NEW DIRECTIONS IN THE USES OF RETINOID THERAPY IN COSMETIC DERMATOLOGY

PHOTODAMAGE
James J. Leyden, MD
Professor Emeritus, Department of Dermatology
University of Pennsylvania School of Medicine, Philadelphia

TOPICAL TREATMENTS FOR PHOTODAMAGE
Leslie S. Baumann, MD
Director, Division of Cosmetic Dermatology
Department of Dermatology, University of Miami

REJUVENATION: SKIN RESURFACING
Tina S. Alster, MD
Director, Washington Institute of Dermatologic Laser Surgery
Clinical Assistant Professor of Dermatology and Pediatrics
Georgetown University Medical Center
Washington, D.C.
NEW DIRECTIONS IN THE USES OF RETINOID THERAPY IN COSMETIC DERMATOLOGY

Photodamage: An Overview
James J. Leyden, MD
Professor Emeritus, Department of Dermatology
University of Pennsylvania School of Medicine
Philadelphia

Topical Treatments for Photodamage
Leslie S. Baumann, MD
Director, Division of Cosmetic Dermatology
Department of Dermatology
University of Miami

Rejuvenation: Skin Resurfacing
Tina S. Alster, MD
Director, Washington Institute of Dermatologic Laser Surgery
Clinical Assistant Professor of Dermatology and Pediatrics
Georgetown University Medical Center
Washington, D.C.

Accreditation
This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Excerpta Medica, Inc., and SKIN & ALLERGY NEWS. Excerpta Medica is accredited by the ACCME to provide continuing medical education for physicians.

CME Credit Statement
Excerpta Medica designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the educational activity. Term of Approval: July 2003 – July 2004.

Target Audience
This activity has been developed for dermatologists and other health care professionals involved in the diagnosis, treatment, and long-term management of patients with photodamaged skin.

Educational Needs
Concern over the visible signs of aging is one of the more common reasons that patients consult dermatologists. Although some of the manifestations of aging are intrinsic and cannot be reversed, prematurely aged skin as a result of photodamage can be treated with myriad techniques that reduce and/or prevent clinical signs such as wrinkles, mottled pigmentation, sallow color, and coarse texture. Dermatologists need to keep abreast of the most current research findings regarding topical therapies, including retinoid agents, topical antioxidants, and alpha hydroxy acid products. They also need to be aware of advancements made in resurfacing technology, especially new-generation laser therapy and chemical peel processes.

Learning Objectives
By reading and studying this supplement, participants should be able to:
• Summarize the histologic changes that occur in photodamaged skin.
• Describe how both UVA and UVB light contribute to photodamage.
• List at least three retinoid agents and three nonretinoid agents used as topical treatments for photodamaged skin.
• Describe the most common side effects associated with retinoid agents and regimens that may be used to help patients minimize them.
• Identify the ideal candidates for superficial, medium, and deep chemical peels.
• Explain how the various laser technologies differ from one another.

Faculty Disclosure
Faculty/authors must disclose any significant financial interest or relationship with proprietary entities that may have a direct relationship to the subject matter. They must also disclose any discussion of investigational or unlabeled uses of products.

Dr. Alster has nothing to disclose. Dr. Baumann has received clinical grants from Galderma, Allergan, and Elan. She discusses the investigational use of retinoids and botulinum toxin for the prevention of aging. Dr. Leyden has received clinical grants from OrthoNeutrogena and is a consultant to Allergan.
PHOTODAMAGE: AN OVERVIEW

James J. Leyden, MD

The cutaneous effects of aging can be categorized as either intrinsic or extrinsic. Generally, intrinsic skin changes associated with chronologic aging are genetically determined. Hallmarks of old age are dermal atrophy, gravity-induced skin sag, permanently etched expression lines from muscle movements, and concavity in the check area from loss of adipose tissue. This discussion will focus primarily on the extrinsic skin changes associated with exposure to sunlight or photoaging, which may appear decades before intrinsic changes manifest. Extrinsic cutaneous injuries are preventable and, to some extent, reversible.

DEGENERATIVE CHANGES CAUSED BY CHRONIC SUN EXPOSURE

Photodamaged skin is often described as dry and leathery, characterized by acinet dyschromia and premature wrinkling. Chronic exposure to ultraviolet (UV) light has been shown to cause major alterations in the papillary dermis, in which large coarse bundles of elastin-like material accumulates. This material is referred to as solar elastosis. Collagen synthesis is decreased, and production of collagen precursor molecules or procollagen is inhibited. Matrix metalloproteinases are enzymes responsible for the degradation of collagen fibers that results in wrinkling. Fisher et al showed that exposure to ultraviolet-B (UVB) light upregulates transcription factors that stimulate these metalloproteinase genes.

