PEDIATRIC DERMATOLOGY

JUNE 2021 A supplement to Pediatric News & Dermatology News

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

New biologics now for atopic dermatitis in preteens

BY LAWRENCE F. EICHENFIELD, MD

There continues to be a tremendous amount of new research on atopic dermatitis (AD) and studies highlighted in this supplement show the breadth of work. From the impact of AD on sleep and attention regulation, to biologic therapies for preteens, there is much to keep abreast of.

Other inflammatory skin disorders are also featured in this year's supplement, including vitiligo.

Vitiligo is a condition that is incredibly impactful on children and teens and their families, and new research on topical and oral JAK inhibitors, in addition to our traditional treatments, may set the stage for more effective disease management.

Preadolescent acne and acneiform conditions are reviewed as well, as something considered in infants and young children with facial eruptions. In addition, a new study showing that a history of depression is an identifiable risk factor for depression development during a course of isotretinoin is helpful in our patient selection and management.

Dr. Eichenfield is chief of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego. He is vice chair of the department of dermatology and professor of dermatology and pediatrics at the University of California, San Diego. He disclosed that he has served as an investigator and/or consultant to AbbVie, Lilly, Pfizer, Regeneron, Sanofi-Genzyme, and Verrica.

Dermatologic emergencies do occur

BY ROBERT SIDBURY, MD, MPH

A wide range of pediatric dermatoses that can affect children are discussed herein.

Pediatricians and dermatologists would be forgiven for thinking they did not really need to "keep up" with eczema therapeutics simply because, until recently, there really was not much to keep up with. In the last several years, however, improved immunologic understanding of eczematous inflammation has led to several novel treatments, with the pipeline promising more on the way.

Patients with AD will continue to be at risk for allergic contact dermatitis (ACD), which tends to hide in plain sight and can be confounded with AD. Two serious pediatric dermatoses that likely present in urgent care or the emergency department are also discussed: eczema herpeticum and staphylococcal scalded skin syndrome. Familiarity with these disorders facilitates rapid diagnosis, which will lead to better outcomes. Though warts are not serious, the presentation about treating them in children here is thorough and serious.

Dr. Sidbury is chief of dermatology at Seattle Children's Hospital and professor, department of pediatrics, University of Washington, Seattle. He is a site principal investigator for dupilumab trials, for which the hospital has a contract with Regeneron.

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Dupilumab curbed itch intensity, frequency in children with severe eczema

BY DOUG BRUNK

REPORTING FROM REVOLUTIONIZING AD 2020

Dupilumab treatment with concomitant topical corticosteroids provided rapid and sustained improvement in itch intensity and frequency in children aged 6-11 years with severe atopic dermatitis.

The findings come from a post hoc analysis of a phase 3 trial known as LIBERTY AD PEDS (NCT03345914) that Gil Yosipovitch, MD, presented during a late-breaking research session at the Revolutionizing Atopic Dermatitis virtual symposium.

Dr. Yosipovitch is a professor of dermatology and director of the Miami Itch Center at the University of Miami. Published data from the double-blind, placebo-controlled, 16-week, LIBERTY AD PEDS trial in children with severe AD showed that dupilumab significantly improved AD signs, symptoms, and quality of life, with an acceptable safety profile (J Am Acad Dermatol. 2020;21:119-31).

For the current analysis, Dr. Yosipovitch and colleagues evaluated the time to onset, magnitude, and sustainability of the effect of dupilumab on different measures of itch using data from approved Food and Drug Administration doses studied in the LIBERTY AD PEDS trial. A total of 243 children aged 6-11 years were randomized to dupilumab 300 mg every 4 weeks (300 mg q4w, baseline weight of less than 30 kg; 600-mg loading dose), 200 mg every 2 weeks (200 mg q2w, baseline weight 30 kg or greater; 400-mg loading dose), or placebo. All patients received concomitant medium-potency topical corticosteroids.

The mean age of patients was 8.4 years and those in the 300–mg q4w group were about 2 years younger than those in the 200–mg q2w group. On the Peak Pruritus Numerical Rating Scale (NRS), treatment with dupilumab was associated with a significant improvement from baseline in daily worst itch score through day 22 in the 300–mg q4w group and the 200–mg q2w group vs. placebo (–29% vs. –30%, respectively; *P* less than or equal to .001 and *P* less than or equal to .05). Treatment with dupilumab was also associated with a significant improvement from baseline in weekly average of daily worst itch score through week 16 vs. placebo (–55% vs. –58%; *P* less than or equal to .001).

By week 16, a higher weekly proportion of dupilumab-treated patients achieved a 2-point or more improvement in worst itch score, compared with placebo (72% in the 300–mg q4w group vs. 74% in the 200–mg q2w group; *P* less than or equal to .001). The same association held true for the daily proportion of dupilumab-treated patients who achieved a 4-point or more improvement in worst itch score, compared with placebo (54% vs. 61%; *P* less than or equal to .001).

Next, the researchers evaluated the proportion of patients reporting the number of days with itchy skin over the previous 7 days as assessed from the Patient-Oriented Eczema Measure (POEM) itch item question: "Over the last week, on how many days has your child's skin been itchy because of their eczema?" By week 16, the majority of children treated with dupilumab achieved a reduction of days experiencing itch from every day at baseline to at most 2 days.

By week 16, the majority of children treated with dupilumab achieved a reduction of days experiencing itch from every day at baseline to at most 2 days.

