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University of Southern California

Marc D. Brown, M.D.  
Professor, Department of Dermatology  
Department of Dermatology  
University of Rochester

Kelly M. Cordoro, M.D.*  
Professor, Dermatology and Pediatrics  
Department of Dermatology,  
Division of Pediatric Dermatology  
University of California, San Francisco

Warren R. Heymann, M.D.  
Head, Division of Dermatology  
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Professor of Pediatrics  
Cooper Medical School of Rowan University  
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Heidi T. Jacobe, M.D., M.S.C.S.*  
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Department of Dermatology  
University of Texas Southwestern

Ginette A. Okoye, M.D.  
Professor and Chair of Dermatology  
Department of Dermatology  
Howard University

Laura B. Pincus, M.D.*  
Associate Professor of Dermatology and Pathology  
Department of Dermatology  
University of California, San Francisco

Brian S. Schwartz, M.D.  
Associate Professor, Medicine  
School of Medicine  
University of California, San Francisco

Jennifer A. Stein, M.D., Ph.D.  
Associate Professor  
Ronald O. Perelman Department of Dermatology  
NYU Langone Health

Rochelle R. Torgerson, M.D., Ph.D.  
Associate Professor of Dermatology  
Departments of Dermatology and Obstetrics & Gynecology  
Mayo Clinic (Rochester)

Hensin Tsao, M.D., Ph.D.*  
Professor, Dermatology  
Harvard Medical School  
Director, MGH Melanoma and Pigmented Lesion Center  
Department of Dermatology  
Massachusetts General Hospital  

Ruth Ann Vleugels, M.D., M.P.H.*  
Associate Professor of Dermatology  
Department of Dermatology  
Harvard Medical School  
Vice Chair for Academic Affairs,  
Department of Dermatology  
Director, Autoimmune Skin Diseases Program  
Director, Connective Tissue Disease Clinics  
Brigham and Women’s Hospital

PROGRAM CO-CHAIRS

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Associate Professor  
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*Former DF research award recipient.

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Dermatology Times has helped to document some of the specialty’s biggest breakthroughs in the last 40 years. We asked the very dermatologist experts who often help us to report on dermatology milestones to weigh in on what they think made the most difference in theirs and their patients’ lives. **ADVANCES CONTINUES ON PAGE 20**

**SKIN CANCER**

**Elderly patients with NMSC increase**

**MANAGEMENT** of non-melanoma skin cancer (NMSC) in the very elderly patient mandates an individualized approach that takes into account multiple factors relating to tumor and patient characteristics along with the risks and benefits of biopsy and treatment options. Providers should utilize techniques of shared decision making with very elderly patients and their caregivers to help them make informed decisions regarding their treatment options.

“According to statistics from the World Health Organization, there are about 125 million people in the world who are aged 80 years or older and the number will reach 434 million by the year 2050,” says Anne Lynn S. Chang, M.D., associate professor of dermatology, Stanford University School of Medicine, Stanford, Calif. “As the incidence rate of NMSCs is increasing, and because age is the strongest risk factor, dermatologists can expect...”

**ATOPIC DERMATITIS**

**Variability by age group**

Differences underlie pathology, indicating efficacy of treatments may vary

**INGRID TORJESEN | Staff Correspondent**

**NOT ONLY** is atopic dermatitis considerably more prevalent in children than adults (12% versus 7.2%), the prevalence of its particular phenotypes and subtypes can also vary markedly across different age groups. For example, in adults, the condition more frequently presents on the hands or feet.

“The key challenge for adult eczema is we often see less flexural disease and more of those other subsets,” says Jonathan Silverberg, associate professor and director of the Northwestern Medicine Multidisciplinary Eczema Center and of the Contact Dermatitis Clinic at Northwestern Memorial Hospital in Chicago. “Couple that with the fact that the differential diagnoses are much broader, and a couple of entities in the differential diagnoses are more common, and atopic dermatitis becomes a very challenging diagnosis.”

Other conditions, such as contact dermatitis, cutaneous T-cell lymphoma and cutaneous/syn...
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Provide practical analysis of recent studies, regulatory updates, techniques, devices & business solutions; and facilitate discussion to optimize practice and improve patient care.

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**Columns**

**Dr. Zoe Diana Draelos**
Dr. Draelos is a consulting professor of dermatology, Duke University School of Medicine, Durham, NC.

**Dr. Elaine Siegfried**
Dr. Siegfried is professor of pediatrics & dermatology, Saint Louis University Health Science Center, St. Louis, Mo.

**Dr. Norman Levine**
Dr. Levine is a private practitioner in Tucson, Ariz.

**Dr. Ronald G. Wheeland**
Dr. Wheeland is a private practitioner in Tucson, Ariz.

---

**Content**

**Vice President, Content & Strategy**
Daniel R. Verdon | dverdon@mmhgroup.com

**Content Channel Director**
Heather O’Toole | heather@mmhgroup.com | 440.836.2868

**Aesthetic Content Editor**
Eliza Cahanes | edcahanes@mmhgroup.com | 440.891.2671

**Associate Editor**
Jessica Barry | jberry@mmhgroup.com | 440.826.2923

**Design Director**
Robert McGarry

**Senior Graphic Designer**
Recia A. Lannidis

**Graphic Designer**
Kimberly Chiracu

**Senior Production Manager**
Karen Lenz | klenzen@mmhgroup.com | 218.740.6371

---

**Sales & Marketing**

**Executive Vice President**
Brian Hong | bhong@mmhgroup.com | 609.325.4780

**Group Publisher, Eye and Skin Care**
Leonardo Avila | laavila@mmhgroup.com | 302.239.5665

**Publisher**
Amy Ammon | aammon@mmhgroup.com | 732.346.3099

**National Sales Manager**
Don Bermann | dbloman@mmhgroup.com | 212.951.6745

**National Accounts Associate**
Bethany Zaccaria | bztaccari@mmhgroup.com | 732.216.4239

**Account Manager, Recruitment Advertising**
Jenina Shappell | jshappell@mmhgroup.com | 440.891.2615

**Permissions**
Megan Rockefeller | mrockefeller@mmhgroup.com

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877.922.2022 | 218.740.6477

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A glass-half-full view of prior authorizations

by ELAINE SIEGFRIED, M.D.

Dr. Siegfried is professor of pediatrics & dermatology, Saint Louis University Health Sciences Center, St. Louis, Mo.

The intended consequence of Prior Authorizations (PAs) is to minimize use of expensive, risky, and inappropriately prescribed medications. Some therapeutic categories have benefitted from this intervention, most notably inpatient antibiotic stewardship. But when broadly applied, most of the policies are about cost, masquerading as safety, resulting in delayed or restricted access to recommended medications, and no comparable alternatives.

The PA process has definitely compromised my ability to treat patients. PAs are now required for the majority of drugs I prescribe, using dumbed-down rationale, most often derived from FDA labelling and inconsistently applied.

Eldel, for example, is FDA-approved for children down to age 2, but access often requires a PA. On the other hand, betamethasone ointment labelling indicates use for only those over age 13, but is readily filled, without question, for infants. Access to newer drugs, like those for itch is denied for many patients. The intrusion of PAs on the physician-patient relationship has surpassed electronic medical records as the leading cause of physician dissatisfaction. A December 2018 American Medical Association survey completed by 1,000 physicians corroborated this impression. The great majority reported that the burden increased over the last five years to “high” or “extremely high,” and has negatively impacted patient outcomes.

Almost one third reported that associated delays lead to serious or life-threatening adverse events for patients. These physicians and their staff spent an average of two business days per week on PAs and over one third have staff members whose time is exclusively spent on this task.

My son was one of those staff members for two years when he worked in a general internist’s office. He was hired as a scribe, but took over PA responsibilities because medical training and experience were not required, and the task was so frustrating and time-consuming for the clinicians.

Delegating PAs to low-paid employees may be the path-of-least resistance, but it also enables perpetuation of this meaningless exercise. My son and my own staff have spent hours struggling with poorly designed platforms unable to access patient information, and waiting on-hold during phone calls to speak with equally untrained and inexperienced payor representatives. In the internist’s office, denials were common for life-saving drugs like insulin. In my office, PAs impact almost all prescriptions I write, from acne to severe inflammatory skin disease. In an attempt to understand and address this issue, we recently reviewed the reasons for our denials.

Age younger than that indicated on the drug label was the most common. Our attorney collaborators found a clause in the Affordable Care Act that bans treatment-related age discrimination, prompting the following statement in my appeal letters: “Restricting access to the medication on the basis of its FDA-approved indication does not excuse the fact that this practice constitutes illegal age discrimination in clear violation of section 1557 of the Affordable Care Act.”

Other reasons for denials applicable to patients seen in a general dermatology practice, is to enforce step-edit requirements or restrict a drug prescribed off-label. My appeal for these decisions includes: “Your attempt to enforce your general criteria without regard to the extenuating factors in this case is essentially the practice of medicine by an organization, which is illegal in several states.”

I also frequently request a peer-to-peer review and inform the reviewer that their name and credentials will be documented in the medical record. Although involving the patient in the PA process is a good idea in theory, neither my office, nor my son’s employer routinely does this, because health literacy in the general population does not support the success of that strategy.

The evolving practice of medicine has always faced obstacles. In the 1980s, dissatisfaction stemmed from the new gatekeeper-controlled, managed care model. Computers were changing the acquisition of information and the physician-dominant power structure was beginning to falter. These menaces have been replaced by electronic data entry, PAs and the consolidation and corporatization of medicine. But medicine remains a great career with relative autonomy, respectable peers and a focus on service to others.

The practice of medicine will continue to evolve, and, hopefully, improve with intelligent voice recognition software that will be able to record beyond verbatim, actually taking notes and learning along the way. One day we will have a system that incentivizes prevention, rewards efficiency and measures true long-term health outcomes.

I strive for a glass-half-full world view and try to make lemonade from bitter lemons. So it occurred to me that a benefit of the PA process is to provide opportunity for experience and a path to medical school for a growing army of medical scribes, including my son, who was not dissuaded by the work. As a first year of medical student, he is looking forward to a rewarding career.

Reference
FIVE DECADES OF ADVANCES
Therapeutic developments have spanned acne, infantile hemangioma, psoriasis and more.

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Am I liable if the patient wasn’t mine?

by DAVID J. GOLDBERG, M.D., J.D.

Dr. Goldberg is director of Skin Laser and Surgery Specialists of New York and New Jersey, past director of Mohs and Laser Research, Icahn School of Medicine at Mt. Sinai; and, adjunct professor of law, Fordham Law School in New York City.

Dr. Wrong has recently been sued in a most disturbing case. Three years ago, an independent nurse practitioner (NP) he supervises by employment contract, saw a young woman with a pigmented lesion, took a photo of it, and showed it to Dr. Wrong. He saw nothing atypical and conveyed this to the nurse practitioner. Unfortunately, the patient died two years later from metastatic melanoma. The estate ultimately sued both the NP and the dermatologist. He does not understand. He tells his lawyer that since he never saw the patient, he never established a patient-physician relationship; therefore, should have no liability. Is he right?

A recently decided case in Minnesota, Warren v. Dinter took a good look at this situation. This case analyzed the essential law underpinning a medical negligence claim – that a doctor-patient relationship must exist for a plaintiff to prevail. Generally, a physician owes no duty to a patient without a physician-patient relationship. Without a physician-patient relationship, with no duty owed, there is no liability for “breach” of that nonexistent duty. In what seemed to be a similar case to that of Dr. Wrong, the physician was found to have liability. Should we now be concerned that a physician can be held liable for malpractice even if there is no physician-patient relationship at all?

Dinter is a case that shows just how important it is to know how that relationship can still form when you never see the patient.

In this case, a patient saw a nurse practitioner for abdominal pain, fever and chills. The NP found that the patient had a high white count and so suspected an infection. The patient also had an elevated blood glucose. The NP tried to get the patient admitted to the hospital, a process which required vetting the case with a hospitalist. The hospitalist attributed the patient’s symptoms to diabetes and refused hospitalization. The patient subsequently died from sepsis caused by an untreated staph infection. Her family sued both the nurse practitioner and the physician for medical malpractice.

The hospitalist sought to be released from the case and a lower court granted it. In this case, although the hospitalist blocked the admission, the lower court nevertheless considered that he was only giving his “thoughts,” treating his interaction with the NP as an informal curbside consult provided as an act of professional courtesy.

It was therefore determined that no physician-patient relationship existed, and no duty of care accrued. Accordingly, the case could not be maintained against the hospitalist.

The appellate court reversed this decision. It said “Most medical malpractice cases involve an express physician-patient relationship. And a physician-patient relationship is a necessary element of malpractice claims in many states. But we have never held that such a relationship is necessary to maintain a malpractice action under Minnesota law. To the contrary: when there is no express physician-patient relationship, we have turned to the traditional inquiry of whether a tort duty has been created by foreseeability of harm.”

The key word here is “express.” It is not that there was no relationship – there was not an express relationship created by a direct agreement between the doctor and the patient; however, the relationship could still be found in an implied fashion.

In this case the patient was reliant on the hospitalist’s decision. A failure by the hospitalist to adhere to the standard of care in carrying out his assessment inevitably harmed the patient. The court said the “decision today should not be misinterpreted as being about informal advice from one medical professional to another. This case is about a formal medical decision.”

Dr. Wrong had a contractual agreement with his NP. Although he never actually saw the deceased patient, he may be found to have liability because of his relationship with the NP.
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“Now is the time to work together to increase clinician engagement in problem-based research and innovation.”

Creative initiative involves clinicians

by LILIT GARIBYAN, M.D., PH.D., FAAD, STEVE XU, M.D., FAAD, AND KACHIU C. LEE, M.D., FAAD

Sometimes innovation feels like a process limited to scientists, engineers or investors. The regular clinician can sometimes feel out of place or out of depth. This should absolutely not be the case. Clinicians are central to innovation – essential in fact.

We have already argued before the need to define great problems as the first step towards meaningful innovation.1 Clinicians are the ones who both deeply understand the problem but also the end users of new innovations. In this issue, we want to highlight clinicians again and the role they play in innovation. Specifically, I am excited to present a great, grassroots initiative to get clinicians more involved in innovation in dermatology.

Focus on the Magic Wand Initiative

The Magic Wand Initiative (MWI) is a creative educational and interactive program designed by-clinicians-for-clinicians to empower physicians to identify and solve unmet patient needs and teach them the process of innovation.2 The MWI cultivates patient-centered innovation where clinicians identify problems worth solving, practice divergent and convergent brainstorming, collaborate with stakeholders, prototype, and possibly commercialize solutions. Throughout this journey of innovation, learners have the opportunity to partner with other expert clinicians and non-physicians (i.e. scientists and engineers) to select which

FOR THOSE INTERESTED IN LEARNING MORE ABOUT THIS PROGRAM Please visit: www.magicwandinitiative.org/togetinvolved
patient problems are worth solving and what solutions are worthy of further development and testing.

This initiative was pioneered, designed and launched by R. Rox Anderson, M.D., and Lilit Garibyan, M.D., Ph.D., at Wellman Center for Photomedicine and Massachusetts General Hospital Department of Dermatology in 2013. The goal and mission were to increase clinician involvement in problem-based research and innovation. Through education and empowerment, clinical dermatologists were the best positioned to identify important unmet medical needs and form teams to solve them (Figure 1).

We partnered with a nonprofit, Advancing Innovation in Dermatology (AID), to provide the education, support and tools needed to solve the identified problems. Since that time, the pilot program has achieved concrete measurable success, affirming that clinicians are empowered to identify and solve existing problems, new and innovative solutions can be brought to the patients. The success has been measured with increased number of publications, awarded grant funding, patient, successful prototype devices and potentially reduced burnout in physicians involved.

Clinician involvement in biomedical innovation is crucial for identifying and solving medical unmet needs and for bringing novel therapies to patients. Physicians are primed to play a pivotal role in innovation because they experience the real-world frustrations experienced in daily practice. Furthermore, their solutions are more likely to directly improve the delivery of healthcare and/or patients' quality of life. These same physicians are end-users of any solution or product created and thus best understand the practical considerations and applicability of the product in daily practice.

The Magic Wand Initiative is not just for academic medical centers like the Massachusetts General Hospital. Clinicians can get involved virtually via a new initiative. The “Virtual Magic Wand” program is a virtual platform program aimed to help early-career clinicians from across the country to deeply understand and define a dermatologic clinical problem worth solving. The goal of the program is to educate and empower residents and early career clinicians to become the next generation of innovators in dermatology.

It is designed as a 10-month-long interactive and versatile course with monthly teleconferences. Each teleconference helps scholars narrow down their problem-worth solving, with several sessions devoted to bringing clinical and industry experts to provide input on the feasibility of the problem posed by the scholars.

At the completion of the program the participants submit a white paper that thoroughly describes a specific clinical problem in dermatology that they have identified and deeply defined. Scholars are also invited to present their findings at the Dermatology Innovation Forum, held prior to the American Academy of Dermatology Annual Meeting each year. This Forum provides a unique opportunity for young innovators to network and find partners within industry to further develop their problem worth solving and associated solutions.

In conclusion, we are calling for more clinicians, universities and industry partners to get involved in innovation. Now is the time to work together to increase clinician engagement and problem-based research and innovation. We need to empower our clinicians to adopt the creative and iterative thinking processes of innovation, and provide them with the tools, and training needed to solve unmet needs. The Magic Wand team is working hard on expanding the program to other sites.

References
Topical options expand

Physicians gain tools to treat inflammatory dermatoses

JOHN JESITUS | Staff Correspondent

Promising topical agents for psoriasis and/or atopic dermatitis (AD) that are commercially available or in late-stage development include tapinarof, JAK inhibitors, phosphodiesterase (PDE) inhibitors and combination products with novel patient-friendly vehicles.

In dealing with inflammatory dermatoses, says George Han, M.D., Ph.D., a patient’s desire for nonsteroidal topical treatments fits into an overall trend toward products perceived as natural. He is an assistant professor of dermatology at the Icahn School of Medicine at Mount Sinai in New York.

However, he noted, patients should beware of Internet “miracle” products. When a colleague had a purported herbal cream brought in by a patient analyzed, its main ingredient was clobetasol.

Fortunately, says Dr. Han, an increasing number of nonsteroidal treatments for psoriasis and AD are becoming available. For starters, he says, many dermatologists are excited about tapinarof.

“Technically it is a natural product, which may satisfy picky patients who only want natural remedies,” he says.

Tapinarof is a small molecule produced by bacteria that live off of nematodes.

MULTIFACETED MECHANISMS

In AD, which is expected to be tapinarof’s first indication, the drug has posted efficacy numbers more impressive than those of the PDE4 inhibitor crisaborole.

“One of the knocks on crisaborole is that while it has a useful place in our non-steroidal armamentarium, the separation between the medication and the vehicle isn’t that great, whereas with tapinarof you’re seeing a much larger delta between the active ingredient and the placebo control vehicle.”

In an early eczema trial, tapinarof achieved investigator global assessment (IGA) reductions of 43% and 56% in treated patients vs. 15% for placebo.1

In phase 2 psoriasis trials, 53% of tapinarof-treated patients achieved IGA 0/1 (with a two-point improvement from baseline) at week 12, versus 24% for placebo.2 Treatment-emergent adverse events affected 56% of the tapinarof group, versus 41% for placebo. Most adverse events were mild.

“Those are the best numbers we’ve seen for any nonsteroidal treatment so far,” says Dr. Han.

Assuming tapinarof earns FDA approval, he says, it will bring the first truly novel mechanism to the eczema and psoriasis markets in quite some time.

LP0133/JTE-052 inhibits JAK 1-3 and tyrosine kinase (Tyk) 2. In a phase 2 AD trial, various concentrations yielded modified eczema area and severity index (mEASI) reductions between 41.7% and 72.9%, vs. 12.2% for placebo (P < 0.001 for all analyses).3

“Topical JAK inhibitors are going to be interesting because not only are we looking for efficacy in eczema and psoriasis, but those drugs might also get a lot of play in other dermatologic conditions such as alopecia areata and vitiligo, for which we lack an efficacious topical treatment outside of steroids. However, these conditions are also a little more difficult to design trials around, especially alopecia areata, which has a high rate of spontaneous recovery.”

One such medication, he adds, failed to meet primary endpoints due to high rates of treatment response in the vehicle treatment group.

Finding the right JAK inhibitor and formulating it into an effective topical vehicle has also proven challenging, he says, partly because some JAK inhibitors’ molecular heft is not ideal for topical application. “Topical JAK inhibitors may debut in four to five years, Dr. Han estimates.

In AD, he adds, crisaborole ointment appears equivalent to a lower-mid-potency steroid.

“It is an intriguing molecule,” Dr. Han says. “If you look closely at the atopic dermatitis trials, the vast majority of patients who responded to treatment remained clear one month later. There are many reasons to believe that tapinarof will be helpful in more than one inflammatory skin condition due to its broad effect on pro-inflammatory cytokines.”

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“In the后面的1/2期的试验中，53%的卡比诺夫治疗患者实现了IGA 0/1（相对于基线改善了2个点），而安慰剂组则为24%。治疗相关的副作用影响了56%的卡比诺夫组，而安慰剂组为41%。大多数的副作用是温和的。”

“这些是我们在脂质性皮炎和银屑病患区取得的最好的数字，”Han说。“我们不仅在脂质性皮炎和银屑病寻找疗效，但这些药物也可能在其他皮肤病中获得应用，比如斑秃和白癜风，对这些疾病我们缺乏有效的外用治疗，除了皮质类固醇。然而，这些条件也有点更难设计临床试验，尤其是斑秃，其有较高的自发性恢复率。”

一种这样的药物，他补充说，未能达到主要端点，由于在车辆治疗组中出现了高的治疗应答率。

找到合适的JAK抑制剂并将其配制为有效的外用药物也颇具挑战，他说，部分原因是因为某些JAK抑制剂的分子重不需要适用于外用应用。“局部JAK抑制剂可能在四到五年内问世。”Han估计。

在AD中，他补充说，克里索巴罗尔乳膏的疗效等同于一种低至中等皮质类固醇。
Niki Vora’s life has changed dramatically for the better since she was a kid with out-of-control and untreated atopic dermatitis. At 26, Vora is a medical student at University of California San Francisco (UCSF). She was enrolled in a dual master’s degree program at Berkeley University of California last year when an essay she wrote about her experience with skin disease earned her a $10,000 Ortho Dermatologics Aspire Higher scholarship.

**WHAT IT WAS LIKE**

Vora grew up with not only atopic dermatitis that she says covered her body, but she also had excessive hair growth, which led to folliculitis.

“You can imagine a teenage girl with a lot of hair on her face and a lot of inflammation on her face. It wasn’t easy. And the eczema, unfortunately due to my constant picking and I’m guessing sun exposure, led to a lot of hyperpigmentation,” Vora said.

But Vora says she just dealt with her skin issues the best she could because she didn’t have health insurance and had no access to a dermatologist. The problem was she wasn’t really dealing with her skin conditions.

