne and compared them to acne-free controls. The difference is, we tried to find a better dietary measurement," than a food frequency recall, which is an unvalidated tool susceptible to recall errors, she said. Instead, they conducted phone interviews to gather 24-hour food intake recall data on three separate occasions (J Am Acad Dermatol. 2016 Aug;75[2]:318-22).



DR. ZAENGLEIN

They found positive associations with total dairy and with nonfat dairy, but not with whole-fat or low-fat dairy. "The association was driven by the nonfat dairy," Dr. Zaenglein said. "When we took nonfat [dairy] out of the total dairy, the association there was no longer significant." "You have to wonder, what could this association between dairy – and skim milk in particular – be? Could dairy actually be involved in the pathogenesis of acne?" There are a number of proposed mechanisms, none of which have ever been confirmed, she said. "Could it be related to steroids? Milk is a very bioactive substance with estrogens and other hormones, but these are fat soluble and would be removed in skim milk." Another theory suggests that insulinlike growth factor-1, either in milk or endogenously stimulated by its consumption, may make a contribution.

"It's really hard to make a firm recommendation to eliminate dairy, because, in this country, it makes up a good portion of the calcium teens need during their bone-building years, and kids are already at high risk for not meeting these requirements."

National nutritional guidelines recommend 1,300 mg of calcium every day, which can be accomplished in three to five servings of dairy. "An 8-ounce glass of milk has 300 mg. Yogurt, cheese, and calcium-fortified juice are all highly accepted by teens. But, to get that same amount from vegetables, for example, you'd have to eat 3 cups of cooked kale. That's a lot of kale," Dr. Zaenglein said. She had no relevant financial disclosures.

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in saturated fats and sugars, which may ameliorate acne by decreasing weight and insulin resistance – especially in patients who already have abnormal metabolic parameters. Patients should also be advised to limit processed foods, meat, and dairy, she added.

As far as dairy and acne, it is too early to say what the impact of intervention would be "because we don't have any great interventional studies that have been done," she said. Moreover, it is unclear how early dietary interventions would need to be started to reduce an individual's risk of acne.

"It could go all the way back to things that happened when you were born that influence your outcome," Dr. Zaenglein said. For example, babies born prematurely are at greater risk for endocrine stressors, which lead to premature adrenarche, increasing their risk for acne.

"We really need new, better intervention studies to be able to give advice to our patients," she said. However, conducting such studies is challenging because it is difficult for people to eliminate dairy or other types of food from their diets for a prolonged period. To date, the majority of dietary studies have been observational and have relied on subjects' recall of what they consumed, so these studies have their own inherent problems, she added.

Dr. Zaenglein's disclosures include serving as an adviser to Anacor Pharmaceuticals and Valeant Pharmaceuticals International, and serving as an investigator and receiving grants/research funding various pharmaceutical companies.

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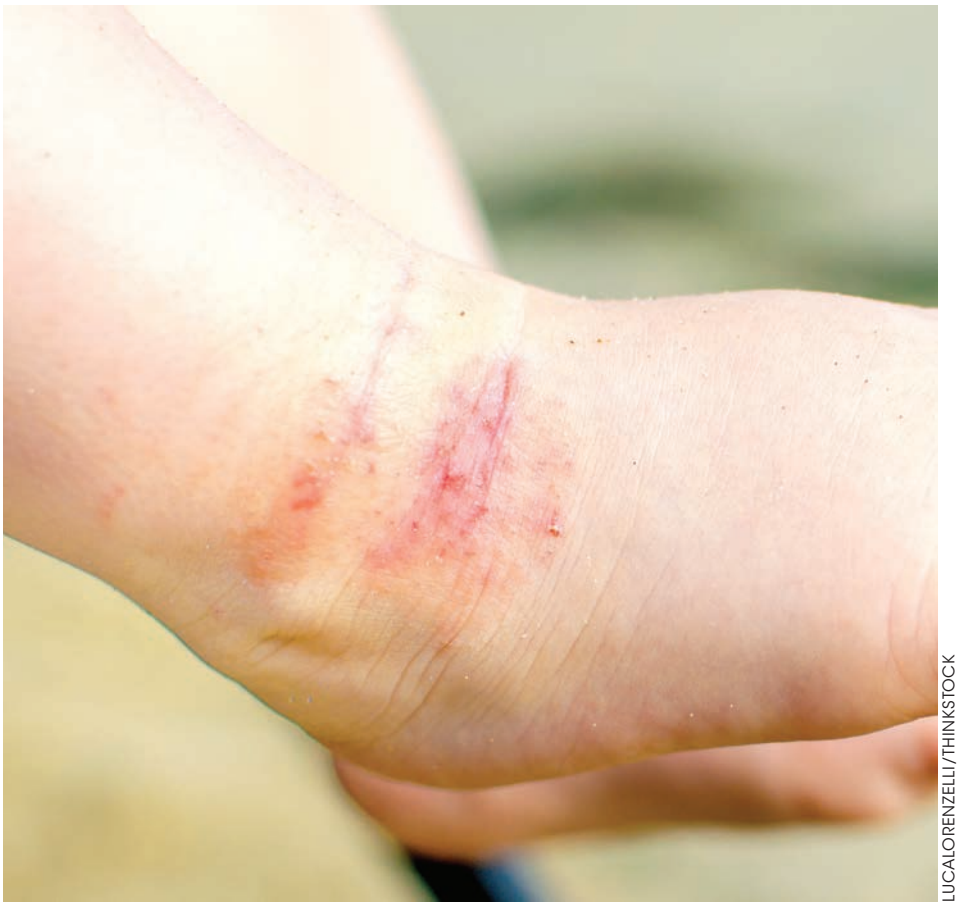
Tips for taming atopic dermatitis

