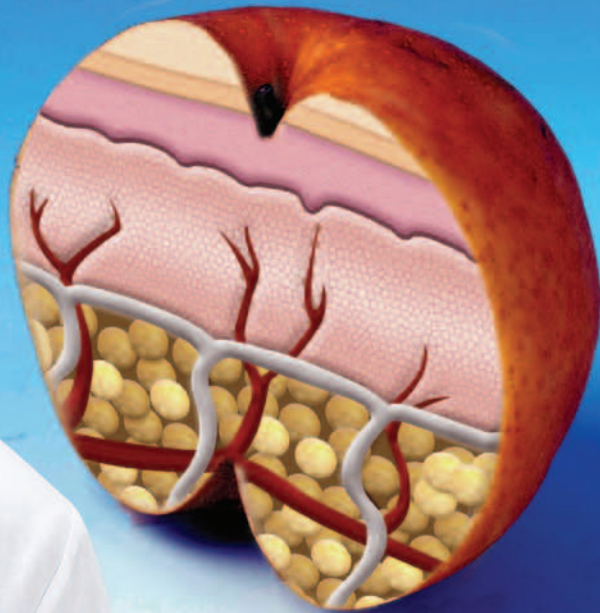


Getting to the Core of Erythema



By Paul Winnington
Editor-in-Chief

Vascular specialists call for a shift in management of moderate to severe rosacea to target the vessels at the heart of the disorder.

Knowledge about the pathogenesis of rosacea remains somewhat hazy despite the prevalence of the disorder—it affects an estimated 14 million Americans. Although dermatologists know that vasodilation, inflammation, cumulative effects of ongoing cutaneous insult, senile skin changes, and perhaps even infective organisms can play a role in development of clinical rosacea, there is much to learn about the etiology of the disease and optimal therapeutic targets.

Largely due to these unknown factors, for years dermatologists lacked reliably effective interventions for rosacea. The pharmacologic landscape has much improved in recent years with several effective topical and oral agents now available to minimize the inflammatory papules and pustules of rosacea and provide a suitable degree of clearance and control to a significant proportion of patients. Nonetheless, some patients continue to grapple with persistent erythema and flushing, even after multiple trials of various therapies. For these individuals, the flushing of rosacea progresses, leading to dramatic cutaneous changes and, in some cases, ocular damage. Targeting the blood vessels that mediate the flushing response (that contributes to subsequent skin changes) may represent an effective method of breaking the cycle of such advanced disease. Growing use of lasers to treat rosacea could point a new direction in treatment. But a proposed laser regimen for rosacea differs markedly from the current laser approach with which most dermatologists are familiar.

Rethinking Rosacea

Rosacea is best conceptualized as a vascular disease, according to Geoffrey Nase, PhD, a rosacea specialist with a Medical Doctorate in Neuro-Vascular Physiology. Dr. Nase works for the Rosacea Treatment Institute of Texas in San Antonio with Medical Director and Laser Treatment Specialist, David H. Nielson, MD.

While dermatologists may think of papules, pustules, and telangiectases as common indicators of rosacea, Drs. Nielson and Nase suggest that these are only secondary signs of the disease; an exaggerated flushing response is really the hallmark of rosacea and precursor to these subsequent cutaneous manifes-

tations. An exaggerated flushing response is often evident in genetically pre-disposed individuals at a very young age—many in pre-adolescence—Dr. Nase says. In some patients, the flushing response remains relatively stable and does not progress into “clinical rosacea.” In others, flushing may progress in intensity and/or duration, leading to vascular hyper-reactivity, structural damage, angiogenesis, and a state of chronic dermal inflammation. Coupled with additional cutaneous insult over time, this environment yields the classic clinical symptoms of rosacea. Dr. Nielson has observed over the past 10 years that severe neural flushing (e.g. blushing) and facial hyperpyrexia (heat and burning sensations) can be present episodically throughout any given day in some rosacea sufferers, which can exacerbate symptoms. There is thought to be a genetic predisposition from a hyperactive sympathetic nervous system that is triggered by emotions (anticipation, anxiety, etc). Of course, untreated or under-treated rosacea may ultimately lead to ocular rosacea with eyelid dysfunction, ocular surface inflammation, blurred vision, loss of vision, and corneal melting.