“I think derm conditions affect us in very insidious ways,” Vora says.

Her skin issues (she also had cystic acne) were visible for the world to see. People would comment constantly, she says, on how she looked.

“And those comments stay with you your whole life,” she says. “When we were kids and people would want to hold hands with each other, people wouldn’t want to hold my hand because it was icky.”

Vora remembers one of her teachers took pictures of every one in her class and posted one photo at a time in a Power Point presentation at the end of the school year. Classmates commented on every photo except Vora’s. When hers was up on the screen, everyone was silent, she says.

**THINGS GOT BETTER WITH THE RIGHT CARE**

Vora finally saw a dermatologist when she was in college. Her mother saved for a decade, she says, so Vora also could get full-body laser hair removal.

“Finally having care and also having laser hair removal helped my conditions a lot. My eczema was under control and because I was removing hair, I had less folliculitis. I used to have bad cystic acne. All of that was decreased. My hyperpigmentation started going away,” Vora says. “It was crazy. In a span of I think two years my skin started to look clear.

“And I feel like people treat you nicer when you have clear skin.”

Vora’s dermatologist prescribed topical triamcinolone and hydrocortisone. It also helped that Vora received guidance on how to moisturize her skin.

Prior to seeing the dermatologist, Vora says she would haphazardly moisturize her skin with whatever fragrance-filled products she had. That didn’t help. What helped was being more conscious of what she put on her skin and moisturizing after showers with moisturizers with ceramides.

“Now I just have a little tube of triamcinolone in case I have a flair up. But everything has been pretty under control for me, which I’m really grateful for,” she says.

The dermatologist helped by being kind and listening. It was the first time, Vora says, that a doctor didn’t just tell Vora to wash her face with soap.

“Can you imagine hearing that for your entire life? It was the first time someone who specialized in skin was looking at me and said I know what you’re going through…. They aren’t down-playing the effect it has on someone,” Vora says.
“We live in an image-based society. So, it is a huge factor in life in how people view you and, therefore, treat you.”

Niki Vora, M.D., medical student at University of California San Francisco, recipient of Ortho Dermatologies Aspire Higher scholarship

Downplaying the effect of skin disease is a problem, according to Vora.

“I think if we take a step back, there are so many psychosocial issues that go hand-in-hand with having a skin disease. It’s not necessarily deadly. That’s why it’s so downplayed in the medical community. But it is a huge factor of life. We live in an image-based society. So, it is a huge factor in life in how people view you and therefore treat you,” she says.

PAYING IT FORWARD
Vora is considering going into dermatology.

She says she loves the specialty because of her experience with skin disease and how a dermatologist helped her. She also did charity work in India, helping to care for patients who had infectious diseases. Vora says skin issues and the need for wound care were common in those patients.

“I always feel like no matter what specialty I’m in, I will notice issues like dermatology that are constantly overlooked. It’s like something small that you could do that would make a big difference in a patient’s life — make them feel human while they’re going through the horrible diseases and difficult treatments,” Vora says.

She encourages other students with skin conditions to apply for the Ortho Dermatologies scholarship program.

“I almost didn’t go for this scholarship. I thought I didn’t have a chance and thought my situation was so common. There wasn’t anything special about it. It was just something that happened to me that continues to stick with me,” she says. “But I think that’s why they gave it to me because it is so common. It is something that sticks with people. I think anyone who is going to college who has a similar story should apply. It’s nice being part of a community that gets it. They’re very supportive. In terms of scholarships that I’ve applied to, Ortho Dermatologies is probably the most supportive after. They keep in touch with you, which makes me feel good.”

Vora is one of several students awarded scholarships each year through Ortho Dermatologies's scholarship program for students with dermatologic conditions. The Aspire Higher scholarship program has awarded 33 scholarships, totaling more than $550,000 toward higher education, since 2013.

Scholarships are open to applicants or current attendees of a two- or four-year college, university or advanced (post-high school) vocational or technical school, and are available in three categories: Undergraduate Scholar Awards; Graduate Scholar Awards; and Today’s Woman Scholar Awards, for students who are mothers pursuing either undergraduate or graduate degrees.
TO TREAT NODULAR ACNE

Isotretinoin (13-cis-retinoic acid), which was approved by the U.S. Food and Drug Administration (FDA) as an oral capsule formulation in 1982 to treat severe recalcitrant nodular acne, has proven to be a major pharmacological breakthrough for acne patients. That’s despite being challenged for its teratogenicity, according to a paper published in 2014 in the Journal of Clinical and Aesthetic Dermatology.1

“In my view, the most significant advance in dermatology has been the development and use of isotretinoin in patients with severe and recalcitrant acne,” according to Tucson, Ariz., dermatologist Norman Levine, M.D. “This one drug has improved the lives of millions of young people. No other drug or device has come close to matching this success in such a prevalent and potentially devastating skin condition.”

Dermatologists have likely felt the greatest impact among medical specialties from isotretinoin, given acne is one of the most common conditions they treat. Acne ranked first among the top 20 conditions seen by dermatologists from 2001 to 2010, according to an article published in 2014 in Cades.2

Acne has far-reaching effects on patients’ physical and psychological wellbeing. Isotretinoin enabled dermatologists to prescribe a drug that offered some of the hardest-to-treat acne patients complete clearance, says Miami, Fla., dermatologist Jill Waibel, M.D.

“This is a type of result that is unheard of in any medical treatment. Isotretinoin has undergone unwarranted demonization in years past and is finally emerging to its rightful role as ‘the drug that got bullied.’ I encourage all of my severe acne patients to try isotretinoin as long as they are not pregnant or breast feeding, as it is the only current way to achieve not only complete but permanent clearance,” she says.

AN AESTHETIC GAMECHANGER FOR SKIN: TRETINOIN

While dermatologists have used tretinoin since the 1960s, dermatologists and others didn’t realize the true potential of the retinoid’s impact on aging skin until the 1980s, researchers reported in paper published 2006 in Clinical Interventions in Aging.3

Old Metairie, La., dermatologist Patricia Ferris, M.D., says the discovery that tretinoin could be used to treat wrinkles and improve the appearance of aging skin was big news for dermatologists and patients.

“I remember being in the back of the room when they were presenting some of the first studies confirming efficacy and thinking, wow, this is a real gamechanger,” Dr. Ferris says. “Up until then, we didn’t really consider topical skincare of value for much beyond moisturization. All of a sudden, we had a cream that patients could apply at home that could actually make them look younger. This really changed the way we thought about skincare and gave way to the development of cosmeceutical products for treating a variety of cosmetic concerns.”

LIDHT ON LASERS

New York City dermatologist Roy G. Geronemus, M.D., says the most significant gamechanger for his practice happened around 1983, when Rox Anderson, M.D., and John Parrish, M.D., published “Mechanism of Selective Vascular Changes Caused by Dye Lasers” — the first article on the use of the pulsed-dye laser’s selective photothermolysis.

“This theory of selective injury of vascular targets in the skin has led to transformative treatments for not only vascular conditions, but also for pigmented lesions, tattoos, hair removal, fractional resurfacing for rejuvenation, scar management and laser assisted drug delivery,” Dr. Geronemus says. “The safety profiles of the technologies developed based on this theory have been extraordinary, leading to widespread acceptance. Selective photothermolysis will likely have an increasing impact on a number of medical conditions in the near future.”

The pulsed-dye laser was an evolution for not only adults but also children, according to Tucson, Ariz., dermatologist Ronald G. Wheeland, M.D.

“The pulsed-dye laser allowed the treatment of port-wine stains or other vascular lesions in children, even babies, without a risk of scar- rying or pigmentary changes unlike all previous devices or treatments,” Dr. Wheeland says. “This was revolutionary in that it could start school without any disfigurement — a real gamechanger.”

Laser techniques in dermatology have been expanded and optimized to allow rapid, low downtime treatment options for the most stubborn of skin pathologies.

ADVANCE OF TUMESCENT LIPOSUCTION

Dermatologist Jeffrey Klein, M.D., published his landmark studies on tumescent anesthesia in the 1980s paving the way for this breakthrough to advance patient care, according to Indianapolis, Ind., dermatologist C. William Hanke, M.D., M.P.H.

“Tumescent anesthesia allowed liposuction and other dermatologic procedures to be performed safely and effectively on awake patients,” Dr. Hanke says.

NEUROTOXINS HIT THE MARKET

Neurotoxins for cosmetic use started with the approval of onabotulinumtoxinA (Botox, Allergan) in 2002 for moderate-to-severe frown lines, according to maker Allergan. Before that in 1990, dermatologist Alastair Carruthers and ophthalmologist Jean Carruthers published their first report on the cosmetic use...
BIOLOGICS FOR PSORIASIS

Finding the best treatment for psoriasis has clearly been top of mind for many dermatologists. One of the most read and cited articles in the Journal of the American Academy of Dermatologists is “The introduction of biologics for psoriasis also has revolutionized treatment for many other diseases,” according to Dr. Matarasso.

With years of experience in using these products, dermatologists are realizing the power of neurotoxins, according to Dr. Matarasso. “I have been using neurotoxins and botulinum toxin for over 25 years, and I think the introduction of neurotoxins has been nothing short of groundbreaking,” Dr. Matarasso says. “In the aesthetic arena, neurotoxins are safe, reliable and so predictable, and patients are universally pleased with the outcomes. These are just some of the therapeutic indications: migraine headaches, temporalomandibular joint syndrome with concomitant bruxism. Just yesterday I treated a 19-year-old boy who was socially ostracized because of profound hyperhidrosis. So, from my perspective, this class of products has had a truly dramatic impact on how we can best treat patients.”

Dermatologists and others are just seeing the tip of the iceberg in terms of potential benefit from neurotoxins, according to Dr. Matarasso. “With years of experience in using these products, dermatologists are realizing the power of neurotoxins, and that could put a black eye on its potential. “This is not a product to be underestimated,” he says.

A FIRST FOR PROLIFERATING INFANTILE HEMANGIOMA

The FDA approved propranolol hydrochloride (Hemangeol, Pierre Fabre Pharmaceuticals) on March 14, 2014 for the treatment for proliferating infantile hemangioma requiring systemic therapy. Hemangeol is the only FDA-approved treatment for the indication.

Infantile hemangiomas are the most common infantile tumor, with a prevalence of infantile hemangiomas in mature neonates around 4.5%, according to a recent article in the Pan African Medical Journal. While most infantile hemangiomas regress spontaneously without therapy, about 10% to 15% of cases have complications.

“Therapeutic effect of propranolol over infantile hemangioma was noted in a child while being treated for hypertrophic cardiomyopathy by this molecule,” the authors write. “Since then, it is being used for infantile hemangioma and currently oral propranolol is the treatment of choice for this condition.”

Hemangeol is among the practice-changers for Saint Louis, Mo., based pediatric dermatologist Elaine C. Siegfried, M.D., whose other picks for biggest dermatology breakthroughs in the last 40 years were isotretinoin, biologics for psoriasis and dupilumab (Dupixent, Sanofi and Regeneron Pharmaceuticals).

“[The advances in dermatology] improve a clinician’s quality of life almost as much as their patients,” Dr. Siegfried says.

Which brings us to dupilumab for atopic dermatitis.

On March 28, 2017, the FDA approved dupilumab injection to treat adults with moderate-to-severe eczema. FDA later approved dupilumab for patients ages 12 to 17 years.

Dermatology Times recently covered a story about how dupilumab is a game-changer for children, like 13-year-old Benjamin Sun, with moderate-to-severe atopic dermatitis.

Biologic drugs for severe psoriasis, melanoma and non-melanoma skin cancer, and severe atopic dermatitis in the current decade have been among the medical breakthroughs in dermatology, according to Dr. Hanke.

“All of these breakthroughs significantly advanced the care of patients by dermatologists,” Dr. Hanke says.

REFERENCES

There are many reasons to believe that tapinarof will be helpful in more than one inflammatory skin condition due to its broad effect on pro-inflammatory cytokines.

George Han, M.D., Ph.D., Icahn School of Medicine at Mount Sinai, New York

Topical options to treat inflammatory dermatoses FROM PAGE 17

“Some proportion of patients experience burning and stinging. I find that if you give crisaborole ointment to a patient who’s having a severe eczema flare who has already been scratching their skin, they’re the ones who are prone to burning and stinging.”

For such patients, he starts with a stronger topical steroid for two weeks.

“Once you calm down the initial severe flare, they’re more likely to be able to maintain on crisaborole, and you optimize the safety and maximize the efficacy of the product in this way,” he says.

Thin-skinned areas such as the perioral area also tend to experience burning and stinging, says Dr. Han. He therefore recommends avoiding crisaborole ointment in such areas during acute disease flares, or refrigerating it or mixing it with a moisturizer to improve tolerability.

“It has good efficacy and is an important part of the long-term treatment arsenal. We need more nonsteroidal topical anti-inflammatory medications like crisaborole to come to market,” Dr. Han says.

Although Pfizer is no longer pursuing a psoriasis indication for crisaborole ointment, Dr. Han sometimes uses it for inverse psoriasis.

“We want to avoid a steroid in areas such as skin folds that are prone to striae or cutaneous atrophy,” he says. “The medication has some utility there.”

COMBINATIONS FOR PSORIASIS

In psoriasis, says Dr. Han, there is room for combinations of existing agents with innovative vehicles. With calcipotriol-betamethasone dipropionate foam (Enstilar, LEO Pharma), he says, a mean reduction of 73% was reported in phase 3 trials, but this data must be interpreted carefully because mean baseline PASI scores were between six and 10, reflecting a more moderate patient than in most randomized controlled trials.

Baseline PASI scores were between six and 10, reflecting a more moderate patient than in most randomized controlled trials.

The product also may have off-label indications such as AA and vitiligo, he says, where previous combinations of retinoids and anti-inflammatory agents have shown some synergy.

Halobetasol propionate 0.01% lotion (Bryhali, Ortho Dermatologics) has shown similar efficacy to halobetasol 0.05% cream.4

“And Bryhali is as efficacious in a once-daily, rather than twice-daily, application,” Dr. Han says. He has been using a fair amount of halobetasol 0.01% in psoriasis and other topical steroid-responsive skin conditions.

“I take heart in the fact that it was tested and approved in a longer treatment course — eight weeks of continuous use. People sometimes forget that some of the early topical clobetasol and betamethasone dipropionate studies had hypothyramic-pituitary-adrenal axis suppression in around 50% of patients, and you’re not supposed to use those longer than two weeks at a time,” he says.

Betamethasone dipropionate emollient spray (Servino, Promius Pharma) appears to have modest efficacy, similar to generic betamethasone dipropionate, says Dr. Han. In a 351-patient randomized clinical trial, 19% of patients met the endpoint of IGA zero or one, including a two-point improvement from baseline, vs. 2.3% for placebo.5 However, the spray showed good tolerability — 13.6% of patients who used a betamethasone lotion comparator experienced burning/stinging, versus 4.1% with the spray (P = 0.006).

Additionally, a calcipotriene-betamethasone cream formulation (MC2-01, MC2 Therapeutics) that has completed phase three psoriasis trials offers a novel vehicle that is said to improve drug delivery partly through a novel oil-in-water dispersion that results in a cosmetically elegant vehicle.

MC2 Therapeutics is expected to file a new drug application this year.

Meeting

Dr. Han has given a presentation titled “Novel and Pending Topicals in Psoriasis and Atopic Dermatitis” at the Atlantic Dermatological Conference. May 5, 2019, New York.

Disclosures

Dr. Han has served as an advisor for Inovio, Janssen, UCSF and Lilly; and an investigator and speaker for Pfizer, and an advisor and speaker for Sanofi Regeneron.

References

Making the Once Impossible, Possible: Innovation in Antibiotic Delivery

The delivery of antibiotics for dermatological conditions represents a unique challenge. Topical antibiotics are generally preferred to oral therapies because they have less systemic absorption. Despite the widespread use of topical antibiotics in dermatology, systemic antibiotics continue to play a significant role in practice, in part, because some antibiotics remain unavailable in topical formulations. Among the most commonly prescribed antibiotics by dermatologists are the tetracycline class, of which doxycycline and minocycline, to date, have proven difficult to formulate topically. Some of the challenges in the development of a topical formulation of tetracyclines include solubility, maintaining stability, and efficiently delivering the active ingredient into the skin. Overcoming the hurdles associated with creating effective topical formulations of tetracyclines has continued to be a challenge since the original development of topical antibiotics more than 50 years ago.13

Foamix is an entrepreneurial, technology-savvy specialty pharmaceutical company that is developing proprietary, innovative, and differentiated delivery systems intended to help solve some of today's most difficult therapeutic challenges in dermatology and beyond. By challenging the status quo, Foamix is reimagining what's possible for conditions with high unmet needs. Created with the formulation of topical tetracyclines in mind, the proprietary Molecule Stabilizing Technology (MST™) platform is the foundation that allows the company to rethink and reengineer topical delivery. MST™ enabled the creation of the first investigational topical antibiotic approach that is formulated without surfactants, using instead natural oils that work with the natural moisturizing oils of human skin. By leveraging foam, a prominent topical delivery system that can be engineered, refined, and elevated, Foamix is taking advantage of an innovative and easy-to-apply investigational alternative to creams and ointments. Potential significant advantages of the foam formulation are that it spreads easily on large skin areas, does not leave an oily film after application, and does not impart a greasy feeling upon, and after, application.45

Through the unique MST™ approach, formulations are in development that may allow for effective topical delivery of tetracyclines. Although some tetracyclines like doxycycline and minocycline are stable in their solid state, they degrade extensively in the presence of water and are sensitive to oxidation, thus preventing their formulation into aqueous compositions. The formulation of these tetracyclines as a suspension in hydrophobic composition was identified as a possible solution to mitigate the risk for degradation. Different carriers were evaluated for solubility and stability; a correlation was found between higher solubility (polar/hydrophilic solvents) and degradation, suggesting a hydrophobic carrier would be favorable. With this in mind, MST™ was designed as a way to formulate a suspension containing these molecules, utilizing an essentially nonaqueous formulation to mitigate degradation risk by reducing the interaction between the active ingredient and the rest of the composition.

Beyond tetracyclines, leveraging MST™ holds promise in the development of additional topical products that deliver proven therapeutic agents. With expertise in topical medicine innovation as its springboard, Foamix is working to develop and commercialize solutions that meet unmet needs in the dermatological market.


Sponsored by Foamix Pharmaceuticals Inc.
Logically, there will probably be differences as some of these pathways are more relevant in adults than children, that is why there is a real rationale to study children separately from adults and not to make assumptions that a child would respond as an adult would, or vice versa.”

Jonathan Silverberg, Northwestern Medicine Multidisciplinary Eczema Center and Northwestern Memorial Hospital, Chicago

Atopic dermatitis prevalence, pathology vary by age

Despite the lower prevalence of atopic dermatitis among adults, an estimated 16.5 million live with the condition in the United States, but if one were to visit a dermatologist’s office and see the number of patients, one might assume that there are far fewer.

Lack of health insurance will keep some patients away from dermatologists’ outpatient clinics, but often patients with insurance coverage will also end up seeking treatment elsewhere.

Atopic dermatitis is an incredibly volatile disease, and there is a subset of patients who experience dramatic flares in their disease that require rapid access. If they can’t get a day off from work during standard outpatient hours, cannot get an appointment with the dermatologist within the next six months, don’t have transportation to get there easily, or have childcare or other caring responsibilities, they will seek more convenient care from the emergency room or a hospital, Dr. Silverberg explains.

Not only does this expose them to potential healthcare infections, but from a cost and economic point of view, treatment in the emergency room or hospital system is “orders of magnitude more expensive” than it would be to be treated in the outpatient setting.

“Many of these patients are actually incurring high expenses both to themselves and to the healthcare system because they are not able to utilise the less expensive outpatient care,” he says. “There are many aspects of the healthcare system that can really be tweaked in order to improve access for the atopic dermatitis patient who is getting that severe itchy flare.”

Quick TAKES

Atopic dermatitis is more prevalent in children, and its phenotypes and subtypes vary considerably.

It is likely that there are differences in the underlying pathological disease process, indicating that different treatment modalities may be more effective.

It is difficult to compare the efficacy of different treatments in children, because, as treatments are first licensed based on studies in adults, very little data often exist on effectiveness in children, and even less from head-to-head comparative trials.

“Logically, there will be differences as some of these pathways are more relevant in adults than children, that is why there is a real rationale to study children separately from adults and not to make assumptions that a child would respond as an adult would, or vice versa,” he explains.

“In reality there may be a variety of different immune mechanisms implicated and some more relevant in children than adults. These are all very theoretical at this point but they may not be for very long. In the next few years I think we will have some really important data to digest between children and adults across a variety of different immune pathways.”

However, right now the assumption is what works in an adult will work in a child, but taking into account safety concerns about use in children.

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Topical retinoid for acne achieves efficacy endpoints

LISETTE HILTON | Staff Correspondent

Two phase three studies suggest once-daily trifarotene 50 μg/g cream effectively and safely treats moderate facial and truncal acne.

Researchers reported on both 12-week double-blind, randomized, vehicle-controlled studies on people ages 9 years and older in a paper published June 2019 in the *Journal of the American Academy of Dermatology (JAAD)*.1 The studies, called PERFECT 1 and PERFECT 2, included 200 sites in the United States, Canada, Europe and Russia and enrolled 2,420 patients with moderate facial and truncal acne who were treated with either trifarotene or vehicle.

Trifarotene (Galderma) is a retinoid receptor agonist that selectively targets retinoic acid receptor gamma (RAR-γ), which distinguishes it from other topical retinoids that target both retinoic acid receptor beta (RAR-β) and RAR-γ, according to the paper.

“Trifarotene is pharmacokinetically stable in keratinocytes but is rapidly metabolized in hepatic microsomes, predicting a favorable safety profile; in addition, it has comedolytic, anti-inflammatory and anti-pigmenting properties,” the authors write. The study design stands out because, while the pathophysiology and presentation of facial and truncal acne are thought to be similar, acne treatment options have not been vigorously studied on truncal acne, the authors write.

The primary efficacy endpoints of the studies were Investigator’s Global Assessment (IGA) success rate on the face, of clear/almost clear and at least a two-grade improvement from baseline at week 12, and absolute change from baseline in facial inflammatory and non-inflammatory lesion counts from baseline to week 12. Secondary efficacy endpoints were Physician Global Assessment (PGA) success rate on the trunk, with clear/almost clear and at least a two-grade improvement from baseline, at week 12, and absolute change in truncal inflammatory and non-inflammatory lesion counts from baseline to week 12, according to a Galderma press release.

Researchers in both studies reported that trifarotene was superior to vehicle in all primary and secondary efficacy assessments. It was superior to vehicle in reducing inflammatory and non-inflammatory lesion counts on the face and trunk. Trifarotene 50 μg/g cream worked quickly, according to the study, significantly reducing inflammatory and non-inflammatory lesion counts in as little as one week of treatment on the face and two weeks of treatment on the trunk.