BY DAMIAN MCNAMARA
At ODAC 2017



LUCALORENZELLI/THINKSTOCK

MIAMI – Tactics for managing patients with atopic dermatitis (AD) can go a long way to educate patients, set realistic expectations, and devise strategies for existing therapies, even as clinicians await some promising agents expected on the market soon.

"The good news is this is the Age of Eczema. In the last couple of years we've seen an explosion in the literature," Adam Friedman, MD, of the department of dermatology, George Washington University, Washington, said at the Orlando Dermatology Aesthetic and Clinical Conference. Some of this research is spurring new therapeutics. a phosphodiesterase 4 inhibitor.

Crisaborole ointment, 2% (Eucrisa), a phosphodiesterase 4 inhibitor, was approved by the Food and Drug Administration in December 2016 for treating patients aged 2 years and older with mild to moderate AD, for example. It is a novel, nonsteroidal anti-inflammatory and the first prescription agent approved in the United States for atopic dermatitis in more than 10 years.

Dr. Friedman has no personal experience with crisaborole, which just became available. "But the data look encouraging. From what I've seen this may be a nonburning alternative to calcineurin inhibitors. It will be interesting to see how this will fit in our practices."

Systemic management of pruritus

There's also promise for patients troubled by one of the top manifestations of AD – the itch. "We have new targeted therapies coming down the pike, some hopefully [gaining approval] in the next few months. We have biologics going after the cytokines of itch. It's a very, very exciting time right now," Dr. Friedman said.

Current clinical trials are focusing not only on AD but also specifically on pruritus, he added.

In the meantime, itch can be managed with prescription and over-the-counter topical agents, as well as systemic therapies such as gabapentin, some antidepressants, and the antiemetic aprepitant. Aprepitant is a substance P antagonist (through blocking neurokinin 1 receptor) and can be effective for some patients when taken three times a week, but it is not indicated for itch, Dr. Friedman said. Because of its off-label indication "it's a little tricky getting [insurance] coverage."

Back to basics

"Even with all the excitement, even with the new therapeutics, you have to stick with the basics," he said. "Put the lotion on, put the cream on. You have to put moisturizer on wet skin and be cautious with soaps." He added, "don't be afraid to ask for help. The National Eczema Association has a wonderful website with research, education, tools – you name it."

Keeping it real

For regional eczemas like hand dermatitis, what are the options? "Tell patients they can glove up, there are various latex alternatives … but it probably won't fly in the real world," Dr. Friedman said. Zinc oxide "works like armor, and patients will probably do well," but the aesthetics are unacceptable for most, he added. "Newer alternatives, such as those with aluminum magnesium hydroxide stearate, have similar protecting power, but are not opaque and rub on easier."