In the LIBERTY AD PEDS trial, data were consistent with the known dupilumab safety profile for adults and adolescents, Dr. Yosipovitch said. "Injection-site reactions and conjunctivitis were more common with dupilumab. Infections and AD exacerbations were more common with placebo."

The study was sponsored by Sanofi and Regeneron Pharmaceuticals. Dr. Yosipovitch and coauthors reported having received financial grants and research grants from numerous pharmaceutical companies.

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Commentary by Dr. Eichenfield

Dupilumab, a biologic agent that targets the cytokines interleukin-4 and IL-13, received expanded indication for moderate to severe atopic dermatitis down to children 6 years of age in May 2020. This has been revolutionary for children with persistent AD and disease that did not have adequate long-term disease control with topical agents. The study that was done in support of this had children with severe AD use dupilumab in varying doses (including placebo injections) along with topical corticosteroids. Analysis of the itch data discussed by Dr. Yosipovitch (one of our national "itch gurus") showed consistent decreases in daily peak itch scores as compared with baseline, and as compared with the placebo group (who had active use of topical corticosteroids). The reporting of "days without itch" means 24 hours without itch, and presumably less sleep disturbance, an important compounder of AD's impact on patients and their families.

Vitiligo treatment options abound but consider patient goals

BY RANDY DOTINGA

FROM MEDSCAPELIVE WOMEN'S & PEDIATRIC DERMATOLOGY SEMINAR

Despite the lack of any Food and Drug Administration–approved medications for vitiligo, there are plenty of treatment options, and therapy can make a big difference in an individual's quality of life, according to Seemal Desai, MD, of the University of Texas, Dallas.

"We have topical steroids. We have vitamin D analogs, calcineurin inhibitors, and depigmentation therapy. We also have systemic therapy, phototherapy, surgical treatment, and even psychological therapy, Dr. Desai said in a presentation at Medscape-Live's virtual Women's & Pediatric Dermatology Seminar.

Head and neck vitiligo, which "tends to respond very nicely to treatment," is one of the affected areas "where we have an important obligation to make sure our patients are effectively and aggressively treated," he said.

According to Dr. Desai, there are three kinds of vitiligo. Active/unstable vitiligo is marked by depigmentation spreading across 1%-2% of body surface area per month, the size of about one to two palms. Refractory vitiligo responds poorly to therapy with less than 25% of affected areas experiencing repigmentation. And the third type is chronic vitiligo. "The majority of patients we see are in this phase, where depigmentation is present for at least 1 year with no history of spontaneous repigmentation."

Before turning to therapy, he said, make sure to understand what the patient wants. "Are they even interested in being treated? I've had some patients with vitiligo, it's only on their chest, and they're always covered. They don't even want anything. Then I have other patients who only want their face and hands treated because those are the only parts of their body that are exposed."

To stabilize vitiligo, Dr. Desai recommends treating patients with "mini-pulse" oral therapy with systemic steroids. "I prescribe 4 mg of dexamethasone to be taken 2 consecutive days per week, such as Saturdays and Sundays. I usually halve the dose in children aged less than 16 years of age, so they'd be taking 2 mg." Make sure, he said, to counsel patients on side effects.

He also recommends antioxidants, particularly polypodium leucotomos, "which has been shown in studies to increase the rates of head and neck repigmentation when combined with narrowband UVB." He recommends

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240 mg or higher, 2 or 3 times a day. He adds that alpha lipoic acid, in combination with vitamin C, vitamin E, and phototherapy, has been shown effective in inducing repigmentation, especially on the head and neck.

As for newer drugs, Dr. Desai said afamelanotide, an analogue of alpha melanocyte–stimulating hormone combined with phototherapy, has shown promise. Like other medications he mentioned, it isn't FDA approved for treating vitiligo.

"Janus kinase [JAK] inhibitors are our new frontier in treating vitiligo," he said. "Tofacitinib can be dosed as an off-label usage in vitiligo in doses of 5 mg every other day, up to 5 mg daily.

Continued on following page ▸

Commentary by Dr. Eichenfield

Vitiligo is a common inflammatory skin disease with a prevalence of up to 2% of the population, and estimates hold that almost half of cases have childhood onset. While asymptomatic, vitiligo can be significantly disfiguring and can have psychological effects on the child and family. Segmental vitiligo usually presents with a "band" or segment and can often stabilize within months. Nonsegmental vitiligo can start anywhere on the body, in multiple parts of the body, and with variable patterns. Dr. Desai's talk at the Women's & Pediatric Dermatology Seminar highlighted that, while we have historically not had any FDA-approved drugs for vitiligo for adults or children, a variety of therapies can be utilized effectively.

Traditional first-line treatments in pediatrics are topical corticosteroids (TCS) of variable potency, dependent on the area of the body involved (milder TCS for more delicate skin), or topical calcineurin inhibitors (pimecrolimus or tacrolimus). Oral therapies such as dexamethasone described by Dr. Desai are uncommonly prescribed for children, while phototherapy (usually with narrowband UVB) may be used more commonly and effectively in cases with high body surface area. It is good to keep an eye out for evolving treatments, with topical ruxolitinib, a topical JAK inhibitor that has already completed phase 3 trials for atopic dermatitis in patients aged 12 or older, is in studies for pediatric vitiligo. Other investigators are exploring topical and oral JAK inhibitors, as well as phototherapy or lasers, in combinations to induce repigmentation.

