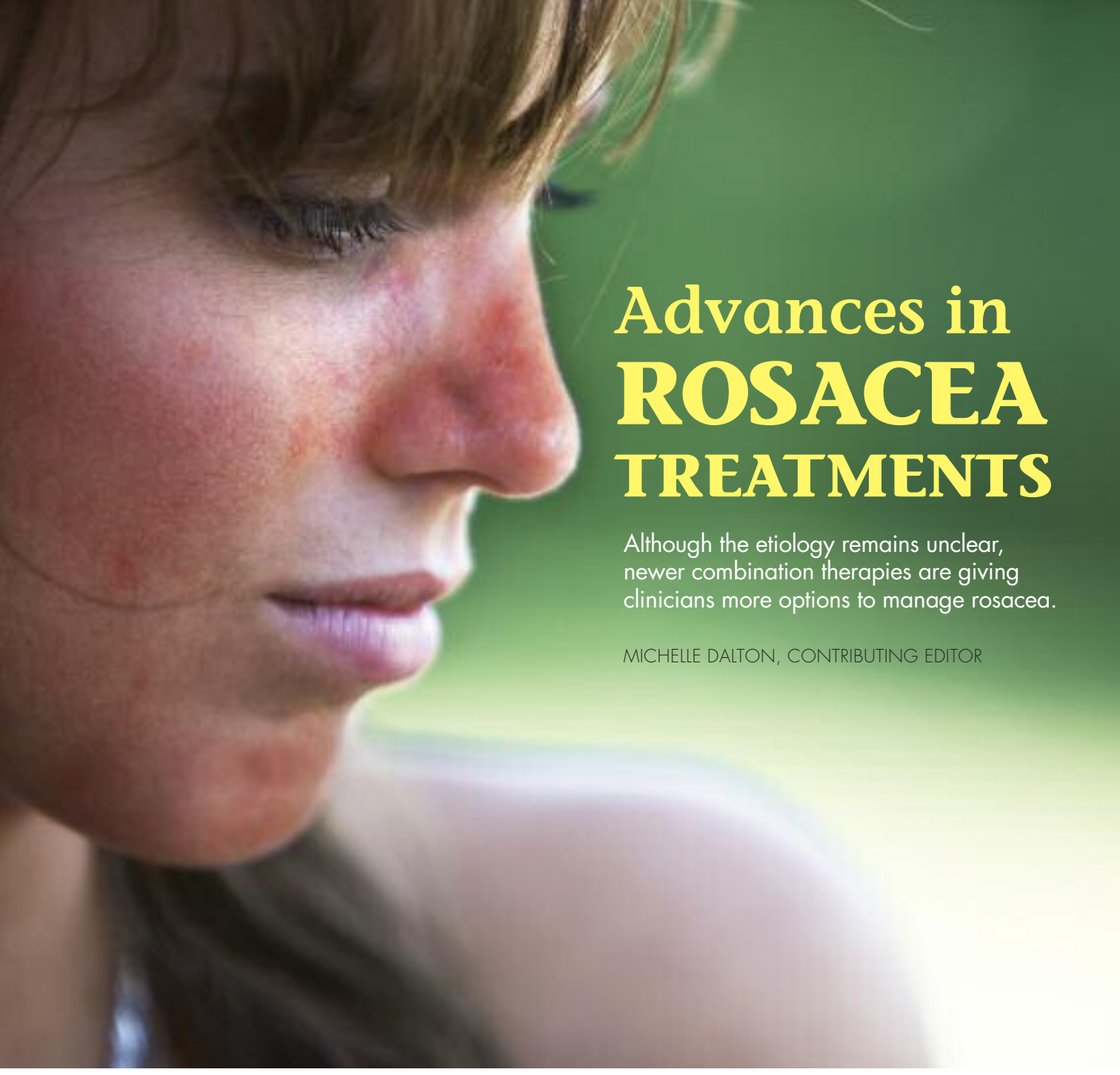

Advances in ROSACEA TREATMENTS

Although the etiology remains unclear, newer combination therapies are giving clinicians more options to manage rosacea.