When the skin sustains an injury from UV radiation, it attempts to repair itself. The repair is imperfect, however, and results in an uneven formation of disorganized collagen fibers in the dermis called a solar scar. Kang et al hypothesized that multiple exposures to UV light cause invisible solar scars to accumulate. At some point, they cross a clinical threshold and become the visible wrinkles that characterize photoaging.

The rough, dry, weathered appearance of photodamaged skin has been attributed to alterations in the distribution of water-retaining glycosaminoglycans (GAGs) in the dermis. A study by Bernstein et al showed that GAG levels actually increase in skin chronically exposed to sunlight; however, GAGs are deposited on the elastic material of the superficial dermis rather than between the collagen and elastic fibers, where they are deposited in nonexposed skin. Thus, due to their relocation, GAGs are not available to hydrate the dermis. The rough surface changes are due to abnormal desquamation of coenocytes, which results in the thickening of the stratum corneum. As the stratum corneum thickens, it also stiffens, and cracks and clumps of uplifted cells are visible as flakes that are rough to the touch.

PHOTODAMAGE AND SKIN CANCER

Sunlight suppresses the immune function of the skin and can promote skin cancer. This sequence of events may be due to the reduced population of Langerhans’ cells in the epidermis of photodamaged skin. Castanet and Ortonne found that melanocyte activity is unpredictable in photodamaged skin: Some melanocytes become hyperstimulated while others cease melanin production. Solar lentigines, ephelides, seborrheic keratoses, and actinic keratoses are the most common pigmented lesions in photodamaged skin.

“Solar lentigines, ephelides, seborrheic keratoses, and actinic keratoses are the most common pigmented lesions in photodamaged skin.”

Photodamaged skin typically has a mottled appearance due to hyper- and hypopigmentation. Irregular distribution of pigment cells, a decrease in melanocytes, and an alteration in melanocyte-keratinocyte interaction are some of the conditions that contribute to uneven pigmentation of the skin. Castanet and Ortonne found that melanocyte activity is unpredictable in photodamaged skin: Some melanocytes become hyperstimulated while others cease melanin production. Solar lentigines, ephelides, seborrheic keratoses, and actinic keratoses are the most common pigmented lesions in photodamaged skin.

Photodamage is a complete carcinogen that has induced squamous cell carcinoma (SCC) in animal models. Actinic keratoses are often described as premalignant lesions of SCC and, as noted previously, are among the most common pigmented lesions in photodamaged skin. Actinic keratoses are transformed, potentially neoplastic keratinocytes, in the epidermal layer that are induced by exposure to UV radiation. They have distinct histologic features of pleomorphism and cytologic atypia. If the cellular atypia progresses, SCC can develop. Exposure to UV radiation is a major factor also in the pathogenesis of basal cell carcinoma.

PREVENTING VERSUS TREATING PHOTODAMAGE IS PREFERABLE

Any discussion a dermatologist has with a patient regarding topical or resurfacing treatments for photoaging should begin with an emphasis on the importance of preventing further skin damage through diligent, daily use of sunscreens; protective clothing; and when possible, sun avoidance during midday.

Both ultraviolet-A (UVA) and UVB light contribute to photodamage. UVB light, the primary cause of sunburn and the most carcinogenic portion of UV, affects primarily the epidermis and upper dermis. Ultraviolet-A, which makes up 95% of UV light, penetrates more deeply into the dermis, causing solar elastosis and other biologic effects. Exposure to UVA light is year-round. UVB light is fundamental to tumor initiation and UVA light causes tumor promotion; compared with UVA light, UVA light generates more oxidative stress and causes more lipid peroxidation.

Sunscreens are considered the gold standard for protecting the skin from the deleterious effects of UV light. Numerous studies have shown, however, that people use sunscreens incorrectly. They typically apply one-fourth to one-half the recommended amount and fail to reapply sunscreens frequently when outdoors for long periods. Although in recent years, sunscreens have evolved from UVB-filters to full-spectrum products that absorb UVB rays plus both short- and long-wave UVA rays, the sun protection factor (SPF) of a product reflects only its ability to block UVB light.

Although sunscreen use is endorsed by numerous health care organizations to help prevent skin cancer, the practice is not without controversy. In fact, some studies have linked the use of sunscreen to increased rates of melanoma. It has been theorized that people at high risk for melanoma use sunscreens to decrease their risk for the acute toxic effect of sunburn, which allows them to accumulate more chronic
injury from UVA. The most current evidence, however, suggests that broad-spectrum sunscreens are helping to reduce rates of melanoma. An important study by Thompson et al showed that regular use of sunscreens prevents development of actinic keratoses and thereby may reduce the risk of SCC.