Beyond the familiar cutaneous symptoms of rosacea—telangiectases, papules, pustules, edema, persistent erythema—some individuals with advanced disease develop rather significant symptoms that many dermatologists may not typically consider. These include neuropathic-type pain and burning that is comparable to a second-degree sunburn or diabetic neuropathy. Though his rosacea is now in full remission, Dr. Nase suffered with the disease himself and recalls the painful burning sensations he experienced for nearly six years. The pain can be so debilitating that patients qualify for medical disability, as is the case for several patients entering treatment at the Rosacea Treatment Institute of Texas. As many dermatologists are aware, this chronic disease can be associated with significant patient distress: “Rosacea can be a constant drain physically and emotionally, and as with any chronic disorder many rosacea sufferers experience clinical depression.” Given the potential impact of the disease, the demand for efficient interventions is obvious, yet the majority of available treatments do not target the root causes of

At the Source of Flushing

Tracing rosacea to its source, Dr. Nase says, leads to the anterior hypothalamus, which modulates hormones and dilator nerves that signal the “fight or flight response.” In simple terms, the anterior hypothalamus is responsible for regulating body temperature, ultimately to protect brain cells from overheating and subsequent death. Neural flushing is one of the primary methods of releasing excess heat, in addition to sweating. In predisposed individuals the anterior hypothalamus essentially is overactive, signaling for flushing when not physiologically necessary. It also helps regulate the release of potent dilators such as cortisol, and if the threshold is offset, it may throw off the circadian rhythm which results in higher internal body temperature and reactive flushing episodes. Therapeutic targeting of the anterior hypothalamus is not practical at this time, although genetic bioengineering and biological response modifiers offer true hope for an outright cure down the road.

rosacea. This led to the collaboration between Dr. Nielson and Dr. Nase and the subsequent formation of the Rosacea Treatment Institute of Texas. Dr. Nielson specializes in treating blushing disorders of the face and several other sympathetically mediated symptoms of the upper chest/face/scalp/hands. Through the collaborative efforts of Dr. Nielson, Dr. Nase, and medical laser physics specialist Patrick Clark, CMLSO, Dr. Nielson has developed a specialized Rosacea Multipass treatment protocol for moderate- to severe-rosacea sufferers and even laser-resistant patients who have been treated unsuccessfully 20 to 35 times.

A Bottom-Up Approach

As a disease of the vasculature, rosacea really begins in the vascular bed of the upper-, mid-, and deep-dermis, contends Dr. Nase, with recent clinical articles showing rosacea pathology all the way down to the adipose cells. Until the advent and subsequent refinement of cutaneous lasers, however, physicians had few options to target the source of the disease. Instead, they emphasized therapies to minimize inflammation and reduce the number of papules and pustules along with avoidance measures aimed to minimize flares. Outcomes of these interventions have varied among patients. Some patients attained suitable clearance and control of rosacea and were satisfied. In many instances, though, patients achieved good clearance of “the bumps” and “pimples” of rosacea but had to rely on camouflage techniques to reduce persistent redness. Avoidance of triggers, while intu-

itively reasonable, simply is not practical, Dr. Nielson and Dr. Nase emphasize, arguing that avoiding many triggers would translate to a significant detrimental impact on quality of life because increased blood flow is the primary trigger for this disorder. For example, the ambient “heat” sufficient to instigate flushing in many rosacea patients is 70 to 72 degrees Fahrenheit—within range of “normal” room temperature for many homes and businesses. For this reason, they believe that any rosacea management plan based on trigger avoidance is simply unacceptable.

By rough estimate, Dr. Nielson and Dr. Nase approximate that about 40 percent of rosacea patients have what is classified as mild rosacea. Another 40 percent have advanced to the moderate stages of the disorder, and the remaining 20 percent have severe rosacea that is debilitating and affects almost every aspect of the patient’s life. Patients with mild rosacea are most likely to achieve satisfactory results from current pharmacologic interventions, including topical antimicrobials and oral antibiotics, they say. Doxycycline monohydrate 40mg (Oracea, CollaGenex), Noritate (Dermik), Metrogel (Galderma), and oral macrolides (Biaxin XL and Azithromycin) have shown benefit as anti-inflammatory agents to help calm the signs and symptoms of rosacea and may improve the quality of life for many patients.

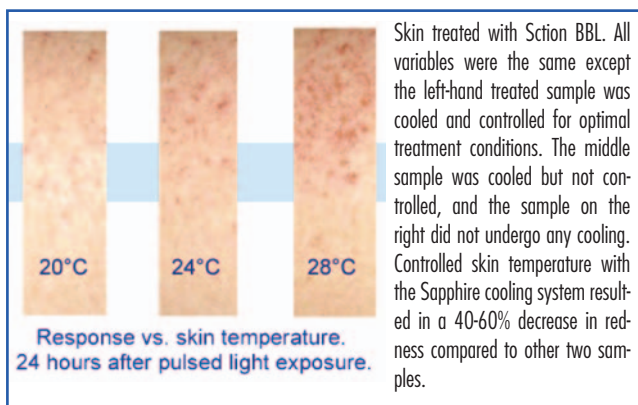
The emergence of effective laser technology may allow dermatologists and other physicians to rethink the treatment of rosacea, particularly for patients with moderate to severe disease. Unlike previous therapies that target the symptoms of the disease without striking the cause, proper administration of laser and light technology targets the vascular components at the heart of rosacea. Dr. Nielson and Dr. Nase agree that treatment of blood vessels is “the single best treatment for Rosacea.”