MICHELLE DALTON, CONTRIBUTING EDITOR

As any physician knows, it is much easier to treat a disease when the underlying pathophysiology is completely understood; with an unknown etiology, several theories on treatment strategies and preferred courses of action are likely. So it goes for rosacea; dermatologists agree that genetics and vascular instability play a significant role, but researchers are still investigating inflammatory and neurovascular mechanisms. Overexposure to the sun, emotional stress and environmental factors — such as repeated exposure to wind, smoking, alcohol, and very hot/cold temperatures — can exacerbate the disease.

Determining the best course of treatment for the patient depends on several factors, but "first you have to differentiate between the different types," says Arielle N.B. Kauvar, MD, clinical professor of dermatology at the NYU School of Medicine in New York.

The National Rosacea Society classifies rosacea according to one of four subtypes: erythematotelangiectatic rosacea, papulopustular, phymatous, and ocular. Rhinophyma may occur as a single, isolated entity, but may be considered a different disease process altogether.

However, Joseph Bikowski, MD, believes up to a third of patients who are diagnosed with rosacea probably don't have true rosacea. Dr. Bikowski, who is in private practice at Bikowski Skin Care Center in Sewickley, PA, says "I think there's a good amount that is actually *Demodex* dermatitis." Additionally, he believes rosacea does not actually have four subtypes, "because one will not progress to the other, so how could they be the same disease?" The question that arises, he says, is what caused them

in the first place. "In my opinion, the only true rosacea is papulopustular rosacea. Red bumps, pus bumps, erythema of the face, telangiectactic, dilated vessels of the face, flushing and blushing. That's rosacea."

During this year's American Academy of Dermatology (AAD), Lisa E. Maier, MD, assistant professor at University of Michigan in Ann Arbor, highlighted some of the recent papers published on the ultraviolet (UV) link to rosacea. She says patients with rosacea tend to be on the lower end of the Fitzpatrick scale, areas not exposed to sunlight are not typically affected, and solar elastosis can be seen in affected skin biopsies. James Q. Del Rosso, DO, dermatology residency director at Valley Hospital Medical Center, in Las Vegas, NV, agrees, noting that UV exposure and rosacea have some shared clinical features, including persistent erythema and telangiectasia; likewise, there are several pathophysiologic features correlated with rosacea. Other areas of research interest include mast cell stabilizers and anti-vascular endothelial growth factor agents.

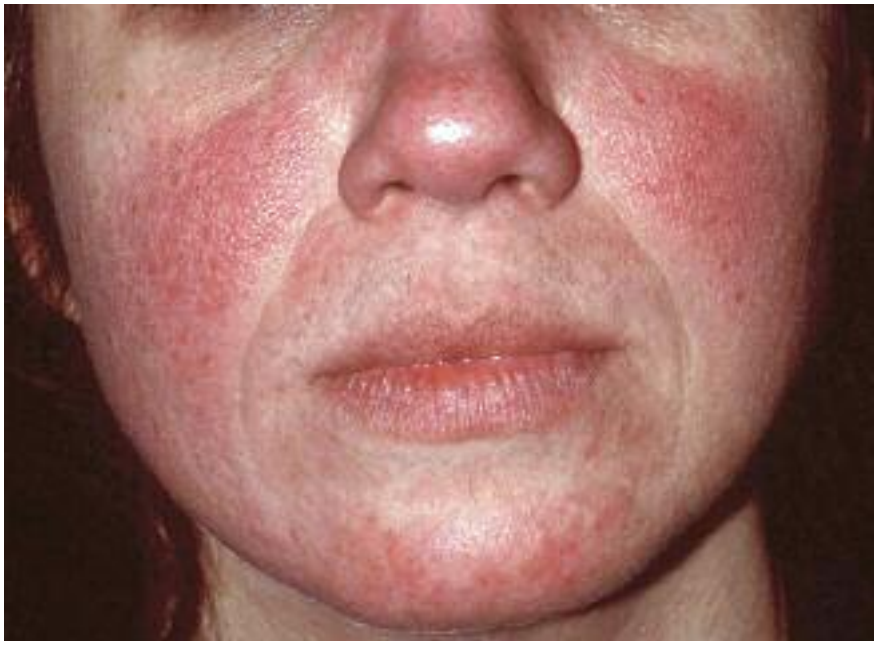

Figure 1. Facial redness (erythematotelangiectatic rosacea) is typified by flushing and persistent redness. Visible blood vessels may also appear. Photo courtesy of the National Rosacea Society.

