Roundup on 
Cosmetic Dermatology 
WINTER 2007

TOPIC HIGHLIGHTS:
Advances in Cellulite Treatment and Dermatologic Use of Mesotherapy
Fractionated Delivery of Laser Energy Continues Evolution, Clinical Expansion
Photodynamic Therapy's Efficacy Draws Strong Testimonials
Proper Technique Delivers Optimal Filler Effects
Tailor Cosmesis to Patients of Color
Patience, Patients: Some Laser Results Are Subtle
Glycerol
Patient Expectations Play a Role in Botox Effects
Small Anesthetic Changes Can Have Big Impact on Blepharoplasty Results

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**Advances in Cellulite Treatment and Dermatologic Use of Mesotherapy**

Over the past decade, laboratory and clinical research has yielded multiple advances in antiaging and skin rejuvenation techniques. During that period of progress, one type of dermatologic malfeasance has defied every attempt at correction: cellulite.

A variety of topical and physical (massage-based) interventions have undergone extensive evaluations as potential solutions to cellulite. However, none has demonstrated the ability to effect long-term changes and improvement, according to New York cosmetic dermatologist David J. Goldberg, M.D., M.D., J.D.

In large part, cellulite’s resistance to modification is a product of a lack of understanding of the condition’s underlying biologic basis, a shortcoming that persists even today.

“It’s not exactly clear what cellulite is,” said Dr. Goldberg, Clinical Professor of Dermatology and Director of Laser Research at Mount Sinai School of Medicine in New York City. “Clearly, it is an abnormality that involves both the fibrous bands deep within the skin and the fat that is connected by these fibrous bands. That understanding has led to the argument behind new approaches to the condition: tighten the skin and lessen the fat.”

Early studies showing some cellulite tightening with diode lasers and/or bipolar radiofrequency devices associated with massage have been followed over the past year, with newer clinical evaluations. These studies have looked at several new devices that aim to address the twofold objective of skin tightening and fat reduction to manage cellulite. Some of the devices already have U.S. Food and Drug Administration approval, and others will likely receive the agency’s approval in the near future, said Dr. Goldberg. Results achieved thus far offer reason for optimism that a long-term solution to cellulite finally is at hand.

The mechanisms of action vary among the new devices and techniques. Some focus on tightening the “cheesy skin” that results in the rippled, uneven surface appearance on the thighs and buttocks, the signature defect of cellulite. One device, which relies on unipolar radiofrequency energy, “clearly tightens the skin,” said Dr. Goldberg.

Other approaches employ ultrasound directed against the fat content of cellulite.

“Instead of tightening the skin, the ultrasound actually disrupts the fat that is out of sync in cellulite,” said Dr. Goldberg. “It creates a smoother appearance in the cellulite skin by smoothening the fat. Some patients who have been treated with the ultrasound approach have even noticed that they can wear smaller clothing sizes because of fat shrinkage.”

The evolution of techniques that disrupt fat content in the body has led to some concern that adverse changes in cholesterol or other blood fats might result. Extensive evaluation of the issue has yielded no evidence of adverse consequences for lipid levels.

Optimal use of the new devices to treat cellulite has yet to be determined. Combined treatment with devices that have different mechanisms of action is a distinct possibility.

“It might turn out that some of these approaches have a synergistic effect on cellulite,” said Dr. Goldberg.

Another area of recent progress in cosmetic dermatology is mesotherapy or injection of a substance into the skin to achieve a specific therapeutic effect. Used extensively in Europe for applications ranging from fat dissolution and skin rejuvenation to rheumatologic disorders and headaches, mesotherapy has begun to make inroads among cosmetic dermatologists in the United States.

“For cosmetic dermatologists, the issue is whether mesotherapy in fact does lessen fatty depositions and have antiaging effects,” said Dr. Goldberg.

Central to successful mesotherapy is the use of appropriate materials for injection. Different substances are used to achieve different effects following injection.

“For dissolving fat, the traditional substance has been phosphatidylcholine,” said Dr. Goldberg. “It now seems that the active component is actually deoxycholate. For antiaging applications, traditional substances for injection have included hyaluronic acid and various types of vitamins.”

Mesotherapy is an umbrella term that refers to the use of multiple superficial injections in the skin to achieve a specific purpose, Dr. Goldberg added. The cosmetic dermatology course will devote considerable time to review and discussion of the advantages and potential disadvantages of the different substances that can be used in mesotherapy.

Dr. Goldberg has received clinical grants from Alma Lasers Inc. He is a consultant to Photo Therapeutics Inc., and Ultrasound Inc. He discusses the off-label use of cellulite treatments.

**References**


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Fractionated Delivery of Laser Energy Continues Evolution, Clinical Expansion

Fractionated delivery of laser energy continues to evolve as a tool for skin rejuvenation and combating the effects of aging. One of the latest advances involves the fractionated delivery of CO₂ laser energy, a wavelength with a long-standing role in the management of dermatologic conditions.

“With fractionated delivery of the CO₂ laser, we’re no longer treating 100% of the skin surface in a flat, two-dimensional manner,” said Christopher B. Zachary, M.B.B.S., F.R.C.P., Professor and Chair of Dermatology at the University of California, Irvine. “Instead, we’re actually delivering energy to about 60% of the skin surface in a vertically oriented ablative manner.

“We’re drilling millions of tiny holes into the skin, which not only will affect the epidermis and superficial dermis, but also allow us to drill to a depth of greater than 1 millimeter in the skin. This has been demonstrated histologically and clinically to have long-lasting benefits in terms of skin tightening and rejuvenation. We might be able to achieve some things that we weren’t able to do with the conventional CO₂ laser.”