Beware a pair of dermatologic emergencies in children

BY RANDY DOTINGA

FROM MEDSCAPELIVE WOMEN'S & PEDIATRIC DERMATOLOGY SEMINAR

Eczema herpeticum and staphylococcal scalded skin syndrome can be emergencies in children and require immediate care, warned dermatologist George Hightower, MD, PhD, in a presentation at MedscapeLive's virtual Women's & Pediatric Dermatology Seminar.

Eczema herpeticum is a condition in which a herpes simplex virus (HSV-1 or HSV-2) is superimposed over preexisting eczema. "The infection may be primary and sustained from a close contact or result in some of our older patients from reactivation and spread through autoinoculation," said Dr. Hightower, of Rady Children's Hospital and the University of California, both in San Diego.

Signs, he said, include acute worsening of atopic dermatitis with new-onset vesicles, pustules, and "punched-out" hemorrhagic crusted erosions. "Presentation ranges from mild to transient to life threatening."

Potential complications include meningitis, encephalitis, hepatitis, and chronic conjunctivitis. "That's why immediate ophthalmological evaluation is needed when there's involvement on the face near the eye," he said.

"Where I have concern for HSV patients, I get HSV [polymerase chain reaction] as well as a bacterial culture," he said. But even before the results are available, empiric treatment with acyclovir can be appropriate. "It's got to be systemic for these kids with severe involvement," he said, and they should also be started on medication for staphylococci and streptococci.

During his presentation, Dr. Hightower also highlighted staphylococcal scalded skin syndrome. Patients with the disease commonly have concurrent skin pain (which can appear to be fussiness), fever, irritability, malaise, and poor feeding. Examination may reveal widespread erythema with accentuation at folds/peeling at hands and large sheets of superficial peeling scale with diffuse erythema.

Widespread skin involvement "results not from the presence of staph throughout the skin, but the exotoxin that it produces that becomes systemic," he said. "Clinical diagnosis is supported by presence of *S. aureus* on bacterial culture, but the presence of staph is not necessary to make the diagnosis. When in doubt, histopathology is helpful."

Cases can be managed with a first- or second-generation cephalosporin, he said. Alternative therapies include antistaphylococcus penicillinase–resistant penicillins (oxacillin or nafcillin) or vancomycin.

Dr. Hightower reported no relevant disclosures. MedscapeLive and this news organization are owned by the same parent company.

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Commentary by Dr. Sidbury

The joke historically has been that the term "dermatologic emergency" is an oxymoron. Dr. Hightower proffers two examples of potentially life- or function-threatening infectious diseases presenting initially in the skin that are anything but laughing matters. Eczema herpeticum (EH) is a condition every provider who takes care of children should be familiar with. If they have not seen it yet, there is a good chance it has seen them – or will. Children with atopic dermatitis, or eczema, experience cutaneous immune dysregulation such that skin infections like herpes simplex virus can present more aggressively. Compounding this challenge is the fact that up to a third of children with EH are superinfected simultaneously with *Staphylococcus aureus*, potentially confounding the clinical picture. Awareness of risk and common presentations, including the telltale "punched out" morphology, will increase the chances of prompt diagnosis and treatment. Dr. Hightower describes another distinctive presentation of *S. aureus* that preferentially affects infants and younger children regardless of eczema history. Staphylococcal scalded skin syndrome is a toxin-mediated process that can progress rapidly and, particularly because of the young age of affected patients, should be diagnosed and treated quickly.

Continued from previous page

It's half of the dose of rheumatoid arthritis, which is 5 mg b.i.d. You can actually start to see repigmentation as soon as 2 months, and then improvement up to 5 months."

The drug requires laboratory monitoring and is expensive, he said, and JAK inhibitor side effects must be discussed with all patients.

Topical JAK inhibitors – tofacitinib 2% cream and ruxolitinib 1.5% cream – are also being evaluated as treatment for vitiligo. "I find that ruxolitinib works a little bit better," said Dr. Desai, who gets these drugs compounded for topical use. He added that he prefers to combine JAK inhibitors with phototherapy when possible.

For resistant vitiligo, he said, "lasers can help, especially Q-switched ruby and Q-switched Alexandrite laser."

Dr. Desai disclosed performing clinical trials and/or consulting for numerous companies, including Pfizer, Allergan, AbbVie, and Dr. Reddy's, among others. MedscapeLive and this news organization are owned by the same parent company.

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†IQVIA, ProVoice Survey, Q1 2018-Q4 2020.

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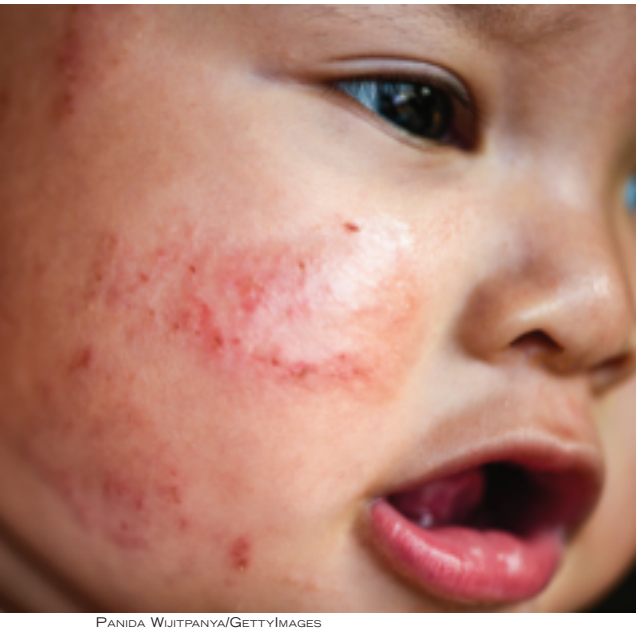
#1 DERMATOLOGIST RECOMMENDED SKINCARE BRAND†

Database offers snapshot of common causes of pediatric allergic contact dermatitis

BY DOUG BRUNK
FROM SPD 2020

The top three contact allergens in patients younger than 18 years of age are hydroperoxides of linalool, nickel sulfate, and methylisothiazolinone, according to an analysis of data from the Pediatric Allergic Contact Dermatitis Registry.



