Treating to Target in Psoriasis: Is the Target Skin Deep or Systemic?

Kevin D. Cooper, MD

Understanding treatment goals. Treating to target defines the treatment goal—ie, the target—as achieving a preset minimum degree of therapeutic benefit, ie, almost clear, or 75% improved. Cycling a given patient through a series of therapies may be required to find the one enabling this. For patients with psoriasis, however, it is not simply an issue of finding the drug that achieves the best PASI score. We know now that roughly 15% of patients with psoriasis are at very high risk for developing one or more comorbidities, including some that cannot revert—psoriatic arthritis, arterial calcification, cardiovascular disease (CVD, eg, heart attacks [MI] and strokes), depression/suicide, renal damage from hypertension or diabetes, brain damage from sleep apnea. Cooper emphasized their permanent consequences, especially of suicide and organ damage. “Although our psoriasis goal is for the skin to clear and look normal,” he said, “it is different with the comorbidities.” Disease prevention is the primary goal, with halting or slowing progression in existing comorbid disease.

Challenges

• Which patients are at most risk for various comorbidities is not known
• The specific level of control of psoriasis needed for each comorbidity is not known
• Whether every drug that results in a psoriasis response produces equally effective treatment of specific comorbidities is not known
• Many comorbidities are not easily monitored, or require serial invasive or risk-associated testing—CT, angiography, brain MRI, joint biopsy, etc
• Practical tests that tell us which patients are at risk for which comorbidities (endotypes), and whether the comorbidity has been rendered inactive (biomarkers or biosensors), are urgently needed

Endotypes and biomarkers. Patient endotypes are subgroups that appear indistinguishable clinically but are clearly identifiable by underlying lab-defined patterns that are also linked to specific future clinical outcomes—comorbid diseases in this setting. “We want to be able to predict the likelihood of a comorbidity so that we can prevent it,” Cooper’s lab is identifying these distinguishing underlying patterns in psoriasis, and exploring how to normalize them.

(Continued on page 3)
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Registration opens mid-September—visit dermatologyfoundation.org
In exploring how these different comorbidities may relate to the skin disease, Cooper explained what led his colleagues to focus initially on monocytes, which are sensitive to mediators circulating in the plasma, able to alter tissues they enter, and are different in people with and without psoriasis. After finding distinctive monocyte profiles that clearly separated patient endotypes, they searched for a far less complex and costly biomarker. Initially, they combined RDW (red cell distribution width) and MPV (mean platelet volume)—two variables in the routine CBC that are each altered in bone marrow dysbiosis, and are significantly associated with CVD when both are high. Cooper described the databases and big data techniques used to identify and explore additional predictive variables. He discussed the evolution from numeric variables to data maps—the distinctive patterns created by integrating variables produced by several different innovative analytic techniques—associated with the respective endotypes. The final map components will come from integrating blood findings, the skin transcriptome, the metabolome, and the microbiome.

The endotype profiles reveal an informative relationship between resistin—an inflammatory adipokine produced by white fat cells—and RDW. In about 50% of patients, resistin molecules from inflamed subdermal adipose tissue are released at high enough levels in the plasma to be detectable as elevated. In a subset of these patients, the bone marrow is also affected and RDW becomes aberrant. "We suspect these are the patients who are most at risk," Cooper said, "if they have the right genetics for CVD."

**What are Endotypes, and Why Should We Care?**

- Clinically indistinguishable subgroups
- Associated with distinct underlying lab-defined patterns (endotypes)
- Linked to specific clinical outcomes in the future
- Some of these outcomes are irreversible once clinically apparent
  - Psoriatic arthritis
  - Renal damage from HTN or diabetes
  - CVD events (MI, stroke)
- Suicide
- Brain damage from sleep apnea
- Arterial calcification

**Defining the target.** "Now that we can begin separating patients into risk groups, we need to know if we can stop the comorbidity." Cooper’s first effort was a yearlong study that set the skin response goal for PASI-50, with the drug used for a given patient changed every 3 months until the target was met. Inflammatory markers—macrophage number, resistin and myeloperoxidase levels—decreased significantly in most patients, and carotid artery inflammation diminished in all. Cooper described the databases and big data techniques used to identify and explore additional predictive variables. He discussed the evolution from numeric variables to data maps—the distinctive patterns created by integrating variables produced by several different innovative analytic techniques—associated with the respective endotypes. The final map components will come from integrating blood findings, the skin transcriptome, the metabolome, and the microbiome.

**Big Data, Bioinformatics, and Biomarkers**

- For patients with psoriasis showing similar clinical external morphology and distributions, how can we distinguish those with emerging comorbidities?
- Can we harness big data and complex data analytics to enable bioinformatics research to help us find biomarkers of endotypes—lab-defined patterns—that link to extreme phenotypes (ie, irreversible comorbidities)?

