OMEGA-3s: A KEY PLAYER IN PREVENTING DISEASE, INCLUDING CANCER PHYSICIAN REV advance for MARCH/APRIL 2009 AGE MANAGEMENT MEDICINE FOR PHYSICIANS VITAMIN D DEBATE **Screen Your Patients** for Deficiencies **BONE HEALTH** Are Bisphosphonates a Double-Edged Sword? ANEW LASERS IN ACNE TREATMENT

ANEW LOOK AT LASERS AND ACNE

ADULT-ONSET ACNE TREATMENT HAS GONE HIGH-TECH, AS LIGHT AND LASER SOURCES PROVIDE ALTERNATIVES TO DRUGS WITH DANGEROUS SIDE EFFECTS.

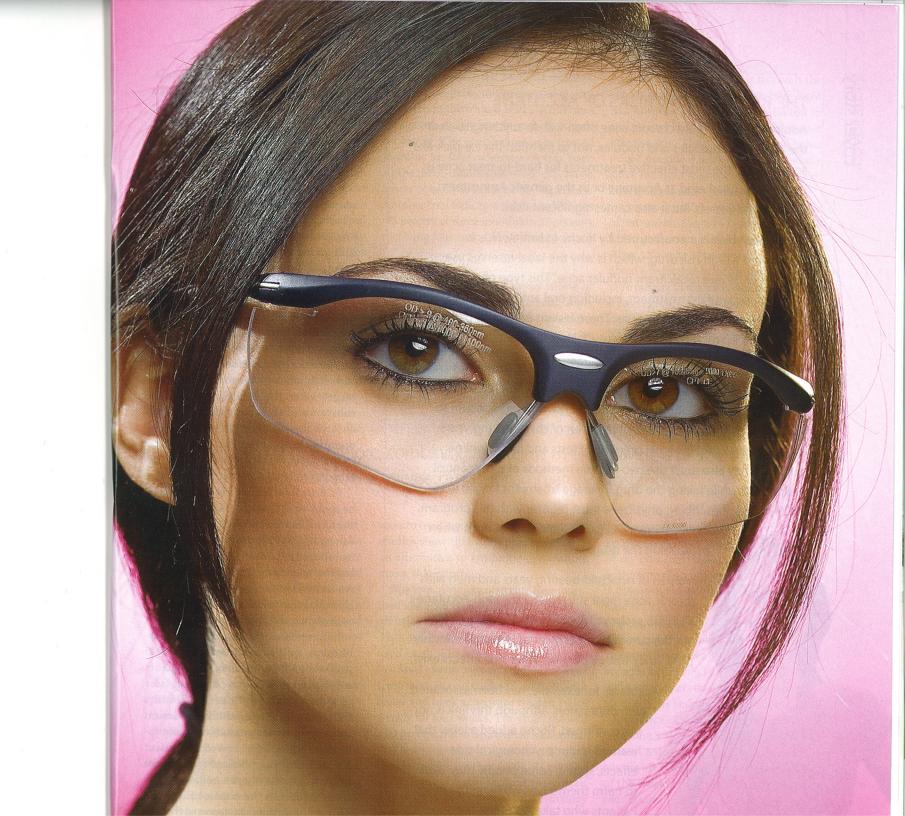
BY DAVID GOLDBERG, MD

Acne is sometimes viewed as an adolescent rite of passage, as common as deepening of the voice or developing curvy hips. Many women are fortunate to dodge the characteristic pimples in their youth only to face stubborn outbreaks of adult-onset acne in their 40s.

Until recently, we could only prescribe a pill, with potentially dangerous side effects, for resistant or moderate to severe forms of this insidious condition. Luckily, times have changed.

ACNE VULGARIS remains one of the most common

Novel therapies, such as light and laser sources, can treat acne and its associated scarring, as well as sidestep the



THE BENEFITS AND RISKS OF ACCUTANE

Adults who suffer from chronic acne often will do anything to clear the condition's pustules and nodules not to mention the ice-pick-like scars. One of the most effective treatments for hard-to-treat acne is isotretinoin (marketed as Accutane or as the generic Amnesteem, Claravis and Sotret). But it also carries significant risks.

Accutane, which is manufactured by Roche in Nutley, N.J., is considered a high-risk drug, which is why the label reserves use to cases of "severe recalcitrant nodular acne." This type of acne is resistant to standard treatment, including oral antibiotics, and is characterized by nodules or cysts. These lesions can cause pain, permanent scarring and negative psychological effects.

This drug has been associated with birth defects, miscarriages and premature births. Patients must register with iPLEDGE, an online risk management program to reduce the risk of fetal exposure to the drug. Under Roche's iPLEDGE, women of child-bearing years must agree to take monthly pregnancy tests and fill out online surveys. They also must use two reliable methods of birth control before and while taking the drug. Average treatment length is 16 to 24 weeks. Prescribing physicians must register with this program,

using a patient's iPLEDGE ID and date of birth when

prescribing the drug.

