Though it represents one of the more commonly seen conditions of dermatology, rosacea remains somewhat enigmatic to practitioners. Key elements of its etiology are obscure, and debate persists regarding the influence of inflammatory mediators and possible contributory factors, such as infectious organisms or chronic sun exposure. Data suggest public knowledge of the disease is even sketchier; the National Rosacea Society says a Gallup survey found that 78 percent of Americans have no knowledge of this condition. Given that rosacea most commonly occurs in individuals over age 30 and may be more common with advanced age, the graying of America may lead to a surge in frustrated patients presenting to dermatologists’ offices.

Despite incomplete understanding of the etiology of rosacea from inception to its most advanced forms (phymas), dermatologists have developed relatively effective strategies for pharmacologic management of the condition. Nonetheless, topical and oral agents cannot eradicate the visible vasculature that is a hallmark of rosacea. In recent years, lasers and light-based systems have emerged as effective...
implements to reduce erythema, erase visible vessels, and help to relieve flushing, sensitivity, and other symptoms of rosacea. When combined with appropriate drug therapy, light-based interventions can yield significant and sustainable control of rosacea for a majority of patients. Key to success is a solid understanding of the role of medical therapy and proper parameters for laser administration and an ability to effectively educate patients about the nature of treatment and the probable need for future re-treatment.

Topical Therapies: The Latest
Rosacea is now widely classified according to four primary subtypes: erythematotelangiectatic (ETR), papulopustular (PPR), phymatous (PR), and granulomatous (GR). Erythema, telangiectases, flushing, and edema characterize ETR rosacea, while papules and pustules against a background of erythema characterize PPR rosacea. These two subtypes, which can appear together, will represent the bulk of discussion for this article. The three primary topical agents indicated for management of ETR and/or PPR rosacea are metronidazole, azelaic acid, and sodium sulfacetamide/sulfur. These agents are generally effective for reducing papules and pustules and calming inflammation to minimize swelling and erythema.

Before more fully describing these various agents, topical sunscreen formulations and good skincare practices warrant mention. Every rosacea patient must apply a broad spectrum moisturizing sunscreen SPF 15 (preferably 30) daily and take appropriate measures to minimize UV exposure on a regular basis and especially during periods of extended sun exposure. The patient must also wash the face only with moisturizing, soap-free cleansers, avoiding harsh cleansers, scrubs, and fragrances. Dermatologists can recommend specific products recommendations for sunscreens and cleansing based on personal research/experience and patient preference.

Metronidazole. Metronidazole has long been a cornerstone of topical rosacea therapy and is effective for both ETR and PPR subtypes. Data have shown that topical application of metronidazole may provide similar efficacy to oral tetracyclines in calming the inflammatory component of the disease. Using a skin lipid model, researchers recently demonstrated that topical metronidazole provides free-radical scavenging actions. One of the newest therapies approved for rosacea is metronidazole 1% (MetroGel 1%, Galderma), the highest available concentration of the drug in a once-daily topical formulation. Topical metronidazole therapy has been associated with application-site irritation, however, a recent study showed that the irritation potential associated with metronidazole 1% gel was similar to that of white petrolatum and was significantly lower than that of metronidazole 0.75% gel.

Azelaic acid. Azelaic acid is credited with antimicrobial, anti-inflammatory, antioxidant, and keratolytic actions. As such, it is most effective for the PRP subtype. A recent systematic review of randomized controlled trials found that azelaic acid 20% cream and 15% gel are effective for inflammatory papulopustular rosacea with particular benefit in decreasing inflammation and erythema. The pooled data suggest that azelaic acid and metronidazole have comparable efficacy. Another study found similar reductions in inflammatory lesion counts among patients treated with metronidazole 1% once daily and those treated with azelaic acid gel 15% twice daily. Both treatment groups had similar and beneficial improvements in global severity scores.
**Sodium sulfacetamide/sulfur.** Due to lack of cosmetic elegance associated with many older formulations of sodium sulfacetamide/sulfur formulations, some patients may be reluctant to use the agent. Yet data support its efficacy in reducing erythema as well as papules and pustules. One study found a significantly greater percentage reduction in inflammatory lesions and a significantly greater percentage of subjects with improved erythema after 12 weeks of treatment with sodium sulfacetamide 10% and sulfur 5% cream with sunscreens compared to metronidazole 0.75%.7

**Other topical therapies.** Interest in the use of pimecrolimus (Elidel, Novartis) continues to increase, although data are limited. One small study documented a substantial improvement of erythema in 10 of 12 patients with ETR or PPR rosacea who applied pimecrolimus cream twice a day for 12 to 18 weeks.8 Five of six PPR patients had at least an 80 percent reduction in lesion counts. However, in a cohort of 40 patients randomized to apply pimecrolimus 1% or vehicle twice daily for four to eight weeks, there was no statistically significant difference in improvement of mean absolute values, mean percentage changes from baseline, or differences from baseline for scores of different clinical signs (erythema, papulation, scaling, and pustules) between the two groups.9 Nonetheless, many clinicians prescribe pimecrolimus for rosacea management, particularly among patients with concomitant seborrheic dermatitis and those who do not respond to standard topical therapies.