**What’s the Best Treatment for this Skin Ulcer?**

**Mark D. P. Davis, MD**

**Introduction.** Dr. Davis emphasized that although conventional wound care is necessary, it is not the key to healing challenging skin ulcerations. "Skin ulcerations should be considered a clinical sign. We need to look for the underlying cause of that ulceration—and treat that cause—for the ulcer to heal," he said. "The key to healing: make the correct diagnosis of the cause of the ulceration, and treat the correct diagnosis." Vascular and neuropathic causes of ulcerations are by far the most common, but many other causes need to be kept in mind. After discussing some of the commonest skin ulcerations and their management—venous ulcers (use compression), arterial insufficiency (revascularize), neuropathic (offload weight), and pressure (remove pressure)—Davis shared examples of patients with uncommon skin ulcers, detailing their presentation, how the underlying cause was identified, and consequent treatment. "The dermatologist comes into play because other specialties may miss some of these causes, and we are the ones who are trained to recognize them," Davis emphasized.

**Uncommon skin ulcers.** Davis began with medication-induced ulcers. First showing arteriolar ulcers caused by hydroxyurea treatment for myelofibrosis. After noting other problem medications,
Dr. Sugarman, an internationally respected pediatric dermatologist, “had the training to be a full-time academician, but he chose a different path, one very much his own,” a close colleague shared. “And we in dermatology—and more broadly in medicine—have benefitted from it greatly.”

Dr. Sugarman has invested his prodigious energies in multiple arenas. He is medical director of Redwood Family Dermatology, the private practice he established in 2002. He is an associate clinical professor (volunteer) at the University of California, San Francisco (UCSF) in the departments of dermatology, and family and community medicine. He actively works to further research in pediatric dermatology, speaks and publishes widely, and provides leadership in several professional associations. In his spare time, he is a highly regarded ceramicist.

Dr. Sugarman first encountered pediatric dermatology during a medical school rotation at UCSD, but it wasn’t until his pediatrics residency at the University of Washington, via his elective in pediatric infectious disease, that he considered it seriously. “I not only discovered a substantial overlap with dermatology—I fell in love with it!” he recalls. He was captured by the visual and tactile elements, the interactive and continuing relationships with patients, the variety of disorders that can be understood through the skin, and the robust research potential. Dr. Sugarman matriculated to UCSF to complete his dermatology residency followed by a pediatric dermatology fellowship.

He works with pediatric and dermatology residents, fellows, and medical students at the UCSF pediatric dermatology clinic. Dr. Sugarman is a key faculty member at UCSF’s outstanding family practice residency at its Santa Rosa campus, and is the cornerstone of its dermatology curriculum. He created the teaching program and established the community clinic shortly after moving there. A colleague notes that “his lectures, precepting, and consultations are uniformly listed as one of the highlights of residency training.”

Dr. Sugarman is the current president of the Society for Pediatric Dermatology. He was instrumental in bringing the Pediatric Dermatology Research Alliance (PeDRA) to life to facilitate collaborative research on rare skin diseases. He founded the Northern California Dermatology Society and has assumed significant leadership responsibilities there. He is a past president of the Sonoma County Medical Association, where he worked to improve access to specialty care for the under- and uninsured. A colleague shares that he is “the kind of leader who draws people to him and earns their respect and trust. His passion for the specialty, his utmost dedication to patients, and his unique intelligence have enabled him to be a key contributor to progress in the specialty.”

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**Clark W. Finnerud Award: Jeffrey Sugarman, MD, PhD**

Honoring the exceptional clinician who is simultaneously a dedicated and highly effective part-time teacher
Dr. Alster took her first step in bringing laser surgery to treating birthmarks and scars—sources of significant anguish for patients—almost 30 years ago, when she founded the Washington Institute of Dermatologic Laser Surgery in Washington, DC. She became a prime mover in the specialty.

“Dr. Alster’s influence on the field of laser use in dermatology has transformed the way we practice,” a colleague remarks. Another notes that “as one of the pioneers of laser, she has changed the face of dermatology and bettered the lives of all dermatology patients via her research and body of work. She is an incredibly gifted dermatologist and surgeon.”

At Duke University School of Medicine, Dr. Alster had been considering plastic surgery until she worked in a dermatology lab. The specialty excited her, and as soon as she began observing a dermatology surgeon at work, she knew this was her direction. During her second year of residency at Yale, “a woman came to me in great distress,” Dr. Alster recalls. This woman was about to change her life. “She had a facial port-wine stain that was so substantial, she had never allowed her husband or adolescent son to see her without her camouflage makeup.” Dr. Alster had just read a newly-published study by a Boston dermatologist describing a laser that could destroy these blood vessels, and promised to research this further. What she learned ignited her lifelong passion, beginning with her laser surgery fellowship at Boston University.

When Dr. Alster chose DC as her home, she pursued an academic setting to work with lasers and found that dermatology departments were not prepared to make the necessary investment. So she redirected her talent, ingenuity, and energy. She worked to build a private practice that now draws patients nationally and internationally, expanded and improved laser treatments, and generously shared her extensive knowledge through multiple avenues. She joined the clinical faculty at Georgetown University Medical Center, where she is now clinical professor of dermatology, and wrote the first textbook on laser surgery. She introduced laser education courses at the AAD and other organizations, continues to teach and lecture worldwide, and publishes widely. Dr. Alster mentors in a myriad of settings that reach medical students, clinicians, and residents who regularly shadow her. A former mentee calls her “a tremendous force in laser education and research, and an amazing mentor. Her teaching and guidance are priceless!”