Panida Wijitpanya/GettyImages

The registry is the first multicenter prospective database in the United States with a focus on pediatric allergic contact dermatitis. JiaDe (Jeff) Yu, MD, a dermatologist at Massachusetts General Hospital, Boston, was awarded a Dermatology Foundation Career Development Grant and formed the registry in 2018, Idy Tam, MS, said during the virtual annual meeting of the Society for Pediatric Dermatology. "There is currently limited data regarding the pediatric allergic contact dermatitis in the U.S., despite as many as 20% of children having allergic contact dermatitis."

To date, the Pediatric Allergic Contact Dermatitis Registry consists of 10 academic medical centers with high-volume pediatric patch testing across the United States: Massachusetts General Hospital, Boston; Brigham and Women's Hospital, Boston; the University of Missouri–Columbia; Stanford (Calif.) University; the Medical University of South Carolina, Charleston; Texas Children's Hospital, Houston; Northwestern University, Chicago; Emory University, Atlanta; Washington University, St. Louis; and the University of California, San Diego.

For the current analysis, Ms. Tam, a research fellow in the department of dermatology at Massachusetts General Hospital and a fourth-year medical student at Tufts University, Boston, and colleagues collected data on 218 patients under age 18 who were referred for an evaluation of allergic contact dermatitis at 1 of the 10 participating sites between January 2016 and June 2020.

The mean age of children at the time of their patch testing was 10 years, 62% were girls, and 66% had a history of atopic dermatitis (AD). Most (75%) were White, 14% were Black, 6% were Asian, the rest were from other racial backgrounds. The distribution of dermatitis varied; the top five most commonly affected sites were the face (62%), arms (35%), legs (29%), hands (27%), and neck (20%).

Ms. Tam reported that the mean number of allergens patch tested per child was 78. In all, 81% of children had one or more positive patch test reactions, with a similar rate among those with and without a history of AD (80% vs. 82%, respectively; $P = .21$). The five most common allergens were hydroperoxides of linalool (22%), nickel sulfate (19%), methylisothiazolinone (17%), cobalt chloride (13%), and fragrance mix I (12%).

The top two treatments at the time of patch testing were a topical corticosteroid (78%) and a topical calcineurin inhibitor (26%).

The work was recognized as one of the top poster abstracts at the meeting. The researchers reported having no relevant disclosures.

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Commentary by Dr. Sidbury

"Allergy testing," to most parents and many providers, means either blood-based radioallergosorbent testing or skin-prick testing. These important modalities help identify type I IgE-mediated hypersensitivity such as milk or dust mite allergy. Conversely, allergic contact dermatitis (ACD) – the classic example being poison ivy – is diagnosed by patch testing. ACD is more prevalent in adults; however, up to 20% of children may have a contact sensitivity, perhaps an even greater percentage of patients with concomitant atopic dermatitis (AD). It can be challenging to diagnose ACD in the context of AD, as the rashes are clinically similar and the histopathology identical. Moreover, the allergen in question may be in a product used to treat the AD, further confounding matters. Patch testing can therefore be an invaluable diagnostic aid. These investigators report on a pediatric ACD database that includes 218 participants under the age of 18 years. Eighty-one percent of children had at least one positive patch test reaction. More than 60% had AD, and the head or neck was involved in the vast majority (81%). These data can help pediatricians assess which patients might most benefit from referral for patch testing.

FDA approves topical antiandrogen for acne

BY HEIDI SPLETE

The Food and Drug Administration has approved clascoterone 1% cream for the topical therapy of acne, providing a treatment with a novel mechanism of action for acne.

Clascoterone is a topical androgen receptor inhibitor indicated for treatment of acne vulgaris in patients aged 12 years and older, according to the labeling from manufacturer Cassiopea. Clascoterone, which will be marketed as Winlevi, targets the androgen hormones that contribute to acne by inhibiting serum production and inflammation, according to a company press release.

"Although clascoterone's exact mechanism of action is unknown, laboratory studies suggest clascoterone competes with androgens, specifically dihydrotestosterone, for binding to the androgen receptors within the sebaceous gland and hair follicles," according to the release.

Approval was based in part on a pair of phase 3, double-blind, vehicle-controlled, 12-week, randomized trials including 1,440 patients aged 9 years and older with moderate to severe facial acne. The findings were published on April 22, 2020, in JAMA Dermatology (156[6]:1-10).

Participants were randomized to twice-daily application of clascoterone or a control vehicle; treatment success was defined as having an Investigator's Global Assessment score of 0 (clear) or 1 (almost clear), as well as at least a 2-grade improvement from baseline, and absolute change in noninflammatory and inflammatory lesion counts at week 12.

At 12 weeks, treatment success rates were 18.4% and 20.3% among those on clascoterone, compared with 9% and 6.5%, respectively, among controls. There were also significant reductions in noninflammatory and inflammatory lesions from baseline at 12 weeks, compared with controls.

