



A SUPPLEMENT TO

Skin & Allergy News®



SKIN DISEASE
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Proceedings from Skin Disease Education Foundation's 34th Annual *Hawaii Dermatology Seminar™*



Based on selected presentations held in Waikoloa, Hawaii

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Introduction

Advances in the field of dermatology have a direct impact in helping clinicians achieve optimal outcomes in the care of their patients. Sharing information about recent developments that are relevant to clinical practice—including new techniques, technologies, and treatment strategies—is critical in increasing awareness of these advances.

As part of its commitment to providing continuing medical education to dermatologists and other health care professionals about conditions of the skin and cosmetic dermatology, the Skin Disease Education Foundation's 34th Annual Hawaii Dermatology Seminar™ held in February 2010 brought together leading experts in the field of dermatology to discuss the latest clinical developments in dermatology. This publication features highlights from presentations made at this conference in the areas of pediatric dermatology, aesthetic dermatology, and medical dermatology. This information can be useful to clinicians who seek to determine effective individualized treatment and disease management strategies for their patients.

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Acne From an Expert—Drugs, Diet, and More

Guy Webster, MD, PhD

Providing care to patients with acne represents a substantial proportion of the daily caseload for many clinicians in the field of dermatology. Dr Guy Webster, a dermatologist who has a private practice in Delaware, shared various clinical insights based on his experiences in helping patients with acne achieve optimal outcomes.

“In acne, there are good reasons to avoid overuse of antibiotics,” said Dr Webster. He explained that acne is harder to treat because of antibiotic resistance, resistant strains are becoming more common in the environment (due to the use of antibiotics in food sources and other issues), and infections with resistant bacteria (eg, methicillin-resistant *Staphylococcus aureus* [MRSA] and vancomycin-resistant *Enterococcus* [VRE] infections) are common.

“If you use retinoids properly, you can minimize the use of antibiotics,” said Dr Webster, noting that the use of topical retinoids in patients with acne can be effective maintenance treatment. “If using a retinoid from day 1, you can discontinue the use of antibiotics at 12 weeks in most patients and improvements in acne will hold, if not continue to improve.”

Acne antibiotics are generally regarded as safe, although some common reactions may include dose-dependent phototoxicity, gastrointestinal upset, and dizziness (“dizziness can be avoided with slow-release formulations”). Uncommon reactions include pigmentation (especially with minocycline use), hypersensitivity, and pseudotumor cerebri (“instruct patients to tell you if they have a bad headache”).

Clinicians need to be aware that their patients may ask questions about studies relating to acne treatments. For example, with respect to reviewing studies that report associations linking antibiotic use and breast cancer (eg, *JAMA*. 2004;291:827-835), Dr Webster cautions clinicians to keep in mind that “statistical correlations aren’t always true.” He noted that, in this particular study, no control for chronic infection or inflammation as an independent risk was applied (ie, long-term antibiotic use may merely be a marker of another underlying predisposition) and raised the question of whether all antibiotic treatments of differing structures and mechanisms had an equivalent risk for cancer.

Clinicians need to determine which antibiotics are most effective for acne treatment in their patients on an

individualized basis, according to Dr Webster. Based on his clinical experiences, using erythromycin plus benzoyl peroxide or clindamycin plus benzoyl peroxide for the treatment of infection with *Propionibacterium acnes* has been more effective than have benzoyl peroxide monotherapy, clindamycin monotherapy, erythromycin monotherapy, and azelaic acid monotherapy.

Key considerations in treating acne in adult women include an understanding that adult women may have higher standards than do teenagers and that acne in adult women is characterized by typically fewer but more resistant lesions and greater hormonal influence, and that acne may overlap with rosacea. Treatment options for acne in adult women include retinoid-containing combination agents, retinoids alone, and spironolactone. Adult women with acne may also have less tolerance of irritation than do other patients with acne, which may be addressed by taking measures to control cleaning regimens, the use of topical dapsone (which is nonirritating), and/or the use of oral treatments rather than topical treatments.

“As we all know, cleanliness does not help acne,” said Dr Webster. “I ask every grown-up with acne this question, ‘Are you someone who burns and stings when you put on cosmetics, moisturizers, or sunscreens?’ If the answer is ‘yes,’ I do not generally use retinoids for such patients.”

“The role of diet in acne has not been studied well,” said Dr Webster. “I tell my patients that the benefits of diet changes for acne seem small, based on study results so far, and that diet changes are not as strong as the weakest of drugs available for the treatment of acne. Some patients may want to try a diet low in carbohydrates to see if there is any effect on their acne.”

Many treatments are available to address the needs of patients with acne. These insights from Dr Webster may be useful to others in clinical practice. ■

Dr Webster discloses industry affiliations with Allergan, Amgen, Astellas, Aventis, Bristol-Myers Squibb, Cipher, Coria, Cutanea Life Sciences, Dermik, Galderma, GlaxoSmithKline, Graceway, Johnson & Johnson, Medicus, Merck, Micrologix, NitricBio, Onset Therapeutics, Ortho, Ranbaxy, SkinMedica, Stiefel, Valocor Therapeutics, Wyeth, and Xoma.

Reference:

Velicer CM, Heckbert SR, Lampe JW, Potter JD, Robertson CA, Taplin CH. Antibiotic use in relation to the risk of breast cancer. *JAMA*. 2004;291:827-835.

New-Generation Topical Medications Harness Mighty Vehicles

Leon H. Kircik, MD

The highly sophisticated vehicles employed in the latest generation of dermatologic topical medications are a boon to patient care, but a headache for researchers.

“At this point in dermatology, in the clinical trials for topical therapies, there is no placebo arm anymore. You're dealing with vehicles that have some activity beyond the placebo effect,” Dr Leon H. Kircik said at the annual Hawaii dermatology seminar sponsored by Skin Disease Education Foundation.

Case in point: dapsone 5% gel (Aczone). The vehicle uses diethylene glycol monoethyl ether (DGME) to facilitate permeation of dapsone into the skin.

In the large, multicenter, pivotal phase III clinical trials, mean reduction in inflammatory lesion count after 12 weeks was 48% with dapsone 5% gel and 42% with vehicle. The proportion of patients who were clear or almost clear was 40.5% with dapsone and 32.8% with the vehicle.