Dr. Alster was a founding member of the International Academy for Laser Medicine & Surgery. She has also held leadership roles with the Women’s Dermatologic Society, the American Society for Dermatologic Surgery, and the American Society for Laser Medicine & Surgery.

For Dr. Alster, her primary focus has always been her patients. “The most rewarding aspect of my job is being able to give hope to children and adults with extensive birthmarks or who have suffered extensive scarring.” This includes the many such patients she treats without charge. “For me, medicine is a profession that allows me to give something of myself. My patients give me a lot—their trust and confidence—and I am personally gratified that I’m able to help them.”

Practitioner of the Year: Tina S. Alster, MD
Recognizing dermatologists for exemplary service as a private practitioner combined with significant contributions to the specialty through leadership and teaching.
he presented ulcers due to cosmetic procedures (deoxycholate injections for a buttocks reduction procedure, and ulcers due to shifting mineral oil used in a buttocks enhancement procedure). Several patients illustrated infectious causes (HSV type II, sporotrichosis, invasive candidiasis). Patients with ulcerations secondary to malignancy included those with BCC and ulcerative cutaneous lymphoma. Vasculitis-caused ulcers included one patient with Henoch-Schönlein purpura, another with ANCA-associated vasculitis, and another with calciphylaxis-caused infarctive ulcers. Davis also discussed ulcers due to trauma and excoriations, and to pyoderma gangrenosum.

Skin Ulcerations are a Clinical Sign, With Multiple Possible Etiologies

- Vascular—most common causes
  - Venous
  - Arterial
  - Vasculitis
- Neuropathic
- Other
  - Trauma, infection, inflammation, collagen vascular disease, coagulopathy, malignancy, hematologic, drug-induced, metabolic, pyoderma gangrenosum

The Key to Healing

- Make the right diagnosis
- Treat the right diagnosis
- Keep it clean
- Keep it moist
- Use adjunctive methods if necessary

Take-home. The best treatment to heal a skin ulceration is not just good wound care. Look for the underlying cause, make the correct diagnosis of that underlying cause, then treat that cause.

The Best Treatment?—A Diverse Array!

- Compress
- Revascularize
- Offload
- Behavioral modification
- Antimicrobials
- Anticoagulants
- Stop medications
- Systemic immunosuppression
- Mohs surgery
- Chemotherapy
- Excise

Nail Procedures for the General Dermatologist

Adam I. Rubin, MD

Introduction. “General dermatologists can offer a lot to our nail patients,” Dr. Rubin noted. To assist this, he shared a range of helpful tips for providing biopsy specimens for pathology that enable the most accurate results, and for facilitating post-biopsy healing and minimizing postoperative dystrophy. For each technique he profiled, Rubin noted the specific application and carefully depicted each step. He set the stage by reviewing normal nail anatomy and identifying areas that heal easily and those vulnerable to injury. He described the basic inventory of nail-specific instruments and his preferred anesthetics and blocks.

Nail Procedures for the General Dermatologist

- Know the anatomy
- Nail-specific instruments
- Distal digital block
- Basic Procedures
  - Nail bed biopsy with onycholysis
  - Nail bed biopsy with intact nail plate
  - Nail matrix punch biopsy
- Advanced Procedures
  - Matrix shave biopsy: longitudinal melanonychia
  - Nail bed excision: longitudinal erythronychia
  - Lateral longitudinal excision

Basic nail unit procedures. Rubin began with the easiest, nail bed biopsy with onycholysis. He described the steps to produce “the perfect specimen” for pathology analysis. Nail bed biopsy with intact nail plate addressed pigmentation and a possible melanoma under a toenail. With the double punch technique, Rubin takes as little as possible, leaving the nail bed intact to enable faster healing (especially with toenails). He described how to know you are in the matrix when an abnormal nail obscures the lunula. The nail matrix punch biopsy can be employed for suspected inflammatory disorders.

Nail Procedures for the General Dermatologist

- English Action Nail Splitter
- Dual Action Nail Nipper
- Platypus Nail Pulling Forceps

Advanced techniques. Rubin uses a matrix shave biopsy/tangential excision for longitudinal melanonychia to remove the entire lesion for the pathologist (which he submits on a nail map), and to minimize the risk of postoperative nail dystrophy. He described a nail bed and distal matrix excision for longitudinal erythronychia. Rubin’s choice enables a more thorough excision, thus producing greater accuracy. He leaves much of the nail plate in place to help in healing, and submits the separated segment to pathology. Rubin uses a lateral longitudinal biopsy not only for neoplastic disorders, but also for difficult-to-diagnose inflammatory disorders. “Because the pathologist will be looking at all anatomic areas of the nail unit, you will get the most definitive diagnosis.”
Transplant Skin Cancer Network