A goal of topical therapy is to get rid of the inflammation, and steroids have

a long history of evidence supporting their use, but "topical steroid phobia in parents" is a problem, he said. To counter the reluctance or refusal to use topical steroids, he suggested exploring reasons for noncompliance, dispelling any myths, and working with parent to make it easier to apply the steroids to their child.

Interestingly, there is some evidence that a simpler regimen may work well for some patients. "We always say 'apply twice a day.' Why? Because all the clinical trials had participants apply steroids twice a day. But there is no evidence to show twice a day is better than once a day, and in fact, a meta-analysis suggests once a day works just as well" (Br J Dermatol. 2005 Jan;152[1]:130-41).

Topical calcineurin inhibitors are another option. In general, Dr. Friedman prescribes these agents for delicate areas, for patients with thin skin, or for patients who use a topical steroid "on and on and on and can't seem to get off it." Calcineurin inhibitors can also be used on in-between days during steroid maintenance therapy, he added.

COMMENTARY
BY DR. SIDBURY

▶ The saying goes, "People don't care how much you know until they know how much you care." Dr. Friedman's advice to "educate and empathize" aligns well with this sentiment. AD is a complex, multifactorial disease without a known cure. This is a set up for misinformation and therapeutic misadventure. Education has as strong an evidence base as any available AD intervention. Dr. Friedman details specifics including the need to address corticosteroid phobia, as well as awareness of support groups like the National Eczema Association. The common theme is properly directed focus and access to good evidence-based information; this is the linchpin of successful AD care.

When prescribing, warn patients about the initial burn (due to substance P release) that commonly occurs so that they have realistic expectations.

Education remains essential

"I encourage you to educate your patients and empathize with them," he said. "Show them how to apply a moisturizer. Also, use your nurses and assistants to help with education – really empower them to be part of the process."

DR. FRIEDMAN

"Explain, explain, explain, so they have realistic expectations," and know that there is no cure, so that when they experience a flare, they understand that "it's not that the steroid didn't work – this is a chronic disease," added Dr. Friedman, who recommends providing patients with handouts that answer many of their questions.

Maximize moisturizing

When it comes to moisturizing, more is usually better. Effective products contain all the key ingredients: emollients to soften the skin, an occlusive to keep the water there, and a humectant to bond the water. "Just one or two is not going to cut it," he said.

"Something we now know is that starting early is key," he pointed out, referring to recent studies that have shown that in babies at high risk for AD, starting moisturizers early can decrease their risk for developing AD later (J Allergy Clin Immunol. 2014 Oct; 134[4]: 818-23).

"Another study that received a ton of press was in JAMA Pediatrics recently," Dr. Friedman said. The study concluded that the use of different moisturizers to prevent AD in high-risk babies was likely to be cost effective (JAMA Pediatr. 2017 Feb 6;171[2]:e163909. doi: 10.1001/jamapediatrics.2016.3909). Although some news reports claimed starting babies with Vaseline as a moisturizer will prevent AD, "that's actually not what the study showed. All the over-the-counter moisturizers they used worked, but Vaseline was the least expensive," Dr. Friedman noted

Help patients select the right soap

Educate patients to avoid "true soaps" such as Dial, Ivory, Irish Spring, or Lever 2000. "Soaps can be a real enemy here. You want lower pH types of soaps. Depending on skin type, our skin is somewhere between 5.5 and 6.5 pH," Dr. Friedman explained. "The paradigm shift for your patients is to hydrate, not to clean. Showers are okay if they're not blaring hot. Baths are okay ... but you should not be sitting in a sudsy bath."

Also, instruct patients to avoid irritating fabrics, dryer sheets, or harsh laundry detergents that could exacerbate AD.

'You're not alone'

Sometimes it's helpful to assure patients with AD that they're not alone, and that many researchers and clinicians are working on effective treatment strategies. "We're all familiar with atopic dermatitis because there's so much of it. The numbers are surprisingly high," Dr. Friedman said. Compared with the estimated 2.2 million Americans with psoriasis, AD eclipses their numbers substantially, affecting about 17 million people.

Dr. Friedman disclosed that he is a speaker for Amgen, Janssen, and Promius; receives research grants from Valeant; and is a consultant and/or advisory board member for Amgen, Aveeno, Biogen, Encore, Exeltis, Ferndale, Galderma, G&W Laboratories, Intraderm, La Roche-Posay, Loreal, Microcures, Nano Bio-Med, Novartis, Oakstone Institute, Occulus, Onset, Pfizer, Promius, Sanova Works, and Valeant. Dr. Friedman is also an editorial advisory board member for Dermatology News.