“The vehicle itself is doing really well here. We see almost one third of patients getting substantially better just with the vehicle. Most vehicles don't help the active drug like that,” observed Dr Kircik of Indiana University, Indianapolis.

Although DGME has been utilized in some cosmetic products, dapsone 5% gel is the first prescription medicine in which it has been employed.

“I think it's a great vehicle. Hopefully the people who own it will use it for topical steroids, topical antifungals—whatever active agent you can put in it—because it really does help permeate into the stratum corneum,” he said.

DGME is a nontoxic liquid that is freely miscible with both polar and nonpolar solvents, which is why it is effective as an enhancer of transdermal permeation. It is also believed to exert beneficial effects on the sebum barrier, as evidenced by the 12-week results on the secondary end points of skin oiliness and erythema.

At baseline, 18.6% of patients in the dapsone arm exhibited significant skin oiliness and 14.8% had erythema; after 12 weeks, these figures dropped to 5.6% and 6.2%, respectively. The vehicle-only group did almost as well: a 19.2% prevalence of oiliness at baseline, improving to 7.2% after 12 weeks, and a reduction in the prevalence of erythema from 15.6% at baseline to 8% (*J Am Acad Dermatol.* 2007;56:439 e1-10).

After decades of 12- to 16-week clinical trials for acne therapies, the Food and Drug Administration now routinely requires 52-week safety data on new products, such as dapsone 5% gel. Dapsone patients showed a mean 49% reduction in total lesion count after 12 weeks, a 56% reduction at 6 months, and a 58% reduction at 1 year (*J Drugs Dermatol.* 2007; 6:981-987).

“Acne patients often come back to see us after 3 to 6 months and say, ‘Hey doc, this isn't working anymore. Give me something else.’ We're always struggling to give them something new or different. I think it's very reassuring to know we can tell patients that if you keep using dapsone for a year, you're going to continue seeing better results,” Dr Kircik said.

Physicians prescribing dapsone 5% gel are likely to hear from their well-intentioned local pharmacist cautioning that a patient has a sulfa-drug allergy. Reassurance can be offered that there is no cross-reactivity between the sulfonamides, which are antimicrobials, and anti-inflammatory sulfones such as dapsone, he said.

Dr Kircik noted that DGME is just one of many sophisticated vehicles being harnessed to help create improved topical medications. Polymeric microsphere technology holds drugs like tiny sponges, delivering medications into the skin with less dryness and irritation than earlier products employing the same drugs with older vehicles. ■

Dr Kircik serves as a consultant, speaker, and research investigator for Allergan, which markets dapsone 5% gel, as well as close to 50 other pharmaceutical companies.

Effects of Uncontrolled Psoriasis Inflammation Are More Than Skin Deep

Jeffrey Sobell, MD

Evidence indicating the serious effects of psoriasis inflammation on the rest of the body and not just the skin is starting to accumulate, noted Dr Jeffrey Sobell.

“We are just beginning to understand the impact of uncontrolled inflammation on the body, separate from the effects we’re seeing in the skin and joints,” Dr Sobell of the Department of Dermatology, Tufts University, Boston, said in an interview. This evidence has raised the question of whether conditions, such as cardiovascular disease (CVD), improve by “treating an individual’s underlying psoriasis and controlling that tremendous inflammation” that characterizes the disease.

In addition to CVD, psoriasis patients are at an increased risk for depression and other conditions such as Crohn’s disease, certain cancers, and chronic obstructive pulmonary disease. In his presentation at the seminar, Dr Sobell focused on psoriatic arthritis (PsA), depression, and CVD.

PsA

PsA usually appears an average of 10 years after the onset of skin disease (*Q J Med.* 1987;62:127-141); about 70% of patients have skin manifestations initially, while 15% develop joint symptoms first and 15% develop joint and skin symptoms simultaneously, he noted.

Dermatologists should screen for arthritis in their psoriasis patients because a prompt diagnosis is critical. Early intervention, particularly with a tumor necrosis factor (TNF) blocker, can reduce the potential for joint deformities and disability, in addition to helping alleviate the signs and symptoms of arthritis, he noted.

The Food and Drug Administration–approved biologic treatments for PsA—etanercept, infliximab, adalimumab, and golimumab— are approved for reducing the signs and symptoms of active arthritis,

including the progression of structural damage, and improving physical function.

“I encourage dermatologists when seeing psoriasis patients to ask questions about arthritis symptoms,” such as joint stiffness in the morning, and performing a physical examination that includes looking for asymmetric inflammatory arthritis and tender or swollen joints, said Dr Sobell. Patients should also be asked about whether they have a family history of PsA and, if they have joint pain, whether it fluctuates with psoriasis exacerbations, he said, noting that only about 35% of patients with PsA have simultaneous flares of skin and joints.

Depression

Depression affects about 25% of people with psoriasis, and it can be debilitating, sometimes leading to suicidal thoughts, particularly in younger patients, Dr Sobell said. Although the disease itself has a psychological impact on patients, TNF levels are known to be elevated in depression. This “may be part of the pathogenesis of depression” in people with psoriasis, and, therefore, TNF levels are a possible target of treatment, he said.

Evidence that treatment with an anti-TNF agent improves symptoms of depression and fatigue includes a phase III study evaluating the efficacy of etanercept, compared with placebo, in over 600 patients with moderate to severe psoriasis (*Lancet.* 2006;367:29-35). At week 12, treatment was associated with improved symptoms of depression and fatigue. Improvements were not strongly correlated with improvements in Psoriasis Area and Severity Index scores and were also seen in patients with little improvement of psoriasis. This “may be a detectable effect of neutralization of TNF” on depression, Dr Sobell said.

Although these results are intriguing, he added that more studies are needed to further investigate the relationship between TNF levels and depression, and that



Psoriasis patients are more likely to have comorbid diseases that are CVD risk factors, such as obesity, hypertension, hyperlipidemia, and insulin resistance.

conclusions cannot be made about the impact of anti-TNF treatment and depression in the general population.

CVD

Psoriasis patients are more likely to have comorbid diseases that are CVD risk factors, such as obesity, hypertension, hyperlipidemia, and insulin resistance. However, psoriasis is also an independent risk factor for myocardial infarction and CVD, which is thought to be related to the immune and inflammatory activity of skin disease, Dr Sobell said.