- A research network funded by the AAD and focused on multicenter studies of skin cancer in organ transplant recipients (OTR)
  - **Initial goal:** to determine the population-based incidence and predictors of post-transplant skin cancer in the U.S.
    - Retrospective review of all OTR transplanted at 26 centers in 2003, 2008
    - 10,649 OTR contributed 59,923 years of follow-up
  - **Long-term goal:** targeting screening to the OTR most likely to benefit
    - Risk prediction algorithm and formal consensus on skin cancer screening based on U.S. incidence and risk factors

Important Considerations for Screening Tool Use

- **Screening** applies only to asymptomatic patients with no active lesions
  - Subjects with pretransplant skin cancer should have an FBSC within the recommended time period at a minimum, or sooner, as directed by their dermatologist
  - Any patient with a concerning lesion should be referred immediately for evaluation
  - This tool does not incorporate risk for Kaposi’s sarcoma or genital dysplasia, both of which may be higher in OTR of color or HIV-positive OTR

For Patients: skincancer.ucsf.edu

**Adolescent Dermatology**

Vikash S. Oza, MD

**Introduction.** “Adolescents are navigating the world with a brain in imbalance and under development. The limbic system governing reward and risk-taking behavior is developed early in adolescence, but the prefrontal cortex—governing executive function—often doesn’t fully mature until one’s mid-20s,” Dr. Oza pointed out. Thus they are different, and effectively communicating with and understanding them requires an awareness of these differences and...
familiarity with core tenets in adolescent medicine. For adolescent patients requiring long-term care, dermatologists are “an important touch point in their medical lives. So we also need to be aware of certain issues that are more common in adolescence and be able to screen effectively for them. We need to know how to identify/assess abnormalities in pubertal development. And we have to become comfortable talking about identity and create a fully accepting environment.”

**Take-Home Points**

- The dermatology visit serves as an important “touch point” in adolescent health
- **Adolescent depression:**
  - Common, and more common in chronic dermatologic disorders
  - Risk factors: obesity, LGBT youth, substance abuse
  - Isotretinoin may not cause depression, but it provides an opportunity to discuss it
  - PHQ-2 is a validated screening tool
- **PCOS in adolescence:**
  - can be a challenging diagnosis
  - >45 days between periods and irregular periods 2 years post-menarche is a red flag
- **Sexual and gender identity in adolescence:**
  - don’t assume; emphasize confidentiality; be supportive
  - 1 in 137 teenagers (13–17) identify as transgender

**Common issues with adolescent patients.**

**Depression**—one of the most common health conditions overall in the adolescent community—rises disproportionately with age, most steeply in girls. Suicide rates are also increasing. Depression is even higher in skin conditions affecting quality of life—psoriasis, hidradenitis suppurativa, and acne. Other risk factors include obesity, LGBT identity, and a history of substance abuse. Be alert. Screen with the PHQ-2, follow up with the PHQ-9. Interestingly strong data have now overturned the initial conviction that isotretinoin heightens the risk for mental health disorders. In reality, it reduces depression scores. **Acne** is one of the clinical signs of puberty, so we have to be able to identify the red flags indicating what is abnormal. Oza often encounters 6- to 7-yo children with early signs. This is *premature adrenarche*—prematurity of the adrenal glands’ androgen precursor secretion—and bone age should be assessed to rule out an underlying endocrinopathy. Oza discussed hormonal imbalance in young women and the trio—hirsutism + obesity + acanthosis nigricans—suggesting PCOS. Additional red flags are irregular period more than 2 years post-menarche, and more than 45 days between periods. Oza also discussed the prolific adolescent use of personal care products and the potential for contact allergens—especially with eczematous issues—and endocrine disrupters. He concluded with the importance of being comfortable discussing sexual and gender identity.

**Cosmetic Procedures in Darker Skin Types:**

**Pearls & Pitfalls**

**Andrew F. Alexis, MD, MPH**

**Background.** Dr. Alexis treats a highly diverse patient population. Addressing their range of concerns has led him to incorporate a number of cosmetic procedures, which “can be transformative in improving common conditions in skin of color.” Unfortunately, most literature and discussions address only lighter skin types, with relatively limited information regarding the management of risks inherent to darker skin. Closing this knowledge gap is particularly important given the increasing proportion of nonwhite racial and ethnic groups undergoing cosmetic procedures in the U.S.—which is approaching one-third and rising. Alexis discussed “safe and effective approaches to the most common procedures we consider in darker-skinned patient populations.”