Treatment with the investigational cream was relatively tolerable, manageable and consistent with topical retinoid dermatitis. Adverse events led to 1.9% of patients in the PERFECT 1 trial and 1.2% of those in the PERFECT 2 trial to discontinue trifarotene treatment. No patients in the vehicle groups discontinued due to adverse events.

“Trifarotene represents a novel topical retinoid with demonstrated efficacy in patients with moderate facial or truncal acne,” says Diane Thiboutot, M.D., an investigator in the phase 3 clinical trials for trifarotene and professor of dermatology at Penn State College of Medicine, Hershey, Pa.

Dr. Thiboutot says she thinks trifarotene’s role in acne treatment would be for patients with moderate acne comprised of comedones with papules, pustules or both.

It’s not so much that trifarotene would replace current acne treatments because there’s so much variability to patient response from treatment, she says.

“Rather I view [trifarotene] as an effective option for patients that haven’t responded to other topical retinoids. I also view it as an alternative to topical antibiotics and in some cases an alternative to oral antibiotics,” Dr. Thiboutot says.

Like with other retinoids, clinicians prescribing trifarotene should educate patients about typical topical retinoid side effects. This includes educating patients about the proper amount of medication to use, how to apply it and how to incorporate the use of moisturizers into their skincare regimens, she says.

Trifarotene is in clinical development for the treatment of moderate facial and truncal acne, including large body surface areas, according to a Galderma press release.

Disclosures: Nestle Skin Health Care-Galderma funded the phase 3 studies. Galderma employees were among the studies’ authors. Dr. Thiboutot was an investigator in the Phase 3 clinical trials for trifarotene at Penn State and attended one advisory meeting for trifarotene. She also served as an investigator for Botanix, Foamix and Cassiopea.

Reference

Patients report low treatment satisfaction

DAVID OZERI, M.D. | Staff Correspondent

Several novel medications have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of psoriasis in the past 20 years. While these have ushered in an era of improved disease control, patient-reported outcomes still suggest failure to meet treatment goals.

Experts from the International Psoriasis Council (IPC) discussed the goals of psoriasis treatment and barriers to receiving optimal care during a day-long roundtable. Their conclusions were published in *Dermatology Therapeutics* in March. The authors speculated there may be several factors causing the perceived disparity, including:

**1. Patient-Perceived Improvement.** Physicians use validated objective measures of treatment efficacy such as PASI scores; however, these measures differ with patient-perceived improvement. For example, “some patients have found itch to be most bothersome, while dermatologists reported the location and size of the skin lesions as paramount.”

**2. The Mild-to-Moderate Patient Population.** Another factor is that new therapies tend to focus on advanced disease. “Part of the problem is that the majority of recent innovation has been targeted to the moderate-to-severe patient population, with little new successful development for those psoriasis patients with mild and moderate disease,” the authors write.

**3. Differing Treatment Goals.** The authors also note that patients may have higher goals than their physicians, citing the results of a Japanese study where physician-patient misalignment was present in nearly 70% of surveys conducted. Furthermore, the authors state, “many patients are unaware that there is a possibility of attaining 100% clearance over both the short-term and long-term,” and that “this finding again highlights the importance of dermatologists recognizing patient expectations in order to reach clinical goals.”

**4. Disease Burden on Family Members.** Psoriasis can have a widespread impact on a patient’s relationships with others. The authors state, “the impact of psoriasis extends beyond the patient. Disease burden on family members and partners has garnered little attention in the past and, due to this lack of consideration, is a hidden and often ignored important aspect of the disease.”

**5. Over-treatment vs. Under-treatment.** With the current medication advancements in psoriasis therapies, sustained remission is a strong possibility. Once patients reach remission, deciding whether to continue treatment can become a serious physician-patient dilemma. This may contribute to poor patient satisfaction, as overtreatment can lead to complications associated with immunosuppression, and undertreatment can lead to increased morbidity from psoriasis.

**6. Delayed Referral to a Specialist.** The authors quoted a study that suggests patients may not seek expert opinion soon enough. Delay in seeking help can be attributed to several barriers, including familial experience of the disease (acceptance that many family members have psoriasis); previous failed therapies and thus a sense of hopelessness; lack of follow-up to assess treatment response after initiation; and difficulty in obtaining a secondary care referral, the authors write.

While the main goal of psoriasis treatment is to restore the patient’s normal daily activities, the authors note that patient-reported outcomes may complement objective skin scores and improve patient satisfaction.

The International Dermatology Outcome Measures Group is working to establish a validated patient-reported outcome based on the Dermatology Life Quality Index (DLQI) that is psoriasis specific. The combination of a tool with objective measures and patient-reported outcomes that is psoriasis specific will enhance physician-patient communication and improve outcomes.

Additionally, experts agree that using treat-to-target strategies is the first step to improve patient satisfaction. However, the strategies may be difficult to implement on a global scale. A “feasible approach” needs to be developed to help achieve treatment goals and patient satisfaction, the authors conclude.

Ultimately, patient education and improved physician-patient communication must be improved to advance psoriasis care and remission maintenance.

**References**

INDICATION
DUPIXENT is indicated for the treatment of patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATION: DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.

WARNINGS AND PRECAUTIONS
Hypersensitivity: Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

Conjunctivitis and Keratitis: Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder in these patients. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

Reduction of Corticosteroid Dosage: Do not discontinue systemic, topical or inhaled corticosteroids abruptly upon initiation with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Atopic Dermatitis Patients with Comorbid Asthma: Advise patients not to adjust or stop their asthma treatments without consultation with their physicians.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.
TRIAL RESULTS: A total of 917 adult patients in Trials 1 and 2 (16-week trials), 251 adolescent patients in Trial 6 (16-week trial), and 421 adult patients in Trial 3 (52-week trial) with moderate- to severe atopic dermatitis not adequately controlled with topical prescription treatments were randomized to DUXENIX or placebo. For all patients in Trial 3, lesions were treated with concomitant TCS. All adults received 300 mg QW following a 600 mg loading dose. Adolescents ≥ 18 kg also received this dose, while adolescents ≤ 18 kg received 200 mg QW following a 400 mg loading dose. Eligible patients had an IGA score ≥ 3 (overall atopic dermatitis lesion severity scale of 0 to 4), an EASI score ≥ 16 on a scale of 0 to 72, and body surface area involvement of ≥ 10%. At baseline, 52% of adults and 46% of adolescents had an IGA score of 3 (moderate atopic dermatitis), 48% of adults and 54% of adolescents had an IGA of 4 (severe atopic dermatitis), mean EASI score was 33 for adults and 36 for adolescents, and weekly averaged peak pruritus NRS was 7 on a scale of 0 to 10 for adults and 8 for adolescents.

TRIAL RESULTS: The primary endpoint was the change from baseline in the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and ≥ 2-point improvement at Week 16 (38% and 36% of adults treated with DUXENIX vs 10% and 9% with placebo in Trials 1 and 2, respectively, P=0.0001; 24% of adolescents treated with DUXENIX vs 2% with placebo in Trial 6, P<0.0001; 39% of adults treated with DUXENIX + TCS vs 12% with placebo + TCS in Trial 3, P=0.0001). Other endpoints included change from baseline in the proportion of subjects with EASI-75 at Week 16 (improvement of ≥ 75%; 51% and 44% of adults treated DUXENIX vs 15% and 12% with placebo in Trials 1 and 2, respectively, P<0.0001; 42% of adolescents treated with DUXENIX vs 8% with placebo in Trial 6, P<0.0001; 69% of adults treated with DUXENIX + TCS vs 23% with placebo + TCS in Trial 3, P<0.0001) and reduction in itch as defined by ≥ 4-point improvement in the Peak Pruritus NRS at Week 16 (41% and 36% of adults treated with DUXENIX vs 12% and 10% with placebo in Trials 1 and 2, respectively, P<0.0001; 57% of adolescents treated with DUXENIX vs 5% with placebo in Trial 6, P<0.0001; 59% of adults with DUXENIX + TCS vs 20% with placebo + TCS in Trial 3, P=0.00001).

EASI, Eczema Area and Severity Index; IGA, Investigator’s Global Assessment; NRS, numerical rating scale; QW, once every 2 weeks; TCS, topical corticosteroids.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS (cont’d)
Parasitic (Helminth) Infections: It is unknown if DUXENIX will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUXENIX. If patients become infected while receiving treatment with DUXENIX and do not respond to anti-helminth treatment, discontinue treatment with DUXENIX until the infection resolves.
SHARE RELIEF

▶ Itch reduction
▶ A biologic—not a steroid treatment or an immunosuppressant
▶ Clear or almost-clear skin
▶ No requirement for initial lab testing or ongoing lab monitoring, according to the full Prescribing Information

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS: The most common adverse reactions (incidence ≥1% at Week 16) in adult patients with atopic dermatitis are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, dry eye. The safety profile in adolescents through Week 16 was similar to that of adults with atopic dermatitis. In an open-label extension study, the long-term safety profile observed in adolescents through Week 52 was consistent with that seen in adults with atopic dermatitis.

DRUG INTERACTIONS: Avoid use of live vaccines in patients treated with DUPIXENT.

USE IN SPECIFIC POPULATIONS

▶ Pregnancy: Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus.

▶ Lactation: There are no data on the presence of DUPIXENT in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DUPIXENT and any potential adverse effects on the breastfed child from DUPIXENT or from the underlying maternal condition.

Please see brief summary of full Prescribing Information on the following pages.

Visit DupixentHCP.com/AtopicDermatitis to learn more
**DUPIXENT** (dupilumab) injection, for subcutaneous use  Rx only

**Brief Summary of Prescribing Information**

**1 INDICATIONS AND USAGE**

**1.1 Atopic Dermatitis**

Atopic dermatitis is indicated as an add-on maintenance treatment in patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

**1.2 Asthma**

Dupilumab is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma.

**1.3 Chronic Rhinosinusitis with Nasal Polyps**

DUPIXENT is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSsNP).

**4 CONTRAINDICATIONS**

DUPIXENT is contraindicated in patients who have known hypersensitivity to dupilumab or any of its excipients (see Warnings and Precautions (5.1)).

**5 WARNINGS AND PRECAUTIONS**

**5.1 Hypersensitivity**

Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum and serum sickness or serum sickness-like reactions, were reported in less than 1% of subjects who received DUPIXENT in clinical trials. Two subjects in the atopic dermatitis development program experienced serum sickness or serum sickness-like reactions that were associated with high titters of antibodies to dupilumab. One subject in the asthma development program experienced anaphylaxis (see Adverse Reactions (6.2)). If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT (see Adverse Reactions (6.1, 6.2)).

**5.2 Conjunctivitis and Keratitis**

Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis recovered or were recovering during the treatment period. Keratitis was reported in <1% of the DUPIXENT group (1 per 100 subject-years) and in 0% of the placebo group (0 per 100 subject-years) in the 16-week atopic dermatitis monotherapy trials. In the 52-week DUPIXENT + topical corticosteroids (TCS) atopic dermatitis trial, keratitis was reported in 4% of the DUPIXENT + TCS group (12 per 100 subject-years) and in 0% of the placebo + TCS group (0 per 100 subject-years). Most subjects with keratitis recovered or were recovering during the treatment period (see Adverse Reactions (6.1)).

Among asthma subjects, the frequencies of conjunctivitis and keratitis were similar between DUPIXENT and placebo (see Adverse Reactions (6.1)). In subjects with CRSsNP, the frequency of conjunctivitis was 2% in the DUPIXENT group compared to 1% in the placebo group in the 24-week safety pool; these subjects recovered. There were no cases of keratitis reported in the CRSsNP development program (see Adverse Reactions (6.1)). Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

**5.3 Eosinophilic Conditions**

Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroid therapy. These events may be associated with the reduction of oral corticosteroid therapy. Physicians should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Cases of eosinophilic pneumonia were reported in adult patients who participated in the asthma development program and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with DUPIXENT in adult patients who participated in the asthma development program as well as in adult patients with co-morbid asthma in the CRSsNP development program. A causal association between DUPIXENT and these conditions has not been established.

**5.4 Acute Asthma Symptoms or Deteriorating Disease**

DUPIXENT should not be used to treat acute asthma symptoms or acute exacerbations. Do not use DUPIXENT to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT.

**5.5 Reduction of Corticosteroid Dosage**

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

**5.6 Patients with Comorbid Asthma**

Advise patients with atopic dermatitis or CRSsNP who have co-morbid asthma not to adjust or stop their asthma treatments without consultation with their physicians.

**5.7 Parasitic (Helminth) Infections**

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if DUPIXENT will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to antihelminth treatment, discontinue treatment with DUPIXENT if the infection resolves.

**6 ADVERSE REACTIONS**

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

• Hypersensitivity [see Warnings and Precautions (5.1)]
• Conjunctivitis and Keratitis [see Warnings and Precautions (5.2)]

**6.1 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.

**6.2 Adverse Reactions Occurring in 2% or More in the DUPLEX MONOTHERAPY GROUP or the Atopic Dermatitis Trials**

**Atopic Dermatitis Trials**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DUPLEX MONOTHERAPY</th>
<th>DUPLEX + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site reactions</td>
<td>51 (10)</td>
<td>28 (5)</td>
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<tr>
<td>Oral herpes</td>
<td>20 (4)</td>
<td>8 (2)</td>
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<tr>
<td>Keratitis</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Dry eye</td>
<td>3 (1)</td>
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</tr>
<tr>
<td>Other herpes simplex virus infection</td>
<td>10 (2)</td>
<td>6 (1)</td>
</tr>
</tbody>
</table>

**Safety through Week 52 (Trials 1)**

*Pooled analysis of Trials 1, 2, and 3 and one dose-ranging trial (Trial 4) evaluated the safety of DUPLEX in subjects with moderate-to-severe atopic dermatitis. The safety population had a mean age of 38 years; 41% of subjects were female, 67% were white, 24% were Asian, and 8% were black; in terms of comorbid conditions, 48% of the subjects had asthma, 49% had allergic rhinitis, 37% had food allergy, and 27% had allergic conjunctivitis. In these 4 trials, 1472 subjects were treated with subcutaneous injections of DUPLEX, with or without concomitant topical corticosteroids (TCS). A total of 739 subjects were treated with DUPLEX for at least 1 year in the development program for moderate-to-severe atopic dermatitis. Trials 1, 2, and 4 compared the safety of DUPLEX monotherapy to placebo through Week 52. Table 1 compared the safety of DUPLEX + TCS to placebo + TCS through Week 52.

**Safety through Week 52 (Trials 1 to 4)**

In DUPLEX monotherapy trials (Trials 1, 2, and 4) through Week 16, the proportion of subjects with discontinuation because of adverse events was 1.9% in both the DUPLEX 300 mg Q2W and placebo groups. Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% in the DUPLEX 300 mg Q2W monotherapy group, and in the DUPLEX + TCS group, all at a higher rate than in their respective comparator groups during the first 16 weeks of treatment.

**7 ADVERSE REACTIONS Occurring in 2% or More in the DUPLEX MONOTHERAPY Group or the Atopic Dermatitis Trials**

**Atopic Dermatitis Trials**

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</table>

*Analysis of Trial 3 where subjects were on background TCS therapy.

**Safety through Week 52 (Trials 1 to 4)**

In the DUPLEX + TCS group, the proportion of subjects who discontinued treatment because of adverse events was 1.8% in DUPLEX 300 mg Q2W + TCS group and 7.6% in the placebo + TCS group. Two subjects discontinued DUPLEX because of adverse reactions: atopic dermatitis (1 subject) and exfoliative dermatitis (1 subject).

**Safety profile of DUPLEX + TCS through Week 52**

The safety profile of DUPLEX + TCS through Week 52 was generally consistent with the safety profile observed at Week 16.

**Adolescents with Atopic Dermatitis**

The safety of DUPLEX was assessed in a trial of 250 subjects 12 to 17 years of age with moderate-to-severe
atopic dermatitis (Trial 7). The safety profile of DUXIPENT in subjects followed through Week 52 was similar to the safety profile observed at Week 16 in Trial 6. The long-term safety profile of DUXIPENT observed in adolescents was consistent with that seen in adults with atopic dermatitis.

**Asthma**

A total of 2888 adult and adolescent subjects with moderate-to-severe asthma (AS) were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (AS Trials 1 and 2). A total of 270 subjects with oral corticosteroid-dependent asthma receiving high-dose inhaled corticosteroids plus up to two additional controllers were enrolled (AS Trial 3). The safety profile (AS Trials 1 and 2) was 12-87 years of age, of which 63% were female, and 52% were white. DUPIXENT 200 mg or 300 mg was administered subcutaneously Q2W, following an initial dose of 400 mg or 600 mg, respectively.

In AS Trials 1 and 2, the proportion of subjects who discontinued treatment due to adverse events was 4% of the placebo group, 3% of the DUPIXENT 200 mg Q2W group, and 6% of the DUPIXENT 300 mg Q2W group. Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator groups in Asthma Trials 1 and 2.

**Injection site reactions**

Injection site reactions included erythema, edema, pruritus, pain, and inflammation.

**Eosinophilia**

Eosinophilia = blood eosinophils ≥3,000 cells/mL, or deemed by the investigator to be an adverse event. None met the criteria for serious eosinophilic conditions [see Section 5.3 Warnings and Precautions]. Injection site reactions were most common with the loading (initial) dose. The safety profile of DUPIXENT through Week 52 was generally consistent with the safety profile observed at Week 24.

**Chronic Rhinosinusitis with Nasal Polyposis**

A total of 722 adult subjects with chronic rhinosinusitis with nasal polyposis (CRSwNP) were evaluated in 2 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (CSNP Trials 1 and 2). The safety profile consisted of data from the first 24 weeks of treatment from both studies. In the safety pool, the proportion of subjects who discontinued treatment due to adverse events was 5% of the placebo group and 2% of the DUPIXENT 300 mg Q2W group. Table 3 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUXIPENT and at a higher rate than in their respective comparator group in CSNP Trials 1 and 2.

**Injection site reactions**

Injection site reactions cluster includes injection site reaction, pain, bruising and swelling.

**Conjunctivitis**

During the 52-week treatment period of concomitant therapy atopic dermatitis trial (Trial 3), conjunctivitis was reported in 16% of the DUPIXENT 300 mg Q2W + TCS group (20% of DUPIXENT subjects) and in 9% of the placebo + TCS group (10 per 100 subject-years). Among asthma subjects, the frequency of conjunctivitis was similar between DUPIXENT and placebo. In the 52-week CRSwNP study (CSNP Trial 2), the frequency of conjunctivitis was 3% in the DUPIXENT subjects and 1% in the placebo subjects; all of these subjects recovered [see Warnings and Precautions (5.2)].

**Eczea Herpetica and Herpes Zoster**

The rate of eczea herpetica was similar in the placebo and DUXIPENT groups in the atopic dermatitis trials. Herpes zoster was reported in <0.1% of the DUXIPENT groups (<1 per 100 subject-years) and in <1% of the placebo group (1 per 100 subject-years) in the 16-week atopic dermatitis trials. In the 52-week DUXIPENT + TCS atopic dermatitis trial, herpes zoster was reported in 1% of the DUXIPENT + TCS group (1 per 100 subject-years) and 2% of the placebo + TCS group (2 per 100 subject-years). Among asthma subjects, the frequency of herpes zoster was similar between DUPIXENT and placebo. Among CRSwNP subjects there were no reported cases of herpes zoster or eczea herpetica.

**Hypersensitivity Reactions**

Hypersensitivity reactions were reported in <1% of DUXIPENT-treated subjects. These included serum sickness reaction, serum sickness-like reaction, generalized urticaria, rash, erythema nodosum, and anaphylaxis [see Contraindications (4), Warnings and Precautions (5.1), and Adverse Reactions (6.2)].

**Eosinophil**

DUPIXENT-treated subjects had a greater initial increase from baseline in blood eosinophil count compared to subjects treated with placebo. In subjects with atopic dermatitis, the mean and median increases in blood eosinophils from baseline to Week 4 were 1004 and 670 cells/mL, respectively. In subjects with asthma, the mean and median increases in blood eosinophils from baseline to Week 4 were 130 and 70 cells/mL, respectively. In subjects with atopic dermatitis, the mean and median increases in blood eosinophils from baseline to Week 52 were 1,000 and 500 cells/mL, respectively. Across all indications, the incidence of treatment-emergent eosinophilia (≥500 cells/mL) was similar in DUXIPENT and placebo groups. Treatment-emergent eosinophilia (≥500 cells/mL) was reported in <2% of DUPIXENT-treated patients and <0.5% in placebo-treated patients. Blood eosinophil counts declined to near baseline levels during study treatment [see Warnings and Precautions (5.3)].

**Cardiovascular (CV)**

In the 1-year placebo controlled trial in subjects with asthma (AS Trial 2), CV thromboembolic events (CV deaths, non-fatal myocardial infarctions [MI], and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT 200 mg Q2W group, 4 (0.6%) of the DUPIXENT 300 mg Q2W group, and 2 (0.3%) of the placebo group.

In the 1-year placebo controlled trial in subjects with atopic dermatitis (Trial 3), CV thromboembolic events (CV deaths, non-fatal MIs, and non-fatal strokes) were reported in 1 (0.9%) of the DUPIXENT + TCS 300 mg Q2W group, 0 (0.0%) of the DUPIXENT + TCS 300 mg QW group, and 1 (0.3%) of the placebo + TCS group.

In the 24-week placebo controlled trial in subjects with CRSwNP (CSNP Trial 1), CV thromboembolic events (CV deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT group and 0 (0.0%) of the placebo group. In the 1-year placebo controlled trial in subjects with asthma (AS Trial 2), CV thromboembolic events (CV deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT group and 0 (0.0%) of the placebo group.

In the 24-week placebo controlled trial in subjects with CRSwNP (CSNP Trial 2), there were no cases of CV thromboembolic events (CV deaths, non-fatal myocardial infarctions, and non-fatal strokes) reported in any treatment arm.

**Immuneogenicity**

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to dupilumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Approximately 5% of subjects with atopic dermatitis, asthma, or CRSwNP who received DUXIPENT 300 mg Q2W for 52 weeks developed antibodies to dupilumab; ~2% exhibited persistent ADA responses, and ~2% had neutralizing antibodies.

Approximately 9% of subjects with asthma who received DUXIPENT 200 mg Q2W for 52 weeks developed antibodies to dupilumab; ~4% exhibited persistent ADA responses, and ~4% had neutralizing antibodies.

Approximately 4% of subjects in the placebo groups in the 52-week studies were positive for antibodies to DUXIPENT; ~2% exhibited persistent ADA responses, and ~1% had neutralizing antibodies.

Approximately 16% of adolescent subjects with atopic dermatitis who received DUXIPENT 300 mg or 200 mg Q2W for 16 weeks developed antibodies to dupilumab; ~3% exhibited persistent ADA responses, and ~5% had neutralizing antibodies.

Approximately 4% of adolescent subjects with atopic dermatitis in the placebo group were positive for antibodies to DUXIPENT; ~1% exhibited persistent ADA responses, and ~1% had neutralizing antibodies.