He referred to evidence that TNF, which has a major role in the pathogenesis of rheumatoid arthritis (RA) and psoriasis, also plays a role in CVD, including TNF effects on promoting insulin resistance. TNF also induces the cytokine interleukin-6, which increases C-reactive protein (CRP), an inflammatory biomarker that is associated with an increased CVD risk.

This type of evidence raises the issue of whether treatment with systemic psoriasis treatments can reduce cardiovascular risk in these patients, and whether biologic agents improve CVD risk factors and markers, Dr Sobell said.

Most of the data that have found an association between anti-TNF therapy and improvements in CVD risk factors and markers have been in people with RA, he said. In a small study of RA patients, those treated

with adalimumab had significant increases in high-density lipoprotein cholesterol and reduced CRP levels after 2 weeks, compared with those in the placebo group (*Ann Rheum Dis* 2005;64:303-305).

Evidence that systemic treatment of RA and psoriasis reduced cardiovascular events was provided in a retrospective study of over 6,000 patients with RA and over 7,000 patients with psoriasis treated between 1998 and 2003 (*J Am Acad Dermatol*. 2005;52:262-267). The risk of CVD was significantly lower in patients who were treated with methotrexate in both groups, compared with the risk in those who were not (risk was reduced by 23% in those with psoriasis). The addition of folic acid further reduced the risk.

Data on the impact of anti-TNF therapies on cardiovascular events include two studies suggesting that cardiovascular events in RA patients were reduced during treatment, he said. These include a Swedish registry study of almost 1,000 RA patients, which found a significantly lower risk of cardiovascular events in those treated with an anti-TNF agent compared with the risk in controls (*J Rheumatol*. 2005;32:1213-1218). The impact of treatment in patients with psoriasis is unknown, he pointed out. ■

Dr Sobell disclosed that he is a speaker and consultant for Abbott, Amgen, and Centocor, and is an investigator for Abbott and Centocor. The companies are manufacturers of biologic treatments for psoriasis.

Quick Diagnosis Key to Photodermatosis Outcomes

Vincent DeLeo, MD

While the diagnostic challenges of photodermatoses are multiple, one thing is certain: a proper and rapid diagnosis is essential to optimizing patient management and outcomes, according to Dr Vincent DeLeo.

The diagnostic challenges of photodermatoses include increasing clinical suspicion to recognize the less common forms, ruling out dermatologic mimics in the differential diagnosis, and identifying etiology to guide therapy and speed patient recovery, Dr DeLeo noted at the seminar.

Photodermatosis incidence varies from relatively common to relatively rare, he said. Specific presentations include porphyria, idiopathic photodermatitis, polymorphic light eruption, solar urticaria, chronic actinic dermatitis, exogenous chemical photosensitivity, and photocontact dermatitis.

Consider age at onset, timing of the skin eruption, and occupation, medication, or plant exposures when taking a patient's history. Ask about products used for personal care, particularly any sunscreens or colognes. Clinical workup should include a review of systems that focuses on cutaneous and neurologic effects and a complete physical examination, said Dr DeLeo, Chairman of the Department of Dermatology at St Luke's–Roosevelt Hospital Center and Beth Israel Medical Center in New York.

Porphyrias present in two specific patterns—immediate, with skin burning within a day of exposure, or delayed, with blistering, hirsutism, or hyperpigmentation. With an immediate form, such as erythropoietic protoporphyria (EPP), rule out solar urticaria and lupus erythematosus, Dr DeLeo suggested.

With a delayed presentation, such as porphyria cutanea tarda (PCT), consider pseudo-PCT and epidermolysis bullosa acquisita in your differential diagnosis, he said. A blood test for plasma porphyrins is usually diagnostic in all porphyrias, but a red blood cell porphyrin assay will diagnose EPP and a 24-hour urine assay will diagnose PCT.

Among the sporadic presentations of PCT, it is important to check for a diagnosis of hemochromatosis early to prevent serious tissue damage, especially

dysfunction of the liver, Dr DeLeo said. A test for the culprit gene mutations can be ordered from any major diagnostic laboratory.

Idiopathic photodermatoses include polymorphous light eruption (PMLE), chronic actinic dermatitis, and solar urticaria. Dermatologists are most likely to encounter PMLE, the most common form of photosensitivity, Dr DeLeo said.

PMLE tends to arise in young adults and in women more than men. Symptoms usually occur within days of exposure—during springtime or while on vacation, for example. Look for a symmetrical distribution on exposed areas only. The histologic differential with suspected PMLE includes lupus erythematosus, lymphocytic infiltrate of Jessner, and cutaneous lymphoid hyperplasia.

Solar urticaria also occurs more often in women than in men. A sudden onset of erythema, edema, urticaria, and pruritus in exposed areas is characteristic. Systemic involvement is rare, Dr DeLeo said. Careful photoprovocation can aid in the definitive diagnosis of this condition. Treatment options include H₁ antihistamines and proper photoprotection.

Chronic actinic dermatitis, on the other hand, is more persistent and not related to a specific acute exposure. Patients typically present with patchy eczema and may have erythroderma or lymphoma-like plaques in sun-exposed areas.

This form of photosensitivity is much more common in men and tends to present in older patients, at a mean age of 65 years, Dr DeLeo said. Rigorous photoprotection is warranted. Consider patch testing and photopatch testing to rule out underlying contact or photocontact allergy. PUVA (psoralen plus ultraviolet A light therapy) or immunosuppressants can be used in severe cases.

Some patients can experience photoirritant contact dermatitis from plants. A number of plants can cause this, including celery, dill, lemon, lime, and St John's wort, he concluded. ■

Dr DeLeo disclosed being a consultant for Estée Lauder, Goodyear, Limited Brands, L'Oréal, Neutrogena, Orfagen, Pfizer, and Schering-Plough.

Scientific Treatment of Photoaging

Leon H. Kircik, MD

Clinicians in the field of dermatology are finding that their patients are expressing a growing concern about aging skin. Interest in this area will continue to increase, given the changing demographics of aging in the United States so that the population distribution is skewed more toward people 50 years of age or older than toward children and young adults.

“Everyone is trying to look better and younger,” said Leon H. Kircik, MD, a dermatologist based in Louisville, Kentucky, who tries to help his patients make sense of the benefits of various antiaging treatments. “As a society, we value better looks and younger-looking skin. Sun exposure and the effects of smoking accelerate aging.”