**Procedures.** Electrodessication is very safe and effective for removing benign epidermal neoplasms (eg, dermatosis papulosa nigra). The key is using the lowest effective setting: in Alexis’s experience, 0.6–1.0 watt. For very small lesions (eg, 1 mm diameter), use an epilating needle to confine damage. Liquid nitrogen, which carries a high risk for hypopigmentation, should be used with caution and is generally less favorable than electrodessication. **Chemical peels** are a great adjunct for a range of aesthetic issues in darker-skinned patients that include disorders of hyperpigmentation, acne, and pseudofolliculitis barbae. To reduce risk of complications, use only superficial peeling agents, especially salicylic acid (20% and 30%), glycolic acid (30% to 50%), or Jessner peels. Stop all exfoliating treatments (including topical retinoids) 1 week before peeling. Alexis avoids trichloroacetic peels in skin of color due to their risk of hypopigmentation. He listed a “host of conditions in skin of color for which laser hair removal is transformative.” The key to safe use is longer wavelengths (in the near infrared spectrum), lower fluences, and longer pulse durations—plus excellent epidermal cooling. He uses the long pulse 1064-nm Nd:YAG laser, beginning with very low fluences. As hair presence diminishes, reducing the chromophore, he can raise fluences. Nonablative lasers—especially nonablative fractional lasers—have opened the door to laser resurfacing for treating acne scars, among other conditions, in darker skin, although considerable hyperpigmentation risk remains. Reducing treatment density—the microthermal zones of injury—is the primary risk-lowering parameter. Also essential: good cooling technique, strict sun-protective behavior and sunscreen use, and hydroquinone use pre- and post-treatment.

**Critical preparation.** “Get to know your devices. With any new device in your practice—do not blindly follow the manufacturer’s settings and advice from the literature. Perform many test spots at different settings to familiarize yourself with the range of safe and effective parameters.”

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**Aesthetic Procedures—Skin of Color**

**Total Ethnic Minority Population = 32%**


**Minimize Risk for Epidermal and Dermal Injury**

- Choose appropriate treatment for given skin type
- Use appropriate device
  - Use with conservative parameters
  - Use with good technique
- Take necessary pre/post treatment precautions
Misha A. Rosenbach, MD

Patient 1: A woman in her 60s came to dermatology with painful burning skin lesions primarily on her legs, especially her severely affected feet. She complained of malaise, noted dark tea-colored urine, had a 1-year history of sinusitis and epistaxis, and was audibly wheezing. Dr. Rosenbach found bilateral lesions on her upper extremities, and was struck by a dusky finger and pronounced saddle-nose deformity. The picture pointed to “a form of vasculitis, but this is a broad term,” he noted. “You identify a patient’s vasculitis based on the size of blood vessels affected, the organs involved, and supportive lab tests.” The biopsy supported cutaneous vasculitis, but the dusky finger was concerning for involvement of larger vessels. Rosenbach admitted the patient for workup, which showed pulmonary nodules, blood in the urine, and kidney involvement. The combination of vasculitis, epistaxis, pulmonary nodules, blood in the urine, and saddle-nose deformity pointed to granulomatosis with polyangiitis. (Her ANCA serologies were negative, which occurs with 10–20% of patients.) The patient has been in remission after treatment with high-dose steroids followed by rituximab.

Patient 2: This man in his 70s with COPD had been repeatedly hospitalized for flares and treated with high-dose prednisone. A slow taper had never progressed below 10–20 mg for the previous 6 months. During his most recent hospitalization, his peripheral IV had infiltrated and he developed a persistent lesion at the site. Culture grew coagulase-negative Staphylococcus and Streptococcus, but multiple courses of skin-pathogen-targeting oral and IV antibiotics had failed. The patient presented with a very indurated pustular-nodular plaque and boggy skin over the entire dorsal hand, but no other lesions. Skin biopsy demonstrated dermal organisms suspicious for a fungal infection. The alga Prototheca fit the histological morphology, but testing was negative (~30% of cases resist culturing) and the organism’s identity could not be confirmed. Prednisone was halted, and the patient was treated with amphotericin, local debridement, and alternate antimicrobial agents. Due to disease progression, amputation was discussed, but the patient passed away from unrelated comorbidities. Autopsy showed the infection isolated to his arm, and confirmation of the pathogen’s identity remains pending.

Andrew F. Alexis, MD, MPH

Patient 1. An 85-yo African American woman presented to the clinic with a dark growth on her forehead that had grown in size since appearing 6 months earlier, itched occasionally, and scabbed easily. A shave biopsy revealed nodular proliferation, basaloid cells emanating from the epidermis, and melanophages, with a diagnosis of pigmented basal cell carcinoma (BCC)—a nodular BCC that is pigmented. Although BCC is the most common skin cancer in Caucasian, Hispanic, Chinese, and Japanese populations, “the key here is that while it is much less common in darker-skinned patients—which includes
better efficacy. Such as terbinafine, which involves a shorter treatment course and significant hair regrowth. Alexis discussed treatment alternatives.

The patient was treated with oral griseofulvin for 3 months (after which the fungal culture was negative), and demonstrated significant hair regrowth. Alexis discussed treatment alternatives such as terbinafine, which involves a shorter treatment course and better efficacy.

Tinea Capitis

- Consider tinea capitis in the differential of hair loss in African American women.
- Look carefully for “black dot” appearance of the scalp in affected area; if present, perform KOH/culture.
- Treat with griseofulvin or terbinafine.