Sunscreens are not the only means of preventing photodamage. According to Kang et al, tretinoin, a topical retinoid, may provide some protective benefits: Applied to human skin before UV irradiation, tretinoin inhibits induction of activator protein-1 as well as matrix metalloproteinases. Tretinoin also prevents procollagen loss. There is preliminary evidence that topical antioxidants, such as vitamin C and vitamin E, may provide some photoprotection, but more research is needed in this area.

Why Treat Photodamage?

As Kligman and Koblenzer have stated, “no one dies of old skin,” so why treat it? It is true that photoaged skin is not a debilitating condition in the way that heart disease, diabetes, and arthritis can be. In photodamaged skin, symptomatic lesions are common, and lesions that are potentially malignant should be treated before more serious sequelae develop.

The psychological distress, particularly among women, of having premature old-looking skin in our youth- and beauty-obsessed culture is not insignificant. Kligman and Koblenzer detail many of the discriminations faced by people who look old and the many psychological benefits that an attractive appearance affords, including greater self-esteem, a more successful career, and improved physical well-being. It is evident from a walk down the skin care aisle of any drugstore that women are keenly interested in maintaining a youthful appearance. Consequently, the cosmetics industry eagerly markets a plethora of unregulated “antiaging” products to women. According to a 2001 survey by the Association for the Advancement of Retired Persons, 61% of women say they apply cosmetics to hide age marks, and 71% of women 45 to 54 years of age have used hair coloring to hide gray hair. The survey also found that 1 in 10 women 55 to 64 years of age has had cosmetic surgery.

Choosing Among Therapies

Elsewhere in this supplement, Dr. Baumann discusses in detail the many topical agents available for treatment of photodamage, and Dr. Alster reviews surgical resurfacing procedures, including chemical peels, dermabrasion, and the various laser surgery techniques.

Selecting therapy depends on individual patient assessment and the severity of the photodamage. Minimal photodamage with mild periorbital wrinkles may be treated with topical therapy or superficial peels. Of the topical therapies, tretinoin is the only treatment to date that has been shown to be effective as an antiaging agent in multiple, double-blind, vehicle-controlled clinical studies. Tazorotene, another retinoid agent, is emerging as a promising alternative to tretinoin.

“Selecting therapy depends on individual patient assessment and the severity of the photodamage.”

Other topical therapies include alpha hydroxy acids, which are often used in conjunction with retinoid therapy, and topical 5-fluorouracil (5-FU). A pyrimidine analog, 5-FU is frequently used to treat widespread actinic keratoses, and it is the opinion of this dermatologist that it is often underused in the treatment of photodamage. Patient compliance with traditional use of 5-FU (twice-daily application for 3 weeks or longer) can be poor, however, because it results in substantial irritation and unsightly inflammation equivalent to laser abrasion. A pulse regimen, in which patients applied the medication 1 to 2 days per week for 6 to 7 weeks, was shown to achieve clearance of 98% of actinic lesions with minimal irritation and erythema.

Moderate wrinkling and photodamage respond best to medium-depth peels, soft tissue augmentation (such as collagen injections), or erbium:ytrrium-aluminum-garnet (Er:YAG) laser resurfacing. The deep wrinkles that characterize severe photodamage are best treated with carbon dioxide laser resurfacing, botulinum toxin injections, and surgical procedures, such as rhytidectomies and blepharoplasties. When other skin rejuvenation procedures are performed, retinoids are often recommended preoperatively because they have been shown to hasten healing and postoperatively to maintain results.

Future Therapies

Some therapies described in this supplement have been studied for decades while others are relatively new, with no long-term evidence of efficacy. The family of retinoid agents continues to expand as molecular biologists seek to develop compounds with less irritancy and greater efficacy for treatment of a broad range of dermatologic disorders. Kang et al suggest that mapping of the UV signaling cascade has identified several potential strategies for preventing photodamage. One of these strategies includes using antioxidants to block the generation of reactive oxygen species, which is one of the earliest measurable UV responses in human skin. In the quest for the ideal sunscreen, new and better products are being introduced every year. Lastly, new understanding of the hormonal effects of aging on women may lead to development of estrogen-based therapies specifically for treating photoaging.

References

TOPICAL TREATMENTS FOR PHOTODAMAGE

Leslie S. Baumann, MD

 Dermatologists have a choice among a wide range of topical agents when selecting treatment for their patients with photodamaged skin. Compared with chemical peels or laser surgery, topical agents require a longer period of time for patients to see results (typically 3 to 6 months or more); however, topical therapy is certainly less invasive and has fewer complications. In addition, following the use of peels or lasers, topical agents are often used preoperatively to hasten healing or postoperatively to maintain results.