Dr Kircik explained how imperfect collagen repair that accompanies aging will lead to wrinkles, which is how individuals develop wrinkles in photoaging skin. He described various clinical studies and the ways photodamage is often determined, including such measures as tactile roughness, fine wrinkling, coarse wrinkling, sallowness, laxity, and mottled hyperpigmentation.

Treatment options that are available for postinflammatory hyperpigmentation include bleaching agents, topical retinoids, azelaic acid, combination products, and physical modalities (eg, chemical peels, microdermabrasion, cryotherapy). He noted that irritation (eg, redness, dryness, peeling, burning/ stinging, itching) can be a limiting factor in treating some patients with retinoids but that such irritation may subside over time (sometimes in as little as 3 months). He explained that antioxidants, anti-inflammatory agents, retinoids, and growth factors improving extracellular matrix quality may all serve various roles in blocking pathways to skin damage.

The emergence of cosmeceuticals (defined as topical agents that lie “somewhere between pure cosmetics and pure drugs...that do something beyond improving appearance...and have some interactive effect”) in the marketplace has caused some confusion for dermatologists in terms of assessing what products can be recommended for their patients. In some cases, there is some science behind these products (eg, the antioxidant properties of coffee berry).

“Skin aging is like a chronic wound,” said Dr Kircik. “Aging produces a chronic wound that affects a large area of skin. Over time, the body loses its ability to complete the healing process in that the repair mechanism becomes slower, resulting in a reduction in collagen, excessive amounts of type 3 collagen, loss of stored antioxidants, loss of skin elasticity, and wrinkle and fine-line formation.” He noted that replenishing growth factors in the skin can induce remodeling and reversal of skin aging, adding that precise three-dimensional structure is essential for binding growth factors to cell surface receptors.

Dr Kircik encouraged others to stay informed about further developments and findings from clinical studies that may offer guidance on which treatment options, determined on an individualized basis, may lead to optimal results for their patients. ■

Dr Kircik has worked as an investigator, consultant, or speaker with the following pharmaceutical companies: Abbott, Acambis, Allergan, Amgen, Astellas, Asubio, Berlex, Biogen Idec, BioLife, Breckenridge Pharmaceutical, Centocor, ColBar LifeScience, CollaGenex Pharmaceuticals, Combinatrix, Connetics, Coria, Dermik, Dow, DUSA Pharmaceuticals, EOS Pharmaceutical, Ferndale, Galderma, Genentech, GlaxoSmithKline, Healthpoint, Innovail, Intendis, Johnson & Johnson, LEO Pharma, Medicis, NanoBio, Novartis, Nucryst, Obagi, Onset Therapeutics, OrthoNeutrogena, Pfizer, PharmaDerm, QLT, QuatRx, Quinova Pharmaceuticals, Serono, SkinMedica, Stiefel, 3M, Tolere, Triax Pharmaceuticals, UCB, Valeant, and Warner Chilcott.



Aging produces a chronic wound that affects a large area of skin. Over time, the body loses its ability to complete the healing process in that the repair mechanism becomes slower, resulting in a reduction in collagen, excessive amounts of type 3 collagen, loss of stored antioxidants, loss of skin elasticity, and wrinkle and fine-line formation.

Periprocedure Considerations

Joel L. Cohen, MD

Minimizing bruising and purpura is one of the goals of clinicians who work in aesthetic dermatology—performing various surgical and laser procedures, as well as administering injectables—to help minimize downtime for patients. Therefore, acquiring the latest information about factors that can minimize or decrease postprocedure bruising is of particular interest to these clinicians.

Dr Joel L. Cohen, a dermatologic surgeon based in Colorado, spends the majority of his time performing Mohs surgery as well as facial aesthetic procedures. He recently shared a number of clinical insights for the care of patients having cutaneous procedures that may be helpful considerations for many patients in terms of minimizing downtime.

With respect to preprocedure considerations, aspirin is an irreversible inhibitor of platelets of cyclooxygenase, explained Dr Cohen, adding that “it takes about 5-plus days to typically recover functional platelets.” Therefore, unless patients are taking “therapeutic” aspirin based on a history of myocardial infarction, cerebrovascular accident, or blood clots, most of his patients are instructed to discontinue their use of aspirin for 5 to 7 days prior to the procedure if agreeable with either their cardiologist or their primary care physician. Regarding nonsteroidal anti-inflammatory drugs, which are reversible inhibitors of platelet aggregation (for headaches, muscle aches, minor pain, and perimenstrual cramping), patients are instructed to discontinue their use for 3 to 5 days prior to the procedure. With respect to various vitamins and herbal agents, patients are instructed that not only “the Gs” (namely, ginseng, garlic, ginger, and *Ginkgo biloba*), but also many other vitamins and herbals such as vitamin E, kava, celery root, fish oils/omegas, glucosamine, chondroitin, Saint John’s wort, licorice, and horseradish are known to have anticoagulant properties. Because “alcohol can cause oozing and swelling” and may inhibit platelet activation, Dr Cohen advises patients to generally try to avoid the use of alcohol for a few days prior to some procedures as well.

Across the spectrum of dermatologic surgical procedures, considerations for reducing bruising during the procedure include using longer pulse durations with pulsed dye lasers (6–10 ms), slow injection and often avoiding fanning for fillers, and the prudent use of epinephrine in local anesthesia, as well as careful slow dissection and meticulous hemostasis for surgical procedures. The intraprocedural use of ice, compressed air, and contact cooling devices all may help reduce pain, swelling, bruising, and thermal injury for various cutaneous procedures from lasers to surgery to injectables.

Postprocedure considerations for reducing bruising include the use of ice, oral arnica (likely not topical arnica due to lack of significant data), possibly bromelain, and topical vitamin K oxide (which studies show may be more effective than topical vitamin K).

Dr Cohen also shared some lessons learned about the limitations of split-face studies based on his recent experiences in conducting a randomized, double-blind, placebo-controlled split-face study (*J Drugs Dermatol.* 2009;8:1020-1024), highlighting that “even small differences in reduced severity or bruising are clinically relevant to patients.”