The antibody titers detected in both DUXIPENT and placebo subjects were neutral. In subjects who received DUPIXENT, development of high titer antibodies to dupilumab was associated with lower serum dupilumab concentrations [see Clinical Pharmacology (12.3) in the full prescribing information].

Two subjects who experienced high titer antibody responses developed serum sickness or serum sickness-like reactions during DUXIPENT therapy [see Warnings and Precautions (5.2)].

7 DRUG INTERACTIONS

7.1 Live Vaccines

Avoid use of live vaccines in patients treated with DUXIPENT.

Manufactured by: Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591 U.S. License # 1760; Marketed by sanofi-aventis U.S. LLC, (Bridgewater, NJ 08807) and Regeneron Pharmaceuticals, Inc. (Tarrytown, NY 10591). DUPIXENT® is a registered trademark of Sanofi Biotechology© 2019 Regeneron Pharmaceuticals, Inc./sanofi-aventis U.S. LLC. All rights reserved. Issue Date: June 2019 US-DUP-1104(2)
IL-17 inhibitors may fill treatment gap in rosacea

LISETTE HILTON | Staff Correspondent

There’s need for therapies to address treatment-resistant and severe of papulopustular rosacea, and interleukin (IL) 17 inhibitors might just fit the bill, Canadian researchers report in a new review published August 12, 2019 in the *Journal of Cutaneous Medicine and Surgery.*

Dermatologists primarily use standard rosacea treatments, including metronidazole, ivermectin, azelaic acid and low-dose oral antibiotics, to control symptoms with the medications' anti-inflammatory effects. But these therapies also have this in common: they act at various stages along the IL-17 pathway, inhibiting IL-17’s downstream products or cytokines responsible for T helper (Th) 17 cell differentiation, according to the authors.

“Until recently, abnormal functioning of the innate immune system and neurovascular dysregulation have been at the forefront of the proposed [rosacea] pathophysiologys,” they write. “However, the role of adaptive immunity, IL-17 in particular, is slowly emerging.”

Among the findings that support IL-17’s role in rosacea, research by Buhl et al found Th1 and Th17 dominance in erythematotelangiectatic papulopustular and phymatous rosacea, with highest T-cell activity and IL-17 immunostaining in papulopustular rosacea. The same authors reported on increased IL-6, tumor necrosis factor (TNF), IL-20 and CCL 29 gene expression—all of which are involved in IL-17 and IL-22 induction.

Researchers also have reported that the skin of rosacea patients tends to have an increased density of Demodex folliculorum (D. folliculorum), which can lead to the release of IL-17, according to the paper in the *Journal of Cutaneous Medicine and Surgery.*

The authors point to gaps in treatment efficacy, including that there is no cure for rosacea and current treatment options lose effectiveness with increasing disease severity. Today’s topical and oral treatments relieve symptoms and slow disease progression, but they are associated with relapse when discontinued and treatments are lacking for severe and treatment-resistant papulopustular rosacea, they write.

Since IL-17 plays a pivotal role in papulopustular rosacea development and there are therapies on the market that target the IL-17 pathway, including secukinumab (Cosentyx, Novartis), ixekizumab (Talz, Lilly) and brodalumab (Siliq, Bausch Medical), IL-17 inhibitor drugs should be considered for the treatment of severe and treatment-resistant papulopustular rosacea, the authors reason.

First approved in January 2015, secukinumab has been available the longest, according to the paper. But Stanford University researchers are studying secukinumab, an antibody that binds specifically to IL-17A and has been shown to be effective in treating moderate-to-severe psoriasis, in a proof-of-concept study for moderate to severe papulopustular rosacea. The study was completed earlier this year but results have not yet been posted, according to ClinicalTrials.gov.

Secukinumab might also be the safest of the three IL-17 inhibitors, according to the paper in the *Journal of Cutaneous Medicine and Surgery.* Brodalumab, a human monoclonal IgG2 antibody that binds to IL-17RA, has a black box warning for suicidal ideation and behavior; however, it might also show promise in the treatment of severe rosacea because it blocks the action of several IL-17 cytokines, according to the paper.

The high costs of these medications could prevent their use in diseases other than psoriasis and psoriatic arthritis—that’s even if further research reveals they are effective and safe for treatment of severe and treatment-resistant papulopustular rosacea, the authors write.

**Disclosures**
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**References**

**Quick TAKES**

There is no cure for rosacea and current treatment options lose effectiveness with increasing disease severity.

Today’s topical and oral treatments relieve symptoms and slow disease progression, but they are associated with relapse when discontinued.

IL-17 plays a pivotal role in papulopustular rosacea development and should be considered for the treatment of severe and treatment-resistant papulopustular rosacea, reason authors of a recent study.
Clinical observations improve pathology report

ILYA PETROU, M.D. | Staff Correspondent

Making an accurate diagnosis of actinic keratosis (AK) based on the histology is crucial as it can directly influence treatment decisions. However, one expert says it can sometimes be challenging for a pathologist to distinguish between AK and squamous cell carcinoma (SCC) in situ.

While the definitions of actinic keratosis, SCC in situ and invasive SCC are well-defined and agreed upon, the interpretation of the histology can be very subjective and may differ among pathologists and their individual judgement of key histologic parameters. Therefore, it is crucial for clinicians to include clinical information regarding the lesion for correlation. This will help a pathologist arrive at an accurate diagnosis, which enables the dermatologist to prescribe the most appropriate therapy, says Travis Vandergriff, M.D., associate professor in the department of dermatology, and dermatopathologist at UT Southwestern Medical Center, Dallas.

“There is a clear consensus regarding the definitions of these lesions but then making the judgement of whether or not some of the criteria that we use to distinguish them are actually fulfilled is a lot more subjective than I think people realize,” he notes.

The main difference between SCC in situ and AK is that in SCC in situ, the full thickness of the epidermis is involved with atypical proliferation of keratinocytes; whereas, in AK, the atypia is limited to lower levels of the epidermis and not its full thickness. The critical point is making the histopathologic judgement on whether the full thickness is involved with atypia or perhaps just the lower two-thirds of the epidermis. This judgement differs among individual pathologists and, according to Dr. Vandergriff, there is some discretion that pathologists use to decide whether or not the criteria are met.

Similar to the assessment of dysplastic nevi and other melanocytic neoplasms, there is a certain amount of interpretation that is involved by the pathologist and, as such, the inter-observer agreement can often diverge. Dr. Vandergriff stresses that this is not due to a lack of education or knowledge about the criteria, but more about the subjective interpretation of the individual pathologist if the criteria are being met.

“When the AK under scrutiny is meeting all the classic features like basal layer atypia and intermittent parakeratosis, you would generally have a really high level of agreement among pathologists. However, when it gets closer to SCC carcinoma in situ and the lines start to blur between our definition of AK and SCC in situ, that’s when there is more dispute among pathologists,” Dr. Vandergriff says.

When pathologists can incorporate clinical information into interpreting a case they can arrive at a more accurate diagnosis, Dr. Vandergriff says. For example, including
The clinical information about the patient and the lesion in question can be key in helping influence the pathologist’s interpretation of the lesion, directly impacting the therapeutic choices of the clinician.”

Travis Vandergriff, M.D., UT Southwestern Medical Center, Dallas

detailed information not only regarding the lesion specifics but also about the patient, such as noting patients who are immunosuppressed or have significant sun damage and therefore may have a higher risk of developing SCC, are data points that may inform a pathologist if a lesion appears to be borderline.

“The clinical information about the patient and the lesion in question can be key in helping influence the pathologist’s interpretation of the lesion, directly impacting the therapeutic choices of the clinician,” Dr. Vandergriff says. “It is important to correlate with clinical information and to recognize that there are these borderline or in-between lesions, and that is where some discretion is needed and where clinical correlation becomes important.”

According to Dr. Vandergriff, the problem relates to the fact that clinicians and pathologists are trying to put labels on specific lesions and make them binary diagnoses when, in reality, these lesions are part of a spectrum, and they can fall anywhere along that spectrum. Trying to decide exactly where the lesion falls on the spectrum relies on the discretion of the individual pathologist, along with clinical correlation.

Most dermatologists and pathologists would agree that borderline lesions or advanced AKs or any lesion that is concerning for early SCC in situ development are lesions that definitely require some form of treatment. Surgery is not often the first choice, as other less invasive destructive therapies including liquid nitrogen cryotherapy and topical chemotherapy treatment (i.e., 5-fluorouracil) work very well in many cases.

“We always try to convey in the pathological report if the lesion is advanced or borderline SCC in situ and, accordingly, the clinician can implement a measured and appropriate therapy,” Dr. Vandergriff says. ▶

Disclosures
Dr. Vandergriff reports no relevant disclosures.

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Head and neck melanoma characteristics

ILYA PETROU, M.D. | Staff Correspondent

Quick Takes
Cutaneous head and neck melanomas have been reported to constitute approximately 12% to 21% of melanomas annually. CHNM are known to have poorer outcomes than melanomas occurring on other anatomic regions.

In a recent study, researchers found specific factors linked with peripherally located CHNM lesions.

Clinicians should be aware of higher risk cutaneous head and neck melanoma (CHNM) lesions and their potentially worse prognosis when considering appropriate therapies for their patients. According to recent data, CHNM have poorer outcomes relative to melanoma on alternate anatomical sites. And, more specifically, peripherally located CHNM appear to have poorer outcomes than centrally located CHNM, a new study indicates.

Cutaneous head and neck melanomas have distinct characteristics and have been reported to constitute approximately 12% to 21% of melanomas annually. The primary environmental risk factor for the development of melanoma is sun exposure, particularly intermittent and intense exposures in childhood that lead to blistering sunburns. This may, in part, explain the high incidence of melanoma in the head and neck region.

There are several factors that are thought to play a role in the poorer outcomes seen in CHNM. Compared with melanomas that occur on other anatomic locations, this subset of tumors may be thicker at the time of diagnosis and may present at a more advanced stage.

In addition, the optimal tumor resection margins in the head and neck region are often times very challenging to achieve due to anatomic constraints. And, lymphatic drainage of this region is variable and complex.

Although epidemiologic and clinical-histological differences according to sublocations (peripheral vs. central) have been reported in the literature, their impact on survival has not been largely explored.

In a recent retrospective study, José Antonio Avilés-Izquierdo, M.D., and fellow colleagues from the department of dermatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain, evaluated the epidemiological, clinical, histological and survival characteristics in a cohort of patients with CHNM.

A total of 371 patients (female: n=191; male: n=180) with a histological diagnosis of CHNM were included in the study and were followed up for a mean of 93.6 months. CHNM were classified according to ultraviolet radiation exposure into peripheral (i.e., scalp, ear and neck) or central (i.e., forehead, eyelids, nose, cheeks, and perioral region) lesions.

Researchers found that peripheral melanomas were much more common in men, were diagnosed at a younger age, had deeper tumor thickness, were more frequently ulcerated, and had a higher (≥6) number of mitoses than those melanomas located centrally.

Data also showed that patients with peripherally located melanomas developed more metastasis, had a higher melanoma-specific mortality, as well as a lower 10-year survival rate (50% vs. 90%; p<0.001) than those with centrally located melanomas.

“Cutaneous head and neck melanomas have been associated with poor outcomes, especially those located on the scalp. The reason for this difference, and whether it is applicable to all locations within the head and neck, remains unclear to this date,” wrote José Antonio Avilés-Izquierdo, M.D., Ph.D., Enrique Rodríguez-Lomba, M.D., and colleagues, in the study to soon be published in The Journal of the American Academy of Dermatology.

Several different factors in the study remained as independent predictors for melanoma-specific survival (p<0.001) including peripheral location of the lesion, tumor thickness, high mitotic rate (≥6/mm2) as well as patient age (≤65 years). Study data also showed that peripheral location had the strongest association with melanoma-specific mortality (OR 11.93; CI 95% 4.77-29.86).

“The reasons underlying differences between peripheral and central CHNM are still unknown. The uneven distribution of CHNM between sexes could be due to the protective role of the hair in the scalp, neck and ears, which are generally covered by hair, even in elderly women. Another possible explanation is a greater delay in diagnosis of peripheral CHNM, as lesions located on the scalp or ears are not easily visible to the patient,” the study authors wrote.

Disclosures
No relevant disclosures reported.

References

“Cutaneous head and neck melanomas have been associated with poor outcomes, especially those located on the scalp. The reason for this difference, … remains unclear to this date.” José Antonio Avilés-Izquierdo, M.D., Ph.D., Enrique Rodríguez-Lomba, M.D., and colleagues, The Journal of the American Academy of Dermatology
Clinical Trial Update

Molluscum Contagiosum and Other Common Skin Conditions

Not representative of all patients.

As many as 6 million people are infected with molluscum, primarily kids under 16; however, many patients do not receive treatment. Quality of life can be negatively affected by a molluscum infection. Children with the disease may become stigmatized and experience teasing, embarrassment, and social isolation. Up to 82% of parents and caregivers express moderate to great concern about molluscum. Lesions may sometimes be asymptomatic, but patients do complain about itching, burning, and tenderness.

Although lesions can resolve within 6 to 9 months, patients typically have the infection for 13 months, and some infections can persist for 2 years or more. Treatment at the time of diagnosis provides the best chance of decreasing the number of lesions and spread of the disease.

No FDA-approved treatment currently exists for molluscum contagiosum.

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    Phase 3 (completed) | CAMP-1 and CAMP-2
  - Verruca vulgaris (common warts)
    Phase 2 (completed) | COVE-1
  - Genital warts
    Phase 2 (enrolling, results expected 2020) | CARE

to see a dramatic increase in very elderly patients with NMSCs.”

In the very elderly, NMSCs are often detected as an incidental finding during a visit when a patient is being seen for another reason, according to Molly Moye, M.D., a fellowship-trained Mohs surgeon in private practice, Forefront Dermatology, Louisville, Ky. She posed the question of whether basal cell carcinomas (BCCs) are being overdiagnosed and overtreated in this advanced age population.

An argument that favors biopsy of all suspicious lesions is that it is the only way to avoid missing the diagnosis of a more serious tumor, such as an amelanotic melanoma or Merkel cell carcinoma. To limit that risk, patients and their families can be educated to watch for worrisome changes and about the importance of returning for regular follow-up, Dr. Moye says.

“There is reason to intervene if a lesion is symptomatic, such that it is bleeding, itching or painful, or if it is reported to be growing rapidly,” she says. “In the case of a lesion that is likely to be an indolent BCC and not bothersome to the patient, however, I consider the patient’s overall health status, life expectancy and the likely consequences of treatment versus no treatment, and I have a conversation with the patient and his or her family to achieve shared decision making,” she says.

Dr. Moye recommends performing a biopsy whenever there is suspicion of squamous cell carcinoma (SCC). The pathology report will then guide the treatment decision. The choice of surgical options depends on tumor size, pathologic features, anatomic location and patient characteristics. Mohs surgery is generally indicated for any tumor that is larger than 2 cm, moderately or poorly differentiated, or when there is presence of acantholysis or perineural or perivascular invasion.

“Some of my toughest Mohs surgery cases involve patients who present with recurrence of an aggressive NMSC that was initially treated with electrodessication and curettage or some other less definitive technique. These tumors can grow back very quickly, and, consequently, the area of involvement may be much larger than it was at the time of initial treatment. In this situation, surgery results in much greater morbidity than if the tumor was treated appropriately with surgery at the outset.”

Simple surgical excision, however, may be preferred in some elderly patients given certain circumstances.

“If, in the clinician’s judgment, an elderly patient is unlikely to be able to sit for the lengthy procedure, standard excision can be an acceptable alternative,” Dr. Moye says.

ALTERNATIVES TO SURGERY

In some cases of high-risk or advanced NMSC, surgery may be declined or contraindicated for reasons that include comorbidity or the likelihood of causing significant disfigurement or functional impairment. Surgery itself may also not be enough if there is metastasis to lymph nodes or distant organs.

Systemic treatment options for advanced NMSC include oral Hedgehog pathway inhibitors, vismodegib (Erivedge, Genentech) and sonidegib (Odomzo, SUN Pharma) for advanced BCC and IV cremiplimab (Libtayo, Regeneron)/Sanofi-Aventis), a programmed death-1 inhibitor, for advanced cutaneous SCC. The use of platinum-based chemotherapy as well as other chemotherapies have also been described in small clinical trials, case series or case reports as treatments for advanced NMSCs.

Radiotherapy can be considered for palliative vs. curative intent. “The lack of data about efficacy, safety and quality-of-life impact in the very elderly (age ≥80 years) is an issue for all of these interventions,” Dr. Chang says.

“There is not a good evidence base to guide decisions about the use of these treatments for NMSC in the very elderly. Although the clinical trials that led to approval of the newer medical options included participants age 65 and older, the number of such patients is fairly low,” she explains.

“Functional and health status affects the ability of patients to tolerate potential side effects of systemic treatments, and there is a real need for more data,” she says.

When considering the use of a systemic medication for treating NMSC in very elderly patients, Dr. Chang suggests using the Eastern Cooperative Oncology Group performance status scale or the Karnofsky score to assess functional status and ordering laboratory tests to evaluate major organ function.

Individual goals of care and the potential for treatment and follow-up adherence are also taken into account.

“Patients need to remember to take their medications, watch for side effects, and return for appointments. Therefore, it is important to assess the patient’s living situation because they may need a caregiver or family member to assist them in these areas. It is also helpful to provide written instructions using large font and simple verbiage that is easy to understand,” Dr. Chang says.

SHARED DECISION MAKING

Eleni Linos, M.D., Dr.P.H., professor of dermatology, Stanford University School of Medicine, Stanford, Calif., advocates for shared decision making and incorporating principles of geriatrics to the care of older adults with skin cancer.

“We need to apply principles of geriatrics to the practice of dermatology when caring for older patients. This type of approach is something our colleagues in pediatric dermatology have been doing for decades when caring for younger patients. It is time to do the same for geriatric dermatology,” Dr. Linos says. “When caring for an older patient with skin cancer, we cannot only focus on removing skin cancer cells. Instead, we need to think about the patient’s overall health, multimorbidity, polypharmacy, function, cognition, mobility, social support, life expectancy and, especially, the patient’s preferences.”

Doctors need to balance the benefits and harms of treatment for each patient, she adds.

“Older adults are a diverse group with varying medical needs, values, life expectancies and preferences, and the relative weight of benefits and harms will often be swayed by the patient’s preferences. Therefore, we cannot follow a one-size-fits-all recommendation for the treatment of NMSCs in this population. The relative weight of benefits and harms will often be swayed by the patient’s preferences.”

Disclosures:

Dr. Moye and Dr. Linos have no relevant financial interests to disclose. Dr. Chang receives grants and research funding from Genentech and Regeneron.
Radiodermatitis is increasingly common

WHITNEY J. PALMER | Staff Correspondent

With more female breast cancer survivors living longer, radiodermatitis is increasingly common. Consequently, dermatologists worldwide are investigating better ways to identify and alleviate it.

In a commentary published in *Breast Cancer — Targets and Therapy*, a team led by Rene-Jean Bensadoun, M.D., a radiation oncologist with the Centre de Haute Energie in France, discussed not only how providers can recognize the types of radiodermatitis, but also some treatment options.

“Radiodermatitis is still a pregnant problem for patients receiving radiation for cancer,” he says. “Radiation oncology is having brilliant results, but acute and late skin toxicity remains an inherent side effect of most radiation treatments, especially in breast cancer, gynecological and rectal cancers.”

In female breast cancer patients, radiodermatitis presents in acute and chronic ways. Not only can these forms present differently, but therapeutic options also vary, he says.

**ACUTE DERMATITIS**
Acute dermatitis is identified by symptoms that appear within six months of treatment. Patients experience dry, itchy skin that can be red, feel warm, and peel along the skin folds of the breasts, clavicle, and periauricular areas.

To date, there have been few evidence-based recommendations on preventing acute radiodermatitis. However, Bensadoun says, new data points to dermocosmetics.

“The role of dermocosmetics has to be highlighted in the preventive management of these skin toxicities,” he says. “Previously, they were not prescribed by most physicians, but recent international guidelines have highlighted their important role.”

For treatment, he says, lasers are preferred. Both animal and clinical studies suggest low level light therapy (LLLT), also known as photobiomodulation or “soft laser” (red light or infrared with <150 mW power), can reduce inflammation and prevent fibrosis. Bensadoun’s group recommends initiating this treatment after a few radiation sessions and before significant redness appears, if possible. However, don’t forego treatment if redness already exists.

**CHRONIC DERMATITIS**
With similar symptoms, chronic dermatitis appears after six months and up to 30 years post-treatment.

New data suggests dermocosmetics may prevent radiodermatitis.

Light therapy has also proved effective to treat both acute and chronic cases.

Quick TAKES

- Acute dermatitis is identified by symptoms that appear within six months of treatment. Chronic dermatitis appears after six months and up to 30 years post-treatment.
- Light therapy has also proved effective to treat both acute and chronic cases.

“Radiodermatitis is still a pregnant problem for patients receiving radiation for cancer.” Rene-Jean Bensadoun, M.D., Centre de Haute Energie, Nice, France
Radiodermatitis affects approximately 95% of all patients who receive radiation therapy for cancer. Many of these individuals are women undergoing breast cancer treatment, and they report developing the condition has significant detrimental impacts on their overall quality-of-life.

In a study published recently in the Journal of Pain and Symptom Management, Yara Christina da Paiva Maia, a professor with the Universidade Federal de Uberlandia, and her colleagues investigated how radiodermatitis affected these patients, finding a significant need for methods to reduce the impact on quality-of-life exists.

“The impact of radiation therapy on functionality and the daily lives of the patients is sometimes underestimated when compared with the chemotherapy period,” de Paiva Maia writes. “However, our study and the literature show that this period presents unique changes, including modifications in their daily routine due to the treatment plan, an increase in physical discomfort, and changes in the breast appearance.”

According to Laura Beamer, Ph.D., associate professor of nursing at Northern Illinois University, affected women reveal the itching, burning, stinging, pain, irritation, embarrassment, depression, reduced social interaction and diminished ability to show affection all chip away at their happiness with their daily lives. The effects can be significant enough to prompt some women to halt treatment, making it critical for dermatologists to find ways to reduce the impact as much as possible.

Tracey Gosselin, chief nursing officer at Duke University Hospital, agrees.

“Knowing how radiodermatitis impacts our patients is integral to supportive treatment,” she says. “We know dermatologists want to do whatever they can to improve symptoms and quality-of-life for women treated for breast cancer who develop this condition.”

Active treatment is one way dermatologists can augment quality-of-life. Topical products that contain emu oil can rehydrate the dry skin, relieving the itching associated with radiodermatitis. Additionally, these products have been shown to reduce inflammation and promote faster healing. Recent research also indicates low level light therapy — red or infrared light with power less than 150 megawatts — can reduce inflammation, pain, swelling, and help save adjacent tissues and nerves. Short pulse dye lasers can also help alleviate symptoms in radiodermatitis that emerges long after treatment ends.