Sarah T. Arron, MD, PhD

Patient 1. This patient came in requesting cosmetic revision for a thickened scar after Mohs surgery 2 years prior for an SCC (classified as T1) on the left side of his nose. He had eventually developed numbness and pain in his left upper lip and cheek, which had been evaluated by dermatology, then neurology, then ENT, where a diagnosis of exclusion concluded trigeminal neuralgia. After a series of ineffective medications, anesthesiology had carried out gasserian ganglion nerve blocks providing pain relief for ~1 year. Recent imaging and the pre-revision biopsy showed no evidence of neoplasm, but tissue removed during debulking revealed perineural SCC, which was confirmed by repeat MRI (the most sensitive imaging for PNI). “It is well known in the head-and-neck neuroradiology literature that signs and symptoms of neurologic disease precede clinical and radiologic evidence of metastasis,” Dr. Arron said. “Send such patients for pain control but maintain a very high level of suspicion for metastatic disease that has not yet declared itself.”

Patient 2. An 8-year-old boy from a nearby rural community was 4 years out from a cord blood transplant for acute lymphoblastic leukemia when he came to the transplant clinic with a 1-year history of cutaneous graft-vs-host disease (GVHD) unresponsive to systemic prednisone and topical tacrolimus. Arron suspected that this was not GVHD, as this intense skin activity was restricted to his face and ears, ending at the neck of his shirt. It was a not-yet-publicized adverse effect of long-term voriconazole (used to prevent/treat invasive fungal infections in immunocompromised patients), involving photosensitivity and consequent risk for SCC and melanoma. The shave biopsy of a lesion Arron had noticed protruding on the back of the boy’s neck identified SCC in situ.

Vikash S. Oza, MD

Patient 1. A 13-yr-old girl with atopic dermatitis (AD) came in with multiple nodules scattered throughout her skin, complaining of intractable pruritus for more than 2 years. “Her case is pertinent because we will soon have access to biologic therapies for younger patients.” After discussing treatment options, Oza explained that his goal for patients with significant prurigo nodularis is to clear them as soon as possible. “As pediatric dermatologists, we need to think about what we should prescribe as systemic medications for AD.” Cyclosporin has been the go-to medication, with methotrexate next in line. This patient was ultimately transitioned to dupilumab, already approved for children ≥12 with moderate persistent asthma. “Given dupilumab’s safety profile, and the toxicity of drugs such as cyclosporin, it may become one of our go-to medications in the setting of the erythrodermic child.” The response is quick, with similar efficacy/safety profiles to those in adults. Oza discussed the tricky off-label dosing.

Patient 2. A 6-yr-old boy came in whose psoriasis-like plaques had appeared before age 1. Many were localized to his face. His palms and soles showed some thickening. “When a very young child presents with psoriasis-like features, especially with thickening of the palms and soles, we should consider the possibility of a monogenetic condition.” Oza noted the relevance here of Keith Choate’s study profiling pediatric patients with CARD14. A central feature is early psoriasis, often before age 1. “With a very young child who also gives the flavor of an overlap with pityriasis rubra pilaris, test for the CARD14 mutation.” Ustekinumab may prove to be an efficacious biologic for CARD14 patients.

MINI-SYMPOSIUM: Cutaneous Oncology

Lymphomas and Lymphoproliferative Disorders

Kevin D. Cooper, MD

Introduction. Dr. Cooper cares for a substantial number of patients with cutaneous lymphomas. He shared cases that exemplify important diagnostic, mechanistic, and/or therapeutic points.

(Continued on page 13)
For adults with plaque psoriasis

**better together**

The first and only steroid/retinoid therapy, allowing halobetasol and tazarotene to work together in an advanced, once-daily lotion that can be dosed to clearance³⁻⁵

**Halobetasol (0.01%)**

Provides powerful antinflammatory effects and reduces skin irritation, which is often associated with retinoids²⁻⁴⁻⁵

**Tazarotene (0.045%)**

Regulates cell growth and specialization to reduce hyperproliferation, increases collagen, and extends remission post treatment⁶⁻⁷

American Academy of Dermatology (AAD) Guidelines give the combination of a corticosteroid and a retinoid an A rating with Evidence Level I for the treatment of psoriasis⁴

The only FDA-approved treatment with a potent-to-superpotent steroid that can be used until control is achieved

**Indication**

DUOBRII™ (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045%, is indicated for the topical treatment of plaque psoriasis in adults.

**Important Safety Information**

**Contraindication**

DUOBRII Lotion is contraindicated in pregnancy.

**Warnings and Precautions**

- Women of child-bearing potential should be warned of the potential risk of fetal harm from DUOBRII and use adequate birth control. A negative result for pregnancy should be obtained within 2 weeks prior to treatment. If the patient becomes pregnant during treatment, discontinue DUOBRII Lotion and advise patient of the potential hazard to the fetus.
- DUOBRII Lotion has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis during or after treatment and may require that patients be evaluated periodically during treatment. Discontinue DUOBRII Lotion if a HPA axis suppression is identified.
- DUOBRII Lotion should not be used on eczematous skin, as it may cause severe irritation.
- Avoid exposure to sunlight, sunlamps and weather extremes. Patients with sunburn should be advised not to use DUOBRII Lotion until fully recovered. DUOBRII Lotion should be administered with caution if the patient is also taking drugs known to be photosensitizers because of the increased potential for photosensitivity.
- Topical corticosteroids may increase the risk of cataracts and glaucoma, advise patients to report any visual symptoms and refer to an ophthalmologist if needed.