“Many options are available for treating the effects of aging on skin,” said Dr Cohen. “Along with the rising demand for these procedures, there may be a parallel need for complementary products as pretreatment conditioning or posttreatment recovery-type products. Complementary formulas may help by minimizing postprocedure skin issues such as bruising, swelling, and overall downtime.” The use of growth factors for posttreatment wound healing may be particularly useful, especially after ablative procedures, and are available in the form of human growth factors as well as a new agent that contains snail-derived factors. ■

Dr Cohen has industry affiliations as a consultant and clinical trials investigator with Allergan, Biopelle, Medicis, Merz, Neocutis, and Obagi.

Reference:

Cohen JL, Bhatia AC. The role of topical vitamin K oxide gel in the resolution of postprocedural purpura. *J Drugs Dermatol.* 2009; 8:1020-1024.

Look Beyond the Wrinkles in the Aging Face

W. Philip Werschler, MD

Tomorrow's approach to the aging face is all about restoring volume and moving away from filling in lines and wrinkles, according to Dr W. Philip Werschler.

Advances in nonsurgical options such as fillers, toxins, lasers, peels, and topical products make it possible to address the volume loss and change in facial shape that come with aging. Volume loss is cumulative through the decades and consists of several components including dermal and muscle atrophy, shifts in fat deposits, and skeletal thinning and remodeling including flattening of the maxilla, expansion of the occipital orbit, and shrinking of the mandible, he said at the seminar.

The heart-shaped or triangular appearance of a youthful face, which peaks in the mid-twenties, inverts

patients, but they will still have a flat face, lacking in contour and dimension. If, however, nasolabial folds are tackled by volumizing the cheeks, it will lift the face and fill in the nasolabial folds, resulting in a more youthful, balanced, and natural appearance. Similarly, botulinum toxin A can be used to change the shape of the orbital opening, thus affecting crow's feet and softening eyebrows.

It is helpful to divide the face into three facial treatment zones when planning a nonsurgical total facial rejuvenation (NSTFR)—upper, mid, and lower. Facial treatment zones are useful terms in patient education because they are easy to remember and easy to comprehend.

When analyzing the treatment zones, look for changes in balance, proportion, and symmetry, and



To address wrinkles only is to address only half of the problem.

to the pyramid of age with volumetric loss and alteration, said Dr Werschler, an assistant clinical professor of dermatology at the University of Washington in Seattle. In women, this occurs earlier, typically in the late 40s and 50s, than in men, in the 60s and 70s. The bottom of the face appears heavier, often jowly; there is loss of the mandibular sweep; and the nose, instead of the chin, serves as the apex of the inverted triangle. Ultimately, as we age, we take on facial proportions that make us look more like infants than adults, he said.

To address wrinkles only is to address only half of the problem, Dr Werschler said. For example, laser resurfacing can produce smooth skin in aging

consider what the patient hopes to achieve. There are many approaches to NSTFR. However, they don't exist in isolation, and frequently the combination of NSTFR and surgery is best, according to Dr Werschler. A good example of this is a brow lift along with laser or filler on the lips or lower part of the face. That may mean referring or collaborating with a surgeon in your practice, but the patient will thank you for the result, he said. ■

Dr Werschler is a speaker, consultant, and clinical investigator for Allergan and Medicis, and has relationships with numerous other pharmaceutical companies.

Fractionated Nonablative Lasers

E. Victor Ross, MD | Christopher B. Zachary, MBBS, FRCP | David J. Goldberg, MD, JD

Several different types of laser technologies are now available for use in achieving cosmetic enhancements in patients. E. Victor Ross, MD, Director of the Scripps Clinic Laser and Cosmetic Dermatology Center based in San Diego, California, shared some of his clinical experiences and expertise regarding laser applications in dermatology.

“Overall, the use of nonablative technologies is more tolerable for patients who want results with little or no downtime,” said Dr Ross, who noted that the use of conventional carbon dioxide (CO₂) lasers for skin resurfacing in the late 1990s sometimes was associated with scarring, infection, hypopigmentation, redness, and worsening of melasma, as well as generating a telltale line of demarcation after CO₂ treatment.

Different wavelength ranges can be used with fractionated ablative technologies. “At reasonable fluences, fractionated nonablative lasers penetrate enough in tissue water so as to heat a cylinder of collagen but not remove it,” said Dr Ross, adding that new “aggressive” fractional nonablative technologies are close to replicating one-pass CO₂ laser treatment results without epidermal damage and at low risk. Reasons for doing fractional rather than confluent resurfacing are to decrease infection risk, increase the quality of recovery for the patient, and decrease the risk of delayed hypopigmentation.

In comparing stamping techniques to a continuous-motion random scanning technique, Dr Ross explained that “stamping techniques have been accused of creating areas of undertreatment and overtreatment so that the skin appears mottled, similar to faux painting a wall with a sponge.” However, in his experience, “stamping techniques create an even pattern of injury if one is careful. On the other hand, a continuous-motion random scanning technique creates a uniform pattern of coverage, similar to painting a wall with a roller brush.” He concluded that “whatever device a clinician is comfortable with (ie, stamping versus scanning) is the one that the clinician is going to be quite adept in using.”

Combination ablative and nonablative fractional technology may work best in some circumstances, where working sequentially is appropriate, according to Dr Ross. “If a patient can tolerate downtime, ablative

may be appropriate, and if the patient cannot tolerate downtime, nonablative may be appropriate.”

Regarding imprinting, Dr Ross noted that “sometimes we see this imprinting phenomenon (pattern of spots), which typically goes away in a few weeks; my experience is that imprinting is never seen to last more than a few months.”

The pitfalls that apply in all fractional laser resurfacing treatments include (1) there are no real clinical end points (“we are treating by recipe”); (2) the parameter sets must be accurate and not result in overtreatment; (3) with more passes, clinicians can approach 100% coverage, but will never achieve 100% coverage; and (4) improvements in pigment are made, but often are incomplete and temporary resolution occurs.

According to Dr Ross, the top reasons for embracing nonablative remodeling are minimal to no downtime, no bleeding, little or no wound care, and the ability to combine nonablative remodeling with other modalities. “Nonablative technologies are known for being more tolerable for patients, as well as for their ease of use for practitioners,” said Dr Ross.

Fractionated Ablative Technologies

Using lawn care repair (ie, aeration of the lawn will allow the grass to grow thicker as new growth spreads and becomes rejuvenated) as an analogy to describe fractionation in the broadest sense, Christopher B. Zachary, MBBS, FRCP, Professor and Chair of the Department of Dermatology at the University of California, Irvine, discussed the skin’s reaction to fractional treatment and showed a series of slides to illustrate his experiences working with ablative technologies. His major point about the use of fractionated ablative technologies was that “you don’t have to treat 100% of the skin to achieve the desired result.”