BOY_ANUPONG/GETTYIMAGES

In the studies, treatment was well tolerated, with a safety profile similar to safety in controls. Adverse events thought to be related to clascoterone in the studies (a total of 13) included application-site pain; erythema; oropharyngeal pain; hypersensitivity, dryness, or hypertrichosis at the application site; eye irritation; headache; and hair color changes.

"Clascoterone targets androgen receptors at the site of application and is quickly metabolized to an inactive form, thus limiting systemic activity," the authors of the study wrote.

Clascoterone is expected to be available in the United States early this year, according to the manufacturer.

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Commentary by Dr. Sidbury

Over the course of my career, acne therapeutics have been much like the nightly weather report in my hometown of Seattle: predictable. While I can expect a forecast of rain tomorrow, I can just as easily predict the next "new" acne topical agent will contain either a benzoyl peroxide, a retinoid, or an antibiotic, if not all of the above. Rinse. Repeat. Clascoterone 1% cream therefore is something of a ray of sunshine. A topical antiandrogen, clascoterone cream competitively inhibits androgen binding on hair follicles, thereby decreasing sebum production. Though the mechanism is different, the result of decreased sebum production is one of the primary reasons isotretinoin (Accutane) is so efficacious. Clascoterone is not a "topical Accutane," but its novel mechanism of action and impressive safety and efficacy results in this phase 3 trial could portend sunny days ahead for kids with acne.

Who's at risk for depression on isotretinoin?

MOTORTION/GETTYIMAGES

BY BRUCE JANCIN

FROM THE EADV CONGRESS

A history of prior depressive illness conferred a sevenfold increased risk of developing treatment-limiting mood symptoms in patients on isotretinoin for acne in a large Scottish observational study, Sanaa Butt, MD, reported at the virtual annual congress of the European Academy of Dermatology and Venereology.

This was, however, the sole identifiable risk factor for treatment-limiting depressive symptoms in acne patients on isotretinoin in the study of 3,151 consecutive acne patients taking isotretinoin. There was no significant difference between those who did or did not develop depression on the oral retinoid in terms of age, gender, or daily dose of the drug at the time it was discontinued.

"Depressive symptoms occurred at any time from the date of initiation of isotretinoin up to 6 months into therapy, with no identifiable peak time period," said Dr. Butt, a dermatologist with the U.K. National Health Service Tayside district at Ninewells Hospital, Dundee, Scotland. "Lower doses appear not to be protective," she added.

The Tayside district has a catchment of roughly 450,000 people. The local population tends to stay put because Tayside is an economically disadvantaged and remote part of Scotland. There are very few private practice dermatologists in the area, so Dr. Butt and coinvestigators are confident their observational study of NHS patients captured the great majority of isotretinoin users in northern Scotland.

The investigators utilized software to analyze the contents of more than 8,000 digitized letters exchanged between NHS Tayside dermatologists and general practitioners during 2005-2018, zeroing in on 3,151 consecutive patients on isotretinoin for acne and 158 on the drug for other conditions, most often rosacea or folliculitis. They then drilled down further through the letters, electronically searching for key words such as suicide, depression, and anxiety. In this way, they ultimately identified 30 patients who discontinued the drug because they developed depressive symptoms. All 30 were on the drug for acne.

The annual incidence of treatment-limiting depressive mood changes was 0.96%, a figure that remained steady over the 13-year study period, even though prescribing of isotretinoin increased over time. This flat incidence rate effectively rules out the potential for confounding because of assessor bias, especially since many different NHS dermatologists were prescribing the drug, Dr. Butt said.

The patients were equally split between males and females. And 15 cases of treatment discontinuation caused by development of depressive symptoms occurred in females, 15 in males. A history of past depressive illness was present in 9.3% of females who started on isotretinoin and in 4.5% of the males. The relative risk of treatment-limiting depressive mood changes was increased 790% among females with a prior history of depressive illness and 440% in males with such a history.

Dr. Butt reported having no financial conflicts regarding her NHS-funded study.

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Commentary by Dr. Eichenfield

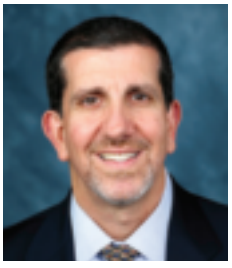
The association of the use of isotretinoin with depression and suicide has created concerns for decades, with an uncertain relationship. Meta-analyses and systematic reviews have concluded there are inadequate data to establish a causal relationship, while it is clear that depression is higher in patients with acne than in the general population without acne, independent of isotretinoin use. However, we consider the possible relationship is real, and prescribing labels for isotretinoin list warnings of potential depression, psychosis, suicidal thoughts and behavior, and aggressive and/or violent behavior. The large observational study presented by Dr. Butt at the EADV meeting is very helpful, finding strong evidence that the history of prior depressive illness was a strong risk predictor (seven times) for mood symptoms requiring discontinuation of isotretinoin treatment. Along with a consistent rate over 13 years of 0.96% annual incidence of depression requiring discontinuation of treatment, the study makes us more comfortable that keeping those patients with a history of past depressive illness under more careful watch is a reasonable strategy. Our policy at Rady Children's Hospital–San Diego is that those with a history of depression have to be cleared by their mental health professional to be stable enough to enter into a course of isotretinoin. We also screen teens for depression at each monthly visit, which helps us feel more comfortable that we are following our patient's mental state.