Topical tretinoin and other retinoids have been recommended for use in rosacea management, though there is concern about associated irritation. Whether topical retinoids confer benefits by improving associated signs of photodamage (such as coarseness, enlarged pores, and mottled pigmentation, including erythema) that are common in patients with rosacea or by reducing inflammation and other pathogenic elements of rosacea remains controversial. Some clinicians advocate topical tretinoin to manage phymatous rosacea, and it appears to provide greatest benefit in the condition’s early stages.

**Systemic Therapies.** Dermatologists are very familiar with the use of oral antibiotics to manage advanced, highly inflammatory, or refractory rosacea. Due to concerns about bacterial resistance, physicians and researchers continue to seek novel effective oral therapies. The most recent systemic agent to arrive on the market is anti-inflammatory dose doxycycline 40mg delayed released (Oracea, CollaGenex). Phase III study data confirm the efficacy of once-daily dosing of anti-inflammatory dose doxycycline over 16 weeks.10 In trials, treated patients had a mean change in lesion counts from baseline of -11.8 in one study and -9.5 in the other (versus -5.9 and -4.3, respectively, for controls). Of note, another analysis of data from phase III trials confirmed that higher doses of doxycycline (as measured in mg/kg) did not provide increased clinical efficacy compared to the 40mg dose, but they did lead to higher plasma concentrations.11 Such findings confirm that Oracea is able to confer anti-inflammatory effects without providing antimicrobial action.

The combined use of anti-inflammatory dose doxycycline along with standard topical therapies has garnered interest, with early data confirming efficacy.12 In a 16-week, placebo-controlled, double-blind study, patients in the treatment group received once-daily anti-inflammatory dose doxycycline plus once daily topical metronidazole gel 1%. Controls received oral placebo plus once daily topical metronidazole gel 1%. At week 12, both group discontinued topical therapy and maintained oral protocols. Combination therapy produced a significant reduction in lesion counts evident at week four through week 12 compared to monotherapy.

Also relatively new to the market, a once-daily extended-release formulation of minocycline (Solodyn, Medicis) approved for the treatment of acne vulgaris may be a convenient option for rosacea patients and is especially suited to patients who have complained of vestibular adverse effects.

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associated with standard minocycline formulations. An analysis of data from phase 2 and 3 trials concluded that concluded that ER-minocycline delivers consistent levels of drug at a 1mg/kg dose while reducing dose-dependent acute vestibular adverse effects.\textsuperscript{13}

**Incorporating Lights and Lasers**

As described, rosacea’s primary clinical components can be generally classified as inflammatory—papules, pustules—or vascular—blushing, erythema, telangiectases. Although topical and systemic therapies are effective at reducing the inflammatory component of the disease and, to some extent, background erythema, no medication effectively targets vasculature. Evidence shows that intense pulsed light and pulsed dye laser systems can effectively target diffuse erythema and visible blood vessels to diminish their appearance. Improvement is not simply cosmetic; One study found that pulsed dye laser treatment led to statistically significant improvements in overall quality of life as well as specific rosacea symptoms, including flushing, burning, itching, dryness, swelling, and skin sensitivity among treated patients.\textsuperscript{14}

Optical therapy does not replace pharmacologic interventions. In fact, the two work synergistically. Topical and/or systemic medical therapy is an important first step in the light-based approach to rosacea management. A treatment period of at least four weeks helps to calm inflammatory components of rosacea, allowing the physician who will administer laser therapy to more accurately assess remaining vascular targets. Many patients present for laser therapy precisely because they are dissatisfied with the results of current, ongoing therapy. However, in the event that a patient has not actively treated rosacea with pharmacologic interventions for the last month or so, prescribe an appropriate topical and/or systemic regimen (based on the specific presentation) to be used by that patient in the period prior to and following laser administration.

Patients need not discontinue topical or oral therapies in the time immediately before light or laser treatment. In fact, they should maintain these therapies throughout the course of laser/light treatment. Some post-op regimen modification may be necessary for patients with very sensitive skin who may not tolerate topical therapy in the days immediately following laser application.

Sunscreen application and sun avoidance are crucial elements of rosacea management but strict adherence is particularly important in the period immediately following laser therapy. Patients should faithfully re-apply sunscreen every few hours and practice careful sun avoidance for the first few days following laser therapy. Daily use of broad-spectrum sunscreens and standard sun avoidance protocols are sufficient in the long-term.

The following discussion will address the role and benefits of IPL and pulsed dye laser therapy for rosacea. It is worth noting that photodynamic therapy for rosacea shows promise according to reports in the literature\textsuperscript{15–17} although these have largely involved small treatment groups. The most recent case series involved 17 patients receiving methylaminolevulinate and red light (MAL-PDT) one to four times. Evaluation at one to two months post-procedure found good results in 10 of 17 patients and fair results in another four patients. PDT may yet prove effective for both the inflammatory and non-inflammatory elements of rosacea, and we await further study.