Dr Zachary identified a wide range of energy-based devices for skin rejuvenation, including ablative devices, fractional thermal devices, larger bulk-heating devices, intense pulsed light devices, light-emitting diodes, Q-switched lasers, long-pulsed lasers, and pulsed dye lasers. Volumetric reduction and dermal plumping are regarded as key features of ablative fractionated rejuvenation.

Fractional treatment approaches for dermal ablation were described as the “delivery of energy in such a fashion as to create wounds that are deeper than they are wide, and with normal skin interspersed.” Fractional treatment approaches for epidermal ablation were described as “any partial-density spot or dot matrix treatment confined to the epidermis.”

In evaluating the results of any skin rejuvenation treatment, clinically visible changes are necessary to be considered valid, according to Dr Zachary. In clinical practice, he prefers using such terminology as “minor improvement,” “moderate improvement,” and “very significant improvement” as meaningful ways to communicate treatment outcomes with patients and others.

“In practice, my go-to device for fractional laser surgery of acne scarring and tissue tightening is the CO₂ laser because it has better natural parameters,” said Dr Zachary.

In assessing the usefulness of fractionated laser resurfacing technologies, Dr Zachary encourages others to consider these factors: they have fewer complications; have off-the-face indications (“great for scars”); produce little postoperative pain; result in less downtime with faster healing; approach the benefits of traditional CO₂ lasers; can be used in combination with other procedures; and may be used as a drug delivery system.

Fractional Radiofrequency

A new technology called fractionated bipolar radiofrequency has recently become available. By using radiofrequency sublation, heat energy is placed into the dermis where it can produce substantial dermal impact with minimal epidermal disruption. The device uses radiofrequency energy that generates deep dermal heating in the region of the 64-electrode matrix to induce skin injury, which elicits a wound-healing response. Less affected tissues around the matrix points may be stimulated by the heat, which can help accelerate the healing process and lead to the appearance of tighter, rejuvenated skin.

David J. Goldberg, MD, JD, provided an overview of this technology and encouraged others in clinical practice to become familiar with its characteristics. This skin rejuvenation treatment may result in the

improvement of wrinkles, skin laxity, scars, acne scars, textural irregularities, tone, and superficial skin lesions.

“The gold standard will always be traditional CO₂ ablation laser resurfacing,” said Dr Goldberg. “Fractional radiofrequency resurfacing can now be added to the list of options available for consideration.”

He identified the characteristics of treatment in terms of minimal epidermal disruption, deep volumetric heating into the dermis, subsequent dermal remodeling, minimal downtime, and optimal results for wrinkles, laxity, tone, and texture. The mechanism of action is based on fractionated and tunable bipolar radiofrequency energy delivered to skin tissue that modifies the connective tissue in the skin via a controlled thermal impact. Applying thermal energy to the skin activates a cascade of physiologic healing responses to promote full recovery.

“The skin doesn’t know the difference as to whether a laser-based or heat-based device is used,” he said, noting that the skin’s healing process involves three phases that overlap in time: inflammation, re-epithelialization, and extracellular matrix remodeling.

He compared the healing response to sublative versus ablative treatments as having the same initiating event of inflammation, but different predominant events (re-epithelialization versus tissue remodeling), a different proportion of dermal/epidermal involvement, and different desired impacts (epidermal re-epithelialization versus dermal collagen regeneration).

“It’s all very early,” he said, noting that some of the unanswered questions include determining how safe fractional radiofrequency treatments are for darker skin types and what happens 6 months after treatment and 12 months after treatment. “We don’t have all the answers.” ■

Dr Goldberg, who works with Skin & Laser Surgery Specialists of New York/New Jersey, Mount Sinai School of Medicine, and Sanctuary Medical Aesthetic Center, has also worked with Syneron™ (the manufacturers of the skin rejuvenation treatment Sublative Rejuvenation™).

Dr Ross has worked as a consultant for and received a research grant from Palomar; has received research support and equipment from Cutera; and has received research support from Candela, Lumenis, Sciton, and Ulthera.

Dr Zachary has received grant support, honoraria, and discounted equipment from Cutera, Lumenis, Sciton, and Solta. He also discloses working with Allergan, Biopelle, Candela, Iridex, Primaeva, Reliant, Rhytec, Sciton, SkinMedica, Thermage, and Through the Lens.

What's Erupting: Acne Update

Lawrence F. Eichenfield, MD

Tremendous variation exists in acne among adolescents and teenagers. Dermatologists often observe a remarkable difference in psychological impact on different individuals, ranging from patients with significant inflammatory acne who may be reluctant to discuss its impact to patients with a single inflammatory papule on their bodies who regard this pimple analogous to a volcano erupting.

Lawrence F. Eichenfield, MD, Professor of Pediatrics and Dermatology at the University of California, San Diego, discussed key considerations in providing dermatologic care to adolescents and teenagers. He noted that although researchers have conducted extensive studies on acne pathophysiology, "the inter-relatedness of the development of *Propionibacterium acnes*, inflammation, and hyperkeratinization has gotten trickier." So far, it is not known how to mediate sebaceous gland activity using the neuroendocrine inflammatory apparatus, which is an area for potential research in the future. Some of the research in the area of acne pathophysiology has yet to be translated into clinically useful material.

With regard to the relationship between food and pediatric acne, Dr Eichenfield noted that "there are essentially no specific pediatric studies on the influence of food." Although he acknowledged that many acne experts include dietary discussion in their management of acne, he has become less dogmatic in discussing the role of food as an influence on acne. "With or without dietary intervention, we have other tools that can generally control acne in our adolescent patients," said Dr Eichenfield.