Still in an early stage of investigation, ablative fractionated rejuvenation (AFR) has produced encouraging results in short-term clinical studies with follow-up of about 6 months. Current machines remain prototypes that are subject to changes in treatment parameters to achieve the greatest efficacy with the least risk of complications. A production model probably is still at least a year away, according to Dr. Zachary.

Even with the caveats associated with an investigational intervention, AFR has produced some impressive results.

“I’m excited because we actually have some hard clinical data,” said Dr. Zachary. “I’m also excited because there is no guessing between pre- and postoperative slides of treated patients. The difference is pretty obvious. When we show a video, everyone can see tissue shrinkage occurring. There is no doubt that we are achieving something quite different from all of the so-called nonablative devices.”

When dermatologists have access to the device, they likely will find multiple applications for it, Dr. Zachary continued. Potential uses include treatment of superficial and deeper wrinkles, acne scarring, and melasma. Additionally, the device’s clinical application will not be limited to conditions affecting the face, a limitation of conventional CO₂ lasers.

AFR with a CO₂ laser also will complement other therapies, such as fillers and injection of botulinum toxin for wrinkling around the eyes. AFR will not negate the benefits offered by traditional tools of cosmetic dermatology, including chemical peels, pulse-dye laser, and KTP (potassium-titanyl-phosphate) laser.

“Clinicians who are offering comprehensive laser surgery will still need other devices, but I think AFR will be a major feather in the cap for people who are interested in causing real tissue tightening,” said Dr. Zachary.

Evaluation of the CO₂ AFR prototype machine has yet to define the full range of beneficial effects and potential adverse effects or complications. Every new device has “quirks that need to be sorted out” and the CO₂ AFR is no exception, said Dr. Zachary. For example, the hand piece has been modified to make it more ergonomic.

“I think if you put this particular device into physicians’ hands right now, they would find certain aspects of the treatment to be complicated,” he said. “The machine is still a prototype, and I am sure that major improvements in the design will occur before the device is ready for production.”

Even after the machine is available to clinicians, instruction in appropriate use will be essential, Dr. Zachary continued. Inappropriate or overly aggressive use of the device will create a potential for persistent redness, swelling, and other complications seen with a traditional CO₂ laser.

The CO₂ AFR device (Reliant Technologies, Inc., Mountain View, Calif.) is farthest along in the evaluation process. However, other companies have begun development of ablative fractional devices. Sciton (Palo Alto, Calif.) is developing an erbium-YAG laser for fractionated laser delivery, and Lumenis (Santa Clara, Calif.) is modifying its CO₂ laser and CPG in an attempt to create similar tissue tightening responses. Other players in the laser industry will likely enter the picture in the future.

The evolution of AFR has occurred within an environment of laudable ethical behavior within the laser industry, Dr. Zachary stated. Companies are pursuing a course of due diligence to ensure the safety and efficacy of machines before they become available to clinicians.

“It’s inappropriate and inefficient for physicians to be given devices prematurely before they have been carefully tested and developed,” said Dr. Zachary. “This might indeed shift the cost of development from the laser companies to the physicians’ practices. But it might also result in unintended side effects, prevent the delivery of good medicine, and besmirch the good name of the manufacturing laser company.”

Dr. Zachary has nothing to disclose.
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Advances in photodynamic therapy (PDT) using 5-aminolevulinic acid (ALA) have led dermatologists to increasingly extol its virtues as a practical, versatile, and highly effective therapy for actinic keratoses, nonmelanoma skin cancer, acne, and photorejuvenation.

For example, at the annual meeting of the Noah Worcester Dermatological Society, several dermatologists described ALA-PDT with a degree of enthusiasm pointedly absent from presentations concerning many new lasers, skin smoothers, and nonablative, all-purpose devices.

“It has...changed the way I practice,” Dr. C. William Hanke said at the meeting.

Dr. Hanke said he recalled hearing about ALA-PDT at an American Academy of Dermatology meeting 5 years ago. His impression of the therapy then was “how terrible it was. There was a lot of hand-holding ... because the patient needed it.”

Still, it seemed to work pretty well in eradicating actinic keratoses (AKs), and a 2003 study showed that it had the potential to be equal to 5-fluorouracil in efficacy and was preferred by most patients, despite the painful recovery required after a 1-4- to 18-hour ALA incubation period and subsequent exposure to a specialized light source (J. Drugs Dermatol. 2003;2:629-35).

Since then, ALA-PDT has changed dramatically in the following ways:

- **Short-contact ALA-PDT is now standard.** ALA remains on the skin just 15-60 minutes, profoundly affecting the side-effect profile and reducing pain. Instead of enduring a week of raw skin, erosions, and inflammation, most patients today note only minor stinging, erythema, and scaling that resolve within a few days. Many studies show that short-contact ALA-PDT does not reduce its effectiveness.

- **Numerous light sources are being used.** Although blue light emits a wavelength (405-420 nm) that conforms precisely to the absorption peak for ALA (marketed as the Levulan Kerastick by DUSA Pharmaceuticals Inc.), intense pulsed light (IPL), pulsed dye lasers, and other light sources also are proving effective. Exposure time will vary: 22-25 minutes for an intense pulsed light source according to the patient’s condition and severity.

- **The versatility of ALA-PDT is expanding.** Approved for nonhyperkeratotic AKs of the face and scalp, it also is being used on the trunk and extremities for AKs, nonmelanoma skin cancer, pigmented lesions, rosacea, and, especially, acne.

- **Competition is on the horizon.** An American launch is imminent for the photosensitizer methyl aminolevulinate, marketed as Mervix by the Norwegian company PhotoCare ASA. Widely used in Europe, Mervix is incubated for 3 hours under occlusion and activated by red light (630-660 nm) from a diode laser. Besides treating AKs and nonmelanoma skin cancer, the system is used to treat psoriasis.