Many of these topical agents may cause irritation that some patients cannot tolerate and, therefore, compliance is often problematic. When patient compliance can be maintained, however, results with retinoid-based topical agents, based on the clinical experience of this dermatologist, are superior or at least equivalent to results associated with superficial chemical peels. To maintain the efficacy of topical agents, they must be used indefinitely.

THE RETINOIDS: AN EVER-EXPANDING FAMILY OF TOPICAL TREATMENTS

Of the topical treatments available, those in the retinoid class, such as tretinoin and tazarotene, are perhaps the products most commonly used by dermatologists. Originally, retinoids were compounds whose structures resembled vitamin A, or retinol, the parent compound from which they were derived. The newest generation of retinoids, however, has been substantially modified and thus bears little resemblance to retinol.

Tretinoin

Topical tretinoin has been used to treat acne vulgaris for more than three decades. In 1986, Kligman et al\(^1\) were the first to report on the efficacy of tretinoin in reversing damage to facial skin caused by excessive exposure to sunlight. Efficacy of the 0.05% tretinoin cream in reversing photodamage has since been demonstrated in numerous long-term, large-scale, double-blind clinical studies. Several of these trials have been summarized in an overview by Gilchrest.\(^2\)

The mechanism of action of tretinoin is attributed to a number of histologic changes in the skin, including increased epidermal and granular layer thickness; decreased melanin content; and compaction of the stratum corneum.\(^3\) Furthermore, tretinoin increases collagen synthesis. This change in the skin associated with tretinoin use is particularly important because a deficiency of superficial dermal collagen, as shown by Kang et al,\(^4\) is the key contributing factor to photoaging of the skin. In addition, Woodley et al\(^5\) found that topical tretinoin increases the number of collagenous anchoring fibrils within the papillary dermis and thereby improves the dermal-epidermal junction. Tretinoin is also associated with an increased number of blood vessels in the skin, which is believed to be responsible for the “rosy glow” that characterizes the facial appearance of patients using the topical agent.

The erythema and desquamation that most patients experience when they initiate tretinoin therapy can make compliance difficult. Although the retinoid irritation subsides after several weeks, many patients cannot tolerate the peeling and redness and, therefore, abandon therapy before they see positive results. In an attempt to counteract these effects, the base of a newer formulation of tretinoin is more emollient than the base of previous retinoid products.

Because compliance failure due to skin irritation is the main concern of patients who use retinoid products, patient education and support are absolutely essential during the early stage of treatment. Successful use of topical retinoids can be achieved by counseling patients to apply the product after using a moisturizer every third night to build up tolerance. Even using retinoid products once a week will eventually help patients to build up tolerance.

Early studies of tretinoin raised concerns that it may increase photosensitivity, and possibly, photocarcinogenicity. These concerns, however, have generally been discounted by subsequent research. In 1996, Fisher et al\(^6\) demonstrated that

**Histologic Changes Associated With Tretinoin Use**

- Compaction of the stratum corneum
- Epidermal spongiosis
- Hyaluronic acid within spongiotic areas
- Increase in granular layer
- Decrease in melanin, more uniform dispersion of melanin
- Decrease in cytologic atypia
- Improved dermal-epidermal junction

**Clinical Changes That Accompany Histologic Changes**

- Increased tactile smoothness of the skin
- Decreased skin mottling
- Decrease in actinic keratoses
- Decrease in skin fragility

Tretinoin has no phototoxic activity. Results of early studies in animals suggested that tretinoin could potentially be photocarcinogenic; however, studies in humans found that tretinoin is noncarcinogenic and may, in fact, provide protection from ultraviolet (UV)-induced lesions. Doses of UV light that are too low to cause skin reddening are still capable of activating the enzymatic activity that sets off the photoaging cascade, and tretinoin has been shown to inhibit this process.4,6

Tretinoin Plus Hydroxyanisole

Solar lentigines on the face and hands are a sign of photodamage that distress patients. Tretinoin is a depigmenting agent that has been used to treat solar lentigines. Another depigmenting agent commonly used in Europe is 4-hydroxyanisole (4HA), which is less irritating than hydroquinone. A formulation combining the two agents (2% 4HA and 0.01% tretinoin) was evaluated in two large phase III, controlled, double-blind clinical trials.1 The combination product was found to be superior to either tretinoin or 4HA used alone, was well tolerated, and had an excellent safety profile.