**Intense Pulsed Light (IPL).** IPL has proven effective for reducing redness and flushing and improving skin texture in rosacea patients.\textsuperscript{18} Quantifying reduction of facial vascular lesions specifically, one study demonstrated a mean clearance of 77.8 percent maintained for an average of 51.6 months among 60 patients receiving a mean of 4.1 IPL treatments.\textsuperscript{19} As a photorejuvenation intervention for patients with normal skin, IPL has been shown to provide microscopic changes in the dermis and epidermis and to produce clinical improvement in wrinkles, oiliness, thickness, dilated pores, and general appearance.\textsuperscript{20} These findings coupled with clinical experience have led to the use of IPL primarily for rosacea patients with background erythema and small telangiectases as well as for those concerned about the appearance of concomitant photodamage.

IPL therapy for rosacea is generally associated with minimal downtime, though most patients should expect to have some treatment-induced erythema for the remainder of the day. Patients with more extensive photodamage may have more prolonged mild erythema for the remainder of the day. Patients had presented with an active papulo-pustular component to their presentation.

Pulsed dye lasers. The pulsed dye laser has been shown to effectively target telangiectases and erythema,\textsuperscript{21,22} and may be preferable to IPL for vessels of somewhat larger diameter. Results of therapy may be long-lasting. In one trial involving 40 patients followed for six to 55.5 months, no patient required medical therapy during this period; 13 of these patients had presented with an active papulo-pustular component to their presentation.\textsuperscript{21}

Flare of rosacea symptoms is possible following pulsed dye laser therapy,\textsuperscript{21} which concomitant pharmacologic therapy may help to prevent or minimize. Compared to IPL, patients will have a more significant reaction to pulsed dye laser therapy with erythema that may persist for several days, as well as swelling. The degree of swelling is most notable when treating the upper cheek/peri-orbital area. Application of ice to the treatment site immediately following therapy and for 10-15 minutes every hour through the remainder of the day can help to minimize and resolve swelling. The sooner and more consistently patients apply ice after treatment, the greater the benefit. Provide disposable ice packs to patients as a physical reminder to encourage compliance. In rare cases, patients may have a robust sunburn-
like reaction following pulsed-dye treatment. Cool compresses and bland emollients may provide relief.

Despite notions to the contrary, clinical purpura is not necessary for clearance of many vessels, though patients are likely to improve more quickly if purpuric settings are used. Most patients tolerate purpura poorly and should be treated with longer pulse durations to reduce the risk of purpura. Appropriate treatment parameters will change depending on the patient and may vary within a session depending on the treatment sites. To determine the appropriate pulse duration to initiate therapy, physicians should choose test sites at least visible sites, such as the lateral cheek or chin. Choose the lowest pulse duration the patient can tolerate that does not induce purpura. A nearly purpuric fluence and pulse duration is an ideal compromise of efficacy and tolerability. Note that certain anatomic targets, such as periorbital skin or areas with large concentrations of vascular targets, are more susceptible to purpura than others.

A Dynamic Process
Regardless of the laser system selected, patients should anticipate requiring a total of about two to four total treatments provided four to six weeks apart for maximum effect. Patients must understand that treatment of rosacea with lights and lasers is a dynamic process; parameters and even laser systems may change from one treatment to the next. In some instances, for example, initial treatment with IPL may improve erythema and provide notable improvement of signs of photodamage, but the patient may require subsequent treatment with the pulsed dye laser to target residual vessels.

Patients should also anticipate future courses of re-treatment. It may be helpful to equate the vasculature with a tree, noting that laser therapy is "pruning the branches," but that re-growth is anticipated. Some patients will require treatment in as few as three months, while others can go several months or even years before requiring re-treatment.

Finally, dermatologists must avoid the most common pitfall of light therapy for rosacea: applying the same treatment parameters to all patients. It is neither appropriate nor effective to establish one or a few treatment parameters for use in all rosacea patients. Rather, parameters must be fully adjustable and determined for each patient and treatment site. Comfort grows with experience, and it is important to recognize that there is often only a fine line between efficacy and inducing pain/purpura. Establish appropriate parameters by considering the:

1. Patient’s skin type
2. Amount of vascular target
3. Anticipated/patient-acceptable downtime.

In some instances (consider perhaps an older gentleman who “just wants it over with”), a more aggressive treatment with attendant significant downtime may be acceptable. However, each patient must clearly understand the degree of anticipated downtime before therapy commences.

An Evolving Approach
Accumulating data coupled with clinical experience suggest that for a wide array of patients, achieving the best results in rosacea management requires the union of pharmacologic therapy and light-based interventions. Patients equipped with proper expectations—those who understand what to expect from light-based interventions, understand the need for multiple treatments and maintenance courses, and recognize that technology does not replace medications—are typically pleased with the results of properly-administered therapy.

References