Dr. Neil S. Sadick voiced a common complaint when he noted that nonablative therapies have now been used for 3 years to treat everything from rosacea to scars, “and we’re still not sure [they’re] effective or worth it.”

In contrast, he said that IPL, which targets chromophores, has become a mainstay in his practice, “providing the greatest amount of clinical satisfaction, consistently, for [the] patients.”

When he’s treating more than telangiectasias, age spots, and minimal actinic damage, Dr. Sadick said he relies on ALA to amplify the impact of IPL. “I can decrease five treatments to two or three treatments with IPL ... for significant actinic damage. It’s not nonablative; I would call it microablative,” said Dr. Sadick, who practices in New York City and Great Neck, N.Y.

Dr. Mitchel P. Goldman said short-contact ALA-PDT using IPL is “incredibly impressive” for acne and a convenient and “very mildly painful” option for patients with actinic keratoses, telangiectasias, and skin texture problems. He even used the modality to treat his own facial squamous cell carcinoma.

He uses a pulsed dye laser rather than IPL on hair-bearing areas because IPL can remove hair. Like Dr. Sadick, Dr. Goldman uses ALA-PDT to “boost” the effectiveness of IPL, reducing the number of treatments required.

After one or two treatments of ALA-PDT with IPL for actinic keratoses, “I think that’s when you need to biopsy,” said Dr. Hanke.

### Getting the Most from PDT

The following steps can maximize the effects of ALA-PDT:

1. **Discontinue topical retinoids several weeks before treatment with 5-aminolevulinic acid photodynamic therapy (ALA-PDT).**
2. **Prepare the skin using gentle microdermabrasion or isopropyl alcohol (to minimize the PDT reaction).**
3. **Use a fresh ampule of Levulan Kerastick (ALA).** The drug becomes inactive 4 hours after being opened.
4. **Apply two coats of ALA with a cotton swab.** Take extra care to avoid getting the solution in the patient’s eyes.
5. **Adjust exposure to ALA and to the light or laser source according to the patient’s condition and severity.** For example, the photosensitizer should remain on the skin 60 minutes prior to PDT for treatment of photoaging. Exposure time will vary: 22-25 minutes for an intense pulsed light source or 16 minutes and 40 seconds for a blue light source.
6. **Use cool airflow, rest periods, and, possibly, topical anesthesia or diazepam (5-10 mg) for pain management.**
7. **Observe the patient post phototherapy, and wash the area thoroughly with soap and water to ensure that all of the photosensitizer has been removed.** Apply sunscreen in the office.
8. **Be adamantly instructing the patient to avoid sun exposure altogether for 24 hours and to wear heavy sunscreen for 3-4 days.** Patients can have extreme reactions to sun exposure in the days following phototherapy.

Source: Dr. Hanke
Proper Technique Delivers Optimal Filler Effects

Proper technique is paramount to optimize outcome and avoid complications with either calcium hydroxyapatite or poly-L-lactic acid fillers, according to a presentation at a Dermatology Foundation-sponsored symposium.

Infiltration of local anesthesia, needle size, injection technique, multiple treatment sessions, and tips to avoid complications are among clinical pearls for optimal use of calcium hydroxyapatite (Radiesse, BioForm Medical) and poly-L-lactic acid (Sculptra, Sanofi-Aventis). “Radiesse is for structure and support and Sculptra is for diffuse volume,” said Dr. Ken K. Lee, director of dermatologic surgery at Oregon Health and Science University in Portland. The two fillers are not mutually exclusive, he added. “I use these two together all the time.”

Focal treatment is the goal with these fillers, Dr. Lee said. “There is a paradigm shift from filling to contouring. Contouring really was only available before with fat transfer.” The gauge of needles typically used to inject calcium hydroxyapatite (27G) or poly-L-lactic acid (25G or 26G) can hurt. He recommended local infiltration with lidocaine with epinephrine prior to injection to reduce pain and bruising.

Dr. Lee does not have a disclosure regarding either filler product. The goal with calcium hydroxyapatite is not to fill in fine lines, but to give more structure, he explained. The synthetic particles form scaffolding for tissue in-growth. “It is off label for cosmetic use—I do tell patients that.”

Radiesse is packaged in 1.3-cc and 0.3-cc syringes. Inject into “deep dermis and a little bit into subcutaneous fat,” Dr. Lee said. He recommended a threading and fanning technique, injecting only a small amount at each pass, such as 0.05 cc. Stop injection before exiting the skin and knead or mold any firm nodules after injection, he suggested.

“I don’t just thread the material along the nasolabial line, I also crisscross to enhance the volume effect,” Dr. Lee said. “This stuff is really thick and hard to get out of the needle, which is good. You don’t want a lot of material in any one area.”

Dr. Lee informs patients in advance that if they have prominent nasolabial lines or marionette lines they will likely need three syringes over two treatment sessions. “Then it doesn’t look like you’ve failed them.” Volume from a single injection typically lasts about 9 months, he said. The double session strategy extends duration of effect to 1 year or longer. “Somehow getting it to last up to a year is much more appealing to patients. The downside is that complications last a long time, too.”