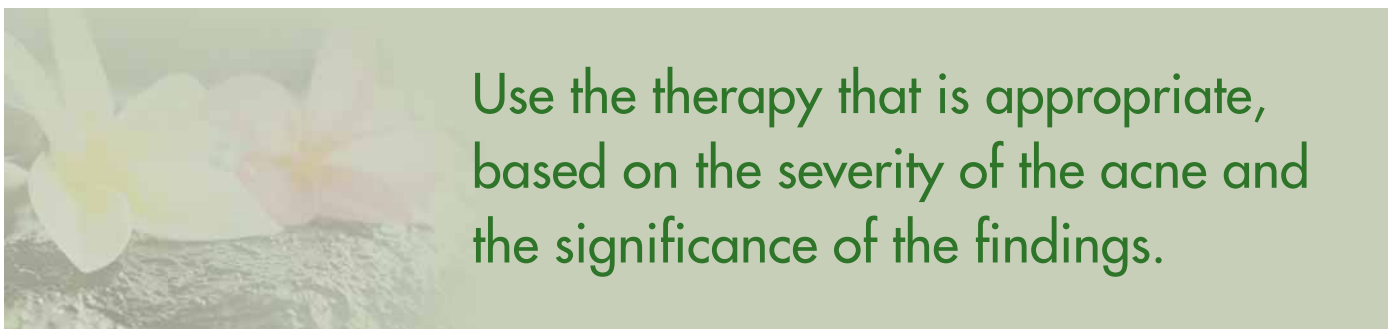
Based on his review of studies focusing on the onset of acne, he concludes that the number of active sebaceous follicles generally correlates with pubertal status, which means "sebaceous gland activity is the prerequisite for *P acnes* in the skin and acne vulgaris in our preadolescents and adolescents."

His recommendation to clinicians who provide care to adolescents with acne is to "use the therapy that is appropriate, based on the severity of the acne and the significance of the findings."

Adherence to and compliance with most acne regimens can often be poor among adolescents. Ongoing monitoring is important to assess the effectiveness of an individual's treatment plan, making adjustments as needed to achieve the desired outcomes. For example, the use of symptom surveys that include questions about mood swings and depressive symptomatology can be helpful in making clinical assessments about individual patients, especially for patients on isotretinoin. These surveys can be administered to individuals in the waiting room prior to their interaction with their clinician and provide useful information for the clinician to find out more details as part of the follow-up visit.

Keeping informed about new developments in the field of dermatology for adolescents and teenagers is essential in delivering optimal care for these patients, according to Dr Eichenfield. ■

Dr Eichenfield has worked on numerous clinical trials for various companies; he is an investigator for/has received grant/research support (no personal compensation received) from Galderma, Ortho Dermatologics, and Stiefel, a GlaxoSmithKline company. He is a consultant/advisor for Coria, Galderma, and Ortho Dermatologics.



Use the therapy that is appropriate, based on the severity of the acne and the significance of the findings.

Calm Parents' Fears About Kids' Sunscreens

Sheila Fallon Friedlander, MD

The benefits of sun protection clearly outweigh the risks," said Dr Sheila Fallon Friedlander, but the debate continues over how to balance the benefits of outdoor activities for children with protection against skin cancer.

Some studies suggest outdoor activity is protective against melanoma, Dr Friedlander noted at the seminar. She cited a case-control study of 583 cases of cutaneous malignant melanoma and 608 controls (*Int J Epidemiol.* 1999;28:418-427). Intermittent sun exposure, such as beach vacations during adolescence and the use of tanning beds and sunlamps, was associated with a significantly greater risk for melanoma, whereas chronic exposure, indicated by days of outdoor activity during adolescence and by outdoor jobs in adulthood, was associated with a significantly reduced risk for melanoma.

But sun protection and patient education do appear to play a role in reducing the number of nevi in children. Dr Friedlander, Clinical Professor of Pediatrics and Medicine at the University of California, San Diego, cited another study in which 458 children in first to fourth grades in Canada were randomized to receive sunscreen and counseling about sun protection. Three years later, the sunscreen group had significantly fewer new nevi compared with the control group (*JAMA.* 2000;283:2955-2960).

What's a dermatologist to do? "Common sense prevails," Dr Friedlander said. She advised dermatologists

to counsel children and their parents to protect against sunburns by using sunscreens and sun-protective clothing. Also, "identify high-risk patients and follow them" so that any problems can be spotted early, she said.

But once parents and children are on board with sun protection, what should they use? The Environmental Working Group (EWG), a nonprofit organization that reviews and disseminates information about contaminants in consumer products and the environment, has come down in favor of physical sunscreens, based on a review of 400 studies and 2,000 sunscreens, Dr Friedlander said.

Some parents and children prefer organic sunscreens, which contain oxybenzones, but the EWG rates these products as more dangerous than physical sunscreens. Some research suggests that oxybenzones can be absorbed into the skin in a way that the nano-particles of zinc oxide and titanium dioxide in physical sunscreens cannot, Dr Friedlander said.

Be aware of what sunscreen characteristics raise concerns in your patients and their parents, Dr Friedlander said. Share information with them, refer them to the EWG Web site, and come up with a reasonable plan for sun protection. ■

Dr Friedlander has served as a clinical investigator for Johnson & Johnson, which manufactures sunscreen products.



Sun protection and patient education do appear to play a role in reducing the number of nevi in children.

Persistent Diaper Dermatitis Could Signal More Serious Skin Condition

Ilona Frieden, MD

Persistent or unusual diaper dermatitis may be a sign of a serious skin disease or systemic illness in infant patients.

Because rare and uncommon skin eruptions in the diaper area can appear to be a conventional rash caused by prolonged skin exposure to wetness, dermatologists should closely examine each referral they receive for diaper dermatitis and look for the warning signs of a more serious skin condition, according to Dr Ilona Frieden.

“When pediatricians ask a dermatologist to see a patient with a diaper rash, it is usually an unusual one. Diaper rashes are common and most never require referral. Thus, if asked, dermatologists should always say ‘Yes’ to these referrals,” said Dr Frieden, Director of Pediatric Dermatology at the University of California San Francisco Children’s Hospital.

Among the unusual eruptions she discussed in her presentation at the seminar were psoriasis, granular parakeratosis, and clear cell papulosis. Diaper rash can also be a manifestation of a systemic illness such as group A streptococcal infection, Langerhans cell histiocytosis, a zinc or other nutritional deficiency, or an asymmetric periflexural exanthem.

Group A streptococcal infection can cause a perianal rash, but may also occur at other intertriginous sites. It is typically characterized by intense, bright-red colors; satellite lesions are usually absent. Treatment requires oral antibiotics, and repeat courses are sometimes necessary, noted Dr Frieden.