But, dermatologists can do more than offer medical interventions to alleviate symptoms. They can also recommend various steps patients can implement to reduce the daily impact of radiodermatitis.

For example, Gosselin says, teaching patients how to care for their skin at home can have a great benefit. First, she recommends teaching patients proper hygiene. Instruct them to gently wash the skin, but never to scrub it. Encourage patients to wear cotton clothing as much as possible and to never wear tight-fitting underwear because they can rub and chafe, exacerbating existing symptoms. This can be a particular problem for women with large, pendulous breasts, she says.

Additionally, caution patients against getting in hot tubs or using heating pads on the impacted skin. They should limit sun exposure as much as possible, either staying out of the sun or wearing clothing that provides proper coverage. And, they should only use alcohol-free products on the skin to limit any burning or stinging.

Overall, Gosselin says, dermatologists must be sure to keep the lines of communication open with their patients to discuss any changes in their radiodermatitis. Open conversation can help patients learn how to augment their own comfort on a daily basis even when they can’t see their provider.

“We must encourage good self-care. To me, that’s the key piece,” she says. “Dermatologists must have a really good understanding of dealing with this condition from the patient’s perspective. They might need our help finding different treatments or different activities that can best support them during this time.”

References
ABOUT FACE
Navigating Neuromodulators and Injection Techniques for Optimal Results

CME/CE ONLINE MONOGRAPH

Highlights include:
• Concise review of the literature on neuromodulators
• Practice perspectives and approaches from leading experts
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• Case summaries featuring real patients and injection procedures
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Can the lips be augmented without dermal filler injections? According to Carlos Wambier, M.D., Ph.D., the answer is a resounding “yes.” And we’re not talking about Kylie’s infamous glass challenge. When reviewing results over time of full-face deep chemical peels that included the lips, dermatologists discovered that the lip tissues weren’t just rejuvenated, they were more defined and voluminous.¹

Peeling offers anti-aging benefits that lip injections do not. “There are epidermal changes that take place [after peeling]. You make the lips look younger,” says Dr. Wambier, department of dermatology, Yale University School of Medicine. Not to mention, peeling the lips also stimulates collagen production and enhances lip definition, he says. Notably, however, peeling compared with injectable fillers doesn’t offer the same amount of control of the size and shape of the augmented lips.

Dr. Wambier presented on the topic of peeling the lips at the Peeling Around the World educational session that preceded the AAD Annual Meeting in Washington D.C. earlier this year. The session was hosted by the International Peeling Society. Dr. Wambier’s presentation follows up research published last year in the Journal of the American Academy of Dermatology (JAAD).¹ In the article, Wambier et al. offer a perspective on the phenol-croton oil chemical peel compared with HA fillers, today’s standard for lip augmentation. But why simply fill wrinkled, photodamaged lips when you could fully rejuvenate and naturally augment them?²

Simply injecting the lips is like filling an old wrinkled pillow, says Dr. Wambier. In keeping with the analogy, one could say that the peeling procedure delivers pillow fluffing service along with a fresh new pillowcase. You could argue that peeling the lips is the ultimate way to rejuvenate and enhance their natural shape.

“The degree of lip augmentation achieved depends mainly on the individual size of the lips and croton oil concentration,” write the authors. Other lip anomalies, including actinic cheilitis and actinic dysplasia, can also be treated with the phenol-croton oil peel.

While some may use the classic Baker-Gordon phenol-croton oil peel with harshly stripping the skin of wrinkles and pigmentation, the formulas can be — and currently are — modified, using lower concentrations (with Hetter’s formulas [phenol + croton oil]) to improve the safety profile while also delivering more natural-looking results.²

In Brazil, says Dr. Wambier, physicians classify chemical applications over the skin into two different categories: It’s “chemical cauterization” when used to destroy something, like actinic cheilitis, and it’s “chemical peel” for cosmetic applications.

“There are three things the peel does,” explains Dr. Wambier.

#1 – IT CHANGES THE SKIN
Skin is fresh, new, revitalized, and importantly, without mutated cells.
Dr. Wambier believes the phenol-croton oil peel is a viable alternative to photodynamic therapy and other more expensive, painful and time-consuming treatments for treating precancerous lesions on the lips and around the mouth. He also notes, however, that there’s a need for studies to compare these treatment options.

#2 - IT EVERTS THE LIPS BY VERMILION RETRACTION.

Similar to the “Botox Lip Flip,” the peel creates the illusion of fuller lips by rolling out the upper and lower vermilion.

#3 - IT CREATES VOLUME.

“Volume is related to the surface area of the peel,” says Dr. Wambier. “So, if you peel a small surface area, there would be less collagen formation. More surface area, more collagen.”

In other words, if a patient has thin lips with a straight surface, they don’t have enough surface for noticeable results.

In such cases, an injectable filler may be appropriate as an add-on procedure if the patient desires larger or differently shaped lips.

The perfect candidate, he says, is someone that has aging lip skin, with a large surface area. “They will get a lot of volume and get eversion,” he says.

But the lip peel isn’t for everyone. Dr. Wambier says it’s contraindicated in those with auto-immune diseases, active cancer or any carcinogen exposure, including smokers.

Although phorbol esters found in croton oil are known to trigger cell differentiation and also have anti-cancer and pro-inflammatory properties, they are mainly mediated by protein kinase C activation, the same pharmacological mechanism of ingenol mebutate (topical treatment for actinic keratosis).3

Protein Kinase C also causes cell proliferation (like a fertilizer). If used in the wrong environment, such as co-exposure to carcinogenic chemicals or radiation, phorbol esters promote tumor growth.4

LEARNING ABOUT THE LIP PEEL

Dr. Wambier says he doesn’t believe the active ingredient in these deep peels is part of the general knowledge in dermatology. “The formula that we use that creates this magic — it’s not because of the phenol; it’s not because of water; it’s not because of soap — it’s the croton oil.”

Derived from the seeds of the Croton tiglium tree, which is native to Indonesia, Dr. Wambier describes croton oil as a stem cell stimulant and says this property is what’s responsible for rejuvenating the skin. Phenol, he says, is the ingredient needed to carry the active properties of croton oil deep into the tissues. Phenol is very effective at coagulating old superficial cells and the superficial drainage system: capillaries and lymphatic. Without phenol, the croton oil would only have very superficial effects, and its active substances would be instantly absorbed to the systemic circulation.

When performing the lip peel, Dr. Wambier uses Hetter’s formulas after applying topical anesthesia with 2% to 4% lidocaine. After degreasing the skin to get optimal penetration, Dr. Wambier spreads the solution on the lips using a swab.

Technique considerations include saturation, pressure and number of passes. Saturation can be wet, moist, semi-dry. The drier the saturation, the better the result. The harder you press, the more the peel is absorbed. For lip eversion, the peel needs to be applied to the vermilion boarder.

Although Dr. Wambier uses a wet technique, he says this should be reserved for the experienced lip peeler. “The dry technique is safer, but you have to apply more layers, do more rubbing.”

But the extra work far outweighs the possibility of complications, he stresses. If the solution gets in the mouth, the tongue swells and is very painful for the patient.

“Rubbing,” adds Dr. Wambier, “is part of the art of peeling.”

GETTING STARTED

According to Dr. Wambier, many dermatology residency programs do not have a history of teaching the chemical peel.

“For those who haven’t had that [hands-on training] in residency, they should look for a hands-on workshop,” says Dr. Wambier.

There are many, he says. Before coming to the United States, Dr. Wambier gave monthly workshops on peeling in Brazil. He knows of a plastic surgeon in the Portland, Ore., area and another in Germany who give regular workshops. Then there’s the big theoretical plus hands-on workshop provided by the International Peeling Society annually in conjunction with the AAD. Dr. Wambier has plans to begin offering lip peel training in 2020.

Physician or resident, he says hands-on, supervised training helps to avoid the potential for mistakes when mixing and using chemical peel formulas.

“Dermatology residency programs should teach chemical peeling in general, and the lips are a good place to start because the area is so small, and healing is fast,” says Dr. Wambier.

References


Disclosure: Dr. Wambier has been an advisor for Allergan and Young Pharmaceuticals, a speaker for Galderma and Cynosure, and an investigator for Pfizer, Concert and Eli Lilly.

Carlos Wambier, M.D., Ph.D., Yale University School of Medicine, New Haven, Conn.
Next-level injectable tips

Dr. Heidi Waldorf offers dos and don’ts for toxins and fillers

LISETTE HILTON | Staff Correspondent

Competition for aesthetic patients is increasing, making it necessary for most cosmetic practices to stand out or stand back. Using botulinum toxin, fillers and energy devices creatively can differentiate cosmetic practice, according to dermatologist Heidi A. Waldorf, M.D., of Waldorf Dermatology Aesthetics in Nanuet, N.Y.

“In this day and age when everyone — including docs from other non-cosmetic specialties, no specialty and every NP, PA, RN and esthetician (depending on the state) — is advertising every procedure in our armamentarium, the only way to build a thriving aesthetic practice is the old way: be better,” says Dr. Waldorf. “Distinguishing yourself as an aesthetic expert is as much about what you do as [what] you don’t do.”

Dr. Waldorf says there are dos and don’ts to show “esthetic sophistication” when using botulinum toxin, fillers and energy-based devices. These tips can help aesthetic practices thrive despite the growing competition.

BOTULINUM TOXIN DON'TS

Don't treat the forehead and glabella simultaneously. Dermatologists shouldn’t think they need to treat the forehead at the same time as the glabella for first-time patients, according to Dr. Waldorf.

“The number one complaint I hear from patients who have had toxin elsewhere is that their lines were gone but their brows were heavy,” Dr. Waldorf says. “On a first-time toxin patient who has any brow ptosis or lid hooiding, treat the glabella first then bring the patient back in two to three weeks to assess the frontalis and treat if appropriate.”

Also: Don't overtreat the periorbital area.

“A sincere smile of enjoyment, called the Duchenne smile, requires some movement of the periorbital muscles — smiling with the eyes or ‘smizing.’ If you overtreat the orbicularis oculi in order to remove all the movement that causes crow’s feet, the smile appears fake,” Dr. Waldorf says.

BOTULINUM TOXIN DOS

BUNNY LINES Dr. Waldorf says do treat bunny lines that appear on the sides of the nose during frowning.

CHIN Do treat depressors of the chin — the depressor anguli oris or mentalis, where a few units of botulinum toxin can make a big difference.

PLATYSMA BANDS Do treat the platysma preventively to reduce pull on the jawline, she says.

MASETERS And do treat the masseters in a patient with obvious squaring of the jaw and palpable strong muscles.

“Nine out of ten times, if you ask the patient if he or she has TMJ or teeth grinding, the answer will be yes. The patient gets the benefit of an aesthetic and symptomatic improvement,” Dr. Waldorf says.

FILLER DON'TS

When treating patients with fillers, Don't paint by numbers, according to Dr. Waldorf.

“There is no ‘right’ amount to inject or injection point that works for every patient,” she says. “Look at the patient’s face and keep looking as you treat.”

Also: Don't treat lips on a patient who doesn't have the perioral appearance and holds earring up more evenly, Dr. Waldorf says.

Radiesse and Sculptra for the neck and chest, according to Dr. Waldorf.

Another area that’s a do: the necklace lines of the neck. Dr. Waldorf recommends using a superficial filler like diluted Belotero (hyaluronic acid, Merz Aesthetics). To treat the crepey skin on the neck and chest, she uses hyperdilute Radiesse (calcium hydroxylapatite [CaHA], Merz Aesthetics) or Sculptra (injectable poly-L-lactic acid [PLLA]/Galdermo), which are biostimulators. Do combine tightening treatments like Ultherapy (ultrasound therapy, Merz Aesthetics) with biostimulatory fillers, such as hyperdilute Radiesse and Sculptra for the neck and chest, according to Dr. Waldorf.

DO treat the NOSE

FILLER DOS

HANDS Treat the hands, according to Dr. Waldorf. “Patients are more likely to ask about hands in terms of brown spots and texture, but introduce the idea of hand filler when they complain of getting their mother’s hands,” she says.

NECK & CHEST Another area that’s a do: the periorbital lines of the neck. Dr. Waldorf recommends using a superficial filler like diluted Belotero (hyaluronic acid, Merz Aesthetics). To treat the crepey skin on the neck and chest, she uses hyperdilute Radiesse (calcium hydroxylapatite [CaHA], Merz Aesthetics) or Sculptra (injectable poly-L-lactic acid [PLLA]/Galdermo), which are biostimulators. Do combine tightening treatments like Ultherapy (ultrasound therapy, Merz Aesthetics) with biostimulatory fillers, such as hyperdilute Radiesse and Sculptra for the neck and chest, according to Dr. Waldorf.

EARLOBES Do pay attention to the earlobes. Dr. Waldorf’s tip is to save a little of the hyaluronic acid or CaHA filler that one might use on a patient’s face to re-plump and reshape the earlobes. The added touch is especially satisfying for the older patient or the post-facelift patient. It gives a more youthful appearance and holds earning up more evenly, Dr. Waldorf says.

NOSE Treat the nose. Filler treatment for noses is called a noninvasive rhinoplasty or liquid rhinoplasty. While fillers won’t mimic the results of a surgical rhinoplasty, a liquid rhinoplasty can be used to reshape the nose by narrowing and raising the bridge and dorsum, camouflaging a dorsal hump and raising the tip, according to Dr. Waldorf. Dermatologists might introduce the option of a liquid rhinoplasty as part of a holistic facial rejuvenation, she says.

JAWLINE & CHIN A final filler do: Treat the jawline and chin. Treat not only the pre-jowl sulcus, which can square the bottom of the face, but extend the chin anteriorly and create definition, Dr. Waldorf says. Using botulinum toxin, fillers and energy devices creatively differentiates cosmetic practices, according to Dr. Waldorf. But to get the most out of these dos and don’ts, Dr. Waldorf says dermatologists should be sure to remember one general don’t: “Whatever you do, don’t promise surgical results without surgery,” she says.

Disclosures

Dr. Waldorf is a Merz advisory board member; speaker; Allergan advisory board member; speaker; Galderma advisory board member; Evolus advisory board member; Revance advisory board member, investigator; and Sinclair advisory board member, speaker.
The Overall Landscape for the Treatment of Melasma

Melasma is a chronic skin disease, yet patients often approach dermatologists for immediate improvement, or even a cure. How do you best manage symptoms and expectations?

In this Dermatology Times podcast, featured physician Seema Desai, MD, FAAD, outlines his multidisciplinary approach to the treatment of melasma. Learn about Dr. Desai’s range of therapeutic combinations — including specific uses of hydroquinone, oral tranexamic acid and chemical peels — as well as guidance for patients to maximize adherence and minimize relapse.

Listen Now: dermatologytimes.com/melasma-podcast
Advancements in laser technology

LISETTE HILTON | Staff Correspondent

Aesthetic laser devices are changing rapidly to improve efficacy and safety — some with features straight out of a sci-fi movie.

“We’re seeing a lot more tools that aid the physician to get better results; a lot more automation and more application-driven menus,” according to E. Victor Ross, M.D., skin laser surgery specialist at Scripps Clinic Carmel Valley in San Diego. “There are more navigational features in laser technology, where the end user is going to be able to do assessments based on monitoring of the device with built-in diagnostics.”

In essence, the devices are becoming more automated. Some examples: Sciton is using optical coherence tomography to “pre-look” at the skin from the inside out. The non-invasive imaging technology helps medical professionals assess the skin and provides feedback about what settings might be good for resurfacing. Cynosure has a pigment meter that gives providers proper guidelines for settings based on the color of the skin, according to Dr. Ross.

LASER DEVICE INNOVATIONS
Laser technology advancements present the opportunity to improve nearly every skin aging concern.

The Dermastat handpiece (Cutera) is one such advance on Cutera’s excel V, a 532 nm and 1064 nm device to treat vascular and pigmented lesions. The excel V is a great time-tested technology — it’s been around for about a decade. The technology turned new again and has been made better, according to Dr. Ross.

“The company has done three things to make it better over the last year. They’ve increased the power, which means it has a larger spot size; they have a thicker cooling window, which means it’s more comfortable and safer; and they’ve added this small handpiece, the Dermastat handpiece, which was the handpiece available on the very first model of the Gemini, the precursor to the excel V,” Dr. Ross says.

Using the pencil-sized Dermastat handpiece, dermatologists can navigate easily around the nooks and cervices, like the corners of the nose or the corner of the eye.

For facial rejuvenation, dermatologic surgeon Suneel Chilukuri, M.D., of Refresh Dermatology in Houston, often turns to the 1927 nm thulium laser Lase MD by Lutronic.

“It’s remarkable in terms of what we can do with this laser because we can limit the downtime to a day or less and really see nice changes in terms of skin quality and fine lines. I call it kind of a ‘polisher’ with minimal to no downtime,” Dr. Chilukuri says.

The 1927 nm thulium is a strong contender for patients who aren’t willing to endure the downtime that comes with laser skin resurfacing with a carbon dioxide (CO2) or erbium YAG (er:YAG) laser, he says.

Dr. Chilukuri says that treatment with the Lase MD isn’t painful and there’s no numbing involved. Patients usually are red for about a day.

“Occasionally, if I’m going more aggressively with it, they’ll be a little bit more red and slightly swollen for about three days,” he says. “The Lase MD is not going to be for the deep rhytids or deep static lines that are on the face because it’s not powerful enough unless you do multiple treatments.”

FAT, SKIN TIGHTENING & COLLAGEN
Dr. Chilukuri also has experience with the recently released Accutite (InMode), which he says is an upgrade from earlier radiofrequency (RF) devices.

“Accutite really works well for skin tightening but also for melting small pockets of fat, like the submental fat. For those patients who don’t want the downtime from Kybella (Allergan), Accutite works great. It’s often a one and done. Results continue to improve over six to nine months. We’re also using this device for the lower eyelid for skin tightening. I’m involved with some research on this indication with an oculoplastic surgeon to determine the ideal depth of treatment and the best protocol,” Dr. Chilukuri says.

One of Dr. Chilukuri’s favorite and most utilized devices is BTL’s Exilis Ultra, which is the first technology to combine radiofrequency (RF) and ultrasound in one handpiece, according to Dr. Chilukuri. There isn’t any downtime, although patients might be red for 30 minutes after treatment. Exilis Ultra works well for stimulating collagen production, reaching the ideal temperature whether it’s on the face, the neck, the body — from 41 to 43 degrees Celsius — quickly and painlessly.
“We think its rapid and more evenly spread head is due to the ultrasound energy. It’s an unfocused ultrasound with a unipolar monopolar RF. It’s a fantastic device that I use multiple times a day,” Dr. Chilukuri says.

BTL’s Entone is among the newest devices in the aesthetic realm. It combines acoustic wave and radiofrequency. Dr. Chilukuri says BTL is marketing the Entone for cellulite and is seeking FDA clearance for other indications.

“What we’re seeing in our practice is that Entone works really well for skin tightening especially on abdomen, the décolletage, arms and legs. The biggest advantage of putting both of those technologies inside one handpiece is that you’re able to get to higher temperatures more comfortably for the patient than ever before,” Dr. Chilukuri says.

LONGER LIFE, DUAL WAVELENGTHS & INTERROGATION SYSTEMS

Another hot topic and technological advancement is microneedling with radiofrequency primarily for skin tightening, according to Dr. Ross.

“We’ve done a lot of work with the Genius device (Lutronic). It has a so-called intelligence design where it actually constantly interrogates the skin to look for the maximal deposition of energy,” Dr. Ross says.

There are several problems with radiofrequency microneedling devices, including that the needles oftentimes don’t go in all the way, according to Dr. Ross.

“Lutronic worked on that in two ways. They have a more powerful motor and sharper needles, but more importantly they have this interrogation system,” Dr. Ross says. “If you don’t deliver all the energy that you’re supposed to, it gives you a warning.”

Candela has its new Vbeam Prima pulsed dye laser device. That’s an important advancement because it does things pulsed dye lasers couldn’t do before, according to Dr. Ross.

“It has a longer dye life. It has two wavelengths versus one wavelength,” Dr. Ross says.

ACNE, STRETCH MARKS & SKIN TIGHTENING

One of the lesser known companies that has a good track record is Fotona, which manufactures the multi-application aesthetic laser system, SP Dynamis. The Fotona aesthetic laser is a versatile and powerful device, according to Dr. Chilukuri.

“That’s one of the devices where I think dermatologists — especially those with fellowships in lasers and cosmetics — are going to hit a homerun because there are so many options with this laser. You can use it to treat acne, to treat stretch marks and for skin tightening,” he says.

The Aerolase Neo (Aerolase) is another example of a device that’s revolutionizing acne treatment, according Dr. Chilukuri.

Dermatologists can use the Aerolase Neo on patients with active acne to generate high energy at a safe level to reach the dermis and significantly clear lesions within 24 to 48 hours after treatment, Dr. Chilukuri says.

“The difference between this and the original nd:YAG lasers that we’ve used for ever and ever is the microsecond pulse. This utilizes 650 microseconds which is longer than nanosecond and picosecond pulse durations,” he says.

“Even though the device is physically small — it looks like a little suitcase — the Aerolase Neo is extremely powerful. We use it most often for acne, but we also use it for telangiectasias, rosacea, PIH and for what I call a laser toning procedure where you can tighten up the skin. It’s not as powerful as the Exilis Ultra or the Accutite with a single treatment, but it works quite well with no downtime and is safe for all skin types.”

MULTIPLE SINGLE-SESSION TREATMENTS

Sonia Batra, M.D., M.Sc., M.P.H., medical director at Batra Dermatology in Santa Monica, Calif., and co-host of The Doctors, says she is using multiple devices on the same day to consolidate downtime and give patients more dramatic results. For example, Dr. Batra has several devices from the Venus company and offers patients the company’s Tribella protocol.

“We do intense pulsed light (IPL) which is more for discoloration. We do radiofrequency, which is more for toning and tightening the skin. Then, on the same day we also do Venus’s nanofractional radiofrequency which is a resurfacing handpiece,” Dr. Batra says. “We’re doing this with other lasers and devices in our practice too, where we try to have the patient come in and address a couple of different concerns with different devices on the same day. For example, I frequently will treat vascular lesions with a VBeam pulsed dye laser on the same day as I treat pigment and texture with a PicoSure.”

Dr. Batra says that she sets the energy of each device a bit lower than she might if she were using one device, alone. She does that to avoid complications from stacking heat in the skin.

“We’ve also become much more precise about how we allot our time as our patients and I have to have enough time to do multiple devices in one visit. In the Tribella protocol, for example, the radiofrequency I delegate that to my registered nurse. But the nano-fractional RF and IPL I perform myself,” Dr. Batra says.

As a result of combining devices, patients get results that approach much more aggressive treatments and devices with much less downtime.

“For example, the Tribella protocol addresses both color as well as texture as well as some aspects of laxity, with usually about three days of being pink and puffy. Many patients would prefer a series with this protocol as compared to a full blown fractional CO2 laser, which would be 7 to 10 days of downtime,” Dr. Batra says.

