



The Role of Skin Care and Maintaining Proper Barrier Function in the Management of Rosacea

James Q. Del Rosso, DO

Rosacea is a chronic dermatologic condition characterized by central facial erythema, flushing, and, in many cases, inflammatory lesions. An inherent component of rosacea is sensitive skin, with patients commonly reporting symptoms such as burning, stinging, and pruritus. Although many medical therapies and physical modalities are available for the treatment of rosacea, an important component of effective rosacea management is skin care. This article discusses the importance of proper skin care selection as an integral component of successful treatment for rosacea.

Patients with rosacea generally present with central facial signs and symptoms, such as erythema, papules, pustules, and blushing or flushing.¹ Transient blushing or flushing may progress to more persistent facial erythema.¹ Erythema and inflammatory lesions cycle chronically through phases of exacerbation and remission. Another hallmark of rosacea is sensitive skin, with patients commonly reporting symptoms such as burning, stinging, and itching.²

Pathogenic Factors in Rosacea

Although the pathogenic mechanisms of rosacea are not fully understood, theories regarding the pathophysiology of rosacea implicate 3 components: vascular, inflammatory, and microbial. Chronic vasodilation may be triggered by photodamage. UV light exposure

can initiate processes that produce harmful reactive oxygen species (ROS) and upregulation of matrix metalloproteinase (MMP) enzymes, which increase degradation of the dermal matrix.³⁻⁶ These, in turn, can weaken vasculature,³⁻⁶ permitting the escape of inflammatory mediators into surrounding tissues, which results in damage of perivascular collagen and elastic tissue.^{1,5} Inflammatory mediators, such as nitric oxide, histamine, and prostaglandins, appear to be associated with the vasodilation often seen in rosacea.^{1,6}

The possible role of microbes in the pathophysiology of rosacea is controversial. Microorganisms can provoke immune-mediated inflammatory reactions common to rosacea. Selected patients with rosacea tend to have greater numbers of *Demodex* mites than those without rosacea.⁷ *Demodex* mites may then stimulate production of inflammation.

One theory suggests that *Demodex* mites contain commensal bacteria, which may be spread as the mites migrate across the face and which may also serve to promote inflammation.⁷ Evidence for this theory is seen in findings from a recent study in which investigators found that *Bacillus oleronius*, a bacterium associated with *Demodex* mites, stimulated an immune system response in more patients with erythematotelangiectatic, or subtype 1, rosacea than in controls.⁸ Further study is needed to confirm whether there is a true link between *B oleronius* and development of rosacea.

Disruption of the integrity and function of the epidermal stratum corneum, coupled with various triggering events, appears to contribute to the disorder and leads to the signs and symptoms of rosacea.^{1,2,9,10} The impaired skin barrier allows heightened transepidermal water loss (TEWL), which may account at least partially for stinging, burning, pruritus, dryness, and scaling.^{10,11} Skin barrier disruption may also permit increased penetration of external irritants, which can contribute to exacerbation of the signs and symptoms of rosacea.¹²

Dr. Del Rosso is Clinical Associate Professor, Dermatology, University of Nevada School of Medicine, Las Vegas, Clinical Associate Professor, Dermatology, Touro University College of Osteopathic Medicine, Las Vegas, and Dermatology Residency Director, Valley Hospital Medical Center, Las Vegas.

Dr. Del Rosso is a consultant, researcher, and speaker for Intendis, Galderma S.A., and OrthoNeutrogena, a consultant for Doak Dermatologics, Medicis Pharmaceutical Corporation, and Stiefel Laboratories, Inc, and a speaker for Unilever.

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An appropriate skin care regimen, concomitant with pharmacologic and physical treatment strategies, is essential in the management of rosacea. A properly selected skin care regimen can aid in both repairing the disrupted epidermal barrier and maintaining its integrity. The avoidance of harsh cleansers, which can damage the epidermal barrier and promote TEWL, and the judicious use of moisturizers help maintain stratum corneum integrity. The use of photoprotectants (ie, sunblocks) also reduces photodamage, which is implicated as a potential pathogenic factor in rosacea. The following presents an overview of various pharmacologic strategies and the role of proper skin care in the optimal management of rosacea.