Expert shares his approach to treating warts in children

BY DOUG BRUNK
FROM PEDIATRIC DERMATOLOGY 2020

In the clinical experience of Anthony J. Mancini, MD, one option for children and adolescents who present with common warts is to do nothing, since they may resolve on their own.

"Many effective treatments that we have are painful and poorly tolerated, especially in younger children," Dr. Mancini, professor of pediatrics and dermatology at Northwestern University, Chicago, said during the virtual Pediatric Dermatology 2020: Best Practices and Innovations Conference. "However, while they're harmless and often self-limited, warts often form a social stigma, and parents often desire therapy."


Dr. Mancini

He characterized classic warts as verrucous, flesh-colored papules that are sometimes extensive in immunocompromised patients and that can be associated with maceration and nail dystrophy. Even though warts may spontaneously resolve in up to 65% of patients at 2 years and 80% at 4 years, the goals of treatment are to eradicate them, minimize pain, avoid scarring, and help prevent recurrence.

One effective topical therapy he highlighted is WartPEEL cream, which is a proprietary, compounded formulation of 17% salicylic acid and 2% 5-fluorouracil. "It's in a sustained-release vehicle called Remedium, and is available from a compounding pharmacy, but not FDA approved," said Dr. Mancini, who is also head of pediatric dermatology at Lurie Children's Hospital of Chicago. "It's applied nightly with plastic tape occlusion and rinsed off each morning."

"It is very effective, tends to be totally painless, and has a much quicker response than over-the-counter salicylic acid–based treatments for warts," he said.

Another treatment option is oral cimetidine, especially in patients who have multiple or recalcitrant warts. The recommended dosing is 30-40 mg/kg per day, divided into twice-daily dosing. "You have to give it for at least 8-12 weeks to determine whether it's working or not," Dr. Mancini said. "In the initial report, [investigators] described an 81% complete response rate, but subsequent randomized, controlled trials were not able to confirm that data against placebo or topical treatments."

For flat warts, verrucous papules that commonly occur on the face, Dr. Mancini recommends off-label treatment with 5% 5-fluorouracil cream (Efudex), which is normally indicated for actinic keratoses in adults. "I have patients apply this for 3 nights per week and work their way up gradually to nightly application," he said. "It's really important that parents and patients understand the importance of sun protection when they're using Efudex, and they need to know that some irritation is possible."

Other treatment options for common warts, in addition to over-the-counter products that contain salicylic acid, are home cryotherapy kits that contain a mixture of diethyl ether and propane. "These can be effective for small warts," Dr. Mancini said.

Treatment options best reserved for dermatologists, he continued, include in-office liquid nitrogen cryotherapy, "if it's tolerated," he said. He also mentioned topical immunotherapy with agents like squaric acid dibutylester. "This is almost like putting poison ivy on your warts to get the immune system revved up," he said. "It can be very effective." Other treatment options include intralesional immune therapy, topical cidofovir, and even pulsed-dye laser.

Dr. Mancini disclosed that he is a consultant to and a member of the scientific advisory board for Verrica Pharmaceuticals.

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Commentary by Dr. Sidbury

It is telling that, at a conference titled "Best Practices and Innovations in Therapy," one of the wart treatments prominently mentioned was no treatment at all. Dr. Mancini, the presenter, was one of my fellowship mentors 20 years ago, and none of the therapies he outlines are fundamentally different from those he taught me to consider way back when. Wart therapy falls into one of two buckets: First, locally destructive techniques employed through physical (for instance, liquid nitrogen) or chemical (salicylic acid, 5-flurouracil, among others) means; and second, immune-based therapies (for instance, cimetidine, squaric acid) that encourage host defenses to recognize and eradicate the causal human papilloma virus. The key to wart therapy is matching the therapy to the patient. In a younger child completely unbothered by warts, often the best intervention is no treatment at all. Parents, typically far more motivated to treat than their afflicted children, must know that nearly all warts spontaneously resolve in healthy kids, so not treating is not the same as doing nothing. In older children who are directly affected by their warts, because of pain, embarrassment, or social stigmatization, the full range of treatment options should be discussed.

Merino wool clothing tied to improved atopic dermatitis, study finds

BY BRUCE JANCIN

FROM MEDSCAPELIVE LAS VEGAS DERMATOLOGY SEMINAR

Conventional wisdom holds that patients with atopic dermatitis (AD) should shun wool clothing in favor of cotton or silk, because wool is said to be irritating and promote itching. Not so when the garments are made of fine-diameter fibers of merino wool, Joseph F. Fowler, Jr., MD, a dermatologist at the University of Louisville (Ky) said at MedscapeLive's annual Las Vegas Dermatology Seminar, held virtually last year.

He was first author of a randomized, 12-week, crossover, assessor-blinded clinical trial which showed precisely that.The study by Dr. Fowler and coinvestigators included 50 children and adults with mild or moderate AD who either wore top-and-bottom base layer merino wool ensembles for 6 weeks and then switched to their regular nonwoolen clothing, or vice versa. The mean Eczema Area and Severity Index (EASI) score in those initially randomized to merino wool improved from a mean baseline of 4.5 to 1.7 at week 6, a significantly greater improvement than in the group wearing their regular clothing. Similarly, those who switched to merino wool after 6 weeks experienced a significant decrease in EASI scores from that point on to week 12, while those who switched from merino wool to their regular clothing did not.