These technologies are catching up with aesthetic providers’ and patients’ wishes, according to Dr. Chilukuri.

“I think the next steps are more automation and interaction between the operator and the device. A lot of things are happening, I think we’ll see things happen even faster in the next five years than in the last five years,” Dr. Ross says.

Disclosures

Dr. Batra has worked as a consultant for Venus. Dr. Ross is a consultant with and has done research for Lutronic and has received honoraria from Candela. Dr. Chilukuri has worked as a consultant and speaker for Alastin. Aerolase, Allergan, BTL, Cynosure, Eurosmed, Goldstarma, InMode, Lutronic, PCA Skin, Sander, Thermavant, Under the Skin, and ZO Skin.
Looming changes in healthcare policy

BOB KRONEMYER | Staff Correspondent

A change in government payment policy for dermatologists and other physicians in selecting office coding and billing for evaluation and management (E/M) is scheduled to begin January 2021.

“The Centers for Medicare & Medicaid Services (CMS) decided over a year ago that it wanted a decrease in the documentation burden on the physician,” said Mark Kaufmann, M.D., an associate clinical professor of dermatology at Icahn School of Medicine at Mount Sinai in New York. “CMS proposed creating a new coding system with fewer codes, thereby creating less of a differential and less work that would need to be done by the physician to choose a code when it came to judging a patient’s office visit and the way they would bill that visit.”

CMS provided a timeline to institute the change, in order to allow the American Medical Association (AMA), the Current Procedural Terminology (CPT) code and the AMA’s Relative Value Scale Update Committee (RUC) to come up with an alternative plan. This past July, CMS proposed to institute this alternative plan.

“The codes remain the same, except for the deletion of one of the E/M codes, but the way that we choose the codes has changed,” says Dr. Kaufmann, who spoke on pending healthcare policy changes relevant to the practicing dermatologist in August at the annual meeting of the Pacific Dermatologic Association in San Diego. “The change in coding will require a re-education of all clinicians in the country over the next 12 months. However, I believe this change in the paradigm for the way we code office visits will be a net positive for the specialty.”

Dr. Kaufmann expects the coding changes to be finalized in November; yet they will likely not take effect until January 2021.

The new coding will be predicated on either time or medical decision making (MDM). “Currently, everyone counts the number of bullet points in their notes that are related to patient history and physical examination,” Dr. Kaufmann said. “Those bullet points will no longer be necessary for billing purposes, although some may be required for good medical care and for medical liability reasons.”

Dr. Kaufmann expects that most dermatologists will use MDM rather than time as their code determinant.

Modifier 25 is a second potential hurdle for the field of dermatology. “This is a billing situation when we do a procedure on the same day as an office visit,” Dr. Kaufmann says. “Currently, everyone counts the number of bullet points in their notes that are related to patient history and physical examination.”

CMS has decided not to finalize changes in reimbursement for Modifier 25 visits, for the time being, in response to

The change in coding will require a re-education of all clinicians in the country over the next 12 months. However, I believe this change in the paradigm for the way we code office visits will be a net positive for the specialty.”

Mark Kaufmann, M.D., Icahn School of Medicine, Mount Sinai, New York
Periorbital Resurfacing: Dos and Don’ts

Compared to alternatives, CO2 lasers are the most functional and comprehensive treatment for periorbital wrinkles and other signs of aging. But as with any approach, there are risks to overtreatment. So how do you most effectively use this tool?

In this Dermatology Times podcast, Dr. Joe Niamtu describes his success with using the CO2RE laser system, advises how to set reasonable expectations for both you and your patients, and offers guidance on taking full advantage of the CO2RE laser’s capabilities.

Listen now: dermatologytimes.com/lasertherapy
smart thermostats, home security systems, fitness watches and other devices that connect with each other and the internet make up what is called the Internet of Things (IoT). And these devices are ubiquitous these days.

There is another world of internet-connected devices that has not caught on quite so quickly: The Internet of Medical Things (IoMT). Andrew Keller, M.D., chief medical officer and chief medical information officer for Western Connecticut Medical Group describes the IoMT as “devices that can collect and exchange data — either with users or other devices — via the internet, and are used to allow doctors to be more aware of a patient’s condition on a real-time basis.”

The IoMT could potentially make managing chronic conditions more efficient and more cost-effective, once they can be used safely and effectively.

Clinical trials are just beginning to prove the benefits of some of these devices. A May 2018 study in JAMA Cardiology found that an Apple watch with an app called Cardiogram could detect abnormal heart rhythms with close to 97% accuracy.

“When this data is transmitted via the internet to the doctor — or someone at the monitoring station — the doctor can adjust medicines or take whatever steps he or she feels necessary,” Keller says.

Clinical trials are beginning to prove the benefits of some of these devices.
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Better Instagram results
Expert discusses 8 ways to grow your practice following

JUSTIN KNOTT | President, Intrepy Healthcare Marketing

Instagram has quickly become a titan in the world of social media marketing. This has been no truer a case than in the health and medical industry. People are taking their health into their own hands, and in doing so, are actively looking to connect with providers and practices that can aid them in their journey.

Practices have long since realized the benefits an active and engaged social community could have on their practice or hospital system. Yet, they often struggle to ever realize that value and achieve success. One of the most common questions I receive from clients and acquaintances in the healthcare world alike is: “how do I grow an active following on Instagram?”

It can seem like a real head scratcher: Do people care about what we are doing in our medical practice? I understand them liking, following and engaging with a clothing or product company, but us?

Well, fear no more. I am going to walk you through eight different proven tactics that we use week-in and week-out to grow medical Instagram accounts.

Don’t just take my word for it, you can see lots of practices and providers killing it on Instagram using these same tactics.

Step #1–
CREATE YOUR PERFECT PATIENT AVATAR
Before you start any marketing or advertising initiative, much less in social media, you need to define who your ideal target patient is and create that patient profile, or avatar. Just like you would target a specific audience to whom to sell a product, every practice or specialty has a specific type that tends to walk through the doors. Some practices may have a broader patient scope than others. For instance, a dermatologist may have two avatars or patient profiles: one for dermatologic procedures and one for cosmetic/aesthetic procedures.

Thus, to find where your patients are on social media, you need to understand them:

- Where do they hang out?
- What types of restaurants do they like?
- What do they do for hobbies?
- What type of fitness are they into? Yoga? Crossfit?

Answering these questions will allow you to know where to go on Instagram to leverage profiles that have these types of followers.

Step #2–
FOLLOW & ENGAGE — GET SOCIAL!
Now that you have developed those patient profiles, it’s time to start creating a list of hashtags and handles that closely align with the lifestyles of the people in your target demographic.

Instagram is about being proactive, not passive. You need to be on the platform daily following, liking, commenting and engaging in your community. The more you do this, the faster your account will grow. For instance, if you are trying to grow your patient base of post-college graduate women, checking out who your local barre or cycling studio is following and who is following them is a great place to look.

Step #3–
LEVERAGE INSTAGRAM STORIES
Instagram stories are all the rage. Practices have been late to jump into the game of leveraging them.

Generally, any new tool or product releases that major social media platforms come out with can be to your advantage and it’s worth figuring out a way to leverage them. The reason? The platforms want to push adoption so they will usually give preferential treatment to those tools in terms of feed placement, increased organic reach and engagement.

The same holds true for Instagram Stories. Instagram wants a continuous stream of new and live content and the best way to do so is with Stories. Therefore, if you really want to explode your organic reach you need to extend beyond just posting on your wall and start adding content regularly to Instagram Stories.

Step #4–
GET YOUR PROVIDERS INVOLVED
Long-term social media success ultimately takes buy-in by all the providers in your office. You will struggle to gain traction over time if you don’t succeed in getting everyone involved.

Take a look around Instagram at the medical practices having significant success. The providers tend to play a critical role in the content that is being produced.

Getting your providers involved has a two-fold effect:

- It will continue to establish each as a thought leader in their space online, making it more likely for patients to find or seek them out.
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Step #5—BRING PATIENTS INTO THE OFFICE & OPERATING ROOM
People love seeing authenticity on social media. By inviting them into your office and showcasing what you do, whether it is in the clinic or the operating room is big.

Take a look at what Sandra Lee M.D., a.k.a. Dr. Pimple Popper, has been able to accomplish with a camera and some dermatologic tools. She has amassed millions of YouTube, and Instagram followers, her own television show and quickly become one of the most sought-after dermatologists in the country, simply by letting people into her office to see her in action. Come to find out, people really, really like to watch gross pimples being popped.

If the idea of shooting video is overwhelming, consider this:

Jump on Amazon and purchase a ring light and lapel mic to ensure the lighting and sound quality are good and then point and shoot with your phone. Then hire an agency to create some professional video animation templates that include an intro, lower-third overlay and outro with a clear call to action.

High-end templates will add a level of professionalism to your videos and ensure brand consistency.

Step #6—GET ON THE INFLUENCER MARKETING TRAIN
Why battle uphill trying to grow your account when you can leverage people that are already there and serving your target audience? That is where influencer marketing comes in. Influencer marketing is essential leveraging someone else’s already established audience to get your brand message in front of their followers. It works so well because they have already established trust with their audience. Pick the right people, and it will do wonders to drive new brand awareness and patient growth.

There are a few keys to consider when leveraging influencer marketing:

- Follower count does not always matter. You would rather have a local account with 2,000 super-targeted, local, potential patients than an account with 1 million followers from all over the world.
- Make sure the terms of your arrangement are very clear for what they get and what you receive in return. A contract is recommended here.

Influencer marketing can be utilized in many different ways for the benefit of the practice. Including: promoting a product or service, showing a demo, sharing a REAL patient success story your audience can connect with and much more.

Step #7—USE THE RIGHT HASHTAGS
Hashtags are a core component of how Instagram information is disseminated, found, and consumed. All too often, however, practices are using the wrong hashtags or not using them at all, and it is killing their reach.

When searching for the right hashtags, it is beneficial to leverage a free tool. There are several that are out there that can help you see what hashtags are trending and being used for particular topics.

My general rule of thumb when it comes to the right mix of hashtags is this:

- Make sure you use the full allotted 30 hashtags that Instagram allows per post.
- Have a blend of tags related to post topic, your city, target demographic as well as anything that may be trending.
- Try to stay away from hashtags that are so popular that your post will be buried in a matter of seconds by a flood of new content from bigger accounts than yours, for instance, #beauty #love #happy.

Influencer marketing can be utilized in many different ways for the benefit of the practice. Including:

- Promoting a product or service, showing a demo, sharing a REAL patient success story your audience can connect with and much more.

Let’s say you’re a dermatology practice located in Atlanta and posting a video demonstration of a new laser skin resurfacing procedure. You could incorporate a blend of these types of hashtag:

- #laserskincare #laserskinresurfacing #laserandinjection #atlanta #atlantafamilies #atlantafitness #momsknowmakeover #buckheadatl #aesthetics

There are not 30 here, but you get the general idea of the ideal blend that should be used.

Step #8—ENCOURAGE EMPLOYEE INVOLVEMENT
Last, but certainly not least, is get your employees involved and excited about the success of the Instagram program.

You would be hard-pressed not to be able to find several of your employees that are very active on their social media in their personal life. Put a program in place that not only encourages but rewards your employees for getting onboard with helping promote the practice to their sphere of influence. You could even try a monthly employee takeover day where they handle content creation for the day on the account.

Make sure you set guidelines and parameters, but this can be a great way to gain access to new audiences in the local community. Consider having signs or posters created that the employees can use to have fun with patients and to create more visual content.

WRAPPING UP
Instagram marketing for medical practices is one of the most effective ways to reach new patients and broadcast your content. Be patient but proactive with the growth and don’t be afraid to try new things. But, most importantly, be engaged, be consistent and create a structure for provider involvement.

Follow these tips, and your practice will be well on its way to cultivating an active community of loyal patients.

If you are looking for more tips to grow your Instagram following make sure to check out this 13 Instagram Marketing Tools Every Practice Needs ASAP eBook. &nbsp;&nbsp;▼

Disclosures
Justin Knott is the president of an award-winning healthcare marketing agency, Intrepy Healthcare Marketing. He founded the agency in 2014 to bring a specialized approach to marketing for medical and dental practices. His primary focus is in digital marketing, social media marketing, medical SEO strategy, and advertising to help practices generate new, targeted patients. Justin has been published as an SEO and marketing thought leader in dozens of online publications.

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“Hashtags are a core component of how Instagram information is disseminated, found and consumed. All too often, however, practices are using the wrong hashtags or not using them at all, and it is killing their reach.” Justin Knott, President, Intrepy Healthcare Marketing, Atlanta
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In an interview with Cardiology Today, Jagneet P. Singh, M.D., Ph.D., Cardiology Today editorial board member and associate chief of the cardiology division at Massachusetts General Hospital, described this technology as a “game changer.”

“Since the sensor and its ability to record ECGs and classify the heart rhythm is FDA-approved, it will begin to find its way into clinical practice and potentially into the electronic health record,” he says. “It will certainly create a heightened awareness about rhythm disturbances and atrial fibrillation.”

In a separate editorial, Dr. Singh expressed cautious optimism about trends in digital health, writing that “both [artificial intelligence] and digital strategies will make the delivery of care both more patient-centric and cost-effective. The advances in mobile and wearable devices and sensors will help initiate the transition from conventional transactional care to a more continuous form of managing our patients.”

A PRESCRIPTION FOR VALUE-BASED CARE
The IoMT could also improve physicians’ bottom line. According to data published in 2017 in the American Journal of Preventive Medicine, 86% of healthcare expenditures are for people with chronic conditions, including cardiovascular disease, diabetes, obesity and dementia.

And these patients are far more likely than others to end up in the emergency department. A 2015 study in American Journal of Managed Care found that patients with the highest care utilization rates, particularly those with multiple chronic conditions, were five times more likely to visit the emergency department than patients with low utilization rates.

Being able to proactively manage these time- and resource-intensive conditions could save money as well as lives. “A device that signals when the patient’s health is changing and alerts the doctor could make it possible to intervene early and reduce hospitalizations and improve patient outcomes,” says Steven Waldren, M.D., vice president and chief medical informatics officer at the American Academy of Family Physicians.

“This technology allows you to manage people with chronic conditions more efficiently and effectively without them having to come into the office,” he says. “As folks are moving toward value-based care, being able to manage patients with chronic conditions at home could help practices be more profitable.”

IoMT technologies can also improve patient engagement. According to Accenture’s 2019 Digital Health Survey, 53% of patients surveyed would be more likely to choose a primary care provider who uses remote or telemonitoring devices to monitor and record health indicators. That’s up from 39% in 2016, and the trend is more noticeable in younger patients. “There’s a lot of push now for this type of care from a subgroup of patients who want to have their health data themselves,” says Dr. Waldren.

Payers are pushing for it, too. “If Medicare will pay doctors to use these technologies, then they’re more likely to use them,” says Dr. Waldren. And Medicare is doing just that. The CMS 2019 Fee Schedule includes three additional CPT codes for remote patient monitoring devices.

According to the Center for Connected Health Policy 2019 State Telehealth Laws and Reimbursement Policies Report, there has been a slight increase in state Medicare programs that reimburse for at least some remote patient monitoring.

SECURE AND STANDARDIZED
This world of increased connectivity does pose challenges. However, Healthcare data is a prime target for hackers, and any internet-connected device poses a risk. “If you’re going to use these devices with your patients, you need to make sure that the devices are HIPAA-compliant and being used in a HIPAA-compliant way,” says Ron Sterling, a consultant who specializes in health-care IT.

Consumer-oriented devices — fitness trackers, nutritional programs, and so on — are not necessarily HIPAA compliant, and patients are under no obligation to use these new technologies not only responsibly, but effectively. “Doctors need to understand that just adopting a piece of technology is not that helpful,” says Dr. Waldren. “You need to identify a particular problem you have with your patient population and find a solution to address that. Don’t just be enchanted by bright and shiny new tech; make sure it’s something that has clinical value.”

Dr. Keller recommends assessing clinical value the same way as any other treatment. “I would ask the normal questions about sensitivity and specificity,” he says. “There is lots of information available at presentations and sessions at national conventions, and vendors usually have displays set up.”

The IoMT may not be as widespread as the IoT, but it is growing. “The fact of the matter is these devices are here, they’re going to be here, and patients want to use them,” says Mr. Sterling. Savvy physicians will be prepared.

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SOCIAL MEDIA PERSONAS | Continued FROM PAGE 52

put all the ingredients together. And their procedures are often trademarked — get over yourself.”

THE MULTI-LEVEL MAMA
These people push multilevel marketing lines at the expense of science. “There’s a very creative use of photography, and I say that very nicely. We all know what Photoshop is.” When Dr. Buford sees such posts, he’s been known to call out those doing the posting, and he encourages colleagues to do likewise.

To understand where social media is heading, he suggests reading The Death of Expertise: The Campaign against Established Knowledge and Why It Matters by Tom Nichols. “You have the anti-vaxers arguing with you online, even though you went to medical school or nursing school and know 100,000 times more than they do.”

CUTTING THROUGH THE CLUTTER
To cut through social media clutter, he recommends combining the credibility of the expert with the eye candy of an authority. An expert has verifiable credentials, peer recognition and a client-centric online presence, says Dr. Buford, but often a small following. “It’s like having a Picasso in the basement.”

Conversely, self-appointed healthcare gurus often have huge, but not well-educated, followings. “If you look at who follows them, it’s not other medical professionals — it’s bots and consumers.” Melding the best of the expert and authority personas allows one’s online presence to strike a happy medium, says Dr. Buford.

He also recommends educating patients about what to look for online. “Tell them just because someone makes a claim doesn’t necessarily make it true.”
strong pushback from medical advocacy groups. But CMS has not ruled out potential changes in the future.

In addition, several commercial payers have already instituted a decrease in reimbursement for Modifier 25 visits, according to Dr. Kaufmann. Global period codes are a third challenge faced by dermatologists. “For instance, packaged into the payment for destroying a wart on a patient’s arm is an office visit, which is assumed to take place over the next 10 days,” Dr. Kaufmann said.

Previously, CMS has sought to eliminate the global visits included in the global period codes commonly used by dermatologists. But it was only prevented by an act of Congress. “CMS is currently revisiting this issue,” Dr. Kaufmann says.

There are also efforts by medical advocacy groups to lessen physician regulatory burden imposed by the Medicare Access and CHIP Reauthorization Act (MACRA) and CHIP (Children’s Health Insurance Program) and the Merit-based Incentive Payment System (MIPS), in order to delivery both more efficient care and decrease rates of physician burnout.

The MIPS program will probably have some changes next year. The minimum MIPS score required to be exempt from the 9% penalty in 2022 will likely be 50% higher than this year, which will make it more difficult to simply “avoid the penalty.”

“The time has arrived for dermatologists to decide if they will be ‘all in’ in the MIPS program or just ‘take the penalty,’” Dr. Kaufmann says.

“Overall, there are a number of challenges in the reimbursement landscape that we face in the field of dermatology,” Dr. Kaufmann says. “None of them are insurmountable, and it is important that people are aware of the issues, as well as the areas that we are advocating for and against.”

Dermatologists should become advocates for these issues, whether on the local, state or national level, according to Dr. Kaufmann.

“CMSG’s ultimate goal is to decrease the cost of healthcare in the country by shifting from volume-based to value-based healthcare,” he says. “We all know where we are going to end up, but the road has been a long and winding one. Each detour that goes up leads to unintended consequences, and we need to be prepared for anything that comes our way.”

Disclosures

Dr. Kaufmann reports no relevant financial disclosures.
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FACE CREAM BRIGHTENS DULL SKIN
Neutrogena’s BRIGHT BOOST BRIGHTENING GEL MOISTURIZING FACE CREAM WITH NEOGLUCOSAMINE improves skin tone and texture, and reduces the appearance of fine lines, says the company. The formula contains neoglucoamin, AHA, PHA and mandelie acid, which work together to resurface skin and boost cell turnover.

FOR MORE INFORMATION: Neutrogena.com

A DIFFERENT SPOT TREATMENT FOR ACNE
Hero Cosmetics’ MIGHTY PATCH offers patients the ability to spot treat pimples as they appear. The 12-mm circle acne patches are clear and designed for all skin types. Users can apply the patch overnight or wear them during the day. In addition to deterring picking or touching, the latex-free patch contains hydrocolloid, which draws out impurities and reduces redness and inflammation, according to the company.

FOR MORE INFORMATION: heroocosmeticsus.com

EYE CREAM BRIGHTENS DARK CIRCLES
The Inkey List recently added BRIGHTEN-I CREAM to its skincare line. The formula features hyaluronic acid to hydrate undereye skin, and a potent vitamin C alternative called Brightenyl to brighten dark circles and even skin tone, the company says. The product can be used alone or in combination with eye makeup.

FOR MORE INFORMATION: beforebeauty.co.uk

MOISTURIZER MAY HELP LIGHTEN SKIN
Sesderma’s HIDRADERM TRX BODY MILK 400 ML hydrates skin with hyaluronic acid and lightens skin with ingredients that block the synthesis of melanin, according to the company. Its lightening ingredients include 4-BuHi-resorcinol (which acts directly on melanogenesis and inhibits TRP-1) and franexamic acid (which blocks other enzymatic steps during the melanin synthesis process).

FOR MORE INFORMATION: sesdermausa.com

FOOT MASK RELIEVES DRY FEET
Aveeno’s REPAIRING CICA FOOT MASK may help patients with dry or sensitive skin on their feet. Containing shea butter and prebiotic oat, the mask is designed to hydrate the skin and improve skin barrier function by healing problem skin. The product is paraben- and fragrance-free and is packaged to include one pair of foot masks for single use.

FOR MORE INFORMATION: aveeno.com
PSORIASIS/SKIN CANCER ADVANCES

Methotrexate was approved for the treatment of psoriasis in the 1970s, but its widespread adoption for the treatment of severe psoriasis was slow to gain traction.

Theodore Tromovitch, M.D., and Sam Stegman, M.D., present skin cancer cases using a fresh tissue Mohs technique at the annual Chemosurgery Conference in December 1970. They subsequently published an 8-year study reporting a 97.2% cure rate for 532 lesions.

SKIN TYPING
Harvard dermatologist, Thomas B. Fitzpatrick, M.D., created a phototyping scale to classify human skin color, which is used today to determine how different types of skin respond to sun exposure.

DERMAL FILLERS
Collagen (Zyderm, Allergan), approved in September for the correction of contour deficiencies, leading the way for other filler materials to join the market.

PHOTOTHERMALYSIS
R. Rox Anderson, M.D., and John Parrish, M.D., published the first article on the use of the pulsed dye laser's selective photothermolysis “Mechanisms of Selective Vascular Changes Caused By Dye Lasers.”

TATTOO REMOVAL
Q- Switched Ruby, approved for tattoo removal in 1989, followed by approvals for Nd:YAG (1991), and Alexandrite (mid-1990s) for tattoo removal.

