

Facial Hygiene and Comprehensive Management of Rosacea

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The skin of patients with rosacea is exquisitely sensitive to various dietary, environmental, and topical factors that initiate the facial erythema characteristic of this sensitive skin condition. This sensitivity is probably due to epidermal barrier dysfunction. Overall management of rosacea involves the avoidance of dietary and environmental triggers, concurrent with the use of prescription therapies. The appropriate selection of over-the-counter and prescription skin care products is equally important. This article reviews the use of therapeutic skin cleansers, including the newest category of prescription antimicrobial cleansers, which can enhance the overall management of this inflammatory dermatologic disorder.

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Rosacea is a chronic dermatologic disorder that predominantly affects the central facial area.^{1,2} A recent consensus document from the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea has determined that there are 4 subtypes of rosacea and one variant (Table 1).³

The pathophysiology of rosacea is elusive. It is hypothesized that rosacea is a vascular and immune disorder initiated by the pathophysiologic changes associated with photodamage.⁴⁻⁶ Both the vascular system and the immune system are intimately related, thus it is plausible that the interaction between both systems accounts for many of the stigmata of rosacea.⁶ The vascular instability characteristic of rosacea flushing initiates the release of

inflammatory mediators into the surrounding dermis, thereby bringing about the chronic inflammation that is a hallmark of progressive rosacea.⁶⁻⁸ These inflammatory mediators include substance P, histamine, serotonin, bradykinin, and prostaglandins.^{4,6-8}

Recent rosacea research suggests that reactive oxygen species (ROS) also may be implicated in the pathogenesis and clinical manifestations of rosacea.⁹ A clinical study comparing biopsies from the faces of people with mild to moderate rosacea with controls showed that levels of superoxide dismutase, the key enzyme involved in defending against ROS, were higher in patients with mild rosacea (subtypes 1 and 2) compared with controls ($P < .05$). In addition, levels of the key ROS, malondialdehyde, were significantly higher in patients with more severe rosacea (subtype 3) compared with both controls and patients with mild rosacea ($P < .05$).⁹ The roles of inflammatory mediators and ROS in the pathogenesis of rosacea are supported by observations about the condition itself and by the efficacy of certain therapeutic interventions. People with progressive rosacea also have accompanying photodamage, which induces the production of ROS.⁴ This finding may explain the efficacy of topical metronidazole in rosacea because it possesses both anti-inflammatory and antioxidant effects.^{10,11}

Other evidence supports the role of *Demodex folliculorum* mites, a frequent commensal found in hair follicles and sebaceous glands or their products, as an inciting factor in rosacea.¹² Individuals with rosacea may evidence a hypersensitivity reaction to this commensal. A recent immunohistochemical study documented an infiltration of lymphocytes in rosacea patients with *Demodex* infestation. These immunologic reactions could contribute to the formation of the inflammatory lesions (papules and pustules) seen in subtype-2 rosacea.¹²

Rosacea as a Disorder of Skin Barrier Function

Rosacea also has been characterized as a disorder of the stratum corneum barrier, allowing irritants to affect the viable epidermis and dermis causing

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Table 1.

Subtypes of Rosacea

| Subtype | Clinical Presentation |
|----------------------------|---|
| 1—Erythematotelangiectatic | Flushing and persistent central facial erythema, with or without telangiectasia |
| 2—Papulopustular | Persistent central facial erythema with transient central facial papules or pustules, or both |
| 3—Phymatous | Thickening skin, irregular surface nodularities, and enlargement. May occur on the nose, chin, forehead, cheeks, or ears |
| 4—Ocular | Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema |
| Variant—Granulomatous | Noninflammatory; hard; brown, yellow, or red cutaneous papules; or nodules of uniform size |