Mean Dermatology Life Quality Index (DLQI) scores in patients who wore merino wool first improved from 6.9 at baseline to 3.4 at week 6. Those who wore their regular clothing first went from a mean baseline DLQI of 6.7 to 6.2 at week 6 – a nonsignificant change – but then improved to a week 12 mean DLQI of 3.7 while wearing wool. There was no improvement in DLQI scores while participants were wearing their regular clothing.

Static Investigator's Global Assessment scores showed significantly greater improvement while patients wore merino wool garments than their regular clothing (Dermatitis. 2019 May/Jun;30[3]:198-206).

The Australian study included 39 patients with mild to moderate AD aged between 4 weeks and 3 years. This, too, was a 12-week, randomized, crossover, assessor-blinded clinical trial. Participating children wore merino wool for 6 weeks and cotton ensembles chosen by their parents for an equal time. The primary endpoint was change in the SCORing Atopic Dermatitis (SCORAD) index after each 6-week period. The mean 7.6-point greater SCORAD reduction at 6 weeks while wearing merino wool, compared with cotton, was "a pretty impressive reduction," Dr. Fowler observed.

Reductions in the secondary endpoints of Atopic Dermatitis Severity Index and Infants' Dermatitis Quality of Life Index while wearing merino wool followed suit. In contrast, switching from wool to cotton resulted in an increase in both scores. Also, use of topical corticosteroids was significantly reduced while patients wore merino wool (Br J Dermatol. 2017 Jul;177[1]:125-33). Wool harvested from merino sheep is characterized by fine-diameter fibers. In Dr. Fowler's study the mean fiber diameter was 17.5 mcm. This makes for a soft fabric with outstanding moisture absorbance capacity, a quality that's beneficial in patients with AD, since their lesional skin loses the ability to regulate moisture, the dermatologist explained.

> Those who switched to merino wool after 6 weeks experienced a significant decrease in EASI scores from that point on to week 12.

Both randomized trials were funded by Australian Wool Innovation and the Australian government.

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Commentary by Dr. Eichenfield

Atopic dermatitis patients have a mixture of skin barrier disruption and a dysregulated immune response, with pruritus as a significant driver of disease. Traditionally, recommendations have been that wool clothing should be avoided, with smooth cotton and silk clothing used, to minimize irritation and itch. But new data on merino wool clothing from two crossover studies, one from the United States (Kentucky) and one from Australia, showed improvement in objective AD scores with the use of the clothing in patients with moderate to severe AD, along with reductions in use of topical corticosteroids. Dr. Fowler explained that merino wool is very soft and "breathable," allowing natural temperature regulation and has an excellent ability to absorb moisture. While these studies were funded by agencies with a desire to show the utility of their clothing (Australian Wool Innovation and the Australian government), the results were consistent and impressive.

Preadolescent acne: Management from birth requires increasing vigilance

BY RANDY DOTINGA

FROM MEDSCAPELIVE WOMEN'S & PEDIATRIC DERMATOLOGY SEMINAR

Treat acne from near birth to adulthood with a growing level of aggressiveness as a child ages, a dermatologist urged colleagues.

Dr. Zaenglein

No treatment may be necessary for acne in the first few months of life, but the condition can leave scars in children as young as ages 3-6 months, said Andrea L. Zaenglein, MD, professor of dermatology and pediatric dermatology, Penn State University, Hershey, said in a presentation at MedscapeLive's virtual Women's & Pediatric Dermatology Seminar.

Neonatal acne occurs in more than 20% of newborns aged 2 weeks to 3 months. "Typically we don't need to treat it. But if you do, you could use a topical antifungal like clotrimazole cream twice a day."

Infantile acne begins about 3-6 months of age typically, or a little bit older, and lasts up to 2 years of age, Dr. Zaenglein said. "You will see comedones in infantile acne, so this is actually a true form of acne. It's due to increased adrenal production of androgens."

She added: "The scarring can be permanent. It's important that you recognize infantile acne and treat it, even though it seems pretty mild."

For infantile acne, she recommends performing a full-skin exam to rule out hyperandrogenic disorders such as Cushing syndrome, congenital adrenal hyperplasia, premature adrenarche, a gonadal/adrenal tumor and precocious puberty.

Treatments are similar to those in teenagers, she said, "but make sure you use baby-friendly formulations," with lower concentrations of active ingredients – and avoid tetracyclines and benzoyl peroxide (BPO) washes. BPO can be used in leave-on formulations/creams at lower strengths (2.5%-5%).

One possible combination option is tretinoin 0.025% cream or adapalene 0.1% gel plus BPO 2.5% cream or clindamycin/BPO gel. Another combination is adapalene/BPO 2.5% gel.

Erythromycin can be appropriate at 30-50 mg/kg per day divided in two or three doses a day, but beware of possible gastrointestinal upset. Azithromycin at 5 mg/kg per day is another option.

"Rarely do we have to go to isotretinoin," Dr. Zaenglein said. "I think in all my years, I've only treated one baby with isotretinoin for infantile acne. But severe forms can occur."

Midchildhood and preadolescent acne conditions occur in children starting at ages 1 up to 10 years, she said. In this population, she also recommends ruling out hyperandrogenism by looking for secondary sexual characteristics with full-body skin exams. "The workup can be broad and includes looking at adrenal androgens and total and free testosterone, as well as looking at growth charts and bone age. Typically, you'll refer these kids to pediatric endocrinology."

Keep in mind, she said, that early adrenarche starts at ages 6-7 years in girls and 7-8 years in boys. "That's when we expect to start seeing that very early acne. You can see it even earlier in patients with elevated BMI, and it's more common in Hispanic and Black children as well."