The Role of Lasers and Light

Mild Rosacea. When they think of laser or light technology for the treatment of rosacea, many dermatologists immediately call to mind IPL or pulsed dye lasers, such as Candela’s 595nm V-beam laser, which Dr. Nase says can effectively reduce superficial erythema and remove visible vessels in patients with mild to moderate disease. “You can achieve good results with these machines, but they can only treat the first and second layer of blood vessels in the face and cannot treat the third and fourth vascular layers that are key to reduction of rosacea symptoms, facial flushing and rosacea triggers. He also suggests that treatments are spaced too far apart, resulting in a sub-optimal treatment regimen.

Dr. Nielson has found that using a multilaser device (Sciton Profile) that uses active contact cooling sapphire crystals and laser energy with a square wave-form so that all laser energy is delivered in the therapeutic range allows him

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to perform treatments in more rapid succession without blistering, edema, severe redness or other damage to the skin. Using the specialized Rosacea Multipass technique, the chance of fully treating culprit vessels is enhanced, where waiting times of three to five weeks between single pass treatments is condensed into typically three passes per treatment session. Dr. Nielsen also incorporates natural angiogenesis inhibitors and natural anti-inflammatory agents, such as a special bioavailable preparation of Zinc, for a multi-faceted approach to treat this inflammatory disorder. One other key to treatment, they say, is the use of Dr. Nielsen's post-laser proprietary gel that contains a potent constrictor to enhance photocoagulation and blunt any inflammatory skin reaction that may be evoked by laser treatment. The gel also contains skin cooling agents, healing agents, anti-edematous agents, and repair enzymes.

Treatment failure or discontinuation of response to therapy should be a sign that the patient requires a different, more comprehensive laser strategy and not a sign to stop treatment. Discontinuing therapy "is absolutely the worst thing to do," Drs. Nielsen and Nase state, because it simply leaves the vessels "aggravated" and only partially treated by the energy—not destroyed. "No one gets worse after you stop laser therapy unless you've only aggravated blood vessels," they emphasize. "You've aggravated the beast!" Frequently, non-response or discontinuation of response indicates the need for an increase in fluence or pulse duration. "We've had too many doctors stop therapy when they should have said, 'Ah-ha, we need something more aggressive,'" they say. Physicians must match the pulse duration to the size of the blood vessels being targeted—the single most overlooked and important treatment parameter, they note.

Moderate to Severe Rosacea. One more aggressive approach involving light/laser technology is the Rosacea Multipass technique devised by Dr. Nielsen and currently used only at the Rosacea Treatment Institute of Texas. It targets ves-

sels in the deepest parts of the dermis and emphasizes anti-inflammatory methods through the use of three different energy sources and a total of three to four passes per treatment session. "With the right lasers it is possible to treat superficial redness and edema and also treat rosacea flushing and eliminate many rosacea triggers," Dr. Nielsen says.

The Rosacea Multipass technique begins with an IPL system (Sciton BBL, 560, 590 and/or 645nm) that targets the upper levels of the dermis. The squared-off pulse optimizes energy delivery. Novel use of the 420nm filter has shown promise in reducing treatment edema allowing full Rosacea Multipass sessions to be given every other day. A next-generation sapphire cooling system helps provide epidermal cooling to superficial and deep targets, protects each layer of the skin before, during and after each laser pulse, actively removes heat from the skin, controls skin temperature within one degree Celsius, and eliminates treatment-associated pain, they say. Most patients do not require anesthetics with this technology. Lasers and IPL work much better when the skin temperature is "precisely controlled."

Physicians also need to understand that continuous monitoring of vascular reactions to laser and real-time changes are also key to excellent results. During light application, settings are continuously readjusted to optimize safety and efficacy of treatment depending on patient's response to treatment.

Next comes treatment with the 1064nm Nd:YAG laser, which Dr. Nielsen notes has been dubbed "the blood vessel eraser." The protocol calls for a relatively high fluence and special hand piece sizes that target deeper culprit vessels. The system incorporates LAPG computer scanning to speed up treatment for certain areas of the skin. Nd:YAG is the cornerstone of treatment at the Rosacea Institute.