Avoid filling thin eyelids and lips with calcium hydroxyapatite, Dr. Lee advised. Deposits can be seen in these areas. Dr. Lee said, “I really recommend collagen or hyaluronic acid for lips.” Poly-L-lactic acid, similar to calcium hydroxyapatite, is injected into the deep dermis or subcutaneous layer. Do not inject this filler superficially, Dr. Lee cautioned. “I aim for the subcutaneous layer. It is more difficult to consistently place in deep dermis and

Continued on page 18
For the temporary treatment of moderate to severe glabellar lines in patients 18 to 65 years of age

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**Hypersensitivity Reactions**

Serious and/or immediate hypersensitivity reactions have been rarely reported. These reactions include anaphylaxis, urticaria, or serious local reactions. Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects due to dysautonomia and respiratory compromise from typical doses of BOTOX® COSMETIC. Published medical literature has reported rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of these cases, the localized ocular side effects outbalanced the systemic event. A parenteral route of administration is recommended in these cases.

**Pre-Existing Neuromuscular Disorders**

Caution should be exercised when administering BOTOX® COSMETIC to individuals with peripheral motor neuromuscular diseases (e.g., amyotrophic lateral sclerosis, or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects due to dysautonomia and respiratory compromise from typical doses of BOTOX® COSMETIC. Published medical literature has reported rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of these cases, the localized ocular side effects outbalanced the systemic event. A parenteral route of administration is recommended in these cases.

**Dysphagia**

Dysphagia is a commonly reported adverse event following treatment of cervical dystonia patients with all botulinum toxins. In these patients, there are reports of rare cases of dysphagia severe enough to warrant the insertion of a gastric feeding tube. There is also a case report where a patient developed aspiration pneumonia following dysphagia subsequent to the finding of dysphagia.

**Cardiovascular System**

There have also been rare reports following administration of BOTOX® of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease.

**Human Albumin**

This product contains albumin, a derivative of human blood. Based on effective donor screening and product formulation, the risk of transmission of viral disease is extremely low. However, even well-screened donors may be infected with rare, normally latent agents, such as the Creutzfeldt-Jakob disease (CJD) virus. The CJD virus is a slowly multiplying prion that can cause vesi- cular atrophy or an altered estrous cycle in female rats. There were no adverse effects on the viability of the embryos.

**Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when BOTOX® COSMETIC is administered to a nursing woman.

**Geriatric use:** The clinical studies of BOTOX® COSMETIC did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. However, the elderly patients tended to be predisposed to experiencing these events. The exact relationship of these events to the botulinum toxin injection has not been established. Additionally, a report of acute angle closure glaucoma one day after receiving an injection of botulinum toxin for blepharospasm was received, with recovery four months later after laser iridotomy and trabeculectomy.

**Glaucoma**

In clinical trials of BOTOX® COSMETIC the most frequently reported adverse events following injection of BOTOX® COSMETIC were: eyelid ptosis, blepharoptosis, ptosis, and upper lid drooping.

**Adverse Events Reported at Higher Frequency (>1%) in the BOTOX® COSMETIC Group**

<table>
<thead>
<tr>
<th>Body System</th>
<th>BOTOX® COSMETIC (N=405)</th>
<th>Placebo (N=130)</th>
<th>Percent of Patients Reporting Adverse Events</th>
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<tr>
<td>Body as a Whole</td>
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**Adverse Events Reported at Higher Frequency (>1%) in the BOTOX® COSMETIC Group Compared to the Placebo**

**Immunogenicity**

Treatment with BOTOX® COSMETIC may result in the formation of neutralizing antibodies that may reduce the effectiveness of subsequent treatments with BOTOX® COSMETIC by inactivating the biological activity of the toxin. The rate of formation of neutralizing antibodies in patients receiving BOTOX® COSMETIC has not been well studied.

The critical factors for neutralizing antibody formation have not been well characterized. The results from some studies suggest that botulinum toxin injections at more frequent intervals or at higher doses may lead to greater incidence of antibody formation. The potential for antibody formation may be minimized by injecting the lowest effective dose given at the longest feasible intervals between injections.

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References:
Tailor Cosmesis to Patients of Color

People of color make up an increasing proportion of patients seeking skin rejuvenation treatments. The changing face of the clientele for cosmetic procedures means that clinicians must adapt their skin management approaches for best results, a panel of experts said at an international symposium of facial plastic surgery.

Among patients seeking skin rejuvenation treatments in 1999 and 2005, the proportion of Hispanics increased 89%, the proportion of African Americans increased 49%, and the proportion of Asian Americans increased 27%, according to a survey of 145 board-certified members of the American Academy of Facial Plastic and Reconstructive Surgery, which sponsored the symposium. Close to a third of the current U.S. population is nonwhite, and the number is expected to rise to approximately half by 2050.

People with Fitzpatrick skin types IV, V, and VI tend to have thicker, oilier skin with increased melanin than those with lighter skin types. These darker skin types may be more prone to acne and may have an increased risk of developing hypertrophic scars, so it’s important to take a good history of previous scars, Dr. Devinder S. Mangat said.

The extra pigmentation in darker skin types is a double-edged sword: It means slower aging and decreased actinic effect, but the skin is less amenable to more aggressive rejuvenation procedures. Darker skin is more likely to develop postinflammatory pigmentation problems after acne therapy, resurfacing, laser hair removal, and other procedures, said Dr. Harris, a facial plastic surgeon in private practice in Vail, Colo., and Cincinnati.

Common themes among people of color seeking skin rejuvenation therapy are proptosis (especially in African Americans and people of Asian descent), intraorbital maxillary hypoplasia, and thick skin, said Dr. Monte O. Harris, who is a facial plastic surgeon and is with the department of dermatology at Howard University, in Washington.

In African Americans, the jawline can be relatively well preserved, even in the eighth decade of life. Intraorbital hollowing is not necessarily a sign of aging but may be present from birth, he noted. Cosmetic management in darker skin types is “less about lines and wrinkles and more about soft tissue and bony relationships,” he said.