Pharmacologic Strategies

The appropriate pharmacologic choice is first determined by the subtype of rosacea being treated.¹³ Although data are limited, therapy for patients with erythematotelangiectatic rosacea has usually involved monotherapy with a topical agent, often coupled with use of physical modalities, such as intense pulse light (IPL). Therapy for patients with papulopustular rosacea has been studied extensively and has classically involved use of topical therapy with or without an oral tetracycline agent, depending on the severity of rosacea.¹³ Conventionally, once signs and symptoms begin to subside, the oral antibiotic has usually been tapered or discontinued in favor of a topical maintenance regimen.⁹

Topical Agents

Current clinical strategies for rosacea involve the use of effective topical agents to reduce the number and severity of inflammatory lesions and perilesional erythema. The choice of topical agents is based on various criteria, including mechanism of action, clinical evidence supporting efficacy and tolerability, and patient factors such as skin type.

The primary topical therapies are sulfacetamide 10%–sulfur 5% (sulfacetamide-sulfur), metronidazole, and azelaic acid (AzA). The topical antibiotics clindamycin and erythromycin have been employed in a secondary capacity, but data supporting their use are limited.¹⁴ In addition, chronic application of clindamycin or erythromycin as topical monotherapy may lead to emergence of resistant bacterial strains due to selection pressure. More recently, anti-inflammatory dose doxycycline (doxycycline 40-mg controlled-release capsule) was approved by the US Food and Drug Administration (FDA) for the treatment of rosacea. This latter agent is administered

orally once daily and is devoid of antibiotic activity, even with prolonged administration.

Sulfacetamide-Sulfur

First employed in 1956 for the management of acne vulgaris, sulfacetamide-sulfur was later used to manage seborrheic dermatitis and rosacea.^{15,16} It is effective in reducing the inflammatory lesions and erythema of rosacea but is often used in combination with another topical agent. Sulfacetamide-sulfur is commonly recommended for rosacea-seborrhea overlap, observed in approximately 20% of patients with rosacea.^{14,17} This agent appears to demonstrate an anti-inflammatory activity, although the exact mechanisms of action are unknown.^{14,17} Sulfacetamide-sulfur is available in both cleanser and “leave-on” formulations. More recently, a cleanser formulation of sulfacetamide-sulfur containing sulfur 1% (as opposed to 5%) has been released for treatment of rosacea, potentially allowing for reduced malodor, which is sometimes reported by patients as a result of the sulfur content.

Metronidazole

Released in 1989, metronidazole is also approved by the FDA for the treatment of rosacea and is available in various formulations (gel, lotion, and cream) and 2 concentrations (0.75% and 1%). Although the exact mode of action of metronidazole is unknown, its efficacy may be due to anti-inflammatory and antioxidant mechanisms.^{18,19} Its efficacy and safety in the treatment of rosacea have been confirmed by multiple controlled studies demonstrating reductions in inflammatory lesions, erythema, and symptomatology.^{14,17}

Azelaic Acid

AzA, a naturally occurring dicarboxylic acid, is the latest FDA-approved topical medication for the management of rosacea, available in a newer 15% water-based gel. AzA gel has shown efficacy in controlled randomized trials, demonstrating continuous improvement in the resolution of inflammatory lesions and in erythema reduction in rosacea.^{9,11,20,21} Although the 15% gel formulation has a lower concentration than its predecessor, a 20% cream vehicle, the gel provides superior percutaneous drug delivery.²² The exact mechanism of action of AzA is not fully understood, but its efficacy is most likely due to its anti-inflammatory, antioxidant, and possibly antimicrobial actions.^{21,23,24}

Oral Agents

Anti-inflammatory dose doxycycline is the only FDA-approved oral treatment for rosacea. However, oral

antibiotics that have been used for rosacea include other formulations of tetracyclines, macrolides, and ampicillin, which are associated with selection pressure and antibiotic resistance, especially with long-term use. Concerns surrounding antibiotic overuse and the development of resistant strains of microorganisms secondary to chronic oral antibiotic therapy for rosacea have underscored the conventional thinking that topical agents be used for long-term maintenance therapy for rosacea.

Oral antibiotics, especially tetracyclines, have commonly been used in combination with topical agents, primarily for the treatment of inflammatory lesions. Oral antibiotic agents have usually been discontinued or the dose lowered once the signs and symptoms of rosacea abate. The effectiveness of oral antibiotic therapy in rosacea is probably due to anti-inflammatory rather than antimicrobial effects. The availability of anti-inflammatory dose doxycycline may alter the paradigm on the use of oral therapy for rosacea, allowing for systemic therapy without antibiotic activity and for potentially augmented benefit when used in combination with topical therapy.