CURRENT TREATMENT APPROACHES

Systemic antibiotic use is declining, while topical agent use is increasing, and combining topical antibiotics with anti-inflammatory agents is gaining acceptance as well. Targeting anti-inflammatory mediators, such as toll-like receptor 2, may prove useful, as their expression seems to be associated more with rosacea than other skin disorders. According to Dr. Bikowski, some research has indicated low-dose aspirin (81 mg) once daily may decrease the flush and blush aspects by inhibiting Substance P.

"It's possible people are presenting with two diseases — say, rosacea and seborrheic dermatitis. If the patient has been on systemic and topical [therapies] for the rosacea, but is still affected, it's likely the underlying disease is not rosacea at all," Dr. Bikowski says. "The redness of true rosacea is very difficult to treat, although medication will help the red bumps and pus bumps."

"Many rosacea patients also have seborrheic dermatitis," maintains Julian Mackay-Wiggan, MD, MS, assistant clinical professor at Columbia University in New York. "If so, the seborrheic dermatitis must be separately addressed and the patient must be counseled about the differences in the two disorders."

First-line therapy for those with severe papulopustular rosacea is a short course of an oral antibiotic like docycycline, Dr. Kauvar says. Some patients may also require maintenance therapy with low-dose oral antibiotics, such as doxycyline (Oracea), which is also prescribed because of its anti-inflammatory properties. She additionally advocates laser treatment. "From my perspective, all rosacea types can benefit from adjunctive treatment with laser. Topical and oral medications will control inflammatory lesions, but they won't treat the telangiectasia and erythema. For most people with mild rosacea, that's the main problem." She says "a much higher percentage" of patients have rosacea limited to erythema and telangiectasia than those who also have a papular/pustular component, and for them, "the vascular component doesn't go away with topical or oral medications."

Dr. Mackay-Wiggan calls topicals such as metronidazole, clindamycin and erythromycin "the mainstay of treatment for many patients in my office," and notes that some patients may benefit from combination therapy with azelaic acid gel 15% (Finacea). "Patients with moderate to severe rosacea with inflammatory papules often benefit from a short (3- to 4-week) course of oral antibiotics and some require long-term low-dose oral antibiotics for ongoing control. Naturally, the treatment regimen must be tailored to the clinical severity and variant of disease as well as the patient's preferences regarding treatment."

Dr. Bikowski says most patients with classic presentations will "respond well to systemic therapy," and he typically begins patients on a regimen of Oracea 40

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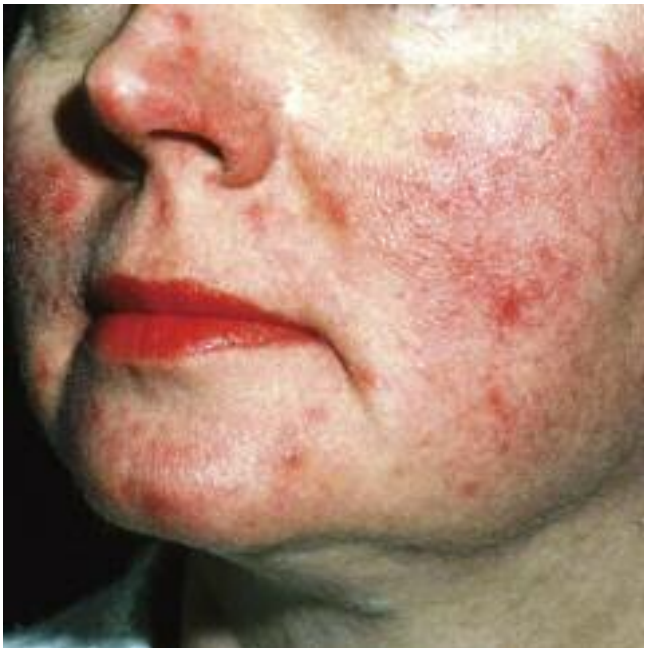

Figure 2. Bumps and pimples (papulopustular rosacea) is often seen following or with subtype 1, and includes persistent facial redness with the addition of bumps or pimples. Photo courtesy of the National Rosacea Society.