Langerhans cell histiocytosis may present as persistent diaper dermatitis that may also occur in other

sites, particularly the scalp, ear canal, and oral mucosa. Be on the lookout for petechiae, atrophy, or deep ulcerations, said Dr Frieden; a biopsy is necessary to make a diagnosis.

Diaper dermatitis due to zinc deficiency is most commonly seen in preterm breast-fed infants. Metabolic disturbances and cystic fibrosis can cause similar eruptions.

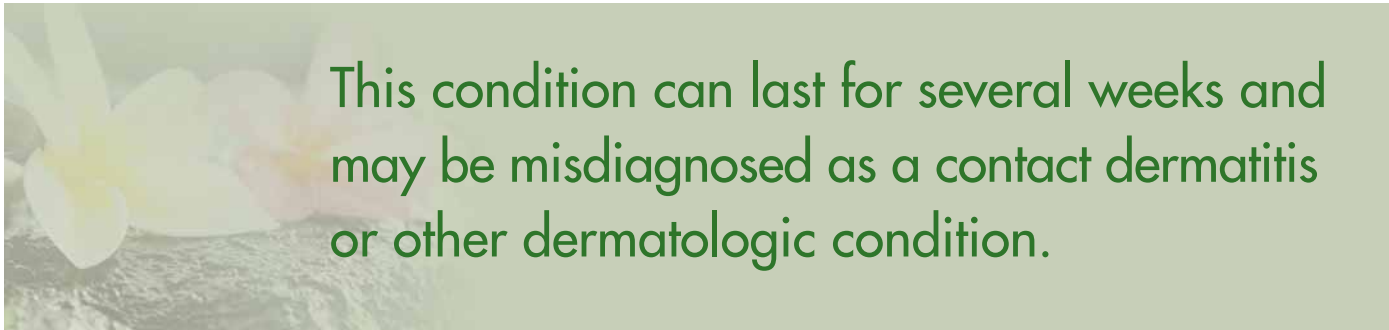
Asymmetric periflexural exanthema typically starts in a flexure, often at the axilla, but it can also begin in the posterior of the thigh, leading to confusion with diaper rash. It is characterized by small red papules at the periphery with a slightly dusky, scaly center, said Dr Frieden.

“This condition can last for several weeks and may be misdiagnosed as a contact dermatitis or other dermatologic condition,” she said. “Eventually, many cases begin to become bilateral and more generalized.” The cause of this exanthema is not known.

An obvious tip for preventing diaper dermatitis, or decreasing its prevalence, is frequent diaper changes to minimize skin exposure to urine and feces. Barrier creams can also be helpful as a preventative measure, she noted.

“It is also important to note that the differential diagnosis of diaper rash during the newborn period differs from that of older infants in that the rash is less likely to be caused by an irritant and more likely to represent an infection or other condition,” said Dr Frieden. ■

Dr Frieden reported having no relevant conflicts of interest.



This condition can last for several weeks and may be misdiagnosed as a contact dermatitis or other dermatologic condition.

What's All the Pus About? Bacterial Infection Update

Moise L. Levy, MD

Dermatologists are seeing a growing number of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) in their caseloads. Dr Moise L. Levy, a pediatric dermatologist based in Austin, Texas, discussed key considerations in clinical practice relating to the care of these patients.

“Community-acquired MRSA is a global problem,” said Dr Levy, noting that US300 is the predominant strain of MRSA in the United States that appears to be responsible for an increase in so-called community-acquired (CA) staph infections and represents a majority of skin and soft-tissue infections (SSTIs) treated in many US emergency rooms. “CA-MRSA is a condition where many patients may end up in the hospital. For those who are not seeing large numbers of CA-MRSA cases at this point, I promise you that you will see many cases once it does come into your community because it spreads rapidly.”

First identified by the Centers for Disease Control and Prevention in 2000 among football players in Pennsylvania, “CA-MRSA is generally community-based and is generally found in healthy, young individuals. In the pediatric population, one study found that the highest rates of CA-MRSA were in children under 1 year of age,” said Dr Levy (*Pediatr Infect Dis J.* 2008;27:925-926).

Risk factors for CA-MRSA include the sharing of towels, razors, and other fomites; skin-to-skin contact; prior use of any antimicrobials; and pet ownership. CA-MRSA is often found in individuals with SSTIs.

Increasing antibiotic resistance (relating to the use of clindamycin, tetracycline, fluoroquinolones, and other antibiotics) is also of importance. The presence or absence of the *mecA* gene is a key diagnostic feature of methicillin-resistant species. With respect to clindamycin resistance, most treatment failures are due to inducibly resistant macrolide-lincosamide-streptogramin B (MLS_{Bi}) strains. Because MLS_{Bi} resistance is not readily detected by standard laboratory sensitivity testing, Dr Levy believes that D-zone testing is necessary. D-zone testing is a practical disk

diffusion method for the detection of MLS_{Bi} strains in which inducible resistance to clindamycin is manifested by a flattening or blunting of the clindamycin zone of inhibition adjacent to the erythromycin disk, giving a D shape to the zone of inhibited growth.

Dr Levy cautions other dermatologists to keep in mind that although MRSA presents predominantly as SSTIs, invasive cases of the disease can occur, including pneumonia, musculoskeletal infections, and osteomyelitis. Other characteristics of CA-MRSA are that it has underlying disease associations with atopic dermatitis and asthma, infections found in more than one member of the family are common, and outbreaks among students in contact sports may occur. Recurrences of CA-MRSA may occur in up to approximately 20% of children with CA-MRSA.

For the management of CA-MRSA, “hand washing cannot be overemphasized with patients and family members,” according to Dr Levy.

In addition to disinfection, the use of topical, parenteral, and/or oral formulations of antibiotics, and various decolonization strategies, incision/drainage is regarded as curative to address the infection that is “screaming for release,” as described by Dr Levy. Of special note is consideration of the use of sodium hypochlorite for antiseptic via diluted “bleach baths” (typically 2 teaspoons of sodium hypochlorite [also known as Clorox] per 1 gallon of water) that are taken two to three times weekly as a means to prevent recurrent infection (*Pediatr Infect Dis J.* 2008;27:934-935). These measures can be useful in addressing the clinical challenges related to the care of patients with CA-MRSA. ■

Dr Levy discloses that he has worked as an investigator, consultant, and speaker for SkinMedica.

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