Proper Skin Care in Rosacea Management

The majority of patients with rosacea report having uncomfortable, sensitive skin that burns, stings, or itches and flushes easily with minimal stimulation. These symptoms are at least partially due to disrupted barrier function, frequently seen in patients with both erythematotelangiectatic (subtype 1) rosacea and papulopustular (subtype 2) rosacea; the latter is also referred to as inflammatory rosacea.¹⁰ Evidence for this is seen in the measurement of TEWL in patients with rosacea as compared with controls. Investigators found TEWL to be significantly increased at 2 facial sites (perinasal cheek, $P=.001$; side of the nose, $P=.006$).¹⁰ Skin irritation testing results also suggest epidermal barrier dysfunction in rosacea (Figure 1). Positive reactions were observed in 100% of untreated patients with erythematotelangiectatic rosacea and 68% of patients with papulopustular rosacea, while only 19% of control patients had positive reactions.¹⁰

A predisposition to skin irritation in patients with rosacea may be compounded by the use of irritating cleansers and other skin care products. An assessment of several commonly used soaps and cleansers found that all but 1 had considerable irritant effects.²⁵

Patients with rosacea have a compromised microvascular system in the dermis owing to the effects of UV light. Photodamage from exposure to UV light over the

long term is believed to be a factor in the pathophysiology of rosacea.^{6,26} Chronic skin exposure to UV light can damage superficial dermal vasculature^{6,27-29} owing to the release of harmful ROS and degradative MMPs.³⁻⁶ An impaired epidermal barrier may also allow irritants to gain entry, which may precipitate some symptoms of rosacea, such as stinging and burning.¹⁰

In double-blind, randomized trials that included 915 patients with papulopustular rosacea, baseline (pre-treatment) symptomatology was captured prior to initiation of topical therapies. As seborrheic dermatitis was one of the exclusion criteria in these trials, an overlap with rosacea did not account for the skin findings at baseline. Prior to initiation of therapy, the findings demonstrated that signs and symptoms commonly inherent to rosacea include scaling, edema, pruritus, stinging, and burning, reflecting underlying impaired epidermal barrier function as a contributing pathophysiologic component (Table).

Thus, optimal management of rosacea warrants use of a total skin care regimen that includes a gentle cleanser, a moisturizer, and a broad-spectrum photoprotectant, such as a physical sunblock.^{2,30,31}

Skin Cleanser Selection in Rosacea

The epidermal barrier can be thought of as a wall, where corneocytes are layered like bricks and intercellular lipids are the mortar.³² These intercellular lipids are vital to skin barrier integrity and maintenance but can be removed or disrupted by cleansers containing irritating detergents and emulsifiers.² Therefore, select skin cleansers carefully in the management of rosacea with regard to ingredients. Avoid products with sensory stimulants, such as menthol, and volatile solvents.¹² Also, avoid common skin irritants, such as sodium lauryl sulfate and sorbic acid.¹²

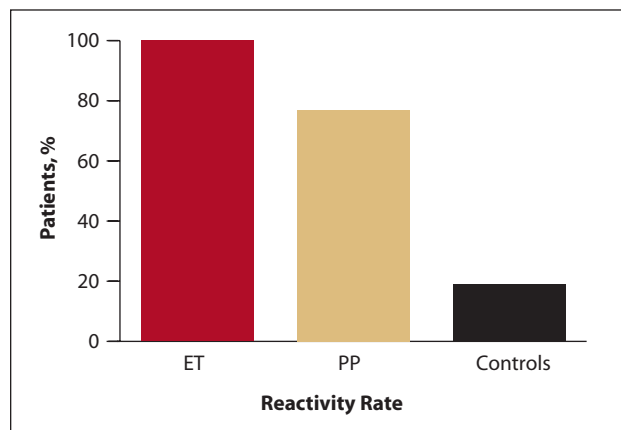


Figure 1. Rates of reactivity to skin-irritation test: rosacea patients versus control patients. ET indicates erythematotelangiectatic rosacea; PP, papulopustular rosacea.

Skin Sensitivity Parameters in Patients With Rosacea: Pretreatment Signs and Symptoms

Clinical Characteristics	Group 1, % (n=457) ^{11,20}	Group 2, % (n=127) ¹¹	Group 3, % (n=331) ²⁰
Skin dryness	65	66	69
Scaling	51	58	57
Itching	49	51	52
Edema	36	32	38
Burning	34	33	36
Stinging	29	34	29
Pain	17	14	21
Other	6	8	4