Tazarotene

Tazarotene was the only agent approved for the treatment of facial wrinkles until the U.S. Food and Drug Administration (FDA) approved tazarotene for the same indication in October 2002. Tazarotene was previously used to treat psoriasis and acne. Histologic changes associated with retinoids are believed to result from their regulation of gene transcription and influence on cellular differentiation and proliferation.”

Similar to therapy with tretinoin, tazarotene treatment requires patient education and support to ensure successful clinical outcomes. Patients need to be advised that the burning, peeling, and erythema will subside in approximately four weeks. Application of tazarotene every third night as described previously for patients using tretinoin is appropriate to enhance compliance.

It should be noted that tazarotene may be better tolerated in humid environments, such as Miami, the location of this dermatologist, than in cooler, drier environments. In more arid climates, the tretinoin emollient cream may be a better choice due to the moisturizing properties of the base cream.

Tazarotene also offers an alternative product for patients who come to the dermatologist insisting that they have tried tretinoin and could not tolerate it. Tazarotene can be presented as another option.

Other Retinoids

Adapalene, like tazarotene and tretinoin, is an acne medication that is being evaluated for possible treatment of photodamaged skin. Early evidence suggests that adapalene, a third-generation retinoid, may be less irritating than other retinoids.13

Topical retinol, the parent compound of all these derivative agents, has gained new interest among dermatologists after being rejected decades ago because oxidation rendered it inactive. Pharmaceutical companies have since succeeded in creating retinol formulations that are much more shelf-stable. While products containing retinol are available over-the-counter (OTC), the amount of the active agent in these unregulated products is difficult to determine. Many products use biologically inactive forms, such as retinyl palmitate.

Alpha Hydroxy Acids

Alpha hydroxy acids (AHAs), especially glycolic acid and lactic acid, have become very popular additives to a host of OTC skin products. Dr. Alster discusses the use of these agents in chemical peels elsewhere in this supplement. This discussion concerns the use of AHAs in topical applications. AHAs have been shown to increase epidermal thickness, increase synthesis of glycosaminoglycans, and decrease stratum corneum thickness.12 There is concern, however, that use of AHAs may increase photosensitivity in patients.13 The FDA is considering requiring products containing AHAs to include a warning label stating that users should wear sunscreen when applying them. Furthermore, AHAs can be irritating to patients with rosacea or sensitive skin. For patients of this dermatologist, salicylic acid, a beta hydroxy acid, is preferred. It has antiinflammatory and comedolytic properties and has been well studied as an acne treatment.

Despite the widespread popularity of AHAs, there are insufficient data to support their efficacy, especially compared to retinoid agents. (Despite a paucity of controlled studies validating the use of AHAs in combination with retinoid products, many dermatologists have tried this technique.)

OTHER TOPICAL THERAPIES

A plethora of other topical therapies exist that have been evaluated for their potential to counter the effects of
photoaging. Some of these products will be addressed briefly.

**Topical Estrogen**

Women begin losing collagen in their skin at menopause when estrogen levels plummet. Although the effects of systemic estrogen (as part of hormone replacement therapy [HRT]) on skin has been the subject of many studies, the effects of topically applied estrogen have received considerably less scrutiny. Schmidt et al.14 conducted several studies using topical estradiol and estriol compounds to counter skin aging. Results showed that they improved skin elasticity and firmness and decreased wrinkle depth, with no systemic hormonal side effects.

It is the practice of this dermatologist to prescribe topical estrogen cream for patients who are not receiving HRT and not at risk for estrogen-responsive cancers. Patients use vaginal creams because there are no estrogen formulations specifically for facial skin. Patients report that their skin appears more hydrated after approximately two weeks of treatment.

**Topical Antioxidants**

Vitamin C, vitamin E, and selenium are popular additions to OTC products for the skin. When skin is exposed to UV radiation, oxygen radicals are created. Antioxidants, such as vitamin C and vitamin E, have been shown to neutralize these free radicals. Data are lacking, however, as to whether they protect against photodamage when applied topically. It is also unclear whether they are absorbed into the skin or remain stable in topical formulations. Yet, there are data showing that taking antioxidants orally raises their levels in the skin.

Plant antioxidants, such as soy isoflavones and green tea polyphenols, have also been studied for photoprotective properties.15 Soy milk has been shown to have depigmenting effects. Furthermore, because soy milk is estrogenic, it may mitigate the depletion of estrogen in women during menopause. Topically applied tea polyphenols decreased UV-induced skin tumors in animal models.16 Copper peptide, niacinamide, and coenzyme Q10 are other antioxidants currently under investigation as agents that may counteract some of the degenerative changes brought about by excessive sunlight exposure.