**Adverse Events**

- The most common adverse events in clinical trials were contact dermatitis (7%), application site pain (3%), folliculitis (2%), skin atrophy (2%), and excoriation (2%).

To report SUSPECTED ADVERSE REACTIONS, contact Ortho Dermatologics at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.
is teratogenic, and it is not known what level of exposure is required for teratogenicity in humans. (see Contraindications and Clinical Pharmacology). Tazarotene elicits teratogenic and developmental effects associated with retinoids after topical or systemic administration in rats and rabbits. Advise females of reproductive potential to use effective contraception during treatment with DUOBRII Lotion (see Use in Specific Populations). It is unknown whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. There is no information on the effects of DUOBRII Lotion therapy on the mother’s clinical need for DUOBRII Lotion and any potential adverse effects on the breastfed child from DUOBRII Lotion. Clinical studies of DUOBRII Lotion have not been conducted in breastfeeding women to not apply DUOBRII Lotion directly to the nipple and areola to avoid direct infant exposure. Adverse reactions involving the eye should be managed with the mother’s clinical need for DUOBRII Lotion and any potential adverse effects on the breastfed child from DUOBRII Lotion. Clinical studies of DUOBRII Lotion have not been conducted in breastfeeding women to not apply DUOBRII Lotion directly to the nipple and areola to avoid direct infant exposure.

BRIEF SUMMARY OF PRESCRIBING INFORMATION
This Brief Summary does not include all the information needed to prescribe DUOBRII safely and effectively. For full Prescribing Information see DUOBRII (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% for topical use INDICATIONS AND USAGE
DUOBRII (halobetasol propionate and tazarotene) Lotion, 0.01%/0.045% is indicated for the topical treatment of plaque psoriasis in adults.

CONTRAINDICATIONS
DUOBRII Lotion is contraindicated in pregnant women. Females of reproductive potential should be warned of the potential risk and use adequate birth-control measures during treatment with DUOBRII Lotion. The possibility that a female of reproductive potential is pregnant at the time of institution of therapy should be considered. A negative pregnancy test should be obtained within 2 weeks prior to DUOBRII Lotion therapy, which should begin during menstruation.

Contraception
Based on animal studies, DUOBRII Lotion may cause fetal harm when administered to a pregnant female (see Use in Specific Populations). Advise females of reproductive potential to use effective contraception during treatment with DUOBRII Lotion.

Pediatric Use
Safety and effectiveness of DUOBRII Lotion in pediatrics under the age of 18 years have not been evaluated. Because of higher skin surface area to body mass ratios, pediatric patients are at a greater risk of systemic absorption. Topical corticosteroids are therefore at greater risk of adrenal insufficiency during or after withdrawal of treatment. Adverse reactions involving the eye should be managed with the mother’s clinical need for DUOBRII Lotion and any potential adverse effects on the breastfed child from DUOBRII Lotion. Clinical studies of DUOBRII Lotion have not been conducted in breastfeeding women to not apply DUOBRII Lotion directly to the nipple and areola to avoid direct infant exposure.

Females and Males of Reproductive Potential

Pregnancy

Precautions

WARNINGS AND PRECAUTIONS

Emphysematous Risk
Based on data from animal reproduction studies, retinoid pharmacology, and the potential for systemic absorption, DUOBRII Lotion may cause fetal harm when administered to a pregnant female and is contraindicated in pregnant women. Tazarotene is teratogenic, and it is not known what level of exposure is required for teratogenicity in humans. (see Contraindications and Clinical Pharmacology). Tazarotene elicits teratogenic and developmental effects associated with retinoids after topical or systemic administration in rats and rabbits. Advise females of reproductive potential to use effective contraception during treatment with DUOBRII Lotion Therapy (see Use in Specific Populations).

Advise pregnant females of the potential risk to the fetus. DOBRII Lotion is a pregnancy category C drug. Advise pregnant women to not apply DUOBRII Lotion directly to the nipple and areola to avoid direct infant exposure.

Adverse reactions involving the eye should be managed with the mother’s clinical need for DUOBRII Lotion and any potential adverse effects on the breastfed child from DUOBRII Lotion. Clinical studies of DUOBRII Lotion have not been conducted in breastfeeding women to not apply DUOBRII Lotion directly to the nipple and areola to avoid direct infant exposure.

很大的文件，可能对理解和阅读造成困难。
The Dermatology Foundation is grateful to the following corporations for their generous contributions last year. Their support furthers the DF’s ability to fund innovative research that shapes the future of dermatology.