Dr. Pearl E. Grimes agreed. She surveyed 100 patients of color (80 African Americans, 17 Hispanics, and 3 Asian Americans) and found that their top three facial cosmetic concerns were pigmentation, skin texture and pore size, and sensitive skin.

Repetitive, less-invasive treatments provide the safest management for darker skin types, said Dr. Grimes, a dermatologist in Los Angeles.

A multidisciplinary approach to darker skin types begins with a strong foundation of cosmeceutical and pharmaceutical agents. “I can’t overemphasize sunscreens to treat hyperpigmentation,” she said.

Among the hyperpigmentation therapies used in her practice for clients of color, she prefers a triple-combination bleaching protocol using hydroquinone 4%, fluocinolone 0.01%, and tretinoin 0.05% applied once a night for up to 3 months, then decreasing applications to once or twice a week or switching therapies.

Another option for hyperpigmentation is application of a sustained-release combination of micro-entrapped 4% hydroquinone and 0.15% tretinoin. Patients can continue this treatment for longer periods of time. Also popular among patients in her practice is a pre-saturated pad containing 4% hydroquinone and a melanin-containing sunscreen.

More difficult to treat is periorbital hyperpigmentation, which Dr. Grimes called “my albatross.” The periorbital skin is thin and easily irritated. Treatment should begin gently with a low dose of hydroquinone that gets titrated upward or a low dose of retinoids or retinol applied initially every third day and then titrated upward, she suggested. A combination of vitamin K and retinol is another option.

Microdermabrasion can be used to treat hyperpigmentation effectively in darker skin types, especially when combined with topical preventive agents. Chemical peels should be limited to superficial peels to avoid postinflammatory pigmentation complications. Retinoids induce a deeper peel with an increased risk of complications and so require more caution. Use extreme caution with laser therapies to avoid scarring or postinflammatory hyperpigmentation in these patients, Dr. Grimes said.

Dr. Harris agreed. Laser therapy “can be devastating in darker skin,” he said.

Just as it’s important to understand proper techniques in darker skin, he says he believes it is equally important to adapt one’s approach to this new demographic of patients. Dr. Harris and his business partner, a cosmetic dermatologist, designed their clinic exterior to look like a storefront in a mall, putting prospective Continued on page 18
Patience, Patients: Some Laser Results Are Subtle

Make sure that patients treated with nonablative lasers have reasonable expectations of what their skin will look like after rejuvenation therapy, Dr. Thomas E. Rohrer said at a symposium sponsored by the American Society of Ophthalmologic Plastic and Reconstructive Surgery.

“Improvement is gradual and subtle, but it is real,” Dr. Rohrer said, warning that patients expecting dramatic skin changes after each treatment could be disappointed.

Dr. Rohrer, a Mohs and dermatologic surgeon in Chestnut Hill, Mass., described nonablative skin rejuvenation as one of the fastest-growing areas of dermatologic surgery, with a 60% increase in 2 years’ time. “What we're talking about is creating a controlled dermal injury—a thermal injury 100-400 microns deep—to get collagen remodeling,” he said at the meeting, which was also sponsored by the American Society for Dermatologic Surgery and the American Academy of Facial Plastic and Reconstructive Surgery. Infrared lasers heat the dermis to get this effect, according to Dr. Rohrer. Heating the dermis results in a wound-healing response: inflammation, proliferation, and remodeling. The process can take months.

“You are effectively changing the dermis without affecting the epidermis,” he said.

The infrared lasers available today vary only slightly and have produced similar outcomes in the studies reported so far. The amount of improvement varies from patient to patient, but most do improve. Despite the use of anesthetic creams and cryogenic cooling, infrared laser treatment does hurt, he said. In his practice, attempts to limit pain have involved vibratory anesthesia, the application of anesthetic cream for about an hour, and the Zimtec treatment, attempts to limit pain have involved vibratory anesthesia, the application of anesthetic cream for about an hour, and the Zimmer cooler, which he said was the most effective.

Multiple tactile pass techniques—going over the same area twice at a lower fluence—also can reduce pain. “It hurts a little bit less at each pass, but you are doubling treatment time,” he said, “so I am not sure how effective or practical that is going to be.”

In what may be the longest study of a nonablative therapy, patients were followed for 35 months. The investigators found that improvement peaked at 6 months after the last treatment, but at 35 months patients still had almost 30% improvement in the texture of the skin, Dr. Rohrer said.

Many patients are combining nonablative lasers with botulinum toxin treatments. Because Botox is known to work, this has raised a question as to the role of the lasers in any improvement that is seen.

“Certainly Botox works faster than nonablative [therapy] and jump starts” rejuvenation, he said, showing photographs of patients whose improvements lasted months after the Botox effect would have worn off. He recommended infrared lasers for the treatment of scars, but again cautioned that patients have to understand that improvement will require multiple treatments over a long time. “We should let our patients know they cannot expect a whole lot after just three treatments,” he said.

Visible light lasers are another nonablative option that has improved pigmentation and vascularity. They also have produced histologic changes and changes in skin texture over time. Intense pulsed light systems deliver a broad band of wavelengths, some of which help with pigment while others increase collagen, according to Dr. Rohrer. He said that he is preparing to publish a series of studies on this option.

Photomodulation light-emitting diodes offer another nonablative therapy that has produced improvement in most patients studied. “Improvement is subtle, but it is there if you measure it,” he said.

Dr. Rohrer disclosed that he receives compensation for research from laser manufacturers Candela Corp., Laserscope, and Palomar Medical Technologies Inc.


Photodynamic Therapy

Continued from page 8

Goldman, who is in private practice in La Jolla, Calif.