**Botulinum Toxin and Photodamage**

Although administered by injection, not topically, botulinum toxin (BTX) is discussed briefly here because it is often used in conjunction with topical therapies as well as with the resurfacing techniques described by Dr. Alster.

Botulinum toxin blocks the release of acetylcholine from the presynaptic terminal of the neuromuscular junction, causing flaccid muscle paralysis and preventing contractions.17 More simply, BTX is effective for wrinkles in motion, such as the glabellar frown lines, but not for those at rest that are associated with photodamage. It is the opinion of this dermatologist that use of BTX may prevent wrinkles in motion from progressing to wrinkles at rest, although this has not been proven.

**REFERENCES**

7. Fleischer AB, Schwarttz EH, Colby SI, Alman DJ. The combination of 2% 4-hydroxyanisole (Mequinol) and 0.01% tretinoin is effective in improving the appearance of solar lentigines and related hyperpigmented lesions in two double-blind multicenter clinical studies. J Am Acad Dermatol. 2000;42:459-467.
S
kin rejuvenation is achieved through selective damage and replacement of photodamaged skin. Mild cutaneous photodamage with minimal rhytides may respond well to topical acid therapy or superficial chemical peels. Moderate to severe photodamage and rhytides typically require deeper chemical peels and ablative laser skin resurfacing. Injections with fillers or botulinum toxin can be used to reverse or prevent rhytides at any stage.

CHEMICAL PEELS
A chemical peel is one of the most common procedures performed for skin rejuvenation and involves application of a caustic chemical to the skin surface. To prepare the stratum corneum for a chemical peel, tretinoin or hydroquinone is often applied for 4 to 6 weeks prior to the procedure. The depth of the resulting injury depends primarily on the type and strength of the chemical agent used and the duration of exposure. While damage associated with superficial peels affects only the epidermis, damage associated with medium-depth peels may be evident as deep as the upper reticular dermis; deep peels penetrate to the mid-reticular dermis.

Superficial peels with Jessner’s solution (resorcinol, salicylic acid, and lactic acid), glycolic acid (20% to 70%), or trichloroacetic acid (15% to 25%), are appropriate for most skin types and require minimal recovery time. Jessner’s solution separates the stratum corneum but does not affect the dermis, whereas glycolic and trichloroacetic acids have been shown to thicken collagen and elastic fibers in the papillary dermis. Superficial peels with Jessner’s solution are associated with longer healing periods. In addition, they pose an increased risk of complications related to the marked inflammatory response and keratocogulative necrosis of the epidermis that extends into the papillary dermis. Epidermal regeneration occurs within approximately 1 week. Studies have demonstrated that topical tretinoin hastens the regenerative process.

“Dermabrasion can also be used to treat photodamaged skin… Pretreatment with tretinoin accelerates postoperative wound healing.”

Reversible erythema and postinflammatory hyperpigmentation are the primary negative effects possible following superficial and medium-depth chemical peels. Deep phenol peels can induce liver, kidney, and cardiac toxicity. Since irreversible hypopigmentation can also result from deep peels, this procedure is not recommended for darker skin tones.

DERMABRASION
Dermabrasion can also be used to treat photodamaged skin. The procedure involves removal of the epidermis and upper- to mid-dermis with a rotating wire brush or diamond fraise. Pretreatment with tretinoin accelerates postoperative wound healing.

Poor intraoperative visualization related to lack of hemostasis and bulky instrumentation make it difficult to achieve fine control during this procedure. Consequently, there is an increase in severe complications, such as permanent dyspigmentation and scarring. It is, therefore, nearly impossible to treat delicate tissue, such as the periorbital and upper lip areas.

ABLATIVE LASERS
Compared with chemical peels and dermabrasion, ablative skin resurfacing with either carbon dioxide (CO₂) or erbium:yttrium-aluminum-garnet (Er:YAG) lasers has been shown to produce more predictable clinical and histologic results. The laser procedure is performed in a char-free and bloodless operative field, permitting clear visualization during surgery. Layer-by-layer, tissue ablation is achieved, permitting treatment titration as appropriate in delicate tissue areas.

The far infrared wavelengths of the CO₂ and Er:YAG lasers (10,600 nm and 2940 nm, respectively) are absorbed in water-containing tissue, allowing precise skin ablation with predictable collateral damage to normal tissue.

Contraindications to Laser Resurfacing

- Active bacterial, viral, or fungal infection
- Inflammatory skin condition
- History of abnormal wound healing
- Keloids or hypertrophic scars
- Isotretinoin use within the previous 6-12 months
- Prior radiation therapy to the target area
- Scleroderma or other collagen vascular disease

thermal damage. The depth of ablation and degree of thermal damage are directly correlated with the energy and number of laser passes applied.25,18,19,20

The CO2 and Er:YAG lasers have been used successfully for facial rhytides; atrophic and surgical or traumatic scars; various epidermal and dermal lesions; and photodamaged skin.12,13 Controlled thermal injury in the papillary and superficial reticular dermis triggers improvements in elastotic skin and induces long-term collagen remodeling.