Finally, patients undergo exposure to a blue light laser source that targets the neutrophils and phagocytes that produce free-radicals and result in local inflammation. Decreasing neutrophils decreases post-procedural inflammation and irritation and may also contribute to a calming of the underlying disease process. Also, the neck of the sebaceous glands is affected by blue light (420nm wavelength), which decreases the size of the infundibular canal and improves papules and pustules. Dr. Nielsen has been so impressed with the decrease in treatment edema by the Blue light, that he has incorporated it into his Rosacea Multipass treatment protocol.

Each treatment session involves application of each of the three energy sources. Treatments are generally given as a series of six sessions over two weeks. For example, a patient may present for treatment on Monday, Wednesday, and Friday each week for two weeks. This would not be possible without active skin contact cooling using Sapphire crystals, Dr. Nielsen

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explains. Patients with less severe disease may require fewer than six total treatments. Alternative application schedules may include two long weekends (Thursday, Saturday, Monday treatment) or another variation that may favor a business professional, for example. Patients experience transient photocoagulation marks but do not experience the dreaded purpura and edema that older systems often evoke.


Ultimate reduction of dermal vessels by 50 to 60 percent is the goal of treatment in order to provide remission of rosacea without additional medical therapy. And, says Dr. Nase, the goal is attainable—he has been in remission for seven years. Though a reduction of vessels by more than half may sound extreme, he says, “You can do this safely because rosacea patients have significantly increased vasculature compared to normal skin, about 100-250 percent greater than control subjects.”

General Principles. Whatever laser technology the physician employs to treat rosacea, he or she should not rely on laser presets, Dr. Nielson and Dr. Nase emphasize. It is important to assess the individual patient and the response to laser application and to tailor treatment parameters accordingly, including during the actual treatment session, Dr. Nielson says. Dr. Nielson and Dr. Nase have formulated a “pre-flush” technique, using topical and/or systemic vasodilators and thermoregulatory heating devices to enhance the laser targets. They also institute oral treatment with a purified extract of Chinese Sea Cucumber extract following laser treatment for four to eight weeks. This agent helps to block angiogenesis by up to 90 percent, countering the body’s natural repair and revascularization processes in response to treatment, they say.

Medical Necessity. Emphasizing the potentially significant impact of rosacea on a patient, Dr. Nase notes that many insurers have agreed to cover laser therapy as a medical necessity (70 to 100 percent reimbursement), particularly for patients with significant inflammation, flushing, or neuropathic burning and pain.

Apart from the Crowd

Perhaps the greatest difficulty in managing rosacea with lasers is standing apart from those who would dabble. “The problem is that everybody has a laser,” Dr. Nase warns. Even dentists and podiatrists in his area have claimed they can treat rosacea with lasers—they often purchase used lasers off of e-Bay. Dermatologists who use IPL or pulsed-dye laser to treat the erythema of rosacea can quickly distinguish themselves by providing effective and efficient treatments. Best results may come from individualized treatments (for energy selectivity and depth) and proper treatment schedules (sessions more closely spaced). “Some people rent a laser one time a month, and that just won’t work on most rosacea cases,” Dr. Nase contends.

When patients fail to respond or hit a plateau, a more aggressive laser intervention may be indicated. “The real secret is getting to all the vascular layers that show pathology, because it’s like an iceberg,” noting that the bulk of the vasculature contributing to rosacea lies deep in the dermis. “Collaboration is key,” Dr. Nielson and Dr. Nase suggest, urging dermatologists to consider referring patients with moderate to severe rosacea to a vascular specialist who may be able to help target the source of the disease by offering a multi-faceted treatment approach that focuses on the many aspects of rosacea. 

Taking a Toll

Dermatologists know that rosacea can have significant negative physical as well as psychological and emotional effects on patients. A recent survey by the National Rosacea Society (rosacea.org) explored the impact of rosacea on patients and their responses to the disease. The survey involved 603 rosacea patients, 76 percent of whom reported that rosacea’s effect on their appearance had lowered their self-confidence and self-esteem.

Not surprisingly, the impact may be greatest among those with more severe disease. Among individuals with severe disease, 94 percent said rosacea had damaged their self-confidence, and 77 percent said it had negatively affected their outlook on life. Nearly half of all respondents said that rosacea had diminished their outlook on life. Sixty-five percent of all respondents reported frustration with rosacea. While 35 percent of rosacea patients report having felt helpless, 25 percent said they suffered depression. Anxiety affected 41 percent of respondents, and 18 percent said they had felt isolated.

One encouraging finding from the study: 80 percent of respondents said the results of medical therapy have improved their emotional well-being.