Appropriate skin cleansers for patients with rosacea are not soap based; instead, they use synthetic detergent (syndet) surfactants that interact minimally with skin lipids and protein.³³ Syndets are less irritating and drying, exhibit a more favorable pH, and thus represent a preferred choice of cleanser for patients with rosacea.³⁴ Soaps, which are alkaline, disrupt the lipid barrier and should be avoided.³¹ Foaming face washes and lipid-free cleansers are also appropriate cleansing agents for people with rosacea.² Some syndet cleaners have been shown to be compatible with topical pharmacologic regimens.^{35,36}

Patients should also be instructed in proper cleansing techniques: vigorous scrubbing should be avoided in favor of gentle washing.³⁴ Advise patients to wash the face with lukewarm water, as hot or cold water may trigger a flush.³⁷

Moisturizer Use in Rosacea

A comprehensive therapeutic skin care regimen for patients with rosacea requires daily moisturizer use. Moisturizers have the potential not only to replenish depleted lipid within the impaired epidermal barrier but also to restore its ability to retain moisture through the incorporation of humectants and occlusive agents in the formulation.³⁴ Humectants (eg, glycerin) attract and hold moisture within the epidermis. This increases hydration and may allow for enhanced penetration of topical pharmacologic agents.^{32,38} Occlusives (eg, petrolatum,

silicates) minimize desiccation by reducing evaporative and transepidermal water loss.³⁴

Photoprotectants

As noted, rosacea is thought to be a photoaggravated condition.³⁴ Long-term photodamage is regarded as a probable pathogenetic factor in rosacea.³⁴ In a survey of more than 1000 patients with rosacea, 81% noted that exposure to sunlight was a trigger factor for flare-ups.³⁹ For these reasons, it is recommended that rosacea patients avoid sun exposure as much as possible and consistently use a photoprotectant formulation (sun protection factor ≥ 15) to avoid the UV-light-induced dermal matrix degradation attributed, at least in part, to upregulation of ROS and MMPs.^{9,40} The selected photoprotectant should be a broad-spectrum formulation capable of filtering both UVA and UVB wavelengths.⁹

Benefits of Proper Skin Care in Rosacea

A study of patients with highly sensitive, dermatologist-assessed skin, most of whom had rosacea, with some cases of atopic background, evaluated the therapeutic impact of a skin care regimen. After a regimen incorporating a designated mild skin cleanser and moisturizer, significant improvements in objective parameters of skin hydration and skin sensitivity were observed for 3 weeks. Improvements in signs of skin irritation parameters were noted for 4 weeks based on investigator and subject assessments and objective measurements.⁴¹

Figure Not Available Online

Figure 2. Change in the intensity of itching and stinging in patients treated with azelaic acid 15% gel in combination with a professionally selected skin care regimen versus azelaic acid 15% gel in combination with a patient-selected regimen for management of rosacea. Asterisk indicates $P=.045$; dagger, $P=.029$. Reproduced from Draelos ZD, Green BA, Edison BL. An evaluation of a polyhydroxy acid skin care regimen in combination with azelaic acid 15% gel in rosacea patients. *J Cosmet Dermatol.* 2006;5:23-29,⁴² with permission from Blackwell Publishing.

Another trial of patients with papulopustular rosacea evaluated AzA 15% gel in combination with a professionally selected skin care regimen versus AzA 15% gel in combination with the patient's self-selected cleansing and moisturizing agents. The investigator observed greater improvements in those patients using a dermatologist-selected skin care regimen. Improvements in skin sensitivity, dryness, texture, smoothness, and overall skin condition were statistically significant ($P<.05$) for patients using the prescribed skin care regimen. This was not the case for patients using a self-selected skin care program. These differences were also pronounced with regard to tolerability. A statistically significant reduction was seen in the intensity of itching (week 8, $P=.045$) and stinging (week 12, $P=.029$) in the group using the dermatologist-recommended skin care regimen (Figure 2).⁴²

These findings suggest that the dermatologist should (1) educate rosacea patients as to the importance of a skin care regimen, (2) direct which skin care products and medications are to be used, and (3) provide detailed usage and application instructions for all products.

Conclusions

The pathophysiology of rosacea is not fully understood. Multiple factors appear to be operative, including vascular, inflammatory, microbial components, and skin barrier. Pharmacologic management, studied primarily

in papulopustular (inflammatory [subtype 2]) rosacea, has been shown to reduce the inflammatory lesions and erythema. Epidermal barrier disruption contributes markedly to the signs and symptoms of rosacea. Proper selection and use of skin care products (cleansers, moisturizers, photoprotectants) are integral components of the overall rosacea management program. Several studies discussed in this article scientifically support the therapeutic benefit of proper skin care in the management of rosacea, including augmentation of positive results provided by medical therapies.

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