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Nasal hemangiomas: More complications

BY MARY ANN MOON
From Pediatric Dermatology

Infantile hemangiomas of the nose develop more complications than those at all other body sites combined, according to a report.

In what they described as the largest study to date to assess nasal infantile hemangiomas, researchers assessed which traits are associated with complications and predict residual skin changes at the age of 5 years.

"Nasal infantile hemangiomas pose an immediate risk of airway obstruction because infants are obligate nasal breathers, and may have long-term functional and psychosocial consequences if involution is incomplete or development of surrounding structures, such as nasal cartilage, is compromised," said Maria S. Kryatova of the departments of pediatrics and dermatology, Johns Hopkins University, Baltimore, and her associates.

The investigators identified all patients younger than 18 years who had been treated at their academic referral center for nasal infantile hemangiomas between 2001 and 2014. They performed retrospective chart reviews, which included photographs, for 89 participants. The parents of 63 of these children were interviewed when the participants reached a median age of 5 years and provided comparison photographs taken at their entry into kindergarten.

Thirty-five children (39%) developed one or more complications at some time during follow-up, including airway compromise, compression, or functional impairment; ulceration; visual obstruction or ocular compression; and infection.

In comparison, the Hemangioma Investigator Group has previously reported a 24% overall rate of complications at all body sites.

"Our study is the first to report a significant association between [the hemangioma's location on the nose] and depth. Lesions on the nasal dorsum are unlikely to be deep, whereas nasal tip lesions are unlikely to be superficial. Deep vertical growth may be limited by underlying nasal bone in the dorsum but less so by the soft tissue of the nasal tip," Ms. Kryatova and her associates reported (Ped Dermatol. 2016;33[6]:652-8).

Segmental- and indeterminate-type lesions were more likely than focal-type lesions to develop ulceration, compression, or functional obstruction, and mixed-depth hemangiomas were more likely than deep or superficial hemangiomas to ulcerate. Overall, the lesions had involuted by kindergarten age in 70% of the study participants but persisted in 30%.

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COMMENTARY
BY DR. SIDBURY

▶ I was taught very early in dermatology training that there are two sites on the body where the size of a hemangioma belies its potential significance: the upper eyelid and the nasal tip. In both of these locations, relatively small lesions can cause big problems. This article validates this lesson with regard to the nasal tip, as nearly 40% of affected patients in this study developed complications, and 80% went on to treatment. Nearly one-third still had their hemangioma at 5 years of age or just when kids were entering kindergarten. Given the sensitive cosmetic location, to say nothing of potential medical morbidity such as ulceration, obstruction in an obligate nose breather, and less commonly bleeding, this is a clarion call for early aggressive treatment of nasal tip hemangiomas.

ECG not always needed before propranolol

BY RANDY DOTINGA
From Pediatric Dermatology

Routine ECG screening in infants before they receive propranolol for hemangiomas is "not likely to be an effective screening tool in patients with otherwise normal physical examination and family history" and may even cause harmful delays in treatment, study authors concluded.

"As previously published guidelines suggest, it is likely that an indication-driven ECG strategy is a better approach, because there is a low incidence of ECG abnormalities that would limit propranolol use in children," wrote Kevin B. Yarbrough, MD, of Phoenix Children's Hospital, and his associates (Pediatr Dermatol. 2016 Nov;33[6]:615-20).

They tracked 162 patients (median age, 5.2 months) who underwent routine ECG screening at several clinics before propranolol treatment for hemangiomas from 2008 to 2013. The ECGs were read as abnormal in 69 cases (43%); the most common abnormality was left ventricular hypertrophy (16 patients), followed by right ventricular hypertrophy (8), sinus bradycardia (6), and sinus tachycardia (5). Cardiologists cleared all 69 patients for propranolol treatment, which they received. "No patients in our cohort experienced an adverse effect during treatment that could have been predicted or prevented by ECG before initiation of the propranolol," they said.

"Routine ECG adds to the cost of

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Pediatric psoriasis is linked to multiple psychiatric comorbidities

BY BRUCE JANCIN
At the EADV Congress

VIENNA – Psoriasis in children and adolescents is associated with significantly increased risk of a variety of psychiatric comorbidities, according to a large Danish national study.