Women of nonchild-bearing years and men with chronic acne must still register through Accutane's iPLEDGE program. But they do not need to fill out the surveys or take birth control and monthly pregnancy tests. However, other side effects exist.

Accutane, for example, has been associated with depression. Although this link is not yet confirmed, Roche added a label that warned about psychological side effects, stating some people may wish to harm themselves while on the drug. Patients who take Accutane need to be closely monitored for psychological well-being. In addition, depressive symptoms may continue after people stop taking the drug.

Source: www.fda.gov/cder/drug/infopage/accutane/default.htm

Sebaceous Gland Targeted Lasers

Sebaceous gland oil production plays a major role in acne formation. In the past, this made treatments, such as systemic isotretinoin, the standard because the drug decreases the size of the sebaceous gland as well as sebum production.

Unfortunately, isotretinoin is also associated with serious potential side effects, including dry skin and eyes, liver and joint abnormalities, and possible mood changes. One of the most dramatic, however, is the risk of fetus deformity in pregnant woman.

Circumventing these side effects, mid-infrared lasers (1064 nm to 1540 nm), which were originally developed for nonablative facial skin rejuvenation, can decrease the size of sebaceous glands as well as sebum secretion. These lasers target water, the dominant absorbing substance of sebaceous glands. Water absorbs the laser energy, which subsequently causes a thermal injury zone in the upper dermis, exactly where the sebaceous glands are located.

1320 nm laser. Among the first lasers to be approved to treat acne vulgaris in 2003, the CoolTouch (Laser Aesthetics Inc., Roseville, CA) 1320 nm laser system uses its infrared light energy to improve acne lesions by altering the sebaceous gland. As an added benefit, this laser remodels collagen, yielding a more youthful appearance and fewer acne scars.

In a randomized, controlled, single-blinded, split-face clinical trial of 46 patients with facial acne, participants received a series of three 1320 nm laser treatments to half of the face. Results were assessed by serial blinded lesion counts and sebum production measurements. Treated skin showed a transient but statistically significant improvement in lesion counts of open comedones as compared with the control side. The majority of patients also reported that the treatments were at least mildly effective for acne and oiliness.¹

The procedure is fast and safe in all skin types. However, treatments are mildly uncomfortable and not generally covered by medical insurance policies.

1450 nm laser. Another similar midinfrared laser, the Smoothbeam (Candela



Corp., Wayland, MA) diode laser also induces thermal damage to the sebaceous gland. One study noted a statistically and clinically significant reduction in acne lesions. In fact, after a 24-week follow-up, 14 of the 15 subjects had no lesions on the treated area. These results, although fantastic, are not the norm. We can expect improvement, but not total clearance. In addition, patients commonly reported transient erythema, edema and hyperpigmentation. All of these side effects resolved without scarring.²

Another study analyzed the 1450 nm laser to treat inflammatory facial acne in 30 subjects. After one treatment, patients in the study saw their acne lesions decrease by 31 percent. They also experienced a 58 percent reduction after two treatments and an 83 percent reduction after three.

nm Aramis (Quantel Medical, France), was first available in Europe and is now also used in the United States. It has been evaluated on 25 patients with facial and back, acne. The acne lesions were treated monthly for four months with this laser. At the three-month follow-up visit, mean lesion count was reduced by 78 percent. Another trial indicated similar reductions (83 percent at three months) in 20 patients receiving four twice-weekly treatments. ⁵

Bacterial Targets

Because the bacteria *P. acnes* is one of the main etiologic factors in acne, topical and systemic antibiotics have been the major bastions of treatment for acne vulgaris. The theoretical emergence of resistant strains, however, has increased the demand for alternative, more effective to penetrate the epidermis to reach the sebaceous glands. Although blue light has now been extensively evaluated to treat acne, red light penetrates deeper into the skin. Thus, combining two lights might provide a better result, especially since red light may lead to the release of anti-inflammatory substances.

One study analyzed the simultaneous use of red and blue light to treat acne vulgaris in 140 patients with mild to moderate acne. After 12 weeks of treatment, researchers noted a reduction in inflammatory lesions of 76 percent in the combined blue-red light treated group. This is significantly better than the group treated solely with blue light. These results may be due to a synergistic effect that combines both antibacterial and anti-inflammatory mechanisms of action. This study was among the first to show

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Treatments were performed at four- to sixweek intervals. Patients were 100 percent satisfied, even in those subjects who were previously refractory to treatment with oral isotretinoin. However, some limitations of this study existed. For example, the length of improvement was not established, and most patients were on topical and/or oral acne regimens.³

Another trial investigated the efficacy of a combined bacteria-destroying 595 nm pulsed dye laser (PDL) and the aforementioned sebaceous gland-injuring 1450 nm diode laser. Fifteen patients with inflammatory acne were initially treated with the PDL, followed by treatment with the 1450 nm diode laser. Four to six weeks after each treatment, researchers noted acne lesion reductions to be 52 percent, 63 percent and 84 percent, respectively. This study elucidates the synergy that can occur when combining acne treatment laser technologies.4 The PDL effect decreases acne-causing bacteria while the thermal effect of the 1450 nm mid-infrared laser shrinks sebaceous glands.