Three distinct zones of tissue alteration result from CO2 laser resurfacing. Most superficial is the zone of direct impact where vaporization of intracellular water and tissue ablation occur. Underlying this zone is a layer of irreversible tissue necrosis. The apparent tissue tightening of loose skin results from heat-induced collagen shrinkage in the dermis.21 The laser-induced dermal injury is thought to promote collagen deposition, with a wider zone of post-treatment fibroplasia. The clinical improvement is attributed to the combination of vaporization, collagen shrinkage, and collagen deposition. Treatment benefits persist for at least 24 months and may be extended by prolonged use of topical tretinoin postoperatively.21

BEFORE AND AFTER LASER RESURFACING

Preoperative treatment for a variable period of time with a range of topical agents, including furfuryladenine, L-ascorbic acid (vitamin C), tretinoin, and glycolic acid, helps to evaluate how a patient’s skin will respond postoperatively and to assess patient compliance. Choice of active agent to administer, in addition to a good sunscreen, depends on the patient’s skin care history and skin type.22,23

Regardless of which wound care technique (wound-healing ointments or semiconfluent dressings) is used postoperatively, the laser-treated skin should be kept moist and iced. Initially, when the skin surface is raw and without epithelium, antibiotic ointments are avoided because irritant or allergic contact dermatitis may develop.22,24 One week after surgery, following reepithelialization, a nonchemical sunscreen, such as zinc or titanium oxide, and fragrance-free moisturizer are introduced. By 1 month postoperatively, the pretreatment product mix is typically resumed.

POTENTIAL LASER ADVERSE EFFECTS

In the hands of an experienced laser surgeon using conservative treatment parameters, laser skin resurfacing is a relatively safe procedure with a low risk of serious adverse sequelae.24,25 As with all skin resurfacing techniques, however, complications are related to depth of dermal wounding, intrinsic patient variables (including patient skin type), and postoperative management. Potential adverse effects after laser resurfacing include prolonged erythema, infections, scarring, and dyspigmentation.24,25

Erythema is an expected outcome from ablative laser treatment and can persist for months. Application of topical L-ascorbic acid in an aqueous formulation has been reported to decrease postoperative erythema significantly.26 Latent herpes simplex virus can be reactivated by laser resurfacing, typically occurring during the first postoperative week. Thus, a 10-day course of an antiviral should be administered concomitantly with the reepithelialization process.27 Bacterial infections may also ensue. The role of perioperative and postoperative antibiotic prophylaxis, however, is uncertain because use of antibiotics may not affect the rate of bacterial infections.28 Due to the moist wound environment, postoperative candidiasis has also occurred. Scarring from infection is largely preventable by close observation of the laser-tissue interaction and by early diagnosis and treatment of suspected postoperative infections. If scarring does occur, the use of a 585-nm pulsed-dye laser for laser-induced burn scars is widely accepted as the treatment of choice.29,30

Pigmentary changes can be reduced or limited by appropriate attention to the depth of resurfacing.31 Transient laser-induced hyperpigmentation occurs in approximately one-third of patients (more frequently among patients with darker skin tones) but can be decreased in severity and duration by postoperative use of topical hydroquinone, tretinoin, or glycolic acid. While preoperative use of tretinoin is often recommended to hasten post-laser reepithelialization, it was not shown to be beneficial in decreasing the incidence of hyperpigmentation. Thus, it was hypothesized that post-laser reepithelialization includes follicular melanocytes that were not affected by pretreatment.31

NONABLATIVE LASERS

Collagen remodeling is also accepted as a key element in the successful treatment of photodamage. Since both the epidermis and dermal collagen absorb energy from infrared- and far-infrared wavelengths due to their relatively high water content, it was necessary to develop systems that were epidermal-sparing. To accomplish “nonablative” regeneration wherein avoidance of epidermal vaporization is achieved on laser impact, systems were developed that incorporate a cooling device to protect the overlying epidermis.

Nonablative systems include the 1320-nm neodymium:YAG, 1450-nm diode, and 1540-nm erbium:glass lasers. They emit far-infrared wavelengths that pass harmlessly through the epidermis to penetrate the dermis and heat collagen above 60° C, thereby inducing collagen contraction and initiating collagen remodeling.32,33 The ideal candidate for nonablative therapy has pale skin, mild
rhytides, and minimal epidermal damage. Because the results are gradual and progressive, other rejuvenative treatments may be more appropriate for patients who desire extreme changes. Frequently, 3 to 5 monthly treatments are required, and the final results are not apparent for several months. On the other hand, since there is no external wound, postoperative recovery is not a concern and patients’ active lifestyles are not interrupted.