Psoriasis is a common skin disease, and 30% of cases have their onset in childhood or adolescence, Tanja Todberg, MD, observed at the annual congress of the European Academy of Dermatology and Venereology.

She presented a retrospective case-control study of national registry data on all children and adolescents diagnosed with psoriasis during 1997-2012. This amounted to 4,410 patients with a mean age of 12.4 years, 10.7% of whom had psoriasis sufficiently severe that they went on methotrexate. Each pediatric psoriasis patient was matched by age, sex, and calendar year with 10 controls.

Diagnosis of psoriasis was based upon medical records and documentation that at least a second prescription for a topical vitamin D derivative had been filled. Those agents are the overwhelming choice as first-line therapy in the pediatric population, explained Dr. Todberg of the University of Copenhagen.

The pediatric psoriasis patients proved to be at significantly increased risk of being diagnosed with depression, eating disorders, drug abuse, and alcohol abuse. They were also more likely than controls to be prescribed antidepressants, antipsychotic agents, and benzodiazepines. That was every prespecified psychiatric outcome that Dr. Todberg and her coinvestigators included in the study except for one: Anxiety disorders occurred at a similar rate in the pediatric psoriasis patients and controls.

She reported no financial disclosures regarding this study, which was supported by Danish medical research funding.

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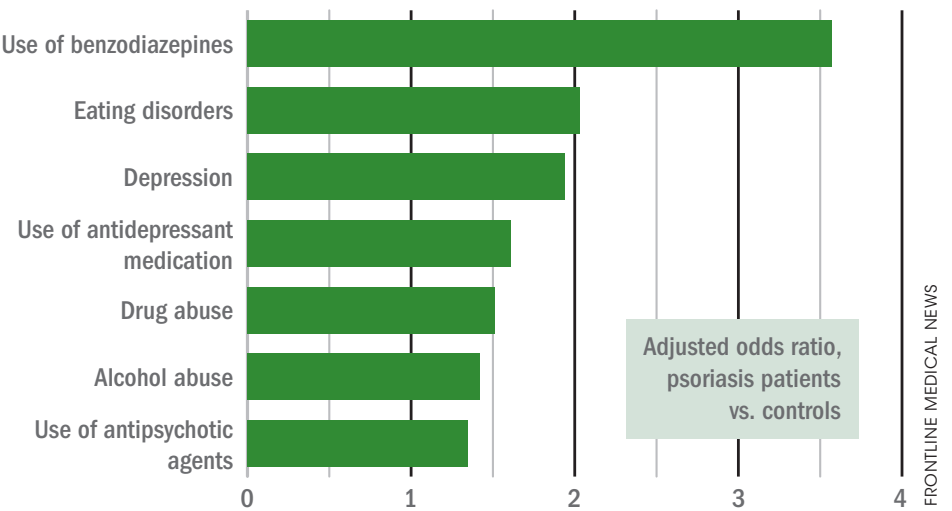
Psychiatric comorbidities in Danish pediatric psoriasis patients



Note: Based on data from 4,410 psoriasis patients and over 41,000 controls.
Source: Dr. Todberg

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treating hemangiomas and leads to unnecessary consultations and testing. Even more importantly, abnormalities detected on ECG can lead to delays in treatment initiation, which in turn can lead to greater patient morbidity, as seen in the case of our patient whose hemangioma ulcerated while awaiting cardiology consultation," they added.

Still, they noted that ECG tests should still be performed on "infants with bradycardia or cardiac arrhythmia found during initial physical examination, a family history of congenital heart disease or arrhythmias, and a maternal history of connective tissue disease."

One researcher reported that he was a clinical investigator for Pierre Fabre Dermatologie, the manufacturer of the oral propranolol product Hemangeol.

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COMMENTARY **BY DR. SIDBURY**

▶ Although propranolol is universally accepted as first-line therapy, protocols for screening and initiation have garnered less consensus. An ongoing question has been whether pretreatment ECG screening is necessary in all infants. In this article, Yarbrough et al. show that, in most cases, the answer is no. If there is a personal or family history of bradycardia, arrhythmia, congenital heart disease, or a maternal history of autoimmune disease, then ECG screening is warranted; otherwise, this step only adds cost and delays appropriate care.

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