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vasodilation, flushing, and inflammation.^{13,14} As noted previously, people with various subtypes of rosacea are exquisitely sensitive to numerous environmental factors; both irritant and allergic contact skin reactions are more common in patients with rosacea than in persons with normal skin.^{15,16} Tests to measure sensory or subjective skin irritation (eg, lactic acid test) constitute a clinical measure of barrier function.¹⁷ Based on the cumulative score from a skin sensation scale, one study showed that 100% of patients with subtype-1 rosacea showed a positive reaction to the lactic acid skin sensory test, whereas 68% of patients with subtype-2 rosacea had positive test reactions.¹⁵ This test showed positive results in only 19% of patients with normal skin, suggesting that epidermal barrier defects may be operative in rosacea. It is unknown whether an initial barrier defect eventually triggers derangements in the vascular and immune systems leading to the clinical manifestations of rosacea or whether inflammatory mediators can lead to barrier defects.

Potential Skin Irritants in Patients With Rosacea

A survey of 1023 patients with rosacea showed that 82% reported hyperirritability, burning, stinging, and general sensitivity to common skin care products, including cleansers (Table 2).^{18,19} Both male and female patients frequently cite alcohols, witch

Table 2.

Skin Irritation Associated With Use of Skin Care Products*¹⁹

| Product | Women, % | Men, % |
|------------------------|----------|--------|
| Astringents and toners | 49.5 | NR |
| Soaps | 40 | 24 |
| Exfoliating agents | 34 | NR |
| Makeup | 29 | NR |
| Perfume and/or cologne | 27 | 19 |
| Moisturizers | 25.5 | NR |
| Hair sprays | 20 | NR |
| Shampoos | 12 | 12 |
| Shaving lotions | NR | 24 |
| Sunscreens | NR | 13 |

*NR indicates no responders.

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Table 3.

Chemical Classes Associated with Skin Irritation

| Chemical Class | Representative Agents |
|-----------------|---|
| Solvents | Alcohol, acetone |
| Aromatics | Menthol, benzyl alcohol, cinnamates |
| Penetrants | Propylene glycol, butylene glycol, α -hydroxy acids |
| Surfactants | Sodium lauryl sulfate, quaternary ammonium compounds |
| Sunscreens | Para-aminobenzoic acid (PABA), benzophenones, cinnamates |
| Abrasives | Polyethylene beads, bismuth oxychloride, mica, silica (especially on the eyelids) |
| Pharmaceuticals | Tretinoin, benzoyl peroxide, urea |

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hazel, fragrances found in cleansers, topical moisturizers, makeup, menthol, peppermint oil, and eucalyptus oil as ingredients that cause skin irritation.¹⁷

Based on 20 years of clinical experience, Scheman²⁰ compiled a list of chemical classes commonly found in skin care products that he proposed were associated with the greatest incidence of skin irritation in patients with sensitive skin (Table 3).

The Use of Cleansers in Patients With Rosacea

The skin hyperreactivity seen in patients with rosacea warrants careful selection of any skin care products, especially cleansers, because they are the most frequent topical cause of barrier damage. For decades, dermatologists have sought cleansers that provide optimal skin cleansing while minimizing barrier damage.²¹ Recognition of the importance of mildness as a property of cleansers has spawned the development of therapeutic cleansers that are compatible with patient skin types and topical

Table 4.

Categories of Surfactants and Representative Examples^{24,25}

| Category | Compounds |
|------------|--|
| Anionic | Sodium lauryl sulfate, sodium laureth sulfate, sodium cocoyl isethionate, sodium tallowate, sodium cocoate |
| Cationic | Acrylates/steareth-20 methacrylate copolymer, sodium triethanolamine |
| Amphoteric | Cocamidopropylbetaine |
| Nonionic | Propylene glycol |

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therapies. There are 4 categories of cleansing agents: soaps; synthetic detergents; lipid-free lotions, which contain fatty alcohols that serve as emollients or humectants, or both, to counter the irritancy or drying of some surfactants; and the newest category, prescription antimicrobials. Among the factors affecting skin compatibility are pH and type of surfactant.^{21,22}

The normal pH of the skin surface is in the acidic range, with estimates ranging from 4.0 to 6.5.²³ Traditional soaps are alkaline and are thought to impair the lipid bilayer of the stratum corneum barrier, leading to the potential for irritation by removing intercellular lipids. Synthetic detergent cleansers are formulated to have a neutral (7.0) or slightly acidic pH to ensure skin compatibility. Some researchers and practitioners, however, opine that the potential for skin irritation associated with cleansing agents is predicated on factors other than pH.²³ This is an area of ongoing controversy.