Dr. Hanke, director of a dermatologic surgery practice in Carmel, Ind., says that ALA-PDT has become ever more useful in his practice over time, for cosmetic as well as medical dermatology. If a patient’s goal is to have smoother, cleaner skin, with less blotchiness and redness, “we can do that,” he said. There are conditions, such as wrinkles, that do not respond well to ALA-PDT, the speakers agreed.

In addition, Dr. Hanke said he was unimpressed by its results in a renal transplant patient with extreme sun damage that included a history of skin cancers and many keratoses.

It also doesn’t work for disseminated superficial actinic porokeratosis or granulomatous rosacea, he concluded.

Its record in treating warts is erratic, he said, although he has had luck sometimes by paring the wart down, applying several coats of ALA, and then occluding the wart overnight prior to exposure to a light source.

Dr. Hanke has conducted clinical trials for DUSA Pharmaceuticals.

Dr. Goldman has been a consultant for DUSA and for the Luminis LightSheer diode laser system, which can be used for phototherapy.

Dr. Sadick has conducted research and/or consulted with Synonor, Thermage Inc., and Omnilux Inc., companies that manufacture lasers and light sources that can be used in phototherapy.

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Glycerol

Derived from the saponification of fats, glycerin (also spelled glycerine and usually referred to in the literature as glycerol) is a strong, nonvolatile trihydroxylated humectant that exhibits hygroscopic ability very similar to that associated with natural moisturizing factor (J. Soc. Cosmet. Chem. 1976;27:65; Acta Derm. Venereol. 1999;79:418-21). Natural moisturizing factor is found in corneocytes and can absorb large quantities of water, even when humidity levels are low, which allows the stratum corneum (SC) to maintain a sufficient hydration level in dry environments. Numerous ingredients have been used in moisturizing products to mimic the activity of natural moisturizing factor, and glycerol is one of the more successful.

Carl Wilhelm Scheele discovered glycerol in 1779, and since that time it has been widely incorporated into cosmetics. About 160,000 tons of the compound are used annually in the United States alone (J. Cosmet. Sci. 2002;53:229-36; Proc. Natl. Acad. Sci. USA 2003;100:7360-5). Glycerol is considered to be the most effective humectant (Skin Therapy Lett. 2005;10(5):1-8), and has recently been shown to provide other benefits.

Mechanism of Action

It is known that skin xerosis is linked to incomplete desmosome degradation. In an in vitro study conducted a decade ago of moisturizers that facilitate desmosome digestion, investigators observed via electron microscopy that desmosomes treated with glycerol were in more advanced stages of degradation than was control tissue. In two other in vitro models evaluated by the same team, glycerol raised the corneocyte loss rate from the superficial surface of human skin biopsies and significantly reduced intercorneocyte forces (Arch. Dermatol. Res. 1995;287:457-64).


In a 5-year study comparing two high-glycerol moisturizers with 16 other popular moisturizers in 394 patients with severe xerosis, the high-glycerol products outperformed the rest by more rapidly restoring normal hydration and preventing the resumption of dryness for a longer period—longer even than petrolatum. Glycerol also was shown to stabilize and fluidize cell membranes, as well as hydrate enzymes required for desmosome degradation (M. Loden and H. I. Maibach, eds. “Dry Skin and Moisturizers: Chemistry and Function,” 2000, Boca Raton, Fla.: CRC Press, p. 217). Ultrastructural analysis of skin treated with high-glycerol formulations has shown that glycerol expands not only corneocytes but also the space between layers of corneocytes, which results in expansion of the SC (Poster presentation, 53rd Annual Meeting of the American Academy of Dermatology, February 1995). These findings indicate that glycerol endows skin with the capacity to hold a reservoir of moisture that makes it more resistant to drying.

In a recent study of mice deficient in the epidermal water/glycerol transporter aquaporin-3 (AQP3), glycerol replacement alleviated several defects, including diminished SC hydration and skin elasticity, as well as poor barrier recovery after SC removal. Notably, SC water content, which was measured as threefold lower in the AQP3-null mice than in wild-type mice, was restored by administration of topical or systemic glycerol, but administration of glycerol-like osmolytes, such as xylitol, erythritol, and propane-diol, was unsuccessful. In addition to concluding that glycerol is an important determinant of SC water retention, the investigators suggested that their data provide a strong scientific foundation for the centuries-old practice of including glycerol in skin formulations for medicinal and cosmetic purposes (Proc. Natl. Acad. Sci. USA 2003;100:7360-5).

The authors also noted that when glycerol is added to SC lipids in vitro, it is thought to combine with lipid lamellae, foster water absorption, and hinder the conversion of lipid lamellar structures from liquid to solid crystal, thereby inhibiting or preventing water loss (J. Soc. Cosmet. Chem. 1990;41:51-65; Proc. Natl. Acad. Sci. USA 2003;100:7360-5). This hypothesis, the data from this study, and the fact that pure glycerol absorbs its own weight in water in 3 days led the authors to speculate that glycerol likely improves SC water absorption and retention.

A recent study of asebia mice with profound sebaceous gland hypoplasia revealed that the topical application of glycerol (which is believed to be endogenously produced in sebaceous glands by triglyceride hydrolysis) restored normal SC hydration, whereas the endogenous humectant urea did not. The investigators also showed that glycerol from triglycerides in sebaceous glands contributes significantly to SC hydration (J. Invest. Dermatol. 2003;120:728-37).

In a more recent study, researchers found that endogenous glycerol, from the circulation into the epidermis via AQP3 and from triglyceride hydrolysis in sebaceous glands, is associated with SC hydration in humans. Indeed, they observed that glycerol from both sources forms a water reservoir that affects such hydration. The authors also noted that other findings in their study support the use of therapeutic moisturizers that contain glycerol (J. Invest. Dermatol. 2005;125:288-93).