LASER HAIR REMOVAL

BILOGICS FOR PSORIASIS
While biologics were discovered decades earlier, biologics made a splash in the specialty starting in 2003 for the treatment of moderate-to-severe psoriasis. The first biologic for psoriasis, alefacept (Amevive, Astellas Pharma US), was approved by the FDA in 2003 and was later withdrawn from the market, but many others followed.

INJECTABLE FILLER MATERIALS BECOME APPROVED
Injectable filler materials became approved and were introduced to restore the aging face. Collagen, approved in 1981, lead the way. The first hyaluronic acid filler, approved in 2003 for the correction of moderate-to-severe facial wrinkles and folds, became a game changer.

DERMAL FILLERS
Hyaluronic acid, Poly-L-lactic acid, and HA with lidocaine became approved in 2006.

TRETINOIN CREAM
“Tretinoin happens to be the retinoid that is investigated more than any other retinoid implicated in the treatment of intrinsic or photoaging. Although tretinoin has been used in dermatology since the 1960s, its potential in the treatment of aging was realized no earlier than in the 1980s,” according to a paper published 2006 in Clinical Interventions in Aging.

ISOTRETINOIN
FDA approved Isotretinoin in 1982 for treatment of severe recalcitrant nodular acne.

TUMESCENT LIPOSUCTION
Jeffrey Klein, M.D., first described the tumescent technique for liposuction at a scientific meeting in 1986 and published his result in the Journal of the American Academy of Cosmetic Surgery in 1987.

BOTULINUM TOXIN TYPE A
Ophthalmologist Jean Carruthers M.D. and dermatologist, Alastair Carruthers M.D., published their first report on the cosmetic use of botulinum toxin.

BOTOX
Neurotoxins for cosmetic use started with the approval of Botox (onabotulinumtoxinA) in 2002 to temporarily improve the appearance of moderate-to-severe frown lines, according to maker Allergan.

DERMAL FILLER
Poly-L-lactic acid approved in 2004 for correcting signs of facial lipatrophy.

HEMANGIOMA TREATMENT
The FDA approved propranolol hydrochloride (Hemangiot, Pierre Fabre Pharmaceuticals) on March 14, 2014, for the treatment for proliferating infantile hemangioma requiring systemic therapy.

BILOGICS FOR ATOPIC DERMATITIS
On March 28, 2017, the FDA approved dupilumab (Dupixent, Sanofi and Regeneron Pharmaceuticals) injection to treat adults with moderate-to-severe eczema.

REFERENCES
THE MANAGEMENT OF
ATOPIC DERMATITIS
ACROSS GENERATIONS
THE MANAGEMENT OF 
ATOPIC DERMATITIS 
ACROSS GENERATIONS

PANELISTS

Peter Lio, MD, is a clinical assistant professor of dermatology and pediatrics at Northwestern University Feinberg School of Medicine in Chicago, IL. He received his medical degree from Harvard Medical School and completed his internship in pediatrics at Boston Children's Hospital and his dermatology training at Harvard, where he served as chief resident in dermatology. Dr. Lio is the founding director of the Chicago Integrative Eczema Center and currently serves as a board member and scientific advisory committee member for the National Eczema Association. He has authored more than 100 publications and has contributed to the publication of two textbooks.

Robert Sidbury, MD, MPH, is a professor in the department of pediatrics at the University of Washington School of Medicine in Seattle, WA, and chief of the division of dermatology at Seattle Children's Hospital. His clinical and research interests include atopic dermatitis, vascular tumors of infancy, vitamin D, and pediatric health services. Dr. Sidbury was co-chair of the American Academy of Dermatology Consensus Guideline Committee for the management of atopic dermatitis.

Emma Guttman, MD, PhD, is the Sol and Clara Kest professor of dermatology, vice chair for research in the department of dermatology, director of the Center for Excellence in Eczema, and director of the Laboratory of Inflammatory Skin Diseases at the Icahn School of Medicine at Mount Sinai Medical Center in New York. Dr. Guttman's major areas of clinical focus include atopic dermatitis and contact/occupational dermatitis. She has done groundbreaking research and published extensively on inflammatory skin diseases.
ATOPIC DERMATITIS (AD) is a chronic, relapsing skin disease commonly seen by pediatricians and dermatologists, although its prevalence in older populations is on the rise. The management of AD has traditionally involved corticosteroids, nonsteroidals, and other topical agents. In recent years, however, systemic biologic therapy has been introduced. New-onset AD is relatively straightforward to diagnose in young children, but it can be more complicated in older patients.

In this supplement, three physician experts discuss the differences in presentation and treatment of new-onset AD across generations.

AGE-BASED DIFFERENCES IN AD

DERMATOLOGY TIMES: How common is new-onset AD after early childhood (ie, after age 5 years)?

Peter Lio, MD: Certainly, most cases of new-onset AD will appear before age 5 years, somewhere in the neighborhood of 90%.1 The remaining group of individuals develop de novo AD later, even into adulthood, and we know a lot less about what drives the onset of their condition. There certainly are some adults who have had AD in a mild form since childhood but just never had it recognized as such until they became older and sought medical help for their symptoms.

DERMATOLOGY TIMES: How often do young children diagnosed with AD have a family history of the condition?

Robert Sidbury, MD, MPH: In approximately 80% of all cases, patients diagnosed with AD will have a family history of AD, asthma, hay fever, allergies, or immunoglobulin-E reactivity to certain foods.2 That said, the manifestation of the condition doesn’t really differ in young children with and without a relevant family history. The rash itches the same way, manifests and progresses in the same areas, and seems to react similarly to triggers such as temperature and humidity.

DERMATOLOGY TIMES: What is different about the diagnostic workup for new-onset AD when you are dealing with teens, adults, or the elderly population compared to young children?

Dr. Lio: It’s also important to remember that AD can change its appearance and distribution in a given patient over time. That may, as Dr. Sidbury noted, be related to exposure to something like pityrosporum yeast on the skin. It may also have to do with occupational or environmental exposures, changes to the microbiome, or perhaps other factors that we do not yet fully understand.

DERMATOLOGY TIMES: Is the diagnosis of AD often delayed in older patients whose primary care physician or other provider simply doesn’t have the condition on their diagnostic radar screen?

Dr. Lio: When I did my medical training, AD was considered almost exclusively a pediatric disease. New-onset adult AD was considered unique and interesting. As residents, those were the patients we would all want to look in on and discuss because they were such fascinating cases.

In today’s environment, new-onset adult AD is beginning to be recognized as an important disease in its own right, with an incidence as high as 10% of all cases of new-onset AD.4

But there are still some unresolved questions. Is that increasing incidence a real trend, or is it an epiphenomenon? Is this something where now that we’re talking...
about it more, we’re finding it more in the general pop- 
ulation? It’s hard to know whether the incidence of 
new-onset adult AD is actually on the rise or whether it’s 
been there all along.

The reason why AD is more difficult to diagnose in 
adults compared to young children is because there are 
a variety of other entities that mimic the condition that 
are uncommon in young children but more common in 

**TABLE**  HANIFIN AND RAJKA CRITERIA FOR THE 
DIAGNOSIS OF AD

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<tr>
<td>□ Itch when sweating</td>
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<tr>
<td>□ Intolerance to wool and lipid solvents</td>
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<tr>
<td>□ Perifollicular accentuation</td>
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<tr>
<td>□ Food intolerance</td>
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<td>□ Course influenced by environmental and emotional factors</td>
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<tr>
<td>□ White dermographism, delayed blanch</td>
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IgE = immunoglobulin E.

Source: Hanifin JM, Rajka G.3

adults. In particular, cutaneous T-cell lymphoma can look a lot like severe AD. That is an extremely rare condition in children. Contact dermatitis may be a mimicking diagnosis, but it also can be a comorbidity of AD, exacerbat- ing the condition and making the rash and itching worse than it would be otherwise. Again, although it can be seen in the pediatric office, it is much more common in adults exposed to a broader environment.

**Dr. Sidbury:** Pediatricians certainly are seeing babies with diaper dermatitis due to contact allergies with products in the baby’s diaper. Additionally, there are children who are allergic to nickel, which is a common juvenile expo- sure. Perhaps the pediatric community should be thinking more about contact dermatitis as a possible diagnosis, but it is clearly still more of an issue for adult patients.

**DERMATOLOGY TIMES:** How long do older patients display some of the primary symptoms of new-onset AD before they will eventually end up in your practices?

**Dr. Lio:** There’s no doubt that I see a range, although there is a personal bias because I tend to see more se- vere cases referred to my practice. That said, I see many individuals who have been suffering for a few months and are frustrated that they’re not getting the proper diagnosis or proper treatment plan, but I also have many patients who have been suffering for years.

When I’m talking to pediatricians or primary care phys- sicians, I’ll tell them there is a broad misconception that everyone who has new-onset AD as a young child is go- ing to grow out of the disease. I see a lot of these patients 25 or 30 years later who are now angry because they were told for years that the disease would simply go away with age and yet they have never “grown out of it.” It is true that most young children with AD will eventually grow out of it, but that is not a justification to avoid treating the condition. It is not yet possible to predict how long an individual patient’s symptoms are going to last.

**Dr. Sidbury:** Do you have adult patients who had given up on dermatology, perhaps because we had nothing sub- stantial to offer them, who are coming back into the fold now that there are treatments that can make a difference?

**Dr. Lio:** Absolutely. A lot of times, it’s the parents of children I am seeing who are the ones I will eventually treat. They have their children with them who are miser- able, but when we start talking about the new options available to treat their child’s AD, mom or dad will pull
up their sleeve to show me their eczema and ask if they could come in for a separate assessment on their own.

DERMATOLOGY TIMES: Because of the unpredictable nature of AD, what do you tell young children and their parents about the likely progression of the condition? Do you avoid telling them it is something they will likely grow out of naturally?

Dr. Sidbury: I do avoid that language. Now, I don’t avoid the idea that there’s hope, because parents are typically distraught and not sleeping and everyone’s stressed out. To take away the idea that their child will likely grow out of the condition is just cruel. The language I use is that their child’s condition will likely evolve. Some parents may already see an evolution from a condition that was more extensor based and facial when their child was a baby but then becomes more flexural as their child gets a bit older. I will often tell parents that this evolution will likely continue with the hope that, by the time their child turns age 5 or 6 years, they may be able to simply use occasional moisturizer to manage any lingering rash.

Dr. Lio: There are families who come to us looking really despondent and discouraged, so we do need to give them hope. I don’t think there is anything wrong with telling a family, “Don’t worry. Time is on our side. It is probably going to get better.”

DEVELOPMENT OF NEW-ONSET AD

DERMATOLOGY TIMES: In a general sense, how does AD develop in babies and toddlers?

Dr. Sidbury: The classic presentation of AD is when the infant will start to have facial redness on the cheeks that gets bumpy. Initially, parents will often link this to food, which is logical in babies when half of their food ends up on their face. Food allergies are therefore often the first thought. But then the infant will start getting the same sort of itchy, extensor-based rash on their arms and sometimes on the trunk. The rash typically spares the underarm and diaper region. The elbows and knees may be involved in a little bit older child.

DERMATOLOGY TIMES: How does the developmental process differ in adult patients?

Dr. Lio: In adults who have had the condition since childhood, their severity of disease tends to follow a J-shaped curve. Their symptoms were bad when they were young children, but then these go into a relatively quiet phase for a few years before picking up again. In my experience, it’s typically patients in their late teens or early 20s who notice their symptoms getting worse. That’s one group of patients.

A second group of patients, those with true new-onset or de novo disease, will often trace back the onset of their symptoms to some sort of specific trigger. I find that if I question these patients long enough, a lot of them will remember getting an itchy rash on their arms or legs that they figured was due to some sort of irritation, such as a contactant. But then that rash either didn’t go away or went away and flared up a few weeks later. For this group of patients, it does seem that there was a triggering event, either a contact dermatitis, allergic reaction, viral exanthem, or some other type of insult that triggered the onset of symptoms. Many patients will often tell you they had sensitive skin as a child, but it was only after this triggering event that they demonstrated signs of AD.

DERMATOLOGY TIMES: What about new-onset elderly AD? How does the condition develop in those patients?

Dr. Lio: New-onset elderly AD is a relatively recent phenomenon, but it’s a real thing. These are generally patients older than age 60 or 65 years. In my experience, these are patients who tell me they never had any symptoms consistent with AD as adults.

Their symptoms typically start out with dry skin and itching. That often naturally occurs as we age because our lipid synthesis is down and our skin barrier decreases. Once the dry skin and itching start, that’s when immune activity will begin in some of these individuals. Elderly patients have immunosenescence, which refers to the gradual deterioration of the immune system brought on by natural aging. It becomes a paradox. These are patients whose immune system is a bit weakened, yet they develop what is considered to be an inflammatory disease. It’s an interesting phenomenon that we don’t yet fully understand.
TREATING AD: AGE-BASED APPROACHES

DERMATOLOGY TIMES: What do you typically set as the primary goal of treatment when talking to the families of babies and young children with AD?

Dr. Sidbury: My primary goal is to decrease the itch. A lot of the secondary issues such as sleep deprivation stem from the itchiness of eczema, so if you solve that one problem, you’ve solved other downstream problems as well. You need to make the child more comfortable. A secondary goal, when appropriate, is to focus the parents’ attention on the value of proper skin care as a first priority and less on potential contributors such as food allergies absent a compelling history.

DERMATOLOGY TIMES: How do those goals potentially change in teenagers and adults?

Dr. Lio: My first goal in my older patients with AD is to relieve the discomfort, which almost always involves itch but can sometimes include pain as well, especially among patients with more severe disease. As Dr. Sidbury noted, relieving that itch and discomfort can impact many other issues such as sleep discomfort and the inability to concentrate.

I always talk about the three great hurdles of treating AD: The first hurdle is, “Can I get you clear?” That is fairly easy for many patients today if we get them on the right treatment. The second hurdle is, “Can I keep you clear safely?” That’s where things get a bit trickier. Many less experienced clinicians and especially nondermatologists who don’t see a lot of AD get stuck. They know to prescribe triamcinolone, which will often clear up a patient’s symptoms, but then they will stop treatment and the patient will flare again. So the patient gets confused. Their physician tells them not to use this medication for an extended duration of time, but whenever they stop, their symptoms come back. It takes careful planning to keep a patient clear for an extended period.

And then the third hurdle is, “Can you keep up with your treatment regimen?” The proper skin care necessary to keep AD at bay can be complicated, and some patients simply get overwhelmed having to constantly apply moisturizers, nonsteroidals, and cortisones depending on the ups and downs of their symptoms. Some patients simply tell me they need to find a way to get out of the exhausting loop of constantly monitoring and adjusting medications for their AD symptoms.

DERMATOLOGY TIMES: What do you do for those patients?

Dr. Lio: Those are the patients for whom we need to think about systemic therapies and treating the whole person instead of just the skin. In many of them, their immune system is highly compromised and there is such a wide surface area of eczema or their disease is so severe that topicals are not enough.

Dr. Sidbury: I deal with a lot of parents and their children as they get older who absolutely hate putting all of these topical agents on their skin every day. Parents especially are fearful of the long-term impact of these topicals, no matter how much we reassure them of their safety. So you have both the inconvenience of using these medications and this underlying fear of them that makes some of the treatment recommendations, even when successful, fraught with difficulties.

DERMATOLOGY TIMES: What are the primary safety concerns that you typically hear about from parents?

Dr. Sidbury: These are mostly related to the use of steroids. Just the term “steroid” has become such a loaded term in our culture because of its association with athletes, body builders, and the like. It can be a challenge to get parents to realize that not all steroids are the same, and topical steroids are significantly different than those they hear about on television.

The second big concern I hear about is the potential thinning of the skin that can be caused by topical steroids. This perhaps is more legitimate, but it’s something we absolutely can manage. I always make an effort to talk with families about the signs of thinning skin, how it can be avoided, and how it can be reversed in its early stages. The boxed warnings on some of the nonsteroidals that we often use to treat AD can be frightening. So, it’s important to walk patients and parents through which risks are real and, for the ones that are, how we can avoid them.

Dr. Lio: It’s a narrow tightrope in our patients with AD to maximize the benefits of topical steroids and avoid some of those more common side effects. One thing I am hearing about more and more from my older patients is the concept of topical steroid withdrawal. To me, the secret when using steroids is to use them intermittently. I will often use them for a short time until we see some
improvement and then switch to a nonsteroidal alternative. I’ll then go back and forth with that regimen pretty much indefinitely, maybe 2 weeks on, 2 weeks off. I think that is a fairly safe approach for most patients, although there are some patients for whom even 1 week a month of a steroid makes them concerned about long-term effects.

Historically, we have been really limited beyond corticosteroids in patients with AD, but now that there is a U.S. Food and Drug Administration (FDA)-approved systemic therapy and more in the pipeline, we can offer patients better options.

**SYSTEMIC TREATMENTS FOR AD**

**DERMATOLOGY TIMES:** What are some of the more common safety concerns related to systemic therapies commonly used to treat AD?

**Emma Guttman, MD, PhD:** I find anything that needs to be ingested or injected is associated in patients’ minds with greater safety concerns than something that they use topically. I often have to spend considerable time explaining to my patients that these systemic therapies actually have fewer safety issues than a strong topical steroid used for an extended period of time.

Total avoidance of, or inadequate, treatment in young children is another issue I often have to combat. Often due to parental safety concerns, I will see children referred to me who are being treated with hydrocortisone 1% or 2.5% despite having severe AD from head to toe, and they are failing to thrive. These are the families I talk to about studies showing that children can have systemic inflammation that can lead to downstream manifestations such as asthma, hay fever, eosinophilic esophagitis, and food allergies. Systemic therapies are clearly a viable option in these patients.

**Dr. Lio:** In general, there is a much greater fear about using systemic therapies among my pediatric patients compared to adolescents and adults. Parents are just nervous, and understandably so. Every side effect is magnified, because we have to look beyond the immediate effects and consider potential impact on growth and development. Of course, it should also be mentioned that these systemic therapies are currently off-label in pediatric patients younger than age 12 years, which is another concern for many parents. Those are among the reasons why I try to avoid or at least minimize immunosuppressants in my pediatric patients with AD whenever I can. Even in the best scenario, you will likely need an immunosuppressant for many months or even years, and there are too many unknowns at play. The FDA has taken a positive step by pushing for more pediatric studies with these systemic therapies so that we can hopefully have formal data and potential extended approvals in the future.

Route of administration is another significant issue with pediatric patients. You can’t use pills in the same manner in young children as you do in adults, and shots can be scary. When I suggest the use of dupilumab in young children, for instance, I often have to deal with needle phobia. Although that can still be an issue in older patients, it is particularly pronounced in pediatric patients.

**Dr. Guttman:** I will sometimes prescribe dupilumab for my adolescent patients after a thorough discussion about the drug and then receive a call from the pharmacy a few weeks later telling me that the drug was never picked up. It’s almost always due to a fear of needles, even in this older population. I almost feel like an injectable is easier for younger patients whose parents can hold them still and give them the injection.

**DERMATOLOGY TIMES:** When you are contemplating a proposed treatment regimen for a 6 month old with AD, what are the primary factors you are considering and discussing with the child’s parents?

**Dr. Sidbury:** I start by going through the same foundational things that I cover with any patient with AD: proper moisturization, proper bathing, and trigger avoidance. I’ll also talk about the appropriate use of our first-line agents, the topical anti-inflammatories, where the skin is inflamed. There is always a discussion of food and its role in the development of AD, usually triggered by parents. We tend to focus on skin care first and allergy care second, unless there is a reason to do otherwise.

**DERMATOLOGY TIMES:** What is the youngest age at which you will consider offering dupilumab in a patient with AD?
Dr. Guttman: I consider dupilumab in any patient for whom I would have previously had to settle for cyclosporine. I would rather have a young child on dupilumab than cyclosporine any day.

Dr. Lio: I feel the same way. I have children all the way down to 6 to 8 months whom I have treated with cyclosporine just because I had no other option. I haven’t treated anyone quite that young with dupilumab, although I have treated children ages 4 to 6 years with severe cases of AD who have failed everything else we currently have available.

What’s important to discuss with parents of any young child initiating treatment for AD is the importance not only of making the skin clearer but also the impact that can have on preventing the development of future comorbidities.

Dr. Sidbury: There are many medications that are not FDA approved in our youngest patients, including crisaborole and topical calcineurin inhibitors. Those, of course, are used commonly in patients younger than age 2 years, but when you tell parents that these agents are not approved at that age, alarm bells start going off in their heads. And then if there is a boxed warning with the calcineurin inhibitors that you have to review, things become even more complicated.

When you are dealing with young children, it’s always important to talk about any medication being prescribed, whether it is FDA approved or not, regarding our experience with the medication, dosing requirements, and other issues. For example, an infant at age 4 months is going to absorb a topical medication differently than a child at age 4 years due to differences in weight/surface area ratio, which needs to be taken into consideration.

DERMATOLOGY TIMES: What do you start seeing some of the common psychological problems that are typically attributed to AD?

Dr. Sidbury: One of the comorbidities that we are seeing more in patients with untreated or suboptimally treated AD is attention-deficit hyperactivity disorder (ADHD) among young children between the ages of about 5 and 7 years. Historically, we have usually looked at these children and said, “Oh gosh, you are losing sleep because of your eczema. That must be why you are having trouble concentrating at school and are so fidgety.” Now we are recognizing that there may be a separate diagnosis of ADHD that needs to be made in some of these patients.

As you get into early adolescence and the teenage years, that’s where some of the more well-publicized psychological issues such as depression and suicidal ideation become a problem. I have certainly seen my share of children with intractable eczema who have been depressed and suicidal, so it is a very real problem many of us have to face. It’s incumbent upon our profession not to ignore these issues.

DERMATOLOGY TIMES: What are some of the specific red flags that you look for?

Dr. Sidbury: I have started having all of my teenage patients with eczema complete the Public Health Questionnaire 2 (PHQ-2) form at every visit. It’s a very simple 2-question form that asks, “Over the last 2 weeks, how often have you had little interest or pleasure in doing things?” and then, “Over the last 2 weeks, how often have you felt down, depressed, or hopeless?” They rate themselves on a 0 to 6 scale, with a score of 3 or greater indicating the need for further intervention. I have found that to be pretty good at flushing out those patients who need to be referred for appropriate management.

Dr. Guttman: What I find interesting is that I am getting calls from psychiatry and psychology colleagues who are involved in the care of some of my teenage patients with AD and they are telling me that patients whose disease is well controlled on dupilumab or on some newer agents in clinical trials are no longer displaying suicidal ideation. These colleagues feel that their improvement in symptoms directly corresponds to their demeanor, which makes sense.

Think about it. When you are a teenager and appearance is so important among your peers and you aren’t sleeping, your entire social life is out of balance. Your academics suffer. Now you take away the impediment to sleep and appearance, and your grades improve and you start hanging out with your friends again. In turn, your depression and suicidal ideation subside. In a sense, among these teenage patients with AD, it’s almost as if they have a reactive depression that may go away or at least dissipate with proper treatment of their AD.