CONCLUSION

Several dermatologic procedures effectively resurface and rejuvenate photodamaged skin. The major advantage of ablative cutaneous laser resurfacing is control of skin vaporization in a relatively clear operative field. With proper laser technique and postoperative management, the risk of scarring or other complications is minimized. Furthermore, clinical results are often superior to those obtained after chemical peels or dermabrasion. Recently, nonablative skin rejuvenation techniques have become more popular than ablative procedures due to the technical learning curve required of surgeons as well as the expense and prolonged recovery time associated with ablative laser therapy.

REFERENCES

NEW DIRECTIONS IN THE USES OF RETINOID THERAPY IN COSMETIC DERMATOLOGY

CME TEST AND POST-TEST EVALUATION

Copyright 2003 International Medical News Group, An Elsevier company

CONTINUING EDUCATION INSTRUCTIONS: There is no fee to participate in this activity.

Please forward the Test Answer Sheet and Evaluation Form to:
Excerpta Medica/Elsevier
Office of Continuing Medical Education, Department SKIN
105 Raider Blvd., Suite 101, Hillsborough, NJ 08844-1528
FAX: (908) 874-5633

Response for AMA Physician’s Recognition Award credit must be submitted by July 2004.

INSTRUCTIONS: Please circle the most appropriate response. Six of eight correct responses are required for credit.

1. The dry, weathered look of photodamaged skin is believed to be caused by alterations in the distribution of:
   a) matrix metalloproteinases
   b) glycosaminoglycans
   c) keratinocytes
   d) procollagen

2. Which of the following statements regarding ultraviolet (UV) light is true?
   a) UVA generates more oxidative stress than UVA.
   b) UVA penetrates more deeply into the dermis than UVA.
   c) UVA is the most carcinogenic portion of UV light.
   d) A sunscreen product’s sun protection factor (SPF) rating now reflects its ability to shield against UVA as well as UVB radiation.
   e) All of the above are true.

3. Which of the following retinoid agents is/are used to treat psoriasis as well as photodamage?
   a) tretinoin
   b) tazarotene
   c) adapalene
   d) retinol
   e) All of the above

4. Which of the following is a beta hydroxy acid?
   a) lactic acid
   b) tartaric acid
   c) malic acid
   d) salicylic acid

5. An early concern that tretinoin may increase __________ has now largely been discounted.
   a) collagen loss
   b) melanin production
   c) photosensitivity
   d) All of the above

6. Which of the following agents is/are used preoperatively to treat patients before laser surgery?
   a) L-ascorbic acid
   b) tretinoin
   c) glycolic acid
   d) furfurylidenine
   e) All of the above

7. Which therapy would be best to treat severe rhytides?
   a) Botulinum toxin
   b) Jessner’s solution peels
   c) Tretinoin plus hydroxyanisole
   d) Tretinoin plus alpha hydroxy acids

8. Which characteristic best describes the ideal candidate for nonablative laser therapy?
   a) A patient who has minimal epidermal damage.
   b) A patient who would not be inconvenienced by a lengthy postoperative recovery period.
   c) A patient who has dark skin that is not suitable for deep peels.
   d) All of the above

Release Date of Activity: July 2003
Expiration Date of Activity: July 2004
Estimated Time to Complete this Activity: 1 hour

PLEASE PRINT

Name ____________________________ Degree ____________________________ Specialty ____________________________
Address __________________________ State ________ ZIP __________ Phone ____________________________ Fax __________
E-mail ____________________________ Signature ____________________________

PLEASE INDICATE AMOUNT OF TIME SPENT ON THIS ACTIVITY: AMA Category 1 credit (maximum 1 hour): ______ hrs ______ min spent on activity

Please check here if you would like to receive future CME publications from Excerpta Medica/Elsevier

CME ACTIVITY EVALUATION:

1. Were you able to meet the objectives of this CME activity? (CIRCLE ONE) YES NO
   If no, please note which objectives you were not able to meet:

2. Will the information presented in this issue be useful in your practice setting? YES NO
   Comments: ____________________________________________________________

3. Did you find the information presented in this publication to be objective, balanced, and free of commercial bias? YES NO
   Comments: ____________________________________________________________

Copyright 2003 International Medical News Group, An Elsevier company
Supported by an unrestricted educational grant from

OrthoNeutrogena®