Skin Barrier Stabilization

The capacity of glycerol as a barrier stabilizer and moisturizing compound is supported by two studies conducted by the same team in 1999. In the first study, barrier repair was found to be more rapid in glycerol-treated sites. Significant differences were noted 3 days after treatment between glycerol open vs. untreated.
**Small Anesthetic Changes Can Have Big Impact on Blepharoplasty Results**

The difference between acceptable and unacceptable results for a blepharoplasty can be as little as a millimeter, so small improvements in anesthetic control and precision can have a large effect, Dr. Marc Cohen said at the annual meeting of the American Academy of Cosmetic Surgery.

“A tolerance of 1 mm or less is a very high standard to live up to,” said Dr. Cohen, a cosmetic surgeon at Wills Eye Hospital in Philadelphia. “The simple truth is that you cannot make the type of intraoperative decisions that give you that type of precision unless the surgery at each step is performed under tremendous control.”

Dr. Cohen offered tips that can make a big difference in results when it comes to maintaining patient comfort and giving the anesthetic block. “Every surgery has a weakest link in terms of surgical control... ”

Avoid injecting in the upper end of the zygomatic muscle—stay close to the orbital rim below the eye, he advised. “Otherwise you will get an unusual crease the patients really do not like.”

Botulinum toxin can correct “bunny lines” on a patient’s nose or a gummy smile. “Ask patients if they have ever noticed they show a lot of gum when the smile. If they say, ‘Yeah, I hate that,’ botulinum toxin can be a good, cheap fix,” he said.

Botulinum toxin can correct facial asymmetry resulting from trauma. Dr. Mandy said that he treated one woman after she had a traumatic injury to the maxillary branch of her seventh cranial nerve. Botulinum toxin corrected contralateral compensatory hyperkinesis and CosmoPlast corrected atrophy of the orbicularis oris and loss of the melolabial fold.

**$300 Is the Magic First-Time Number**

The financial “ouch factor” for patients considering botulinum injections is $300, Dr. Mandy said. “Allergan has done a tremendous amount of research with consumers about what the ‘ouch factor’ is,” he added.

Any charge greater than $300 for botulinum toxin treatment begins to dissuade a first-time patient. Any charge below $300 and the patient begins to perceive the botulinum toxin treatment as less valuable. Don’t treat too much too soon with new patients, Dr. Mandy advised. “A good tactic is to treat one area for $300 and have them come back. If they leave the first time with a $900 bill, they won’t come back.”

**Patient Expectations Play a Role in Botox Effects**

A scertain and address patient expectations before inject- ing botulinum toxin, Dr. Stephen H. Mandy ad- vised during a symposium sponsored by the Dermatology Foundation.

Inform patients up front how long they can expect the results to last. Tell them the botulinum toxin will last 2.5-3 months, he said. “If you don’t tell them, they will come back... and say it didn’t work.” Duration is dose related, so a higher dose might yield longer-last- ing results, between 3 months and 3.5 months, for example.

However, Dr. Mandy advised starting new patients at a lower dose. “If you aren’t certain, tell patients you’re going to go a little light and have them come back in 2 weeks. The patient appreci- ates it.” Dr. Mandy is a voluntary professor in the department of dermatology and cutaneous surgery at the University of Miami.

“Ask for their expectations,” Dr. Mandy said. “If a patient is from Los Angeles, they want to look like a statue. Most other people want some muted movement.”

Keep in mind that in general men require twice the dose of botulinum toxin, compared with women, Dr. Mandy said. Another tip is to offer new patients a free touch-up at 2 weeks if they are unhappy, he said, but be cautious. “You get very savvy patients who try to come in for free touch-ups every 6 weeks.”

Although some dermatologists administer botulinum toxin with a 1-cc syringe, Dr. Mandy prefers a 31-gauge insulin syringe. “The injection amount is easier to control than with a 1-cc syringe,” he said. “There is no hub so you don’t waste valuable product.”

Dr. Mandy typically injects 4-6 units of botulinum toxin around each eye. “Other dermatologists use up to 12-15 units on each eye,” he said. “I don’t think I need that much.”

Although most botulinum toxin injections are intramuscular, he prefers a subepidermal technique for periorbital injections to avoid bruising. “Patients don’t like having a black eye,” Dr. Mandy said. “People will ask them: ‘What happened to you?’”
Proper Technique
Continued from page 9

there are more complications.” Inject a small amount on withdrawal.
Poly-L-lactic acid is a synthetic, biodegradable, biocompatible polymer that stimulates a patient’s own collagen. Dr. Lee reconstitutes the filler with sterile water and 2% lidocaine. It is stable up to 72 hours after reconstitution. The vial is stored at room temperature but should be warmed prior to use, Dr. Lee suggested. “I have the patient hold the vial prior to injection. It helps to avoid clogging of the needle.”
Massaging right after injections is very important, Dr. Lee said. “I tell patients to massage five times a day for 5 minutes for 5 days for distribution of the Sculptra.”
Up to six treatment sessions may be necessary for full effect. Schedule treatment sessions about 4-6 weeks apart, Dr. Lee suggested. Volume enhancement with poly-L-lactic acid can last 2 years or more.
Hematoma is the most commonly reported complication in studies, Dr. Lee said. Subcutaneous papules are another potential problem. “You really have to be careful,” he said. “Sculptra in cosmetic patients has really shown me how much volume affects the drooping of the skin.”