Dr. Lio: Could depression be related directly to a patient’s inflammation? For a long time, we tied a patient’s depression to the fact that their skin was bad, but we are beginning to wonder if there is also a direct psycholog-
ical effect of inflammation in the body. It’s an interesting theory that is gaining traction within some circles.

**DERMATOLOGY TIMES:** Are there any unique problems related to polypharmacy, especially in adult and elderly patients with new-onset AD?

**Dr. Lio:** There are two major issues. The first is that in adult patients who are taking multiple medicines, sometimes we have to rule out an eczematous drug eruption before we can make a diagnosis of AD, and that can be difficult. There are patients who often have a medication list that is 2 pages long, with frequent additions and dosage changes to follow. Pediatric patients, generally speaking, have a much cleaner medical history and are taking few, if any, other medications when they come to see us for help with their AD.

The second issue is that conventional immunosuppressants we use to treat AD have a number of drug–drug interactions. Cyclosporine, for example, can be particularly problematic. For instance, it raises a patient’s blood pressure, which can be a problem for many adult patients who have hypertension. If cyclosporine is our best option, the patient will likely need to work with their primary care physician or cardiologist to modify the dosage of their hypertension medicine. A lot of our patients are obese and may have fatty liver disease. You may want to avoid methotrexate in those patients.

Those factors are among the reasons why dupilumab is often the best choice in adult and older patients with AD. Biologics in general don’t often have any direct interactions with other medicines, and because dupilumab is not an immunosuppressant, you can use it in circumstances in which a traditional immunosuppressant would be otherwise contraindicated.

**Dr. Guttman:** I typically explain to patients that dupilumab is an immune corrector rather than an immune suppressant. Cyclosporine and oral prednisone affect T cells, B cells, and other cells. Dupilumab affects only one molecule, and that is why the only significant safety concerns are ocular. As Dr. Lio said, there aren’t typically concerns about drug–drug reactions in our youngest patients being treated with AD, but there are still safety concerns with long-term use of cyclosporine such as impaired kidney function that can become permanent after a year of use.

**LOOKING TO THE FUTURE OF TREATMENT FOR AD**

**DERMATOLOGY TIMES:** How has your treatment paradigm changed in the last 5 years for children with AD who are age 5 years or younger?

**Dr. Sidbury:** The biggest difference in the last couple of years was the introduction of crisaborole, which is approved for use in children age 2 years and older. It’s a nonsteroidal that does not have a boxed warning, both of which are positives. However, I have not used crisaborole as much as I might have initially expected in young children for a combination of reasons. It’s almost expected these days that any new medication is going to be expensive, and crisaborole is no exception, so it’s been inaccessible for some of my patients from a financial standpoint. In addition, I have witnessed a fair amount of application-site stinging, especially on the face, which has been a barrier. So while crisaborole has worked well for some of my patients and it’s of course good to have another option to consider for patients with AD, it hasn’t had a profound approach on how I treat my patients age 5 years or younger.

**DERMATOLOGY TIMES:** How about any changes in older children and adults with AD? What changes have you noted in your approach to their treatment?

**Dr. Guttman:** The introduction of crisaborole has had an impact, particularly in areas where we don’t like administering topical steroids such as folds in the genital areas as well as in areas such as the back of the hands. I do, however, agree with Dr. Sidbury about the stinging, particularly on the face. I find that if you tell the patient about the expected stinging, it is tolerable and typically subsides in about 20 minutes. But if you don’t warn the patient in advance, they will not use the drug after the first application.

Of course, the biggest change in the last 5 years has been the introduction of dupilumab to treat moderate-to-severe AD. That has revolutionized our ability to control these patients for whom we previously had little to offer.

**Dr. Sidbury:** My approach to treatment has completely changed in my 12- to 18-year-old patients in recent years.
When I can get it approved, dupilumab is my first and best option for those teenagers with moderate-to-severe AD who need systemic therapy. And even in children under age 5 years for whom I’m not yet using dupilumab, just the idea that we have these new medicines being approved and a robust clinical trial pipeline gives patients the promise of a better future.

**DERMATOLOGY TIMES:** What about elderly patients with new-onset AD? How has their treatment evolved in recent years?

**Dr. Lio:** My biggest change conceptually has been the target to which I’m treating. I feel like I have really raised the bar. My goal now is to try to get people clear or almost clear and hold them there for at least a few months. I find that if I can keep a patient clear for several months, they seem to enter a state of partial or full remission where their disease severity stays quiet even after I have de-escalated therapy. That’s a concept I employ not only in my elderly patients but also for all of my patients with AD.

The other piece for elderly patients with AD is that I try to avoid immunosuppression whenever possible by excluding medications that may interact with other medicines they are taking. Now that we have dupilumab as an option, it has become my first-line systemic therapy in those elderly patients who do not respond to phototherapy. I still try to use phototherapy whenever I can, but because it can be cumbersome and difficult to get patients to stay with over the long term, it does not end up being utilized by as many patients.

**DERMATOLOGY TIMES:** What specific research currently under way in AD do you find particularly promising?

**Dr. Guttmann:** I’m excited to see if early treatment with either dupilumab or other systemic agents can prevent the atopic march we see so often, especially in children. I think we also will learn more about whether these treatments, again given early in the disease process, can halt or reverse disease progression. If we can tell a child and/or a parent that, “Listen, we’re going to use an injectable systemic therapy, but we’ll only need to use it for X amount of time and then you are done,” that is going to be a huge breakthrough. Today, we can’t assure them that they won’t need these injectables for a lifetime.

**Dr. Lio:** I have been thinking a lot about the microbiome. We know the microbiome is abnormal in the gut and on the skin of children and adults with AD, and many of our current treatments impact the microbiome in some manner. I’m fascinated with the idea that perhaps we can affect the disease by manipulating the microbiome. We have always been taught that microbiome changes are really secondary with these medications, but I wonder if Staphylococcus aureus is the primary driver of AD, at least in a subgroup of patients. Right now, we have not really stratified patients with AD into subgroups like we have, for instance, with asthma patients, but perhaps we’ll begin to do that in the near future and develop unique treatment pathways.

**DERMATOLOGY TIMES:** This has been a terrific discussion. We want to thank you all for your insights. I hope that our audience is able to take away some helpful information from our discussion to inform their practice’s approach to the treatment of AD across the various age groups affected by this condition.

**REFERENCES**


INDICATION

DUPIXENT is indicated for the treatment of patients aged 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

Conjunctivitis and Keratitis: Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder in these patients. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

Reduction of Corticosteroid Dosage: Do not discontinue systemic, topical or inhaled corticosteroids abruptly upon initiation with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

Atopic Dermatitis Patients with Comorbid Asthma: Advise patients not to adjust or stop their asthma treatments without consultation with their physicians.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.
**TRIAL DESIGNS:** A total of 917 adult patients in Trials 1 and 2 (16-week trials), 251 adolescent patients in Trial 6 (16-week trial), and 421 adult patients in Trial 3 (52-week trial) with moderate-to-severe atopic dermatitis not adequately controlled with topical prescription treatments were randomized to DUPIXENT or placebo. For all patients in Trial 3, lesions were treated with concomitant TCS. All adults received 300 mg O2W following a 600 mg loading dose. Adolescents ≥60 kg also received this dose, while adolescents <60 kg received 200 mg O2W following a 400 mg loading dose. Eligible patients had an IGA score ≥3 (overall atopic dermatitis lesion severity scale of 0 to 4), an EASI score ≥10 on a scale of 0 to 72, and body surface area involvement of ≥10%. At baseline, 52% of adults and 46% of adolescents had an IGA score of 3 (moderate atopic dermatitis), 48% of adults and 54% of adolescents had an IGA of 4 (severe atopic dermatitis), mean EASI score was 33 for adults and 36 for adolescents, and weekly averaged peak pruritus NRS was 7 on a scale of 0 to 10 for adults and 8 for adolescents. 

**TRIAL RESULTS:** The primary endpoint was the change from baseline in the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and ≥2-point improvement at Week 16 (38% and 36% of adults treated with DUPIXENT vs 10% and 9% with placebo in Trials 1 and 2, respectively, P<0.0001; 24% of adolescents treated with DUPIXENT vs 2% with placebo in Trial 6, P<0.0001; 39% of adults treated with DUPIXENT + TCS vs 12% with placebo + TCS in Trial 3, P<0.0001). Other endpoints included change from baseline in the proportion of subjects with EASI-75 at Week 16 (improvement of ≥75%; 51% and 44% of adults treated DUPIXENT vs 15% and 12% with placebo in Trials 1 and 2, respectively, P<0.0001; 42% of adolescents treated with DUPIXENT vs 8% with placebo in Trial 6, P<0.0001; 69% of adults treated with DUPIXENT + TCS vs 29% with placebo + TCS in Trial 3, P<0.0001) and reduction in itch as defined by ≥4-point improvement in the Peak Pruritus NRS at Week 16 (41% and 36% of adults treated with DUPIXENT vs 12% and 10% with placebo in Trials 1 and 2, respectively, P<0.0001; 57% of adolescents treated with DUPIXENT vs 5% with placebo in Trial 6, P<0.0001; 59% of adults with DUPIXENT + TCS vs 20% with placebo + TCS in Trial 3, P<0.0001).

**EASI:** Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, numerical rating scale; O2W, once every 2 weeks; TCS, topical corticosteroids.

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (cont’d)**

**Parasitic (Helminth) Infections:** It is unknown if DUPIXENT will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves.
SHARED RELIEF

- Itch reduction\(^1\)
- Clear or almost-clear skin\(^1\)
- A biologic—not a steroid treatment or an immunosuppressant\(^4\)
- No requirement for initial lab testing or ongoing lab monitoring, according to the full Prescribing Information\(^1\)

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS: The most common adverse reactions (incidence ≥1% at Week 16) in adult patients with atopic dermatitis are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, and dry eye. The safety profile in adolescents through Week 16 was similar to that of adults with atopic dermatitis. In an open-label extension study, the long-term safety profile observed in adolescents through Week 52 was consistent with that seen in adults with atopic dermatitis.

DRUG INTERACTIONS: Avoid use of live vaccines in patients treated with DUPIXENT.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus.

- **Lactation:** There are no data on the presence of DUPIXENT in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DUPIXENT and any potential adverse effects on the breastfed child from DUPIXENT or from the underlying maternal condition.

Please see brief summary of full Prescribing Information on the following pages.

Visit DupixentHCP.com/AtopicDermatitis to learn more
1.1 Atopic Dermatitis

Brief Summary of Prescribing Information

4 CONTRAINDICATIONS

polyposis (CRSwNP).

patients with inadequately controlled chronic rhinosinusitis with nasal polyps.

DUPIXENT is not indicated for the relief of acute bronchospasm or status asthmaticus.

5.1 Hypersensitivity

Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum and serum sickness or serum sickness-like reactions, were reported in less than 1% of subjects who received DUPIXENT in clinical trials. Subjects in the development programs who experienced serum sickness or serum sickness-like reactions were associated with high titers of antibodies to dupilumab. One subject in the asthma development program experienced anaphylaxis [see Adverse Reactions (6.2)]. If a clinical use for a hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT [see Adverse Reactions (6.1, 6.2)].

5.2 Conjunctivitis and Keratitis

Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis recovered or were recovering during the treatment period. Keratitis was reported in <1% of the DUPIXENT group (1 per 100 subject-years) in the 16-week atopic dermatitis monotherapy trials. In the 52-week DUPIXENT + topical corticosteroids (TCS) atopic dermatitis trial, keratitis was reported in 4% of the DUPIXENT + TCS group (12 per 100 subject-years) and in 0% of the placebo + TCS group (0 per 100 subject-years). Most subjects with keratitis recovered or were recovering during the treatment period [see Adverse Reactions (6.1)].

Among asthma subjects, the frequencies of conjunctivitis and keratitis were similar between DUPIXENT and placebo [see Adverse Reactions (6.1)]. In subjects with CRSwNP, the frequency of conjunctivitis was 2% in the DUPIXENT group compared to 1% in the placebo group in the 24-week safety pool; these subjects recovered. There were no cases of keratitis reported in the CRSwNP development program [see Adverse Reactions (6.1)].

Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

5.3 Eosinophilic Conditions

Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroids. These events may be associated with the reduction of oral corticosteroid therapy. Physicians should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Cases of eosinophilic pneumonia were reported in adult patients who participated in the asthma development program and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis have been reported with DUPIXENT in adult patients who participated in the asthma development program as well as in patients with co-morbid asthma in the CRSwNP development program. A causal association between DUPIXENT and these conditions has not been established.

5.4 Acute Asthma Symptoms or Deteriorating Disease

DUPIXENT should not be used to treat acute asthma symptoms or acute exacerbations. Do not use DUPIXENT to treat acute bronchospasm or status asthmaticus. Patients should seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with DUPIXENT.

5.5 Reduction of Corticosteroid Dosage

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Reductions in corticosteroid dose should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.6 Patients with Comorbid Asthma

Advise patients with atopic dermatitis or CRSwNP who have co-morbid asthma not to adjust or stop their asthma treatments without consultation with their physicians.

7.7 Parasitic (Helminth) Infections

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if DUPIXENT will influence the immune response against helminth infections.

Treatment of patients with pre-existing helminth infections before initiating therapy with DUPIXENT is recommended. In subjects who discontinued treatment because of adverse events, 1.8% in DUPIXENT 300 mg Q2W + TCS group and 7.6% in the placebo + TCS group. Two subjects discontinued DUPIXENT because of adverse reactions: atopic dermatitis (1 subject) and exfoliative dermatitis (1 subject).

The safety profile of DUPIXENT + TCS through Week 52 was generally consistent with the safety profile observed at Week 16.

Adolescents with Atopic Dermatitis

The safety of DUPIXENT was assessed in a trial of 250 subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis (Trial 6). The safety profile of DUPIXENT in these subjects through Week 16 was similar to the safety profile from studies in adults with atopic dermatitis. The long-term safety of DUPIXENT was assessed in an open-label extension study in subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis...
atopic dermatitis (Trial 7). The safety profile of DUPIXENT in subjects followed through Week 52 was similar to the safety profile observed at Week 16 in Trial 6. The long-term safety profile of DUPIXENT observed in adolescents was consistent with that seen in adults with atopic dermatitis.

**Asthma**

A total of 2888 adult and adolescent subjects with moderate-to-severe asthma (AS) were evaluated in 3 randomized, placebo-controlled, multicenter trials of 24 to 52 weeks duration (AS Trials 1, 2, and 3). Of these, 2678 had a history of 1 or more severe exacerbations in the year prior to enrollment despite regular use of medium- to high-dose inhaled corticosteroids plus an additional controller(s) (AS Trials 1 and 2). A total of 210 subjects with oral corticosteroid-dependent asthma receiving high-dose inhaled corticosteroids plus up to two additional controllers were enrolled (AS Trial 3). The safety population (AS Trials 1 and 2) was 12-87 years of age, of which 63% were female, and 82% were white. DUPIXENT 200 mg or 300 mg was administered subcutaneously Q2W, following an initial dose of 400 mg or 600 mg, respectively.

In AS Trials 1 and 2, the proportion of subjects who discontinued treatment due to adverse events was 4% of the placebo group, 3% of the DUPIXENT 200 mg Q2W group, and 6% of the DUPIXENT 300 mg Q2W group. Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% in subjects treated with DUPIXENT and at a higher rate than in their respective comparator groups in AS Asthma Trials 1 and 2.

**Hypersensitivity Reactions**

Hypersensitivity reactions were reported in <1% of DUPIXENT-treated subjects. These included serum sickness reaction, serum sickness-like reaction, generalized urticaria, rash, erythema nodosum, and anaphylaxis [see Contraindications (4), Warnings and Precautions (5.1), and Adverse Reactions (6.2)].

**Eosinophilia**

DUPIXENT-treated subjects had a greater initial increase from baseline in blood eosinophil counts compared to subjects treated with placebo. In subjects with atopic dermatitis, the mean and median increases in blood eosinophils from baseline to Week 4 were 100 and 0 cells/mcL, respectively. In subjects with asthma, the mean and median increases in blood eosinophils from baseline to Week 4 were 130 and 10 cells/mcL, respectively. In subjects with CRSwNP, the mean and median increases in blood eosinophils from baseline to Week 16 were 150 and 50 cells/mcL, respectively. Across all indications, the incidence of treatment-emergent eosinophilia (≥500 cells/mcL) was similar in DUPIXENT and placebo groups. Treatment-emergent eosinophilia (≥5,000 cells/mcL) was reported in <2% of DUPIXENT-treated patients and ≥5% in placebo-treated patients. Blood eosinophil counts declined to near baseline levels during study treatment [see Warnings and Precautions (5.3)].

**Cardiovascular (CV)**

In the 1-year placebo controlled trial in subjects with asthma (AS Trial 2), CV thromboembolic events (CV death, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.2%) of the DUPIXENT 200 mg Q2W group, 4 (0.6%) of the DUPIXENT 300 mg Q2W group, and 2 (0.3%) of the placebo group.

In the 1-year placebo controlled trial in subjects with atopic dermatitis (Trial 3), CV thromboembolic events (CV death, non-fatal MIs, and non-fatal strokes) were reported in 1 (0.9%) of the DUPIXENT + TCS 300 mg Q2W group, 0 (0.0%) of the DUPIXENT + TCS 300 mg QW group, and 1 (0.3%) of the placebo + TCS group.

In the 24-week placebo controlled trial in subjects with CRSwNP (CSNP Trial 1), CV thromboembolic events (CV deaths, non-fatal myocardial infarctions, and non-fatal strokes) were reported in 1 (0.7%) of the DUPIXENT group and 0 (0.0%) of the placebo group. In the 1-year placebo controlled trial in subjects with CRSwNP (CSNP Trial 2), there were no cases of CV thromboembolic events (CV deaths, non-fatal myocardial infarctions, and non-fatal strokes) reported in any treatment arm.

**6.2 Immunogenicity**

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to dupilumab in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Approximately 5% of subjects with atopic dermatitis, asthma, or CRSwNP who received DUPIXENT 300 mg Q2W for 52 weeks developed antibodies to dupilumab; ~2% exhibited persistent ADA responses, and ~2% had neutralizing antibodies. Approximately 9% of subjects with asthma who received DUPIXENT 200 mg Q2W for 52 weeks developed antibodies to dupilumab; ~4% exhibited persistent ADA responses, and ~4% had neutralizing antibodies. Approximately 4% of subjects in the placebo groups in the 52-week studies were positive for antibodies to DUPIXENT; ~2% exhibited persistent ADA responses, and ~1% had neutralizing antibodies. Approximately 16% of adolescent subjects with atopic dermatitis who received DUPLEXENT 300 mg Q2W or 400 mg QW for 16 weeks developed antibodies to dupilumab; ~3% exhibited persistent ADA responses, and ~5% had neutralizing antibodies. Approximately 4% of adolescent subjects with atopic dermatitis in the placebo group were positive for antibodies to DUPLEXENT; ~1% exhibited persistent ADA responses, and ~1% had neutralizing antibodies. The antibody titers detected in both DUPLEXENT and placebo subjects were mostly low. In subjects who received DUPLEXENT, development of high titer antibodies to dupilumab was associated with lower serum dupilumab concentrations [see Clinical Pharmacology (12.3) in the full prescribing information].

**7 DRUG INTERACTIONS**

7.1 Live Vaccines

Avoid use of live vaccines in patients treated with DUPLEXENT.
7.2 Non-Live Vaccines

Immune responses to vaccination were assessed in a study in which subjects with atopic dermatitis were treated once weekly for 16 weeks with 300 mg of dupilumab (twice the recommended dosing frequency). After 12 weeks of DUPLEXNT administration, subjects were vaccinated with a Tdap vaccine (Adacel®) and a meningococcal polysaccharide vaccine (Menomune®). Antibody responses to tetanus toxoid and serogroup C meningococcal polysaccharide were assessed 4 weeks later. Antibody responses to both tetanus toxoid and meningococcal polysaccharide vaccine were similar in dupilumab-treated and placebo-treated subjects. Immune responses to the other active components of the Adacel and Menomune vaccines were not assessed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPLEXNT during pregnancy. Please contact 1-877-311-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/ to enroll in or to obtain information about the registry.

Risk Summary

Available data from case reports and case series with DUPLEXNT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPLEXNT may be transmitted from the mother to the developing fetus. There are adverse effects on maternal and fetal outcomes associated with asthma in pregnancy (see Clinical Considerations). In an enhanced pre- and post-natal developmental study, no adverse developmental effects were observed in offspring born to pregnant monkeys after subcutaneous administration of a homologous antibody against interleukin–4 receptor alpha (IL-4Rα) during organogenesis through parturition at doses up to 10–times the maximum recommended human dose (MRHD) (see Data). The estimated background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defects and other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-fetal Risk

In women with poorly or moderately controlled asthma, evidence demonstrates that there is an increased risk of preeclampsia in the mother and premature, low birth weight, and small for gestational age in the neonate. The level of asthma control should be closely monitored in pregnant women and treatment adjusted as necessary to maintain optimal control.

Data

Animal Data

In an enhanced pre- and post-natal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of homologous antibody against IL-4Rα up to 10 times the MRHD (on a mg/kg basis of 100 mg/kg) from the beginning of organogenesis through parturition. No treatment-related adverse effects on embryofetal toxicity or malformations, or on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age.

8.2 Lactation

Risk Summary

There are no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal and limited systemic exposure to dupilumab on the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DUPLEXNT and any potential adverse effects on the breastfed child from DUPLEXNT or from the underlying maternal condition.

8.4 Pediatric Use

Atopic Dermatitis

The safety and efficacy of DUPLEXNT have been established in pediatric patients 12 years of age and older with moderate-to-severe atopic dermatitis. A total of 251 adolescents ages 12 to 17 years old with moderate-to-severe atopic dermatitis were enrolled in Trial 6. The safety and efficacy were generally consistent between adolescents and adults [see Adverse Reactions (6.1) and Clinical Studies (14.2) in the full prescribing information]. Safety and efficacy in pediatric patients (<12 years of age) with atopic dermatitis have not been established.

Asthma

A total of 107 adolescents aged 12 to 17 years with moderate to severe asthma were enrolled in AS Trial 2 and received either 200 mg (N=21) or 300 mg (N=18) DUPLEXNT (or matching placebo either 200 mg [N=34] or 300 mg [N=34]) Q2W. Asthma exacerbations and lung function were assessed in both adolescents and adults. For both the 200 mg and 300 mg Q2W doses, improvements in FEV1 (LS mean change from baseline at Week 12) were observed (0.36 L and 0.27 L, respectively). For the 200 mg Q2W dose, subjects had a reduction in the rate of severe exacerbations that was consistent with adults. Safety and efficacy in pediatric patients (<12 years of age) with asthma have not yet been established.

References:
1. DUPLEXNT Prescribing Information.

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