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What You Need to Know About Nail Melanoma
Adam I. Rubin, MD

Introduction. Although longitudinal melanonychia is generally benign, nail melanoma is included in the differential diagnosis. Two-thirds of nail unit melanomas present clinically as pigmented streaks in the nail. Nail melanoma has a higher mortality rate than other... (Continued on page 14)
cutaneous melanomas because biopsies are often delayed, “so although we want to be cautious,” Dr. Rubin said, “we do not want to miss a nail unit melanoma.” (Amelanotic nail melanomas, on the other hand, can be highly challenging to detect.)

What You Need To Know About Nail Melanoma

- Concerning clinical and epidemiologic factors
- ABC rule for longitudinal melanonychia
- Dermoscopy evaluation of the nail plate
- Intraoperative dermoscopy of longitudinal melanonychia
- Nail clipping for surgical planning of longitudinal melanonychia
- Nonmelanocytic lesions presenting as longitudinal melanonychia
- Nail Unit Melanoma: functional surgery vs amputation

Assessing longitudinal melanonychia. Rubin discussed the variables associated with nail melanoma: age (5th–7th decades); single affected nail (especially thumb or great toe); band characteristics (darker, irregular borders, nonhomogeneous, >3 mm width); Hutchinson sign; nail plate dystrophy; bleeding or ulceration; failure to respond to prior diagnosis-based therapy; as well as family and/or personal history of malignant melanoma. The matrix shave/tangential excision is generally the preferred sampling method for longitudinal melanonychia, but a punch biopsy can be employed for small lesions located in the distal matrix. Rubin discussed the unique value of dermoscopy both before and during the biopsy procedure.

Nail unit melanoma. It is important not to delay a nail unit biopsy. The detection of amelanotic nail melanomas can be substantially delayed because detection is so difficult, and Rubin emphasized the need to consider this possibility whenever a nail is not responding to seemingly appropriate therapy. Surgical excision is the treatment of choice for nail melanoma. Other than for in situ tumors, however, there are no specific therapeutic guidelines for a given tumor thickness. Rubin discussed data clearly supporting the value of functional surgery above amputation except in cases where the tumor is very deep and involves the bone.

2019 DF Clinical Symposia Faculty Disclosures (Part I)

Andrew F. Alexis, MD, MPH: Almirall, Beiersdorf, BiopharmX, Bristol-Myers-Squibb, Celgene, Cipla, Dermavant, Galderma, Leo Pharma, Menlo, Novartis, RxI, Pfizer, Sanofi-Regeneron, Trevi, Unilever, Bausch Health.

2019 DF Clinical Symposia—Thank You to All

Held in Naples, Florida earlier this year, the 2019 program drew nearly 400 physicians who came ready to learn and interact with today’s experts. Over three days, the Clinical Symposia’s 11 distinguished faculty members—several who are former DF award recipients—presented a range of cutting edge topics for the practicing dermatologist.

The Foundation extends its thanks to its Program Co-Chairs, Janet A. Fairley, MD, and Jack S. Resneck, Jr., MD, and the faculty who are responsible for the success of this year’s exciting set of talks. The DF is also grateful to Unilever for its educational grant that enabled 50 residents to attend the program, and the corporate supporters who made this annual meeting possible.
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www.dermatologyfoundation.org
Spring/Summer 2019  15
Skin microbiome expert Elizabeth A. Grice, PhD, Associate Professor of Dermatology at the University of Pennsylvania, is the first recipient of the DF’s new Sun Pharma Award. This mid-career award is enabling her to launch highly insightful research into microbially derived molecules with the potential for a totally new type of therapeutic for inflammatory skin diseases. Dr. Grice’s inspiration took shape as she pursued her research to understand interactions between the skin and its microbiome constituents.

Dr. Grice has been studying the skin microbiome—comprising the skin’s highly complex communities of resident microorganisms—since 2007, when this research first began at the NIH. “We have learned that microbes modulate barrier function and immune and inflammatory processes,” she notes. It is essential to skin health. As Dr. Grice has probed the microbiome’s interactions with the skin, she realized that individual commensal bugs must be secreting small molecules to achieve their effects—and she recognized the strong potential for harnessing their mechanisms to treat inflammatory and infectious skin diseases. Already accurately and effectively targeted, these molecules would act with significantly greater selectivity than current systemic immunotherapy approaches that sometimes have undesirable side effects.

Dr. Grice is deeply grateful for her Sun Pharma Research Award. Her research is well underway with a screen of >4,000 human skin commensal bacterial strains to identify those with anti-inflammatory activity. She and her lab are currently working to identify the most promising candidates for changing the course of atopic dermatitis (AD), which will be tested in mouse models of AD and skin inflammation.

“My Sun Pharma award is allowing me to take my research in a new and exciting direction, and identify microbially derived molecules with therapeutic value,” Dr. Grice explains. “This unique approach to treating inflammatory skin disease holds the potential to impact the way medicine is practiced.”

The Foundation thanks Sun Pharma for their generous gift of $1 million to fund three mid-career awards for outstanding scientists driving progress in treating inflammatory skin diseases. The DF is now accepting applications for the 2020 award: dermatologysfoundation.org