Tailor Cosmesis
Continued from page 13

clients at ease to come in and ask questions. “There has to be some level of comfort for how they walk in the door,” he said.
He offers clients an integrated approach to cosmetic care starting with a complexion analysis, followed by what he called “Skin Care 101” with the simpler, least-invasive aesthetic treatments. Patients may choose to proceed to such targeted spa treatments as microdermabrasion and, beyond that, to targeted surgical treatments, injectables, rhinoplasty, or other procedures.

Anesthetic Changes
Continued from page 17

“One once the needle is in place, it’s not moved and a 2- to 3-cc bolus injection is given,” Dr. Cohen explained. Remove the needle and massage the bolus immediately.
A transconjunctival block poses more of a bruising problem because the conjunctiva is highly vascular. Dr. Cohen’s trick is to constrict the blood vessels before giving the block by using a drop of 2.5% phenylephrine.
There are, however, patients for whom it just is not prudent to have heavy sedation. “You’re at a significant disadvantage with these people because they are much more likely to bleed and bruise during surgery,” said Dr. Cohen. This is especially true for performing a block. “We go to great lengths to ensure that the block is painless so there is no bruising.”
For these patients, Dr. Cohen uses a syringe device called the Wand (Milestone Scientific), which has a microprocessor. The microprocessor controls the rate of flow so there is a constant pressure that is below the pain threshold. When using this device, Dr. Cohen uses the same technique as for a standard block. He reported no conflict of interest with the device.


Glycerol
Continued from page 16

ed and glycerol occluded vs. untreated sites, and SC hydration was superior in the glycerol plus occlusion sites.
In the second study, barrier repair was again more rapid in glycerol-treated areas, with significant differences, compared with untreated and base-treated areas at day 7, and SC hydration was superior in glycerol-treated areas after 3 days of treatment. The authors concluded that glycerol promotes barrier repair, notably after acute exogenous disturbance, and enhances hydration of the SC (Acta Derm. Venereol. 1999;79:418-21).
In a study of dermatologic vehicles and their effect on the horny layer, investigators found that adding glycerol to oil-in-water (O/W) emulsions eliminated the barrier-damaging effect of such formulations. O/W emulsions containing glycerol also decreased horny layer damage in stress tests with wash solutions, and were deemed to be appropriate for atopic dermatitis therapy (Skin Pharmacol. Physiol. 2004;17:267-73). More recently, combining glycerol with occlusive agents has been shown to confer a synergistic amelioration of xerotic symptoms (Skin Therapy Lett. 2005;10[5]:1-8; J. Soc. Cosmet. Chem. 1996;47:39).

On the Market
Glycerol, which helps condition the skin, is the most widely used hydrating agent and, as such, is a common ingredient in skin cleansers, creams, lotions, cosmetics, and cosmeceuticals. Its importance stems from its efficacy, long history of use (it has a veritable classic status among cosmetic raw materials), and pervasiveness in the skin care product market.
Recent research has indicated that glycerol exhibits multiple mechanisms of action, and its efficacy depends on the choice of vehicle and emulsifying agent. These considerations are especially important when making proper recommendations to patients and for helping consumers select over-the-counter products.


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Roundup on Cosmetic Dermatology Winter 2007
RENOVA (tretinoin cream) 0.02%

FOR TOPICAL USE ON THE FACE, NOT FOR ORAL, OR INTRAVAGINAL USE.

Brief Summary
RENOVA 0.02% contains the active ingredient tretinoin in a cream base.

IMPORTANT NOTE—This information is a BRIEF SUMMARY of the complete prescribing information. It is not intended to be a substitute for the complete prescribing information. The physician should be thoroughly familiar with the complete prescribing information before prescribing the product.

INDICATIONS AND USAGE:
(RENOVA is not indicated for use on the scalp. If you need to use it on your scalp, please read the entire INDICATIONS AND USAGE section. See pages 19 through 22.)

RENOVA (tretinoin cream) 0.02% is indicated as an auxiliary measure of the treatment of certain conditions of the skin, including, but not limited to:

- Acne vulgaris
- Keratosis pilaris
- Photodamaged skin
- Molluscum contagiosum

It is not indicated for use in children 12 years and younger. Patients who use RENOVA should be counseled about the potential for skin adverse effects. The physician should be familiar with the complete prescribing information before prescribing the product.

INDICATIONS AND USAGE:
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A Picture-Perfect Combination

Efficacy With Cosmetic Elegance

The power of tretinoin with everyday appeal

• 60% of patients treated with RENOVA® (tretinoin cream) 0.02% experienced an improvement in fine facial wrinkling after 24 weeks of treatment*1
• Reduces fine lines and wrinkles, with clinical benefits often seen in 4 to 12 weeks2,3
• Lightweight, non-greasy cream is ideal for daily use2

See the difference RENOVA 0.02% can make after 24 weeks3,4

Continuous improvement over 52 weeks2
85% of patients treated with RENOVA 0.02% showed improvement in fine wrinkling (N=108)2

RENOVA 0.02% is indicated as an adjunctive agent for use in the mitigation (palliation) of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs. RENOVA 0.02% does not eliminate wrinkles, repair sun-damaged skin, reverse photoaging, or restore more youthful or younger skin. The safety and efficacy of using RENOVA 0.02% daily for greater than 12 months have not been established. RENOVA 0.02% is proven effective on lightly pigmented skin, Fitzpatrick skin types I, II, and III. Do not use RENOVA 0.02% if the patient is taking drugs known to be photosensitizers, pregnant, attempting pregnancy, or nursing. RENOVA 0.02% is a dermal irritant. Almost all patients experience skin reactions, including dryness, peeling, burning/stinging, erythema, and itching. In some patients this may be severe.

Please see brief prescribing information on the next page.

References:
1. RENOVA 0.02% [prescribing information]. Skillman, NJ: Ortho Dermatological; September 2000.

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