1540 nm laser. Another laser, the 1540

ways to treat acne. Bacteria-targeted laser studies show that this approach may be an alternative to antibiotic use without major side effects.

Blue light. A variety of studies have examined low level blue light (415 nm) and its abilities to eradicate *P. acnes* colonies. This approach is painless and can be used in all skin types. It is also the first low level energy system studied for acne treatment. In one study, 35 subjects with facial and back acne were treated twice weekly for four weeks. The study showed a 70 percent mean decrease in inflammatory lesion count two weeks after the last treatment. In another study, 87 percent of the treated areas showed more than a 20 percent reduction of inflammatory acne lesions.

These results remained steady at two, four and eight weeks after the end of therapy. This promising study showed that results can last for at least two months after treatment.⁷

Combination blue and red light. One of the main limitations of light therapy for acne is that it can be difficult to get light that several acne-clearing devices may be more effective when used together.⁸ Many clinicians now treat their patients with more than one device.

Pulsed dye yellow laser. The pulsed dye laser (PDL) also has been used successfully to treat acne. This laser's yellow light may be particularly suitable to treat the dilated vascular component of acne inflammation because its 585 nm to 595 nm wavelength is absorbed by erythema-associated hemoglobin. This reduces the erythema-like appearance of the lesions.

In one study, authors reported a 49 percent reduction in inflammatory lesion counts after one treatment. Almost half of the treated patients had a 50 percent reduction in lesion counts by 12 weeks when compared to the control group. Unfortunately, these results were not substantiated in another study using the same laser.⁹

The reasons for the discrepancy are unclear. One possibility for the difference may be that more laser treatment pulses (which were not defined) were delivered during a session in the positive study.

Photodynamic Therapy

Another adjunctive treatment for acne vulgaris is photodynamic therapy (PDT), which uses a variety of light and laser sources with aminolevulinic acid (ALA). ALA is a light-sensitizing agent that can penetrate through the skin into the sebaceous glands.

Often used to prevent and treat non-melanoma skin cancer, ALA can target the sebaceous glands and kill *P. acnes*—providing a dual strike. This approach has been increasingly used over the last two to three years.

Studies have shown a decrease in acne lesion counts that persisted for 10 to 20 months. These results occurred after one to four treatments. Additionally, studies show a reduction in sebum excretion rate, sebaceous gland size and follicular bacterial counts. The treatment, though, can be associated with some discomfort, transient hyperpigmentation, and redness and scabbing. This will be exaggerated in those who have extensive sun damage. However, some investigators suggest PDT may ultimately be the way to cure acne. ¹⁰

One study delved further by analyzing three different light sources' ability to activate ALA. In this investigation, 22 patients with moderate to severe acne vulgaris were randomly assigned to receive ALA-PDT photoactivation by intense pulsed light (IPL), a combination of IPL and bipolar radiofrequency (RF) energies, or blue light. Each patient received three ALA-PDT sessions at two-week intervals. Follow-up at one and three months after the final treatment indicated that ALA-PDT with IPL activation provides greater, longer-lasting and more consistent improvement than either RF-IPL or blue light activation.¹¹

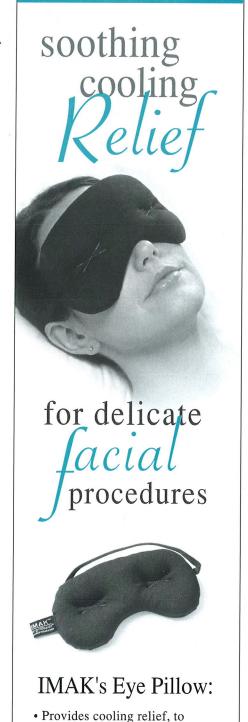
The study, however, did not evaluate a red light source. The red light source penetrates deeper into the dermis than a blue light source. Therefore, ALA and red light, or a combination of red and blue light, might yield the best results. But this

Whether used alone or as adjuvant therapy with other more conventional treatments, lasers and light-based devices are effective and becoming increasingly popular in treating adult acne vulgaris. Treatments are generally well tolerated, convenient, noninvasive and free of potential serious side effects or antibiotic resistance. Additionally, several lasers provide the added benefit of reducing the appearance of acne scarring and improving skin texture, a feature every patient desires.

Laser treatments for acne do not provide a cure. In fact, most patients still receive standard topical or oral acne treatment before they consider laser therapy. However, for that patient who seeks an alternative to systemic agents, laser treatment has evolved into a reasonable consideration. As laser and PDT approaches become better, the cure for acne may someday be at hand.

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