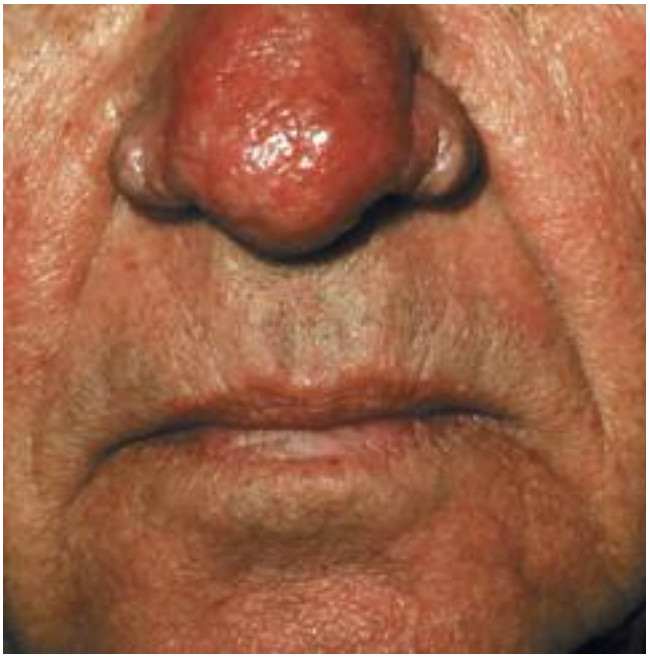

Figure 3. Phymatous rosacea involves skin thickening and enlargement, usually around the nasal area. Photo courtesy of the National Rosacea Society.

mg daily because "there's no antibiotic effect, it's an anti-inflammatory that's been thoroughly evaluated in the literature." In his practice — which is solely medical dermatology — Dr. Bikowski will use topical treatments, but believes there should be adjunctive therapies. When he does prescribe metronidazole gel 1% (Metrogel), Dr. Bikowski avoids the generic formulation "because the vehicles in which they come have not been worked out very well."

Dr. Kauvar considers lasers to be "the most fundamental treatment for the vascular component of rosacea."

"We don't understand a lot about the pathophysiology [of rosacea]. There are many different theories about what contributes to rosacea, but there's really no consensus," she says. "What we do know — and is very clear cut — is that if we treat with laser, even with severe papules and pustules, the vascular component improves and the acneiform component goes into remission as well."

Without eliminating the vascular component, she says, dermatologists will be hard-pressed to eliminate the other aspects. "With laser therapy, however, even granulomous rosacea unresponsive to oral antibiotics, will improve with one or two laser treatments."

Naturally, the treatment regimen must be tailored to the clinical severity and variant of disease as well as the patient's preferences regarding treatment.

~Julian Mackay-Wiggan, MD

She treats patients with erythematotelangiectatic rosacea and papulopustular rosacea with a pulsed dye laser, such as the Vbeam from Candela, a KTP laser, such as the Gemini from Iridex, or with intense-pulsed light therapy (IPL). Depending on the severity, two to five monthly treatment sessions are usually required, she says. In her opinion, the pulsed dye laser and KTP lasers "will dramatically reduce severe flushing/blushing symptoms, which usually do not respond to other interventions."

If there are numerous sebaceous hyperplasia or an early phymatous component, Dr. Kauvar will use combination therapy. She will combine pulsed dye Vbeam laser treatment with 1450 nm diode laser treatment with the Smoothbeam from Candela, or use the Gemini 532 nm KTP with the 1064 nm Nd:YAG. The vascular lasers improve the erythema and telangiectasia, and the infrared lasers improve the appearance of large pores, sebaceous hyperplasia and early phymatous change by heating the dermis and remodeling the collagen.

Ongoing research includes the use of brimonidine to treat background erythema, Dr. Bikowski says, although the drug is still in very early stages of development. (Brimonidine is currently approved for the treatment of open-angle glaucoma or ocular hypertension and marketed under the brand name Alphagan.)