The type of surfactant used is considered to have a major effect on a cleansing agent's irritancy potential. Surfactants, defined as chemicals that lower the surface tension or free energy at the interface of a 2-phase system (eg, liquid-solid system), are key to removing excess facial sebum, desquamated cells, and environmental debris from the skin's surface.²¹ There are 4 categories of surfactants based on their molecular charge or lack of molecular charge: anionic, cationic, amphoteric, and nonionic (Table 4).^{21,24,25} Although some anionic surfactants (eg, sodium lauryl sulfate) are



Patient with moderately severe subtype-2 rosacea at baseline (A) and after (B) 8 weeks of treatment with topical metronidazole gel 0.75% and sodium sulfacetamide and sulfur cleanser. Photographs courtesy of Joseph Bikowski, MD. Reprinted with permission from *Cutis*. 2004;73(suppl 1):29-33. ©2004, Quadrant HealthCom Inc.

associated with the greatest potential for skin penetration and skin irritation,²¹ other anionic surfactants, such as the salts of the isethionates, show excellent skin compatibility.^{21,26} On the other hand, nonionic surfactants, which penetrate least into the skin, also can cause epidermal barrier disruption by changing the composition and content of epidermal phospholipids.²²

Antimicrobial Cleansers for Patients With Rosacea

The newest category of therapeutic cleansers are the prescription antimicrobials that contain both sodium sulfacetamide (10%) and sulfur (5%), with sodium cocoyl isethionate as the major surfactant. Several antimicrobial cleansers are presently available: Rosanil™, Plexion®, and Clenia™. These formulations contain a solution of purified water. The use of water-based solutions can enhance penetration of both sodium sulfacetamide and sulfur, as well as other topical drugs.²⁷ All these agents have a slightly acidic-to-neutral pH and lack the odor

seen in older sulfur-containing formulations, which leads to greater patient acceptability. The major difference between Rosanil and the other 2 cleansers is that Rosanil is fragrance free.

The rationale for developing this category of antimicrobial therapeutic cleansers is to provide both a complementary mechanism of action to standard topical rosacea therapies, such as metronidazole formulations, and cleansing properties with a low potential for skin irritation. The Figure shows a patient with moderately severe subtype-2 rosacea before and after treatment with metronidazole gel 0.75% (MetroGel®) and sodium sulfacetamide and sulfur cleanser (Rosanil).

Rare, local irritation with topical sodium sulfacetamide and sulfur therapy has been reported. Furthermore, this category of cleansers should not be used in patients with hypersensitivity to sulfur and sulfonamides.

Both sodium sulfacetamide and sulfur have antimicrobial and anti-inflammatory properties.²⁸ Sulfur has antiodemodectic properties, as well as a

mild keratolytic action that can facilitate penetration of topical therapies.²⁸ A double-blind, randomized, vehicle-controlled study of 94 patients with subtype-1 and subtype-2 rosacea found that sodium sulfacetamide (10%) and sulfur (5%) in a lotion formulation provided significant efficacy in reducing erythema and inflammatory lesions.²⁸ When used for the treatment of rosacea²⁸ and acne vulgaris,²⁹ this sulfacetamide and sulfur formulation was associated with minimal skin irritation.

Conclusion

Patients in various stages of rosacea show increased skin sensitivity to numerous skin care products. This increased sensitivity is probably due to a defect in stratum corneum barrier function. The barrier dysfunction may be due to an underlying disorder in the immune system, leading to a release of inflammatory mediators. The choice of therapeutic cleanser is a critical factor in the overall management of patients with rosacea. A new class of prescription therapeutic cleansers, the antimicrobials, offers dermatologists a new option for optimal management of this condition.

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