She added that it's important to remember that early adrenarche is a risk factor for polycystic ovarian syndrome (PCOS). "So ask patients about their family history and look for other signs of PCOS as they move further into adolescence."

Milder cases of acne in this age group can be treated with "salicylic acid wipes and things that are kind of a rite of passage. But if they have any more severe acne, you're going to want to treat it more or less like you do adolescent acne."

MedscapeLive and this news organization are owned by the same parent company. Dr. Zaenglein disclosed receiving consulting fees from Cassiopea, Dermata, and Regeneron and fees for contracted research support from Incyte.

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Commentary by Dr. Eichenfield

While acne is most prevalent in teens, the presentation by Dr. Zaenglein, renowned pediatric dermatologist, "acneologist," and coeditor-in-chief of the journal Pediatric Dermatology, reminds about acne across the pediatric age spectrum, starting near birth. She points out that the earliest "acne" in infants probably isn't true acne vulgaris; we know the superficial pustules called neonatal acne are usually a condition termed neonatal cephalic pustulosis, which is self-limited and quite responsive to topical antifungal agents. Infantile acne, starting later, can be tremendously variable in severity, in some cases causing permanent scarring. Next up is midchildhood acne, occurring before early adrenarche, and of concern because of possible pathologic causes; this usually requires a workup, as mentioned by Dr. Zaenglein. Preadolescent acne at 7 years plus is often normal physiologic adrenarche and can be treated effectively in a similar way to adolescents but being conscious that many cases will be mild. Reassurance or suggestions on over-the-counter therapies would be a reasonable therapeutic approach.

More severe AD correlates with worse sleep health and attention problems in children

BY DOUG BRUNK
FROM REVOLUTIONIZING AD 2020

Poor sleep health and attention regulation problems are common in young children with atopic dermatitis (AD), and the burden intensifies with worse severity, results from a national survey demonstrated.

"We think it's important for dermatologists and pediatricians to be monitoring children with AD for sleep and attention dysregulation," Nina Y. Zhou said during a late-breaking research session at the Revolutionizing Atopic Dermatitis virtual symposium. "It's also important to highlight sleep hygiene habits to improve sleep health overall."

In an effort to determine the impact of AD severity on these symptoms in young children with AD and characterize sleep health and attention regulation behaviors, Ms. Zhou, a medical student at Northwestern University, Chicago, and colleagues drew from a national survey distributed via panel company OP4G and the National Eczema Association that was conducted with parents of 60 children with AD aged 1-5 years.

Questionnaires included the Patient Reported Outcomes Measurement Information System (PROMIS) Early Childhood Sleep Health Measures to assess sleep health, the Peak Pruritus NRS to measure itch severity, and the Multidimensional Assessment Profile of Attention Regulation (MAPS-AR) to measure attention dysregulation related to inattention and hyperactivity. The researchers performed linear regression to determine the predictors of sleep health and attention dysregulation.

The mean age of the 60 children was 3 years, 55% were male, 32% were black, 42% had severe disease, 42% had moderate disease, and 16% had mild disease. Children with more severe AD were significantly more likely to report worse sleep disturbance. The proportion of children who reported sleep disturbance on at least 5 nights per week was 67% among those with severe AD, 24% among those with moderate AD, and 0% among those with mild AD.

In addition, 72% of parents of children with severe AD reported they had trouble paying attention at least 3 times per week "no matter what was going on," compared with 24% of those with moderate AD and none of those with mild AD.

Parents of children with more severe AD reported more itch-related burden and significantly decreased quality of life for their children. For example, 76% of parents with children who had severe AD reported "because of itch, their child was frustrated," compared with 44% of those with moderate AD and 10% with mild AD.

In fully adjusted linear regression analysis, the strongest predictors of sleep disturbance were AD severity (unstandardized beta-value = 0.79, *P* less than .01) and being Black (unstandardized beta-value = 3.89, *P* = .03). AD severity (unstandardized beta-value = 1.22, *P* less than .01) and being Black (unstandardized beta-value = 7.79, *P* less than .01) also predicted more attention dysregulation.

Parents of children with more severe AD reported more itch-related burden and significantly decreased quality of life for their children.

Household income appeared to differ significantly based on AD severity groups. "If you have mild AD, you are more likely to come from a higher income household," Ms. Zhou said.

She concluded her presentation by calling for future studies with larger samples sizes.

The study was funded by the Agency for Healthcare Research and Quality. Ms. Zhou reported having no financial disclosures.

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Commentary by Dr. Eichenfield

The impact of sleep disturbance on children with AD was really brought home in the study presented by Ms. Zhou, a national survey of 60 children 1-15 years of age. More extensive disease was correlated with worse sleep disturbance! And severe disturbance on at least 5 nights a week was reported by 67% of those with severe AD. Almost 75% of parents of children with severe AD reported their child having trouble paying attention at least three times a week (versus none with mild AD). Prior studies by Ramirez and colleagues have reported nearly 50% higher odds of sleep-quality disturbances with AD (versus not having AD), and cohort data from more than 11,500 mother-child pairs showed mothers of AD patients reporting problems falling asleep, having insufficient sleep, and experiencing daytime exhaustion through the first 11 years of childhood (JAMA Dermatol. 2019;155:556-63; JAMA Pediatr. 2019;173:e190025). The association of mental health effects with AD is clear, with higher rates of attention-deficit hyperactivity disorder, depression, and anxiety.

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