Other current clinical studies include investigation of tretinoin gel 0.05% (Atralin); apremilast; a topical minocycline foam (Foamix); combination therapy with calcium dobesilate and pulsed dye laser treatment; and clindamycin phosphate 1.2%/tretinoin 0.025% gel (Ziana).

DEALING WITH CHRONICITY

The National Rosacea Society found more than 76% of patients with rosacea said the condition lowered self-esteem and self-confidence, and 41% reported that they avoided public contact or canceled social outings as a result of a recurrence.

"Patients need to be counseled that rosacea is a chronic disease and that the goal of treatment is control versus cure," Dr. Mackay-Wiggan says. "In addition, patients are advised that occasional flares may occur and, if necessary, therapy can be tailored to treat flares when they occur."

"The number one thing a patient with rosacea who walks into my office gets is instructions in skin care," Dr. Bikowski says. He recommends ceramide-based products and instructs patients to use cleansers and moisturizers twice daily, as well as "any SPF that's 15 or higher."

Because "almost all" rosacea patients have sensitive skin, Dr. Mackay-Wiggan recommends avoiding "irritating skin care products. Sun protection and sunscreens are also a mainstay of treatment and maintenance," she says.

Dr. Kauvar stresses to patients that although laser and other therapies will induce a remission, "we can't prevent a recurrence. If someone has had success with three to four laser treatments initially, they may only need to come back once or twice a year to keep the outbreaks under control." If laser therapy appears to be working, Dr. Kauvar says she will wean the patient off oral antibiotics and off topicals as well, if possible.

"What we do know — and is very clear cut — is that if we treat with laser, even with severe papules and pustules, the vascular component improves and the acneiform component goes into remission as well."

~Arielle N.B. Kauvar, MD

"It's common to keep them on topical therapy, but once laser treatment has induced a remission, we can wean them off oral antibiotics," she explains.

If patients have an acne overlap, "low-dose isotretinoin or topical retinoids may be of benefit in selected patients with those clinical features," Dr. Mackay-Wiggan says.

Some cosmeceuticals are also showing promise in the treatment of rosacea, according to Diane S. Berson, MD, FAAD, assistant clinical professor of dermatology at Weill Medical College of Cornell University, in a news release from the AAD.

"When the skin is stripped of lipids, which are part of its protective outer layer, the skin barrier is compromised and can worsen acne and rosacea," she said in the release. "By keeping the skin well hydrated with the proper skin care products, the barrier will stay intact, allowing patients to better tolerate their medications." Moisturizers should include lipids (such as ceramides), which are usually well-tolerated "and improve the barrier that is often compromised in patients with this condition." ■

Disclosures: Dr. Bikowski consults for Coria, Galderma and Intendis. Dr. Kauvar has served as an investigator for Candela, and is on the advisory board for Iridex. Dr. Mackay-Wiggan is a clinical investigator in a study supported by Celgene.

Rosacea Smart Phone App Launched

According to the National Rosacea Society, upwards of 16 million people in the United States are affected by rosacea. During this year's American Academy of Dermatology meeting, Intendis announced that it has developed the first free smart phone application for people with rosacea. The app will be available on the iPhone, Blackberry and Android platforms, according to the company. It "can help a rosacea patient gain a better understanding of their disease, track their own specific symptoms, identify potential triggers and create a personal rosacea trigger tracker that may be used as part of a dialogue with one's healthcare provider," explains William Griffing, president and chief executive officer of Intendis.

The app includes a trigger tracker, a weather tracker — complete with live satellite to provide temperature, humidity, etc., to help patients predict weather-related outbreaks — and a treatment plan. A question-and-answer section for people who do not yet have a confirmed diagnosis should help foster a better understanding of the disease, according to the company, and allow them to track some triggers so they can discuss those with their dermatologists. Users can fill out a questionnaire on the app that may help facilitate a conversation with their doctors about their condition. The app also offers a substitution finder, so, for example, if a patient realizes a certain spice triggers rosacea, the substitution finder will offer an idea for an alternative spice that may not cause the patient to react. The app will also include news updates from the National Rosacea Society, which has designated April as Rosacea Awareness Month. The Rosacea App also offers users a coupon for azelaic acid gel 15% (Finacea) that can be used at the pharmacy directly from their smart phone, and the ability to register for special offers as well as for a monthly newsletter.